Virchows Archiv (2023) 483 (Suppl 1):S1–S391
https://doi.org/10.1007/s00428-023-03602-w

ABSTRACTS

35th European Congress of Pathology – Abstracts

Published online: 2 September 2023

Oral Free Paper Sessions

OFP-01 | Oral Free Paper Session Digestive Diseases Pathology – GI

OFP-01-001

Results of the "Uniform Noting for International application of the tumour-stroma ratio as easy diagnostic tool" (UNITED): a multicentre prospective validation study

M. Polack*, A.G. Roodvoets, E. Meershoek-Klein Kranenbarg, H.A. Gelderblom, V. Terpstra, G. Petrushevska, G. Gasljevic, S. Kjær-Frifeldt, E.M. de Cuba, N. Bulkmans, G.R. Vink, R. Al Dieri, R.A. Tollenaar, H.J. van Krieken, W.E. Mesker
*Department of Surgery, Leiden University Medical Center, Leiden, The Netherlands

Background & objectives: As advised by the UICC and CAP, the prospective multicentre UNITED study was initiated to validate the tumour-stroma ratio (TSR) as prognostic independent parameter, predicting patient-related outcomes for stage II-III colon cancer (CC) patients and subsequently aid in personalized treatment.
Methods: The UNITED study was enrolled in 27 participating centres in 12 countries worldwide. The effect of TSR, categorized as stroma-high (>50%) or stroma-low (≤50%) through standardized histopathology microscopic assessment by certified pathologists, was evaluated on disease-free survival (DFS) as primary endpoint for a 3-year median follow-up period. Secondary endpoints were response to adjuvant chemotherapy and overall survival (OS).
Results: A total of 1537 patients were included, of which 1388 were deemed eligible and operated between 2015-2021. DFS was significantly shorter ($p<0.001$) in stroma-high CC patients (n=428) than in stroma-low CC patients (n=960). In multivariate analysis, the TSR was an independent prognosticator for DFS ($p=0.001$; hazard ratio 1.498, 95% confidence interval 1.180-1.903) as well. As secondary outcomes, stroma-high stage II-high risk and stage III CC patients also notably had a worse DFS despite receiving adjuvant chemotherapy ($p<0.001$). For OS, although the follow-up period was relatively short, already a slight trend towards worse OS in stroma-high CC patients was visible ($p=0.102$).
Conclusion: The multicentre UNITED study hereby unequivocally validates the TSR as an independent, prognostic factor for DFS in stage II-III CC patients, proving that stroma-high CC patients have a worse survival. Furthermore, these patients were also observed to respond worse to adjuvant chemotherapy. As the TSR can thus aid in shared decision-making and personalized treatment, future implementation in the tumour-node-metastasis-classification is aimed.
This work was supported by grants from the Dutch Cancer Society (KWF Kankerbestrijding; project 10174) and the Stichting Fonds Oncologie Holland, as well as the Bollenstreekfonds, Lisse, the Netherlands. These funders had no role in study design, data collection and analysis, nor in the decision to publish, nor in the preparation of the manuscript.

OFP-01-002

Multi-site multi reader study on artificial intelligence-assisted primary diagnosis of gastric biopsies

M. Rodriguez-Justo*, G.Y. Lauwers, A.L. Booth, A.P. Levine, W. Jervis, K. Kantekure, L. Aherfi, E. Lanteri, L. Apple, A. Arat, R. Mikulinsky, T. Amit, M. Vecsler, M. Grinwald, J. Sandbank
*Cancer Institute, University College London, United Kingdom

Background & objectives: This study aimed to clinically validate the use of an artificial intelligence (AI)-based solution by pathologists for reviewing and reporting gastric biopsies.
Methods: A two-arm prospective reader study comparing the performance of pathologists supported by AI with pathologists reviewing digital slides was performed at multiple sites (varied staining protocols & different scanners). Both arms were compared to ground truth (GT) established by a consensus of 2 GI-pathologists. Rates of major discrepancies between each arm and GT, as determined by an adjudicating-pathologist, were compared.
Results: 6 pathologists reported on 235 cases (426 H&E-slides), each case being reported twice, once in each study arm. Pathologists first reviewed only slides and IHC after request, while the AI results were rendered on H&E-slides only. The AI solution demonstrated high performance for the detection of gastric-neoplasia (Carcinoma/HGD/ HG-Lymphoma):AUC of 0.98 (95% CI: 0.967,0.994), sensitivity 96%, specificity 90%, NPV 100% and PPV 94%. High performance was demonstrated for H Pylori detection: AUC of 0.93 (95% CI: 0.88,0.97) sensitivity 91%, specificity 80%. Pathologists' feedback showed the AI solution is user friendly (92.5%), adds confidence to the cases review (80%) and a majority (83%) would prefer continuing to work with the system.
Conclusion: This multi-site multi-reader study reports high accuracy for the detection of gastric neoplasia by the AI solution. The AI solution performed accurately and equally well with slides issued from different staining platforms and scanners. Thus, AI solutions have the potential to be a significant helping tool for pathologists in various clinical decision-making in routine pathology practice, enhancing the quality and reproducibility of diagnoses.

OFP-01-003

Quantitative and qualitative analyses of exosomes derived from cancer-associated fibroblasts (CAFs) according to the desmoplastic reaction (DR) patterns in colorectal cancer

K. Tashiro*, K. Okamoto, S. Mochizuki, E. Shinto, Y. Kajiwara, M. Yamadera, H. Abe, Y. Sota, K. Kikuya, T. Kawauchi, K. Aihara, H. Ueno
*Department of Surgery, National Defense Medical College, Japan

Background & objectives: DR pattern is a novel prognostic factor in colorectal cancer (CRC) and CAFs derived from intra-tumorous lesion generating the "Immature" pattern, an independent poor prognostic histopathological feature of CRC patients, are shown to behave in a pro-tumour manner.
Methods: CAFs were isolated and cultured from resected tumour's tissue with "Mature" pattern (CAF-A) or that with "Immature" pattern (CAF-C) and exosomes released from CAFs were collected with the ultracentrifugation method. After confirming the exosomal proteins levels being sufficient by silver staining, the expression of programmed cell death ligand 1 on exosomes (PD-L1Ex) were also evaluated by western blotting.
Results: In a total of 22 cases (CAF-A, 11; CAF-C, 11), all of CD9, an exosomal surface antigen, or exosome-derived miRNAs were successfully detected in exosome derived from CAFs. The total protein level of exosomes evaluated with a microvolume spectrophotometer was significantly higher in CAF-C (40.5 ng/ul) than in CAF-A (17.7ng/ul) (p=0.024; Welch test). Among 10 cases with sufficient exosomal proteins (5 CAF-A cases and 5 CAF-C cases, respectively), the expression of PD-L1Ex was identified in 2 cases, both of which were from the CAF-C exosomes and none of the 5 cases of CAF-A had PD-L1Ex.
Conclusion: We reported previously that immature DR pattern was significantly relevant to the suppressed CD8+ T-cell infiltration, suggesting the pivotal association between fibrotic stromal environment and immune escape of tumour cells. Recently, exosomes derived from tumour cells, including PD-L1Ex, have intensively been investigated, however, exosomes derived from CAFs could also effectively induce immune escape of a tumour. The present study suggested that PD-L1Ex might be a factor contributing to the development of immune escape in the "Immature" DR environment of CRC.

OFP-01-004

NTRK gene alterations are enriched in gastric cancer with hepatoid differentiation but not in those with DNA mismatch repair protein deficiency

Y. Fu*, X. Pu, X. Fan
*Department of Pathology, Affiliated Drum Tower Hospital, Medical School of Nanjing University, China

Background & objectives: Gastric cancer is a heterogeneous disease, and identifying the molecular characteristics of specific subtypes can aid in the development of targeted therapies. In this study, we aimed to investigate the clinicopathologic profile of gastric cancer with oncogenic NTRK alterations.
Methods: We used NTRK break-apart probes and gene-specific probes for fluorescence in situ hybridization (FISH) to screen for NTRK fusion and amplification in 491 gastric cancer cases. We also collected additional samples from duodenal adenocarcinomas, endometrioid carcinomas, and colorectal cancers with dMMR to investigate the relationship between NTRK alterations and DNA MMR proteins.
Results: Our analysis revealed that only four cases had NTRK alterations, including two cases with NTRK fusions and two cases with NTRK amplifications. Interestingly, all four cases were enriched in a specific subtype of gastric cancer, hepatoid adenocarcinomas of the stomach, and were all adenocarcinomas with enteroblastic differentiation. Furthermore, our analysis revealed that all five cases with NTRK gene fusions were found exclusively in colorectal cancer with dMMR. We also identified seven genes that were highly expressed in all three groups: CACNA1A, FGF18, BMP7, CHRNA7, CCKAR, BIRC3, and CXCL6. FGF18 and BMP7 in particular may play a role in the interaction between the MMR system and NTRK gene alterations in HAS.
Conclusion: Our study provides valuable insights into the molecular characteristics of gastric cancer with NTRK alterations. Our findings suggest that NTRK gene alterations are enriched in a specific subtype of gastric cancer, HAS, and are not enriched in gastric cancer with dMMR. Furthermore, we identified common genes that may be involved in the interaction between the MMR system and NTRK gene alterations in HAS. These results may have important implications for the development of targeted therapies for gastric cancer.

OFP-01-005

What is the value of lymph node regression after neoadjuvant chemoradiotherapy in rectal cancer?

S. Kus Ozturk*, C. Graham Martinez, K. Verhoef, M. Tosetto, K. Sheahan, G.A. Hospers, C. van de Velde, C.A. Marijnen, C.S. van der Post, I. Nagtegaal
*Radboud University Medical Centre (Radboudumc), The Netherlands

Background & objectives: Following neoadjuvant therapy, regression may also be seen in lymph nodes and affect nodal stage. Our aim is to determine the role of regression of lymph nodes on outcome in patients with rectal cancer.
Methods: All the lymph node slides were evaluated for metastasis (ypN) and regression (REG) (fibrosis and acellular mucin) in a cohort of 469 rectal cancer patients following chemoradiotherapy. According to ypN and REG status, a three-tiered (ypN0 REG+, ypN0 REG-, ypN+) and a four-tiered (ypN0 REG+, ypN0 REG-, ypN+ REG+, ypN+ REG-) classifications were generated and subgroups compared to each other.
Results: In our cohort, the distribution of ypN0 REG+, ypN0 REG-, ypN+ REG+ and ypN+ REG- was 20%, 49%, 15%, and 16%, respectively. We found significantly better overall survival in ypN0 REG+ and worse overall survival in ypN+ group in both three-tiered (p=0.002) and four-tiered classifications (p=0.005). ypN0 REG+ group remained as the best prognostic group in DFS (three-tiered; p=0.004, four-tiered; p=0.01) and even outperformed ypN0 REG- group (p=0.008).
Conclusion: Regression in lymph nodes is frequent and results in significantly better outcome compared to patients with remaining lymph node metastases.

OFP-01-006

Intratumoral budding assessment in biopsies supports the preoperative management of colorectal cancer patients

S. Kus Ozturk*, J. Bokhorst, K. Sheahan, M. Vieth, A. Lugli, I. Nagtegaal
*Radboud University Medical Centre (Radboudumc), The Netherlands

Background & objectives: We aim to define the sufficiency criteria of a biopsy for an effective intratumoral budding (ITB) evaluation by using AI. We focus on the characteristics of the biopsy and its representation of tumour budding (TB) in the whole tumour.
Methods: We examined the biopsy and corresponding resection specimens of 571 CRC patients. A tissue segmentation algorithm was used to quantify the amount of biopsy, tumour, and necrosis in biopsy materials. The TBs were evaluated with an AI algorithm in H&E stained biopsy and resection slides. TB distribution was investigated within the first five millimetres from the lumen in 30 resections.
Results: The average biopsy size, tumour, and necrosis were 71mm2, 7mm2, and 2mm2, respectively. Our preliminary analyses (n = 175) showed an increased gap between TB counts in biopsies and resections with smaller amounts of tumour in biopsies (rho= -0.13, p=0.07). The difference disappeared in biopsies with over 12 mm2 tumour.
Within 1 mm from the tumour surface, 87% of the resections already contained TBs. ITB scores within five millimetres from the surface

were associated with the peritumoral budding category in 70% of the tumours. The complete data will be presented at the congress.
Conclusion: ITB can be reliably scored on biopsies, based on the presence of TB in the superficial portion of the tumour, provided that sufficient tumour is captured in those biopsies.

OFP-01-007
A real-time histologic evaluation of gastric cancer tissue by using artificial intelligence-assisted confocal laser endomicroscopic system
S. Kim*, H. Bae, H. Cho, J. Chu, S. Choi, S.M. Heo, K. Hwang, Y. Jo, K. Kim, D. Lee
*Ajou University School of Medicine, Republic of Korea

Background & objectives: The processing time and preparation artifacts of frozen sections demand a novel technique for the instant histologic evaluation. A confocal laser endomicroscopic system provides real-time imaging of the tissue without glass slide preparation. We evaluated its applicability in gastric cancer.
Methods: A confocal laser endomicroscopic system using light laser scanning was developed. Forty-five advanced gastric cancer tissues and the normal tissues were obtained from fourteen patients. Five pathologists interpreted 200 images and detected histologic locations and the presence of cancer. An artificial intelligence (AI)-based tumour detection algorithm was developed with 1,305 tumour and 1,137 normal tissue images, by using EfficientNet V2.
Results: Pathologists initially detect the histologic location of the images with 65.7% accuracy and differentiate cancer tissue from normal with 74.7% accuracy. The sensitivity and specificity of cancer detection were 71.9% and 76.1%. The interpretation time per image was 12.0 seconds. Following the review of matched H&E images, the accuracy of identifying the histologic location was increased to 92.8% ($P<0.0001$), and that of detecting cancer tissue was also increased to 90.9% ($P<0.001$). The sensitivity and specificity of cancer detection were enhanced to 89.1% and 93.2% ($P<0.0001$). The interpretation time per image was decreased to 5.3 seconds ($P<0.001$). The AI algorithm revealed 94% accuracy, 96% sensitivity, and 93% specificity for detecting cancer.
Conclusion: High-quality histologic images were immediately acquired by the confocal laser endomicroscopic system. The trained pathologists could accurately detect cancers and histologic location and the developed AI algorithm showed high performance in detecting cancer, raising its potential applicability as a real-time tissue imaging modality.
Funding: Korea Medical Device Development Fund (RS-2022-00140721)

OFP-01-008
Characteristics of a modern, screened UICC stage II colon cancer cohort
M. Pihlmann Kristensen*, U. Korsgaard, I. Zlobec, T. Frøstrup Hansen, H. Hager, S. Kjær-Frifeldt
*Department of Pathology, Lillebaelt Hospital, University Hospital of Southern Denmark, Denmark

Background & objectives: Current high-risk factors used for selecting stage II colon cancer patients to adjuvant chemotherapy are based on outdated cohorts. The aim of this study was to establish a modern cohort of stage II colon cancer patients, post-screening.
Methods: A cohort consisting of resected colon cancers from 2014-2016 in the Region of Southern Denmark was collected retrospectively using the Danish Colorectal Cancer Group database and the Danish Pathology Registry. All diagnostic slides were reviewed, and the tumours re-staged according to the UICC TNM Classification, 8th edition. A comprehensive histopathological characterization was performed, and clinical data extracted from medical journals.
Results: In total, 497 patients met the inclusion criteria of which 20% were diagnosed through the Danish colorectal cancer screening. Adjuvant chemotherapy was administered to 14 % of the patients. Sufficient lymph node sampling ($\geq$ 12) was obtained in 98% of the tumours and lymphatic, venous and perineural invasion was confirmed in 5, 23 and 12% of the tumours respectively. A test of prognostic biomarkers revealed a high stroma content (>50%) in 52% of tumours and a distribution of tumour budding as low, intermediate and high in 53, 22 and 25% of the tumours respectively. Local or distant relapse was determined in barely 9% of patients. The survival analyses are ongoing.
Conclusion: This screened cohort of stage II colon cancers is thoroughly characterized and brought up to current pathological evaluation. The relapse rate is notable lower than in other cohorts reflecting the contemporary approach in this cohort. Consequently, we propose that it is highly relevant to examine high risk factors in modern cohorts in order to select the right patients for adjuvant chemotherapy.
Funding: Lillebaelt Hospital Region of Southern Denmark

OFP-01-009
A new algorithm for coeliac disease based on gamma delta intraepithelial lymphocytes detected with an antibody working on FFPE sections
E.N. Kozan*, C. Tuna Kirsaclioglu, A. Kansu, A.I. Soykan, D. Gokmen, B. Savaş, A. Ensari
*Ankara University Medical School, Pathology Department, Turkey

Background & objectives: Diagnosis of coeliac disease (CD) with mild mucosal changes is difficult for all parties involved. We aimed to determine the power of γδ+ IELs in discriminating CD from other causes of intraepithelial lymphocytosis using a new monoclonal antibody.
Methods: A total of 167 cases comprising coeliacs with 117 active CD (29 type 1, 29 type 2, 39 type 3) and 20 treated CD, and non-coeliacs including 24 controls and 26 non-coeliac IELosis were studied. IEL counts were evaluated on H&E, CD3, TCRδ-stained (with moAb H-41) sections. Morphometric features were evaluated on digitalized images. Discriminant analysis was applied for statistics.
Results: γδ+ IELs were significantly higher in CD (24.83 ± 16.13) compared to non-CD (6.72 ± 6.32) and were positively correlated with the degree of mucosal damage (type $1=20.41\pm13.57$, type $2=24.24\pm12.65$, type $3=33.69\pm19.15$). Both γδ+ IEL count and γδ+/CD3+IEL ratio showed higher performance in differentiating coeliacs from non-coeliacs with a sensitivity of 89,69; 84,62 and specificity of 87,5; 76,00, respectively. γδ+ IEL counts also differentiated groups showing normal villus/crypt architecture including type 1 CD (20.41 ± 13.57) and non-coeliac IELosis (9.42 ± 7.28) with great significance ($p=0.001$). Discriminant analysis revealed that villus/crypt ratio, IEL distribution pattern, γδ+/CD3+IEL ratio were the most potent discriminants. Discriminant function correctly classified 82.3% of study cases; 97.5% of new cases and was therefore validated.
Conclusion: The new antibody detecting γδ+IELs in FFPE sections allowed us to determine thresholds to discriminate coeliacs from non-coeliacs. Using 10.5 for γδ+ IELs and 14% for γδ+/CD3+IEL ratio proved highly sensitive and specific in correctly classifying cases with normal villus/crypt axis as Type1 CD, non-CD IELosis and controls. γδ+ IEL counts also correlated with Marsh classification. We propose a 'histopathological algorithm' based on γδ+IELs and hope that it will be used as a simple diagnostic test by our fellow pathologists.

OFP-01-010

Specific morphological characteristics predict microsatellite instability status in gastric cancer

J. Almeida*, J.R. Silva, L. Mascarenhas-Lemos, C. Neto do Nascimento, D. Sousa Marques, X. Wen, L. Pinho, R. Maio, P. Pontes, L. Cirnes, M. Cravo, F. Carneiro, I. Gullo
*Department of Pathology, Centro Hospitalar Universitário de São João (CHUSJ), Porto, Portugal

Background & objectives: The evaluation of microsatellite instability (MSI) status in gastric cancer (GC) is pivotal for the definition of prognosis and optimal treatment approach. In this study, we aimed at identifying morphological features that might be associated to MSI-high status in GC.
Methods: The series encompassed 140 GCs. Tumour morphology was evaluated in endoscopic biopsies (EB) and surgical specimens (SS) according to Laurén and WHO classification. Specific morphological features were evaluated, including tumour grade, presence of solid component, extracellular mucin pools, areas with prominent lymphoplasmacytic and/or neutrophilic inflammatory infiltrate (distant from ulceration/perforation). MSI status was evaluated by multiplex-PCR and immunohistochemistry for mismatch-repair proteins.
Results: The series encompassed 38 MSI-high GC (27,1%). MSI-high GCs occurred more frequently in older (median age=73 years, $p<0.01$) females (57.9%, $p=0.012$) and in the distal third of the stomach (89.5%, $p=0.037$), when compared with microsatellite stable (MSS) tumours. No statistically significant association was found between MSI-high status and Laurén or WHO classifications. The evaluation of specific morphologic characteristics in SS revealed that MSI-high GC showed more frequently solid and/or mucinous components ($p=0.034$ and $p<0.001$, respectively), as well as the presence of "neutrophil-rich stroma" ($p<0.001$). Both solid areas and extracellular mucin lakes were discriminating features for the identification of MSI-high cases also in EB ($p=0.002$ and $p=0.045$, respectively).
Conclusion: GC is a highly heterogenous tumour and few studies have assessed possible morpho-molecular correlations. Despite the morphological heterogeneity of GC harbouring MSI-high status, we identified specific histopathological features that should prompt the search for this molecular subtype both in EB and SS, namely solid component and extracellular mucin lakes. To our knowledge, this is the first study describing a neutrophilic-rich inflammatory infiltrate in MSI-high GC, a feature which predicted MSI-high status in up to 85% of GC cases.
This research was partially co-financed by Hospital da Luz under the initiative "Luz Investigação" in the context of the Group GENIUS (Reference LH.INV.F2019015). Part of IdyllaTM reagents have been provided free of charge by Biocartis. The funding source did not have any influence on the design, conduction, analysis and interpretation of data and report of the results for this study.

OFP-01-011

The complexity of shapes; how the circularity of tumour nodules impacts prognosis in colorectal cancer

N. Brouwer*, A. Khan, J. Bokhorst, F. Ayatollahi, J. Hay, F. Doubrava-Simmer, N. Hugen, H. de Wilt, I. Zlobec, J. Edwards, I.D. Nagtegaal
*Radboud University Medical Center, The Netherlands

Background & objectives: The current definition of tumour deposits (TDs) in colorectal cancer (CRC) staging is subjective and leads to high interobserver variability. In this study, objective assessment of the shape of lymph node metastases (LNMs) and TDs was correlated with outcome.
Methods: 190 cases of stage III CRC from IGMP (Bern) were included in the test cohort. Slides with LNMs and TDs were roughly annotated and processed using a segmentation algorithm to determine their shape. The complexity ratio was calculated for every shape and correlated with outcome. A cohort of 169 stage III CRC cases from QEUH (Glasgow) was used as validation.
Results: A significantly higher disease-free survival (DFS) for N1 than N2 cases was observed in both cohorts, as to be expected. TDs showed a significantly more complex shape than LNMs with extranodal extension (ENE), which were again more complex than LNMs without ENE ($p<0.001$). In the test cohort, patients with the highest sum of complexity ratios had a significantly lower DFS ($p<0.01$), which remained when only the nodule with the highest complexity was taken into account ($p<0.001$). This maximum complexity ratio per patient was identified as an independent prognostic factor in the multivariate analysis (HR 3.12, $p<0.05$). The validation cohort confirmed these results.
Conclusion: More complex nodules in stage III CRC were correlated with a significantly worse DFS, even if only the most complex nodule was taken into account. These results suggest that more complex nodules are a reflection of a more aggressive tumour biology. Since most of the more complex nodules were diagnosed as TDs, we suggest to provide a more prominent role for TDs in the nodal stage and possibly include an objective complexity measure in their definition.

OFP-01-012

Tumour deposits - a heterogeneous group of lesions with different metastatic potential

A.S. Oguz Erdogan*, N. Brouwer, V. Angerilli, T. Haddad, S. Lent-vanVliet, N. Rutgers, F. Doubrava-Simmer, I.D. Nagtegaal
*Radboud University Medical Center, The Netherlands

Background & objectives: Tumour deposits (TDs) are tumour aggregates in the mesocolon. Several possible pathways including lymphovascular invasion, lymph nodes and perineural invasion have been suggested. This study aims to identify the TDs by evaluating them in terms of well-known metastatic pathways.
Methods: We examined histopathological specimens from 646 colorectal cancer patients and identified 136 patients with 329 tumour deposits (TDs). We conducted serial sectioning and staining of TDs using HE, EVG, CD34, D2-40 and S100.
Results: Based on the presence or absence of haematovascular invasion, lymphovascular invasion, lymph node involvement, and perineural invasion we classified TDs into three groups: those with a single metastatic origin (171, 52%), those with multiple metastatic origins (115, 35%), and an unknown group (43, 13%) where no metastatic pathway was evident. Haematovascular pathway is the most common route for TDs.
Conclusion: Our findings illustrate that, TDs are a highly heterogeneous group of lesions and the haematovascular pathway plays a significant role in TDs formation.
Funding: KWF

OFP-01-013

Stroma AReactive Invasion Front Area (SARIFA) as novel prognostic biomarker in colorectal cancer is characterized by a distinct transcriptional signature associated with stromal cell infiltration and lipid metabolism

N.G. Reitsam*, V. Grozdanov, B. Grosser, C.M.L. Löffler, H.S. Muti, J.N. Kather, B. Märkl
*Pathology, Medical Faculty, University of Augsburg, Germany

Background & objectives: Recently, we established Stroma AReactive Invasion Front Areas (SARIFA), defined as direct contact between tumour cells and adipocytes, as novel hematoxylin-and-eosin (H&E) based prognostic biomarker in gastrointestinal cancers. We now comprehensively evaluated gene expression signatures with regards to SARIFA-status.

Methods: We screened 627 colorectal cancer (CRC) cases in the The-Cancer-Genome-Atlas (TCGA) datasets, and could establish SARIFA-status based on available diagnostic H&E whole-slide-images (https://portal.gdc.cancer.gov) in 215 cases, of which 207 classified cases could be eventually included in final analysis. Consecutively, we performed differential gene expression analysis, gene set enrichment analysis as well as treatment prediction based on RNA-expression data.
Results: 72 (33.5%) of all analysed cases were SARIFA-positive CRCs. Beyond again proving the prognostic value of SARIFA-status in this cohort, we could further show that survival differences seem not to be driven by alterations on a genomic level. However, SARIFA-positive CRCs were characterized by a distinct transcriptional profile. Even though SARIFA-positive CRCs were more likely to be of consensus-molecular-subtype (CMS) 4 and displayed a higher stromal-cell-infiltration-score (SIIS), SARIFA-positive CRCs were additionally again characterized by upregulation of genes associated with lipid metabolism (FABP4, CD36). Additionally, gene set enrichment analysis uncovered extracellular matrix organization as relevant SARIFA-dependent biological process. Lastly, RNA-based treatment response prediction revealed differential drug sensitivity in SARIFA-positive CRCs.
Conclusion: Based on the TCGA, our study confirms the high prognostic value of H&E-based SARIFA-classification in CRC. SARIFA represents the H&E correlate of an aggressive tumour biology, partly showing an overlap with mesenchymal CMS4-subtype and SIIS score but furthermore being associated with lipid metabolism and possessing an 'own' transcriptional identity, which opens the window for new therapeutic approaches. Hence, SARIFA is an easy-to-implement biomarker in diagnostic routine that could also be beneficial for more detailed patient stratification in prospective clinical trials.
JNK is supported by the German Federal Ministry of Health (DEEP LIVER, ZMVI1-2520DAT111) and the Max-Eder-Programme of the German Cancer Aid (grant #70113864), the German Federal Ministry of Education and Research (PEARL, 01KD2104C), and the German Academic Exchange Service (SECAI, 57616814). This research was funded/supported by the National Institute for Health and Care Research (NIHR, NIHR213331) Leeds Biomedical Research Centre. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

OFP-01-014

Tumour stroma ratio and tumour budding in colorectal adenocarcinoma and its association with clinico-pathological parameters

A.A. Khan*, S. Zaheer
*Vardhman Mahavir Medical College, India

Background & objectives: The pTNM classification in colorectal carcinoma is based on anatomical evaluation and lacks predictive accuracy. We aimed to study the association of tumour stroma ratio (TSR) and tumour budding (TB) with pTNM and histopathological grading in patients of colorectal adenocarcinoma.
Methods: 40 patients, who underwent curative surgery for colorectal adenocarcinoma (CRC) were retrospectively included in this study. Hematoxylin and eosin stained sections of tumour were examined and TSR was calculated using a Java based open access image processing software (Image-J) and TB was calculated in hot spot region. These values were correlated with pTNM and histopathological grade.
Results: Low TSR value i.e. < 0.5 was found in 26 patients (65%). We observed that low TSR (< 0.5) and high TB were significantly associated with poorly differentiated CRC ($p < 0.0001$ and $p = 0.0001$ respectively). A higher T and N stage and perineural invasion were significantly associated with low TSR ($p<0.005$ and $p<0.013$, respectively) . Overall, TSR showed higher sensitivity (100% versus 93.75%), specificity (50% versus 45%), positive predictive value (61.54% versus 57.69%), negative predictive value (100% versus 90%) and diagnostic accuracy (72.22% versus 66.67%) than TB in differentiating poorly differentiated colorectal carcinoma from moderately differentiated ones.
Conclusion: The significance of tumour microenvironment is being increasingly recognized in various aspects including tumour progression, prognosis and response to therapy. TSR is a relatively new, simple and promising histological biomarker which can be used as an independent prognostic marker along with TB in CRC for better clinical patients. The present study was limited to smaller number of patients and also needed more follow up of the patients for a comment on overall survival were the limitations of this study.

OFP-01-015

Early invasive (pT1) colorectal cancer: low PD-L1 expression in immune cells predicts the presence of nodal metastasis

G. Trucco*, G.M. Benazzo, A.A. Ricci, L. Mangherini, E. Falco, A. Gambella, L. Bertero, P. Cassoni
*Pathology Unit, Department of Medical Sciences, University of Turin, Italy

Background & objectives: Nodal involvement in pT1 colorectal carcinoma (CRC) is rarely present resulting in unnecessary surgeries. This study investigates the effectiveness of PD-L1 expression as a marker of lymph node metastasis for tailoring surgical treatment after endoscopic removal of pT1 CRC.
Methods: Histopathological features of 19 metastatic and 62 non-metastatic surgically resected pT1 CRCs were assessed. Immunohistochemical expression of PD-L1 (clone 22C3) was evaluated using Tumour Proportion Score (TPS), Combined Positive Score (CPS), and Immune Cell Score (ICS). The correlation between PD-L1 expression and nodal metastasis, the optimal cut-off values, interobserver agreement and the potential impact on patients' surgical management were determined.
Results: PD-L1 expression in terms of CPS and ICS independently correlated with lymph node metastasis (PD-L1CPS: OR -2.5, 95%CI: -4.11 to -0.97, p=0.008 and PD-L1ICS: OR -1.85, 95%CI: -2.90 to -0.79, p=0.004) and <1.2 CPS and <1.3% ICS were identified as the optimal cut-off values to discriminate between metastatic and non-metastatic patients. In our cohort, the implementation of these cut-off values would have avoided a significant rate of unnecessary surgeries in pN0 patients (PD-L1CPS: 43.2; PD-L1ICS: 51.9%). Ultimately, PD-L1 evaluation showed good inter-pathologist concordance in absolute terms (PD-L1CPS Interclass correlation coefficient, ICC: 0.91; PD-L1ICS ICC: 0.793) and using the identified cut-off values (PD-L1CPS ICC: 0.848; PD-L1ICS ICC: 0.756).
Conclusion: Our study shows that PD-L1 expression is an effective predictor of nodal status and could improve patient selection for surgery after endoscopic removal of pT1 CRCs. Good inter-pathologist concordance supports the potential reproducibility of PD-L1 immunohistochemical evaluation in routine diagnostics.

OFP-02 | Joint Oral Free Paper Session Gynaecological Pathology / Cytopathology

OFP-02-001

CK17 and SOX2 immunohistochemistry in the distinction of HPV-independent p53 wild-type verruciform acanthotic vulvar intraepithelial neoplasia (vaVIN) from its mimickers and margin assessment

E. Cook*, K.K. Van de Vijver, C. Parra-Herran
*Brigham and Women's Hospital, USA

Background & objectives: vaVIN is a lesion with altered architecture, bland cytology and risk of recurrence and cancer progression, shown to be often CK17 and SOX2 positive. We document the performance

of these markers in vaVIN versus its wide differential of benign conditions.
Methods: CK17 and SOX2 immunohistochemistry was evaluated on 13 vaVINs (lesion and adjacent normal mucosa) and 38 acanthotic mimickers including verruciform xanthoma (n=6), lichen simplex chronicus (LSC), lichen sclerosus, psoriasis & pseudoepitheliomatous hyperplasia (n=5 each), syphilis, granular cell tumour, and differentiated VIN (n=4 each). Stains were recorded as negative (absent=0/patchy=1+) or positive (continuous moderate/strong, partial=2+ or full thickness=3+).
Results: 13/13 (100%) vaVINs were positive for CK17 (92%=3+) while 6/7 (85%) were positive for SOX2 (17%=3+). The normal mucosa adjacent to vaVIN was CK17-positive in only 1/10 (10%) cases, whereas it was SOX2-positive in 5/5 (100%) cases. Among mimickers, 28/38 (74%) were CK17-positive (43%=3+) and 20/38 (53%) SOX2-positive (25%=3+). CK17 showed higher rates of positivity than SOX2 in most categories including pseudoepitheliomatous hyperplasia (100% vs 0%), LSC (100% vs 40%), psoriasis (100% vs 40%), lichen sclerosus (83% vs 40%), and syphilis (50% vs 25%). CK17 sensitivity and specificity for vaVIN diagnosis was 100% and 26% if 2+/3+ were considered positive, and 92% and 69% if only 3+ was considered positive.
Conclusion: CK17 and SOX2, portended as useful distinguishing vaVIN from non-dysplastic vulva, have limitations when acanthotic lesions are included in the differential. They are frequently positive in vaVIN but are also often expressed in benign lesions, although in the latter CK17 staining is more frequently partial-thickness. Full-thickness CK17 staining has good performance in vaVIN diagnosis, whereas negative CK17&SOX2 argues against it. CK17 also has value in margin assessment, as histologically normal mucosa next to vaVIN is consistently negative (unlike SOX2).

OFP-02-002
Opening the black box: validating AI-based findings with spatial transcriptomics in high-grade serous ovarian carcinoma
A. Laury*, S. Zheng, O. Youssef, N. Aho, S. Hänninen, J. Tang, O. Carpen
*University of Helsinki, Finland

Background & objectives: H&E images of high-grade serous ovarian carcinoma (HGSC) contain prognostic information detectable only by artificial intelligence (AI). These regions can predict patient outcome using H&Es alone, and now we aim to reveal the biology behind these regions via spatial transcriptomics.
Methods: A deep learning neural network tool identified novel tumour regions most indicative of outcome in high-grade serous carcinoma. These novel (HC) regions, and background tumour (BG) tissue, were probed with 10x Visium for FFPE spatial transcriptomics. Gradient boosting machines were trained, and differential gene expression and pathway enrichment analyses were performed. Individual transcripts were validated by RNA in-situ hybridization.
Results: Data was successfully obtained for 35/36 tumour samples from 16 patients, identifying 17,866 genes across 9,129 capture locations. Gradient boosting machines confirm that prediction accuracy for outcome is higher using transcript profiles from HC regions (0.68) as compared to BG regions (0.44)($p = 0.0133$).
Pathway analyses show significant enrichment of inflammatory signalling pathways in poor outcome HC regions (interferon alpha response), while cell cycle control and replication pathways (Hallmark DNA repair) are enriched in improved outcome tumour HC regions.
1Differential gene expression analyses reveal that 142 genes (0.78%) show significant differential expression exclusively in HC regions. RNA-ISH validation of one such gene (JUN) confirms the transcriptomics finding.
Conclusion: Artificial intelligence-based image-analysis (AI-IA) of diagnostic HGSC slides can identify morphologic patterns invisible to the human eye and guide selection of biologically meaningful regions. Spatial transcriptomics confirms improved outcome prediction in HC tumour regions, as well as biologically relevant pathway enrichment and differential gene expression, which can be validated using standard techniques.
AI-IA together with spatial transcriptomics offers a promising toolkit to identify biological features associated with cancer behaviour, making AI-based findings more interpretable and clinically relevant.
Funding: University of Helsinki Doctoral Programme in Clinical Research, Suomen Lääketieteen Säätiö, HUS Diagnostic Center, the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 965193 for DECIDER, Finnish Cancer Foundation, Sigrid Juselius Foundation and Finska Läkaresälskapet.

OFP-02-003
Is it time to move towards a new classification of high grade endometrial stromal sarcoma?
D. Arciuolo*, S. Patrizi, S. Vallese, R. Alaggio, S. Sfregola, B. Padial Urtueta, A. Travaglino, M. Valente, I. Giovannoni, G.M. Milano, L. Pedace, C. Nardini, L. Pedone Anchora, G.F. Zannoni, E. Miele
*Pathology Unit, Department of Woman and Child's Health and Public Health Sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background & objectives: High-grade endometrial stromal sarcoma (ESS-HG), paediatric BCOR-rearranged sarcoma and clear cell sarcoma of the kidney share common molecular drivers. We investigated their methylation profile to better define the classification and the potential relationship among these entities with clinical impact.
Methods: Fifty-one cases of morphologically and molecularly confirmed tumours, including 6 ESS-HG, 10 undifferentiated uterine sarcomas (UUS), 27 paediatric BCOR-rearranged sarcoma (pBS) and 8 clear cell sarcoma of the kidney (CCSK), underwent DNA methylation profiling.
For the hierarchical clustering we included 19 Ewing sarcomas as control group and an external cohort of 32 previously published pBS/CCSK and low/high grade-ESS.
Results: DNA methylation profiling. All ESS-HG were classified into ESS-HG class with calibrated scores (CS) >0.9 in 5/6 cases and pBS/CCSK as "sarcoma with BCOR alterations" with CS> 0.9 in 26/27 cases. UUS were classified into several groups with low CS except 2 that were classified as malignant rhabdoid tumour and undifferentiated sarcoma (CS>0.9).
CNV analysis. Fifteen out of 27 pBS/CCSK and 1/16 uterine sarcoma cases showed a flat profile. The remaining cases exhibit several alterations, mostly 1q gain and loss of 9p- 13q- 10q.
The hierarchical clustering revealed two main clusters, the "BCOR-altered family" composed of pBS/CCSK and ESS-HG and a second group with ESS-LG, UUS, and Ewing sarcoma
Conclusion: ESS-HG and pBS/CCSK are epigenetically and closely related entities and could have a common progenitor cell. The variation in CNV could be related to the higher genetic instability in tumour of adult patients. These findings, combined with the histological and molecular similarity, allow us to speculate that in the future ESS-HG and pBS/CCSK might be grouped as BCOR-sarcoma.
Moreover, the proximity between ESS-LG and UUS suggests the possibility of common histogenesis to be further investigated.

OFP-02-004
Is Mandard's tumour regression score able to assess the response to chemo-radiotherapy in patients with locally advanced cervical cancer?
G. Scaglione*, D. Arciuolo, A. Travaglino, A. Santoro, N. D'Alessandris, M. Valente, G. Angelico, F. Inzani, A. Muccilli, S. Sfregola, B. Padial Urtueta, S. Spadola, L. Pedone Anchora, M.G. Ferrandina, G.F. Zannoni

*Pathology Unit, Department of Woman and Child's Health and Public Health Sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background & objectives: Locally advanced cervical cancer (LACC) represents 37% of worldwide cervical cancer. Chemo-radiotherapy followed by surgery is an alternative to standard treatment. We aimed to assess the prognostic role of the therapeutic response in LACC using Mandard tumour regression score.
Methods: We enrolled 244 patients with LACC treated with CT-RT followed by surgery. Histopathologic response was assessed according to Mandard-score system: 1-complete fibrosis; 2- rare residual cancer cells scattered through the fibrosis; 3- increased number of cancer cells, fibrosis predominating; 4- residual cancer outgrowing fibrosis; 5- no fibrosis. Kaplan–Meier and Cox regression were used for survival analysis.
Results: We found a complete pathological response in 118 patients (48.4%), tumour regression score (TRG) 2 in 49 cases (20.1%), TRG3 in 35 cases (14.3%), and 42 (17.2%) were classifies as non-responders (TRG4-5). TRG was significantly associated with OS ($p<0.001$) and PFS ($p<0.001$). Main responders (TRG1-2) showed a 92% 5-year overall survival (5y-OS) and a 75% 5-year disease free survival (5y-DFS). Minor or no responders showed a 48% 5y-OS and a 39% 5y-DFS. Kaplan-Meier curves for OS and PFS showed two prognostic groups: TRG1-TRG2 cases had a better outcome than TRG3-TRG4-5 cases. The 2-tiered TRG was independently associated with both DFS and OS in Cox regression analysis.
Conclusion: Currently there is not a standard method to classify tumour regression in LACC. We showed that Mandard TRG is strongly associated with OS and PFS. Moreover, 2-tier TRG (TRG1-2 vs TRG3-4-5) is an independent prognostic factor in post-CT/RT LACC, with potential benefits in defining post-treatment adjuvant therapy. Lastly, 2-tier TRG is an easier method to assess tumour regression overcoming the difficulty of 5-tier TRG in distinguishing regressive fibrosis from the dense fibrous cervical stroma.

OFP-02-005

Mutational profiling of recurrent endometrial endometrioid carcinoma with no specific molecular profile (NSMP)/p53wt using endometrial brush sampling

A. Khatib*, T. Revil, L. Jiang, L. Gilbert, B. Tessier-Cloutier
*Division of Gynaecologic Oncology, McGill University Health Centre, Montreal, Canada

Background & objectives: The NSMP/p53wt endometrial carcinoma (EC) is defined by the exclusion of POLE mutation, mismatch repair protein loss and aberrant p53 protein expression. We set to study clinicopathological features of NSMP/p53wt EC using a targeted DNA sequencing panel.
Methods: Endometrial brush samples were collected at the time of hysterectomy in patients with low-grade (FIGO grade 1-2) and low stage (pT1-2) EC NSMP/p53 between 2015 and 2019. Clinicopathology review was performed for each case. Mutational profiling assay included low-pass whole genome DNA sequencing, as well as targeted sequencing for 19 common EC genes.
Results: We included 180 NSMP/p53 cases, 13 of which recurred. The median age was 60-year-old, and all patients were treated with surgery. The most common site of recurrence was the vaginal apex. Logistic regression analyses showed that positive intra-operative cytology ($p=0.006$), grade 2 ($p=0.027$), and tumour size ($p=0.037$) were independently associated with a higher rate of recurrence. All tumours expressed ER and PR by immunohistochemistry. Mutational analysis, currently available for 99 cases (seven with recurrence), showed that 1q gain was associated with tumour recurrence ($p=0.0247$), none of which had a PTEN mutation. One recurrent tumour had an APC mutation ($p=0.0173$). No other alterations were significantly associated with recurrence.
Conclusion: Our analysis supports that, along high-risk clinicopathologic metrics, 1q gain is a helpful marker of more aggressive disease in low-grade and ER positive EC. As we lean further into the molecular classification for the diagnosis of EC, DNA sequencing approaches for NSMP/p53wt subgroup may be necessary for adequate for clinical stratification. Sequencing is ongoing to validate our results in the remaining cases.
Funding: Henry R. Shibata Cedars Cancer Fellowship/Cedars Cancer Foundation

OFP-02-006

Proficiency testing of p53 IHC pattern interpretation in vulvar biopsies shows overcalling of the mutant basal overexpression pattern in TP53 wild-type cases

M. Kinloch*, C. Parra-Herran, G. Focchi, B. Howitt, S.L. Skala, S. Strickland, J. Watkins, R. Wong, E. Torlakovic, R. Crawford, B. Gilks, L. Anderson, N. Singh, K. Wei, L. Hoang
*University of Saskatchewan, Canada

Background & objectives: Recently, criteria for p53 immunohistochemistry (IHC) interpretation was described in the vulva. However, proficiency of pathologist read out has not been studied. We used a read-out module to assess proficiency variation in a set of gynaecologic pathologists.
Methods: Scanned images of p53 IHC on 90 vulvar biopsies (diagnoses of non-neoplastic dermatoses, high-grade squamous intraepithelial lesion, differentiated vulvar intraepithelial neoplasia, verruciform acanthotic vulvar intraepithelial neoplasia) were provided. Scoring completed by pathologists as wild-type or mutational via 6 p53 IHC patterns. Following 45 cases in Module A and given TP53 sequencing data, a second 45-case Module B was completed.
Results: Eleven gynaecologic pathologists participated in module A with a mean accuracy of 67.04% (concordant p53 IHC pattern and NGS result), that ranged from 55.56% to 86.67%. Accuracy improved for 75% pathologists from Module A to Module B with a mean of 77.22%. The mean improvement was 10.2%. Null pattern (100% case accuracy) and parabasal/diffuse overexpression patterns (66% case accuracy) were the most accurate in pathologist readout (where $\geq$9 pathologists accurately predicted the mutation). Remarkably, the basal overexpression pattern had only 20% case accuracy. There were 21 cases where $\geq$4 pathologists overcalled basal overexpression and 2 cases where all 12 pathologists overcalled a basal overexpression mutant pattern in a wild-type setting.
Conclusion: Proficiency readout improved from Module A to Module B with the educational intervention of TP53 sequencing data. However, pathologists must exhibit caution in overcalling the mutant basal overexpression pattern. Given basal overexpression can occur in both wild-type and TP53 mutation settings, pathologists may not be able to recognize a mutant basal overexpression, even with training. Limitations of this study are small sample size and pathologist's blinding to H&E and p16.
Funding: Carraresi Foundation and Sumiko Kobayashi Marks Memorial OVCARE Research Grants

OFP-02-007

Prognostic impact of pathological parameters in molecular subgroups of endometrial carcinoma

A. De Leo*, M. Ruscelli, F. Rosini, A.G. Corradini, T. Maloberti, S. Coluccelli, A. Costantino, C. Ceccarelli, D. de Biase, D. Santini, G. Tallini
*University of Bologna, Italy

Background & objectives: Molecular characterization of endometrial carcinoma (EC) has recently included in the ESGO/ESTRO/ESP

guidelines. The study aims to evaluate the impact of integrated molecular and pathologic risk stratification and the relevance of pathologic parameters in predicting prognosis in each molecular subgroup.
Methods: ECs were classified using immunohistochemistry and next-generation sequencing into the four molecular classes: POLE mutant (POLE), mismatch repair deficient (MMRd), p53 mutant (p53abn), and no specific molecular profile (NSMP).
Results: According to WHO algorithm, 219 ECs were subdivided into the following molecular subgroups: 7.2% POLE, 32.8% MMRd, 21% p53abn, 39.2% NSMP. Molecular classes as well as pathological parameters and ESGO/ESTRO/ESP 2020 risk groups were statistically correlated with disease-free survival. At multivariable analysis, the independent parameters associated with recurrence for the entire cohort were: stage, grade, and tumour budding. Refining the analysis to NSMP tumours, several pathological features were correlated with recurrence: histotype, grade, stage, necrosis, tumour budding and substantial lymphovascular space invasion (LVSI). At multivariable analysis in NSMP subgroup, the independent parameters predictive of recurrence were: necrosis and tumour budding.
Conclusion: Our study supports the prognostic importance of EC molecular classification and demonstrated the essential role of accurate assessment of pathological parameters predictive of recurrence that are still crucial for appropriate patient management.

OFP-02-008
Endometrial stromal sarcomas with BCOR alterations: clinicopathological and molecular study of a rare subgroup
C. Alves-Vale*, M. Varela dos Santos, N. Maida Méndez, C. Martins, F. Silva, S. Lérias, A. Felix, J. Ferreira
*CUF Descobertas Hospital, Faculdade de Medicina da Universidade de Lisboa, Portugal

Background & objectives: Endometrial stromal sarcomas (ESS) are rare uterine neoplasms. *BCOR* alterations occur in a small subset of those. *MDM2* and *CDK4* pathway alterations have recently been described. We review the clinicopathological and molecular features of a series of ESS with *BCOR* alterations.
Methods: Four *BCOR*-associated ESS were retrieved: one with *BCOR* internal tandem duplication (*BCOR*-ITD) and three with *BCOR* rearrangements (*ZC3H7B* rearranged in 2 cases; no rearrangements of *MAML3*, *CCNB3*, or *JAZF1* detected). Clinical, morphological and immunohistochemical data were collected and reviewed. Comparative genomic hybridization (CGH) was performed, followed by FISH analysis of *MDM2*, *CDK4*, *CDKN2A*, and *RB1* genes in selected cases.
Results: Age at diagnosis ranged from 49 to 71y. FIGO stages were IA, IB and IVB. Neoplasms were myxoid and composed of round-to-spindle cells, with mitotic activity: 3-12/mm2. Collagen plaques (3/4), staghorn-shaped vessels (3/4), lymphovascular invasion (2/4) and necrosis (2/4) were found. Tumours showed an infiltrative pattern or a tongue-like infiltration with intravascular plugs. CD10 expression was strong and diffuse (*BCOR*-rearranged ESS) or focal and weak (*BCOR*-ITD). Cyclin D1 positivity was variable (60-90%). In two cases, CGH analysis revealed gain of 12q13-q21.1, corresponding to *MDM2*/*CDK4* amplification (confirmed by FISH), and deletions affecting 9p and 13q (with corresponding *CDKN2A* and *RB1* deletion by FISH). Despite different follow-up durations (1-42mo), outcomes varied from disease-free to death.
Conclusion: Our cases present several similarities to those previously described, namely the myxoid background, frequently with staghorn-shaped vessels. The case without *ZC3H7B* rearrangement shares morphology and immunoprofile with *ZC3H7B-BCOR* rearranged neoplasms. We also detected a subset of cases with *MDM2* and *CDK4* amplification, along with *CDKN2A* and/or *RB1* deletion. This emphasizes the clinical relevance of detailed molecular characterization of *BCOR*-associated ESS to identify potential candidates to CDK4/6 inhibitors.

OFP-02-009
Genomic profile analysis of leiomyomas with bizarre nuclei and fumarate hydratase deficient leiomyomas: strengths, weaknesses, and limitations of array-CGH interpretation
Q. Fontanges*, P. Dubos, T. Lesluyes, Y. Laizet, V. Velasco, L. Mayeur, E. Oliva, R.H. Young, M. Devouassoux-Shisheboran, S. Isabelle, G. Frédéric, J.C. Noël, M. Barbara, F. Chibon, S. Croce
*Cliniques Universitaires de St Luc, Belgium

Background & objectives: Array-CGH analysis of uterine smooth muscle tumours is becoming part of diagnosis routine. The aim of this study is to investigate the genomic profiles of two challenging leiomyoma variants: leiomyoma with Bizarre Nuclei (LMBN) and Fumarate Hydratase deficient leiomyoma (FHLM).
Methods: Genomic profiles of 28 FHLM and 37 LMBN from 64 patients were analysed by array-CGH. Genomic complexity was evaluated from a quantitative (Genomic Index (GI)) and qualitative (tumour suppressor gene analysis) perspective. Clinical data included patient's age, type of surgery and follow-up. We tested 9 tumours with Nanocind CINSARC®, a transcriptomic signature reflecting genomic complexity and demonstrated to be prognostic.
Results: Follow-up was available for 46 patients (mean 87,3 months). All were alive without disease. For 51 array-CGH interpretable tumours, mean GI was 16.4, lower than LMS (mean GI 51.8, $p<0.001$). Three groups emerged: 1) FH deleted (24/58) with low GI (mean 11), 2)TP53 deleted (17/58) with higher GI (mean 22.4), and 3)no event on FH or TP53 (17/58) (mean 18.3). FH deleted and TP53 deleted genomic groups were associated with distinct clinical and pathological profiles. Patients harbouring FH deletion were younger than those with TP53 deleted tumour (mean 44,1 y. vs 51,8 y., $p=0.006$. The 9 tested tumours were classified C1 with Nanocind CINSARC® signature (lowest risk of recurrence).
Conclusion: Our findings indicate that a GI>10 or alterations in tumour suppressor genes in isolation should not warrant a diagnosis of malignancy and can be observed among LMBN and FHLM with long follow up and no recurrences. Although a GI <10 remains a predictor of benign behaviour, the GI at the cut off of 10 is not applicable in these LM variants. LMBN and FHLM are challenging entities, GI and genomic profile should be interpreted with caution in these morphological settings.

OFP-02-010
Diagnostic value of pan-TRK immunohistochemistry in NTRK-rearranged gynaecological sarcomas and morphological mimics. A study of 473 gynaecological mesenchymal tumours
S. Croce*, M. Souto, V. Velasco, F. Kommos, E. Oliva, I. Treilleux, M. Devouassoux-Shisheboran, I. Hostein, I. Soubeyran, E. Khalifa, G. Mccluggage, C. Hartog, F. Le Loarer, J. Costa
*Institut Bergonié, France

Background & objectives: NTRK-rearranged sarcomas of the uterus show a "fibrosarcoma-like" morphology, harbour NTRK rearrangements and they strongly express pan-TRK. The aim of this study is to investigate pan-TRK immunohistochemistry in a large cohort of gynaecological mesenchymal neoplasms, including NTRK-rearranged sarcomas and mimics.
Methods: A total of 473 gynaecological mesenchymal tumours (461 without NTRK fusions and 12 NTRK-rearranged sarcomas) were included. Pan-TRK immunohistochemistry (EPR17341, Abcam on Ventana Benchmark platform) was performed on whole tissue sections and tissue microarrays. Molecular study of pan-TRK positive tumours was performed by RNA sequencing or FISH.
Results: Of the 12 NTRK-rearranged sarcomas, 11 (92%) exhibited pan-TRK staining, mostly diffuse (≥70%) and cytoplasmic with

moderate/strong intensity and one (with SPECCL1::NTRK3 fusion) was negative. Eleven of 461 (2.4%) cases without NTRK rearrangements also exhibited pan-TRK expression: 3 low-grade and 7 high-grade endometrial stromal sarcomas and 1 undifferentiated uterine sarcoma. Molecular confirmation of the absence of NTRK rearrangements was possible in 9 tumours; molecular testing was not successful in the other 2 cases. Of the 9 pan-TRK positive neoplasms without NTRK-rearrangements, 7 exhibited focal/multifocal (<70%) cytoplasmic staining with weak/moderate positivity. None exhibited strong and diffuse staining.

Conclusion: Even though pan-TRK immunohistochemistry is not entirely sensitive or specific for NTRK-rearranged sarcomas, these neoplasms tend to exhibit diffuse staining with moderate/strong intensity, unlike the positive staining in neoplasms without NTRK-rearrangements. Pan-TRK should be performed in uterine monomorphic spindle neoplasms negative for smooth muscle markers and hormone receptors and variably positive for CD34 and S100. The diagnosis of an NTRK-rearranged sarcoma requires molecular confirmation but pan-TRK immunohistochemistry is a useful screening tool to direct which cases require molecular testing

OFP-02-011

Oestrogen receptor expression in endometrial adenocarcinomas of no specific molecular profile shows a bimodal distribution

B. Gilks*, L. Hoang, B. Howitt, T. Longacre, J. McAlpine, A. Jamieson, N. Singh, J. Pors
*Canada

Background & objectives: Decreased Oestrogen receptor (ER) expression is a poor prognostic marker in endometrial carcinomas of no specific molecular profile (NSMP), but the optimal cut-off for low ER (high-risk) versus high ER (low-risk) expression has not been defined.

Methods: Endometrial biopsy specimens from 120 cases of endometrial carcinoma of NSMP molecular subtype were stained for ER and Allred score was assigned (sum of staining intensity score, with 0, 1=weak, 2=moderate and 3=strong staining, and distribution score, with 0=negative, 1=<1% of cells staining, 2=1-10%, 3=11-33%, 4=34-66% and 5=67-100%). Histotype and grade was available for every case. Clinical follow-up data pending.

Results: The Allred score distribution is bimodal with a small peak at 0 and larger peak for scores 7/8. Twelve tumours had an Allred score of 0-3, including four endometrioid carcinomas, four clear cell carcinomas, and one each of: mesonephric-like adenocarcinoma, gastric-type adenocarcinoma, carcinosarcoma and endometrioid carcinoma with yolk sac differentiation. One mesonephric-like adenocarcinoma had an Allred score of 4 and the two tumours with an Allred score of 5 were a mesonephric-like adenocarcinoma and an endometrioid carcinoma. Five tumours had an Allred score of 6: 4 endometrioid carcinomas and 1 mixed clear cell and endometrioid carcinoma. 99% of tumours with an Allred score of 7 or 8 (99/100) were endometrioid.

Conclusion: The distribution of ER expression in NSMP endometrial carcinoma is bimodal, with most (>80%) showing high level ER expression (Allred score 7 or 8) when staining is performed in well-fixed endometrial biopsy specimens. All non-endometrioid carcinomas and a few endometrioid carcinomas had lower-level ER expression (Allred score of 6 or less). These results suggest an Allred score cut-off of 6 separates high from low ER expressing NSMP endometrial carcinomas, with potential implications for risk stratification and clinical management.

Funding: Terry Fox Research Institute

OFP-02-012

Cytology evaluation of neuroblastic tumours

E. Dvidenko*, F. Santos, M.M. Lemos
*Instituto Português de Oncologia de Lisboa Francisco Gentil, Portugal

Background & objectives: Neuroblastic tumours (NTs) arise from neural crest-derived tissues and are divided in four categories by International Neuroblastoma Pathology Committee (INPC). We aim to describe our cytological experience with NTs as a useful tool for initial diagnostic approach and molecular characterization.

Methods: NTs diagnosed in our institution from 2010 to 2022 with pre-treatment cytological and histological first diagnosis were reviewed. Air-dried touch preparations from fine-needle aspirations and biopsy imprints were available. Flow cytometry, segmental chromosomal alterations analysis and MYC amplification by fluorescence in situ hybridization (FISH) were performed in both smears and fresh tissue. Cytological and histological findings were correlated.

Results: Twenty-nine NTs were included. Mean patient age was 38.7 months (2 – 132 months). Fifteen were females (51,7%). Adrenal gland was the main primary site (55,2%). A diagnosis of NT was achieved in 22 smears (75,9%): 14 poorly differentiated NTs, 4 undifferentiated NTs and 4 were reported as unclassifiable NTs. The remaining 7 cases were cytologically diagnosed as small round cell tumours. Undifferentiated and poorly differentiated NTs were concordant with final histological diagnosis. Molecular studies and FISH results were available in 25 cases (86.2%): 12 had segmental chromosomal aberrations; 4 had MYC amplification; none had ALK gene alterations. DNA index was feasible in 23 cases (79.3%) with seven diploid tumours.

Conclusion: Cytology, a minimally invasive technique, reliably yields material for diagnosis and molecular studies of NTs. Nevertheless, due to tumour heterogeneity, definitive cytological evaluation and tumour subtyping according to INPC is not widely recommended. Our study confirms the suitability of cytological samples for molecular characterization, but also demonstrates that a rapid diagnosis and subtype assessment of non-treated NTs is possible in these specimens, providing they are adequately handled and evaluated by an experienced cytopathologist.

OFP-02-013

Application of the new WHO reporting system for lung cytopathology on bronchial wash samples: a cytohistological correlation study from a tertiary hospital

J. Vaz Silva*, L. Leça, C. Lobo, N. Coimbra, A.L. Cunha, P. Monteiro
*Pathology Department, Portuguese Oncology Institute of Porto (IPO-Porto), School of Medicine, University of Minho, Braga, Portugal

Background & objectives: Bronchial wash(BW) is a minimally invasive method to sample mucosal surfaces of the bronchial tree to assist in the diagnosis of infection and malignancy. Several studies report a wide range of sensitivity for malignancy detection, with different factors influencing sensitivity.

Methods: Recently, WHO introduced a new reporting system for lung cytopathology. Our aim was to assess the new system accuracy for BW samples, through cytohistological correlation, while characterizing BW performance in lung diagnosis.

We retrieved all BW from 2021-2022 with an available histological diagnosis. Cytology reports were divided into negative- and positive-tiers (including suspicious/atypical categories). BW-performance parameters were calculated following histological correlation.

Results: We assessed a total of 440 cytological and 440 histological samples. Each biopsy/histologic diagnosis correlated with a BW performed either simultaneously or prior.

BW performance analysis demonstrated a sensitivity of 37,9% and a specificity of 93,3%; positive predictive value of 95,6% and a negative predictive value of 28,5%. Overall diagnostic accuracy was 49,5%. Sensitivity was slightly higher in patients with a diagnosis of squamous cell carcinoma than in patients with adenocarcinoma diagnosis.

When applying the new WHO reporting system (WHO-RS), risk of malignancy(ROM) ranged from 71% in the benign/negative category to 97% in the malignant category. However, as an oncological centre, the ROM of our population can present a sampling bias.
Conclusion: With the growing need for multiple testing (histologic, molecular) of lung malignant neoplasms and the decreasing size of histological samples, it is essential to determine diagnostic accuracy of additional tests that can be performed concomitantly.
Studies demonstrate a BW sensitivity range from 29-78% in central lesions, thus our results in overall lesions are within expected.
Regarding WHO-RS, we observed higher ROM than expected for most categories. However estimated ROMs are based on few retrospective studies, thus further studies are needed.

OFP-02-014
Routine next generation sequencing testing on lung adenocarcinoma pap-stained (OH-fixed) cytological samples
T. Labiano*, E. Almudevar, D. Guerrero-Setas
*Hospital Universitario de Navarra, Spain

Background & objectives: Minimally invasive methods are used for diagnosis and staging in patients of suspected lung cancer. In Lung Adenocarcinoma (L-ADC) biomarkers testing is mandatory for a comprehensive diagnosis. Aim of this study is to describe clinico-pathological characteristics and NGS results.
Methods: We selected 125 L-ADC cytological cases diagnosed in 2021.Oncomine-Focus Assay,52-genes panel (Thermo-Fisher) was used after ADN/ARN extraction from OH-fixed pap-stained slides. Sample procurement techniques were: EBUS-FNA 45.6% (57/125);US-FNA 24% (30/125); CT-FNA 13.6%; Pleural fluid 7.2% and EUS-FNA 5.6% and other 7.2%.Location of tumour was both primary (16%)and metastatic disease (84%).ROSE and Tumour Fraction(T%) and Cellularity were assess in all cases by cytopathologists.
Results: We included 125 patients (83 M/42F), mean age 66.7 yo (range 46-89).Valid test rate was 89.6% (112/125).In 15 cases we obtained not valid results:7 studies were invalid for both AND & RNA, in 5 for DNA, one for ARN and in two cases without CNV detection. T% median was 90%(mean 75.4%). Among patients with invalid results 10 were rebiopsied. Thirty two patients have no genomic aberrations (24.4%).Co-ocurring molecular alterations-rate was 47,5%.Molecular alterations in KRAS and EGFR genes were the most frequent identified in 37(33%) and 22(16%) cases respectively. Included 2 Insertions in exon 20 and two cases with concomitant KRAS+EGFR mutations . We found also 6MET alterations, 5BRAF and 2 fusion (EML4-ALK and KIF5B-RET).
Conclusion: Cytological samples obtained by minimally invasive procedures are a good source for routine NGS testing. The routine use of these samples for NGS has the potential to improve detection of biomarkers, essential for lung cancer patients treatment management and better survival in lung ADC patients. Co-ocurring molecular alterations are frequent. Rapid on-site assessment is a useful tool to ensure adequate material is present and to check tumour fraction. Low T% and/or low cellularity are related factors with invalid results and required rebiopsy.

OFP-02-015
Immediate and long-term risk of preneoplastic or neoplastic cervical lesion with a low-grade cytology after a positive mRNA-HPV test. The protective role of a negative HPV test result in the first round of a primary HPV screening programme
R. Granados*, J. Duarte, A. Gutierrez-Pecharromán, D. Luján, B. Raposo, I. Solís, L. Molpeceres, P. Bajo
*Hospital Universitario de Getafe, Spain

Background & objectives: Although screening guidelines calculate CIN2+ risks considering previous test results, data is scarce due to the newness of primary HPV programmes. This study analyses the value of a previous HPV test result for managing women with a low-grade cytology test.
Methods: A prospective longitudinal study of 2,112 women, aged 25-65. Cotest was performed with ThinPrep cytology and mRNA Aptima HPV-test (AHPV). CIN2+ risks were measured and compared among the following subsets:1) interventional group (IG,n=1,975) recruited for a second cotest 3-5 years later; 2) positive cotest (n=75) with AHPV+ and low-grade (ASCUS/LSIL) cytology; 3) mixed cotest (n=62) with AHPV negative and ASCUS/LSIL.
Results: From the IG group, 19 women had positive AHPV and low-grade cytology in the new cotest and a 1-4 year follow-up (FU). Immediate (<12 month) and long-term risks for CIN2+ were 0 and 5,3%, respectively. Cases with low-grade cytology but negative AHPV in second cotest had a 0% 0-6y risk. Women with positive initial cotest had an immediate risk of 24% and a 4,4y risk of 33,3%. The group with mixed cotest (ASCUS/LSIL but negative AHPV) had immediate and 4,6y risks of 0% and 3,2%. Risk differences between AHPV positive and negative cases with ASCUS/LSIL and those of AHPV-positive women with or without a previous negative AHPV, were statistically significant.
Conclusion: The risk of developing a preneoplastic or a neoplastic (CIN2+) lesion in women with a low-grade cytology and a positive AHPV test is significantly higher when there is no previous history of HPV testing, warranting a colposcopic study and/or biopsy. However, a previous negative AHPV test confers a protective effect, lowering the risk of CIN2+ below the threshold of colposcopy referral. These findings, verified in a longitudinal study, are relevant and pertinent for patient management in primary HPV screening programmes.

OFP-03 | Oral Free Paper Session Digestive Diseases Pathology – Liver/Pancreas

OFP-03-001
Spatial heterogeneity of immune drivers coordinates the organisation of antitumor immunity in pancreatic cancer, affecting patient outcome
A.S. Wenning*, I. Marinoni, P. Aeschbacher, B. Gloor, A. Perren, E. Karamitopoulou
*Department of Visceral Surgery, University Hospital Bern, Switzerland

Background & objectives: Pancreatic ductal adenocarcinoma (PDAC) is considered low immunogenic with "cold" tumour microenvironment (TME) and is mostly unresponsive to immune checkpoint blockade therapies. Here we decipher the impact of intratumoral heterogeneity of immune determinants on antitumor response.
Methods: Each four regions from tumour centre (TC) and invasive front (IF) from 130 PDACs, including long-term survivors (LTSs, n=29, overall survival≥60 months) and short-term survivors (STSs, n=101, overall survival<60 months), were examined by transcriptomic and proteomic analysis (Nanostring platform). Spatial compartments (tumour, leukocytes, stroma) were defined by fluorescent imaging. Additionally, 20 tumours from each group were immunophenotyped by multiplex immunofluorescence.
Results: LTSs displayed mostly homogeneous morphology with extended glandular differentiation and immunogenic TME both at TC and IF, with increasing gradient towards the IF. There was higher presence of immune checkpoint-associated and immunogenic genes and proteins at the IF as compared to the TC, including CD40, CD3, CD8, CD4, GZMB and PD-L1. In contrast, STSs were characterized by morphologic heterogeneity, including areas with reduced glandular differentiation and high tumour budding and a mostly immunosuppressive TME with negative gradient towards the IF. Moreover, there was decreased presence of several genes and proteins, including CD3, CD8, CXCL10, GZMB, IFNG, HLA-DR and CD40, at the IF as compared to the TC.

Conclusion: LTSs display a significantly more immunogenic TME underscoring their effective antitumor immunity, especially at the area of IF compared with STSs. Furthermore, we detected significant intratumoral heterogeneity between TC and IF on the expression of immune determinants, both in LTSs and STSs, which might explain the different antitumor immune responses, affecting patient outcome. The differential expression of immune drivers may help selecting patients for combination therapies to improve antitumor immunity and harness the responsiveness to immune checkpoint inhibitors in PDAC.

OFP-03-002

Negative prognostic impact of PD-L1 expression in tumour cells of undifferentiated (anaplastic) carcinoma with osteoclast-like giant cells of the pancreas

J. Hrudka*, K. Lawrie, P. Waldauf, V. Ciprová, J. Moravcová, R. Matej
*UH Kralovske Vinohrady, Czech Republic

Background & objectives: Pancreatic carcinoma is generally characterized by a dismal prognosis. A rare subvariant of pancreatic cancer, undifferentiated carcinoma with osteoclast-like giant cells (UCOGC), has an unpredictable prognosis according to many previous studies, with unexpectedly long survival in individual cases.
Methods: We examined 13 cases of UCOGCs and performed immunohistochemistry focused on the expression of the programmed death-ligand 1 (PD-L1) and several other potential predictive markers (PanTRK, p53, MSH2, PMS2, and the number of tumour-infiltrating lymphocytes), to explore their correlation with the follow-up of the patients. As a control group, we examined 24 cases of conventional pancreatic ductal adenocarcinoma (PDAC).
Results: PanTRK was negative in all 24 cases. P53 did not show any significant differences between UCOGCs and PDACs, and the entire cohort was MSH2, MLH1, PMS2, and MSH6 positive. Significant differences were present in the analysis of PD-L1: UCOGCs were found to express PD-L1 significantly more frequently and have a higher number of tumour-infiltrating lymphocytes than PDAC. The expression of PD-L1 was related to significantly shorter survival in patients with UCOGC and in the entire cohort. Patients with PD-L1 negative UCOGCs displayed surprisingly long survival in comparison to PD-L1 positive UCOGCs and PDACs (both PD-L1+ and PD-L1-).
Conclusion: We compared our results with previously published data, and, after statistical analysis, we were able to identify PD-L1 as an effective prognostic marker of UCOGC and suggest a strong need for a clinical trial of immune checkpoint immunotherapy in patients with advanced PD-L1 positive UCOGCs.

OFP-03-003

Non-ductal pancreatic tumour classification by whole genome DNA methylation profiling

A.V. Verschuur*, F. Westerbeke, J.K. Benhamida, O. Basturk, D.S. Klimstra, S. Yachida, P. Selenica, W.M. Hackeng, C. Geisenberger, L.A. Brosens
*Department of Pathology, University Medical Center Utrecht, Utrecht University, The Netherlands

Background & objectives: Cytological and histopathological diagnosis of pancreatic neuroendocrine neoplasms, acinar cell carcinoma, solid pseudopapillary neoplasms and pancreatoblastomas can be challenging while it is crucial for therapeutic decision making. This study investigates if methylation profiling can assist in differentiating non-ductal pancreatic cancers.
Methods: DNA methylation profiles were obtained from 306 primary pancreatic cancer samples and 20 normal pancreas cases. Machine learning methods including Neural Networks, Random Forest and Gradient Boosting were trained to distinguish between cancer types. Methylation data obtained from The Cancer Genome Atlas spanning 29 different tumour types were used to develop an algorithm capable of detecting tumours of non-pancreatic origin.
Results: The Neural Networks, Random Forest and Gradient Boosting models achieved accuracies of 96%, 9% and 91% respectively in 100% of cases. When modifying the threshold for minimally required probability scores for classification, the Random Forest model demonstrated highest accuracies for the majority of cases. Non-pancreatic tumour detection based on prediction scores achieved an AUC of > 0.99.
Conclusion: Highly accurate differentiation between non-ductal pancreatic cancers can be achieved with whole genome DNA methylation profiling. At the same time, non-pancreatic entities are identified with near perfect precision preventing false positive diagnoses.

OFP-03-004

Morphological spectrum of gallbladder cancer and its precursors

V. Angerilli*, T. de Bitter, M.E. Vink-Börger, P.R. de Reuver, M. Fassan, I.D. Nagtegaal, R.S. van der Post
*Department of Medicine, Surgical Pathology Unit, University of Padua, Italy

Background & objectives: Gallbladder cancer (GBC) is a rare neoplasm in Western countries with a dismal prognosis and its pathological evaluation remains a challenge. Here, we performed a comparative histopathologic analysis of a large multi-institutional series of GBC cases and associated precursor lesions.
Methods: Specimens and clinicopathological data of 670 GBC patients, diagnosed between 2000 and 2019 were collected using the Dutch Nationwide Pathology Database (PALGA) and the Netherlands Cancer Registry. Histopathology of precursor lesions and carcinomas was reviewed. The entire cohort was investigated for the immunohistochemical expression of EMA, MUC2, MUC5AC, MUC6, CK7, CK20, and p53. Univariate and multivariate survival analyses were performed.
Results: Precursor lesions were reported in 41.8% (280/670) of cases, either intracholecystic papillary-tubular neoplasm (ICPTN) (n=192), biliary intraepithelial neoplasia (BilIN) (n=81), or mixed lesions (n=7). Histopathological subtypes comprised biliary-type adenocarcinoma (AC, 64.8%), intestinal-type AC (13.6%), and other subtypes (21.6%) including adenosquamous, diffuse, undifferentiated, mucinous, neuroendocrine, squamous, clear cell and carcinosarcoma. The presence of BilIN was associated with biliary-type AC (p=0.040), while ICPTN was associated with intestinal-type AC (p=0.002). At univariate analysis, carcinoma histotype, grading, T and N stage, lymphatic, vascular, and perineural invasion were associated with overall survival (OS) ($p<0.05$). At multivariate analysis, carcinoma histotype, grading, and T stage proved to be independent prognostic factors ($p<0.05$).
Conclusion: This work sheds light on the morphologic spectrum of GBC and precursor lesions. The histopathologic and immunophenotypic features of GBC represent valuable information and must be taken into account in the prognostic stratification of GBC patients.

OFP-03-005

Diagnostic accuracy of cell blocks in bile duct carcinomas. A pilot study

L.P. Mocan*, I. Rusu, T. Mocan, C.S. Melincovici, C.M. Mihu
*Department of Histology, "Iuliu Haţieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Background & objectives: Cholangiocarcinoma (CCA), a highly aggressive malignancy has a rising incidence and a deficient diagnostic accuracy, of around 50%. The aim of this study was to assess the diagnostic performance of cell blocks from bile samples in patients with biliary carcinomas.

Methods: The study group included 55 patients previously diagnosed with CCA or gallbladder carcinoma, using imaging studies and/or conventional pathology. The control group included 15 patients with choledocholithiasis. Bile samples were collected for cell block analysis during therapeutic endoscopic retrograde cholangiopancreatography or percutaneous biliary drainage. Cell blocks were assessed by pathologists blinded to clinical data, in a tertiary hepatobiliary healthcare facility.
Results: The median age of the patients was 66.98 years and 30 patients (54.54%) were women. The average tumour size was 4.72 ± 2.63 cm (standard deviation). In our study group, there were 9 cases of intrahepatic CCA, 31 perihilar CCAs, 2 distal CCAs and 13 gallbladder carcinomas. Overall, the diagnostic accuracy between cell blocks and the final clinical diagnosis was 63.63%. In 61.29% cases, the interpretation of cell block correlated with conventional pathology and in 58.53%, it correlated with imaging conclusions. Cell block interpretation was aided by immunohistochemical stains in 11 cases (20%). In the control group, all cell blocks were negative for malignancy.
Conclusion: We showed that evaluation of cell blocks from bile distinguished malignant cases with a reasonable sensibility, thus representing an adequate method for positive pathologic diagnosis of biliary cancers. Moreover, if positive for malignancy, cell block interpretation can counteract delayed diagnosis in cases where tumour biopsies are not attainable for conventional pathology or cases with recurrent false negative results. This would offer earlier access to oncologic therapy for a significant subgroup of patients. Larger studies are needed to validate the results.

OFP-03-006

Morphological subtypes of pancreatic ductal adenocarcinoma have quite unique features and prognostic values

A. Yavas*, L. Haeberle, I. Esposito
*Heinrich-Heine University and University Hospital of Düsseldorf, Germany

Background & objectives: Despite the improvements in molecular subtyping of pancreatic ductal adenocarcinoma (PDAC), the relevance of histomorphological subtyping is still not known. In our study, we aimed to classify PDACs according to tumour morphology and investigate the association with clinicopathological parameters.
Methods: An extensive histomorphological analysis of 164 PDACs was performed. Based on the presence of a special histologic component in >30% of the tumour, PDACs were classified as conventional, complex with small solid nests or large solid sheets, papillary and cribriform. Moreover, recognized PDAC variants, presence of clear cells (>30%) and pleomorphic single cells were noted. Clinicopathological comparisons were performed.
Results: 35% of cases were classified as conventional PDACs,13% were variants (8% adenosquamous,4% undifferentiated,1% micropapillary), 36% had complex,14% papillary and 2% cribriform patterns. In contrast to conventional and papillary tumours, all complex PDACs were WHO grade 3($p<0.05$) and a higher proportion of them revealed pleomorphic single cells (61%) and clear cells (27%) ($p<0.05$). 65% of tumours with >30% clear cells were grade 3 complex PDACs with large solid sheets.
Papillary PDACs revealed longer overall survival (median 30.2 months) than conventional, complex and cribriform subtypes (median 19.3, 16 and 13 months, respectively), with significant difference between complex and papillary PDACs($p<0.05$). Surgical margin status, N, M and TNM stages were related to overall survival($p<0.05$).
Conclusion: Our preliminary results confirm that PDAC is a highly heterogeneous entity. PDACs with >30% complex morphology, characterized by abortive glands, cribriform structures, small solid nests or large solid sheets, tend to exhibit more aggressive behaviour, in contrast to PDACs with >30% papillary structures. Morphological classification is useful to better understand the characteristics of PDAC and to predict the clinical outcome. Further analyses are required to elucidate the association between morphological and molecular subtypes of PDAC.

OFP-03-007

Beyond histology: mutation of TERT promoter among the predictors of post-surgical recurrence of resected hepatocellular carcinomas

F. Vasuri*, S. Chillotti, T. Maloberti, E. Albertini, G. Germinario, M. Cescon, M. Ravaioli, D. de Biase, A. D'Errico
*Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy

Background & objectives: Surgical resection is the first option in advanced hepatocellular carcinoma (HCC), albeit burdened with a high recurrence rate. Aim of this study was to integrate the HCC pathological features with gene mutations to improve the prognostic role of pathological analysis.
Methods: In this monocentric prospective study, 67 patients resected for HCC were enrolled. All histological features were collected, including tumour grade, architecture, margins, microvascular invasion (MVI) and portal microvascular invasion (PMVI). Next-generation sequencing (NGS) was applied with a custom panel analysing 330 amplicons. Patients' clinical data and follow-up were recorded as well. Disease-free survival was analysed by multivariate and univariate tests.
Results: At follow-up, 13 (19.4%) patients experienced HCC recurrence. The most represented mutations were TERT promoter (n=41, 61.2%), TP53 (n=18, 26.9%) and CTNNB1 (n=17, 25.4%). At multivariate analysis, tumour dimensions (p=0.040, Exp(B) 1.13), PMVI (p=0.010, Exp(B) 36.29), and TERT mutation (p=0.034, Exp(B) 6.95) correlated with recurrence. Univariate analyses (Kaplan-Meier curves) confirmed the prognostic value of these variables: tumour dimensions ≥4.5 cm (very close to AJCC stage pT3; 9 recurrences, p=0.041, odd-ratio=3.7), PMVI (9 recurrences, p=0.062, OR=3.3), and TERT (11 recurrences, p=0.049, OR=4.4) confirmed the correlation with post-surgical HCC recurrence. The concomitant occurrence of these three variables was present in 7 cases, among which 5 recurrence cases were recorded (p=0.002, OR=15.94).
Conclusion: Our results show that NGS analysis in resected HCC could not only be used for future therapeutic options, but it should be integrated with histopathological analysis in order to predict the risk of tumour recurrence after surgical resection: indeed, in resected patients, TERT mutation is among the strongest predictors of tumour recurrence, together with tumour dimensions (i.e. pathological stage) and the occurrence of portal microvascular invasion, which should always be reported separately from the classic MVI.
This work was funded by Fondazione Cassa di Risparmio di Bologna (Carisbo).

OFP-03-008

Biliary atresia; do histopathological insights predict clinical outcomes?

A.T. Bol Serttürk*
*Ankara University Medical School, Pathology Department, Turkey

Background & objectives: Biliary atresia (BA) is an idiopathic, progressive inflammatory disease of the biliary tract. Kasai Procedure (KP-Hepatoportoenterostomy) should be performed to maintain biliary drainage and decelerate cirrhotic progression. Here, we aimed to evaluate the histopathological findings in liver related to clinical outcomes.
Methods: 26 BA cases with clinical follow-up were reevaluated. Portal fibrosis, edema and expansion, severity and distribution of biliary duct proliferation, bile plugs, pseudorosette formation, giant cell transformation (GCT), hepatocyte damage, extramedullary haematopoiesis, ductal plate malformation were examined in liver biopsies which were obtained during

KP. Clinical information about attacks of cholangitis, native-liver survival, need for transplantation were obtained from the database.
Results: Among the 26 cases, 23 had Kasai in 90 days after birth, involved in the statistical analysis. 8 (%34.8) cases were operated in the first 45 days (Group 1) whereas 15 (Group 2) between 45-90 days. Severe fibrosis was significantly more common in Group 2(p=0,009). Biliary duct proliferation was more commonly intense(p=0,008) and diffuse(p=0,032) in Group 2. There was no significant difference between groups for GTC. Additionally, no difference was found between the groups in terms of clinical outcomes. However, patients with shorter than two-years native-liver survival(n=6) were all in Group 2. Besides, patients with at least four years native-liver survival had had Kasai before 60 days.
Conclusion: BA is, by its nature, a progressive disease that results in liver cirrhosis. It has been demonstrated by clinical outcomes and pathological parameters that surgery performed at an early age offers a longer native-liver survival. It is seen that findings from pathological examination are directly related to time until KP is performed, these findings can provide preliminary information about the course of the disease.

OFP-03-009
Correlations between morphology and mutational profile in hepatocellular carcinoma: time for routine molecular biology?
S. Chillotti*, T. Maloberti, G. Germinario, M. Carroli, M. Ravaioli, D. de Biase, A. D'Errico, F. Vasuri
*Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy., School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: The mutational profiling could be a useful tool to better stratify risk in patients with hepatocellular carcinoma (HCC). Our aim is to evaluate how and if next-generation sequencing (NGS) results, immunohistochemistry (IHC) and morphology correlate each other.
Methods: We enrolled 76 consecutive resected HCCs on which we reviewed the histology and recorded various morphological parameters such as grade, architecture, variant, presence of overt cirrhosis and microvascular invasion. We then performed NGS with a panel spanning 330 amplicons and IHC analysis for the proteins p53, beta-catenin and glutamine synthase (GS).
Results: The most commonly found mutations were TERT-promoter (61%), TP53(32%) and CTNNB1(28%). Less frequent mutations were found: SMAD; KIT; PI3K and IDH1. TP53-mut correlated with higher grade tumours (p=0.029), and with macrotrabecular/solid architecture(p=0.004) while TERT-mut was found in 50% of non-cirrhotic cases and 72% of cirrhotic cases (p=0.040). CTNNB1 didn't correlate with a specific pattern. IHC for p53 was not useful in recognizing TP53-mut. IHC for GS was strongly and diffusely positive only in CTNNB1-mut cases, but with 3 negative cases. Beta-catenin expression in non-CTNNB1-mut cases was strong membranous while in CTNNB1-mut cases it showed a variable staining with 10 showing a nuclear translocation, 17 cytoplasmic positivity and 14 lost the membrane positivity.
Conclusion: Our results show a variegated mutational landscape: TP53-mut correlates with histological appearance, but in absence of a clear IHC positivity. CTNNB1-mut cases were recognizable using beta-catenin and GS: GS positivity is today used as a diagnostic tool in early HCCs, but as we showed it can be negative also in CTNNB1-mutated cases. Considering that we found HCCs with potentially targetable mutations but lacking specific morphology, it could be time to include NGS in the routine practice of HCCs.
Funding: Fondazione Cassa di Risparmio in Bologna

OFP-03-010
Keratin filaments deficiency in ischemia-reperfusion liver injury
T.S. Driva*, A. Pergaris, G. Sotiropoulos, E. Antoniou, I. Delladetsima, S. Sakellariou
*1st Department of Pathology, General Hospital of Athens "Laiko", Medical School, National and Kapodistrian University of Athens, Greece

Background & objectives: Keratin (K) 7 is expressed by hepatocytes in ischemic states, while attenuation of K8/18 expression has been observed in ballooned hepatocytes in various liver diseases. Herein we investigate the expression of K8/18 and K7 in ballooned hepatocytes of ischemia/reperfusion injury.
Methods: K7 and K8/18 expression was immunohistochemically assessed and semiquantitatively evaluated in 8 graft biopsies with ischemia /reperfusion injury showing minimal/mild (3 cases) to moderate/severe (5 cases) degree of hepatocellular ballooning and cholestasis (6 cases). Liver samples were obtained 1 to 9 days post-transplantation.
Results: A significant reduction to elimination of the cytoplasmic expression of K8/18 was observed in ballooned hepatocytes in the cases with prominent hepatocellular ballooning in zones 3 and 2. Slight attenuation and occasionally loss were demonstrated in those with milder cell swelling. Hepatocellular expression of K7 was observed in zone 3 only in 2 cases with minimal hepatocellular ballooning.
Conclusion: In ischemia/reperfusion injury hepatocellular ballooning is associated with disorders of keratin filaments 8/18. Attenuation and loss of their cytoplasmic expression are related to the degree of ballooning. Lack of K7 appearance in hepatocytes with prominent ballooning suggests generalized intermediate keratin filaments disarray or arrest of liver cell metaplastic mechanisms, while an independent to ischemia pathogenetic process cannot be excluded.

OFP-03-011
Hepatic histopathological lesions and study of liver stiffness in a case series of patients with Fontan procedure
M.R. Meléndez Gispert*, L. Téllez, C. Ariño-Palao, D. Bueno-Sacristán, A. Tenelanda-Santillán, A. Veliz Dominguez, C. Perna Monroy
*Ramón y Cajal University Hospital, Spain

Background & objectives: Fontan procedure (FP) is performed in single ventricle defects patients and produces long-term liver damage. Liver stiffness, several grades of fibrosis and even hepatocellular carcinoma (HCC) may occur. Time from surgery is an important issue.
Methods: Liver biopsies and clinical data including transient elastography (FibroScan®) from patients with FP were reviewed between 2017 and 2023. The hepatic congestive fibrosis index was used to classify fibrosis into F0, F1, F2A, F2B, F3 and F4.
Results: Fifty-nine patients, 38 males (64.40%) and 21 females (35.59%) were found. Mean age was 30.79 years. Patients were categorized into F0 (1.69%), F1 (8.47%), F2A (20.33%), F2B (8.47%), F3 (32.2%) and F4 (28.81%). Elapsed time from surgery in these groups were 20, 21.2, 22.83, 20.8, 23.31 and 25.35 years respectively. Four patients (6.77%) developed HCC (3,38% F4, 1,69% F2A). The mean value of liver stiffness was 17.5 KPa in F0, 20.26 KPa in F1, 26.43 KPa in F2A, 15.40 KPa in F2B, 23.77 KPa in F3 and 40.38 KPa in F4.
Conclusion: Nearly 90% of biopsies disclosed significant hepatic fibrosis (≥F2) which confirms that fibrosis is practically universal in FP patients. A common potential complication of chronic liver damage is the development of HCC. All patients except three, presented severe liver stiffness values on FibroScan®(≥F3). F4 patients showed marked increase in stiffness compared with F2 and F3 patients. Non-invasive methods of monitoring liver fibrosis are usually used in FP patients. However, only congestive fibrosis index in biopsy remains validated as the gold standard.

OFP-03-012
Expression of fibroblast activation protein (FAP) in pancreatic neuroendocrine tumours
F. Kellers*, V. Stoll, C. Röcken, B. Konukiewitz

*University Medical Center Schleswig-Holstein, Campus Kiel, Department of Pathology, Kiel, Germany

Background & objectives: Fibroblast activation protein (FAP) expressed by cancer-associated fibroblasts can be targeted in theranostics in various solid tumours. We investigated the immunohistochemical expression of FAP in stroma and tumour cells of pancreatic neuroendocrine tumours (PanNETs) in relation to hormone expression.
Methods: 31 PanNETs were analysed. Histological and immunohistochemical (synaptophysin, chromogranin A, Ki67, islet hormones, SSTR2) classification was conducted. Semiquantitative analysis of hormone expression was performed. Percentage of FAP expression and staining intensity was measured semiquantitatively in tumour and stroma cells and confirmed using digital image analysis (QuPath). FAP expression was correlated with hormone expression and clinicopathological characteristics.
Results: 27 (87 %) of PanNETs showed hormone expression (26 % insulin, 48 % glucagon, 58 % PP, 13 % somatostatin, 13 % gastrin, 10 % serotonin). 84 % of PanNETs showed membranous positivity (2+ or 3+) for SSTR2. Membranous and cytoplasmatic FAP expression in tumour cells was observed in 45 % of PanNETs. All FAP-positive PanNETs expressed glucagon. FAP was detected in stroma fibroblast in 87 % of PanNETs (39 % positivity in 1 % - 10 % of stromal cells; 19 % positivity in 11 % - 50 % of stromal cells; 29 % positivity in > 50 % of stromal cells in PanNETs), including SSTR2-negative tumours.
Conclusion: Membranous FAP expression was observed in cancer-associated fibroblasts in the stroma of PanNETs with varying intensity. Moreover, tumour cells of glucagon-positive PanNETs displayed cytoplasmatic positivity. Targeting FAP broadens imaging options and therefore could be a promising approach in glucagon-positive PanNETs as well as in insulin-positive, SSTR2-negative PanNETs.
Funding: Franziska Kellers participates in the Clinician Scientist Program in Evolutionary Medicine (CSEM) at University Medical Center Schleswig-Holstein supported by the DFG (Deutsche Forschungsgemeinschaft).

OFP-04 | Joint Oral Free Paper Session Uropathology / Nephropathology

OFP-04-001
For those who like to see numbers in pathology reports when histological grading is blurry...

E.D. Serbes*, M.C. Karaburun, K. Obaid, M. Babayigit, M.C. Gogus, S. Baltaci, E. Suer, S. Kiremitci, D. Enneli
*Ankara University Medicine School, Pathology Department, Turkey

Background & objectives: In this study, we aimed to investigate the prognostic significance of the ratio of accompanying low-grade areas in high-grade non-muscle invasive bladder carcinomas (NMIBC), which are at the intermediate/high-risk group and received intravesical BCG therapy.
Methods: A preliminary cohort of 148 patients diagnosed as high-grade NMIBC at transurethral resection (TUR) specimens and completed at least one cycle of induction and maintenance BCG therapy at our institution between 2010-2020 was included. The percentage of low-grade areas of the tumour was determined in the initial TUR specimens of every case. Clinical follow-up information (recurrence/progression, survival data) were obtained.
Results: While 70% (104/148) of the tumours had pure high-grade morphology(group-1), 30% had low-grade component ranging from 5 to 80%(group-2). The median follow-up time of the group-1 and 2 were 32 and 35 months, respectively. The progression rate in the group-1(10,5%) was significantly higher than group-2 (4,54%)(p=0.033), whereas no such significant difference was found regarding recurrence rate (p=0.098). Within group-2, 23/44 cases <=20% low-grade areas (group-2a) and 21/44 cases had >20% (group-2b). There was no statistical difference between group-2a and group-2b regarding recurrence rates, but progression rate was higher in the group-2a (p=0.019). Kaplan-Meier survival analysis, univariate/multivariate regression analysis were planned to be done after the evaluation of the whole cohort.
Conclusion: According to the latest World Health Organization (WHO) classification, urothelial carcinomas with 5% high-grade histology are considered as high-grade. However, high-grade NMIBCs containing 0% and 95% low-grade components are tumours located at two different ends in terms of the low-grade component ratio and our preliminary study revealed that the risk of progression rate significantly increases when low grade areas were limited in a percentage of 20% in the initial TUR specimens of high-grade NMIBC.

OFP-04-002
Molecular subtyping of upper urinary tract urothelial carcinomas with surrogate immunohistochemical markers

E.D. Serbes*, M. Babayigit, S. Sevim, E. Suer, M.C. Gogus, S. Kiremitci, D. Enneli
*Ankara University Medicine School, Pathology Department, Turkey

Background & objectives: Studies on molecular subtyping of upper urinary tract urothelial carcinomas (UTUC) are limited, which is a distinct entity from urinary bladder carcinomas (UBC). We aimed to perform basal/luminal phenotyping of UTUCs by using surrogate immunohistochemical markers and to investigate its prognostic significance.
Methods: Fifty patients diagnosed with UTUC on radical nephroureterectomy specimens at our institution between 2009-2019 were included in the study. Tumours were all high grade conventional urothelial carcinomas. Those with any concomitant/previous diagnosis of UBC were excluded. An antibody panel of CK5/6, CD44, CK20, p53 was applied immunohistochemically, to identify basal/luminal molecular subtypes and investigate their prognostic role in UTUCs.
Results: The mean follow-up time of the patients (mean age:67,range:37-81) was 42.6 months (±21.4). 18/50 (36%) patients showed intravesical recurrence after a mean follow-up period of 7.94 months. Twenty-six cases (52%) died, of which 20(76.9%) were cancer-related. Twenty-five(50%), 19(38%), 4(8%) cases showed basal-like, luminal-like and mixed(basal and luminal-like) immunophenotypes, respectively, 2(4%) cases showed null-phenotype. Univariate-Cox-analysis of disease-free survival (DFS) revealed that CD44(hazard-ratio:0.14, p=0.004) or CK5/6(hazard-ratio:0.108, p=0.001) expression indicating basal-like phenotype were favourable prognostic factors, whereas CK20(hazard-ratio:26.159,p=0.001) and p53(hazard-ratio:4.394,p=0.004) expression were poor prognostic factors. Significantly higher intravesical recurrence was observed in CK5/6-negative UTUCs (p=0.035), despite of no correlation with other markers. In multivariate-cox-analysis of DFS, CK20-positivity in UTUCs indicated 9.5 times increased risk (p=0.047) and basal-like immunophenotype indicated better prognosis (p=0.006).
Conclusion: In the present study, we investigated the prognostic role of basal/luminal immunophenotyping and p53 expression in UTUCs. CK20 and p53 expression indicated poor prognosis, whereas basal-like phenotype correlated with significantly more favourable prognosis, in contrary to its poor prognostic effect in UBC. CK5/6 negativity was found to be correlated with a significantly increased risk of intravesical recurrence. Although these results look promising in predicting prognosis and risk of intravesical recurrence in UTUCs, they need to be confirmed by further studies.

OFP-04-003
Does GATA3 expression contribute to diagnosis in renal tumours with eosinophilic/oncocytic features?

C. Utku*, B. Sarsik Kumbaraci, B. Yaman, M.S. Kalemci, S. Sen
*Department of Pathology, Ege University Faculty of Medicine, Izmir, Turkey

Background & objectives: There is a limited number of studies investigating GATA3 expression in eosinophilic renal tumours. We aimed to assess GATA-3 expression in newly defined eosinophilic renal tumours that have overlapping morphological features between oncocytoma and chromophobe renal cell carcinoma (CRCC).
Methods: Thirty eosinophilic tumours from 29 cases that have radical/partial nephrectomy or needle biopsy materials between 2021 and 2023 have been reevaluated retrospectively by their morphological and immunohistochemical findings. The morphological features and expressions of GATA3, CK7, CK20, vimentin, SDHB, FH, HMB45, Melan A, and CD117 were evaluated.
Results: The mean age was 58,17±17,07 years (range; 13-87) with a slight predominance of men over women (1.2:1 ratio). There were 13 (45%) CRCCs, 8 (28%) oncocytomas, two (7%) eosinophilic solid cystic RCCs (ESC-RCC), and three (10%) low-grade oncocytic tumours (LOT). Papillary tumour with reverse polarity (RP-PT) coexisted with one of the LOT cases. The other three tumours were SDHB-deficient RCC, FH-deficient RCC, and TFEB-rearranged RCC. LOTs, SDHB-deficient RCC, FH-deficient RCC, and RP-PT showed diffuse, 10 of 13 CRCCs, and 2 of 8 oncocytomas showed focal GATA3 positivity. SDHB-RCC, FH-RCC, TFEB-RCC, ESC-RCC, and oncocytomas didn't express CK7. The newly identified LOT and RP-PT (provisional entity) showed GATA3 and CK7 expressions.
Conclusion: Morphological similarity of CRCC, oncocytoma, and newly defined eosinophilic tumours in nephrectomy and kidney needle biopsy materials can cause diagnostic problems. Our results show that diffuse CK7/GATA-3 coexpression contributes to identifying eosinophilic renal tumour types in routine practice. Awareness of this immunohistochemical profile in eosinophilic renal tumours may help to avoid misdiagnosis.

OFP-04-004

Investigating the prognostic value of invasive cribriform gland size and percentage in grade group 2 and grade group 3 prostate adenocarcinoma

E. Tekin*, N.S. Şeker, A. Ozen, M.F. Açıkalın, C. Can, E. Çolak
*Eskişehir Osmangazi University, Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Gleason scores guide clinical management in prostate adenocarcinoma. Cribriform glands are linked to poorer outcomes. Our study aims to assess the prognostic role of invasive cribriform gland size and percentage in low-intermediate risk group adenocarcinomas.
Methods: Our study enrolled 177 male patients with Grade Group 2 and 3 prostate adenocarcinomas. All cases were re-evaluated and recorded clinical and pathological data. The largest invasive cribriform gland was identified, and its diameter measured. P63 was used as a basal marker for all cases.
Results: The mean age of the patients was 67.8 years. Lymph node metastasis was not detected in cases without cribriform pattern, whereas it was noted in 22.5% of cases with cribriform pattern ($p=0.014$). The mean percentage of cribriform glands and the mean largest invasive cribriform gland size were significantly higher in cases with lymph node metastasis compared to cases without lymph node metastasis (34.3% - 2.98 mm vs. 17.5% - 1.98 mm, respectively; $p<0.001$ and $p=0.003$, respectively). Biochemical recurrence-free survival was significantly lower in cases with a maximum invasive cribriform gland diameter of >0.5 mm ($p<0.001$) and in cases with a cribriform pattern percentage of >10% ($p<0.001$).
Conclusion: Mean cribriform gland sizes and percentages were significantly associated with more advanced pT status, a higher rate of extraprostatic extension, lymph node metastasis, biochemical recurrence, higher preoperative PSA values, surgical margin positivity, and lower biochemical recurrence-free survival. Our findings suggest that a more aggressive clinical approach may be needed in grade group 2 and 3 cases with invasive cribriform glands larger than 0.5 mm and a cribriform gland percentage of >10% in prostate needle biopsies.
Funding: Eskişehir Osmangazi University Scientific Research Project Unit

OFP-04-005

Intraepithelial CD8+ cytotoxic T-cells are the main component of the immune tumour microenvironment that drive prognosis in muscle-invasive bladder cancer

N. Blessin*, N.F. Debatin, E. Bady, T. Mandelkow, H. Samtleben, D. Horst, A.H. Marx, M. Fisch, M. Slojewski, T. Ecke, S. Koch, N. Adamini, G. Sauter, T. Schlomm, H. Zecha
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: Quantity and the spatial relationship of individual immune cell (sub)types can provide prognostic information in muscle-invasive bladder cancer.
Methods: To study the prognostic role of different immune cell subpopulations in muscle-invasive bladder cancer, we stained 521 muscle-invasive urothelial bladder carcinomas with 21 antibodies using BLEACH&STAIN multiplex fluorescence immunohistochemistry (mfIHC) in a tissue microarray format. A framework of neuronal networks was trained and used for image analysis.
Results: The identification of more than 300 different immune cell subpopulations and the characterization of their spatial relationship resulted in numerous spatial interaction patterns. 40 immune parameters showed prognostic significance in univariate analyses of which 15 were independent from pT, pN, and histologic grade. The strongest association to clinical outcome was identified for intraepithelial CD8+cytotoxic T-cells (tAUC: 0.70) compared to all other 15 independent prognosis parameters (AUC: ≤0.68,0.039). Deeper spatial analysis revealed an increased expression levels of TIM3, CTLA-4 and PD-1 on CD8+ T cells that were located in the intraepithelial compartment. Furthermore, the cell-to-cell interaction profile of intraepithelial CD8+T-cells was dominated by intraepithelial dendritic cells as well as intraepithelial M1-macrophages.
Conclusion: The intraepithelial CD8+T-cells that showed the highest expression level of TIM-3, PD-1 and CTLA-4 and were strongly interacting with M1-macrophages as well as dendritic cells and represented the strongest prognostic parameter in muscle-invasive bladder cancer. This can be explained by the fact that tumour cell destruction by CD8+cytotoxic T-lymphocytes through direct cell-to-cell-contacts represents the "terminal-end-route" of anti-tumour immunity. The strongest prognostic immune-factor –intraepithelial CD8+T-cells– can be measured straightaway in routine pathology as the CD8-labelling index using conventional bright field immunohistochemistry.

OFP-04-006

Evaluation of PBRM1, PD-L1, CD31 and CD4/CD8 ratio as a predictive signature of response to VEGFR-TKI-based therapy in metastatic renal cell carcinoma (mRCC) patients with IMDC intermediate prognosis: results from the APAChE-I study

M. Martini*, C. Ciccarese, V. Fiorentino, F. Pierconti, G. Tortora, R. Iacovelli, A. Ieni
*Università di Messina, Italy

Background & objectives: Current first-line (1L) therapy options for intermediate IMDC group mRCC patients (pts) are based on anti-angiogenic agent (VEGFR-TKI) and/or immunotherapy. No biomarkers (BM) for selecting the most effective regimen have been identified so far.
Methods: Immunohistochemical expression of PBRM1, PD-L1, CD31, and CD4/CD8 ratio was evaluated on 156 histological samples of intermediate-risk mRCC pts treated withVEGFR-TKI monotherapy. Cox model was used to assess the correlation between BM and outcomes; PFS and OS were estimated by Kaplan-Meier method.

Results: In pts treated with VEGFR-TKI monotherapy, a significant correlation with PFS was observed with loss of PBRM1 expression (p=0.035), PD-L1 negativity (p=0.048), and high CD4/CD8 ratio (p=0.073). CD31 expression did not significantly correlate with PFS. A profile potentially predictive of angiogenesis (AP+) was defined based on the PBRM1 loss, PD-L1 negative, and high CD4/CD8. In pts treated with VEGFR-TKI monotherapy, tumours with the AP+ had a significantly longer median PFS (p=0.003) and mOS (p=0.024) compared to the others. The AP+ retained its significant correlation with PFS (p<0.001) and OS (p=0.006) in pts receiving VEGFR-TKI-based therapies.
Conclusion: The AP+ signature (loss of PBRM1, PD-L1 negative, and CD4/CD8 highratio) was associated with improved clinical outcomes in mRCC pts at IMDC intermediate prognosis treated with VEGFR-TKI-based therapy; this correlation was significant regardless from the addition of IO to VEGFR-TKI monotherapy. Prospective validation of this signature is required for guiding the selection of the most appropriate 1L therapy.

OFP-04-007

Basal phenotype is a peculiar feature of urothelial bladder carcinoma of young adults: a cohort analysis

M. Valeri*, M. Iuzzolino, M. Cieri, L. Dore, A. Bressan, F. De Napoli, C. De Carlo, C. Rebecchini, L.M. Terracciano, P. Colombo
*Humanitas University, Department of Biomedical Science, Pieve Emanuele, Milan, Department of Pathology, ASST Bergamo Est, Bolognini Hospital, Seriate, Bergamo, Italy

Background & objectives: Urothelial carcinoma (UC) in young adults (YA, 18-40 years) is an uncommon, poorly understood and challenging disease for the clinical impact of potential recurrence and progression. Here we investigated the molecular phenotype and the genomic profile of a YAUC cohort.
Methods: All YAUCs diagnosed in our department between 1998 and 2021 were reviewed. As surrogate of molecular subtyping, we employed immunohistochemical markers (CD44, CK5/6, CK20, GATA3) and a score system to stratify into Luminal and Basal phenotype. Additionally, expression of Androgen receptor (AR) and RB1 was evaluated. In a subset of cases, NGS analysis was performed to search for genomic alterations.
Results: Of the 51 cases collected, median age was 35 years and 42 patients were male; tumour grading was as follow: 36 low-grade (LG), 5 high-grade (HG), and 10 low malignant potential (PUNLMP) or papilloma (UP). All but 2 cases were pTa. Basal phenotype was the most common finding (44/51; 86,3%), with 43 cases both CK5/6+ and CD44+. Three HGUC were Luminal. AR and RB1 were expressed in 26 and 48 cases, irrespective of grading. NGS analysis of 10 cases showed FGFR2 mutation in 40% of tumours, while mutations in HRAS, KRAS, PIK3CA, CDKN2A, p53 were uncommon. Phenotype did not correlate with recurrence, possibly due to the limited number of events.
Conclusion: The recent classification in molecular phenotypes and genomic alterations are still poorly investigated in YAUC. Our cohort showed a clear Basal phenotype and retention of RB1, although our data may be biased by the predominance of LGUC. In contrast to previous published data, GATA3 did not act as a Luminal marker since all cases were positive. These results should be validated on a larger cohort of YAUC with a deeper investigation of molecular events related to this challenging category.

OFP-04-008

Expanding the spectrum of eosinophilic solid and cystic renal cell carcinoma: molecular characterisation of borderline neoplasms from 25 patients reveals frequent alterations of TSC1, TSC2, and MTOR

S. Williamson*, J. Van Arnam, K. Al-Obaidy, R. Humble, C. Kao, L. Schwartz, M. Tretiakova, T. Antic, L. Cheng, N. Gupta, J. McKenney, J. Nguyen, C. Przybycin, R. Alaghehbandan, S. Mohanty
*Cleveland Clinic, USA

Background & objectives: Eosinophilic solid and cystic (ESC) renal cell carcinoma (RCC) is accepted as a distinct renal neoplasm, with eosinophilic cell morphology, frequent keratin 20 positivity, and *TSC1/TSC2* gene alterations. We studied tumours with overlapping morphology for immunohistochemistry and genetics.
Methods: We selected tumours (n=25) with partial features of ESC RCC: voluminous eosinophilic cells, solid architecture, keratin 20 positivity, cytoplasmic stippling, or hobnail-shaped cells, combined with atypical features, including papillary/tubular architecture, clear cells, foamy macrophages, psammoma bodies, end-stage renal disease (ESRD), concurrent papillary RCC, strong AMACR, or negative keratin 20. A next generation sequencing cancer gene panel was performed on 19.
Results: Patients were 15:10 F:M, 48 to 76y. Unusual findings included ESRD (6) or multiple tumours (7 papillary/ESC-like). Only 3 were originally diagnosed as ESC. Keratin 20 most often was rare positive, 1-5% of cells. Five were negative and 3 showed higher percentages of cells positive. Sequencing revealed alterations of *TSC1*, *TSC2*, or *MTOR* in 11 of 19, and one additional *PIK3CA* mutation. Eleven were reclassified as ESC or likely ESC. Seven were indeterminate, either suggestive morphology/negative genetics or positive genetics/atypical morphology. One in an ESRD patient had *KMT2C* mutation (reported in ACKD RCC, although morphology was not classic). Three were considered other entities: unclassified, papillary, and clear cell RCC.
Conclusion: A substantial fraction of tumours with eosinophilic cells showing overlapping features of ESC RCC and papillary RCC are likely best classified as true ESC RCC, often with only rare keratin 20 positive cells. However, keratin 20 positivity can also be found in occasional non-ESC tumours. The morphologic spectrum of ESC is probably broader than previously thought, as only 3 of the most convincing 11 ESC tumours were originally diagnosed as such.

OFP-04-009

Immune cell infiltration, tumour budding, and the p53 expression pattern are important predictors in penile squamous cell carcinoma: a retrospective study of 152 cases

J. Hrudka*, Z. Prouzová, M. Kendall Bártů, J. Hojný, D. Čapka, N. Zavillová, R. Matej, P. Waldauf
*UH Kralovske Vinohrady, Czech Republic

Background & objectives: Penile squamous cell carcinoma is a rare malignancy with a slowly increasing incidence and variable prognosis. Regional lymph node involvement signifies poor prognosis but represents a late sign, and more prognostic markers for effective patient risk stratification are urgently needed.
Methods: 152 tumour samples were analysed for traditional pathological variables; tumour budding, p53, and p16 immunohistochemistry. The density of tumour lymphocytic infiltrate was subjectively determined by two pathologists (brisk/non-brisk/absent) and also using the immunoscore method, which categorized the cohort into five groups according to the number of CD3+ and CD8+ T-cells in both the tumour centre and tumour invasion front.
Results: Tumour budding count $\geq$ 5 tumour buds/20x power field and non-brisk/absent lymphocytic infiltrate were significant negative predictors of both the overall survival(OS) and cancer-specific survival(CSS), whereas a low immunoscore was a significant marker of shorter OS but not CSS. Advanced pT stage (3+4) was a significant marker of shorter CSS but not OS. In the multivariate analysis, high-grade budding was a significant parameter if adjusted for the patient`s age and associated variables, except for the pN stage. The lymphocytic infiltrate retained its prognostic significance if adjusted for age and associated variables. The negative prognostic significance of lymphatic, venous, and perineural invasion, lymph node metastasis, and p53 mutated profile was confirmed.

Conclusion: High-grade tumour budding, low immunoscore, non-brisk or absent lymphocytic infiltrate, and mutated p53 immunoprofile are negative prognostic markers in penile squamous cell carcinoma. Grade, histological subtype, and HPV status (as determined by p16 immunohistochemistry) showed, surprisingly, little or no prognostic significance.
This work was supported by the Czech Health Research Council (Grant number NU21J-03-00019).

OFP-04-010

Detection of muscularis propria invasion in urothelial carcinoma using artificial intelligence

I. Fahoum*, R. Naamneh, R. Hagege, K. Pragier, D. Hershkovitz
*Institute of Pathology, Tel-Aviv Sourasky Medical Center, Israel

Background & objectives: Muscularis propria invasion in urothelial carcinoma indicates surgical treatment and chemotherapy. Detecting muscularis propria invasion in transurethral resection specimens can be time consuming for pathologists. We aim to develop an algorithm to identify muscularis propria invasion in urothelial carcinoma.
Methods: Training the algorithm involved manual segmentation of muscularis propria and tumour using 925 images from 50 cases of urothelial carcinoma. Analytical validation was performed using 97 additional manually segmented images from 10 new cases, and the algorithm was compared to annotations of pathologist for tumour and muscularis propria. Detection rate, false alarm rate and intersection over union were calculated.
Results: In the validation cohort the detection rates of the algorithm for muscularis propria and tumour were 85% and 90%, respectively. On the other hand, the false alarm rates were 21% for tumour and 30% for muscularis propria. Causes of false alarms included thick muscular wall of blood vessels in the lamina propria and urothelium with reactive changes. When we defined event as muscle and tumour tissue were in nearest proximity, the algorithm showed lower false alarm rates.
Conclusion: Artificial intelligence can be an efficient tool and assist pathologists identifying urothelial carcinoma invasion into the muscularis propria. Our algorithmic approach yielded good results based on a relatively small training cohort. Inclusion of the proximity factor between the tumour and the muscularis propria significantly reduced the false alarm rate.

OFP-04-011

Assessing the robustness of a glomerular segmentation tool: characterization and automatic detection of annotation errors

H. Weishaupt*, N. Mola, J. Besusparis, S. Sund, S. Leh
*Department of Pathology, Haukeland University Hospital, Bergen, Norway

Background & objectives: In nephropathology, segmentation of glomeruli is one of the tasks most extensively studied using artificial intelligence. While some software applications are already becoming publicly available, it remains largely unclear how robust such tools are when applied to new cases.
Methods: To address this open question, the current study investigated the performance of a publicly available glomerular segmentation tool when applied to over 1000 whole slide images, yielding more than 125000 glomerular predictions. A combination of qualitative and quantitative measures was employed to determine the types and prevalence of annotation errors and how to automatically detect them.
Results: Through visual inspection, the project revealed that, in addition to false-positive and false-negative predictions, there were three major categories of annotation errors reflecting different segmentation mistakes. Furthermore, utilizing a wide range of morphometric features, i.e., applied quantitative metrics characterizing the shape of annotations, these errors could be detected automatically and were estimated to account for about 5% of all predictions.
Conclusion: Having investigated a large number of glomerular annotations predicted by a publicly available segmentation tool, the project demonstrates what kind of mistakes can occur, how often they occur, and how they can be automatically detected. We believe that the results of the study are highly relevant for future use of segmentation tools by raising awareness of different segmentation mistakes and how they can be identified, thus enabling their subsequent correction.

OFP-04-012

Digital pathology and gene expression analysis as potential tools of standardisation for renal transplant pathology

D. Dobi*, A. Edwards, Z.G. Laszik
*Semmelweis University, Hungary

Background & objectives: Renal transplant diagnostics is based on semi-quantitative assessment of the biopsy sample. This method is prone to inter-, and intraobserver variability. Here, we used the tools of digital and molecular pathology to explore ways to improve the current diagnostic system.
Methods: The enrolled kidney biopsies covered the entire spectrum of the T-cell alloimmune response, from normal morphology to borderline changes to T-cell-mediated rejection (n = 96). Histological sections from formalin-fixed, paraffin-embedded (FFPE) tissue blocks were stained with multiplexed immunohistochemistry, then were digitized and analysed using machine learning. Gene expression studies were performed on sections from FFPE tissue on the Nanostring platform.
Results: The F-score, recall and precision for the glomeruli were 0.91, 0.89 and 0.94 respectively. Similarly excellent parameters could be achieved for the tubules (0.93, 0.95 and 0.91). Object recognition capacity for inflammatory cells (0.79, 0.84 and 0.74) and peritubular capillaries (0.66, 0.82 and 0.60) were fair. The variables generated with the help of the algorithm showed a moderate to strong correlation with the gene sets characteristic of T cell-mediated rejection.
Conclusion: Digital pathology methods and gene expression testing are useful additional tools for semiquantitative kidney biopsy evaluation.

OFP-04-013

Hepatitis E virus infection mimics T-cell mediated rejection in transplanted kidneys

J. Schmitz*, J. Kracht, K. Evert, J.J. Wenzel, M. Schemmerer, M. Panning, L. Pape, M. Pohl, J.H. Bräsen
*Hannover Medical School, Institute of Pathology, Nephropathology, Germany

Background & objectives: Immunocompromised patients are at risk of chronic hepatitis E (HEV) infection, which can be treated with ribavirin. Recurrent T-cell and borderline rejections in a paediatric patient with high HEV copy numbers led us to study HEV infection within renal transplants.
Methods: To investigate frequency of HEV infection in renal allografts, we identified a total of 15 samples from patients with contemporaneous diagnosis of HEV-infection (diagnosed by PCR of blood/stool) at Hannover Medical School. Ten samples had sufficient residual paraffin tissue for immunofluorescence (IF) and fluorescence-in-situ-hybridization (RNA-FISH). The biopsy of the paediatric index patient was additionally sufficient for tissue-PCR and electron microscopy.
Results: We detected HEV virus RNA in paraffin tissue of the paediatric index patient by tissue-PCR. Subsequently, we localized HEV infection in tubular epithelial cells by immunofluorescence and RNA-FISH (HEV Oligo-FISH) within residual paraffin tissue as well as in electron microscopy using a routinely embedded epon block. One of

the additionally stained biopsies from an adult was also positive for HEV RNA by RNA-FISH and IF. Focal IF positivity for HEV peptide was observed in eight allografts. Ribavirin therapy was not successful in paediatric index patient: after a relapse of HEV infection rivavirin is still administered. In the second patient successful elimination of HEV was achieved after short-course ribavirin therapy.
Conclusion: HEV infection is an important differential diagnosis for T-cell rejection within transplanted kidneys, but detailed data on incidence are missing. Immunostaining of HEV peptide does not necessarily prove acute infection of renal tissues since RNA-FISH for HEV was positive only in two of the ten cases with positive tubular epithelial staining for HEV peptide by immunofluorescence. RNA-FISH seems to be a reliable and quick method to localize HEV and requires only a small amount of tissue.

OFP-04-014
Caveolin-1 expression in glomerular and peritubular capillaries as diagnostic support for doubtful cases of kidney rejection: a proof of concept
M. Carroli*, S. Chillotti, D. Malvi, E. Albertini, B. Fabbrizio, A. D'Errico, G. Pasquinelli, F. Vasuri
*Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy., School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: Caveolin-1 has been described as a useful immunohistochemical marker of antibody-mediated rejection after kidney transplantation. Aim of the present study was to evaluate the diagnostic utility of Caveolin-1 in borderline cases, i.e., with doubtful morphology between antibody-mediated and T-cell-mediated rejection.
Methods: Thirty-nine renal biopsies were evaluated, 14 post-reperfusion biopsies (controls), 15 histologically-proven rejections (6 T-cell-mediated and 9 antibody-mediated), and 10 morphological borderline rejection cases. Histology was revised, and immunohistochemistry (IHC) for Caveolin-1 and C4d was automatically performed. Caveolin-1 expression was semi-quantitatively assessed as the percentage of positive glomeruli and the density of positive peritubular capillaries/mm2.
Results: In the T-cell-mediated rejections (TCMR) and antibody-mediated rejection (AMR) groups, the mean percentage of Caveolin-1-positive glomerular capillaries was 0.0%, and 70.0%±34.2% respectively, meaning that no positive glomeruli were observed among TCMR ($p<0.001$). The mean density of peritubular capillaries/mm2 was 5.2±3.1 and 21.2±22.1, showing the highest value in AMR group ($p=0.019$). In the 10 borderline cases the mean percentage of positive glomeruli was 21.9±25.1% and the mean density of peritubular capillaries was 12.5±8.2/mm2; however, 4 had completely negative glomeruli, 2 less than 30% positive glomeruli and 4 more than 30% positive glomeruli, suggesting a different immunological pathogenesis for the borderline group. Notably, no correlation between Caveolin-1 and C4d was observed.
Conclusion: Our results confirm that Caveolin-1 immunohistochemistry is a valid tool in diagnosing AMR, even when C4d is not determinant. In particular, Caveolin-1 expression in more than 30% of glomeruli distinguishes AMR, while TCMR cases show no positive glomeruli. Most important, in those borderline cases in which the rejection has not a clear histological classification, an alleged role of Caveolin-1 IHC is suggested by the fact that some of them are strongly positive, while others are completely negative.

OFP-04-015
Modified method of histological scoring and grading of renal amyloidosis correlates with renal outcome: an Indian experience
V. Agrawal*, I. Singh, R. Pandey, M. Jain, N. Prasad, A. Kaul
*SGPGIMS, India

Background & objectives: Renal amyloidosis is usually associated with poor renal outcome. We studied the typing of amyloid and the extent of amyloid deposition in renal biopsies and correlated it with the clinical presentation and renal outcome.
Methods: Renal biopsies diagnosed as renal amyloidosis over a period of ten years were reviewed. Amyloid typing was done using a multimodality approach including clinical history, bone marrow examination, tests for monoclonal proteins, renal tissue immunofluorescence and immunohistochemistry. Renal amyloid deposits were scored and graded by a slight modification of the previously described method (Şen S and Sarsik B (2010).
Results: The study included 147 patients diagnosed as amyloidosis on renal biopsy, with M:F ratio of 2.3:1 and mean age 51.3±14.5years. 24-hour proteinuria was 6.6 ± 4.7gm/day (range 0.146-35gm/day). Renal failure was present in one-third at diagnosis. Glomerular pattern of involvement was diffuse mesangio-capillary in 77% biopsies. AA (58.8%) type was commonest, followed by AL (38.7%; AL-lambda-96%). On Renal Amyloid Prognostic Score (RAPS) scoring, two-third of the biopsies showed advanced stage (grade 3). 50 patients died due to disease (average 6.2months; range 0.1-30.5 months). The factors associated with a poor outcome were serum creatinine, cardiomyopathy, degree of IFTA on histology, high RAPS score and grade and AL amyloidosis.
Conclusion: We found AA to be the most common type of renal amyloidosis and most of our patients were diagnosed at an advanced stage of renal amyloidosis. We describe a modified histopathological scoring and grading system for renal amyloidosis which shows correlation with clinical presentation at diagnosis and with overall survival.

OFP-05 | Oral Free Paper Session Pulmonary Pathology

OFP-05-001
A single centre re-evaluation of the correlation of pleural fluid cytology and pleural biopsies in malignant mesothelioma and investigation of inter-observer variability
G. Raghuram*, A. Loona, I. Soomro
*Nottingham University Hospitals NHS, United Kingdom

Background & objectives: The RCPath dataset sets a positive predictive value (PPV) of 50% for the diagnosis of malignant mesothelioma in cytology. Previous auditing within our institution showed a PPV of 53%. Here, we re-evaluate this and investigate inter-observer variability in cytology reporting.
Methods: A search was conducted on our laboratory information system 'WinPath' to find cases of mesothelioma reported between 2016 to 2021. Clinicopathological information from the histology reports was collated including dates between cytology and biopsy sampling. Cases where there was a diagnosis of mesothelioma on biopsy but a negative cytology report were reassessed by two experienced pathologists.
Results: Of 179 cases, 129 had both cytology and biopsy specimens and PPV was 55.5%. Rarer histological subtypes; desmoplastic, lymphohistiocytoid and well differentiated papillary mesothelioma were associated with negative cytology results. One case of 'Mesothelioma-in-situ' was seen for which the cytology specimen was reported as atypia (not otherwise specified). Of 50 cases originally reported as negative cytology, 7 (14%) were upgraded, 24 (48%) remained negative and in 15 (30%) there was differing opinions between the two pathologists. Immunohistochemistry was primarily used as an adjunct for malignant effusions to determine cell phenotype, with no cases being sent for molecular analysis. The average delay between a cytology and biopsy specimen was 13 days.
Conclusion: Despite increased awareness of pitfalls of cytology, PPV of pleural fluid cytology appears to inherently be approximately 50%.

Although BAP1 loss and homozygous P16 loss on FISH are considered to be useful in pleural fluid cytology, molecular analysis is still not commonly practiced within our centre. Based on this re-audit we make the following recommendations; double reporting in cases where there is clinical concern and discussion with clinicians regarding simultaneous cytology and biopsy sampling to reduce delays in diagnosis.

OFP-05-002

Reproducibility of c-MET immunohistochemistry (clone SP44) interpretation in non-small cell lung carcinoma

C. Bontoux*, V. Hofman, E. Chamorey, R. Schiappa, S. Lassalle, E. Long-Mira, J. Fayada, C. Bonnetaud, S. Goffinet, M. Ilié, P. Hofman
*Laboratory of Clinical and Experimental Pathology, Hospital-Integrated Biobank (BB- 0033-00025), Pasteur Hospital, IRCAN Team 4, Inserm U1081, CNRS 7284, FHU OncoAge, Université Côte d'Azur, Nice, France

Background & objectives: Emerging therapies for non-small cell lung carcinoma (NSCLC) with MET overexpression have shown promise. However, MET expression evaluation is challenging. We aim to help standardizing MET expression evaluation among pathologists for a better understanding of its role as a biomarker.
Methods: 110 cases diagnosed with NSCLC and routinely evaluated for cMET expression in the Laboratory of Clinical and experimental Pathology (Nice, France) in 2022/2023 were selected. All cMET stained-slides were digitized. Six pathologists (junior and senior) performed a H-score and grading assessment of cMET expression for all cases, both under the microscope and on screen. We analysed inter and intra-rater reproducibility.
Results: Global intraclass correlation coefficient (ICC) for H-score classification (cut-off of 150) was 0.668 (IC95%[0.552-0.773]) with an ICC of 0.812 (IC95%[0.691-0.907] in biopsy samples.
Global ICC for cMET group grading (using a semi-quantitative evaluation according to the % of 3+ stained cells) was 0.671 (IC95%[0.555-0.776]) with an ICC of 0.888 (IC95%[0.805-0.947]) in biopsy samples and 0.959 (IC95%[0.914-0.986]) for squamous cell histology. ICC was similar for junior and senior pathologists.
Regarding intra-rater reproducibility, Cohen's kappa coefficient varies from 0.348 to 1.0 and from 0.538 to 1.0 for H-score and group grading assessment, respectively. Cohen's kappa coefficient was lower for junior versus senior pathologists using both methods.
Data from digital assessment are awaiting.
Conclusion: We demonstrate that the reproducibility of assessing cMET expression ranges from moderate to good. Certain factors, such as squamous cell histology or biopsy samples, can significantly improve reproducibility. Additionally, we showed that intra-rater reproducibility seems to be lower for junior pathologists. Our findings support the notion of tumour heterogeneity in cMET expression both within and between tumours, highlighting the importance of establishing a consensus definition and providing further training in cMET expression evaluation, particularly for inexperienced pathologists.

OFP-05-003

Novel ALK Dako-CD246 assay proves to be as competent as the FDA-approved ALK Ventana-D5F3 assay in identifying lung adenocarcinomas with ALK alterations: real-life validation of 188 cases (2011-2023)

O.C. Eren*, C. Aydin Mericoz, P. Bulutay, A. Baygul, I. Kulac
*Koç University Hospital, Department of Pathology, Turkey

Background & objectives: Affordable and reliable, immunohistochemistry-based biomarkers show promise. FDA-approved ALK Ventana-D5F3 assay is a valid alternative to molecular tests for non-small-cell lung cancer. Recently introduced ALK Dako-CD246 assay may offer similar benefit. We present the first validation study on the latter.
Methods: Primary lung adenocarcinomas between 2011-2023 were retrieved from archives of Koç University Hospital. Representative tumour blocks for each case were stained with Ventana-D5F3 and Dako-CD246 and evaluated by 3 independent reviewers. For a subset, Next Generation Sequencing (NGS) / Fluorescence in situ Hybridization (FISH) was carried out to verify results of IHC-based assays.
Results: 188 primary lung adenocarcinomas were evaluated. Inter-assay agreement was found to be K=0.885 ($p<0.001$, "near perfect" category). In Ventana-D5F3 assay, 14 of cases were interpreted as positive and 171 as negative. In Dako-CD246 assay, 16 and 169 cases were allocated in the respective categories. Three cases (%1.6) in both assays could not be reliably evaluated. Concerning molecularly confirmed cases (n=38), concordant results were obtained in 92.1% (35/38, Ventana®) and 94.7% (36/38, Dako®) of cases, achieving high sensitivity (84.6%, Ventana®; 92.2%, Dako®) and specificity (96% for both). With NGS/FISH results taken gold standard, Kappa scores were K=0.875 ($p<0.001$) for Ventana-D5F3 and K=0.940 ($p<0.001$) for Dako-CD246, both in "near perfect" category.
Conclusion: IHC-based assays provide a valid and reasonably priced alternative, especially in settings where molecular confirmatory tests such as NGS/FISH are not offered or accessible. In this regard, Dako-CD246 proves to yield concordant results with Ventana-D5F3, which is already promptly used in routine pathology practice. The present study being the first in the field, given its high inter-assay and molecular concordance, we propose that novel Dako-CD246 assay can be reliably used in identifying cases for ALK-targeted therapy.

OFP-05-004

Discrimination of multiple primary lung adenocarcinomas from the intrapulmonary metastasis by using pathologic, radiologic, and molecular correlations

P. Bulutay, B.K. Aktas*, G.E. Cecikoglu, C. Aydin Mericoz, I. Kulac, K.B. Ozer, S. Erus, S. Tanju, S. Dilege, C. Atasoy, P. Fırat
*Koç University Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Accurately differentiating between "multiple primary lung cancers (MPLC)" and "intrapulmonary metastasis (IPM)" is essential for prognosis and treatment. Given that histology-based discrimination can be prone to misinterpretation, molecular evidence can provide a valuable adjunct in reducing errors in selected cases.
Methods: The study included seventeen cases, each of which had at least two synchronous or metachronous lung adenocarcinomas and all underwent molecular testing. Cases were evaluated blindly for the morphologic features, radiologic interpretation, and molecular alterations, and diagnosed as MPLC or IPM for each parameter. The results were brought together and their compatibility with each other was investigated.
Results: Twelve cases (70%) were evaluated with next-generation sequencing (NGS) and 5 with single gene analysis (30%). At least one driver mutation was detected in 77% (13/17) of the cases. Among them, 2 cases supported IPM due to the same mutation types, while the remaining 11 cases were classified as MPLC due to different mutation types. Morphologic classification of 85% (11/13) of those was compatible with their molecular findings. Molecular findings were consistent with radiologic classification in the remaining 2 cases. Four cases were molecularly inconclusive, among them 2 cases were evaluated using single gene analysis. Radiological and morphological diagnoses were consistent in 74% of the cases, and inconsistent in 26%.
Conclusion: The histology-based approach can accurately discriminate MPAC and IPM in most cases. Radiologic correlation enhances the reliability of morphological diagnosis and can assist in categorizing morphologically indeterminate cases into a specific direction. Revealing the molecular alterations of each tumour focus enables evidence-based differentiation of MPACs and IPMs. However, since performing molecular tests on each

tumour focus separately would not be cost-effective, the radiological-pathological correlation would be the most appropriate approach to distinguish morphologically indeterminate cases.

OFP-05-005

Endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA) and EBUS-guided transbronchial mediastinal cryobiopsy (EBUS-TMC) in the diagnosis of mediastinal lymphadenopathy: our experience with the technique and proposal on its indication

J. Martin Lopez*, G. Diaz Nuevo, E. Tejerina Gonzalez, D. Garcia Fresnadillo, C. Lopez García-Gallo, C. Salas Anton
*Department of Pathology. Hospital U. Puerta de Hierro, Spain

Background & objectives: EBUS-TBNA is the technique most frequently used in the study of mediastinal lymph nodes. In some cases, EBUS-TBNA fails to accurately diagnose (lymphoma-sarcoidosis) or obtains insufficient material to molecular testing (MT) and EBUS-TMC has proposed to resolve this situation.
Methods: To evaluate the role of EBUS-TMC we present a case-series of eighteen patients from November 2022 to April 2023 who underwent EBUS-TBNA and TMC in a single procedure for diagnostic purposes of mediastinal lesions. Three cryobiopsies were performed per lymph node. All procedures were performed by the same two operators. Rapid onsite evaluation (ROSE) was done in all cases.
Results: Of the cases, 2 cases were reactive lymphadenopathy with both techniques, 2 sarcoidosis, 2 SCLC and 12 NSCLC (3 SCC, 5 ADC, 2 TC and 2 NSCLC, NOS). In 2 cases a previous EBUS-TBNA was performed with a negative result and with the second procedure an SCLC and sarcoidosis was confirmed both in EBUS-TBNA and EBUS-TMC. In 2 cases EBUS-TMC confirmed a previous EBUS-TBNA diagnosis (2 cases of typical carcinoid). EBUS-TMC got sufficient material to MT in 9 cases but also the EBUS-TBNA performed during the second procedure obtained enough in cell-block cytology (only 1 EBUS-TBNA was insufficient). EBUS-TBNA allowed the MT in one case that was insufficient with EBUS-TMC.
Conclusion: EBUS-TMC following EBUS-TBNA reports a minimal increased of diagnostic yield than EBUS-TBNA alone. In our experience, molecular testing in lung cancer was possible in most of the samples obtained from EBUS-TBNA. EBUS-TMC allowed us to identify patients with sarcoidosis and perform PCR techniques for microorganisms in cases with a previous EBUS-TBNA that was negative. We consider that the indication to perform EBUS-TMC should be in certain patients with previous insufficient EBUS-TBNA or selected in the setting of a multidisciplinary committee.

OFP-05-006

Histological, immunohistological and molecular characterisation of congenital pulmonary airway malformation (CPAM)

M. von Laffert*, S. Schweitzer, M. Lacher, O. Aubert, F.W. Hirsch, D. Gräfe, K. Hauptmann, A. Arnold, D. Horst, M. Chirica, F. Klauschen, U. Obeck, M. Boeschen, M. Stiller, H. Bläker
*Institute of Pathology UKL University of Leipzig, Germany

Background & objectives: CPAM is a hamartomatous cystic lesion of the lung. Possible histological findings are foci of goblet cell hyperplasia (GCH),showing KRAS-mutations. Recently, KRAS-mutations were also described in the non-GCH regions. However, morphological studies, linking molecular data with immunohistochemistry (IHC) are scarce.
Methods: We re-evaluated 39 cases (Stocker type I-III) and performed IHC (18 marker panel) with regards to cytokeratin expression, cell cycle, transcription factors (i.a. TTF1, PAX8, Napsin, Surfactant, CK5/6, CK7, CK20, p16, p53) and Next Generation Sequencing (NGS: 40 gene panel; 113 fusion genes panel). In samples with GCH, NGS was performed in cystic and non-cystic regions.
Results: Type I was found in 28% (11/39), type II in 18% (7/39), type III in 3% (1/39). The majority of cases (51%) showed a mixed pattern (mainly type I and II). CPAM showed different expressions by means of CK5/6 (56% positive), Napsin (46% positive), Surfactant (44% positive) and CK20 (41% positive). Combined positivity of all 4 IHC-markers was only seen in 10% (4/39). 23% (9/39) showed KRAS mutations (7xG12D, 1xG12V, 1x G12D/V co-mutation). Mutations were detected in GCH and non-GCH cystic areas. One CPAM with KRAS G12D mutation had a further TP53 mutation. No fusions were detected.
Conclusion: We were able to confirm recent data, showing that KRAS-mutations also occur in non-mucinous regions. To the best of our knowledge, we are the first group to report a KRAS G12D/TP53 co-mutation and a CPAM harbouring a KRAS double mutation (G12D+V). Our preliminary data suggest a subclassification based on conventional histology, protein expression and molecular data (KRAS-status) to be more appropriate. The different expression patterns of CK5/6, Napsin, Surfactant and CK20 might reflect different stages during lung morphogenesis.

OFP-05-007

National testing rate and prevalence of MET exon 14 skipping mutations in NSCLC in the Netherlands

V.D. de Jager*, B. Cajiao Garcia, A.J. van der Wekken, L. van Kempen, E. Schuuring, S.M. Willems
*Department of pathology and medical biology, University of Groningen, University Medical Center Groningen, The Netherlands

Background & objectives: Mesenchymal-epithelial transition (*MET*) exon 14 skipping mutations are uncommon, but targetable oncogenic alterations in non-small cell lung cancer (NSCLC). This study aimed to determine the testing rate and prevalence of these mutations in patients with metastatic NSCLC in the Netherlands.
Methods: After linkage of clinical data of the Netherlands Cancer Registry (NCR) and pathology reports of the Dutch Pathology Registry (PALGA), molecular test status of *MET* exon 14 skipping mutations, molecular test type(s), and test outcome were manually extracted from pathology reports of patients diagnosed with metastatic non-squamous NSCLC between January 1st and December 31st 2019 in the Netherlands.
Results: Among 3,803 patients included in this preliminary analysis, 71.9% received molecular testing for *MET* exon 14 skipping mutations within three months of diagnosis (2,734/3,803). Testing was not performed in 18.2% of cases (692/3,803) and *MET* testing status was unknown in 8.3% (316/3,803). Among *MET*-untested patients, 49.9% did not receive molecular testing for any predictive biomarker (345/692). In total, 47 patients had positive *MET* exon 14 skipping mutation test results, resulting in a prevalence of 1.7% in the *MET*-tested population (47/2,734). Among patients with confirmed *EGFR*/*KRAS*wt, 88.8% were simultaneously or sequentially tested for *MET* (1,438/1,620).
Conclusion: In the Netherlands, the predictive molecular testing rate for *MET* exon 14 skipping mutations in metastatic NSCLC was 71.9% in 2019. The prevalence of *MET* exon 14 skipping mutations was 1.7% in the *MET*-tested population. About half of all *MET*-untested patients did not receive molecular testing for any predictive biomarker, but the vast majority (88.8%) of patients with *EGFR*/*KRAS*wt did receive molecular testing for *MET*. Routine use of direct (i.e. non-sequential) next-generation sequencing (NGS) may increase the latter percentage.
Funding: This work was supported by MSD, Pfizer, Astrazeneca, and Roche. The funders had no role in the design of the study, in the collection, analyses, interpretation of data, or in the writing of the abstract (All fees transferred to UMCG account).

OFP-05-008

Predicting the evolution of lung squamous cell carcinoma in situ using deep learning

A. Vigdorovits*, G. Olteanu, O. Tica, M. Boros, O. Pop

*County Clinical Emergency Hospital of Oradea, Romania

Background & objectives: Only half of lung squamous cell carcinoma in situ (SCIS) lesions progress to squamous cell carcinoma (SCC), while a third undergo spontaneous regression. The objective of this study was to predict the evolution of SCIS lesions using deep learning.
Methods: The dataset consisted of 112 H&E stained WSI from patients that underwent biopsies of SCIS lesions and were subsequently followed up for progression to SCC. Tiles of 256 x 256 pixels were extracted from the WSI and a deep learning model was trained to obtain tile-level predictions. A probability-weighted aggregation module was created in order to generate WSI-level predictions.
Results: The model achieved a per-tile AUC of 0.78 on the test set, an F1 score of 0.84 and a sensitivity of 0.94. After applying the probability-weighted tile aggregation module, the model achieved an accuracy of 0.75, an F1 score of 0.8 and a sensitivity of 0.90 on the WSI-classification task.
Conclusion: To our knowledge, this study is the first to demonstrate that deep learning has the ability to predict the evolution of SCIS from H&E stained WSI. Deep learning has the potential to be used as a low-cost method that could provide prognostic information for patients with preinvasive lesions.

OFP-05-009

The role and importance of BAP1, MTAP and 5-HMC immunohistochemical markers in diagnosis and prognosis in pleural malignant mesothelioma

B.N. Ateş*, E. Kilic Bagir, I.C. Karacaoglu, D. Gümürdülü
*Department of Pathology, Faculty of Medicine, Cukurova University, Adana, Turkey

Background & objectives: Mesotheliomas are the most common primary pleural tumours. They should be distinguished from benign mesothelial lesions, especially. The aim of this study is to investigate the role of the current markers BAP1, MTAP and 5-hmC, in the diagnosis and prognosis of mesothelioma.
Methods: 65 mesothelioma and 28 reactive mesothelial lesions diagnosed in Çukurova University Faculty of Medicine, Department of Medical Pathology between 2010-2017 were included in the study. BAP1, MTAP and 5-hmC antibodies were immunohistochemically applied to the formalin-fixed paraffin embedded block of the cases, the loss of markers was evaluated. The effects of these markers on survival in mesothelioma cases were also examined.
Results: BAP1, MTAP and 5-hmC were 100% specific in distinguishing pleural mesotheliomas from the benign group; the sensitivity of the markers was determined as 67.7%, 61.5% and 52.3%, respectively. When all three markers are used together, the sensitivity reached 95.4%. BAP1, MTAP and 5-hmC were not found to be statistically significantly associated with survival in all or subtypes of mesothelioma.
Conclusion: Most of the mesothelioma cases have to be diagnosed from small biopsy materials. It is difficult to make the differential diagnosis of reactive lesion and mesothelioma, especially where the surrounding adipose tissue cannot be observed. Current immunohistochemical markers BAP1, MTAP and 5-hmC are highly specific for mesothelioma. The combined use of these markers has higher sensitivity than their individual use. Therefore, the algorithmic application of these markers to use BAP1 in the first line will enable the diagnosis of the majority of mesothelioma cases.

OFP-05-010

Small samples, big insights: evaluating PD-L1 expression and inter-observer variability in NSCLC

N. Tezcan*, L.S. Gucer, C. Aydin Mericoz, P. Bulutay, P. Firat, I. Kulac
*Koç University Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Immunohistochemical PD-L1 expression evaluation poses challenges with adequacy of specimens and inter-observer variability. We aim to evaluate the efficiency of small samples and inter-observer variability with the changes in time over assessment in non-small cell lung cancer (NSCLC) cases.
Methods: All PD-L1 studies were retrieved from Koç University Hospital, Pathology Laboratory System. PD-L1 tests that were performed on thoracic samples with the diagnosis of NSCLC were included to this study. Type of procedure and tumour, PD-L1 tumour proportion score (TPS), and assessor's name were recorded. In total, 494 tests were included in the study. Positive TPS corresponded to TPS>0.
Results: Of 494 specimens, 152 (30.8%) were resections and 342 (69.2%) were small samples, including tru-cuts and cell-blocks. Tumour types comprised adenocarcinoma (61.3%; n=303), squamous-cell carcinoma (18.6%; n=92), large-cell neuroendocrine carcinoma (2.6%; n=13), and NSCLC-NOS (17.4%; n=86). A total of 275 positive TPS (55%) were recorded. TPS results were categorized into three groups: <1% (44.3%), 1-49% (33%), and >49% (22.7%). There was no difference in the distribution of TPS between small samples and resections, assessors or 1-year periods. Overall positive TPS was 30% (median). Assessors' positive TPS was ranging between 15-35% (median). There was no significant difference in median positive TPS values between small/large samples, tumour types, assessors or 1-year periods.
Conclusion: This study demonstrates the adequacy of small samples (including cell blocks) for immunohistochemical PD-L1 expression evaluation in NSCLC, with no significant difference in median TPS between tumour types, small samples, and resections. Furthermore, TPS distribution showed no statistically significant difference across small samples-resections, years or assessors, with the latter indicating interobserver consistency. These findings support the reliability of the PD-L1 test in small samples and reveal that inter-observer variability does not make a significant difference in the PD-L1 assessment.

OFP-05-011

Surgically resected adenocarcinoma in situ and minimally invasive adenocarcinoma of the lung – a case series with follow-up

V. Almeida*, L. Veloso, L. Carvalho
*Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Portugal, CIMAGO – Research Center for Environment, Genetics and Oncobiology, Faculty of Medicine, University of Coimbra, Portugal, Pathology Service, University Hospital Anatomical Pathology Coimbra, Portugal

Background & objectives: Pulmonary adenocarcinoma in situ (AIS) and minimally invasive adenocarcinoma (MIA) are the pre-invasive forms of pulmonary adenocarcinoma, with an excellent prognosis.
We aim to report our Hospital´s casuistic on surgically treated AIS and MIAs, with clinicopathological and follow-up data.
Methods: We reviewed the clinicopathologic findings of surgically treated AIS and MIAs diagnosed between 2015 and 2019 at Centro Hospitalar e Universitário de Coimbra.
The median postoperative follow-up period was 58 months (range: 22 - 98 months) and the recurrence-free survival (RFS) and lung cancer-specific survival (LCSS) are the outcomes of interest.
Results: We identified 14 cases - 6 AIS and 8 MIAs. Most patients were female (8/14), and the majority were non-smokers (10/14).
The patient´s median age was 65 yo (55-76). Seven were previously biopsied and were subsequently subjected to lobectomy, while the others (7/14) had an intraoperative frozen section study, completed by lobectomy in 5 cases. All were R0 surgeries.
The median tumour size was 11 mm (6-29). For MIAs, the invasive component was acinar (5/8), papillary (2/8), and micropapillary (1/8).

No recurrences were reported during follow-up. One AIS patient died 22 months after surgery, while another developed a lung adenocarcinoma after 65 months (LCSS=92,9% for AIS and MIA cases together).
Conclusion: Our casuistic aligns with most publications that report a near 100% rate of RFS, even with longer follow-ups. This result highlights the importance of distinguishing AIS and MIA from other pulmonary adenocarcinoma stages.
Moreover, we report the occurrence of one metachronous lung carcinoma during follow-up. This finding is also in line with the recent recognition of high rates of secondary lung tumours in patients with previous AIS and MIA, supporting long-term follow-ups after surgery.

OFP-05-012
A comparative analysis of proficiency testing for the biomarkers ALK, ROS1, EGFR, KRAS and BRAF in non-small cell lung cancer (NSCLC) using the IHC,ISH and MolPath methodologies
A. Ryška, S. Merkelbach-Bruse*, D. Jonigk, E. Schuuring, I. Kern, D. Dawodu, K. Ilm, K. Jöhrens
*University Hospital Cologne, Germany

Background & objectives: NSCLC accounts for about 85% of all lung cancer cases. Accurate and reliable identification of several biomarkers are critical for guiding the treatment decisions. We present the outcomes of the proficiency-test programs that involved participation of over 100 European laboratories.
Methods: QuIP GmbH provided 5 cases of 1 FFPE section to the participating laboratories for the IHC&ISH (ALK&ROS1) testing and 5 cases of 2 FFPE sections for the molecular pathology testing (EGFR, KRAS and BRAF).The anonymized results and reports were reviewed by experts and sent to participants to help improve their diagnostic performance and facilitate benchmarking of their results.
Results: The number of participation and the error rate in % for each sub-scheme of the proficiency tests are: 60 and 20 % for ALK (IHC), 42 and 12 % for ALK (ISH), 46 and 37 % for ROS1 (IHC), 41 and 7 % for ROS1 (ISH), 79 and 9 % for EGFR, 48 and 2 % for KRAS and 51 and 2 % for BRAF. A broad range of methodologies were used by participants making it challenging to correlate specific methodologies with the pass / fail rates.
Conclusion: The number of participation indicates a growing recognition of the importance of proficiency testing. The unsuccessful participants commonly faced issues related to the use of inadequate controls, staining inconsistencies, incorrect interpretation of results, and inaccurate labelling and documentation of results. Despite the promising results of the proficiency tests, these issues could have significant consequences for patient care highlighting the importance of regular proficiency testing and continuous monitoring to ensure high standards of quality and accuracy.

OFP-05-013
ROS1 SP384 clone and ROS1 FISH concordance in non-small cell lung cancer: a clue for oncogenic driver mutations
C.A. Gomez Gonzalez*, B. Yaman, G. Serin, A. Veral, D. Nart
*Department of Pathology, Ege University Faculty of Medicine, Turkey

Background & objectives: In Turkey, lung cancer is the most common cancer type in men and women. For molecular diagnosis, local guidelines have been developed. We present the status of ROS1 gene mutation by comparing immunohistochemistry (IHC) and FISH in a single centre in Turkey.
Methods: 201 biopsies performed in Ege University Hospital and consultation material referred for molecular studies during the period of 2019 and 2022 were evaluated. Tissue and cytology specimens with the diagnosis of NSCLC were included. Demographic information, histologic type, ROS1 SP384 immunohistochemistry staining pattern (H-Score), and at least reflex molecular testing of three genes (EGFR, ALK, and ROS1) were recorded.
Results: 34 cases (16,9%) had positive results for ROS1 IHC. ROS1 FISH was positive in 7 cases from the cohort (3,48%);5 cases with positive ROS1 IHC staining (5/34; 14,7%) and 2 cases without staining (2/167; 1,19%). The average H-score for FISH-positive cases was 152. Additionally, ROS1 IHC was positive in cases with ALK, EGFR, and KRAS mutation; one case had synchronous EGFR and ROS1 mutation. ROS1 SP328 clone sensitivity and specificity were 71,43%(95%CI 29,04 to 96,33%) and 85,05%(95%CI 79,24% to 89,75%) respectively, NPV of 98.80%(95%CI: 96.23% to 99.63%); adjusting H-scores above or equal to 150, sensitivity and specificity values were 42,86%(95%CI 9,9% to 81,59%) and 97,42%(95%CI 94,09% to 99,16%) respectively, NPV 97,93%(95%CI: 94,78% to 97,93%).
Conclusion: ROS1 IHC assessment in lung cancer as a screening tool is helpful to suspect molecular alterations in positive cases, revealing ROS1 rearrangement and/or other oncogenic driver mutations. Evaluation with the FISH technique should be performed. In discordant cases with no molecular correlation of ROS1, ALK, KRAS, or EGFR; NGS or RT-PCR for ROS1 can be run to exclude rare mutations or undetected fusion partners with FISH. ROS-1 rearrangement can have co-mutations with EGFR, KRAS, and ALK setting a challenge for medical treatment.

OFP-05-014
Ki-67 and PHH3 score in grading mesothelioma: comparison between cytological and surgical specimens
D. Vurallı Bakkaloğlu*, Y. Ozluk
*Istanbul Faculty of Medicine, Pathology Department, Turkey

Background & objectives: Grading mesothelioma can be challenging especially in cytological and limited tissue biopsies. We aimed to investigate the role of Kİ-67 and PHH3 scores in distinguishing poor outcome patients by evaluating cytological and surgical specimens.
Methods: Twenty-one pleural mesothelioma cases that has been diagnosed both by cytology and surgical specimens were included in the study. Descriptive data, nuclear atypia, mitosis count, necrosis, nuclear grade, tumour grade, histologic subtype, Ki-67 and PHH3 score were evaluated. Material adequacy for evaluation was noted as high power fields for cytology. Comparison tests and survival analysis were performed.
Results: Seventy-six percent of the patients were male. Mean age was 57.52±10.31 years. Median survival time was 20.00±4.94 months. Histologic subtypes were as follows: 66.7% epithelioid, 23.8% biphasic and 9.5% sarcomatoid. High grade mesothelioma was diagnosed only by resection materials, but not by cytology. PHH3 scores (0.62±0.81, 2.10±1.61), mitosis count (13.76±15.36, 27.05±24.05) and Ki-67 scores (19.57±18.89, 35.81±24.87) were found higher in surgical specimens ($p<0.002$). High mitotic count (≥2) and Ki-67 score of ≥30% were found as poor prognostic factors in both cytological and surgical materials ($p<0.05$).
Conclusion: High mitosis count (≥2) and ≥30% Ki-67 score can be a useful tool to predict prognosis both in cytology and surgical materials. Reporting these findings may help the clinician to manage the poor outcome patients.

OFP-06 | Joint Oral Free Paper Session Endocrine Pathology / Head and Neck Pathology

OFP-06-001
Papillary microcarcinoma – does size still matter?
G. Fontinha*, M.J. Martins
*Centro Hospitalar e Universitário de Coimbra, Portugal

Background & objectives: Papillary microcarcinoma of the thyroid is a papillary carcinoma with ≤10 mm. Although it carries an excellent prognosis it may metastasize, and this behaviour is difficult to predict.

Methods: Retrospective study assessing papillary carcinomas diagnosed in surgical specimens from 2005 to 2020 in a central university hospital. We recorded sex, age and tumour size. The clinical evolution of tumours with ≤5 mm and their clinical evolution was registered. Those associated with other thyroid neoplasms (malignant or low-risk) were excluded.
Results: 1288 total cases of papillary carcinoma 557 of which were microcarcinomas. Of those 20 were excluded due to a concurrent malignant or low-risk thyroid neoplasm. 311 of the remaining cases had ≤5 mm. 265 patients were female and 46 male. The follow-up average period was 70.8 months and the age 58.2. 32 died during the follow-up, all unrelated to the microcarcinoma. 10 had focal invasion of extrathyroid tissue and 3 were pN1 at the diagnosis. During the follow-up there were 0 recurrences, 1 lymph node and 1 lymph node and bone metastasizing averaging 7 months after diagnosis. All of these patients were female. One case of pN1 showed tall cells.
Conclusion: In this series of 311 cases of papillary microcarcinoma with ≤5 mm 1.6% of patients developed lymph node or distant metastasis. Despite these cases no patient died due to thyroid disease.
No matter the size it seems that papillary carcinoma of the thyroid gland can spread and some aspects like the presence of tall cell component should be searched when studying this specimens as they are known predictors of worse prognosis.

OFP-06-002
Utility of HAND2 immunohistochemistry in the differential diagnosis of neuroendocrine neoplasms
M. Manethova*, V. Stejskal, J. Drugda, M. Hácová, H. Hornychová, D. Netuka, T. Česák, F. Gabalec, A. Ryška, J. Soukup
*The Fingerland Department of Pathology, Charles University, Faculty of Medicine in Hradec Králové and University Hospital Hradec Králové, Czech Republic

Background & objectives: Together with Phox2B and GATA3, Hand2 is a transcription factor responsible for terminal chromaffin differentiation of neuroendocrine cells. However, there are no data to this date addressing the immunoreactivity of Hand2 in different neuroendocrine neoplasms.
Methods: Tissue microarrays or whole sections of 64 well differentiated neuroendocrine tumours (WDNET), 29 neuroendocrine carcinomas (NEC), 47 paragangliomas (PG), 6 olfactory neuroblastomas (ONB) and 21 cauda equina neuroendocrine tumours (CENET) were stained with Hand2 antibody (EPR19451, 1:150, Abcam). The percentage of positive cells and staining intensity was assessed as H-score by two independent observer pathologists.
Results: All examined PGs (100%, 47/47) were Hand2+ (median H-score 175; IQR 90-280), while only 12.5% (8/64) of WDNETs were Hand2+ (5 lung and 3 appendix tumours, median 11; IQR 5.7-15.3). Rare positive cells were noted in 9.5% (2/21) of CENETs and 3.2% (1/29) NECs (all H-score 2), while all ONBs were negative. Compared to WDNETs, PGs showed significantly higher H-score ($P<0.001$) and parasympathetic PGs had significantly higher H-score, compared to sympathetic PGs (median 280 vs 122.8; $p<0.001$). For a positive identification of PG, the ROC analysis proposed cut off values of H-score 21,5 (sensitivity 89,4%, specificity 100%) and cut off values of positive cell percentage 8,3% (sensitivity 95,8%, specificity 100%).
Conclusion: In neuroendocrine neoplasms, Hand2 is consistently observed in paragangliomas, while it is only rarely seen in other neuroendocrine tumours. This might be of diagnostic use.
Funding: BBMRI-CZ LM2023033; Charles University Cooperatio Program, research area DIAG and METD; Czech Ministry of Defense MO 1012; The European Regional Development Fund-Project BBMRI-CZ Biobank network – a versatile platform for the research of the etiopathogenesis of diseases, No: EF16_013/0001674.

OFP-06-003
How far can we go grading medullary thyroid carcinoma on fine needle aspiration?
C. Ariño-Palao*, A. Ferrer-Gomez, M.R. Meléndez Gispert, H. Pian-Arias, A. Benito-Berlinches, I. Ruz-Caracuel
*Pathology, Ramón y Cajal University Hospital, IRYCIS, Madrid, Spain

Background & objectives: Latest WHO Classification of Endocrine Tumours has included histopathological grading of medullary thyroid carcinoma (MTC) but its use is still discouraged on fine needle aspiration (FNA) due to the absence of studies. We aim to study grading features on FNA.
Methods: FNA smears from 18 patients with MTC diagnosed on surgical specimens, were blindly reviewed. We annotated cytological features such as predominant pattern, necrosis, mitosis, amyloid, and pleomorphic cells. The value of different cytological stains was also assessed. Lastly, we compared our findings with histopathological grade and other features of their surgical counterparts.
Results: Our series comprises 4 high-grade and 14 low-grade MTC. At FNA, we identified mitosis in 2 out of 4 samples from high-grade carcinomas. Necrosis was identified in only one of these two FNA. We didn't find any mitotic figures in low-grade cases. Nuclear characteristics and mitosis were easier to identify on Papanicolaou smears. Spindle cell pattern was predominant in 5 cases while 13 showed epithelioid/plasmacytoid morphology, with no distinction between grades. Amyloid was present on 14 resections, while we only identified it on 9 FNA cases with no clear difference on grade. Occasional pleomorphic and multinucleated cells were present in both categories but appeared on all high-grade cases.
Conclusion: We were not able to identify all high-grade carcinomas on FNA. However, the two cases with the highest proliferation index (above 6%) in the surgical specimen, were identified by the presence of few mitosis on smears. Although MTC grading cannot be performed on FNA, the identification of mitotic figures should be highlighted as suspicious of high grade MTC. In this setting, Papanicolau staining can facilitate mitosis identification.

OFP-06-004
Are prognostic cutoff values for WHO grade parameters and foci of vascular invasion accurate when applied to papillary thyroid carcinoma? A case control validation analysis
G. Tallini*, P. Mancuso, G. Besutti, A. De Leo, S. Coluccelli, T. Maloberti, F. Chiarucci, D. Giordano, F. Torricelli, A. Ciarrocchi, D. de Biase, A. Frasoldati, S. Piana, P. Giorgi Rossi, M. Ragazzi
*Department of Medical and Surgical Sciences (DIMEC), University of Bologna Medical Center, Bologna, Pathology-IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy

Background & objectives: Necrosis and/or mitoses define high-grade papillary thyroid carcinoma (PTC). It is unclear whether extent of angioinvasion is prognostic. Cutoffs at ≥5 mitoses/2mm2 and >4 angioinvasive foci are empirically defined. We aim to identify optimal cutoff values predictive of distant metastases.
Methods: We analysed 50 consecutive PTC cases with distant metastases (DM-PTC): 16 synchronous, 34 metachronous. One-hundred-eight matched cases with non-metastatic PTC (N-DM-PTC, 10-year minimum follow-up) were used as controls. Necrosis, mitoses, and angioinvasion were quantified. ROC analysis was performed and area under the curve (AUC) values determined to define the best sensitivity and specificity cutoffs predictive of distant metastases.
Results: Metastases were associated with necrosis (any, no cutoff: 43.8% all DM-PTC, 53.1% metachronous DM-PTC vs 5% N-DM-PTC; $p<0.001$), mitoses ($p<0.001$), angioinvasion ($p<0.001$). Cutoff ≥5 has optimal parameters based on sensitivity/specificity AUC values for

mitoses: sensitivity/specificity 42.9%/97.2% all DM-PTC, 18.8%/97.2% synchronous DM-PTC, 54.6%/97.2% metachronous DM-PTC. Cutoff ≥5 has optimal parameters based on sensitivity/specificity AUC values for angioinvasion: sensitivity/specificity 36.2%/91.7% all DM-PTC, 25%/91.7% synchronous DM-PTC, 41.9%/91.7% metachronous DM-PTC. Positive/negative predictive values (PPV, NPV) were: necrosis 21.2% (PPV), 98.2% (NPV); ≥5 mitoses 32.3% (PPV), 98.2% (NPV); ≥5 angioinvasive foci 11.8% (PPV), 97.9% (NPV). After multivariable analysis only necrosis and ≥5 mitoses remained associated with DM-PTC, necrosis also to synchronous and metachronous DM-PTC.
Conclusion: Necrosis of any extent and mitoses (cutoff ≥5) are the best predictors of DM-PTC, including those cases in which metastases develop after initial diagnosis and staging (metachronous DM-PTC). Angioinvasion (cutoff ≥5 foci) predicts DM-PTC, but it is not independent after multivariable analysis. Our data statistically validate empirically established criteria to identify poor prognosis PTC.

OFP-06-005

MCT4 expression correlates with tumour progression and highlights metabolic heterogeneity in Pancreatic Neuroendocrine Tumours (PanNETs)

K. Bräutigam*, J. Straub, P. Kirchner, V. Andreasi, C. Saganas, R. Maire, M. Falconi, I. Marinoni, M. Sadowski, A. Perren
*Institute of Pathology, University of Bern, Switzerland

Background & objectives: Recent transcriptome and epigenome analyses suggest that epigenetic and metabolic changes are associated with progression, increased proliferation and aggressiveness of Pancreatic Neuroendocrine Tumours (PanNETs). However, specific metabolic markers, their role and therapeutic potential are currently unknown.
Methods: Monocarboxylate transporters (MCT) 1 and 4, carboanhydrase 9 (CA9), Glucose transporter 1 (GLUT1) were analysed in two independent PanNET cohorts (n(Bern)=110; n(Milano)=71) by immunohistochemistry. Metabolism of 2D and 3D models of PanNET cell lines as well as patient-derived tumoroids was functionally assessed by PrestoBlue assay and quantitative fluorescence microscopy. MCT1/4 were investigated as potential therapeutic targets with small molecule inhibitors.
Results: Immunohistochemistry of metabolic enzymes demonstrates three protein expression patterns in both PanNET cohorts: homogeneous, heterogeneous and absent expression. Homogeneous and heterogeneous expression of MCT4 and/or CA9 significantly correlate with higher tumour stage and size, as well as relapse. Lower microvessel density is associated with heterogenous expression and shorter time to relapse and presence of metastasis. Similar to PanNET tumours, our 3D PanNET models show regional hypoxia and spatial metabolic heterogeneity. Inhibition of MCT1/4 leads to reduced metabolic activity in PanNET cell lines, i.e. blockage of glycolysis and diminished uptake of oxidative fuels. Finally, through these mechanisms, MCT1/4 inhibition results in lower proliferation of PanNET spheroids and patient-derived tumoroids.
Conclusion: PanNETs exhibit considerable metabolic heterogeneity. Protein data suggest that metabolic enzymes are robust prognostic and predictive markers of PanNET aggression. MCT4 stratifies subtypes according to their expression pattern. Interestingly, in our in vitro 2D and 3D models, metabolic inhibitory agents show similar to better effects in reducing tumour growth compared to conventional inhibitors (e.g. mTOR). MCT4 is a prognostic biomarker and a potential surrogate for promising anti-metabolic therapies.

OFP-06-006

Considerable interlaboratory variation in PD-L1 assessment for head and neck squamous cell carcinoma in the Netherlands – a nationwide evaluation study

M.A. Hempenius*, B.M. Koomen, I.A. Deckers, S.M. Willems, B. van der Vegt
*University Medical Center Groningen, The Netherlands

Background & objectives: Patients with recurrent or metastasized head and neck squamous cell carcinoma (HNSCC) are selected for pembrolizumab treatment by determining the PD-L1 combined positive score (CPS). This nationwide study, using real-world data, investigates interlaboratory variation in PD-L1 assessment for HNSCC.
Methods: Pathology reports of HNSCC patients mentioning PD-L1 testing between 1/7/2019 and 31/6/2022 were extracted from the Dutch nationwide pathology databank Palga. Pseudonymized tumour and PD-L1 testing characteristics were analysed per year to evaluate the testing landscape. Using CPS≥1 and CPS≥20 cutoffs, variation in PD-L1 positivity between laboratories was assessed using funnel plots with 95% confidence limits around the overall mean.
Results: A total of 640 PD-L1 tests were reported in 561 HNSCC patients across 20 laboratories. 83.4% of the tests were positive using the ≥1 cutoff. There were no differences in national PD-L1 positivity rates between the three years ($p = 0.581$). In these years, use of the recommended scoring method CPS increased from 80.0% to 98.0% and 22C3 antibody use increased from 51.7% to 75.2%. 529 PD-L1 tests on histological specimens from 12 laboratories were analysed to evaluate interlaboratory variation. Three (25%) out of 12 laboratories significantly deviated from the national mean of PD-L1 positive cases while using the CPS≥1 cutoff; 2 (16.7%) laboratories significantly deviated for the CPS≥20 cutoff.
Conclusion: In the first 36 months after introduction of PD-L1 testing in HNSCC, assessment has become more uniform in the Netherlands, regarding the used PD-L1 scoring method and antibody. However, interlaboratory variation in PD-L1 positivity between Dutch laboratories was substantial. Guidelines and additional training in PD-L1 scoring for pathologists might help to further reduce this variation.
This work was supported by MSD (grant number not applicable). MSD had no role in study design, data collection and analysis, writing the manuscript or the decision to submit this abstract for publication.

OFP-06-007

Comparative analysis of PLAG1 rearranged cutaneous mixed tumours and pleomorphic adenomas of salivary glands: identification of distinct recurrent TRPS1::PLAG1 gene fusion in cutaneous mixed tumours

Z. Alsugair*, N. Macagno, J. Tantot, O. Harou, M. Battistella, P. Sohier, T. Kervarrec, A. de la Fouchardière, A. Champagnec, D. Pissaloux, J. Lopez, M. Laé, F. Descotes, V. Costes-Martineau, N. Benzerdjeb
*Department of Pathology, Institut of Pathologie Multisite, Groupement Hospitalier Sud, Hospices Civils de Lyon, Pierre-Bénite, France

Background & objectives: PA (pleomorphic adenomas) and CMT (cutaneous mixed tumours) are virtually indistinguishable histologically, making the distinction difficult in certain head & neck regions. Determining the tumour origin in a metastatic context of carcinoma ex-PA or malignant CMT is equally difficult.
Methods: Two cohorts consisting of 34 cases of CMT and 39 cases of PA of the salivary glands were obtained from French institutions and reviewed by specialists in each subspecialty. RNA sequencing analysis was conducted to identify molecular features of cases harbouring PLAG1. Clinical, pathological, and molecular data were collected.
Results: CMT were mainly located on the head (mean: age 61yo/size 11mm). Positive PLAG1 immunostaining was found in 33/34 cases (97%), associated with PLAG1 gene fusion with mainly TRPS1::PLAG1 in 25/33 (75.7%); and BUB1B::TRPS1 in one case. PA were mainly located in the parotid gland (mean: age 60yo/size 77mm) with different histological variants including conventional (66%,N=26), oncocytic (25%,N=10) and canalicular-like variants

(9%,N=3). PA harbored in 12 cases (30%) CTNNB1::PLAG1 fusion, and ZBTB47-AS1::PLAG1 in 6 cases (N=15%). Others fusion partners of PLAG1 included CHCHD7, NCALD, ACTA2, LIFR, BOC, CARMN, CRISPLD1, EIF4G2, FBXO32, GEM, OSR1, TGFBR3, and in one case TRPS1. Both CMT and PA shared same histological features. Statistically, gene fusion involving TRPS1 was more frequent in CMT($p<0.001$).

Conclusion: This study highlights that although CMT and PA share almost the same morphological features and PLAG1 gene fusions, fusion partners are different between the 2 tumour groups. CMT are mainly characterized by TRPS1::PLAG1 gene fusion, while PA exhibit a broad spectrum of PLAG1 gene fusion partners, with exceptional TRPS1 usage. This study provides the first detailed comparison between CMT and PA, emphasizing on their molecular distinctiveness and its potential diagnostic utility in clinical practice to determine the tumour origin.

OFP-06-008

MicroRNA expression in oropharyngeal squamous cell carcinoma – searching for novel prognostic biomarkers in a clinico-pathological and molecular genetic study of 73 patients

J. Laco*, H. Parova, N. Birknerova, I. Baranova, H. Vosmikova, B. Gajdosova, M. Hodek, M. Vosmik, M. Chmelarova, P. Celakovsky, A. Ryska
*Faculty of Medicine Hradec Kralove Department of Pathology, Czech Republic

Background & objectives: MicroRNAs (miRNAs) have been recognized as key molecules in cancer development and progression. The aim of our study was to determine relative miRNA expression in metastasizing oropharyngeal squamous cell carcinoma (OPSCC) and to find correlation with clinico-pathological characteristics.

Methods: A total of 190 samples were analysed in the study (73 primary tumours with 73 corresponding lymph node metastases, and 44 control samples). In every patient, classical clinicopathological parameters were recorded. For miRNA expression, both miRNA microarray analysis and small RNA sequencing were performed to select significantly dysregulated miRNAs, which relative expression was subsequently verified using qPCR analysis.

Results: The study sample comprised 55 males and 18 females, aged 41–80 years (median 58 years). A total of 81% of tumours were HPV-DNA/p16-positive. During the follow-up period (range 3–200 months; median 97 months), 18% of tumours recurred and 14% of patients died due to the tumour. We observed significant upregulation of both miR-206 and miR-3656 and downregulation of miR-150-5p in primary tumours compared to controls ($p < 0.05$). The trend for more prominent downregulation of miR-150-5p in HPV-negative OPSCC was found ($p = 0.07$). Kaplan-Meier survival curve showed that patients with lower expression of miR-150-5p had impaired overall survival compared to patients with higher expression ($p = 0.01$).

Conclusion: In summary, both significant dysregulation of selected miRNAs in tumour samples versus controls and correlation with recorded clinico-pathological parameters was observed in our OPSCC study sample. Notably, miR-150-5p might become a novel prognostic marker in these malignancies. In general, our promising results unravel novel potential biomarkers which, if confirmed by further studies, could be used as prognostic markers in the sense of tailored therapy and treatment individualization of patients with OPSCC.

Funding: Supported by the project BBMRI-CZ LM2018125, by the European Regional Development Fund-Project BBMRI-CZ.: Biobank network – a versatile platform for the research of the etiopathogenesis of diseases, No: EF16_013/0001674, and by the Cooperatio Program of Charles University (research area DIAG).

OFP-06-009

Sinonasal DEK/AFF2 carcinoma: 11 additional cases with new histological features

A. Trinquet*, M. Laé, M. Hourseau, V. Costes-Martineau
*CHU Gui de Chauliac, France

Background & objectives: Sinonasal carcinoma with DEK/AFF2 rearrangement is an entity of recent discovery with few described cases. We described the morphological and immunophenotypic characteristics of eleven additional cases in order to better recognize them and to investigate their prognosis.

Methods: We studied a cohort of 11 patients diagnosed with DEK/AFF2 carcinoma, within the framework of RefCor network.

Epidemiological data (gender, age), tumour-, treatment-related and prognostic data (location, extension, treatment, relapse, death) were retrospectively analysed.

Morphological and immunophenotypic features were reviewed by two pathologists.

We then combined these data with data of the 29 previously published cases.

Results: In our cohort, these tumours displayed several recurrent aspects, the most constant ones being the presence of a mixed exo-endophytic pattern, cytological monotony and the most striking aspect being the presence of an abundant inflammatory infiltrate rich in neutrophils. We also described one case with an unusual biphasic pattern. All tumours expressed P40. CK7, PDL1 and P53 expression were variable, and P16 was not overexpressed.

On the prognostic level, when combined to other published cases, 57% of patients showed local recurrence or tumour progression, 24%, lymph node involvement, 21% distant metastatic involvement and 14% disease-related death.

Conclusion: Carcinomas with DEK/AFF2 rearrangement show some particular histological features. Few cases have been described so far and the follow-up time of patients is still too short to evaluate the prognostic impact or the theranostic interest of this molecular anomaly. Thus, a research of this translocation on a larger number of sinonasal papillary P16 negative tumours would be desirable to clarify these aspects and could also be a diagnostic aid because malignancy is sometimes difficult to assert in these cases.

OFP-06-010

Independent validation of somatostatin receptor 2 as a sensitive and specific biomarker for Epstein-Barr virus status in sinonasal/nasopharyngeal squamous cell carcinoma

K. Viswanathan*, C. Marcus, S. Muzahir, S. Steward-Tharp
*Emory University Hospital Midtown, USA

Background & objectives: Epstein-Barr virus (EBV), a known nasopharyngeal carcinoma (NPC) driver, promotes somatostatin receptor 2 (SSTR2) expression via NF-KB. SSTR2 is detectable by immunohistochemistry, however, validation data on whether SSTR2 immunohistochemistry can distinguish EBVNPC from non-EBV squamous cell carcinoma (SCC) is limited.

Methods: SSTR2 immunohistochemistry was performed on our cohort of EBVNPC (n=15), HPV-positive sinonasal SCC (n=7, HPVSCC), and virus-negative sinonasal SCC (n=8, VNSCC). Slides were reviewed by two board-certified pathologists and an H-score was calculated using the intensity and extent of tumour staining. Cases were also scored as positive or negative. Clinical outcomes and demographic information were obtained from the medical charts.

Results: Using a positive/negative system, 93.3% EBVNPC (n=14/15), 14% HPVSCC (n=1/7), and 25% VNSCC (n=2/8) demonstrated multifocal to diffuse strong SSTR2 expression. The sensitivity, specificity, negative predictive value, and positive predictive values for SSTR2 IHC were 93.3%, 80%, 92.3%, and 82.4%, respectively. The median

H-score for EBVNPC was 180 (range 12-295; mean 179), whereas the median H-scores for HPVSCC and VNSCC were 0 (range 0-56; mean 8) and 0 (range 0-125; mean 31), respectively (p<0.001 for EBVNPC compared to either).
Conclusion: Our study validates the strong correlation between SSTR2 immunohistochemistry and EBV status in NPCs, supports its use in clinical practice as a highly sensitive and specific surrogate biomarker, and lends credence to exploring SSTR2-targeted imaging and therapy.
The study does not have its own funding. However, the research was supported in part by the Cancer Tissue and Pathology shared resource of Winship Cancer Institute of Emory University and NIH/NCI under award number P30CA138292. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

OFP-06-011
Mapping viral integration sites in human papillomavirus positive head and neck squamous cell carcinomas using proximity ligation-based sequencing
E.J. Speel*, I. Demers, H. Balaji, N. Wuerdemann, S. Wagner, B. Kremer, C. Huebbers, J. Klussmann
*Maastricht UMC, The Netherlands

Background & objectives: Human papillomavirus (HPV) integration may affect HNSCC carcinogenesis and prognosis. Study aim was to assess HPV integration in HPV-positive HNSCC cell lines and FFPE tissue comparing the new Targeted Locus Amplification (TLA) technology with previously used PCR technology (APOT/DIPS).
Methods: Seven HPV-positive cell lines and FFPE material of 27 HPV-positive HNSCCs were used for HPV integration detection by TLA, a proximity ligation-based NGS technique. Crosslinked DNA is digested with restriction enzymes, and re-ligated into chimeric DNA molecules. For cell lines a PCR-based and for FFPE material a capture-based target enrichment was performed for HPV16 sequences, followed by Illumina sequencing.
Results: TLA was able to sequence up to 100 kb around the target, detecting exact HPV integration loci, structural variants, and chromosomal rearrangements. In all cell lines, one or more integration sites were identified, in accordance with APOT/DIPS PCR data and the literature. In the FFPE tissue samples, TLA identified integrated HPV in 15 out of 27 tumours, with simple and more complex integration patterns, confirmed by qPCR data. TLA confirmed known PCR data, identified additional integration sites, and proved useful in establishing clonal relationships of multiple tumours within a patient.
Conclusion: TLA provides the opportunity for reliable and robust detection of HPV integration in HNSCC cell lines and FFPE tissue. This new sequencing technology will be a useful tool for further research on HPV integration in disease and patient outcome and clonality analysis of multiple tumours within a patient.

OFP-06-012
Molecular profiling and classification of odontogenic lesions
S.E. Gultekin*, B. Tokozlu, C. Heydt, R. Aziz-Heiloun, O. Gunhan, R. Buettner
*Gazi University, Faculty of Dentistry, Turkey

Background & objectives: Odontogenic tumours (OTs) comprise a group of heterogeneous lesions. There are various types of OTs and still different views exist as to their correct classification. Therefore, we here performed comprehensive molecular profiling of odontogenic lesions, to identify genomic alterations.
Methods: We analysed a cohort of 70 odontogenic lesions with cysts and benign or malignant tumours. NGS was performed with an in-house specified, customized hybrid capture-based primer panel of 31 different genes. Mutational patterns were compared with histological diagnosis for each entity. The correlation of genomic profiles with classification of the tumours and clinical parameters (age, gender, location, recurrence) was statistically analysed.
Results: Mutations were identified in 46 of 70 available odontogenic lesions (66.7%) while 23 lesions were classified as wild-type. Odontogenic epithelial tumours significantly harboured more mutations than mixed or mesenchymal types (p=0.008). In malignant tumours, mutations were observed in 75% of cases which was statistically significant (p=0.05). Among our 46 cases with mutations, 11 cases harboured two simultaneous genetic alterations. With respect to KRAS, the c.35G>T p.G12Vs mutation was the most prevalent alteration detected in 14 and 12 cases, respectively. The PATCHED-1 mutation, which was the third most common mutation, was exclusively detected in 9 out of 10 OKC cases (90%) (p≤0.000).
Conclusion: Our data strongly suggest that histological classification and mutational status in OTs consistently coincide and that obtaining the mutational status may facilitate histological typing in difficult incisional biopsies.

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OFP-07-001
Epidermal ELAFIN expression for diagnosis and differentiation of acute cutaneous graft-versus-host disease
E. Kuzucular*, F. Özden
*Istanbul Medipol University, Turkey

Background & objectives: Graft versus host disease (GVHD) is a severe complication observed following approximately 40-60% of allogeneic hematopoietic stem cell transplants. We aimed to evaluate the utility of elafin expression in skin by immunohistochemistry for accurate diagnosis of acute skin GvHD.
Methods: We performed the histological examination of biopsy samples from acute GvHD (aGvHD; n = 69), Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN; n = 18), drug reaction (DR; n = 31), and healthy controls (n = 23). Elafin was applied immunohistochemically and staining of ≥ 50% of the epidermis was considered positive.
Results: In total, 141 patients were included in the study. In aGVHD cases, 56/69 biopsies, elafin positivity was observed; in only 13 cases, expression was not seen. SJS/TEN patients, with 6/18 biopsies focally showing 50% positivity. In 11 samples, elafin expression was found only in single cells; one biopsy was negative. In DR patients, 2/31 biopsies exhibited 50% staining in some parts of the epidermis; 15 showed staining only single cells in the granular layer; 14 were negative. Twenty-three healthy control biopsies were entirely elafin negative; in four samples, only single cells in the granular layer were stained.
Conclusion: Specific markers cannot exclude clinical mimics of acute skin GVHD (such as drug reaction and SJS/TEN). It is difficult to distinguish between clinical mimics based on histopathology alone because they may present with similar clinical/histological symptoms. We conclude that elafin has a high rate of positivity in aGVHD cases. Tissue elafin is a useful immunohistochemical marker for acute skin GVHD. However, more extensive studies are needed to validate these results.

OFP-07-002
Overexpression of MicroRNAs 21 and 199 related to the synthesis of collagen V in patients with keloid scars
V. Berton Liguori Zacchi*, A. Sousa Santos, L. Henrique Gomes Matheus, T. de Matos Lobo, Z.A. de Jesus Queiroz, C. Machado Baldavira, V. Elias Contini, S. de Morais Fernezlian, A.P. Pereira Velosa, V.L. Capelozzi, W. Rosolia Teodoro
*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: Keloids are hyper-proliferative scars whose mechanism is still poorly understood. The aim of this study was to investigate the regulatory role of microRNAs (21 and 199) in the synthesis of collagen V (Col V) related to the progression of keloid.
Methods: Skin biopsies from 14 patients and 6 healthy controls were studied. Keloid histologic assessment was performed with a graduation score from zero to 4. Semi-automated microscopic evaluation of keloid, immunohistochemistry, immunofluorescence, and quantitative RT-qPCR were performed.
Results: Col V was overexpressed in keloid, mainly in Grade 4 compared to normal subjects and the remaining grades. A positive association was found between Col V and thickened basement membrane of the dermo-epidermal junction and the number of dermal immune cells. Significant association ($\rho>0.50$, $P<0.01$) was found between Col V in the papillary dermis, miR21, miR199, and lymphatic vessels; Col V in the reticular dermis and miR21. When correlated with the clinical-pathological characteristics, there was a significant association ($\rho>0.45$, $P<0.05$) between Col V in the papillary dermis and gender, fibrosis follow-up, and ethnicity; between Col V in the reticular dermis and ethnicity.
Conclusion: Increased deposition of Col V and its correlation with histological graduation, miR21, and miR199 expression, suggest that Col V may affect the regulatory pathway of keloid through the control of miRNAs. These findings highlight the pathogenesis of keloid scars and the perspective of future treatment options.
This work was supported by the Sao Paulo Research Foundation - FAPESP [Process numbers: 2018/20403-6, 2018/00415-0, and 2021/13220-5] and Foundation Faculty of Medicine.

OFP-07-003
Hypoxia and ezrin expression in primary melanoma have high prognostic relevance
U. Maccio*, A. Mihic, D. Lenggenhager, I. Kolm, C. Mittmann, M. Heikenwälder, A. Lorentzen, D. Mihic-Probst
*Universitätsspital Zürich, Institut für Pathologie, Switzerland

Background & objectives: Hypoxia affects tumour aggressiveness and activates pathways associated with epithelial mesenchymal transition (EMT) which are crucial for tumour progress. The study investigates the correlation of hypoxia and EMT with sentinel lymph node status and tumour-specific survival in primary melanomas.
Methods: CD34 for capillary count and Hypoxia inducible factor-1α (HIF-1α) as hypoxia indicators as well as Ezrin and L1-Cell Adhesion Molecule (L1CAM), both critical proteins contributing to EMT, were analysed using immunohistochemistry in 49 melanoma patients with long follow-up (F/U, mean 110 months; range 12-263 months).
Results: We found a significant correlation between Breslow tumour thickness and Ezrin expression ($p = 0.018$). L1CAM expression in primary melanoma was significantly associated with HIF-1α expression ($p<0.0001$) and sentinel lymph node metastasis ($p=0.011$). Furthermore, low capillary count, reflecting hypoxic condition, was significantly associated with Ezrin expression ($p=0.047$) and decreased tumour-specific survival ($p=0.035$). In addition, patients with high Ezrin expression in their primary melanoma had a dramatic loss of life early in their F/U period (mean survival time 29 months; range 15-44 month).
Conclusion: Our results highlight the relevance of Ezrin, L1CAM and HIF-1α as prognostic markers in melanoma patients. Additionally, we demonstrate that hypoxia in primary melanoma affects epithelial mesenchymal transition and is at least partly responsible for early metastatic dissemination.

OFP-07-004
Does size matter in positive sentinel lymph nodes in melanoma?
C. Lightner Ferrer*, C. Heffron
*Cork University Hospital, Ireland

Background & objectives: Sentinel lymph node (SLN) in melanoma is a core part of management of cutaneous malignant melanoma. Tumour burden within the SLN has been the subject of much debate. Our aim was to assess impact of tumour burden in our cohort.
Methods: SLN received in our laboratory over a 10 year period were retrieved from our files. Data including size of metastases, Breslow thickness of original melanoma, subsequent completion lymphadenectomy, recurrence (local or distal), metastases (local or distal) was recorded and analysed. Any pathologically documented follow up was also noted.
Results: A total of 380 cases were retrieved, 296 (77.9%) were negative while 84 (22.1%) were positive with the size of the metastatic deposits ranging from isolated tumour cells to a 13mm deposit. As expected, positive cases had a higher average Breslow thickness (4mm v 2.4mm), higher stage (pT4 35.7% v 15.2%) as well as higher rate of recurrence or metastases (46.9% v 13.5%). A comparison of metastatic deposit size >1mm v 1mm or less (53.1% v 46.9%) showed both groups to have a similar rate of documented recurrence or metastases, 46.5% v 47.4% with an average Breslow thickness of 4.6mm and 3.4mm respectively. Both had similar rates of completion lymphadenectomy.
Conclusion: Size >1mm has been used as cut off to determine further management decisions eg completion lymphadenectomy. Our data does not show any major differences when this cut off is used. There is now data suggesting giving adjuvant immunotherapy to patients with a deposit >0.3mm. It is clear that careful recording of the size of metastatic deposits in SLNs will be vital in determining the next stage of treatment in melanoma and thus analysis of any follow up data is merited.

OFP-07-005
Immunohistological study of melanocyte stem cells
A.A. Khan*, A.K. Yadav
*Vardhman Mahavir Medical College, India

Background & objectives: Vitiligo is characterized by marked reduction of melanocytes. Re-pigmentation in vitiligo depends on the viable melanocyte stem cells (MelSCs) in lesional and perilesional skin. The objective was to evaluate the presence of MelSCs using CD34 and C-kit immunohistochemical markers.
Methods: It's a cross-sectional study in a tertiary care hospital. A 3mm punch biopsy from lesional and perilesional skin from 33 clinically diagnosed vitiligo patients were sent for histopathological examination. The specimens were formalin fixed and paraffin processed. Sections of 3-4 micron were taken and stained with haematoxylin and eosin for vitiligo histological scoring and immunohistochemistry was performed for MelSCs evaluation.
Results: In this study, male to female ratio was 0.83:1 with mean age at appearance of first lesion being 22.09 years. Mean histological score in lesional and perilesional skin in study subjects was 2.7 and 1.18 respectively. Vitiligo histological score was significantly higher in lesional skin as compared to perilesional skin ($p < .0001$) suggesting an increased disease activity in lesional skin. Histological examination revealed presence of melanocytes and melanin pigment in many of the vitiliginous lesion but in significantly less number and concentration. We were unable to observe MelSCs due to decreased expression of CD34 and c-kit in lesional and perilesional skin and hence no correlation was established.
Conclusion: Detection of melanocyte stem cells in vitiliginous lesion is important in understanding the pathogenesis and development of novel therapeutic models in this cell based era. The current study highlights the importance of histopathology and immunohistochemistry in the assessment of disease activity in vitiligo. However, CD34 and C-kit

failed to demonstrate the presence of MelSCs due to their decreased expression. Hence, role of alternative markers like DCT, TRP1, and TYR needs to be explored in order to identify MelSCs.

OFP-07-006
Clinicopathological evaluation of nail lesions: a single-centre experience
S.K. Dursun*, B. Çalım Gürbüz, O. Erdem, F. Kuşku Çabuk
*Basaksehir Cam and Sakura City Hospital, Turkey

Background & objectives: The nail region consists of a complex anatomy with surrounding structures. Trauma-induced lesions of this region are frequently confronted in childhood and adulthood. Besides this, infections, systemic disease involvement, and neoplastic lesions are also conditions that can be encountered.
Methods: This study aimed to assess the clinicopathological findings in the materials of the patients who had a complaint in the nail area and underwent a biopsy. Biopsy materials of 116 patients diagnosed in our department between June 2020 and December 2022 were retrospectively analysed. Clinical presentation type, localization, lesion diameter, age, gender, and pathological diagnosis were evaluated statistically.
Results: 66% were female and the median age was 30.9 years old (range 6-71). 67% were adults, and 64% were localized to the foot. The most common clinical presentations were; granulation tissue development (58%), keratotic papules (14%), melanonychia (11%). Pathological diagnoses were; vascular lesions (54%), epithelial lesions (22%), infections (12%), stromal lesions (9%), systemic disease involvement (2%). The vascular lesions were seen statistically significantly more frequent in adulthood&toenail region ($p<0.001$). Among the epithelial lesions, the most common ones were melanocytic hyperplasia (n=9) and keratoacanthoma/squamous cell carcinoma (n=6). They were seen significantly higher in adulthood ($p=0.01$). The systemic disease involvement was in adults, while their diagnoses were lichen planus and psoriasis vulgaris.
Conclusion: Nail lesions are frequently seen in clinics, but the role of pathology in this process is still unclear. The development of traumatic lesions is the most remarkable condition in the nail region. It is stated that the more frequent occurrence of these lesions is associated with the long-term use of the wrong shoes. Especially in adulthood, hyperkeratotic papules and melanonychia on the nails should be carefully examined clinicopathologically. Systemic disease involvement should also be kept in mind in nail lesions.

OFP-07-007
Diagnostic utility of PRAME in melanocytic lesions, particularly in spitzoid ones
Z. Gahramanli*, A. Okcu Heper, B.A. Kirmizi
*Ankara University School of Medicine, Turkey

Background & objectives: Distinguishing between melanoma and nevi is usually straightforward, whereas differential diagnosis can sometimes be problematic. Therefore, additional reliable methods to help differentiate benign from malignant are crucial. We aimed to investigate the role of PRAME in challenging melanocytic lesions.
Methods: Our study included 119 cases; 27 atypical Spitz tumours (AST), 12 spitzoid melanoma, 20 conventional melanoma, and 60 nevi (Spitz, melanocytic, dysplastic). All tissue sections were analysed for PRAME, BRAF, BAP1, p16, and MelanA/Ki67. Staining above 75% was accepted as a threshold for PRAME. We also investigated the usefulness of PRAME together with BRAF(VE1) positivity, Ki67 proliferation, p16, and BAP1 loss.
Results: PRAME showed diffuse positivity in twelve conventional and three spitzoid melanoma cases. Benign nevi showed no staining at all. However, we detected PRAME expression in one AST, three Spitz nevi, and two dysplastic nevi. For melanoma, sensitivity was 60%, specificity was 100%; for spitzoid melanoma, sensitivity was 25%, and specificity was 100%. When we lowered the threshold to 50%, sensitivity increased to 70% for melanoma and 33.3% for spitzoid melanoma, with no change in specificity. There was no statistically significant correlation between PRAME expression and the degree of dysplasia. However, as the degree of dysplasia increased, the percentage and severity of PRAME expression correspondingly increased.
Conclusion: The absence of PRAME staining in melanocytic nevi and its characteristic staining pattern in melanomas demonstrated that PRAME is useful in distinguishing malignant from benign/borderline melanocytic lesions. Furthermore, decreasing the previously reported PRAME cut-off from 76% to 70% in conventional melanoma and 50% in spitzoid melanoma would enhance the sensitivity of PRAME as an ancillary tool. However, a diagnosis based solely on PRAME expression should be avoided, and any expression pattern must be evaluated in light of histologic findings.

OFP-07-008
Large-scale dermatopathology dataset for AI: construction, annotation, and segmentation of cutaneous neoplastic lesions
Y. Chong*, M. Alam, B. Kim, G. Park
*The Catholic University of Korea, Republic of Korea

Background & objectives: Artificial intelligence (AI) has shown great potential in dermatology and dermatopathology, particularly in segmenting various cutaneous malignant lesions. However, AI application in dermatopathology mainly focused on malignant melanoma and the dataset was limited without enough external validation.
Methods: This study aimed to address previous limitations by constructing a large-scale, multi-institutional dermatopathology dataset and exploring the potential of AI in segmenting six types of skin lesions. We collected 34,376 whole slide images from multiple medical institutions, including Seoul National University Hospital, Catholic Medical Center, National Cancer Center, and Samsung Medical Center. Multiple segmentation models were employed and compared.
Results: Included skin lesions were epidermal inclusion cyst (EIC), seborrheic keratosis, Bowen disease/squamous cell carcinoma (BWN/SqCC), basal cell carcinoma, melanocytic nevus (MN), malignant melanoma, normal skin tissue. The model achieved relatively high performance in segmenting skin lesions, with the highest patch-level performance of 90.08% in EIC and the lowest of 81.98% in BWN/SqCC, and the highest slide-level performance of 90.78% in MN and the lowest of 81.31% in BWN/SqCC, as measured by dice coefficient score.
Conclusion: Our study demonstrates the potential of AI in segmenting cutaneous malignant lesions using a large-scale, multi-institutional dataset. However, further research is needed to address limitations such as racial diversity and external validation.

OFP-07-009
Do multidisciplinary team meetings make a difference in the reporting of dermatopathology?
M. Craughwell*, A. Dorman, E. Kay, K. Sheehan
*Blackrock Clinic, Ireland

Background & objectives: There is increasing evidence around the benefits of multi-disciplinary teams (MDT) in the practice of Histopathology. The objectives of this study were to evaluate the impact that discussion at a Dermatopathology MDT had on the final pathology report.
Methods: All patients who were listed for discussion at an MDT attended by Dermatologists, Plastic surgeons and Pathologists, between January and December 2022 were analysed retrospectively. The nature of pathology was divided into 3 categories. Any additional work that was performed as part of the 2nd review or MDT discussion was documented, including any changes to the final diagnostic report.

Results: 431 patients were discussed at MDTs over the 12-month period, including melanocytic (47%), non-melanocytic neoplasia (27%) and inflammatory lesions (26%). After 2nd review/MDT discussion, 155 (36%) of these required further investigation including 102 requiring additional immunohistochemistry/special stains, 5 molecular analysis and 7 external opinions.
Of the 155 requiring investigation, this did not change the final conclusion in 67 (43%), but half these reports required supplementary clarifications. In the remaining 88 (57%) where discrepancies were identified, this included measurement of margins (28%), a change in grade of atypia/depth of invasion (24%), including upgrading from benign to malignant or vice versa (10%). The final diagnosis was altered in 9% of inflammatory lesions.
Conclusion: This study confirms the value of 2nd review and MDT discussion in improving the diagnostic accuracy of Dermatopathology reporting. In particular, melanocytic lesions required more additional work (59%) in comparison to non-melanocytic neoplasia or inflammatory pathology. Further studies are required to assess how the changes identified reflect the overall clinical management of these patients.

OFP-07-010

Collagen V mediates the fibrillar organisation in the time course of skin fibrosis in experimental systemic sclerosis

Z.A. de Jesus Queiroz, A.P. Pereira Velosa, J. Sampaio Silva, S. Catanozi, A. dos Santos Filho, S. de Morais Fernezlian, V. Elias Contini, L.K. Ramos da Silveira, S. Carrasco, V. Berton Liguori Zacchi*, D. Levy, V.L. Capelozzi, W. Rosolia Teodoro
*Division of Rheumatology, Faculdade de Medicina da Universidade de São Paulo, Brazil

Background & objectives: The formation of cutaneous fibrosis in the Systemic Sclerosis (SSc) model induced by collagen V (Col V) remains unknown. Our objective was to characterize skin fibrosis in this model and to evaluate the effect of Col V in fibroblast culture.
Methods: SSc model was induced in C57BL/6 mice by Col V immunization. The animals were euthanized on 15-, 30-, 45-, and 120-days post-immunization. Histology, immunofluorescence, and histomorphometry were employed to evaluate cutaneous fibrosis. The synthesis of fibrillar collagens I, III, V, and α-SMA in healthy mouse skin fibroblasts stimulated with 25,50, 100μg/mL of Col V was evaluated by immunofluorescence.
Results: The temporal analysis showed an increase of collagen I expression in the 45- and 120-days groups in comparison with the 15 and 30 ($P<0.01$) days groups. Furthermore, we observed a significantly increased expression of collagen III in the skin from 120 days group compared to the 15, 30, and 45 ($P<0.01$) days groups. Additionally, 45 and 120 days, showed a significant increase in collagen V ($P<0.01$). Fibroblasts stimulated with Col V showed increased expression of collagen I and α-SMA ($P<0.05$), collagen III, and collagen V ($P<0.01$).
Conclusion: Our study indicates that the increase in Col V alters skin fibrillogenesis, contributing to the onset of the cutaneous fibrosis process in the SSc model, after 45 and 120 days of immunization. In addition, Col V in vitro stimulates fibroblast differentiation and collagen production. These data suggest that Col V stimulates a signalling pathway that could result in fibrosis.
This work was supported by the Sao Paulo Research Foundation - FAPESP [Process numbers: 2018/20403-6, 2018/00415-0, and 2021/13220-5] and Foundation Faculty of Medicine.

OFP-07-011

Immunohistochemistry of NTRK in atypical fibroxanthoma and pleomorphic dermal sarcoma: a five-year study

N. Cadavid-Fernández*, A. Tenelanda-Santillán, M.R. Meléndez Gispert, C. Ariño-Palao, A. Veliz Dominguez, S. Foncueva-Casado, D. Bueno-Sacristán, A. Navarro-Cantero, C. Perna-Monroy, M.E. Reguero-Callejas, C. Moreno-Garcia-del-Real
*Ramón y Cajal University Hospital, Spain

Background & objectives: Atypical fibroxanthoma (AFX) and pleomorphic dermal sarcoma (PDS) are spindle-shaped malignant cutaneous neoplasms (clinicopathological spectrum) of mesenchymal origin. We propose that they may present NTRK fusions as the new emerging group of soft tissue tumours called NTRK-rearranged spindle cell neoplasms.
Methods: All AFX/PDS diagnosed at our institution (January 2018-March 2023) were collected, reviewed and stained with pan-TRK antibody (clone EPR17341). We evaluated the presence or absence of staining and the percentage of positive tumour cells. Positive staining was defined as staining above background in at least 1% of tumour cells in any pattern including membranous, cytoplasmic, perinuclear or nuclear.
Results: We studied a total of 21 cases diagnosed as AFX/PDS [16 (76%)/ 5 (24%)]. Four (19%) were punch biopsies and 17 (81%) were complete excisions. Pan-TRK (+) was positive in 4 (19%) cases, with medium intensity cytoplasmatic and focal expression pattern in spindle-shaped cells; 3 (14%) cases were considered to have borderline positivity for pan-TRK defined as mild cytoplasmatic positivity not clearly in spindle-shaped cells and the remaining cases were negative. The 4 positive cases were FXA and among the borderline cases 2 were diagnosed as PDS and 1 as FXA. In positive/borderline cases we will perform molecular techniques (FISH) to support our results.
Conclusion: AFX/PDS tumours develop in sun-damaged skin of the elderly. They both are diagnosis of exclusion and their treatment is surgical tumour extirpation except in high-risk cases in which multidisciplinary treatment is considered. After reviewing the literature, possible NTRK fusions justified by their spindle-shaped morphology have not been studied. We carried out this study not for diagnostic purposes but to analyse possible new molecular associations and treatment targets.

OFP-07-012

SATB2, CKAE1/AE3, and synaptophysin as a sensitive immunohistochemical panel for the detection of lymph node metastases of Merkel cell carcinoma – a multicentre study

P. Donizy*, D. Massi, A. Cassisa, M. Krzyzinski, M. Dudzisz-Sledz, P. Biecek, P. Rutkowski, A. Marszalek, M.P. Hoang, A. Szumera-Cieckiewicz
*Department of Clinical and Experimental Pathology, Wroclaw Medical University, Poland; Department of Pathology and Clinical Cytology, Jan Mikulicz-Radecki University Hospital, Wroclaw, Poland

Background & objectives: This study was undertaken to determine the most sensitive immunohistochemical panel for the detection of nodal metastases in Merkel cell carcinoma (MCC) patients.
Methods: 102 metastatic MCC lymph nodes were tested with 7 antibodies, including cytokeratin (CKAE1/AE3), CK20, chromogranin A, synaptophysin, INSM1, SATB2, and neurofilament (NF). The 5-tier scoring system was used for analysed markers (0: 0% of positive MCC cells; 1: <25%; 2: 25-74% ; 3: 75-99%; 4: 100% of MCC cells with moderate to strong reactivity).
Results: SATB2, CKAE1/AE3, and synaptophysin are the top three markers with the highest cumulative percentage of positive reaction. 91/102 (89.2%) of metastatic nodes were characterized by a moderate to strong expression of SATB2 in ≥75% tumoral cells; 85/102 (83.3%) and 80/102 (78.4%) for CKAE1/AE3 and synaptophysin, respectively. There were no entirely negative cases for these markers. SATB2 and CKAE1/AE3 were the stains with the highest rate of 100% positivity. SATB2 and CKAE1/AE3 presented a significant additive effect on detecting MCC metastases. 10/11 (91%) of SATB2-low metastatic lymph nodes revealed high CKAE1/AE3 expression. Fisher's exact test showed the similar distribution of SATB2, CKAE1/AE3 and synaptophysin among MCPyV-negative and MCPyV-positive cases.

Conclusion: Simultaneous evaluation of SATB2, CKAE1/AE3, and synaptophysin detects nodal metastatic MCC cells with the highest diagnostic sensitivity, independently of MCPyV status. We propose including them in the routine MCC sentinel lymph node biopsy/lymphadenectomy protocol of histopathologic evaluation.
This research was funded by a statutory subsidy by the Polish Ministry of Science and Higher Education as part of Wroclaw Medical University's grants SUBZ.A430.22.089 and SUBZ.A430.23.075 (records number in the Simple system) granted to Piotr Donizy.

OFP-08 | Joint Oral Free Paper Session Paediatric and Perinatal Pathology / Autopsy Pathology

OFP-08-001
CD34 immunostain increases the sensitivity of placental examination for distal foetal vascular malperfusion in liveborn children

J. Stanek*
*Division of Pathology, Cincinnati Children's Hospital, USA

Background & objectives: Placental foetal vascular malperfusion (FVM) is associated with increased perinatal morbidity and mortality. This retrospective observational analysis was performed to compare the impact of large proximal vessel, remote distal villous, and recent FVM diagnosed by endothelial fragmentation by CD34 immunostaining.
Methods: Clinical and placental phenotypes (expanded Amsterdam criteria) of 581 live births were compared: Group 1 73 cases without FVM, Group 2 220 cases with large vessel FVM without distal vessel changes, Group 3 132 cases with remote distal vessel FVM, Group 4 87 cases with recent FVM, and Group 5 69 cases with combined remote and recent features of FVM.
Results: FVM was present in 88% of placentas from high-risk pregnancy dominated by congenital anomalies. 43% of those were global (partial, large proximal vessel) FVM without distal villous changes, least commonly high-grade (13%), least commonly with complicated perinatal outcome (except for congenital anomalies (79%), and with least common other abnormal placental phenotypes, particularly maternal vascular malperfusion, chronic villitis and plasma cell deciduitis; however, large vessel FVM lesions were commonly associated with distal FVM. Remote distal villous FVM and particularly on-going FVM with temporal heterogeneity is statistically significantly associated with preterm births, preeclampsia, abnormal umbilical artery Dopplers, foetal growth restriction, highest caesarean section rate and high grade FVM overall.
Conclusion: Lesions of global FVM feature relatively low sensitivity for perinatal complications. Isolated recent distal villous (segmental) FVM diagnosed by clustered endothelial fragmentation by CD34 immunostaining without avascular villi on hematoxylin-eosin (remote changes) does not feature significant perinatal morbidity/mortality either, likely because of its short duration. Remote FVM (long lasting), and particularly on-going lesions with temporal heterogeneity portend the most complicated perinatal outcome, low placental weight, postuterine pattern of placental injury, villous infarction, chronic villitis, and are most frequently high grade.

OFP-08-002
Histopathological findings in placentas and adverse perinatal outcomes from pregnant patients with autoimmune diseases

A. Nadal*, A.S. Castellanos-Gutierrez, F. Figueras, G. Espinosa, L. Youssef, F. Crispi, M. Santana, N. Baños
*Hospital Clinic, Spain

Background & objectives: To describe the pattern of placental lesions in women with autoimmune diseases (AID) and correlate the placental findings with the occurrence of adverse perinatal outcomes (APO).
Methods: 91 women with AID (42 SLE, 21 NC-OAPS, and 28 APS) and 91 controls were included. The perinatal outcomes and placental findings of pregnancies with AID (systemic lupus erythematosus [SLE], antiphospholipid syndrome [APS], and non-criteria obstetric APS [NC-OAPS]) and gestational-age matched healthy controls were analysed and classified according to the 2015 Redline - Classification of placental lesions.
Results: Placental weights were significantly lower in NC-OAPS and APS groups compared to controls. 14.3% of placentas in the APS group was < 3rd percentile which was exceedingly higher than in other groups.
Maternal malperfusion was significantly increased in APS (46.4%) compared to NC-OAPS (14.3%) and SLE (9.5%). Foetal vascular-stromal maldevelopment was significantly increased in NC-OAPS (19.1%) compared to controls (1.1%) and SLE (2.4%). APOs were more frequent in all AIDs compared to controls (3.3% vs 52.4-64.3%). Overall, both maternal (OR 6.8, 95%CI 2.1-22) and foetal-side (OR 4.1, 95%CI 1.3-13.5) lesions were associated with APO. Maternal malperfusion and developmental foetal vascular-stromal lesions were the lesions most strongly associated with APO.
Conclusion: Pregnant women with SLE, APS, or NC-OAPS showed a different pattern of histopathological findings. Compared to controls, all AID conferred an increased risk of APO that was strongly associated with placental maternal-side malperfusion and foetal-side maldevelopment vascular-stromal lesions.

OFP-08-003
Sarcina colonization in three paediatric patients with delayed gastric emptying, and esophagitis with increased intraepithelial eosinophils (EIEo)

C. Salgado*, Y. Hadjiyannis, S. Ali, Q. Wang, E.V. Zambrano Tola, M. Reyes Mugica
*University of Pittsburgh, Pathology, USA

Background & objectives: Sarcina organisms are rare, gram-positive, sugar fermenting cocci, identifiable by molecular testing or histomorphologic examination. The pathologic potential and relevance of Sarcina identification in gastrointestinal tract biopsies is ill-defined, but complications such as emphysematous gastritis, and gastric perforation are described.
Methods: Following institutional review board approval, the cases were selected at Children's hospital using retrospective search of the pathology archives (1/1/2020 to 4/1/2023). The original slides were reviewed by two pathologists (CMS and MRM); clinical information and image studies were obtained from electronic medical records. The presence of Sarcina was confirmed in three cases; their clinical and histological features were described.
Results: Three boys (9, 11 and 16 years-old); two of them having developmental delay (one in the autism spectrum and the other with chronic epilepsy). All patients presented with variable degrees of abdominal pain and reflux-related symptoms (vomit/ regurgitation/ dyspepsia) associated with delayed gastric emptying. In one case, the Sarcina colonization was diagnosed after treatment of Helicobacter pylori gastritis with associated duodenal lesion/ obstruction. Histologically, all patients demonstrate variable reactive gastropathy and EIEo. Duodenal inflammatory changes were present in two cases. The bacteria arranged in tetrads or octets, consistent with the morphologic diagnosis of a Sarcina organism present in the surface of the oesophagus and stomach in all three cases.
Conclusion: Previous reports of paediatric cases linking clinical symptoms with findings of Sarcina on histology are scant and rarely associated with EIEo. These three paediatric cases presented with previously reported Sarcina-related symptoms including abdominal pain and vomiting. Because of the ubiquitous environmental presence of Sarcina, the clinical significance of this finding is not well characterized, and the decision to treat, along with the chosen regimen, remain

debatable. Additional studies to better characterize the importance of this finding are needed.

OFP-08-004

Paediatric cystic lesions of the kidney: a review of 54 cases

E. Benammou*, R. Honnla, S. Gharbi, T. Ravelomampitoniainarivony, S. Irtan, D. Berrebi, L. Galmiche, F. Dijoud, S. Boudjemaa, A. Coulomb
*Department of Pathology, Armand Trousseau Hospital-Sorbonne University, France

Background & objectives: Paediatric renal cystic lesions are rare and various neoplastic and non-neoplastic entities, often displaying similar and confusing radiologic and macroscopic features. The aim of this study is to analyse the characteristics and repartition of these different entities.
Methods: This series includes 54 patients, aged 3 months to 14 years, treated for renal cystic lesions in the period extending between the years 2009 and 2023. It includes six bilateral cases. These cases were retrieved from the French Renal Tumour Study Group.
Results: Cystic-Nephroma(CN) represented 37%(n=20) of all cases, with a size range of 2 to 16cm, intrapelvic growth in 47% of the cases and DICER1-mutation in some. Cystic-Partially-Differentiated-Nephroblastoma(CPDN) represented 7%(n=4) of the diagnoses. Tumour size ranged between 9 and 21cm. None featured intrapelvic growth. Intralobar-Nephrogenic-Rest was found in 13%(n=7) of the cases, in association with a predisposition syndrome 4 times. Perilobar-Nephrogenic-Rest was identified once. Congenital-Mesoblastic-Nephroma(CMN), mainly of cellular subtype, was found in 9%(n=5) of all cases. Cystic-Wilms-Tumour and Eosinophilic Solid and Cystic Renal Cell Carcinoma were each diagnosed once. Unilateral segmental or total Multicystic Dysplasia was reported in 24%(n=13) of the cases, associated with Wilms-Tumour twice. Cystic uropathies were identified twice.
Conclusion: In conclusion, paediatric renal cystic masses are often challenging as the diagnoses may correspond to various neoplastic, malformative, benign or malignant entities, requiring different therapeutic approaches. Histological examination key to correctly diagnose and treat those lesions.

OFP-08-005

Placental pathology in 3rd-trimester stillbirths and neonatal deaths: comparison between preterm and term cases - are they different? A retrospective study in Centro Hospitalar e Universitário de Coimbra

A. Lai*, C. Cerdeira, R. Pina
*Pathology Department, Coimbra Hospital and University Centre (CHUC), Portugal

Background & objectives: During 3rdtrimester, maternal vascular malperfusion(MVM) is the most common cause of stillbirth, and infection after 37week-gestational (WG) age. In preterm cases, the reasons can be varied.
Our objective was to evaluate possible differences between preterm/term periods concerning placental pathology.
Methods: We retrospectively reviewed 389 autopsy reports, over the last 3 years, excluding those associated with medical termination of pregnancy, those below 23+6 WG-age and those without placental reports. We reviewed the maternal history and placental/autopsy reports.
Results: We obtained 50cases (12.9%) divided into, preterm (24-36+6WG) and term (37-42WG), respectively, 37cases (74%) and 13cases (26%).
The preterm cases have a mean of 29.5 WG-age and a mean maternal age of 30.9years-old; 12cases were live-born (32.4%). The term cases have a mean of 38.6WG-age and a mean maternal age of 31.9years; 3cases were live-born (8.1%).
MVM and infection were the commonest diagnosis in both groups. Concerning women without prior history, we found 12cases in the first group (32.4%) and 8cases in the second group (61.5%). MVM was still predominant, but the second diagnosis was different: infection in the term group and foetal vascular malperfusion (FVM) in preterm cases.
Conclusion: Despite healthcare programs and vigilance, we still have late stillbirths/neonatal deaths which have a colossal impact on families.
Our study didn't find any differences between preterm/term groups regarding the most prevalent placental diseases: MVM and infection - reflecting the need for equal vigilance programs during the 3rdtrimester.
However, looking at healthy women, not all cases were maternal-dependent during the preterm period; some were associated with FVM, possibly indicating concurrent etiologies which are challenging to assess in routine vigilance programs.

OFP-08-006

Chorioamnionitis and pregnancy fatal outcomes: three-year case series of foetal and newborn autopsies

C. Courelas*, S. Bárbara, A. Alves, J. Gama, J.L. Amaral, V. Almeida, C. Cerdeira, A. Lai, R. Pina
*Pathology Department, Coimbra Hospital and University Centre (CHUC), Portugal

Background & objectives: Chorioamnionitis is a maternal inflammatory response associated with foetal/neonatal adverse outcomes. This study aims to describe the experience with foetal and newborn autopsies associated with chorioamnionitis by the Surgical Pathology Department from Coimbra Hospital and University Centre.
Methods: Between 2020 and 2022, chorioamnionitis cases associated with fatal foetal/newborn outcomes were retrieved. Medical termination of pregnancy (MTP) or autopsy not performed (ANP) were excluded. In the scope of analysis were: maternal age, gestational age, grade and stage of maternal and foetal inflammatory response, type of pregnancy delivery/loss, prenatal care, microbiology studies and foetal/neonatal infection in autopsy.
Results: From a total of 37 patients retrieved, 11 were excluded (7 MTP, 4 ANP). Maternal age ranged from 21-44-year-old, mean 32±5.92 years: 50% aged under 32 and 33.3% above 35 years. Except for one patient, all had prenatal care. Gestational age ranged 14-41-weeks: 11.54% full-term and 88.44% preterm (76.92% extreme preterm). Microbiology analysis of placenta was available in 4 out of 26 patients: 2 negatives; 2 positives (E.coli and L.monocytogenes). Severe maternal Inflammatory response was dominant (69.23%), with severe and mild/moderate foetal inflammatory response equally distributed. Signs of Infection were present in 65.38% of foetus/newborns in autopsy.
Conclusion: As expected, most of the patients concerned extremely preterm pregnancies. The limited sample size makes it difficult to further explore the distribution pattern of foetal response, but the maternal response is predominantly severe. In most cases there are direct signs of infection in the foetus/newborn. The retrospective nature of the study poses several limitations and a large sample and control group will be important.

OFP-08-007

Malignant ovarian neoplasms in children and adolescents: a series of 52 cases

G. Pereira*, E. Dvidenko, F. Silva, A. Félix, J. Ferreira
*Instituto Português de Oncologia de Lisboa Francisco Gentil, Portugal

Background & objectives: Paediatric ovarian cancer is an extremely rare event, despite being the most common gynaecological cancer in children. Paediatric ovarian cancer has a much better prognosis than adult ovarian cancer, due to the difference in the distribution of histological types.

Methods: All borderline or malignant ovarian tumours diagnosed in paediatric patients (under 18 years old) and treated at IPOLFG between 2000 and 2021 were retrieved. Clinical data was collected, and all histological slides were reviewed. Pre-diagnostic clinical data was missing in two patients and follow-up data was missing in another two patients who were excluded from the series.
Results: A total of 52 patients aged 2-17 years old were included (median 12 years; follow-up mean: 88.3 months). Most (77%) had FIGO stage I disease. Two girls had DICER1 syndrome (4%) and another 2 had Turner syndrome (4%). The most common neoplasms were germ cell tumours (GCT)(52%) followed by sex cord-stromal tumours (SCST) (37%), with immature teratomas (n=12) and juvenile granulosa cell tumour(n=14), the most frequent. SCST and GCT were most frequent below the age of 10 and in the 10-14 age group, respectively. Three malignant and three borderline epithelial neoplasm were diagnosed (11.5%), with only one borderline diagnosed under 10 years of age. Seven patients developed disease recurrence/persistence. Two patients died (recurrent juvenile granulosa cell tumour; unrelated cause).
Conclusion: Irrespective of histological type, most patients in our series had an excellent prognosis. Tumour-predisposing syndromes are frequent in this age group (8%). Epithelial malignant neoplasms can occur in this age group and be exceptionally diagnosed below the age of 10.

OFP-08-008
From morphology to genetics in syndromic craniosynostosis: two cases of a rare diagnosis in foetal autopsy
J. Vaz Silva*, C. Mora, A. Costa Braga
*Pathology Department, Portuguese Oncology Institute of Porto (IPO-Porto), School of Medicine, University of Minho, Braga, Portugal

Background & objectives: Disruption of embryological craniofacial differentiation leads to a variety of craniofacial abnormalities. Craniosynostosis occurs most commonly as an isolated event. However, when it involves multi-sutures and/or arises in a set of associated anomalies, a syndromic craniosynostosis should be suspected.
Methods: Syndromic craniosynostoses are rare conditions, with the incidence varying between 1:25,000-1:100,000 live births. We describe two autopsy cases of foetuses presenting with craniosynostosis and multiple other malformations associated, which were suspicious of a syndromic context.
Results: Regarding the autopsies, both foetuses presented with bilateral coronal craniosynostosis, conditioning craniofacial changes, as well as with syndactyly of both hands and feet, hypoplasia of nasal bones, and intestinal malrotation. Additional malformations were detected, namely cardiovascular malformations (interventricular septal defect; persistent left superior vena cava), central nervous system anomalies (corpus callosum and vermis hypoplasia, anomalous gyration) and additional craniofacial abnormalities.
Due to the presence of multi-sutures craniosynostosis along with additional foetal malformations, the possibility of a syndromic context was raised, and genetic counselling was advised. In one of the cases presented, a pathological variant in FGFR2 was identified, consistent with Apert syndrome. Genetic counselling is ongoing in the other case.
Conclusion: Syndromic craniosynostoses are often sporadic, arising from de novo autosomal dominant mutations in FGFR and TWIST genes. Genetic counselling should be considered. We highlight the importance of craniosynostosis recognition during autopsy since it could prompt the diagnosis of these rare genetic syndromes, with possible clinical implications for subsequent pregnancies.

OFP-08-009
Discrepancies between clinical diagnosis and autopsy findings - 77 consecutive autopsies
B. Sepodes*, V. Almeida, M.A. Cipriano
*Centro Hospitalar e Universitário de Coimbra, Portugal

Background & objectives: The clinical autopsy is a procedure in decline that guarantees medical care quality and assesses the global rate of health services. The studies pointed to discrepancies of around 30%. We aim to determine this rate at our hospital.
Methods: We reviewed 77 autopsy reports performed at our hospital from 2017 to 2021 and evaluated diagnostic discrepancies between clinical diagnosis and autopsy findings. The major diagnostic errors were classified: Class I - misdiagnoses that directly impacted survival; Class II - findings that would not have changed the course of the disease. Association with the length of hospitalization was also determined.
Results: Of the 77 autopsy cases, 56% were male and 44% female, with a median age of 61 years. We identified discrepancies in 45,3% of the cases: 29,8% belonged to class I and 15,5% to class II. Pulmonary embolism and pneumonia were the most frequent misdiagnosis in class I. Occult neoplasias and infectious diseases played a significant role in class II. Postoperative complications were common but not always described in clinical reports. The rate of diagnostic discrepancy remained constant over time, and the length of hospitalization was inversely proportional to the discrepancy rate, particularly in the diagnosis of class I.
Conclusion: Despite technological modernization, many erroneous/incomplete diagnoses remain to identify. The results stress the importance of the autopsy to clarify the cause of death accurately. The length of hospitalization suggests that lack of time for accurate diagnosis has an essential role. Our findings are consistent with the literature. We must consider the autopsy a potent research tool to understand the disease and face it as a crucial opportunity to improve clinical practice and medical training.

OFP-08-010
COVID-19 postmortem evaluation by minimal invasive tissue sampling: histological findings, role of coinfections and genomic profiles
P. De la Iglesia, A. Martinez, S. Segura, S. Villaroel, M. Garbarini, D. Alvarez Paggi, S. Esperante, J. Pollan, H. Michelangelo, M. Caballero*
*Hospital Italiano de Buenos Aires, Argentina

Background & objectives: Minimally invasive tissue sampling (MITS) can be used as an alternative to clinical autopsy. Our aim is to assess the histological findings, the prevalence of coinfections and the role of immune complexes in hospital deaths due to COVID-19 infection.
Methods: We designed a cross-sectional study, based on MITS and medical record review of adults who died due to COVID19 at a tertiary hospital in Buenos Aires. Sampling was performed >6 hours after death. Lung, heart, bone marrow, liver, brain, cerebrospinal fluid and blood samples were obtained. RNA extraction and Nanostring was performed in tissue samples.
Results: 17 patients were enrolled. Hypertension (11/17) and diabetes (8/17) were the most frequent comorbidities. Frequent histological findings were diffuse alveolar damage (DAD) (13/17), organizing pneumonia (8/17), capillaritis (14/17), liver steatosis (12/17), liver mild sinusoidal inflammation (14/17) and hemophagocytosis 9/14. 10/17 patients had coinfection and 6 had histological evidence of bacterial coinfection in the lung (one lung abscess, 5 cases of exudative pneumonia). Patients had significantly higher titers of neutralizing antibodies than controls ($p<0.05$). RNA extraction was successfully performed, and gene expression profiles related to patients' previous conditions were observed.
Conclusion: MITS can be safely performed and can be a useful tool in assessing superimposed infections in the context of long hospitalizations both for histological and genomic analysis. Immune complexes do not seem to be relevant in COVID-19 related deaths. Histological findings of COVID 19 infection are similar to previously reported cases. RNA expression profiles were related pre-existing conditions of patients.
This project was funded by MITS Surveillance Alliance.

OFP-08-011

SARS-CoV-2-related mortality – an autopsy study

C. Schwab*, U. Merle, P. Schirmacher, T. Longerich
*University of Heidelberg, Institute of Pathology, Germany

Background & objectives: For the management of the COVID-19 pandemic it is important to discriminate who died due to COVID-19 or due to another disease while being infected. We addressed this question and compared COVID-19-related lung damage during the course of the pandemic.
Methods: From March 2020 to December 2023 a total of 117 autopsies were performed according to a standardized protocol on decedents with proven SARS-CoV-2 infection. COVID-19-related lung damage was semiquantitatively assessed for the exudative, proliferating and fibrosing component, respectively. The cause of death was assessed in synopsis of all autopsy findings and clinicopathological data.
Results: The characteristic sequence of COVID-19-related lung injury was preserved during the pandemic, but there were differences between the individual waves of infection related to the evolution of various virus variants. In decedents infected by an Omicron variant the lung damage was less severe and significantly less often the cause of death compared to precedent variants ($p<0.05$). COVID-19-related death was not recorded in patients being re-infected or having received a booster vaccination.
Conclusion: Autopsy is a valuable tool for evaluating the outcome of a SARS-CoV-2 infection. According to our findings infections with an omicron variant is rarely causative of death, which is highly relevant for the management of the COVID-19 pandemic.
The study was funded by the Ministry of Science, Research and Art of Baden-Württemberg (Baden-Württemberg Corona Autopsy Biobank and Registry).

OFP-08-012

Sudden death due to hydatid disease: a histopathological analysis

E. Gun*, M.C. Yazici, B. Gun, T. Das, I. Coban
*Basildon University Hospital, Mid and South Essex NHS Foundation Trust, Basildon, Essex, United Kingdom

Background & objectives: Caused by the parasite Echinococcus granulosus, hydatid disease (HD) is an important public health problem in endemic regions. Rarely, cysts may rupture, leading to anaphylactic shock and sudden death. We aimed to identify cases of sudden death caused by HDs.
Methods: Cases that underwent autopsy between January 2010 and July 2022 and were diagnosed with HD based on histopathological examination were retrospectively examined along with their histopathological findings. The demographics, the localization and characteristics of the cysts, and the causes of death were reviewed. Cases that resulted in sudden death due to HD were identified.
Results: Of the 91 cases identified with HD, 64 were males and 27 were females, with a mean age of 42.1 years (8-89). The majority of the cysts were located only in the liver (n=67), and cysts were found in multiple organs in 12 cases, including the lungs, heart, kidney, bladder, pancreas, spleen, and gallbladder. Fifteen cases (16.4%) were attributed to HD and its complications as the cause of death. Anaphylactic reaction caused sudden death in nine cases, and histopathological examination revealed scolices in the pulmonary vessels in eight of these cases. Five sudden death cases had a cyst in the heart, and two had scolex emboli in the cerebral vessels.
Conclusion: Even though HD most commonly affects the liver and lungs, it can affect many other organs. In conclusion, the present study suggests that HD can lead to serious complications including sudden death, particularly when the scolices enter the circulation causing anaphylactic shock. Histopathological examination of autopsy cases is important in determining the cause of death in HD. The findings of this study may contribute to raising awareness of the risks associated with HD and its potential complications, especially in endemic regions.

OFP-09 | Oral Free Paper Session Breast Pathology

OFP-09-001

Breast-conserving surgery in invasive lobular carcinoma of the breast after neoadjuvant chemotherapy

J. Azevedo*, M. Alzamora, A. Coutada, A. Lapa, L. Gonçalves, N. Coimbra, C. Leal
*Pathology Department, IPO-Porto, Portugal

Background & objectives: The surgical management of invasive lobular carcinoma (ILC) after neoadjuvant chemotherapy (NAC) is controversial due to its distinctive characteristics, which may lead to preoperative underestimation of disease extent. We evaluated frequency of breast-conserving surgery (BCS) and need of surgical re-intervention.
Methods: Cases diagnosed with ILC who underwent surgery following NAC between 2011 and 2021 were identified through a review of internal records. Data recorded included patient age, radiological findings (pre- and post-chemotherapy) and type of surgery. The need for re-excision lumpectomy (with margin status) or complementary mastectomy was recorded.
Results: In total, 115 cases were included with 29 (25.2%) undergoing BCS and 86 (74.8%) mastectomy. In the cases of BCS, 11 (37.9%) showed radiological complete response and 8 (27.6%) marked reduction in size. Eleven cases (37.9%) performed margin widening intraoperatively. In the final pathology report, 2 cases (6.9%) had pathological complete response. Regarding margin status, 14 (48.3%) were positive and 9 (31.0%) were close (<1mm). Subsequently, 7 (24.1%) patients were submitted to re-excision lumpectomy and 10 (34.5%) to mastectomy. Of these 17 patients, 11 presented residual invasive carcinoma (RIC). One patient required a third surgery, modified radical mastectomy, still showing RIC.
Conclusion: NAC is a well-established treatment option in breast cancer in order to obtain tumour downsizing, allowing BCS, and achieve tumour downsizing/pathological complete response, however its role in ILC is controversial. Additionally, accurate preoperative staging and monitoring NAC response in ILC remains challenging. More than half of the patients require a second surgery either re-excision lumpectomy or complementary mastectomy, to achieve tumour-free margins. Also, intraoperative margin widening during BCS does not reduce the need for further surgeries in patients with RIC.

OFP-09-002

Analysis of discordant cases between tumour grade and risk categorisation using EndoPredict® in breast cancer

V. Macarrón Aguilera*, A. Peláez-García, J.I. Sánchez-Méndez, L. Yébenes, A. Berjón, D. Hardisson
*La Paz University Hospital, Spain

Background & objectives: EndoPredict® is a genetic test that predicts relapse risk in ER+/HER2- breast cancer by combining genetic and clinicopathological data (EpClin). We aim to assess cases where there is a discrepancy between tumour grade and genomic risk classification (EPClin high/low-risk).
Methods: EndoPredict® has been utilized in our centre on 323 patients since 2015. We reviewed the EP (genomic index), EPClin (EP combined with tumour size and lymph node status, pN), and tumour grade to identify discordant cases. Furthermore, we examined the proliferation index (Ki67) and genomic profile (proliferation genes of EP index).
Results: In total, we identified 20 cases with low tumour grade and high-risk EPClin (G1 HR) and 15 cases with high tumour grade and low-risk EPClin (G3 LR). In G1 HR, the genomic profile was high-risk in 19 cases (95%). 45% of these tumours were >20 mm, and 70% were pN+. However, Ki67 index was ≥20% in only 9 cases (45%). On the other hand, in G3 LR, 87% of tumours had a high-risk genomic profile. In these cases, the clinicopathological features of the tumours shifted

EPClin towards a LR, with only 13% of pN+ cases. Ki67 index was ≥20% in 67% of cases.
Conclusion: In G1 HR breast cancer, despite the presence of poor clinicopathological features, most tumours already have a high genomic profile (proliferation genes of EP index). Therefore, Ki67 index is a poor predictor of the genomic profile of the tumour in these cases. Conversely, G3 LR identifies a subset of tumours with high expression of proliferation genes. In these cases, favourable clinicopathological features often modify the EPClin index. Here, the Ki67 index is a more reliable marker of the genomic profile.

OFP-09-003
Intraoperative evaluation of sentinel lymph nodes after neoadjuvant therapy in breast cancer patients has low accuracy rate due to unique challenges
S. Sahoo*, M. Huerta-Rosario, R. Zhang, Y. Fang
*UT Southwestern Medical Center, USA

Background & objectives: Intraoperative evaluation (IOE) of sentinel lymph nodes (SLNs) to detect metastases in breast cancer patients after neoadjuvant therapy is challenging due to therapy related changes. The objective of the study is to determine the accuracy of IOE of SLNs.
Methods: This retrospective study included a total of 1098 SLNs from 294 patients treated between January of 2020 through March of 2023. The intraoperative results (13 patients had touch preps and 281 patients had frozen sections) were compared with the final pathology results.
Results: Of the 294 patients, 191 patients had negative results and 103 had positive results on IOE. Of the 191 patients with negative results, 32 had false negative results. Of the 32 false negative cases, 10 were macrometastases, 19 were micrometastases and 3 were isolated tumour cells. There were no false positive results. The overall sensitivity, specificity, positive predictive value and negative predictive value are 76.3%, 100%, 100% and 83.2%, respectively. The sensitivity rate for detecting macrometastasis was higher (89.9%) than micro-metastasis (38.9%).
Conclusion: The sensitivity of detecting metastasis intra-operatively is lower after neoadjuvant systemic therapy (NST). Our results of high false negative rates in detecting micro-metastasis is consistent with previous studies. The major reason of missing metastasis (including macro-metastasis) is due to partial response to therapy where residual tumour cells scattered in a larger fibro-inflammatory background are difficult to recognize. Therefore, it may not be possible to attain the same level of sensitivity in the NST setting when compared with primary surgery setting.

OFP-09-004
TRPS1 is a highly sensitive marker for breast cancer: a tissue microarray study evaluating more than 19,000 tumours from 152 different tumour entities
M. Lennartz*, N. Blessin, C. Hube-Magg, T. Krech, A. Hinsch, E. Burandt, G. Sauter, R. Simon, P. Lebok, D. Dum, S. Minner, F. Jacobsen, T.S. Clauditz, C. Bernreuther, S. Steurer
*University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: TRPS1 (Trichorhinophalangeal syndrome 1) is a nuclear protein expressed in breast epithelial cells. TRPS1 immunohistochemistry (IHC) has thus been suggested as a marker for breast cancer. However, reports on TRPS1 positivity in other cancer types are piling up.
Methods: To comprehensively determine the diagnostic utility of TRPS1 IHC, tissue microarrays containing 19,201 samples from 152 different tumour types and subtypes were analysed. GATA3 IHC data were available from 11,891 of these tumours from a previous study.
Results: TRPS1 positivity occurred in 86 of 152 tumour categories of which 36 contained at least one strongly positive case. TRPS1 staining predominated in various types of breast carcinomas (51%-100%) and was also seen in various subtypes of soft tissue tumours (up to 100%), salivary gland tumours (up to 46%), squamous cell carcinomas (up to 35%), and gynaecological cancers (up to 40%) as well as in other tumours. TRPS1 positivity occurred in only 1.8% of 1,083 urothelial neoplasms. Positivity for both TRPS1 and GATA3 occurred in 47.4%-100% of breast cancers, up to 30% of salivary gland tumours, but in only 29 (0.3%) of 9,835 tumours from 134 other cancer entities.
Conclusion: Although TRPS1 expression can be seen in many different tumour types, TRPS1 Immunohistochemistry has high utility for the identification of cancers of breast or salivary gland origin, especially in combination with GATA3. The virtual absence of TRPS1 positivity in urothelial neoplasms is useful for the distinction of GATA3 positive urothelial carcinoma from breast cancer.

OFP-09-005
Risk stratification in invasive lobular carcinoma of the breast by clinicopathological features and Prosigna-PAM50 multigene assay characterisation
J. Vaz Silva*, A. Varelas, C. Escudeiro, M.R. Teixeira, C. Leal, N. Coimbra
*Pathology Department, Portuguese Oncology Institute of Porto (IPO-Porto), Porto, School of Medicine, University of Minho, Braga, Portugal

Background & objectives: Invasive lobular carcinoma(ILC), the second most common type of invasive breast carcinoma(IBC), is reported to have good short-term prognosis. However, several studies demonstrate that long-term outcome is similar or worse than IBC-NST, hindering therapeutic decision in early and intermediate-risk tumours.
Methods: Prosigna-PAM50, a multigene assay that encompasses tumour size and nodal metastasis, determines intrinsic subtype and risk of recurrence(ROR), assigning a probability for 10-year distant recurrence(ROR10). In our institution, selected patients with intermediate risk criteria undergo Prosigna-PAM50 characterization to aid therapeutic decision. Here, we compared Prosigna-PAM50 ROR results with different clinicopathological characteristics of patients diagnosed with ILC, thus characterizing this population.
Results: Tumours were <2cm in 49(52%) cases and node metastases (LNM) were present in 22(23%). All were ER-positive and HER-2-negative. PR expression was negative/low(<20%) in 22(23%). Ki-67 proliferation-index(Ki-67) was >15% in 28(30%).
Prosigna-PAM50 classified 85(89%) as Luminal-A and 10(11%) as Luminal-B. Overall ROR10 average was 7,25%, with 55(58%) classified as low-ROR, 34(36%) as intermediate-ROR and 6(6%) as high-ROR.
Low-ROR tumours were >2cm in 23(41,8%), LNM were present in 4(7,4%), and Ki-67 was >15% in 11(20%) cases.
Intermediate-ROR tumours were >2cm in 18(52,9%), LNM present in 11(32,4%), while Ki-67 was >15% in 13(44,8%) cases.
High-ROR tumours were >2cm in 5(83,3%) case, LNM present in 4(66,7%), while Ki-67 was >15% in 4(66,7%) cases.
Conclusion: Despite ILC being associated with favourable prognostic features, there is still ongoing debate regarding its long-term outcome, making risk stratification and therapeutic decision difficult.
Many cases demonstrated overlap between clinicopathological risk assessment and Prosigna-PAM50 characterization. However, Prosigna-PAM50 provides additional risk discrimination, for example in cases with LNM but low-ROR.
Although multigene risk assays are validated for IBC, extended clinical follow-up will be essential to further refine their prognostic value and clinical application in the setting of ILC.

OFP-09-006
Dako HercepTest (poly) allocates more cases to HER2-low group compared to ventana PATHWAY 4B5 anti-HER2 assay: a multicentre study on 116 invasive breast cancer cases
O.C. Eren*, O.C. Taskin, M. Oktay, A. Baygul, F. Aktepe, N. Kapucuoglu
*Koç University Hospital, Department of Pathology, Turkey

Background & objectives: Treatment of breast cancer revolves around HER2 protein, via targeted antibodies or antibody-drug conjugates. As

target population expands to include the HER2-low group, immunohistochemistry-based assays' power in distinguishing HER2-low from HER2-negative cases acquires substantial therapy-guiding relevance.
Methods: 116 cases covering HER2 0 (n=39), 1+ (n=25), 2+ (n=26) and 3+ (n=26) groups were scored via HercepTest (poly) and PATHWAY 4B5 assays by 5 blinded pathologists. Amplification status of cases were further verified with Brightfield Dual in situ Hybridization (BDISH). Segregation of HER2-positive, HER2-low and HER2-negative cases was evaluated, as well as inter-assay and inter-observer concordance.
Results: Identical IHC scores were achieved in both assays for 63.8% (74/116, Kappa=0.522, p<0.001) of cases. Among remaining, difference was mainly due to higher HER2-status scores in HercepTest assay (37/42). Number of HER2-positive cases was 34 in HercepTest and 31 in PATHWAY 4B5. All 3 discordant cases were overscored (IHC 3+) by HercepTest, as they were 2+ according to PATHWAY 4B5 and further found to lack amplification in BDISH. Number of HER2-low (IHC 1+ and 2+/BDISH-) cases was also higher in HercepTest (57 vs 41). Inter-observer agreement was substantial in both assays, with Fleiss' kappa 0.63 (p<0.001) in HercepTest and 0.62 (p<0.001) in PATHWAY 4B5 assay.
Conclusion: Both assays have high sensitivity in detecting HER2 amplification, however more cases are allocated to HER2-positive and HER2-low group in HercepTest (poly). As clinical consequences in HER2-low group are not yet fully established, different segregation profiles among different IHC-based assays should be acknowledged. Probability of a case being overscored in one assay or underscored in another should be considered while therapeutic translations are made from pathology reports.

OFP-09-007
Multi-reader study of a fully automated artificial intelligence solution for HER2 IHC scoring in breast cancer biopsies
S. Krishnamurthy*, S. Schnitt, A. Vincent-Salomon, R. Canas-Marques, E. Colon, K. Kantekure, M. Maklakovski, W. Finck, J. Thomassin, Y. Globerson, L. Bien, M. Grinwald, M. Vecsler, C. Linhart, J. Sandbank
*MD Anderson Cancer Center, USA

Background & objectives: Recent proven efficacy of HER2-targeted therapy on HER2-low expressing tumours raise the need for accurate and reproducible HER2 scoring. We aimed to validate pathologists' use of an artificial intelligence (AI) solution for interpreting HER2 scores in breast samples.
Methods: Two-arm multi-reader study on 120 cases, containing H&E and complementary HER2 IHC, from four sites, compared HER2 scoring performance of 4 pathologists with an AI HER2 solution versus manual interpretation. Both arms were compared to rigorous ground truth (GT) established according to ASCO/CAP 2018 guidelines by five breast subspecialists, i.e. agreement of at least 4 out of 5 pathologists.
Results: The AI solution demonstrated high accuracy for HER2 scoring of 92% on slides with a robust GT majority (N=92). Average inter-observer agreement among GT pathologists for across all HER2 scores was 72.8%; for each HER2 score, 0/ 1+/ 2+/ 3+, their agreement was 80.1%, 65.9%, 69.2% and 96.4%, respectively. Pathologists supported by AI showed significantly better performance with higher consistency (88.8% vs 81.9%), and accuracy (87.4% vs. 69.8%) for HER2 0/1+, while across all HER2 scores a trend of better performance was observed (83.7% vs. 75% for consistency, and 88% vs. 85% for accuracy).
Conclusion: This study demonstrated the developed automated AI solution scored HER2 accurately according to 2018 ASCO/CAP guidelines. Pathologists supported by AI showed improvements in HER2 IHC scoring consistency and accuracy, especially for HER2 0 and 1+. AI solutions could be used as decision-support tools for pathologists, enhancing the reproducibility and consistency of HER2 scoring, thus enabling optimal treatment pathways and better patient outcomes.

OFP-09-008
Agreement among 4 observers and 4 reading modalities for HER2 Low designation of breast carcinoma
S. Nofech-Mozes*, E. Olkhov-Mitsel, A. Plotkin, E. Slodkowska, F. Lu
*Precision Diagnostics and Therapeutics Program, Sunnybrook Health Sciences Centre, Toronto, Department of Laboratory Medicine and Pathobiology, University of Toronto, Canada

Background & objectives: Accurate designation of HER2 Low (HER2L) (IHC 1+ or 2+/ISH-) in breast carcinomas (BC) is critical due to recently approved antibody drug conjugate in the metastatic setting. We examined the agreement among 4 breast pathologists using different slide viewing modalities.
Methods: Array with 51 cores enriched for HER2L, stained with 4B5, was independently scored using the 2018 ASCO/CAP guidelines by 4 breast pathologists with 4 slide viewing modalities:
SC1-Scanned slide.
SC2- Scanned slide after consensus discussion (and washout).
GSM- Glass slide using a microscope.
GSTV- Glass slide projected to HDTV screen.
Concordance between modalities, observers and assessments was evaluated.
Results: Among 46 cores with BC adequate for scoring, there was complete agreement among raters and modalities in 39 (84.8%) cores. Seven (15.2%) cores had at least one discordant score, all HER2-0 vs HER2-1+ ($\kappa = 0.792$-0.894). The interrater agreement for each modality was SC1 - $\kappa = 0.860$, p<0.001; SC2 - $\kappa = 0.905$, p<0.001; GSM - $\kappa = 0.890$, p<0.001 and GSTV - $\kappa = 0.903$, p<0.001. The agreement on HER2-0 improved from 0.844 on SC1 to 0.894 on SC2 (p<0.001). 6/7 discordant cores were scored as HER2-0 with GSM and HER2-1+ with scanned slides.
Conclusion: Post analytical variables including interobserver, intraobserver and modality used for HER2 immunohistochemistry assessment are critical for the distinction between HER2-1+ and HER2-0 BC, particularly for cases bordering the 10% faint membranous staining cutoff. We observed more HER2 1+ scores with scanned slides vs other modalities, raising a need for modality-specific validation as many pathology departments are transitioning to digital platforms for primary diagnosis. The effect of different scanners, focal points, white balance and computer monitors should be studied further.

OFP-09-009
Upgrade rate and predictive factors of fibroepithelial lesions of the breast to phyllodes tumour
R. Alaghehbandan*, T. Salisbury, M. Zokaei Nikoo, G. Sokhanran, S. Koonmee
*Cleveland Clinic, USA

Background & objectives: Fibroepithelial lesions (FELs) of the breast are heterogenous neoplasms that can present diagnostic challenges, particularly on core biopsies. The aim of this study was to determine the upgrade rate of FELs to phyllodes tumour on surgical follow-up and associated factors.
Methods: This is a retrospective population-based study of FELs of the breast (fibroadenoma [FA], phyllodes tumour [PT]) on core biopsies over a three-year period (2017-2019) in Vancouver, BC, Canada. The data were obtained from the laboratory information system and patient's chart. Core biopsy diagnoses were correlated with surgical pathology resection findings. Clinical and radiologic factors were compared to identify PT-related features.
Results: Of 425 core biopsies of FELs (369 FA, 9 PT, and 47 indeterminate), 91 underwent excisional biopsy, with an upgrade rate of 24.2% to PT. Of 44 core biopsies diagnosed/favoured as FA, 3 were PT on excisional biopsy (NPV=93.2%). Of 9 PT diagnosed (or favoured) on core biopsies, 7 were confirmed on excisional biopsy (PPV=77.8%). Mean age and mass size were significantly higher in the PT group (51

yr, 3.3 cm) than FA (37.7 yr, 2.4 cm) (p=0.02). Logistic regression model showed older age and larger tumour size were strong predictors of PT. BIRAD, needle gauge, clinical presentation, and history of breast cancer were not associated with upgrade to PT.
Conclusion: Core biopsy is sufficiently sensitive and specific in stratifying FELs of the breast and can effectively optimize and reduce the need for surgical management in FELs. In indeterminant core biopsies, pertinent clinical information such as age and tumour size can potentially aid in appropriate decision making. Core biopsy plays a crucial role in safe avoidance of unnecessary surgical procedures of FELs of the breast, given the vast majority of FAs can be observed.

OFP-09-010
The assessment of tumour-infiltrating lymphocytes in invasive apocrine carcinoma of the breast in relation to the Her2 status
S. Vranic*, N. Kuzumova, I. Rose, Z. Gatalica
*College of Medicine, Qatar

Background & objectives: Tumour-infiltrating lymphocytes (TIL) represent a robust immunologic biomarker mediating chemotherapy and immunotherapy responses. In the current study, we assessed the tumour-infiltrating lymphocytes (TIL) in invasive apocrine carcinomas of the breast (Apoca) in relation to the Her2 status.
Methods: The current study used a cohort of 54 well-characterized, naïve Apoca. All patients were women, with a mean age of 64 years (range 39–83 years). The TIL distribution was assessed using the hematoxylin and eosin whole slide/scanned images following the recommendations of the international TILs working group 2014 [Ann Oncol 26(2), 2015].
Results: Forty carcinomas were "pure apocrine" [PAC; ER-/AR+)], and the remaining 13 were classified as "apocrine-like" [ALC; ER+/-, AR+/-]. HER-2/neu was positive (score 3+ by IHC and/or amplified by FISH) in 18/40 (45%) PAC and 3/13 ALC (23%). The prevalence of HER2-low expression (scores 1+ and 2+ without HER2 amplification) in Apoca was high (21/53, 40%); the HER2-low phenotype was more prevalent in "triple-negative" PAC than in ALC (68% vs. 46% p<0.001). Levels of TIL were low (≤10%) in 75% Apoca (median: 5%, range 0–50%). TIL levels were significantly higher in ALC than in PAC (p = 0.05). Her2 status had no impact on the TIL distribution (p=0.45).
Conclusion: Invasive apocrine carcinomas of the breast have predominantly low TIL, particularly PAC. The prevalence of the HER2-low phenotype in apocrine carcinomas is high, which should have therapeutic and clinical implications given the recently approved therapies with antibody-drug conjugates for Her2-low breast cancers.

OFP-09-011
Heterogenous HER2 inter- and intra-laboratory lower limit of detection
N. 't Hart*, S. Sompuram, M. Eenkhoorn, D. Dabbs, S. Bogen
*Isala, The Netherlands

Background & objectives: HER2 (4B5) immunohistochemistry (IHC) was used in the Destiny/Breast04 study. Accurate patient stratification depends on whether the assay can be consistently replicated from one lab to the next. The objective is to quantitatively measure inter-laboratory reproducibility using HER2 calibrators.
Methods: To quantify reproducibility of HER2 IHC assays, three calibrator slides (Boston Cell Standards Inc, Boston, USA) were sent to 42 labs. The calibrator incorporates 10 HER2-coated cell-sized microbeads at HER2 concentrations ranging 38.000 – 2.7 million copies. Linear range formalin-fixed microbead controls were also included. Slides were stained on three consecutive days, analysed and the coefficient of variation was calculated.
Results: Four antibodies were used by 32 labs: 59.4% clone 4B5, 9.4% Herceptest monoclonal (DG44), 15.6% SP3 and 15.6% C-erbB-2. The calibrator was evaluable for 4B5 and DG44 (22 laboratories), allowing calculation of the lower limit of detection (LOD). The inter-laboratory coefficient of variation (CV) for the LODs was 55% (4B5 labs) and 5% (DG44 labs). In addition to LOD, we also evaluated the CV in stain intensity with a mid-range control: 32% (4B5) and 22% (DG44). Within-lab variability in LODs were: 25% (4B5) and 18% (DG44). Within-lab variability with a single mid-range control was 23% (4B5) and 12% (DG44).
Conclusion: HER2 IHC assays are more heterogenous than commonly appreciated, sometimes with poor inter- and intra-laboratory reproducibility. DG44 showed the highest consistency, followed by 4B5. The fact that there were only 3 participating IHC labs using the DG44 is a limitation in the findings. Laboratories need to re-validate HER2 IHC assays to ensure accurate identification of HER2-low and address poor reproducibility issues in order to reliably assess HER2-low in clinical practice.

OFP-09-012
A multi-feature AI solution for diagnosis support of breast excisions: a clinical validation study
G. Broeckx*, F. Deman, R. Salgado, I. Krasnitsky, D. Mevorach, J. Theunissen, M. Vecsler
*GZA-ZNA Antwerp, Belgium

Background & objectives: This study aimed to clinically validate the performance of an artificial intelligence (AI)-based solution on detection of invasive and in-situ carcinomas in breast excisions compared to a robust ground truth (GT) established by multiple expert pathologists.
Methods: An AI algorithm previously validated on biopsies was tested in a prospective standalone performance study on an external cohort comprising 248 retrospectively collected breast excisions. AI results on invasive and in-situ carcinoma were compared with GT diagnosis that was reached by concordance between two blinded pathologists who prospectively reviewed the slides. Discrepancies were adjudicated by a third expert pathologist.
Results: The AI demonstrated high performance when compared with the GT with an AUC of 0.986 (95% CI: 0.973-0.998) for the detection of invasive carcinoma (specificity and sensitivity of 96.3% and 89.9% respectively) and with an AUC of 0.994 (95% CI: 0.987-1) for the detection of DCIS (sensitivity and specificity of 95.6% and 95%, respectively). The AI differentiated well between subtypes/grades of invasive and in-situ cancers with an AUC of 0.963 (95% CI: 0.922-1) for IDC vs. ILC and AUC of 0.970 (95% CI: 0.931-1) for DCIS high grade vs. low grade.
Conclusion: This blinded study reports the successful clinical validation of an AI-based solution in the accurate detection of clinically relevant diagnostic parameters regarding invasive and in situ breast carcinoma, offering an important tool for computer-aided diagnosis in routine pathology practice, supporting pathologists in their diagnostic work.
This research is sponsered by Ibex Medical Analytics.

OFP-09-013
Interplatform and interobserver reproducibility of PD-L1 CPS testing in mTNBC using 22C3 and SP263 assays
M. Ivanova*, C. Frascarelli, B. Cerbelli, G. Pignataro, C. Criscitiello, G. Curigliano, K. Venetis, E. Sajjadi, E. Guerini Rocco, P. Graziano, M. Martini, G. D'amati, N. Fusco
*IEO, European Institute of Oncology, Milan, Italy

Background & objectives: Pembrolizumab+chemotherapy is a first-line treatment option for metastatic triple-negative breast cancer (mTNBC) with PD-L1 combined positive score (CPS)≥10. The available validated assays lack standardization. We aimed to characterize the reproducibility of PD-L1 CPS in mTNBC using CE-IVD tests.
Methods: 60 mTNBC samples were tested for PD-L1 IHC using 22C3 pharmDx on a Dako Autostainer Link 48 and SP263 on a Ventana BenchMark Ultra. Five pathologists assessed the CPS. The intraclass correlation coefficient (ICC) for each assay and inter-rater/inter-platform

agreement (Fleiss's κ; 95% confidence interval, CI) were performed by R Software (v 4.2.2) and irr (interrater reliability package).
Results: Both assays have demonstrated a significant ICC (p<0.001) using CPS≥10 as a cut-off value: 22C3=0.939 (CI:0.913-0.96); SP263=0.972 (CI:0.96-0.982); combined 22C3-SP263=0.909 (CI:0.874-0.938). Fleiss's κ confirmed an almost perfect agreement among pathologists and assays: 22C3=0.938 (CI:0.857-1.018); SP263=0.972 (CI:0.890-1.052); combined 22C3-SP263=0.907 (CI:0.869-0.945).
Conclusion: Both 22C3 pharmDx, which was used in the KEYNOTE studies, and SP263 are approved in Europe and can be reliably performed in mTNBC, providing that each assay is used on the dedicated platform (Dako and Ventana, respectively). The inter-observer reproducibility ranges from perfect to almost perfect in both assays, confirming that PD-L1 with CPS should be assessed by specifically trained pathologists. The validation and harmonization of the assays is warranted to provide a high-quality PD-L1 CPS test in mTNBC.
This work was partially supported by the Italian Ministry of Health with Ricerca Corrente 5 x 1000 funds Mariia Ivanova was supported by Fondazione Umberto Veronesi. Konstantinos Venetis was supported by Fondazione IEO – MONZINO.

OFP-09-014
Tumour infiltrating lymphocytes and neutrophil-to-lymphocyte ratio before neoadjuvant therapy in relation to prognosis of triple negative breast cancer
Y. Liu*, M. Zhao
*The Fourth Hospital of Hebei Medical University, China

Background & objectives: To explore the correlation between the peripheral blood neutrophil-to-lymphocyte ratio (NLR) and tumour infiltrating lymphocyte (TIL) before neoadjuvant therapy (NAT) and the prognosis of patients with triple negative breast cancer.
Methods: A total of 126 patients with TNBC who received NAT were screened out. PD-L1 (22C3), TILs, CD8+TIL and FOXP3+TIL were detected by immunohistochemistry in core needle biopsy specimens before treatment, and NLR was calculated. Kaplan-Meier analysis was used to estimate survival rates. Univariate and multivariate analyses were performed using Cox proportional hazards regression.
Results: Univariate analysis showed that high T stage, lymph node involvement, lymphovascular invasion, high NLR, low TILs density and high CD8+ TIL were associated with poor overall survival (OS) and breast cancer-specific survival (BCSS). Multivariate Cox regression analysis showed that high NLR (HR= 36.182, 95%CI: 4.120-317.759, P=0.001) and high CD8+ TIL density (HR=0.182, 95%CI: 0.044-0.754, P=0.019) were independently associated with poor OS. Similarly, high NLR (HR=23.989, 95%CI: 2.275-252.131, P = 0.008) was independently associated with worse BCSS.
Conclusion: NLR may be able to predict the prognosis of patients with triple negative breast cancer after neoadjuvant therapy.

OFP-09-015
Frozen section vs touch imprint for intraoperative evaluation of sentinel lymph nodes of breast cancer patients in neoadjuvant setting: a systematic review and meta-analysis
M. Huerta-Rosario*, C. Quispe-Vicuña, D. Julca-Marin, L.M. Acuña-Chavez, F. Medina-Navia, H.K. Baltazar-Ñahui, C.J. Zumarán-Nuñez
*Universidad Señor de Sipán, Red de Eficacia Clínica y Sanitaria, REDECS, Lima, Peru

Background & objectives: Evaluation of frozen section (FS) or touch imprint (TP) in neoadjuvant setting is challenging due to therapy effect. Some studies suggested that TP may not be the appropriate method. Our objective is summarizing evidence on these techniques after neoadjuvant therapy.
Methods: PubMed, Embase, Scopus and Web of Science were systematically searched until September 2022 for studies evaluating the diagnostic accuracy of FS and TP in BC patients who underwent neoadjuvant therapy. A meta-analysis was planned using a random-effects model to estimate pooled effects. Study quality was assessed using the QUADAS-2 tool. GRADE criteria were used to identify the certainty of evidence.
Results: 17 studies were included. Regarding TP, at lymph node level the pooled sensitivity and specificity was 0.55 (96% CI) (0.33-0.76) and 1.0 (0.98 -1.0), respectively. At patient level, TP had a pooled sensitivity and specificity of 0.74 (0.50 - 0.89) and 0.99 (0.82-1.00), respectively. Regarding the FS, at lymph node level, the pooled sensitivity and specificity was 0.86 (0.81- 0.90) and 1.00 (0.94 -1.00), respectively. At patient level, FS reports a sensitivity and specificity of 0.79 (0.72-0.84) and 1.0 (0.0-1.0), respectively. For most studies, risk of bias was low. Also, for both techniques, the sensitivity had a very low to moderate certainty and the specificity had a high certainty.
Conclusion: Both diagnostic techniques showed very high specificity. Although at lymph node TP had a low sensitivity, at patient level the sensitivity was comparable for both technics. The low certainty in some results would indicate the need for future methodologically better studies.

OFP-10 | Joint Oral Free Paper Session Digital and Computational Pathology and Other Topics (EM / DEVEL / CARD)

OFP-10-001
Diagnostic electron microscopy of endomyocardial biopsies
V. Papa*, C. Baldovini, M. Riefolo, O. Leone, G. Cenacchi
*Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: Endomyocardial biopsy is an important invasive procedure in suspected non-ischemic cardiomyopathy patients. Histological data can need ultrastructural examination for a more detailed differential diagnosis. We aimed at clarifying the diagnostic role of Electron Microscopy (EM) in primary and secondary cardiomyopathies.
Methods: Endomyocardial biopsies obtained from patients with suspected non-ischemic cardiomyopathy between January 2001 and March 2023 at S. Orsola Hospital were studied. For EM analysis, the samples were fixed in 2.5% glutaraldehyde and post-fixed in 1% osmium tetroxide, then dehydrated in ethanol and embedded in epoxic resins. Ultrathin sections were examined under a transmission EM Philips 410.
Results: Altogether 466 biopsies were analysed, 123 of which revealed non-specific changes as presence of glycogen, lipid and mitochondrial accumulations. In 122 cases EM confirmed the histological signs of amyloidosis showing extracellular 7-10 nm non-branched fibrils, while in 34 cases the diagnostic ultrastructural markers were useful for the differential diagnosis as follows: mitochondrial paracristalline inclusions and/or shape and size abnormalities (mitochondrial cardiomyopathy); lysosomal lamellated zebra-bodies inclusions in cardiomyocytes (Fabry disease); basal membrane in the inner side of autophagic vacuoles (Danon disease); ovoidal/polygonal extracellular deposits (cardiac ochronosis); many electrondense iron-containing particles (sized <12 nm) free in the cytoplasm or in single-membrane-bound lysosomal bodies (haemocromatosis); curvilinear bodies and concentric mielin figures (hydroxychloroquine cardiotoxicity).
Conclusion: The diagnostic role of EM was especially evaluated in the vacuolar degeneration of cardiomyocytes, commonly encountered during routine histological examination, in which EM can often reveal their content to differentially diagnose various lysosomal storage diseases, mitochondrial cardiomyopathy or autophagic degeneration; moreover EM can be useful in overcoming histological sensitivity

limitations when pathognomonic signs are in too small areas and scattered in the sample. But even under an EM, undiagnosed cases remain.

OFP-10-002

Brazilian pathology teaching forum: teaching-learning tool

G. Brasileiro Filho, D. Nunes Oliveira*, L.C. Lima Ferreira, M. Freire Santana, F. Toledo Bueno Pereira, D. Masashi Sugita, S. Correia Leão, G. Pozzan, A.C. Siquara de Sousa, R. Vilar Lima, J. Carneiro Melo
*University of Fortaleza, Brazil

Background & objectives: Supported by the Brazilian Society of Pathology (SBP), Pathology teachers from all over Brazil came together to stablish a forum (FEP) aimed at improving the academic work of professors and the teaching-learning of medical students.
Methods: The forum actions are conducted by 4 working groups: 1-Metacognition (didactic strategies and resources, which deals with the bases of learning and didactic-pedagogical actions, including computational tools); 2- Pedagogical bases (educational objectives, courses contents, expected competences and teaching-learning methodology); 3-Learning assessment; 4 - Elaboration of instructional materials (macro and microcopy figures, clinical cases, autopsies and others).
Results: Since 2019, the forum has make available: a) videoclasses on several topics: medical education, general pathology and many aspects of COVID-19; b) recomendations about curricular contents and competences (general and specific) in Pathology, for broad use by medical schools in the whole country; c) macroscopic and microscopic figures of around a hundred cases (general Pathology, cytopathology, infectious diseases and many cancer types).
Conclusion: Providing effective Pathology learning, especially in a very large and diverse country (350 medical schools), is really challenging. Sharing basic educational rules and successful experiences to thousands of professors all over the country can make a notorious difference. The initial good adherence from dozens of colleagues, from different parts of the country, has make possible steps ahead. The potential achievement for this group is promising, so we are convinced that this work can really improve medical education in Brazil.

OFP-10-003

Truncated titin is incorporated into the sarcomere in human cardiac samples of dilated cardiomyopathy

D. Kellermayer*, H. Tordai, B. Kiss, G. Török, A.A. Sayour, M. Pólos, I. Hartyánszky, B. Szilveszter, S. Labeit, A. Gángó, G. Bedics, C. Bödör, T. Radovits, B. Merkely, M. Kellermayer
*Department of Pathology, University of Pécs, Hungary

Background & objectives: Heterozygous (HET) truncating mutations in the TTN gene (TTNtv) encoding the giant titin protein are the most common genetic cause of dilated cardiomyopathy (DCM). However, the molecular mechanisms by which TTNtv mutations induce DCM are controversial.
Methods: Here we investigated 127 clinically identified DCM human cardiac samples with next-generation sequencing (NGS), high-resolution gel electrophoresis, Western blot analysis and super-resolution microscopy in order to dissect the structural and functional consequences of TTNtv mutations.
Results: The occurrence of TTNtv was found to be 15% in the DCM cohort. Truncated titin proteins were detected in the majority of the TTNtv samples. The total amount of expressed titin, which includes the truncated fragments, was comparable in the TTNtv+ and TTNtv- samples. Proteomic analysis of washed myofibrils and Stimulated Emission Depletion (STED) super-resolution microscopy of myocardial sarcomeres labelled with sequence-specific anti-titin antibodies revealed that truncated titin is structurally integrated in the sarcomere. Sarcomere length-dependent anti-titin epitope position, shape and intensity analysis pointed at structural defects in the I/A junction and the M-band of TTNtv+ sarcomeres.
Conclusion: The comparable amount of titin in the TTNtv+ and TTNtv- samples indicates that titin haploinsufficiency may not be the leading cause of the pathogenesis. The sarcomeric integration of TTNtv may contribute, via faulty mechanosensor function, to the development of manifest DCM.
Funding: NVKP_16-1-2016-0017, K135076 (B.M.), K135360 (M.K.)

OFP-10-004

Cardiac amyloidosis: the role of endomyocardial biopsy to assess the myocardial damage

M. De Gaspari*, L. De Michieli, E. Barbieri, S. Rizzo, T. Berno, M. Perazzolo Marra, M. Della Barbera, D. Mele, C. Basso, A. Cipriani
*Cardiovascular Pathology Unit, Department of Cardiac, Thoracic, Vascular Sciences and Public Health, University of Padua - Azienda Ospedaliera, Padova, Italy

Background & objectives: The two most common forms of cardiac amyloidosis (CA) are immunoglobulin light chains (AL-CA) and transthyretin (ATTR-CA), with diverse clinical course and prognosis. Our aim was to compare clinical and pathological data of CA patients who underwent endomyocardial biopsy (EMB).
Methods: An observational retrospective study was performed on patients with a diagnosis of CA who underwent comprehensive clinical evaluation in our centre from 2012 to 2022, including histological confirmation of cardiac involvement by EMB. Clinical parameters including high sensitivity cardiac troponin I (hs-cTnI) values and echocardiographic data were compared to histological findings.
Results: A total of 40 patients were included (66% males, mean age 67 years). Fourteen patients were affected by ATTR-CA (35%) and 26 by AL-CA (65%). At histology, mean amyloid burden was 25.9% (range 3%–85%). A perivascular pattern of amyloid deposition was demonstrated in 50% of EMB, being more frequent in AL- than ATTR-CA (62% vs 29%, p=0.047). Myocyte vacuolization was present in 60% of EMB, replacement-type fibrosis in 40% whereas myocyte necrosis, edema and inflammation in less than 10%. An increase in myocyte diameter and amyloid burden corresponded to worse morphofunctional parameters. The perivascular deposition pattern was associated with altered longitudinal strain, reduced ejection fraction and higher hs-cTnI values.
Conclusion: In CA significant correlations between the clinical parameters and the histological changes on EMB are found. Cardiomyocyte diameter, amyloid burden and perivascular deposition were associated with relevant laboratory and echocardiographic morphofunctional alterations reflecting myocardial injury caused by amyloid deposition. These data support the role of EMB in clarifying the mechanisms of myocardial injury responsible for worse prognosis in CA patients.

OFP-10-005

Morphological cardiac phenotyping with automated quantification of fibrosis, fat and myocardial tissue using QuPath software

P.H. Holm*, K.B. Olsen, B.G. Winkel, J. Tfelt-Hansen, J. Banner
*Section of Forensic Pathology, Department of Forensic Medicine, University of Copenhagen, Denmark

Background & objectives: Cardiac diseases like arrhythmogenic cardiomyopathy are linked to structural abnormalities like fibrosis and fat replacement. Assessments by pathologists are somewhat subjective and using state-of-the-art stereology is time-consuming. We aimed to develop a standardized semi-automated method for cardiac phenotyping using QuPath.
Methods: Whole-slide samples of Picro Sirius Red-stained myocardial tissue were used to develop a pipeline in QuPath. Five cases (25 regions) were used for training. The process included training a pixel classifier to annotate the tissue sample, semi-automatically dividing the tissue into regions, training a different pixel classifier to differentiate

between fibrosis and myocardium, and using Cellpose to detect single adipocytes.
Results: The accuracy of the pixel classifiers was estimated to be over 96% on the separate set of training images, and the preliminary tests look promising. We will annotate ground-truth regions in five randomly selected samples from different cases and compare them blinded with automated classification. Similarity will be calculated using the Jaccard coefficient, and performance will be measured using the F1-score. The method will be further tested by applying it to five arrhythmogenic cardiomyopathy cases and matched controls in a blinded manner, and the results will be compared with the established diagnostic criteria of arrhythmogenic cardiomyopathy. The results of the study are pending and will be presented at the conference.
Conclusion: The expected outcome is an automated method for estimating fibrosis, fat, and residual myocytes in Picro Sirius Red-stained myocardial tissue. We expect that this method will contribute to a standardized and reproducible tool that can be used to establish a cardiac phenotype in cardiac pathological research projects and, hopefully, in future daily diagnostics.

OFP-10-006
IDH status prediction in gliomas using H&E slides and deep learning
Y. Friedmann*, D. Roitman, N. Shelestovich, I. Barshack, S. Ben Amitay
*Sheba Medical Center, Israel

Background & objectives: Determination of IDH mutation status is essential for glioma diagnosis and management. Yet, the limited availability and time-consuming nature of IDH tests pose significant challenges. We aim to develop a deep learning approach for IDH status prediction using H&E slides.
Methods: Our pipeline comprised tissue detection and tile extraction from 1819 H&E slides from Sheba Medical Center and TCGA. We used these tiles to train a self-supervised vision transformer to extract features, which were subsequently used to train a DeepMIL classifier for IDH status prediction. The classifier was trained using 5-fold cross-validation on H&E slides and their corresponding IDH status.
Results: The dataset for IDH classification comprised 323 histologically confirmed glioma cases with known IDH status obtained from Sheba MC, consisting of 378 H&E stained slides. The dataset included 302 IDH wildtype and 76 IDH mutant slides, which were divided into training and testing sets. Our DeepMIL classifier achieved a mean AUC score of 0.88 in cross-validation. Further evaluation on the test set achieved an AUC score of 0.94. Adding TCGA slides with the same mutant/wild-type ratio achieved similar AUC scores. To enhance performance, we incorporated age and sex information into the model using logistic regression, resulting in AUC scores of 0.94 and 0.95 in cross-validation and test sets, respectively.
Conclusion: Our study demonstrates the potential of deep learning in accurately predicting IDH status from H&E slides, achieving high AUC in cross-validation and test sets, which was further validated using TCGA slides. Incorporating patient information improved the model's performance. This approach could significantly reduce the time and cost associated with traditional molecular testing, particularly in resource-limited settings, thus improving patient outcomes. We further plan to expand the dataset, incorporate stain normalization techniques, predict additional biomarkers and evaluate the model's clinical utility.

OFP-10-007
A look at scanner introduced variation in contrast, resolution, and colour across 10 different models of whole slide imaging (WSI) scanner
H. Pye*, D. Brettle, D. Kaye, C. Dunn, M. Humphries, D. Treanor
*National Pathology Imaging Co-operativel, Leeds Teaching Hospitals NHS Trust, Leeds, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

Background & objectives: Variation in images is introduced across the digital pathology pathway. The WSI scanner is a source of this variation; for example: variation in illumination, colour space, and/or signal to noise ratio will be reflected in image colour, contrast and resolution.
Methods: We measured the range of introduced variation across 10 different makes and models of WSI scanner. Ground truth slides were prepared representing a range of contrast (neutral density filters; ranging from 100% transmission to 7% transmission), colour in relation to H&E (stained biopolymer; 3 intensities of each haematoxylin and eosin) and a resolution test pattern (line pairs down to 1um).
Results: Max and min contrast were shifted and the linear relationship with % transmission stretched differently between resultant images across scanners, in some cases resulting in a logarithmic-style relationship. These contrast patterns were reflected in H&E colour variation across all channels, apart from Eosin red which was saturated. Shifts were also seen within the colour space for some, the extent and direction varying across scanners. No scanners could reproduce all the line pairs perfectly, with variation seen both between and within the images. The measured variabilities shown in this work will be reflected in any image data set that uses a range of different scanners, impacting the value of that dataset.
Conclusion: Some believe computation techniques may be able to overcome image variability. However, if data is compromised or missing, in many cases it cannot be compensated for afterwards. We believe as a minimum, the variation in image generation must be described to allow users of image processing and artificial intelligence applications to assess any impact. The introduction of quality processes and test tools is key to this measurement and assessment and could be used to reduce image variability where needed.
Funding: National Pathology Imaging Co-operative, NPIC (Project no. 104687) supported by a £50m investment from the Data to Early Diagnosis and Precision Medicine challenge, managed and delivered by UK Research and Innovation (UKRI)

OFP-10-008
Towards an open-source Transformer-based multiclass segmentation pipeline for basic kidney histology
J. He, P. Valkema*, J. Long, J. Li, S. Florquin, M. Naesens, T. Nguygen, S. Meziyerh, A. de Vries, O. de Boer, F. Verbeek, Z. Xiong, J. Kers
*Pathology, LUMC, Leiden, Pathology, Amsterdam UMC, The Netherlands

Background & objectives: Multiclass segmentation of the microanatomy of kidney biopsies is an important and non-trivial task in computational renal pathology, forming the basis for development of more complex tools. In a multicentre study, we tested the performance of a novel Transformer-based workflow.
Methods: We densely annotated basic anatomical objects (glomeruli, tubules and vessels) in 261 regions of interest of kidney biopsies from Amsterdam, Utrecht and Leiden (the Netherlands). Test performance was assessed on 24 annotated biopsies from Leuven (Belgium) with subgroup analysis for the extent of fibrosis and inflammation (<25%, 26-50%, >50%). We compared models trained with CNN-based U-Net and the Transformer-based Mask2Former.
Results: Mask2Former with the Swin-B encoder (SB-M2F) showed the highest mean (IoU 0.75 vs 0.69) and per-class external test set performance (IoU 0.92 vs 0.88 for glomeruli, 0.89 vs 0.85 for tubules and 0.59 vs 0.48 for vessels) compared to the best-performing U-Net with a ResNet18 encoder (R18-U-Net). SB-M2F compared to R18-U-Net performed particularly better for each class with increasing

degrees of fibrosis and inflammation (overall IoU 0.76 vs 0.66 for >50% inflammation/fibrosis). Vessels were the hardest to segment in severely fibrotic/inflamed biopsies where SB-M2F increased the IoU to 0.58 compared to 0.35 for R18-U-Net (IoU 0.22 for R50 U-Net backbone). SB-M2F resulted in visibly crisper and more uniform segmentations.

Conclusion: We show that the widely used U-Net architecture with various ResNet encoders is outperformed by the recently released Transformer-based architecture Mask2Former for multiclass segmentation of kidney histology. Importantly, we show improved performance in test biopsies with increasing extent of fibrosis and inflammation, lesions that are known to deteriorate segmentation performance. We have written code to extract object-based annotations from the SB-M2F output for further segmentation improvement in a Human-AI-Loop (HAIL) setting and easy object labeling in the open-source software "Slidescape".

Funding: JK is financially supported by grants from the Dutch Kidney Foundation (17OKG23) and the Research Priority Area Human(e) Ai of the University of Amsterdam.

OFP-10-009

Computationally-derived stromal phenotypes, along with tumour-infiltrating lymphocytes, are associated with progression-free survival in high-grade serous ovarian carcinoma digital pathology slides

C. Walker*, L. van Wagensveld, J. Sanders, R.F. Kruitwagen, M.A. van der Aa, G.S. Sonke, K.K. Van de Vijver, S. Rottenberg, H.M. Horlings, A. Janowczyk

* Institute of Animal Pathology, University of Bern, Switzerland

Background & objectives: Tumour development is critically dependent on the supporting stroma and tumour-microenvironment. Here we investigate the prognostic significance of stroma phenotypes and the spatial arrangement of tumour-infiltrating lymphocytes (TIL) in high-grade serous ovarian cancer (HGSOC) using a fully-automated digital pathology pipeline.

Methods: n=360 patients with advanced-stage HGSOC, treated with primary debulking surgery(PDS), or neo-adjuvant chemotherapy(NACT) and interval debulking(IDS). Stroma was delineated using a DeepLabv3 segmentation model, with subsequent extraction of texture features. TILs were detected using nuclei detection followed by an optimized ResNet18 for cell classification and analysed using graph-based features. Features were selected and validated using a 50:50 training/validation split.

Results: Visual inspection showed high accuracy for stroma delineation and TIL detection. Using feature forward selection, 10 features were selected based on progression free survival (PFS) for stroma and TIL respectively. Partial log hazard estimation based on the stromal texture features and TIL graph and density features were both significantly associated with PFS (HR=1.07, CI=1.03-1.12; HR=1.09, CI=1.03-1.16) on the validation set. Furthermore, learning of a combined risk score on the training set based on the stromal and TIL based partial log hazard scores leads to a significant risk score (HR=1.16, CI=1.09-1.17, $p<0.005$), which remained significant in multivariable analysis (HR=1.12, CI=1.04 -1.23, $p<0.005$).

Conclusion: Stroma composition may be an independent prognostic biomarker in HGSOC for PFS. Furthermore, combining stroma texture features with TIL graph features is associated with PFS when adjusted for treatment, patient age and FIGO stage. Interestingly, visual assessment of these phenotypes is likely challenging and subject to large inter-observer variability. Consequently, computational assessment of stroma phenotypes and TIL graph features provides the high-reproducibility needed for imaging-based biomarkers that may further help in stratifying risk of recurrence in HGSOC patients.

OFP-10-010

Automated diagnostic coding (SNOMED-CT) from narrative pathology reports using natural language processing

G. Cazzaniga*, V. L'Imperio, F. Pagni

*Università di Milano-Bicocca - Department of Pathology, IRCCS San Gerardo, Monza, Italy

Background & objectives: Pathology reports contain a wealth of information, but their unstructured and free-text format presents challenges for analysis and knowledge extraction. In this study, we aim to automate the diagnostic coding (SNOMED-CT) from narrative reports with Natural Language Processing (NLP).

Methods: We extracted the diagnosis text and corresponding SNOMED-CT over the past four years from the Laboratory Information System (LIS) of the IRCCS San Gerardo Pathology Department, Monza, Italy, excluding uncoded cases and retaining only the D (diagnosis) or M (morphology) codes. The diagnoses associated with the 70 most frequent codes were selected to train a 3-layer LSTM (Long-Short-Term-Memory) network model.

Results: The final dataset consisted of 36,855 well-balanced labelled diagnoses, with most represented categories being generic codes like "Chronic Inflammation" and "Negative for Tumour Cells". The LSTM model was trained on 6 epochs and 64 batch size, showing an accuracy of 0.83 for the training set and 0.78 for the test set, with precision and recall of 0.78, and an F1-score of 0.77. Notably, best results were achieved in malignancies, while confounding factors were the presence of adjectives as in the case of tubular vs tubulo-villous adenomas. Explainability graphs were used to identify influential monograms and bigrams for each category and fine-tune the model by identifying outliers.

Conclusion: The present study demonstrates the feasibility of retrospective classification and coding of a large dataset of narrative reports using NLP, which has potential applications in identifying unlabelled cases, automating the diagnostic process and monitoring disease trends in real-time. This approach, along with the prospective introduction of synoptic reports, can represent the basis to build an invaluable resource for the patients, especially through the desirable integration with commercially available LIS.

OFP-10-011

Resizing and recompression of pathology whole slide images for affordable long term storage

L. Alfaro*, M.J. Roca

*Hospital Vithas 9 de Octubre, Spain

Background & objectives: Digital pathology has spread to healthcare practice with innumerable advantages. However, its implementation is limited by high financial investment required in storage systems. In order to optimise its use, we designed an image recompression system to reduce long-term storage costs.

Methods: Pathology cases are scanned for diagnosis at high resolution according to the specifications of manufacturers, with three scanners from different companies in .ndpi, .svs and .mrxs formats. Three months after the diagnosis, digital files are moved from the diagnosis server to a storage repository, after a recompression and resizing process.

Results: We use three different software: Hammatsu NDP Convert, Aperio-Leica Digital Slide Studio and Objective Converter. JPEG2000 compression systems used at rates 10-20 (originally 80-90) and files are reduced to 25--33% of their original size.

Depending on the degree of compression and resizing, resulting files weight varies between 5 and 15% with average of 10%.

To assess the quality of these files, authors submitted the cases to pathologists with experience in digital diagnosis for re-evaluation. In all cases the overall assessment of the diagnosis was possible, and files were found to be valid for review in practice and for decision making. Only details requiring high resolution at maximum magnification presented limitations.

Conclusion: The organisation of storage in digital pathology with redundant systems and backups that guarantee the integrity of information requires large and expensive storage environments.

Long-term storage of information on already diagnosed cases doesn't need maintaining the highest resolution for most of them, which will only occasionally be consulted again in future. With our recompression system, we reduce original size to 10%, which allows long-term storage at affordable prices and with quality if not optimal sufficient for re-evaluation of old cases.

OFP-10-012

HPV detection in oropharyngeal squamous cell carcinoma: comparison of morphology and artificial intelligence

S. Craig*, V. Gaborieau, R. Gault, K. McCombe, A. Moyes, Y. Sun, T. Wang, A. Schache, T. Jones, J. Risk, P. Gunning, P. Brennan, J. James, B. Abedi-Ardekani
*Queens University Belfast, United Kingdom

Background & objectives: HPV infection has a key role in the pathogenesis and prognosis of oropharyngeal squamous cell carcinoma (OPSCC). This study compares pathological assessment of HPV based on morphological features in H&E and p16-stained slides, against a novel artificial intelligence (AI) model.
Methods: Based on an EfficentNet-b4 architecture, H&E images from a UK cohort were used to develop a deep-learning model for predicting HPV status. This model was independently tested in an unseen cohort of OPSCC in European, and American patients (n=418). HPV statuses were reported as positive when non-keratinising morphology with p16 strong expression in >70% of tumour cells was met.
Results: Using p16 immunohistochemistry as a surrogate biomarker for HPV status, p16-related OPSCC was identified in 45% (190/418) of European and American patients assessed. Non-keratinising morphology was observed in 37% of cases (156/418). Morphological features accurately predicted p16-related OPSCC in 77% (95% CI: 72-81) of cases with a sensitivity of 65% (95% CI: 81-90) and specificity of 86% (95% CI: 81-91). In contrast, by using a deep learning AI model to assess tumour morphology we were able to accurately predict 85% (95% CI: 82-89) of p16-related European and American OPSCC cases with a sensitivity of 85% (95% CI: 79-90) and specificity of 86% (95% CI: 81-90).
Conclusion: This study highlights the subtly of phenotypic differences in tumour morphology driven by high-risk HPV infection in malignant disease and the difficulty in recognising these features reliably by eye. Our AI model demonstrated significantly better accuracy in identifying p16-related disease compared to manual assessment of non-keratinising morphology. This model has the potential to be tested for usability in HPV-related squamous cell carcinomas from other sites and organs and offers a potentially clinically relevant tool for determining HPV status.

OFP-10-013

Artificial intelligence's impact on prostatic needle biopsies' diagnostics

E. Torresani*, L. Cima, M. Gentilini, E. Bragantini, F.G. Carbone, L. Maccio, M.G. Disanto, C. Sartori, S. Grassi, L. Morelli, T. Cai, M. Brunelli, C. Doglioni, M. Barbareschi
*Department of Laboratory Medicine, Unit of Surgical Pathology, Ospedale Santa Chiara di Trento, APSS, Trento, Italy

Background & objectives: Artificial intelligence algorithms applied to digital slides is promising to have huge impact on work's quality and workflow in pathology.
Aim of our study is to compare the performance of Paige Prostate AI to human performance in a routine setting.
Methods: We selected 106 consecutive patients who underwent prostatic needle biopsies (1431 cores and consequently slides overall).
Glass slides were digitalized with 3DHistech P1000 scanner and analysed with Paige Prostate AI.
We compared AI analysis with the diagnostic reports already provided by seven expert uropathologists and by one junior pathologist, considering cancer status and Gleason Score grading as parameters of interest.
Results: We compared AI analysis to three datasets: expert uropathologists' diagnosis, junior pathologist's diagnosis on glass slides, junior pathologist's diagnosis on digital slides.
Agreement on cancer detection, considering each core individually, ranged from AC1=0.929 (CI 0.912-0.946) (expert pathologists vs AI) to AC1=0.937 (CI 0.912-0.946) (junior pathologist on digital slides vs AI).
Agreement on Gleason Score grading, considering each core individually, ranged from AC2=0.881 (CI 0.851-0.911) (junior pathologist on digital slides vs AI) to AC2=0.923 (CI 0.898-0.947) (expert pathologists vs AI).
AI's sensitivity was 0.975 (IC 0.958-0.992) and specificity was 0.973 (IC 0.963-0.982).
Conclusion: Paige Prostate AI has almost perfect agreement with pathologists' performance, with excellent sensitivity and specificity values, supporting its eligibility for a routine use in pathology departments with a dedicated uropathology service.
Its implementation in a laboratory workflow could have a great impact in standardizing prostate needle biopsies' diagnostics. Moreover, it could ensure the dropping of inter- and intraobserver variability and finally could be used as a quality control tool.
Funding: Internal APSS research funding.

OFP-10-014

OvarIA: a deep learning approach for BRCA somatic mutations detection in high-grade ovarian cancer based on an innovative tumour segmentation method from whole-slide images

R. Bourgade*, N. Rabilloud, T. Perennec, T. Pecot, C. Garrec, C. Delnatte, S. Bézieau, A. Lespagnol, M. De Tayrac, S. Henno, C. Sagan, C. Toquet, J. Mosnier, S. Kammerer-Jacquet, D. Loussouarn
*Department of Pathology, University Hospital of Nantes, France

Background & objectives: BRCA mutations represent an effective predictor of sensitivity of high-grade ovarian cancer to PARP inhibitors. However, their testing by NGS is costly and time-consuming. This work presents a novel approach for predicting BRCA mutations in ovarian cancer using deep learning.
Methods: We included 775 patients with high-grade ovarian cancer and BRCA mutational status. A first step of tumour segmentation based on an innovative deep learning technique was performed and a total of 1,69M tumour tiles were predicted. We used 599K tiles to train a ResNet-50 with momentum contrast while 1,087M tiles were used to train the BRCA classifier with multiple-instance learning.
Results: The tumour segmentation model trained on 8 whole-slide images obtained a Dice Score of 0.915 (± 0.05) and an IoU of 0.847 (± 0.079) on a testing set of 50 whole-slide images. The BRCA classifier achieved the state-of-the-art AUC of 0.739 (± 0.024) in 5-fold cross-validation, 0.681 (± 0.014) over the testing set, and 0.631 (± 0.03) over an external cohort from The Cancer Genome Atlas. We performed an additional multi-scales approach whose results have suggested that the relevant information for predicting BRCA mutations seems to reside more in the tumour spatial conformation than in the cell morphology.
Conclusion: Our results suggest that somatic mutations of BRCA have a phenotypic impact in high-grade ovarian cancer and this information lies more in the tumour context than in the cell morphology. Even if this study needs to be validated on a larger and multicentre cohort with homologous recombination deficiency, it paves the way to clinical application with the future implementation of pre-screening tools for a more personalized medicine.

OFP-10-015

An international multi-institutional validation study of deep learning-based classifier for prostate cancer detection and Gleason grading in biopsy samples

Y. Tolkach*, V. Ovtcharov, A. Pryalukhin, M. Eich, N. Gaisa, M. Braun, W. Hulla, G. Netto, P. Caie, R. Büttner
*University Hospital Cologne, Germany

Background & objectives: Pathologic examination of prostate biopsies is time consuming due to the large number of slides per case. In this study, we develop and validate a deep learning-based classifier for prostate cancer (PCA) detection and Gleason grading in biopsy samples.
Methods: Five external cohorts of patients with prostate biopsy were analysed. A total of 5922 H&E sections (7473 biopsy cores, 423 patient cases) were assessed concerning tumour detection. Whole Slide Images (WSI) were digitized using three scanners. Two datasets (core n=227 and 159) were graded by international group of pathologists including expert urologic pathologists (n=11) to validate the Gleason Grading classifier.
Results: The sensitivity, specificity, and NPV for the detection of tumour-bearing biopsy slides was in a range of 0.971-1.000, 0.875-0.976, and 0.988-1.000, respectively, across the different test cohorts. In several biopsy slides tumour tissue was correctly detected by the AI tool that was missed by pathologists during initial evaluation. Most false positive misclassifications represented lesions suspicious for carcinoma or cancer mimickers. The quadratically weighted kappa levels for Gleason grading agreement for single pathologists was 0.62-0.80 (0.77 for AI tool) and 0.64-0.76 (0.72 for AI tool) for the two grading datasets, respectively. In cases where consensus for grading was reached among pathologists, kappa levels for AI tool were 0.903 and 0.855.
Conclusion: The PCA detection classifier showed high accuracy for PCA detection in biopsy cases during external validation, independent of the institute, scanner or magnification used. High levels of agreement for Gleason grading were indistinguishable between experienced genitourinary pathologists and the AI tool.

OFP-11 | Joint Oral Free Paper Session Neuropathology / Ophthalmic Pathology

OFP-11-001

Use of immunohistochemical surrogate biomarkers as an alternative to molecular methods in classifying adult-type diffuse gliomas

F. Gundogdu*, B. Babaoglu, F. Soylemezoglu
*Hacettepe University Department of Pathology, Turkey

Background & objectives: Nowadays, the use of difficult-to-access and expensive molecular methods has become mandatory in the diagnosis and grading of IDH-mutant diffuse gliomas. In this study, we aimed to find immunohistochemical (IHC) surrogate biomarkers that could be an alternative to molecular methods.
Methods: Tissue microarrays were prepared using 93 astrocytoma and 73 oligodendroglioma cases diagnosed between 2014-2021. 1p/19q and CDKN2A FISH, and H3K27me3 and MTAP IHC studies were performed. The stainings were evaluated independently by two observers. The relationship between CDKN2A HD and loss of MTAP expression and the relationship between 1p/19q codeletion and loss of H3K27me3 expression were investigated for two observers.
Results: CDKN2A HD was detected in 25 (15.1%) of 161 diffuse gliomas, while the first observer detected MTAP loss in 30 tumours (18.1%), and the second observer in 29 (17.5%). As a surrogate marker for CDKN2A FISH, the sensitivity of MTAP was 88% for both observers, and the specificity was 95.52%-96.27% respectively. Loss of H3K27me3 expression was observed in 67.1-68.5% of oligodendrogliomas, and 21.1-22.6% of astrocytomas. As an alternative to 1p/19q FISH, the sensitivity of H3K27me3 was 77.42-76.34%, and the specificity was 65.75%-67.12%. In both biomarkers, an almost perfect agreement with a 0.938 Kappa coefficient was recorded among observers.
Conclusion: MTAP IHC appears to be a reliable surrogate biomarker with high sensitivity and specificity as an alternative to CDKN2A FISH. However, the loss of H3K27me3 expression is not sensitive and specific enough as an alternative to 1p/19q FISH although it is more frequently seen in oligodendroglioma.

OFP-11-002

Prognostic value of the Ki-67 proliferative index in paediatric medulloblastoma, in relation to histology and molecular subgroups

M. Al-Hussaini*, A. Abu Shanab, J. Amarin, A. Al-Ani, N. Amayiri
*KHCC, Jordan

Background & objectives: A high proliferative index, as measured by Ki-67, has been shown to predict poor prognosis in adult medulloblastoma. This study explores the prognostic significance of Ki-67 proliferative index in paediatric medulloblastoma and its relation to molecular subgroups.
Methods: Medulloblastoma specimens from paediatric patients (3 – 18 years) were stained with Ki-67/ MIB-1 immunostain. At a mean cut-off of 30.0%, we correlated the Ki-67 proliferative index with histology and molecular subgroups. Kaplan Meier analysis and Cox proportional hazard analysis were conducted to examine the relationship between Ki-67 proliferative index and clinicopathological characteristics including molecular subgroups.
Results: We included 85 patients (mean age of 7.7 years). There were 17 (20.0%) WNT-activated, 21 (24.7%) SHH-activated, 20 (23.5%) group-3, and 27 (31.8%) group-4 tumours. There were 45 (52.9%) classic, 17 (20%) desmoplastic/ nodular, and 23 (27.1%) large cell/ anaplastic medulloblastoma. Mean Ki-67 score correlated with molecular subgroups (p-value = 0.016). Group-4 has the lowest mean Ki-67 score. It also correlated with histology (p-value = 0.006). Large cell/anaplastic has the highest mean Ki-67 score.
The 5-year OS and PFS rates were 70.2% (SE, 5.5%) and 67.9% (SE, 5.8%), respectively. There was no significant survival difference between patients stratified by Ki67 mean score (PFS: p-value = 0.529; OS: p-value = 0.493).
Conclusion: Unlike its adult counterpart, the Ki-67 proliferative index mean score failed to be associated with survival outcomes in paediatric medulloblastoma. However, Ki-67 proliferative index correlated with histology and molecular subgroups.
Funding: Intra-mural grant from King Hussein Cancer Center

OFP-11-003

Colorectal cancer brain metastases, the use of immunohistochemistry markers in the assessment of prognosis

J. Gama*, R. Caetano Oliveira, P. Teixeira, F. Silva, Â. Jesus, O. Rebelo, M.A. Cipriano
*Centro Hospitalar e Universitário, Portugal

Background & objectives: Brain metastases in colorectal cancer patients are common and are associated with a dismal prognosis. Immunohistochemistry assessment of biomarkers may predict prognosis and guide therapy. Our goal was to investigate the role of different immunohistochemistry makers in prognosis.
Methods: A retrospective transversal study of 77 patients (diagnosed between 2001-2016) with colorectal cancer brain metastases was carried out using archival biological material.
Expression of CD44, HER2, MLH1, MSH2, MSH6, PMS2, BerEp4, EGFR, NTRK, HIF1-alfa and PD-L1 was assessed by immunohistochemistry.
Clinical and pathological data was retrieved from the hospital database. The local ethical committee approved this study.
Results: Of the 77 patients (44 male and 33 female) enrolled in the study, the median age at diagnosis was 65 years (33-84). After a median follow-up

of six months (0-2408 months), the median overall survival was of 6±0.5 months.
No difference in overall survival was seen associated with the expression of CD44 (p=0,504), HER2 (p=0,599), BerEp4 (p=0,899), EGFR (p=0,081), mismatch repair proteins (p=0.197) and HIF1 (p=0,65). PD-L1 and NTRK was negative in all cases.
Conclusion: Colorectal brain metastases are associated with a poor prognosis. In our study, no association was found between CD44, HER, mismatch repair proteins, BerEp4, EGFR, PD-L1, HIF1 and NTRK. Although not showing statistical significance there seems to be a possibility for CD44 and EGFR to predict prognosis and guide therapy. These findings should be confirmed in further multicentric studies.

OFP-11-004
Diagnostic accuracy and feasibility of an ultra-fast digital confocal microscopy scanner for real-time intra-operative brain tumour diagnosis
W. Bolton, P. Ramakrishnan, D. Reveendran, V. Crispi, O. Adebola, R. Sinha, R. Digby*, A. Chakrabarty, R. Mathew
*Leeds Teaching Hositals NHS Trust, United Kingdom

Background & objectives: Real-time intra-operative brain tumour tissue analysis shortens turnaround times and facilitates repeated sampling, improving diagnostic accuracy and guidance to maximise resection. The aim of this present study is to evaluate the diagnostic accuracy of Histolog® within 50 brain tumour patients.
Methods: Varying brain tumour types was conducted in adult patients undergoing brain biopsies or tumour debulking surgery. Multiple, freshly excised tissue samples were stained, and scanned via Histolog® confocal microscopy (60 seconds) in parallel to standard diagnostic pathways including frozen section and smear cytology. Blinded concordance analysis between Histolog® images and gold standard histopathology was performed by a Consultant Neuropathologist.
Results: A total of 50 cases are included in this analysis. Cases studied included glioma, metastasis, meningioma, schwannoma, and pituitary adenoma. Blinded concordance analysis revealed that in every case (n=50; 100%) the Histolog® image was able to confirm the presence of abnormal vs normal tissue, and in n=34 (68%) of instances the diagnosis was precisely confirmed with Histolog® alone. Histolog® images demonstrated specific diagnostic features such as clusters of cohesive epithelioid cells (metastatic carcinoma), sheet-like variably cellular and pleomorphic cells (gliomas), diffuse sheet-like monomorphic round nuclei (pituitary adenoma), elongated spindle cells (schwannoma), and nodular architecture and oval nuclei (meningioma).
Conclusion: Ultra-fast confocal microscopy scanning with Histolog® demonstrates non-inferior diagnostic accuracy when compared to current gold standard but significantly reduces the intra-operative time to achieve diagnosis. We are the first team in the world to demonstrate the feasibility of this technology for real-time intra-operative brain tumour tissue diagnosis. Future studies will investigate the effect of real-time margin zone analysis and explore the use of machine learning applied to the Histolog® images for automatic computer aided diagnosis.

OFP-11-005
In the molecular era, is histopathological examination still effective in demonstrating the relationship with recurrence in meningiomas?
Y. Adali*, S. Ekmekci, Ü. Küçük, Y. Pekçevik, E.E. Pala
*Izmir University of Economics Faculty of Medicine, Turkey

Background & objectives: Meningiomas are usually slow growing tumours which are divided into three grades according to their histopathological and some molecular findings. In this study, it was aimed to document the meningiomas and to investigate the relationship between histopathological findings and recurrence.
Methods: 266 cases diagnosed with meningioma between 2017-2022 were included in the study. Sections of the cases were re-evaluated by 2 pathologists in terms of histological type, grade, number of mitosis, Ki-67 proliferation index (Ki-67); and presence of necrosis, pattern-free pattern, small cell change, hypercellularity, macronucleolus, brain invasion. Tumours diagnosed in 2022 were not included in the recurrence focused analysis.
Results: 111(41.7%) cases were meningothelial, 67(25.2%) atypical, 45(16.9%) transitional, 18(6.8%) fibrous, 8(3.0%) anaplastic, 6(2.3%) angiomatous, 4(1.5%) psammomatous, 3(1.1%) microcystic, 2(0.8%) metaplastic, and 2(0.8%) clear cell histological type of meningiomas. It was noted that the grade, mitosis, and Ki-67 were statistically significant with the presence of necrosis, pattern-free pattern, small cell changes, hypercellularity, macronucleolus, and brain invasion (all p values 0.000). The presence parameters other than grade, mitosis and Ki-67 shows a statistically significant correlation with the absence of necrosis, patternless pattern, small cell changes, hypercellularity, macronucleolus, and brain invasion (all p values less than 0.001). Similarly, a statistically significant correlation was found with recurrence with increased grade, mitosis and Ki-67.
Conclusion: The most common subtypes are defined as meningothelial, fibrous (replaced by atypical in our study) and transitional. Meningiomas are graded according to the mitosis, hypercellularity, macronucleolus, small cell changes, pattern and necrosis. In the present study, a significant relationship between grade and mitosis and Ki-67 was shown, while a negative correlation with other histopathological findings was noted. In this context, it should be underlined that not only histopathological findings, but also molecular features should be included in the grading of meningioma in daily practice.

OFP-11-006
Histologic definition of enhancing nodule and FLAIR hyperintensity region of glioblastoma, IDH-wild type: a clinico-pathologic study on a single-institution series
G. Broggi*, R. Altieri, V. Barresi, F. Certo, G. Barbagallo, M. Zanelli, A. Palicelli, G. Magro, R. Caltabiano
*Department of Medical and Surgical Sciences and Advanced Technologies "G. F. Ingrassia", Anatomic Pathology, University of Catania, 95123 Catania, Italy

Background & objectives: Since the extent of resection beyond the enhancing nodule (EN) in glioblastoma IDH-wild type (GBM, IDHwt) is a highly-debated topic in neuro-oncology, we aimed to provide a comprehensive description of the histopathology of EN and FLAIR hyperintensity regions.
Methods: 33 patients (20 males and 13 females with a mean age at diagnosis of 56 years) affected by GBM, IDHwt were enrolled in this study; for each of them EC and FLAIR hyperintensity regions were sampled intraoperatively using neuronavigation and 5-aminolevulinic acid (5-ALA) fluorescence. A total of 109 histological samples were collected and evaluated.
Results: In 29/33 (88%) cases, the samples from ECs exhibited classic GBM morphology, consisting of hypercellularity, increased mitotic activity, necrosis and/or microvascular proliferation (MVP). In 4/33 cases (12%), the specimens from the ECs showed hypercellular and mitotically-active high-grade diffuse astrocytic tumours, IDHwt, lacking both necrosis and MVP. We also found that FLAIR hyperintensity regions consisted of: (i) fragments of white matter focally to diffusely infiltrated by tumour cells in 76% of cases; (ii) a mixture of white matter with reactive astrogliosis and grey matter with perineuronal satellitosis in 15% and (iii) tumour tissue in 9%.
Conclusion: Since it has been demonstrated that local disease recurrence often arises in peritumoral areas of GBM, IDhwt and that radiologically-defined FLAIR hyperintensity areas of GBM IDHwt are often visible beyond the conventional EN, a deeper knowledge of the histology of FLAIR hyperintensity areas in GBM, IDHwt may serve

to better guide neurosurgeons on the choice of the most appropriate surgical approach.

OFP-11-007

Neuroanatomical location of common brain metastases by primary site with assessment of provided history

M. Bonert*, A. Berzins, H. Begum, J. Lu, A. Swaminath, A. Naqvi
*McMaster University / St. Joseph's Healthcare Hamilton, Canada

Background & objectives: Brain metastases are a frequent occurrence in neuropathology practices and are known to favour certain neuroanatomical locations based on their primary site. This work examines metastases through the lens of pathologic specimens only and the primary site per pathology report.
Methods: All brain pathology cases accessioned 2011-2020 were retrieved from a regional centre. Specimens were classified by neuroanatomical location (frontal /temporal/ occipital/ parietal/ cerebellum/ other), diagnosis, diagnostic category and clinical history in relation to the final diagnosis with a hierarchical free text string-matching algorithm (HFTSMA) and pathologist review. Randomly selected cases were reviewed to assess the HFTSMA.
Results: The cohort had 4,625 cases. 843/4,625 were metastases per HFTSMA; 96% were correctly classified as per 200/4,625 randomly selected cases. 493 were classified as metastases with a single defined primary site on report review from 472 patients. Primaries from breast (38%), gynaecologic tract (35%), and gastrointestinal tract not otherwise specified (33%) most frequently spread to the cerebellum. Kidney metastases (35%) were most frequently found in the occipital lobe. Lung (35%), metastatic melanoma (44%) and colorectal primaries (29%) were mostly commonly found in the frontal lobe. The provided clinical history predicted the primary in 198 patients (42%), was discordant in 16 patients (3%) and non-contributory in 258 patients (55%).
Conclusion: The hierarchical free text string-matching algorithm assisted categorization facilitated the analysis; however, it was not sufficiently accurate without pathologist review. In the majority of brain metastases, the provided clinical history was non-contributory; this suggests surgeon-neuropathologist communication may have the potential for optimization. The distribution of the metastatic tumours in the brain is dependent on the primary cancer.

OFP-11-008

Characterization of the protein expression of the promising immunotherapy targets VISTA, LAG-3 and PRAME in a cohort of southern French patients with primary uveal melanoma

N. Lamas*, S. Lassalle, A. Martel, S. Nahon-Estève, A. Macocco, K. Zahaf, S. Lalvee, J. Fayada, V. Lespinet-Fabre, O. Bordone, F. Pedeutour, S. Baillif, P. Hofman
*Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Campus de Gualtar, Braga, Portugal; Anatomic Pathology Service, Pathology Department, Centro Hospitalar Universitário de Santo António (CHUdSA), Porto, Portugal

Background & objectives: Novel cancer therapies based on immunotherapy have changed the treatment landscape and overall survival prospects for patients. VISTA, LAG-3 and PRAME are emerging targets of immunotherapy for different solid tumours, but their relevance in primary uveal melanoma (pUM) is unknown.
Methods: Using immunohistochemistry in representative whole sections of pUM cases of a cohort of 30 patients from one single centre (Nice University Hospital, Nice, France), we studied and characterized the protein expression of VISTA, LAG-3 and PRAME. The expression of each of these markers was correlated with different clinical and pathological parameters, including metastases onset and overall survival.
Results: VISTA and LAG-3 protein expression was identified in small lymphocytes infiltrating the pUM cases, while no expression of both proteins was detected in uveal melanoma cells. Contrarily, PRAME nuclear expression was identified in uveal melanoma cells, while no expression in the tumour infiltrating immune cells was observed. Increased levels of VISTA expression in tumour infiltrating lymphocytes (TILs) were associated with BAP1 nuclear preservation and a better prognosis for patients. Higher levels of LAG-3 in TILs were associated with higher levels of CD8-positive TILs. PRAME nuclear positivity in uveal melanoma cells was associated with epithelioid cell uveal melanoma histologic subtype, higher mitotic numbers and a higher percentage of chromosome 8q gain.
Conclusion: Our study demonstrates that VISTA is a novel relevant immune checkpoint molecule in pUM. In addition, we further confirm that LAG-3 and PRAME are potentially important immunotherapy targets in the treatment of uveal melanoma patients. Together, our results help to expand the range of immunotherapy candidate molecules that are relevant to modulate in uveal melanoma, which currently has a dismal prognosis once metastases develop, since therapeutic options for the metastatic disease are mostly ineffective.

OFP-11-009

Prognostic significance of BAP1 protein expression in uveal melanoma in comparison to The American Joint Committee on Cancer (AJCC) staging and The Cancer Genome Atlas (TCGA) system

S. Owens*, C. Hegarty, N. Walsh, N. Horgan, V. O'Neill, J. O'Neill, L. Ivers, S. Kennedy
*Research Foundation, Royal Victoria Eye and Ear Hospital, Dublin, National Ophthalmic Pathology Laboratory, Royal Victoria Eye and Ear Hospital, Dublin, School of Biotechnology, Dublin City University, Ireland

Background & objectives: Uveal Melanoma (UM) is a rare and aggressive malignancy that metastasises in approximately 50% of cases. This study aimed to evaluate the role of nuclear BAP1 (nBAP1) expression in overall survival of UM compared to AJCC staging and TCGA system.
Methods: A detailed review of pathology files, cancer registry files and death certs were accessioned and tabulated for UM patients who received enucleation between 1974 and 2022.
BAP1 immunohistochemistry (IHC) results were obtained from stained BAP1 IHC slides or UM tissue microarrays. nBAP1 expression was correlated with metastasis free survival to compare the prognostic value of AJCC staging and TCGA system.
Results: 308 UM patients aged 11-96 [median age: 63] were analysed by IHC for nBAP1 expression. Loss of nBAP1 protein expression was detected in 144/308 (47%) of patients. 124/308 (40%) developed metastasis, 71/124 (57%) were nBAP1 negative.
Clinical, pathological, and genomic characteristics were correlated to identify the best prognostic indicators for overall survival (OS). Through multivariate analysis (95% confidence interval) of clinicopathological features with OS, nBAP1 negative expression [P=0.030] was shown to be an independent factor along with older age and presence of metastasis whereas AJCC and TCGA fell out of significance.
When correlated with clinicopathological features, loss of nBAP1 expression was significantly [Log rank, P=0.0008] associated with poor survival.
Conclusion: In this study, nBAP1 protein expression proved to be a more reliable prognostic indicator for overall survival than AJCC staging or TCGA classification.
This study also provides support for accurate prognostication of UM patients in routine histology laboratories by means of immunohistochemistry for BAP1 alone, without the need to refer all cases for genetic studies, when this is not readily available. It provides further evidence that BAP1 protein expression is a more powerful prognosticator for overall survival than chromosomal studies.

OFP-11-010

ATRX loss suggestive for adverse clinical behaviour in conjunctival melanocytic lesions

J. van Ipenburg*, Q. van den Bosch, D. Paridaens, N. Naus, R.M. Verdijk
*Radboud University Medical Center, The Netherlands

Background & objectives: Conjunctival melanoma (CM) with TERT promoter mutations are associated with metastatic disease. Both ATRX mutations and TERT promoter mutations are associated with faulty telomere maintenance. This study aimed to determine the prognostic value of ATRX loss in conjunctival melanocytic lesions.
Methods: Conjunctival melanocytic lesions (nevi (n=16), primary acquired melanosis (PAM) without atypia (n= 6), PAM with atypia without associated melanoma (n=5) and CM with/without associated PAM with atypia (n=58)) from the Rotterdam Ocular Melanoma Study group were collected. ATRX status was determined using immunohistochemical staining. The TERT promoter status was determined by SNaPshot analysis and/or targeted next-generation sequencing.
Results: None of the nevi and PAM without atypia showed ATRX loss, while ATRX loss was found in 40% (2/5) of the PAM with atypia without associated CM and in 14% (8/58) CM. Twenty-six of the 57 (46%) CM with known TERT promoter status harboured a TERT promoter mutation, with none of these cases showing ATRX loss. Eleven CM developed metastases, including 8 CM harbouring a TERT promoter mutation, 2 other CM showing ATRX loss and one case showing neither a TERT promoter mutation nor ATRX loss. For 2 metastasized CM cases with a TERT promoter mutation the ATRX status was unknown. Correction for adverse clinicohistopathological parameters was not possible.
Conclusion: ATRX loss was found in (pre-)malignant and not in benign conjunctival melanocytic lesions, comparable to TERT promoter mutations, suggesting that both alterations are associated with adverse clinical behaviour. This is emphasized by the finding that most cases with metastatic disease revealed either ATRX loss or a TERT promoter mutation. Similar to TERT promoter mutations ATRX loss may be used as a diagnostic tool in determining whether a conjunctival melanocytic lesion is prone to have an adverse clinical course.

OFP-11-012

Prognostic risk stratification of orbital solitary fibrous tumours using Phosphohistone H3 (PHH3)

D. O'Dwyer*, L. Hendrie, F. Roberts
*Queen Elizabeth University Hospital, NHS Greater Glasgow and Clyde, United Kingdom

Background & objectives: Orbital solitary fibrous tumour (OSFT) is an uncommon and unpredictable tumour. Risk stratification models employ mitotic count to predict outcome. Recently PHH3 has been validated as a mitotic count biomarker. This study assessed PHH3 as a prognostic marker in OSFT.
Methods: A retrospective review was performed to identify all patients diagnosed with OSFT (Mar 2003 – Dec 2021). Clinicopathological details were recorded from clinical records and OSFTs were classified according to the previously published Demicco and Thompson risk stratification models. Following PHH3 immunohistochemistry and interpretation by two independent observers, OSFTs were reclassified and outcomes were analysed using SPSS.
Results: Sixteen patients diagnosed with OSFT were identified. The average age at diagnosis was 50 years (range 25 – 84 years) and 8/16 were female. Median follow-up time was 45.4 months (range 5.2 – 212.5 months) and 25% of patients developed a recurrence. One patient died during the study period. Overall outcome was predicted by older age (p=0.01) whilst risk stratification by the Demicco and Thompson models did not significantly predict prognosis. Following reclassification of tumours using PHH3 mitotic counts the Demicco risk stratification model successfully categorised patients according to risk (p=0.008). Additionally, PHH3 mitotic count alone predicted prognosis when using both Demicco (p=0.02) and Thompson (p=0.03) mitotic count categorical values.
Conclusion: This is a small study of 16 OSFTs with limited follow-up time. However, OSFT is a rare tumour and our recurrence rate of 25% reflects other studies. In this cohort the currently validated risk stratification models failed to predict OSFT outcomes. Following PHH3 staining we successfully predicted prognosis. These findings are consistent with studies reporting PHH3 as an independent prognostic marker. To our knowledge this is the first study to describe PHH3 as a putative prognostic marker in OSFT.

OFP-12 | Joint Oral Free Paper Session Soft Tissue and Bone Pathology / Infectious Diseases Pathology

OFP-12-001

Prognostic risk stratification of 150 solitary fibrous tumours – a single centre experience

D. O'Dwyer*, L. Hendrie, F. Roberts
*Queen Elizabeth University Hospital, NHS Greater Glasgow and Clyde, United Kingdom

Background & objectives: Solitary fibrous tumour (SFT) is an uncommon and unpredictable tumour. The prognostic stratification model developed by Demicco et al helps predict risk. Here we describe a single centre experience of SFT risk stratification and identification of factors associated with outcome.
Methods: A retrospective review was performed to identify all patients diagnosed with SFT (Jul 1997 – Dec 2021). Clinicopathological details were recorded from clinical records and SFTs were classified according to the previously published Demicco risk stratification models. The association between individual clinicopathological variables and outcome was analysed using SPSS.
Results: One-hundred and fifty patients diagnosed with SFT were identified. Mean age at diagnosis was 55.7 years (range 21 – 85 years) and 54% were female (n=81). The primary anatomical sites were: 68 intra-thoracic (45.3%), 46 soft tissue (30.7%), 16 orbital (10.7%) and 20 miscellaneous (13.3%). Median follow-up time was 51.7 months (range 0.6 – 293.0 months). Seventeen patients (11.3%) developed recurrence - orbital SFTs had higher recurrence rates compared to other sites (p=0.07). Risk stratification according to the Demicco model was as follows: 82 low risk (54.7%), 49 moderate risk (32.7%) and 19 high risk (12.7%). Orbital SFTs were predominantly categorised as low risk compared to other sites (p=<0.05).
Conclusion: This is a descriptive study of 150 SFTs with long term follow-up. SFTs can have an unpredictable clinical course and our recurrence rate of 11.3% is similar to other studies. Despite orbital SFTs tending to have higher recurrence rates compared to SFTs from other sites they were also likely to be categorised as "low risk" according to the Demicco risk stratification model. These findings highlight the ongoing necessity to further characterise this uncommon tumour and identify putative clinicopathological prognostic markers.

OFP-12-002

Multiregional whole genome sequencing to decipher the evolution of complex structural events in osteosarcoma

S. De Noon*, J. Espejo Valle-Inclan, A. Flanagan, I. Cortes-Ciriano
*UCL Cancer Institute, Royal National Orthopaedic Hospital NHS Trust, United Kingdom

Background & objectives: Osteosarcoma is an uncommon malignant bone forming tumour with complex genomes due to genomic instability. Large-scale studies of their evolution are lacking due to their

rarity. Our aim was to characterise key events in osteosarcoma using multiregional whole genome sequencing.
Methods: We uniformly processed 185 osteosarcoma whole genomes from 41 patients generated via two sequencing projects (100,000 Genome Project and Gabriella Miller Kids First Paediatric Data Resource). Intratumoral diversity was characterised based on driver alterations, mutational signatures, and complex rearrangements including chromothripsis. Phylogenetic and timing analyses were then employed to determine the order of these genomic features in osteosarcoma development.
Results: Our analyses reveal commonly reported drivers in osteosarcoma are frequently subclonal (NF1-58%, PTEN- 60%, ATRX- 72%). In addition, while chromothripsis and complex genomic rearrangements (CGRs) are typically clonal, a significant number of subclonal structural alterations make up these CGRs, adding to regional diversity. Whole genome duplication (WGD) are late events in these tumours, and CGRs are found to occur mainly after WGD, providing evidence for their role as driver-like events triggering clonal diversification. Finally applying timing approaches to determine the order of structural alterations within these complex rearrangements reveals foldback inversions as an important initiator of amplifications in osteosarcoma.
Conclusion: Our work highlights the extent of genetic subclonal diversity in osteosarcoma. Here we also demonstrate that CGRs are not static events but continue to evolve throughout a tumour lifespan, priming the genome for further instability. These findings have important implications for therapeutic approaches to osteosarcoma and other genomically unstable cancers. Through timing of complex structural events, we reveal common initiating mechanisms of driver events, furthering our understanding of osteosarcoma development.

OFP-12-003
Calcified chondroid mesenchymal neoplasms: expanding the molecular and morphological spectrum
C. Bouvier*, C. Benard, F. Le Loarer, R. Azmani, J. Garcia, I. Hostein, M. Karanian, A. Meurgey, F. Tirode, N. Macagno
*Hôpital de la Timone, France

Background & objectives: Soft tissue tumours with chondroid matrix and calcifications are frequently found at the extremities or the temporomandibular joint. Recently FN1 fusions to genes encoding RTK (receptor tyrosine kinases) were identified in close mimics: «calcified chondroid mesenchymal neoplasms (CCMT)».
Methods: In order to define the morphological spectrum of these tumours we gathered together 41 tumours diagnosed in the french network of soft tissue and bone tumours. The final diagnosis was done with morphological and clinicoradiological data. We performed whole RNA sequencing, transcriptomic and methylome profiling.
Results: We found 6 synovial chondromatoses, 2 mesenchymal phosphaturic tumours and 33 CCMT which encompassed 15 soft tissue chondromas (CD), 10 tophaceous pseudogouts (TPG) and 8 chondroid tenosynovial giant cell tumours (TCGT). 28/33 had fusions with FN1 gene, with varied partners including FGFR2 (13 cases) and TEK (8 cases). All the FN1::TEK-fused tumours were located in the temporomandibular joint and had morphological features of TCGT. They formed a distinct subgroup on unsupervised trancriptomic and methylome clustering analyses. CD and TPG were located in a distinct molecular subgroup aside from other chondroid neoplasms such as synovial chondromatosis and acral fibrochondromyxoid tumours.
Conclusion: FN1-fused CCMT share several morphological features that overlap with CD, TPG and TCGT. Interestingly some TCGT located in the temporomandibular joint were devoid of chondroid matrix and harboured a FN1::TEK fusion expanding the molecular spectrum of TCGT. Surgical resection is the rule but in cases of recurrence or bone erosion tyrosine kinase inhibitors could be an alternative treatment.

OFP-12-004
Unravelling homologous recombination repair deficiency and therapeutic opportunities in soft tissue and bone sarcoma
C. Pauli*, L. Planas-Paz, A. Pliego Mendieta
*USZ and UZH, Switzerland

Background & objectives: Homologous Recombination Deficiency (HRDness) has become of major clinical relevancein cancer therapy but remains poorly investigated in sarcoma. We here broaden the understanding of HRDness in soft tissue and bone sarcoma by performing a comprehensive molecular and functional analysis.
Methods: We investigated genomic and transcriptomic features of HRDness in sarcoma and cross-validated our findings from different sarcoma subtypes among several datasets. We established patient-derived ex vivo sarcoma cell models and functionally tested the sensitivity of our models to several targeted therapies including PARPi as gold standard treatment for HRDness and chemotherapies in monotherapy or in combination.
Results: We show that specific sarcoma entities exhibit high levels of genomic instability signatures and molecular alterations in HRR genes, while harbouring a complex pattern of chromosomal instability. Furthermore, sarcomas carrying HRDness traits exhibit a distinct SARC-HRD transcriptional signature that predicts PARPi sensitivity in patient-derived sarcoma cell models. Concomitantly, HRDhigh sarcoma cells lack RAD51 nuclear foci formation upon DNA damage, further evidencing defects in HRR. We further identify the WEE1 kinase as a therapeutic vulnerability for sarcomas with HRDness and demonstrate the clinical benefit of combining DNA damaging agents and inhibitors of DNA repair pathways ex vivo and in the clinic.
Conclusion: HRDness in tumours correlate with poor prognosis and has become of major clinical relevance as it is associated with therapeutic vulnerabilities and remains poorly investigated in sarcoma. We show that a subset of sarcoma entities exhibit features of HRDness at the genomic and transcriptomic level and highlight the need to characterize sarcoma patients with multiple parameters to better identify those with HRDness. In summary, we provide a personalized oncological approach to treat sarcoma patients successfully.
Funding: Swiss Cancer League KFS 5270-03-2021

OFP-12-005
Recurrent USP6 rearrangement in a subset of low grade myofibroblastic sarcomas of the soft tissues
G. Arcovito*, S. Crucitta, M. Del Re, C. Caporalini, A. Palomba, F. Nozzoli, A. Franchi
*University of Pisa, Italy

Background & objectives: USP6 gene rearrangement typically occurs in benign entities like nodular fasciitis. Nevertheless, rare cases of USP6-rearranged myofibroblastic neoplasms with locally aggressive behaviour have been described. The role of USP6 in low grade myofibroblastic sarcomas (LGMSs) has not yet been investigated.
Methods: On the basis of 2 index cases of LGMS which presented USP6 rearrangement by RNA sequencing (Archer FusionPlex panel), we extended our analysis to a series of 10 cases of low-grade sarcoma with similar morphology and immunohistochemical features, performing fluorescent in situ hybridization (FISH) analysis with USP6 break-apart probe. All the available histological and immunohistochemical slides were reviewed.
Results: In the 2 index cases, RNA sequencing identified USP6::THBS2 and USP6::RRBP1 fusions, and rearrangement of USP6 was confirmed by FISH. One further case presented USP6 rearrangement by FISH. Six tumours showed no rearrangement of USP6, while in 3 cases results were not evaluated due to poor DNA quality. USP6-rearranged tumours arose in deep soft tissues of the extremities in adults. Histologically, they presented

similar features including infiltrative growth, variable multinodular/plexiform architecture, intersecting fascicles of spindle cells, prominent thick-walled vessels, scattered osteoclast-like giant cells, peripheral lymphoid aggregates. All tumours expressed smooth muscle actin and one showed desmin positivity, while beta-catenin, CD34, S100, SOX10 and ALK were negative.
Conclusion: We report a subset of low-grade sarcomas with myofibroblastic features harbouring recurrent USP6 rearrangement. Our findings support the notion that among soft tissue tumours with fibroblastic/myofibroblastic phenotype, USP6 rearrangement is not limited to benign tumours, and warrant further investigation of genetic changes in myofibroblastic sarcomas.

OFP-12-006
Characterisation of immune cells in dysplastic neurofibromas: identification of PD1 and the TIM-3/Galectine 9 pathway as potential targets for immunotherapy
A. Brunet*, L. Lacroix, V. Aftimos, O. Hermeziu, P. Maille, K. Radomska, A. Rapinat, P. Wolkenstein, P. Topilko, N. Ortonne
*APHP, France

Background & objectives: Neurofibromatosis 1 predispose to the development of malignant peripheral nerve sheath tumours (MPNSTs). Dysplastic neurofibromas (DysNF) precedes the transformation of plexiform neurofibromas (pNFs) into MPNSTs. We characterize the immune infiltrates in DysNFs as compared to MPNSTs and NFs.
Methods: The study cohort includes 32 cutaneous neurofibromas (cNFs), 49 pNFs, 31 DysNFs, 20 MPNSTs. We quantify the immune cells of the infiltrates, and characterize them using immunohistochemistry/immunofluorescence. We perform a transcriptomic study using Nanostring technology (panel IO360 pan-Cancer) on a sub-group of the cohort, to identify immune check points and validate their protein expression using immunohistochemistry and immunofluorescence.
Results: We identified higher levels of mononuclear cells infiltration in DysNFs in comparison with cNFs, pNFs and MPNSTs ($p<0.0001$), and more specifically CD3+ T-lymphocytes and CD163+ macrophages ($p<0.0001$). Transcriptomic analysis showed a pro-inflammatory and immune signature in DysNFs with an overexpression of various immune checkpoints, in particular HAVCR2-mRNA encoding for Tim-3. Multiplex immunofluorescence showed that PD1 was mostly expressed by CD8+ T lymphocytes, and Tim-3/Gal9 by CD163+ macrophages, in all tumour types, while PD-L1 was rarely expressed by tumour cells. We found a higher expression of HLA-ABC by tumour cells in MPNSTs, whereas the expression of cleaved caspase 3 was more important in DysNFs and MPNSTs than in pNFs.
Conclusion: Our results suggest the development of an anti-tumour immune response in DysNFs, involving both T-lymphocytes and macrophages, which might control malignant transformation of DysNFs into MPNST. Because Gal9 is one of the main ligand of Tim-3, an autocrine/paracrine loop may play a role in regulating macrophage functions downstream of Tim-3 activation. Whether the blocking of the PD-L1/PD1 and Tim-3/Gal9 pathways may represent targets for an effective immunotherapy to prevent malignant transformation of DysNF remains to be confirmed by further studies.

OFP-12-007
Clinicopathological features of five ultra-rare cases of CIC::DUX4 positive sarcomas
B. Rekhi*, R. Rumde, O. Shetty
*Department of Pathology Tata Memorial Hospital, Parel, India

Background & objectives: According to the recent World Health Organization (WHO) classification, CIC-rearranged sarcomas, including CIC::DUX4-positive constitute an aggressive subtype of undifferentiated round cell sarcomas. There a single study on these tumours from our subcontinent. We present 5 additional cases of this tumour.
Methods: Thirty-nine undifferentiated round cell sarcomas, excluding Ewing sarcomas (ES), were tested for CIC::DUX4 fusion, including Type I (165 base pair size) and II(230 bp) by reverse transcription-polymerase chain reaction. Twenty-seven of those cases were tested for EWSR1 gene rearrangement, 5 for SS18 and 4 for SS18::SSX fusion, and were negative for those tests. Five tumours (12.8%) were positive for CIC::DUX4(Type II) fusion.
Results: Five CIC::DUX4-positive sarcomas occurred in 4 males and one female; of 25-43 years of age, in soft tissues, including thigh (n=2), chest wall(n=1), iliac region(n=1) and foot(n=1). Tumour size varied from 2.2-19 cm. Microscopically, the tumours were composed of nodules and sheets of malignant round to epithelioid cells, including "rhabdoid-like" (n=2) and spindle-shaped (n=2) with eosinophilic to vacuolated cytoplasm (4/5), distinct nucleoli (4/5), brisk mitoses, focal myxoid stroma (4/5) and necrosis (5/5). Immunohistochemically, tumour cells were positive for WT1 (5/5), calretinin (3/4), pan-keratin (1/4), CD99/MIC2 ("dot-like" to cytoplasmic membranous) (4/4), while negative for desmin (0/4), S100P (0/4) and NKX2.2(0/5). INI1/SMARCB1 was retained (3/3). All patients underwent excision with adjuvant radiotherapy and chemotherapy (ES regimen). One patient developed recurrence, while 2 developed pulmonary, including one brain metastasis.
Conclusion: CIC::DUX4-positive sarcomas are ultra-rare tumours, that mainly occur in the soft tissues and in young adult patients. Histopathologically, these tumours display a wide spectrum, including round to epithelioid cells, variable amount of cytoplasmic vacuolization and myxoid stroma with necrosis.
Immunohistochemically, these tumours express WT1 and calretinin. Despite adjuvant therapies, these tumours have dismal outcomes, especially in large-sized tumours. CIC::DUX4-positive sarcomas need to be differentiated from their histopathological mimics, in view of significant treatment-related implications.
Funding: This constitutes a part of an intramural-funded study at our Institution, Tata Memorial Hospital, Mumbai.

OFP-12-008
Solitary fibrous tumour occurring in unusual sites: a clinico-pathological series of 40 cases
M. Mazzucchelli*, G. Angelico, G.N. Rosano, S. Poidomani, G. Magro
*Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", Anatomic Pathology, University of Catania, Italy

Background & objectives: Extrapleural Solitary fibrous tumour is a rare fibroblastic tumour arising in superficial and deep soft tissues. Herein, we present a clinico-pathologic study of SFTs arising in unusual sites, emphasizing the uncommon morphological, clinical and pathological features that cause diagnostic problems.
Methods: A series of 40 SFTs were selected from the pathology files of the University of Catania, Italy.
Immunohistochemical studies were performed with the labelled streptavidin–biotin peroxidase detection system. The following antibodies were tested: vimentin; alpha-smooth muscle actin; desmin; CD34; and STAT6. Pleural SFT with typical morphology, diffusely positive (nuclear immunoreactivity) for STAT6, served as external positive control.
Results: In the present series of SFTs, the following unusual clinico-pathological morphological features were observed: i) unusual sites; ii) tumours with a predominant leiomyomatous-like pattern and only focal tumour areas with the classic-type SFT morphology; iii) tumour with a variable epithelioid cell component; iv) myxoid stromal changes; v) focal to absent vasculature characteristic of SFT; tumours without alternating hypocellular and hypercellular areas; vi) tumours with multinucleated floret-like cells; vii) tumour with sarcomatous overgrowth consisting of atypical spindle to epithelioid

cells and multinucleated giant cells with pleomorphic nuclei; viii) S100 protein immunoreactivity.
Regardless of the histopathological findings and risk stratification models, all tumours showed a benign clinical behaviour.
Conclusion: Although the pathological diagnosis of SFT is usually straightforward, some difficulties may occasionally arise mainly due to the wide morphologic spectrum exhibited by this tumour. The key histological features for a correct diagnosis of SFT are: (i) tumour circumscription; (ii) bland-looking spindle-to ovoid-shaped cells; (iii) "patternless" growth pattern (haphazard arrangement of neoplastic cells); (iv) alternating hypercellular and hypocellular areas; (v) prominent vasculature with hemangiopericytoma-like pattern and/or perivascular hyalinization; (vi) thin to thick collagen fibres; (vii) low mitotic index (<3/10 HPF).

OFP-12-009
Comparative study of diagnostic tools for the detection of MDM2 amplification: fluorescent in situ hybridization, immunohistochemistry, MLPA and massive sequencing
C.M. Ortega Albiach*, J. González, P. Masia Minguez, A. Ferrandez Izquierdo, S. Navarro Fos, C. Martinez Ciarpaglini
*INCLIVA, Spain

Background & objectives: MDM2 targets the tumour suppressor gene p53. Although MDM2 amplification is useful for the diagnosis of lipomatous tumours, there is no clear evidence on how the results of different methods for the study of MDM2 copy-number are correlated.
Methods: We assessed the state of M2M2 amplification through NGS (Oncomine Childhood panel, Thermofisher), IHC (MDM2 clone 1B10, Gennova), FISH (ON MDM2 (12q15) / SE 12, Leica Biosystems) and MLPA (SALSA MLPA Probemix P105 Glioma-2, MRC Holland) in a retrospective series of mesenchymal tumours diagnosed in our institution.
Results: We evaluated 98 cases. We built two cohorts of amplified (10%) and non-amplified cases (57%) in which the results of FISH and NGS were concordant. Amplified cases showed MLPA ratio ≥ 3, IHC expression in ≥ 70% tumour cells with moderate to strong staining intensity, and HScore ≥ 140. Non-amplified cases had: MLPA ratio < 2, IHC expression in ≤ 20% of cells with weak to moderate intensity and HScore ≤ 60.
Based on this results for MLPA and IHC, we analysed the cases where FISH and NGS were initially discordant, to understand better the reasons and potential pitfalls to be considered in clinical routine practice.
Conclusion: The IHC study of MDM2 is a cost-effective subrogate marker for the prediction of amplification if adequate cut-off points are established. In cases with intermediate degrees of staining, it is desirable to use a molecular technique to discern the state of the gene. NGS and MLPA show excellent agreement with FISH, however, cases with low levels of amplification or samples with low concentration of tumour cells, may show false negative results.

OFP-12-010
Characteristics of pulmonary artery wall remodeling in patients who died of COVID-19
S. Nikolaienko*, S. Gychka, T. Amalyan, V. Vasylyk, M.S.A. Tuffaha, Y. Suzuki
*Bogomolets National Medical, Ukraine

Background & objectives: Lung damage and the development of respiratory failure are the major cause of death in COVID-19. The aim of this research is to characterize lung arterial smooth muscle cells in the course of COVID-19.
Methods: 22 lung tissue samples from patients died of COVID-19 were divided in two groups (group 1 – death up to 7th day, group 2 – on 14-16 day) and studied with light microscopy, Masson's trichrome stain, immunohistochemistry (alpha-smooth muscle actin). Morphometry included arterial wall thickness, AWT, (ImageJ software). Statistical analysis included descriptive statistics and Mann–Whitney test (SPSS Statistics v. 28).
Results: In group 1, lung changes included signs of ARDS. Thickening of the lung arterial walls was caused mainly due to the edema and initial fibrosis as well as angiomatosis of the adventitia. In group 2, thickening of the arterial walls was related to the media and combined with pronounced fibrosis of the adventitia and perivascular areas. Results for group 1: AWT Average=8,19 μm (SD=2,23 μm), in group 2: AWT Average=16,49 μm (SD=4,26 μm). Mann–Whitney U test showed statistically significant difference in distribution of AWT between groups (p<0,001).
Conclusion: Severe course of COVID-19 is associated with the thickening of pulmonary arterial walls due to the proliferation of smooth muscle cells as well as the development of fibrosis in the adventitia. The development of remodelling is a characteristic of a longer course of the disease. This factor should be taken into account in the rehabilitation of COVID-19 convalescents who have had a long course of disease.
Funding: Funded by NIH (R03AG71596)

OFP-12-011
Dynamics of SARS-CoV-2 spike protein and nucleocapsid protein in lung tissue of patients died of COVID-19
S. Gychka*, S. Nikolaienko, T. Amalyan, V. Vasylyk, M.S.A. Tuffaha, Y. Suzuki
*Bogomolets National Medical University, Ukraine

Background & objectives: SARS-CoV-2 infection causes lung damage with the development of acute respiratory distress syndrome (ARDS), pneumonia, pneumofibrosis, and respiratory failure. Rate of elimination of the virus from the lung tissue is one of the factors affecting the degree of lung damage.
Methods: 22 lung tissue samples form patients died of COVID-19 were divided in two groups (group 1 – death up to 7th day, group 2 – on 14-16 day) and studied with light microscopy, immunohistochemistry (spike glycoprotein, SG; nucleocapsid protein, NP). Expression levels were scored as 0-3; for SG both in intima, SGI, and media, SGM; NP only in intima.
Results: Morphological changes of the lungs during the severe course of COVID-19 transformed mainly from ARDS in group 1 to secondary bacterial pneumonia and pneumofibrosis with remodelling of the arterial walls in group 2. Statistical analysis included descriptive statistics and Mann–Whitney U test (IBM SPSS Statistics v. 28). Results for group 1: SGI AV=1,5 (SD=0,53), SGM AV=0,7 (SD=0,48), NP AV=1,2 (SD=0,42). For group 2: SGI AV=0,64 (SD=0,39), SGM AV=0,64 (SD=0,32), NP AV=0,91 (SD=0,63). Mann-Whitney U test showed statistically significant difference in distribution of SGI between groups (p=0,002). No difference in SGM and NP between groups were found.
Conclusion: A decrease in the expression of spike glycoprotein in the intima of the pulmonary arteries was detected in patients who died on the 14th-16th day of the course of the disease. The low expression of spike glycoprotein during the third week of the disease indicates the leading role of secondary complications in the cause of mortality.
Funding: Funded by NIH (R03AG71596)

OFP-12-012
Primary Ewing sarcoma/Primitive neuroectodermal tumour of the kidney: Experience from a rural teaching hospital in South India
V.M. Godkhindi*, R. Kudva, K. Pai, S. Sharma, M. Mathew, G. V, A. C K Rao, V. Monappa, S. P S, B. Nayal, D. Nayak M, B.M.K. Singh, C.B. K Udupa, D. H C
*Department of Pathology, Kasturba Medical College, Manipal, Manipal Academy of Higher Education (MAHE), Karnataka, India

Background & objectives: Primary renal Ewing sarcoma is a rare subset and often requires a multimodal approach synergising between

surgery, chemotherapy, radiotherapy & palliative care. This study aims to review the clinicopathologic features & outcomes in a resource-constrained setting of LMICs.
Methods: Hospital-based retrospective analysis of all cases of primary renal Ewing sarcoma/PNET registered between 2014 & 2022.
Results: A total of eight patients were identified, of which 4 [50%] were males & 4 females, and the median age: 19.5 years [Range, 12-59 years]. The most common presenting complaint: Haematuria [87.5%], flank pain [62.5%], abdominal mass [25%]. The median tumour size: 9.65 cm [Range, 4.7-31 cm] with RV involvement identified in 3 [37.5%] & IVC in a single case. 75% were non-metastatic at presentation. Upfront nephrectomy: 5 [62.5%] cases. Tumour cells were immunopositive for NKX2.2, CD99, FLI1 & synaptophysin. Cytogenetic analysis for EWSR1 translocation: 4 cases. The chemotherapy used a combination of 3-weekly ifosfamide, and etoposide, alternating with vincristine, doxorubicin/dactinomycin, cyclophosphamide. All patients received neoadjuvant/adjuvant chemotherapy & local site radiotherapy in one case. On the last follow up 3 patients [37.5%] were alive with progressive disease, 3 succumbed to metastatic disease, one alive with stable disease, one lost to follow-up.
Conclusion: Primary renal Ewing sarcoma carries a guarded prognosis and warrants an aggressive multimodal approach. The diagnosis & management needs to be tailored & modified for every individual and resource-constrained setting.

OFP-13 | Joint Oral Free Paper Session Molecular Pathology / Haematopathology

OFP-13-001
Comprehensive genomic profiling for precision oncology: the Belgian Approach for Local Laboratory Extensive Tumour Testing study (BALLETT)

B. Maes*, F. Dedeurwaerdere, I. Vanden Bempt, J. Van Huysse, S. Rottey, J. Vermeij, S. Lambin, J. Van der Meulen, F. Vaeyens, G. Beniuga, K. Punie, C. Van Marcke, D. Schröder, G. Froyen, P. Aftimos
*Jessa Hospital Hasselt, Belgium

Background & objectives: Comprehensive Genomic Profiling (CGP) in cancer diagnostics is gaining interest but broad access is still limited. The nationwide BALLETT study aims to have a fully standardized CGP analysis available, potentially increasing access to innovative drugs for Belgian cancer patients.
Methods: BALLETT is recruiting about 900 patients with a metastatic solid tumour in 12 Belgian hospitals. CGP is weekly performed on pooled samples using the TSO500® kit (Illumina) by one of the 9 hospital labs collaborating in the BALLETT lab consortium. Results are discussed weekly in a virtual, national Molecular Tumour Board (nMTB) resulting in CGP-based treatment recommendations.
Results: Since June 2021, tumour samples of 630 patients with 32 different tumour types have been successfully tested by CGP, with a final test success rate of 94 %. Median turnaround time from informed consent to nMTB discussion was 25 days. For the 30 tumour types with more than 1 case, actionable genomic alterations were recorded in 55 % to 100 % of cases. The nMTB discussions resulted in a CGP-guided treatment recommendation in 441 patients (70 %): reimbursed treatments (n=46), participation to a clinical trial (n=355) or a medical need program (n=8) or off-label drug use (n=32). Follow-up on potential hereditary cancer predisposition was recommended for 74 patients (11,7 %).
Conclusion: BALLETT has resulted in a broad access to CGP for patients with metastatic cancer in Belgium. Clinically relevant biomarkers were identified, and CGP-based treatment recommendations were made for the large majority of patients. The uptake of these treatment recommendations and the outcome of the patients will be followed up within the project. Furthermore, the BALLETT laboratory consortium combined with the nMTB is a valuable platform for reducing turnaround time, exchanging expertise and standardization of CGP methodology and treatment recommendation. ClinicalTrials.gov:NCT05058937
Funding: European Union (CAN.HEAL grant) Belgian Society of Medical Oncologists

OFP-13-002
Molecular profiling of advanced urothelial carcinoma in Ireland through next generation sequencing

J. Maguire*, S. McCarron, A. Dunne, R. McDermott, C. O'Brien, S. Finn
*Histopathology Department, St James's Hospital, Dublin, Ireland

Background & objectives: Mutational burden of urothelial carcinoma (UC) is variable and complex, with therapeutic targets for certain molecular alterations (eg. FGFR3). Our aim was to describe the molecular profile of UC in our centre with a focus on the occurrence of co-mutations.
Methods: All cases of UC that were referred for Next Generation Sequencing (NGS) analysis since its commencement in our centre (December 2021–March 2023) were drawn from the Cancer Molecular Diagnostics Laboratory database (n=77), and the molecular profile of each tumour was analysed using the OncomineTM Focus targeted NGS panel, comprising common driver mutations and oncogenic fusions.
Results: As expected, FGFR3 mutations (all variants of strong clinical significance) and fusions (FGFR3::TACC3) were most commonly identified (15% of cases). No FGFR1/2 mutations were identified. All remaining mutations were of potential/unknown clinical significance. PIK3CA mutations were identified in 13% of cases, ERBB2 in 8%, KRAS 6%, CTNNB1 3%, KIT 3% and EGFR in 1%. 4 cases had more than one gene implicated in mutational pathways; MAP2K1/HRAS (both potentially clinically significant), FGFR3 with a potentially clinically significant PIK3CA mutation, KRAS/KIT mutation of unknown clinical significance and finally one case with 3 mutations PIK3CA, ERBB2 and KIT. 7% of cases were insufficient for analysis, 56% had no mutation identified by this panel.
Conclusion: While the identification of 11 cases of UC with FGFR3 alterations is in keeping with published research and of potential therapeutic benefit, this study also supports the evidence of a spectrum of other genetic mutations of potential clinical significance, including co-mutations, most notably PIK3CA and ERBB2. The location of the mutations identified in our study is in keeping with The Cancer Genome Atlas (TCGA) findings and suggestive of APOBEC mutagenic activity, potentially predictive of prognosis and therapeutic response.

OFP-13-003
Predicting survival from whole-slide images in lung cancer patients treated with immune checkpoint inhibitors

M. Ilié*, P. Tourniaire, J. Mazières, A. Vigier, F. Ghiringhelli, N. Piton, J. Sabourin, F. Bibeau, N. Ayache, P. Hofman, H. Delingette
*CHU Nice LPCE, Pavillon J, France

Background & objectives: PD-L1 expression is currently the only approved biomarker for the selection of NSCLC patients for treatment with immune checkpoint inhibitors (ICIs). However, it lacks both efficiency and robustness. We aimed to construct a new solely based on whole-slide image analysis.
Methods: First, we used a clustering method based on a deep learning model to cluster patches within the images. After the clustering step, for each slide, we measured the interactions between clusters by counting the occurrence of neighbouring patches. Finally, these interaction measures were used to train a Cox Proportional Hazard (PH) model to predict patient overall survival.
Results: 149 NSCLC patients from five centres were included in the study. A 5-fold cross-validation of the Cox PH model using PD-L1 expression alone yielded a mean c-index of 0.617 (0.558, 0.676). No statistically significant difference between low- and high-risk groups was found (HR=1.46,

p-value=0.06). When using cluster interactions as features for the Cox regression, we obtained a mean c-index of 0.615 (0.567, 0.662) with statistically significant difference between low- and high-risk groups (HR=1.54, p-value=0.03). Combining PD-L1 expression with cluster-based features increased the mean c-index to 0.666 (0.654, 0.678) with a sharper difference between low- and high-risk groups (HR=2.06, p-value<0.001).
Conclusion: Using whole-slide images only, we were able to devise a new set of features to predict survival for patients receiving ICI treatment consequent to lung cancer. Our method combines a deep learning-based clustering approach with a Cox PH regression to output the survival probability after treatment. We show that the newly created features had a predictive power comparable to PD-L1 expression. The combination of the two showed even more promising results to distinguish low- and high-risk groups.

OFP-13-004
N-glycomic signature of microsatellite unstable colorectal cancer
I. Ukkola*, P. Nummela, A. Heiskanen, M. Holm, S. Zafar, M. Kero, C. Haglund, T. Satomaa, S. Kytölä, A. Ristimäki
*Department of Pathology - HUSLAB, Helsinki University Hospital and University of Helsinki, Finland, Applied Tumour Genomics Research Program – Faculty of Medicine, University of Helsinki, Finland

Background & objectives: Approximately 15% of colorectal cancers (CRCs) display microsatellite instability (MSI) and show major differences in outcome and therapeutic responses as compared to microsatellite stable (MSS) CRCs. The molecular CRC subtypes have been largely ignored in previous glycomics studies.
Methods: We compared the N-glycan profiles of stage II and IV MSI CRCs, further subdivided into BRAFV600E mutated (mt) or wild-type (wt) subgroups (n=10 in each group), with each other and with non-neoplastic colon control samples using MALDI-TOF mass spectrometry. In addition, the N-glycan profiles of the stage II BRAFwt MSI tumours were compared to corresponding MSS tumours analysed previously (n=9).
Results: In line with previous CRC reports, MSI CRC tumours displayed higher relative abundance of neutral pauci-mannose but in contrast lower abundance of high-mannose N-glycans than the control tissues. Between stage II MSI and MSS CRCs, especially the acidic N-glycan profiles markedly differed, MSI tumours showing lower relative abundances of large, sulfated, terminal N-acetylhexosamine (HexNAc) containing, and fucosylated N-glycans. Striking differences were also seen in the acidic N-glycans of MSI subgroups. Most interestingly, the large, sulfated, and terminal HexNAc containing N-glycans were more abundant in BRAFmut than BRAFwt stage IV MSI tumours, whereas in stage II they were less abundant in BRAFmut than BRAFwt tumours.
Conclusion: In conclusion, the neutral and acidic N-glycan profiles of stage II MSI CRC tumours differ from the corresponding MSS tumours. Most importantly, the acidic N-glycan profiles show a clear dependency on tumour stage and BRAF mutation status in MSI CRC. Our results show that the molecular subgroups of CRC have unique glycan profiles, which may partly explain their tumorigenic and immunogenic properties. These glycosylation alterations could thus predict the progression and therapy responses of MSI CRCs after further validation.
Funding: Cancer Foundation Finland, Finska Läkaresällskapet, Helsinki University Central Hospital Research Funds, Medicinska Understödsföreningen Liv & Hälsa, Orion Research Foundation, Sigrid Juselius Foundation, and University of Helsinki.

OFP-13-005
Detection of tumour DNA in bronchoscopic fluids in confirmed or suspected lung cancer: a proof-of-concept study
N. Piton, G. Arhant, S. Lachkar, P. Thiebaut*, F. Marguet, A. Lamy, L. Thiberville, M. Salaün, F. Guisier, J. Sabourin
*Rouen University Hospital, France

Background & objectives: Genotyping of circulating tumour DNA is a useful tool for characterization of lung cancer, but with low sensitivity. Our aim was to detect tumour DNA in the supernatant of guide sheath flush fluids collected during bronchoscopy.
Methods: Total DNA was extracted and genotyped using high-throughput sequencing or the COBAS® EGFR Mutation Test. Thirty-three paired samples (supernatant of guide sheath flush + plasma) from 24 newly diagnosed patients and 9 progressive non-small cell lung cancer patients were analysed.
Results: Guide sheath flush-based genotyping yielded a mutation detection rate of 61.8% (17/24 EGFR, 1/2 ERBB2, 1/1 KRAS, 1/1 MAP2K, 1/4 MET, and 0/1 STK11), compared to 33% in plasma-based genotyping ($p = 0.0151$).
Conclusion: The detection of tumour DNA in the supernatant of guide sheath flush fluid collected during bronchoscopy represents a feasible and more sensitive alternative to circulating tumour DNA genotyping in non-small cell lung cancer.
This work was mainly funded by Boehringer Ingelheim® ("Bourse Régionale Profil Onco 2015" awarded to Nicolas Piton).

OFP-13-006
Molecular characterization of metastatic breast carcinomas by NGS on circulating tumour DNA
P. Santiago Díaz*, S. Clavé Safont, R. Longarón Rozalen, A. Escobar Tejeda, G. Piquer Velasco, I. Vázquez de las Heras, L. Comerma Blesa, B. Lloveras Rubio, B. Bellosillo Paricio
*Hospital del Mar, Barcelona, Spain

Background & objectives: Cell-free DNA (cfDNA) analysis is useful to identify actionable alterations, monitor treatment response and evaluate clonal heterogeneity. The aim of this study was to evaluate the clinical utility of cfDNA analysis in breast cancer patients by next-generation sequencing (NGS).
Methods: 26 cases of metastatic breast cancer were prospectively selected and analysed using Oncomine Breast cfDNA Research Assay v2 NGS panel (ThermoFisher) on cfDNA (24 blood samples, 1 pleural fluid and 1 cerebrospinal fluid). Cases with no alterations detected on cfDNA were studied performing NGS on DNA from FFPE tumour tissue. cfDNA concentration (ng/ml) and limit of detection (LoD%) were annotated.
Results: Molecular alterations were detected in 18 out of 26 cases. 16 cases harboured 1-2 alterations, with 6 being the maximum number detected in a single case. PIK3CA was mutated in 13 of 18 cases, followed by TP53 (8 cases, 6 showed coexistence with PIK3CA). Other alterations were found on ESR1, SF3B1 and FGFR1. No cfDNA abnormalities were observed in 8 cases (31%). FFPE tumour tissue characterization showed gene mutations (PIK3CA, ERBB2 and FGFR1) in 4 of them, and no alterations in the other 4 cases. Cases with detectable alterations showed higher cfDNA concentration (73.1 vs. 63 ng/ml), and higher sensitivity (LoD%: 0.3% vs. 0.9%).
Conclusion: The application of NGS panels on cfDNA allowed the molecular characterization of patients with metastatic breast cancer in combination with the study of tumour tissue samples in 22 out of 26 (85%) cases. Despite the limitation of the low number of cases in our series, this work suggests that the detection of gene mutations in cfDNA correlates with cfDNA concentration.

OFP-13-007
Lineage-specific molecular differences in the development of brain metastasis from lung adenocarcinoma and breast cancer
J. Kros*, S. Najjary, w. de Koning, C. van Eijck, D. Mustafa
*Dept. of Pathology, Erasmus Medical Center, The Netherlands

Background & objectives: In order to find drugs preventing the formation of cerebral metastases, or interfere with outgrowth in brain, we aimed to identify the involvement of molecules or pathways in tumours of different lineages.

Methods: Sample pairs (primary tumours and their brain metastasis) of 11 LUAD and 11 BC (total 44 samples) were investigated in this study. RNA was extracted from the FFPE samples and the targeted gene expression profiles were measured using the PanCancer IO360™ Panel that includes 770 cancer-related genes (NanoString technology). Data were analysed using the nSolver software.
Results: LUAD and BC show differences in genes and pathways to reach the brain. We identified 12 common up-regulated genes in the brain metastases irrespective of their origin (LUAD or BC). Pathway analysis revealed higher metabolic stress in the BC-derived brain metastases compared to LUAD. In addition, we found the immune regulatory molecule VISTA to be highly expressed in the primary tumours of LUAD and their matched brain metastases.
Conclusion: Our study demonstrates that LUAD and BC utilize different genes/pathways to metastasize into the brain. However, once in brain there are particular genes upregulated that are common for the seedings of both primary lineages. LUAD and their brain metastasis express high levels of VISTA. The results urge the development of lineage-tailored therapeutic approaches to successfully prevent or treat brain metastases.
Funding: Foundation "Help Casper".

OFP-13-008
A simple, low-cost pipeline for patient specific, cell free DNA based liquid biopsy
S. Tsuriel*, V. Hannes, A. Refael, D. Mirelman, D. Hershkovitz
*Tel Aviv Sourasky Medical Centre, Israel

Background & objectives: Liquid biopsy (LB) can identifies relapse with before visible in imaging. Detecting a small fraction of tumour somatic DNA variants is required, and testing a large mutation panel improves sensitivity. We developed a pipe-line for tumour-specific multiplex based LB.
Methods: This pipeline is based on tumour mutational profile driven from commercial, ~500 genes panel that is part of the standard of care in Israel for a number of malignancies. It includes the selection of variants, primers design, *in-silico* PCR testing against the human genome and reduction of potential primer dimers. The pipeline can be based on online free bioinformatics tools.
Results: We used this pipeline to design costume panels for 30 patients with 2- 25 variations. We tested the panels on urine and plasma DNA and got high uniformity and low limit of detection enabling us to detect changes in ctDNA level following treatment.
Conclusion: We present the method's applicability to clinical practice. This pipeline is based on ion-torrent platform, it has a relatively lower costs and user-friendly bioinformatics tools can be applied for the analysis. The library preparation process is simple and short which make it feasible in many pathology institute.

OFP-13-009
Oculo-cerebral lymphoma: a monocentric retrospective study of 56 cases
M. Quintyn-Ranty*, R. Bouchoucha, P. Marty, E. Cornet, E. Emery, G. Damaj, J. Quintyn
*Caen University Hospital, France

Background & objectives: We described the characteristics of patients with oculo-cerebral lymphoma (all types) in our institution and evaluated the prognostic value of cell of origin (COO), MYC and BCL2 in primary diffuse large cell B-cell lymphoma (CNS-PDLBCL).
Methods: Retrospective study of lymphomas with a primary cerebral localization according to the French oculo-cerebral lymphoma network at Caen University Hospital from January 2011 to September 2019 (collection of clinical, imaging, biological and treatment data). Immunophenotypic evaluation on FFPE of CNS-PDLBCL. COO subtyping was determinated thanks to Hans algorithm. A report was made to the local ethics committee.
Results: 56 patients had CNS lymphoma, of which 15 had ocular involvement. The median age was 66 years (32% under 60 years), with mostly focal neurological signs (60%), neuropsychiatric signs and intracranial hypertension (36%), comital crisis (11%). The median time from diagnosis to the start of treatment was 18 days. The median overall survival was 29.7 months with a three-year overall survival rate of 47%.
We had FFPE material for 38 patients with CNS-PDLBCL. The GC phenotype was in the minority (6/38).
There was no no difference in overall (OS, p=0.84) or progression-free survival (PFS, p=0.46) with COO stratification, or neither with ocular involvement or not (OS, p=0.816; PFS, p=0.373).
Conclusion: Patients without ophthalmologic involvement were more likely (71% versus 33%, p=0.043) to have a single lesion on MRI.
The lymphoma diagnosis was made on flow cytometry alone in 12% of cases.
There were no significant differences in clinical data and treatment response between the GC and non-GC groups.
Dual expression of MYC and BCL2 was associated with a OS decreased (median of 5.34 months for dual expressors and 12 months for other patients, p=0.009).

OFP-13-010
Lymphoma classification using the World Health Organisation (WHO) 5th edition and International Consensus Classification 2022: an audit of cases diagnosed in Cork University Hospital in 2021
G. Crilly*, B. D. Hayes
*Pathology Department, Cork University Hospital, Ireland

Background & objectives: Lymphomas are classified using the World Health Organisation 5th edition (WHO-HAEM5) or International Consensus Classification 2022 (ICC). These divergent systems reflect advances in immunophenotypic and molecular lymphoma classification, defining new/emerging entities and redefining existing ones.
Methods: All lymphomas cases diagnosed in Cork University Hospital in 2021 were identified by SNOMED search. Each diagnosis was compared using WHO-HAEM5 and ICC 2022.
Results: 190 lymphomas were identified - 33 Hodgkin-lymphoma, 142 B-cell and 11 T-cell lymphomas. Diffuse large B-cell lymphoma was the most frequent diagnosis (42 cases). In 96% of cases the diagnosis according to WHO-HAEM5 and ICC was identical. Divergent diagnoses included four cases of nodal TFH lymphoma, angioimmunoblastic type (WHO-HAEM5) / follicular helper T-cell lymphoma, angioimmunoblastic type (ICC), and a case of primary cutaneous marginal zone lymphoma (WHO-HAEM5) / primary cutaneous marginal zone lymphoproliferative disorder (ICC). Among DLBCL cases, 10% were classified as DLBCL / high grade B-cell lymphoma with MYC-and BCL2-rearrangements (WHO-HAEM5) / high grade B-cell lymphoma with MYC-and BCL2-rearrangements (ICC). No "triple hit" DLBCLs or MYC/BCL6-rearranged DLBCLs were identified.
Conclusion: Our audit showed that WHO 5th edition and ICC 2022 lymphoma classification mirror each other for the most part. However, there is now a deviation in how the WHO and ICC recommends DLBCL classification. This is the most commonly encountered lymphoma which requires immunohistochemistry / molecular work-up. Follow-up studies will be necessary to see if this has any treatment/prognostic implications. Additionally, new entities have been added to the WHO 5th edition which are not necessarily reflected in the ICC.
Conclusion: A wide spectrum of TKD mutation was noted in 25% of the patients tested. T315I was the most common TKD mutation and was found to be associated with advanced disease. The finding from our study was in conjunction with similar studies.

OFP-13-011

Comparison of cell of origin (COO) classification of DLBCL patients using HTG EdgeSeq platform with conventional Han's algorithm

S. Feldstein (Davydov)*, J. Ben-Ezra, D. Hershkovitz, A. Erental
*Tel Aviv Medical Center, Israel

Background & objectives: This study compares the RNA-based HTG EdgeSeq assay with Immunohistochemistry (IHC)-based Han's algorithm for subtyping diffuse large B-cell lymphoma (DLBCL) into GCB and ABC types, where ABC subtype correlates with shorter survival and poor conventional treatment response.
Methods: The HTG EdgeSeq DLBCL COO Assay was used to evaluate 20 cases, including 15 previously analysed by Han's algorithm and 5 reference samples. After RNA extraction and automatic library preparation, sequencing was performed on the IonTorrent platform. Eventually, the HTG EdgeSeq System was used to analyse the data. The assessment of agreement between techniques was performed by Fisher's exact test.
Results: The study found 100% agreement in the 5 reference samples. Among the 15 cases previously analysed by Han's algorithm, 7 were classified as ABC and 8 as GCB. Of the seven IHC-based ABC cases, 6 were confirmed by the HTG assay, but one was discordant and classified as GCB. Of the 8 IHC-based GCB cases, 3 were discordant and classified as ABC by the RNA expression assay. FISH analysis showed double-hit involving c-MYC and BCL-6 in 2 of the 4 discordant cases, which are more commonly found in ABC, suggesting possible misclassification by Han's algorithm. Overall, 11 out of 15 (73%) samples showed concordant results.
Conclusion: The combined diagnostic approach is used for DLBCL patients including immunophenotyping, FISH and COO classification, which are required for tailored treatment. The widely used Han's algorithm reported 78% concordance with the gold standard Nanostring assay for COO classification. Our study demonstrated similar concordance with the HTG assay. As NGS platforms become more widely available in pathology, RNA expression-based assays are expected to become more significant in diagnostics and replace IHC-based methods of classification.

CP-01 | Computational pathology – Where do we stand?

CP-01-004

Deep learning-based multi-organ cancer and site classification using pathologic whole slide images of public datasets

Y. Chong*, K. Yim, K.J. Seo, M. Alam, B. Kim, G. Hwang, D. Kim, O.R. Shin
*The Catholic University of Korea, Republic of Korea

Background & objectives: Accurate classification of cancer and its primary site is crucial for effective diagnosis and treatment planning. However, current artificial intelligence (AI) application in pathology focuses on the classification and subtyping within a certain organs or cancers.
Methods: This study aims to develop a deep learning-based AI model for multi-organ/tumour-origin cancer and subtype classification using TCGA and CPTAC datasets, including 14 types of cancer samples. The dataset was divided into training, validation, and test sets for each organ and cancer subtype. Model performance was assessed using sensitivity, specificity, and accuracy metrics for each organ and cancer subtype.
Results: Our model achieved an overall class classification accuracy of 89.98% and a cancer site classification accuracy of 97.83% (Ranged 97.23-99.60%). Overall sensitivity and specificity of cancer site classification were 88.46% and 99.88%, respectively (Ranged 63.93-97.00% and 97.90-99.73%, respectively).
Conclusion: Our model exhibits promising performance for most organs and cancer subtypes, assisting pathologists in diagnosing and treating cancer patients. However, further improvements can be made for specific organs with lower performance and external validation with real-world data should follow. This model can be incorporated into the general AI system as an ensemble with many preexisting or upcoming organ-specific/task-based models.

CP-01-005

Metastatic melanoma immunotherapy response prediction from routine histopathology slides using digital pathology

J. Bonjour*, A. Wicky, A.H. Seipel, S. Latifyan, P. Liakopoulos, M. Beaussart, O. Michielin, M.A. Cuendet, A.R. Janowczyk
*Precision Oncology Center, Department of Oncology, Lausanne University Hospital, Switzerland

Background & objectives: A clinically actionable biomarker identifying which patients with metastatic melanoma may benefit from immunotherapy is sorely needed. Tumour-infiltrating lymphocyte (TIL) patterns may lead to such a biomarker. Here, we precisely characterized them at scale using digital pathology.
Methods: In n=48 metastatic melanoma biopsies from patients treated with immunotherapy, deep-learning models identified TILs in pre-treatment 40x magnification Hematoxylin and Eosin (H&E) whole slide images. Hand-crafted TIL spatial organization features were extracted and assessed against overall survival (OS). Using leave-one-out-cross-validation, feature selection using Maximum Relevance Minimum Redundancy (MRMR) led to development of a predictive immunotherapy benefit score via logistic regression.
Results: Several features showed significant OS association: kurtosis of lymphocyte cluster areas (dichotomized at the median: HR=0.225, p=0.001, 95% CI=0.089-0.568), fraction of 500x500-pixel tiles with at least one lymphocyte (HR=0.308, p=0.006, 95% CI=0.127-0.742), and median distance between non-lymphocyte cells and nearest lymphocyte cluster (HR=0.390, p=0.023, 95% CI=0.168-0.907). These computer-only derivable features performed significantly better than those typically assessable visually by pathologists, such as TIL density (HR=0.500, p=0.089, 95% CI=0.220-1.130) and TILs to-all-cells ratio (HR=0.539, p=0.133, 95% CI=0.238-1.223). In a multivariate setting with clinical characteristics, TIL features remained independently predictive. The logistic regression-based prediction of immunotherapy benefit using six MRMR-selected features yielded an AUC of 0.78 (95% CI=0.61-0.93).
Conclusion: Initial findings suggest that H&E TIL-based biomarkers hold promise in stratifying patient overall survival after immunotherapy. Computational digital pathology allows precise quantification of complex TIL features inaccessible via visual assessment, offering a novel opportunity for inexpensive, rapid, and non-destructive image-based biomarkers. These promising results indicate that an image-based biomarker using routine histopathology slides may aid in clinical treatment optimization, though further large-scale multi-site validation is necessary.

CP-01-006

A roadmap for single-cell annotation using artificial intelligence algorithms – analysis of PD-L1 IHC expression analysis in gastric cancer biopsies

S. Badve[1], G. Kumar[2], J. Ruschoff, H. Schildhaus, T. Lang, F. Faber, K. Daifallla, M. Karasarides
[1]Emory University School of Medicine, USA, [2]Bristol Meyers Squibb, USA

Background & objectives: There are no clear guidelines at a single cell level to annotate tumour, immune, and stromal cells in gastric biopsies for PD-L1 AI-assisted combined positive scoring. To resolve this, we have developed a roadmap to guide scoring consistency and accuracy.

Methods: A single pathologist selected 31 difficult-to-annotate regions of interest (ROIs) from gastric biopsies. The ROIs were independently reviewed by three pathologists in-person gathering, and individual cells were classified into 5 categories (positive/negative tumour cell, positive/negative immune cell, and unclear). Fibroblasts/endothelial cells were excluded. Discrepancies were resolved by consensus among the three pathologists, and output was used to inform the roadmap.
Results: Consensus building and discussions produced the following principles: a) nuclear size, shape, and chromatin are helpful for the recognition of epithelial cells and require assessment of tumour architecture and potential reference to the H&E stain; b) in cases with shared membrane positivity only one cell is considered positive; c) at the tumour-immune boundary, distinct membranous staining is required for tumour cell positivity; d) scoring of regions with extensive granular membranous staining should be avoided or staining repeated; e) multinucleated cells are considered as single cells; in case of uncertainty the least number of overlapping cells should be counted; f) cytoplasmic positivity in immune cells needs to be convincing at 20x.
Conclusion: The roadmap outlined here provides the basis for standardized cell annotations to train AI algorithms and produce accurate scoring. This will provide a consistent framework for clinical usage. While PD-L1 is used as a case study, the principles may be generally applied to assist in a variety of single-cell annotations necessary to advance AI-based analysis of single or multiplex immunohistochemical stains.
Funding: Bristol Meyers Squibb

CP-01-007
Deep-learning model multiplexing CD68 virtual stain with digital whole slide images of scanned PD-L1 22C3 pharmDx immunostained non-small cell lung cancer tissue slides
S. Aviel-Ronen*, O. Ben-David, E. Arbel, F. Aidt, K. Kersch, T. Hagedorn-Olsen, D. Rabkin, I. Remer, A. Ben-Dor, L. Jacobsen, A. Tsalenko
*Adelson School of Medicine, Ariel University, Pathology Department, Sheba Medical Center, Tel Hashomer, Israel

Background & objectives: Tumour Proportion Score (TPS) of PD-L1 22C3 pharmDx (GE006) immunostaining in non-small cell lung cancer (NSCLC) excludes all immune cells including macrophages which is challenging.
Our objective is to provide virtual stain multiplexing CD68 and PD-L1 to support accurate scoring.
Methods: Forty-nine NSCLC tissues were sequentially stained and scanned with CD68 PG-M1 (GA613)-Envision FLEX HRP Magenta chromogen (GV925) on top of PD-L1 IHC 22C3 pharmDx and the whole slide images (WSI) were aligned.
A deep convolutional neural-network model was trained and validated using matched pairs of PD-L1 (input) & PD-L1+CD68 (ground-truth) patches to create CD68 virtual stain based on PD-L1 stain.
Results: CD68 staining highlights surprisingly more PD-L1 positive macrophages infiltrating the tumour than on initial estimation. Our model produced virtual CD68 staining resembling the actual CD68 stain, as qualitatively assessed by pathologist. Most macrophages in the validation set were stained by the virtual CD68 stain. To quantitatively evaluate the contribution of the model to pathologist detection of macrophages we compared pathologist cell annotations as macrophages/not macrophage performed on PD-L1 stain only vs. multiplexed PD-L1/virtual CD68 stain, using annotations performed on PD-L1/CD68 sequentially stained slides as the ground truth. In ~4000 cells annotated, sensitivity/positive predictive value increased from 0.32/0.44 to 0.79/0.67 respectively. Paired McNemar's test yielded a p-value of less than 10E-30.
Conclusion: We demonstrated a promising CD68 virtual stain-multiplexing model in NSCLC digital WSI, able to identify and virtually stain macrophages on an internal validation set. The model can be extended to virtually multiplex additional stains, including for other types of immune cells. Such virtual stain multiplexing could serve in the future as an assistive layer, allowing pathologists to score PD-L1 slides more accurately and reliably, and present an opportunity for studying the spatial relations between tumour and immune cells.
Funding: Agilent Technologies

CP-02 | Oral free presentations and Best Abstract Award

CP-02-002
Transformer-based automated biomarker prediction from colorectal cancer histology
S.J. Wagner*, D. Reisenbüchler, J.M. Niehues, J.A. Schnabel, M. Boxberg, T. Peng, J.N. Kather
*Helmholtz Munich, Germany

Background & objectives: Deep learning (DL) can extract predictive and prognostic biomarkers from routine pathology slides in colorectal cancer. However, current approaches rely on convolutional neural networks (CNNs). More recently, transformer networks are outperforming CNNs in many computer vision tasks.
Methods: We developed a new fully transformer-based pipeline for end-to-end biomarker prediction from pathology slides. We combine a pretrained transformer encoder and a transformer network for patch aggregation, capable of yielding single and multi-target prediction at patient level. In contrast to previous methods, the transformer-based aggregation relates all tiles to each other instead of considering each tile individually.
Results: A fully transformer-based approach massively improves performance, generalizability, data efficiency, and interpretability as compared with current state-of-the-art algorithms. By using the transformer-based aggregation module and stain colour augmentation during the preprocessing, we can improve the prediction of MSI in colorectal cancer on the public dataset TCGA from 0.79 to 0.9 AUROC score compared to existing attention-based models. External validation on the public dataset CPTAC improves from 0.66 to 0.85 AUROC compared to state-of-the-art methods showing significantly better generalization capabilities. The approach learns faster from fewer data samples than existing methods. Furthermore, multiple attention heads attribute high scores to different medical features increasing the interpretability of the model.
Conclusion: A fully transformer-based end-to-end pipeline yields clinical-grade performance for biomarker prediction. Using a feature extractor pretrained on millions of pathology patches, stain color augmentation, and a new transformer-based aggregation module for MSI prediction on colorectal cancer histology significantly outperforms current state-of-the-art methods. Notably, our approach improves generalization to unseen cohorts, important for translation to clinical application.
Funding: SJW and DR are supported by the Helmholtz Association under the joint research school "Munich School for Data Science - MUDS" and SJW is supported by the Add-on Fellowship of the Joachim Herz Foundation. JNK is supported by the German Federal Ministry of Health (DEEP LIVER, ZMVI1-2520DAT111), the Max-Eder-Programme of the German Cancer Aid (grant #70113864) and the German Academic Exchange Service (SECAI, 57616814). JNK and JNK is supported in part by the National Institute for Health and Care Research (NIHR) Leeds Biomedical Research Centre.

CP-02-003
Automated Ki67 hot-spot detection and analysis leads to higher Ki67 proliferation indices
M. Zwager*, T. Koopman, H. Buikema, T. Ramsing, J. Thagaard, B. van der Vegt
*Department of Pathology, University of Groningen, University Medical Center Groningen, The Netherlands

Background & objectives: Visual identification and manual scoring of Ki67 hot spots is difficult and prone to inter- and intra-observer

variability. We compared the performance of two Ki67 hot-spot detection and scoring digital image analysis (DIA) algorithms.
Methods: Ki67 hot spots were manually scored on whole tissue sections of 135 consecutive invasive breast carcinomas. Two DIA algorithms, based on deep learning (DL) and virtual dual staining (VDS), an image processing technique virtually combining two or more serial stains, respectively, were used to automatically determine Ki67. Correlations between manual and automated scoring of Ki67 hot spots were assessed using Spearman correlation.
Results: 135 cases were available for analysis. Automated detection and assessment of hot-spots using VDS could be performed in 98 (73%) out of 135 cases, while Ki67 hot-spot detection and scoring with the DL based algorithm could be performed in all 135 cases. Assessment by using VDS and DL led to higher hot-spot Ki67 scores (mean 39.6% (range 0.7-98.8%) and mean 38.4% (range 0.7-95.4%), respectively) compared to manual scoring (mean 30.4% (range 0-99.5%)). Correlation between manual and VDS Ki67 scores was substantial (r=0.86). Correlation between manual and DL based Ki67 scores was high (r=0.91).
Conclusion: Automated Ki67 hot-spot detection and analysis correlates strongly with manual Ki67 assessment. Automated Ki67 hot-spot assessment leads to more accurate hot spot detection and higher proliferation indices, compared to manual scoring. The DL based algorithm outperforms the VDS based algorithm in clinical applicability, because it does not depend on virtual overlay of slides. The DL based method correlates stronger with manual scores. Using a DL based algorithm may allow to set a clearer Ki67 cut-off, thereby better aiding clinical decision making.

CP-02-004

Artificial intelligence may help to differentiate morphological characteristics of preoperatively detected and incidentally diagnosed hepatocellular carcinoma ≤ 2 cm in diameter

N. Tezcan*, A. Armutlu, B.L. Cesur, M.N. Ozates, F.U. Kasapoglu, M. Seker, A. Durur Karakaya, C. Gunduz Demir, B. Saka
*Koç University Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: The detectability of hepatocellular carcinoma (HCC) in radiology is limited for ≤2 cm. By comparing multiple morphologic features of incidental and nonincidental foci, factors that provide visibility in radiology were investigated. Microscopic examination was supported with artificial intelligence (AI).
Methods: 102 explants with HCC were evaluated. Nodules not defined as HCC in the last 6 months of preoperative period were re-evaluated by liver radiologists, the ones other than LIRADS4&5 were defined as "incidental". Microscopy & AI were employed. For AI, binary classification task was defined to differentiate nonneoplastic-periphery/HCC and incidental/nonincidental. Features were extracted for each cropped patch, using a pretrained neural network, and an SVM was used for classification.
Results: 73 HCC nodules of 35 patients [M/F=8, Mean Age:51(20-70), mean diameter:1.1 cm (0.3-2)] met criteria.
All were cirrhotic, mostly result of HBV (31%). 29 nodules were defined as HCC on preoperative MRI and 60% (n=44) were incidental. The most common features were detected as: pT2 (21/35), noninfiltrative borders (58/73), Grade 2/3 (54/73), predominantly microtrabeculated (70%). 22% have ≥5% steatosis. The mean nodule diameters were different between incidental and nonincidental (p=0.0001), even grouped as ≤1cm and >1cm(p=0.007). None of the aforementioned microscopic features were different.
AI classifier tested on 26000 patches for each task. Differentiation accuracy was 84% and 67% for nonneoplastic peripheral parenchyma vs HCC and incidental vs nonincidental nodules, respectively.
Conclusion: For preoperative HCC diagnosis, radiological recognizability was related to tumour diameter, even for tumours ≤2 cm.AI recognized HCC with high accuracy and was able to distinguish incidental and non-incidental nodules. By working with different AI methods and expanding our case series, we aim to get the chance to lead radiologic detectability.

CP-02-005

Self-supervised learning-based analysis of colon cancer histopathology uncovers morphological features associated with overall survival

M. Polack*, B. Liu, A. Claudio Quiros, N. Coudray, H.J. van Krieken, R.A. Tollenaar, W.E. Mesker, A. Tsirigos
*Department of Surgery, Leiden University Medical Center, The Netherlands

Background & objectives: Self-supervised learning (SSL) in artificial intelligence, requiring no histopathology annotations, efficiently extracts features from hematoxylin and eosin-stained whole slide images (WSIs). SSL enables exploring the potential of histopathology to predict colon cancer overall survival (OS) in an interpretable manner.
Methods: The Barlow-Twins-encoder was trained on 435 TCGA-colon adenocarcinoma WSIs to extract features from small image patches (tiles). From the extracted features, tiles were grouped into distinct clusters, used to predict OS. Pathologists analysed the histopathology tissue composition of each cluster and linked them to immune and gene expression profiles. Prediction performance was validated in 1213 WSIs from the AVANT-trial.
Results: We derived 47 morphology clusters displaying unique tissue types through blinded histopathological analysis. Clusters with immune cells, healthy colon tissue, and aligned tumour stroma associated with better OS, while mucinous, poorly differentiated tumours or disorganized tumour stroma were linked to worse OS. Furthermore, the immune profile with high leukocyte fractions were correlated with immune cell-rich clusters. Notably, in the AVANT-bevacizumab group, clusters linked to better survival showed enrichment in gene pathways promoting VEGFa production, the target for bevacizumab. Overall, the prediction of OS from our SSL-based histopathology model achieved the state-of-art performance and outperformed the clinical baseline model including the variables age, sex, tumour-node-metastasis staging, and tumour-stroma-ratio.
Conclusion: The SSL Barlow-Twins model effectively formed distinct morphology clusters of WSIs from well-documented cohorts. Utilizing the clinical AVANT-trial, we validated clusters linked to OS in standard-treated colon cancer patients and those treated with bevacizumab, revealing novel histopathology insights and emphasizing the significance of tissue type quantity and tumour stroma architecture in relation to OS.

CP-02-006

A novel deep neural network for the histologic diagnosis of breast specimens

A. Lagree*, L. Itert, A. Sadeghi-Naini, S. Nofech-Mozes, A.L. Martel, W.T. Tran, F. Lu
*Biological Sciences Platform, Sunnybrook Research Institute, Canada

Background & objectives: Accurate histologic diagnosis is key to the correct prognostication and treatment of breast carcinoma. In this study, we developed a deep neural network to classify invasive breast carcinoma (IBC), carcinoma in-situ (CIS) and normal tissue (NT) on breast specimens.
Methods: An ensemble ResNet50 model containing three concatenated ResNet50 models was trained using whole slide images (WSI) of multiresolution (magnification=5X, 10X and 20X), digitized and annotated Hematoxylin & Eosin-stained slides of breast core needle biopsy and excisional specimens. The WSI were split (80:20) to create training and hold-out test sets.

Results: Data included 988,272 tiles (size=256x256 pixels) containing 303,318 IBC, 348,945 CIS, and 336,000 NT tiles from 403 WSI. Classification performances of the independent test set containing 134,760 tiles yielded an average accuracy of 89%, average precision score of 0.89, average recall score of 0.89 and average F1 score of 0.89. The area under the curve computing each class against the rest was 0.98 for IBC, 0.99 for CIS, and 0.95 for NT.
Conclusion: Our results suggest that this novel deep neural network model can accurately diagnose IBC, CIS and NT on breast core needle biopsies and excisional specimens. If validated, this computational framework could be incorporated into digital pathology workflows to facilitate the diagnostic workup of breast specimens and integrated in biomarkers scoring algorithms. In addition, the learning frameworks of this model may be transferred to applications in other disease sites.

CP-02-007
NPIC AI FORGE: a unique multi-scanner digital pathology testbed for artificial intelligence development and evaluation
M. Humphries*, D. Kaye, G. Stankeviciute, C. Dunn, H. Pye, A. Wright, D. Brettle, D. Bansal, D. Treanor
*Leeds Teaching Hospitals NHS Trust and National Pathology Imaging Cooperative, Leeds, United Kingdom

Background & objectives: Artificial intelligence (AI) has potential to revolutionize pathology diagnosis; accuracy is dependent on the training dataset. Sensitivity to input changes reduces real-world performance. Generalizable AI requires diverse data obtained from multiple sources, scanners, and staining platforms.
Methods: To address this problem, NPIC have created a unique multi-scanner facility, the NPIC AI FORGE (Facilitating Opportunities for Robust Generalisable data Emulation). This facility comprises 15 scanners from 8 vendors as follows:
Results: The NPIC AI FORGE has broad capabilities including high-capacity WSI brightfield scanning of 1x3 inch slides; 3x2 inch slides; multiple magnification capture; z-stacking across 3 instruments, and WSI fluorescence scanning. The NPIC AI FORGE can generate over 3000 WSI images per day, equating to over 5Tb of data. The NPIC AI FORGE is supported by a research image management system, and secure research data repository with 15 petabytes of backed up storage, and disaster recovery mitigations, ensuring the safety, security and longevity of all digital pathology data generated. Our PACS system presents as an easy to access online portal for rapid QC, viewing, annotation, project creation and sharing, and download.
Conclusion: The ability to compare multiple scanning platforms provides an opportunity to map differences between data sets, to accurately measure the impact this has on AI specificity. We are able to accurately QC each system to specific calibration settings, ensuring robust and reliable data for AI training. Furthermore, unlike other areas of healthcare, slides can be re-scanned multiple times, which offers an opportunity develop high-quality cross-platform AI. To our knowledge, this is the only such digital pathology facility in the world.
All authors are funded by NPIC (Project no. 104687), supported by a £50m investment from the Data to Early Diagnosis and Precision Medicine strand of the government's Industrial Strategy Challenge Fund, managed and delivered by UK Research and Innovation. (UKRI).

MD-01 | Selected Abstracts

MD-01-001
External Quality Assessment (EQA) for PIK3CA testing in breast cancer: lessons learned and the need for continued quality improvement
V. Williams*, M.H. Cheetham, A. Maqsood, N.L. Wolstenholme, S. Patton
*EMQN CIC, United Kingdom

Background & objectives: Breast cancer is the most common cancer in women and may also occur in men. We present 3 years (2020-2022) of data from an EQA scheme designed to assess the quality of clinical testing for *PIK3CA* testing in breast cancer.
Methods: EMQN sent artificial FFPE reference materials and/or patient derived FFPE tumour samples to each EQA participant for testing of clinically actionable *PIK3CA* variants using their routine methodologies. Anonymised results were assessed and peer reviewed. Individual laboratory and overall summary scheme reports were fed back to laboratories to help improve their performance and to enable comparison (benchmarking) of results and reporting.
Results: Over the three years, there has been an improvement in the quality of testing, the clinical reporting of results, and standardisation of variant nomenclature used for reporting sequence variants. Improvement in the clinical interpretation of the impact of the analytical result is also evident; further work is still required to raise standards.
Conclusion: Although errors persist, we conclude that annual participation in this EQA scheme can improve the quality of clinical diagnostic testing for breast cancer and contribute to the realisation of accurate personalised medicine.

MD-01-002
Health care providers' knowledge, confidence and practice of molecular pathology testing for oncology, within an Irish university hospital setting
S. Kearney*
*University College Dublin, St Vincent's University Hospital, Innopharma Education, Ireland

Background & objectives: Healthcare providers' (HCPs) pathology knowledge was measured, via both a subjective appraisal alongside an objective assessment. Self-confidence and practice ordering, interpreting and explaining molecular pathology tests were evaluated, alongside HCPs' views on clinical versus research utility of molecular pathology testing.
Methods: The survey was conducted via electronic means, utilising Google Forms, which was distributed to a wide variety of HCPs. 30 HCPs from a large academic teaching hospital in Ireland replied, including nurses, doctors in training, qualified consultants from a variety of specialities and general practitioners.
Results: More than half of respondents (65.6%) thought they knew less than enough about molecular pathology to do their jobs. Regarding confidence in the steps of ordering, interpreting and explaining molecular pathology tests, only a minority were fully or somewhat confident. Most HCPs were positively predisposed to utilising clinical informatics tools, genetic counsellors, second opinions services and molecular tumour boards (MTBs) in their molecular pathology workflows. Finally, the majority (83.9%) were supportive or strongly supportive that molecular pathology testing was important to their clinical practice, rather than research.
Conclusion: Despite a small subset of respondents having high self-appraisals of their molecular pathology knowledge, when objectively measured most Irish HCPs lack knowledge and confidence in molecular pathology. This is important, given the growing prominence of molecular pathology in mainstream clinical practice, as reported by respondents.

MD-01-003
Retrospective blind assessment of SOPHiA DDM™ Dx HRD solution for evaluation of olaparib maintenance treatment efficacy in ovarian cancer patients from the randomized, phase III PAOLA-1 trial
A. Buisson*, M. Lamkhioued, P. Constantoulakis, K. Oikonomak, P. Harter, S. Pignata, A. Gonzalez-Martin, C. Schauer, K. Fujiwara, I. Vergote, N. Colombo, E. Pujade-Lauraine, I. Treilleux, P. Saintigny, I. Ray-Coquard
*Centre Léon Bérard, Lyon, France

Background & objectives: SOPHiA DDM™ Dx HRD Solution combines analysis of genomic instability and homologous recombination

repair gene mutation status to predict homologous recombination deficiency (HRD) in ovarian cancer (OvCa). As part of the ENGOT HRD initiative, we present updated clinical relevance results.
Methods: Using SOPHiA DDM™ Dx HRD Solution, DNA from a subcohort of 359 patients (pts) from the GINECO/ENGOT-Ov25 PAOLA-1 trial (NCT02477644) was re-analysed in a multicentre study. We compared the results to those previously obtained using Myriad myChoice CDx. We investigated differences in progression-free (PFS) and overall (OS) survival in the olaparib+bevacizumab and placebo+bevacizumab arms between HRD-positive and HRD-negative pts.
Results: HRD status was determined in 98.9% of pts using SOPHiA DDM™ Dx HRD Solution. The overall concordance with Myriad myChoice CDx was 98.1% (95% confidence interval [CI], 96.0%-99.1%) and highly reproducible across laboratories (r=0.987). In HRD-positive pts, the PFS and OS time were 55.7 months and 75.2 months respectively in the olaparib+bevacizumab arm versus 18.7 and 56.4 months respectively in the placebo+bevacizumab arm (hazard ratio [HR] PFS, 0.32; 95% CI, 0.22-0.45, p<0.001; HR OS, 0.49; 95% CI, 0.32-0.77, p=0.002). No significant difference in PFS or OS was observed between treatment arms in pts with HRD-negative test (HR PFS, 1.04; 95% CI, 0.71-1.52; p=0.8; HR OS, 1.19; 95% CI, 0.78-1.80; p=0.4).
Conclusion: The analytical performance and the potential clinical relevance results of SOPHiA DDM™ Dx HRD Solution from PAOLA-1 samples support the value of combining low-pass whole genome and targeted sequencing in a unique workflow for reliable and decentralized HRD testing and future patient stratification.

MD-01-004
Optical genome mapping for comprehensive cytogenetic analysis of soft tissue and bone tumours
J. Baelen*, I. Vanden Bempt, P. Schöffski, R. Sciot, B. Dewaele
*KU Leuven, Belgium

Background & objectives: In soft tissue and bone tumours (ST&BT), identification of structural variants (SV) and copy number alterations (CNA) is challenging but essential for accurate diagnosis. We introduce optical genome mapping (OGM) for comprehensive SV and CNA detection in diagnostic ST&BT samples.
Methods: Ultra-high molecular weight DNA was extracted from a series of 55 snap-frozen diagnostic ST&BT samples, diagnosed between 2015 and 2022 at the University Hospitals Leuven. DNA was labelled and optically imaged; data was analysed using the rare variant analysis/de novo assembly pipeline (Bionano Genomics). Results were compared to karyotyping, fluorescent in situ hybridization (FISH) and/or RNA sequencing.
Results: In total, 39 samples comprising 20 ST&BT subtypes were successfully analysed by OGM (39/55, 71%). Highest success rates were obtained in undifferentiated small round cell sarcomas (USRCS) of bone and soft tissue (6/6, 100%). OGM identified diagnostic SV/CNA in 36 out of 39 samples (92% concordance to standard-of-care). In those 39 samples, 3 out of 20 unique SV/CNA were not detected by OGM: CIC::DUX4, STAT6::NAB2 and heterogeneous MDM2 amplification. Of interest, OGM identified additional SV/CNA, including the recently described EWSR1::COLCA2 fusion in an USRCS and a novel TGFBR3::CLPTM1L translocation in a myxoinflammatory fibroblastic sarcoma. No false positive diagnostic SV/CNA were found by OGM. Reproducibility was demonstrated in 3 duplicate analyses.
Conclusion: OGM was successful in a variety of ST&BT subtypes with highest success rates obtained in USRCS of soft tissue and bone (100%). OGM identified diagnostic SV/CNA in 92% of cases, compared to combined state-of-the-art diagnostic testing. Importantly, OGM allowed identification of additional SV and CNA that remained undetected by current cytogenetic tools. We conclude that OGM has the potential to improve diagnostic cytogenetic testing for ST&BT, allowing more comprehensive and highly sensitive and specific detection of SV and CNA.
Funding: JB receives funding via "Kom Op Tegen Kanker/Fonds Wetenschappelijk Onderzoek IVB is recipient of a post-doctoral mandate from the Klinische onderzoeks- en opleidingsraad (KOOR) of the University Hospitals Leuven

Poster Sessions

PS-01 | Poster Session Breast Pathology

PS-01-001
Inter-laboratory variability of HER2-low analysis using artificial intelligence
N. 't Hart*, M. Eenkhoorn, H. Høeg, D. Dabbs
*Isala, The Netherlands

Background & objectives: Treatment of HER2-positive breast carcinoma is emerging for HER2-low expressing tumours. In this study, immunohistochemical detection of HER2-low is tested for inter-and intra-laboratory reproducibility in The Netherlands.
Methods: To define reproducibility of HER2-low, three blanc slides with a dynamic range cell line (HistoCyte, Newcastle,UK) were send to 42 labs. Participants were asked to stain slides in three consecutive days. After staining, slides were scanned and analysed using AI-software (Qualitopix, Visiopharm, Hoersholm,DK). Membrane staining intensity was measured for all cells and a score (0-100) was determined for each core.
Results: Four antibodies were used by 32 laboratories: 59.4% clone 4B5, 9.4% Herceptest (DG44), 15.6% SP3 and 15.6% C-erbB-2. Summary statistics are calculated across different antibodies per core. The middle core of the cell line showed the most variation and is shown here as a striking example. Clone 4B5 scored 44.07+/-9.45% (mean+/-SD) and DG44 scored 72.57+/-3.99%. Both 4B5 and DG44 are monoclonal antibodies of Ready To Use kits. Monoclonal SP3 is used at dilutions ranging from 1:200 to 1:1000, polyclonal C-erbB-2 dilutions varied between 1:200 and 1:500. The negative core showed a positive result for both SP3 and C-erbB-2. The middle core scored 42.83+/-11.01% for SP3 and 71.20+/-20.11% for C-erbB-2.
Conclusion: Four HER2 antibodies were used in Dutch laboratories. 4B5 and DG44 showed consistent HER2 results. C-erbB-2 and SP3, however, demonstrated HER2-positive results in negative controls. Furthermore, C-erbB-2 and SP3 were used with different antibody concentrations showing inconsistent HER2-expression. Overall, HER2 antibodies need to be re-validated and the use of a standardized reference material (e.g. cell lines) with AI is a promising method to determine HER2-low for clinical use.
Funding: AstraZeneca Nederland

PS-01-002
Androgen receptor mRNA is associated with better survival outcomes in triple negative breast cancer
S.S. Ahmed*, D.Y. Lee, C.H.C. Ong, B. Lee, J.P.S. Yeong, J. Iqbal
*Singapore General Hospital, Department of Anatomical Pathology, Singapore

Background & objectives: This study aims to evaluate the gene expression of AR in triple negative breast cancers (TNBC), analyse the relationship between AR transcriptional expression with clinicopathological parameters and survival outcomes and to spot a panel of AR-correlated hub-genes with prognostic value.
Methods: Tissue microarrays (TMA) were constructed from formalin fixed paraffin (FFPE) embedded tissue of 389 TNBCs diagnosed at Singapore General Hospital. NanoString mRNA extraction and Digital mRNA quantification using NanoString assay were performed on TMA and analysed.

Statistical analysis was performed in correlation with clinicopathological parameters, protein and mRNA expression.
Results: 55% of TNBCs expressed AR mRNA levels. Low AR mRNA expression was associated with younger age (p=0.017), high histological grade (p<0.001) and poor overall-survival rates (p=0.032) and adjusted with age, tumour size histological grade (p=0.023).
Conclusion: Low AR mRNA expression is associated with poorer survival outcome
AR mRNA correlated hub-gene panel and its regulatory role in immune cell infiltrations (CCNB2, H2AFZ) and drug resistance (AURKB) provide novel insights into the immune microenvironment role in AR+ TNBCs.
AR inhibitors increase recruitment of cytotoxic T cells that may enhance sensitivity and susceptibility to immunotherapy.

PS-01-003
Ki67 quantitation in breast cancer: a comparative analysis of four counting methods
C. Albarracin*, Y. Wu, M. Mersereau, H. Chen
*University of Texas, MD Anderson Cancer Center, USA

Background & objectives: There is increasing use of Ki67 as a prognostic and predictive marker in breast cancer. Quantitation of immunostains for Ki67 is limited by lack of standard scoring methods. Our goal is to compare four different methods of evaluating Ki67 staining.
Methods: 100 cases selected from database of ER+/HER2- invasive breast carcinomas. Immunohistochemical stains using MIB-1/Ki67 antibody were evaluated using four methods. Visual total count microscopically estimated Ki67 in the entire tumour. It served as "gold standard" and compared to Digital total count, Hotspot count and the International Ki67 Working Group Unweighted (IKWG-U) methods. Time utilized for analysis was noted.
Results: Visual count was used to classify the 100 cases into Low Ki67 (<17%), Moderate Ki67 (17-35%), and High Ki67 (>35%). Digital count quantified Ki67 in the entire tumour by digital analysis. IKWG-U quantified four areas of different staining densities. In comparison to Visual, Digital and IKWG-U each altered Ki67 categories in 3 of 100 cases. Hotspot quantified areas with highest Ki67 labelling resulting in altered Ki67 categories in 16 of 100 cases. Comparison to Visual count yielded linear regression R2 values of 0.9756 for Digital, 0.9776 for IKWG-U, and 0.8678 for Hotspot. Average time <2 mins for Visual, 28 mins for Digital, 10 mins for IKWG-U, 6 mins for Hotspot.
Conclusion: Our study successfully demonstrated that Visual count, Digital count and IKWG-U are reliable and reproducible methods for Ki67 evaluation. While these methods yielded comparable results, Visual count required the least amount of time and can be easily utilized in a clinical setting. In contrast, Hotspot had a lower correlation with Visual count, and its use in clinical practice may be limited. In summary, these results validate the use of Visual count as a viable and effective method to quantify Ki67.

PS-01-004
Concordance of Nottingham histologic and neuroendocrine grading schemes in mammary neuroendocrine neoplasms
C. Albarracin*, J. Wen, K. Sweeney, Q. Ding, Y. Wu
*University of Texas, MD Anderson Cancer Center, USA

Background & objectives: IARC/WHO expert panel has proposed a uniform diagnostic scheme for neuroendocrine neoplasm (NEN) of all the organs including breast. The objective of the current study is to compare the Nottingham histologic grading and NEN grading scheme in mammary NEN.
Methods: Eighty NENs (15 NEC and 65 NET) were identified from surgical pathology file at University of Texas MD Anderson Cancer Center between 2008 and 2020. The histologic grade of those cases was compared using Nottingham histologic grading scheme (glandular formation + nuclear pleomorphism + mitosis) and NEN grading scheme (mitosis and Ki67 proliferation rate). Kendall's co-efficiency concordance was calculated.
Results: There was overall good agreement between Nottingham histologic grading and NEN grading scheme (Kendall's co-efficiency of 0.844) for all the cases. There was complete concordance of the two grading schemes in neuroendocrine carcinoma (NEC) (Kendall's co-efficiency of 1). The concordance co-efficiency for neuroendocrine tumour (NET) is 0.72.
Conclusion: NEN is a unique pathologic and clinical entity of the breast. Although WHO recommends using Nottingham histologic grading scheme for this type of tumour in breast, Nottingham histologic grading scheme has a high concordance with NEN grading scheme.

PS-01-005
TRPS1 expression in cytokeratin 5 expressing triple negative breast cancers, its value as a marker of breast origin
S. Almási*, L. Kuthi, A. Sejben, A. Voros, Á. Nagy, T. Zombori, G. Cserni
*University of Szeged, Hungary

Background & objectives: Triple negative breast cancer (TNBC) lack the expression of ER, PR, and HER2. The majority of them do not express breast markers either, such as GCDFP-15, GATA3, MGB and SOX10, therefore identification could present as a major challenge.
Methods: Our aim was to evaluate trichorhinophalangeal syndrome type 1 (TRPS1) protein as a breast marker in a series of cytokeratin-5-expressing TNBC, mostly corresponding to basal-like TNBCs, previously characterized for the expression of other breast markers. One hundred seventeen TNBCs in tissue microarrays were immunostained for TRPS1. The cut-off for positivity was ≥ 10%. The reproducibility of this classification was also assessed.
Results: TRPS1 positivity was detected in 92/117 (79%) cases, and this exceeded the expression of previously tested markers like SOX10: 82(70%), GATA3: 11(9%), MGB: 10(9%) and GCDFP-15: 7(6%). Of the 25 TRPS1-negative cases, 11 were positive with SOX10, whereas 5 to 6 dual negatives displayed positivity for the other makers. The evaluation showed substantial agreement.
Conclusion: Based on our results, of the five markers compared, TRPS1 seems the most sensitive marker for the mammary origin of CK5-expressing TNBCs. Cases that are negative are most often labelled with SOX10, and the remainder may still demonstrate positivity for any of the three other markers. TRPS1 has a place in breast marker panels.
This research was funded by the University of Szeged, Faculty of Medicine Research Fund-Hetényi Géza Grant (Grant No. 5S 340 A202)

PS-01-006
NGS mutational status on first diagnostic tissue and liquid biopsy in breast cancer
C.M. Ardeleanu*, M. Olinca, B. Galateanu, H. Muresan, A. Tecuceanu Vulpe, I. Gune, G. Manole, M. Bugeanu, A. Hudita
*Onco Team Diagnostic, Romania

Background & objectives: Breast cancer mutations modify the tumour aggressiveness, drug resistance, residual disease. Aim: to assess by NGS the mutational status of G2-G3 breast tumours in evolution, on tissue and liquid biopsies at the first diagnostic and after mastectomy, on residual tumour.
Methods: From primary breast tumours (24), core biopsies were formalin fixed, paraffin embedded, Haematoxilin-Eosine stained; Ventana-Benchmark-Ultra (ER-Ventana-6F11, PGR-Ventana-16, cerbB2-Ventana-4B5), Bond-III Leica (Ki67-Leica-MM1), assured immunohistochemistry; results: ER/PGR/Ki67 percentage; cerbB2 ASCO/CAP/2018score.

Tissue biopsies (24) and plasma (8) served for DNA/RNA extraction: RecoverAll/Total/Nucleic/Acid/Isolation/kit and Thermo-Fisher, MagMAXCell-free/Total/Nucleic/Acid/Kit. DNA/RNA concentration: Invitrogen, Qubit/RNA/HS/Assay/kit, Qubit-1X-ds-DNA-HS-Assay and Qubit-4-Fluorometer. RNA reverse-transcription: Superscript-IV-Vilo-Master-Mix. Libraries: Oncomine-Focus-Assay-Chef-Ready-Library and Oncomine-Pan-Cancer-Cell-Free-Assay. Ion-GeneStudio-S5-Prime-sequencer and Ion-Reporter-software served for pathogenic-variants (PV)and variants-of-uncertain-significance (VUS) selection.
Results: Age of patients:38-86years, average of 56,2, present previous clinic and imaging and Ethic Committee approval. All 24 cases had G2/G3 mammary invasive carcinomas NST, Nottingham score 6-9; molecular subtypes: 8 cases LuminalA (LA), 9-LuminalB (LB) (Ki67>25%), 2-LuminalB-like(LB-l), 3-Her2-enriched(Her2-enr) and 2-triple negative(TN). Thirteen tissue biopsies had Her2-low. NGS analysis showed PV/VUS in 14 cases. From the 6 PV, 4 are PV-PIK3CA(3-LA,1-LB,1-LB-l,1-her2-enr) and 2, AKT(1-LA,1-LB), and all in Her2-low cases. The 2 PV-PIK3CA in liquid biopsies are present also in the corresponding tissue biopsies. The VUS- RET, SMO, MYC, appeared in tissue biopsies; a VUS-TP53 appeared in a plasma LB case, PV-negative. The PV-PIK3CA and PV-AKT do not appear together having actually common signalling pathway (PI3K/AKT/mTOR).
Conclusion: These preliminary results are suggesting that NGS positive PV-PIK3CA cases could be a therapy target in early breast cancer. The PV-PIK3CA appearing in the tissue and liquid biopsies of the same 2 patients, is showing that liquid biopsy is a promising tool in cancer monitoring. The association PV-PIK3CA and hormonal receptor in our cases is similar to other studies; PV-PIK3CA and PV-AKT apparently are in mutual exclusion. Her2 low cases, unexpectedly, had the major part of PV in our series.
The poster was supported by the Project PN-III-P2-CERC-CO-PTE-3-2021, ONCOGUARD (Validation and implementation of the liquid biopsy as an actual method of NGS molecular profile assessment for the prognostic and therapy modulation in breast cancer), Bucuresti

PS-01-007
Successful deployment of an artificial intelligence solution for primary diagnosis of breast biopsies in clinical practice
M. Aslam*, A. Gunavardhan, A. Phillips, A. Savage, P. Huey, R. Nicholson, I. Krasnitsky, D. Ignatov, M. Grinwald, M. Vecsler
*Betsi Cadwaladr University Health Board, NHS Wales, United Kingdom

Background & objectives: We present the analysis of a clinically deployed artificial intelligence (AI) decision support solution for breast biopsies primary diagnosis utilized as first read within a digital pathology workflow in a hospital pathology laboratory setting.
Methods: 7 pathologists underwent training and used the solution for prospective primary diagnosis of consecutive breast biopsies, reporting on 355 cases (460 H&E slides), 178 cancer (50%) and 177 benign (50%). All the slides were digitized and blindly processed by the AI solution. Pathologists were presented with the AI pre-classifications on invasive, in-situ and other features, reviewed and reported the cases.
Results: The AI solution demonstrated high performance when pre-classifying cases with high likelihood for cancer, with AUC = 0.99 (95% CI: 0.988, 0.999), NPV = 99% (95% CI: 0.956, 1) and PPV = 84% (95% CI: 784, 0. 888), respectively. 19 % of parts have been classified as suspicious by AI. The AI performance for invasive carcinoma was very high with AUC = 0.99 (95% CI: 0.988, 0.999), NPV = 99% (95% CI: 0.956, 1), and PPV = 91% (95% CI: 0.858, 0.950), respectively. Additional performance metrics on detection of DCIS and other features will be presented.
Conclusion: We report here the successful implementation of a multi-feature AI solution that automatically imparts clinically relevant diagnostic parameters regarding breast cancer such as subtypes/grades of invasive and in-situ cancers and other pathologic features. The solution demonstrated the ability to accurately pre-classify cancer and contribute to workflow efficiency and that it be used as a significant aiding tool for pathologists in decision-making in routine pathology practice.

PS-01-008
Impact of analytic factors of immunohistochemistry (IHC) on the incidence of human epidermal growth factor receptor 2 (HER2)-low breast cancer
Y.K. Bae*, S.Y. Kwon, M.C. Kim
*Department of Pathology, Yeungnam University College of Medicine, Daegu, Republic of Korea

Background & objectives: HER2-low breast cancers (IHC 1+ or 2+ without gene amplification) have demonstrated efficacy for the newly developed HER2-targeting antibody-drug conjugates (ADCs). We investigated the frequency of HER2-low breast cancer and compared the IHC conditions used in different laboratories.
Methods: We retrospectively reviewed primary breast cancers diagnosed at the Yeungnam University Hospital (YUH) and Keimyung University Dongsan Hospital (KUDH) between January 2022 and December 2022. The data on specimen type, HER2 status (IHC and in situ hybridization (ISH) results), and IHC conditions were collected. HER2 status was defined according to the most updated ASCO/CAP HER2 testing guidelines.
Results: The pathology laboratories at YUH and KUDH performed HER2 IHC staining using the 4B5 antibody and HER2 ISH testing with the INFORM® HER2 dual ISH DNA probe (Ventana). However, there were differences in the IHC conditions, including antigen retrieval time (16 min vs 30 min), incubation time (28 min vs 32 min), temperature (42˚C vs 37˚C), type of detection kit (OptiView vs UltraView), and staining platform between the two laboratories. Of the 623 cases diagnosed at YUH, 465 (74.6%) were HER2-negative, 81 (13%) were HER2-low, and 77 (12.4%) were HER2-positive. Of the 290 cases diagnosed at KUDH, 135 (46.6%) were HER2-negative, 82 (28.3%) were HER2-low, and 73 (25.2%) were HER2-positive.
Conclusion: The frequencies of HER2-positive and HER2-low breast cancers showed a difference of nearly two times between the two laboratories. We adjusted staining conditions using PATHWAY HER2 4 in 1 control slides to achieve the intended staining. Unlike HER2 positivity, there is no gold standard or reflex test to confirm HER2-low expression. Before conducting clinical trials or applying the new ADCs, each pathology laboratory should verify IHC conditions to accurately identify HER2-low breast cancer.

PS-01-009
HER2-low breast cancer and response to neoadjuvant chemotherapy: a population-based cohort study
X. Baez Navarro*, C. van Deurzen, M.R. van Bockstal
*Erasmus MC, The Netherlands

Background & objectives: The clinical impact of low expression of HER2 (HER2-low) breast cancer (BC) and its relation to response to neoadjuvant chemotherapy (NAC) is not well understood. We aimed to study the association between HER2-low BC and the pathological response on NAC.
Methods: Data from the Dutch Pathology Registry was collected from BC patients treated with NAC between 2014-2022. HER2-low BC was considered as immunohistochemical (IHC) score of 1+ or 2+ with negative reflex test. We compared clinicopathologic features of HER2-0 versus HER2-low BC and assessed the correlation between HER2 status and the pathological complete response (pCR) rate after NAC, including overall survival.
Results: In total 11,988 patients were retrieved. Among oestrogen receptor (ER)+ tumours (n=6,886), 67% were HER2-low, compared to 46% (n=2566) in the ER- group. Around 32% (n=207) of patients had

a discordant HER2 status between the pre-NAC biopsy and the corresponding post-NAC resection, from which 87% (n=165) changed from HER2-0 to HER2-low or vice versa. pCR rate was significantly lower in HER2-low BC compared to HER2-0 BC within the ER+ group (4% versus 5%; p=0.022). In ER- cases, the pCR rate was also lower in HER2-low compared to HER2-0 cases, but not significant (32% versus 34%; p=0.266). There was no statistical difference in overall survival between HER2-low and HER2-0 tumours.

Conclusion: Around one third of the BC patients in this study had a discordant HER2 status (0, low, positive) between the pre-NAC biopsy and the post-NAC resection specimen, which could impact clinical decision making if T-DXd gets a role in the treatment of early breast cancer. In this study, HER2-low BC was associated with a lower pCR rate compared to HER2-0 cases in the ER+ group, although these absolute difference was limited and the clinical relevance is questionable.

Research funded by Aztrazeneca

PS-01-010

Alteration of HER2 status during metastatic progression of breast cancer in the HER2-low population

K. Bai*, H. Kwon, K. Suh, S. Kim, J. Kim, S. Park
*Department of Pathology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Gyeonggi, Republic of Korea

Background & objectives: Recent studies show that novel antibody–drug conjugates (ADCs) can improve clinical outcomes of patients with HER2-low breast cancers. This study aimed to investigate the changes of HER2 status during metastatic progression of breast cancer, focusing on HER2-low status.

Methods: We analysed 321 paired samples of primary and recurrent/metastatic breast cancer diagnosed between 2017 and 2022. HER2 status was classified to negative [immunohistochemistry (IHC) score of 0), low (IHC score 1+ or 2+/in situ hybridization-negative) and positive. Discordance rate between primary and matched metastatic samples was calculated in relation to the type of recurrence, site of metastasis and molecular subtype.

Results: As a whole, HER2 discordance rate between primary and first recurrent/metastatic breast cancers was 28.0% (k=0.542) with mostly negative-to-low (11.5%) or low-to-negative (10.6%) conversion. HER2 discordance between primary tumour and second metastasis was 38.5%. Discordance rate was significantly higher in distant metastasis than in loco-regional recurrence (33.2% vs 10.7%). When classified to metastatic sites, discordance rates ranged from 44.4% in bone metastasis to 20.0% in central nervous system metastasis, but with no statistical difference. Luminal A subtype had the highest discordance rate (32.9%) and HER2-positive subtype had the lowest rate (12.1%). Discordant cases revealed significantly higher progesterone receptor (PR) positivity and HER2 negativity in primary tumour, compared to concordant cases.

Conclusion: HER2 status changed during metastatic progression in some portion, mostly between negative and low status. HER2 discordance between primary tumour and metastases differed by metastatic sites and molecular subtypes and was associated with PR and HER2 status in primary tumour. As HER2 instability increases during metastatic progression, re-evaluation of HER2 needs to be performed when considering ADCs in metastatic settings.

PS-01-012

CD47 and CD68 expression in breast cancer is associated with tumour-infiltrating lymphocytes, blood vessel invasion, detection mode and prognosis

Y. Chen*, T.A. Klingen, H. Aas, E. Wik, L. Akslen
*Fürst medisinske lab., Norway

Background & objectives: CD47 expressed on tumour cells binds to SIRPα on macrophages, initiating an inhibition of phagocytosis. We investigated the relation between tumour expression of CD47 and CD68 macrophage content, subsets of tumour infiltrating lymphocytes (TILs), and vascular invasion in breast cancer.

Methods: A population-based series of 282 cases from Norwegian Breast Cancer Screening Program was examined. Immunohistochemical staining for CD47 and CD68 was evaluated on TMA-slides. For CD47 evaluation, a staining index (SI) was used. CD68 and TIL subsets (CD45, CD3, CD4, CD8, FOXP3) were counted and dichotomized using immunohistochemistry on TMA-slides. Vascular invasion was determined on whole tissue slides.

Results: High CD47 tumour cell expression or high counts of CD68 macrophages were significantly associated with elevated levels of all TIL subsets (p<0.02), CD163 macrophages (p<0.001), blood vessel invasion (p<0.01), and high tumour cell Ki67 (p<0.004). High CD47 expression was associated with ER negativity (p<0.001), HER2 positive status (p=0.03), and interval detected tumours (p=0.03). Combined high expression of CD47-CD68 was associated with a shorter recurrence-free survival (RFS) by multivariate analysis (HR 2.37, p=0.018), adjusting for tumour diameter, histologic grade, lymph node status and molecular subtype. Cases with luminal A tumours showed a shorter RFS for CD47-CD68 high cases by multivariate assessment (HR 5.73, p=0.004).

Conclusion: This study demonstrated an association of concurrent high CD47 tumour cell expression and high CD68 macrophage counts with various TIL subsets, blood vessel invasion, other aggressive tumour features, and interval presenting breast cancer. Our findings suggest a link between CD47, tumour immune response, and blood vascular invasion. Combined high expression of CD47-CD68 was an independent prognostic factor associated with poor prognosis in all cases, as well as in the luminal A category.

This work was partly supported by the Research Council of Norway through its Centres of Excellence funding scheme, project number 223250, and by grants from Helse Vest Research Fund (L.A.A.) and Vestfold Hospital Research Fund (Y.C and T.A.K).

PS-01-013

The importance of establishing ground truth when building clinical-grade artificial intelligence tools for breast cancer

C. Conway*, S. Ali Arshad, P. Khorramshahi, H. Eslami Manoochehri, D. Miller, J. Wang, R. Millican-Slater, A. Hanby, J. Stephenson, D. Bansal, C. Colquhoun, A. Wright, O. Colgan, D. Treanor, C. Salinas
*Leica Biosystems, USA

Background & objectives: Artificial Intelligence (AI) holds potential to aid pathologists in routine diagnostics and address increasing imbalances in pathology demand versus capacity. Herein, we describe the approach and initial results in a study detecting breast cancer using AI.

Methods: > 1500 Hematoxylin and Eosin (H&E) slides from multiple global locations were annotated at pixel-level detail. A 25+ breast pathologist network was established ensuring each slide is reviewed/annotated by 3 specialists, accounting for discordance in breast tissue classification into clinically relevant subcategories.
Slides are scanned at 40x on Aperio GT 450/450DX scanners and annotated using mouse, stylus and touchscreen technology.

Results: To develop a ground truth platform for clinical AI development, consideration should be given to ethical patient slide/data access, sample size, number of specialist reviews for each slide, and variation in tissue preparation/staining. Herein, we describe the results in a study detecting breast cancer using AI.
Automatically combining annotation inputs and extracting concordant areas is critical to developing a strong data pipeline. Early

analysis revealed 12% discordance for 2 pathologists and 22% for 3, supporting a multi-reviewer approach.
Early prototype models achieved 87.5% - 97.1% accuracy at a tile level in detecting diagnostically significant areas against the test set.
Conclusion: Definition of ground truth provides a platform to investigate methodologies for reviewing and analysing pathology cases, magnification levels, architectural changes and feature extraction. Careful definition of the annotation protocol and pathology tool will ultimately enable development of the best aids to the pathologist.
Funding: National Pathology Imaging Co-operative, NPIC (Project no. 104687) funded from the £50m investment from the Data to Early Diagnosis and Precision Medicine strand of the government's Industrial Strategy Challenge Fund, managed and delivered by UK Research and Innovation (UKRI)

PS-01-014
Cytological features of breast ductal adenoma
F. Di Donato*, M. Cattani, A. Tafa', M.C. Cucchi, L. Saragoni, M.P. Foschini
*School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: Ductal Adenoma (DA) of the breast is a benign tumour with a high overdiagnoses risk especially in preoperative procedures. The purpose of this study is to describe specific cytological features of a series of DAs to avoid misdiagnoses of malignancy.
Methods: Fourteen cases having a histological diagnosis of DA and a previous cytological examination by Nipple Discharge (ND) or Fine Needle Aspiration Cytology (FNAC) were selected. Clinical and ultrasound data were collected. Cytological features were evaluated with quantitative and morphological systems. Histological samples of the lesions were reviewed. Cytological and histological aspects were compared to identify the spectrum of DA's cytology.
Results: All patients were women, with a mean age of 59 years. Lesions appeared on ultrasound as hypoechoic or anechoic, the range size was 1-10 mm. The three cases of ND were characterized by numerous red blood cells, conspicuous fluid, poor cellularity and mild/moderate cellular atypia. A diagnosis of suspicion of malignancy was made.
The eleven cases studied by ultrasound guided FNAC showed: scarce fluid, high cellularity, mild/moderate atypia, rare stromal fragments, presence of blood, myoepithelial cells, mono/multilayered tissue fragments, dispersed bipolar nuclei and singular cells. Cytological reports based on the Yokohama System resulted principally C3 and C4. Histological examination of the lesions confirmed the main diagnosis of DA.
Conclusion: DA is a benign tumour, composed of distorted glands in a sclerotic stroma surrounded by a fibrous capsule, that can mimic carcinoma on preoperative procedures. Therefore, knowledge of its cytological features is important to avoid misdiagnoses. High cellularity and nuclear atypia may lead to a misdiagnosis of malignancy, but the presence of myoepithelial cells and apocrine changes suggests a benign lesion. Cytology, together with clinical and ultrasound data, allows DA diagnosis avoiding overtreatment.

PS-01-015
HER2 assessment in breast cancer – routine diagnostics vs. segment-based annotations in multi-institutional raters
J. Steenpass*, M. Öttl, C. Schmidt, M. Ruebner, P.A. Fasching, M.W. Beckmann, C. Taverna, F. Tava, C. Lang-Schwarz, A. Hartmann, K. Breininger, R. Erber*
*Institute of Pathology, University Hospital Erlangen, Comprehensive Cancer Center Erlangen-EMN, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Germany

Background & objectives: Human epidermal growth factor receptor 2 (HER2) status is a crucial prognostic and predictive biomarker in invasive breast cancer (IBC). We investigated manual HER2 scoring as performed in routine diagnostics versus exact annotations by five multi-institutional raters with different experience.
Methods: HER2 immunohistochemical (IHC) expression was analysed using 80 regions-of-interest (ROIs) out of eight digitized HER2 IHC whole slide images (WSIs) of IBC. After estimating the tumour distribution across the HER2 scores within each ROI, the ROIs were annotated on the open-source image analysis platform EXACT by assigning the correct HER2 score according to the ASCO/CAP guidelines to pre-segmented tissue structures.
Results: The Earth Mover's Distance (EMD) was used to assess the intra-/interrater agreement on the distributions of HER2 scores: the intra-rater reliability comparing estimated and annotated HER2 scores ranged from 0.059 to 0.155 (mean 0.119) which indicates a certain consistency for each of the five raters. Regarding the inter-rater agreement, the median of the EMD was 0.317 for the estimated scores and 0.236 for the exact annotations. In all eight cases, at least three of the five pathologists agreed on the total HER2 score of the WSI. Clinically significant difference in HER2 status may occur in up to three estimated and two annotated cases depending on a follow-up in situ hybridization.
Conclusion: The study indicates that HER2 scoring is subject to variability; fine-grained annotations resulted in better agreement than estimates. Although assessment of HER2 overexpression using IHC is standardized by the ASCO/CAP guidelines, there are concerns about reproducibility and reliability potentially leading to different scores and treatment decisions. Accurate evaluation, especially in HER2-low tumours, has become more important due to the development of new therapeutic options such as antibody-drug conjugates. Further analysis is needed to handle upcoming challenges in HER2 scoring.
This project is supported by the Bavarian State Ministry of Health and Care, project grant No. G81d-A1070-2020/257-10 (MGP-2008-0003 and MGP-2010-0004). Katharina Breininger is supported by d.hip campus - Bavarian aim in form of a faculty endowment. Jana Steenpass is supported by the German Cancer Aid (Deutsche Krebshilfe, Mildred-Scheel Doktorandenprogramm).

PS-01-016
Residual lymphovascular invasion after neoadjuvant chemotherapy is associated with poor prognosis in breast carcinoma
G. Gasljevic*, N. Pislar, A. Perhavec
*Institute of Oncology Ljubljana, Slovenia

Background & objectives: The poor prognostic significance of lymphovascular invasion (LVI) in breast carcinoma (BC)is recognized in several studies. Its prognostic role in post-neoadjuvant chemotherapy (NACT) remains unclear. We wanted to evaluate prognostic importance of residual LVI (rLVI) after NACT and surgery.
Methods: 01.01.2008-31.12.2021, 655 BC patients were treated by NACT and surgery. Clinical history and primary tumour characteristics were obtained from database. Residual cancer burden (RCB) system was used for evaluation. Complete pathologic response (pCR) was defined as ypT0/isN0, rLVI as carcinoma cells within endothelial-lined space (H&E). Survival analysis was performed using Kaplan-Meier and covariates were tested with Cox proportional hazards model.
Results: Out of 654 tumours (data missing for 1 case), rLVI was present in 28.9% of patients. Ten out of the 176 patients with pCR had isolated rLVI. rLVI was associated with poor disease-free survival (DFS) in univariate analysis (HR 2.36 (95% CI 1.69–3.31), p <0.001) (Figure 1). Tumour size (T1 vs T2 and T3), presence of lymph node (LN) metastases, Her2 positivity and RCB categories II and III were also predictors of poor DFS in univariate analysis. In multivariant analysis, T stage and RCB categories II and III remained significantly associated with poor DFS. Patients' characteristics as well as the results of uni-and multivariate analyses are summarized in Table 1.

Conclusion: We identified post-NACT rLVI as a strong factor predictive of poor DFS in retrospective series of 655 BC patient treated by NACT and surgery and evaluated by RCB prognostic scoring system. The effect was lost on multivariate analysis, while RCB status remained significant. Residual LVI should be systematically reported in post-NACT pathology reports and could serve as indicator of poor survival in cases where RCB score cannot be calculated with certainty (e.g., in false negative sentinel lymph node biopsy).

PS-01-017

Lack of deletion of 1p36 in primary adenoid cystic carcinoma of the breast

G. Gasljevic*, B. Grcar-Kuzmanov, S. Borstnar, J.A. Contreras Bandres
*Institute of Oncology Ljubljana, Slovenia

Background & objectives: Breast adenoid cystic carcinoma (B-AdCC) is a rare salivary gland-type tumour. In salivary gland AdCC, deletion 1p36 associates with solid histology and aggressive course. The aim of the study was to investigate its existence and prognostic value in 21 B-AdCCs.
Methods: Twenty-one B-AdCC diagnosed from 1985-2022. were included in the study. Tissue microarrays were constructed by sampling cores of 2-mm diameter from area of conventional and/or solid basaloid type as well as from high grade transformation. For the detection of 1p36 locus deletion by FISH, ZytoLight® SPEC 1p36/1q25 Dual Color Probe (ZytoVision GmbH) was used.
Results: Seven tumours (33.3%) were pure conventional B-AdCC, 4 (19%) were pure basaloid B-AdCC while 9 (42.8%) had between 10-90% of solid basaloid component. One (4.7%) was AdCC with high grade transformation. All 21 cases were analysable by FISH. Follow-up was available for all patients. All the cases, including 2 patients who died of metastatic disease as well as the patient with B-AdCC with high grade transformation, proved to be negative for 1p36 deletion.
Conclusion: Our results show that the deletion of 1p36 is not a feature of B-AdCC and cannot be used as a prognostic marker. Further studies on larger series are needed to confirm this assumption.

PS-01-019

Hypoxia and immune evasion in young women with breast cancer: a population-based study

R. Humlevik*, A. Svanøe, G. Knutsvik, A. Sæle, C. Askeland, L. Ingebriktsen, U. Hugaas, A. Kvamme, K. Krüger, B. Davidsen, T. Aas, I. Stefansson, E. Hoivik, L. Akslen, E. Wik
*University of Bergen, Norway

Background & objectives: Young women, below 40 years, present higher frequency of aggressive tumour features and poor prognosis. We aimed to investigate the relationship between age and breast cancer related biomarkers and biology, with emphasis on hypoxia and immune evasion.
Methods: Clinico-pathologic variables was obtained from of a population-based cohort of women aged under 50 (n=355) and compared to a previously described cohort of breast cancer patients aged 50-69 (n=543). The tumour infiltrating lymphocyte (TIL) markers CD45 and CD8 were stained by immunohistochemistry. Data from the METABRIC cohorts was applied for analyses of stemness, immune, and hypoxia-related gene expression signatures.
Results: Young patients presented with aggressive tumour features and shorter survival. Ki67 showed a weaker prognostic value within the young group. Young age was associated with gene-scores reflecting increased hypoxia. High levels of CD45+ and CD8+ TILs were associated with the triple negative and basal-like subtypes, and there was a trend towards higher levels of CD45+ TILs in young women. Age below 40 was significantly associated with transcriptional patterns of stemness and the basal-like marker CK5/6. Young women showed significantly higher expression of genes contributing to an immune evasive environment, including CTLA4 and PD1, and lower expression of B7-H4. High expression of CTLA4 and PD1 mRNA was associated with poor survival.
Conclusion: Our population-based study confirms previous findings of a more aggressive breast cancer phenotype in patients below 40 years. We demonstrate increased expression of markers tumour cell proliferation, stemness, hypoxia, and an immune evasive environment in young breast cancer patients. Hence, tumours of young breast cancer patients may have a unique biology that may open for new clinical opportunities stratifying treatment by age.
The work was supported by the University of Bergen and the Research Council of Norway through its Center of Excellence funding scheme (project number 223250), and through the Helse Vest Research Fund (F-12143 and F-12596).

PS-01-020

Assessment of PD-L1 expression in triple-negative breast carcinoma: the first north African case series

M. Khmou*
*National Institute of Oncology, Morocco

Background & objectives: TNBC are not sensitive to endocrine therapy or HER2 treatment. Recent advances have led to the development of immune-checkpoint-inhibitors and have shown survival improvements. The aim of this study is to report PD-L1 expression in TNBC among the Moroccan population.
Methods: We investigated PD-L1 expression by immunohistochemistry in TNBC, without neoadjuvant chemoradiotherapy, diagnosed at the department of pathology at the National Institute of Oncology in Rabat, from January 1st, 2021, to December 1st, 2021. Fifty-four biopsy samples with sufficient tumour tissue were selected. Antibody clone 22C3 was used and PD-L1 expression was evaluated using the Combined positive score (CPS).
Results: The study included 54 cases of TNBC. 15 out of 54 cases (27.8%) had PD-L1 CPS score $\geq$10. The mean age of our patients was 53 years, with extremes ranging from 32 to 81 years. The most common histological type was invasive carcinoma of no special type (90.7%). PD-L1 expression was significantly correlated with high tumour-infiltrating lymphocytes (TILs). There was no statistically significant relationship between PD-L1 expression and other clinicopathological parameters.
Conclusion: Our study showed that 27.8% of our patients had PD-L1 CPS score $\geq$10, and higher TILs were significantly correlated with the PD-L1 expression CPS score. Thus, these findings may be useful for setting new therapeutic guidelines in our country, aiming for a better outcome. Our study is the first to report PD-L1 expression in TNBC among the Moroccan population and has several main limitations, as it is a retrospective analysis with a small-sized sample which may lead to selection bias.

PS-01-021

A Canadian experience in proficiency testing for HER2-low breast cancers

Z. Kos*, J. Garratt, J. Won, B. Sheffield, B. Gilks
*BC Cancer Vancouver Centre, Canada

Background & objectives: Novel anti-HER2 compounds are transforming the traditional dichotomy of HER2 status in breast cancer, commonly defined by immunostaining and *in situ* hybridization assays. We share findings from a proficiency testing scheme for HER2-low breast cancers in which 35 laboratories participated.
Methods: The CPQA-AQCP provided an unstained section of a 43-core breast carcinoma tissue microarray to participating laboratories for HER2 immunostaining as per routine testing methodologies. Results were

self-assessed by each participant then anonymized for assessment by the CPQA-AQCP in direct comparison to results obtained from a laboratory with validated testing for detection of HER2-low expression.
Results: This pilot scheme for HER2 immunostaining in HER2-low breast cancers ran in November 2022, with 35 participating laboratories. Two general observations will be discussed: 1) many participants applied a very conservative approach to diagnosis of 1+ HER2 immunostaining in their self-assessment that was corrected upon review by the CPQA-AQCP, and 2) the overall technical quality of staining was generally sufficient to detect HER2-low expressing breast cancers as defined by reference laboratory staining. Lack of sensitivity in detection of low expression was not a problem for most laboratories if cores were interpreted correctly. Detection of additional HER2-low expressing tumours compared to the reference laboratory led to poor specificity for many participants.
Conclusion: As the treatment landscape has changed, so too has assessment of relevant biomarkers. Reporting of HER2 immunostaining must include the IHC score (0, 1+, 2+, 3+). Laboratories and pathologists may wish to reconsider their reporting terminology and specifically indicate "HER2-low" for cases showing IHC 1+ or IHC 2+ not amplified by ISH. At this early point in validation of immunostaining to detect HER2-low expressing breast cancers, continued participation in external quality assurance and proficiency testing will be vital.
Funding: AstraZeneca

PS-01-022
MHC class I and PD-L1 expression in ductal carcinoma in situ subtypes of the breast: impact on T-cell infiltration and clinical outcome
J.S. Lee*, M.H. Park, N.I. Kim
*Department of Pathology, Chonnam National University Hwasun Hospital, Republic of Korea

Background & objectives: PD-L1 expression and MHC class I downregulation are essential mechanisms of tumour escape from the host's immune system. We examined MHC class I expression in ductal carcinoma in situ (DCIS) subtypes with attention to PD-L1 expression and T cell infiltration.
Methods: MHC class I and PD-L1 expression and CD3+ and CD8+ T lymphocytes were detected with immunohistochemistry in 131 pure DCIS samples using tissue microarrays. DCISs were classified into hormone receptor (HR)+/ human epidermal growth factor 2 (HER2)-, HR+/HER2+, HR-/HER2+, and triple-negative (TN) subtype.
Results: Loss of MHC class I expression was found in 16.4% (21/128) cases and was highest in the HR+/HER2- subtype (29.2%). PD-L1 expression in immune cells (≥1%) was seen in 18.8% (24/128). PD-L1 expression was higher in HER2+ (HR+/HER2+ and HR-/HER2+) subtypes than in HR+/HER2- subtype. In PD-L1 positive DCIS, MHC class I expression was intact in most cases (95.8%), whereas only one case (4.2%) lost MHC I expression in HR-/HER2+ subtype. In HR+/HER2- and HR-/HER2+ subtypes, the numbers of stromal CD3+ and CD+8 T cells was highest in MHC class I intact and PD-L1 positive cases. MHC class I expression and PD-L1 expression were not associated with tumour recurrence.
Conclusion: We demonstrated differential patterns of MHC class I and PD-L1 expression and T-cell infiltration in distinct subtype of DCIS. Increased knowledge regarding MHC class I, PD-L1, and immune subset including CD8+ T cells could contribute to future development of immune modulating therapies in DCIS, especially HER2+ subtype.

PS-01-023
Impact of HER2 assay sensitivity on the ability to detect tumours with low to ultra-low HER2 expression: a TMA study on more than 10,000 tumours from more than 100 tumour entities
M. Lennartz*, N. Blessin, D. Dum, D. Hoeflmayer, S. Weidemann, G. Sauter, T.S. Clauditz, F. Jacobsen, T. Krech, A.H. Marx, S. Minner, R. Simon, N. Gorbokon, S. Steurer, E. Burandt
*University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: Detection of low level HER2 expression is important for therapy with new HER2 inhibitors in breast cancer. HER2 assays with high sensitivity are therefore needed. These may identify low level HER2 expression in various types other than breast cancer.
Methods: A tissue microarray containing >10,000 tissue samples from more than 100 different tumour types and subtypes was analysed for immunohistochemical expression of HER2 using different immunohistochemistry protocols and anti-HER2 antibodies, including the HercepTest and laboratory developed tests designed for high sensitivity. HER2 IHC evaluation included the recording of HER2 low (1+), ultralow (any staining, less than 1+), and 0 (negative).
Results: Irrespective of the assay sensitivity all assays showed the expected/tolerable association with HER2 FISH data in 308 breast cancers. In non-breast cancers, the use of different assays yielded variable rates of low or ultra-low HER2 expression in different tumour entities. For example, low (1+) and ultra-low (+) expression was observed in 7-24% (1+) and 11-28% (+) of serous ovarian cancers, 6.2-24% (1+) and 3.4-19% (+) of endometrioid endometrial cancers, 5.5-14% (1+) and 7.7-13% (+) of intestinal gastric cancers, 1.8-9.2% (1+) and 4.5-11% (+) of ductal adenocarcinomas of the pancreas, 19-33% (1+) and 5.5-11% (+) of muscle invasive urinary bladder cancers, 2.9-16% (1+) and 4.3-12% (+) of adenocarcinomas of the colon.
Conclusion: Low level HER2 expression occurs commonly in many cancer types. The rate of identifiable tumours with HER2 low or HER2 ultra-low expression varies depending on assay parameters that can easily be modified. Irrespective of assay sensitivity, our data identify various tumour entities with significant fractions of "HER2-low" cases that might benefit from therapy with new antibody drug conjugates.

PS-01-024
Discordance in molecular (Prosigna ®) and surrogate (immunohistochemistry) subtyping of breast carcinoma
G.A. Martín Small*, A. Castillo, L. Pons, C. Perelló-Fabregat, P. Rodríguez-Martínez, E. Castellà, A.M. Muñoz-Mármol, A. Urbizu, L. Arnaldo, M. Martín-Céspedes, R. Marginet-Flinch, M. Jimeno, M. Margelí, C. Sanz, P.L. Fernández
*Hospital Universitari Germans Trias i Pujol, Spain

Background & objectives: Prosigna is a genetic test that analyses the expression of 50 genes estimating a 10-year risk of relapse classifying the tumours in one molecular subtype of breast cancer (BC). This classification doesn't always correlate with the immunohistochemistry (IHC) surrogate subtype.
Methods: 199 invasive BC were studied with Prosigna. They had been classified as Luminal A (LA), Luminal B/Her2- (LB/HER2-), LB/HER2+, HER2+ and Triple Negative (TN) by IHC (St Gallen 2021 guidelines). A Ki67 cut-off point of 24% (institutional mean) and 20% for progesterone receptors (PR) was used to categorized luminal subtypes. Agreement between both methods was estimated with kappa coefficient.
Results: There were 77 discordant cases (38.7%). Most of them (n=39) were tumours classified as LA by Prosigna but as LB/HER2- by IHC due to low progesterone receptors (PR) (n=20), high Ki67 index (n=16) or both (n=3). The majority of the LB cases correctly classified had a Ki67≥24%.
We also identified 20 LB cases (Prosigna), classified as LA by IHC.
Concordance rate between both methods was poor in Luminal subtypes (Cohen's kappa, k=0,32).
Moreover, 7 of the discordant cases classified as HER2enriched by Prosigna were LB/HER2- (4), LB/HER2+ (1) and TN (2) by IHC. This may be due to HER2 activating mutation that doesn't overexpress HER2 protein.

Conclusion: BC Molecular subtypes from IHC and Prosigna show limited concordance in Luminal tumours, suggesting that Ki67 and especially PR used for IHC classification might be reconsidered when approaching LA and LB diagnosis.
Precise Ki67 labelling remains an important biomarker in spite its limited reproducibility.
More research in these parameters is requested in order to better understand the correlation between both methods in breast pathology.

PS-01-025
Atlas of ex vivo breast tissue and carcinomas images by ultra-fast large field-of-view fluorescence confocal microscopy of lumpectomy
M. Mathieu*, M. Ragazzi, P. Van Diest, M. Ferchiou, O. Casiraghi, N. Labaied, A. Conversano, M. Abbaci
*Gustave Roussy, Université Paris-Saclay, France

Background & objectives: New generation ultra-fast fluorescence confocal microscopy (UFCM) allows ex-vivo intraoperative analysis of fresh breast tissue.
Objective: To create an atlas of ex vivo UFCM images of breast tissues and carcinomas based on large field-of-view UFCM breast cancer images.
Methods: One hundred sixty patients who underwent breast conserving surgery were included. Their fresh surgical specimens were sectioned, stained with acridine orange and imaged with large-field-of-view UFCM. The resulting images were digitally false coloured in purple gradient. Each UFCM image was correlated with the corresponding definitive histology. The images of normal tissue, inflammation, benign and cancer lesions have been collected.
Results: UFCM images in a quality closely resembling frozen sections were recorded from 103 invasive carcinoma (58 no special type, 44 lobular, 1 mucinous), 49 carcinomas in situ (47 ductal, 2 lobular) and 8 specimens without cancer. The UFCM image corresponds to a large-section histology and allows the evaluation of the global architecture of the tissue at low and intermediate magnification and could then be zoomed in at higher magnifications to identify cellular features. With an axial resolution of 30 µm, UFCM images were richer in cells than histological sections. Representative images of the normal, non-tumoral and carcinomatous tissues were annotated to establish an UFCM atlas and will be available online.
Conclusion: UFCM enables the fast imaging of fresh breast surgical specimens. Main morphological criteria defined in traditional histopathology such as tissue architecture and cell features can be applied to describe UFCM images content. However, the cell density is higher than in histological sections and needs training. The created atlas of the main normal or tumoral tissues could become a reference for the introduction of the technique for intraoperative UFCM examination of breast specimens. Further studies will introduce more rare breast lesions.
Funding: Samantree Medical

PS-01-026
Association of serum inflammatory profiles with breast cancer immunophenotypes and clinicopathological factors
Y.G. Montoyo Pujol*, S. Pascual-García, P. Martínez-Peinado, A.B. López-Jaén, J. Ponce, I. Lozano, T. Martín-Bayón, H. Ballester, A. Ramos, S. Delgado, E. Castellón-Mollá, J.M. Sempere-Ortells, G. Peiró
*Alicante Institute for Health and Biomedical Research (ISABIAL), Spain

Background & objectives: Inflammation can inhibit tumorigenesis. However, maintaining serum cytokines (SC) in breast cancer (BC) is linked to immunosuppression, tumour growth, metastasis, and drug resistance. Therefore, our objective was to evaluate the relationship between clinicopathological factors and SC in BC.
Methods: We collected serum from 229 pretreated BC patients (17.9% Luminal A, 17.9% Luminal B/HER2, 17.9% Luminal B/HER2+, 10.4% HER2-enriched, 17.9% Triple-Negative/Basal-like -TN/BL-) and 50 healthy donors (HD). Using LEGENDplex immunoassay, we measured 62 SC through flow cytometry. The results were correlated with clinicopathological factors (age, tumour size and grade, vascular invasion, necrosis, immunophenotype, tumour-infiltrating lymphocytes (TILs), lymph-node status, and Ki67).
Results: Compared to HD, BC patients had higher levels of SCF, MIP3α, VEGF, and EPO but lower levels of PDGF-AA, Galectin-9, PDGF-BB, and MCP-1, IL-2RA, IL-18, IL-8, B7.2, IL-27, MIP-1β, IL-11, IL-1β, and PD-1. Moreover, EPO correlated with younger age ($p<0.001$), in contrast to Galectin-9, MCP-1, IL-2RA, B7.2, MIP1β, and IL-8 ($p\leq0.013$). IL-27 was elevated in tumours ≤20mm ($p=0.043$) and, along with B7.2 and IL-1β, in low Ki67 tumours ($p\leq0.044$). Contrary, MIP-3α was associated with a high Ki67% ($p=0.022$). Increased PDGF-BB, MIP3-α, and MIP-1β were detected in non-Luminal tumours ($p\leq0.049$), but only EPO in Luminal ones ($p=0.046$).
Conclusion: Our results showed that BC patients had a specific profile of SC compared to HD. This profile differs among BC immunophenotypes, with IL-27, B7.2, and IL-1β on the one hand and MIP-3α on the other, being associated with favourable and unfavourable clinicopathological features, respectively.
Supported by Grant (SEAP-Proyecto Semilla; Expt. 200042); Biobank HGUA (21-154) and HUB-ICO-IDIBELL (PT17/0015/0024).

PS-01-027
HER2-Low breast cancer: incidence and observer variability
F. Ramalhosa*, G. Fontinha, S. Bárbara, C. Faria, R. Celestino, M.A. Cipriano, M.J. Martins
*Centro Hospitalar e Universitário de Coimbra, Portugal

Background & objectives: Human Epidermal Growth Factor Receptor 2 (HER2) status is a biomarker in breast cancer for therapeutic stratification and prognosis. Recent trials showed favourable results when using Trastuzumab Deruxtecan in previously treated HER2-low advanced breast cancers.
Methods: HER2 status of diagnostic core biopsies of breast invasive carcinomas from 2020 and 2021 in a central university hospital was reviewed to estimate the incidence of HER2-low breast cancer. 20 randomly picked cases were blindly assessed by two breast expert pathologists and two residents to evaluate observer variability.
Results: A total of 421 diagnostic core biopsies were observed. The HER2 status at the time of diagnosis was analysed: 150 negative 0 (35.7%), 132 low 1+ (31.3%), 66 equivocal (15.7%); 73 positive 3+ (17.3%).
The blind assessment by two breast expert pathologists and two residents showed a concordance of 50% in the HER2 status determination. When only the experts were considered the concordance rose to 65%. The lowest concordance - 22.2% and 40% - were found in low 1+ (9 cases) and negative 0 (5 cases), while the positive 3+ cases showed a higher concordance (75% in 4 cases).
Conclusion: The results of HER2 status at the time of diagnosis in our institution are roughly equivalent to what is found in the literature. The HER2-low corresponds to one-third of the total cases that are, now, potentially treated by Trastuzumab Deruxtecan. The implementation of software support for HER2 status determination is essential since the interobserver variability is high, particularly in HER2 negative 0 and HER2-low cases.
This work had the financial support of AstraZeneca Portugal.

PS-01-028
Clinicopathological spectrum of adenomyoepithelioma: a tertiary care cancer centre experience of a rare entity
A. Sahay*, M. Aziz, A. Patil, T. Shet, S. Desai
*Tata Memorial Center, Mumbai, India

Background & objectives: Biphasic breast tumours with myoepithelial cell (MEC) predominance constitute heterogeneous group, ranging from benign adenomyopeithelioma (AME) to malignant AME (M-AME). However, definition of M-AME not clear due to rarity. We reviewed clinicopathological features of AME at our tertiary-care cancer institute.
Methods: All 61 AME diagnosed between 2012-2022 were retrieved from departmental archives, of which 43 were benign (70.5%), 18 were M-AME (29.5%). Diagnosis of M-AME was based on increased mitoses (>3/10HPF), marked atypia, prominent nucleoli, necrosis, and infiltration. M-AME were further classified as M-AME in-situ (AME+DCIS), M-AME invasive (malignant epithelial and/or myeoepithelial component), and AME with invasive breast carcinoma (IBC).
Results: Benign AME: median age 41 years (range:11-67 years), median size 2.6cm (range:0.6-12.4cm), predominantly unilateral (Left:23; right:17; bilateral:3). Core biopsy (CB) diagnosis was AME in 9, while 7 called other benign entities. M-AME: median age 48 years (range 34-90), median size 4cm (range 0.7-22cm), predominantly unilateral (right:9; left:8; 1:bilateral). Among M-AME, 3 were M-AME in-situ, 6 M-AME invasive, while 9 AME with IBC. Of the latter, 6 were hormone receptor (HR)+HER2-; 2 HR-HER2+ and 1 triple negative. CB (8/18) showed M-AME (1), and IBC (4) while rest benign. All AME showed bilayered epithelial-MEC (immunohistochemically confirmed). M-AME showed nodal metastasis (3/18), lung metastasis (2/18) & local recurrence (3/18). Eight patients received adjuvant therapy.
Conclusion: M-AME are larger and occur at an older age than benign AME. They may be misdiagnosed on CB and carry a potential for metastasis and recurrence. Complete excision with clear margins and adjuvant therapy may be indicated. Recognition of biphasic elements, confirmation with immunohistochemistry, and identification of aggressive histology are essential for an accurate diagnosis.

PS-01-029

Assessment of intra-laboratory mitoses counting reproducibility in breast cancer using telemedicine platform

I. Telezhnikova*, G. Setdikova, A. Abduraimov, S. Khomeriki, L. Zhukova
*Loginov Moscow Clinical Research Center, Russia

Background & objectives: Counting mitotic figures (MF) in histologic sections is an integral part of the diagnostic pathologist's tumour evaluation. However, level of concordance of MF among pathologists remains low. The aim of this study was to evaluate of level concordance for MF.
Methods: The slides were scanned at 40x magnification by 3DHISTECH®. Slides were uploaded to the OneCell telemedicine platform for pathology laboratories. For each slide, 10 fields of view 0.264 mm^2 were selected using markup tools. The evaluation was performed by 3 pathologists specializing in breast cancer. Convergence on mitosis detection and grading deviations were assessed.
Results: The sample was 100 fields of view from 20 patients. Categories MF were distinguished (1 – mitosis inconclusive, 2 – mitosis yes). MF categories defined as 2 in 32.8% pathologist markup 1, 35.9% pathologist markup 2, 44.3% pathologist markup 3. The mean deviation ± MF between pathologists on the convergence coefficient was 0.66 (0.55±0.78). The total absolute deviation by category on the inverted augmented slides was 0.7 for pathologist markup 1, 1 for pathologist markup 2, and 0.65 for pathologist markup 3. Grade of tumour changed in 8/20 of patients by pathologist markup 2. Overestimation of grading were a statistically significantly difference (higher) than understatement ($p < 0.001$).
Conclusion: Level concordance for counting mitoses among pathologists was low, level of category concordance on the inverted augmented slides was also low. The authors feel it advisable to conduct training on mitoses counting using telemedicine platforms. Training of MF will improve reproducibility and accuracy.

PS-01-030

Presence of crown-like structures in breast adipose tissue; differences between healthy controls, breast cancer patients and BRCA1/2 gene mutation carriers

M. Zwager, I. Holt-Kedde*, H. Timmer-Bosscha, G. de Bock, C. Schröder, B. van der Vegt, M. Arjaans
*Department of Plastic Surgery, University of Groningen, University Medical Center Groningen, The Netherlands

Background & objectives: Crown-like structures (CLS) might influence breast cancer behaviour. Therefore, we compared CLS presence between adipose tissue of breast cancer patients, BRCA1/2 gene mutation carriers and healthy controls, and assessed the relation of CLS numbers with clinical outcome.
Methods: Breast adipose tissue sections from 259 breast cancer patients, 78 BRCA1/2 gene mutation carriers after mastectomy and 48 healthy controls after breast reduction were immunohistochemically stained for CD68. CLS presence and index (CLS/cm2) were determined and correlated with BMI, BRCA status, tumour presence and intrinsic tumour subtype with logistic regression analyses. Correlations with tumour characteristics and clinical outcome were assessed.
Results: CLS were more often present in breast cancer patients compared to BRCA carriers and healthy controls (OR:3.2; 95% CI:1.4-7.5; p=0.005). In the total study population, CLS presence was associated with the presence of breast cancer (OR:2.2; 95% CI:1.3-3.8; p=0.005) and high BMI (overweight OR: 2.1; 95% CI:1.3-3.6; p=0.004; obese OR:3.3; 95% CI:1.8-5.8; p<0.001). The same was found in the breast cancer subgroup (overweight OR:2.3; 95% CI:1.2-4.2; p=0.010; obese OR:4.2; 95% CI:2.1-8.4; p<0.001). No association with BRCA status was found. CLS presence was higher in Luminal-B-like tumours compared to the other subtypes (OR:2.5; 95% CI=1.3-5.2; p=0.010). In TNBC, CLS were related to lymphovascular invasion (p=0.013). No association with survival was found.
Conclusion: In conclusion, CLS were more frequently present in breast adipose tissue of breast cancer patients compared to BRCA1/2 gene mutation carriers and healthy controls. Furthermore, our study provides further evidence of the association between obesity and presence of CLS. The prognostic significance and impact on clinical outcome of differences in CLS numbers should be further assessed in prospective studies.

PS-02 | Poster Session Digital and Computational Pathology

PS-02-001

Automatic discrimination between neuroendocrine carcinomas and neuroendocrine tumours of grade 3 by deep learning analysis of H&E staining images

A. Arrieta*, J. Bohoyo, M.J. Araúzo Bravo, M.R. Bella, J.C. Ferreres
*Consorci Corporació Sanitària Parc Taulí, I3PT, Universidad Autónoma de Barcelona, Spain

Background & objectives: Deep learning (DL) is a machine learning technology based on artificial neural networks (ANN). We have shown DL as an aid to make a selection between Neuroendocrine tumours (NETs) and Neuroendocrine carcinomas (NECs) from Neuroendocrine neoplasms (NENs).
Methods: 95 cases of NENs were selected from 2015 to 2018 from Parc Tauli Hospital database. These cases were used to develop, train and validate an ANN using the Keras DL learning Application Program Interface written in Python, running on top of the DL platform TensorFlow on a High Performance Cluster with 10 Graphic Processing Units

Results: The system was evaluated with 119 new images. The results were satisfactory for the four resolutions tested. The accuracy achieved for the resolutions of 64x64, 128x128, 256x256, and 512x512 pixels were 0.74, 0.98, 0.98 and 1, respectively. Since the required computational capacity increases considerably with image size, the optimal resolution might be between 64 and 128 pixels, depending on the available computational resources and accuracy requirements. Most of the misclassifications have been false negatives, i.e., the NET1 type images have been classified as NEC type.
Conclusion: We have demonstrated that a diagnosis algorithm based on DL has been effective in discriminating between NET and NEC with results similar to those of the pathologist. Our software can be adapted to integrate more than one ANN and therefore, this opens a range of possibilities to combine DL and histological diagnosis. A further goal is to be able to classify not only a NET but the three-tier system (NET1, NET2 and NET3) attending exclusively to the tissue differentiation information.

PS-02-002
Digital analysis of well-differentiated hepatocellular carcinoma
W. Cao*
*Rhode Island Hospital, USA

Background & objectives: The diagnosis of well-differentiated hepatocellular carcinoma (WDHCC) can be challenging. In this study, we performed digital analysis of well-differentiated hepatocellular carcinoma by using the software QuPath to see whether some parameters may be helpful for the diagnosis of WDHCC.
Methods: We queried our records for the biopsies of WDHCC from 2018 to 2022. Thirty cases were included. Nineteen cases had adjacent benign liver parenchyma. Thirteen cases had Ki-67 and CD34 immunostainings. We used QuPath to analyse the nuclear hematoxylin optical density, nucleus/cell area (N/C) ratio, maximum cell calibre, Ki-67 and the percentage of the positive area of CD34 staining.
Results: The nuclear OD was significantly higher, and the tumour cell size was remarkably smaller in WDHCC than in benign hepatocytes (BH). N/C ratio was markedly higher in WDHCC (0.2 ± 0.01) than in BH (0.12 ± 0.003). If N/C ratio cutoff was >0.15, the sensitivity was 89.5% and specificity was 94.7%. Ki-67 index was significantly higher in WDHCC ($14.3 \pm 6.0\%$) than in BH ($1.3 \pm 0.4\%$). If Ki67 index cutoff was >4%, the sensitivity was 63.6% and specificity was 100%. CD34+ area was significantly higher in WDHCC ($15.2 \pm 1.8\%$) than in BH ($1.8 \pm 0.3\%$). If CD34+ cutoff was >4%, the sensitivity was 92.3% and specificity was 100%.
Conclusion: Digital analysis may be helpful in assisting the diagnosis of WDHCC. N/C ratio >0.15, Ki-67 proliferation index >4% and CD34 positive area >4% may support the diagnosis of WDHCC.

PS-02-003
Digital analysis of lung cancer whole slide images – part 1 of the INGENIO multicentre ring trial
I. Carretero*, A. Illarramendi, D. Curto, S. Granados-Aparici, A. Compañ, M.L. Cagigal, Á. Estebánez, C. Bejarano-Jurado, J. Castellvi Vives, L. Pijuan, I. Esteban Rodríguez, I. Sánchez Güerri, M.J. Ledesma, J. Palacios Calvo
*Hospital Universitario Ramon y Cajal, Spain

Background & objectives: INGENIO is a multicentre project aimed at standardizing digital pathology for routine clinical care. After providing training in digital analysis to pathologists, we conducted a ring trial to evaluate their agreement in the analysis of lung cancer whole slide images (WSI).
Methods: Participants received 4 WSI. They were tasked with obtaining on each WSI the number of non-tumour cells and tumour cells (epithelial and stromal). They used QuPath to annotate tissue, perform cell segmentation, and classify cells. The results were exported and analysed to assess agreement on the number and percentage of cells in each category using the intraclass correlation coefficient (ICC).
Results: Nine centres participated in the ring trial. By visual examination, the annotations made in QuPath by the different pathologists were similar. One WSI mostly contained necrosis, resulting in higher annotation subjectivity for this image among centres. The remaining 3 WSI had differing numbers of epithelial, stromal, and non-tumour cells. Interobserver agreement was moderate for the absolute number of epithelial and stromal cells (ICC 0.73 and 0.75, respectively) and poor for non-tumour cells (ICC 0.06). Regarding percentages, there was moderate agreement for stromal cells (ICC 0.76) and poor agreement for non-tumour and epithelial cells (ICC 0.40 and 0.09, respectively).
Conclusion: Although digital pathology is considered a more objective way to quantify different pathology features, it still has some degree of subjectivity, mostly in the annotation phase. This ring trial demonstrates that with a little training pathologists are able to reach moderate agreement on digital image quantification. However, further training sessions and an additional ring trial with more WSI are planned to better standardize our results, with the ultimate goal being for each centre to analyse their own WSI.
This work has been developed with the financial support of Instituto de Salud Carlos III (ISCIII) project INGENIO (PMP21/00107) and the Next Generation EU funds.

PS-02-004
Digital pathology implementation in routine breast cancer pathology clinical service: how we made it work and what we gained
E. Colon*, L. Kis, E. Andersson
*UNILABS SWEDEN, Sweden

Background & objectives: The use of digital slides shows advantages over microscopy, but validation is needed to allow its use in clinical practice. The aim was to support the quality and advantages of using digital pathology in breast pathology clinical practice.
Methods: Different steps included verifying pre-analytical procedures and validation of interpretation. All pathologists had access to a Digital workstation and microscope. Cases were diagnosed on WSI and confirmed on physical slides before signing out. Comments on diagnostic pitfalls were collected in a list. A total of 217 consecutive breast cancer were included. Ground truth was established on physical slides before MDT.
Results: Primary diagnoses on WSI showed a high average agreement of 99% with final diagnoses. The pathologists using Digital experienced reduced barriers to asking for a second opinion on challenging cases with rare morphology through the live share function. Discussions with peers resulted in a decrease in IHC orders in 20% of cases. The production per pathologist increased between 12-50 % compared to production before the implementation. The interobserver agreement, measured as a reduced number of cases with revised diagnoses at review before MDT, increased from 71 % to 94.4%. The production measured as the number of signed-out cases per pathologist per week increased between two- to three-fold.
Conclusion: The entire group chose to continue using digital pathology in routine practice. In 2022 the group signed out a total of 2017 breast pathology samples using Digital pathology.
Individual training and validation increase confidence in the use of Digital Pathology. This study reports a productivity increase between 2x-3x, reduction of supporting immunostainings, enhanced collaboration with live sharing, and reduced need for revision of diagnoses before MDT.

PS-02-005
Validation of a quantitative image analysis algorithm for HER2 status determination in breast cancer by immunohistochemistry as positive, low or ultra-low
M. Cossutta*, J. Bellocq, C. Egele, A. Papine, E. B. Tatarinova, K. Socha, M. Soussaline, C. Homsy, F. Soussaline
*IMSTAR Dx, France

Background & objectives: Breast carcinoma (BC) treatment relies on HER2 status using immunohistochemistry (IHC) to identify

HER2-positive BCs. New therapies raised diagnostic issues with the emergence of HER2-low and HER2-ultralow categories. Our objective was to design an adapted Quantitative Image Analysis (QIA) algorithm.
Methods: The evaluation used 133 slides providing from 2 external proficiency testing schemes (2021, n=52; 2022, n=81) conducted by the french interlaboratory comparison organization (AFAQAP) and comprising 8 different BCs with HER2 scores ranging from 0 to 3+. All statuses were assessed by 2 independent methods: visually by 3 expert pathologists, and by QIA using the IMSTAR PathoScan Tumour-Marker HER2 algorithm.
Results: Expert pathologists identified 48 HER2 IHC slides receiving an "optimal technique" appreciation for each 4 BCs (2021, n=19 slides; 2022, n=29 slides). HER2-QIA algorithm performed an accurate evaluation of HER2 scores with an overall concordance of 94% with the experts for all optimal slides.
The concordance between QIA and the experts was of 100% for HER2-positive BCs, 94% for IHC 1+ BCs, and 85% for IHC 0 BCs. Of note, concordance for the conventional IHC 0 BCs decreased from 100% in 2021 to 76% in 2022 with 7/29 BCs scored as 1+ by QIA, raising the question of the proper visual identification of HER2-physiological expression BCs, and HER2-ultralow BCs.
Conclusion: Our QIA solution was efficient to identify HER2 expression on technically optimal slides despite multiple laboratories IHC techniques being applied, highlighting the need for IHC standardization to obtain robust digital evaluations. HER2-QIA algorithm is accurate for the proper identification of HER2-positive BCs, while providing an objective, quantitative method discriminating between HER2-physiological expression, HER2-ultralow, and HER2-low BCs. In the lowest range of HER2 expression, it allows to generate HER2 new thresholds related to drug efficacy revealed by future clinical studies.

PS-02-006
A colorectal AI model for triage and a second opinion in a digital workflow
C. Girleanu*, R. Chetty, J. Weldon, M. Morrissey, R. Sykes, M. Colleluori, J. Fitzgerald, C. Durnin-White, S. Hutton, N. Mulligan

*Mater Misericordiae University Hospital Pathology Dept, Ireland

Background & objectives: Delayed diagnosis of advanced colorectal polyps result in increased morbidity and mortality. Rising workloads and pathologist shortages mean screening cases have reduced priority. A.I. driven case prioritisation within colorectal screening programmes may reduce turnaround time for clinically significant cases.
Methods: A proprietary, weakly supervised learning classifier for slide-level, colorectal biopsy classification was created. The model was trained on over 15,000 whole slide images (WSI) of H&E colon biopsies obtained from The Mater Misericordiae University Hospital, Dublin (MMUH) at 20x magnification. This training cohort consisted of 32 unique biopsy diagnoses which were also provided by MMUH.
Results: The model successfully triaged an unseen test cohort of 241 colon biopsies. This test cohort consisted of 156 urgent biopsies and 85 non-urgent biopsies. Of the 156 urgent biopsies, 20 contained colorectal cancer. The model classified each biopsy as urgent or non-urgent with 96% sensitivity and 92% specificity. Pathologist feedback on the 4% false negatives indicated that the majority were mislabelled ground truth and/or borderline cases. 100% of the biopsies containing colorectal cancer were classified as urgent.
Conclusion: There is applicability of this A.I. for case triage and as a second opinion for decisions within a digital pathology platform that connects laboratories worldwide to an international network, where subspeciality pathologists can apply their expertise to clinical cases.
This project received funding from the Enterprise Ireland Disruptive Technologies Innovation Fund (DTIF Project 2018_164)

PS-02-007
Developing an efficient digital pathology cloud platform for collaborative image annotation and management
C.K. Jung*, M. Yook, S.H. Lee, S.K. Yoon, I.Y. Choi
*Department of Hospital Pathology, College of Medicine, The Catholic University of Korea, Cancer Research Institute, College of Medicine, The Catholic University of Korea, Republic of Korea

Background & objectives: To integrate digital pathology into routine diagnostic practice, efficient storage and processing of whole slide images (WSIs) data is crucial. Our objective was to develop a cloud platform with collaborative image annotation, multiple-user support, and managing large imaging datasets.
Methods: Our dataset included mrxs, svs, ndpi, and tiff file formats scanned at 40x magnification. We customized Cytomine, incorporating annotation tools, clinical information, and pathology reports management. We tested a system that uses both cloud and on-premise servers to see how well it works for accessibility, cost-effectiveness, and how quickly images are displayed.
Results: We compressed original WSI formats to tiff files using pyvips python, maintaining the same number of pixels as in the native WSIs. Compression with Q=50 reduced the file size by an average of 69% without significantly affecting visual quality, enabling data annotation. Using a hybrid cloud server system, native WSIs were stored on an on-premise server, while compressed tiff files were uploaded on object storage of a public cloud server. When used for annotation or viewed on demand, they were moved to the Network-Attached Storage (NAS). Annotations can be made directly on tiff WSIs in the NAS, accessible on any internet-connected device. XML ingestion/export options were added for local annotation.
Conclusion: Our hybrid cloud system is cost-effective, sustainable, and offers fast and memory-efficient processing of large WSIs, with support for annotation, visualization, and machine learning. Its flexibility, scalability, and ease of use make it a valuable tool for collaborative annotation, with options for multiple users and annotation types and for managing and analysing large imaging datasets. Its ability to support collaborative annotation across different platforms and to ingest and export annotations in XML provides additional user benefits.
This research was supported by a grant (HI21C0940) from the Korean Health Technology R&D Project, Ministry of Health and Welfare, Republic of Korea.

PS-02-008
Minimum cell counts for single gene testing – implications for tissue curation in molecular testing
F. Kaar*, S. Conneely, A. O'Keefe, G. Callagy, S. Hynes
*Anatomic Pathology, University Hospital, Galway, Ireland

Background & objectives: Thresholds for molecular assessment of tumours vary depending on the technology used. The working threshold for single gene testing in most laboratories is 10%. However, the minimum number of tumour cells required for detection of a variant is not known.
Methods: We analysed both colorectal and malignant melanoma cases with using a PCR based clinical assay for single gene assessment. Sensitivity was assessed using varying dilutions of the tumour cells. Absolute tumour cell and stromal counts were done using whole slide image assessment and QuPATH open-source software.
Results: A colorectal cancer slide with known G12X and A146X variants had 748,858 cells detected of which 441,962 cells were tumour cells. Based on dilutions of the target DNA a final minimal threshold of 189-2511 cells was estimated to be required for detection of these variants. A similar analysis of a BRAF V600E mutation in malignant melanoma was not able to find a dilution cut off point in order to illustrate the threshold.

Conclusion: These results suggest the minimal threshold required to detect variants using a single gene test is much lower than the working threshold of 10%. When biopsy tissue is limited, this may have significant implications in the responsible curation of tissue for molecular testing.
Funding: Pathological Society of Great Britain and Ireland Undergraduate Elective Bursary

PS-02-009
Deep learning for multi-class cell detection in H&E-stained slides of diffuse gastric cancer
R. Lomans*, J. van der Laak, I.D. Nagtegaal, F. Ciompi, R.S. van der Post
*Radboud university medical centre, The Netherlands

Background & objectives: Diffuse gastric cancer (DGC) is characterized by poorly cohesive cells which are difficult to detect. We propose the first deep learning model to detect classical signet ring cells (SRCs), atypical SRCs, and poorly differentiated cells in H&E-stained slides of DGC.
Methods: We collected slides from 9 patients with hereditary DGC, resulting in 105 and 3 whole-slide images (WSIs) of gastric resections and biopsies, respectively. The three target cell types were annotated, resulting in 24,695 cell-level annotations. We trained a deep learning model with the Faster-RCNN architecture using 99 WSIs in the development set.
Results: The algorithm was tested on 9 WSIs in the independent validation set. Model predictions were counted as correct if they were within a 15-micron radius from the expert reference annotations. For evaluation, we split the detection task into two components: class-independent cell localization (recognition of any tumour cell type) and cell-type classification (categorizing localized cells as the correct types). We found (average) F1 scores of 0.69 and 0.93 for the localization and classification tasks, respectively. Thus, we observe that the algorithm does not generally misclassify cells, but rather, the errors mainly arise from missing cells or false positive predictions of cells that do not belong to the three target classes.
Conclusion: Future work will focus on improving the cell localization performance of the algorithm. Cell localization of the three target classes will be an important task in a clinical application of our model, in which it could be used to improve the detection of DGC lesions among large sets of slides. Moreover, the algorithm will allow for quantitative assessment of DGC patterns, potentially giving new insights in specific morphological features of DGC such as patterns of spatial cell distributions.
This research was supported by an unrestricted grant of Stichting Hanarth Fonds, The Netherlands

PS-02-010
IMSeg: a clinically deployable tool for the detection of intestinal metaplasia in gallbladder using digital pathology slides and deep learning
J. Massonnet*, K. Egervari, M. Kreutzfeldt, D. Merkler, A. Janowczyk
*Department of Pathology, Division of Clinical Pathology Geneva University and University Hospitals, France

Background & objectives: Early detection of gallbladder intestinal metaplasia (IM) is critical for improving patient outcomes, as IM can ultimately progress to dysplasia and cancer. To ease pathologist's exhaustive high-magnification screening, a deep learning tool identifying IM on H&E-stained slides, IMSeg, was developed.
Methods: Emergence of goblet cells in the epithelium is a defining feature of IM. Consequently, IMSeg takes a 2-step filtering approach: 1) segmentation (UNet) of epithelial regions at 5x magnification, 2) subsequent segmentation of masked regions for goblet cell detection (UNet) at 10x. Patient-level diagnostic accuracy, and goblet cell level F1 scores were computed using n=50 patients (10 IM-positive).
Results: Calibrated using 80/20 training/testing split, patient-level diagnostic accuracy of 100% was observed. At the goblet cell level, an F1-score of 0.95 was observed, with successful detection determined by a Dice coefficient ≥ 0.85. IMseg's output directs pathologist attention directly to IM regions, eliminating the need to manually review the entire slide, and resulting in a 50% (2.5 minutes) reduction in patient diagnostic time. This translates to an anticipated yearly time saving of 40 hours in our institution. Furthermore, detection of IM by IMSeg will automatically prompt the preparation of additional tissue blocks, necessary for ruling out dysplasia in such cases, ultimately reducing patient case turn-around time by approximately one day.
Conclusion: Automated detection of IM provides a powerful, highly accurate, tool for pathologists. IMseg was designed to be seamlessly integrated into our hospital's primary digital diagnostic workflow, helping streamline the diagnostic process and improve lab efficiency. Future work will focus on performing that integration while evaluating the accommodation of pathologists using IMSeg in their daily practice, as well as maintenance to ensure its performance remains sufficient for clinical usage over time.

PS-02-011
IBAPAT project: the unified digital pathology laboratory of the Balearic Islands
G. Matheu Capó*, D. Laguna Macarrilla, A. Forteza Valadés, F.A. Miguel Gayá, C. Fernández Palomeque
*Servei d'Anatomia Patològica. Hospital Universitari Son Espases, Spain

Background & objectives: The Balearic Islands (BI) have six Pathology Departments spread over three islands, with variable technology and specialization. Digital pathology can facilitate the creation of a single pathology laboratory to minimize accessibility and care equity problems owing to insularity.
Methods: The IBAPAT project is based on three axes that are being developed sequentially: 1. the implementation of a Laboratory Information System (LIS) for the six Departments of Pathology in the BI; 2. Whole-slide imaging (WSI) of all histological preparations for routine diagnosis; 3. The centralization of laboratory processes in a single digitized and highly productive laboratory for all the BI.
Results: An LIS has been acquired; it is a single database for all pathology departments, with a traceability system adapted to digital pathology, allowing networking and management of a central laboratory. Scanners covering all histological activities (single laboratory model), storage hardware, image viewer software, and basic algorithms for diagnosis in digital pathology have been developed. The central laboratory building is in the construction project phase, from tissue processing to stained slides and their scanning, and other ancillary studies (FISH, PCR, NGS, etc.) will be performed in this laboratory. Pathologists maintain their work activities in their pathology departments.
Conclusion: Taking into account the insular geographical context and the need to give patients equal and universal access to health care and technology, the IBAPAT project pursues the modernization of IB Pathology departments by improving information systems, the WSI, and centralization of the laboratory, improving the global efficiency of the diagnostic process in pathology, and improving patient care in terms of equity, safety, and quality of diagnosis.

PS-02-012
Predicting cell-of-origin for diffuse large B-cell lymphoma patients (DLBCL) using explainable feature-based model
P. Lin, N. Shaikh, P. Porwal, S. Jayachandran, Q. Gu, X. Li, K. Korski*, Y. Nie
*Department of Personalized Healthcare, Data, Analytics and Imaging group, Genentech, Inc., USA

Background & objectives: Determining cell-of-origin (COO) subtypes in DLBCL has been only possible by genomic testing or multiple

immunohistochemistry assays requiring expert visual assessment. We aim for standardized and automated tissue-saving COO prediction using H&E whole-slide-images (WSIs) and interpretable machine learning methods.
Methods: Multiple field-of-view (FOV) images were randomly extracted from tumour regions in WSIs. For each FOV, cellular features characterizing tissue morphologies were extracted and used to train a random-forest (RF) model for FOV prediction. The averaged FOV prediction is reported per WSI. As a comparison, an attention-multi-instance-learning (AMIL) network using FOV image embeddings generated by a pre-trained ResNet50 is also investigated.
Results: The RF and AMIL models were developed using a 40X WSI dataset, which contained 120 activated-B-cell-like (ABC) and 236 germinal-centre-B-cell-like (GCB) subtype cases determined by genomic testing. The RF model achieved an average ROC-AUC of 0.675 on a 5-fold cross validation, and the AMIL model achieved an average ROC-AUC of 0.687. On a separate test dataset containing 22 ABC and 32 GCB cases, the RF model achieved a ROC-AUC of 0.715, and the AMIL model achieved a ROC-AUC of 0.737. In addition, RF model's feature importance revealed that tumour cell spatial distribution features consistently had high impact on the model prediction across training and testing.
Conclusion: In this work we demonstrate that tissue morphological features are correlating to the biology driving COO determination. A RF model employing explicit morphological features and an AMIL model using image embeddings from a convolutional neural network can achieve comparable COO prediction performance. While the AMIL model provides interpretability through locating high attention regions in a WSI, the RF model enables identifying impactful cellular level features and provides insights for further investigation of model trustworthiness.
This study was funded by F. Hoffmann-La Roche AG, Basel, Switzerland. Support with compliance and the abstract submission process was provided by PharmaGenesis Cardiff, Cardiff, UK, and funded by F. Hoffmann-La Roche AG.

PS-02-013
Automated PD-L1 tumour proportion scoring algorithm in non-small cell lung cancer for multiple companion diagnostic assays
D. Rodrigues*, C. Neppl, D. Dorward, T. Losmanová, R. Wyatt, D. Mulkern, S. Pattle, R. Oberson, S. Reinhard, T. Waldburger, I. Zlobec, P. Caie
*Indica Labs, USA

Background & objectives: High interobserver disagreement when reporting programmed cell death ligand 1 (PD-L1) expression, may result in suboptimal treatment decisions. HALO PD-L1 AI aims to support pathologist quantification for PD-L1 companion diagnostics SP263 and 22c3 assays in non-small cell lung cancer (NSCLC).
Methods: HALO PD-L1 AI was trained with 146984 expert annotations to identify PD-L1 tumour-positive cells, within segmented tumour regions. The algorithm's Tumour Proportion Score (TPS) was validated on 203 SP263-stained whole slide images (WSI), assessing its agreement with the TPS scores of three pathologists. For the 22c3 clone, we gathered agreement metrics from the algorithm and the reported TPS score.
Results: For SP263-stained images (n=203), pairwise pathologist agreement ranged from 74.9% to 77.3%. Algorithm agreement with the pathologists' mode was 75.4%, with agreement at the clinically relevant cut-offs (<1%, 1-49% and >50%) ranging from 0.71 to 0.78. Intraclass correlation coefficient (ICC) between the algorithm and pathologists' TPS scores was 0.95 (95% CI 0.93 – 0.97).
Preliminary results on 22c3-stained slides (n=243), show that the overall percent agreement with the reported TPS score was 74.1%, with the agreement at the clinically relevant cut-offs ranging from 0.68 to 0.82. The ICC agreement was 0.95 (95% CI 0.94 – 0.96).
Conclusion: Immunotherapy has revolutionized advanced NSCLC treatment and several companion diagnostic assays are available to determine eligibility for this therapy. However, reporting of PD-L1 expression suffers from high interobserver disagreement. We developed HALO PD-L1 AI to support pathologists PD-L1 scoring with the aim of saving pathologists time and ensuring consistency in the reported results. The algorithm is highly concordant with the pathologist TPS scores for SP263 and 22c3 companion diagnostic assays.

PS-02-014
An automated deep learning artifact detection tool for quality control of whole-slide digital pathology images
D. Rodrigues*, E. Burlingame, C. Babcock, V. Ovtcharov, S. Reinhard, T. Waldburger, D. Martin, S. Couto, I. Zlobec, P. Caie
*Indica Labs, USA

Background & objectives: Mechanical and digital artifacts have a negative impact on digital pathology workflows. Image focusing issues can be a critical bottleneck during slide digitisation. We developed SlideQC to automatically segment tissue artifacts in haematoxylin and eosin (H&E) and immunohistochemistry (IHC)-stained slides.
Methods: SlideQC was developed using 2499 artifact annotations across 302 H&E and IHC stained slides, alongside 2048 synthetically generated out-of-focus images. SlideQC performance was evaluated on 432 annotations across external H&E (HistoQC Repo) and IHC (LYON19) test images. SlideQC's ability to distinguish in-focus from out-of-focus was assessed on 4954 patches from the TCGA@Focus dataset.
Results: For the external H&E and IHC test sets, SlideQC showed high precision, recall, and F1-score with average values of 0.94, 0.90, and 0.91, respectively, over pixel-level annotations. Recall per artifact type was 0.84 for air bubbles, 0.91 for debris/dust, 0.84 for folds, 0.98 for pen marker, and 0.97 for out-of-focus regions. For the TCGA@Focus dataset, the median percent of artifact reported for the 2461 out-of-focus labelled patches was 76.7 [IQR 41.3 – 97.6] and for the 2493 in-focus labelled patches was 3.3 [IQR 0.8 – 8.4].
Conclusion: SlideQC can alleviate the bottleneck of manual quality control in both clinical and research based digital pathology workflows, thereby bringing efficiency gains to both fields. Slide QC achieved high precision, recall, and F1-score in H&E and IHC external test cohorts. Furthermore, SlideQC showed a good ability to distinguish out-of-focus from in-focus patches in the TCGA@Focus dataset. By identifying and reporting the percentage of artifacts on each slide, SlideQC could provide an automated, measurable quality control procedure.

PS-02-015
Interpretable artificial intelligence to predict lymph node metastasis in early gastric cancer
Y. Sung*, Y.J. Lee, S.H. Lee, S. Ahn
*Republic of Korea

Background & objectives: When early gastric cancer (EGC) shows high-risk features, current guidelines recommend surgery due to the risk of lymph node metastasis (LNM). We aimed to develop machine learning algorithm that can predict LNM status using H&E-stained histopathology images from multiple institution.
Methods: Our pipeline consists of two sequential approaches; a feature extractor and a risk classifier. For the feature extractor, segmentation network (DeepLabV3+) was trained on 243 WSIs across 5 datasets to differentiate each histologic subtype. UMAP was employed to visualize the quality of encoder. After that, risk classifier was trained with XGBoost using 70 morphologic features inferred from trained feature extractor.

Results: The trained segmentation network, the feature extractor achieved high performances with an accuracy, recall, precision, F1-score and mIOU of 0.987, 0.9742, 0.9742, 0.9742, and 0.95 respectively on the external validation sets. We further verified the disentangled representation of the encoder of the segmentation network using UMAP. The risk classifier achieved an AUROC of 0.7487 (± 0.0021) in predicting LNM status. The top features which affect LNM status were mostly geometric features from the total tumour and the undifferentiated tumour, including the area, and diameter of the total tumour and the perimeter of undifferentiated one.
Conclusion: This is the first multi-institution study to develop machine learning algorithm for predicting LNM status in patients with EGC using H&E-stained histopathology images. Our findings have the potential to better help in selecting patients who need surgery among EGC patients showing high-risk histologic features.

PS-02-016

Artificial intelligence-assisted daily quality control system for histologic diagnosis of gastrointestinal endoscopic biopsies: 1-year experience

S. Yoo*, Y. Park, J. Jang, S. Yun, Y. Hwang, Y.S. Ko
*Pathology Center, Seegene Medical Foundation (SMF), Republic of Korea

Background & objectives: In March 2022, SMF has launched an artificial intelligence (AI)-based quality control system (SeeDP) that double-checks all gastrointestinal endoscopic biopsy (EB) slides for possible incorrect diagnosis. We aim to review its operational records and clinical impact over the past year.
Methods: Operational records were retrieved for the total number of EB specimens submitted, slides scanned and assessed by AI models, and cases with discordant assessments between the AI and pathologists' diagnoses. Cases of which the diagnosis was revised after SeeDP's suggestion were collected and compared to revised cases identified by conventional routes such as random review and clinician's enquiry.
Results: From 2022-03-01 to 2023-02-28, 67.7% (572,254/844,906) of EB slides were scanned. SeeDP failed to analyse 0.8% (4,531/562,203) of gastrointestinal EB slides due to various technical errors. AI's judgement differed from pathologist's diagnoses in 7.7% (42,760/557.672) of the cases assessed by SeeDP. Review of discordant cases revealed that true misdiagnosis accounted only for 5.1% (21/410) of the disagreement, with most discordance attributable to inherent limitation of the current AI models. Compared to conventional error recognition routes, SeeDP detected more misdiagnosed cases (14 versus 8) in significantly shorter interval of time (average of 3.6 days versus 38.8 days; P<0.001), including one signet ring cell carcinoma case initially diagnosed as gastritis.
Conclusion: This is the first report of implementation and utilization of AI-based daily QC system for histologic diagnosis, and demonstration of its usefulness in routine clinical practice. Promising results were yielded over the past one year, but technical errors and unexpected events compromised 100% coverage of the QC system. The accuracy of AI models may not be improved under the current patch-based framework. Further effort is needed to systematically manage SeeDP coverage and to construct a more histologically relevant AI framework.

PS-02-017

Interobserver variability in semantic segmentation for urothelial carcinoma

S. Zurac*, B. Ceachi, L. Nichita, M. Cioplea, C. Popp, A. Cioroianu, L. Sticlaru, M. Busca, A. Vilaia, J. Dcruz, P. Mustatea, C. Mogodici
*Colentina University Hospital, Carol Davila University of Medicine, Romania

Background & objectives: Artificial intelligence (AI)-based algorithms for automatic detection in urothelial carcinoma (UC) are not available yet. Semantic segmentation for creating a dataset for UC requires heavily annotation on pixel level. We analysed the interobserver variability and its consequences for annotation process.
Methods: We selected 307 areas of interest (AOI) of minimum 1028x1028 pixels originating in 3 whole slide images (high-grade invasive UC; high-grade non-invasive UC; low-grade non-invasive UC); we used Cytomine application (Cytomine Corporation); 8 pathologists with various expertise in UC diagnosis & seniority annotated 13 different classes on each AOI (tumour-related, stroma-related, non-diagnostic, no_tissue, electrocoagulation). We evaluate annotations similarity with Sørensen–Dice coefficient (SDC).
Results: SDC varied largely: low-grade tumour 0.91-0.93, smooth muscle 0.88-0.90, high-grade tumour 0.86-0.88, no_tissue 0.81-0.84, stroma 0.80-0.81, electrocoagulation 0.74-0.79, vessels 0.71-0.74, emboli 0.70-0.91, non-diagnostic 0.66-0.744, interstitial haemorrhage 0.55-0.78, invasion 0.47-0.73, inflammation 0.45-0.6. For invasion, the most similar pair of annotators (MSPA) had 40.74% annotations with similarity <0.5. Image analysis reveal an issue of interpretation: large tumoral areas were labelled as invasive in context. Different cut-off levels for inflammation gave the lowest SDC score. Higher cut-off levels for electrocoagulation influence less-experienced pathologists labelling of "non-diagnostic". Low-grade UC annotations differed by pixel-level inconsistencies (manual delineation). Stroma differences (32.37% similarity <0.5 for MSPA) arise from delicate strands of collagen (pixels-wide) in low-grade non-invasive UC.
Conclusion: Interobserver variability is significant when manual annotations are performed. Two main causes were identified: interpretations problems (with similarity scores less than 0.75) and technical problems due to manual delineation of each area (with similarity scores approx. 0.9). Interpretation issues (with considerable larger discrepancies between pathologists) must be mitigated in consensus debates in order to establish similar method of approach (i.e., "invasion" category) and similar cut-off levels ("inflammation", "electrocoagulation" etc).
This work was partially supported by a grant of the Ministry of Research, Innovation and Digitization, CNCS - UEFISCDI, project number PN-III-P4-PCE-2021-0546, PCE 109/2022, within PNCDI III

PS-02-018

Quantitative aspects of neutrophils, Paneth cells, and adipocytes in digital H&E slides from uninvolved proximal ileal resection margins can predict post-operative recurrence in Crohn's disease

N. Zurek, D. Shiramizu, P. Gu, A. Mujukian, Y.J. Lee, K. Nurzynska, E. Chang, A.E. Walts, P. Fleshner, D.P. McGovern, A. Gertych*
*Cedars-Sinai Medical Center, USA

Background & objectives: Evidence suggests that histology at the proximal ileal resection margin (PIRM) has prognostic significance in post-operative recurrence (POR) of Crohn's disease (CD). In this prospective study we used AI to analyse histologic features in PIRMs and to predict POR.
Methods: Our AI pipeline identified neutrophils, Paneth cell granules, stroma/smooth muscle, and submucosal fat in H&E slides from 139 PIRMs with no evidence of active CD per pathologist review. Extracted relevant features, and fractal dimension and adipocyte flattening in ROIs were analysed using Kaplan-Meier (K-M) plots and/or the rank sum test. Post-resection follow-up was >6 months in each case.
Results: Utilizing average neutrophil density in the stroma/muscle, the K-M estimator significantly stratified patients into low- and high-risk groups for POR (HR=1.7, CI (1.11-2.61), p=0.0138). The stratification improved when this feature was combined with median Paneth cell granule count (HR=1.83, CI (1.19-2.81), p=0.0042), and when these two features were further combined with the percentage of submucosal fat pixels in the digital slides (HR=2.06, CI (1.34-3.17), p=0.00067). Analysis of submucosal fat ROIs from recurrent (n=17)

and non-recurrent (n=37) cases (based on evidence of early endoscopic POR, Rutgeerts score >i2 on colonoscopy <15 months after resection) revealed differences in median adipocyte flattening (p=0.045) and median capacity fractal dimension (p=0.006).
Conclusion: AI provides an objective and in-depth assessment of PIRMs. Based on our findings, elevated neutrophil density in stroma/muscle might be a novel risk factor for time-to-POR. High count and small size of Paneth cell granules, less flattened adipocytes and low fractal dimension in submucosal fat were observed in digital slides from high-risk PIRMs. Our results suggest that digitized H&E PIRM slides can be used to predict early and time to POR. Validation of these findings, currently in progress, is warranted.
Funding: A grant from The Leona M. and Harry B. Helmsley Charitable Trust.

PS-03 | Poster Session Electron Microscopy

PS-03-001
Understanding the quality of your electron microscopy provider in this era of outsourcing of services.
T. de Haro*
*UK NEQAS - CPT, United Kingdom

Background & objectives: Electron Microscopy remains vital to the diagnostic repertoire for the diagnosis of pathologies. A large amount of EM is now outsourced to units away from the originating trust so how can you ensure your EM provider is fit for purpose?
Methods: Methods of evaluating the following were considered.
Results: To ensure that the EM service you are sending your samples to is 'fit for purpose'
Conclusion: Access to EM services remains vital but is increasingly being outsourced to units remote from the originating trust. here, the pathologist is reliant on the images and ultrastructural report being accurate to inform diagnosis.
To ensure accuracy, the EM unit should participate in a quality EQA scheme and the staff should be experienced and educated to a high level in ultrastructural pathology. Without this the referring trust cannot be guaranteed the service they are paying for is fit for purpose.

PS-04 | Poster Session Head and Neck Pathology

PS-04-001
Tumour-infiltrating lymphocytes in oral cavity squamous cell carcinoma and its association with clinicopathological parameters
S. Ahuja*, A.A. Khan, S. Zaheer
*Department of Pathology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

Background & objectives: Oral squamous cell carcinomas (SCC) is one of the most common cancers of the head and neck region. The aim of the present study is to evaluate the significance of tumour-infiltrating lymphocytes (TILs) in oral squamous cell carcinoma.
Methods: All patients of oral cavity SCC who underwent resection were included in the study. Assessment of the stromal TILs was done on H&E-stained sections using the International Immuno-Oncology Biomarker Working Group scoring criteria. TILs were categorised as low TILs (<20%) and high TILs (>=20%). The association between TILs and clinicopathological parameters was evaluated using the Fischer exact test.
Results: Among the 51 cases evaluated in the present study, majority (76.4%) were <60 years of age. 48 patients (94.1%) were males while the remaining (5.9%) were females. In the oral cavity, the most frequently involved sites included buccal mucosa and tongue. Moderately differentiated squamous cell carcinomas were the most prevalent according to grade. Low and high TILs were found in 25.5% and 74.5% cases respectively. TILs were found to show a significant association with tumour size and lymphovascular invasion. However, no significant association was found with age, gender, nodal status, grade, perineural invasion and site in the oral cavity.
Conclusion: The evaluation of TILs as proposed by the International Immuno-Oncology Biomarker Working Group is an simple, inexpensive test. Morphological evaluation of TIL can provide valuable prognostic information in oral cavity squamous cell carcinoma cases and can be incorporated as a part of routine histopathological reporting.

PS-04-004
ETV6::NTRK3 translocation- associated papillary adenocarcinoma: let's play it by ear
D. Bell*, E. Maghami, R. Bakkar, M. Afkhami
*City of Hope National Cancer Center, Department of Pathology, USA

Background & objectives: Ceruminous glands are modified apocrine glands, situated in the external auditory canal (EAC), that, together with sebaceous glands, produce cerumen. The neoplastic transformation of these structures is very rare.
We encounter 2 cases of EAC adenocarcinoma with ETV6::NTRK3 fusion.
Methods: Index case 1
73 years old female with admitting diagnosis of cellulitis of external ear canal. Diagnostic excisional biopsy submitted for expert opinion.
Index case 260 years old male with intermittent bloody otorrhea and ear pain. CT films EAC tumour invading TMJ and extending into parotid. Diagnostic biopsy submitted for expert opinion.
Results: Histologically, a papillary glandular pattern was common to both biopsies. The neoplastic cells were diffusely positive for keratins AE1/AE3, Cam5.2 (#1), CK7 (#2),SOX10, scattered p63 (#1); both biopsies were negative for neuroendocrine markers and S100; DOG1, AR (#1); Ki-67 15% (#1) and 60% (#2).
Molecular genetic testing using targeted next-generation sequencing (NGS) with solid tumour comprehensive platform targeting DNA (523 genes panel) to detect SNVs, CNV, MSI and TMB; and RNA sequencing platform (165 gene panel) to detect fusion with unknown gene partners was performed. A fusion ETV6::NTRK3 was detected in both cases.
Despite this genetic overlap, the morphology and immunophenotype delineate its clear separation from secretory carcinoma.
Conclusion: These cases demonstrate novel primary EAC adenocarcinoma with papillary morphology, which expand the ever-increasing list of ETV6::NTRK3-positive malignancies and which we would like to term ETV6::NTRK3-translocation associated papillary adenocarcinoma.
We also advocate the use of molecular techniques in rare tumours of uncertain type or differentiation, to increase understanding and possibilities of reproducible classification of these rare neoplasms.
Pathologists and oncologists should recognize this entity, which leads to a direct approach for detecting NTRK fusion for appropriate treatment.

PS-04-005
Addition of tumour microenvironment immune cell composition to conventional prognostic factors improves the performance of a locoregional recurrence predictive model for oral squamous cell carcinoma
S. Bisheshar*, M.F. van der Kamp, J. de Vries, L. Slagter-Menkema, E. Schuuring, G.A. Lunter, G.B. Halmos, B. van der Vegt
*Department Pathology and Medical Biology, University Medical Center Groningen, The Netherlands

Background & objectives: Conventional clinicopathological characteristics insufficiently predict a patients' unfavourable oncological outcome (UOO) after surgical treatment for oral squamous cell carcinoma (OSCC). We aimed to assess the added predictive value of tumour environment immune cell composition (TMICC) in addition to conventional clinicopathological characteristics.
Methods: Clinicopathological data of 290 OSCC patients was obtained. Primary tumour samples underwent immunohistochemical staining for CD4, CD8, CD20, CD68, CD163, CD57, FoxP3 and PD-L1. Least Absolute Shrinkage and Selection Operator (LASSO) regression analyses with cross-validation were conducted to train and validate predictive models. Receiver operating characteristic (ROC) analyses were used to quantify the added predictive power of TMICC within models. UOO was defined as loco-regional recurrence, distant metastasis and second primary tumours.
Results: UOO occurred in 32.1% of the 290 patients. The LASSO regression-based predictive model contained conventional clinicopathologic variables: tumour localisation, T-stage, N-stage, resection margin, differentiation grade and perineural invasion. The area under the ROC curve (AUC) of training and test cohorts were: 0.72 (± 0.01) and 0.67 (± 0.01), respectively. Addition of TMICC to the model improved the AUC to respectively 0.80 (± 0.01) and 0.74 (± 0.01). The model showed that CD163 and FoxP3 were positively, whereas CD4 and CD8 were negatively correlated with UOO.
Conclusion: This is the first study showing that addition of TMICC to conventional clinicopathological characteristics improves the performance of predictive models for UOO of OSCC after surgery. This may give guidance in clinical decision making.

PS-04-006
Investigation into the potential role of R-loops in cisplatin resistant oropharyngeal squamous cell carcinoma (OPSCC)
H. Crane*, K. Hunter, S. El-Khamisy
*University of Sheffield, United Kingdom

Background & objectives: OPSCC is frequently treated with a chemoradiotherapy regime including cisplatin, but resistance can develop. R-loops are three-stranded DNA:RNA hybrids which modulate gene expression as well as being a source of genomic instability, however their role in cisplatin resistance is unknown.
Methods: A HPV-positive (HPV+) and HPV-negative (HPV-) head and neck cell line were subjected to long term treatment with cisplatin and single cell clones were selected. Alterations in R-loop dynamics were explored using S9.6 slot blots and DRIP-qPCR. The effect of depleting a known R-loop regulator on cell viability and DNA damage was assessed using MTS assays and immunofluorescence respectively.
Results: In both HPV+ and HPV- cisplatin sensitive cells, R-loops increased with cisplatin treatment. Interestingly, in HPV+ resistant cells, there was an increase in R-loops at baseline when compared to sensitive cells. This increase was also seen at specific genomic loci with DRIP-qPCR. HPV+ resistant cells were also found to upregulate a known R-loop resolving protein known as senataxin. When senataxin was depleted using siRNA, both HPV- and HPV+ resistant cells showed reduced cell viability in response to cisplatin treatment, however the effect was greater in the HPV+ resistant cells. Following depletion of senataxin and cisplatin treatment in HPV+ resistant cells there were higher levels of DNA damage and increased R-loops.
Conclusion: R-loops can modulate sensitivity to cisplatin in resistant cells and the effect is greater in cells which upregulate senataxin. This may represent a potential therapeutic target which warrants further investigation.
Funded by a Cancer Research UK (CRUK) and the Pathological Society Joint Predoctoral Research Bursary and Wellcome Trust Clinical PhD Fellowship.

PS-04-007
Technical external quality assessment schemes for p16 and high-risk human papilloma virus detection in head and neck squamous cell carcinoma: report of year-one results
A. Dodson*, D. Nayar, S. Parry
*UK NEQAS ICC & ISH, United Kingdom

Background & objectives: p16 immunohistochemistry is an aid to identifying HPV-positive oropharyngeal squamous cell carcinoma (SCC), which has distinct clinicopathological features and a favourable prognosis. We report results from external quality assessment (EQA) programmes for p16 and HPV testing in this clinical setting.
Methods: Sections from two FFPE Head & Neck SCC specimens positive for the expression of p16 and HPV, together with a tumour in which neither marker was demonstrable, and a piece of tonsil showing reactive changes, were prepared onto microscope slides and circulated to participating laboratories. Stained slides were returned for central assessment by an expert panel of assessors.
Results: Summated data are presented from four runs conducted at regular intervals in 2022-23.
p16: 143 participations, of which 140 (97.9%) were assessed as acceptable (inter-run-range, IRR=94.3-100.0%). 126 (88.1%) were further categorised as good/excellent (IRR=83.3-90.0%). The most used antibody was CINtec E6H4 (Ventana), used by 78 (81.3%) of 96 laboratories reporting methodology. All 78 (100.0%) produced submissions of acceptable stain quality.
HPV: 43 submissions, of which 42 (85.7%) were assessed as acceptable (IRR=75.0-92.3%). 31 (63.3%) were of good/excellent quality (IRR=46.2-84.6%). The probe set most used was the HPV III Family 16 Probe (Ventana), used by 34 (82.9%) of 41 laboratories that reported their method. 29 (85.7%) produced submissions of acceptable quality.
Conclusion: In the H&N SCC setting, p16 IHC is done exceptionally well in most laboratories submitting material to the EQA. Similarly, detection of HPV in the same type of material is also performed well, albeit with slightly more variability. The most commonly used primary markers in each of the EQAs both produced superior results when compared to the aggregate for all the alternatives.

PS-04-008
Study of CTNNB1 mutations in a case series of 25 basal cell neoplasms of the salivary gland
M. Gómez Tena*, N. Fullana Llinas, I. BLAZQUEZ, M. Gomà Gallego, M. Vazquez Pariente
*Hospital Universitari de Bellvitge, Spain

Background & objectives: Basal cell adenoma (BCA) and basal cell adenocarcinoma (BCAC) are infrequent neoplasms that mimic other basaloid salivary gland tumours. Nuclear expression of β-catenin and CTNNB1 mutations are useful in distinguishing BCA from other neoplasms.
Methods: We reviewed 23 BCA and 2 BCAC diagnosed at our institution between 1994 and 2022, assessing histological pattern (tubular-trabecular, solid, membranous), presence of biphasic cellularity, presence of nuclear of β-catenin expression and of CTNNB1 mutations.
Results: After reviewing the cases, two BCAs were reclassified as pleomorphic adenomas and two as myoepitheliomas. The most common pattern in BCA was tubular-trabecular (70%), followed by solid (12%) and membranous (18%). 16 cases exhibited biphasic cellularity. Nuclear β-catenin staining was demonstrated in 15 cases (focal in 10, diffuse in 5), in 6 of them only epithelial cells showed positivity while in 9 it was present also in the stroma. CTNNB1 mutations were present in 12 out of the 17 BCA: six I35T, four T41I and one S45C. Membranous BCA didn't show biphasic cellularity, nuclear β-catenin or CTNNB1 mutations. β-catenin nuclear expression and CTNNB1 mutations were absent in the two BCAC.

Conclusion: The presence of CTNNB1 was a common finding in the BCAs of our sample, which is consistent with the current literature. Membranous BCAs lack biphasic cellular pattern, nuclear β-catenin expression and CTNNB1 mutations in contrast to other morphologic subtypes of BCA.

PS-04-009

Determination of vimentin 3 (Vim3) and miR-15a expression profile in ameloblastomas: a preliminary study

S.E. Gultekin*, H. Goebel, E. Baris, B. Koditz, İ. Atak Secen, M. Freifrau von Brandenstein
*Gazi University Faculty of Dentistry, Turkey

Background & objectives: Ameloblastoma is a mostly benign but locally aggressive odontogenic tumour. Vim3 was defined as a different protein with a unique C-terminal ending and proposed as a differential marker for kidney tumours. We aimed to determine Vim3 expression profile in ameloblastomas.
Methods: The study was conducted immunohistochemically on a total of 45 paraffin-embedded tissue samples including conventional ameloblastoma (n:15), unicystic (n:15) and dental follicle as control (n: 15). The expression of Vim3 and Full - length (FL-vimentin) and related miRs (mir 498 and mir 15a) was detected by using immunohistochemistry and q RT- PCR.
Results: The positive staining with Vim3 was seen in parenchymal cells (ameloblastoma-like cells) whereas FL- vimentin was solely positive in the stroma. The tumour cells were not stained by FL- vimentin. A significant, increase of Vim3 ($p<0.05$) and mir 15a ($p<0.0001$) and a slight increase of mir 498 in the samples of conventional ameloblastoma cases were detected compared to unicystic and controls.
Conclusion: Here, we identified the first time Vim 3 expression in ameloblastomas which is structurally and functionally different from full-length (FL) vimentin. Our preliminary data displayed the expression pattern of Vim3 in ameloblastomas which may have the potential to be used as a biomarker in the future.
Funding: The Scientific and Technological Research Council of Türkiye (TÜBİTAK) and German Academic Exchange Service (DAAD) Bilateral Cooperation Travel Support Program

PS-04-010

Multiple primary carcinoma in the oral cavitiy: new insights into clinicopathological and molecular characteristics

A.B. Larqué Daza*, J. de la Oliva, P. Jares, P. Castillo, G. Frigola, C. Marti, A. Ferrer, E. Garcia, L. Alos
*Hospital Clínic of Barcelona, Spain

Background & objectives: The development of multiple primary carcinomas in the oral cavity is attributed to the field cancerization phenomenon. The objective of this study was to determine similarities or differences in gene mutations between the primary (index) tumours and the subsequent lesions.
Methods: A retrospective pathology database search was performed to identify all oral squamous cell carcinomas diagnosed at our institution from the last 15 years. Patients' demographics, clinical history, and microscopic findings were reviewed to identify multiples primary oral carcinomas. Eight samples corresponding to four index tumours, two second primary tumours and two recurrences were sequenced by next generation sequencing.
Results: 501 patients were diagnosed with oral squamous cell carcinomas in our hospital. Among these, 43 patients (8.6%) developed two or more primary tumours. Multiple primary tumours frequently affected older women and appeared preferentially in the tongue. The next generation sequencing panel showed a totally different molecular profile between the first tumours (index tumours) and second primary tumours, whereas common molecular alterations, consistent with clonality, were found in the index tumours and their tumour recurrences. Moreover, three separate TP53 mutations was found in a recurrent tumour.
Conclusion: In conclusion, the development of multiple primary tumours in the oral cavity is a frequent event that occurs predominantly in older women. The next generation sequencing cancer panels can be useful to differentiate second primary tumours from tumoral recurrences. The finding of three separate TP53 mutations in one of the recurrence tumour could suggest that it is a recurrent polyclonal tumour.

PS-04-011

Primary osteosarcoma of the mandible: a report of seven cases

W. Majdoub*, K. Ben Lazreg, S. Mestiri, A. Baccouche, L. Jaidane, D. Benletaifa, M. Krifa, A. Bdioui, S. Hmissa
*Pathology Department Sahloul Hospital, Tunisia

Background & objectives: Osteosarcomas account for 40-60% of primary malignant bone tumours and can arise in any bone. The localization in the mandibula is extremely rare. We aim to provide a clinicopathological description of 7 cases of osteosarcoma of the mandibule (MOS).
Methods: We conduct a retrospective study of 7 patients diagnosed with MOS listed in the Cancer Registry of Center Tunisia during a period of 15 years from 2006 to 2021. MOS were diagnosed on biopsy or on hemimandibulectomy specimen.
Results: The mean age was 46 years with extremes of 16 and 87 ans. There were 4 females and 3 males. All tumours have an osteolytic aspect on imaging consistent with malignancy. Two cases were diagnosed on biopsy and five cases on hemimandibulectomy specimen. The tumour was localized in the mandibular body in three cases and in the horizontal branch in four cases. Median size was 4.7 cm and ranged from 3 to 7.5 cm. All tumours were of high grade with a chondroblastic osteosarcoma in two cases and an osteoblastic chondrosarcoma in four cases. Chemotherapy was administrated in 6 cases and radiotherapy in a case.
Conclusion: Osteosarcoma has a large histomorphological spectrum and can be classified into 3 groups: low-grade (paraosteal or central), intermediate grade (periosteal) and high grade (conventional, telangiectasic and small cell). The conventional subgroup includes osteoblastic, chondroblastic and fibroblastic osteosarcoma. There is no specific tumour classification system for MOS. Two common misdiagnoses are benign tumours and chondrosarcomas on biopsy samples. Immunohistochemistry lacks diagnostic specificity but might be helpful in some cases. The prognosis is poor and deaths are frequently due to local relapse.

PS-04-012

PD-L1 immunohistochemistry in head and neck squamous cell carcinoma: an audit of positivity rates and turnaround times at a referral centre in the United Kingdom

K. Moutasim*, B. Templer
*University Hospital Southampton, United Kingdom

Background & objectives: PD-L1 immunohistochemistry is employed to identify patients that might respond to anti-PD1 immunotherapy.
The principal aim of this audit was to compare the positivity rates at a large referral centre (University Hospital Southampton) with those in published clinical trials.
Methods: This was a retrospective audit of hospital records of 100 PD-L1 cases (2021-2022), that had been stained with the 22C3 PharmDx Dako antibody. Scoring was performed using the combined positive score (CPS). Turnaround times of test results were also recorded, in addition to histopathological data from individual tumours.
Results: Over 90% of cases tested had a CPS of 1 or more and were therefore regarded as being positive. The remaining cases had a CPS of <1 and were regarded as negative. These 'real life' data are

comparable (if slightly higher) than those from published clinical trials.
More than 75% of cases were reported in 10 days, as per the department's policy.
Conclusion: The KEYNOTE-048 trial found 85% of cases had a CPS of 1 or more which is exceeded by our local 'real life' rate of 92%. Our local PD-L1 positivity rates for head and neck squamous cell carcinoma were comparable to those in published clinical trials. Turnaround times were similarly deemed to be satisfactory.

PS-04-013
Nodular fasciitis of parotid gland: an uncommon lesion and a mimic of pleomorphic adenoma - a case series
S. Naresh Shah*, S. Kar
*Apollo hospitals, India

Background & objectives: Nodular fasciitis (NF) is a self-limiting, pseudosarcomatous process composed of fibroblasts and myofibroblasts. It commonly affects the upper extremity, head and neck region and lower extremity. Uncommon in parotid gland it mimicks pleomorphic adenoma (PA) cytologically.
Methods: We retrieved cases of NF of parotid gland from the laboratory interface system from 2016 to 2021 in Apollo hospital, Chennai, India.
Results: We report 8 cases of NF of parotid gland. The age of the patients ranged from 4 to 72 years, with male preponderance. Fine needle aspiration (FNA) was performed in 6 cases which was followed up by biopsy. A diagnosis of PA was made in 3 cases on cytology, which turned out to be NF on histology. Subsequent cases raised a suspicion of NF on cytology itself, which was confirmed by histopathological examination. Two cases did not have cytological evaluation and were excised with a clinical diagnosis of PA.
Conclusion: NF is a self -regressive benign lesion which can be left alone or treated by conservative surgery. It can mimic PA and few other benign and malignant lesions cytologically. We report these cases to familiarize the practicing pathologists with this entity, with a special emphasis on the importance of cytological analysis of these lesions, so that a presurgical diagnosis of NF may be rendered and unwarranted surgeries be avoided.

PS-04-014
Tumour immune microenvironment in odontogenic carcinomas
K. Oh*, S. Cho, J. Lee, H. Yoon, S. Hong
*Dankook University, Republic of Korea

Background & objectives: This study aimed to investigate the tumour immune microenvironment in odontogenic carcinomas and ultimately determine the applicability of immunotherapy as a novel therapeutic strategy and the prognostic significance of immune markers in patients with odontogenic carcinomas.
Methods: The expression of T-cell markers including CD3, CD8, and FOXP3 was visualized by immunohistochemistry in 21 tissue samples of odontogenic carcinomas. Immune profiles were determined for each tumour type, and the density of T-cell subsets was calculated based on their spatial distribution. The associations of these immune markers with clinicopathological factors were statistically analysed.
Results: 57.1% (12/21) of the cases studied were the immune-inflamed phenotype, which was defined as the presence of T cells in the tumour parenchyma. Among tumour types, the frequency of the immune-inflamed phenotype was highest in ameloblastic carcinoma (87.5%; 7/8) and lowest in clear cell odontogenic carcinoma (25.0%; 1/4). The densities of CD3+ and CD8+ T cells were significantly higher in the stroma than in the parenchyma (both, $P < 0.001$), and no correlations were observed between the densities of intratumoral and stromal CD3+, CD8+, and FOXP3+ T cells (all, Pearson correlation coefficient < 0.3). The intratumoral CD8+/CD3+ cell ratio was inversely associated with tumour size ($P = 0.048$).
Conclusion: Taken together with the results of our previous study on PD-L1 expression in odontogenic carcinomas, this study further supports the therapeutic potential of immune checkpoint blockade in patients with odontogenic carcinomas, especially in those with advanced ameloblastic carcinoma. Among T-cell subsets, the immune response by intratumoral CD8+ T cells may primarily inhibit tumour progression in odontogenic carcinomas.
This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. RS-2023-00212868).

PS-04-015
Diagnostic algorithm for salivary gland carcinomas
B. Othman*
*Charles University, Czech Republic

Background & objectives: The newly emerging salivary gland carcinomas (SGC) have demonstrated diverse differentiation, while specific molecular mutations have been verified in a few neoplasms We propose a diagnostic algorithm that is based on molecular and immunohistochemical findings for each salivary gland carcinoma.
Methods: After mining the medical literature for all SGCs published from 2015, we annotated each SGC for the marker(s) used and the level of evidence attained for diagnosing each published case. Questionable diagnoses were discarded. All SGCs were converted into nodes to which immunohistochemical markers were aligned to the right while molecular investigations were aligned to the left for clustering computationally.
Results: We proposed a diagnostic algorithm a diagnostic that is based mainly on morphologic features and immunohistochemical investigations and supported by molecular analysis. The generated results were compared to the findings retrieved from a reliable registry in which 1428 cases were diagnosed molecularly (using FISH analysis next-generation sequencing, PCR or a mixture of all). The accuracy of the diagnostic algorithm was 92%. The proposed algorithm was illustrated as a flowchart, which combines the use of principal immunohistochemical markers (IHC), complimentary ones and confirmatory molecular investigations. The SGCs which could be diagnosed with the listed markers were labeled for further consultation with expert pathologists.
Conclusion: Our algorithm helps with diagnosing 19 SGCs, which present either monomorphous neoplastic spindle cells (e.g., myoepithelial carcinoma), biphasic populations (e.g., adenoid cystic carcinoma) or more (e.g., mucoepidermoid carcinoma). It also covers the morphologic features, including cellular differentiation (e.g., clear cells or oncocytes), growth patterns (e.g., cribriform or mucinous), and high-grade transformation (e.g., dedifferentiation and undifferentiation). It also highlights some markers whose expression could distinguish malignancies arising in benign lesions (e.g., Warthin-like mucoepidermoid carcinoma) from benign neoplasms masquerading as malignancies.

PS-04-016
Effect of SMARCA4 in anaplastic thyroid cancer
C. Wang*, U. Bhawal, H. Okada
*Department of Histology and Embryology, Nihon University Graduate School of Dentistry at Matsudo, Japan

Background & objectives: Anaplastic thyroid cancer is one of the most aggressive and deadliest malignancies. This study aimed to investigate the biological roles and underlying molecular mechanisms of SMARCA4 in anaplastic thyroid cancer.
Methods: Western blot analysis, transwell assay, flow cytometry and quantitative real-time PCR has been carried out to evaluate the changes

in multiple cellular functions after SMARCA4 knockdown in an anaplastic thyroid cancer cell line, ASH-3. DNA microarray was used to uncover biologically coherent gene sets. Immunohistochemical analysis was performed to detect the expression level of SMARCA4 in 19 anaplastic thyroid patients.
Results: In vitro, SMARCA4 knockdown significantly altered the cell proliferation, migration, invasion, and apoptosis of ASH-3 cells. Silencing of SMARCA4 also markedly amended the sensitivity of cisplatin in ASH-3 cells. Knockdown of SMARCA4 influenced the expression of HOX proteins. Ingenuity pathway analysis suggested that the effect of SMARCA4 is regulated by immunogenic cell death signalling pathway, ferroptosis pathway etc. Abundant giant cells with mitotic figures and pleomorphic spindle cells accompanied by inflammatory infiltration were present in anaplastic thyroid cancer. Immunohistochemical results revealed that SMARCA4 is highly expressed in anaplastic thyroid cancer tissues. Positive p53 expression was observed in these tissues while cyclinD1 and p63 were negative.
Conclusion: Taken together, these results provide new insights into the biological impacts of SMARCA4 in anaplastic thyroid cancer. Furthermore, we provide clues to examine SMARCA4 as an imperative biomarker for predicting anaplastic thyroid cancer. Additional research is underway to ascertain functional regulation of SMARCA4 in anaplastic thyroid cancer.

PS-05 | Poster Session Infectious Diseases Pathology

PS-05-001
Histopathological characteristics of lesions suspected of Leishmaniasis: report of a series of patients

D. Nunes Oliveira*, J. Carneiro Melo, G. Ferreira Morgantetti, G. Alencar Medeiros, H. Neves Feitosa Filho, V. Queirós Calheiros Campelo Maia, F.R. Oliveira Cavalcante Júnior, J.S. Pereira Filgueira, J. Silva Pinheiro Firmino, N. Pinheiro Rodrigues
*University of Fortaleza, Brazil

Background & objectives: Leishmaniasis is a parasitic disease caused by Leishmania parasites, transmitted through the bites of infected sandflies. Our aim was to analyse the histopathological findings of biopsies from patients suspected to have leishmaniasis.
Methods: This was a retrospective, descriptive study of histopathological reports of biopsies of patients with suspected leishmaniasis, carried out in a pathology laboratory, in northeastern Brazil, from January 2020 to March 2023. The variables age, sex, histopathological subtype, clinical picture and what was the conclusion of diagnosis were analysed.
Results: 39 histopathological reports (36 skin biopsies, 3 gastric) with suspected leishmaniasis with a mean age of 37.4 years and 51.2% men. 84.6% with a single lesion located mainly on the lower limb (53.8%). Lesion types included ulcer (46.1%), papule (28.2%) and nodule (25.6%). The main histopathological changes observed were lymphoplasmacytic inflammatory infiltrate, well-formed epithelioid granuloma (43.7%), malformed granuloma (56.2%) and focal necrosis (15.3%). Leishmania amastigotes in 17 biopsies (82.3% in the dermis and 17.6% in the gastric mucosa) and Giemsa was positive in 11 (skin) and 3 (stomach). Granuloma ($P = 0.030$), ulcer formation ($P = 0.036$) and Giemsa positive ($p = 0.0007$) were significantly associated with body load.
Conclusion: This study investigated suspected cases of leishmaniasis in 39 patients and found that the disease mainly affects adult men with a single lesion on the lower limb, characterized by ulcers, papules or nodules. Significant associations were found between organism load and granuloma ,ulcer formation and giemsa positive.It is important to remember that the immunocompromised are not only more susceptible to infection, but also to disseminated disease, including gastric leishmaniasis.

PS-05-002
Clinical and morphological features of acute respiratory distress syndrome in lethal cases of COVID-19

D. Shtyrts*, O. Reshetnikova, A. Ermakov, L. Rudiuk
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: Acute respiratory distress syndrome(ARDS) is one of the most severe clinical complications of the COVID-19. The aim of this study was to reveal pathomorphological and clinical peculiarities of the fatal outcomes of ARDS in COVID-19 patients of various age groups.
Methods: Autopsy examinations were performed in 106 fatal cases of COVID-19. Medical histories and full post-mortem examinations data were analysed with emphasis the morphogenesis of the structural changes in the lung parenchyma in correlation with the patient's age and the length of stay in the hospital. Gross pictures of the internal organs were examined and their tissue samples studied histologically.
Results: Studies revealed that 52% of patients with a fatal outcome of ARDS were over 70 y.o., the minimum number was occupied by the age group 31-50 years (12%) and 36% were included in the 51-70 y.o. group. Lung tissue's histology showed that intra alveolar edema, formation of hyaline membranes, desquamation of the alveolar epithelium and haemorrhagic syndrome were observed in all corpses, with prolonged duration (up to 21 days) in older patients. On the 8th day of hospital stay, all individuals older than 50 years had proliferative features in the lung tissue. Their combination with exudative changes, were recorded for the longest time (up to 30 days) in elderly individuals.
Conclusion: The lungs parenchyma' morphological features in the fatal outcomes of the COVID-19 infection depend on the age of the patient and the duration of the disease (stay in the hospital). The change of acute exudative processes to proliferative ones in most cases is characterized by a long-term combined manifestation of both. The morphogenesis of damage and repair of the lung parenchyma in COVID-19 with an emphasis on the patient's age should be investigated in order to develop adequate therapeutic strategies.

PS-06 | Poster Session Nephropathology

PS-06-001
Peritubular capillaritis in lupus nephritis: frequency and relationship with disease activity

B.B. Cengiz*, E. Tekin, M.F. Açıkalın, Ş.B. Yaşar
*Eskişehir Osmangazi University, Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Lupus nephritis (LN) is associated with a shorter time to death in systemic lupus erythematosus. The objective of this study was to determine the frequency of peritubular capillaritis (PTC) and its relationship with active and chronic lesions in LN.
Methods: The specimens of 57 patients diagnosed with LN were re-evaluated using revised 2018 ISN/RPS classification and the modified NIH scoring system. Peritubular capillary inflammation was evaluated according to the Banff classification and cases with PTC scores of 2 and 3 were defined as positive for PTC. The patients were grouped by high/low activity and chronicity index scores.
Results: 45 (78.9%) patients were female and 12 (21.1%) were male, with a mean age of 27.43 years (range 8–71). PTC was captured in 45 (78.9%) patients, with PTC scores of 1, 2 and 3 in 20 (35.08%), 20 (35.08%), and 5 (8.7%) patients, respectively. Higher severity of PTC was detected in cases with elevated serum creatinine levels ($p<0.001$). The severity of PTC was higher in class 4 patients than in class 3 patients ($p=0.005$). The rate of detection of PTC score 2-3 was higher in patients with an activity index of 6 and above ($p=0,032$). However, no significant correlation was found between the chronicity index and PTC.

Conclusion: The findings of this study suggest that PTC is a frequently observed pathological feature in patients with LN. In addition, the severity of PTC appears to be positively associated with high serum creatinine levels, while higher PTC scores are detected in cases with a high activity index.

PS-06-002

Investigating viruses as potential causative agents for tubulointerstitial nephritis

M. Nackenhorst*, L. Leiendecker, A. Kousanadis, T. Wiesner, K. Smith, P. Lyons, W. Weninger, R. Kain
*Medical University of Vienna, Austria

Background & objectives: Tubulointerstitial diseases pose a particular challenge within the spectrum of renal diseases, as often no specific causative agents can be identified. There is a significant number of cases where morphological characteristics suspicious for a viral aetiology are seen.
Methods: 19 FFPE samples were selected for analysis based on histomorphological signs of viral infection from the tissue archive of the Department of Pathology at the Medical University of Vienna. DNA and RNA were isolated. We custom build a metagenomic pipeline to adapt to the specific challenge of identifying viral sequences which are small in an abundance of host contamination.
Results: The quantity and quality of the resulting DNA and RNA was low, presumably because formalin fixation and paraffin embedding cause fracturing of nucleic acids and protein crosslinking. Library generation was possible for DNA samples exclusively.
BK-Polyomavirus was identified in 19/19 cases with our custom pipeline. Two other established pipelines showed comparable results. While all metagenomic pipeline results indicated Polyomavirus as a potential candidate, qPCR did not confirm these results.
Potential errors such as multiplexing errors and uneven distribution of reads over the genome were investigated in great detail with no indication of having taken place.
Conclusion: Finding the underlying cause for tubulointerstitial nephritis (TIN) without proven aetiology could pave the path for implementing future targeted treatments and can be considered an important goal - not least from a health economical point of view.
Viral agents are, however, most likely not a causative agent in TIN. Viruses remain elusive and difficult to identify in metagenomic approaches and there are several caveats to consider when virus hunting.

PS-06-003

Direct infiltration of the kidney by clonal lymphocytic or plasmacytic populations in the context of haematologic abnormalities: a probably underestimated condition

K. Palamaris*, P. Korkolopoulou, P. Foukas, E. Lakiotaki, A. Stofas, M. Kaniadaki, A. Chalkia, A. Gerakis, E. Dermitzaki, E. Theodoropoulou, M. Papasotiriou, K. Stylianou, E. Papachristou, E. Kastritis, H. Gakiopoulou
*First Department of Pathology, National and Kapodistrian University of Athens School of Medicine, Greece

Background & objectives: Direct infiltration of the renal parenchyma represents a less frequently reported but probably underestimated mode of renal involvement in the context of lymphoproliferative disorders or plasma cell dyscrasias. We present 20 patients with kidney infiltration by a hematologic neoplastic population.
Methods: Light microscopy with histochemical and immunohistochemical stains (B-cell/T-cell/plasma-cell markers), immunofluorescence, and electron-microscopy. IgG-subclasses and DNAJB9 investigations. Clonality-testing was used to confirm the clonal nature of the lesions. Main indications of renal biopsies included acute kidney injury and/or proteinuria/nephrotic syndrome. Of note that in 25% of patients there was not known hematologic abnormality before biopsy, while only one patient had multiple-myeloma(MM).
Results: Most biopsies showed infiltration by clonal B-cell or plasma-cell populations compatible with chronic-lymphocytic-leukaemia, marginal-zone-lymphoma, Waldenström-macroglobulinemia, diffuse-large-B-cell lymphoma, mantle-cell-lymphoma or MM. In four cases, defined as either B-cell or plasma-cell malignancy, further typing was unattainable and additional investigations including control for MYD88L265P-mutation, were suggested. In 2 biopsies, renal infiltration by chronic-myelomonocytic-leukaemia (CMML) and a T-cell lymphoproliferative disorder was diagnosed, respectively. Clonality-testing confirmed the clonal nature of the populations observed. Besides direct infiltration, in ~40% of patients, additional patterns of monoclonal kidney injury were observed, including monoclonal-immunoglobulin-deposition-disease, proliferative-glomerulonephritis-with-monoclonal-immunoglobulin-deposits, immunotactoid, fibrillary, cryoglobulinemic glomerulonephritis, and two membranous cases, one with IgG1-restriction and one in the context of CMML, reported for the first time.
Conclusion: Direct renal invasion by neoplastic lympho- or plasmacytic populations in the context of hematologic abnormalities is probably underestimated. Sometimes, the infiltrates are mild and focal and can be easily overlooked and mistaken for inflammation. In cases without coexistent glomerular/tubular involvement missing of these infiltrates may lead to erroneous therapeutic decisions. On the other hand, despite the presence of glomerular/tubular monoclonal involvement, infiltrates also deserve further investigation to reveal their neoplastic nature leading to a more appropriate disease staging and therapy.

PS-06-004

Macrophage densities in native kidney biopsies correlate with renal dysfunction and predict end-stage renal disease

J. Schmitz*, M.B. Pfenning, I. Scheffner, K. Schulte, A. Khalifa, H. Tezval, A. Weidemann, A. Kulschewski, U. Kunzendorf, S. Dietrich, H. Haller, J.T. Kielstein, W. Gwinner, J.H. Bräsen
*Hannover Medical School, Institute of Pathology, Nephropathology, Germany

Background & objectives: Renal macrophages and monocytes are main players in inflammation. Their relevance on clinical outcomes remains to be determined in native kidney diseases. Precise quantification of innate immune cell infiltration can support morphological diagnostics.
Methods: In our cross-sectional study 324 renal biopsies comprising 17 disease entities and normal renal tissues for comparison were included. Samples were stained for CD68+ macrophages, CD14+ monocytes and CD163+ alternatively activated macrophages. Cell densities in cortex, medulla and whole renal tissue were precisely quantified by a pixel-based approach (QuPath). Clinical data at time of biopsy and follow-up data were accessible.
Results: Biopsies with native kidney diseases presented higher CD68+- and CD163+-macrophage densities than controls (whole renal tissue, cortex, medulla, $P<0.001$). CD68+-macrophage densities correlated with eGFR and risk of ESRD (defined as requirement of permanent dialysis) in whole cohort and separate diseases (Spearman's/Chi Square test, $P<0.05$): a high cortical CD68+-macrophage density (>median 0.875%) predicted a higher risk of ESRD at follow-up. Multivariable Cox regression revealed a 4-fold higher risk of ESRD when macrophage density was >median (hazard ratio=3.911, $P<0.05$), whereas % interstitial atrophy/fibrosis had minimal effect (hazard ratio = 1.032, $P<0.001$). Patient age, global glomerulosclerosis, presentation (acute kidney injury (AKI), AKI on chronic kidney injury (CKD), CKD) and sex had no effect.
Conclusion: Innovative predictive data can be generated by increasing precision and objectivity using digitally-based morphologic analyses. Patients

with high risk for ESRD can be identified by quantification of macrophages in native renal biopsies. Further studies will show whether macrophages have a bystander or independent role in renal injury. Macrophages might be a promising therapeutic target in different renal diseases.
JS and JHB received funding from German Federal Ministry of Education and Research (BMBF No. 13GW0399B).

PS-07 | Poster Session Other Topics

PS-07-001
HPV infection is linked to enriched T- and dendritic cell infiltration in squamous cell carcinomas from 8 different origins

N. Blessin*, N.F. Debatin, E. Bady, J.H. Müller, T. Mandelkow, R. Simon, M. Lennartz, G. Sauter, E. Burandt, S. Steurer, T.S. Clauditz, C. Bernreuther, A. Menz
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: Given that HPV infection is generally accompanied by gene alterations, epigenetic changes, and altered microRNA expression in squamous cell carcinomas (SCCs), the composition and degree of immune checkpoint expression on immune cell subtypes might be linked to the HPV status.
Methods: To study differences between 199 (51%) HPV-associated and 194 (49%) HPV-independent squamous cell carcinomas from 8 different origins, the spatial interplay of more than 30 TIM3, CTLA-4, PD-1/-L1 expressing leukocyte subpopulations was analysed in a tissue microarray format using our 21-marker-BLEACH&STAIN multiplex fluorescence immunohistochemistry approach and analysed using a deep learning-based image analysis framework.
Results: The density of CD8+ cytotoxic T-cells, CD4+ T-helper cells, and CD11c+ dendritic cells, irrespective of the tissue compartment, was significantly linked to HPV-positivity ($p \leq 0.006$ each), while the density of FOXP3+ T-cell, CD20+ B-cells, M1/ M2 macrophages showed no difference between HPV positive and negative cases. Interestingly, except for reduced CTLA-4 expression on CD4+ T-cells in HPV positive cases, no other link between immune checkpoint expression and HPV status was found. A significantly higher interaction pattern between CD8+/ CD4+ T-cell and CD11c+ dendritic cells ($p<0.001$) as well as between CD8+ cytotoxic T-cells and CD4+ T-helper cells ($p=0.005$) was found in HPV-associated SCCs.
Conclusion: HPV-associated squamous cell carcinomas of various origins were characterized by a higher degree of cytotoxic and helper T-cell as well as dendritic cell density and a reduced CTLA-4 expression on T-helper cells compared to HPV independent cases. In addition, a stronger interaction network between non-regulatory T-cells and dendritic cells was linked to HPV-associated SCCs.

PS-07-002
An evaluation of physician's knowledge and practices about pre-analytical phase in pathology: the first survey-based study in Morocco

S. Chaib*, J. Kharmoum, M. El jiar, I. Eliahiai, M. Chraibi
*University Hospital Mohammed VI, Morocco

Background & objectives: The pre-analytical phase in pathology is crucial in obtaining reliable analysis results. Mismanagement of this phase can compromise the quality of results, which may impact clinical decisions and patient treatments.
Methods: We conducted a national cross-sectional anonymous survey among Moroccan physicians regarding the pre-analytical phase in pathology, designed on the Google Forms platform. The target population is physicians practicing in the public, academic, and private sectors, responded to questionnaire covering various aspects of the pre-analytical phase. A total of 341 participants were surveyed including 52,4% resident, 22,7% interns, and 4,5% professors.
Results: Results found 94,5% of participating physicians didn't receive any training on the pre-analytical phase. Specific knowledge was also limited, with a percentage of ignorance regarding the fixative (20.3%), and the required volume to fix samples (80%). 13.7% don't routinely orient their specimens, while 16.2% always open specimens. 15% believe that not all tissue samples need to be sent for histological examination. 47.4% think that it is acceptable to store specimens without fixative in a refrigerator for more 24H. We noticed that inadequate practices in case of fixative unavailability; using plastic bags (38.2%). Poor contact with pathologists were reported (95.1%). 80,7% were unaware of the effect of fixation on anatomopathological study.
Conclusion: This study revealed significant gaps in the management of specimens. Solutions such as practical workshops, practical guides posters in departments, and a platform to facilitate communication between physicians and pathologists have been proposed to address these gaps and ensure quality healthcare.

PS-07-003
Using propidium iodide instead of DAPI can expand the use of stored tissue samples for immunofluorescence

K. Cizkova*, K. Koubova, Z. Tauber
*Department of Histology and Embryology, Faculty of Medicine and Dentistry, Palacky University, Olomouc, Czech Republic

Background & objectives: Archival tissues are a rich source of potential material for retrospective and comparative studies. Clear detection of nuclei is crucial in immunofluorescence however we observed blurred, poor quality DAPI staining of nuclei in several archival specimens.
Methods: We investigated the effect of aging of tissue blocks on the quality of nuclear staining. Placental tissue samples stored for 1, 5, 18 and 26 years were examined for DAPI and propidium iodide staining. ImageJ software was used to detect nuclei. In addition, the same samples were stained with haematoxylin to confirm tissue integrity.
Results: Although haematoxylin staining showed good quality in all samples, DAPI staining deteriorated with increasing age of the tissue blocks, a phenomenon that could be improved by using propidium iodide. Replacing DAPI with propidium iodide significantly increased the detectability of nuclei in tissue blocks stored for 18 or 26 years using ImageJ software.
Conclusion: Based on our results, we suggest that replacing DAPI with propidium iodide could extend the use of immunofluorescence techniques to archival tissue samples.

PS-07-004
Comparison of INSM1 immunostaining with established neuroendocrine markers Synaptophysin and Chromogranin A in over 14,000 neuroendocrine and non-neuroendocrine tumours

K. Möller*, N. Gorbokon, D. Dum, C. Hube-Magg, C. Fraune, M. Lennartz, N. Blessin, E. Burandt, R. Krech, T. Krech, A.H. Marx, G. Sauter, R. Simon, C. Bernreuther, S. Minner
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: INSM1 is a transcription factor protein which is increasingly used as an immunohistochemical marker for neuroendocrine differentiation.
Methods: To determine the prevalence of INSM1 expression in tumours and its expression pattern in normal tissues, tissue microarrays containing 14,908 samples from 117 different tumour types/ subtypes as well as 76 different normal tissues were analysed by immunohistochemistry.
Results: INSM1 was positive in 89.2% of 471 neuroendocrine neoplasms (NEN) and in 3.5% of 11,815 non-neuroendocrine neoplasms

that were successfully analysed. INSM1 positivity occurred in 59 non-neuroendocrine tumour entities, of which 15 entities contained at least one strongly positive case. Comparison with synaptophysin and chromogranin A revealed that in NEN, synaptophysin showed the highest sensitivity (93.3%), followed by INSM1 (89.2%) and chromogranin A (87.5%). In neuroendocrine carcinomas (NEC), sensitivity was highest for INSM1 (88.0%), followed by synaptophysin (86.5%) and chromogranin A (66.4%). The additional use of INSM1 increased the sensitivity for detecting neuroendocrine differentiation in NEN from 88.2% (synaptophysin and chromogranin A) to 91.2% (synaptophysin, chromogranin A and INSM1).
Conclusion: Our study shows that INSM1 is a useful additional marker for neuroendocrine differentiation that shows a particularly high sensitivity in NEC. The additional use of INSM1 results in a higher sensitivity for the identification of a neuroendocrine differentiation than what can be obtained by using only synaptophysin and chromogranin A.

PS-07-005
PD-L1 IHC 22C3 pharmDx: real time study for stained slide stability on multiple tumour types
D. Moquin*, S. Tabuena-Frolli, S. Hund, L. Peltz, M. Adams, J. Vasquez, G. Toland, B. Watts, K. Kersch, M. Kalpakoff
*Agilent Technologies, Inc., USA

Background & objectives: PD-L1 22C3 IHC pharmDx (SK006) is a qualitative immunohistochemical (IHC) assay to detect PD-L1 expression in formalin-fixed, paraffin-embedded (FFPE) tissues. Studies have been conducted to evaluate the stability of the PD-L1 IHC 22C3 pharmDx stain on multiple FFPE tumour types.
Methods: Slides stained using PD-L1 IHC 22C3 pharmDx from 10 different tumour types were aged in the dark at ambient temperature and assessed at pre-determined time intervals. Slides were blinded, randomized, and scored using Combined Positive Score (CPS). Slides stained at time zero (T0) were used as reference for remaining time points. Each tumour type was studied and analysed separately.
Results: Stability was determined using regression analysis and was based on the specimen in the cohort exhibiting the shortest stability. Analysis performed on CPS results indicated the following stained slide stabilities for each tumour type when stored in the dark at ambient temperature: 810 days for Urothelial Carcinoma (UC), 550 days for Gastric Carcinoma (GC), 735 days for Triple-negative Breast Cancer (TNBC), 763 days for Head and Neck Squamous Cell Carcinoma (HNSCC), 951 days for Esophageal Cancer (EC), 660 days for Ovarian Carcinoma (OC), 738 days for Biliary Tract Adeno Cancer (BTAC), 597 days for Colorectal Carcinoma (CRC), 735 days for Cervical Cancer (CC) and 1085 days for Prostate Cancer (PC).
Conclusion: Stability of PD-L1 IHC 22C3 pharmDx stained slides is of interest when patient specimens are re-scored for a different cutoff or for research purposes. These studies demonstrated a minimum stained slide stability of 550 days across the 10 tumour types studied, providing high confidence in the assay performance on aged, stained slides when stored in the dark at ambient temperature. The stability of slides stained with PD-L1 IHC 22C3 pharmDx remains a parameter specific to tumour type.

PS-07-006
A way to teach pathology through gamification: Clue and Escape 60
S. Maria Macêdo, R. Barreira Pitombeira, L. Barreira Pitombeira, G. Machado Nepomuceno Correia Lima, C. Albuquerque Colares, C.C. Rodrigues Augusto Gonçalves, I. Castelo Branco Fontenele Costa, V. Veras Pereira de Matos Filho, A.D. Muniz de Sousa, V. Vieira Freitas Araujo, J. Carneiro Melo, E. Tome de Sousa, D. Nunes Oliveira*
*University of Fortaleza, Brazil

Background & objectives: Gamification is a game thinking-based strategy, proven by studies to enhance learning in academic contexts, by increasing apprenticeship efficiency and engagement. This paper aims to report the experience with gamification as a teaching tool in pathology.Gamification is a game thinking-based strategy, proven by studies to enhance learning in academic contexts, by increasing apprenticeship efficiency and engagement. This paper aims to report the experience with gamification as a teaching tool in pathology.
Methods: Two games were created as tools for teaching pathology in the sixth semester of the medical course at a private university. One of the games was about chronic obstructive pulmonary disease and incorporated elements from the "Clue" game, while the second one, addressed Hodgkin's and non-Hodgkin's lymphoma, based on the game "escape 60".
Results: Regarding the clue game, 48 responses were received, with 97.9% (47) stating that the game aided in knowledge fixation and met learning objectives. Ratings were as follows: 58.3% gave it a 10, 25% gave a 9, 4.1% gave an 8, 4.1% gave a 7, and 2.08% gave a 5, averaging 9.3. Additionally, 95.8% want the game to continue being applied. For "Escape 60," 23 responses were received, with a consensus that this strategy aided in knowledge fixation, met learning objectives and should continue being used. Ratings were: 65.2% gave a 10, 30.4% gave a 9, and 4.3% gave an 8.
Regarding the clue game, 48 responses were received, with 97.9% (47) stating that the game aided in knowledge fixation and met learning objectives. Ratings were as follows: 58.3% gave it a 10, 25% gave a 9, 4.1% gave an 8, 4.1% gave a 7, and 2.08% gave a 5, averaging 9.3. Additionally, 95.8% want the game to continue being applied. For "Escape 60," 23 responses were received, with a consensus that this strategy aided in knowledge fixation, met learning objectives and should continue being used. Ratings were: 65.2% gave a 10, 30.4% gave a 9, and 4.3% gave an 8.
Conclusion: This study demonstrated that the use of gamification resulted in positive results, supporting the validity of this innovative approach in the teaching-learning process. Furthermore, this study highlighted scholarly perspectives on creating and utilizing dynamic resources aimed at increasing student engagement.

PS-07-007
Effects of ischemia and fixation time on specimens stained with PD-L1 IHC 22C3 pharmDx (Code SK006)
C. Roach*, J. Musser, S. Tabuena-Frolli, S. Hund, K. Kulangara
*Agilent Technologies, USA

Background & objectives: PD-L1 IHC 22C3 pharmDx is a qualitative immunohistochemical (IHC) assay for PD-L1 expression in FFPE specimens routinely processed for diagnostic evaluation. A pre-analytical variable study has been performed to assess the effects of ischemia and fixation time on PD-L1 expression.
Methods: Normal human placenta tissue was used as a model since syncytiotrophoblastic cells have features similar to malignant cells. Fresh tissue was procured, prepared and then subjected to ischemic times of 0- 24 hours. Specimens were then fixed in 10% NBF for 6 - 72 hours. A cohort of 216 placenta blocks were stained by IHC using PD-L1 IHC 22C3 pharmDx.
Results: Stained slides were evaluated and assessed for any changes in PD-L1 expression and overall staining intensity by comparing specimens prepared with various ischemic and fixation times. This data demonstrated average IHC intensity of PD-L1 expression differences of ≤ 0.5 grade between sections processed with ischemic times 0-24h and fixation times 6-72h. To leverage these results for neoplastic specimens, a titration study was performed to compare PD-L1 expression on placenta and non-small cell lung cancer (NSCLC) to assess similarities in sensitivity. Similar sensitivity to titrations was observed between placenta and NSCLC.

Conclusion: Pre-analytical effects in IHC can be minimized with standardization of specimen handling leading to enhanced specimen quality and antigen preservation. FFPE tissues prepared with various ischemic times ranging from 0-24 hours and fixation times ranging from 6-72 hours demonstrated negligible variability in intensity between conditions and was well within the expectations of IHC staining.

PS-07-008

Prostein expression in human tumours: a tissue microarray study on 19,202 tumours

F. Viehweger*, M. Lennartz, N. Blessin, C. Hube-Magg, D. Dum, A. Menz, R. Uhlig, E. Burandt, G. Sauter, R. Simon, M. Kluth, S. Steurer, T.S. Clauditz, C. Bernreuther, S. Kind
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: Prostein (P501S), also termed solute carrier family 45 member 3 (SLC45A3) is an androgen regulated protein which is preferentially expressed in prostate epithelial cells. Because of its frequent expression in prostate cancer, prostein was suggested a diagnostic prostate cancer marker.
Methods: In order to comprehensively assess the diagnostic utility of prostein immunohistochemistry, a tissue microarray containing 19,202 samples from 152 different tumour types and subtypes as well as 608 samples of 76 different normal tissue types was analysed by immunohistochemistry.
Results: Prostein immunostaining was typically cytoplasmic, granular and perinuclear and predominated in prostate cancer. Prostein positivity was seen in 96.7% of 419 prostate cancers including 78.3% with a strong staining. In 12,233 extra-prostatic tumours, prostein positivity was observed in 9.8% of cases but only 0.4% had a strong staining. Extra-prostatic prostein positive tumours were 50 different tumour categories, 12 of which included at least one strongly positive case. Extra-prostatic tumours with highest rates of prostein positivity included salivary gland tumours (7.6%-44.4%), neuroendocrine neoplasms (15.8%-44.4%), adenocarcinomas of the gastrointestinal tract (7.3%-14.8%), biliopancreatic adenocarcinomas (3.6%-38.7%), hepatocellular carcinomas (8.1%), and adenocarcinomas of other organs (up to 21%).
Conclusion: In summary, our data provide a comprehensive overview on prostein expression in human cancers. Prostein is a highly sensitive prostate cancer marker occurring in >96% of prostate cancers. Because prostein can also be expressed in various other tumour entities, labelling of a tumour mass as a prostate cancer should not be based on prostein positivity alone.

PS-08 | Poster Session Dermatopathology

PS-08-001

PRAME expression and its relationship between clinicopathological parameters and immunological markers in melanoma: an in-silico analysis

Y. Cakir*, Z. Sağnak Yılmaz, B. Lebe
*Dokuz Eylül University, The Institute of Health Sciences, Department of Molecular Pathology, Turkey

Background & objectives: PRAME is a cancer-testis antigene which showed differential expression in cancers compared to normal tissue. However, its role in immune infiltration and immunotherapy is controversial. We investigated the association between PRAME expression and clinicopathological/immunological characteristics in melanoma with bioinformatic tools.
Methods: The cBio Cancer Genomics Portal (cBioPortal), The University of Alabama at Birmingham Cancer data analysis Portal (UALCAN), Tumour Immune Estimation Resource (TIMER2.0), Gene Expression Profiling Interactive Analysis (GEPIA2), the Tumour–Immune System Interactions and Drug Bank (TISIDB) databases were used to explore the effect of PRAME expression on clinicopathologic features, immune infiltration, survival, the correlation with immune checkpoint genes expression.
Results: TCGA and metastatic melanoma (DFCI, UCLA) datasets were investigated in UALCAN and cBioPortal databases. The higher PRAME expression levels were detected in cases with higher T/N stage, metastatic and p53 non-mutant cases (p<0,001). There was no statistically significant relationship with tumour mutation burden, total neoantigen or survival status. PRAME expression was positively correlated with CD8+ T cells and follicular helper T cells infiltration and negatively correlated with CD4+ T cells, regulatory T cells, neutrophils, monocytes, CAFs and endothelial cells (p<0,05). The analyses performed with TISIDB and GEPIA2 showed that PRAME expression was negatively correlated to the expression of many immune checkpoint genes (PDCD1, PDCD1LG2, TIGIT, CD274, CTLA4, HAVCR2, LAG3) (p<0,001).
Conclusion: PRAME expression was associated with immune infiltration and immune modulator or immune check points genes. Our results suggested that it can be a potential biomarker for predicting immunotherapy response in melanoma.

PS-08-002

Genetic and epigenetic changes in melanoma progression: a TCGA based study

Y. Cakir*, M.H. Toper, B. Lebe, S. Sarıoğlu
*Dokuz Eylül University, The Institute of Health Sciences, Department of Molecular Pathology, Turkey

Background & objectives: We aimed to investigate molecular mechanisms affecting melanoma progression by comparing genetic/epigenetic features between melanoma having different Breslow thicknesses and stages via TCGA data.
Methods: Data were collected from "cBioPortal" bioinformatic service. Cases having complete information were included, metastatic cases were excluded. Cases were compared in terms of copy number variations (CNV), DNA mutations, mRNA/protein expression, agnostic biomarkers (tumour mutation burden, NTRK, HER2, NRG, RET, BRCA, KRAS, FGFR). Gene set enrichment analysis were performed with g:Profiler. p and q<0.05 were accepted as statistically significant.
Results: Breslow thickness was ≤1mm in 41 cases, >1mm in 159 cases. 230 and 34 differentially expressed genes were detected in thin and thick melanomas, respectively. g: Profiler analysis showed that these genes have roles in immune response/regulation and keratinocyte differentiation, respectively. 10 genes were hypermethylated in thick melanomas.
T stages were; Tis:7, T1:27, T2:62, T3:57, T4:51. In Tis, 252 genes had significant CNV, 147 and 3 genes showed DNA mutation with higher frequency in Tis and T1, respectively. Hypermethylation was detected for a gene in T1 and T3; 7 genes in Tis. One gene (OR10G3) had higher mRNA expression in Tis (p,q<0,05 for genes mentioned).
Other parameters weren't statistically significant.
Conclusion: Melanoma progression is a complex process comprising many genetic/epigenetic changes. Understanding these changes is essential for diagnosis and predicting melanocytic lesions' prognosis. Our results can light subsequent studies to identify the steps in melanoma progression.

PS-08-003

Feasibility and impact of embedding a larger DNA and RNA tissue-based sequencing panel for the routine care of patients with advanced melanoma in Spain

A. Carrasco Lorenzo*, N. Castrejon, M. García, M. Marginet, P. Jares, C. Montironi, J. Navarro, A. Arance, L. Alos, C. Teixido
*Department of Pathology, Hospital Clinic, IDIBAPS, University of Barcelona, Spain

Background & objectives: Targeted NGS allows a fast and efficient multi-gene analysis in melanoma. The main objective of this study is to describe the genetic alterations of melanoma cases using an NGS DNA and RNA panel, relating these results with the clinicopathological features.
Methods: Patients diagnosed with advanced melanoma at our centre from 2020 to 2022 were included. Total genomic DNA and RNA were extracted from formalin-fixed and paraffin-embedded samples for sequencing.
Results: A series of 87 advanced melanoma cases were selected for the study. The most prevalent mutated genes were BRAF (29%), NRAS (28%), ALK, KIT, and MAP2K1 (5% of each three). Co-occurrence of oncogenic mutations was detected in 24/82 (29%) of the samples, such as BRAF with CTNNB1, EGFR, ALK, HRAS, and MAP2K1; and the combination of NRAS with IDH2, IDH1, KIT, and JAK2. Amplifications and rearrangements were detected in 4 cases (5%). Significant statistical association between BRAF mutation and sun exposition was found. However, no other significant statistical associations were identified.
Conclusion: Targeted NGS testing is an essential tool in advanced melanoma patients' evaluation since it provides complete molecular genetic information required for their proper therapeutic management. This expanded knowledge about the molecular alterations of advanced melanoma could underlie the development of new effective targeted treatments.

PS-08-004
Clinicopathological features, cell cycle regulators and Ki 67 in dermatofibrosarcoma protuberans
M.S. Chang*, S. Byeon, S. Park, S. Yoo, C. Lee
*Seoul National University College of Medicine, Boramae Hospital, Republic of Korea

Background & objectives: Little is known about cell cycle regulators in dermatofibrosarcoma protuberance (DFSP). We aimed to determine key variables for adverse outcome of patients with DFSP.
Methods: We reviewed clinicopathological features for 127 cases of DFSPs having wide local excision with clear resection margin. Immunohistochemistry was conducted for p53; cyclin D1/cyclin-dependent kinase (CDK)4 and cyclin E/CDK2 as cell cycle activator; p16INK4A and p21CIP1 as CDK inhibitors; phospho-retinoblastoma (pRB), and Ki67 (a proliferation marker).
Results: Compared to 97 non-recurrent DFSPs, 30 recurrent DFSPs revealed a predilection for head and neck in location, larger tumour size, deeper invasion beyond the subcutis, more frequent mitotic figures, more diverse histologic subtype, and more frequent CDK4+ and combined CDK4+/p16INK4A-. Four metastatic DFSPs (three of fibrosarcomatous type and one of myxoid type) disclosed nil, one, four or eleven instances of local recurrence. Metastatic DFSPs showed larger tumour size, deeper invasion beyond the subcutis, and more frequent mitotic figures than non-metastatic DFSPs. Cyclin D1 and Ki67 expression tended to differ from "low" in primary skin lesion to "high" in corresponding metastatic sites. None of 127 DFSPs presented p53 overexpression.
Conclusion: CDK4+ and p16INK4A- in tumour cells may be useful as biomarkers predicting local recurrence of DFSP. Cyclin D1 and Ki67 may be associated with DFSP progression, and further, metastasis. p53 may be not involved in development of DFSP.
Funding: Basic Science Research Program through The National Research Foundation of Korea, funded by the Ministry of Education under award number 2016R1D1A1B01010316.

PS-08-005
Analysis of the corelations between PRAME expression and melanoma subtypes
A. Georgescu*, T. Georgescu, M. Sajin, F. Pop
*Department of Pathology, "Carol Davila" University of Medicine and Pharmacy Bucharest, Department of Pathology, Nephrology Clinical Hospital "Dr. Carol Davila", Bucharest, Romania

Background & objectives: Preferentially Expressed Antigen in Melanoma (PRAME) is an antigen from the Cancer testis family, normally expressed in the gonads, which has been proved to be expressed in different malignant lesions and which is now widely used to immunohistochemically identify melanoma.
Methods: We have reevaluated 59 cases of cutaneous melanoma (3 lentigo maligna melanoma, 5 acral melanoma, 12 nodular melanoma, 34 low-CSD melanoma and 5 Spitz melanoma) which were diagnosed between June 2021 and December 2022. PRAME immunoreactivity has been evaluated using a 4-tiered grading system, incorporating both intensity and percentage of positive cells. Collected data has been analysed using SPSS software.
Results: PRAME immunoreactivity strongly correlated with the subtypes of melanoma (p=0,003), with all lentigo maligna melanoma as well as acral melanomas, showing strong and diffuse immunoreactivity for PRAME (4+). 66,6% of all nodular melanoma showed a 3+ pattern of PRAME immunoreactivity, while the other 33,3% displayed 4+ immunoreactivity. Regarding low-CSD melanoma, the distribution of the patterns of immunoreactivity was most diverse, with 14,7% showing pattern 2+, 47,05% showing pattern 3+ and 38% showing pattern 4+. Regarding Spitz melanoma, pattern 4+ was observed in 20% of all cases and 60% showed pattern 3+, while the remaining showed no immunoreactivity for PRAME (adequate on-slide control was present in sebaceous glands).
Conclusion: In conclusion, 100% of all acral melanomas and lentigo maligna melanomas showed diffuse and strong immunoreactivity for PRAME melanoma, with a statistically significant correlation between the histopathological subtype of melanoma and PRAME immunoreactivity. The most variable pattern of expression was observed in low-CSD melanoma, which also represented the most common subtype of malignant melanoma in our study. A pattern of immunoreactivity of 3+ and 4+ was observed in 89,84% of all malignant melanomas included in our database.

PS-08-006
The role of PRAME for the differential diagnosis between nevus with regression-like fibrosis/sclerosing nevus with pseudomelanomatous features and its malignant mimickers
A. Orsatti*, B. Corti, F. Ambrosi, E. Dika, M. Lambertini, M. Grillini, A.A.P. De Leo, M. Fiorentino, C. Ricci
*Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, University of Bologna, Bologna, Italy, School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: Nevus with regression-like fibrosis/sclerosing nevus with pseudomelanomatous features (NRLF/SNPMF) is a clinical and histologic simulator of well-defined melanoma (M) histotypes. Herein, we tested PRAME for the differential diagnosis between NRLF/SNPMF and its malignant mimickers.
Methods: We retrospectively collected 20 NRLF/SNPMF and 25 M mimickers, namely 11 M with extensive regression of fibrous-type (MERF), 7 recurrent M (RM), and 7 nevus-associated M (NAM). We adopted a double stain (DS) for Melan A/PRAME and the score 4+ sec. Lezcano C et al. (≥75% of positive nuclei) has been chosen to dichotomize the cases in positive and negative.
Results: The sensitivity (SE), specificity (SP), and accuracy (AC) of PRAME for the distinction of NRLF/SNPMF from the globally- and singly-evaluated M histotypes were: all M mimickers (SE: 76%, SP: 100%, AC: 86.6%), MERF (SE: 90.9%, SP: 100%,

AC: 96.8%), RM (SE: 100%, SP: 100%, AC: 100%), and NAM (SE: 28.6%, SP: 100%, AC: 81.5%) if PRAME was scored in the whole lesions (including N component for NAM and the dermal benign-looking component for NRLF/SNPMF). By contrast, if the PRAME was scored only in the M component for NAM and the atypical superficial component in NRLF/SNPMF, the diagnostic performance of PRAME remarkably improved (SE: 100%, SP: 100%, AC: 100%).
Conclusion: Our results indicate that PRAME is a useful tool for the appropriate diagnosis of NRLF/SNPMF and its M mimickers (MERF, RM, and NAM). Furthermore, we found that in NAM, the accurate PRAME assessment restricted only to the histologically suspicious/atypical components (M component for NAM and atypical superficial component in NRLF/SNPMF) is crucial to obtain satisfactory diagnostic performance, especially for SE.

PS-08-007
A decision support system for the detection of cutaneous fungal infections using artificial intelligence
N. Rappoport Levin, G. Goldinger*, A. Debby, J. Gildenblat, C. Sagiv, A. Barzilai
*Sheba Medical Center, Israel

Background & objectives: Fungal infections of the skin are very common. We use the DeePathology STUDIO to create a proof of concept for an AI based decision support system for the diagnosis of fungal infection of the skin.
Methods: We used skin biopsies of patients that were diagnosed for cutaneous fungal infection at the Sheba Medical Center between 2014-2023. Samples were stained with PAS stain and digitized using the Philips IntelliSite scanner. With the DeePathology STUDIO fungal elements were annotated and used for the creation of the AI solution. The study was approved by the local IRB committee.
Results: Two WSI (whole slide images) were used to train the AI solution that detects tiles that contain fungal structures. We used 162 annotations of tiles that contain fungal elements and 74 tiles which were negative for fungi. All tiles were annotated in association with the stratum corneum. For validation, the AI solution was deployed on 146 regions of interest in five slides. Accuracy metrics were calculated using the Validation Tool of the DeePathology STUDIO: Precision=0.8391, Recall=0.8441 and F1 score of 0.841. The AI solution was trained to be more tolerant to false positives than to false negatives as the main aim is to provide a screening tool.
Conclusion: In this study, we provide the first evidence of an AI decision support algorithm for the detection of cutaneous fungal infection. Further work is planned for validating the algorithm on more cases and extend this work by automating the epidermal layer segmentation.

PS-08-008
Comparison of the clinicopathological characteristics of NRAS- and BRAF-mutated primary cutaneous melanoma: a 7-year review from a tertiary referral centre
P. Reddy*, D. Martin, A. Fabre, S.V.H.G. Strategic Skin Cancer Network
*Histopathology Department, St Vincent's University Hospital, Ireland

Background & objectives: NRAS and BRAF mutations in primary cutaneous melanoma (PCM) show distinct characteristics such as thicker tumours and older age in NRAS-mutated cases. Our 7-year review compares the clinicopathological features of patients with PCM who underwent genetic testing at our institution.
Methods: Our study included 123 patients who underwent genetic testing for PCM between January 2016 and December 2022. We analysed clinical and pathological parameters including age, Clark level, Breslow thickness, ulceration, mitotic rate, and origin from a naevus. Categorical variables were analysed with a chi-square test and continuous variables with a Mann Whitney U test.
Results: In our NRAS PCMs, NRASQ61X was the most common mutation (57/61) and V600E was the most common in the BRAF PCMs (52/62). NRAS PCMs were frequently observed on the leg (25/61) and had a nodular subtype (34/61). BRAF PCMs were more evenly distributed between the leg (19/62) and the back (17/62) and both nodular (30/62) and superficial spreading (27/62) subtypes were commonly observed. Age, Breslow thickness, and mitotic rate were significantly associated with NRAS mutations ($U=1048$, $p<0.05$; $U=150$, $p<0.05$; $U=183$, $p<0.05$). Differences in Clark level and ulceration were not found to be significant. ($p=0.054$; $p=0.23$). BRAF mutated PCMs were more likely to originate from a naevus (17/62 vs 8/61, $p=0.048$).
Conclusion: Our retrospective review is consistent with previous studies showing that NRAS PCMs are more commonly diagnosed in older patients, with greater Breslow thickness and higher mitotic rates. Additionally, we observed BRAF PCMs more commonly originated from naevi. These distinct clinicopathological characteristics may be associated with more aggressive tumour behaviour and as such can assist management decisions taken at multidisciplinary team meetings.

PS-08-009
Lower frequency of cutaneous melanoma BRAF mutations in an Irish population
S. Staunton*, R. Cummins, C. Ryan, M. Redmond
*Beaumont Hospital, Ireland

Background & objectives: Activating BRAF oncogene mutations in melanoma carry a worse prognosis. Management of advanced BRAF mutation-positive melanoma is changing rapidly. While BRAF mutations occur in 50% of advanced melanomas worldwide, there is emerging evidence of lower frequency in an Irish population.
Methods: A retrospective audit using the Laboratory Information System of melanoma cases from 2018-2022 on which BRAF testing via next generation sequencing was performed using data from a single tertiary referral centre for melanoma mutation testing in Ireland. Both in-house and referred material was analysed.
Results: Data from 508 cases was analysed. Mean age was 66.9 years. The most common specimen types were skin (44.3%, n=225), lymph nodes (17.7%, n=90), and brain (10.6%, n=54). BRAF mutations were present in 27.1% (n=138) of which 85.5% (n=118) were V600 mutations. NRAS and KIT mutations were present in 41.7% (n=212) and 23.6% (n=120) respectively, though not all cases were tested. Younger age was a significant predictor of BRAF mutation ($p<0.00001$) while gender was not ($p=0.49$). Superficial spreading melanoma was more likely than other subtypes to harbour a BRAF mutation (44.7%, $p=0.001$). BRAF mutation-positive melanomas were less likely to display ulceration ($p=0.033$) but more likely to display lymphovascular invasion ($p=0.029$).
Conclusion: NICE states that standard treatment for advanced/metastatic melanoma is either immunotherapies or targeted therapy (alone or in combination). Patients with BRAF V600 mutation-positive melanoma are likely to be offered a targeted therapy at some point in the treatment pathway, particularly if resistance occurs. As the prevalence of BRAF mutations in our centre is lower than that seen internationally, less treatment options may be available to our patient cohort, potentially leading to worse outcomes.

PS-08-010
Brightfield multiplex immunohistochemistry assay for PD-L1 evaluation in challenging melanoma samples
F. Ugolini*, S. Simi, L. Tinunin, G. Baroni, D. Massi
*Section of Anatomic Pathology, Department of Health Sciences, University of Florence, Italy

Background & objectives: PD-L1 testing in melanoma tissue samples may be challenging, due to morphological features and technical issues. The aim of the study was to develop and validate a new immunohistochemistry (IHC) multiplex technique to facilitate interpretation and scoring of PD-L1.
Methods: Formalin-fixed paraffin-embedded (FFPE) melanoma samples (n=315) were retrospectively selected. We tested PD-L1 expression in 92 primary cutaneous melanoma and 223 melanoma metastases. Sections were incubated with anti-PD-L1 (Clone E1L3N) with RED chromogen. Any intensity of membranous staining on tumour cells was considered, and samples where membrane staining was obscured by high cytoplasmic staining or melanin content were be deemed indeterminate.
Results: We observed that 93/315 (29.5%) melanoma cases were characterized by a difficult interpretation of the PD-L1 staining. This complexity was mainly due to the majority of tested samples 52/315 (16.5%) falling across the cutoff (1%). Additionally, 8/315 (2.5%) cases showed wide areas of necrosis and/or fibrosis and 33/315 (10.5%) were highly pigmented, both conditions that complicate the staining's evaluation. To overcome these challenges, we developed a highly standardized multiplexing protocol using the RED/DAB chromogens combination. This double staining was coupled with a previously published bleaching pretreatment technique (Ugolini; 2021), in selected highly pigmented samples.
Conclusion: Our results showed that brightfield multiplex PD-L1/SOX10 double labelling could be a useful tool in challenging melanoma specimens, which may be used to colocalize SOX10+/PD-L1+cells. This technique could help pathologists in daily practices to recognize more accurately melanoma cells positive to PD-L1 membranous stain, particularly at the host-tumour interface. Finally, this technique could be useful in training phase of development of AI power tools that in future could standardize and autonomize the PD-L1 assessments.
This work was funded by the Fondazione AIRC "Programma di ricerca 5 per Mille 2018—ID#21073"

PS-09 | Poster Session Endocrine Pathology

PS-09-001
Thyroid papillary carcinoma and multifocality
Y. Adali*, S. Ekmekci, M. Üstün, Ü. Küçük, E.E. Pala
*Izmir University of Economics Faculty of Medicine, Turkey

Background & objectives: Papillary thyroid cancer (PTC) is the most common endocrine malignancy with an increasing incidence. Multifocality is frequently detected in PTC, but its prognostic significance is controversial. In this study, it was aimed to determine the relationship between multifocality and histopathological prognostic parameters.
Methods: In the study, 513 PTC cases between the years 2012-2022 were examined. Sections of the cases were re-evaluated by 2 pathologists. In addition to age and gender, multifocality was compared with parameters which are known to show histopathological and prognostic importance like lymphovascular invasion (LVI), blood vessel invasion (BVI), perineural invasion (PNI), and lymph node metastasis (LN).
Results: The mean age of the cases was 46.86+13.17, and 394 (76.8%) cases were female and 119 (23.2%) were male. Multifocal tumour was observed in 237(46.0%) cases. Of the multifocal cases, 128(25%) had 2 foci, 57(11.1%) had 3 foci, 29(7.7%) had 4 foci, 23(4.5%) contains 5 foci or more. No statistically significant correlation was found between multifocality and gender (p=0.372), LVI (p=0.461), BVI (p=0.191), PNI (p=0.523) and LN (p=0.156).However, in cases with multifocality, PTC was observed statistically significantly higher than microcarcinoma (PTMC) when compared with unifocal's (p=0.000).Although follicular carcinoma (FC) is the most common subgroup in both groups; FC was found to be statistically significantly higher in unifocal tumours compared to multifocal tumours (p=0.000).
Conclusion: Different potential prognostic factors such as patient age, tumour grade, regional and distant metastasis have been demonstrated in PT. Multifocality has been reported to be associated with increased vascular invasion, LN, advanced stage, increased risk of recurrence, and the need for more extensive treatment. In the current study, although these relationships could not be demonstrated, it was noted that multifocality was observed with PTC rather than PTMC. It seems that the controversial effect of multifocality in the management of these tumours will continue.

PS-09-002
Three new gene fusions in radio-iodine refractory differentiated thyroid cancer
Z. Alsugair*, F. Descotes, J. Lopez, M. Decaussin-Petrucci
*Department of Pathology, Institut of Pathologie Multisite, Groupement Hospitalier Sud, Hospices Civils de Lyon, Pierre-Bénite, France

Background & objectives: Radio-iodine refractory differentiated thyroid cancer is challenging to treat, with need for effective diagnostic and therapeutic strategies. Extensive molecular testing became essential for identifying genetic alterations, discovering new therapeutic targets, we report three metastatic refractory thyroid cancers with new gene fusions never described before in thyroid.
Methods: We performed pan-cancer DNA- and RNA-sequencing on tumour samples from 85 patients with Radio-iodine refractory differentiated thyroid cancer. We used bioinformatics tools to identify genetic alterations, including gene fusions, single nucleotide variants, and copy number alterations. The histological slides were reviewed to reclassify all the cases according to the 2022 WHO classification of thyroid neoplasms.
Results: Among the 85 cases, we identified 13 fusions (15%) including three new gene fusions never described in the thyroid gland: UGGT1::TERT, BTBD9::TERT, and TG::IGF1R. These fusions were all associated with high-grade DTCs. The first case, a tall cell subtype of papillary thyroid carcinoma (PTC), presented a UGGT1::TERT fusion associated with a BRAF V600E mutation. In the second case, a high-grade follicular subtype of PTC, we identified a BTBD9::TERT fusion associated with a biallelic inactivation of the ATM gene and a NRAS Q61R mutation. The third case, an angioinvasive oncocytic carcinoma, harboured a TG::IGF1R fusion and was associated with a TERT promoter mutation.
Conclusion: Our study highlights three novel fusions UGGT1::TERT, BTBD9::TERT and TG::IGF1R in RAI-R-DTC . These newly detected alterations extend the molecular spectrum of thyroid carcinomas and provide a novel insight into their oncogenesis and prognosis. Further investigations are needed to confirm if these fusions represent a unique subtype entity or a genotype-phenotype correlation.

PS-09-003
Immature PIT1-lineage pituitary neuroendocrine tumour/adenoma
E. Athanasiou*, G. Kyriakopoulos, A. Therapontos, F. Dolkiras, P. Vlachou, I. Galonakis, M. Chrisoulaki, E. Spiteri, N. Stavrinou
*Department of Pathology, Evaggelismos General Hospital Athens, Greece

Background & objectives: Immature PIT1-lineage pituitary neuroendocrine tumour/adenoma corresponds to a recently identified entity with distinctive immunohistological features, characterized by more aggressive biological behaviour.
Methods: Three female patients aged 33, 44 and 53 years with macroadenomas in the Sella Turcica underwent transsphenoidal resection of the tumours.
Results: The histological characteristics consisted of a neuroendocrine cell tumour with a bold eosinophilic nucleus with pseudo-inclusions, multilobulated nuclei with an abnormal nuclear membrane and a

chromophobe/amphophilic cytoplasm. The Ki-67 proliferation index ranged between 7-12%. Immunohistochemically, full expression of the transcription factor PIT-1 was observed, with an accompanying limited expression of GH, TSH and PRL hormones as well as α-subunit expression. Overexpression of the cell cycle protein Cyclin D1 was observed in one patient. Loss of nuclear expression of ATRX protein was observed in 2 patients. Menin protein expression was retained in all patients. In all patients there was recurrence of the neuroendocrine tumour within a two-year period.
Conclusion: PIT1-lineage pituitary neuroendocrine tumours include a wide spectrum of neuroendocrine tumours, the most aggressive of which is the Immature PIT1-lineage tumour/adenoma. The differential diagnosis is based mainly on the morphological features of the tumour and the representation of all three hormones of the PIT-1 cellular lineage.

PS-09-004
NKX2.2 expression in several tumour types
M.A. Bani*, P. Khneisser*, C. Ngo, A. Al Ghuzlan, M. Faron, J. Scoazec
*Department of Medical Biology and Pathology, Morphological pathology laboratory, Gustave Roussy Cancer Campus, Villejuif, France; Paris-Saclay University, Gustave Roussy Cancer Centre, Inserm US23, CNRS UMS3655, AMMICa, Villejuif, France

Background & objectives: NKX2.2 is a transcription factor that plays a role in cell differentiation in many tissues. It has been proposed as a marker for Ewing sarcoma. This study aims to determine the spectrum of expression of NKX2.2 in several tumour types.
Methods: We evaluated, by immunohistochemistry, the expression of NKX2.2, neuroendocrine markers, and various transcription factors (chromogranin A and B, synaptophysin, INSM1, CD56, CDX2; PDX1, GATA3, PAX8 and TTF1) in several tumour types including neuroendocrine neoplasms and other epithelial or mesenchymal tumours, originating in different organs, diagnosed in our institution between 2021-2023.
Results: We evaluated 154 cases, including 72 neuroendocrine neoplasms (NEN), 19 Ewing sarcomas, 10 carcinomas with neuroendocrine differentiation, 6 adenocarcinomas, 5 osteosarcomas, 4 neuroblastomas, 3 olfactory neuroblastomas, 4 paragangliomas, 2 Merkel cell carcinomas, 2 rhabdomyosarcomas, 2 mesenchymal chondrosarcomas. NKX2.2 showed variable expression intensity in 71 cases (49.3%). Strong diffuse staining was observed in 20 neuroendocrine tumours, 13 Ewing sarcomas, all olfactory neuroblastomas, 1 mesenchymal chondrosarcoma, [SJ1]2 poorly differentiated carcinomas. NKX2.2 expression was correlated with specific tumour types ($p<0.001$), the expression of INSM1 ($p=0.005$), chromogranin A ($p=0.045$), and other neuroendocrine markers. Among all NEN, NKX2.2 expression was predominantly seen in tumours originating from the pancreas and small intestines ($p=0.004$).
Conclusion: Our preliminary results show that NKX2.2 is significantly expressed in Ewing sarcomas, NEN, olfactory neuroblastomas and mesenchymal chondrosarcoma. Among all NEN, pancreatic and small intestinal primaries were the most positive. Breast carcinomas with neuroendocrine differentiation were usually negative despite the expression of chromogranin A and synaptophysin. Correlation of NKX2.2 expression with clinicopathological features is under investigation.

PS-09-005
Clinicopathological characteristics of non-syndromic familial non-medullary thyroid cancer in Santiago de Compostela (northwest Spain)
J.M. Cameselle-Teijeiro*, G. Rodríguez-Carnero, C. Beiras-Sarasquete, I. Abdulkader-Nallib, M. Sánchez-Ares, M. Piso Neira, V. Pubul-Núñez, J.M. Cabezas-Agrícola, J.A. Puñal-Rodríguez
*Clinical University Hospital of Santiago de Compostela, Universidad de Santiago de Compostela and Galician Healthcare Service (SERGAS), Santiago de Compostela, Spain

Background & objectives: Non-syndromic familial non-medullary thyroid cancer (NSFNMTC) is a group of hereditary carcinomas whose aetiology remains poorly understood. We investigate the characteristics of a case series of NSFNMTCs in comparison with sporadic follicular-derived thyroid carcinomas (SFTCs) from the same geographical area.
Methods: From our institution's records of diagnosed thyroid carcinoma (TCs) (1991-2015), all NSFNMTCs were selected following the 5th edition WHO thyroid tumour classification (follicular cell derived carcinoma in ≥3 first-degree relatives or papillary carcinoma [PTC] in ≥2 first-degree relatives, in the absence of radiation exposure and inherited cancer syndromes). The clinicopathological features of NSFNMTCs were compared with those of the SFTCs.
Results: Of the 880 follicular-derived TCs reviewed, 44 cases (5%) were NSFNMTCs and 836 (95%) SFTCs. The mean age was 42.8 years in NSFNMTCs and 52.2 in the SFTCs ($p=0.006$). The NSFNMTCs included 93.2% PTCs, 4.5% follicular carcinomas (FTCs) and 2.3% oncocytic carcinoma (OTC), while the SFTC group included 81.5% PTCs, 9.2% FTCs, 5.9% OTCs, 1.7% poorly differentiated carcinomas and 1.8% anaplastic carcinomas. PTCs measuring ≤1 cm were more common in the SFTC group (45.5% versus 22.7%, $p=0.001$). Multifocality and bilaterality were more common in NSFNMTCs (24[54.6%] and 20[45.5%] versus 199[25.4%] and 149[19%] respectively, $p=0.000$). No significant differences were detected in tumour size, angioinvasion or associated thyroid pathology.
Conclusion: NSFNMTC accounts for 5% of follicular-derived thyroid carcinomas. These patients usually present at a younger age (average ≈9 years) than with SFTCs. NSFNMTC are differentiated carcinomas, mainly PTCs, with a higher rate of multicentricity and bilaterality than SFTCs.
This study has been funded by Instituto de Salud Carlos III (ISCIII) through the project PI19/01316 and co-funded by the European Union.

PS-09-006
Papillary thyroid carcinoma and thyroid follicular nodular disease: a retrospective cross-sectional study of 672 cases
M. de Brito Pereira*, É. Almeida, R. Ilgenfritz, A. Alves
*CUF Descobertas Hospital, Portugal

Background & objectives: Thyroid follicular nodular disease (FND) is a benign proliferation composed of multiple clonal and nonclonal nodules (1). This study aims to study the coexistence of clinicopathological features of papillary thyroid carcinoma (PTC) and FND.
Methods: In a 3-year period (from 2019 to 2022), in one institution, papillary thyroid carcinoma was diagnosed in 672 cases. Those reports were revalued, the epidemiological data and the information on the anatomopathological report was collected. The epidemiological data of PTC with associated FND was compared to the cases of PTC without associated FND.
The data was analysed through JASP software.
Results: Of the 672 cases, 282 cases (42,0%) had PTC with FND. The average age was 54.6 years with FND vs. 46.6 without FND. The patients were predominantly women in both groups (82,7% in FND vs 76,1%).
The most common presentation of PTC was unifocal lesions (61,7% in FND vs 66,2%), followed by multifocal lesions and bifocal lesions. The rate of extra-thyroidal extension was 14.2% in FND vs 18.7% without FND. The rate of metastases in central lymph nodes was 12.1% in FND vs 21.3%.Regarding the staging, 71.6% cases with FND vs. 62.6%

without were pT1 and 16.3% vs. 24.4% were pT2. Similar rate of pT3 and pT4 was present.
Conclusion: Papillary thyroid carcinoma with FND was related to a diagnosis in older patients and a more indolent course, documented by a lower rate of extra-thyroidal extension, metastization to local lymph nodes and a lower staging (higher rate of pT1 staging vs lower rate of pT2) when compared to PTC alone.

PS-09-007
Identification of NIFTP-specific mRNA markers for reliable molecular diagnosis of thyroid tumours
C.K. Jung*, S. Lee, J. Park, K. Kim, J.S. Bae, S. Kim
*Department of Hospital Pathology, College of Medicine, The Catholic University of Korea, Cancer Research Institute, College of Medicine, The Catholic University of Korea, Republic of Korea

Background & objectives: Distinguishing non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) from other thyroid tumours can pose diagnostic challenges, even with molecular testing. This study aimed to identify NIFTP-specific mRNA markers for improved diagnostic accuracy.
Methods: Using RNA sequencing analysis of fresh thyroid tumour tissues from 74 cases, we identified differentially expressed genes and pathways in NIFTP/malignancy compared to benign tumours. We utilized Venn diagrams to identify significantly further dysregulated mRNAs in NIFTP. We selected mRNA markers using the Akaike information criterion (AIC) analysis and performed receiver operating characteristic analysis to estimate their accuracy.
Results: Our analysis revealed 255 downregulated and 737 upregulated genes in NIFTP/malignancy compared to benign tumours. KEGG pathway enrichment analysis further showed several cancer-associated pathways in NIFTP/malignancy. Using Venn diagrams, we identified 19 significantly upregulated and 7 downregulated mRNAs in NIFTP. After validating our results in The Cancer Genome Atlas (TCGA) dataset, we selected OCLN, ZNF423, LYG1, and AQP5 mRNA markers using AIC analysis and developed a prediction model that exhibited good accuracy in predicting NIFTP in both our cohort and the TCGA cohort.
Conclusion: Our study suggests that the identified four mRNA markers can serve as reliable molecular markers for identifying NIFTP among other thyroid tumours, thus aiding in the accurate diagnosis and management of NIFTP patients.
This research was supported by "Systemic Industrial Infrastructure Projects" through the Ministry of Trade, Industry, and Energy (MOTIE) (P0009796, 2019) and the KRIBB Research Initiative Program (KGM5192322). This research was also supported by a grant (HI21C0940) from the Korean Health Technology R&D Project, Ministry of Health and Welfare, and a grant (NRF-2020R1F1A1070028) from the Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Science and ICT.

PS-09-008
A comprehensive clinico-pathological study of carcinoma and atypical adenomas from parathyroid in a series of patients with long-term follow-up
J. Machuca Aguado*, P. Rodríguez de Vera Gómez, Á. Gutiérrez, T. Martín Hernández, J.J. Rios Martin, M.A. Idoate Gastearena
*Virgen Macarena University Hospital, Seville, Spain

Background & objectives: Parathyroid carcinomas (PC) are rare neoplasms with histopathological differences from atypical parathyroid adenomas (APA), with a rather similar clinical course, excepting the very unusual PC metastases. Our aim was to identify variables for a better characterisation of both tumour types.
Methods: It is a retrospective observational clinicopathological study of a series of 7 PC and 10 APA which were diagnosed according to the WHO 2022 criteria with a median follow-up of 11 years. Immunohistochemistry was performed for parafibromin, PGP 9.5 and galectin 3. Post-surgical tumour recurrence was determined using clinical imaging and/or by elevation of parathormone (PTH) in blood.
Results: No statistically significant differences were observed between PC and APA in terms of age, sex, pre-surgical blood tests (PTH and calcaemia), ultrasound characteristics, percentage of post-surgical cure and tumour recurrence (29% vs 20%; p=0.63). No metastases were identified. Immunohistochemically, no differences in parafibromin, PGP 9.5 or galectin-3 expression were observed between PC and APA. Tumours with loss of parafibromin expression (5/17, 29.4%), 2 APA and 3 PC, were associated with older age (74 years vs 54 years, p=0.04), negative PGP 9.5 expression (80% vs 16%, p=0.02), infiltration of adjacent structures (60% vs 33.3%, p=0.05) and capsular invasion (100% vs 58.3%, p=0.06)
Conclusion: It can be concluded that no analytical or clinical behavioural differences were observed between PC and APA. Furthermore, no metastatic PC were found in a systematic follow-up under close scrutiny. Interestingly, parathyroid tumours with loss of parafibromin showed locally more aggressive behaviour and should therefore undertake continuous clinical monitoring.

PS-09-009
Prognostic impact of fibrosclerotic changes in (non-papillary) follicular cell-derived thyroid carcinomas
G. Orlando*, G. Capella, E. Vissio, G. Trucco, J. Metovic, F. Maletta, M. Volante, M. Papotti
*Pathology Unit, Department of Oncology, University of Turin, Italy

Background & objectives: Prognostic factors in thyroid carcinomas, with special reference to non-papillary histotypes, are scarce. Intratumoral fibrosis was identified as an adverse prognostic factor in papillary carcinomas but has not been investigated in other subtypes, including follicular, oncocytic and poorly differentiated carcinomas.
Methods: The presence of intratumoral fibrosis and its correlation with clinical outcome was analysed in 132 non-papillary follicular cell-derived thyroid carcinomas (53 follicular carcinomas, 31 oncocytic carcinomas and 48 poorly differentiated carcinomas). The percentage of fibrosis x tumour area was assessed on Hematoxylin & Eosin slides by two independent pathologists and, in 65 selected cases, using digital image analysis.
Results: Spearman's correlation agreement between the two observers and with digital image quantification was very high ($p<0.0001$). The presence of intratumoral fibrosis (scored as absent, mild if <10% or extensive if >10%) was significantly associated with poorly differentiated carcinoma histology, large tumour size, extensive vascular invasion, presence of necrosis, high mitotic index, positive nodal status and aggressive clinical outcome (all $p<0.01$). Moreover, fibrosclerotic changes, either mild or extensive, were associated in the whole series with a significantly shorter disease-free and disease-specific survival ($p<0.0001$ in Log Rank test), retaining statistical significance also in differentiated (follicular and oncocytic) and poorly differentiated carcinomas analysed separately.
Conclusion: Intratumoral fibrosis is a potential novel prognostic factor in non-papillary follicular cell-derived thyroid carcinomas. It is associated significantly with the presence of parameters of aggressiveness, and with a decreased survival rate independently from the tumour histotype. It is also easily assessable, with a very high interobserver agreement, thus supporting its potential use in the clinical diagnostic practice.

PS-09-010

Clinicopathologic characteristics and succinate dehydrogenase deficiency in paragangliomas: a 10-year retrospective study from a tertiary care centre

M.L. Sacramento*, E. Rios
*Serviço de Anatomia Patológica, Centro Hospitalar Universitário de São João, Porto, Portugal

Background & objectives: Paragangliomas are extra-adrenal neuroendocrine tumours associated with underlying germline mutations in up to 80%, especially involving succinate dehydrogenase complex (SDHx) genes. SDHB immunohistochemistry (IHC) can predict SDHx mutations that have prognostic implications.
This study aimed to characterize a paraganglioma series.
Methods: A total of 36 paragangliomas were diagnosed retrospectively at our hospital over the last ten years (2012-2022). The clinical characteristics of the patients were collected, and all slides were reviewed. SDHB protein expression was examined on all tumours. Genetic results were available in 17 patients. Grading system for Adrenal Pheochromocytoma and Paraganglioma (GAPP) score was calculated whenever possible.
Results: Among 36 cases, 26 were diagnosed in females (Male:Female = 1:2.6) . The median age at diagnosis was 48 years (range, 12–80 years). The most frequent location was the carotid body (13 cases). Tumour sizes were 0.4 to 11.6 cm (mean, 4 cm). SDHB expression loss occurred in 16 (44%) paragangliomas. Genetic study was available in 7 SDHB-deficient tumours: 6 SDHB mutations and 1 SDHD mutation. From these, 4 (in a total of 5) showed malignant behaviour.
GAPP score was calculated in 17 tumours. In the well differentiated group (n=12), 4 were SDHB-deficient. In the moderately differentiated group (n=5), 2 were SDHB-deficient.
Conclusion: Our study revealed a female predominance of paragangliomas and clinicopathologic characteristics that fit into the existing literature. SDHB-deficiency was observed in 80% of paragangliomas with malignant behaviour, highlighting that SDHB IHC can be regarded as a biomarker of prognosis in paragangliomas. A higher GAPP score correlates with malignant behaviour and syndromic background, reinforcing that GAPP score is a useful tool for risk stratification in paragangliomas.

PS-09-011

GATA3 and SF1 in silent gonadotroph tumours of the pituitary: do we really need both?

J. Soukup*, H. Faistova, L. Gerykova, P. Poczos, T. Česák, M. Kosak, D. Netuka, F. Gabalec
*University Hospital Hradec Kralove, Czech Republic

Background & objectives: Detection of transcription factors is a crucial part pituitary neuroendocrine tumours (PitNETs) work-up. However, SF1 antibodies can be costly and difficult to implement. Thus, we were interested in added value of detection of GATA3 for diagnosis of gonadotroph tumours.
Methods: A total of 148 nonfunctional PitNETs diagnosed over 15-year period were analysed for immunohistochemical expression of Pit1, Tpit, SF1 and GATA3. In selected cases, additional pituitary hormones, and cytokeratin 8/18 were evaluated.
Results: The cohort consisted of 120 (81.6%) gonadotroph PitNETs, 14 (9.5%) corticotroph PitNETs, 9 (6.1%) Pit1+ PitNETs, 3 (2%) null-cell tumours and 1 (0.7%) plurihormonal PitNETs. Pit1-lineage tumours were exclusively Pit1-positive. Among ACTH+/Tpit+ corticotroph PitNETs, 3 out of 14 demonstrated weak GATA3 positivity. Among 120 gonadotroph tumours, 105 (87.5%) were GATA3+/SF1+; 10 tumours were GATA3+ (8.3%) and only 5 (4.2%) were SF1+. GATA3 exhibited 95.8% sensitivity and 85.7% specificity for diagnosis of gonadotroph PitNET, while SF1 showed lower sensitivity (91.7%) but higher specificity (96.4%). The use of Pit1/Tpit/GATA3 panel resulted in diagnosis of 8 (5.4%) null cell tumours, compared to 13 (8.8%) null cell tumours identified by Pit1/Tpit/SF1 panel.
Conclusion: GATA3 is a more sensitive marker of gonadotroph PitNETs compared to SF1. Applying a Pit1/Tpit/GATA3 panel led to a misdiagnosis of 3.4% of PitNETs as null-cell tumours, while a Pit1/Tpit/SF1 panel resulted in a 6.8% misdiagnosis rate. However, GATA3 immunoreactivity was observed in a subset of corticotroph tumours, and it can be also present in a subset of Pit1+ tumours with thyrotroph differentiation. Thus, it should be always included with additional PitNET lineage markers (at least Pit1 and Tpit).
Funding: BBMRI-CZ LM2023033; Charles University Cooperatio Program DIAG and METD; Czech Ministry of Defense MO 1012; European Regional Development Fund-Project BBMRI-CZ Biobank network – a versatile platform for the research of the etiopathogenesis of diseases, No: EF16_013/0001674

PS-09-012

A prognostic marker panel (OTP, CD44, Ki-67) predicts relapse free survival in patients with surgically resected pulmonary carcinoid

E.J. Speel*, L. Moonen, J. Derks, M. Den Bakker, L. Hillen, J. von der Thüsen, R.J. van Suylen, R. Damhuis, K. Smits, W. Buikhuizen, G. PALGA, A. Dingemans
*Maastricht UMC, The Netherlands

Background & objectives: Relapse occurs in 10% of patients with resected pulmonary carcinoid (PC). Aim was to examine if an immunohistochemical (IHC) marker panel (OTP, CD44, Ki-67) improves 1) uniformity among pathologists (compared with WHO classification) and 2) prediction of relapse-free survival (RFS).
Methods: All surgically resected PC (2003-2012) were identified from the Dutch cancer/pathology registry. A case-control cohort (2:1 for relapse, N=170) was established. 4 pathologists independently revised cases and assessed IHC-markers (OTP&CD44 H-score, Ki-67 eyeball). IHC cut-off values were determined using ROC curves. Agreement between pathologists for classification and IHC was determined using kappa. The remaining total cohort (N=396/566) was scored similarly.
Results: Median FU of 2:1 cohort was 86.7 months and 61% (n=35/57) of relapsed patients had TC diagnosis. Revision showed poor kappa among pathologists (necrosis:0.48; mitotic count:0.38), whereas IHC markers showed high kappa (OTP:0.98, CD44:0.98, Ki-67:0.92). ROC analysis for relapse identified optimal cut-off for OTP (<50), CD44 (<30), and Ki-67 (≥5). Mean negative predictive value (NPV) for relapse increased from 0.74 (TC diagnosis) to 0.85 (IHC low-risk [OTP≥50 & CD44≥30 & Ki-67<5]). IHC risk stratification of total cohort (high-risk [n=220] and low-risk [n=314]) showed a NPV of 96%.
Conclusion: Our study shows that the IHC marker panel including OTP, CD44, and Ki67 increases diagnostic uniformity among pathologists and reveals a high NPV (96%) for relapse, indicating that a biomarker driven FU management for PC patients may be used to identify patients who can be excluded from long-term FU. Further studies are warranted to validate our findings, also in the light of the recently identified clinically relevant molecular PC subtypes.
Funding: Dutch Cancer Society

PS-09-013

Mature fat containing thyroid lesions: report of five cases

A. Yavuz*, B. Altunay, E. Ocak Gedik, C. Arıcı, G.A. Ocak, I.E. Gurer
*Akdeniz University Department of Pathology, Turkey

Background & objectives: The thyroid gland does not normally consist adipose tissue. Rarely, non-neoplastic and neoplastic thyroid

gland lesions can contain mature fat tissue. In this report, we present an uncommon thyroid phenomenon, termed lipomatous metaplasia in 5 different patients.
Methods: Pathological examination was performed by routine hematoxylin-eosin and histochemical staining. For the detection of amyloid, congo red stain, and crystal violet histochemical markers were used.
Results: Five patients between the ages of 36 and 70 (mean age 54 years) were documented, including two male and three female patients. All patients presented with dyspnea. T3, T4, and thyroid-stimulating hormone levels were within the normal range in all cases. Three of the patients had a history of renal transplantation, and two of them had already been diagnosed with Familial Mediterranean fever (FMF). Macroscopically, all thyroid specimens showed a marked increase in weight and size, ranging from 84 to 203 grams. Microscopically, four cases showed amyloid deposition with crystal violet staining. Four cases were ultimately diagnosed as amyloid goiter.
Conclusion: The majority of the available literature on lipomatous metaplasia of the thyroid gland is limited because of its rare occurrence in surgical pathology. Patients with Cowden syndrome and those who have been exposed to radiation have both been documented to have lipomatous metaplasia in the thyroid gland. Secondary amyloidosis should also be considered in the differential diagnosis of lipomatous metaplasia of the thyroid gland in patients who have a history of chronic inflammatory disorders or long-term infections.

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PS-10-001
Histomorphological evaluation of desmoplastic tumour stroma in malignant ovarian surface epithelial tumours

S. Ahuja*, S. Zaheer, S. Ranga
*Department of Pathology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

Background & objectives: A reactive stroma rich in cancer associated fibroblasts is associated poorer prognosis in breast, colorectal and oral cancers.
The present study was conducted to highlight the prognostic significance of tumour budding and fibrotic stroma in malignant ovarian surface epithelial tumours.
Methods: This was a cross-sectional study in which all histologically diagnosed cases of malignant ovarian surface epithelial tumours were included. The fibrotic stroma was classified into three distinct categories- mature, intermediate and immature. The number of tumour buds were counted at the invasive front of the tumour and graded based on the number of buds- 0-5, 5-9 and >=10 buds.
Results: Among the 50 cases, 32% (16 cases) had mature stroma while 30% (15 cases) and 38% (19 cases) had intermediate and immature stroma respectively. Though, a significant association could not be established between tumour budding and stroma grade, fair agreement was established between them. However, a significant association could be established between histological grade with both tumour budding (p value=0.03) and fibrotic stroma grade (p value=0.02).
Conclusion: The study highlighted the role of stromal response in malignant surface epithelial tumours of the ovary since a higher grade tumour was associated with an immature stroma while a lower grade tumour was associated with a mature stroma.

PS-10-002
Optimization of diagnostic yield from macroscopically inadequate endometrial histological specimens: cytology cell block preparation permits histological diagnosis in 70% of cases

S. Al Mandhari*, N. Conlon
*Cork university hospital, Ireland

Background & objectives: The study objective was to assess the impact of the introduction of cytology cell-block preparation into the management protocol of low/no volume endometrial specimens at our laboratory on the proportion of these cases which are labelled as "inadequate for diagnosis".
Methods: A new protocol was introduced in our laboratory, whereby on receipt of an endometrial specimen containing no or minimal visible tissue/mucoid material only, the specimen was submitted for cytology cell block preparation and a H&E-stained slide was produced. A retrospective audit of this practice was conducted for the period 2018-2021 (4 years) via analysis of the final pathology report.
Results: The study cohort involved 70 patients over 4 years. 87.5% of patients were post-menopausal, with 67% presenting with post-menopausal bleeding. In 73% of cases no tissue was identified grossly; 11% contained mucin only and 16% had tiny tissue fragments too small for routine processing.
On microscopic examination, 70% of cases had sufficient endometrial tissue present to allow a descriptive diagnosis and avoid an "inadequate for diagnosis" report. The most common histological diagnoses was endometrial atrophy (39% of cases) or inactive endometrium (33%). No cases of atypical hyperplasia or malignancy were made. With follow-up of between 1 to 4 years, none of these patients had developed evidence of endometrial neoplasia.
Conclusion: Low/no volume endometrial specimens frequently contain sufficient microscopic diagnostic material to produce a clinically-useful histological report, if the specimen is submitted for cytology cell block preparation. This retrospective audit provides evidence that this processing method does not provide false reassurance on endometrial status, as no patient subsequently presented with evidence of endometrial neoplasia during follow-up. This method represents an effective way to reduce the number of "inadequate for diagnosis" histological reports, particularly in the postmenopausal patient population.

PS-10-003
SATB2 cytoplasmic expression is characteristic of a subset of ovarian stromal cells and sex cord-stromal tumours

M. Al-Hussaini*, G. McCluggage
*KHCC, Jordan

Background & objectives: SATB2 is a transcription factor that shows consistent nuclear staining in colorectal adenocarcinoma and osteosarcoma. Following the observation of cytoplasmic staining in luteinized ovarian stromal cells, we studied the expression of SATB2 in ovarian stromal cells and sex cord-stromal tumours.
Methods: 82 cases were stained for SATB2. These included hilar Leydig cells, corpora lutea, follicular cysts, stromal hyperthecosis, and a variety of sex cord-stromal tumours.
Results: Ovarian hilar Leydig cells (n=12), luteinized stromal cells (n=9), corpora lutea (n=4), luteinized follicular cysts (n=3), stromal hyperthecosis (n=6), Leydig cell tumours (n=1) and steroid cell tumours (n=3) mostly showed diffuse granular cytoplasmic staining. SATB2 also highlighted Leydig cells in Sertoli-Leydig cell tumours (n=15) and gynandroblastomas (n=3). SATB2 was essentially negative in adult granulosa cell tumours (n=14), apart from positivity in scattered luteinized cells, juvenile granulosa cell tumours (n=3), sex cord tumour with annular tubules (n=4), cellular fibromas (n=2), sclerosing stromal tumours (n=1), thecomas (n=1) and uterine tumours resembling ovarian sex cord tumour (n=1).
Conclusion: SATB2 granular cytoplasmic staining has not been previously described but is characteristic of a variety of ovarian stromal cells and sex cord-stromal tumours, in particular those exhibiting steroidogenic differentiation. SATB2 staining may be of value in identifying luteinised or Leydig cells when these are morphologically inconspicuous.

PS-10-004

Tumour budding characterisation of endometrial carcinoma in molecular groups

A. Alpsoy*, G. Koca Yilmaz, G. Erdogan, H.E. Pestereli
*Akdeniz University Department of Pathology, Turkey

Background & objectives: Endometrial carcinomas, being the most frequent gynaecologic neoplasms, are now classified into molecular groups. Tumour budding can be a helpful indicator of epithelial-mesenchymal transition. We evaluated tumour budding to understand the relationship between tumour budding and endometrial carcinoma molecular groups.
Methods: We used 55 endometrial carcinoma cases previously molecularly classified. We examined the H&E slides of the 55 cases with an Olympus Bx53 microscope and counted the intratumoral and peritumoral buds. We later converted the intratumoral and peritumoral bud counts into the International Tumour Budding Consensus Conference (ITBCC) tumour budding score and the ITBCC tumour budding score with the "0 score".
Results: Our cases consisted of 13 FIGO Grade 2 and 42 FIGO Grade 3 cases. Molecular characterization of endometrial carcinoma cases revealed 11 POLE mutant, 14 MSI, 15 no specific molecular profile (NSMP), and 15 P53 mutant cases. Average peritumoral tumour budding was found to be higher in the NSMP group compared with other molecular groups. Average tumour budding was also higher in cases with cervix invasion (p=0,031). The average ITBCC tumour budding score was significantly higher in 15 NSMP cases compared to the other 40 cases' average ITBCC score (p=0,036).
Conclusion: In conclusion, the successful application of the ITBCC tumour scoring system to the endometrial carcinoma cases uncovered that NSMP cases had higher ITBCC peritumoral budding scores than the other molecular groups.

PS-10-005

Potential immunohistochemical markers to find pole mutant endometrial carcinomas: AMF and AMFR

A. Alpsoy*, G. Koca Yilmaz, C. Karadag, O. Birge, T. Simsek, G. Erdogan, H.E. Pestereli
*Akdeniz University Department of Pathology, Turkey

Background & objectives: Molecular techniques are the sole way of assessing the POLE status of endometrial carcinomas, making molecular classification challenging. Previous study found higher AMF/PGI and AMFR/gp78 in POLE mutant endometrial carcinomas. We utilized AMF/PGI and AMFR/gp78 immunohistochemistry to address this issue.
Methods: We used 55 molecularly classified endometrial carcinomas in our institution. We applied AMF/PGI and AMFR/gp78 immunohistochemistry. The staining intensity was scored as 0 (negative), 1 (weak), 2 (medium), or 3 (strong) and the extent was scored as 0 (0%), 1 (1–25%), 2 (26–50%), 3 (51–75%), or 4 (76–100%). The final score is the sum of intensity and extent scores.
Results: The average AMF/PGI score (p=0,003) and average AMFR/gp78 score (p=0,043) of the POLE mutant group were found to be significantly higher than the POLE wild-type group. AMF/PGI antibody reached a score of 6 and more on 9 out of 11 POLE mutant cases. Furthermore, the AMF/PGI antibody showed a sensitivity of 81.8% and a specificity of 61.4%. Lower AMF/PGI and AMFR/gp78 scores were observed in cases with malignant peritoneal cytology (p=0,042, p=0,026). The analysis of the AMFR/gp78 score revealed a statistically significant decrease in recurrent cases (p=0.029). Furthermore, AMFR/gp78 antibody had a low expression in cases with a high peritumoral tumour budding score (p=0,043).
Conclusion: In conclusion, our findings point to the possibility of using the immunohistochemical application of AMF/PGI to prioritize high-potential POLE mutant cases in practice.

Our project is funded by Akdeniz University BAP(Scientific Research Projects Coordination) Unit with the TTU-2022-5893 project number.

PS-10-008

Next-generation sequencing analysis of mixed epithelial carcinomas of the endometrium and ovary

J. Betenbuk*, I. Vereczkey, Z.B. Melegh, E. Tóth, A. Simon, A. Kohánka
*National Institute of Oncology, Hungary

Background & objectives: Mixed carcinoma of the female genital tract is a tumour that comprises two or more distinct histotypes. These tumours can develop along three different pathways, but most of them represent divergent differentiation or transdifferentiation. Collision tumours are rare.
Methods: Between 2017 and 2023, 1208 endometrial and 757 ovarian tumours were investigated. After the exclusion of carcinosarcomas, 16 endometrial and 10 ovarian mixed epithelial carcinomas were identified. Following a morphological examination, ER, PR, p53, mismatch repair (MMR) immunohistochemistry was performed, supplemented with PAX8 for ovarian carcinomas. From both localisations, 8 cases were analysed by next-generation sequencing (Oncomime Comprehensive Assay v3).
Results: 1.32% of both endometrial and ovarian carcinomas were found to be mixed epithelial carcinomas. Of the 8 endometrial tumours we examined, 4 were dedifferentiated carcinomas (DDE), 3 mixed clear cell and low-grade endometrioid carcinomas (CCC/LGEC), 1 mixed CCC and undifferentiated carcinoma (CCC/UC). All of these tumours were MMR deficient in at least one component. Of the 8 mixed ovarian tumours, three were endometriosis-associated, all of which showed PIK3CA mutation. The remaining tumours were 1 mixed borderline mucinous tumour and low-grade serous carcinoma (BMT/LGSC), 2 mixed LGSC and high-grade serous carcinoma (LGSC/HGSC). Two contained mixed high grade carcinoma components. The components had shared pathogenic mutations in all 16 examined tumours.
Conclusion: In summary, our results show that mixed epithelial endometrial and ovarian carcinomas are rare, but thorough morphological and immunohistochemical examination is a reliable tool for their detection. In the samples we examined, synchronous, biologically unrelated, so-called collision tumours did not occur. The distinction of tumours showing transdifferentiation of one histological type to another, from those arising through divergence of two or more histological types from a common progenitor is not always clear.

PS-10-009

Improving the diagnosis of serous tubal intraepithelial carcinoma (STIC) using deep learning

J. Bogaerts*, J. Bokhorst, M. van Bommel, M. Steenbeek, J. de Hullu, M. Simons, J. van der Laak
*Radboud University Medical Center, The Netherlands

Background & objectives: Diagnosing Serous Tubal Intraepithelial Carcinoma (STIC), a precursor of high-grade serous carcinoma, is important for individual patient care and investigating new risk-reducing strategies. However, reproducibility of STIC among pathologists is suboptimal, and many pathologists have limited experience with the diagnosis.
Methods: We collected, digitalized, and annotated 496 cases. The reference standard was set by a panel of five gynaecologic pathologists. An automated deep-learning algorithm was developed to detect regions that potentially contained STIC. Discrimination of STIC from normal was assessed by analysis of area under the curve (AUC) in ROC curve analyses. Mapped areas of STIC were highlighted for visual review.
Results: The deep learning model was evaluated on two independent test sets, one which was acquired from the same data sources as the

training set and one from fully external sources. The first set achieved an AUC of 0.981 (0.96 - 0.99) on slide level. The second, fully external test set, containing 78 cases with STIC/STIL lesions and 112 control cases, reached an AUC of 0.949 (0.90-0.99), showing an overall underlining robustness of the algorithm. Subsequent visual inspection confirmed accurate detection of STIC/STIL lesions in relation to the morphology, immunohistochemistry and the reference standard set by the expert panel.
Conclusion: Reliably diagnosing STIC is critical for the safety of patients who opt for alternative risk-reducing surgery. Moreover, women with STIC seem to be at an increased risk of developing peritoneal carcinoma, raising issues about management and follow-up. Accurate detection of STIC is therefore essential but is constrained by limited experience and observer variability. In this study, we demonstrate that a deep-learning algorithm has the potential to identify STIC automatically and thus may improve the accuracy of this difficult diagnosis.
Funding: Dutch Cancer Society (KWF)

PS-10-010
Change in the incidence trend of early miscarriages during the COVID-19 pandemic: Single-centre retrospective cohort study
D.P. Burlacu*, A. Burlacu, B. Szabo, T. Mezei
*Department of Pathology of Emergency Clinical Hospital of Targu-Mures, Romania, Romania

Background & objectives: Pregnant women, especially during the first trimester, are considered more vulnerable to viral infections due to their pro-inflammatory state. This study aims to assess the incidence trend of early miscarriages and the influence of the COVID-19 pandemic on pregnancy outcomes.
Methods: A retrospective-cohort study was conducted including all pregnant women admitted to Targu-Mures Clinical Hospital, Romania, between January 2018-December 2022. Early miscarriages percentage recorded during pre-pandemic was compared with those registered during the COVID-19-pandemic, March 11th 2020 being officially declared the pandemic beginning. Early pregnancy outcomes (viable and ectopic pregnancies, medical and spontaneous abortions) were measured as total number and percentage.
Results: The annual incidence of registry-identified early miscarriages has declined from 5.4% 12– 46-year-old women in 2018 to 3.6% in 2022 (p=0.008). An overall incidence rate of 3.66% [95% C.I. 3.26-4.05] was calculated, with 4.25% [95% C.I. 3.35-4.41] in the pre-pandemic period and 3.24% [95% C.I. 2.82-3.57] during the pandemic. A higher incidence rate was identified among nulliparous (36.9%), followed by multiparous (35.9%) and primiparous women (27.2%) (p<0.0001). It mostly occurred during the 8th gestational week (14.1%, p<0.0001), in women aged > 30 years (23.8%), > 20 years (19.9%), and < 20 years (17.5%), (p<0.0001). 0.9% of early miscarriages and one maternal death were associated to Sars-COV2 infection (p= 0.978).
Conclusion: Our study demonstrates that the increase of early miscarriages incidence rate is attributable to advanced maternal age. To our knowledge, the present study is the first European study that proves the incidence rate of early miscarriages during the COVID-19 pandemic was not significantly increased, suggesting that this viral infection does not alter the risk of miscarriages. These findings should help women to cope with any additional emotional stress caused by pregnancy during periods of pandemics.

PS-10-011
panTRK is expressed in a variety of malignant uterine mesenchymal tumours without identifiable NTRK-associated gene fusions
C. Connolly*, C. Murray, A. Hodgson
*Toronto General Hospital, Canada

Background & objectives: Previous work has documented panTRK immunohistochemical positivity in a subset of uterine leiomyosarcomas and high grade endometrial stromal sarcomas. We aimed to assess panTRK expression in a wider spectrum of uterine mesenchymal neoplasms.
Methods: Malignant uterine mesenchymal neoplasms diagnosed at our institution which had previously undergone targeted next generation sequencing (assessment of fusions +/- mutations) were immunohistochemically evaluated with panTRK immunohistochemistry (clone EPR17341). Whole tumour sections from resection specimens were stained and pattern (cytoplasmic, nuclear, membranous), extent (focal, patchy, diffuse) and intensity (weak, moderate, strong) of expression was recorded.
Results: 12 uterine mesenchymal tumours were studied: 6 endometrial stromal sarcomas (3 low grade, 3 high grade), 2 inflammatory myofibroblastic tumours, 2 adenosarcomas, and 2 leiomyosarcomas. All tumours had typical disease-defining fusions or no detectable fusion (i.e., no identifiable fusion involving NTRK genes). panTRK immunoexpression was identified in 11/12 tumours and the neoplasm that showed no expression was a low grade endometrial stromal sarcoma with a EPC1::EED fusion. Diffuse strong cytoplasmic staining was seen in 3/3 high grade endometrial stromal sarcomas as well as 1/2 adenosarcomas. The remaining positive tumours (n = 7) showed focal to patchy often weak cytoplasmic expression and 2/7 showed focal or patchy strong nuclear staining.
Conclusion: This study supports the known conclusion that the diagnosis of a NTRK-related fusion-driven neoplasm cannot be made based solely on the immunohistochemical expression of panTRK. The significance of panTRK immunohistochemical expression in multiple different uterine mesenchymal neoplasms without NTRK-related fusions is, as of yet, not entirely clear but continues to raise questions regarding a) the exact mechanisms causing this, and b) the possible therapeutic utility of selective TRK inhibitors in the treatment of these neoplasms.

PS-10-012
Complex genomic and transcriptomic analysis in uterine tumours resembling ovarian sex cord tumour (UTROSCT)
M. Flídrová*, N. Hájková, K. Němejcová, J. Hojný, J. Dvořák, R. Jakša, Q.H. Bui, J. Laco, J. Škarda, G. Mccluggage, G. Giordano, E.M. Silini, P. Dundr, M. Kendall Bártů
*Department of Pathology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic

Background & objectives: UTROSCT is a rare entity. Most tumours behave in a benign fashion, but clinically aggressive neoplasms have been described. Our aim was to perform a comprehensive genomic and transcriptomic analysis in a series of UTROSCT to reveal clinically relevant alterations.
Methods: DNA and RNA isolated from 30 UTROSCT were analysed using capture DNA NGS analysis (KAPA HyperPlus kit and a panel of 788 genes/gene parts; 2044 kbp; Roche) and transcriptome RNA-Seq (KAPA RNA HyperPrep kit; Roche), and pair-end sequenced on NextSeq 500 or NovaSeq (Illumina). Only likely pathogenic or pathogenic (class 4/5) mutations and gene fusions were evaluated.
Results: The analyses of our sample set revealed the presence of several recurrent gene fusions in the majority of the cases, including NCOA2/3. Moreover, whole transcriptome RNA-Seq revealed additional rare gene fusions such as COL6A3::FAM13B. Other alterations detected included rare class 4/5 mutations in CHEK2 and RECQL4.
Conclusion: Our complex study of the molecular alterations in UTROSCT has revealed potentially significant gene fusions and genetic alterations in these tumours, some of which may be clinically actionable.
Supported by Ministry of Health of the Czech Republic (project no. NU21-03-00122 and RVO64165, General University Hospital in Prague) and by Charles University (Project UNCE204065).

PS-10-013

A clinicopathologic analysis of somatically derived germ cell tumours of the female genital tract

M. Fukunaga*
*Shin-yurigaoka General Hospital, Japan

Background & objectives: Female genital tract malignant epithelial neoplasms with germ cell tumours (GCTs) are very rare and pose diagnostic and therapeutic challenges. This type of neoplasm usually arises in postmenopausal females. The objective is to clarify the clinicopathologic features and its histogenesis.
Methods: A total 18 cases of these neoplasms with GCTs in patients aged 40 years or over, except one of 31 years, were clinicopathologically and immunohistochemically studied.
Results: The age of the patients ranged from 31 to 79 years. Eight tumours were in the endometrium, 6 in the ovary, 2 in the tube, one each in the cervix or peritoneum. Five each had choriocarcinoma, hepatoid carcinoma, or yolk sac tumours (YSTs), two had immature teratomas and one had YST and hepatoid carcinoma. There were malignant epithelial tumours comprising high-grade serous carcinoma (n=7), endometrioid carcinoma (n=3), large cell neuroendocrine carcinoma (n=3), clear cell carcinoma (n=3), and gastric type mucinous carcinoma (n=2). There was some immunophenotypic overlap with carcinomas and YSTs. Follow-up data were available in 11 cases. Six died of the disease within 12 months (mean: 8.5) after surgery.
Conclusion: The findings suggest the association between GCT and epithelial malignant neoplasm, with the former probably arising from the latter through a process of neometaplasia or retrodifferentiation in the female genital track. Somatic epithelial neoplasm can be of various histologic types. This type of tumour can occur in young patients. Its recognition is necessary in view of its unusually aggressive behaviour and associated poor prognosis. Adjuvant chemotherapy regimens should include platinum-based chemotherapy, aiming at treatment for both carcinoma and GCT.

PS-10-014

Histologic findings in hysterectomy and oophorectomy specimens in individuals undergoing gender-affirming surgery

J. Gama*, F. Ramalhosa, J. Madeira, V. Almeida, C. Courelas, J.L. Amaral, B. Sepodes, A. Alves, J. Pimentel, M.A. Cipriano
*Centro Hospitalar e Universitário, Portugal

Background & objectives: Gender-affirming surgery is increasingly common and it is part of the process of gender transitioning. Histological changes that may happen under hormonal treatment are important to recognize and are not yet fully described.
Methods: A retrospective study (2016-21) was carried out. Clinical and pathological data were retrieved from the hospital database. Histological evaluation of the surgical specimens was performed, all surgical gynaecologic pathology and cytology slides were reviewed.
Results: A total of 28 patients were included, which represented 28 hysterectomy and bilateral salpingo-oophorectomy specimens, 2 vaginectomy specimens and 5 cervical cytologies. The median age at surgery was 29 years and all patients were under treatment with testosterone.
Twenty-one patients (75%) exhibited transitional cell metaplasia of the cervix and 2 of the vagina (100%). Prostatic-type glands were identified in two patients (7.1%). Inactive endometrium was present in 17 (60.7%) patients, active in 10 (35.7%), disordered proliferative in 1 case (3.5%). In two patients (7.1%) adenomyosis was found. The ovaries were mostly multifollicular (27 patients, 96,4%). Of note, one of the patients had a serous borderline tumour of the ovary.
Conclusion: Histological changes after hormonal treatment are mostly related to transitional metaplasia of the cervix and vagina. The awareness of these changes, in this population, is important in order to avoid a potential misdiagnosis. The presence, although rare, of pre-neoplastic and neoplastic lesions prompts a careful study of these specimens.

PS-10-015

NK cell-mediated antitumour immunity in endometrial carcinoma

P. Janega*, M. Kuhnel, A. Janegova
*Institute of Pathological Anatomy, Comenius University in Bratislava, Medirex Group Academy, n.p.o., Nitra, Slovakia

Background & objectives: Natural killer cells are lymphocytes with cytotoxic and immunomodulatory activity. In endometrium, they are involved in angiogenesis, nidation of the embryo and its tolerance by the maternal immune system. Their role in tumour transformation in endometrium is not entirely clear.
Methods: The pilot study included patients with endometroid carcinoma who met specific criteria (MSS, pT1a). Tumour tissue was assessed for the presence of natural killer cells using immunohistochemistry. CD56+ and CD57+ lymphocytes were quantified in 5 random fields in neoplastic tissue and in surrounding endometrial tissue. Results were compared and correlated with hormone receptor positivity, tumour grade, and patient age.
Results: Results of our study showed no significant difference in the presence of CD56+ NK cells between tumour and surrounding non-tumour tissue. However, there was a significant correlation between the number of CD56+ NK cells in both areas. CD56+ NK cell presence was not correlated with tumour grading or hormone receptor positivity but was negatively correlated with patient age. In contrast, CD57+ NK cells were significantly increased in the tumour bed compared to surrounding non-tumour tissue. CD57+ NK cell presence was not related to tumour grading, hormone receptor positivity, nor patient age.
Conclusion: The study's findings indicate that NK cells are involved in endometrial tumour transformation. CD56+ NK cells appear to reflect general immune activation, as their upregulation is seen in both tumour and surrounding tissue. Notably, this activation significantly decreases with patient age. In contrast, CD57+ NK cells are more associated with local immune system activation, suggesting more targeted immune response.
Funding: BIOMEDIRES II. phase, 313011W428

PS-10-016

Somatic neoplasms arising from teratomas - a quaternary care centre experience

A. Lakshmanan*, N. Mulchandani, S. Naresh Shah, M. Menon, A. Subramanyam
*Apollo Hospitals, India

Background & objectives: Somatic-type neoplasms (SN) arising from any of the germ-cell elements of teratomas can either be benign or malignant. SNs are mostly associated with mature teratoma (MT) and less commonly with immature teratomas (IT) and mixed germ cell tumours (MGCT).
Methods: Over an 8-year-period (January 2014 to December 2022), 1198 reported cases of teratomas, arising at gonadal and extra-gonadal locations were retrieved from the database. We studied 80 cases of SN arising in teratomas to evaluate their morphology and immunohistochemistry (IHC) features. The SNs were further categorized as benign, borderline, and malignant.
Results: The age range was 10 months - 79 years with a M:F ratio of 1:8. Teratomas were seen most commonly in the ovaries (87.5%), followed by testis (5.8%), mediastinum (2.5%) and the rest in other sites. Pure MT was the commonest diagnosis (90.4%), followed by MGCT (6.3%) and IT (3.3%).
The SNs were categorized as benign (n=51; 63.8%), borderline (n=5; 6.2%), and malignant (n=22; 27.5%). Remaining 2 cases (2.5%) showed immature glial proliferation.
Mucinous cystadenoma was the commonest benign SN and atypical proliferative serous tumour was the commonest borderline neoplasm.

Somatic malignancies included carcinomas, sarcomas, neuroblastoma and high-grade glioma with squamous cell carcinoma and adenocarcinoma being the commonest entities.
Conclusion: Ours is the largest study from India to study the SNs arising in teratomas. Development of somatic-type malignancies in germ cell tumours represents a significant challenge in diagnosis and treatment. They are often resistant to chemotherapy and are mostly amenable to surgical treatment. Hence, adequate sampling of teratoma with appropriate use of IHC in cases wherever deemed necessary is recommended to not miss and to correctly diagnose the associated somatic-type malignancies.

PS-10-017
Phosphohistone H3 (PHH3) expression in the risk rating for endometriosis
L. Lozneanu*, I.D. Căruntu, S.E. Giușcă, R. Balan, B. Toma, R.D. Matasariu
*U.M.F. "Grigore T. Popa" Iasi, Romania

Background & objectives: Endometriosis represents a chronic inflammatory disease. Phosphohistone H3 (PHH3) facilitates cellular damage and inflammation in endometriosis. As the prevalence endometriosis in Romania is high, we aim to to analyse PHH3 expression in both groups with and without Progesterone (hormonal) treatment.
Methods: 30 patients with endometriosis followed up at Obstetrics and Gynaecology, Cuza Vodă Hospital, Iaşi, Romania, between 2021-2022 were retrospectively selected. Clinicopathological features and gynaecologic examinations were assessed. Immunohistochemistry analysis for the evaluation of PHH3 expression status in endometriotic foci of both groups was performed. PHH3 was expressed in the glandular epithelium and endometrial stroma of both groups.
Results: Our series included 18 (60%) cases without hormonal treatment and 12 (40%) cases with hormone therapy. The PHH3 negative expression was found in 16 (53%) cases, being in equal distribution in both groups, while from 14 (47%) positive expression, 10 (71%) were without hormonal treatment, and 4 (29%) with hormone therapy.
Conclusion: To our knowledge, this is the first Romanian case series showing high prevalence of PHH3 in endometriosis patients with and without hormonal treatment. Positive PHH3 expression was found in the non-treatment group, showing an increasing trend compared to treatment group. PHH3 might be involved in the progression of endometriosis in patients without hormonal treatment. Progesterone is likely responsible for this difference. Since PHH3 showed less expression in hormone therapy group, blocking PHH3 can inhibit the progression of endometriosis.

PS-10-018
"Deciduoid" change in uterine leiomyomas in pregnancy: aberrant expression of sex cord markers inhibin and calretinin
J. Machuca Aguado*, G. McCluggage
*Virgen Macarena University Hospital, Seville, Spain

Background & objectives: Leiomyomas are common hormone responsive uterine neoplasms which can exhibit a variety of morphological changes secondary to hormonal agents such as progestogens. Surprisingly the morphological features of leiomyomas in pregnancy are not well described in the literature.
Methods: Retrospective observational clinicopathological study of a series of 29 uterine leiomyomas in pregnancy. Clinicopathological features were collated.
Results: The morphological features included, in decreasing order of frequency, infarct-type necrosis, decidualisation of the serosal surface, hyalinisation, myxoid alteration of the stroma, oedema (sometimes with cyst formation) and dystrophic calcification. We also report a feature which we term "deciduoid" change (seen in 10 of 29 leiomyomas) which takes the form of altered smooth muscle cells with an epithelioid morphology with abundant eosinophilic or clear cytoplasm. Furthermore, we show that the "deciduoid" cells commonly exhibit expression of sex cord markers inhibin and calretinin. We speculate on the pathogenesis of the "deciduoid" change which together with its "aberrant" immunophenotype may result in diagnostic problems and consideration of other neoplasms.
Conclusion: We report the histological features in a series of leiomyomas in pregnancy. These include an alteration which we term "deciduoid" change because of the resemblance to decidualised stromal cells. We believe these "deciduoid" cells represent modified smooth muscle cells probably altered by the hormonal milieu of pregnancy. These "deciduoid" cells can exhibit an unusual immunophenotype, including aberrant expression of inhibin and calretinin; the morphological alterations and aberrant immunophenotype may result in diagnostic problems if pathologists are unaware of this phenomenon.

PS-10-019
Tumour-infiltrating lymphocytes (TILs) digital quantification as a relevant prognostic biomarker in high-grade serous ovarian cancer
J. Machuca Aguado*, A.F. Conde-Martín, A. Álvarez-Muñoz, E. Rodríguez-Zarco, J.J. Rios Martin, M.A. Idoate Gastearena
*Virgen Macarena University Hospital, Seville, Spain

Background & objectives: It is postulated that Tumour Infiltrating Lymphocytes (TILs) can have a significant prognostic and predictive role in high-grade serous ovarian carcinoma (HGSOC). However, only three studies have reported the prognostic value of TILs in HE-stained sections in this tumour type.
Methods: 76 molecularly and clinically, well characterized HGSOC III/IV staged (FIGO) cases were studied. HE-stained sections were evaluated digitally using learning image analysis algorithms. IeTILs (ratio intrachordonal immune cells number/tumour cells number) and sTILs (immune cells number in the stroma/total stromal area) were quantified and correlated with disease free survival (DFS) and overall survival (OS).
Results: Interestingly, 40% of cases showed intense colonisation of tumour chords by TILs, especially in cases which had received neoadjuvant treatment. A correlation between DFS with ieTILs (r=0.252; p=0.028) and sTILs (r=0.231; p=0.045) was observed.
Furthermore, this correlation showed greater significance when tumours were assessed by median, with high-ieTILs showing longer DFS than low-ieTILs (median 33 months vs. 20 months; p=0.008). The same was found for high-sTILs when compared to low-sTILs (median 31 months vs. 18 months; p=0.033).
In addition, high-ieTILs demonstrated a longer five-year survival when compared to low-ieTILs (77% versus 29.9%; p=0.028). However, this was not observed in sTILs.
Conclusion: We consider that the quantification of TILs on H&E-stained sections using a digital quantification is an appropriate approach for clinical purposes. We have shown that quantification of TILs, especially TILs location, could be a relevant prognostic parameter in HGSOC, supporting the role of antitumour effect of immune response in ovarian cancer.

PS-10-020
Molecular classification of endometrial carcinoma (EC): a single institution experience with 144 ECs exclusively tested by NGS
K. Michalova*, O. Ondic, J. Presl, P. Martinek, N. Hejhalova, A. Hluchy, A. Strakova-Peterikova, M. Michal, M. Michal
*Department of Pathology, Faculty of Medicine in Pilsen, Charles University, Pilsen, Czech Republic

Background & objectives: POLEmut ECs have excellent prognosis requiring no adjuvant therapy. Sanger sequencing is used for

POLEmut detection but in comparison with NGS has 50% sensitivity, leading to overtreatment of POLEmut patients. We share our experience with molecular classification performed by NGS.
Methods: All molecularly classified EC from Pilsen Faculty hospital were included. All cases were examined by morphology, IHC (MSH2, MSH6, PMS2, MLH1, p53) and by NGS with GynCore oncopanel (Archer, Inc) specifically designed for EC and containing 16 genes of interest. Clinical data were obtained from the electronic database of the hospital.
Results: The cohort included 144 patients and was composed of 7 POLEmut EC (4.99%; 3 endometroid EC grade 3, 4 endometroid EC (grades 1-2)), 41 MMRd EC (28.5%; 31 sporadic EC, 10 suspicious of Lynch syndrome), 80 NSPM EC (55,6%) and 16 TP53mut EC (11,1%). The mean follow-up time was 45 months. Ninety-seven patients were alive, with no signs of recurrence, including 5/7 POLEmut EC, 26/41 MMRd EC, 63/80 NSMP and 3/16 TP53mut. The remaining 2 POLEmut patients are alive with disease, both were diagnosed at stage 3 (FIGO IIIA and IIIC1, respectively), the time of follow-up was 28 and 30 months, and patients aged 59 and 88 years, respectively.
Conclusion: Our large cohort encompassing 144 prospectively studied EC classified exclusively by NGS into 4 molecular groups further highlights the importance of incorporation of routine molecular classification of EC as it has a high impact on patient´s management. Furthermore, the importance of using NGS for detection of POLE mutations needs to be emphasized as this method is far more reliable than Sanger sequencing.

PS-10-021

Tumour infiltrating lymphocytes in early-stage high grade serous ovarian cancer: prognosis significance of visual and digital analysis

S. Molés Caparrós*, A. Veliz Dominguez, J.C. Corredor-García, A. Tenelanda-Santillán, N. Cadavid-Fernández, I. Romero, J.A. López-Guerrero, A. Poveda, I. Carretero-Barrio, B. Pérez-Mies, J. Palacios Calvo
*Ramón y Cajal University Hospital, Spain

Background & objectives: The aim of this study is to determine the prognosis significance of CD4 and CD8 tumour infiltrating lymphocytes (TILs) in early-stage high grade serous ovarian carcinoma (HGSOC) and determine whether digital quantification can improve prognosis stratification in those patients.
Methods: We studied TILs in HGSOC tissue microarrays cores stained with CD4 and CD8. We counted intraepithelial and stromal TILs visually and with digital analysis, establishing >20 TILs/core as high TILs. We used QuPath to perform the digital analysis. We studied the correlation between visual and digital count and performed a survival analysis comparing tumours with high and low TILs.
Results: We evaluated 109 patients: 51 for intraepithelial (i) and stromal (s) CD4 and CD8 TILs, 29 for CD4, and another 29 for CD8. We found statistically significant differences in mean TILs between visual and digital analysis in all settings (iCD4, iCD8, sCD4, SCD8 TILs). For example, visually the average iCD8 count was of 25.5 TILs/core, whereas digitally it reached 46.5. We also found a positive linear correlation between visual and digital count. With both visual and digital analysis, high iCD8 TILs were associated with better survival. However, only with visual analysis we found better survival in patients with low iCD4 TILs.
Conclusion: There is an association between TILs and prognosis in early stages of HGOC: higher iCD8 TILs, as well as lower iCD4 TILs, entail better outcomes. Digital analysis showed a good correlation with visual analysis, proving its value as an assistant diagnostic tool. However, more studies should be done in order to improve its usefulness for prognosis stratification in HGSOC.
This research was supported by CIBERONC (CB16/12/00316), Instituto de Salud Carlos III, Ministerio de Ciencia e Innovación and Unión Europea – European Regional Development Fund. This study has been funded by Instituto de Salud Carlos III (ISCIII) through the project "PI22/01892" and co-funded by the European Union. Developed with the financial support of Immune4ALL Project (PMP22/00054), with European funds of the Recovery, Transformation and Resilence Plan, and financed by the Instituto de Salud Carlos IIII. Supported by the Spanish Group of Research in Ovarian Cancer (GEICO group).

PS-10-022

Clinicopathological and molecular features of mesonephric-like adenocarcinoma of uterine corpus

C. Mora*, J. Ferreira, F. Cunha, F. Silva, P. Silva, C. Albuquerque, A. Félix
*Serviço de Anatomia Patológica, Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisbon, Portugal

Background & objectives: Mesonephric-like adenocarcinomas (MLA) are rare tumours of the uterine corpus with a poor prognosis. Differential diagnosis can be difficult. Frequent KRAS mutations have been described. We report the clinicopathological and molecular findings in a series of MLA.
Methods: Five MLA cases were included. Clinical data was retrieved. H&E and immunohistochemistry (GATA3,TTF1,CCD10,p53,ER,PR) slides were reviewed. NGS targeting *KRAS, NRAS, PIK3CA, PTEN, POLE, TP53, EGFR, BAP1* and *CTNNB1* mutations was performed.
Results: Patients' median age was 72 years old(48-75yrs). FIGO stage distribution was IA(1),IB(1),II(2),IVB(1). Patients were treated with surgery(n=5) and adjuvant chemo/radiotherapy(n=4). All neoplasms showed a variety of histological patterns. Numerous LVI were observed in 4 cases. Tumours were GATA3+(5/5), TTF1+(4/5), CD10+ apical staining(4/5), p53 wild-type(4/5), ER/PR negative(5/5). In one tumour, p53 null pattern was observed. Inverted GATA3/TTF1 staining was observed in 3 cases. All tumours were MMR proficient(3/3). Four cases harboured pathogenic *KRAS* mutations, three with c.35G>T p.(Gly12Val), and one with c.35G>C p.(Gly12Ala). No mutations were found in the other genes analysed. During a median follow-up of 21 months (11-46), three patients developed recurrence/distant metastasis, and two died of the disease.
Conclusion: In our series, all but one case had at least 2 mesonephric markers expression. One case only had GATA3 expression but had typical morphology and was *KRAS* mutated. *KRAS* mutations are a frequent event. p53 mutated pattern was observed in one case with otherwise typical morphology and immunohistochemical findings, which can aggravate diagnostic challenge. Irrespective of stage, MLA is a highly aggressive neoplasm.

PS-10-023

Endocervical adenocarcinoma (ECA): Reclassification as per IECC into HPV associated(HPVA) and HPV independent(HPVI) using morphology, P16INK4a immunohistochemistry and HR-HPV RNA in situ hybridization(ISH)

A. Mundada, K. Deodhar*, B. Rekhi, S. Menon, N. Mittal, O. Shetty, O. Salvi
*Tata Memorial Hospital, Homi Bhabha National University, India

Background & objectives: The year 2018 witnessed a breakthrough in the field of cervical adenocarcinoma when Stolnicu and colleagues proposed a new pathogenetic classification for endocervical adenocarcinomas based on their association with HPV which was adopted by the WHO in the 2020 update.
Methods: Retrospective study was undertaken at a tertiary care oncology centre in India to study the clinical and pathological features of cases of ECA whose resection specimens were received at the department of pathology from 2016 to 2020. Cases were classified as HPVA or HPVI based on morphology by two pathologists and compared with results of immunohistochemistry for p16INK4a and HR-HPVISH.
Results: The IECC morphologic classification had perfect interobserver agreement in 76/79 (96.2%) cases. HPVA cases n=68 (86%) with usual 77.9%, mucinous 10.2%, intestinal 4.4%, ISMC 4.4% and

n=11 (13.9%) HPVI cases with gastric 45.4%, clear cell 27.3%, mesonephric 18.2%, endometrioid 9.1%. 87.7% HPVA were positive for P16. HR-HPV RNA ISH was performed for 10 cases (HPVA 85.71% positive, HPVI 100% negative). Silva pattern of invasion(POI) for HPVA was Type A 14.7%; Type B 39.7%; Type C 45.6%. Nodal metastasis was observed in 21.9% HPVA, 28.6% HPVI cases. The mean follow-up time was 41.68 months (range 0.9–96). Recurrence free survival was 56.97 and 37.97 months for HPVA and HPVI cases respectively.

Conclusion: IECC by morphology is highly reproducible. Sensitivity of P16 was 87.7% with PPV of 96.6%.HR-HPV RNA ISH remains a costlier approach and is highly dependent on tissue preservation and viral load. None of the cases with type A POI had nodal metastasis as compared to 45.5% with type B and 54.5% with type C POI. With respect to overall survival and recurrence free survival, HPVI cases (HR 1.84, 1.45,) as compared to the HPVA cases (HR 1.0, 1.0) (95% CI,p=0.3,0.4)respectively.

Funding: Institutional intramural funding was received for this project.

PS-10-024

Characterisation of uterine leiomyosarcomas: a single-centre retrospective study of 19 tumours

D. Piñol Ballús*, A. Prat, S. Acosta, M. Miralles, M.C. Campos, E. Lerma, A. Gallardo
*Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Background & objectives: Uterine leiomyosarcomas (ULMS) are rare and aggressive tumours with a poor clinical outcome. The genetic complexity of ULMS is well-established. The objective of this study was to retrospectively analyse the molecular profile using surrogate immunohistochemical stains.

Methods: We analysed the molecular profile of 19 patients with ULMS diagnosed at our institution between 2013 and 2023.

Results: The study included 19 women aged 46-67 years with a recent diagnosis of ULMS. Thirteen patients presented with locally advanced metastatic disease at diagnosis, and seven patients died during follow-up. The tumours were located in the uterine corpus and ranged in size from 63-180 mm. All ULMSs showed smooth muscle differentiation and presented necrosis, severe pleomorphism, and lymphovascular invasion. Tumour mitotic rate ranged from 7-70 mitosis/mm2. 12 tumours showed variable expression of hormone receptors. 4 tumours were focally positive for cytokeratin markers. IHC analysis revealed mutations in TP53 (53%), ATRX (63%) and CDKN2A/p16 (89%). However, these molecular alterations did not correlate with patient survival or mortality.

Conclusion: TP53, ATRX, and CDKN2A/p16 are frequently mutated genes in ULMS. Hormone receptor expression and molecular alterations showed no correlation with patient survival. The frequent mutations in TP53, ATRX, and CDKN2A/p16 identified in our cohort support their potential as biomarkers for ULMS diagnosis and prognosis. Further studies with larger sample sizes and longer follow-up periods are needed to confirm these findings and explore the clinical utility of these biomarkers.

PS-10-025

HER2 testing in endometrial carcinoma, a summary of real world initial experience in a large tertiary cancer centre

A. Plotkin*, E. Olkhov-Mitsel, S. Nofech-Mozes
*Precision Diagnostics and Therapeutics Program, Sunnybrook Health Sciences Centre, Toronto, Department of Laboratory Medicine and Pathobiology, University of Toronto, Canada

Background & objectives: Trastuzumab has been approved for treatment in HER2 positive endometrial serous carcinoma (ESC) based on results of randomized clinical trials. We audited our experience in a tertiary care centre where testing is performed by clinician's request.

Methods: Endometrial carcinoma cases were tested by HER2 immunohistochemistry (IHC) using Ventana 4B5 antibody (Roche). Cases with equivocal IHC (score 2+) were further tested by dual-probe FISH assay (PathVysionHER2 DNA Probe kit). All cases were reported by one of two experienced HER2 FISH readers gynepathologists based on the practical recommendations proposed by ISGyP. Tumour characteristics were extracted from the pathology reports.

Results: Over 18 months we tested 48 samples (from 47 patients); 47.9% were biopsies, 83.3% primary tumours, 52% serous and 48% non-serous endometrial cancer (EC) including 8.3% low grade endometrioid adenocarcinoma. Six cases were evaluated by two readers. HER2 was positive in 29.2% (35.7%- had IHC score 3+ and 64.3% showed HER2/neu gene amplification). The majority (78.6%) of positive cases showed heterogenous signal by either IHC or FISH. Among HER2 positive cases, 8 were ESC, 3 carcinosarcomas, 2 (high grade) HG-NOS and 1 ambiguous. P53 was abnormal in 8 cases and unknown in 6.

Conclusion: In our institution, about half of the requests for HER2 testing occurred in non-serous EC cases reflecting the notion that histologic subtyping of high grade EC is challenging as well as the limited management options for advanced EC. The frequent observation of intratumoral heterogeneity raises the need to further study its potential role in trastuzumab resistance, benchmarking and possible rational of testing antibody drug conjugates in endometrial carcinoma.

PS-10-026

Clinicopathological features of 231 endocervical adenocarcinomas, including p16INK4a immunostaining results: a study at a tertiary cancer referral centre, India

B. Rekhi*, A. Duggad, K. Deodhar, S. Menon, J. Ghosh, S. Gulia, T. Shylasree, A. Maheshwari
*Department of Pathology Tata Memorial Hospital, Parel, India

Background & objectives: There is no comprehensive study on clinicopathological features of endocervical adenocarcinomas (ECAs), including HPV-related features and p16INK4a immunostaining from our country. This study was aimed at evaluating 231 ECAs, focusing on HPV-related morphological features and p16INK4a immunostaining with other parameters.

Methods: Cases of ECA from Jan 2010-Dec 2015, including biopsies and/ or resections were evaluated for HPV-associated morphological features. p16INK4a(E6H4,Roche,USA) immunostaining was performed in 87(37.6%) tumours. Diffuse nuclear and cytoplasmic staining in >80% of tumour cells was considered as block-like/positive result. Histopathologically, there were 174/231(75.3%) usual-type ECAs; 14(6.1%) gastric-type; 13(5.6%) villoglandular; 8(3.4%) endometrioid; 7(3%) mucinous/signet-ring cell and 15(6.4%) other types.

Results: Age-range was 18-76 years (median=48). Stage-wise(n=142/231, 61.5%), most cases (67/142, 47.2%) were stage2, followed by stage1(45, 31.7%) and stage3(21,15%). There were 201/231(87%) tumours with HPV-associated morphological features. Most common HPV-associated was usual-type(174/201, 86.5%). The most common non-HPV-associated type was gastric-type(14/27, 51.8%). 63/87(72.4%) tested ECAs were p16INK4a-positive. 54/63(85.7%) tumours with HPV features were p16INK4a-positive.

Most patients underwent concurrent chemoradiotherapy. Silva pattern C was commonest (68/89,76.4%), was frequently associated with lymphovascular emboli(LVE)(85.7%) and nodal metastases (81.8%). On univariate analysis, larger tumour size, higher stage and lack of HPV-associated features were significantly associated with lower progression-free survival(PFS) ($p<0.001$, $p=0.003$, $p=0.011$). Nodal metastases and higher tumour stages led to lower overall survival (OS) ($p=0.049$, $p=0.017$).
Conclusion: Histopathologic features of HPV and block-like p16INK4a staining were useful in subtyping ECAs into HPV-dependent vs. non-HPV dependent. Tumours with HPV-associated features displayed improved PFS. Larger tumour size and higher stage were also associated with lower PFS.
Funding: Intramural, Institutional funding.

PS-10-027
DNA NGS and immunohistochemical analysis of a large cohort of adult granulosa cell tumours focusing on predictive aberrations.
A. Safanda*, P. Dundr, N. Hájková, J. Hojný, E. Krkavcová, R. Michálková, J. Laco, J. Škarda, J. Drozenová, R. Matěj, M. Hácová, K. Němejcová
*Department of Pathology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic

Background & objectives: We analysed a large cohort of adult granulosa cell tumours of the ovary (AGCT) with aim to perform a complex DNA analysis and reveal potentially clinically relevant alterations and immunohistochemical analysis of selected predictors of immunotherapy.
Methods: Paired-end capture DNA NGS analysis (KAPA HyperPlus kit; 788 genes, 2044 kbp; Roche) using NextSeq500 (Illumina) was performed with 87 FFPE AGCTs. The constructed pipeline in CLC Genomics Workbench (Qiagen) were used for evaluation of mutations, tumour mutation burden (TMB; TMB≥10 mut/Mb were considered as TMB-High) and microsatellite stability. Immunohistochemical analysis of HER2 and PD-L1 were performed on 120 samples.
Results: TMB in AGCTs ranged between 2-20 mut/Mb (median 6). 7/87 (8%) were TMB-High, and two of these were MSI-High. FOXL2 recurrent mutation (C134W) was found in 81/87 (93%) AGCTs. Moreover, in 8 of those was detected also second FOXL2 mutation (V261fs, *377fs, P332A, G240S, M220fs or K366fs). Other detected mutations included TERT, CHEK2, and TP53 (all found in ≥3 cases). The expression of HER2 was negative in the entire cohort. The expression of PD-L1 showed a similar result, with a single exception of a case with CPS slightly above 1.
Conclusion: Our complex DNA analysis of AGCT revealed potentially significant genetic alterations with possible impact on clinical practice. Regarding predictive immunohistochemical markers, our results may provide valuable knowledge for future immunotherapy research.
Supported by Ministry of Health of the Czech Republic (project no. NU21-03-00238 and RVO64165, General University Hospital in Prague) and by Charles University (Project UNCE204065).

PS-10-028
Association of PD-L1 expression with clinicopathological and prognostic characteristics in cervical cancer: a single-institution study
G. Sahraoui*, F. Sassi, M. Manai, R. Mchiri, R. Doghri, L. Charfi, K. Mrad
*Salah Azaiez Institute, Tunisia

Background & objectives: The immune checkpoint PD-L1 plays a crucial role in immunosuppression in cervical cancer (CC). This study aimed to determine the expression profile of the PD-L1 protein in CC and investigate the correlations between PD-L1 status and clinicopathological and prognostic characteristics.
Methods: This retrospective descriptive study collected 146 cases of CCs from medical records and pathological reports. The expression of PD-L1 was assessed through immunohistochemistry using the laboratory's protocol. The mean age of the patients was 54 years (23-87 years), and the average tumour size was 40.7 mm (5-90 mm).
Results: Squamous cell carcinoma was the most common histological type (88.3%). CCs were well-differentiated in 62.6% of cases, and stage 2B was observed in 49% of cases. Vascular emboli were seen in 7.1% of cases. Concomitant radio-chemotherapy was recommended in 86.8% of patients, and brachytherapy was indicated in 79.7% of patients. More than half of the patients underwent surgery. Distant recurrence occurred in 17.3%, while pelvic recurrence occurred in 20.4% of cases. The evolution was favourable in 39.3% of cases. Immunohistochemical analysis revealed PD-L1 expression in 32.4% of tumour cells and 47.1% of immune cells. The expression of PD-L1 in tumour cells was associated with endometrial invasion ($p=0.014$).
Conclusion: PD-L1 is expressed in CCs, and the expression of PD-L1 in tumour cells was associated with endometrial invasion. Larger studies with a higher number of samples are required to evaluate the correlation between PD-L1 and histoprognostic factors to support the role of this biomarker in the progression of CCs.

PS-10-029
TLR4 down-regulation identifies high risk HPV infection and integration in cervical squamous cell carcinomas
A. Santoro*, M.C. Pedicillo, I.S. De Stefano, G. Aquino, M.L. Tornesello, F. Miele, N. D'Alessandris, G. Scaglione, F. Addante, G.F. Zannoni, G. Pannone
*Pathology Unit, Department of Woman and Child's Health and Public Health Sciences, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Background & objectives: There are few studies on TLRs mediated HPV-clearance in cervical oncology. We evaluated whether TLR4 expression identifies HPV infection and HR-HPV integration in 40 bioptical samples of cervical squamous cell carcinoma (CSCC) and 20 HSIL bioptical samples.
Methods: TLR4 levels was studied by IHC, HR-HPV integration by ISH, and viral typing by RT-PCR-based assay. TLR4 staining intensity (TLR4-SI), TLR4 percentage of expression and Combo Score (TLR4-CS) has been evaluated. Similarly, by IHC also CK19 and p16 expression were studied.
Results: TLR4-SI and TLR4-CS are downregulated in HSIL and CSCCs, compared to normal cervix ($p=.001$, ANOVA; $p=.004$; Kruskal-Wallis test). Significant differences have been observed between TLR4 % expression in normal epithelium and HSIL and between HSIL and CSCCs ($p<0.05$; ANOVA). ISH HPV+ samples reported TLR4-SI lower levels than negative samples ($p = .002$). Pointbiserial correlation revealed association between TLR4 expression and HR-HPV integration ($p = .0001$) and between TLR4 expression and HPV16 infection ($p = .001$). An inverse significant relationship between TLR4-SI, CK19 ($R=-0.4906$; $p=0.0001$, ANOVA) and p16 has been observed. A correlation between TLR4 downregulation and inflammatory microenvironment has been demonstrated ($R=0.5341$; $p=0.001$, ANOVA).
Conclusion: TLRs are main actors of the immune-response against HPV transformed cancer cells. In the present study, TLR4 downregulation is strongly associated with HR-HPV (HPV16+) integration in CSCCs, CK19 and p16 over-expression, in this way acting as an important biological actor for immuno-escape. This study reveals important implications for diagnostic approach, immunotarget therapy, and vaccination strategies.

PS-10-030

Risk stratification of endometrioid endometrial carcinoma (EEC) of no specific molecular profile (NSMP) utilizing E2F1 and CCNA2 RNA expression and PPP2R1A/FBXW7 mutation status

M. Shahi*, S. Yadav, S. Jenkins, J. Bakkum-Gamez, N. Kanwar, J. Gonzalez Bosquet, K. Halling, K. Podratz
*Mayo Clinic, USA

Background & objectives: NSMP molecular subgroup consists of EEC with predominantly FIGO grade 1/2 histology with at least intermediate risk of recurrence. Intermediate/high-risk disease in histomorphologic low-grade EEC imposes prognostic/therapeutic challenges. We assessed the performance of a novel molecular risk-classifier in NSMP EEC.
Methods: The Cancer Genomic Atlas (TCGA) data was utilized. Three molecular profiles (MP) within the NSMP subgroup (N=89) were evaluated and correlated with clinical outcomes: MP1-E2F1+CCNA2 log2 expression low (L) (<4.75); MP2-. E2F1+CCNA2 log2 expression high (H) (≥4.75); and MP3- PP2R1Amu/FBXW7mu. Tumour grade, stage, L1CAM log2 expression, and CTNNB1mu, PIK3CAmu, ARID1Amu, KRASmu were studied in each MP.
Results: The 3-year recurrence free survival (RFS) for MP1, MP2 and MP3 was 93.6%, 36.7% and 61.1%, respectively; corresponding Cox univariate hazard ratios for recurrence(95% CI) were 14.329 for MP2 (3.6, 71.5) and 9.7 for MP3 (2.1, 49.6) respectively (MP1 reference, overall P=0.0002). No significant associations with PFS were found in univariate analysis of tumour grade, stage, L1CAM expression tertile, CTNNB1mu, PIK3CAmu, ARID1Amu, or KRASmu. RFS in FIGO grade 1 EEC with <75% Myoinvasion and MP1 vs. MP2/MP3 was 100% vs. 49.3%, respectively (p<0.0001).
Conclusion: We present molecular profiles (E2F1+CCNA2-H and FBXW7mu/PPP2R1Am vs. E2F1+CCNA2-L) that i) selectively identifies occult high-risk disease among histomorphologic low-grade EEC, ii) efficiently risk-stratified TCGA NSMP EEC, and iii) suggests potential value in molecular-surgical staging.

PS-10-031

Endometrial clear cell carcinoma mimickers (CCCM): morphologic, immunophenotypic and molecular evaluation of an enigmatic and diverse group of tumours

M. Shahi*, F. Reyes-Baez, K. Schoolmeester, M. McGree, A. Fought, L. Grcevich, G. Schivardi, G. Glaser, A. Mariani
*Mayo Clinic, USA

Background & objectives: Endometrial clear cell carcinoma (ECCC) is associated with aggressive behaviour. Besides its diverse molecular landscape and clinical behaviour, controversy regarding risk stratification can be due to overdiagnosis. A subset of non-ECCC (CCCM) exhibits histologic characteristics resembling ECCC, imposing diagnostic difficulties.
Methods: Cases diagnosed as ECCC or carcinoma with clear cell changes (1999-2017) were re-examined by two gynaecologic pathologists and re-classified as ECCC and CCCM. Histologic [histotype, grade, myoinvasion, LVSI, peritumoral stromal tumour-infiltrating lymphocytes (sTILs)], IHC assessment [p53, mismatch repair (MMR) proteins and L1CAM] and *POLE* sequencing performed. Overall and Progression-free survival (OS/PFS) of CCCM and ECCC per molecular subclass were evaluated.
Results: Upon curated pathology review, 37 of 125 (29.5%) cases were reclassified as CCCM, further classified as high-grade (n=14) (including serous, FIGO grade 3 endometrioid carcinoma with clear cell changes and yolk sac tumour) and low-grade morphology (n=23) including FIGO grade 1 and 2 endometrioid carcinoma with clear cell changes. CCCMs are enriched with MMRd (n=16/35, 46%), followed by NSMP (n=11/35, 31%) and p53abn (n=8/35, 23%). No pathologic POLE mutations were identified. MMRd cases demonstrated a higher rate of extensive LVSI (7/16 vs. 3/19) and more extensive sTIL (mean 2.3 vs.1.6). The prognosis of NSMP was significantly better in CCCM vs. ECCC (90% vs. 54% OS at 5-year).
Conclusion: CCCM is composed of morphologically, biologically and prognostically heterogeneous groups of cases enriched with MMRd molecular subclass. Comprehensive pathologic assessment for the segregation of this group from the unequivocal ECCC is necessary for better risk stratification of such patients.

PS-10-032

Vitamin E inhibits heavy metals accumulation in the uterus during short- and long-time exposure

K. Sikora*, Y. Lyndina, N. Hyriavenko, A. Awuah Wireko, T. Abdul-Rahman, D. Tsepochko, O. Romaniuk, M. Lyndin, A. Romaniuk
*Sumy State University, Ukraine

Background & objectives: Vitamin E demonstrates benefits for reproductive health protection against pollutants. Therefore, we aimed to study the protective effect of vitamin E treatment on the heavy metals (HMs) accumulation in rats' uterus under 30 and 90 days of HMs exposure.
Methods: Female rats were randomly divided into three groups: untreated animals (control group); animals orally treated with HMs (Zn,Cu,Fe,Mn,Pb,Cr) mixture (HM group); and animals treated simultaneously with HMs and vitamin E (HM+E group) during 30 and 90 days. The chemical composition of uteruses was studied by Scanning-electron microscopy with elemental analysis and atomic absorption spectrometer.
Results: Our previous results demonstrated a considerable (p<0.01) bioaccumulative potential of Zn, Cu, Fe, Mn, Pb, and Cr in the rat uterine within 30 and 90 days in the HM group compared to the control. Herewith, HMs levels in the HM+E group were also significantly (p<0.01) higher on the 30th and 90th days (Zn–x1.18/1.29, Cu–x1.31/1.46, Fe–x1.45/1.59, Mn–x1.26/1.45, Pb–x1.39/1.62, Cr–x1.36/1.56) compared to control. Combining all the results, vitamin E treatment showed a decrease (p<0.01) in HMs accumulation on x1.12/1.13 for Zn, x1.1/1.09 for Cu, x1.11/1.15 for Fe, x1.09/1.12 for Mn, x1.09/1.14 for Pb, x1.08/1.1 for Cr in the uterus against to HM group, respectively.
Conclusion: Vitamin E has not provided complete protection against HMs accumulation. However, this treatment significantly reduced the bioaccumulative potential of pollutants. Moreover, the positive effect of vitamin E was confirmed by the intensity reduction of Zn, Cu, Fe, Mn, Pb, and Cr accumulation with the treatment prolongation to 90 days.

PS-10-033

Incidence of high-risk and low-risk human papilloma virus subtypes in invasive squamous cell carcinomas of the cervix: a molecular international multi-institutional study on 448 cases

S. Stolnicu*, D. Allison, A. Momeni Boroujeni, L. Hoang, C. Terinte, A. Pesci, C. Mateoiu, R.R. Lastra, T. Kiyokawa, R. Ali-Fehmi, M. Kheil, E. Oliva, K.M. Devins, N.R. Abu-Rustum, R.A. Soslow
*Department of Pathology, UMFST Gh E Palade of Targu Mures, Romania

Background & objectives: Squamous carcinoma of the cervix (SCC) is the fourth most common malignancy to affect women worldwide, historically attributed to High-risk Human Papilloma Virus (HR-HPV) infection. We aimed to determine the incidence of HR-HPV and Low-risk HPV (LR-HPV)-associated SCCs.
Methods: 448 surgically treated (conization/trachelectomy/hysterectomy) SCCs with readily available tissue to construct tissue microarrays were retrospectively assessed to confirm the microscopic diagnosis, tumour growth patterns, associated precursor lesion and further studied by in situ hybridization for HR-HPV and LR- HPV. Cases were considered as positive for either HR- or LR-HPV if any nuclear or cytoplasmatic signal was encountered within tumour cells.
Results: A total of 10 (2.2%) HPV-independent (HPVI) SCCs and 437 (97.8%) HPV-associated (HPVA) SCCs were identified with significant

difference in median age between two groups (67.8y in HPVIs vs 50y in HPVAs) and HPVIs presenting at higher stage. Most HPVAs were of non-keratinizing growth pattern while most HPVIs were keratinizing. We have also observed differences regarding associated precursor lesions between HPVIs versus HPVAs with HPVI precursor lesions presenting either as undifferentiated basaloid high grade squamous intraepithelial lesion (HSIL-like) or as high grade differentiated keratinizing (similar to differentiated vulvar intraepithelial neoplasia (d-VIN). Among the HPVA SCC cases, none (0%) was associated with LR-HPV while all (100%) were positive for HR-HPV.
Conclusion: Most cervical SCCs are associated with HR-HPV however, rare HPVI SCCs tumours can be encountered, with important clinical and histologic differences from their HPVA counterparts. The present study failed to identify SCCs associated with LR-HPV.

PS-10-034
In silico methods investigation of molecular changes in adenoid cystic carcinomas
M.H. Toper*, S. Sarioglu
*Dokuz Eylul University, Turkey

Background & objectives: MYB/MYBL1-NFIB rearrangements can be seen frequently in adenoid cystic carcinomas (ACC), along with low frequency mutations in different genes. In this study, we aimed to investigate molecular changes at the genomic/transcriptional level in ACCs by in silico methods.
Methods: Open access data in the cBioPortal database were used for DNA alterations. GSE153283-dataset from the NCBI-GEO database was evaluated with the Geo2R online-tool to detect differentially expressed genes (DEG) between normal/tumour tissues. In addition, using these data, gene-set enrichment analysis with GSEA program and functional-enrichment analysis with David tool were performed. Protein-protein association analysis was evaluated in String database/Cytoscape.
Results: In cBioPortal, common structural changes (N=239) were seen in NFIB(71%), MYB(58%), MYBL1(20%) genes, and the most frequent sequence mutations were at KDM6A(9.5%), SPEN(9.4%), SLC9C2(8.3%) genes. 387 DEGs were observed by Geo2R-mediated; the highest expression were seen BMP7, TLX1, COL27A1 genes; decreased expression were ETV1, WNT5A, WIF1. GSEA analysis demontrated that E2F targets, Notch pathway, Estrogen-early response, Wnt-βcatenin pathway, G2M-checkpoint, MYC targets-V1. David functional-enrichment analysis has revealed PI3K-Akt pathway, signal transduction, breast cancer, MAPK pathway, and transcriptional misregulation. In the protein-protein relationship analysis revealed that the most interacted protein were TP53, MYC, CTNNB1. DEGs interacting with MYB protein were E2F1, TCF3, MYC.
Conclusion: In our study, along with MYB/MYBL1 translocation, other genomic/transcriptional changes that affect transcriptional regulation, cell cycle and Notch/PI3K/Wnt-β-catenin/MAPK pathways are observed in ACCs, and it provides pioneering information for future studies in terms of pathogenesis or treatment targets.

PS-10-035
Prognostic significance and computer aided quantitative analysis of tumour-stroma ratio in high-grade serous ovarian cancer using routine H&E digital pathology slides
L. van Wagensveld*, C. Walker, K. Hahn, J. Sanders, R.F. Kruitwagen, M.A. van der Aa, G.S. Sonke, S. Rottenberg, K.K. Van de Vijver, A. Janowczyk, H.M. Horlings
*Department of Research and Development, Department of Molecular Pathology, The Netherlands Cancer Institute, The Netherlands, GROW, School for Oncology and Reproduction, Maastricht, The Netherlands

Background & objectives: Tumour-stroma ratio (TSR) is prognostic in multiple cancers, but remains understudied in high-grade serous ovarian cancer(HGSOC). We investigated the prognostic significance of TSR in HGSOC and developed a deep-learning based, fully-automated, scoring algorithm(OTSR), and evaluated its relationship with tumour-infiltrating lymphocytes (TILs).
Methods: N=360 patients with advanced-stage HGSOC, treated with primary debulking surgery(PDS) or neo-adjuvant chemotherapy(NACT) and interval debulking (IDS), were scored for TSR in both the most invasive(MI) and whole tumour(WT) region of hematoxylin-and-eosin-stained tissue. TSR was scored by two independent pathologists and quantified with OTSR. Patients were classified as High-TSR (≥50% stroma) or Low-TSR(<50%). TILs were assessed with immunohistochemical staining.
Results: In PDS, TSR-high, compared to TSR-low, was significantly associated with papillar growth pattern(60% vs 34%). In NACT it was associated with a lower Mandart-score(score 4&5, 21% vs 57%) and pleural metastasis (25% vs 16%). High TSR depicted a significantly shorter overall and progression-free survival(31 versus 45 months; and 38 versus 44) in WT and MI. Grouping TSR and TILs (based on the median) led to three distinct survival groups with good(Low TSR, high TIL), medium(High TSR, high TIL. Or; Low TSR, Low TIL) and poor(High TSR, low TIL) survival, which remained significant for CD8 and CD103 in multivariable analysis. OTSR depicted similar significant results and demonstrated high concordance with pathologists (correlation = 0.83).
Conclusion: TSR is an independent prognostic biomarker for OS in HGSOC in both whole tumour and most invasive region. High TSR showed a worse prognosis and a higher likelihood of pleural metastasis in case of NACT and may serve as a prognostic parameter in HGSOC. OTSR could provide a cost and time-efficient way of determining TSR, with a high reproducibility and reduced inter-observer variability.
This research was funded by the Dutch Cancer Society [IKNL2014-6838].

PS-10-036
ß-catenin and L1CAM expression further stratify endometrial carcinoma patients in no specific molecular profile group and p53 abnormal group respectively
H. Yoon*, H. Kim
*Department of Pathology, Seoul National Bundang Hospital, Seongnam, Republic of Korea

Background & objectives: The Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE-POLE; MMR-D; p53 wt/NSMP; p53 abn) has consistently been shown to be prognostically significant in endometrial carcinomas (EC). This study investigated the prognostic effect of ß-catenin and L1CAM expression on ProMisE classification.
Methods: 240 EC specimens from the Seoul National University Bundang Hospital database were classified according to the ProMisE classification. ß-catenin and L1CAM were evaluated by immunohistochemistry on tissue microarray. We defined ß-catenin positive, if ≥10% of tumour cells showed nuclear staining and L1CAM positive, if ≥10% of tumour cells showed membranous staining. Correlations between clinicopathological data and survival were calculated.
Results: 8.8% showed ß-catenin expression and 12.5% showed L1CAM expression. Both markers were expressed mutually exclusive pattern except for one case. L1CAM expression was associated with non-endometrioid histology and high tumour grade (p<0.001). ß-catenin and L1CAM expression were most frequent in NSMP group (76.2%) and p53 abnormal group (63.3%), respectively. In survival analysis, ß-catenin expressing patients showed shorter progression free survival(PFS) in NSMP group than ß-catenin wild type, whereas L1CAM expressing patients showed longer PFS in p53 abnormal group compared to negative patients (p<0.001). In multivariate analysis, the modified ProMisE classification applied with

ß-catenin and L1CAM was confirmed as an independent prognostic factor affecting recurrence (p=0.004) along with FIGO stage (p=0.001).
Conclusion: We showed that ß-catenin expression could stratify no specific molecular profile group by identifying EC patients with higher risk for severe outcomes and L1CAM expression could stratify p53 abnormal subgroup by identifying EC patients with more favourable prognosis. Thus, we propose the modified molecular classification that integrates the ß-catenin expression within NSMP subgroup and L1CAM expression within p53 abnormal subgroup into the ProMisE classification.

PS-11 | Poster Session Haematopathology

PS-11-001
Correlation between tumour infiltrating lymphocytes and prognostic factors in mantle cell lymphoma

J. Chabla Jaramillo*, A. Diazgranados Daza, J.T. Zuñiga Gaitan, M. Diaz Guillen, S. Ramón y Cajal Agüeras, J. Castellvi Vives
*Hospital Universitari Vall d'Hebron, Spain

Background & objectives: In mantle cell lymphoma (MCL) there are variable numbers of T cells admixed with tumour cells which role in its behaviour is not well known. Therefore, we wanted to know if they correlate with known morphological prognostic factors.
Methods: We selected 37 lymph nodes with MCL from the files of our department, and the morphologic type, p53 immunohistochemistry result and ki67 expression were recorded. To quantify TILs, CD3 immunohistochemical slides were scanned and evaluated with the cell quant algorithm of 3D-Histech QuantCenter, and the results were analysed with SPSS.
Results: The series was composed of 32 classic and 5 blastoid MCL. Only one of theme showed overexpression of p53. Ki67 cases were grouped in cases with <30% (17 cases) and >30% (20 cases) of positive cells. The number of TILs varied from 177% to 7% of the total cells. This result correlated with Ki67, with higher number of TILs in Ki67 low cases (p=0.044). No correlation was found with morphologic variants.
Conclusion: Although it is a short series of MCL, there is a correlation of TILs and one of the most used prognostic factors in MCL. Interestingly, the cases with higher TILs showed less proliferation index, and therefore better prognosis. The case p53 positive was the one with more TILs of the series, but a larger series is necessary to evaluate if there is a correlation between them.

PS-11-002
High level of tumour-infiltrating T lymphocytes predicts better prognosis in diffuse large B-cell lymphoma

Y. Cho*, J. Cho
*Department of Pathology and Translational Genomics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Republic of Korea

Background & objectives: The implication of tumour-infiltrating T lymphocytes (TIL-T) in diffuse large B-cell lymphoma (DLBCL) is yet to be elucidated. We aimed to investigate the effect of the degree of TIL-T on the prognosis of DLBCL patients.
Methods: Ninety-six patients with DLBCL, not otherwise specified were enrolled in the study. The ratio of TIL-T was measured as the ratio of CD3-positive cells to total cells using QuPath, a digital pathology software. The TIL-T ratio was investigated in three foci (high, intermediate, and low) in each case and the relationship between TIL-T ratio and overall survival was investigated.
Results: Among 96 patients, 44 (45.8%) were Ann Arbor stage III-IV, and 64 (66.7%) were non germinal centre B-cell in cell-of-origin. When a TIL-T ratio of 25% was used as the cutoff value, high TIL-T and low TIL-T patients were 62 (64.6%) and 34 (35.4%), respectively. High TIL-T ratio was significantly associated with lower Ann Arbor stage (p=0.011). Upon univariate analysis, patients with low TIL-T ratio had a significantly worse prognosis in overall survival compared to those with high TIL-T ratio (p<0.001); this difference remained significant in a multivariate analysis with Cox proportional hazards (hazard ratio, 6.52; 95% confidence interval, 2.30 to 18.51; p<0.001).
Conclusion: DLBCL patients with high TIL-T ratio showed a significantly better prognosis than those with low TIL-T ratio, and the level of TIL-T ratio was an independent indicator for overall survival. These results suggest that TIL-T may play a critical role in the disease progression of DLBCL and evaluating the degree of TIL-T in DLBCL specimen using digital pathology software may become useful in predicting the clinical behaviour and the response to immunotherapy in DLBCL patients.

PS-11-003
Molecular classification of systemic diffuse large B-cell lymphoma in Korea

Y.A. Kim*, J. Yim, B. Han, S. Lim, Y.K. Jeon
*SMG-SNU Boramae Medical Center, Republic of Korea

Background & objectives: Diffuse large B-cell lymphoma(DLBCL) features medium to large B-cells with a diffuse growth pattern, diverse morphology and molecular profiles. This study aimed to categorize systemic DLBCL in Korea via the LymphGen classifier and analyse distinct clinicopathological features of each subgroup.
Methods: We conducted customized targeted gene sequencing for 121 lymphoma-related genes and immunohistochemistry in 151 systemic DLBCL patients including EBV+ DLBCL, THRLBCL, PMBL, and IVLBCL. For 135 DLBCL, NOS cases, clinical data, including gender, age, symptoms, serum LDH level, stage, IPI risk group, and treatment response were obtained. We analysed clinicopathologic and molecular differences and outcomes according to the LymphGen subgroups.
Results: DLBCL, NOS were categorized into MCD(23%), A53(17%), EZB(9%), BN2(6%), and unclassified ("Other")(39%) by LymphGen classifier. EBV+ DLBCL were classified as ST2 and other subgroups, while TCRLBL as MCD and other subgroups, and all PMBL were unclassifiable. The BN2 had a higher proportion of older patients, and the EZB had higher GCB subtype proportion. The A53 frequently showed mutations in TP53, and IRF4; EZB exhibited mutations in BCL2, MYC, KMT2D, SGK1, and EZH2; MCD showed mutations in PIM1, BTG1, CD79B, HIST1H1E, MYD88, and PRDM1; ST2 exhibited mutations in ITPKB and SOCS1, mostly consistent with previous studies. In the unclassified ("Other") group, frequent mutations were observed in TET2, KMT2C, PIM1, and IRF4.
Conclusion: This study classified systemic DLBCL cases in Korea using the LymphGen classifier and analysed the unique clinicopathological characteristics of each subgroup. The distribution of the LymphGen subgroups varied among different types of DLBCL. The identification of specific mutations in each subgroup, which were largely consistent with previous studies, indicates that the LymphGen classifier may be valuable in individualized treatment approaches for DLBCL patients. Additionally, this study demonstrates that unclassified group ("Other") may potentially be established as a distinct subgroup.

PS-11-004
NGS testing practices and molecular profile of KIT in systemic mastocytosis: real-world insights from France, Italy, and Spain

N. Lamontagne*, S. Cheloni, S. Lima, T. Green, Z. Crouch, A. Kim
*Blueprint Medicines, Switzerland

Background & objectives: ~95% of systemic mastocytosis (SM) cases are driven by the *KIT* D816V mutation (Ungerstedt, et al. Cancers. 2022;14(16):3942). We examine next-generation sequencing (NGS) *KIT* testing practices in France, Italy, and Spain to investigate molecular profiles potentially associated with SM cases.
Methods: The SOPHiA DDM™ Platform (SOPHiA GENETICS SA, Switzerland) was used to analyse pseudonymized real-world genomic

profiles (Q1 2019 – Q4 2022) across 71 Institutions. Aggregated anonymized statistical data were obtained from 30 SOPHiA GENETICS somatic onco-hematological (HemOnc) NGS panels capable of detecting *KIT* alterations from RNA or DNA.
Results: 71,755 individuals were tested with somatic HemOnc panels capable of detecting *KIT* alterations, with the European testing footprint increasing over the >3-year time period. 50,611 *KIT* gene variants were identified amongst 23,007 *KIT* mutation-positive profiles (32% of the total tested individuals). Of the *KIT* mutation-positive profiles, more than 400 (>1.5%) had a *KIT* D816V mutation; in >50% of these cases, the *KIT* D816V mutation was associated with a myeloid/myeloproliferative malignancy. The analysis of *KIT* drivers within *KIT* or other genes found that a substantial proportion of *KIT* D816V mutation-positive cases had a co-occurring oncogenic alteration in *KIT*, *SRSF2*, *ASXL1*, *TET2*, or *RUNX1*.
Conclusion: These data provide new insights into the occurrence of *KIT* alterations and co-occurring oncogenic mutations in systemic mastocytosis profiles, and NGS testing practices across France, Italy, and Spain. The comprehensive characterization of the molecular epidemiology of *KIT* variants and co-mutations is crucial to better define SM prognosis and treatment strategies.

PS-11-005
Chronic lymphocytic leukaemia with Reed–Sternberg cells. Review of this rare entity in a tertiarty university hospital
P. Pérez-Montero*, E.P. Sánchez López, G. Olmedilla Arregui, E.M. Fernandez
*La Paz University Hospital, Spain

Background & objectives: Chronic lymphocytic leukaemia (CLL) may transform into an aggressive lymphoma. CLL progresses to Diffuse Large B Cell Lymphoma (DLBCL) in 2-8% and less than <1% to Classic Hodgkin Lymphoma (CHL). CLL with RS cells is yet a poorly understood entity.
Methods: We reviewed all our cases diagnosed as Richter's Syndrome (RS) and CLL with RS cells from 2007 to 2023. We revised the histopathological, immunohistochemical slides and molecular studies. We looked at the clinical records, searching for clinical variables as age of diagnosis, gender, time from CLL diagnostic to RS, therapy and vital status.
Results: We found 2 cases with Reed-Stemberg cells (RSC) or CD30+ cells without other characteristics of CHL and 10 cases of transformation from CLL to DLBCL or CHL. As expected, the majority of them consisted in a progression to DLBCL (80%) and only 2 cases were CHL. Mean age of CLL diagnosis was 64 and mean time to transformation was 7.2 years. Every CLL was positive for CD5 and CD23 and every DLBCL was non germinal centre, none of them showed BCL6, BCL2 nor MYC translocation by FISH analysis. Mean DLBCL Ki-67 proliferation index was 62.5%. CHL cases showed positivity for CD15, CD30 and Epstein-Barr in RSC.
Conclusion: CLL progression to high grade lymphoma is a rare phenomenon which diagnosis may be a challenging task. Those with isolated CD30 + cells or Reed-Stemberg cells lacking mixed inflammatory background should not be considered as Richter Syndrome. Accelerated CLL with high Ki-67 index also must be ruled out. DLBCL cases are more likely non germinal centre (100% in our study) and usually keep a similar immunophenotype as the previous CLL (CD5 and CD23 typically).

PS-12 | Poster Session History of Pathology

PS-12-001
Museum of anatomical pathology – last century gynaecology
G. Fontinha*, V. Sousa, M. Viseu, C. Eliseu, T. Ferreira, R.H. Henriques De Gouveia, M. Pinheiro Lourenço, L. Carvalho
*Centro Hospitalar e Universitário de Coimbra, Portugal

Background & objectives: Hysterectomy the second most prevalent non-outpatient surgery, most commonly due to leiomyomas. An increase in hysterectomies being performed for malignant diseases has been happening in recent years. The authors propose a comparison with a museum collection representative of gynaecology specimens.
Methods: It is estimated that by the age of 59 and 79 about 25% and 40% of women respectively have had a hysterectomy. The Museum of Anatomical Pathology of the Institute of Anatomical and Molecular Pathology has been collecting surgery specimens since 1822 most of them being from the first half of the 20th century. It holds 289 hysterectomy specimens.
Results: The collection reports to 198 leiomyomas, 22 carcinomas, 16 sarcomas, 45 inflammatory entities such as endometritis and 7 cases without definite interpretation. Of the 22 carcinomas, 3 are labelled as adenocarcinoma, 3 as coriocarcinoma, 1 as squamous cell carcinoma and 1 as papillary carcinoma. The papillary carcinoma might have been a serous carcinoma according to today's standard classification and macroscopic characteristics. The squamous cell carcinoma is perhaps an endometrioid carcinoma with extensive squamous metaplasia or a true cervical tumour. The not otherwise specified cases are endometrioid carcinomas macroscopically. Excluding the unknown cases, non-malignant issues account for 86.4% of the causes for the hysterectomy specimens kept in the Museum.
Conclusion: Medical Students look into the Museum collection as a window to the past as it seems that the main cause for hysterectomy remains actual. There has been however a more preponderance in the malignant causes for this surgery lately. Actual data show that leiomyosarcoma accounts for 1-2% of uterine malignancies. Sarcomas representing 42% of the uterine cancer cases in the collection are probably related to the selection bias of the rarer specimens and to today's early diagnosis recognition of carcinomas.

PS-12-002
Museum of anatomical pathology – embryological errors revised
G. Fontinha*, V. Sousa, M. Viseu, C. Eliseu, T. Ferreira, R.H. Henriques De Gouveia, M. Pinheiro Lourenço, L. Carvalho
*Centro Hospitalar e Universitário de Coimbra, Portugal

Background & objectives: Since the introduction of prenatal screening and legal pregnancy interruption, the rate of congenital anomalies in livebirths have dwindled. For EUROCAT, the main reason for medical pregnancy interruption comprises genetic disorders and nervous system anomalies. The Museum collection is revisited.
Methods: The Museum of Anatomical Pathology–Institute of Anatomical and Molecular Pathology of the Faculty of Medicine of the University of Coimbra retains a collection of cases dating from late XIX century and collected during the XX century, kept in liquid fixative solution. There are eighteen relevant cases, "monsters" as they were called in the past, concerning visible defects.
Results: The nervous system embryological understandable malformations are predominant in the collection mainly consisting of neural tube defects, the more spectacular comprising two cases of anencephaly, two of iniencephaly and one of encephalocele. There are also two cases of severe holoprosencephaly with cyclopia, one of which with a proboscis. Abdominal wall defects are the second most prevalent cases with two gastrochisis and one omphalocele. There are seven cases of conjoined twins as well, a condition corresponding actually to 0,04 cases per 10000 livebirths, registered in 2020 in the EU zone.
Conclusion: Neural anomalies will keep crossing time as common congenital defects. Prenatal screening programs have however lowered the observation of these in neonates as these pregnancies are medically interrupted. High prevalence of conjoined twins in

the museum collection is most likely due to selection bias. This collection and the whole Museum of Anatomical is integrated in Pathology Program contents of Medical Students of the Faculty of Medicine of the University of Coimbra and open to other Scientific Institutions.

PS-12-003

The VII th European Congress of Pathology. 1979: an historical overview

A. Llombart-Bosch*
*Dep Pathology, University of Valencia, Spain

Background & objectives: An overview of the activities and participants.
Methods: The Congress took place in Valencia, Spain from the 17 to the 21 September 1979 while the ESP presidency of Prof Christian Nezeloff (Paris). The Congress took place in the Convention Hall at the Colegio de Medicos of Valencia. The assistance was of over 700 delegates from 38 countries all over the Word with presence of members from East Europe.
Results: Scientific activities complied Symeonides lecture ,5 Plenary Sessions,4 Scientific Sessions, one Symposium oriented to "Training programmes in Pathology", 6 slide seminars and 340 free oral presentations. Many outstanding pathologists were lectures.
The abstract book was edited by the journal "Pathology Research and Practice vol 165,1-2.1979". A book over the "Spanish Classics in Pathology before Cajal" J.M. Lopez Piñero el col., was edited and distributed among all delegates.
Conclusion: Prof Antonio Llombart Bosch (president of the European Society of Pathology,1987-89), assume the local presidency of the Organizing Committee and carried out a large and very much appreciated social events.

PS-12-004

Paleopathology survey of an ancient female monastic community: the Hermit Poor Clares mummies of Fara in Sabina, central Italy (17th-18th century)

L. Ventura*, F. Bruno, A. Avitabile, A. Risdonna, A. Ventura, E. Petrella, A. Biselli, E. Cilli, M. Traversari
*ASL 1 Division of Pathology, Italy

Background & objectives: The mummified bodies held in the Monastery of the Hermit Poor Clares of Fara in Sabina are occasionally mentioned in paleopathological literature. Actually, it represents a rather numerous series, including extremely well-preserved bodies dating back to 17th-18th century.
Methods: The investigation included external examination, anthropometric and paleopathological studies through CT scanning, and minimally invasive sampling addressed to further laboratory analyses. The textile fragments recovered from the bodies were submitted to commodity study. Textual sources were also examined in order to highlight significant information about daily activities and mortuary practices in force at the time when the nuns lived.
Results: The mummies were extremely well-preserved, with limited examples of posterior and facial soft tissues decay. The presence of dehydrated internal organs without skin cuts/sutures indicated spontaneous mummification, possibly enhanced by external treatments. Anthropological age at death of the subjects ranged from 40 to 64 years old. The main paleopathological findings included lung calcified nodules possibly related to pulmonary tuberculosis in 6 individuals and gallstones in 3 subjects. Tarso-metatarsal and/or patello-femoral osteoarthritis was widely detected, with prolonged kneeling supposed as a causal role in the development of such degenerative lesions. Single cases of concha bullosa, vertebral body haemangioma, pelvic organ prolapse, and monostotic Paget's disease of the pelvis were also observed.
Conclusion: The study provided important information on the diseases suffered by these silent nuns from the past. Their health status was closely related to daily activities, most of which were connected with prayer, meditation, and corporal mortification. Further investigation on genetic features and nutritional status of the individuals will help to shed further light on the secret life of this small community, which lived away from the affairs of the external world.

PS-13 | Poster Session Ophthalmic Pathology

PS-13-001

Ocular rhinosporodiosis: a report of 15 cases from Uganda

M. Odida*, R. Schmauz
*Department of Pathology, Faculty of Medicine, Gulu University, Uganda

Background & objectives: Rhinosporodiosis mainly affects the nasal cavity, with few cases reported from ocular sites.
The objective was to assess the occurrence and sites of ocular rhinosporodiosis in Uganda.
Methods: We reviewed biopsy records for the period 2008 to December 2021 from Multisystem Clinical Laboratories, a private histopathology laboratory in Kampala, Uganda which receives specimens from many health facilities in Uganda. All cases reported as rhinoporodiosis were retrieved and the clinical information and slides were reviewed. Cases of ocular rhinosporodiosis are hereby presented.
Results: Fifteen cases of ocular rhinosporodiosis were encountered, aged between one year and 63 years. There were ten males and five females. Eight cases were from conjunctiva, four were from the eyelids and in three remaining cases, the sites were not indicated. Histology of all cases showed chronic granulomatous inflammation with spherules containing spores.
Conclusion: Ocular rhinosporodiosis appears to be common in Uganda and tends to affect all age groups. Rhinoporodiosis needs to be considered in differential diagnosis of inflammatory ocular lesions.

PS-14 | Poster Session Soft Tissue and Bone Pathology

PS-14-001

Low-grade fibromyxoid sarcoma: Clinicopathological and immunohistochemical features of 12 cases

Y. Cakir*, B. Bambul Sığırcı, E. Hacıhasanoğlu, Y.B. Kök, C.K. Kayhan, G. Başdemir, K. Behzatoğlu
*Dokuz Eylül University, The Institute of Health Sciences, Department of Molecular Pathology, Turkey

Background & objectives: Low-Grade Fibromyxoid Sarcoma (LGFS) is a rare type of sarcoma, typically located within deep soft tissue of the body. Although it shows bland histology, it has risk of local recurrence/metastasis. We aimed to present 12 LGFS cases with clinicopathologic findings.
Methods: Twelve cases were diagnosed with LGFS in 13 years in our department. The clinical findings of the patients were recorded, and the slides were re-evaluated.
Results: Age ranged from 9 to 70 (median:32), and eight were male. Tumours were located in the gluteal region (8), pelvis (2), and upper extremities (2). Microscopically, myxoid and collagen-rich fibrous areas including bland spindle cells with mild to moderate cellularity were seen. There was epithelioid morphology in two cases and large collagen rosettes in one case. The mitotic index was low, nuclear pleomorphism was occasional. There was no necrosis. MUC4

immunoreactivity, accepted as the gold standard for diagnosis, was detected in all cases. 3 of the 12 cases (25%) had lymph node metastasis at the initial diagnosis. In follow-up, lung metastasis was detected in 4 cases (33%).
Conclusion: LGFS is a rare sarcoma with local recurrence and metastasis risk although it reveals bland morphology. It can result in differential diagnosis problems with other fibroblastic tumours.

PS-14-002
Importance of transthyretin-derived amyloidosis (ATTR) detection in carpal tunnel syndrome (CTS)
C. Girleanu*, J. Bissonnette, P. Fleming, N. Bermingham, L. Burke
*Department of Pathology, Cork University Hospital, Cork, Ireland

Background & objectives: Transthyretin-derived amyloidosis (ATTR) is a rare progressive multisystemic disease. Advancements in therapy warrant attention to its indentification. Carpal tunnel syndrome (CTS) is a known symptom manifestation. An institutional audit was performed to evaluate the detection of ATTR in CTS cases.
Methods: A COGNOS database search of CTS samples containing amyloid at the Pathology Department. CUH from 2008 to 2022 was performed. Data analysed for these cases included age, gender, localization of amyloid deposits (confirmed by Congo Red stain) within the tissue, and results of Amyloid sub-type classification performed at the National Amyloidosis Centre, UK.
Results: 126 cases of CTS were identified over a 14-year period (2008-2022). 21 cases displayed amyloid appropriate birefringence on Congo Red analysis with an average age of 75 years (age range- 57 to 91 years). There was a slight excess in males (11/21). In 20 cases amyloid deposits were identified within the stroma with only one case having a known Monoclonal IgM Kappa Band paraprotein. One case incorporated amyloid deposits in both the stroma and vessels.
In the 11 cases subtyped, including the case with a known paraprotein, all contained transthyretin (TTR) amyloid subtype.
Conclusion: Given the therapeutic advances in management of ATTR amyloid and its known associations with other disease processes such as cardiomyopathy, neurological disorders, etc., its detection is very important. Our results indicate that all samples of CTS with positive Congo Red amyloid deposits could act as an early histological diagnosis for this entity and therefore subtype analysis should be performed on all cases.

PS-14-004
Osteosarcoma of the toe: a clinicopathologic study of 4 cases
O. Houghton*, V. Sumathi, A. Rosenberg
*Royal Group of Hospitals, Belfast, Ireland

Background & objectives: Osteosarcoma of the toe is extremely rare with only 10 well described cases in the literature. It is often unexpected clinically and radiologically, and the histological diagnosis may be challenging. We describe the clinicopathologic features of four cases.
Methods: The consultation files of one of the authors and the surgical pathology files of the Department of Musculo-Skeletal Pathology, Royal Orthopaedic Hospital, Birmingham, were searched for toe osteosarcoma. Available H&E slides on each case were retrieved and reviewed. Radiographs were available for review in 1 case. Relevant clinical information was obtained by written questionnaires with referring pathologists and treating physicians.
Results: The patients included 3 males and 1 female, ranging in age from 15 to 54 (mean age 32). The tumours arose in the proximal phalanges, occurring in the first, third and fifth toe, respectively. The specific phalanx of origin in one case was not known. One tumour was a parosteal osteosarcoma and 3 were intramedullary osteosarcomas. The intramedullary tumours included a conventional low-grade central osteosarcoma, an osteoblastoma-like osteosarcoma and a conventional high-grade osteosarcoma. Of the two patients with known follow-up data (the parosteal osteosarcoma and the osteoblastoma-like osteosarcoma) there was no evidence of recurrence or metastasis after a period of 84 months (range 21 to 147 months).
Conclusion: This is the largest series of osteosarcoma of the toe. As osteosarcoma is often unexpected clinically and radiologically in this location and as low-grade osteosarcoma subtypes, which are more common in the toe, can be confused histologically with benign fibroosseous lesions or with the chondrosseous lesions which have a predilection for the toes, there is potential for diagnostic delay. Pathologists should be aware of osteosarcoma of the toe to ensure prompt diagnosis and appropriate treatment.

PS-14-005
Prognostic and diagnostic significance of mitotic activity between low grade dedifferentiated liposarcoma and cellular well differentiated liposarcoma
J. Lee*, H.J. Kwon, G. Choe, K.S. Lee
*Seoul National University Bundang Hospital, Republic of Korea

Background & objectives: Morphologically ambiguous lesions of overlap between well differentiated liposarcoma (WDL) and dedifferentiated liposarcoma (DDL) are not infrequently encountered. Interpretative difficulties arise when the low-grade sarcoma component that does not meet the criteria for typical DDL.
Methods: Tumours of this feature are considered to represent "low-grade (LG) DDL" or "cellular WDL". Some studies suggested that at least 5 mitotic figures per 10 high-power fields (≥5/10 HPF) are required for diagnosis of DDL. In our study, liposarcoma contains LG sarcomatous lesion with mitotic count <5/10 HPF were considered as LG DDL.
Results: A total of 244 patients with liposarcoma (average age=60, range=18-91years) were evaluated. The MDM2 amplification was determined using fluorescence in situ hybridization in all cases. The study included 46 (20.53%) typical DDL,28 (11.47%) LG DDL, and 170 (69.67%)WDL. Sixty-nine (28.27%) liposarcoma originated from the retroperitoneum and 175 (72.72%) were observed in limbs and trunk, etc. Kaplan–Meier analysis indicated that DDL was significantly associated with poor recurrence free survival compared (RFS) to WDL (P< 0.001).LG DDL was significantly correlated with a worse RFS compared to WDL (P=0.013). However, LG DDL was not correlated with a better RFS compared to typical DDL (P=0.704).
Conclusion: We investigated the clinical relevance of mitotic activity in MDM2 amplified liposarcoma. There is a suggestion that liposarcoma with LG sarcoma component (mitotic count <5/10 HPF) should be included in the WDL or cellular WDL. However, LG DDL definitely shows poor RFS compare to WDL and does not significantly have a better RFS than typical DDL. Thus, LG DDL should not be underestimated as cellular WDL.

PS-14-006
Clear cell chondrosarcoma, an aggressive low grade chondroid neoplasm - a case series
S. Naresh Shah*, A. Parameswaran
*Apollo hospitals, India

Background & objectives: Clear cell chondrosarcoma is a low grade chondroid neoplasm which constitutes 2-4% of conventional chondrosarcomas and 0.4% of primary bone neoplasms. They radiologically mimic a benign lesion and therefore pathological examination is the gold standard for diagnosing this entity.
Methods: We retrieved 109 chondrosarcomas from Apollo hospital laboratory database from 2012-2022, of which only 7 cases were of Clear cell chondrosarcoma. Histopathological examination was the mainstay of diagnosing this entity with immunohistochemistry when indicated.

Results: Out of 7 cases of CCC, 6 were males and 1 was female. Five cases occurred in femur, one in humerus and one in vertebral body. All these cases were diagnosed a benign lesion on radiology and turned out to be malignant CCC on histology. Two of these cases had aneurysmal one cyst-like areas. Immunohistochemistry was done in 2 cases. Bone curettage with grafting was done in all cases, followed by wide local excision in three cases. There is no evidence of recurrence or metastasis in these patients till the last follow up.
Conclusion: Clear cell chondrosarcoma almost always mimics a benign lesion clinically and radiologically, with a mortality rate of 15% and metastatic potential of 20% in 10 years. We emphasize the importance of clinical, radiological and pathological integration to diagnose this lesion and always look out for the clear cells on pathological examination, when one comes across a clinical diagnosis of benign lesions such as chondroblastoma, giant cell tumour or aneurysmal bone cyst in slightly older patients.

PS-14-007
Data analysis of synovial specimens in a Portuguese tertiary centre – prevalence, diagnostic and prognostic significance
M. Pinho Fialho*, C. Ochôa Matos, V. Fernandes, R. Moiteiro da Cruz, J. Boavida, E. Vieira-Sousa, M.E. Vitorino, R. Luís
*Serviço de Anatomia Patológica, Centro Hospitalar Universitário de Lisboa Norte, Faculdade de Medicina da Universidade de Lisboa, Portugal

Background & objectives: Joint pathology encompasses a broad group of diseases, often with overlapping features. Our aim was to assess whether the histopathological study of synovial samples could complement suspected clinical diagnoses or clarify therapeutic failure scenarios, allowing for a precise management.
Methods: We analysed the reports of all synovial specimens received at our Department between 2010-2022. The specimens were mainly submitted for diagnosis and/or management guidance, especially in the context of therapeutic failure. Clinical and histological diagnoses were both categorized into tumour-like, degenerative/non-inflammatory and inflammatory lesions, further subclassified by the Krenn score; the categories were then matched for comparison.
Results: A total of 599 reports pertaining to 535 patients (335 female, 264 male; 0-93y.o.) were reviewed. Most specimens were collected by the Rheumatology and Orthopedics Departments. Histologically, the samples were classified as low-grade synovitis (36%), high-grade synovitis (15%, with 5% further established as rheumatoid arthritis), septic arthritis (10%), microcrystalline arthritis (3%) and granulomatous synovitis (3%); tumour-like lesions were diagnosed in 18%, mainly encompassing cysts (10%); the remainder were mostly non-informative. Clarification of clinical diagnosis and/or differential diagnosis was possible in the majority and in some cases, microscopic evaluation gathered unforeseen information, allowing for a definitive diagnosis of immune-related, septic, granulomatous and microcrystalline arthritis or revealing (pseudo)tumoral lesions.
Conclusion: Synovial histopathological evaluation may benefit patients in select cases, namely when a clinical differential requires clarification or, after a diagnosis is established, a secondary diagnosis or infection must be excluded. Nevertheless, integration of clinical, laboratorial, radiological and histological data through multidisciplinary discussion is the ultimate approach to improve patient care.

PS-14-008
A retrospective analysis of 116 patients with chordoma: morphologic and clinical characteristics
M. Ramadwar*, S. Lashkar, N. Khanna, D. Sharma, B. Rekhi, P. Panjwani, V. Raje, M. Patel, M. Pruthi, P. Nayak, A. Janu
*Tata Memorial Hospital, India

Background & objectives: Chordoma is a malignant tumour of notochordal origin arising in sacrococcygeal or clival region. Histologic variants of chordoma are associated with different biologic, morphologic and clinical characteristics. We aim to study the histopathological spectrum of chordoma along with clinical features.
Methods: We studied 116 patients diagnosed with chordoma. Clinical features including treatment details and follow up information were derived from electronic medical records. Histopathology and immunohistochemistry were reviewed.
Results: 116 patients with chordoma had age range of 1 to 75 years. Sacrococcygeal region was the commonest site followed by base skull. Conventional morphology was seen in 88% while poorly differentiated chordomas (PDC) were seen in 8.6% patients. Dedifferentiation was seen in 1.6%. All tumours were positive for brachyury, EMA and S100. All PDCs contained rhabdoid cells with loss of INI1. 27% patients underwent surgery, 44% patients had radiotherapy, 22% were treated with combination therapy. 41% patients had incomplete surgical resection. None of the patients had complete response to radiotherapy. 5 patients died of disease; 3 were patients with PDC. 16% patients experienced disease relapse; 3 had metastases.
Conclusion: Results of our study of 116 patients have highlighted chordomas as aggressive malignant tumours with bulky, locally destructive tumours. They were refractory to therapy with high rates of incomplete surgery, poor control on radiotherapy and high relapse rates. Sacrococcygeal site was the commonest. A consistent morphologic and immunohistochemistry profile was observed with brachyury being highly specific marker for notochordal differentiation. PDCs emerged as distinctive tumours showing rhabdoid phenotype and loss of INI1. Aggressive behaviour of PDCs was also clearly evident.

PS-14-009
Fusion gene rearrangements in nodular fasciitis: a study of rare and novel USP6 fusion partners
J. Zamecnik*, J. Balko, M. Stanek, L. Krskova
*Department of Pathology and Molecular Medicine, 2nd Faculty of Medicine, Charles University and Motol University Hospital, Prague, Czech Republic

Background & objectives: In this retrospective non-randomised study we aimed to identify new and rare fusion partners with *USP6* gene in nodular fasciitis. Nodular fasciitis can harbour different variants of *USP6* fusions, which can be used in diagnostics and determine the biological behaviour.
Methods: A total of 19 cases of nodular fasciitis examined between 2011 and 2022 at Motol University Hospital in Prague, Czech Republic were enrolled into this study. Next to the histopathological evaluation, all cases were assessed using immunohistochemistry, RT-PCR and Anchored multiplex RNA methods. Patient's main demographic characteristics and corresponding clinical data were also analysed.
Results: This study presents one novel (*KIF1A*) and five rare examples (*TMP4, SPARC, EIF5A, MIR22HG, COL1A2*) of fusion partners with *USP6* gene among the 19 cases of nodular fasciitis.
Conclusion: Identification of USP6 fusion partners in nodular fasciitis helps to understand the biology of the lesions. Moreover, it can be useful in routine histopathological practice of soft-tissues diagnostics, especially in preventing possible misdiagnosis of malignancy.
Funding: Research Project of the Ministry of Health of the Czech Republic No. 00064203.

PS-15 | Poster Session Thymic and Mediastinal Pathology

PS-15-001
Mediastinal gray zone lymphoma: unclassifiable lymphomas with intermediate features

H. Ichrak*, R. Ayadi, E. Brahem, L. Farah, S. Hamza, O. Ismail, A. Ayadi
*CHU abderrahmen Mami, Tunisia

Background & objectives: Gray-zone lymphoma (GZL), or B-cell lymphoma unclassifiable with features intermediate between diffuse large B-cell lymphoma (DLBCL) and classical Hodgkin lymphoma (CHL), is a challenging diagnosis. They are generally more aggressive than either CHL and DLBCL, hence the need to be distinguished.
Methods: We report a retrospective study of 8 cases of GZL diagnosed at our department of pathology between 2008 and 2022.
Results: There were 3 male and 5 female patients, aged between 21 and 43 years with a mean age of 32. The diagnosis was made on transparietal biopsies (n=1), on surgical biopsies (n=3), on lymph node biopsies (n=2) and multiple biopsies (n=2). An intraoperative frozen section was performed (n=2) showing a lymphoma in two cases. The histological examination revealed diffuse sheets of lymphomatous tumour cells with a moderately abundant clear cytoplasm, intermixed with a moderate inflammatory infiltrate. Immunohistochemistry (IHC) revealed diffuse positivity for CD20, focal positivity for CD30, rare CD15-positive cells and CD3-negative cells. Based on these histologic and IHC findings, the final diagnosis of mediastinal gray zone lymphoma was made.
Conclusion: The pathological diagnosis of GZLs remains challenging due to their heterogeneous histology and ambiguous histogenesis. However, recognition and diagnosis is crucial for the initiation of an optimal treatment.

PS-16 | Poster Session Cytopathology

PS-16-001
Results of the first year of implementation of cervical cancer screening with human papilloma virus (HPV) testing using self-sampling in Catalonia (Spain)

I. Blazquez*, L. Pijuan, E. Roura, N. Baixeras, C. Robles, R. Llatjòs, R. Font, A. Matrero, E. Rodiño, X. Matias-Guiu, J.A. Espinàs, L. Bruni, P. Peremiquel-Trillas
*Hospital Universitari de Bellvitge, Spain

Background & objectives: A pilot test with the self-sampling for the Human Papilloma Virus test (HPV) for cervical cancer screening among women aged 30 to 65 years, was established in one area of Health Primary Care.
Methods: An eligible population of women aged 30-65 are invited by SMS. At the laboratory, the samples (Floqswabs, Copan) are resuspended with 5 ml of Preservcyt (Hologic). HR-HPV testing is performed using cobas® HPV-Test (Roche). HPV positive women are recalled and taken a liquid base cytology (ThinPrep, Hologic) to be processed with T5000 (Hologic) and stained with Papanicolaou for cytological diagnosis.
Results: Out of 3425 women requesting opportunistic screening at the ASSIR, 3255 women met eligibility criteria and were invited to the pilot. 2719 women (84%) collected the self-sampling device at the pharmacy and 2470 (76 %) returned the collected sample. Among the 2470 samples processed at the laboratory, 260 (10,5%) tested positive for HR-HPV. The type of the HR-HPV in 260 patients was 17.3 % HPV-16, 3.1 % HPV-18 and 79.6 % non16non18. 251 out of 260 patients have performed a triage cytology: 142 with a normal result, 34 ASCUS, 48 L-SIL, 11 ASC-H, 13 H-SIL, 3 AGC/AGC-NOS.
Conclusion: HPV detection in self-collected samples using a non-liquid base system at the time of collection can be used as an alternative screening method to determine the presence of HR-HPV. It is necessary to have a laboratory solution to automate the process. Self-sampling in cervical cancer screening has been widely accepted among female participants, which is expected to translate into increased participation and eventually coverage.

PS-16-002
Implementation of the Milan System in a cytopathologist-performed US-guided FNA practice

A. Carillo*, M. Salatiello, P. Pisapia, E. Vigliar, G. Troncone, C. Bellevicine
*Università degli studi di Napoli Federico II, Italy

Background & objectives: The Milan System (MSRSGC) was introduced as standard classification in our salivary gland FNAs reporting. In this study we evaluate the added value of the MSRSGC implementation in our Institution, where these FNAs are performed by interventional cytopathologists.
Methods: We searched for salivary gland FNAs performed from 2018 to 2021 with 23-gauge needles by an experienced interventional cytopathologist under US-guidance. For each FNA, we searched for subsequent histologic reports. Overall sensitivity, specificity, positive predictive value and negative predictive value were calculated. The risk of neoplasm and risk of malignancy were also calculated for each category of the MSRSGC.
Results: A total of 642 salivary gland FNAs were retrieved: 118 cases were as non-diagnostic (ND), 107 non-neoplastic (NN), 64 atypia of undetermined significance (AUS), 254 neoplasm-benign (NB), 45 salivary gland neoplasm of uncertain malignant potential (SUMP), 19 suspicious for malignancy (SFM) and 35 malignant (M). 40,59% of FNAs had an available surgical follow-up: 14,56% ND; 4,60% NN; 8,43% AUS; 50,19% NB; 13,41% SUMP; 3,07% SFM; 5,75% M. RON and ROM were respectively: 44,74% and 7,90% for ND; 33,33% and 0 for NN; 77,27% and 22,73% for AUS; 98,47% and 0,76% for NB; 94,29% and 20% for SUMP; 100% and 87,50% for SFM; 100% and 93,33% for M.
Conclusion: The MSRSGC is a valuable tool that can help to standardize reporting and stratify cases preoperatively. In our study, we observed some differences in terms of ROM compared with MSRSGC that reflect some constant problems in diagnosis of salivary gland FNA, such as the ability of the operator who performs the FNA, the scant cellularity on the smear and the sovrapposition of features common both in non-neoplastic lesions and in neoplastic ones.

PS-16-003
Morphological detection of non-invasive follicular thyroid neoplasm with papillary-like features (NIFTP) from papillary thyroid carcinoma on cytology using a scoring system

G. Heuston*, D. Gibbons
*University Hospital Galway, Ireland

Background & objectives: Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is a non-invasive follicular cell derived tumour with low malignant potential. Separation from papillary thyroid carcinoma (PTC) on fine needle aspiration cytology is challenging. Accurate diagnosis is essential in planning management.
Methods: Cytology slides from patients diagnosed with NIFTP on surgical resection between 2015 and 2022 were identified. PTC cases designated as THY5, THY4 and THY3 were randomly selected with the pathologist blinded to the outcome. Specific cytologic features were scored from 0 to 2 and summated for each case. A student T test was used to compare mean scores.
Results: A total of 6 cases of NIFTP were identified along with 7 cases of Thy 5, 8 cases of THY4 and 6 cases of THY3 FNA's that on surgery were PTC's. Five of six NIFTP cases were Thy3 or Thy4 on FNA. The

final morphologic scores for cases of NIFTP ranged from 2 to 7 with a mean of 4.33 with those of THY5 PTC ranging from 6 to 8 with a mean of 6.57 giving a significant p value of 0.0109. A comparison of NIFTP cytology scores with scores of surgically proven PTC with THY3 and THY4 preoperative diagnoses was non-significant (P= 0.8442).
Conclusion: The morphological detection of NIFTP on FNA is supported by the identification and scoring of key cytological features. The scoring system is most effective at distinguishing NIFTPs from Thy 5 PTCs on FNA. The separation of NIFTPs, predominantly Thy3 and Thy4, from Thy 3 and Thy 4 FNA's that turned out to be papillary cancer using the scoring system is not possible. Combination with other testing modalities, including molecular, is required.

PS-16-004
Spectrum of RAS and BRAF mutational analysis in indeterminate thyroid nodules
N. Kumari*, N. Krishnani, R. Paturu
*All India Institute of Medical Sciences, Raebareli, India

Background & objectives: The role of molecular testing in indeterminate thyroid aspirates have become increasingly important in cases of indeterminate cytology (Bethesda category III, IV and V). Molecular testing helps to decide predicting the risk if malignancy and decide about the surgical management.
Methods: 135 cases of indeterminate Bethesda cytology were retrieved from the pathology records in 50 months duration. All cases were reviewed by two experienced pathologists. Thirty-one cases were excluded because of inadequate material or reclassification into category II or VI. Remaining 104 cases were included for molecular testing of RAS (NRAS, HRAS, KRAS) and BRAF mutations by real time PCR.
Results: Cytomorphologically there were 27.9% Bethesda III, 60.6% IV, and 11.5% category V. Histopathologically malignancy was confirmed in 35.6% cases. 64.4% cases were benign. RAS was common than BRAF mutation (53.3% vs 7.7%). NRAS was predominant mutation (33.7%) followed by HRAS (16.3%) and KRAS (1.9%). Prevalence of mutations in each Bethesda category followed the order of NRAS > HRAS > BRAF > KRAS except in category V where BRAF (25%) was greater than NRAS (16.7%), HRAS (8.3 %) and KRAS (8.3%). Overall risk of malignancy in indeterminate nodules was 35.6%. 66.7% risk highest in category V followed by IV (36.5%) and III (20.7%). NRAS significantly predicted malignancy (p=0.005) in 54% cases.
Conclusion: The sensitivity, specificity, positive predictive value, and negative predictive value of NRAS mutations to predict malignancy in indeterminate thyroid nodules is 51.35%, 76.12%, 54.31%, 73.89%, respectively. Despite, predicting malignancy significantly (p=0.005), NRAS had a low diagnostic accuracy of malignancy of 67.3%.

PS-16-005
UKNEQAS CPT Cell Block Scheme
A. Patterson*
*UKNEQAS CPT, United Kingdom

Background & objectives: Currently there is no External Quality Assurance scheme for assessing the quality of Cell Blocks prepared from cytology samples. It was decided by UKNEQAS CPT to investigate the need for such a service.
Methods: Increase in the number of Haematoxylin and Eosin slides from cell blocks and number of inquiries regarding preparation methods suggested a need for such a scheme. A survey UKNEQAS CPT circulated indicated that there is a need for such a scheme. In response to the survey responses it was decided to perform 2 pilots which were well supported.
Results: Previously cell block slides were considered to be covered by the Tissue Diagnostics scheme. However, this is not entirely appropriate as cytology departments use a variety of preparation methods and fixatives for cell blocks.
The 2 pilots were well supported and successful leading to the launch of the new scheme in April 2023. Participants are asked to provide details about the sample types and preparation methods used for the samples they submit for assessment. This presentation will cover the results of the 2 pilots and how the scheme intend to collate the information gathered and share this with our users.
Conclusion: The UKNEQAS CPT Cell Block scheme is not intended to be merely a 'tick box' exercise for UKAS. or other accreditation bodies. lt will enable enable gathering valuable information about 'best methods' which can be circulated to laboratories experiencing problems. It will be an advisory service which aims to improve diagnostic practices and therefore be of benefit to patients and clinicians.

PS-16-006
High positive predictive value of atypical glandular cells in cytology for a preneoplastic or neoplastic squamous and/or glandular cervical lesion
H. Piña-Giménez*, B. Raposo, R. Granados
*Hospital Universitario de Getafe, Spain

Background & objectives: Reproducibility of cytological glandular cell atypia (AGC/AGC-H) is low and carries an elevated risk of CIN2+ cervical lesions, warranting immediate colposcopy. This study analyses the positive predictive value (PPV) of the AGC/AGC-H cytological diagnosis in our population for CIN2+ lesions.
Methods: A retrospective study with the analysis of liquid-based cytology (LBC) samples, human papillomavirus (HPV) status, histological correlation and clinical follow-up of women from our archives in the past 10 years. The incidence of AGC/AGC-H in our population and the presence of either glandular, squamous or mixed lesions associated with this diagnosis was reviewed. Statistical analysis of PPV was calculated.
Results: From 163.033 LBC samples, 94 (0,06%) showed AGCs (76 AGC and 18 AGC-H). Twenty-two had additional cytological squamous atypia. From 81 biopsies, 66,7% showed CIN2+ (average age of 41 years), 27,2% glandular lesions, 11 of them with infiltrating adenocarcinoma. Mixed squamous/glandular lesions co-existed in 16,7% of cases, but 59,3% of CIN2+ lesions were purely squamous. There were 21 women with negative biopsies, accounting for 25,9% of cases with AGCs. No biopsy was performed in 13 cases, followed-up with cytologies from 1-10 years. The PPV of AGCs in cytology was 66,7% when all, squamous and glandular, CIN2+ lesions were considered. PPV decreased to 27,2% for adenocarcinoma in situ (AIS) or adenocarcinoma.
Conclusion: Although a very unusual cytological diagnosis in our population, the presence of AGC or AGC-H poses a high risk (66,7%) for a preneoplastic or neoplastic cervical lesion in women aged 41 years in average. Most associated CIN2+ cases are squamous or mixed squamous/glandular. However, the PPV of atypical glandular cells in cytology for AIS or adenocarcinoma reaches 27,2%, justifying the immediate referral of these women for colposcopy in most cervical cancer screening programmes.

PS-16-007
Immunocytochemical determination of hormonal receptor and CerbB2 status in metastatic breast carcinoma in axillary lymph nodes (via SurePath experience) and correlation with synchronous breast mass core needle biopsies
S.R. Ramazanoglu*, H. Eren, S. Bagbudar, T. Soylemez Akkurt, H. Izol Ozmen, M.A. Nazli
*Başakşehir Çam and Sakura City Hospital, Department of Pathology, Division of Cytopathology, Turkey

Background & objectives: Determination of ER and CerbB2 status have pivotal role in patients with breast cancer. We aimed to find out the significance of ER, CerbB2 antibodies' efficiency and accuracy in metastatic axillary lymph nodes, all of which were diagnosed via FNAC.

Methods: From October 2020-December 2022; 31 FNAC cases of metastatic breast carcinoma -devoid of cell blocks- were retrospectively analysed and compared with synchronous breast mass CNB results. All cases were prepared via Liquid Based Cytology technique (SurePath-BD). ER and CerbB2 antibodies were applied to Papanicolaou stained slides by Ventana. Statistical analysis was performed by using SPSS.
Results: Examination of the slides revealed that, nine of 31 cases were negative and 22 were positive for ER. For CerbB2, two cases were inadequate for interpretation. Fifteen cases were negative (Score 0/1+), 5 cases equivocal (Score 2+) and 9 positive (Score 3+/Amplification identified via in-situ hybridization). When all the FNAC data were compared to CNB, the positive predictive value (PPV) of ER was 100%; negative predictive value (NPV) was 66.7%. For CerbB2, PPV was 77.8%; NPV was 93.3%. Consequently, the sensitivity of ER and CerbB2 were 88%, 87.5%, respectively ($p<0.001$). The specificity of ER and CerB2 were 100%, 90.5%, respectively ($p<0.001$).
Conclusion: The results of our study showed that FNAC is an efficient and accurate method both in the diagnosis and evaluation of ER and CerbB2 status in metastatic axillary lymph nodes in patients with breast cancer.

PS-16-008
Rapid toluidine blue staining for on-site evaluation of cytological specimens: the Lausanne experience
C. Royer*, M. Maillard, E. Dubruc, E. Hewer
*CHUV Lausanne, Switzerland

Background & objectives: Rapid toluidine blue staining for on-site evaluation (ROSE) of cytological specimens takes less than a minute, while offering excellent morphology. Here, we assess the performance of ROSE using toluidine blue staining in our institution and illustrate its morphological characteristics.
Methods: We evaluated a series of consecutive thyroid, lung, head and neck FNA specimens with ROSE performed for assessment adequacy, for triage for ancillary testing and/or for preliminary diagnosis. Additionally, we illustrated the morphological features identified in toluidine-blue stained slides as compared to the definitive Papanicolaou staining.
Results: Adequate material was obtained in 110 of 118 (93.2%) consecutive samples. In only a single case (0.8%), ROSE had erroneously suggested an adequate specimen. In 4 samples (3.3%), the specimen was inadequate according to ROSE, but adequate according to the final evaluation. Among the 106 specimens with adequate material on both ROSE and definite evaluation, both were positive in 47 samples (39.8%), both were negative in 40 samples (33.9%). For 2 samples (1.7%) tumour cells were not identified during ROSE, but present in the definite samples, corresponding to 100% specificity and a 95.8% sensitivity of the ROSE. Evaluation for the presence of neoplastic cells was deferred for 5 samples (4.2%).
Conclusion: The previously described rapid toluidine blue staining protocols allows for reliable ROSE of thyroid, head and neck, and pulmonary FNA specimens with high concordance between rapid and final evaluation and in particular without risk of false positive ROSE. The staining protocol provides excellent nuclear morphology, very similar to a Papanicolaou staining. As the staining is non-permanent, it is fully compatible with subsequent Papanicolaou staining of the same slides.

PS-16-009
The value of p16/Ki-67 double staining in the diagnostic triage of the abnormal Pap test
S. Stemberger-Papic*, D. Vrdoljak-Mozetic, D. Versa Ostojic, R. Rubesa-Mihaljevic, M. Dinter
*Department of Pathology and Cytology, Clinical Hospital Centre Rijeka, Department of Pathology, Medical Faculty, University of Rijeka, Croatia

Background & objectives: Dual p16/Ki-67 immunocytochemical staining is used for the detection of the HSIL that require further treatment. The aim of this work is to evaluate the value of p16/Ki-67 as a predictive marker in patients with ASCUS, LSIL and ASC-H cytology.
Methods: 312 samples of conventional cytology were analysed and p16/Ki-67 double staining (CINtec PLUS, Roche, Switzerland) was performed on the same smear. The results were compared with the findings of histological examinations (conization, LLETZ, biopsy and endocervical curettage) or with clinical follow-up of patients for at least 12 months.
Results: p16/Ki-67 staining was positive in 154 (49.4%) samples. In the p16/Ki-67 positive group, 83(53.9%) HSIL+ lesions were confirmed, and in the p16/Ki-67 negative only 10(6.3%). In the ASCUS category, out of 133 samples, 39(29.3%) were p16/Ki-67 positive and 4(10.3%) HSIL+ lesions were detected. In the LSIL category 37 samples was analysed, p16/Ki-67 was positive in 14(37.8%) and HSIL+ lesions were confirmed in 4(28.6%). In the ASC-H group, 142 samples were analysed, p16/Ki-67 were positive in 101(71.1%) and 75(74.3%) HSIL+ lesions were confirmed.
Based on the correlation of p16/Ki-67 and histology or clinical follow-up, an overall sensitivity, specificity, positive and negative predictive value were 89.3%, 67.6%, 53.9% and 93.7%. respectively.
Conclusion: The results of the study show a high negative predictive value of p16/Ki-67 immunocytochemical staining in the detection of HSIL+ lesions in patients with ASCUS, LSIL and ASC-H cytology. The use of p16/Ki-67 staining could lead to more accurate and efficient management of patients with abnormal Pap test results, potentially reducing the need for unnecessary interventions and improving patient outcomes.

PS-16-010
Comparison of risk of malignancy and predictive value of diagnostic categories defined by Papanicolaou Society of Cytopathology System and WHO Reporting System for Pancreaticobiliary Cytopathology in solid pancreatic lesions
B. Vasas*, A. Fábián, Z. Bősze, S. Hamar, L. Kaizer, P. Bacsur, T. Resál, K. Farkas, T. Molnár, R. Bor, Z. Szepes
*University of Szeged, Department of Pathology, Hungary

Background & objectives: The standardized diagnostic categories defined by the new WHO Reporting System support the interdisciplinary interpretation of cytological findings in the management of pancreatic cancer.
Methods: Aim of the study was to compare this classification to the Papanicolaou Society of Cytopathology (PSC) system in terms of predictive value and risk of malignancy (ROM) in solid pancreatic lesions. All consecutive patients with solid pancreatic lesions were retrospectively enrolled who underwent endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) sampling in University of Szeged from 2014 to 2021.
Results: 521 EUS-FNA samplings were performed with a malignancy rate of 81.76%. In both systems, the ROM of "non-diagnostic", "negative for malignancy", "atypical", "suspicious for malignancy" and "malignant" categories were 48.2%, 2.3%, 78.1%, 100.0% and 99.4%. Despite the heterogeneous "neoplastic: other" category of PSC system, the ROM for solid lesions was 100%. PaN-high including only 2 endosonographically solid cases of high-grade IPMNs showed 100% ROM. There were no differences between PSC and WHO systems in sensitivity, specificity, NPV and PPV: excluding the "atypical" category, these were 99.7%, 95.6%, 97.7%, 99.5%. "Atypial" category considered as benign resulted in higher decrease in validity compared to "atypical" considered as true malignant (93.6% vs. 97.7%).
Conclusion: For solid pancreatic lesions, the WHO system was identical to the PSC system in terms of ROM and predictive values.
This work was supported by the research grants of the National Research, Development and Innovation Office (Grant ID: 125377, 129266 and 134863), by the New National Excellence Program of the Ministry of Human Capacities (UNKP-21-5-SZTE-552 to FK, UNKP-22-5-SZTE-545 to BR, UNKP-22-4-SZTE-296 to FA) and Janos Bolyai

Research Grant (BO/00723/22 to BR). The funding body did not play roles in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

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PS-17-001

A weakly supervised learning approach based on multiple instance-learning and self-supervised contrastive learning for gastric cancer classification using whole slide images.

A., S. Ali*, T.P. Theodore Armand, H. Kim
*Inje University, Republic of Korea

Background & objectives: The whole slide image classification is a challenging task in digital histopathology because they are big in size and have high resolution. It is very difficult and time-consuming to annotate WSI. We used multiple instance learning (MIL) for gastric cancer.
Methods: To deal with the WSI classification of gastric cancer, we applied dual-stream MIL. Since WSI contains only a small portion with disease-positive instances resulting in data imbalance between positive and negative bags, therefore, to address this problem, we introduced self-supervised contrastive learning. It extracts useful representations for MIL and addresses the issue of prohibitive memory costs for large bags.
Results: We collected gastric cancer data from five different hospitals in South Korea. The dataset consists of 220 training and 54 testing WSI images which produced 1.2 million patches of size 224 x 224 at 10x magnification. Each slide contains pixel-level annotations of the tumour regions and is weakly annotated. However, we consider slide-level annotations. We trained the backbone model resnet18 on 500 epochs. Moreover, for contrastive learning, the SimCLR model was trained on 100 epochs. We calculated the accuracy and area under the curve (AUC) of our model for the classification of poorly differentiated (PD) and well-moderately differentiated (WMD) classes. The model achieved 73% accuracy and 80.5% AUC.
Conclusion: In this research study, we introduced a weakly supervised-based dual-stream MIL approach for the classification of WSI. We integrated self-supervised contrastive learning with MIL. In DS-MIL, the highest-scored instance is determined by the first stream using standard max pooling, while by determining each instance's distance from the highest-scored instance, the second stream calculates an attention score for each instance. We think that our approach represents a significant advancement in the diagnosis of gastric cancer using WSI.
This research was supported by the MSIT(Ministry of Science ICT), Korea, under the National Program for Excellence in SW, supervised by the IITP(Institute of Information & Communications Technology Planning & Evaluation) in 2022 (2022-0-01091, 1711175863).

PS-17-002

Does the morphology of Helicobacter pylori matters for the histopathology in gastric endoscopic biopsies?

Y. Adali*, Ö. Ertener, H. Beşeren, G. Yıldız
*Izmir University of Economics Faculty of Medicine, Turkey

Background & objectives: The histopathological changes in the presence of Helicobacter pylori (H. pylori) in the stomach are well defined. In this study, it is aimed to evaluate the relationship between the main morphological types of H. Pylori and histopathological findings observed in gastric endoscopic biopsies.
Methods: The study included 791 gastric endoscopic biopsies evaluated by a single pathologist over a 2-year period. In addition to the morphological findings re-evaluated according to the updated Sydney classification by two separate pathologists, the morphological appearances of H. Pylori was categorized as bacillus, coccoid, bacillus+coccoid forms. Afterwards, H. Pylori morphology, demographic information and histomorphological findings were compared.
Results: Active chronic gastritis was observed in 442(55.9%) cases and chronic gastritis was observed in 338(42.7%) cases. The presence of H. Pylori was observed in 604(76.4%) cases. The morphology was bacillus in 456(57.7%) cases, coccoid in 70(8.8%), and bacillus+coccoid in 78(9.9%). In cases with active chronic gastritis, the most statistically significant morphology is bacillus, then bacillus+coccoid, and lastly coccoid form (p=0.000). In cases with chronic gastritis, bacillus+coccoid, then bacillus and then coccoid morphologies are observed most (p=0.015). While no statistical significance was observed between intestinal metaplasia and dysplasia and morphology, the presence of lymphoid aggregates was mostly observed in bacillus, then bacillus+coccoid and last coccoid forms (p values 0.317, 0.402, 0.000, respectively).
Conclusion: The relationship between the bacillus form and active chronic gastritis has been shown, as expected from routine pathology practice. However, the change in this morphological order, which is expected in chronic gastritis, indicates that the history of anti-gastritis and anti-acid drugs should be carefully examined. In addition, it is thought that no statistically significant relationship was found between H. Pylori morphology compared to intestinal metaplasia and dysplasia due to the low number of cases with these histopathological findings.

PS-17-003

Clinicopathological spectrum of primary anorectal melanoma: a single centre experience of 36 resected cases

T. Agrawal*, M. Bal, K. Deodhar, M. Ramadwar, A. Saklani, S. Yadav, R. Kumar
*Tata Memorial Hospital, India

Background & objectives: Anorectal melanoma is an uncommon and aggressive malignancy with poor median survival rates. In this study we aimed to evaluate the clinical and histopathological parameters and to correlate these clinic-pathologic parameters with prognosis.
Methods: Operated cases of anorectal melanoma from 2013 to 2019 were included. Clinical and treatment details were obtained from the electronic medical record. Pathological parameters evaluated included histological type, tumour depth, level of anorectal wall invasion, vertical and radial growth phase, mitotic rate, surface ulceration, lymphovascular invasion, perineural invasion, microscopic satellitosis, tumour infiltrating lymphocytes, and lymph node status.
Results: A total of 36 cases were assessed. The median age was 53.5 years. Tumour epicentre was anorectal junction(24), rectum(7) and anal canal(5). Median tumour dimension was 40 mm(7-150mm) and histologic depth of 13.5 mm(1-23mm). Histomorphology was epithelioid (44.5%, n=16), spindled (11%, n=4) and mixed (44.5%, n=16). Invasion into muscularis propria and beyond was seen in 22 patients (61%). Radial growth phase was seen in 50%(n=17/34), pagetoid spread(26%, n=9/34), junctional activity(35%, n=11/31), lymphovascular invasion(22%, n=8), perineural invasion(11%, n=4), and microsatellitosis (17%, n=6). Amelanotic cases were 19%(n=7). Lymph node metastasis was seen in 55%(17/31), whereas 85%(22/26) developed distant metastasis. Follow-up data was available for 22 patients and 7(32%) were alive (median follow-up: 13 months).
Conclusion: Anorectal melanoma is an aggressive neoplasm and patients present at an advanced stage. These patients have a higher frequency of lymph node metastasis and distant metastasis, and an overall poor survival rate.

PS-17-004

TempO-Seq Detects Fusobacterium nucleatum in formalin-fixed paraffin-embedded patient tissue from a bowel screening population

S.S.F. Al-Badran*, S. McSorley, M. Johnstone, J. Hay, J. Jawny, N. Maka, D. Andersen, G. Lynch, J. Edwards
*School of Cancer Sciences, University of Glasgow, United Kingdom

Background & objectives: *Fusobacterium nucleatum* is an oral pathogen implicated in colorectal cancer (CRC) progression. Colorectal polyps are thought to initiate colorectal carcinogenesis. This study aimed to investigate novel targeted RNA sequencing technology TempO-Seq for detecting bacteria in formalin-fixed paraffin-embedded (FFPE) polyp tissue.
Methods: TempO-Seq depends on hybridizing detector oligos (DOs) to proximal sequences. Excess DOs are enzymatically removed, the juxtapositional DOs ligated, and amplified by PCR before sequencing. DOs were designed to target *F. nucleatum*'s (ATCC 10953) 16S region. DOs were quality checked (QC) on purified human and *Fusobacterium* RNA, before TempO-Seq analysis of a pilot study of 120 polyp samples.
Results: Eight probes were designed, and five passed *in silico* QC. Three probes passed *in assay* QC. TempO-Seq analysis using *Fusobacterium* DOs was performed on FFPE tissue lysates from 120 screened patients. Human DOs were added as assay controls. 8% were *F. nucleatum*+ for Probe 1, 23% for Probe 2 and 9% for Probe 3. Samples were stratified for metachronous polyps (MPs) development as an outcome, and 3%, 24%, and 6% of those who developed MPs were *F. nucleatum*+ for Probe 1, Probe 2, and Probe 3 respectively. Alternatively, 12% of patients that didn't develop MPs were *F. nucleatum*+ for Probe 1, 21% for Probe 2, and 12% for Probe 3.
Conclusion: These results suggest that TempO-Seq is a robust technology that detects bacterial RNA in archival FFPE tissue. Three probes displayed different trends based on their specificity. Since *F. nucleatum* has been associated with poor prognostic factors in CRC, this technology can be investigated as a prognostic technique. Up-scaled future work will use TempO-Seq to detect *F. nucleatum* in FFPE polyp lysates and will use that information to predict the development of MPs and explore any associations with other clinical characteristics.
Funders of this work include Medical Research Scotland BioClavis Ltd. Innovate UK

PS-17-005
Immunohistochemical assessment of Ki67 and pathway analysis in pre-malignant colonic polyps suggest Ki67 as a potential prognostic maker for metachronous disease
A. Ammar*
*University of Glasgow, United Kingdom

Background & objectives: Bowel screening program risk stratification tool uses polyps' number and size to assess the need for surveillance colonoscopy following polypectomy. The prognostic significance of index polyps Ki67 for metachronous disease and molecular differences between normal and dysplastic epithelia were explored.
Methods: Whole tissue index polyps (n=153) were stained for Ki67 using immunohistochemistry. 48.4% developed metachronous polyps (median time 36.5 months (2006-2019)) and 63% had BSG20 high risk score. QuPath software was used to quantify Ki67 in annotations of luminal/basal epithelium. Temp-O-Seq RNA sequencing for normal and dysplastic epithelium (n=40) and ssGSEA/GSEA methods for pathways and leading- edge gene analyses were applied.
Results: Ki67 percentages were higher in luminal (46.4%) vs basal (24.8%) epithelium ($p<0.0001$). High luminal Ki67 significantly associated with metachronous disease ($p=0.013$) and polyp histology ($p=0.051$) and was an independent prognostic factor for metachronous disease (HR=2.6, CI(1.238-5.46), $p=0.012$; compared to number of polyps and BSG20 risk score using Cox-regression analysis). Myc targets-V1, G2M checkpoint and E2F-targets were enriched in dysplastic epithelium (NES=2.98, 2.88 and 2.7; respectively) whereas epithelial-mesenchymal transition was mostly enriched in normal epithelium (NES=2.33) and that was confirmed on single sample level (ssGSEA $p<0.0001$). Ki67 gene expression was higher in dysplastic than in normal epithelium ($p<0.001$). Myc, MAD2L1, KPNA2, CDK4 and MCM5/MCM6 genes were highly enriched in dysplastic regions.
Conclusion: Ki67 is an independent prognostic marker for metachronous polyps and may help improve the current BSG20 criteria. Ki67 scores can be combined with BSG20 risk score and number of polyps excised at index colonoscopy to better stratify patients who are at a higher risk of developing metachronous polyps. Dysplasia-enriched pathway and leading-edge genes suggest an active biological process relating to cell cycle and replication. Genes enriched in dysplastic polyps require further validation on the protein level using INCISE polyp cohorts.
Funding: Title: Integrated Technologies for Improved Polyp Surveillance Project number: 42497 Funder: Innovate UK 2022 – 2023 Title: Risk Stratification Tool for Colorectal Polyp Surveillance Project number: 10054829 Funder: Innovate UK 2023 – 2025

PS-17-006
Dysplasia in sessile serrated lesions: prevalence, interobserver variability and value of immunohistochemistry
V. Angerilli*, M.E. Vink-Börger, G. van Lijnschoten, N.C. van Grieken, M. Fassan, R.S. van der Post, I.D. Nagtegaal
*Department of Medicine, Surgical Pathology Unit, University of Padua, Italy

Background & objectives: Sessile serrated lesions with dysplasia (SSLd) are the precursors of 15% of colorectal carcinomas (CRCs). We aim to estimate the prevalence of dysplasia in sessile serrated lesions (SSLs), (ii) evaluate interobserver variability, and (iii) assess additional value of immunohistochemistry (IHC).
Methods: (i) We retrieved histology reports from colonoscopy patients between 2014 and 2022 from the Dutch Nationwide Pathology Database. (ii) Histological slides of SSLd from all laboratories were reviewed by the pathology panel of the Dutch CRC screening program. (iii) A cohort of 212 SSLs/SSLd of >=1cm was reviewed to assess dysplasia and expression of MLH1, beta-catenin, Myc, p16, and p53.
Results: (i) Out of the 186,427 SSLs 17,456 showed dysplasia (9.4%). (ii) Twelve laboratories submitted their SSLd cases. No IHC stain was originally performed in any of the cases. The diagnosis of SSLd was confirmed by the pathology panel in 44 cases (75.9%). The remaining 14 cases were reclassified as SSL (n=8), traditional serrated adenoma (n=5), and serrated adenocarcinoma (n=1). (iii) The hematoxylin and eosin (HE) slides of SSL/SSLd cohort were subject to an IHC-blinded and IHC-unblinded revision. The IHC-blinded and IHC-unblinded revisions revealed the presence of dysplasia in 20/212 (9.4%) and 26/212 (12.3%) cases, respectively. The six additional SSLd had minimal deviation dysplasia and were identified by loss of MLH1.
Conclusion: This study shows that considerable variability is present in the histopathological assessment of SSLd. The accurate diagnosis of subtle dysplasia can be challenging and MLH1 expression should be used when suspected on routine stains.

PS-17-007
Early-onset small bowel adenocarcinomas (EO-SBAs) are more frequently associated with a predisposing condition compared to late-onset SBAs: an international multicentre study
G. Arpa*, C. Guerini, M.V. Lenti, E. Quaquarini, F. Grillo, F. Antoci, E. Travaglino, M. Fassan, R.P. Graham, A. Casadei Gardini, M. Ferrante, A. Moens, G. De Hertog, A. Di Sabatino, A. Vanoli
*Department of Molecular Medicine, Unit of Anatomic Pathology, University of Pavia, Unit of Anatomic Pathology, ICS Maugeri-IRCCS SpA SB, Pavia, Italy

Background & objectives: The incidence of early-onset gastrointestinal cancers (i.e., age at diagnosis <50 years) is increasing and most of them are supposedly sporadic. However, data on early-onset small

bowel adenocarcinoma (EO-SBA) are lacking. We aimed to investigate EO-SBA clinico-pathologic features.
Methods: A retrospective study was conducted on an international multicentric cohort of 208 SBA patients. EO-SBAs (i.e., SBAs with age at cancer diagnosis <50 years) were compared to late-onset SBAs (LO-SBAs) (i.e., age at diagnosis ≥50 years) in terms of predisposing conditions (hereditary syndromes and immune-mediated disorders), other clinico-pathological features, and cancer-specific survival. Mismatch repair status was assessed by immunohistochemistry.
Results: Forty-one EO-SBAs (mean age: 40 years; 20 males) and 167 LO-SBAs (mean age: 66.9 years, 109 males) were identified. A predisposing condition was significantly more common in EO-SBAs (76%) compared to LO-SBAs (52%, p=0.008). Association with celiac disease, Crohn's disease, familial adenomatous polyposis and Lynch syndrome was reported in 13 (32%), 13 (32%), 2 (5%), and 3 (7%) EO-SBAs, and in 28 (17%), 45 (27%), 0, 14 (8%) LO-SBAs, respectively. Among such predisposing conditions, only celiac disease proved to be significantly more frequent in EO-SBAs compared to LO-SBAs (p=0.047). No significant difference was found between the two groups for remaining clinico-pathologic features, cancer-specific survival, or mismatch repair status.
Conclusion: When compared to LO-SBAs, EO-SBAs showed a higher rate of cases associated with predisposing conditions, and the difference was mainly due to the association of EO-SBAs with celiac disease. The present study emphasizes the importance of assessing potential predisposing conditions in all EO-SBA patients.

PS-17-008
Mucinous carcinoma: pathomolecular and microenvironment characterisation - a trans organ study
M.A. Bani*, P. Dartigues, C. Genestie, M. Classe, A. Boileve, M. Ducreux, J. Scoazec
*Department of Medical Biology and Pathology, Morphological pathology laboratory, Gustave Roussy Cancer Campus, Villejuif, France, Paris-Saclay university, Gustave Roussy Cancer Centre, Inserm US23, CNRS UMS3655, AMMICa, Villejuif, France

Background & objectives: Mucinous carcinomas (MC) can arise in any type of epithelial tissue. Previous studies focused only on specific organs. This is a trans-organ study aiming to establish the molecular profile and to reveal the different components of tumour immune microenvironment.
Methods: Descriptive, retrospective and monocentric study on patients treated in our institution between 2015 and 2021 for MC. Clinical data were collected from medical records and histological samples re-examined for histoprognostic factors. Tissue hypoxia in tumours and the proportions of immune cells were studied by immunohistochemical methods and digital image analysis. A molecular study was done by Next Generation Sequencing.
Results: The study involved 206 CM from 13 different organs. In the univariate study for overall survival: gender(male), size(>6cm), tumour site, vascular invasion, perineural invasion, signet ring cells, nodal invasion and T3/T4 TNM stages were significantly associated with poor prognosis. In the multivariate study, only perineural invasion (p=0.001) and T stage (p=0.018) remained statistically significant. More frequent mutations were found in the ERK-pathway (65.21%) and less frequently in TP53 (24%) and PIK3CA (15%). The highest hypoxia score was found in ovary and head and neck. There was a predominant infiltration by macrophages in the mucin and by T lymphocytes in the peri-tumoral areas. These factors had no impact on overall survival.
Conclusion: Our preliminary results do not show any significant difference in the molecular profile of the sequenced MC as well as the composition of immune infiltrates. Mutations on the ERK-pathway seem to be predominant in all different sites. We also demonstrate the spatial heterogeneity of the immune microenvironment of MC in different organs. A significant difference in the hypoxia score between different organs could explain some different biology.

PS-17-009
Small intestinal metaplasia in indefinite for dysplasia, dysplasia, and adenocarcinoma in patients with inflammatory bowel disease
A. del Portillo*, A. Koehne de Gonzalez, L. Fazlollahi
*Columbia University Irving Medical Center, USA

Background & objectives: Recent studies show loss of the colonic marker SATB2 in inflammatory bowel disease (IBD)-associated dysplasia and carcinoma. We tested whether this represents small intestinal metaplasia by examining these lesions for expression of SATB2 and other small intestinal markers.
Methods: We searched for cases of IBD with dysplasia, carcinoma, and indefinite for dysplasia from 2010-2022. We tested 30 colon samples (biopsies and resections) from 26 patients with IBD with diagnoses of indefinite for dysplasia (6), low-grade dysplasia (10), high-grade dysplasia (8), and carcinoma (6) for the small intestinal markers CD10, HepPar1, and colon marker SATB2 by immunohistochemistry.
Results: At least one marker of small intestinal metaplasia was seen in lesional cells in colon samples of 85% (11/13) of patients with high-grade dysplasia or carcinoma. CD10 was expressed in the lesional cells in 30% (9/30) of cases and in 35% (9/26) of patients. SATB2 was lost or showed reduced/patchy expression in 38% (11/29) of cases tested (one case was not stained) and 42% (11/26) of patients. HepPar1 was expressed in at least 47% (14/30) of cases (5 cases failed, 11 cases were negative in the lesion) and 50% (13/26) of patients. When SATB2 was lost/reduced, at least one other small intestinal marker was expressed in 82% (9/11) of cases/patients.
Conclusion: IBD-associated dysplasia and carcinoma often exhibit small intestinal metaplasia. We previously found that small intestinal metaplasia occurs in non-neoplastic colonic mucosa from patients with IBD at a lower rate (5.3% CD10 expression, 13.8% HepPar1 expression, 3.2% lost/reduced SATB2 expression). Thus, IBD-associated dysplasia enriches small intestinal metaplasia. These findings suggest that small intestinal metaplasia in colonic mucosa of patients with IBD may represent a marker of progression to IBD-associated dysplasia and carcinoma.

PS-17-010
Prognostic value of tumour infiltrating lymphocytes in colon cancer
S. Gharbi*, D. Bacha, I. Mallek, E. Benammou, M. Hajri, H. Mestiri, A. Lahmar, S. Ben Slama
*Department of Pathology, Armand Trousseau Hospital-Sorbonne University, France

Background & objectives: Tumour-infiltrating-lymphocytes (TILs) are currently considered as a prognostic factor in several cancers. For stageII colon cancer(CC), studies are underway to validate the prognostic value of this parameter. The objective of this study was to assess the prognostic value of TILs in stageII CC.
Methods: It was a retrospective and descriptive study. It involved 70 patients, who underwent curative surgery for stage II colonic adenocarcinoma. The data was collected over a period of 15 years with a mean follow-up of 24 months.
Results: The mean age of the patients was 60years. The most frequent circumstances of discovery were abdominal pain (48%), followed by digestive tansit disorder(26%) and digestive bleeding(20%). All patients (n=51) at "high risk" of recurrence had received adjuvant chemotherapy except for seven patients. The mean overall survival and recurrence-free survival rates were 51 and 56 months, respectively. TILs rate varied between 3% and 80%. TILs rate <50% significantly decreased recurrence-free survival in univariate analysis (p=0.001). In multivariate analysis, it was identified as an independent factor for

the recurrence-free survival. We found a correlation between the rate of TILs<50% and the lymphatic invasion(p=0.022), the high grade of the tumour(p=0.02) and the tumour size>3cm(p=0.009).
Conclusion: ILs represent an important prognostic and predictive factor for stage II CC. It should be introduced in clinical practice, to identify patients with "high risk" stage II CC, justifying the benefit of adjuvant chemotherapy.

PS-17-011
In-house validated approach of gastric cancer: a tool for a better evaluation of HER2 heterogeneity
S. Gurzu*, C. Satala, Z. Kovacs, I. Jung
*George Emil Palade University Of Medicine, Pharmacy, Sciences And Technology Of Târgu Mureş, Romania

Background & objectives: As HER2 is a target for therapy with trastuzumab, different methodologies were proposed for detection of HER2 expression/amplification. The aim of this study is to present the challenges encountered by pathologists in evaluation of HER-2 expression in gastric cancer.
Methods: In 90 consecutive gastro-oesophageal adenocarcinomas, HER2 immunophenotype was checked with the polyclonal antibody c-ErbB-2 (HER2) from Dako (dilution 1:800). To test the tumour heterogeneity, three different slides were stained for each case, two from tumour core, and one from invasion front. Fluorescence in situ hybridization (FISH) was done in cases with equivocal results.
Results: In 6 of the seven cases with HER2 3+ expression, the three sections showed diffuse positivity, in both core and front. One of the cases revealed 2+ equivocal result in the front, with further HER2 amplification. In 5 cases equivocal HER2 (2+) was seen in tumour tissue sampled from tumour core. Three out of the five cases presented low HER-2 (1+) in the front and no FISH amplification. After examination of the 10 cases with low HER2 (1+) in both core and front, no differences were observed between the two tumoral areas. One of the cases was amplified. The other 68 cases did not express HER2 and were predominantly dedifferentiated.
Conclusion: HER2 heterogeneity should be checked in the tumour core, using at least two full slides per case, especially for tumours that show equivocal results (2+). Further data needs to elucidate the prognostic or therapeutic impact of low HER2 in gastric cancer.
This research was funded by George Emil Palade University of Medicine, Pharmacy, Science and Technology, Targu Mures, Romania - grant number 10127/13/17.12.2020.

PS-17-012
IL-17-positive cells in gastric cancer
M. Hadzhi*, P. Petkova, K. Dinkova, M. Gulubova
*Dept. General and clinical pathology, Trakia University, Medical Faculty, Bulgaria

Background & objectives: Gastric cancer is one of the most common cancers. IL-17 is produced by Th17 cells but also by innate T-cell subsets such as T regulatory cells, CD8 T cells, NK T cells, γδ T-cells, NK cells, neutrophils and eosinophils.
Methods: The study includes 32 operated gastric cancer patients. We used immunohistochemistry with antibodies against IL-17, chromogranin A and tryptase, and combined staining with toluidine blue and IL-17.
Results: The IL-17-positive immune cells has been counted in the invasive front (IF), tumour stroma (TS), and in tertiary lymphoid structures (TLS). MCs-positive for IL-17, tryptase and toluidine blue are detected. IL-17-positive endocrine cells (EC) have been observed in antral, corpus mucosa and in some tumour cells.
Conclusion: We demonstrate that the IL-17 tumour-promoting cytokine is secreted not only by innate immune cells and mast cells but also by IL-17+ ECs. New investigation are necessary to determine the precise mechanisms of IL-17 production and the connection of Th17 cells, MCs and ECs in gastric cancer development.

PS-17-013
Ki67 is a good prognosis marker in colorectal carcinoma
S. Hidouri*, M. Walha, D. Jamai, S. Aloulou, A. Khabir, K. Bel Hadj Ali, M. Hamdani
*Department of Pathology, Habib Bourguiba University Hospital, Medenine, Tunisia

Background & objectives: Colorectal cancer (CRC) with same stage has different behaviour. Using a score based on staining intensity and frequency, we analysed the prognostic value of ki67-expression in Tunisian CRC and we addressed its expression relation with patient survival and clinicopathological factors.
Methods: One hundred CRC-patient were enrolled in this study collected from the pathology department of Medenine during six years. The immuno-histo-chemistry study was performed with pre-diluted antibodies on multi-tissue blocks prepared from well-targeted donor blocks. For statistical reasons, Ki67 expression was sub-grouped into four groups referring to the Allred score as used in breast carcinoma. The data was analysed on SPSS-software.
Results: The proliferative index was more than 75% in 40% of cases. Allred score was between 5 and 8 in 70 cases. Ki67'over-expression was more frequent in case of absence or low percentage of metastatic lymph-node and in case of stage I and II with respective p 0.028 and 0.01. It was more observed in the presence of a minority poor prognosis component with a $p = 0.05$. An inverse significant correlation was observed in the presence of venous (p=0.02) and lymphatic (p=0.02) vascular invasion and with the abundance of stroma lymphocyte infiltrate (p=0.01). Overall survival at 5 years was better in patients with Ki67score ≤ 4, without statistically significant differences.
Conclusion: Tumours with same stage are heterogeneous if measured by proliferative index. Intra-tumoral LI has not been reported in series studying Ki67 expression in CCR. We report for the first time a significant and inverse correlation with the abundance of the LI. Explaining their better prognosis, tumour cells with high proliferative activity are more sensitive to chemo-radiotherapy and they cause an imbalance between "proapoptotic" and "anti-apoptotic" signals.

PS-17-014
Cyclin D1 is a good prognostic biomarker in colorectal carcinoma
S. Hidouri*, M. Walha, D. Jamai, S. Aloulou, K. Bel Hadj Ali, A. Khabir, M. Hamdani
*Department of Pathology, Habib Bourguiba University Hospital, Medenine, Tunisia

Background & objectives: Colorectal cancer (CRC) with same stage has different behaviour. We analysed the prognostic value of Cyclin D1-expression in CRC Tunisian-patients. Using a score based on staining intensity and frequency, we addressed Cyclin D1 expression relation with patient-survival and clinicopathological factors.
Methods: One hundred patients with CRC were enrolled in this study collected from the pathology department of Medenine during 6 years. The immunohistochemistry study was performed with pre-diluted antibodies on multi-tissue blocks prepared from well-targeted donor blocks. For statistical reasons, the expression of Cyclin D1 was dichotomized into "negative" or "positive". The data was analysed on SPSS software.
Results: Cyclin D1 was positive in 42 cases. pT1-pT2 tumours had a clear tendency to express Cyclin D1($p = 0.090$). For lymph nodes, two inverse significant correlations were found with lymph-node stage (p=0.02) and with the percentage of metastatic lymph node (p=0.008). Two additional significant negative correlations were observed with

distant metastasis and tumour stage with respectively p value 0.005 and 0.007. There was an inverse correlation with vascular invasion (0.052), perineural invasion (0.01) and carcinomatous lymphangitis (0.053). Positive Cyclin D1'tumours were associated with better patient survival at 5 years (p=0.03).
Conclusion: The prognosis value of Cyclin D1 labelling was subject of discussion in CCR. Our results did not match with data based; we did not find a lot of series like us. Some authors explained these results by the fact that cyclin D1 induces apoptosis in tumour cells and therefore has a suppressive effect on tumour growth.

PS-17-015
Oesophageal adenocarcinoma heterogeneity in clinicopathology and prognosis: a single-centre longitudinal cohort study of 146 patients over a 20-year period
Q. Huang*, E. Lew, Y. Cheng, S. Shinagare, V. Deshpande, D. Wiener, J. Gold, H. Weber
*Beth Israel Deaconess Medical CTR, USA

Background & objectives: Recent clinical and genomic studies suggest that oesophageal adenocarcinoma (EAC) is heterogeneous and can be divided into true (tEAC) and probable (pEAC) groups. We investigated and compared clinicopathologic and prognostic features between those two groups of EAC patients.
Methods: We identified 146 consecutive EAC patients treated at our centre over a 20-year period. Tumours with epicentres 2 cm beyond the gastroesophageal junction (GEJ) were assigned to the tEAC group (N=63), while tumour epicentres within 2 cm, but not crossing the GEJ were allocated to the pEAC group (N=83). Clinicopathologic and prognostic features were compared between the two groups.
Results: All patients were elderly male (median age: 70 years) and over 98.6% were White. No significant difference between the two groups was found in gastroesophageal reflux disease, obesity (BMI 27.8), comorbidities, and being diagnosed during endoscopic surveillance. However, compared to pEAC patients, tEAC patients had a lower frequency of cases with no known history of Barrett's oesophagus (p=0.053) but a higher prevalence of hiatal hernia (p=0.003), smaller tumour size (p=0.007), higher prevalence of common adenocarcinoma histology (p=0.001), early stage disease (p=0.012), and better 5-year overall survival (34.9 months versus 16.8 months in pEACs) (p= 0.043).
Conclusion: Determining tumour epicentre location, using clinical, radiologic, endoscopic, surgical, and pathologic studies, demonstrates that tEAC patients had a higher prevalence of hiatal hernia, history of Barrett's oesophagus, smaller tumour size, common adenocarcinoma type, early-stage disease, and better outcomes, compared to pEAC patients. Precise sub-classification of EAC patients based on tumour epicentre location allows the distinction of these two groups of EAC patients with different clinicopathologic and prognostic characteristics, which may help improve clinical management and translational research strategies.

PS-17-016
Lymphovascular invasion in ESD specimens and its clinical significance
J.M. Kim*, J.H. Sohn, M. Cho, The Gastrointestinal Pathology Study Group of Korean Society of Pathologist
*Inha University Hospital, Republic of Korea

Background & objectives: The authors investigated the frequency and significance of LVI in ESD specimens and tried to identify the clinicopathologic factors predicting LVI prior to the ESD.
Methods: Total number of cases was 737 ESD specimens from 712 patients. The clinicopathologic factors analysed were age, gender, tumour location, tumour size, ulcer, differentiation, and depth of invasion.
Results: LVI was observed in 32 cases (4.3%). The age, tumour size, differentiation, depth of invasion were correlated with LVI (p<0.04). The groups ≤2cm vs >2cm showed different risk of LVI (p=0.02), but groups ≤3cm vs >3cm did not (p=0.151). The incidence of LVI in LP, MM, SM1 and SM2 cancers were 0.3% (1/368), 1.2% (3/250), 20.0% (13/65), and 27.8% (15/54), respectively. Confidence interval was more acceptable in LP-MM-SM1 group vs SM2 group rather than LP-MM group vs SM1-SM2 group. The cases satisfying absolute or extended indication, LVI was observed in 1 (0.2%), and 12 (5.6%) cases, respectively. After surgery, lymph node metastases were identified in 2 cases (4.2%, 2/48).
Conclusion: This study will be useful to plan the treatment policy of gastric cancer patient who will undergo the ESD.

PS-17-017
Tyrosine 42-phosphorylated RhoA expression is associated with aggressive behaviour in gastric cancer
J. Kim*, J. Jung, J. Park
*Department of Pathology, Kangnam Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Republic of Korea

Background & objectives: Wnt/β-catenin signalling pathway is commonly activated in gastric cancer. Tyrosine42-phosphorylated (p-Tyr42) RhoA induced by radical oxygen and Wnt3A is bound to β-catenin and transported into nucleus. We investigated the p-Tyr42 RhoA expression in gastric cancer and assessed its clinicopathological significance.
Methods: Expression of p-Tyr42 RhoA was examined using immunohistochemical staining on tissue microarrays consisting of 312 gastric cancer cases. Immunohistochemical expression was evaluated by two pathologists and used to compare clinicopathologic parameters and patients' prognostic outcomes.
Results: Cancer cells frequently showed high p-Tyr42 RhoA expression than normal gastric cells (p<0.001). High p-Tyr42 RhoA expression was associated with advanced gastric cancer (p<0.001), high grade (p<0.001), diffuse type (p<0.001), large tumour size (≥5 cm, p=0.035), lymph node metastasis (p=0.005), and high stage (p=0.035). Poorly differentiated tumours of intestinal-type had a tendency of high p-Tyr42 RhoA expression (p=0.048). In survival analysis, patients with high expression displayed shorter disease-free survival (DFS) time than those with low expression (p=0.014). In intestinal-type cancer, patients with high p-Tyr42 RhoA expression had significantly worse DFS than those with low expression (p=0.019), however in diffuse-type cancer the expression did not relate to DFS (p=0.708).
Conclusion: These findings suggest that p-Tyr42 RhoA is associated with aggressive biologic behaviour. P-Tyr42 PhoA may have value as a prognostic marker and a potential target molecule for gastric cancer treatment.

PS-17-018
Autoimmune gastritis: is it really rare to see incomplete intestinal metaplasia?
K. Kolçak*, G. Menetlioğlu, Ç. Ataizi Çelikel
*Marmara University Pendik Hospital, Turkey

Background & objectives: Recently it has been postulated that gastric adenocarcinoma (GACa) risk in autoimmune gastritis (AIG) is likely to be H. Pylori (HP)-related. Besides, the presence of incomplete intestinal metaplasia (IM) is controversial in HP (-) AIG. This study examines IM, atrophy and dysplasia in HP(-) AIGs.
Methods: Between 2012 and 2022, gastric endoscopic biopsies with AIG were retrospectively collected and re-evaluated. Among 89 clinically verified cases, just 43 antiparietal antibody positive and HP(-) AIG cases were included in the study. Histopathological evaluation focused on the degree of inflammation, atrophy, and IM in accordance with Sydney

System. The type of IM, presence of spasmolytic polypeptide-expressing metaplasia (SPEM) and dysplasia were also recorded.
Results: Atrophy was observed in 41 (95%) of the oxyntic mucosa samples; 7 mild (16.3%), 20 moderate (46.5%) and 14 severe (32.5%). IM and SPEM were detected in 30 (69%) and 5 (11%) cases, respectively. The presence of incomplete IM was found to be significantly low compared to complete intestinal metaplasia (n=12 vs n=27). Among cases with incomplete IM, it was focal and seen in addition to severe complete IM in 8 cases (66.6%). A statistically significant relationship was found between the degree of atrophy and the presence of incomplete IM (p=0.01). No dysplasia was detected in any of the cases.
Conclusion: Our study revealed that despite the presence of widespread atrophy in HP(-)AIG cases, incomplete IM was observed at lower rates. Considering the association of incomplete IM with GACa in previous publications, our study suggests that the low risk of GACa in HP(-)AIG can be explained by the low prevalence of incomplete IM. On the other hand, it may show that gastric atrophy may not be the main determinant of gastric carcinogenesis in these cases. In conclusion, the follow-up of HP(-)AIG patients may deserve a different approach.

PS-17-019
mRNAs, lncRNAs and circRNAs as prognostic biomarkers in stage II colon cancer
U. Korsgaard*, J. Luis Garcia Rodriguez, J. Kjems, H. Hager, L. Sommer Kristensen
*Department of Pathology, Lillebaelt Hospital, University Hospital of Southern Denmark, Denmark

Background & objectives: Treatment of stage II colon cancer is a clinical dilemma and despite treatment, a considerable number suffer from recurrence of disease. We aim to determine differentially expressed mRNAs, lncRNAs and circRNAs that can predict prognosis of stage II colon cancer.
Methods: We performed total RNA sequencing on fresh frozen tissue from a cohort containing 59 patients. DESeq2 was used to detect differentially expressed mRNAs, lncRNAs and circRNAs between stage II colon cancer patients with and without recurrence. Receiver operating characteristics (ROC) analysis was used to determine the biomarker potential of individual RNAs in stage II colon cancer.
Results: In the cohort, 29 patients suffered from stage II colon cancer and 11 of these had recurrence of disease. Using total RNA sequencing, we found 135 differentially expressed mRNAs, 77 differentially expressed lncRNAs and 4 differentially expressed circRNAs between stage II colon cancers with and without recurrence (p-adjusted < 0.05). For mRNA, ROC-analysis showed that PPP1R12A, MRLP30 and UBX2NA had an area under the curve (AUC) of 0.95, 0.93 and 0.92, respectively. For lncRNAs, ROC-analysis showed that HSD17B1-AS1, LOC100129931 and AFAP1-AS1 had an AUC of 0.91, 0.91 and 0.894, respectively. For circRNAs, ROC-analysis showed that circ_SRPK1, circ_MVP and circ_CCDC9 had an AUC of 0.88, 0.83 and 0.82, respectively.
Conclusion: In this study, we found multiple promising and previously undescribed potential prognostic biomarkers in colon cancer. Our data suggest that mRNAs, lncRNAs and circRNAs can be used to distinguish patients with high risk of recurrence in stage II colon cancer, and thus improve decision making when selecting patients that should receive adjuvant chemotherapy. However, further validation is needed to support our findings.
The work was supported by the Region of Southern Denmark and the Research Council of Lillebælt Hospital.

PS-17-020
Childhood florid reactive lymphoid follicular hyperplasia: a potential diagnostic pitfall of a rare disease
D. Laguna*, M.A. Martínez, C. González, C. Calvo, O. Moya, I. Amengual
*Hospital Universitari Son Espases, Spain

Background & objectives: Childhood florid reactive lymphoid follicular hyperplasia (CFRLFH) is a benign lymphoid proliferation that could be mistakenly diagnosed as a lymphoproliferative disorder. The aim of this study is to review the cases in our institution and to make a comparative analysis.
Methods: All the cases diagnosed as CFRLFH in the last 15 years at our institution were selected by database consultation of our informatic program. Furtherly, sex and age, as well as clinical presentation and development, location, endoscopic imaging data, histopathology, immunohistochemical profile and IgH rearrangement results were noted.
Results: A total of 4 cases of CFRLFH were finally recovered: two of them in appendix and the other two in rectum. All 4 cases showed histologically a B-type follicular hyperplasia with large and irregular germinal centre formation, located in submucosa with focal affectation of mucosa, positive for CD20, CD10 and bcl-6 and negative for bcl-2. All cases displayed Lambda light chain restriction (by immunohistochemistry and in situ hybridization); nonetheless, the molecular rearrangement of IgH showed policlonality. The age ranged between 4 and 6 years, with male predominance (3:1). Endoscopically, it was found one case with concomitant oxyurasis.
Conclusion: CFRLFH is a rare disease with unknown aetiology, and histologically may be confused with malignant lymphoid processes such as paediatric-type follicular lymphoma (amongst others). Light chain restriction is not necessarily linked to monoclonality and may lead to misdiagnosis. Therefore, an appropriate clinical context is needed for the correct diagnosis: paediatric patients with consistent clinical, histological and immunohistochemical findings, as well as an indolent development.

PS-17-022
Epigenetic regulation of CDX2 in colorectal cancer cell motility and tumour budding
R. Mehmeti*, N. Bodmer, M.P. Tschan, I. Zlobec
*Institute of Tissue Medicine and Pathology, University of Bern, Switzerland

Background & objectives: CDX2 expression in colorectal cancer (CRC) predicts patient outcome and is often lost in tumour cell dissemination and budding. We examine potential inhibitory effects of histone deacetylase (HDAC) family members on CDX2 expression, cell migration, epithelial-mesenchymal transition (EMT) and budding.
Methods: Pharmacological and genetic inhibition of HDACs was applied to CDX2 negative CRC cells. We used CRISPR technology to knock out CDX2 in CDX2 positive CRC cell lines. These cells were evaluated using transwell migration and *in ovo* assays. Using multiplex immunofluorescence (mIF) we determined CDX2, HDAC and EMT marker expression in primary CRC patient samples.
Results: Our HDAC pharmacological inhibitory screen identified UFO10, an HDAC class I and IIb inhibitor, as a dose dependent CDX2 activator. Using RNAi to validate CDX2 activation revealed HDAC 2,6, and 8 as potential CDX2 repressors. These cell lines and CDX2 knockout CRC cell lines showed decreased or increased cell migration, respectively. The chick embryo chorioallantoic membrane (CAM) *in ovo* assay showed increased invasiveness and tumour budding in CDX2 knockout compared to control cells. mIF analysis showed significantly lower CDX2 and EMT marker levels associated with aberrant HDAC class I/IIb expression in tumour buds compared to nearest primary tumour regions in primary CRC patient samples.
Conclusion: Our study highlights CDX2's critical role in CRC progression and metastasis. We identified HDAC 2, 8 (class I), and 6 (class IIb) as CDX2 repressors. Low CDX2 expression increases CRC cell migration as well as tumour cell dissemination and is associated with tumour budding and EMT in primary CRC patients. Our findings

suggest particular HDAC inhibitors as a promising therapeutic target for CRC management by reactivating CDX2 tumour suppressor expression to counteract metastasis.
Funding: 1. Swiss Government Excellence Scholarship: https://www.sbfi.admin.ch/sbfi/en/home/education/scholarships-and-grants/swiss-government-excellence-scholarships.html
2. Swiss National Science Foundation: https://www.snf.ch/en

PS-17-023
Gastric dysplasia: clinicopathologic features and mucosal characteristics according to morphologic subtypes
G. Menetlioğlu*, K. Kolçak, Ç. Ataizi Çelikel
*Marmara University, Departmant of Pathology, Turkey

Background & objectives: Gastric dysplasia (GD) can be morphologically categorized as adenomatous dysplasia (AD), foveolar dysplasia (FD), hybrid dysplasia (HD), basal crypt dysplasia (BCD), and serrated dysplasia (SD). This study investigates GD subtypes in terms of clinicopathological features and background mucosal characteristics.
Methods: A total of 63 endoscopic biopsies and 65 resection specimens diagnosed as GD between 2018-2023 were retrieved from pathology archives and re-evaluated. GD cases were subtyped (AD, FD, HD, BCD, SD) and degree of dysplasia (low and high grade) was noted. Site of dysplasia, type of gastritis, presence of H Pylori (HP), and intestinal metaplasia (IM) status were assessed.
Results: Cases were grouped as AD (64.84%), FD (17.96%), BCD (10.15%), and HD (7.05%). No significant difference was found between groups in terms of demographic data. Most common site was antrum in AD (57.62%), FD (60.86%), and HD (62.5%), while 55.8% of BCD was located in corpus/fundus. There was no difference between AD and FD in respect to the background mucosa (type of gastritis, presence of HP and IM). Although chronic gastritis (-/+IM) was detected in most AD and FD cases, BCD and HD were associated with multifocal atrophic gastritis and chronic atrophic gastritis, respectively. AD, FD, and BCD had similar rates of complete/incomplete IM, while IM was rare in HD.
Conclusion: Our study revealed no significant difference between AD and FD. Among GD subtypes HD showed distinct background mucosal characteristics, suggesting that it may develop along a different neoplastic pathway. Contrary to the literature, BCD was not rare in our study. Our observation of BCD in the proximal stomach in the background of multifocal atrophic gastritis may implicate a difference in its pathogenesis. This study contributes to a better understanding of GD subtypes and emphasizes the need for more detailed research.

PS-17-024
Digitopathological evaluation of gastroenteropancreatic neuroendocrine tumours
T. Micsik*, L. Csellar, A. Jakab, V. Jonas, B. Molnar
*Department of Pathology and Experimental Cancer Research, Hungary

Background & objectives: Gastro-Entero-Pancreatic NeuroEndocrine Tumours (GEPNETs) have a grading (Grade1 to Grade3) system relying on mitotic (MI) and proliferation indices (PI) defined by WHO. Manual counting is quite laborious, thus we aimed to use a digital pathology approach in grading GEPNETs.
Methods: We scanned 60 GEPNET cases from the archive of the Department of Pathology and Experimental Cancer Research (Semmelweis University, Budapest) with 3DHistech`s (Budapest, Hungary) digital platform and defined exact PIs with manual (MarkerCounter-MC) and automatic (NuclearQuant-NQ) counting on Ki67-stained immunoslides. Tumour-recognition application (PatternQuant-PQ) was applied for fully automated PI-assessment and detailed cellular morphometrical analysis (cell size, perimeter, shape-factor) was also performed.
Results: We found excellent correlations between the PIs, defined by either method. Clinical-PI: defined by the pathologist with visual estimation on glass-slides; MarkerCounter-PI: manually counted on digital slides; NuclearQuant-PI: automatically assessed PI with NuclearQuant on automatically selected tumourous regions by PatternQuant. Correlations: Clinical vs. MarkerCounter =0,897, Clinical vs. PatternQuant =0,913, MarkerCounter vs. PatternQuant =0,963. Furthermore, we found significant differences in the cellular parameters of the various grades of GEPNETs defined by either method (Clinical, MarkerCounter, PatternQuant). The averages and standard deviations of the tumour cell-areas, tumour cell-perimeters and shape factors of the tumour cells significantly differed in more aspects in relation G1/G2, and in all aspects of G1/G3, and G2/G3 groups.
Conclusion: Grading GEPNETs is a laborious work following WHO-guidelines of cell-counting. An exact manual-PI counting on digitized slides is very reliable, but also laborious. Our results showed that manual counting can be replaced by automatic tumour recognition and proliferation index counting, significantly decreasing time and workload and delivering robust data. Furthermore, detailed cellular morphometrical analysis can further increase our accuracy in grading of GEPNETs. Altogether, digital pathological evaluation of GEPNETs is a reliable and robust alternative to ease our everyday routine.

PS-17-025
A tertiary centre experience of reporting extramural vascular invasion in rectal cancers: pathology reporting frequencies and correlations with radiology
A. Mukherjee*, C. Clarke, C. Santos
*University of Nottingham BDI3, University Park, United Kingdom

Background & objectives: Extramural vascular invasion (EMVI), a known prognostic marker in colorectal cancer (CRC), remains underreported histologically. Radiological techniques, especially MRI, diagnose EMVI quite accurately. This study aimed to explore reporting frequencies and histopathology versus radiology correlations for EMVI in rectal adenocarcinomas.
Methods: Rectal adenocarcinoma patients' records at a tertiary institution were interrogated over a five-year span for EMVI status on histopathology and MRI reports. A direct comparison of these investigative modalities was performed, and discrepancies noted. Neo-adjuvant treatment status was noted for confounding effects. Resections from acute presentations with unavailable radiology were excluded from analyses.
Results: Of 107 cases, 83 (~78%) were matched for EMVI status per both modalities [67 negative; 16 positive]. 32 cases (~30%) were positive for EMVI on pathology; 24 cases (~22%) were positive on radiology. 16 cases (~15%), negative on radiology, were positive on histology. In 3 such, pathology matched pre-chemotherapy rather than pre-operative EMVI on MRI; and 2 cases recorded tumour deposits on MRI but not EMVI. 8 cases (~7.5%), reported positive/probable on imaging, were reported negative by pathology. In 1, the MRI report was downgraded to negative on review. Confounding fibrosis (1), movement artefact (1) on radiology, and fibrosis (1) /tumour deposit (1) on pathology, was noted in discrepant reports.
Conclusion: Histopathology reporting frequency for EMVI in this series of rectal cancers achieved the standards recommended by the Royal College of Pathologists' minimum dataset. Strong correlations were observed with radiology detected EMVI status. Comparison across modalities could further fine-tune holistic service provision. Particularly, node negative cancers with EMVI positivity on radiology, but negative on histology, could be investigated further with special stains. Time lapse between the modalities, history of neo-adjuvant treatment and fibrosis may be confounding factors causing discrepancies.

Funding: Innovate UK and Bowel Research UK

PS-17-026

Alterations in p53, microsatellite stability and lack of MUC5AC expression as molecular features of colorectal carcinoma associated with inflammatory bowel disease

E. Musulen*, M. Gené Hijós, M. Cuatrecasas, I. Amat, J.A. Veiga, M.J. Fernández Aceñero, V. Fusté Chimisana, J. Tarragona, I. Jurado, R. Fernández-Victoria, C. Martinez Ciarpaglini, C. Alenda González, C. Zac, P. Ortega de la Obra, M.T. Fernández-Figueras
*Pathology Department, Hospital Universitari General de Catalunya-Grupo Quirónsalud, Sant Cugat del Vallès, Barcelona; Institut de Recerca contra la Leucèmia Josep Carreras, Badalona, Barcelona, Spain

Background & objectives: Colitis-associated colorectal carcinoma(CAC) occurs in inflammatory bowel disease(IBD) as a result of the "chronic inflammation-dysplasia-cancer" carcinogenesis. Gastric metaplasia (GM) has been described as the initial event of serrated colorectal cancer(CRC) process. The objective is to characterize CAC to explore GM.
Methods: A total of 57 CAC were studied from 38 (72%) men and 15 (28%) women, aged between 34 and 90 years (mean 62.6), 34 (64%) with UC and 19 (36%) with CD from a series of 53 IBD colectomies with CAC from 14 hospitals. Immunohistochemistry was performed to assess p53 alterations, MSI, and MUC5AC expression as a surrogate for GM.
Results: The p53 mut-pattern was found in more than half of the CAC, most frequently stable (MSS) and MUC5AC negative. Only 6 tumours were unstable (MSI-H), with p53 wt-pattern (p=0.010) and MUC5AC positive (p=0.005). MUC5AC staining was more frequently observed in intestinal mucosa, inflamed or with chronic changes, than in CAC, especially in those with p53 wt-pattern and MSS.
Conclusion: Based on our results we hypothesize that, as in the serrated pathway of CRC, in IBD GM occurs in inflamed mucosa, persists in those with chronic changes and disappears with the acquisition of p53 mutations. We cannot rule out that the group of MSI-H CRC that appear in IBD, with characteristics similar to MSI-H sporadic tumours with MLH1 hypermethylation, are nothing more than serrated pathway CRC that appear in a context of continuous colon injury.
This research was funded by Roche through a collaboration agreement for research in the area of Oncology (activity code: SP210830002).

PS-17-027

Developing a revised, prognostically significant morphological classification system for gastro-oesophageal adenocarcinoma (EAC)

S. N Kalimuthu*, J. Cotton, R. Zyla, F. Allison, Y. Bach, J. Allen, G. Darling, E. Elimova, G. Wilson, J. Yeung
*University Health Network, Toronto, Canada

Background & objectives: Oesophageal adenocarcinoma (EAC) has a poor prognosis. Methods for stratifying patients into prognostic/treatment-responsive groups are lacking. Presently, the significance of morphological heterogeneity in these tumours is not understood. We aim to develop a prognostically significant morphological classification for EAC.
Methods: All tumour slides were reviewed from 106 patients who underwent resection from 2008 to present. Tumour morphology was quantified by calculating percentage of each pattern per slide and summed across all case slides to determine overall percentage of each morphology. We categorized cases as neoadjuvant-treated or untreated resection specimens and collected survival data for each surgical resection case.
Results: In this study, 70 patients (58 male, 12 female; mean age = 59.26 +/- 11.12 years) received neoadjuvant therapy before resection, while 36 patients (29 male, 7 female; age = 66.36 years +/- 11.85 years) did not receive any treatment. Treated cases had a higher average number of slides reviewed (10.13 +/- 7.43 slides) than untreated cases (9.14 +/- 8.57 slides). In untreated cases, 33% (12/36) showed three [WG1]or more morphologies comprising over 10% of the tumour area compared to 24.2% (16/70) of treated cases. Subgroup analysis revealed cords, single files, and neuroendocrine-like morphologies are present in higher frequency in neoadjuvant treatment-resistant cases and associated with poorer prognosis.
Conclusion: In this study, we have identified new morphological patterns of EAC associated with poor prognosis. This is a first of a kind study focused on identifying new prognostically significant morphological patterns of EAC. We are currently exploring clinical correlations and molecular underpinnings of these different morphological patterns. In addition, we are developing a deep learning pipeline to aid in morphological identification. Our overall goal is to develop a clinically relevant classification system that identifies therapeutic vulnerabilities.

PS-17-028

Analysis of tertiary lymphoid structures (TLSs) in microsatellite stable colorectal cancer (MSS-CRC)

B. Palomar De Lucas*, M. García, N. Tarazona, J. González, M. Huerta, D. Moro, A. Cervantes, C. Martinez-Ciarpaglini
*Incliva, Biomedical Research Institute, Hospital Clínico Universitario de Valencia, Spain

Background & objectives: TLSs have been demonstrated as a promotor of efficacious immune response in solid tumours. We aim to explore the content of TLSs in a series of MSS-CRC and its relationship with the consensus molecular subtype (CMS) and the microenvironment composition.
Methods: We retrospectively evaluated a series of 102 surgically resected colorectal cancer cases. The TLSs content and type were evaluated on HE whole tissue sections. A 96 custom gene panel for nCounter assay was used to classify colon cancer into CMS subtypes. Whole tissue sections were immunostained and scanned for CD3, CD4, CD8, CD163, FOXP3 and PD-L1 evaluation.
Results: We found the CMS4 to have a lower content of TLSs compared to the CMS2/3 subtypes (p=0.042). Tumours showing secondary follicles were associated with low tumour budding grade (p=0.015) and were more frequent in the right colon (p=0.050). The presence of TLSs was associated with a higher concentration of CD3, CD4 and CD8 cells in the tumour front (p=0.031, 0.013, 0.049 respectively) and decreased levels of CD163 positive macrophages (p=0.045). FOXP3 and PD-L1 expressions were not significantly correlated to TLSs content.
Conclusion: Our study suggests that TLSs may potentially help to recognize a subset of MSS-CRC associated with active antitumoral immune response and less aggressive features
Funding: Project PI21/00695 financed by ISCIII and co-financed by FEDER funds

PS-17-029

Features of PDX-1 expression in gastric neuroendocrine tumours, neuroendocrine carcinomas and carcinomas

V. Pechnikova*, L. Mikhaleva, L. Gurevich, O. Vasyukova, A. Birukov, K. Midiber, R. Vandysheva, N. Shakhpazyan, Z. Gioeva, A. Konyukova, L. Kakturskiy
*Avtsyn Research Institute of Human Morphology of Federal State Budgetary Scientific Institution "Petrovsky National Research Centre of Surgery", Russia

Background & objectives: The research aimed at studying the PDX-1 expression features in gastric neuroendocrine tumours (NETs), neuroendocrine carcinomas (NECs) and gastric carcinomas (GC).
Methods: The study included 78 patients with 89 solitary and multiple NETs G1-G3, NECs. Comparison group included 31 GCs including 13 signet-ring cell carcinomas. We used PDX-1 (1:100, EP139) and Ki-67 antibodies. Positive PDX-1 reaction showed nuclear staining in most

tumour cells. Ki-67 index was counted for 500-1000 tumour cells in hot spots, median % of Ki-67 index is presented.
Results: Average age was 54.7±12.6 years (median 55), 55 females, average tumour size – 3.16 cm (0.2-18 cm). 37/89 neoplasms located in the stomach body, 12 – in cardia, 11 – in antrum. In 29 cases the region was not specified. 79 cases were NETs G1-G3 (G1:G2:G3 – 51:24:4), 10 – NECs. Median Ki67 was for NETs G1 – 1.2%, G2 – 7%, G3 – 18; for NECs – 50%. PDX-1 was positive in 36/79 NETs: 27/51 G1, 6/24 G2, 3/4 G3. 7/10 NECs were PDX-1-positive. PDX-1 was positive in 24/31 GCs (13/13 signet-ring). Statistically significant relationship was shown between PDX-1 expression and the NEN grade (p=0.002).
Conclusion: In our study, PDX-1 expression was most often detected in most G3 NETs, NECs and gastric cancers, especially in signet-ring cell carcinomas. Our results indicate the important role of PDX-1 in the malignant transformation of the gastric epithelium and a possible target for treatment.

PS-17-030
Colon neuropathy as a predictor of the development of diverticular disease
V. Pechnikova*, L. Mikhaleva, A. Konyukova, A. Proshchina, O. Vasyukova, K. Bolikhov, A. Shulaev, N. Gutyrchik, A. Mikhalev, S. Shapovalyants
*Avtsyn Research Institute of Human Morphology of Federal State Budgetary Scientific Institution "Petrovsky National Research Centre of Surgery", Russia

Background & objectives: Diverticular disease is one of the most common diseases of the colon, however, the predictors of a complicated course have not been formulated. The aim of our study is to determine the morphological predictors of the complicated diverticulosis
Methods: We analysed 103 consecutive cases of left-sided hemicolectomy, 15 cases were studied comprehensively. Surgical specimens were fixed in 10% neutral buffered formaline and stained by hematoxylin-eosin and immunohistochemistry with S100 and b3-tubulin antibodies. Morphometric evaluation was performed in order to assess the glial index (the ratio of glial cells to neurons) in myenteric plexus of colon.
Results: Among 15 extensively studied cases 6 patients (40.0%) had complicated diverticulosis of the colon, 5 (33.0%) presented with uncomplicated diverticulosis and 4 (27.0%) had no diverticula of the colon (comparison group). We noted an increase in the glial index in observations in patients with complicated and uncomplicated diverticular disease (8.1), in contrast to the comparison group (6,4). However, there was no significant difference comparing the uncomplicated and complicated disease.
Conclusion: The present study demonstrates that the glial index is significantly higher in patients with diverticular disease of the colon (8,1) than in the comparison group (6,4). Our results indicate that the glial index can be considered as a predictor of the development of diverticular disease, however, it is not possible to judge uncomplicated and complicated disease.

PS-17-031
Assessment of intra- and intertumoural heterogeneity of molecular biomarkers in locally advanced gastric cancer
G. Raskin*, N. Beliak, M. Mukhina, M. Kleshev, R. Orlova, S. Kutukova
*Dr. Berezin Medical Insitute, Russia

Background & objectives: Significance of intertumoral heterogeneity of biomarkers in gastric cancer are poor established. The aim of the study was to evaluate the heterogeneity of the main molecular biomarkers in the primary tumour and in metastasis to the regional lymph node.
Methods: A total of 62 patients with primary loco-regional (N+) gastric adenocarcinoma were recruited. The study included 20 women and 42 men. 44 patients had Laurén's intestinal type of cancer, 18 had a diffuse type. One block with primary tumour and one with metastasis to the regional lymph node were selected for HER2, MMR, PD-L1, FGFR2 immunohistochemistry, FISH FGFR2, CISH EBV.
Results: 10 patients (6,2%) showed overexpression of HER2/neu, and heterogeneity was detected in five cases. 4 patients showed dMMR (6,45%), in two cases heterogeneity in dMMR status was also revealed: it was presented in the primary tumour and absent in regional metastasis (pMMR). And in one case, heterogeneity in terms of dMMR was observed both in the primary tumour and in the metastasis. In 12 cases (19,6 %) marked heterogeneity in PD-L1 status between the primary tumour and its regional metastasis (1 case with dMMR heterogeneity) was also revealed. In one case FGFR2 gene amplification was detected in the primary tumour, which was "lost" in the metastasis.
Conclusion: The findings in this paper indicates that the intertumoral heterogeneity of HER2 overexpression is common in GC patients. We highly recommend at least two samples for accurate HER2 assessment. Given the rarity of status detection dMMR, a study in a larger number of patients is required, however, our data also confirm the presence of heterogeneity in dMMR status, and probably the possibility of metastasis of a more aggressive pMMR clone. Heterogeneity in PD-L1 is not rare and has practical significance.

PS-17-032
Expression and amplification of FGFR2 in gastric cancer: a comparative study
G. Raskin*, M. Mukhina, E. Kravtcova, I. Tsimafeyeu, S. Tjulandin, N. Beliak, M. Kleshev, R. Orlova
*Dr. Berezin Medical Insitute, Russia

Background & objectives: FGFR2 status in gastric cancer is an important factor in determining optimal treatment with FGFR2 inhibitors. The question remains how different assays agree on the FGFR2 status of the same patient and whether one test can be substituted by another.
Methods: Pairwise comparison of 4 tests based on the same patient population was performed: 4 IHC assays [Abcam clone EPR24075-418, R&D clone 98706, Santa Cruz clone C-8, Abcam 1G3] and one FISH test. 61 formalin-fixed, paraffin embedded samples (including 61 primary tumours and 61 metastases of same patients) were obtained and were stained with FGFR2 IHC assays.
Results: After evaluating the expression in the first 16 patients, further study was carried out only using the Abcam EPR24075-418 assay due to pronounced nuclear staining with other IHC tests. FGFR2 any level expression was detected in 26 (43%) tumours. The prevalence of FGFR2 amplification was 8% and was accompanied by 3+ expression in 4 cases, 2+ - in 1 case. Discordance between FGFR2 expression in primary tumour and lymph node metastases was revealed in 13 (21%) cases.
Conclusion: EPR24075-418 assay showed the best results among others in FGFR2 immunohistochemical evaluation: concordance with FISH was 100% in 3+ cases. Due to high FGFR2 heterogeneity in tumour, both primary tumour and metastasis must be stained by immunohistochemistry or when it is not possible more material of primary tumour should be evaluated.

PS-17-033
Evaluation of well-known and candidate tumour-agnostic biomarkers with molecular pathological alterations according to tumour localisation in colorectal carcinoma: in silico analysis
Z. Sağnak Yılmaz*, S. Demir Kececi, M.H. Toper, S. Sarioglu
*Dokuz Eylül University, The Institute of Health Sciences, Department of Molecular Pathology, Karadeniz Technical University, Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: To determine the prognostic value of tumour agnostic markers in colorectal carcinoma (CRC) cases by in silico analysis and to evaluate their distribution in anatomical sub-regions of the colon and whether there are genomic differences in rectal carcinomas.

Methods: The prognostic and agnostic biomarkers were evaluated in 3546 CRC cases (324 non-metastatic(M0) and 3222 metastatic(M1), included in the MSK-MetTropism dataset in the "cBioportal"). 1684 cases were evaluated in two groups as right and left colon, and in three groups as right, left, and rectum as well as the anatomical sub-region distribution of biomarkers.
Results: In microsatellite stable (MSS) CRC cases, ARID1A genomic alterations ($p<0.001$) in non-metastatic cases, KRAS genomic alterations ($p=0.043$), and TP53 mutations ($p=0.038$) in metastatic cases were more common. In cases of MSS metastatic CRC, tumour mutational burden(TMB) <10/Mb ($p=0.023$), copy number alterations (CNAs) ($p<0.001$)), CDKN2A genomic alterations ($p<0.001$) and MET amplifications ($p=0.047$) had a shorter overall survival. Targetable fusions were more common in the right colon and MSI, TMB-high, KRAS, and BRAF-wild-type cases. PIK3CA genomic alterations, MSI, and TMB≥10 decreased in the rectosigmoid region, while KRAS genomic alterations increased. The rectum differs from the left colon by higher frequency of KRAS genomic alterations and total amplification and less BRAF genomic alterations.
Conclusion: Our analysis is informative regarding the distribution and prognosis of fusions, CNAs, and other genomic changes in agnostic biomarkers. CNAs, CDKN2A genomic alterations, and MET amplifications have a poor prognosis, while MSS-TMB≥10/Mb cases have a better prognosis, like MSI-TMB≥10/Mb cases. Our findings are remarkable because of the possible importance of ARID1A and CDKN2A in the right colon and some differences in the left colon regarding other agnostic biomarkers, especially amplifications of the rectosigmoid region and rectum.

PS-17-034
Revisiting early gastric cancer in search of a rare entity: "gastric adenocarcinoma of fundic-gland type"
S.N. Sayir*, H.K. Kahraman, A.R. Akur, H. Berber, S. Yüksel, B. Savaş, A. Ensari
*Ankara University, Faculty of Medicine, Turkey

Background & objectives: Gastric adenocarcinoma of fundic-gland type(GA-FG) is a recently defined subtype mostly presenting with early stage and good prognosis. Its biological behaviour as early gastric cancer(EGC) encouraged us to re-examine our EGC cohort with a fresh look in search of GA-FG.
Methods: A total of 100 EGC cases were re-evaluated for gastric cancer subtypes, grade, depth of invasion, lymphovascular invasion(LVI), type of specimen, background mucosa. Presence of GA-FG pattern which is characterized by anastomosing glands lined by cells of oxyntic mucosa in the deeper parts covered with normal foveolar surface was noted. Statistical analysis was performed using Chi-Square and Mann-Whitney tests.
Results: Patient age ranged between 37-93 years and 66% were male. GA-FG pattern was detected in 35 cases 8 of which were purely GA-FG type. Majority(38) showed tubular type, followed by 12 poorly cohesive, 5 mixed, 4 papillary, 2 signet ring, 1 mucinous and 1 MiNEN. Submucosal(42%), lamina propria/muscularis mucosa invasion(36%) and insitu(22%) presentation were observed in the cohort. GA-FG cases were significantly($p=0.012$) older(77.63) than other subtypes (68.27) and most(71.4%) presented with earlier stages (Tis/T1a) compared to others ($p=0.039$). Lymph node metastasis was significantly($p=0.035$) more frequent in GA-FG(20%) compared to other group(6.2%). There was no difference between the groups for grade, LVI, dysplasia in background mucosa which was mostly atrophic with intestinal metaplasia(79%).
Conclusion: In accordance with the recent literature our results revealed that GA-FG type is associated with lower stages, therefore should be considered within the spectrum of EGC. Reviewing EGC cases would provide new insights regarding morphological features of GA-FG presenting either in pure form or as an accompanying pattern. This approach would justify endoscopic treatment as more appropriate for such patients rather than surgery. Thus, it is of paramount importance to recognize and rightfully diagnose GA-FG cases despite its relative rarity.

PS-17-035
STING: the key in dMMR colo-rectal cancer in the era of immunotherapy?
G. Scellier*, M. Bubenheim, N. Piton, F. Di Fiore, J. Sabourin
*CHU Rouen, Department of Pathology, France

Background & objectives: 30% of deficient mismatch repair (dMMR) colorectal cancer (CRC) are primary resistant to immunotherapy (ICI). We hypothesized that STING expression could be predictive of ICI response in CRC.
We aimed to compare STING expression between pMMR and dMMR CRC.
Methods: A single-centre historical cohort of CRC surgically resected between 2017 and 2021 was constituted. MMR status was assessed by both immunohistochemistry (IHC) and PCR. dMMR CRC were matched with proficient MMR CRC according to UICC 2017 stage and date of receipt of the specimen. STING IHC (D2P2F clone, Cell Signaling®) was blindly evaluated with determination of H-score on tumour cells.
Results: The cohort consisted of 96 patients with CRC (48 dMMR and 48 pMMR). STING median Hscores were 80 (Q1-Q3: 10-150) for dMMR CRC, and 10 (Q1-Q3: 0-40) for pMMR CRC ($p < 0.001$).
In our cohort, two patients with dMMR CRC were treated by immunotherapy : the first had a clinical complete response at 2 years (initially STING H-score at 80) and the second had a partial response at 1 year (initially STING H-score at 160).
We also identified a subgroup of pMMR CRC with high STING expression (H-score ≥ 80, n=10/48), which share morphological features. In this subgroup, we did not identify any POLE mutation by targeted PCR (SNaPshot™).
Conclusion: Overall, STING was overexpressed in dMMR CRC compared to pMMR CRC. However, 25% of dMMR CRC patients had a weak or null expression of STING and could represent nonresponders to ICI. Our results support our hypothesis of a major role of STING in the immune response of dMMR CRC. STING immunostaining could be a good predictive biomarker of ICI response in dMMR CRC. Clinical validation is ongoing.

PS-17-036
Comparative analysis of Granzyme B expression in refractory coeliac disease type II, untreated coeliac disease and normal duodenal mucosa
D. Skrobo*, S. Bennett, F. Murray, A. O'Donoghue, A. Hayat, V. Byrnes, C. Brodie
*Galway University Hospital, Ireland

Background & objectives: Refractory coeliac disease type II (RCDII) does not respond to a gluten-free diet. GranzymeB (GrB) is a protease known for its pro-apoptotic function. Its role in RCDII pathogenesis is unclear. We compared the GrB immunohistochemistry in 3 cohorts.
Methods: This retrospective study consisted of 3 cohorts. RCDII, untreated coeliac disease (CD) and a normal control group. N=26 patients, with 8 patients in each group. GrB expression was evaluated using immunohistochemistry (IHC) on duodenal biopsies. Morphology was evaluated on H&E and the number of positive GrB cells in the lamina propria (LP) and intraepithelial lymphocytes (IEL) were counted per/mm2.
Results: The RCD cohort bore 4-42 GrB positive IEL's/mm2 with a median of 19 per/mm2, mean 21. In the LP there were 9-101 GrB positive cells/mm2 with a median of 62, mean 60. The CD cohort bore 1-41 GrB positive IEL's/mm2 with a median of 7per/mm2, mean 14. In the LP there were 11-270 GrB positive cells/mm2 with a median of 51, mean 80. In the normal cohort there were 0-2 GrB positive IEL's/mm2 with a median of 0 per/mm2, mean 0.5. The staining pattern in RCDII and CD cohort was a dot-like cytoplasmic pattern. The staining pattern in NDM was fine-granular cytoplasmic pattern.
Conclusion: In this small hypothesis testing study we noted that there was a different staining pattern in the intraepithelial and lamina propria

lymphocyte population between RCD, untreated CD and the normal patient cohorts. A trend was observed in the RCD cohort with more GrB positive IEL's and fewer GrB positive cells in the LP.

PS-17-037

A closer look at the implications of CD68 in gastrointestinal stromal tumour behaviour

I.A. Spiridon*, A.D. Timofte, I.D. Căruntu
*"Grigore T. Popa" University of Medicine and Pharmacy Iasi, Romania; Institute of Image Guided Surgery IHU-Strasbourg, France

Background & objectives: Macrophages are integral part of the immune response, with primary phagocytosis function. Upregulation of these CD68+ cells is observed in various cancers, with impact on prognosis. Our study focuses on the involvement of intratumoral macrophages in gastrointestinal stromal tumour(GIST) behaviour.
Methods: CD68 immunohistochemical (IHC) evaluation was carried out on 44 cases of small bowel GISTs from adult patients, diagnosed based on histology and the classical panel of markers (CD117, CD34, DOG1). We analysed the spatial distribution of positive cells on WSI of GIST and correlated tissue expression with the clinicopathological factors, while also assessing the impact on survival and disease-free interval.
Results: Quantitative IHC expression of CD68 using automated cell counting software QuPath rendered a more precise evaluation of the number of positive cells/mm2 and revealed marked intratumoral heterogeneity. The distribution in tumour core versus tumour periphery was varied, with immunoreactive cells mostly observed as present in isolated or small groups (<10 cells), some with vasocentric aggregation. Intertumoural heterogeneity revealed marked differences, which correlated with mitotic activity and the presence of myxoid degeneration of the stroma ($p<0.05$). Significant correlations with other clinicopathological factors were not confirmed. However, CD68 expression was correlated with patient survival and disease-free interval ($p<0.05$), as estimated by the Kaplan-Meier method and log-rank test.
Conclusion: Our results show that CD68 positive cells display complex intratumoral spatial distribution that correlates with changes in stroma, indicating intricate interactions with the tumour microenvironment. In this context, we have demonstrated that the CD68 expression profile is also impactful on patient survival. These results can be further capitalized by including this marker into immunoscores aimed at characterizing tumour-associated response in GISTs and refining the currently existing systems used in estimating patient prognosis and survival.
This work was supported by French state funds managed within the "Plan Investissements d'Avenir" and by the ANR (reference ANR-10-IAHU-02).

PS-17-038

Analytical and clinical performance of the VENTANA CLDN18 (43-14A) RxDx Assay in gastric and gastroesophageal junction adenocarcinoma tissue samples for patient identification in two phase 3 trials of zolbetuximab

S. Stratton*, L. Pang, J. Pugh, M. Kouzova, D. Baldwin, J. McDonald, J. Buckmeier, A. Guerrero, D. Moran
*Roche Diagnostics Solutions, USA

Background & objectives: Immunohistochemical detection of tight junction protein Claudin-18 (CLDN18) using the investigational VENTANA CLDN18 (43-14A) RxDx Assay was performed in pivotal trials to help identify patients with gastric or gastroesophageal junction (G/GEJ) adenocarcinoma who may benefit from zolbetuximab, a CLDN18.2-targeted therapy.
Methods: The VENTANA CLDN18 (43-14A) RxDx Assay was designed for high sensitivity/specificity and underwent rigorous interlaboratory, instrument, day, run, and reader precision testing using formalin-fixed, paraffin-embedded, tumour specimens. A clinical cut-off of ≥75% of tumour cells with moderate-to-strong membranous CLDN18 staining was defined as CLDN18.2-positive. Over 4000 samples were analysed from the recent phase 3 SPOTLIGHT and GLOW trials of zolbetuximab.
Results: Analytical performance studies indicated within- and between-reader precision of 98.7% Overall Percent Agreement (OPA) across three readers. Between-day and within-run studies showed 100% agreement. Inter-laboratory reproducibility (3 sites) exceeded 90% in all categories, with inter-site OPA of 91.1%, inter-reader OPA of 94.8%, and overall OPA of 95.0%. Initial (first-pass) and final acceptability rates for overall staining were 94.9% and 98.7%, respectively in SPOTLIGHT. Patients with HER2-negative, locally advanced unresectable or metastatic G/GEJ adenocarcinomas, enrolled in SPOTLIGHT (NCT03504397) or GLOW (NCT03653507), with CLDN18.2-positive tumours had statistically significant prolonged progression-free survival (PFS) and overall survival (OS) when treated with zolbetuximab + chemotherapy versus placebo + chemotherapy, demonstrating clinical performance.
Conclusion: The VENTANA CLDN18 (43-14A) RxDx Assay met all analytical criteria for performance, demonstrating precision scoring of CLDN18 status in G/GEJ adenocarcinomas. The clinically significant improvements in PFS and OS in CLDN18.2-positive patients, identified by the VENTANA CLDN18 (43-14A) RxDx Assay, support the clinical utility of this assay as a companion diagnostic for reliably identifying patients who may benefit from first-line treatment with the CLDN18.2-targeted therapy zolbetuximab in combination with chemotherapy.
This study was funded by Astellas Pharma, Inc., which is the legal entity responsible for governance, coordination, and running of the study. Medical writing support was provided by George Pellegrino, MD, PhD, of Oxford PharmaGenesis Inc., Newtown, PA, USA, and was funded by Astellas Pharma, Inc.

PS-17-039

Insulinoma-associated protein 1 expression in primary neuroendocrine neoplasms of the gastrointestinal and pancreaticobiliary tracts: a study from a tertiary care hospital of Coastal India

P. Suresh*, E. Edwin, S. Rao, S. Sreeram, H. Kini, J. Kini, S. Basavaiah, V. B
*Kasturba Medical College Mangalore, Manipal Academy of Higher education, Manipal, India

Background & objectives: Neuroendocrine neoplasms (NENs) are uncommon tumours that can arise from the gastroenteropancreatic(GEP) system. Insulinoma-Associated Protein 1(INSM1) is a novel marker found in developing neuroendocrine tissues and tumours. We aimed to evaluate INSM1 expression in primary GEP-NENs.
Methods: Retrospective review (2016-2021) was used to assess clinical features and histomorphology of 70 cases of GEP-NENs. Paraffin-embedded tissue was available in 49 GEP-NENs which along with 10 other non-neuroendocrine gastrointestinal neoplasm controls were subsequently stained with INSM1, Syn, CgA and Ki-67.
Results: The patients ranged from 13-87 years of age with the majority of them over 50 years (68.5%) and most men (62.8%). The most common site for GEP-NENs was the duodenum (34.3%), followed by the rectum (20%). INSM1, CgA, and Syn expression were noted in 71.4%, 57.1%, and 87.8% of GEP-NENs respectively. INSM1 was more sensitive than CgA but less sensitive than Syn and as specific as CgA and SYN (Sensitivity – 71.4%, 57.1%, and 87.8% and specificity – 90%, 90%, and 90% of INSM1, CgA, and Syn respectively)
Conclusion: INSM1 is a promising novel marker for GEP-NENs. Compared to traditional neuroendocrine markers, INSM1 is more sensitive and as specific. In addition, we found that INSM1 showed positivity in G3 NETs as compared to CgA and Syn. Further studies on INSM1 in NENs of the entire body are recommended to validate INSM1 as a single neuroendocrine diagnostic marker.

PS-17-040

Cost effectiveness of Helicobacter Pylori testing in gastric biopsies

P. Tilekar*, K. Robertson, M. Elgoweini
*Pathology department, University Hospital Crosshouse, United Kingdom

Background & objectives: The Royal College of Pathologists guidelines do not support biopsy of normal stomach or gastritis for histological categorisation as neither is likely to change management. Here we estimate cost and efficacy of histological detection of Helicobacter pylori in our department.
Methods: An electronic search was made of our departmental database for gastric biopsies received in November 2021. Clinical information such as presenting symptoms, endoscopy findings, clinical request for histological detection of Helicobacter pylori, histopathology diagnosis, number of glass slides and paraffin blocks were collected from clinical portal and Winpath systems. The cost was calculated.
Results: Clinicians requested histological detection of H pylori in 53 (28.3%) out of 187 gastric biopsies received. 10 of these were endoscopically normal while 43 had gastritis. Histologically, Helicobacter pylori was only detected in two biopsies; one from each group. 52 cases had one paraffin block processed and one had two. 51 cases had one glass slide while two had two glass slides processed. The laboratory costs for the 53 cases were £1761.69. This included the cost of receiving, processing, embedding, cutting, staining, quality check and immuno-histochemistry. The cost of the consultants reporting time was £1176. Therefore, the total cost was £2937.69.
Conclusion: The estimated cost for a diagnostic endoscopy is £398, making the cost of detecting two cases of Helicobacter pylori infection, in our lab, for one month £24,031.69. Other, non-invasive techniques, such as faecal antigen testing or urea-breath testing, with comparable sensitivity and specificity, are likely to be cheaper and safer alternatives.

PS-17-041

Clinicopathological significance of LAG3+ immune cells in gastric cancer

D. Ulase*, H. Behrens, S. Krüger, C. Röcken
*Department of Pathology, CAU / UKSH Campus Kiel, Germany

Background & objectives: Lymphocyte activation gene 3 (LAG3) is an immune checkpoint that is linked to T-cell exhaustion within tumour microenvironment. This study analysed spatial distribution of LAG3+ immune cells in relation to clinicopathological data in a set of 441 therapy-naive gastric cancers.
Methods: LAG3 expression was evaluated in tumour centre (TC) and invasive front (IF) using immunohistochemistry and whole-slide digital image analysis using Definiens Tissue Studio. Cases were divided into LAG3-low and LAG3-high groups based on median LAG3+ cell density. Associations with clinicopathological variables were analysed using cross-tabulation analysis and Kendall's tau test for ordinal variables or Fischer's exact test for non-ordinal variables.
Results: Median density of LAG3+ cells differed significantly between both compartments ($p<0.001$): 55.15 cells/mm2 in TC (range 3.57–1687.63) vs. 70.35 cells/mm2 in IF (1.91–1858.35). Patients with high LAG3 expression at IF were more likely males (56.3% vs. 39.6% females, $p=0.002$) with proximally located tumours (58.5% vs. 46.2% distal, $p=0.025$). LAG3+ cell density at both compartments correlated with Lauren phenotype ($p=0.001$, TC; $p<0.0001$, IF) and was inversely associated with tumour budding ($p=0.004$, TC; $p<0.0001$, IF). Higher LAG3 expression correlated with EBV-positive ($p<0.0001$, both compartments) and microsatellite instable ($p=0.003$, TC; $p=0.005$, IF) cancers. Tumours with lower LAG3+ cell infiltration in TC tended to have advanced pT ($p=0.075$) and pN ($p=0.079$) categories.
Conclusion: Our findings demonstrate differences in tumour microenvironment of the main histological and molecular subtypes of gastric cancer. Inverse relationship between LAG3+ cell density and tumour microinvasion (as demonstrated by budding) suggests that LAG3 expression could rather be a sign of crosstalk between cancer and immune cells than a sign of exhausted, dysfunctional T cells. Our results support the need for extended analysis of both LAG3 and microenvironment of IF, as it appears to be more active compartment in gastric cancer.

PS-17-042

Biological background of colorectal polyps and carcinomas with heterotopic ossification

A. Vos*, L. Pijnenborg, S. van Lent-van Vliet, L. Kodach, F. Ciompi, C.S. van der Post, F. Simmer, I. Nagtegaal
*Radboud University Medical Center, Nijmegen, The Netherlands

Background & objectives: The molecular and cell biological mechanisms and the prognostic impact of heterotopic ossification in neoplasms is not fully understood. This study will generate insight into the potential pathway by which heterotopic ossification develops in colorectal neoplasms.
Methods: Via the Dutch nationwide Pathology databank 77 cases were collected. A literature search yielded an additional 96 case reports. Clinicopathological characteristics and several histological traits were scored for all these cases. To investigate the involvement of the TGFβ/BMP pathway, our cases were stained immunohistochemically for BMP2, SMAD4, and Osterix. Using an artificial intelligence algorithm, the tumour-stroma ratio was determined.
Results: The polyps consisted mainly of juvenile polyps (25%), tubulovillous adenomas (25%), and traditional serrated adenomas (25%). The carcinomas comprised mostly conventional (62.9%) and mucinous adenocarcinomas (32.3%), with a few serrated adenocarcinomas (4.8%). Many of the neoplasms showed fibrosis, both surrounding bone as in other parts of the tumour. Immunohistochemistry for BMP2, SMAD4, and Osterix frequently showed a gradient with more pronounced expression in tumour and/or stromal cells directly surrounding bone. Eighteen cases (26.9%), showed such a gradient in two or more stains, indicating activation of the BMP pathway. The tumour-stroma analysis classified more than half of the cases as the mesenchymal subtype (CMS4).
Conclusion: Heterotopic ossification is seen often in serrated and mucinous tumours as well as in juvenile/inflammatory polyps. Based on the enrichment of fibrosis, CMS4 and the observed staining patterns, it seems likely that induction of bone formation is due to activation of the BMP pathway.

PS-17-043

Prognostic significance of tumour budding, desmoplastic reaction, and lymphocytic infiltration in patients with gastric adenocarcinoma

A. Yavuz*, K. Şimşek, A. Alpsoy, B. Altunay, E. Ocak Gedik, B. Ünal, C.I. Bassorgun, A.M. Tatli, G.Ö. Elpek
*Akdeniz University Department of Pathology, Turkey

Background & objectives: In gastric adenocarcinoma (GAC), the relationship among tumour budding (TB), desmoplasia, and the tumour microenvironment remains unclear. This study aims to determine the correlation among TB and desmoplasia and lymphocytic infiltration in patients with GAC and their impact on prognosis.
Methods: Our study group consisted of 101 patients diagnosed with GAC. TB was defined according to the International Tumour Budding Consensus Conference (ITBCC). Desmoplastic reaction (DR) was classified into three groups based on the maturation of tumour stroma. The evaluation of TIL was determined semi-quantitatively based on a 5% cutoff value. Statistical analysis was performed using SPSS version 27.
Results: In our study group, peritumoral budding (PTB) was strongly correlated with intratumoral budding (ITB) (r: 0.970). Immature DR and low TILs were more frequently observed in tumours with high PTB

(p<0.001). While both PTB and ITB were found to be associated with histological subtype, grade, and lymph node metastasis (LNM), PTB was also correlated with the level of invasion and metastasis (p<0.005). Univariate survival analysis revealed that ITB, PTB (p<0.001), LNM (p values <0.001), DR, and stage (p<0.03) as risk factors for poor prognosis. ITB, PTB, and lymph node metastasis were independent prognostic factors in multivariate Cox-regression analysis.
Conclusion: Our findings support that the evaluation of TB according to ITBCC criteria can be performed to stratify patients with gastric cancers for treatment and prognosis.
In addition, the relationship among TB, DR, and lymphocyte infiltration in the tumour area observed in our study warrants further research with larger patient series to determine the role of a scoring system consisting of these three parameters in determining the behaviour of gastric cancers.

PS-18 | Poster Session Neuropathology

PS-18-001
Morphological analysis of intraepithelial nerve fibre density in Parkinson's disease patients treated with levodopa-carbidopa intestinal gel infusion (Duodopa system)
E. Izycka-Swieszewska*, K. Buczkowski, R. Piekarski, J. Slawek
*Medical University of Gdansk, Poland

Background & objectives: A prevalence of small fibre neuropathy in Parkinson's disease patients treated with Duodopa system is higher than in general population. An objective is to determine the nerve fibre density and the influence of vitamin supplementation on development of neuropathy.
Methods: 21 patients (age:50-78) with Parkinson's disease (duration 6-25y) treated with Duodopa System for one year. Skin punch biopsies (3mm core) taken from thigh and lower leg at the onset and after one year. Ten randomized patients received supplementation of B vitamins and folic acid. Histological slides were stained with H-E and immunohistochemically with PGP 9.5 with a routine procedure.
Results: Intraepidermal nerve fibre density (IEND) was assessed according to the European Federation of Neurological Societies guidelines. Groups with and without vitamin supplementation presented no significant differences in initial IEND (thigh: 0,76±0,28/mm vs 1,18±0,62/mm, p=0,09; calf: 0,39±0,26/mm vs 0,59±0,42/mm, p=0,32) . The group without supplementation showed a statistically significant decrease of IEND in the skin after one year (0,48±0,25/mm vs 1,18±0,62/mm, p=0,003), compared to the baseline biopsy. Such differences were not found in the lower leg sections in this group (0,39±0,35mm vs 0,59±0,42/mm, p=0,18). However, no statistically significant differences in density were observed in the group with vitamin B supplementation (thigh: 0,78±0,43/mm vs 0,76±0,28/mm, p=0,51; lower leg: 0,46±0,36/mm vs 0,39±0,26/mm, p=0,51).
Conclusion: The observed reduction of IEND may reflect the progression of a small fibre neuropathy in Parkinsonian patients treated with Duodopa system. In parallel, oral supplementation of B-group vitamins possibly has a preventive effect for neuropathy progression. The longer observation on the bigger group of patients is needed.

PS-18-002
The impact of methylome implementation on neuropathology: experience of two referral hospitals
S. López*, C. Rodríguez Jiménez, L. Fernandez Ariati, E. Rubio Martín, R. Moreno Velasco, M. Burdiel Herencia, O. Pernía Arias, I. Ibáñez de Cáceres, N. Rodríguez Salas, A. Patiño García, I. Esteban Rodríguez, J.I. Echeveste, C. Lavarino, Á. López Janeiro, C. Rodríguez Antolín
*Hospital Universitario La Paz, Spain

Background & objectives: Genome-wide DNA methylation profiling is valuable tool to refine diagnosis in neuro-oncology, although they are not universally available. We investigated the impact of DNA methylation-based classification on neuropathological diagnosis in two tertiary referral hospitals.
Methods: We analysed brain tumours diagnosed from January 2022 to March 2023 at University Hospital La Paz (Madrid, Spain) and Clínica Universidad de Navarra (Pamplona, Spain). Tumours submitted to DNA methylation-based (EPIC-850K-BeadChip-Array, Illumina) classification (Brain tumour classifier v12.5 https://www.molecularneuropathology.org), were selected for further analysis. We recorded pre-test histopathologic diagnosis and associated WHO-grade and additional diagnostic information provided by the methylome analysis.
Results: Ten out of 103 (9.7%) brain tumours underwent DNA methylation analysis. Most patients were younger than 30 years of age (mean = 22 years p25-p75=13-24,75). Inability to perform a specific entity diagnosis was the reason to perform methylome analysis in all tumours. Histologically, three tumours were classified as glioneuronal tumours, 2 were diffuse gliomas and 5 were found to be unclassifiable. Nine out of 10 tumours were low grade (G1 or G2), none harboured IDH1/2 or ATRX mutations. The Brain tumour classifier score was greater than 0.5 in 8 out of 10 cases. The diagnosis of 5 cases was refined after methylome analysis. Of note, tumour grades remained unchanged.
Conclusion: DNA methylation-based classification was required in a small subset of all brain tumours diagnosed, mostly for difficult-to-diagnose tumours in paediatric or young adult patients. Methylation analysis improved diagnostic accuracy in 50% of cases, demonstrating its utility as complementary tool to refine diagnosis in a subset of highly selected patients. Importantly, methylome diagnostic refinement did not modify the final WHO tumour grade.
Funding: GETTHI Ramón de las Peñas Grant

PS-18-003
Clinico-pathological spectrum of intracranial mesenchymal tumours, FET::CREB fusion-positive - case series
T. Pancsa*, R. Laxton, L. Bhaw, C. Fisher, A. Niblett, D. Hughes, E. Maratos, K. Ashkan, M. Gallagher, S. Al-Sarraj, A. King, I. Bodi, Z. Reisz
*University of Szeged, Department of Pathology, Szeged, Hungary

Background & objectives: Intracranial mesenchymal tumour (IMT), FET::CREB fusion-positive is a provisional tumour type in the 2021 WHO Classification of CNS tumours awaiting further clarification. Here, we present the clinicopathological findings, therapeutic management and follow-up data of six cases.
Methods: A retrospective departmental study found six intracranial tumours (9-65 years, M:F=5:1) with molecularly confirmed FET::CREB fusion. All tumours were extensively investigated by immunohistochemistry and further analysed by multimodal panel (covering 305 DNA and 76 RNA targets)/TruSight RNA Pan-Cancer Panel (targeting 1385 genes) and DNA methylation array. Cases were reviewed for histological and radiological features, therapeutic management and follow-up data.
Results: Histologically, most tumours showed vague lobular arrangement, sclerotic/hyalinised areas and pseudo-angiomatous spaces. One case displayed astroblastomatous-type rosettes. Desmin, CD68 and PLAP were positive in all except one case. The most frequent EWSR1 fusion partner was the CREM (3 cases) followed by CREB1 (2 cases) and ATF1 (1 case). One jugular foramen tumour was profiled as "angiomatoid fibrous histiocytoma (AFH)" with multiple CNV alterations, while the rest showed no match by DKFZ Sarcoma classifier (v12.2) and had a relatively balanced genome. Five cases with complete surgical excision showed no tumour recurrence on follow-up. The jugular foramen tumour underwent surgical debulking and it recurred in 16 months with multiple spinal tumour implants.

Conclusion: IMT, FET::CREB fusion-positive may be under-recognized due to its broad morphological presentation, including cases with striking astroblastoma-like pattern and rare desmin negative cases. The diagnosis requires confirmation of FET::CREB fusion. Methylation profiling was inconclusive apart from a histologically typical AFH case with secondary extension into the intracranial space. While most tumours had no recurrence after complete surgical resection, a case with significant residual tumour and instable genome showed cerebrospinal fluid seeding and multiple spinal tumour implants.

PS-18-004

The integrated genomic and epigenomic landscape of gangliogliomas - retrospective analysis of a single-centre case series

Z. Reisz*, R. Laxton, K. Eggleton, L. Bhaw, B. Clark, A. King, S. Al-Sarraj, I. Bodi
*Clinical Neuropathology, King's College Hospital NHS Foundation Trust, London, United Kingdom

Background & objectives: Gangliogliomas are low-grade epilepsy associated tumours (LEAT) with frequent BRAF V600E mutation, however, rare cases with other MAPK pathway alterations or gene fusions have been recently reported. We present here the integrated histo-molecular classification of 47 cases.
Methods: Retrospective analysis of a departmental CNS tumour database identified 47 cases with a histological diagnosis of ganglioglioma. Morphological features and immunostains were reviewed independently by two neuropathologists, and the cases were further investigated by multimodal panel (covering 305 DNA and 76 RNA targets) and methylation array (DKFZ, Brain classifier v12.5). The tumours were reclassified according to the 2021 WHO guidelines.
Results: Most cases occurred in the temporal lobe (66%) with a mean age of 12.3 years and an even gender distribution. Twenty-three cases (48.9%) harboured BRAF p.V600E mutation. Two cases had BRAF insertion (p.V504_R506dup), 2 cases showed KRAS p.Q61K mutation and additional 3 cases harboured SLMAP::NTRK2 and KIAA1549::BRAF fusion. Methylation array profiled 5 of these cases as "MC Pilocytic astrocytoma, hemispheric" and 2 cases as "MC Ganglioglioma". A tumour with FGFR2::SHTN1 fusion was reclassified as polymorphous low-grade neuroepithelial tumour of the young. An FGFR3::SH3GLB1 translocation with concomitant TERT promoter mutation and chr +7/-10 was detected in a long-standing parietal lobe tumour in a 72-year-old male, with a methylation profile of ganglioglioma.
Conclusion: Precise distinction of gangliogliomas from other epilepsy associated tumours may be challenging due to overlapping morphological features. While our study confirmed hotspot BRAF p.V600E mutation in nearly half of the samples, the BRAF-wildtype tumours showed a rather heterogenous molecular spectrum, including BRAF insertions, KRAS mutations and NTRK2 or FGFR2/3 fusions. One case presented with concerning copy number changes and TERT promoter mutation, raising the possibility of glioblastoma. Further studies regarding the biological behaviour of these tumours are needed.

PS-18-005

Whole genome sequencing - a single assay approach in paediatric brain tumour diagnostics

Z. Reisz*, R. Laxton, K. Eggleton, L. Bhaw, S. Nevis, C. Limbachia, S. Allouni, H. Hanson, A. King, I. Bodi, B. Clark, S. Al-Sarraj
*Clinical Neuropathology, King's College Hospital NHS Foundation Trust, London, United Kingdom

Background & objectives: Comprehensive molecular analysis is essential for accurate diagnosis of paediatric central nervous system tumours, which often requires parallel running of diverse testing methods. We evaluated the diagnostic utility of whole genome sequencing (WGS) compared with a standard-of-care molecular panel.
Methods: Fresh brain tumour samples from 40 paediatric patients (30 glial, 7 embryonal, 1 pineal, and 2 germ cell tumours) were analysed by a multimodal panel (covering 305 DNA and 76 RNA targets) and DNA methylation array (DKFZ). Comparative analysis with WGS data was performed including detection of diagnostic small nucleotide (SNVs) and structural variants and loss of heterozygosity (LOH).
Results: Multimodal panel detected diagnostic variants in 77.5% of the cases, with a total of 48 pathogenic SNVs and 15 gene fusions. Nine cases had no driver molecular alterations, but all tumours were confidently profiled by methylation array. WGS confirmed 85.4% of the known pathogenic SNVs and found an additional 21 previously undiscovered variants and one pathogenic germline variant. All the diagnostic fusions were confirmed by WGS. Among the cases with no diagnostic alterations by the standard-of-care panel, WGS found 6 new SNVs and 2 gene fusions. Methylation array appeared sensitive for copy number variation assessment, apart from copy-neutral LOHs. The histological diagnosis was refined in 2 cases after molecular investigation.
Conclusion: WGS offers a single-test molecular approach with improved diagnostic utility over the standard-of-care gene panels, particularly in challenging brain tumour cases. Limitations might include the requirement for fresh tissue, slower turn-around time due to time-consuming data analysis and the large number of variants of unknown clinical significance. The possibility of missed SNVs and complex structural variants cannot be excluded, which may be resolved by future long-read sequencing techniques.

PS-18-006

SOX11 immunohistochemistry in diagnosis of gliomas and reactive glioses

J. Soukup*, L. Gerykova, P. Kasparova, Z. Pleskacova, J. Petera, V. Skarkova
*University Hospital Hradec Kralove, Czech Republic

Background & objectives: SOX11 is a transcription factor involved in neurogenesis. In current study, we assessed SOX11 immunoreactivity in large cohort of different reactive glial processes and neoplasms to evaluate SOX11 utility in diagnostic neuropathology.
Methods: Tissue microarrays were constructed, with samples of reactive glioses (n=46), glioblastomas (GBMs, n=81), IDH1-mutant astrocytomas (IDH1-As, n=17), oligodendroglial tumours with 1p/19q-loss (OGs, n=17), ependymomas (EPs, n=10, including 2 subependymomas), pilocytic astrocytomas (PAs, n=8 including one pilomyxoid astrocytoma) and gangliogliomas (GGs, n=5). SOX11 was detected in TMAs using monoclonal antibody MRQ-58 (1:50) on Ventana Benchmark Ultra and analysed as H-score.
Results: SOX11 was significantly more positive in gliomas compared to glioses (69.9% vs 20.4%, $p<0.001$). However, absence of SOX11+ cells was only 79.5% sensitive and 46.6% specific for diagnosis of reactive gliosis. We observed a consistent positivity of SOX11 in IDH1mt subset of gliomas (100%, 34/34) and a common positivity in GBMs (75%, 57/76). IDH1mt tumours showed significantly higher SOX11 expression compared to GBMs (median H-score 2 vs 25.8, $p<0.001$). There was no difference in SOX11 between IDH1-As and OGs. SOX11 expression in IDH1mt tumours was associated with tumour grade (medians H-score G2=7.5, G3=55, G4=47.6, $p<0.001$). Of other gliomas, SOX11 was observed in one PA and ependymoma (H-scores 1 and 10).
Conclusion: IDH1-mutated tumours and GBMs are commonly SOX11 positive, compared to other glial neoplasms. Although glioses are positive significantly less frequently, low sensitivity and specificity precludes SOX11 use as a general marker of glioma in limited samples.
Funding: Ministry of Health, Czech Republic, project No. NU20-03-00360

PS-18-007

Comprehensive immunohistochemical profiling with hierarchical clustering and self-organising neural maps allows for consistent subtype identification in glioblastomas

J. Soukup*, R. Dolezal, L. Gerykova, P. Kasparova, Z. Pleskacova, J. Petera, V. Skarkova
*University Hospital Hradec Kralove, Czech Republic

Background & objectives: Glioblastomas (GBMs) show divergent biological features. In past, 3 subtypes (mesenchymal, proneural and classical) were consistently identified with comprehensive genomic studies. The aim was to identify these subsets, using simpler and more affordable approaches.
Methods: Tissue microarrays were constructed from 86 GBM samples. Immunohistochemistry was performed for 13 selected subtype-related markers, based on previously published data, and scored for intensity and extent of staining. EGFR ISH (either FISH or SISH) was scored either as normal or amplified. The results were analysed using hierarchical clustering (HC) and self-organising neural maps (SOM) in Matlab 2023 software.
Results: Using HC, the three groups configuration was generated with highest stability. These three groups corresponded to predicted classical subtype (n = 28), mesenchymal subtype (n = 29), and proneural subtype (n = 29). Comparing HC and SOM, a considerably high prediction correspondence in the threefold GBM classification was found (e.g. specificity = 0.95, accuracy = 0.91, F1 = 0.91). According to SOM weight matrix, EGFR+/MEOX2+/p53wt phenotype showed strongest association with classical subtype. Mesenchymal subtype was characterised by Vimentin+/D2-40+/Olig2- profile and Olig2+/p53mt/Vimentin- was characteristic of proneural subtype. The profiles were consistent with previously published data.
Conclusion: The mathematical analyses of the IHC data enabled to design a predictive SOM-based model for the GBM classification the results of which were in strong agreement with HC approach. Moreover, the weight matrix of SOM elucidates quantitatively the marker contributions to each of the typical GBM classes and provides support for the phenotype interpretation.
Funding: Ministry of Health, Czech Republic, project No. NU20-03-00360

PS-19 | Poster Session Paediatric and Perinatal Pathology

PS-19-001

Osteolysis and neurofibromatosis type 1 (NF-1): a rare association scarcely reported in the literature. Synopsis of clinical, radiological, and histopathological findings in a retrospective case series

M. Bronte Anaut*, J. Arredondo Montero, J.J. Pozo Krelinger, J.C. López Guitierrez
*Hospital Universitario Araba, Spain

Background & objectives: 10-20% of patients with NF-1 present skeletal abnormalities such as scoliosis, pseudarthrosis and more rarely osteolytic events. Several theories have been proposed on the etiopathogenesis of the latter such as the presence of vasculo-lymphatic anomalies in neurofibromas.
Methods: A search was made in the institution archives reviewing the records of 7 children with NF-1 who had been evaluated for osseous defects (bone loss) on imaging tests. Among the information collected were socio-demographic variables, clinical-radiological characteristics, accompanying lesions/abnormalities and evolution. Histological sections were analysed for microscopic findings in the resected lesions. The presence of coexisting genetic syndromes was excluded.
Results: Five patients were female. Mean age at diagnosis was 5.6±2.1 years. During follow-up patients presented neurofibromas in multiple locations, mainly cervico-thoracic and in lower extremities, both subcutaneous and in soft tissue. Six patients presented polyostotic bone loss. All osteolytic events were subjacent to a bone loss related plexiform neurofibroma with/without diffuse component (BLRN). All BLRN showed heterogeneous 18F-FDG metabolism with higher uptake foci. Immunohistochemical study (IHS) showed positivity to CD31 (endothelium), CD34 (endothelium, tumour cellularity), and negativity to D2-40, LYVE-1 and WT1. Male patients selectively showed focal WT1 positivity (neurofibroma cellularity). BLRN main locations were cranial base, occipital bone, cervical vertebrae, orbit, mandible and thoracic cage.
Conclusion: BLRN in NF-1 appear to have a female predominance and an early age of onset. The most characteristic presentation was a large cervico-cranial neurofibroma affecting more than one bone with a vasculo-lymphatic IHS pattern. Further studies that deepen in the IHS characterization of these lesions are necessary to define the existing relationship between vascular anomalies and osteolysis in NF-1.

PS-19-003

Expression of ACE2 and TMPRSS2 in human placental tissue during SARS-CoV-2 infection

E. Demaria*, A. Salerno, A. Degiovanni, A. D'Errico, M. Fiorentino
*Department of Medical and Surgical Sciences (DIMEC), University of Bologna, Italy

Background & objectives: ACE2 and TMPRSS2 are the primary cellular receptors involved in SARS-CoV-2 entry, expressed in the lungs but also in the placenta. This case-control study aims to evaluate ACE2 and TMPRSS2 expression during a SARS-CoV-2 infection in first-trimester placental samples.
Methods: We selected a case group of first-trimester miscarriage samples. Sample selection criteria were: SARS-CoV-2 positivity during pregnancy or within 14 days from the miscarriage. Then, a comparable pre-COVID-19 control group was identified. Once collected, all samples were stained with antibodies anti-ACE2 and anti-TMPRSS2 for immunohistochemistry. While, for the case group only, virus detection was performed by In Situ Hybridization.
Results: 300 cases of miscarriage examined at our institute between January 2020 and March 2022, 9 were collected in the case group. One of them was excluded due to the lack of immunoreactivity. Overall, ACE2 expression was widely distributed in both cases and controls, mostly in vessels but also in the decidua and villi. Surprisingly, ACE2 positivity in the villous trophoblast was only observed in the brush border, but not in the stroma. In contrast, TMPRSS2 positivity was stronger in the case group compared to the control group. SARS-CoV-2 spike protein was identified in 6 cases and exclusively in the maternal compartment of the placenta.
Conclusion: These results suggest that, on the one hand, infected tissues overexpress the TMPRSS2 receptor. This may be interpreted as an actual activation of the protein following viral infection. On the other hand, although TMPRSS2 expression increases in the placenta and SARS-CoV-2 entry receptors are exposed in the foetal compartment, there is no sign of vertical transmission. Confirming this, national registry statistics show that the annual abortion rate in the Italian population did not increase during the pandemic years.

PS-19-004

Congenital pulmonary airway malformation: a diagnostic challenge. Usefulness of historical classification

C.E. Haro Haro*, M. Garrido Pontnou, A. Chaachou Charradi, J.T. Zuñiga Gaitan, J. Camacho Soriano, F. Rodríguez Díaz, A. Navarro Jiménez
*Vall d'Hebron University Hospital, Spain

Background & objectives: Congenital pulmonary airway malformation (CPAM) is a rare anomaly of the developing lung. It occurs in <25% of all congenital lung abnormalities in infancy. There will be histologic features that may be useful in classifying them.

Methods: We reviewed the digitalized preparations of 39 cases diagnosed in our centre between 2001 and 2023, as well as the medical history, and prepared a table with the histologic data and relevant characteristics. Stoken's classification was used as a reference.
Results: 39 cases reviewed, 23(59%) were boys and 16(41%) girls. The age range was between 18 weeks of gestation and 16 years, being more frequent in the first year of life. The review diagnoses were: CPAM 1: 6 cases (15.4%), CPAM 2 or bronchial atresia sequence 24 cases (61.6%), in which 4 cases (17.4%) the atresia was identified, CPAM 3: 1 cases (2.5%), CPAM not classifiable: 8 cases (20.5%).
The following differential histopathological features were observed between type 1 and type 2.
Groups of mucinous cells ($p<0.005$) CPAM1 5 cases (83.3%) and CPAM2 2 cases (8.3%). Signs of obstruction ($p<0.001$) CPAM1: 1 case(16.7%) and CPAM2: 16 cases (67%). Presence of lymphoid component ($p<0.001$) CPAM1: 2 cases (5%), CPAM2: 18 cases (46%).
Conclusion: The historical classification of CPAM is confusing and poorly replicable. In our series, We conclude that groups of mucinous cell are important for CPAM 1 and signs of obstruction and lymphoid component for CPAM 2 or bronchial atresia sequence. In foetal lesions the classification is very limited by the maturational stage of the lung. The other histological parameters such as epithelial lining, size of the cyst or wall, presence of smooth muscle in our series were not statistically significant ($p>0.05$).

PS-19-005
Placental pathological assessment in a SARS-CoV2 maternity ward of the Romanian National Institute for Mother and Child Health
T.G. Jaswal*, T. Georgescu, A. Roșulescu, A. Georgescu, A. Cernat-Stefan, R. Pletosu, M. Sajin
*Department of Pathology, University Emergency Hospital Bucharest, Romania

Background & objectives: Since the coronavirus disease outbreak, there was increased interest in the spectrum of inflammatory-hypoxic-thrombotic abnormalities during pregnancy. In this study, our objective was to investigate the placental signs of foetal (FVM) and maternal vascular malperfusion (MVM) contribution to foetal development.
Methods: We analysed 39 placentas delivered between 2020 and 2022 by pregnant women confirmed with SARS-CoV2 infection using RT-PCR. We applied the Amsterdam Placental Workshop Group Consensus recommendations and categorized the histopathological findings into three major groups: MVM, FVM and inflammatory lesions. Statistical analysis was performed using SPSS. T test and Chi-square test were used to compare study and control groups.
Results: All placentas were from third trimester live births, except for one intrauterine foetal demise in the second trimester. Statistically significant differences were observed among MVM findings of SARS-CoV2 placentas and controls: decidual arteriopathy ($p=0.016$), perivillous fibrin deposition ($p=0.033$), Tenney-Parker-Change ($p=0.008$). Among FVM signs there was a higher frequency of avascular villi (AV) ($p=0.001$), foetal-circulation thrombi ($p=0.003$), subchorionic vascular ectasia ($p=0.001$), delayed villous maturation (DVM) ($p=0.036$). Deciduitis was observed in 40% cases ($p=0.021$) and villous oedema in 52.5% ($p=0.004$). We found that in newborns of SARS-CoV-2-positive mothers, the Apgar score was lower in the presence of AV ($p=0.044$) and the weight was lower in the presence of DVM ($p = 0.039$).
Conclusion: Our study revealed that there is an increased prevalence of both maternal and foetal vascular malperfusion as well as inflammatory lesions among the placentas from women infected with SARS-CoV2, compared to the control group. There may be a cascade of pathological anomalies starting with the hypercoagulable state of the SARS-CoV2 positive mothers following hypoxic changes and ending with injury of the placenta. Future research should assess the correlations between these histopathological findings and the impact on pregnancy outcome.

PS-19-006
Placental pathology and clinicopathologic correlation in kidney transplant patients: tertiary centre experience
H.S. Toru*, B. Altunay, D.M. Chiorean, G. Bulbul, C.Y. Sanhal, I. Mendilcioglu
*Akdeniz University, Turkey

Background & objectives: There is a limited number of studies in the literature on whether there is a difference in the histopathological examination of placental findings in pregnancies of kidney transplant patients compared to the average population.
Methods: We aim to contribute to the literature by comparing the placental pathology with control groups. Retrospectively, pathology archive was reviewed, and 16 kidney transplant patients' placenta were included in the study. We selected 32 cases in term placenta control group and 32 cases in control group at the same gestational age in kidney transplant group.
Results: Among 80 cases, 36.3% of mothers had a clinical disease. Mean age was 29.81 (std: $\pm$ 3.33) kidney transplant group, 29.97 (std $\pm$ 8.46) same gestational age control group, 29.88 (std: $\pm$ 6.20) term control group. Placental pseudocysts were significantly higher in the kidney transplant group than in both control groups ($p<0.01$). Chorionic pseudocysts were seen higher in kidney transplant group than control groups, but the difference was insignificant ($p=0.140$). The difference between groups in amniotic fluid infection sequence was insignificant ($p=0.268$). IUGR were similar in kidney transplant group and same gestational age group; both were significantly higher than the term group ($p=0.001$).
Conclusion: Pregnancy complications in kidney transplant patients are higher than in the general population. For this reason, patients with kidney transplantation should be followed carefully, and a multidisciplinary approach should be applied with nephrologists or organ transplant physicians, midwives, and obstetricians. In addition, placenta gives important data related to pregnancy process, maternal and foetal progress.
In conclusion, if placental data are widely evaluated and meta-analyses are made, follow-up and treatment protocols specific to kidney transplant pregnancies can be improved and developed.

PS-20 | Poster Session Pulmonary Pathology

PS-20-001
Correlation between morphology and next generation sequencing in multiple lung adenocarcinomas, our experience in 24 patients
I. Amat Villegas*, D. Guerrero-Setas, A. Panizo Santos, T. Labiano Miravalles, C. Cerezo Aguirre, M.R. Mercado Gutierrez, V. Zelaya Huerta
*Spain

Background & objectives: The distinction between intrapulmonary metastases, synchronous primary tumours and metachronous multiple lung adenocarcinomas are often challenging. Main basis for this purpose are the histological features of the different nodules but next generation sequencing (NGS) is becoming a useful tool too.
Methods: We retrospectively analysed a series of 24 patients with two or more lung adenocarcinomas, synchronous or metachronous. Two pathologists with special interest in thoracic pathology reviewed the histological slides and Focus NGS was performed on all of them. A staging was proposed for each form of evaluation and the correlation between both was studied.
Results: A total of 54 lung adenocarcinomas from 24 patients have been evaluated by reviewing histological slides of resected specimens and a suggested staging for 21 patients was done. Seventeen tumours were synchronous and nine metachronous, three patients had more than two nodules. Concordance between molecular results in different tumour nodules of a patient was found consistent with tumour metastases. Correlation between morphological and molecular staging was found in 19 cases.

Conclusion: The presence of multiple lung adenocarcinomas is an issue for staging. In this setting next Generation Sequencing could bring supplementary information and could be useful in the differentiation between intrapulmonary metastases and multiple primary tumours. A good correlation between histological examination and molecular analysis increases accuracy to assess the right staging for synchronous or metachronous lung adenocarcinomas.

PS-20-002

Small bowel metastasis of lung cancers: clinico-pathological and molecular characterisation

M.A. Bani*, L. El-Khoury, P. Dartigues, C. Smolenschi, I. Sourouille, B. Besse, S. Cotteret, J. Scoazec
*Department of Medical Biology and Pathology, Morphological pathology laboratory, Gustave Roussy Cancer Campus, Villejuif, France, Paris-Saclay university, Gustave Roussy Cancer Centre, Inserm US23, CNRS UMS3655, AMMICa, Villejuif, France

Background & objectives: Metastasis of lung cancer (MLC) is often detected at the time of diagnosis. Small bowel is the most frequent gastrointestinal metastatic site. The aim of this study is to explore the specificity of the involvement of small bowel in MLC.
Methods: This retrospective analysis included 6 patients diagnosed with primary lung carcinoma with small bowel metastasis between 2003 and 2022 identified in our institution. The clinical features for each patient were obtained from the medical file. For each patient an immunohistochemical study and molecular testing using next generation sequencing and RNA sequencing were performed.
Results: The mean age at diagnosis was 66.2 years. 3 patients had synchronous metastasis and for the other 3 patients ileal metastasis was detected in the year following the diagnosis. Four cases were diagnosed with a primary lung adenocarcinoma, while two had a poorly differentiated adenocarcinoma. Only one case had an undifferentiated histology on metastasis with negative TTF1, CK7 and p40 and a loss of BRG1, revealing a SMARCA4 deficient undifferentiated tumour. There was no expression of NUT. KRAS mutations were detected in 3 cases, TP53 in 2 cases, BRAF in one case and SMARCA4 and CTNNB1 in one case. No fusion gene were detected by the RNA-sequencing panel used.
Conclusion: To the best of our knowledge, there have been no studies on the clinicopathological and molecular characteristics of small bowel metastases from the lung. These metastases occur in advanced stage, are associated with unfavourable prognosis. Most of our patients had lung adenocarcinomas and one had a SMARCA4 deficient undifferentiated tumour. There were no peculiar molecular profile since half of our cases harboured KRAS mutations. The characterisation of the immune microenvironment of these tumours is under investigation.

PS-20-003

Anaplastic lymphoma kinase (ALK) status in non-small cell lung cancer (NSCLC), a prospective study/review of 2445 cases

C. Girleanu*, J. Mc Fadden, S. McCarron, A. Dunne, M. Wright, G. Castriciano, S. Nicholson, A. Keogh, A.M. Baird, C. O' Brien, S. Finn
*Dept of Histopathology, LabMed Directorate, SJH, Ireland

Background & objectives: The prevalence of anaplastic lymphoma kinase (ALK) fusion in non-small cell lung cancer (NSCLC) varies by detection method used. In our study we prospectively compared the detection of ALK rearrangements in NSCLC using Next-Generation Sequencing (NGS) and Immunohistochemistry (IHC).
Methods: Analysis of ALK status was performed using NGS (Oncomine Focus panel) VENTANA anti-ALK (clone D5F3) Rabbit Monoclonal Primary Antibody, and IHC in 2475 cases of NSCLC diagnosed in St James's Hospital over the past 5 years. Discrepant cases were also tested using Fluorescence in situ hybridisation. Results were considered to be consensus positive/negative if reproduced across two methods.
Results: 2445 cases of NSCLC were assessed with IHC and NGS. Of these, 216 cases had insufficient RNA for NGS, 32 had insufficient tissue for IHC and 67 cases were insufficient for both techniques, two cases had atypical laboratory findings and were not included in the comparative analysis. A total of 317 cases were excluded. Therefore, we analysed 2126 cases, 2108 cases showed concordance with both methods, 18 cases were discrepant between NGS and IHC. Consensus analysis using FISH demonstrated the NGS result to be consistent with consensus in 17/18 cases. Based on these numbers the accuracy of NGS is 99.9% and the accuracy of IHC 99.2%.
Conclusion: Our study confirms that compared to IHC, NGS is a more accurate first line testing platform for the detection of consensus ALK fusion status. However access to IHC may be required to mitigate the higher tissue requirements of NGS and access to FISH may be beneficial to resolve atypical results.

PS-20-004

Immunohistochemistry assessment of NTRK gene expressions in non-small cell lung cancer

J.M. Gutiérrez Herrera*, M.A. Montero Fernández, G. Kokaraki, L. De Petris, R. Maia Falcão, J.Á. García García, R. Guijarro, S. Ekman, C. Ortíz Villalón
*Karolinska University Hospital, Sweden

Background & objectives: The NTRK gene-fusions has gained importance in understanding tumour development and performance of TRKI inhibitors. The aim of this study was to assess the utility of pan-TRK immunohistochemistry for detecting NTRK gene rearrangements in non-small cell lung cancer.
Methods: We conducted a retrospective analysis of 482 non-small cell lung cancer (NSCLC) cases from Karolinska University Hospital using pan-TRK IHC. Whole Exome Sequencing NGS was performed to confirm the presence of NTRK fusions in pan-TRK IHC positive cases. We also used the IPA software to better understand the molecular pathways of lung cancer and suggest the best treatment option.
Results: We detected TRK overexpression in 4.56% of the NSCLC cohort using pan-TRK IHC. The positive expression of TRK in NSCLC was correlated with histologic subtypes (adenocarcinomas, squamous cell carcinomas and large cell carcinomas), $p < 0.0001$; and grade of differentiation, $p < 0.005$. Overall were15 pan-TRK IHC positive cases, where 7 were confirmed to have NTRK fusions through NGS. NTRK2 and NTRK3 fusions were detected at a lower proportion compared to NTRK1 fusions. Other important somatic mutations were detected. Tumour burden in our cohort was high and there was not NTRK gene amplification but there was KRAS gene amplification in 1/15 samples.
Conclusion: Pan-TRK IHC is a reliable and tissue-efficient method for identifying NTRK fusions in NSCLC. Further research is needed to understand the clinical significance of NTRK fusions in lung cancer and its role as potential targets for therapy. The IPA software is a useful tool for gaining a better understanding of molecular lung cancer pathways and suggesting the best treatment option.
This study was funded in part by Bayer.

PS-20-005

A review of the diagnosis and investigation of pulmonary amyloidosis and an evaluation of current local practice

A. Hennessy*, C. Lightner, C. O'Brien, N. Mayer, L. Burke
*Department of Pathology, Cork University Hospital, Cork, Ireland

Background & objectives: Pulmonary amyloidosis is rare and can involve the tracheobronchial tree, lung and pleural parenchyma. Amyloid subtype analysis is important for patient management. An audit was performed to evaluate detection and pathological management of these cases over a 14-year period.
Methods: A COGNOS database search was performed at the Pathology Department, CUH from 2008-2022 for diagnosed airway and lung parenchymal amyloid. Data evaluated included number of cases, age, gender, localization of deposits (confirmed by Congo Red), disease association, and amyloid sub-type performed at the National Amyloidosis Centre, UK. Amyloid that did not stain with an antibody was termed non-AA amyloid.
Results: 15 patients identified by Congo Red stain from 2489 specimens (0.6%) - 12 male, 3 female patients, mean age 72 (range 51-89 years). Of 12 cases sub-typed, Amyloid light chain (AL), Lambda subtype was the most common.
Tracheobronchial (n=5): 3 AL amyloid sub-type, unassociated with a clonal plasma cell proliferation. 2 non-AA amyloid, one associated with an adenocarcinoma.
Lung parenchyma (n=8): 6 cases sub-typed, 4 AL amyloid sub-type with a nodular distribution pattern, one associated with a plasmacytoma, and one with a squamous cell carcinoma. Two were non-AA amyloid sub-type with an interstitial pattern, one with a known myeloma history.
Pleura (n=2): Both AL amyloid sub-type and previous amyloidosis diagnoses.
Conclusion: Pulmonary amyloidosis can be either localized or systemic and usually presents in one of three different forms – nodular, diffuse alveolar-septal, or tracheobronchial amyloidosis. AL Lambda subtype, unassociated with a systemic clonal plasma cell proliferation, was the dominant subtype similar to current literature. Amyloid subtyping guided management for all of these patients and continues to be standard practise within our laboratory.

PS-20-006
Histological analysis of lung grafts lesions related to cold preservation at 10C
J. Martin Lopez*, P. Gil Bernabé, S. Martin Poza, S. Crowley, G. Silvestre Egea, R. Laporta, C. Salas Anton, J.L. Campo Cañaveral
*Department of Pathology. Hospital U. Puerta de Hierro, Spain

Background & objectives: Cold preservation of the lung graft at 10°C seems a promising method to safely extend the cold ischemia time. We analysed the impact of preservation at 10 °C compared to standard preservation at 4 °C in lung transplants.
Methods: This is a prospective single-arm study of lung transplants (LTx) performed between September 2021 and September 2022. Those with doubts in perfusion and preservation processes, or those subsidiaries of ex vivo assessment were excluded. Biopsies of the lung grafts were taken at different times during the transplant. The presence of neutrophils, alveolar edema and interstitial infiltrate were evaluated and graded.
Results: 41 patients were included (n=20 preserved at 10°C; n=21 at 4°C). There were no differences regarding demographic variables and the indication for transplantation. Total preservation times were statistically longer ($p<0.001$) in the 10°C group [1st lung; 662 min (R 428-807); second lung; 813 (R 620-946)] than in the 4°C group [1st lung; 360 min (R 320-400); second lung; 439 (R 395-490)]. Histologically, no relevant inflammatory or exudative changes were recognized that would make it possible to identify the preservation method chosen. Some samples had intravascular thrombi and scaly changes that will be analysed in a second phase. Mortality at 30 and 90 days was 0% in both groups.
Conclusion: Our study proposes the evaluation of inflammatory mediators and the histological assessment of acute lung injury to study whether preservation methods affect donor lungs. Only a few series have evaluated this previously. We show that preservation at 10°C seems to be a safe and feasible strategy to intentionally prolong cold ischemia time in lung grafts, rendering it advantageous in the logistics of a lung transplant program so it could, in the future, be considered a semi-scheduled procedure.

PS-20-007
Do more and increasing of diagnostic yield with rapid on-site evaluation ROSE in trans-thoracic needle aspiration/biopsy TTNA/B
S. Melotti*, A. Velotti Fino, C. Ricci, N. Nannini, A. De Leo, M. Sirolli, E. Mengozzi, D. Papadopoulos, A. Bruno, M. Fiorentino, F. Ambrosi
*Pathology Unit, Maggiore Hospital-AUSL Bologna, Bologna, Italy, School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: ROSE is a cytological technique that supports sample evaluation during endobronchial procedures. We aim to uncover the extent to which ROSE of TTNA/B samples under CT and US-guided can safely and cost-effectively reduce the necessity for additional procedures.
Methods: Two groups of patients who underwent TTNA/B for thoracic lesions (89% from the lung and 11% from mediastinum) have been compared. The first group-cohort A not supported by ROSE, as well as the latter (cohort B) was supported by a systematic ROSE during the radiological procedures. All data have been retrieved from the digital archives of the Department of Pathology.
Results: 91.04% of cohort A patients' preliminary diagnosis has been rendered during CT or US-guided procedures supported by ROSE, and in 68.7% of cases only a single TTNB pass was sufficient for the diagnosis, the immunohistochemical and the molecular characterization. Furthermore, the number of inadequate procedures reduced from 29.90% in cohort A in contrast to 8.96% in cohort B (<0.005 Fisher exact).
Due to an average improvement in the samples quality, an NGS characterization was carried out in 60% cases in cohort B, as opposed to 45% of cohort A. The PD-L1 immunohistochemistry has been evaluated in 69.04% of non-small cell lung cancer in cohort B versus 25% of cohort A.
Conclusion: Performing ROSE during TTNA/B consistently reduced the number of inadequate samples and increased diagnostic yield. It also allowed the collection in one single procedure of sufficient tissue for further molecular and immunohistochemical diagnostic analysis.

PS-20-008
Wnt3α in a mouse model of bleomycin induced lung fibrosis
A. Ognjenović*, S. Čužić, M. Antolić, V. Milutinović, Ž. Anzulović Šanta, B. Hrvačić, I. Glojnarić
*Selvita Ltd., Croatia

Background & objectives: Wnt signalling pathway plays important role in lung development, regeneration, and disease progression. Aim of the study was to identify cells that are the source of Wnt3α, a member of the canonical Wnt pathway, in naïve and fibrotic murine lungs.
Methods: C57BL/6N mice were divided into naïve control and bleomycin-challenged group. Lung tissue was sampled on days 7, 9, 14 and 21 following intranasal bleomycin challenge. Formalin-fixed paraffin-embedded lung tissue sections were stained by double immunofluorescence (CC10/Wnt3α and CD206/Wnt3α). Slides were scanned using AxioScan.Z1 scanner (Zeiss). Quantification of CC10/Wnt3α positive surface within bronchi surface was performed using Visiopharm software.
Results: The main source of Wnt3α in naïve mice lungs was the bronchial epithelium. In bronchial epithelium, most of the club cells (CC10-positive cells) expressed Wnt3α; approximately 80% of the cells. Bleomycin challenge induced club cell damage and depletion. Despite the subsequent recovery of the club cell population by day 21 post-bleomycin challenge, less than 40% of the club cells expressed Wnt3α. At the same time, Wnt3α became expressed within the areas of pathological bronchiolization (CC10-positive cells). On day 21 post-bleomycin Wnt3α was present within a small portion of M2 macrophages (CD206-positive cells).

Conclusion: Wnt proteins have multiple functions in cell proliferation, migration, and tissue organization. This study showed that the main source of Wnt3α in the lungs of naïve mice are club cells within the bronchial epithelium. Post-bleomycin challenge, club cells within bronchial epithelium are recovering but no longer express Wnt3α in the same amount. Since a small fraction of M2 macrophages expresses Wnt3α in a later stage post-bleomycin challenge, their exact role has to be elucidated further.

PS-20-009

Comparison of PDL1 expression between different tissue samples in non-small cell lung cancer

Z. Radicevic*, N. Kurtović, I. Zagorac, M. Bakula, E. Matuzalem Marinović, J. Rajc
*Department of Pathology and Forensic medicine, Osijek University Hospital, Osijek, Croatia; Faculty of Medicine Osijek, University of Osijek, Croatia

Background & objectives: In many patients with advanced stage of non-small cell lung cancer, only small biopsies or cytology samples are available for the evaluation of PDL1 expression. In this study we compared the average rate of PDL1 positivity between different tissue samples.
Methods: We reviewed 401 case of non-small cell lung cancer stained with PDL1 IHC Ventana SP263 assay between January 2019 and December 2022, assessed as a tumour proportion score (TPS). Samples were divided in four categories: cell blocks, small biopsy samples, surgical resections and distant metastasis. The cross-tabulated statistics of the observed values were performed between the four categories.
Results: Among the 401 specimens, 187 were small biopsies (46,6%), 130 cell blocks (32.4%), 51 lung resections (12,7%) and 33 biopsies taken from distant metastasis (8,2%). Tumour proportion score (TPS) of <1% was detected in 205 cases (51,1%), TPS ≥1-49% in 133 cases (33,2%) and TPS ≥ 50% in 63 cases (15,7%). By using both, continuous and three-category variables of TPS (<1%, ≥1-49% and ≥50%) we found that the average PDL 1 positivity rates were evenly distributed in all examined tissue samples (cell blocks, small biopsies, large surgical resections, and distant metastasis), considering all three TPS categories.
Conclusion: Our study shows that the rates of PDL1 positivity were not significantly different in cell blocks, small biopsy samples, samples from distant metastasis and large surgical resections. Despite of the well know heterogeneity of PDL 1 expression in non-small cell lung cancer that might reflect in inaccurate results, especially if the test is carried in a small tissue specimen, our findings suggests that all above-mentioned materials are equally adequate for immunohistochemical PDL 1 assessment in a daily practice.

PS-20-010

Real-world comparison between PD-L1 SP263 and 22C3 assays in non-small cell lung cancer: interchangeability of two assays and interlaboratory concordance

M.S. Roh*, S.Y. Ha
*Department of Pathology, Dong-A University College of Medicine, Republic of Korea

Background & objectives: The evaluation of PD-L1 expression is critical for the selection of patients for immunotherapy in non-small cell lung cancer (NSCLC). To standardize the effective use of PD-L1 assays, inter-assay concordance for two PD-L1 tests was assessed using real-world data.
Methods: Two histologic sections from 340 NSCLCs were distributed to 2 sites. SP263 testing on Ventana Benchmark platform was performed in-house and interpretated by a pathologist, while 22C3 testing on Dako Link 48 platform was outsourced and evaluated by 10 different pathologists. The concordance rate was evaluated using tumour proportion score (TPS) cutoffs of 1 and 50, respectively.
Results: The overall percentage agreement (OPA) was 89.6% at TPS ≥ 1, whereas the OPA was 98.1% at TPS ≥ 50. The κ coefficient was calculated as 0.653 at TPS ≥ 1 and was 0.864 at TPS ≥ 50. The majority of scoring challenging cases was in TPS 1% borderline samples. When examining variability between pathologists, there was good to strong reliability among pathologists at TPS ≥ 50 (intraclass correlation coefficient [ICC] = 0.78–0.94), whereas moderate-to-strong interobserver agreement (ICC = 0.51-0.81) at TPS ≥ 1. The interobserver reproducibility was improved in the recent 2-year samples compared to the previous samples.
Conclusion: These findings indicated that PD-L1 SP263 and 22C3 assays were highly comparable analytical performance, especially at TPS ≥ 50, although assays were performed at different laboratories and evaluated by differently trained pathologists. Experience gained with real-world analysis supported the potential interchangeability of two PD-L1 assays. By reducing the number of PD-L1 assays in cases displaying an unequivocally TPS ≥ 50, it may aid to save both cost and specimens for subsequent molecular evaluations.

PS-20-011

Comparison of artificial intelligence-assisted and manual assessment of programmed death-ligand 1 (PD-L1) expression

Z. Sağnak Yılmaz*, Z. Turkmen Usta, S. Aydin Mungan
*Dokuz Eylül University, The Institute of Health Sciences, Department of Molecular Pathology, Karadeniz Technical University, Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Programmed cell death ligand 1 (PD-L1) is a critical biomarker for predicting the response to immunotherapy. In this study, we aim to evaluate the agreement in PD-L1 scoring among pathologists and between deep learning (DL)-based artificial intelligence (AI) model.
Methods: One hundred five patients with lung cancer were included in the study. Preparations stained with Ventana PD-L1 (SP263) assay were first evaluated by three pathologists and given tumour proportion score (TPS). All preparations were evaluated with Ventana DP 200 slide scanner and uPath/ PD-L1 algorithm. Statistically, the intraclass correlation test and kappa score were used to evaluate group consistency.
Results: Considering the agreement among pathologists (P1, P2, P3), the highest correlation was between P1 and P2 (P1 vs. P2: R= 0.894; P2 vs. P3: R= 0.879; P1 vs. P3: R= 0.794). Considering the correlations of TPS-AI with pathologists separately, the highest accordance was with P3 (TPS-AI vs. P3: R= 0.772; TPS-AI vs. P2: 0.769; TPS-AI vs. P1: 0.657). Those with TPS <1%, 1-49%, and >50% were categorized separately. The agreement between TPS-AI and pathologists is generally lower than inter-pathologists' agreement (Kappa values: TPS-AI vs. P2: 0.537, TPS-AI vs. P1: 0.500, TPS-AI vs. P3: 0.482; P1 vs. P2: 0.739; P2 vs. P3: 0.702; P1 vs. P3: 0.554).
Conclusion: In general, both the agreement among pathologists and the agreement of individual pathologists with TPS-AI are lower than the literature data. This may be due to the limited number of cases evaluated. It was concluded that manually given scores were higher than TPS-AI. The most important reason for this situation may be the pressure to approach the assumed threshold value for the patient to receive immunotherapy.

PS-20-012

Confocal microscopy and real-time PCR for rapid perioperative molecular profiling of lung cancer: a proof of concept

F. Schmitt*, A.G.M. Sciarra, M. Christodoulou, I. Letovanec, C. Beniere
*SamanTree Medical, Lausanne, Switzerland

Background & objectives: Time reduction between surgery and adjuvant therapy for non-small cell lung cancer improves (NSCLC) patient survival. We have tested the perioperative combination of confocal microscopy and real-time sequencing to provide faster and simpler workflow for the molecular profiling of NSCLC.
Methods: Three fresh lung adenocarcinoma tumour tissue samples were perioperatively imaged with the Histolog® Scanner confocal microscope. Tissue areas relevant for molecular profiling were immediately sampled by the pathologist thanks to confocal images and analysed with the IdyllaTM real-time PCR based molecular testing. Obtained molecular profiles were compared with the output of standard-of-care assessments performed on diagnostic FFPE bioptic materials.
Results: High cellularity tumour areas were identified with confocal imaging and sampled in less than 10 minutes allowing to start molecular profiling right away and get the results of this assessment 2-3h after surgery. Treatment with Histolog® Scanner confocal microscope does not consume tissue nor negatively impact subsequent assessment in histopathology. Results of the molecular assessments obtained through the combination of confocal microscopy and automated sequencing were in complete agreement (100% concordance) with the output of standard-of-care assessment for the three cases. These included one KRAS, one EGFR mutated adenocarcinomas, and one with the absence of ALK, ROS, NTRK, RET fusions, or METex14 skipping.
Conclusion: We report here a promising proof-of-concept for a fast and simple postoperative molecular analysis of NSCLCs. The use of on-site confocal imaging of full NSCLC surgical specimens allows the rapid retrieval of appropriate specimens for a fast automated sequencing. Tumour molecular profiling can be obtained on the day of the surgery. After confirmation on more cases, this approach could be implemented to simplify the molecular pathology workflow and provide in a timely manner useful information for the patient targeted treatment.

PS-20-013
Studying tumour heterogeneity and its functional consequences in tumour growth in vitro and in vivo
I. Vamvakaris*, K. Potaris, K. Tsilingiri, A. Chalari, Z. Kanaki, C. Karakostas, G. Zachou, I. Pateras, P. Constantoulakis, G. Christopoulou, V. Georgoulias, A. Klinakis
*SOTIRIA, Greece

Background & objectives: In recent years it has been shown that tumours are highly heterogeneous "mosaic" tissues. The genetic differences leading to this mosaicism as well as the significance for tumour growth and metastasis are poorly understood.
Methods: Non-small cell lung cancer tumours were used to generate patient-derived xenografts and organoid cultures. We have compared the growth potential of squamous cell carcinomas to that of adenocarcinomas. Furthermore, we have evaluated the capacity of different bits of the same tumour to grow both in mice and in culture. Tumour heterogeneity has been assessed with haematoxylin/eosin and specific staining.
Results: In agreement with others, we have shown that squamous cell carcinomas have significantly higher engraftment rates, with around 80% of squamous cell carcinomas successfully establishing patient derived xenografts for at least 3 passages, compared to less than 50% for adenocarcinomas. Further, we observe that different areas of the same tumour engraft with not only different success rates but also different latencies for those bits that do engraft successfully. This heterogeneity is evident in tumour samples as small as 1cm2 as shown also by the histopathological analyses. The molecular basis of these differences is not yet clear and is the subject of ongoing studies in our laboratory.
Conclusion: We show here that beyond the already described intratumour heterogeneity, to a certain extent there is also important intertumour heterogeneity. Whether this arises from genetic or epigenetic differences and whether invasive clones originate in specific areas of the tumour are important issues that need to addressed.

PS-20-014
Pathomorphological features of AL-amyloidosis of the upper and lower respiratory tract
O. Vasyukova*, Z. Gioeva, L. Mikhaleva, R. Vandysheva, K. Midiber, N. Gutyrchik, V. Pechnikova, D. Areshidze, M. Kozlova
*Avtsyn Research Institute of Human Morphology of Federal State Budgetary Scientific Institution "Petrovsky National Research Centre of Surgery", Russia

Background & objectives: Respiratory system is one of the target organs that can be affected by the pathologic protein aggregation in both systemic and localized forms of the amyloidosis. Objective: to describe pathomorphological features of AL-amyloidosis of the upper and lower respiratory tract.
Methods: In this study, clinical findings, biopsy and surgical specimens were assessed in 17 patients with amyloidosis of the upper and lower respiratory tract. Amyloid deposits were identified in tissue sections using Congo red stain and polarized light microscopy. Immunohistochemical analysis was carried out with monoclonal and polyclonal antibodies against different amyloid types.
Results: Amyloidosis of the respiratory tract was diagnosed in 7 male and 10 female patients, age range 42-88 years. The main clinical manifestations included hoarseness, cough and dyspnea. Six cases were classified as localized laryngeal amyloidosis, including 4 cases of AL-kappa and 2 cases of AL-lambda amyloidosis. Lung involvementwas reported in 8 patients (6 patients with AL-lambda amyloidosis, 2 with AL-kappa amyloidosis). Three cases of diffuse pulmonary amyloidosis demonstrated the deposits within the interstitium and blood vessels. Amyloid tumour-like interstitial deposits were detected in 5 patients. Diffuse tracheal and bronchial involvement in amyloidosis was found in 3 cases (two cases of AL-kappa- and one - AL-lambda amyloidosis).
Conclusion: Amyloidosis of the respiratory system is a rare disease. Localized amyloid deposits in the respiratory tract can be treated surgically, while diffuse interstitial and vascular amyloid deposition which typically occurs in systemic amyloidosis requires combination therapy comprising surgery, transplantation, chemotherapy.
This study was supported by RSF, grant No. 23-15-00138.

PS-20-015
Placental transmogrification of the lung: a clinicopathological analysis of a case series and literature review
C. Vieru*, J.C. Ruiz Tello, M.Á. Tribaldos Villar, M.J. Bonilla Pérez, A. Jiménez García, Á. Panizo Santos, M. García Martos
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Placental Transmogrification of the Lung (PTL), first described in 1979, is a rare benign disease with unclear pathogenesis, frequently associated with emphysematous or cystic lung lesions, pulmonary fibrochondromatous hamartomas and pulmonary lipomatosis. Morphologically resemble immature placental villi without placental properties.
Methods: We reviewed all cases diagnosed as pulmonary hamartoma or bulla over a period of 11 years (2012-2023) in two university Spanish hospitals. We identified several cases of PTL and retrospectively analysed clinical, radiological, histopathological and immunophenotypic features.
Results: 15 cases were retrieved, 9 associated with hamartomas and 6 detected as focal lesions in bullectomy specimens. There were 10 males and 5 females with 55,26 years mean age and 80% smoking background. Hamartomas were detected incidentally on radiology as solitary well-defined lung lesion (0,7-3 cm) and half of bullectomy specimens were obtained in pneumothorax context. Microscopically, pulmonary parenchyma surrounding main lesions focally showed papillary structures resembling immature placental villi, lined by hyperplastic penumocytes and containing myxoid-edematous fibroadipose stroma with a variable

number of bland stromal cells with clear cytoplasm, proliferating vessels and inflammatory cells. Immunohistochemical analysis were CK7 and TTF1 positive in epithelial component and CD10 in stroma.
Conclusion: Placental Transmogrification of the lung (PTL) is a rare benign pulmonary lesion whose morphological pattern mimic placental villus, with approximately 40 cases described in the literature. Its incidentally observation in hamartomas or bullectomy specimens may cause problems for pathologists and clinicians unfamiliar with this lesion. Although immunostaining could be helpful, its morphology awareness will allow an accurate diagnosis and will avoid confusion.

PS-20-016
Proposal of a grading system for squamous cell carcinoma of the lung – the prognostic importance of tumour budding, single cell invasion and nuclear diameter
N. Zombori-Tóth*, F. Hegedűs, S. Almási, A. Sejben, L. Tiszlavicz, J. Furák, G. Cserni, T. Zombori
*Csongrad-Csanád County Hospital of Chest Diseases, Hungary

Background & objectives: The prognostic factors of lung squamous cell carcinoma (LSCC) are less investigated. Therefore we aimed to evaluate the prognostic impact on overall survival (OS) and recurrence-free survival (RFS) of morphologic features and grading systems among patients with resected LSCC.
Methods: Patients who underwent surgical resection at the Department of Surgery, University of Szeged between 2010 and 2016 were included. Follow-up data were collected from medical charts. Morphological characteristics were recorded from histological revision of slides. Kaplan-Meier analysis, log-rank test, and Cox proportional-hazards model were utilized.
Results: Altogether 220 patients were included. In univariate analysis, higher degree of tumour budding, infiltrative tumour border, larger nuclear diameter, presence of single cell invasion and spread through air spaces (STAS) were associated with adverse prognosis. The previously introduced grading schemes failed to separate three clusters of patients. Therefore, based on our results, we proposed an easily applicable grading scheme focusing on tumour budding, nuclear diameter and single cell invasion. In multivariate analysis, the proposed grading system (HR-OS: 3.41, 95%CI:1.89-6.17; HR-RFS: 2.49, 95%CI: 1.66-3.74), infiltrative border (HR-OS: 3.08, 95%CI:1.46-6.50; HR-RFS: 2.04, 95%CI: 1.15-3.6) and STAS (HR-OS: 3.36, 95%CI:1.59-7.16; HR-RFS: 3.19, 95%CI:1.82-5.58) were independent prognosticators.
Conclusion: We validated the prognostic impact of tumour budding, single cell invasion, nuclear diameter, and STAS in LSCC. We recommend a grading system combining tumour budding, single cell invasion and nuclear diameter for proper prognostic stratification of LSCC patients. Further research is required for the validation of this grading scheme and to gather more data about its reproducibility.

PS-20-017
The more extensive the spread through air spaces (STAS), the worse the prognosis is – semi-quantitative evaluation of STAS in pulmonary adenocarcinomas
N. Zombori-Tóth*, D. Paróczai, J. Lantos, S. Almási, A. Sejben, L. Tiszlavicz, G. Cserni, J. Furák, T. Zombori
*Csongrad-Csanád County Hospital of Chest Diseases, Hungary

Background & objectives: The extent of STAS is less investigated among patients with lung adenocarcinoma who underwent sublobar resection. We aimed to evaluate the extent of STAS semi-quantitatively, to assess its prognostic impact on overall survival (OS) and recurrence-free survival (RFS).
Methods: The number of tumour cell clusters and single tumour cells within air spaces were recorded in three different most prominent areas (200x field of view). The extent of STAS was categorized into three groups and the presence of free tumour clusters (FTC) was recorded.
Results: Altogether 61 patients were included. Recurrence was more frequent with higher architectural grade (p=0.027), presence of lymphovascular invasion (p=0.027) and presence of STAS of any extent (p=0.007). In multivariate analysis, presence of FTC (HR: 5.909; 95%CI: 1.72-20.25; p=0.005) and more pronounced STAS (HR: 3.9; 95%CI: 1.54-9.87; p=0.004) had impact on OS and RFS, respectively. Concerning reproducibility, excellent agreement was found among STAS parameters (ICC range: 0.92-0.94).
Conclusion: More extensive STAS is an unfavourable prognostic factor in adenocarcinomas treated with sublobar resection. As the semiquantitative evaluation of extent of STAS is reproducible, we recommend to include it in histopathology reports.

PS-21 | Poster Session Autopsy Pathology

PS-21-001
Attitudes of clinicians toward autopsy in a tertiary hospital
A.C. Ablaza*, A.B. Asanion
*Baguio General Hospital and Medical Center, Philippines

Background & objectives: Hospital autopsies have been decreasing despite their great benefit to healthcare and legal systems. Considered as the most critical factor contributing to this decline is the clinician's attitude. We aim to determine the association between clinicians' attitude and their demographics.
Methods: The attitude was evaluated through a self-administered survey which consisted of 22 validated questions. Attitudes were interpreted as either positive or negative. Demographic profile with emphasis on the respective clinical department, total years of clinical practice, and number of autopsies observed were studied. Statistical analysis was performed using IBM SPSS version 20.
Results: There were 385 respondents (68 internal medicine, 50 surgery, 50 paediatrics, 35 radiology, 32 obstetrics-gynaecology, 31 anaesthesiology, 28 family medicine, 23 otorhinolaryngology, 18 neuroscience, 18 orthopaedics, 18 psychiatry, 14 ophthalmology) with 174 males (45.2%), 211 females (54.8%), and majority belonged to the 25-34 year age group (42.2%). Most had short-term clinical experience (44.8% <5 years, 8.1% >20 years). Overall autopsy exposure was low (52.1% none, 2% >20 autopsies). Majority expressed positive attitude, greatest in orthopaedics (76.0%), those with <5 year clinical experience (64.5%), and those with >20 autopsies (65.5%). There was significant association between attitude and 8 of 12 departments, 1-20 year clinical practice, and 1-20 year autopsy experience ($p<0.05$).
Conclusion: Factors that influence the clinicians' attitudes toward autopsy can be addressed to promote positive attitudes and thereby increased hospital autopsy rates. Knowledge and experience in autopsy can be enhanced by correcting any misinformation and spreading awareness that one can request it without additional financial burden to the patients' family. We recommend to improve the collaboration between pathologists and clinicians regarding autopsy request, informed consent, and issues of interest, as well as the communication of autopsy findings in a timely manner.

PS-21-002
Systemic fungal infection in patients with haematological malignancies, a retrospective autopsy study
W. Cao*
*Rhode Island Hospital, USA

Background & objectives: Invasive fungal infection (IFI) is one of the causes of death in immunocompromised patients. In this study, we

analysed all invasive fungal infection autopsy cases in patients with haematological malignancies over the past twenty years.
Methods: A retrospective study of autopsies was performed on patients with invasive fungal infection and haematological malignancies at Rhode Island Hospital and The Miriam Hospital from 2000 to 2021. The pertinent clinical information was collected and the pathologic data were reviewed in detail.
Results: Seven cases were found to have invasive fungal infection, including 4 males and 3 females. The average age at death was 43.2 years (range 4-79 years). Of 7 cases, invasive candidiasis (2/7, 28.6%), invasive mucormycosis (1/7, 14.3%), invasive scedosporium prolificans (1/7, 14.3%), invasive fusarium (1/7, 14.3%), and mixed candida and mucor or aspergillus and mucor (2/7, 28.6%). Most commonly involved organs were lungs (7/7), heart (5/7), kidneys (5/7), thyroid gland (4/7), brain (4/7), spleen (4/7), liver (3/7), lymph nodes (2/7) and GI tract (2/7). Four cases had acute inflammation and abscess formation. The other three cases did not have acute inflammation. All cases did not have granuloma formation.
Conclusion: The most common organisms of IFI were candida, mucor and aspergillus species. The most commonly involved organs were lungs, heart, kidneys, thyroid gland, brain and spleen. More than 50% cases had acute inflammatory responses.

PS-21-003
Expect unexpected - experiences on neuropathological findings in autopsy material; a case report series
P. Grochowski*, T. Schaller, I. Kleinlein, B. Märkl, F. Liesche-Starnecker
*General Pathology and Molecular Diagnostics, Medical Faculty, University of Augsburg, Germany

Background & objectives: The role of autopsies is gradually decreasing in pathologists' routine. In our experience, they often deliver unexpected, interesting findings, contributing to clinically known disease patterns. We present a case series of patients diagnosed postmortem with relevant, partially unforeseen neuropathological lesions.
Methods: The reports from all autopsies conducted in our institute in 2022 were evaluated for relevant neuropathological findings and compared to available clinical data, focusing on previously undiagnosed pathologies. Age-related and terminal changes, e.g. terminal oedema, as well as common alterations, especially hypertensive microangiopathy, were not taken into account.
Results: Brain examination was performed in 175 of 201 autopsies. In 53 (30,3%), relevant cerebral pathologies were found, of which 33 (18,9%) were not clinically known. For eight (4,5%) deceased, cerebral involvement was main cause of death. For example, seven primary and ten secondary neoplasms were detected, in two cases classified as cause of death (intravascular DLBCL and diffuse midline glioma, H3 K27-altered). We also found five benign incidental tumours. Four cases presented with neurodegenerative diseases, including one with so far undiagnosed Parkinson's disease. Brain autopsy of one case with the very rare Bornavirus encephalitis was included, as well as one limbic encephalopathy and one infant meningocerebral angiodysplasia.
Conclusion: Using the example of brain autopsy, we demonstrate that many unusual and unexpected pathologies are waiting to be found. Standardized procedure and established cooperation with clinical counterparties can contribute to higher prevalence of findings. In broader perspective, if pathologists deliver more accurate information about cerebral pathologies, that often occur in the background of complex clinical pictures, more attention and carefulness can be prompted to clinicians, which could lead to a better standard of care.

PS-21-004
Retrospective study in 20 years of post-mortem and additional clinical examination of (young)adults
M. Hoogland*, T. Wemeijer, N. van Zanten, W. Duijst
*Isala, The Netherlands

Background & objectives: A retrospective study to gain insight into the cause of death in deceased (young) adults, by analysing autopsies and other (post-mortem) clinical examinations (including radiology, toxicology, medical microbiology and clinical chemistry) emphasizing their contribution into finding the cause of death.
Methods: Between January 2000 – October 2022, adults within 18-45 years were included who underwent a clinical autopsy at a hospital in Zwolle, the Netherlands. Inclusions had a natural cause of death. For each patient the post-mortem examination and their contribution to diagnosing the cause of death were determined, among other things. Collected data was processed in a database and analysed.
Results: Within the research period, 2867 autopsies were performed. 212 autopsies were included, 54 (25,5%) expected and 158 (74,5%) unexpected deaths. Post-mortem examination was subdivided into histology, immunohistochemistry, clinical chemistry, medical microbiology, radiology, toxicology and genetics. 116 deceased had an unknown cause of death (7 expected vs. 109 unexpected). After post-mortem examination, this category decreased to 15 deaths (expected 0 vs. unexpected 15). Of the 96 presumed causes of death for autopsy, 16 (16,7%) cases were stated as Goldman score 1 discrepancy, which led to reclassification of the primary diagnose. In order of most to least contributing post-mortem examination is histology, immunohistochemistry, medical microbiology, toxicology radiology, genetics, clinical chemistry.
Conclusion: Performing post-mortem examinations reduces the number of unknown causes of death, both in expected and unexpected deaths. Both categories contain discrepancies between presumed causes of death and established causes after autopsy. A combination of several post-mortem examinations gives the greatest chance of determining/confirming cause of death. Additionally, clarity into causes of death provides a better alignment of national statistics with the actual situation. Over the years, more postmortem examinations have been performed, however, post-mortem examination is not yet standard practice.

PS-21-005
Complications of SARS-Cov-2 infection in cancer patients – an autopsy-based study
É. Kocsmár*, I. Kocsmár, Á. Jakab, T. Várkonyi, T. Glasz, K. Danics, A. Kiss, Z. Schaff, G. Lotz
*Semmelweis University, Department of Pathology, Forensic and Insurance Medicine, Hungary

Background & objectives: Autopsies performed during the severe acute respiratory syndrome-2 (SARS-CoV-2) infection and disease (COVID-19) pandemic provide insights into the specific features of COVID-19 in cancer patients particularly susceptible to infections but whose altered immunological status may affect the disease course.
Methods: Between July 2020 and the end of 2022, a total of 2548 adult autopsies were performed in our department. COVID-19-positive cases were classified as cancer (102 cases) and non-cancer (439 cases) patients and from the second wave onwards, subgrouped as wave 2/3/4/5/5+ according to the course of the pandemic (autopsies were not allowed in the first wave).
Results: COVID-19 was significantly more frequent direct cause of death in non-cancer (77.3%) than in cancer patients (48%,$p<0.0001$), predominantly during waves 2-3 ($p<0.001$). Mild COVID-19 was more common in cancer (33.3%) than non-cancer patients (14,6%,$p<0.0001$). In non-cancer cases, COVID-19 was a significantly more frequent direct cause of death in waves 2-3 (83.8%) than in the second half of the pandemic (67.6%,$p=0.0001$), when mild course of infection/disease was significantly more common (23.7% vs. 8.5% in waves 2-3,$p<0.0001$). In cancer patients, no similar difference was observed

between the initial and later waves. Bacterial over-infection with viral pneumonia was more prevalent in both cancer and non-cancer patients in the later waves of pandemic (p=0.04/p<0.0001).
Conclusion: In cancer patients, the course of COVID-19 was much more balanced during the pandemic than in non-cancer patients, who more often had severe, fatal COVID-19 in the early disease waves. This may be partly due to the relative immunosuppressed status of cancer patients, and to the fact that even early/mild viral infection can more easily upset the balance of their condition, leading to death from their underlying cancer or its other complications.
Funding: K_22 142604 grant of the National Research, Development and Innovation Office (Hungary)

PS-21-006
Expression of calpain 10 in different mechanisms of heart cell death
K. Matušan Ilijaš*, I. Medved, A. Ferenčić, S. Arbanas, L. Kunišek
*Clinical Hospital Center Rijeka, Croatia

Background & objectives: Calpains are cellular proteins involved in different diseases with potentially prophylactic and therapeutic implications. The aim of the study was to analyse calpain 10 expression in heart cells during ischemia, infarction, apoptosis, hyperglycaemia and death by head gunshot.
Methods: Using immunohistochemistry calpain 10 expression was analysed on 205 heart tissue samples taken during forensic autopsies in the case of sudden cardiac death (SCD) caused by myocardial ischemia or infarction in diabetic (D) and non-diabetic (ND) patients as well as in the case of head gunshot. TUNEL method was used to determine the degree of apoptosis.
Results: Cardiomyocytes calpain 10 expression was higher in non-ischemic than in ischemic/infarction region of SCD group (P<0.001) with negative correlation to degree of cardiomyocytes apoptosis (rs=-0.593; P<0.001) in D as well as ND group. The calpain 10 expression was also significantly higher in D than in ND group as well as in head gunshot group (P<0.001) than in SCD group (P<0.001). Among other heart cells, only endothelial cells showed similar results as cardiomyocytes in comparison of non-ischemic region to ischemic/infarction region of SCD group (P<0.001). On the contrary, non-cardiomyocytes followed the results of cardiomyocytes when D and ND group was compared at the statistically significant level.
Conclusion: Calpain 10 upregulation in SCD and death by head gunshot but also diabetes mellitus could be explained by its protective role preventing programmed cell death during homeostasis dysregulation. This is particularly important in the case of cardiomyocytes, but similar results for endothelial cells prove their important role in tissue maintenance through its regeneration. Calpain 10 upregulation in cardiomyocytes as well non-cardiomyocytes in patients with diabetes mellitus confirms previously well-established molecular background of this disease.

PS-21-007
Autopsy findings and thromboembolic complications in patients died with COVID-19
T. Muzashvili*, B. Märkl, P. Adam
*Pathology, Faculty of Medicine, University of Augsburg, Germany

Background & objectives: The symptomology of patients infected with the novel coronavirus disease (SARS-CoV-2 caused COVID-19) shows a great variability. After clinical observations and autopsy findings, it became clear that the disease causes acute respiratory distress syndrome (ARDS) including angiopathy, endotheliitis and thrombosis.
Methods: We have analysed 148 autopsy cases of patients died with COVID-19 infection with a main focus on thromboembolism of central or peripheral lung arteries. Additionally, the presence of associated acute myocardial and cerebral infarcts was investigated. Furthermore, we analysed the application of invasive mechanical ventilation and its correlation with thromboembolic complications.
Results: We compared our findings with a control group (CG-1) of four patients died with respiratory syncytial virus (RSV) pneumonia, 11 patients died with influenza virus and a group of 29 patients with proven SARS-CoV-2 infection but a cause of death which was not related to COVID-19 (CG-2). All statistical tests were performed using SPSS software. Autopsy revealed central lung arterial thrombosis in 8 of 148 patients (5%); peripheral lung artery thromboembolism was seen in 23/148 cases (16%); acute myocardial infarct was detected in 7 (5%) und acute cerebral infarct in 2 cases (1%). In CG-2 we did not find any events of thromboembolism or acute myocardial or cerebral infarct.
Conclusion: In contrast to many previous reports we identified in this large study pulmonary thromboembolic events in a low frequency in fatal cases of COVID-19. Further investigations are currently underway to investigate the occurrence of capillary fibrin thrombi.

PS-21-008
Evolving patterns of drug and alcohol toxicity; a single-institution review
D. O'Connor*, C. Mulvey, E. O'Connor, K. O'Hare
*Coombe Hospital, Ireland

Background & objectives: The use of toxicology as a key ancillary investigation in autopsy practise is of essential importance. The aim was to analyse the patterns of lethal drug and alcohol toxicity at our autopsy practise to assess the importance of toxicological analysis.
Methods: All autopsy reports at our institution between 2018 and 2021 were analysed. The cause of death and the presence of positive toxicology was recorded. Lethal overdoses of non-illicit drugs such as paracetamol were excluded. For any toxicological result that contributed to death, the exact agent was documents.
Results: 599 autopsy reports were analysed. Of these, the cause of death was directly related to lethal drug and/or alcohol toxicity in 12% of cases (n=72). 57.5% (n=23) of drug and alcohol toxicity cases were related to multidrug toxicity. In 22.2% (n=16) of drug and alcohol toxicity cases, a single drug or class of drug present within the lethal range resulted in death. Of these, 81.2% (n=13) were due to opiates, including oxycodone, heroin and methadone. Alcohol toxicity alone was fatal in 9.7% (n=7) of cases, with alcohol and benzodiazepine toxicity combined fatal in 2.7 % (n=2) of cases.
Conclusion: 12% of autopsies at our institution had a cause of death directly related to lethal drug and alcohol overdoses. The majority of single drug overdoses were due to opiates. Autopsy practise is constantly evolving, with the use of ancillary investigations paramount to successfully identifying the causes of death in many situations. Our study highlights the role of toxicology as an essential investigation and details the evolving patterns of drug and alcohol toxicities in our population.

PS-22 | Poster Session Cardiovascular Pathology

PS-22-002
Calcified aortic valve disease (CAVD) in autopsy cases
S. Glumac, R. Janković*, J. Varda, M. Jovanović
*Institute for Pathology, Medical Faculty, University of Belgrade, Serbia

Background & objectives: The calcifications in CAVD represents actively produced osteoid matrix by osteiod producing cells in response to inflammatory milieu. The origin of those cells is still unclear; they are either activated valvular interstitial cells (VICs), or transformed macrophages with osteoblast-like features.

Methods: Prospectively sampled five aortic valves of five adult patients referred to the autopsy at the Institute for Pathology, Medical Faculty, University of Belgrade in period of October to Depscember 2022, in whose CAVD was not diagnosed antemortem. The valves were grossly analysed, measured and sampled for microscopic evaluation in order to immunophenotypically assessed osteoid producing cells.
Results: There were three male and two female patients with mean age 74.9 (66-88). Grossly measured AV circumference averaged 5.72 cm, (5.4-6 cm), while recalculated AVA (Aortic valve area) averaged 2.62 cm2. On von Kossa special staining were detected multiple diffuse calcified nodules, as well as one larger calcified nodule on all valves. In the vicinity of those calcified nodules and osteogenic matrix were present spindle cells which immunohistochemical phenotype was in favour of VICs (Vimentin+/CD68-/CD34-), while CD68+ macrophages were distant and peripherally distributed. Endothelial erosion above the calcified area, as well as CD34+ areas of neoangiogenesis, were found in 2/5 aortic valves.
Conclusion: Nowadays it is known that calcifications in CAVD are not passive and degenerative in nature, but actively produced osteoid matrix. In our study present osteoid producing spindle cells were characterized as activated VICs. However, the origin of osteoid producing cells is still under debate and further research in phenotyping of these cells is needed and highly appreciated in order to better understand underlying pathological mechanisms included in CAVD development and possible medical therapeutic approaches.

PS-22-003
Cardiovascular mortality and autonomic innervation in myocardial sleeves around pulmonary veins
I. Kholova*, D. Depes, A. Mennander, R. Vehniäinen, T. Paavonen
*Tampere University and Fimlab Laboratories, Tampere, Finland

Background & objectives: Autonomic nerve impairment in the myocardium may be associated with an increased risk of cardiovascular morbidity and mortality. We aimed to study autonomic neural remodelling in myocardial sleeves around pulmonary veins (PVs) and atrial-PV ostia with immunohistochemistry and clinicopathological correlations.
Methods: PVs were collected from 37 and atrial-PV ostia from 17 human autopsy hearts. The density of autonomic nerves was quantified by measuring the area of immunohistochemical staining for sympathetic (tyrosine hydroxylase, TH) and parasympathetic (choline acetyltransferase, CHAT) nerves and ganglia. Growth-associated protein 43 (GAP43) was used as a neural growth marker.
Results: In the PV cohort, subjects with immediate cardiovascular cause of death had significantly decreased sympathetic nerve density in fibro-fatty tissue vs. those with non-cardiovascular cause of death (1624.53 µm2/mm2 vs. 2522.05 µm2/mm2, P=0.038).
In the atrial-PV ostia cohort, parasympathetic nerve density in myocardial sleeves was significantly increased in subjects with underlying cardiovascular cause of death (19.48 µm2/mm2) compared to subjects with underlying non-cardiovascular cause of death (P=0.034).
Conclusion: Heterogeneous autonomic innervation around PVs and atrial-PV ostia are associated with cardiovascular morbidity and mortality.
Funding: VTR grant, Aarne Koskelo Foundation

PS-22-004
Histone methyltransferase DOT1L mediates NLRP3 inflammasome priming and activation in atherosclerotic apolipoprotein E knockout mice; potential functional implication in human atherosclerosis
A. Manea*, M. Vlad, A. Lazar, S. Manea
*Institute of Cellular Biology and Pathology "Nicolae Simionescu" of the Romanian Academy, Romania

Background & objectives: Alterations in epigenetic mechanisms induce adverse transcriptomic signatures that are associated with the pathoetiology of atherosclerotic disease. The study aimed at elucidating the potential implication of DOT1L epigenetic enzyme in mediating NLRP3 inflammasome priming and activation in experimental atherosclerosis.
Methods: Non-atherosclerotic and atherosclerotic tissue specimens derived from patients undergoing extended carotid endarterectomy, ApoE-/- mice and polarized pro-inflammatory (M1)/anti-inflammatory/(M2) human macrophages (Mac) were examined employing immunofluorescence microscopy, real-time PCR and Western blot. ApoE-/- mice fed a normal/atherogenic diet were treated with 5 mg/kg EPZ004777, a specific DOT1L inhibitor, or vehicle, for 4 weeks. Resting and M1/M2-Mac underwent EPZ pharmacological interventions.
Results: The mRNA and protein levels of DOT1L, NLRP3, caspase 1 (Cas1), IL1β and IL18 were found significantly elevated in human atherosclerotic lesions, atherosclerotic aorta of ApoE-/- mice and in cultured M1-Mac. The colocalization of DOT1L and NLRP3 inflammasome components with lesional Mac within both human and mouse atherosclerotic plaques was demonstrated by immunofluorescence microscopy. Systemic DOT1L blockade led to significant decreases in mRNA and protein levels of NLRP3, Cas1, IL1β, and IL18 in the atherosclerotic aorta of ApoE-/- mice. Inhibition of DOT1L suppressed the mRNA and protein up-regulation of NLRP3, Cas1, IL1β and IL18 in cultured pro-inflammatory M1-Mac.
Conclusion: DOT1L-induced histone H3 methylation (H3K79me1/me2/me3) generates long-lasting transcriptomic alterations, since unlike other histone methyltransferases, no specific demethylases of these histone modifications have been characterized. Activation of NLRP3 inflammasome leading to increased production of IL1β and IL18 is instrumental in atherogenesis. We provide evidence that DOT1L contributes to NLRP3 inflammasome priming and activation in both in vivo and in vitro experimental settings of atherosclerosis. The data point to DOT1L as a promising therapeutic target to reduce inflammation in atherosclerosis.
This work was supported in part by grants from the Ministry of Research, Innovation and Digitization, CNCS – UEFISCDI (PN-III-P4-ID-PCE-2020-1898, PN-III-P1-1.1-TE-2021-0180), within PNCDI III and from the Romanian Academy.

PS-22-005
Pharmacological inhibition of histone methyltransferase SET7 reduces inflammation and fibrosis in the kidney of diabetic mice
S. Manea*, A. Lazar, M. Vlad, A. Manea
*Institute of Cellular Biology and Pathology "Nicolae Simionescu" of the Romanian Academy, Romania

Background & objectives: Inflammation and fibrosis are important mechanisms leading to renal dysfunction and ultimately kidney failure in diabetic kidney disease (DKD). We aimed to uncover the potential role of histone methyltransferase SET7 in mediating pro-inflammatory and pro-fibrotic responses in diabetic kidney.
Methods: Male non-diabetic and streptozotocin-induced diabetic C57BL/6J mice were treated with 5 mg/kg (R)-PFI 2 hydrochloride, a specific SET7 inhibitor, or its vehicle for 4 weeks. Human endothelial cells (EA.hy926, EC) underwent PFI pharmacological interventions and transient transfection assays employing a human SET7 expression vector. Histochemistry, immunofluorescence microscopy, real-time PCR, and Western blot techniques were used to examine the samples.
Results: Significantly elevated mRNA/protein levels of SET7, pro-inflammatory cell adhesion molecules (E-selectin, ICAM-1, VCAM-1), extracellular matrix proteins (collagen IV/Col IV, fibronectin/FN, laminin/LM), and pro-fibrotic factor TGFβ were determined in the kidney of diabetic mice. SET7 blockade significantly reduced glomerular hypertrophy, and the gene and protein expression levels of E-selectin, ICAM-1, VCAM-1, Col IV, FN, LM and TGFβ in diabetic kidney. The expression of SET7 was significantly induced in high glucose-exposed EC. PFI intervention suppressed the high glucose-induced

up-regulation of the examined pro-inflammatory and pro-fibrotic molecules in cultured human EC. Transient overexpression of SET7 determined significant increases in E-selectin, ICAM-1, VCAM-1, Col IV, FN and LM transcript levels in EC.
Conclusion: Dysregulated epigenetic mechanisms have been increasingly implicated in pathoetiology of diabetes-associated vascular complications. Histone methyltransferase SET7 induces H3K4me1 modification, an epigenetic histone imprint that is associated with a long-lasting transcriptional activation and responsiveness of the target genes. In this study we provide evidence that pharmacological inhibition of SET7 limits the pro-inflammatory and pro-fibrotic responses in diabetic kidney. The data suggest that pharmacological targeting of SET7 could be considered for further pre-/clinical assessment as potential supportive therapeutic strategy in DKD.
This work was supported in part by grants from the Ministry of Research, Innovation and Digitization, CNCS – UEFISCDI (PN-III-P1-1.1-TE-2021-0180, PN-III-P4-ID-PCE-2020-1898), within PNCDI III and from the Romanian Academy.

PS-23 | Poster Session Digestive Diseases Pathology - Liver/ Pancreas

PS-23-001
Metal mining of liver tissues using Laser Ablation-Inductively Coupled Plasma Mass Spectrometry provides multi-elemental resolutive spatial distribution

P. Allaume*, J. Le Maitre, B. Turlin, E. Bardou-Jacquet, O. Loreal, M. Ropert-Bouchet
*Rennes University Hospital, Departement of Pathology, France

Background & objectives: Metal homeostasis disorders contribute to liver disease. Knowledge of metal distribution abnormalities may improve disease understanding. Our objective is to perform metal imaging in paraffin embedded human liver biopsies by using Laser Ablation coupled with Inductively Coupled Mass Spectrometry (LA-ICP-MS).
Methods: Liver biopsy samples were collected in the University Hospital, Rennes from patients exhibiting either a cirrhosis, a genetic hemochromatosis (GH) or a Wilson's disease (WD). Standard histological stains assured a morphological control. LA-ICP-MS was performed on 3µm thick unstained paraffin slides with a high spatial resolution (10µm spot size). Elemental distribution of 56Fe, 65Cu, 66Zn, 78Se and 24Mg was analysed.
Results: LA-ICP-MS analysis of 20 paraffin embedded human liver biopsy samples (5 cirrhosis, 10 GH, 5 WD) enables easy recognition of histological structures including portal tracts, fibrous septa, centrolobular veins and iron-free foci in GH. Iron and copper distribution correlates with the morphological analysis using standard stains (Perl's and rhodanine respectively). Morever, LA-ICP-MS is able to accurately demonstrate local iron and copper distribution in advanced cirrhosis patients, whereas dry weight biochemical quantification may result in misquantification. LA-ICP-MS also enables investigation of the distribution of metals inaccessible to standard histological analysis (66Zn, 78Se and 24Mg). Results are consistent with the known literature.
Conclusion: LA-ICP-MS is an innovative, highly sensitive and resolutive method for simultaneous multi-metal imaging in paraffin embedded human liver samples. The obtained data can be superposed with standard histological procedures. Pre-analytic constraints are few, enabling an easy integration into care workflow. Biochemical determination, current gold standard for liver trace element quantification, does not enable topographical analysis. LA-ICP-MS is therefore a powerful technique that open new opportunities for studying metal homeostasis disorders, and a potential tool in the practice of pathology.

PS-23-002
Evaluation of tumour budding, desmoplastic reaction, and lymphocytic infiltration in predicting survival for pancreatic ductal adenocarcinoma

A. Alpsoy*, K. Şimşek, A. Yavuz, B. Altunay, M. Karaca, B. Ünal, C.I. Bassorgun, A.M. Tatli, G.Ö. Elpek
*Akdeniz University Department of Pathology, Turkey

Background & objectives: Recently morphological assessment of tumour budding(TB) has been revealed as a promising prognostic finding to predict tumour behaviour in Pancreatic Ductal Adenocarcinoma(PDAC). Therefore, this study aims to investigate the prognostic role of TB, desmoplastic reaction(DR), and lymphocytic infiltration in PDAC.
Methods: The study group consisted of 100 patients with PDAC (from 2005 to 2020). Both peritumoral and intratumoral budding was assessed according to the ITBCC. Desmoplastic reaction (DR) was classified into three groups based on the maturation of tumour stroma. The evaluation of TIL was determined semi-quantitatively based on a 5% cutoff value. Statistical analysis was performed using SPSS version 27.
Results: A strong relationship was observed between the intratumoral and peritumoral budding scores (r:0,890). An inverse correlation existed between a high peritumoral budding score and a low TİL ($p<0,001$). The peritumoral budding score and TİL were associated with T, lymphovascular invasion, lymph node metastasis, and stage ($p<0,005$). Univariate analysis indicated poor survival rates were associated with lymphovascular invasion, lymph node metastasis, high peritumoral, and intratumoral budding ($p<0.001$). On multivariate Cox regression analysis, intratumoral and peritumoral budding scores were determined as independent prognostic factors.
Conclusion: Our findings support that the evaluation of TB according to ITBCC criteria can be performed to stratify patients with PDAC for treatment and prognosis. In addition, the close relationship between intratumoral and peritumoral budding warrants further research with larger series to determine whether intratumoral budding assessed in small biopsies provides to determine the behaviour and the treatment strategy for unresectable PDAC.

PS-23-003
Assessment of PD-L1 expression correlated with the MSI status in extrahepatic cholangiocarcinoma

R. Ardeleanu*, S. Zurac, T. Voiosu, C.I. Diaconu, M. Birligea, D. Raduta, A. Cernat-Stefan, M. Matanie, C. Popp
*Colentina Clinical Hospital, Romania

Background & objectives: We aim to predict the prognostic and therapeutic value of the Programmed-death Ligand 1 (PD-L1) marker expression in extrahepatic cholangiocarcinomas, along with a potential correspondence with the microsatellite instability (MSI) status, as a prospect of targeted immunotherapy in these patients.
Methods: This retrospective study included 34 patients who underwent tissue sampling from radiologically proven infiltrative tumours, with a histological diagnosis ranging from atypical biliary epithelium to carcinoma. We performed immunohistochemical stains for the four mismatch repair proteins (MSH2, MSH6, MLH1, PMS2) and evaluated the PD-L1 membranous expression in both atypical and tumour cells, with a positive cutoff point set at 5%.
Results: Five cancer biopsies out of 30 (16,6%) showed PD-L1 positivity, with the highest percentage of expression being 10% and a male sex predominance (80%) within this group. Surprisingly, two of these patients displayed positive staining in biopsy samples of atypical biliary epithelium as well. Four cases demonstrated a microsatellite instability status: two from the PD-L1 positive category, one being a carcinoma with negative labelling for all the four markers and one with MSH6 and MLH1 loss in the abnormal biliary specimen. The remainder of two were PD-L1 negative, comprising a PMS2 and MLH1

negative carcinoma and an atypical biliary epithelium showing absence of staining for all the mismatch repair proteins.
Conclusion: Extrahepatic cholangiocarcinoma is an aggressive neoplasm with a dismal prognosis, partly due to limited treatment options. The PD-L1 positivity in a significant proportion of the cancer cases raises the potential utility of the immunotherapy regimen in this particular pathology. A targeted therapy aimed at immune checkpoint regulators, such as Programmed-death Ligand 1 and correlated with the assessment of the mismatch repair proteins expression, could predict the clinical outcome and improve survival for these patients.
The study was supported by grants of the Ministry of Research, Innovation and Digitization, CCCDI-UEFISCDI, project number PN-III-P1-1.1-TE-2021-0801 .

PS-23-004
Impact of resection margins on recurrence patterns and prognosis in resectable pancreatic ductal adenocarcinoma – a long-term population-based cohort study
H. Blomstrand*, H. Olsson, B. Björnsson, H. Green, N. Elander
*Department of Pathology, Linköping University Hospital, Department of Biomedical and Clinical Sciences, Linköping University, Sweden

Background & objectives: Survival outcomes remain poor following resection of pancreatic cancer. To better guide postoperative management, more accurate prognostic models are needed. Previous studies suggest improved prognostic value when dividing R1 resections with regards to whether mobilization or transection margins were involved.
Methods: In a population-based retrospective study covering 275 pancreatic resections over eleven years, all specimen slides were carefully reviewed. The prognostic impact of pathological, laboratory and surgical factors, including margin clearance with R1 cases divided into affected margin type (mobilization (R1-mob)/transection (R1-trans)) or distance (standard <1mm clearance(R1-1mm)/tumour on ink(R1-ink)), were analysed with Cox regression.
Results: Resection margin status was found to be a significant prognostic factor in the univariable analyses regardless of whether the R1-group was subdivided by margin type (median OS R1-mob 24.1 months, R1-trans 18.7 months and hazard ratio (HR) R1-mob 1.39, R1-trans 1.93, p<0.001 (R0 resections as reference)) or clearance (median OS R1-1mm 22.6 months, R1-ink 14.5 months and HR R1-1mm 1.43, R1-ink 2.40, p<0.001). However, only the latter of the two was an independent prognostic factor in the multivariable analysis (p=0.006) together with year of resection (survival improving over time), lymphovascular invasion, tumour differentiation grade, TNM 8th edition stage and adjuvant treatment.
Conclusion: In the present study resection margin status with subdivision of the R1 group by margin clearance proved to be superior to division by margin type. The study indicates that tumour on ink might convey additional prognostic information and should be highlighted in the pathology report when present.
Funding: FORSS (grant number 941207) County of Östergötland (grant numbers 962449 and 935580)

PS-23-005
Mettl14-mediated m6A modification prevents NASH by regulating endoplasmic reticulum stress and oxidative stress
Y. Chen*, Y. Shi
*Department of Pathology & Institute of clinical Pathology, West China Hospital, Sichuan University, Chengdu, China

Background & objectives: N6-methyladenosine (m6A) mRNA modification plays critical roles in multiple diseases, including Non-alcoholic steatohepatitis (NASH). However, the role of m6A methyltransferase like 14 (Mettl14) in NASH remains largely unknown. Here, we identify Mettl14 as a key negative regulator of NASH pathogenesis.
Methods: The role of Mettl14 was verified in Mettl14 deficient hepatocytes and hepatocyte-specific Mettl14 knockout mice, which were fed with methionine and choline deficient diet (MCD). Western Blot and RNA dot blot were used to determine the expression of Mettl14, as well as global m6A modification. Furthermore, the molecular mechanisms were validated with histopathology, electron microscopy, RNA-sequencing and m6A-sequencing.
Results: An overwhelming proportion of m6A-modified genes with up-regulated m6A levels is identified in the MCD-induced NASH mouse, and Mettl14 is upregulated. Hepatocyte-specific deletion of Mettl14 drives NASH progression, which is histologically characterized by diffuse macrovesicular steatosis of hepatocytes, infiltration of inflammatory cells, and obvious fibrosis in portal areas. And more lipid droplets are deposited in Mettl14 ablated hepatocytes after palmitic acid treatment. mRNA transcripts, such as Stt3a, P4hb, Lman1, GCLC, and SLC7A11, encoding proteins involved in polypeptide processing and the synthesis of GSH, are m6A-hypomethylated, and their mRNA and protein levels are decreased. The hepatocytes are under severe endoplasmic reticulum (ER) stress and oxidative stress.
Conclusion: We demonstrate a mechanism of Mettl14 in inhibiting NASH by negatively modulating ER stress and oxidative stress in an m6A-dependent manner. Mettl14 deficiency directly induces excessive ER stress by inhibiting the expression of ER polypeptide processing proteins, which in turn indirectly induces oxidative stress. On the other hand, Mettl14 inhibits the antioxidant reaction mediated by GSH, resulting in severe oxidative stress, thereby promoting the occurrence and development of NASH.

PS-23-006
Loss of F-Box and leucine rich repeat protein 5 (FBXL5) expression is associated with poor survival in patients with hepatocellular carcinoma
Y.A. Cho*, S. Kim, C.K. Park, S.Y. Ha
*Samsung Medical Center, Republic of Korea

Background & objectives: The deficiency of F-Box and leucine rich repeat protein 5 (FBXL5), an iron-sensing ubiquitin ligase, triggers carcinogenesis of hepatocellular carcinoma (HCC) due to iron overload. However, the expression of FBXL5 and its clinical implication have not been elucidated in HCC.
Methods: We investigated FBXL5 protein expression using immunohistochemistry in HCC tissue samples of two institutes, Samsung Medical Center and Hallym University Sacred Heart Hospital. After setting cut-off value using X-tile software, we evaluated the relation between FBXL5 expression and various clinicopathological parameters. For external validation, the Cancer Genome Atlas (TCGA) cohort was used.
Results: Among 374 cases, 70 cases showed low FBXL5 expression, which is less than 5% of tumour (18.7%). Low FBXL5 expression group showed inferior disease-specific survival (DSS; P = 0.002) and recurrence free survival (RFS; P=0.001) compared to high FBXL5 expression group and associated with non-viral aetiology (P = 0.024). Similar to our cohort, cases with low FBLX5 mRNA level showed inferior DSS and RFS (P<0.001 and P=0.002, respectively) than cases with high FBLX5 mRNA level in TCGA cohort.
Conclusion: Low expression of FBXL5 is associated with inferior DSS and RFS in HCC patients in two institute cohorts and related with non-viral aetiology. FBXL5 can be used as a potential prognostic markers and therapeutic target for HCC.

PS-23-007
Molecular heterogeneity of Primary liver carcinomas: early study
J. Espírito Santo*, A.F. Ladeirinha, A. Alarcão, E. Strelet, M. Reis, R. Santos, L. Carvalho
*Adult Liver Transplantation Unit, Coimbra Hospital and University Centre, Portugal

Background & objectives: Primary liver carcinomas (PLC) comprise hepatocellular carcinoma (HCC), combined hepatocellular-cholangiocarcinoma (cHCC-CCA) and intrahepatic cholangiocarcinoma (iCCA), displaying continuous histopathological features and distinct molecular profiles across PLC spectrum heterogeneity.
We aimed to investigate gene expression profiles in a small series of PLC.
Methods: Seven patients (5 cirrhotic), with main risk factors being alcohol intake and viral hepatitis, undergoing liver transplantation/resection were studied, concerning 7 PLC: 2 HCCs CK19-/CK7- and 2 HCCs CK19+/CK7+, 1 cHCC-CCA and 2 iCCAs, classified according with WHO 2019 histopathological criteria. Gene expression profiling and sequencing of relevant microdissected areas were performed by next-generation sequencing (Genexus, Oncomine Precision Assay Panel).
Results: Mutations in EGFR predominated in HCC CK19-/CK7-; CTNNB1 in HCC CK19+/CK7+; TP53/FGFR3 in cHCC-CCA and ALK in iCCA; TP53 mutations: HCC CK19+/CK7+, cHCC-CCA and iCCA; ALK and EGFR mutations: HCC CK19-/CK7-, HCC CK19+/CK7+ and iCCA. HCC CK19+/CK7+ and iCCA shared RET, ALK, EGFR and TP53 mutations; while PIK3CA mutations were present in HCC CK19-/CK7- and cHCC-CCA. AR and KIT mutations were exclusively seen in cHCC-CCA. HCC CK19+/CK7+ shared more mutations with iCCA than HCC CK19-/CK7- with iCCA; cHCC-CCA and iCCA shared more mutations than HCC and cHCC-CCA. An association ($p<0.05$) was determined between: ERBB3, IDH2, MAPK2 and PDGFRA mutations and HCC CK19+/CK7+; FGFR1/FGFR4 and HCC CK19-/CK7-; AR/KIT mutations and cHCC-CCA.
Conclusion: This preliminary study suggests that HCC with cholangiocytic features and cHCC-CCA share hepatocarcinogenic pathways with iCCA, being genetically closer. Acknowledging a probable continuous mutational landscape might elucidate the interpretation in between histopathological criteria and cell of origin. HCC CK19+/CK7+ targeted therapy might benefit from a CTNNB1, TP53, ALK, EGFR, MAP2K2, RET, PTEN, and IDH2 panel, standardized for PLC spectrum. This knowledge would allow better understanding the clinical course and PLC heterogeneity, together with improving tumour classification and treatment.
Funding: ROCHE-APEF (Portuguese Association for the Study of the Liver) research grant.

PS-23-008

An HE-only workflow for liver fibrosis assessment using HE-predicted collagen

R. Fick*, G. Balezo, C. Bertram, C. Tilmant, S. Petit, S. Ben Hadj
*Tribun Health, France

Background & objectives: To highlight fibrotic collagen in liver disease, special stains like Masson's Trichrome (MT), Sirius Red (SR), or Saffron (HES) are required. This study aims to highlight collagen directly from Hematoxylin and Eosin (HE) stained liver biopsies using deep learning.
Methods: We obtained 11 retrospective liver cases with varying degrees of fibrosis. For each case, we collected three consecutive slides, each stained with HE, and separately overstained with either HES, MT, or SR. We predict the collagen on the HE (c-HE) using deep learning. We validate our approach by having two pathologists do METAVIR scoring on the special stains and c-HE.
Results: Results reveal a strong pixel-wise correlation between c-HE and each registered special stain (HES: 0.87, MT: 0.78, SR: 0.71) with p-value<1e-5, indicating accurate collagen content inference from HE-stained liver biopsies. Pathologist agreement on METAVIR scores was high, with P1 at 10/11 and P2 at 11/11 cases for both special stains and c-HE. This supports the potential for deep learning to replace special stains in detecting fibrosis, maintaining high-quality METAVIR evaluations.
Conclusion: In conclusion, our study demonstrates that deep learning can accurately infer collagen content from HE-stained liver biopsies, both quantitatively and qualitatively, showing a high correlation with the standard special stains traditionally used to highlight collagen. Moreover, the agreement between pathologists on METAVIR scores remains high when using our digital HE-predicted collagen method, suggesting that this approach can potentially replace the need for special stains in detecting fibrosis without compromising the quality of METAVIR evaluations.

PS-23-009

Hepatic resection for colorectal cancer metastases: the role of the histopathologist as a bridge between science and medicine when assessing background liver pathology following chemotherapy

M. Hanks*, L. Khasati, C. Santos, A. Zaitoun
*Nottingham University Hospital NHS Trust, United Kingdom

Background & objectives: The liver is a common site for colorectal metastases; chemotherapy is often administered prior to hepatic resection leading to regimen specific effects on liver parenchyma. We assessed these changes to enable pathologists to produce informative reports to optimise patient care.
Methods: We reviewed hepatic resection cases containing colorectal metastases between 2013-2022. Samples were assessed for chemotherapy associated regression and non-tumour parenchyma for steatosis, lobular inflammation and hepatocyte balloon degeneration using Brunt Scoring; fibrosis was assessed using Metavir grading. Sinusoidal dilatation was assessed using Rubbia-Brandt grading. Presence of focal hepatocyte plate disruption, peliosis, veno-occlusive disease-like changes or parenchymal extinction lesions were recorded.
Results: 100 cases were reviewed; 74 male and 26 female. Sinusoidal dilatation was seen in 100% of cases with 33% involving over 2/3s of the lobule. Steatosis was noted in 79% with 52 cases showing mild steatosis. Ballooning degeneration was present in 57% of cases and fibrosis in 31%, the most grade was F1 (13%). Lobular inflammation was evident in 62 cases. Hepatocyte plate disruption was noted in 58% of cases and nodular regenerative hyperplasia in 57%; this was most often subtle. 1 case showed peliosis. 16 samples showed veno-occlusive disease-like changes. Parenchymal extinction lesions were seen in 16% of cases.
Conclusion: Our findings highlight the variety of background liver parenchymal changes that occur following chemotherapy in the management of hepatic colorectal metastases. It is important to recognise chemotherapy-induced liver injury as these may reduce hepatic functional reserve and increase morbidity and mortality. Our findings emphasise the importance of multidisciplinary team discussions to maximise patient care and highlights the key role of the pathologist as a bridge between Science and Medicine in the management of patients with hepatic metastases from colorectal cancer.

PS-23-010

Digital spital profiling reveals possible predictive and prognostic markers in pancreatic cancer

S.I. Jeong*, K.R. Lee, S. Lee, J.A. Lee, H.Y. Na, J. Kim
*Department of Pathology, Seoul National University Bundang Hospital, Seongnam, Gyeonggi, Republic of Korea; Department of Pathology, Seoul National University College of Medicine, Seoul, Republic of Korea

Background & objectives: Despite improvements in surgical and medical treatment, the prognosis of pancreatic cancer remains poor. We intended to uncover novel predictive or prognostic markers in pancreatic cancer by using digital spatial transcriptomic and immunohistochemical (IHC) analysis.

Methods: A total of 48 cases of pancreatic cancer which were surgically resected with (NAT group, n=24) or without NAT (UFS group, n=24) in Seoul National Bundang Hospital were included. Tissue microarray (TMA) was constructed followed by spatial transcriptomic analysis using NanoString GeoMx Digital Spatial Profiler Transcriptomic Atlas. IHC for CD3, CD20, CD4, CD8, CD68, CD163 were also performed.
Results: When comparing pan-CK-positive cells in NAT and UFS group, FGD6 and CPB1 gene showed increased expression in NAT group, while SUMO4 and FOXN2 gene expression was increased in UFS group (all $q<0.1$). In CD45-positive cells and remainder cells, PPP1R10 and MFAP4 expression was increased in CAP score 3 group compared with CAP score 2 group (all $q<0.1$). IHC analysis revealed higher CD3, CD4, CD8, CD68, and CD163-positive cells in CAP score 2 group compared with CAP score 3 group (all $p<0.05$). Higher CD68-positive cell density was associated with shorter overall survival (OS) ($p=0.020$) while higher CD8-positive cell density was marginally associated with prolonged progression-free survival (PFS) ($p=0.050$).
Conclusion: FGD6 which is known to be related with micropinocytosis, can be considered as possible target in NAT group. Increased PPP1R10 and MFAP4 expression, and a paucity of immune cells could be predictive markers of response to the NAT. In addition, CD8- and CD68-positive cell density can be prognostic indicator of pancreatic cancer.

PS-23-011
Multi-regional analysis of combined hepatocellular-cholangiocarcinoma reveals histologic diversity and molecular clonality
Y.E. Kim*, H.Y. Na, H. Kim, J.H. Kim, S. Ahn
*Department of Pathology, Seegene medical centre, Seoul, Korea, Republic of Korea

Background & objectives: Combined hepatocellular-cholangiocarcinoma (cHCC-CC) is a rare liver tumour that exhibits both hepatocytic and biliary differentiation within the same tumour. The histology and genomic alteration of recurrent/metastatic cHCC-CC are poorly understood.
Methods: We selected six cHCC-CCs of which recurrent or metastatic tumours were histologically confirmed, consisting of four classic cHCC-CCs and two intermediate cell carcinomas. Clinicopathologic features including histology of primary, and recurrent/metastatic tumours were evaluated. Next generation sequencing was performed in 16 multi-regional and longitudinal tumour samples.
Results: Among four classic cHCC-CC patients, three cHCC-CCs had a previous history of HCC, and two of them were developed after transarterial chemoembolization. In a total of 13 samples from four cHCC-CC patients, the most frequent pathologic variants were TP53 (46.2%), TERT promoter (38.5%), ARID1A mutations (23.1%), and MET amplification (30.8%). Large proportion of mutations were shared by each HCC and CC component, suggesting monoclonal origin of this entity. In ICs, ATM mutation was detected in one patient, and genes commonly altered in HCCs or CCs were not detected. Recurrent or metastatic lesions presented more mutations than primary lesions.
Conclusion: The histology of recurrent/metastatic tumour of cHCC-CC was variable. The genomic profiling of cHCC-CCs revealed similar genomic alterations to HCC, and suggested a monoclonal origin of each HCC and CC component. Genetic alterations in ICs were different from either HCC or CC, suggesting the distinct nature of this tumour.

PS-23-013
An immunohistochemical study of MAGE proteins in hepatocellular carcinoma
M. Lambropoulou*, S. Tologkos, V. Papadatou, A. Panagiotopoulos, T. Alexiadis, A. Mitrakas, C. Alexiadi, V. Lampropoulou, C. Nikolaidou, G. Tripsianis
*Histology-Embryology Lab., Medical Department, Democritus University of Thrace, Alexadroupolis, Greece

Background & objectives: The MAGE protein family consists of more than forty members that have been found overexpressed in various malignancies. This study was designed to detect MAGE-C1 and MAGE-C2 expression in hepatocellular carcinoma, and to correlate their expression with clinicohistopathological parameters.
Methods: We used 57 samples from patients with hepatocellular carcinoma. MAGE-C1 and MAGE-C2 expression was evaluated using immunohistochemistry via monoclonal antibodies for both proteins. Statistical data analysis was performed using the SPSS, version 19.0 (IBM). The chi-squared test and multivariate logistic regression were used to assess the association of individual MAGE-C1 and MAGE-C2 expression with patients' clinicopathological parameters.
Results: Higher expression of MAGE-C1 and C2 was found in males ($p<0.001$, $p<0.001$), patients with history of HBV/HCV ($p=0.008$, $p<0.001$), higher grade tumours ($p<0.001$, $p<0.001$), patients with multiple nodules ($p<0.001$, $p<0.001$), patients with higher AFP levels ($p<0.001$, $p<0.001$) and was also correlated with higher chance of death ($p=0,008$, $p=0.008$). When multiple logistic regression was performed age, presence of HBV/HCV, higher grade, more nodules, higher AFP and status remained independent prognostic factors for high MAGE-C1 expression, while all the parameters tested except for age were independent prognostic factors for high MAGE-C2 expression.
Conclusion: Our research is in accordance with limited studies in the literature which have shown that MAGE proteins could be used as prognostic markers in a variety of malignancies. Based on our results MAGE-C1 and MAGE-C2 are potential biomarkers for prognosis and a perspective therapeutic target in hepatocellular carcinoma. However due to the limited literature on the subject and the small samples amount of our study further research would be appropriate.

PS-23-014
GAD2 is a highly specific marker for neuroendocrine neoplasms of the pancreas
M. Lennartz*, N.B. Dünnebier, N. Blessin, D. Hoeflmayer, S. Dwertmann Rico, S. Kind, C. Fraune, N. Gorbokon, C. Hube-Magg, F. Büscheck, A. Menz, G. Sauter, R. Simon, S. Minner, C. Bernreuther
*University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: Glutamate decarboxylase 2 (GAD2) is the most important inhibitory neurotransmitter and plays a role in insulin-producing β-cells of pancreatic islets. The limitation of GAD2 expression to normal brain and pancreatic islet cells makes GAD2 a potential immunohistochemical diagnostic marker.
Methods: To evaluate the diagnostic utility of GAD2 immunohistochemistry (IHC), a tissue microarray containing 19,202 samples from 152 different tumour entities and 608 samples of 76 different normal tissue types was analysed. Data on progesterone receptor (PR) expression were available on 15,232 tumours from a previous study.
Results: GAD2 positivity occurred in 20 of 152 tumour categories including 5 tumour categories with at least one strongly positive case. GAD2 positivity was most frequent in neuroendocrine carcinomas (58.3%) and neuroendocrine tumours (63.2%) of the pancreas, followed by granular cell tumours (37.0%) and neuroendocrine tumours of the lung (11.1%). GAD2 in <10% of cases occurred in 16 other tumour entities including paraganglioma, medullary thyroid carcinoma, and small cell carcinoma of the urinary bladder. In a cohort of 95 pancreatic and 380 extra-pancreatic neuroendocrine neoplasms, GAD2 had a sensitivity of 64.2% and a specificity 96.3% for pancreatic tumour origin while PR had a sensitivity of 56.8% and a specificity of 92.6%.
Conclusion: GAD2 IHC is a highly useful diagnostic tool for the identification of pancreatic origin in case of neuroendocrine neoplasms with unknown site of origin. The particular strength of GAD2 is its high specificity for pancreatic origin. For the distinction of a pancreatic tumour

origin, both sensitivity and specificity is higher for GAD2 than for PR. The combination of PR and GAD2 further increases sensitivity and specificity.

PS-23-015

RNF135 promoter methylation as a potential diagnostic biomarker distinguishing hepatocellular carcinoma from other adenocarcinomas

B. Ranković*, T. Draškovič, N. Zidar, N. Hauptman
*Institute of Pathology, Slovenia

Background & objectives: Differentiation of hepatocellular carcinoma (HCC) from liver metastases can be challenging. We investigated the methylation status of the promoter region of RING finger protein 135 (RNF135) and its significance as DNA methylation biomarker in different adenocarcinomas.
Methods: DNA was isolated from formalin-fixed paraffin-embedded tissue samples from 14 HCCs, 12 cholangiocarcinomas, 15 pancreatic adenocarcinomas, 6 stomach adenocarcinomas, 7 colorectal cancers and their paired normal tissue samples. The methylation status of RNF135 promoter region was determined by methylation-sensitive high-resolution melting analysis. The methylation status was used to determine sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).
Results: Our results show that RNF135 promoter region was hypermetylated in HCC and hypomethylated in other investigated adenocarcinomas and their paired adjacent normal samples. Methylation status of RNF135 promoter region successfully discriminates between HCC and its adjacent normal liver tissue with a sensitivity of 77%, specificity of 93%, PPV of 0.91 and NPV 0.81. Furthermore, this methylation biomarker can differentiate between HCC and investigated adenocarcinomas with a sensitivity of 77%, specificity of 100%, PPV 1, and NPV 0.93. When testing all tumour and normal samples, methylation status of RNF135 promoter showed an overall sensitivity of 77%, specificity of 99%, PPV of 0.91, and NPV of 0.97 for HCC.
Conclusion: DNA methylation in promoter region of gene RNF135 showed high sensitivity, specificity, PV and NPV for discriminating HCC from other adenocarcinomas and normal samples.

PS-23-016

TIMP1 as venous invasion marker in pancreatic ductal adenocarcinoma

Y. Sung*, M. Kim, S. Hong
*Republic of Korea

Background & objectives: Venous invasion is known to be the cause of poor prognosis in pancreatic ductal adenocarcinoma (PDAC), but the exact mechanism is still not well elucidated. In this study, gene expression array was performed and biomarkers of venous invasion were investigated.
Methods: To select venous invasion specific genes, Nanostring nCounter analysis was performed on the following groups: 1) vein with cancer invasion; 2) cancer without vein invasion; and 3) normal vein. The selected genes were validated by immunohistochemical staining in protein level. The role of potential biomarker in venous invasion was investigated by invasion assay and western blot analysis.
Results: Four genes (CXCR4, TIMP1, OLFML2B, CYP1B1) were specifically high expressed in vein with cancer invasion group. Among them, high protein expression of CXCR4 and TIMP1 were validated by immunohistochemical staining and in particular, high TIMP1 expression was confirmed by 3D image in venous invasion areas. TIMP1-expression group was related to lymphovascular invasion ($p < 0.001$) and low 5 year-survival rate ($p = 0.032$). Furthermore, TIMP1 inhibition by siRNA reduced cancer cell invasion ability in the presence of cancer-associated fibroblast (CAF). In co-culture condition, TIMP1 was increased along with PI3Kp110 and phospho-AKT in pancreatic cancer cells. Therefore, TIMP1 in pancreatic cancer cells may induce venous invasion through PI3K/AKT pathway.
Conclusion: This study discovered TIMP1 as a biomarker of venous invasion of pancreatic cancer and revealed that TIMP1/PI3K/AKT pathway affect venous invasion of pancreatic cancer.

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PS-24-001

A real-world experience from a single centre (LPCE, Nice, France) highlights the urgent need to abandon immunohistochemistry for ROS1 rearrangement screening of advanced non-squamous non-small cell lung cancer

C. Bontoux*, V. Hofman, S. Goffinet, E. Long-Mira, S. Lassalle, M. Ilié, P. Hofman
*Laboratory of Clinical and Experimental Pathology, Hospital-Integrated Biobank (BB- 0033-00025), Pasteur Hospital, IRCAN Team 4, Inserm U1081, CNRS 7284, FHU OncoAge, Université Côte d'Azur, Nice, France

Background & objectives: Detection of ROS1 rearrangements in metastatic NSCLC is mostly based on a testing algorithm associating ROS1 immunohistochemistry (IHC) screening followed by mandatory ROS1 FISH and/or next generation sequencing (NGS) analyses in the case of IHC positivity to confirm the results.
Methods: We here evaluated RNA NGS used as reflex testing for ROS1 rearrangement assessment in NS-NSCLC with the aim of replacing ROS1 IHC as a screening method. ROS1 IHC and RNA and DNA NGS were prospectively performed from January 2021 to January 2023 for 810 NS-NSCLC. Positive results were additionally analysed by ROS1 FISH. The turnaround times (TATs) were compared.
Results: ROS1 IHC was positive in 26/810 (3.2%) cases that showed variable staining intensity while NGS detected ROS1 rearrangements in 12/810 (1.5%) cases. ROS1 FISH was positive in 14/26 (54%) of ROS1 IHC positive cases and in all positive ROS1 NGS cases. Obtaining both ROS1 IHC and ROS1 FISH reports took an average of 6 days, while obtaining ROS1 IHC, DNA, and RNA NGS reports took an average of 3 days.
Conclusion: Taken together, these results showed that systematic screening for the ROS1 status using IHC must be replaced by NGS reflex testing in cases of metastatic NS-NSCLC.

PS-24-002

Pulmonary Adenocarcinoma: ALK, ROS1 and RET imbalance sequencing concomitant with other target mutations

L. Carvalho*, M.R. Silva, A. Alarcão, A.F. Ladeirinha, T. Ferreira, C. Eliseu, M. Viseu, V. Almeida, G. Fontinha, V. Sousa
*Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Coimbra, Portugal, CIMAGO – Research Center for Environment, Genetics and Oncobiology, Faculty of Medicine, University of Coimbra, Portugal; Pathology Service, University Hospital Anatomical Pathology Coimbra, Portugal

Background & objectives: Gene fusions have significant prognostic and predictive value being screened as part of molecular pathology testing for patient management. Different approaches have been developed to detect fusion, in next generation sequencing, 3'/5' imbalance value can evaluate novel fusions for diagnosis.
Methods: Oncomine™ Precision Assay Panel workflow applied to fusion detection using expression "imbalance" in Oncomine Reporter™ Software, generates 3'/5' imbalance value, reporting the difference in expression between 5' assay and 3' assay of each driver gene ALK, ROS1 and RET. Fluorescence in situ hybridization (FISH) and Immunohistochemistry (IHC) were applied to 3'/5' imbalance cases to confirm these targets in pulmonary adenocarcinomas.

Results: Genexus sequencing reported ten cases with 3'/5' imbalance values.
Six cases were ALK 3'/5' imbalance and five presented other concomitant driver mutations: EGFR, KRAS, MET exon skipping and ALK-EML4 rearrangement. These five cases were either ALK FISH or IHC negative. One case presented ALK 3'/5' imbalance with FISH negative and IHQ (3+) positive. Four cases presented RET 3'/5' imbalance, three with concomitant mutations; two with EGFR mutations and one with RET fusion CCDC6. All were RET FISH negative. One case presented no other known mutation and RET-FISH was negative.
Conclusion: NGS has brought advantages in multiple genes mutations/fusions detection. This technology is fast, informative and demands less cellular burden to detect novel mutations/fusions. Possible novel fusion mutations (3'/5' imbalance) detections requires confirmatory analyses. Tumoural cells that contain a gene fusion are often expected to have elevated expression of the 3' assay compared to the 5' assay, and these cases have to be confirmed though the other methods – IHC and FISH, to complete Molecular Pathology Reports for target therapies prescription.

PS-24-003
Moving away from reliance on formalin fixed paraffin embedded tissue- can we use circulating tumour DNA to identify driver mutations in diffuse large B-cell lymphoma?
N.H. Cutmore*, I. Moutsopoulos, J. Krupka, C. Trethewey, S. Anand, L. Raso-Barnett, D. Hodson
*Department of Haematology, University of Cambridge, United Kingdom

Background & objectives: Diffuse large B-cell lymphoma is molecularly heterogenous. Genetic profiling is critical to improving future therapeutics. Biopsies have many issues: scant material, artefacts, logistics. Circulating tumour DNA offers an alternative. Objective: Compare mutation profile in paired samples using custom bioinformatics pipeline.
Methods: A custom bioinformatics pipeline, AULE (Automated Ultrasensitive Lymphoma Evaluation) was built. Pre-processing used unique molecular identifiers (UMIs). Somatic variant calling used four callers (SAGE, Strelka2, LoFreq, Mutect2), and only variants called by 3 or more were included in downstream analysis. Mutations were annotated using Variant Effect Predictor. Driver mutations were annotated as previously described (Lacy et al, PMID: 32187361).
Results: Paired samples from 23 patients included 23 plasma (ctDNA) and 24 formalin fixed paraffin embedded (FFPE) biopsies (one patient had two primary biopsies). 2 FFPE and 7 ctDNA samples had no driver mutations. The number of drivers between sample types was similar (FFPE: median = 6, IQR = 3-9, n = 22; ctDNA: median = 7, IQR = 5-9, n = 17), and within published range (6-13). 9/17 patients had 100% concordance between sample types and 13/17 had over 85% concordance (IQR = 87.5- 100%, n = 17). Cases with concordance below 1st IQR or no drivers have lower DNA concentration input into libraries (median [2.7 ng/uL] vs [16.3 ng/uL]).
Conclusion: Genetic profiling is the driver of future improvements in DLBCL treatment. Access to adequate genetic material is vital. ctDNA is attractive and more convenient for patients. Here we demonstrated that ctDNA can be used to genetically profile patient tumours. Caution must be taken when the input DNA concentration is low- this applies to both sample types. We conclude that ctDNA can be used as an alternative to FFPE for genetic profiling in DLBCL.
Funding: Cancer Research UK Clinical Research Fellowship: SEBSTF-2021\100001

PS-24-004
Performance evaluation of different genomic testing workflows for the detection of gene-fusions in non-small cell lung cancer
J. Fairley*, M. Gupta, I. Simon, S. Deans
*GenQA, United Kingdom

Background & objectives: Gene-fusions in *RET*, *NTRK*1/2/3 genes and *ROS*1 are actionable biomarkers in non-small cell lung cancer (NSCLC) and challenging for clinical laboratories to detect. Performance of six different testing workflows in seven independent laboratories to detect these gene-fusions was evaluated.
Methods: FFPE blocks (n=11) from resected NSCLC cases with known fusions [*RET* (n=7), *NTRK3* (n=1), *ROS1* (n=1)] and cases without fusions (n=2) were sourced. These were provided to seven clinical laboratories for testing. Results and various quality metrics were collected. Methods evaluated were Oncomine Precision Assay (OPA), TSO500, custom panels for ArcherDx, Qiagen and Roche DNA hybrid-capture, and Idylla Gene-Fusion assay.
Results: From the 11 samples used for workflow evaluation in seven labs, concordance, discordance and failure rates were: OPA= 11, 0, 0; TSO= 11, 0, 0; ArcherDx= 8, 0, 3; Qiagen= 7, 1, 3; Roche= 8, 3, 0; Idylla-Lab-A= 9, 2, 0; Idylla-Lab-B= 8, 2, 1. The failures on NGS technologies were mainly because of the low RNA quality or quantity. Some of the discordant results on Idylla were because of known limitations in the assay design. Characteristics of tissue samples, RNA metrics, workflows, partner genes and assay design that explain these failures and discordant results will be discussed.
Conclusion: Choosing a genomic technology is difficult and can be impacted by many variables, including sample characteristics typical of the tumour type, the clinically required turn-around-time, and the skill and experience required for each molecular technology in the laboratory. Clinical testing laboratories may benefit from improved understanding of strengths and limitations of different workflows. It is important to keep these in mind when reporting results.

PS-24-005
Development of a novel metric to measure genomic instability using unbalanced copy number changes with fast comprehensive genomic profiling
M. Gupta, P. Jermann*, G. Lowman, D. Cyanam, E. Norris, V. Mittal, S. Bandla, Y. Jin, M. Torro, L. Pickle, P. Williams, E. Wong-Ho, S. Sadis, J.L. Costa
*Thermo Fisher Scientific, Switzerland

Background & objectives: One of the primary causes of Homologous Recombination Deficiency (HRD) is BRCA1/2 pathogenic mutations and the consequence is genomic instability (GI). We developed a novel metric termed genomic instability metric (GIM) to measure GI in FFPE cancer samples.
Methods: We developed an amplicon-based enrichment next-generation sequencing panel (OCA Plus) that enables comprehensive genomic profiling (CGP) by interrogating 500+ genes relevant to precision oncology including 46 genes in the HRR pathway including BRCA1/2 using the Ion Torrent Genexus system that automates library preparation, templating, and sequencing with next day results. A large cohort of ovarian cancer FFPE samples was sequenced.
Results: Genome segmentation was performed using amplicon copy number (CN) log-ratio profiles and allele frequency log odds for thousands of single nucleotide polymorphisms (SNPs) in OCA Plus panel with high minor allele frequencies and GIM was calculated by summarizing unbalanced copy number segments. As expected, we observed GIM could stratify BRCA 1/2 mutated samples from wild type (WT) in the ovarian cancer FFPE cohort. In addition, we noted high GIM values in samples lacking BRCA1/2 mutations and observed over half of the ovarian cancer samples overall exhibited HRD based on BRCA 1/2 mutations and/or high GIM. CGP allowed us to explore associations between mutations in HRR pathway genes and GIM.

Conclusion: We devised a novel method to determine genomic instability for characterizing consequence of HRD using OCA Plus, which was developed for fast CGP of cancer FFPE samples to aid research into precision oncology. By combining genomic instability assessment with DNA repair pathway analysis such as mutations in BRCA1/2 and other genes in HRR pathway, OCA Plus will support research into the mechanisms underlying HRD.

PS-24-006

17p13 deletions are a feature of p53 null phenotype in urothelial bladder cancer and is associated with an aggressive tumour phenotype

M. Kluth*, M. Hitzschke, H. Plage, M. Lennartz, N. Blessin, A.H. Marx, M. Fisch, M. Slojewski, T. Ecke, S. Koch, G. Sauter, T. Klatte, T. Schlomm, D. Horst, H. Zecha
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: 17p13 deletions including p53 and other genes represent a common cause for reduced/lost p53 function in tumour cells. In this study, we analysed the impact of TP53 deletions and p53 expression on tumour aggressiveness and patient prognosis in urothelial carcinoma.
Methods: 17p13 copy number status was analysed by fluorescence in-situ hybridization (FISH) on more than 2,500 urothelial bladder carcinomas in a tissue microarray format. 17p13 deletion data were compared to p53 expression data measured by immunohistochemistry (IHC) which were available from a previous study. Different types of p53 alterations were compared with tumour phenotype and clinical outcome data.
Results: 17p13 deletions occurred in 23% of 2,185 analysable carcinomas. The fraction of tumours with 17p13 deletions increased from pTa G2 low (9%), to pTa G3 (24%, $p<0.0001$). In muscle-invasive carcinomas, 17p13 deletions were associated with advanced pT stage ($p=0.0246$), but unrelated to patient prognosis ($p>0.5$). 17p13 deletions were significantly related to p53 immunostaining ($p=0.0375$). 17p13 deletions were most common in tumours with complete lack of p53 staining (31%), which supports the concept that these tumours have a complete loss of p53 function (p53 null phenotype). 17p13 deletions were also increased in tumours with high p53 staining (26%).
Conclusion: 17p13 deletions were most commonly seen in p53 negative cancers, supporting their role as a cause for p53 null phenotype in urothelial cancer. The association of 17p13 deletions with high grade and advanced pT stage may reflect increasing genomic instability going along with stage and grade progression.

PS-24-007

Performance of microsatellite instability detection using Elio Tissue Complete and Idylla platforms in endometrial cancer

J. Lobo*, M. Hanbazazh, D. Shimoga Chandrashekar, S. Harada, A.C. Mackinnon
*Portuguese Oncology Institute Porto, Portugal

Background & objectives: Low-level microsatellite instability (MSI) phenotypes are common in endometrial cancer (EC) and may be missed with molecular-based testing platforms. We aim to assess the MSI detection performance of the Idylla and the FDA-cleared Elio Tissue Complete (ETC) platforms.
Methods: Immunohistochemistry (IHC) for mismatch repair (MMR) proteins was used as the gold standard for defining MMR status. Tumour DNA was extracted from FFPE tissue blocks, and MSI testing was performed using the Idylla (Biocartis, Mechelen, Belgium) and ETC platforms (PGDx/labcore, Baltimore, MD). Performance was assessed by evaluating concordance between MMR IHC, Idylla, and ETC.
Results: Thirty EC cases were included: 21 MMR deficient (19 MLH1/PMS2, 1 MSH2/MSH6 and 1 MSH6 deficient) and 9 MMR proficient. 20 of 21 cases showed MSI by Idylla and ETC. 1 discordant case (with loss of MLH1/PMS2) was missed by Idylla and ETC using vendor-defined thresholds for MSI detection. Evaluation of the ETC NGS data demonstrated low-level MSI characterized by loss of 1 nucleotide in 15 of 66 microsatellite tracks (23%).
Conclusion: Despite widespread use, PCR analysis for determining MSI has several limitations, and ECs with low-level MSI phenotypes represents a major diagnostic challenge. Increasingly, MSI testing is a component of pan-solid tumour NGS panels allowing simultaneous determination of complex molecular signatures (e.g., MSI, tumour mutation burden) and detection of somatic variants. Despite the inherent challenges with MSI detection across different tumour types, methods for NGS-based MSI testing are reliable provided labs carefully establish and validate interpretation criteria.

PS-24-008

Prognostic significance of epithelial-mesenchymal transition (EMT) markers in stage I-III colorectal cancer

A. Matly*, P. Hatthakarnkul, A. Ammar, M. McFarlane, J. Quinn, N. Maka, J. Park, K. Pennel, J. Edwards
*University of Glasgow, United Kingdom

Background & objectives: Epithelial-mesenchymal transition (EMT) is an important process in the development of metastases and colorectal cancer (CRC) progression. However one marker alone is not sufficient to identify the process. This study assessed expression of six EMT markers in CRC human specimens.
Methods: The study cohort consisted of 787 stage I-III CRC patient specimens. Immunohistochemistry was utilised to determine expression of E-cadherin, β-catenin, Snail, Twist 1, ZEB 1, and SOX 9 in a tissue microarray and expression was assessed using the weighted histoscore method. Full sections from the same cohort were utilised to perform transcriptomic analysis using TempO-Seq technology, Bioclavis.
Results: High expression of Snail ($P=0.007$) and Twist1($P=0.031$) was associated with decreased cancer-specific survival (CSS). When β-catenin and E-cadherin expression were combined, low expression of β-catenin and high expression of E-cadherin associated with good prognosis ($P=0.0027$), inflammation ($p = 0.05$), increased memory T-cells within the stroma ($p = 0.025$), and tumour invasive margin ($p = 0.04$). Cox-regression analysis demonstrated when combined with known clinical variables, the combined β-catenin E-cadherin score was independently associated with CSS (HR 2.379 95% CI 1.435–3.942, $p < 0.001$). Highest differentially expressed genes were CTNNB1 (β-catenin), Myc, NOTCH1 and TCF7 and gene set enrichment analysis demonstrated WNT β-catenin signalling and EMT gene sets were up-regulated.
Conclusion: The combined β-catenin and E-cadherin score stratifies patient's survival and associates with factors relating to metastasis. This combined β-catenin, E-cadherin score could be used to identify patients at risk of micro metastasis, who may benefit from standard adjuvant therapy, potentially in combination with EMT blockade therapy. Gene set enrichment analysis revealed that CTNNB1 (β-catenin) and TCF7 upregulation associated with poor survival in the cohort identifying these genes as promising candidates for targeted therapy and are worthy of further investigation.
Funding: Bowel cancer UK

PS-24-009

Next Generation Sequencing bile study as a pathological diagnostic tool for early diagnosis of cholangiocarcinomas

M.d.R. Mercado Gutierrez*, I. Amat, M. Arechederra, M. Rullan, P. Azcue, I. Fernández De Los Reyes, D. Guerrero-Setas, B. Carmen, M. Avila, A. Córdoba

*Navarra's Universitary Hospital, Spain

Background & objectives: Next generation sequencing (NGS) have identified recurrent mutations in cholangiocarcinomas (CCAs) in tissue samples and recently in bile cell-free DNA
Objective: To test NGS in bile cell free DNA as a tool in the diagnosis of malignant biliary stenosis
Methods: Prospective 68 patient study between January 2017 and December 2020 at Navarra University Hospital(Spain) with clinical malignant bile duct stenosis.
Sixty nine bile duct(BD) cytologies and 12 BD biopsies were pathologicaly evaluated.) 68 bile samples were collected.
NGS panel (Oncomine Pan- Cancer) was performed in bile samples and compared with the pathological diagnosis.Mean follow up was 15. 5 months.
Results: The pathological diagnosis was: n = 32 malignant (24 CCAs and nine pancreatic ductal adenocarcinomas PDACs) , n=26 benign, n=9 indeterminate.
Bile mutations (BM) were identified in all CCAs (sensitivity 100%) and in seven PDACs. Mutations identified were KRAS, TP53, ERBB3, GNAS, FBXW7, ERB2, IDH2, MAPK2K1 and FGFR3.
After follow up 14 of the 23 patient diagnosed as benign, developed a malignant stenosis. BM were identified in 18/23 of these patients.
In indeterminate diagnosis (n=9) BM were identified in eight patients, in the follow up all of these developed a malignant tumour
Conclusion: Pathological diagnosis of malignancy in biliary strictures are very specific (100%).
Bile mutations are the same found in tissue samples of CCAs (KRAS, TP53, ERBB3, GNAS, FBXW7, ERB2, IDH2, MAPK2K1 and FGFR3).
In clinical suspected malignant strictures, diagnosed as benign or indeterminate, assessment for bile mutations could determine the clinical follow up and is a strong indicator for repeating cytology or biopsy in order to avoid a false negative diagnosis.

PS-24-010

BC-miR: monitoring breast cancer-related miRNA profile in blood sera - a prosperous approach for tumour detection

T. Pankotai*, B. Borsos, Z. Páhi, Z. Ujfaludi, F. Sükösd, S. Bankó, G. Pankotai-Bodó, O. Olah-Nemeth
*Hungarian Centre of Excellence, University of Szeged, Albert Szent-Györgyi Medical School, Institute of Pathology, Hungary

Background & objectives: Breast cancer is the most frequent cancer with a high fatality rate amongst women worldwide. Diagnosing at an early stage is challenging, and due to the limitations of the currently used techniques, including mammography and imaging diagnostics, it remains unascertained.
Methods: We monitored the expressional changes of 15 pre-selected miRNAs in a large cohort, including 65 patients with breast cancer and 42 healthy individuals. We performed thorough statistical analyses on the cohort sample set and determined the diagnostic accuracy of individual and multiple miRNAs.
Results: Serum biomarkers can be a solution for this as they can be isolated in a less painful, more cost-effective, and minimally invasive manner. In this study, we shed light on the relevant role of multiple microRNAs (miRNAs) as potential biomarkers in breast cancer diagnosis. We generated a miRNA cluster, including various numbers of correlated miRNAs and monitored which ones seemed to be the most suitable for discriminating the healthy individuals from BC patients. These analyses underlined the promiscuous relevance of miR-15a+miR-16 and miR-15a+miR-16+miR-221 clusters in recognizing breast cancer with high prevalence and specificity.
Conclusion: In our cohort, the miR-15a+miR-16+miR-221 combination turned out to be the most promising multiple miRNAs, which may be suitable for further diagnostic purposes related to breast cancer. According to our data, we believe that if future validation studies supported our data, clinical implementation of miR-15a+miR-16+miR-221 would be of great importance in ameliorating the progression and recurrence of breast cancer.
This research was funded by the National Research, Development and Innovation Office grant NKFI295 FK 132080. T.P. was funded by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences BO/27/20 and UNKP-22-5-SZTE-318, UNKP-22-3-SZTE-274. The project has received funding from the EU's Horizon 2020 research and innovation program under grant agreement No.739593. Project no. TKP-2021-EGA-05 has been implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund, financed under the TKP2021-EGA funding scheme.

PS-24-011

Novel kinase-activating fusions in lung adenocarcinomas

G. Raskin*, E. Preobrazhenskaya, F. Zagrebin, R. Mulkidzhan, E. Saitova, I. Bizin, E. Imyanitov
*Dr. Berezin Medical Insitute, Russia

Background & objectives: Gene fusions involving protein kinases are druggable therapeutic targets, which are characteristic for a subset of lung adenocarcinomas. They are particularly common in young-onset cases, females and non-smokers.
Methods: RNA-based NGS analysis for 650 kinase genes was performed for 87 lung adenocarcinomas obtained from 77 young-onset patients (age range: 33-50 years; median age: 44 years; 53 males and 24 females) and 10 non-smoking females over 50 years old (age range: 58-79 years; median age: 68 years). All these tumours were negative for alterations involving *EGFR/BRAF/MET/ALK/ROS1/RET/NTRK1-3/HER2/KRAS/NRAS* genes.
Results: Kinome RNAseq revealed 84 chimeric transcripts; most of them were frameshifts, with only 26 fusion variants being in-frame. There were 20 interchromosomal and 64 intrachromosomal rearrangements. Kinase domain was completely or partially lost in 6 and 12 out of 26 tumours with in-frame translocations, respectively. Eight rearrangements preserved the entire kinase domain within a chimeric transcript: *MAPK10::RASGEF1B* 4q21.22-23del3.95Mb, *STK38::CDC73* t(4;1)(p21.31;q31.2), *BCR::PKHD1* t(22;6)(q11.23;p12.3), *CLTC::RPS6KB1* 17q23.1del0.2Mb, *CDC42BPG::ATG2A* 11q13.1del0.05Mb, *ATXN2L::SMG1* 16p11.2-12.3del9.9Mb, *WASF::FGR* 1p36.11del0.12Mb and *ZNHIT3::PRKCA* 17q12-24.3del29.8Mb. These gene fusions were analysed in 1059 NSCLCs, which were negative for all known actionable mutations, however no additional instances of these translocations was observed.
Conclusion: This study identified eight novel potentially actionable kinase gene fusions. The spectrum of recurrent kinase-activating tranlocations does not extend beyond *ALK/ROS1/RET/NTRK1-3* gene fusions, with other presumably druggable rearrangements being exceptionally rare and diverse.
Funding: Russian Science Foundation, grant 17-75-30027

PS-24-012

Clinical validation of NTRK gene fusion companion diagnostics (CDx) claims for TruSightTM Oncology Comprehensive (EU) assay

V. Sementchenko*, M. Harris, D. Vavrek, A. Martinez, C. Chen, K. Shen, L. Yun, T. Pawlowski
*Illumina, Inc., USA

Background & objectives: TruSight Oncology Comprehensive (TSO Comp) (EU) assay is a CE-marked comprehensive genomic profiling assay designed to interrogate solid tumours for small variants and gene amplifications from DNA, as well as gene fusions and splice variants from RNA.
Methods: Accuracy and bridging studies to validate NTRK fusion CDx claims were conducted using banked formalin-fixed, paraffin embedded (FFPE) clinical samples from patients enrolled in the larotrectinib clinical trials (NCT02122913, NCT02576431, and NCT02637687) supplemented with FFPE samples from various solid tumours. The agreement between results from TSO Comp and the reference method were compared to evaluate accuracy.
Results: For accuracy, 407 samples were evaluable, of which 118 were CDx NTRK fusion positive and 289 negative by the orthogonal method; of which, 114 (out of 118) were CDx NTRK fusion positive and 273 (out of 289) negative by the TSO Comp assay. PPA was 96.6% (114/118, 95% CI: 91.5% to 99.1%) and NPA was 94.5% (273/289, 95% CI: 91.2% to 96.8%). Clinical effectiveness of the TSO Comp was assessed in the bridging study. For clinical efficacy, within the 164 patients in the larotrectinib extended efficacy analysis (ePAS4) population, 110 had samples available for TSO Comp testing and 97 yielded valid results. The ORR is 78.4% (76/97, 95%CI [69%, 86%]).
Conclusion: Clinical efficacy of larotrectinib for the TSO Comp NTRK fusion positive population (97 patients, ORR=78.4%, 95% CI [69%, 86%]) was similar to the efficacy of larotrectinib in the total extended primary efficacy analysis population (164 patients, ORR=73%, 95%CI [65%, 79%]). Study results support the use of the TSO Comp (EU) assay to aid clinicians in identifying cancer patients with NTRK gene fusions who may be eligible for treatment with larotrectinib.

PS-24-013

Lung cancer molecular approach by NGS/MPS: the experience of IAP-PM using different NGS platforms

V. Sousa*, A.F. Ladeirinha, A. Alarcão, M.R. Silva, T. Ferreira, C. Eliseu, M. Viseu, V. Almeida, R. Almeida, G. Fontinha, L. Carvalho
*IAP-PM - Universidade de Coimbra, CHUC, Portugal

Background & objectives: The identification of therapeutic targets is essential to guide the personalized treatment of lung cancer. Molecular tests and biomarkers evolution in lung cancer requires pathologists to be equipped with better and fast technologies.
Methods: Since 2017, IAP-PM carried out NGS for mutation research in lung cancer. We started with ION PGM, used S5 from 2020 to 2021 and are currently using Genexus. Colon-Lung Panel was used on Ion PGM and S5, with manual library preparation. For Genexus we use Oncomine Precision Assay Panel, allowing DNA/RNA research simultaneously, fully automated from library preparation to sequencing.
Results: Of the 69 cases studied in the Ion PGM, mutations were found in 28.9% of the cases and only in samples with more than 10% of tumour cells. S5 allowed us to identify mutations in about 35% of the cases (18/51 cases) and we were able to detect mutations in samples with less than 10% of tumour cells. With Genexus, we were able to detect mutations in about 74% (142/192 cases) of the cases. We could detect mutations in cases with less than 10% of tumour cells and we have identified one target mutation in a case with only 2% of neoplastic cells and under 100 cells.
Conclusion: Molecular biomarkers optimization is important in lung cancer, in order to obtain more complete information in a shorter time. Genexus, combined with Oncomine Precision Assay, has proven in our practice to be an effective technology for personalized therapy. Enhanced vision of molecular environment was achieved. The frequency of targetable mutations and complex mutation detection increased. The use of more sensitive technologies helps pathologists respond faster, more proficiently, with less likelihood of errors due to automation with less sample requirement.

PS-24-014

Assessment of serum miRNA profiling in metastatic testicular cancer

Z. Ujfaludi*, F.E. Fazekas, T.Z. Beöthe, T. Pankotai
*University of Szeged, Albert Szent-Györgyi Medical School, Institute of Pathology, Hungary

Background & objectives: As the long-term outcome of testicular cancer depends on the formation of metastasis, the follow-up of patients and early diagnosis of such new lesions is essential. We studied the diagnostic value of serum miRNAs in metastatic testicular cancer (MTC).
Methods: Expression patterns of 10 miRNAs were determined by RT-qPCR in blood sera of healthy individuals and MTC patients (n=27+27) and matched surgically removed metastatic retroperitoneal lymph nodes (n=38), respectively. Using descriptive and mathematical-statistical methods, the miRNA expression and clinical data of the patients were further analysed to evaluate the diagnostic value of our miRNA marker panel.
Results: Determining the expression patterns of 10 pre-selected miRNAs from blood sera samples of healthy individuals and MTC patients (prior to surgical resection), we found that using the medians of either the overall marker set or only of the 3 highest distinctive miRNAs, the 2 groups of the cohort can be separated with 93 and 96% probability, respectively. The expression patterns of the same miRNA markers in patient-matched metastatic lymph nodes do not correlate with the sera profiles in great concert with literature data nor reflect statistically significant differences between the subgroups of patients determined by histological evaluation.
Conclusion: Our study showed that profiling the expression of 10 preselected miRNAs, healthy individuals and MTC patients can be distinguished by high confidence. This method might have the potential for the follow-up of TC patients using regular minimal invasive blood test sampling. Although our findings are promising, expanding the cohort is necessary for further testing, strengthening, and possibly increasing the number of included marker miRNAs in developing a reliable clinical test.
The project has received funding from the EU's Horizon 2020 research and innovation program under grant agreement No.739593. Project no. TKP-2021-EGA-05 has been implemented with the support provided by the Ministry of Culture and Innovation of Hungary from the National Research, Development and Innovation Fund, financed under the TKP2021-EGA funding scheme. T.P. was funded by the János Bolyai Research Scholarship of the Hungarian Academy of Sciences BO/27/20 and UNKP-22-5-SZTE-318, UNKP-22-3-SZTE-274.

PS-24-015

Comparison of data from two commercially available tissue-based comprehensive genomic profiling (CGP) solutions using AMP/ASCO/CAP guidelines and ESMO ESCAT

T. Wieland*, K. Hertel, M. Hiemenz, F. Fuhlbrück, J. Oughton, U. Schlecht, M. Cantone, S. Langer, H. Sorensen, D. Gonzalez de Castro, C. Messina, H. Adams
*Foundation Medicine GmbH, Germany

Background & objectives: We compared theoretical clinical significance data from two CGP solutions – the AVENIO Tumour Tissue CGP Kit (for Research Use Only) paired with navify Mutation Profiler (NMP), and TruSight Oncology 500 (TSO) assay paired with PierianDx Clinical Genomics Workspace.
Methods: AVENIO and TSO assays were run on 145 FFPE solid tumour samples (prostate: n=28; breast: 27; colon: 26; lung: 25 [among others]). Variant calls were acquired using manufacturer-provided software. Key variant annotation outputs were variant tiers and ESCAT guideline inclusion per tumour type. AMP/ASCO/CAP tiers were obtained with NMP for AVENIO or PierianDx for TSO. ESCAT inclusion was determined manually.
Results: Tier I/II variants detected by both assays were: 643 short variants (SVs), 408 copy number alterations (CNAs) and 54 gene fusions. For ESCAT variants, none were missed by AVENIO.

Conversely, 1/24 SVs and 5/11 CNAs were missed by TSO. Average positive agreement for CNAs was 28.5%; average negative agreement was 98.0%.
Tumour mutational burden (TMB) with TSO was significantly higher vs AVENIO (regression modelling, p<0.001); TSO called n=41/145 samples TMB-high, vs 31/145 samples for AVENIO. Recent guidance suggests TMB algorithms should account for germline and somatic driver mutations. Differences in bioinformatic approaches raise concerns about TMB overestimation by TSO.
Conclusion: With advances in molecular guided therapy options, CGP solutions should robustly detect guideline-relevant alterations. Two commercially available CGP solutions with tertiary analysis software had differences in the detection of TMB and ESCAT biomarkers, including CNAs. These differences can be largely explained by differences in variant calling and filtering algorithms and are important considerations for any diagnostic CGP offering, raising concern of inaccurate results if not properly controlled.
Funding: F. Hoffmann-La Roche Ltd/Roche Diagnostics International Ltd.

PS-25 | Poster Session Pathology in Favour of Developing Countries

PS-25-001
Evaluation of 70% isopropyl alcohol as a fixative medium in surgical cooperation campaigns: a pilot study
M. Bronte Anaut*, J. Arredondo Montero, E. Carracedo Vega, A. Moreno Ibérico, Y.P. Rodriguez Velandia, Y. Ruiz de Azua-Ciria, C. Bardají Pascual, R. Guarch Troyas
*Hospital Universitario Araba, Spain

Background & objectives: The lack of adequate resources in international cooperation limits the study of anatomopathological specimens. The literature on potential inexpensive and available fixation media is scarce.
Methods: Lesions were prospectively collected during a surgical cooperation campaign in 2022. Lesions were fixed in parallel in 5% formalin (FF) and 70% isopropyl alcohol (AF). H&E sections and immunohistochemistry (IHC) techniques were performed. Images were anonymized and assessed by 2 senior and 2 junior pathologists, evaluating the quality of staining and diagnostic feasibility by means of an anonymized questionnaire.
Results: Three surgical specimens were included: 1 lymph node (3 H&E, 4 HIC), 1 seborrheic keratosis (2 H&E, 5 HIC), 1 branchial remnant (2 H&E, 2 HIC). Fixation times were similar in all the specimens (10-13 days). All FF H&E were diagnostic. AF H&E was 100% diagnostic in 5/7 sections and 75% diagnostic in the two remaining sections. In most cases pathologists preferred FF. CK7 (x2), P40, EMA, CKAE1AE3 and TTF1 were 100% diagnostic in both groups. CD20, CD45 and EMA were 100% diagnostic (FF) and 75% diagnostic (AF). CD10 was 75% diagnostic (FF) and 25% diagnostic (AF). BCL6 was 75% diagnostic (FF) and 100% diagnostic (AF). IHC preferences were inconsistent.
Conclusion: 70% Isopropyl alcohol has a worse fixation profile than 5% formalin but allows diagnosis in most cases. The immunoreactivity observed is variable depending on the tissue and the stain used. Based on these findings, it can be considered an inexpensive, readily available and potential useful fixation medium for diagnosis in developing countries where surgical cooperation campaigns are developed. Future studies of larger sample size and characterizing other histologic subtypes are needed to confirm these findings.

PS-25-002
Opting surgical pathology as a future specialty; student's perspective from Lahore, Pakistan
F. Rehman*, F.N. Alam, M.U. Farooq, R. Saqib, S. Hameed, A. Hamid
*Associate professor Pathology department, Ameerudin medical college/postgraduate medical institute, Lahore, Pakistan

Background & objectives: Choosing a medical specialty is crucial to a medical student's long-term career goals. The aim of this study is to evaluate inclination of medical students towards choosing surgical pathology as a future specialty and various factors that influence their choice.
Methods: A descriptive cross-sectional study was conducted among a random sample of (209) medical students from (time slot) and comprised of 1st year to final year MBBS students at various medical universities in Pakistan. A (web-based) self-administered structured questionnaire after validation from experts, was distributed among the students. The collected data was analysed using SPSS version 21.
Results: Out of the 209 forms that were distributed, 202 students completed the survey with a response rate of 96.65 %. Almost one third of the students were in third and 4th years of their medical education. The top choices opted by respondents were mainly medicine and surgery and allied specialties. Factors for not opting surgical pathology mainly includes lack of awareness of the importance and role of the specialty in deciding patient therapeutic management. Many of the students were of view that its a basic science specialty with less interaction with patients and physicians. In addition, structured curriculum of MBBS lacks rotation in different sections of pathology.
Conclusion: The findings of this multi-institutional study will help us in better understanding the emerging trends among medical students regarding specialty choice. Lack of self-interest in pathology; in particular surgical pathology due to false impression of the subject 'being very tedious with complex histology diagrams'. Interaction with surgical pathology residents & consultants, better understanding of routine workflow by including pathology rotations in curriculum, participation in clinicopathological conferences and multidiscipliniary meetings will help in developing a positive perception in student's mind.

PS-25-003
Haematological indices as potential markers of renal involvement in systemic lupus erythematosus
S. Sharma*, S. Farheen, R. Linghaiah, A. Aggarwal
*Department of Pathology, SGPGIMS, India

Background & objectives: Lupus nephritis develops in approximately 50% of the SLE patients. The study was aimed to evaluate haematological indices i.e., neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, mean platelet volume and red cell distribution width as potential markers of renal involvement in SLE patients.
Methods: In this cross-sectional study of 110 SLE patients, 73 had biopsy proven lupus nephritis (LN). The LN patients were categorized into Class II (n=4), III (n=30), IV (n=16) and Class V (n=23). Univariate and multivariate analysis to predict the haematological indices influencing the renal involvement and ROC curve analysis to discriminate patients with LN were performed.
Results: The median values of NLR (3.26 vs 1.90), PLR 148.36 vs 104.85) and RDW (20.70 vs 14.20) were significantly high (p<0.05) in LN patients as compared to those without LN. Among haematological indices RDW showed a significant correlation with S. creatinine (r=0.290, p=0.013) and NLR with S. uric acid (p=0.259, p=0.027). On multivariable analysis, RDW (Adj. OR: 1.45; 95% CI: 1.219-1.716; p<0.001) and PLR (Adj. OR: 1.01; 95% CI: 1.001-1.017; p=0.011) were independent indicators of renal involvement. RDW was the best predictor of renal dysfunction (AUC: 0.811, Cut-off: 14.25%; sensitivity: 91.70%; specificity: 47.40%) followed by MPV (AUC: 0.754), NLR (AUC: 0.719) and PLR (AUC: 0.686) on ROC curve analysis.
Conclusion: In our study haematological indices (RDW, Platelet-to-Lymphocyte Ratio PLR, Neutrophil-to-Lymphocyte Ratio NLR and MPV) which are derived from complete blood counts were found to

be significantly high in LN patients as compared to those without LN. Among these indices RDW & PLR were independent predictors of renal involvement. These findings suggests that these indices may be used as cost-effective and non-invasive potential markers for predicting renal involvement in SLE patients.

PS-26 | Poster Session Uropathology

PS-26-001

An algorithmic pattern-based practical approach to the new WHO classification of renal cell tumours: emphasis on kidney biopsy specimens

M. Alzamora*, M. Hanbazazh, Â. Rodrigues, J. Loureiro, R. Henrique
*IPO-Porto, Portugal

Background & objectives: Presently, renal cell tumours (RCT) pose significant clinical challenges, warranting accurate biopsy-based diagnosis. We propose a practical approach to the 2022 WHO classification established upon morphology and immunohistochemistry (IHC), testing the algorithm's performance in paired kidney biopsies and surgical specimens.
Methods: As per the WHO Classification of Urinary and Male Genital Tumours 5th edition (2022), we reviewed literature to develop an algorithmic practical approach to RCT classification based on common morphologic features and distinct IHC profiles. We identified consecutive RCC cases spanning 2004-2022 through a query of internal records and compared diagnostic performance in biopsies and corresponding resection specimens.
Results: Overall, we identified 160 eligible RCT cases and reviewed their diagnoses in light of the 2022 WHO classification using the proposed algorithm. The first discriminator consisted of five main morphological categories: clear cell tumours, eosinophilic cell tumours, tumours with a papillary pattern, tumours with a cystic pattern, and high-grade infiltrating tumours. Some tumours, such as clear cell RCC and MiTF-Translocation RCC depicted overlapping features across categories. IHC profiles and molecular techniques were particularly important for diagnosis in challenging cases, especially eosinophilic cell and high-grade infiltrating tumours.
Conclusion: Accurate RCT classification provides clinically relevant information, aiding in patient management and improving communication between pathologists and clinicians. We provide a practical and accurate framework for RCT classification based on the new criteria from the 2022 WHO Classification of Urologic Tumours, facilitating its widespread implementation. This approach may be particularly valuable for diagnosing kidney tumours in biopsies and may improve patient management. Overall, the proposed algorithm could improve accuracy and reliability of pre-operative RCT diagnosis to guide clinical decision-making.

PS-26-002

Diagnostic spectrum of tumours developing in native kidneys of renal transplant recipients

G. Aydogan*, B. Sarsik Kumbaraci, K.E. Ergun, B. Goktepe, A. Celtik, S. Sen
*Ege University Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: The risk of developing de novo malignancy is high in organ transplant recipients receiving long-term immunosuppressive therapy. Although skin and hematopoietic neoplasms are common in general, tumours in native kidneys are also described.
Methods: At our centre, 17 native nephrectomy of 14 patients who underwent kidney transplantation between 1989 and 2019 were examined. Three patients had bilateral nephrectomy. Twenty-one renal tumours detected in native kidneys of these patients were re-evaluated according to World Health Organization (WHO) 2022 renal tumours classification system.
Results: In this study of 14 patients, of which two (14%) were female and twelve (86%) were male. The mean age of the patients was 51 years (range=14-75). The mean interval between transplantation and tumour diagnosis was 88 months (range=1-312). Histologically, these tumours were classified as follows; five (5/21,24%) papillary renal cell carcinoma (RCC), two (2/21,10%) clear cell RCC, two (2/21,10%) acquired cystic disease associated RCC. The other six tumours were TFE3-rearranged RCC, chromophobe RCC, clear cell papillary renal cell tumour, low-grade oncocytic tumour, papillary tumour with reverse polarity (RP-PT), and metanephric adenoma. The five (5/21,24%) tumours were in the morphology of renal papillary adenoma. One tumour could not be classified.
Conclusion: The incidence of malignancy has increased in kidney transplant recipients. As a result, the risk of tumour development in the native kidneys is high. Therefore, clinical follow-up of native kidneys is extremely important.

PS-26-004

IFITM3-mediated activation of TRAF6/MAPK/AP-1 pathways induces acquired TKI resistance in clear cell renal cell carcinoma

Y.M. Cho*, S.U. Jeong, J. Park, S.Y. Yoon, H.S. Hwang, H. Go, J. Lee, G. Jeong, H. Lee
*Asan Medical Center, University of Ulsan College of Medicine, Republic of Korea

Background & objectives: VEGF tyrosine kinase inhibitors (TKIs) have been the standard of care for metastatic clear cell renal cell carcinoma (ccRCC). However, the therapeutic effect of TKI monotherapy remains unsatisfactory due to drug resistance to the TKI therapy.
Methods: To define the TKI-resistance mechanism for TKI-resistant ccRCC, an integrative differential gene expression analysis was performed using paired tumour samples harvested at pre- and post-TKI treatment periods from 10 ccRCC patients and a public dataset. Sunitinib-resistant RCC cell lines were established and used to test their malignant behaviours of TKI resistance through in vitro and in vivo studies.
Results: Integrated differential gene expression analysis revealed increased interferon-induced transmembrane protein 3 (IFITM3) expression in post-TKI samples. IFITM3 expression was increased in ccRCC compared with the normal kidney. TKI-resistant RCC cells showed high expression of IFITM3 compared with TKI-sensitive cells and displayed aggressive biologic features such as higher proliferative ability, clonogenic survival, migration, and invasion while being treated with sunitinib. These aggressive features were suppressed by the inhibition of IFITM3 expression and promoted by IFITM3 overexpression, and these findings were confirmed in a xenograft model. IFITM3-mediated TKI resistance was associated with the TRAF6 and MAPK/AP-1 pathways.
Conclusion: These results demonstrate IFITM3-mediated activation of the TRAF6/MAPK/AP-1 pathways as a mechanism of acquired TKI resistance, and suggest IFITM3 as a new target for TKI-resistant ccRCC.
This work is funded by the Ministry of Science, ICT and Future Planning (2019R1A2C1088246) and a grant (2022IL0018-1) from the Asan Institute for Life Sciences, Asan Medical Centre, Seoul, Korea.

PS-26-005

Deep learning diagnosis of renal cell carcinoma using the largest dataset of whole slide images

Y. Chong*, K. Yim, B. Kim, S. Jung, H. Shin, Z. Xu, S. Lim, M. Alam, Y.J. Choi
*The Catholic University of Korea, Republic of Korea

Background & objectives: The increasing prevalence of renal cancers necessitates accurate detection and subtyping. However, diverse histologic spectrums make this task challenging. Recently, AI has demonstrated potential in histologic image analysis but has been underutilized in renal cancer due to dataset limitations.
Methods: To address this, we aim to create a deep learning model for renal cell carcinoma (RCC) diagnosis by utilizing whole slide images (WSIs) sourced from multiple hospitals, which could enhance the accuracy and efficiency. A total of 1,639 WSIs from two university hospitals, Seoul and Uijeongbu St. Mary's hospital, were used to compare ten convolutional neural network models.
Results: Accuracy, area under the curve (AUC), and F1 score of resnet18, resnet34, resnet50, resnet101, densenet, mobilenet, vgg, efficientnet, inception, squeezenet were compared after normalization and augmentation for efficient learning. Images were divided into training, validation, and test sets for model development and evaluation. The Efficientnet model demonstrated the highest performance, with an accuracy of 96.82%, AUC of 98.67%, and F1 score of 97.80%.
Conclusion: Our study indicates that employing various deep learning models can enhance the accuracy and efficiency of RCC diagnosis using WSIs. These promising results in renal neoplasms detection suggest potential for future advancements in RCC diagnosis and treatment. However, further external validation with larger datasets from multiple institutes and ethnicity is needed to improve performance and generalizability.

PS-26-006
Routine use of an artificial intelligence solution for primary diagnosis of prostate biopsies in clinical practice
R. Dhir*, R. Abou Shaar, G.M. Quiroga-Garza, K. Takeda, D. Hartman, M. O'Leary, R. Ziv, M. Grinwald, M. Vecsler
*University of Pittsburgh Medical Center, USA

Background & objectives: We present the analysis of a clinically deployed artificial intelligence (AI) decision support solution for prostate biopsies primary diagnosis utilized as first read within a digital pathology workflow.
Methods: The AI solution was previously validated in the lab on an independent cohort. Four pathologists underwent training and used the solution for prospective primary diagnosis of consecutive prostate core needle biopsies, reporting on 122 cases (509 parts, 770 H&E slides).
Results: The AI solution demonstrated high performance when preclassifying parts with the likelihood to be benign or malignant, with AUC = 0.99 (95%CI: 0.985, 0.997), NPV = 99.9% (95%CI: 0.966, 0.999) (163/164) and PPV = 97.6% (95%CI: 0.948, 0.991) (244/250), respectively. 19% of parts have been classified as suspicious by AI. The AI performance in Gleason group grading was high, at 90.6% of full agreement or one group difference. User feedback survey, showed high satisfaction marks for the AI solution, particularly for the Gleason scoring (95%), PNI detection (90%), and tissue and tumour length automated measurement (95%). Pathologists felt there is potential to increase diagnostic efficiency by using the AI tool.
Conclusion: We report here the successful implementation of a multifeature AI solution that automatically imparts clinically relevant diagnostic parameters regarding prostate cancer, grading, measurements, and other pathologic features. The solution demonstrated its ability to accurately detect cancer and contribute to diagnostic quality. Thus, the AI solution could be used as a significant aiding tool for pathologists in clinical decision-making in routine pathology practice.

PS-26-007
Characterisation of embryonic-type neuroectodermal tumour and embryonic-type neuroectodermal elements adopting a broad immunohistochemical panel
L. Di Sciascio*, F. Ambrosi, T. Franceschini, F. Giunchi, G. Di Filippo, E. Franchini, F. Massari, V. Mollica, V. Tateo, F. Mineo Bianchi, M. Colecchia, A.M. Acosta, J. Lobo, M. Fiorentino, C. Ricci
*School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: Embryonic-type neuroectodermal tumour (ETNT) is an aggressive somatic-type malignancy of the testis. For its rarity, there're limited data on its immunohistochemical features. Herein, we tested a series of ETNT with a broad panel to clarify the immunohistochemistry aiding the diagnosis.
Methods: Twelve cases including 4 ETNT, 4 teratomas of the testis with embryonic-type neuroectodermal elements (ETNE), and 4 immature teratomas of the ovary and/or the central nervous system were collected. The cases were tested with a broad immunohistochemical panel including SOX2, NF, INI-1/SMARCB1, SMARCA4/BRG1, S-100, SOX10, NeuN, WT-1, CD99, GFAP, Synaptophysin, Chromogranin, and CK AE1/AE3, and adopting a previously-described scoring system.
Results: All cases were reviewed and classified according to the specific WHO classification systems. ETNT displayed a wide range of histological patterns (atypical small round/epithelioid/spindle cells, high mitotic count, solid sheets/fascicular arrangement/multilayered rosettes/anastomosing neural tubules, and necrosis) often merged with mature glial/neural components. SOX2 (mv: 6.4, r: 0-9) and cytoplasmatic WT-1 (mv: 6.3, r: 3-9) were the most frequent and intense stains for the immature neuroepithelial components of all the selected histological entities. Cytoplasmatic WT-1 showed the best values also for the mature glial/neural components. All the other stains were completely negative or focally/weakly positive in the immature neuroepithelial components, with variable results in the mature glial/neural components.
Conclusion: Our study suggests that SOX2 and cytoplasmatic WT-1 are useful diagnostic tools for the identification of immature neuroepithelial components in germ cell tumours of the testis, so aiding the diagnosis of ETNT and quantitative distinction from teratoma with ETNE. In our study, SOX2, a pivotal factor for the development of neuroepithelium, did not stain mature glial/neural components and performed better than cytoplasmatic WT-1 at helping estimate of the amount of immature neuroepithelial components.

PS-26-008
Functional atlas of prostate cancer mesenchyme: a translational approach to untangle the stromal molecular landscape in prostate cancer initiation, progression, and metastatization via single-cell profiling
G.N. Fanelli*, H. Pakula, M. Omar, R. Carelli, F. Pederzoli, T. Pannellini, S. Rodrigues, C. Fidalgo-Ribeiro, P.V. Nuzzo, D.S. Rickman, B.D. Robinson, A.G. Naccarato, C. Scatena, L. Marchionni, M. Loda
*University of Pisa, Italy

Background & objectives: Prostate cancer (PCa) has divergent clinical behaviour that molecular alteration in epithelial cancer cells can only partially justify. Indeed, tumour stroma can deeply influence it. Using scRNA-seq we explored mesenchymal cells' expression programs to untangle stromal impact on PCa carcinogenesis.
Methods: We used four PCa mouse models representing different disease stages: TMPRSS2-ERG (T-ERG) model for PCa initiation; Nkx3.1creERT2;Ptenf/f (NP) model for intraepithelial neoplasm; Tg(ARR2/Pbsn-MYC)7Key (Hi-MYC) for early invasive adenocarcinoma and Pb-Cre4+/-;Ptenf/f;Rb1f/f;LSL-MYCN+/+ (PRN) for advanced adenocarcinoma with neuroendocrine features. Using scRNA-seq we compared their mesenchymal cells' transcriptional program to their wild-type counterparts, and to primary and metastatic human samples with comparable genotypes.

Results: We identified eight transcriptionally different stromal populations: c0-c7. Three were common to all models: c0 expressed contractile marker genes; c1 displayed *Sfrp1, Gpx3,* and complement system-related genes expression, and c2 JNK pathway-related genes. Five were specifically linked to specific epithelial mutations: c3 and c4, enriched in T-ERG, Hi-MYC, and NP models, expressed WNT pathway-related genes; c5, c6, and c7, enriched in PRN model, revealed high levels of proliferative markers, collagen and metalloproteinase genes, adaptive immune responses, TGF-β and WNT pathways-related genes. These clusters extensively map in human primary and metastatic samples: c3 was the most conserved one, whereas stromal transcriptional profiles of PRN model and human metastases were strikingly similar.
Conclusion: We provided clear molecular evidence of stromal changes during PCa carcinogenesis in mouse models, driven in a genotype-specific manner, which can be extended to humans. We demonstrated how *TMPRSS2-ERG* fusion reprograms the mesenchyme in the early phases of PCa; while, in advanced PCa models, transcriptional mesenchymal programs are associated with metastatic potential, and similar to the human bone microenvironment ones. Overall, these findings support mesenchymal changes as major contributors to PCa carcinogenesis and phenotypic heterogeneity, to a previously unrecognized level.
This work was partially supported by the National Cancer Institute (Prostate Cancer SPORE Grant P50CA211024 [M.L., H.P., R.C., M.O., S.R., C.R.], P01 CA265768-01 [M.L., H.P., R.C., M.O., S.R., C.R.], R01CA200859 [L.M.]), by an AIRC Fellowship for Abroad "Ezio, Maria e Bianca Panciera" [F.P.] and by a Junior Assistant Professor/ Temporary Researcher (RTDA) contract - Italian Ministry of University and Research - PON "Research and Innovation" 2014-2020 (PON R&I) Actions IV. 4 "Doctorates and research contracts on innovation topics" [G.N.F.].

PS-26-009
Using AI-powered solution in clinical practice for primary diagnosis of prostate biopsies
R. Grobholz*, P. Nahm, L. McDuffus, D. Mevorach, M. Vecsler
*Medical Faculty, University of Zurich, Institute of Pathology, Cantonal Hospital Aarau, Switzerland

Background & objectives: We aimed to test the accuracy of an artificial intelligence (AI)-based solution for primary diagnosis of prostate carcinoma using real-world data. Emphasis was given on the accuracy of detection of Gleason patterns and assigning to the Gleason grade groups (GG).
Methods: The project included validation of the AI solution in clinical practice prior to deployment. One pathologist used the solution for primary diagnosis of 91 prostate biopsies, reporting on 678 parts (1,563 H&E slides), 19 cases with GG1, 15 with GG2, 16 with GG3, 22 with GG4 and 19 with GG5. Accuracy for adenocarcinoma detection and Gleason grading was assessed.
Results: The AI solution agreed with the ground truth (GT) in 100% of cases for carcinoma, and generated identical or +1/-1 GG to the GT for 98.7% of cases (n=81). The highest levels of agreement were for GG 1 and 5 (100% and 90%, respectively). For GG 2-4, the AI findings were identical or +1/-1 GG to the GT for 100% of cases but had higher disagreement rates with respect to the amount of pattern 4. For GG2 and GG3 concordance rate was 57.1% and 26.6%, respectively. Part-level analysis demonstrated high accuracy, with an AUC of 0.992 (95% CI: 0.9857-0.999), NPV of 98.5% and PPV of 98.7% for carcinoma detection.
Conclusion: This study demonstrates the successful validation of a multi feature AI solution that aids to accurately detect all cancer areas and assign an accurate Gleason score. However, detection and quantifying of Gleason pattern 4 remains challenging, and AI can aid to detect and quantify the amount of this pattern in order to accurately assign the respective GG.

PS-26-010
Assessment of tumour infiltrating lymphocytes in urothelial carcinomas of the bladder and their prognostic value
E. Haddad*, A. Blel, H. Ayed, S. Rammeh
*CHU ROUEN, France

Background & objectives: Analysis of tumour infiltrating lymphocytes (TILs) represents a new immunological marker considered as a prognostic factor in several solid tumours. The aim of our work was to evaluate the level of TILs in muscle-invasive bladder UC and their prognostic value.
Methods: Retrospective and descriptive study including 74 Urothelial Carcinoma collected between 2010 and 2017. TILs were evaluated based on the recommendations of the International TILs Working Group. A rate of TILs <10% was considered low and a rate ≥10% was considered high. The prognostic value of TILs was assessed. The correlation between clinical-pathological parameters and the rate of TILs was evaluated.
Results: A rate of TILs≥10% was observed in 58 cases (78%). The mean follow-up period was 19 months. Mean overall survival was 42 months and progression-free survival was 57 months. Aggressive histologic variants, high tumour stage, perineural neoplastic invasion (p=0.04), tumour surgical limits, lymph node invasion, and a TILs rate of less than 10% were prognostic factors for overall survival. In multivariate analysis, rate of TILs, tumour stage, metastasis were independent factors of overall survival. The rate of TILs was not a prognostic factor in progression-free survival. A low rate of TILs was correlated with the presence of aggressive histological variants (p=0.02), high tumour stage (p=0.02) and tumour surgical limitations (p=0.02).
Conclusion: Our results confirm that TILs in bladder UC are a prognostic factor in overall survival. We recommend the inclusion of this factor among prognostic markers in anatomo-pathological reports.

PS-26-011
Assessment of positive margins on prostatectomy specimens using fluorescence confocal microscopy: the LaserSAFE technique
A. Haider*, R. Almeida-Magana, A. Mathew, T. Al-Hammouri, K. Dinneen, G. Shaw
*Department of Histopathology, University College London Hospital, United Kingdom

Background & objectives: Frozen section of the posterolateral prostatic margins (NeuroSAFE) has been described as a safe method to evaluate positive surgical margins (PSM) during radical prostatectomy to guide nerve-sparing decisions during surgery. However, its associated time and cost requirements prevent widespread adoption.
Methods: We developed a standardised fluorescence confocal microscopy (FCM) method to analyse margins of prostatectomy specimens. The sample cohort included RP specimens from April 2022 to February 2023 from consented patients. Intact specimens were dipped in a photoreactive solution and placed on the microscope for en-face imaging. Specimens were then processed using standard paraffin analysis (PA). FCM images were analysed retrospectively.
Results: Thirty-one patients were included. It took 1 operator less than 10 minutes to produce images of both posterolateral surfaces of the prostate. 60 images were acquired. 59 images had good quality and contrast, and 56 had >90% of the specimen surface analysable. Eight positive surgical margins were identified on both FCM and PA with a median length of 4 mm. We found one false positive (benign glands on PA) and one false negative on FCM. Sensitivity was 87.5% (CI 86.4%-88.6%), specificity was 98.1% (CI 97.6%-98.5%), and Cohen's kappa agreement was 0.86. No artefacts were found on PA attributed to the LaserSAFE technique.
Conclusion: The LaserSAFE technique is easy to perform and demonstrates high accuracy and very good agreement with PA. These

preliminary performance results will be confirmed in a blinded prospective clinical trial comparing findings with NeuroSAFE.

PS-26-012

Hilar vascular changes are associated with adverse outcome in non-seminomatous germ cell tumours: a single institute experience

M. Idrees*, K. Collins, K. Ebare, S. Harari, T. Ulbright, A.M. Acosta, I. Kilic
*Indiana University School of Medicine, USA

Background & objectives: Advanced clinical stage, lymphovascular invasion (LVI) and hilar adipose tissue involvement (HATI) are known important prognostic factors for testicular germ cell tumours (GCT). The aim of this study was to evaluate the prognostic significance of hilar vascular changes in GCTs.
Methods: Our cohort included 112 radical orchiectomies incuding non-seminomatous germ cell tumours (NSGCT) (n=60) and seminomas (n=52) diagnosed from 2005 through 2022. We categorized vascular changes into three groups: vascular proliferation/thickening, stromal/vascular inflammation, and vascular degeneration and scored semiquantitatively for each (0=normal, 1=mild, 2=moderate, and 3=severe). We recorded scores and compared NSGCT versus seminoma for LVI and HATI with concurrent metastasis.
Results: Of the NSGCT, the mean age was 31.3 years and mean tumour size was 4.1 cm. Of the pure seminomas, the mean patient age was 34.6 years and the mean tumour size was 3.9 cm (range, 0.9 to 9.8 cm). In the hilar soft tissue, 41 out of 52 (78.8%) seminoma cases showed vascular thickening alone (34/41, 82.9%), while 59 out of 60 (98.3%) NSGCT cases showed both vascular proliferation/thickening and 20 out of 60 (33.3%) NSGCT cases showed moderate/severe vascular degeneration. On univariate analysis, the following parameters showed statistically significant association between NSGCT and moderate/severe vascular changes ($p<0.00001$): HATI ($p=0.003$), LVI ($p=0.0006$), and metastasis ($p=0.0406$).
Conclusion: In conclusion, moderate/severe vascular changes in addition to LVI and HATI, in the hilar soft tissues are strongly associated with metastatic disease and should be reported in cases with no definitive LVI or HATI, particularly for NSGCT.

PS-26-013

Prostate cancer perineural invasion and bone metastases in the mouse model

E. Izycka-Swieszewska*, D. Sigorski, S. Galli, S. Hong, J. Kitlinska
*Medical University of Gdansk, Poland

Background & objectives: Bone metastases in prostate cancer (PCa) patients, initially develop in the lower part of the spine and pelvis. The retrograde venous spread is the working explanation. The PCa perineural invasion (PNI) links with mechanism of bone dissemination needs investigation.
Methods: The PC3-ML cell line, which triggers bone metastases in the orthotopic xenograft model was used. The PCa cells were injected into the prostates of male SCID/Bg mice, the tumours development and progression was followed by periodic magnetic resonance imaging (MRI). Finally, multiple sections of primary and metastatic lesions were examined with histopathology and IHC for neuronal and endothelial markers.
Results: MRI indicated local invasion of the primary tumour, which later resulted in the formation of multiple secondary lesions along the lower spine. Histopathology revealed that these lesions developed in the soft tissues surrounding the vertebral column, while the subsequent invasion of the vertebra was the secondary event. The neurofilament (NF), tyrosine hydroxylase (TH) and neuropeptide Y (NPY) stainings, revealed that PCa cells created secondary foci spreading longitudinally along the small nerve fibres, particularly in the paraspinal muscle compartment. CD31 staining detected small vessels within PCa clusters. However, no evident angioinvasion of the PCa cells within the blood vessels corresponding to the retrograde venous spread was observed in serial sections.
Conclusion: These results on the suitable and well recognized mouse model suggest PNI as the main route of the initial local invasion/ dissemination of the PCa cells toward the bone, which then causes bone invasion and subsequent hematogenous spread to the distant bones. Further mechanistic studies are required to confirm this hypothesis.

PS-26-014

Hedgehog (Hh) pathway ligands genetic alterations in paediatric and adolescent germ cell tumours

E. Izycka-Swieszewska*, K. Czarnota, M. Jankowski, J. Stefanowicz, W. Grajkowska, J. Gulczynski, B. Lipska-Zietkiewicz
*Medical University of Gdansk, Poland

Background & objectives: New genetic candidates can help to connect the embryology with cancerogenesis in germ cell tumours (GCTs). Hedgehog signalling pathway controls embryonic cell migration, sexual differentiation and postnatal gonadal function. Aim: Hh pathway analysis focused on ligand alterations in paediatric GCTs.
Methods: FFPE tumour samples of 70 childhood and adolescent GCTs. The mutational analysis of the Hh pathway and chosen non-Hh network genes performed using NGS with a designed QIAseq Targeted DNA 25 genes panel (Qiagen). Cannonical Hh pathway: DHH, IHH, SHH, PTCH1, SMO, SUFU, GLI1,2,3; Hh-associated: DISP2, HHIP, LRP2, PTCH2, PTCHD1, ZIC1,2. Moreover: KIT, KRAS, NRAS, HRAS, CBL, mTOR pathway.
Results: The genetic alterations concerned Hh ligands, Hh- cannonical and associated, KRAS/KIT, and PI3K/mTOR genes. According to HH ligands: four tumours presented ultra-rare missense variants in DHH gene- three cases were postpubertal, testicular mixed GCTs. IHH single pathogenic variant was detected in a prepubertal ovarian mixed tumour harboring KRAS pathogenic variant, and IHH variant of unknown significance- in one postpubertal testicular mixed tumour. Missense variants in SHH gene concerned two postpubertal testicular mixed GCTs, including case with coexisting altered IHH and two SHH variants of unknown significance. Five tumours had somatic truncating variants in DISP2: three post-pubertal testicular mixed GCTs and two infantile meoplasms: immature sacrococcygeal teratoma and yolk sac tumour.
Conclusion: Hh pathway ligand genetic alterations were found in 12 / 70 analysed GCTs cases. These alterations can occur in germ cell tumours as isolated event or can coexist with Hh pathway multiple events, KRAS/KIT changes, or PI3K/mTOR pathway mutations. The detected genetic changes in Hh ligands and regulators concern more often postpubertal adolescent testicular mixed GCTs (8/12 tumours). These findings suggest that the dysregulation of Hh signalling on different levels is involved in a complex pathobiology of GCTs.
Funding: Polish National Science Centre grant 2014/15/B/NZ4/04855

PS-26-015

The extent of prostate cancer innervation with different types of nerve filaments

L. Krivošíková*, F. Blasko, P. Babal
*Comenius University Bratislava, Slovakia

Background & objectives: Nerves and catecholaminergic signalling play significant roles in cancer biology and are important microenvironmental components in several cancers. We aimed to analyse nerve types and their distribution in benign prostatic hyperplasia (BPH) and prostate cancer.
Methods: Human samples of BPH (n=10), samples of prostate cancer with Gleason pattern 3 (n=5), and Gleason pattern 5 (n=5) were analysed by immunofluorescence. Antibodies against common neuronal

markers PGP9.5 and S100 were combined with antibodies against tyrosine hydroxylase for the detection of sympathetic nerves, VAChT for parasympathetic nerves, and Substance P and CGRP for sensitive nerves detection.
Results: In BPH were sympathetic filaments in 1/10 of nerves, only a few scattered delicate parasympathetic and rare sensitive fibres in larger nerves. The pattern of innervation in prostate cancer was analogous to BPH. However, there was a considerably lower amount of nerves of all types, especially in high-grade cases. In high-grade prostate cancer, there were no sympathetic fibres in the central areas of the tumour, with increasing positivity in areas of perineural spread. Most cancer cases (8/10) were negative for sensitive fibres, with only occasional fibres on the periphery of the tumour nest.
Conclusion: The presented results may differ from those of other authors. However, the majority of published works are experimental, with minimal data about human prostate cancer. The decrease in nerve density in prostate cancer does not subsidize the role of nerves in it, which has been proven repeatedly. The effects of nerves can be modulated by many factors, including neurotransmitter receptors. Evaluation of nerves distribution in different Gleason patterns is important for further research and assessment of neurotransmitter and nerve-targeted therapy.
Funding: VEGA 1/0684/21

PS-26-017
Analysis of renal cell carcinoma in end-stage renal disease of Hungarian patients
L. Kuthi*, F. Sánta, B. Pósfai, D. Semjén, D. Dénes, Á. Somorácz, A. Fintha, G. Fórika, A. Jenei, T. Micsik, D. Dobi, K. Eizler, N. Giba, B. Iványi, A. Sejben
*University of Szeged, Hungary

Background & objectives: End-stage renal disease (ESRD) and acquired cystic kidney disease (ACKD) are known risk factors of renal cell carcinoma (RCC). In this study, the clinical and pathological characteristics of RCCs developed in ESRD were investigated.
Methods: A database of 2597 nephrectomy cases was built, from 6 pathology departments in Hungary. Then, we identified 42 RCCs in 35 patients that developed in ESRD. Demographic, clinical and pathological parameters, along with the survival data were investigated. RCCs were reclassified according to the current WHO Classification of Urinary and Male Genital Tumours.
Results: Twenty-eight tumours developed in men and 13 in women, with a median age of 57 years (27-75 years). The causes of ESRD were glomerulonephritis (n=7), hypertensive kidney disease (n=6), autosomal dominant polycystic kidney disease (n=6), chronic pyelonephritis (n=4), diabetic nephropathy (n=3), chemotherapy-induced nephropathy (n=1), and undetermined (n=8). ACKD complicated ESRD in 13 patients. The following histological subtypes were identified: clear cell RCC (n=23), papillary RCC (n=8), clear cell papillary tumour (n=5), ACKD RCC (n=3), and eosinophilic solid and cystic RCC (n=2). The median tumour size was 32 mm (10-80 mm), and 39 tumours were kidney-confined (pT1-pT2). No tumour-specific death occurred during the study period. Progression was registered in one patient.
Conclusion: In our cohort, the most common RCC subtype was clear cell RCC (56%), with a frequency that exceeded international data appreciably (14-25%). The incidence of clear cell papillary tumour and ACKD RCC (12.2% and 7.31%) was lower than data reported in the literature (30% and 40%). Our results indicate a favourable outcome of RCC in ESRD.
This research was funded by the University of Szeged, Albert Szent-György Medical School Research Fund-Hetényi Géza Grant (Grant No. 5S 340 A202) and the New National Excellence Program (Grant No. ÚNKP-22-4-SZTE-305).

PS-26-018
Development and validation of a machine learning model for detection and classification of tertiary lymphoid structures (TLS) in renal cell carcinoma (RCC) to predict clinical outcome
I. Laklouk*
*University of Wisconsin Madison, USA

Background & objectives: The prognostic value of TLS in localized RCC is uncertain, and the evaluation of TLSs is hindered by inter-observer variability. To address this, the study aimed to develop a machine-learning model capable of quantifying TLSs automatically using IHC-multiplex whole-slide images.
Methods: TLS maturation was graded using routine H&E slides according to previously published criteria. A HALO platform-based machine learning model was developed and confirmed to automatically identify, tally, and classify TLSs in IHC-multiplex whole-slides. A quantitative scoring scheme for TLSs was proposed and its relationship with survival was investigated in patients with localized RCC.
Results: 88 patients with localized RCC ≥7cm, underwent complete surgical resection at a single institution. Follow-up median of 31 months (IQR 15-62 months). Tumours were categorized into two groups based on the presence of mature TLSs using Brightfield (H&E) staining. Mature TLS (N=38) and no mature TLS (N=50). Using multivariable Cox regression, the impact of TLS on patients' survival rates was analysed while adjusting for prognostic factors (such as sarcomatoid and rhabdoid features, and nuclear grade). The presence of mature TLS was linked with a lower early recurrence likelihood ($P < 0.05$). Furthermore, tumours lacking TLS had significantly worse overall survival rates than those with mature TLS ($P < 0.05$).
Conclusion: In this study, a machine-learning model was developed that is easy to understand and could potentially identify TLSs on IHC-multiplex whole-slides with high precision. This model could be used alongside other methods to assess the risk stratification of localized RCC. To confirm its accuracy, further studies using (H&E) staining whole-slide are needed.

PS-26-019
PD-L1 expression heterogeneity in localized renal cell carcinoma tumours and its prognostic value for predicting metastatic progression: evidence from multi-region sampling
I. Laklouk*, M.H. Lee, D. Jarrard, T. Borza, G. Allen, K. Richards, W. Huang, E.J. Abel, D. Shapiro
*University of Wisconsin Madison, USA

Background & objectives: Prior studies show conflicting evidence regarding the prognostic ability of PD-L1 expression in localized renal cell carcinoma (RCC), likely due to expression heterogeneity throughout RCC tumours. We employed multi-region tumour sampling to evaluate PD-L1 expression heterogeneity and PD-L1 prognostic ability.
Methods: Tumours from 46 patients with localized RCC were used to construct tissue microarrays containing samples from at least 12 locations within each tumour. Patients were matched on clinical variables and divided into two cohorts (progression vs. no progression). PD-L1 expression was quantified with immunofluorescence (Vectra platform). Heterogeneity was assessed using Kernel-density plots. PD-L1 expression was compared using nested t-tests.
Results: 26 patients developed metastatic progression [median follow-up of 7 years (IQR 5-11)], and 20 patients remained disease-free [median follow-up of 11 years (IQR 8-15)]. The median tumour size was 9 cm in both cohorts. There was no statistical difference in age, gender, grade, or stage between cohorts. We observed substantial heterogeneity in PD-L1 expression within all tumours, particularly within tumours that progressed. Additionally, tumours that progressed had higher PD-L1 expression (mean optical density 0.025 vs. 0.011,

P<0.001). PD-L1 was associated with prognosis, and tumours with high PD-L1 expression had a median recurrence-free survival of 11.7 months compared to the median not being reached for low PD-L1 expressing tumours (P<0.001).
Conclusion: These data demonstrate considerable intratumoral PD-L1 expression heterogeneity within localized RCC tumours, which can be mitigated by multi-region sampling. Additionally, PD-L1 expression positively correlates with metastatic progression after radical nephrectomy for localized disease. PD-L1 expression was particularly high for patients who rapidly progressed; thus, PD-L1 may be possible biomarker for patients who should be treated with adjuvant immunotherapy. Currently, no biomarkers are routinely used for localized RCC. Validation using an additional 102 localized RCC patients is currently being performed.

PS-26-020
mTOR mutated eosinophilic renal cell carcinoma: a distinct tumour characterized by mTOR mutation, loss of chromosome 1, and cathepsin K expression responsive to target therapy
S. Marletta*, A. Caliò, G. Settanni, A. Pesci, S. Fratoni, F. Pierconti, M.R. Raspollini, A. Marchetti, G. Martignoni
*Department of Diagnostic and Public Health, Section of Pathology, University of Verona, Department of Pathology, Pederzoli Hospital, Peschiera del Garda, Italy

Background & objectives: In the wide spectrum of oncocytic renal tumours, a subset of neoplasms with high-grade-appearing histologic features harboring pathogenic mutations in mammalian target of rapamycin (MTOR) and hitherto clinical indolent behaviour has been described.
Methods: In the present study, we reported three cases (2F, 1M) of mTOR-mutated eosinophilic renal cell carcinoma with histologically documented metastases (lymph nodes, skull, and liver) and we performed a comprehensive immunohistochemical panel.
Results: All the tumours were composed of eosinophilic cells with prominent nucleoli (G3 by ISUP/WHO) arranged in solid to nested architecture. Additionally, there were larger cells with perinuclear cytoplasmic shrinkage and sparse basophilic Nissl-like granules, superficially resembling the so-called "spider cells" of cardiac rhabdomyomas. Both renal tumours and metastases (skull and liver) were positive for PAX8, CK8-18, and cathepsin K, but not for vimentin. NGS identified mTOR genetic alterations in the three cases (1 deletion in exon 30 p.Tyr1450_Trp1456, 2 mutations in exon 53 p.Leu2427Arg/p.Leu2427Gln), including metastases, and loss of chromosome 1 in all cases. One patient has been treated with Everolimus (mTOR inhibitor) gaining clinical response (metastatic tumours shrinkage).
Conclusion: We present a distinct renal entity characterized by high-grade eosinophilic cells, cathepsin K immunohistochemical expression, and harbouring mTOR gene mutations, demonstrating a malignant potential and showing the responsiveness to mTOR inhibitors. The responsiveness of mTOR inhibitors encourages pathologists to investigate mTOR gene mutations in aggressive high-grade/cathepsin K-positive eosinophilic carcinomas.

PS-26-021
Cathepsin-K immunostaining and eosinophilic renal tumours: two clones in comparison
F.M. Martelli*, A. Caliò, S. Pasinato, S. Marletta, S. Pedron, N. Santonicco, G. Martignoni
*Department of Diagnostic and Public Health, Section of Pathology, University of Verona, Italy

Background & objectives: Cathepsin-K is a lysosomal cysteine protease expressed in translocation renal cell carcinoma, PEComa and in a subgroup of eosinophilic renal neoplasms characterized by TSC/mTOR gene mutations. Recently, staining for Cathepsin-K(EPR19992) has been reported in oncocytoma and chromophobe renal cell carcinoma.
Methods: Cathepsin-K immunohistochemical analysis was performed in 50 oncocytomas, 50 chromophobe renal cell carcinomas and 8 low grade oncocytic tumours (LOT) using two different clones (3F9, mouse monoclonal, dilution 1:2000, ABCAM and EPR19992, rabbit monoclonal, dilution 1:500, ABCAM). The first clone recognized the procathepsin-K, band 37kDa, whereas the second one recognized the mature form, band 27kDa.
Results: Cathepsin-K expression, using clone EPR19992, has been observed in 100% of oncocytomas, in 93% of chromophobe renal cell carcinoma, and in 100% of LOT whereas no staining was seen using cathepsin-K clone 3F9. Immunolabeling of Cathepsin-K clone EPR19992 is also found in the normal distal tubules.
Conclusion: Cathepsin-K has been included in the best practices recommendations on the use of immunohistochemical markers in the differential diagnosis of renal tumours. Staining for Cathepsin-K clone EPR19992 is observed the normal distal tubules and in all eosinophilic renal tumours tested, supporting their origin from distal nephron. Therefore its expression is not helpful in the differential diagnosis of eosinophilic renal tumours whereas Cathepsin-K clone 3F9 is a useful tool.

PS-26-022
PD-L1 expression in clear cell type renal cell carcinoma with immunohistochemical loss of BAP-1
J. Martínez*, D. Fernández-Calvo, I. Ortiz, I. Blázquez, E. Condom, A. Vidal, M. Pujol, M.R. Taco, M. Gomà Gallego, M.Á. López, M. Pané-Foix
*Hospital Universitari de Bellvitge, Spain

Background & objectives: Loss of BAP-1 in clear cell renal cell carcinoma (ccRCC) is associated with increased aggressiveness and histological features like rhabdoid morphology, pleomorphic nuclei and/or eosinophilic cytoplasmic globules . We analysed the expression of PD-L1 in cases of BAP-1 deficient ccRCC.
Methods: We reviewed clinical charts and histological features of cases of ccRCC with loss of immunohistochemical expression of BAP-1 (Clone BSB-109, Gennova) diagnosed in 2021-2022. PD-L1 staining was performed (clones 22C3 from DAKO and SP142 from Ventana-Roche). Results were evaluated calculating the Combined Positive Score (CPS) for 22C3 and the tumour-infiltrating Immune Cells (IC) for SP142.
Results: Fourteen cases with immunohistochemical loss of BAP-1 were identified (13 men and 1 woman; mean age 57,9 years). Most debuted with advanced disease (11/14 stage III-IV; 8/14 metastatic disease within 1 year).
PD-L1 positivity (CPS>10) was detected in 13/14 cases with 22C3 and in 5/14 with SP142 (CI>5%). SP142 expression was borderline in 4 cases (CI 1-5%).
Conclusion: ccRCC with loss of BAP-1 has characteristic phenotypic features. It is associated with aggressive clinical behaviour. Identifying these cases may have clinical relevance for possible therapeutic strategies. The high rate of PD-L1 positivity observed in our series points to the possibility of considering combined treatment with immunotherapy. However, the series is limited and studies with larger numbers of cases are needed.

PS-26-023
Impact of cribriform pattern 4 and intraductal carcinoma on CAPRA-S post-prostatectomy patient stratification
N.J. Nguyen*, K.A. Iczkowski, K. Liu, K. Lajkosz, T.H. van der Kwast, M.R.D. Downes
*University of Toronto, Canada

Background & objectives: We previously demonstrated the impact of cribriform pattern 4 (CC) and intraductal carcinoma (IDC) in biopsies on pre-treatment prostate cancer (PCa) risk stratification

tools. Herein, we assess their impact in prostatectomies on biochemical recurrence (BCR) using CAPRA post-surgical (CAPRA-S) stratification.
Methods: 826 prostatectomy cases diagnosed with PCa between 2010 and 2018 in two North American cohorts were retrospectively assessed for presence of CC/IDC. CAPRA-S scores were calculated and stratified into low (0-2), intermediate (3-5) and high (6-10) risk groups. BCR was compared between cases with and without CC/IDC using Cox model statistics. Prognostic performance was evaluated using Harrell's c-index.
Results: 826 cases: Grade group (GG) 1, n=94; GG2, n=476; GG3, n=185; GG4, n=13; GG5, n=58. Median follow-up time, 4.2 years (range 2.9-6.4). There were 341 (41%) CC/IDC cases, and 166 (20%) BCR. The CAPRA-S low, intermediate, and high risk groups comprised 356 (43%), 329 (40%), and 141 (17%) cases. CAPRA-S scores discriminated the three risk groups for BCR ($p<0.001$). Addition of CC/IDC significantly improved stratification of the CAPRA-S intermediate-risk group for BCR (HR 2.27, 95% CI 1.40-3.66) as well as overall c-index (0.689 vs 0.667, ANOVA $p<0.001$). CC/IDC had no significant impact amongst the low-risk group, and inconclusive effects in the high-risk group likely due to small data volume.
Conclusion: The integration of CC/IDC into the CAPRA-S tool led to substantial improvement of post-surgical patient stratification for BCR in cases with CAPRA-S score 3-5 (intermediate-risk group). This suggests CC and IDC are relevant prognostic biomarkers to be included in future prostate cancer stratification tools. A larger, more diverse cohort with longer follow-up would allow us to better evaluate the impact of CC/IDC in predicting BCR in the CAPRA-S high-risk group and in predicting event-free survival across all risk groups.

PS-26-024
MTAP status in a non-muscle invasive bladder cohort: correlation with grade, subtype and progression
A. Oberc*, E. Olkhov-Mitsel, E. Slodkowska, K.J. Craddock, M.R.D. Downes
*University of Toronto, Canada

Background & objectives: Methylthioadenosine phosphorylase (MTAP) immunohistochemistry (IHC) is a surrogate for *CDKN2A* deletions which have been associated with adverse outcomes in bladder cancer. We assessed how MTAP IHC correlated with grade, molecular subtypes, and clinical outcomes in non-muscle invasive bladder cancer (NMIBC).
Methods: 74 resection and biopsy specimens of NMIBC were graded using a three-tier hybrid system. MTAP IHC (Abnova, clone 2G4) was interpreted as negative when carcinoma completely lacked MTAP expression. Molecular subtype was defined as basal, luminal-URO and luminal-GU using CK5/6, GATA3, and p16 IHC. Progression free (PFS) and recurrence free survival (RFS) were assessed.
Results: There were 56 luminal-URO, 18 luminal-GU, 0 basal and 25 low grade, 21 high grade 2, 28 high grade 3 cases. Luminal-GU was associated with decreased PFS ($p=0.003$) and RFS ($p=0.047$) compared to luminal-URO. High grade 2 and 3 had reduced PFS ($p=0.006$) but no significant change in RFS compared to low grade. Low grade was associated with luminal-URO, whereas high grade 3 was associated with luminal-GU ($p=0.030$). MTAP loss was only identified in luminal-URO (22/56 cases vs 0/18 Luminal-GU). When MTAP status is combined with subtype, luminal-URO with MTAP loss shows an intermediate PFS between MTAP-intact URO and luminal-GU ($p=0.007$).
Conclusion: High grade and luminal-GU subtype were associated with progression to muscle invasion or beyond ($\geq$ pT2). We established MTAP loss occurs exclusively in the luminal-URO subtype, similar to findings in muscle invasive bladder cancer, and that MTAP loss reduces PFS. This suggests that MTAP may be a relevant prognostic biomarker in luminal-URO NMIBC and could help in determining frequency of follow up and management in the most common molecular subgroup of NMIBC.

PS-26-025
Transrectal ultrasound prostate biopsy is associated with higher rates of Gleason grade group concordance in prostatic adenocarcinoma compared with transperineal biopsy: a retrospective cohort series from a tertiary referral centre
P. Reddy*, N. Swan, T. Crotty, D. Galvin
*Histopathology Department, St Vincent's University Hospital, Ireland

Background & objectives: Prostate biopsy (PB) Gleason grade group (GGG) scoring is a key parameter for diagnosis, risk stratification and management decisions in prostate cancer. Our study investigated whether PB method affects the concordance rates of GGG between PB and radical prostatectomy (RP).
Methods: Our study included 588 patients who underwent RP from January 2018 to December 2022. We collected data from histology reports on biopsy method, age, GGG on PB, GGG on RP, surgical margin status and the presence of extra-prostatic extension (EPE). Statistical analysis was performed using a chi-square test for categorical variables and Mann Whitney U test for continuous variables.
Results: The median age at RP was 62 years. Transrectal ultrasound biopsy (TRUS) was performed in 72% of cases, while transperineal biopsy (TP) was used in 21%. Overall concordance was observed in 58% of cases, with 22% upgraded and 20% downgraded. GGG 4 was the least predictive group, with 68% of these cases assigned a different GGG at RP. GGG upgrading was more frequent in TP compared with TRUS biopsy (55% vs 33%) and this method of biopsy was significantly associated with GGG upgrading ($p=0.01$). EPE and seminal vesicle involvement (SVI) were also associated with GGG upgrading ($p=0.01$ and $p=0.01$). Surgical margin status was not significantly related to GGG upgrading ($p=0.48$).
Conclusion: Our study further highlights that GGG discordance between PB and RP is a common occurrence. While our study is limited in size, it demonstrates a significantly higher rate of upgrading in TP compared with TRUS. This finding emphasises the need for further investigation into the relationship between biopsy method and GGG upgrading. We also highlight other factors associated with GGG upgrading, namely the presence of EPE and SVI. These may assist management decisions at multidisciplinary team meetings.

PS-26-026
Predictors of cancer-specific mortality in pT1 urothelial bladder cancer: 50 months follow-up in 284 cases
A. Ristic Petrovic*, S. Stojnev, M. Potic Floranovic, I. Conic, M. Krstic, L. Jankovic Velickovic
*University Clinical Centre Nis, Medical Faculty University of Nis, Serbia

Background & objectives: Treatment of pT1 bladder cancer should be personalized from the beginning in order to preserve functional bladder. Molecular pathways activated in hypoxia personalize response to radio/chemotherapy. NOTCH3 contributes chemotherapy resistance and NOTCH3-HIF1α interaction leads to hypoxia-induced resistance to radiotherapy.
Methods: The immunohistochemical expression of HIF1 alpha, VEGFR1, and NOTCH3 was evaluated in 284 pT1 bladder cancer samples, incorporated in tissue microarrays. HIF1-alpha was assessed through nuclear staining, VEGFR1 through cytoplasmic expression, while for NOTCH3 membranous expression was declared as positive. Micro-vessel density was estimated through counting the CD34 positive micro-vessels.
Results: After a mean follow-up of 50 months, in 284 patients diagnosed with pT1 bladder cancer, we found independent predictors of cancer specific mortality: older age, high grade, presence of divergent differentiation, especially squamous, concomitant carcinoma in situ, smoking, dysuria as the first symptom, all types off treatment

that did not include intravesical BCG instillation after transurethral resection, and absence of recurrence or a lower number of recurrences. The presented study identified HIF1α, VEGFR1, NOTCH3 and micro-vessel density as independent prognostic parameters for overall survival and cancer specific survival of patients. NOTCH3 overexpression, greater micro-vessel density, absence of HIF1α and absence of VEGFR1 expression indicate shorter overall and cancer specific survival.
Conclusion: Complete clinical data, a comprehensive pathohistological report, estimation of HIF1 alpha, VEGFR1, NOTCH3 expression and number of CD34 positive micro-vessels on a 2mm biopsy incorporated in tissue microarray could select pT1 patients that require intensive follow-up and a trimodal approach to treatment. Understanding the role of molecular pathways in chemio/radiotherapy response could bring new possibilities for better controlling and personalized, molecular treatment of bladder cancer.

PS-26-027
Low-grade oncocytic tumour of the kidney – clinical, pathological, and genetic features
F. Sánta*, D. Dénes, Á. Somorácz, A. Jenei, G. Fórika, A. Fintha, N. Kránicz, Z. Mészáros, F. Salamon, K. Eizler, N. Giba, D. Semjén, B. Pósfai, A. Sejben, L. Kuthi
*University of Szeged, Hungary

Background & objectives: Low-grade oncocytic tumour of the kidney (LOT) is a provisional entity categorized as "other oncocytic tumour" in the current World Health Organization classification scheme. In this study, we investigated the clinical, morphological, immunohistochemical, and genetic characteristics of LOT.
Methods: LOTs were collected from 6 pathology departments in Hungary. We recorded the demographic, pathological, and survival data. The immunophenotype of the tumours was characterized by CA9, CK7, CK20, CD10, CD117, AMACR, PAX8, GATA3, FH, and SDHB. By the expression of mismatch repair proteins, we defined the microsatellite status. Whole exome sequencing was carried out in 5 cases.
Results: We identified 12 LOTs in 7 males and 5 females. The median age was 74 (51-83 years). The median tumour size was 33.5 mm (18-105 mm). All LOTs were kidney-confined (10 pT1 and 2 pT2). The growth pattern was solid, and the tumours were composed of eosinophilic tumour cells having mild nuclear atypia and perinuclear halos. All cases harboured a CK7-positive and CD117-negative immunophenotype, furthermore, PAX8, GATA3, FH, and SDHB were diffusely positive in all LOTs. The mismatch repair proteins were retained, indicating a microsatellite stable status. The whole exome sequencing revealed mutations of the TSC1, TSC2, mTOR, and PIK3CA genes. Cancer-specific death was not recorded.
Conclusion: In our tumour set, LOT was a rare neoplasm (0.42%), with an excellent clinical course, and it mainly affected old males. LOTs had a unique immunophenotype (CK7+, CD117-, GATA3+), that could be used to discriminate LOTs from other renal neoplasms with eosinophilic cytoplasm. The presence of the mutations of the mTOR/PIK3CA pathway supports that LOT can be a distinct renal tumour entity.
Funding: Géza Hetényi Grant, Albert Szent-Györgyi Medical School Research Fund, University of Szeged (5S 340 A202) and New National Excellence Programme (ÚNKP-22-4-SZTE-305).

PS-26-028
Prognostic significance of death receptors expression in primary and recurrent T1 bladder cancer
S. Stojnev*, M. Krstic, A. Ristic Petrovic, I. Conic, I. Petkovic, J. Todorovic, M. Mladenovic, L. Jankovic Velickovic
*University Clinical Centre Nis, Medical Faculty University Nis, Serbia

Background & objectives: Stage T1 bladder cancer is a potentially lethal disease with a ten-year progression rate of 40%. A high risk of progression warrants careful endoscopic surveillance. The aim of this study was to assess the prognostic impact of death receptors' expression.
Methods: This study included 224 high grade T1 urothelial bladder cancers, out of which 168 were primary and 56 recurrent cases. Tumour samples were incorporated in tissue microarrays and analysed by immunohistochemistry for expression of DR4, DR5, and FAS receptor. The expression status of death receptors was correlated with pathological parameters and follow-up data. The median follow-up was 60 months.
Results: High expression of DR4, DR5, and FAS was observed in 67%, 72.5%, and 57.1% of the tumours, respectively, and mutually strongly correlated. DR4 was associated with smoking (p=0.045), while FAS expression was more frequent in male patients (p=0.028). FAS stained primary tumours more frequently than recurrent ones (p=0.044). Loss of FAS was significantly associated with cancer-specific death (p=0.046). There was no statistically significant association between death receptors expression and overall survival in the whole group. However, after stratification for primary and recurrent tumours, loss of DR4 expression in recurrent tumours was the predictor of shorter overall survival (p=0.015).

Conclusion: The expression of death receptors may play a significant role in the prediction of T1 bladder cancer prognosis. DR4 loss in recurrent tumours may indicate progression and predict inferior outcome in patients with T1 disease. Death receptors should be included in immunohistochemical biomarkers that require further validation and may potentially aid in personalized decision-making.

PS-26-029
Penile squamous cell carcinoma: prognostic impact of p53 immunohistochemical expression using a pattern-based framework
I. Trias*, R. López, I. Ribera-Cortada, I. De-Torres, C. Ferrándiz, F. Algaba, N. Rakislova
*Hospital Clinic de Barcelona, Spain

Background & objectives: To analyse the prognostic value of p16 and p53 immunohistochemistry (IHC) in 122 patients with primary penile squamous cell carcinomas (PSCC).
Methods: PSCC were classified HPV-associated/HPV-independent based on p16 IHC. p53 IHC was evaluated using "mutated" patterns (diffuse or basal over-expression, null or cytoplasmic staining), and "wild-type" patterns (scattered and mid-epithelial positivity sparing basal layer). Patients were staged using UICC criteria and treated following standard protocols. Mean follow-up was 66.7 months (range 7-237). Disease-free survival (DFS) and overall survival (OS) were analysed.
Results: Thirty-six tumours (29.5%) were HPV-associated (mean age 67y) and 86 (70.5%) HPV-independent (mean age 69y). p53 IHC showed abnormal pattern suggestive of mutation in 55 tumours:51/86 (59.3%) HPV-independent and 4/36 (11%) HPV-associated tumours (p<0.001). 58 of the patients were stage I tumours, 41 stage II, 15 stage III and 8 stage IV. p16 IHC (HPV status) had no impact on stage, DFS or OS. Stage was related to DFS and OS (p=0.001 and p<0.001, respectively). Abnormal p53 IHC showed impaired OS (p=0.002). Moreover, 9/10 patients (90%) in advanced stage (III/IV) with abnormal p53 pattern died of disease, whereas only 2/13 patients (15%) with normal p53 IHC, died of disease (p<0.001).
Conclusion: Patients with PSCC showing an abnormal pattern of staining for p53 evaluated using the pattern-based framework, have an impaired prognosis. This association between abnormal p53 and prognosis is particularly strong for patients with advanced stages. p53 could help to define prognosis and to refine treatment strategies for patients with PSCC.

PS-26-030

PTEN loss in intraductal carcinoma of the prostate has low incidence in Japanese patients

T. Tsuzuki*, T. Takahara, T. Itou, N. Taniguchi, Y. Yamamoto
*Aichi Medical University, Japan

Background & objectives: Clinical and genomic features of prostate cancer (PCa) vary considerably between Asian and Western populations. PTEN loss is a frequent abnormality in intraductal carcinoma of the prostate (IDC-P) in Western populations. We evaluated PTEN expression in IDC-P in Japanese population.
Methods: This study included 45 and 59 patients with PCa with and without IDC-P, respectively, who underwent radical prostatectomy. Representative slides for each case were stained by ERG, PTEN, and high molecular weight cytokeratin.
Results: PTEN loss was observed in ten patients with PCa with IDC-P (22%) and nine patients with PCa without IDC-P (17%). There were no significant differences in age, pathological stage, Gleason grade, presence of Gleason pattern 5, IDC-P, cribriform pattern, lymphovascular infiltration, or frequency of biochemical relapse between patients with PCa with and without PTEN loss. ERG expression was relatively frequent in patients with PCa with PTEN loss, although a significant difference was not observed. PTEN loss and ERG expression co-occurrence were observed in four patients with PCa with IDC-P and one without IDC-P. PTEN loss and ERG expression did not affect progression-free survival, regardless of the presence of IDC-P.
Conclusion: The frequency of PTEN loss in IDC-P is lower in Asian patients than in Western patients. Our results indicate the presence of an unknown mechanism underlying IDC-P in Asian populations.
Funding: Grants-in-aid for Scientific Research (KAKENHI): 21K06933, 22K09497

PS-26-031

Origin and outcome of testicular metastasis: a nationwide study

C. Woortman*, A. Van Leenders, N. Hugen, M.G.H. van Oijen, I.D. Nagtegaal
*Department of Pathology, Radboud University Medical Center, Nijmegen, The Netherlands

Background & objectives: Testicular metastases are rare. Existing studies date back to 1934 and the number of included patients is low. This study aims to increase insight into the origin and timing of testicular metastasis, the occurrence of oligometastases and survival of patients.
Methods: A nationwide retrospective review of pathology reports of all patients diagnosed with testicular metastases between 1991 and 2021 was performed. Data was collected from the Dutch nationwide pathology databank (PALGA) and the Dutch Cancer Registry (NCR). Log-rank testing and Kaplan-Meier analyses were used to assess overall survival, and Cox proportional hazard models were used for multivariate survival analysis.
Results: A total of 175 patients with a testicular metastasis were included. The median age at diagnosis of testicular metastasis was 67 years. Testicular metastases originated from a variety of primary tumours, though most frequently from the prostate (40.6%), kidney (13.7%), colon (10.3%), bladder (7.4%), and skin (5.7%). In 15 patients the primary tumour was unidentified. Solitary metastasis occurred in 42% of patients. Overall survival after the diagnosis of a testicular metastasis was poor with a median survival of 14.2 months (95% CI 10.2 – 18.3). The primary tumour origin was an independent factor for survival, with worst outcome for patients with primary skin, bladder and colon cancer.
Conclusion: Testicular metastases are very uncommon and arise mainly from primary tumours anatomically close to the testes. Patient outcome is dependent on the origin of the primary tumour, although invariably poor.

PS-26-032

A comparative study of holmium laser enucleation of the prostate (HoLEP) and transurethral prostate resection (TUR-P) containing prostatic adenocarcinoma

S. Yilmaz Erozbek*, T.C. Savli, A. Çakır, B. Muezzinoglu
*Department of Pathology, Istanbul Medipol University, Turkey

Background & objectives: Recently, HOLEP(Holmium laser enucleation of the prostate), which obtains more material, has been added to the TUR-Prostate of the treatment of prostatism. In this study, the frequency of prostatic adenocarcinoma(PA), the characteristics of the patients, the sampling methods were investigated.
Methods: Samples of 269 HoLEP patients between 2021-2023 and 770 patients who underwent TUR-P between 2014-2023 evaluated retrospectively. Age, PSA values, material weights, tumour types, histological grades, rate of tumour detected in the excised tissue and number of chips (both initial sampling and resampling) of patients diagnosed with incidental PA were examined. Chi-square and t-test were used for comparisons.
Results: PA was detected in 54(5%) cases,25 in HoLEP (25/269,9%),29 in TUR-P(29/770,4%).The frequency was found to be higher in HoLEP ($p=0.0004$). When tumours within the materials were compared, no difference was found in terms of age($p<0.05$).However, a significant difference was found between mean total PSA (HoLEP:8.42, TUR-P:11.7,$p=0,003$)and mean material weights (HoLEP:61 gr,TUR-P:9 gr, $p<0,001$).When HoLEP with and without tumour were compared, no significant difference was found between age, total PSA, and material weight. Tumour grade group didn't change, in resampled TURP and HoLEP materials. Extra tumours were seen in 10 (71%) of the 14 resampled HoLEP material, with only 2 cases the total tumour percentage and the average cassette count increased.
Conclusion: The number of HoLEP is increasing in pathology laboratories. HoLEPs, where more tissue is obtained compared to TURP, affect the workload, sample size and increase the number of incidental PAs. Searching for clues that will enable us not to miss a possible adenocarcinoma in the HoLEP materials will facilitate the daily pathology routine. In addition, with the data obtained from the study, the patient group that is considered to be applied HoLEP can be determined more clearly.

E-Posters

E-PS-01 | E-Posters Autopsy Pathology

E-PS-01-002

Collaborative digital forensic histopathology whole-slide images library in postgraduate education

C. Amalinei*, A.D. Timofte, I.D. Căruntu, S.E. Giușcă, R.A. Balan, E.R. Avadanei, L. Lozneanu, A. Grigoraș
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: In the context of whole-slide-based imaging techniques improvement driven by COVID-19 pandemic, digital microscopy has become increasingly important in microscopy education, along with remote histopathological diagnosis.
Methods: A consortium-based two-years European project that began in December 2022 is currently developing a section of forensic histopathology within a digital slides library, by joining the work of Morphology teachers and Pathologists, supported by whole-slide-based imaging techniques and software.
Results: The result is a continuously improved cloud-based collection of digital slides containing the main topics in forensic pathology, including fatal cardiac and non-cardiac pathology (central nervous system, respiratory, gastrointestinal, hepatic, pancreatic, adrenal, splenic, genitourinary, and paediatric pathology), along with miscellaneous

injuries, which allows simple visualization, easy navigation, measurements, and areas of interest delimitation. By creating this section of a digital library, postgraduate students, as junior in training or residents of Pathology may have easy access to the dedicated database, with the possibility of self-training and export of their personal annotations. Due to included available software tools, the collection may be also used for testing of their progresses in histopathology learning.
Conclusion: Considering that digital histopathology becomes a reality in many universities and Pathology labs across the world, as it allows remote work, our project creates the base of modernization of the training curricula of future specialists in Pathology, providing also an additional channel of communication between students and teachers. The use of whole-slide-based imaging techniques represents a largely accepted educational method among Medicine undergraduate and postgraduate students and teachers and opens the perspectives of a better and optimized knowledge of microscopy.
This study is supported by Erasmus+, ANPCDEFP - KA220-HED - Cooperation partnerships in higher education, project 2022-1-RO01-KA220-HED-000089017.

E-PS-01-003
Incidental renal angiomyolipomas – autopsy findings
C. Amalinei*, A. Grigoraș, L.A. Riscanu
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: Angiomyolipoma is a relatively rare benign mesenchymal tumour, mainly located in kidneys, but also occurring in extrarenal sites. The aim of our study is to report a miniseries of cases of incidental angiomyolipomas necroptically diagnosed, from our files.
Methods: Six cases have been selected from our files, four men and two women, with age range between 53-79 years-old, in which necroptic examination has been associated to collection of tissue specimens for microscopy. Routine hematoxylin-eosin staining, along with immunohistochemistry, using a panel of markers (HMB45, MelanA, SMA, Desmin, S100, Vimentin, CK AE1/AE3, and CK7) have been performed.
Results: The histopathological examination revealed 0.5-2cm diameter, circumscribed, non-encapsulated renal tumours, with pushing borders, containing a variable triphasic pattern of growth (mature adipose tissue, myoid spindle cells, and large pleomorphic epithelioid cells), with trapped renal tubules, and dysmorphic thick walled hyalinized blood vessels. A variable positive immunoexpression of HMB45, MelanA, SMA, Desmin, S100, Vimentin, along with CK AE1/A3 and CK7 negativity has been observed. The corroboration of histopathological and immunohistochemical findings led to the diagnosis of incidental angiomyolipomas, classic variant. The differentials have been clear cell renal cell carcinoma, well differentiated liposarcoma, leiomyoma, leiomyosarcoma, pleomorphic rhabdomyosarcoma, melanoma, adrenal cortical carcinoma, oncocytoma, and mixed epithelial and stromal cell tumour of the kidney.
Conclusion: Angiomyolipoma, a member of the perivascular epithelioid cell (PEC) tumour family, is usually diagnosed in the second or third decade of life but, due to slow growth and late symptoms, it may represent an incidental finding in autopsy, such as in our miniseries of cases. Despite their rarity, angiomyolipomas should be considered in the differential diagnosis of other renal tumour masses. The microscopic examination associated with immunohistochemistry is important in diagnosis certification.

E-PS-01-004
Unusual autopsy diagnosis in an adrenal tumour
C. Amalinei*, A. Grigoras, L. Lozneanu
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: Metastatic malignancies are relatively frequent in forensic practice. The aim of our study is to report a case with an unusual apparent primary adrenal tumour with multiple metastases, in a 75-year-old man, who has been diagnosed in our department.
Methods: Necroptic examination has been associated with collection of tissue specimens for microscopy. Routine hematoxylin-eosin staining, along with immunohistochemistry using a panel of markers (S100, HMB-45, Melan-A, PRAME, Synaptophysin, Chromogranin A, Inhibin A, and Ki67) have been performed.
Results: The gross examination revealed a pigmented left adrenal mass, of about 2cm diameter, adherent to pancreas, with areas of haemorrhage of 0.1-0.2 cm, leptomeningeal, intra-cerebral, and intra-cerebellar pigmented areas, of 0.3-1cm diameter, calcified coronary atherosclerosis, ischemic myocardial fibrosis, and areas of lung condensation. Adrenal microscopy revealed an irregular distribution of large atypical epithelioid cells, with confluent growth, marked nuclear enlargement, hyperchromasia, irregular coarse chromatin, prominent eosinophilic nucleoli, increased mitotic activity, tumour necrosis, abundant inflammatory infiltrate, haemorrhage, and fibrin deposits. Immunohistochemistry confirmed its melanocytic origin (HMB-45, S100, Melan-A, and PRAME positivity), associated with melanocytic-positive tumour implants in myocardium, leptomeninges, brain, pancreas and retroperitoneal soft tissues. Furthermore, bronchopneumonia has been microscopically diagnosed.
Conclusion: Although a large adrenal tumour may suggest a pheochromocytoma, the variable presence of pigment and immunohistochemical positivity for melanocytic markers confirmed the onset of a metastatic malignant melanoma in left adrenal gland, myocardium, leptomeninges, brain, pancreas, and retroperitoneal soft tissue, in the absence of an usual cutaneous or extracutaneous location of a primary tumour. The unusual autopsy presentation of this malignant melanoma serves as a reminder that melanoma may be always included in variable tumours differential diagnosis.

E-PS-01-005
Aortic invasive fungal infection – a rare case in forensic pathology
C. Amalinei*, R.A. Balan, T.A. Balan, A. Grigoraș
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: Aortic wall invasion of fungal infection is a rare condition, which may occur following cardiac surgery or in immunocompromised patients. The aim of our study is to report an aorta invasive fungal infection, necroptically diagnosed in a 34 years-old men.
Methods: Autopsy examination has been associated to collection of tissue specimens for microscopy. Routine hematoxylin-eosin and Periodic acid Schiff staining have been performed.
Results: The autopsy showed consolidation area of 70/50/40mm, located in the right lung superior lobe and an area of necrosis in the ascending aorta wall, situated at 20mm superior to the sigmoid valves, associated with an intraluminal thrombotic mass. The microscopic examination revealed the fungal hyphae and neutrophils in the alveolar spaces associated with alveolar haemorrhages in the surrounding lung areas and fungal hyphae invasion of the pulmonary blood vessels. Within the ascending aorta, a partially occlusive thrombus covering an area of necrosis located in the media of the aortic wall, associated with fungal hyphae and neutrophils has been observed. Differentials between aspergillus, candida, and mucormycota species have been considered.
Conclusion: Invasive fungal infection of the aorta is a rare and aggressive complication with high mortality. Despite their rarity, fungal aortitis should be considered in the differential diagnosis of other infectious aortitis (tuberculous or luetic aortitis), or non-infectious aortitis, such as giant cell arteritis, Takayasu arteritis, and Ormond's disease. These may be incidentally discovered during the necropsy, the microscopic examination being important in the certification of diagnosis.

E-PS-01-006

Diabetes-induced dementia: review of histopathological changes on autopsy

B.M. Bernal G.*, L.F. Salas
*Universidad Pedagogica y Tecnológica de Colombia, Colombia

Background & objectives: Diabetes-induced dementia diagnosis is frequent by use of glial damage biomarkers. Advanced glycation end products (AGE) affect secretion of brain-derived neurotropic factor-BDNF, cause of cognitive decline In vivo, with limited histopathological data, aims in order to state of the art.
Methods: Systematic review was elaborated with Key words BDNF and Diabetes, BDNF and histopathology, BDNF and Dementia, in order to find morphological characteristics when BDNF is risen; The case definition were articles with the presence of BDNF levels in serum samples or Cerebral spinal fluid and clinicopathological features of Diabetes.
Results: The search results were extracted from 33 randomized controlled trials. Data extracted from abstract and full text reading. Clinicopathological findings showed not relationship between increased BDNF levels and interventions against Hyperglycaemic status except exercise and movement. Only two studies shown unspecific histopathological changes and then we could find a relevant topic to research on Autopsies in order to answer the question that Diabetes damage on cerebral tissue could be prevented earlier.
Conclusion: Despites their pathological changes on glial and biochemical factors, neuroinflammation without microorganisms still being controverted. Injury to blood brain barrier like that observed on aging, occasionally described on autopsy settings, with disfunction in aerobic metabolic pathways, can be related with increase of amyloid B deposits and chronical hyperglycaemia. Histopathological features about these phenomena could be linked.
Funding: 2496-2498 DIN UPTC

E-PS-01-007

Streptococcus pyogenes sepsis in a 3-year-old girl, apropos of an autopsy study

S. Blasco Muñoz*, A. Sánchez Espinosa, A. Ortiz González, C.A. Capozzi, D. Pérez Parra, E. Guillén Saorín, E. Aguilar Navarro, C. López Peña
*Complejo Hospitalario Universitario de Cartagena, Spain

Background & objectives: A 3-year-old girl consulted for fever, vomiting and diarrhoea of 12 hours of evolution. After an emergency room examination, she was discharged with a diagnosis of gastroenteritis, and was readmitted a few hours later in a state of shock.
Methods: After a torpid evolution, the patient died and we performed a postmortem examination. Samples were taken for histological and microbiological study. Macroscopic findings included: petechial exanthema, chin skin erosion, pulmonary oedema and congestion, blackish appearance of the adrenal glands, fibrinoid material in the urinary bladder wall, subgaleal haemorrhage, and meningeal empyema.
Results: Histologically the most relevant findings were: cerebral oedema and hyaline thrombi, meningeal haemorrhage, meningitis focus, pulmonary oedema and haemorrhage, adrenal haemorrhage, renal septic embolisms, cystitis, intravascular leukemoid reaction. Culture results were positive for Streptococcus pyogenes in lung tissue, meningeal and bladder fibrinoid material. The histopathologic and microbiology findings, in the context of systemic multiorgan failure due to sepsis caused by Streptococcus pyogenes, justify the triggering cause of the Exitus.
Conclusion: Streptococcus pyogenes septic shock induces hypovolemic shock, which justifies hypotension, as well as hypoxic-ischemic damage at the multiorgan level. In addition, it can produce toxic shock by means of streptococcal pyrogenic exotoxins that act as superantigens, producing excessive immune response and a state of procoagulation. The accompanying leukemoid reaction, consisting of an increase in the immature-looking leukocyte population in peripheral blood, can occur in response to many diseases, including acute or chronic infectious processes.

E-PS-01-008

An unusual case of disseminated actinomycosis with cardiac, cerebral, and patchy pulmonary involvement

L. Chinezu*, I. Iurian, C. Carasca
*G.E. Palade UMFST Targu Mures, Romania

Background & objectives: Actinomycosis is an infrequent, slowly progressive bacterial infection, with cervico-facial, thoracic, abdominal, or pelvic region involvement. Hematogenous seeding from a primary site could be the cause of disseminated actinomycosis (DA). The sudden death was rarely reported in DA.
Methods: We presented the case of a 77-years-old male found dead at home without previous medical history. The autopsy was performed at the Institute of Forensic Medicine of Targu Mures, Romania.
Results: Gross examination of cerebral and lung tissue was non-specific. Heart examination revealed multiple patchy, discoloured, and haemorrhagic areas on left ventricular sections. Microscopically, abundant suppurative inflammation and characteristic structures composed of central sulphur granules surrounded by an eosinophilic material suggestive for Actinomyces were seen in subarachnoid space, cerebral tissue, and myocardium. The examination of the lungs revealed diffuse acute oedema and small foci of mixed inflammatory infiltrates with only few structures suggestive for Actinomyces. The final diagnosis was DA associated with extensive myocarditis, meningoencephalitis, and patchy bronchopneumonia.
Conclusion: As in our case, sudden cardiac death can occur in DA and it can be related to extensive myocarditis. The better characterisation of this rare disease is needed to improve our understanding, to minimize morbidity, and to prevent death.
Funding: FDI internalization of higher education

E-PS-01-009

A sudden infant death syndrome in a full-term neonate: autopsy findings

S. Emoke-Andrea*, A. Raicea, L. Chinezu
*G.E. Palade UMFST Targu Mures, Romania

Background & objectives: Sudden infant death syndrome (SIDS) of a previously healthy infant occurring within the first postnatal week is a very rare occurrence. We present the case of a full-term neonate who was found unresponsive after breastfeeding.

Methods: A 4 day-old male infant was pronounced dead after cardiopulmonary resuscitation with endotracheal intubation. A complete autopsy was performed at Institute of Forensic Medicine, Targu Mures, Romania.
Results: Gross examination revealed whitish material predominantly in the trachea, bronchi, and in a small amount in the stomach. The organs were congested. Extensive histological examinations of lung tissue identified amorphous material, suspected to be aspirated milk in the bronchi, bronchioles, and alveoli, associated with collapsed and emphysematous alveoli. Inflammation was not evident in lung sections. No other pathological findings were observed at macroscopic and microscopic examinations of the organs. The final diagnosis was SIDS due to a suddenly developed accidental milk aspiration.
Conclusion: In many cases of SIDS, an extensive histopathological assessment is necessary for the identification of the cause of death. As not all infants exhibit respiratory symptoms, when they aspirate, the postmortem diagnosis of milk aspiration can be a challenge for the clinician

and pathologist. Without symptoms, aspiration often goes undetected or is misdiagnosed and may eventually cause morbidity and even mortality.
Funding: FDI internalization of higher education

E-PS-01-010
Massive perivillous fibrin deposition and COVID 19: a neonatal autopsy case report
G. Escuer*, P. Puente López, M. Parron-Pajares, E. Martin-Boado, I. Esteban-Rodríguez, R.M. Regojo-Zapata
*La Paz University Hospital, Spain

Background & objectives: Massive fibrin deposition (MPFD/MFD) causes significant neonatal morbidity and mortality and has a multifactorial aetiology. We present a neonatal autopsy case of this entity in relation to SARS-CoV-2 infection.
Methods: We reviewed the clinical history and performed a radiological examination and a complete study of the internal organs of the newborn. Immunohistochemistry techniques C4d and SARS-CoV-2 spike antibody (1A9) Gene TeX were used for the histological evaluation of the placenta. We performed a literature review of this pathology in Pubmed.
Results: In 2021, we performed an autopsy on a preterm newborn at week 25 who died at 45 min of life, despite resuscitation manoeuvers, after an urgent caesarean section for risk of perinatal death in a threatened preterm labour. The mother was on HIV therapy with an undetectable load and tested positive for COVID-19 PCR in week 23. The only autopsy findings were a low weight percentile, an altered brain/liver ratio and a delayed radiological bone development. The placenta had a massive perivillous fibrin deposition with associated chronic histiocytic intervillositis.
Due to the maternal medical history, spike COVID 19 immunohistochemistry was performed on the placenta with positive result.
Conclusion: Massive fibrin deposition is a placental pathology at the second/third trimester that, although rare, has a great impact on foetal health and risk of recurrence.
Although its pathophysiology is unclear, it has been associated with maternal thrombophilia, antiphospholipid syndrome, autoimmune diseases and a variety of infections such as cytomegalovirus, enterovirus and the newly emerging SARS-CoV-2.

E-PS-01-011
Elements of COVID-19 morphogenesis after the development of viremia in the analysis of sectional cases of early death
G. Gubina-Vakulik*, G. Gradil
*KhNMU, Ukraine

Background & objectives: The causes of death with COVID-19 were analysed and described in numerous publications. The objective was to show the paramount importance of "weakness" of the blood vessel endothelium for lethal outcome development at first days after viremia arising in COVID-19.
Methods: The case histories, autopsy protocols and micropreparations of various organs stained with hematoxylin-eosin of 38 deceased patients with COVID-19 (Regional Clinical Infectious Diseases Hospital, Kharkiv) were studied, among which two patients lived from the onset of the first symptoms to death for 1-1.5 days and 7 patients who died on 5-6-7 days.
Results: Patients who died within 1-1.5 days were patients with a history of prolonged and severe diseases accompanied by frequent and severe damage to the endothelium of blood vessels: arterial hypertension and general atherosclerosis, coronary artery disease with extensive post-infarction cardiosclerosis, type 2 diabetes. The autopsy material revealed signs of DIC followed by shock, without the formation of interstitial pneumonia.
Patients who died on 5-7 days of COVID-19 had a history of the same diseases, but less long, in addition, 1 case - chemotherapy and 1 case - drug user. In them, we have observed pathologically the development of typical interstitial pneumonia with the development.
Conclusion: Early deaths in COVID-19 are directly related to the rapid development of a decompensated state of the blood vessel endothelium due to a decrease in compensatory capabilities in the presence of endothelial-damaging background diseases. The decompensated state of the endothelium is developed very fast (shock) or in some days (interstitial pneumonia). For the pathologist, the possible effectiveness of the use of endothelium-sparing medications is obvious already at the first symptoms of COVID-19 in patients with a history of endothelial-damaging diseases.

E-PS-01-012
Disseminated tuberculosis as a cause of death: an autopsy study
E. Gun*, A. Bugra, S. Yalcinkaya, N. Ziyade
*Basildon University Hospital, Mid and South Essex NHS Foundation Trust, Basildon, Essex, United Kingdom

Background & objectives: Disseminated tuberculosis (DT) is a potentially fatal form of tuberculosis that occurs in 1-2% of all tuberculosis cases, as a result of the lymphohematogenous spread of Mycobacterium tuberculosis. We aimed to investigate DT cases that we encountered during forensic histopathology practice.
Methods: Cases that underwent autopsies between January 2018 and July 2022 and were diagnosed with tuberculosis were reviewed. The demographical characteristics, country of origin, autopsy, histopathological, and microbiological findings of the cases where DT was identified as the cause of death were investigated. The histopathological prediagnosis of tuberculosis infection was confirmed microbiologically in all cases. Acid-fast staining results were graded from 1+ to 4+.
Results: There were a total of 178 tuberculosis cases. Eighty-five of these cases were pulmonary tuberculosis whereas six of them were extra-pulmonary (EP) and 87 were DT. The mean age of DT cases was 35 years (15-86) with 71 males and 16 females. For DT cases, the second most commonly involved organ after the lungs was the liver, followed by the spleen, kidney, and lymph nodes. The majority of the cases had tuberculoid granulomas in multiple organs. There were six DT cases with heart involvement and two EP cases with isolated involvement of the heart. Central nervous system tuberculosis was detected in five cases and tuberculosis meningitis was detected in two.
Conclusion: Tuberculosis infection continues to be a global health problem despite all treatments. According to World Health Organization data from 2021, it is the second most common infection resulting in death worldwide. DT is a severe and potentially fatal form of tuberculosis that affects multiple organs, and its diagnosis requires a high level of suspicion. The findings from this study highlight the importance of histopathological and microbiological examinations in the postmortem period, which can aid in improving diagnostic and treatment approaches.

E-PS-01-013
Conduction system hamartoma – autopsy case series
E. Gun*, B. Keskin Ozturk
*Basildon University Hospital, Mid and South Essex NHS Foundation Trust, Basildon, Essex, United Kingdom

Background & objectives: Conduction system hamartoma is a benign hamartomatous lesion arising from Purkinje and Purkinje-like cells of the heart. It tends to occur in females under two years old. We aimed to investigate the cases that we detected during postmortem histopathological examination.

Methods: The histopathology reports of the cases that were autopsied between 2012 and 2022 were reviewed retrospectively using the keywords "conduction system hamartoma" and "histiocytoid cardiomyopathy". The cases were evaluated in terms of histopathological features, demographic data, autopsy findings, causes of death, microbiological results, and accompanying cardiac anomalies.
Results: There were a total of four cases. The female-to-male ratio was 3/1. The mean age of the cases was 5.8 months. The average heart weight was 36,3 grams and it was found within the normal range when evaluated according to age and gender. No malformations were observed in the heart or great vessels in any of the cases. Endocardial opacification was observed in one case. Microscopy revealed sharply demarcated cell groups or layers with histiocyte-like cells with foamy cytoplasm. The history of the cases regarding arrhythmias is unknown since hospital records could not be reached. Congenital heart disease and lung infection were given as causes of death in all cases.
Conclusion: Previously named histiocytoid cardiomyopathy, infantile cardiomyopathy, arachnocytosis of the myocardium, infantile xanthomatous cardiomyopathy, focal lipid cardiomyopathy, isolated cardiac lipidosis, foamy myocardial transformation, histiocytoid changes with cardiomyopathy, this lesion is now known as "conduction system hamartoma" within the latest WHO classification (5th edition). Being aware of this entity that causes fatal arrhythmias and sudden cardiac deaths is important for pathologists. The autopsy findings should be evaluated by taking extra samples from the heart if necessary especially in suspected cases under two years.

E-PS-01-014
Fatal consequences of adipose tissue manipulation: an autopsy case series of fat embolism syndrome
E. Gun*, A. Bugra, T. Das
*Basildon University Hospital, Mid and South Essex NHS Foundation Trust, Basildon, Essex, United Kingdom

Background & objectives: Although fat embolism in the pulmonary or systemic circulation is usually seen after long bone fractures, it may occur during procedures like liposuction, fat grafting, and joint repair. We aimed to present cases of macro fat embolism that resulted in sudden death.
Methods: Among the cases that underwent medicolegal autopsies, three cases with a history of sudden death due to macro fat embolism during the perioperative period were identified and included in the study. The demographical characteristics, surgical operation types and histories, autopsy and histopathological findings of the cases were evaluated.
Results: Case 1 is a 31-year-old male with a medical history of penile warts who underwent liposuction for gynecomastia and adipose tissue injection to the penis at a private aesthetic surgery clinic. The patient died suddenly following the surgery. The presence of fat globules was identified in the lumens of large and medium-sized vessels in the lungs in the postmortem histopathological examination.
Case 2 is a 60-year-old female with a history of knee osteoarthritis who died suddenly while receiving a stem-cell injection obtained from abdominal adipose tissue at an orthopaedic clinic. Histopathologically, fat globules were observed in the lumens of medium-sized vessels in the lungs.
Conclusion: Case 3 is a 31-year-old female who was admitted to a private aesthetic surgery clinic for abdominal liposuction and died suddenly during the procedure. Fat globules were detected in the medium-sized vessel lumens in the lungs. Grade 4 fat embolism was observed in the capillaries, which stained positively with Oil-Red-O in all cases. Fat embolism syndrome is a rare but life-threatening condition that should be considered in patients with respiratory distress and impaired neurological status in the postoperative period of these procedures.

E-PS-01-015
Autoptic demonstration of clinically undiagnosed diseases: frequency and association with risk factors in a retrospective study on 648 autopsies
U. Maccio*, M. Reinehr, H. Moch, Z. Varga
*Universitätsspital Zürich, Institut für Pathologie, Switzerland

Background & objectives: Clinically undiagnosed diseases (because not investigated or missed), are often disclosed at autopsy. However, few studies have investigated their frequency and no study examined their association with the most common risk factors (increased age, hypertension, smoking, alcohol abuse, etc.).
Methods: Using our electronic report system, we conducted a retrospective study on all complete adult autopsies performed in our institution in a range of time of three years. We compared clinical and autoptic reports to verify which disorders, demonstrated at autopsy, were clinically undiagnosed. Thus, the correlation of their presence with the most common risk factors was analysed.
Results: 648 autopsies were selected. 633 (98%) revealed at least one clinically undiagnosed finding (mode 3, range 1 – 8). Most common non-tumoral entities were bronchopneumonia (31%), coronary artery disease (CAD, 24%) and acute or subacute myocardial ischemia (15%). Most common malignant tumours were prostate cancer in men (3.4%), followed by kidney cancer (1.5%), GIST (gastrointestinal stromal tumour, 1.5%) and lung carcinoma (1.4%) in both sexes.
Increased age, hypertension, chronic kidney disease (CKD) increased the probability of finding clinically undiagnosed diseases at autopsy. Hypertension was associated with autopsy-discovered amyloidosis, smoking with coronary artery disease (CAD), alcohol with undiagnosed liver cirrhosis, CKD with bronchopneumonia and amyloidosis, and age with bronchopneumonia and amyloidosis.
Conclusion: Senile cardiac amyloidosis is clinically underdiagnosed. As the prevalence increases with age and the population demographic shifts toward the elderly, clinicians should be more aware of this disease. Although some associations are well known (i.e., smoking-CAD), our study suggests that some entities (i.e., CAD and liver cirrhosis) are clinically still underdiagnosed though the known presence of a specific risk factor. The association between hypertension and amyloidosis deserves further analyses.

E-PS-01-016
Carcinoma of gallbladder with the stenosis of pylorus that imitates Krukenberg metastasis
S. Nikolaienko*, O. Nikolaienko, M. Plodiienko, O. Orlov, S. Gychka
*Bogomolets National Medical, Ukraine

Background & objectives: Krukenberg tumour is a frequent clinical manifestation of gastric carcinoma. Clinical and CT signs of antral stenosis in combination with CT signs of neoplasia in ovaries may suggest of gastric carcinoma. We described same picture but connected to gallbladder carcinoma.
Methods: Lifetime investigations included cytology and immunocytochemistry (CA125, CDX-2, PAX-8) of ascitic fluid, CT, gastric endoscopy with biopsy. Postmortem studies included light microscopy and immunohistochemistry (CK7, CA125, CDX-2, PAX-8, WT-1).
Results: Cytology of ascitic fluid: IRSSFC – MAL-S. Immunocytochemistry: CDX-2+, CA125+, PAX-8-. Endoscopically and on gastric biopsy – no signs of gastric neoplasia. The autopsy revealed gallstone disease with the presence of several faceted large calculi in the gallbladder, pronounced adhesion fibrosis of the subhepatic area with its spread to the pyloric part of the stomach causing its stenosis. Carcinomatosis of peritoneum, pleura, 8 cm mass in left ovary.
On histology in gallbladder: adenocarcinoma with invasion into gastric wall. In ovary, peritoneum, pleura, lung a histologically similar tumour.

Immunohistochemically tumour phenotype: CK7+, CDX-2+, CA125+, PAX-8-, WT-1-.
Post-mortem diagnosis: biliary type adenocarcinoma of gallbladder with metastasis into left ovary, lungs, pleura, peritoneum.
Conclusion: The described clinical case indicates that clinical and imaging signs of advanced gastric cancer are sometimes incorrectly evaluated and overdiagnosis is possible. Gallbladder cancer can mimic stomach cancer in terms of its clinical picture and spread.

E-PS-01-017
Necropsy in the context of already diagnosed sickle cell anaemia: what are we missing?
D. Nunes de Melo Braga*, M.V. Pereira dos Santos, M. Baquit Reis, D. Ribeiro Cavalcante, R.B. Egídio Miranda de Oliveira, A.L. Grangeiro de Sá Barreto Lima, S. Maria Macêdo, D. Nunes Oliveira, E. Tome de Sousa, J. Carneiro Melo
*University of Fortaleza, Brazil

Background & objectives: This study aimed to report the spectrum of pathological findings in autopsies of a patient with sickle cell anaemia (SCA), diagnosed at the age of five - who died at the age of 22 due to complications of the disease.
This study aimed to report the spectrum of pathological findings in autopsies of a patient with sickle cell anaemia (SCA), diagnosed at the age of five - who died at the age of 22 due to complications of the disease.
Methods: Literature review and evaluation of medical record of a 22-year-old patient who died; autopsy carried out by Service verification of Death.
Literature review and evaluation of medical record of a 22-year-old patient who died; autopsy carried out by Service verification of Death.
Results: Macroscopic and microscopic examinations revealed classic manifestations of ACS, caused by occlusion of the microvasculature around the organs. Areas of infarction in the spleen and liver, cerebral oedema with increased cerebrospinal fluid, and hepatomegaly were observed. The heart showed dilated cardiomyopathy with thrombotic processes and hypertrophy of cardiomyocytes. The lungs showed septic and reddish infarcts and accumulation of fluid in the alveolar space, indicating acute pulmonary oedema. The kidneys showed nephropathy with increased weight and volume in both organs and hypercellularity and lobulation of glomerular tufts seen under the microscope. These findings suggest a systemic pathology with serious consequences, requiring immediate and targeted treatment.
Conclusion: This report elucidates the importance of necropsy even in the context of chronic diseases, such as ACS, highlighting the histopathological findings and their importance to the final diagnosis, as well as helping to fully understand the disease.
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E-PS-01-018
Diagnosis of tuberculosis using minimally invasive autopsy (MIA): case report
D. Nunes de Melo Braga*, K.S. Coelho Gomes, M. Costa Cavalcante, M. Martins Guanabara, V. Pedrosa Fernandes, S. Maria Macêdo, D. Nunes Oliveira, E. Tome de Sousa, J. Carneiro Melo
*University of Fortaleza, Brazil

Background & objectives: The objective is to analyse the importance of minimally invasive autopsies in diagnosing and studying infectious diseases. The analysis came from the case of the patient LMS, who died of hypovolemic shock due to the diagnosis of tuberculosis.
The objective is to analyse the importance of minimally invasive autopsies in diagnosing and studying infectious diseases. The analysis came from the case of the patient LMS, who died of hypovolemic shock due to the diagnosis of tuberculosis.
Methods: In this case report, the patient who died at home was clinically monitored and taken to the Death Verification Service (SVO) in Fortaleza-Brazil to diagnose his death's cause. The main technique used was the Minimally Invasive Autopsy (MIA), which includes the study of histopathology slides and the results of the AFB sputum test done before his death.
In this case report, the patient who died at home was clinically monitored and taken to the Death Verification Service (SVO) in Fortaleza-Brazil to diagnose his death's cause. The main technique used was the Minimally Invasive Autopsy (MIA), which includes the study of histopathology slides and the results of the AFB sputum test done before his death.
Results: The patient received a positive sputum culture shortly before death and could not receive decent treatment for tuberculosis. The MIA (Minimally Invasive Autopsy), performed in this case, allowed the collection of fragments from several organs simultaneously, making it possible to confirm the diagnosis of pulmonary tuberculosis and affirm that the granulomatous inflammation reached the kidneys by microscopic observation of the removed tissues. In cases like this, where the family does not allow a conventional autopsy for various reasons; or when the cause of death is an infectious disease, MIA is the best and safest alternative to continue carrying out studies and data that can improve public health policies.
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Conclusion: The reported case is based on the use of MIA to endorse the patient's hypotheses of death, confirming hypovolemic shock due to pulmonary tuberculosis. The performance of MIA is seen as a useful new technique for obtaining medical data that were previously only obtained by classic autopsy without the need to open the body. Considered relatively recent, the procedure, in addition to being more socially acceptable, also allows for the storage of samples for future research.
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E-PS-01-019
A 61-year-old woman with an incidental retroperitoneal tumour found at autopsy: report case
D. Nunes de Melo Braga*, B. Memória Feitosa, E. de Vasconcelos Lobo, L. Vieira Paz Sampaio, R. Borges de Mello Viana, J.L. Bezerra de Menezes Saraiva, S. Maria Macêdo, D. Nunes Oliveira, E. Tome de Sousa, J. Carneiro Melo
*University of Fortaleza, Brazil

Background & objectives: Autopsy serves as a valuable research tool method. Neoplasia consists of uncontrolled cell proliferation. However, when the offspring's place of the neoplasia is indeterminate, it is important to make immunohistochemical. Thus, this study aims to show the relevance of immunohistochemical.
Autopsy serves as a valuable research tool method. Neoplasia consists of uncontrolled cell proliferation. However, when the offspring's

place of the neoplasia is indeterminate, it is important to make immunohistochemical. Thus, this study aims to show the relevance of immunohistochemical.
Methods: Autopsy case study carried out through the analysis of medical records, macroscopic examination of the organs and observation of histological slides of a female patient, 61 years old, found unconscious, dehydrated and with abdominal distension. She had episodes of vomiting days before her death and arrived at the emergency room with irreversible cardiorespiratory arrest.
Results: On examination, dark secretions were found in the mouth and nostrils, a distended abdomen with the presence of a suture in the lower left quadrant, oedema in the right leg, and a very thin aspect, in addition to the presence of pulmonary and cerebral oedema. In addition, a poorly delimited tumour mass with an infiltrative aspect was found from the retroperitoneum to the left ovary and uterine body, the primary site not being evident. Thus, the macroscopic diagnosis of a wasting syndrome associated with malignant neoplasia was registered as causa mortis. Therefore, immunohistochemistry would be important to detect where the neoplasm began, through biomarkers, leading to the consequences of wasting syndrome.
On examination, dark secretions were found in the mouth and nostrils, a distended abdomen with the presence of a suture in the lower left quadrant, oedema in the right leg, and a very thin aspect, in addition to the presence of pulmonary and cerebral oedema. In addition, a poorly delimited tumour mass with an infiltrative aspect was found from the retroperitoneum to the left ovary and uterine body, the primary site not being evident. Thus, the macroscopic diagnosis of a wasting syndrome associated with malignant neoplasia was registered as causa mortis. Therefore, immunohistochemistry would be important to detect where the neoplasm began, through biomarkers, leading to the consequences of wasting syndrome.
Conclusion: The primary diagnostic hypotheses raised were myocardial infarction, stroke or sepsis with an abdominal focus, mainly due to the patient's presentation (irreversible cardiorespiratory arrest). However, a metastatic malignancy was found, that is, an undetected insidious disease resulting in wasting syndrome. Therefore, the importance of anatomopathological and immunohistochemical analysis is highlighted in the discovery of the local origin of the tumour and in the effective elucidation of the cause of death of each patient.

E-PS-01-020
Infectious complications in a large series of patients with cirrhosis: retrospective study of 386 cases (2016-2023)
J.P. Olano*
*University of Texas Medical Branch, USA

Background & objectives: Cirrhosis is a common disease worldwide. The most common etiologic factors are alcohol abuse, hepatitis C and NASH. Cirrhosis increases the risk of infections. This study analyses a cohort of cirrhotic patients with infections leading to the their demise.
Methods: Retrospective review of 386 cases of cirrhosis from 2016-2023. Complete autopsies were performed on all cases and data was collected regarding cirrhosis aetiology and infectious disease complications including their etiologic agent. Only cases where the infectious disease complication was directly related to the cause of death were included. All autopsies included histologic, microbiologic (pre- or postmortem) and toxicological analysis.

Results: 135 (35%) patients died of infectious disease complications. Hepatitis C was the main aetiology (85.9%) followed by alcohol abuse (7.4%) and both Hepatitis C and alcohol (8.1%). Bacterial bronchopneumonia was the cause of death in 34.8% of cases, followed by cellulitis with septicaemia (14.8%), spontaneous bacterial peritonitis (SBP) with septicaemia (13.3%), bronchopneumonia with septicaemia (9.6%), pyelonephritis (3.7%), infectious endocarditis (3%), septicaemia diagnosed by pre-mortem blood cultures with no evident focus of infection (3%) and phlegmonous colitis (2.2%). The infectious aetiology was as follows: Staphylococcus aureus (15.5%), Klebsiella and Streptococcus spp. (8.1%), Candida spp. (5.2%), Enterococcus spp. (4.4%) and others (14 different bacteria; 14.8%). No etiologic agent was identified in 46.7%.
Conclusion: Infectious disease complications represent an important cause of death in patients with cirrhosis. Our cohort is mostly comprised of inmates, hence the high percentage of cirrhosis due to Hepatitis C. A significant percentage of patients died of infectious complications in whom no etiologic agent was identified. The diagnosis was made histologically and most of them were acute bacterial bronchopneumonias. Cellulitis and SBP were always associated with septicaemia. Cases of sepsis diagnosed by pre-mortem culture were due to unusual bacterial pathogens.

E-PS-01-021
The role of foetal autopsy in understanding the causes of intrauterine death: an interesting illustrative case
A. Raicea*, S. Emoke-Andrea, L. Chinezu
*Pathology Department of Mures County Clinical Hospital, Romania

Background & objectives: Foetal autopsy plays an important role in defining the final diagnosis. The aim was to analyse the extent to which the foetal autopsy and placental examination can provide information to identify the foetal main cause of death.
Methods: A histopathologic examination of a second-trimester stillborn foetus, its placenta, and umbilical cord was performed at Targu Mures Institute of Forensic Medicine, Romania.
Results: Gross examination of foetus and umbilical cord was nonspecific. Macroscopic examination of placenta revealed fibrinous foci. Microscopically, the examined placental tissue had the characteristic appearance of a second trimester of pregnancy placenta, presenting with abundant mixed inflammatory infiltrate (more than 10-20 neutrophils per cluster) in the chorion and amnion, with many neutrophils into decidual tissue and intervillous space setting the diagnosis of acute chorioamnionitis associated with acute deciduitis and intervillositis. At the level of the umbilical cord, both umbilical arteries were involved by the inflammation with confluent collections of neutrophils, that extended out into Wharton's jelly, setting the diagnosis of arteritis and funisitis.
Conclusion: The final diagnosis of the placenta was acute chorioamnionitis, maternal stage 2, grade 2 associated with deciduitis and intervillositis, with foetal vascular involvement, foetal stage 2, grade 2. The feto-placental infection remains a major relevant condition associated to stillbirth, especially in early gestational age.

E-PS-01-022
Case report: CD74-ROS1 translocation lung adenocarcinoma treated by ALK inhibitors
P. Suhaj*, E. Parobkova, T. Olejar, R. Matej
*Thomayer University Hospital, Czech Republic

Background & objectives: 55 years old female, non-smoker, was diagnosed with ROS1 positive generalized pulmonary adenocarcinoma (T3N3M1c). Treatment with ALK inhibitors resulted in CT regression and stabilization of disease for 1.5 years. We performed autopsy and NGS analysis to explain the patient's demise.
Methods: Modified Letulle's autoptic technique and serial sectioning of heart and lungs were used. Findings were compared with radiographic studies.
FFPE blocks of archival bioptic and necroptic material were used for further analysis. We used antibodies against PDL-1 (22C3 pharmDx), ALK and ROS1.

For NGS studies we used XCeloSeq Fusion Research kit (GeneFirst Ltd., UK) on sequencing platforms NextSeq 550/550Dx Illumina.
Results: Diagnosis was established by transbronchial biopsy from the upper lobe of right lung. Tumour was tubular and solid, cells were polymorphous with irregular nuclei, conspicuous nucleoli and amphophilic cytoplasm. Tumorous cells were IHC positive for ROS-1, NGS analysis disclosed translocation t(5;6)(q33;q22), CD74-ROS1. On autopsy we observed pronounced lymphatic drawing of lungs and pericardium, metastases were present in thyroid and lymph nodes (cervical, thoracic, abdominal). Microscopically were present similar tumorous elements with larger polymorphy, but this time were ROS1 negative in IHC and NGS studies. In lungs was prominent fibrosis devoid of tumorous cells at the primary site, in other lobes there were dilated lymphatics with adenocarcinoma and massive alveolar oedema.
Conclusion: ROS1 is tyrosine kinase receptor, CD74 is receptor facilitating permeability of lymphatics. CD74-ROS1 is rare fusion gene, which serves as oncogene and simultaneously enables early lymphangiopathy. Our patient was initially diagnosed in advanced IVB stage with multiple extrathoracic metastases. Treatment with ALK inhibitors eradicated primary tumour and metastases at several locations (brain, adrenals, vertebrae) and stabilized the disease. Unfortunately, the adenocarcinoma became negative for CD74-ROS1, resulting in massive carcinomatous lymphangiopathy. Consequential massive pulmonary oedema caused respiratory failure.
Supported by MH CZ – DRO (Thomayer University Hospital – TUH, 00064190).

E-PS-01-023
Thanatophoric dysplasia: case report and literature review
A. Van Der Biezen*, M.N. Villca Huayta, C. Vieru, M. García Martos
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Thanatophoric dysplasia (TD) is a rare and lethal form of osteochondrodysplasia. It is caused by mutations of the gene encoding fibroblast growth factor receptor 3 (FGFR3). We present one case of TD with genetic confirmation.
Methods: A 24-week gestational-age female foetus with skeletal malformations was delivered to a 37-year-old G2P1 mother. The ultrasound scan at 21 weeks for morphologic evaluation showed micromelia with angulation of the extremities, prompting the diagnosis of skeletal dysplasia. The mother has no personal history of interest or family history of skeletal dysplasia. It concluded with feticide and request for an autopsy.
Results: CT scan showed micromelia, craniofacial disproportion, narrow thorax with hypoplastic lungs, and vertebral body ossification defect. Postmortem examination showed a female foetus, weighing 650 g. The external examination findings revealed macrocephaly, a depressed nasal bridge, low-set ears, a narrow chest with the presence of short ribs, and the upper and lower limbs were symmetrically short.
Histologically slides from the ribs and femur demonstrated atypical endochondral ossification. The epiphyseal growth plate was severely retarded and disorganized, with hypertrophic chondrocytes and absence of column formation. The molecular analysis detected mutation of FGFR3, c.742C>T, p.Arg248Cys.
Conclusion: Thanatophoric dysplasia is the most common lethal skeletal dysplasia with an estimated incidence of 1 in 20.000 to 40.000 births. Although TD is autosomal dominant, the majority occurs sporadically and the recurrence risk is low. We present one case with radiologic, morphologic, histologic, and molecular features, herein described, which were compatible with TD Type 1. Even though TD is a rare condition, skillful antenatal sonographic can be used to obtain an accurate prenatal diagnosis.

E-PS-01-024
Congenital intracranial immature teratoma: presentation of a case and a systematic review of the literature
A. Van Der Biezen*, M.N. Villca Huayta, M.L. Abascal Camacho, F.J. Díaz Crespo, F. Arías
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Congenital intracranial tumours are rare and only account for 0.5-1.5% of all paediatric brain tumours. Teratoma is the most frequently encountered intracranial tumour at birth. We present a case of congenital intracranial immature teratoma to describe clinicopathological correlation.
Methods: Obstetric ultrasonography in a 31 week-old-foetus revealed a large cranial mass with hydrocephalus. An urgent MRI showed a solid, heterogeneous, lobulated mass with extensive cystic and calcified areas, in the left cerebral hemisphere measuring 11 cm, surrounded by markedly dilated lateral ventricles. It concluded with a feticide at 33 weeks and a request for an autopsy.
Results: A 33-week gestational-age foetus was delivered to a 32-year-old G3P2 mother. Postmortem examination showed a male foetus, weighing 3100 g. The external examination findings revealed macrocephaly with wide fontanelle and retrognathia. The brain weighed 251 g and examination showed a replacement of the left side of the brain by a solid and cystic haemorrhagic mass, with no remarkable findings in the remaining organs. Histologically, the mass was composed predominantly of immature neuroepithelial tissue forming rosette-like structures and tubules. It also contained cystic spaces lined by columnar epithelium, immature mesenchyma with rhabdomyoblastic differentiation, cartilage and muscle. Morphologic findings were consistent with an immature teratoma.
Conclusion: We present a congenital intracranial teratoma to further expand our knowledge of this rare pathology which bears a poor prognosis and low survival rate. Since there are no significantly associated risk factors known to date, we emphasize the importance of an early diagnosis and a multidisciplinary approach, as an early termination of pregnancy may avoid obstetric and psychological complications for the mother.

E-PS-02 | E-Posters Breast Pathology

E-PS-02-003
Adenoid cystic carcinoma of the breast: can we predict its aggressiveness?
I. Amat Villegas*, E. Carracedo Vega, Y. Ruiz de Azua, I. Fernández De Los Reyes, R. Beloqui, A. Pasco Pena, A. Córdoba
*Hospital Universitario de Navarra, Spain

Background & objectives: Breast adenoid cystic carcinoma (BACC) is an uncommon neoplasm, typically triple negative, usually with a favourable prognosis although sometimes is aggressive. We apply three different grading schemes and immunohistochemistry antibodies through a series of 14 cases.
Methods: We analysed the clinicopathological and immunohistochemical features of all BACC and grade them according to the different systems proposed in order to distinguish the aggressiveness of each tumour.
Results: Our BACC had an average tumour size of 23.4mm. All patients were women (78.5% over 60 yo.) and underwent surgical resection. Nine women had axillary lymph node staging, one presented micrometastases. One woman developed local recurrence and two died from disease. Nine women underwent radiotherapy and six chemotherapy and four no adjuvant treatment.
None cases have a pure growth pattern, all were mixed, and solid was the most common. Tumour borders were pushing in six cases and infiltrative in eight. All cases were classify according to the Nottingham, Spiro and Perzing grading system. Immunohistochemical profile was 13 cases triple negative, 71.5% positive for MYB and 85.7% for CD117.

Conclusion: The management and prognosis ACC of breast, remains uncertain and novel grading systems and immunohistochemical markers do not improve accuracy in aggressive cases detection. Tumour size over 5 cm seems to be the best prognostic factor in our series.

E-PS-02-004

Upgrading of high-risk breast lesions in patients with multiple biopsies: is surgery essential?

N. Arı*, S.E. Horoz, K. Kolçak, H. Kaya
*Marmara University School of Medicine, Department of Pathology, Turkey

Background & objectives: High risk breast lesions are associated with increased risk of malignancy. Upgrading of these lesions to higher grade lesions is commonly encountered in subsequent biopsies. In this study, upgrading status of these lesions is investigated in patients with multiple biopsies.
Methods: Biopsy reports with initial diagnosis of high-risk breast lesions (atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), lobular carcinoma in-situ (LCIS), intraductal papilloma and sclerosing adenosis) between the years of 2018-2022 were retrieved from the hospital records. Among these patients, 40 patients who underwent more than one biopsy (either multiple core needle biopsies or subsequent surgical excision) were included.
Results: Core needle biopsy results of 40 patients were compared with their subsequent (mainly excisional) biopsies. Upgrading to a higher-grade lesion was seen in 45% (n=18) of the patients. 43,7% (n=14) of the patients who were initially diagnosed as intraductal papilloma (n=32) were found to have a higher-grade lesion in subsequent biopsies, 9,3% (n=3) of them diagnosed as carcinoma and 21,8% (n=7) of them as DCIS. All patients who were initially diagnosed as ALH (n=2) displayed upgrading in their excision specimens. 2 of 3 patients with ADH were upgraded to DCIS whereas no patients with sclerosing adenosis were observed to have an upgraded lesion in subsequent biopsies.
Conclusion: Management of high-risk breast lesions remains as a matter of debate since both surgical excision and patient follow-up constitute the options. Overtreatment with unnecessary surgical interventions should be avoided. However, inadequate sampling with core needle biopsy is a major concern for underdiagnosis of high-grade lesions, especially if radiological-pathological correlation cannot be accomplished. In this study, high upgrade rates in subsequent biopsies highlight the possibility of underdiagnosis of high-risk lesions, including carcinoma, if excisional biopsy is not performed.

E-PS-02-005

Synchronous bilateral breast carcinoma and axillary non-Hodgkin lymphoma: two case reports and literature review

R. Ayadi*, E. Braham, H. Ichrak, F. Loued, O. Ismail, A. Ayadi
*Hôpital Abderrahmane Mami, Tunisia

Background & objectives: Breast cancer is the most prevalent tumour for women worldwide. Synchronous breast carcinoma and lymphoma are rare. It is of high rate of misdiagnosis in clinical practice.
The aim is to describe a clinicopathological data of patients with both diagnoses.
Methods: We report two patients who developed simultaneous breast lymphoma and breast carcinoma aged 74 and 85 years.
Results: Two women presented with a palpable mass in the left breast and a right axillary adenopathy. A CT of the chest showed multiple right axillary nodes and mass in the left breast. They underwent excisional biopsy of a right axillary node which demonstrated diffuse large B-cell lymphoma. IHC showed CD3(–), CD20(+), CD10(–), BCL-6(–), MUM-1(strong+) and CK(–).Ultrasound-guided needle core biopsy of the breast lesions showed infiltrating ductal carcinoma in the left breast, and oestrogen and progesterone receptor (+), HER2 receptor (-).Thoracic CT scan, ultrasound scan of abdominal, pelvic and superficial lymph nodes and bone marrow were performed. No metastasis was found. They received R-CHOP to cover the breast cancer and lymphoma.
Conclusion: These two patients remind us of the coexistence of breast cancer and breast lymphoma. The diagnosis of synchronous malignancies poses challenges for both the diagnosing pathologist and the treating clinician.

E-PS-02-006

Pathologic characteristics and response of invasive lobular carcinoma of the breast after neoadjuvant chemotherapy

J. Azevedo*, M. Alzamora, A. Coutada, A. Lapa, L. Gonçalves, N. Coimbra, C. Leal
*Pathology Department, IPO-Porto, Portugal

Background & objectives: Invasive lobular carcinoma (ILC) is considered a distinct clinical and biological type of breast cancer, being less responsive to neoadjuvant chemotherapy (NAC) compared to ductal invasive carcinoma. We aim to characterize our population with ILC that received NAC.
Methods: Retrospective analysis of all patients diagnosed with ILC treated with NAC followed with surgery in our institution between 2011 and 2021. We evaluated clinical and pathologic features including age, surgery type, histological grade and immunohistochemical profile on biopsy, tumour size with magnetic resonance, before and after NAC, and pathological response. Time of follow-up, recurrence, metastasis and overall survival were recorded.
Results: 115 cases were included, the majority presenting in biopsy with G1/G2 tumours (n=95, 90.87%). Most cases were positive for hormone receptors (HR) and HER2 negative (n=96, 83.5%) with smaller subgroups HR-/HER2+ (n=5, 4.3%), HR+/HER2+ (n=11, 9.6%) and triple negative (n=3, 2.6%). Complete pathological response (pCR) was achieved in 4 (3.5%) cases; all pleomorphic and HER2+ (3 were HR-). All these patients are disease-free. In cases with partial pathological response (n=111, 96.5%), median of tumour size before and after NAC was 3.6cm [0.6-11cm] and 4cm [0.2-12cm], respectively. Additionally, in 13 of pathology partial responders small foci (<0,1cm) with low cellularity were observed throughout the tumour bed.
Conclusion: The vast majority of ILC are low-grade with low proliferative index, oestrogen receptor-positive with poor response to NAC. The few cases of pCR were associated with HER2 positivity, indicating that this relative resistance to NAC may be more related to molecular characteristics than histologic subtype. We believe that assessment of partial response by AJCC ypT can be affected by interobserver heterogeneity, as evaluation of the largest contiguous focus can be difficult due to scattered foci over the tumour bed.

E-PS-02-007

Incidence and clinicopathologic features of human epidermal growth factor receptor 2 (HER2)-low breast cancer

Y.K. Bae*, M.C. Kim
*Department of Pathology, Yeungnam University College of Medicine, Daegu, Republic of Korea

Background & objectives: HER2-low breast cancer (BC), which is defined as immunohistochemistry (IHC) 1+ or 2+ without gene amplification, is a recently proposed HER2 category for new HER2-targeting drugs. We investigated the incidence, clinicopathologic characteristics, and prognosis by comparing HER2-negative and HER2-positive BCs.
Methods: We obtained clinicopathologic information [age at diagnosis, tumour size, histologic type, histologic grade, lymphovascular invasion, lymph node status, IHC results for oestrogen receptor (ER), progesterone receptor (PR), HER2, and Ki-67, and clinical outcomes] from 2,309 patients with primary invasive BC who underwent curative surgery at Yeungnam University Hospital between November 2007 and December 2014.
Results: Of the 2309 cases, 1497 (64.8%) were HER2-negative, 348 (15.1%) were HER2-low, and 464 (20.1%) were HER2-positive. Compared with HER2-negative BCs, HER2-low BCs were associated with

lymphovascular invasion, ER positivity, and PR positivity. Furthermore, HER2-low BCs had a smaller tumour size, lower histologic grade, positive ER and PR status, and low Ki-67 status than HER2-positive BCs. When we stratified the patients based on ER status, there was no difference in overall survival (OS) and disease-free survival (DFS) between the HER2-negative and HER2-low BC groups. However, patients with HER2-low BC had better DFS in ER-positive group and worse OS in ER-negative group than those with HER2-positive BC.
Conclusion: The incidence of HER2-low BCs was lower than expected. They showed higher ER and PR expression than HER2-negative and HER2-positive BCs. There was no survival difference between HER2-low and HER2-negative BC patients regardless of ER status. However, prognosis between HER2-low and HER2-positive BCs depended on ER status. ER status needs to be considered in the therapeutic strategies for the treatment of patients with HER2-low BC.

E-PS-02-008
Two rare cases of adenosis tumour (nodular adenosis)
R. Balan*, I.D. Căruntu, R. Socolov, I. Păvăleanu, L. Toma, L. Lozneanu, A. Grigoraș, T.A. Balan, C. Amalinei
*"Grigore T. Popa" University of Med, Romania

Background & objectives: Adenosis tumour or nodular adenosis (NA) represents a rare entity, in which a benign lobulocentric proliferation of glands compressed by fibrosis, called sclerosing adenosis forms a firm, homogenous, nodular mass. Sometimes clinical and histopathological aspects of NA can mimic carcinoma.
Methods: We report two cases of NA, in two patients, aged 18 and 41 years, respectively, admitted in the Clinical Hospital of Obstetrics and Gynaecology „Elena Doamna" from Iasi, Romania. In both cases lumpectomy was performed. The specimens were referred to Pathology Service and histopathologically examined by routine staining (H&E) and immunohistochemical techniques (SMA, p63, CK5/6) to exclude a carcinoma.
Results: The clinical and ultrasound examination revealed a solid hypoechogenic nodule in both cases, one with central areas of liquefaction. Macroscopically, one case presented a multinodular aspect, with microcystic areas, while the other was a less circumscribed nodular mass. The histopathological diagnosis revealed a well circumscribed nodular proliferation of slightly dilated glandular structures, with predominantly tubular pattern, slightly lined by simple epithelium, with partial preservation of myoepithelial cells, surrounded by collagenous stroma. The other case revealed nodular areas with sclerosing adenosis and florid tubular proliferation, with different growth patterns. The presence of myoepithelial cells was confirmed through immunohistochemical evaluation of p63, SMA, and CK5/6, all markers presenting diffuse positive expression.
Conclusion: Adenosis tumour is a rare entity, which is characterized by a variety of growth patterns, aspects that, along with clinical and imaging characteristics, differentiate NA from other benign entities or carcinomas. The two presented cases, which are notable for the extreme ages of the patients, as well as for the heterogeneous morphological aspects, sometimes requiring immunohistochemical confirmation, provide additional data that can complete the clinical-pathological picture of nodular adenosis.

E-PS-02-009
Vein invasion in breast cancer – a single centre experience
A. Baltan*, S. Costache, A. Gont, A. Chefani, C. D'Arrigo
*Poundbury Cancer Institute, Romania

Background & objectives: There is wide recognition of vein invasion in certain tumours (colorectal, pancreatic, or renal). This has not been adequately distinguished from lymphatic invasion in breast cancer. Nevertheless, vein invasion appears to be a distinct event of uncertain clinical significance.
Methods: We have routinely screened and reported the presence of vein invasion in breast carcinoma in our practice. All positive or suspicious cases on morphological grounds are confirmed with IHC for desmin. To establish prevalence, we reviewed 173 surgical excisions (screening and symptomatic patients) from a single institution between June 2022 and March 2023.
Results: A total of 16 cases with vein invasion were identified (9.24% of all cases). These were mostly present in elderly women (>80 years old), in higher-grade carcinoma and higher tumour burden (size> 20mm). We have observed vein invasion within the primary tumour bed, in perinodal tissue, or in both. Out of the 16 cases, 11 had vein invasion only at the primary site, 3 within the perinodal tissues only and 3 in both sites. In addition, there was no significant association with lymphatic invasion.
Conclusion: Vein invasion is underrecognized in breast cancer. Desmin greatly facilitates its identification since in breast tissue it stains only blood vessels. Lack of correlation with lymphatic invasion points towards these being distinct events of tumour progression. Vein invasion at other tumour sites is associated with worse prognosis and higher rates of systemic metastases. In breast cancer, anecdotal association with brain metastases warrants further studies to assess potential link with systemic disease.

E-PS-02-010
Simultaneous presentation of a giant malignant phyllodes tumour of the breast and high-grade renal cell carcinoma – a rare presentation: a case report
Y. Belogrivtseva*, A. Israh, A. Arriola, M. Mollaee
*Temple University Hospital, USA

Background & objectives: Phyllodes tumours (PTs) are rare, accounting for less than 1% of breast tumours. It is classified into benign, borderline, and malignant based on cellularity, stromal overgrowth, stromal cell atypia, infiltrative borders, and the presence of heterologous component(s).
Methods: We report a case of a 59-year-old female, presenting with a rapidly enlarging 31 cm mass of the right breast with focal skin ulceration and purulent discharge.
Results: Follow-up imaging studies for staging revealed mediastinal adenopathy, and an incidental 9.7 cm exophytic renal mass along with bilateral enlarged inguinal lymph nodes. The patient underwent a mastectomy and subsequent partial nephrectomy within a few weeks apart. Histopathologic examination of the breast mass biopsy showed a fibroepithelial tumour and a phyllodes tumour was favoured. Subsequent mastectomy specimen revealed malignant phyllodes tumour with marked necrosis and positive margins. A partial nephrectomy performed for the renal tumour showed a high-grade papillary renal cell carcinoma with perinephric extension and three positive lymph nodes.
Conclusion: The genomic landscape of PT from sequencing could provide more insight into its molecular pathogenesis, help improve diagnostic accuracy, and identify potential drug targets for malignant PT, however, there are limited published studies with this information. Reporting the simultaneous presentation of these two high-grade tumours would help to better our understanding of potential molecular associations driving these two distinct high-grade processes.

E-PS-02-011
Interobserver agreement between pathologists assessing tumour-infiltrating lymphocytes in breast cancer by applying International TILs Working Group recommendations
E. Benammou*, D. Bacha, I. Mallek, S. Gharbi, M. Hajri, H. Mestiri, A. Lahmar, S. Ben Slama
*Department of Pathology, Armand Trousseau Hospital-Sorbonne University, France

Background & objectives: Several studies highlighted the prognostic and predictive values of tumour-infiltrating lymphocytes (TILs) in

breast cancer (BC). This study aims to determine interobserver agreement between pathologists using the International TILs Working Group recommendations for the assessment of stromal TILs (sTILs) in BC.
Methods: We retrospectively analysed 53 hematoxylin and eosin stained slides of invasive BC, obtained from 26 core needle biopsies and 27 surgical resections. Three pathologists independently reviewed each slide and evaluated sTILs. We used Fleiss's kappa statistics to calculate the overall proportion of interobserver agreement.
Results: The mean of age was 56.5 years. The kappa statistic for sTILs assessment was 0,55 with 15 discrepancies cases. Discordances were mostly noted in surgical resection specimens (37%) compared to micro-biopsies (19%) and interested mainly TILs proportions in intervals (5-10%) and(40-50%). In operative specimen, discrepancies reasons included the difficult distinction between lymphocytes and granulocytes in one side and carcinomatous cells and lymphocytes on the other side. In all samples, there has been a tendency to increasing TILs average rates in the presence of a focal hot spot zone. Artefactual retraction spaces helped to distinguish carcinomatous clusters from stromal inflammatory infiltrate. A weakly contrasting staining increases difficulties to distinguish carcinomatous cells from inflammatory cells.
Conclusion: Acceptable agreement in sTILs assessment was noted when applying the international TILs Working Group recommendations. Sample fixation quality, which is better in micro-biopsies specimen, and a suitable contrasting staining, play an important role in the distinction between cell types.

E-PS-02-012
Nonnecrotising granulomatous lymphadenitis in the context of autoimmune pseudosarcoidotic reaction
S. Blasco Muñoz*, A. Sánchez Espinosa, A. Ortiz González, E. Guillén Saorín, D. Pérez Parra, C.A. Capozzi, J.M. Acosta Ortega, M.J. Sánchez de las Matas Garre
*Complejo Hospitalario Universitario de Cartagena, Spain

Background & objectives: A 36-year-old woman with non-special infiltrating carcinoma (NOS) in the right breast, hormone receptor-negative and HER2-neu positive, associated with intraductal component; and tubular carcinoma in the left breast, hormone receptor-positive and HER2-neu negative.
Methods: In PET-CT, in addition to the breast tumour tissue, multiple axillary, right supra and infraclavicular, right internal mammary, mediastinal, bilateral hilar, presacral/behind the psoas, left obturator and intergluteal lymphadenopathies are evidenced. Treatment with Pertuzumab-Trastuzumab-Docetaxel-Zometa was started. Given the persistence of mediastinal and inguinal adenopathies after completing treatment, it was decided to perform a biopsy.
Results: In both biopsies representative fragments of lymph nodes (structures with capsule and secondary follicles) were confirmed, with abundant medium and large sarcoidosis-like granulomata (naked lymphohistiocytic aggregates with some multinucleated giant cells). No signs of malignancy were observed. Immunohistochemical techniques with CK AE1-AE3 were performed without identifying metastases. A diagnosis of sarcoid granulomatous lymphadenitis is proposed. Recently a new lesion has appeared in the spleen, which has been biopsied, finding the same histological features of non-necrotizing granulomatous reaction.
Conclusion: Sarcoidosis-like reactions have been described in 4-14% of cancer patients and occur more frequently in patients receiving Trastuzumab treatment. Distinguishing these lesions from metastases is complicated without a biopsy, but necessary, as it can avoid overtreatment of patients. It should especially be suspected in patients in whom chemotherapy reduces tumour size but lymph nodes remain enlarged.

E-PS-02-013
Artificial intelligence-based breast cancer detection facilitates automated prognosis marker assessment using multiplex fluorescence immunohistochemistry
N. Blessin*, T. Mandelkow, E. Bady, M. Lennartz, A. Lebeau, S. Steurer, E. Burandt, T.S. Clauditz, G. Sauter, M. Graefen, S. Minner, C. Bernreuther
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: Prognostic markers in routine clinical practice of breast cancer are often assessed using RNA based multi-gene panels that are depending on a fluctuating tumour purity. Multiplex fluorescence immunohistochemistry (mfIHC) holds the potential for improved risk assessment.
Methods: To enable automated prognosis marker quantification, we have developed and validated a framework for automated breast cancer detection involving three different artificial intelligence analysis steps and an algorithm for cell-distance analysis using BLEACH&STAIN multiplex fluorescence immunohistochemistry. Pan-cytokeratin (panCK) antibodies were used to detect epithelial cells and antibodies directed against Myosin and p63 were used to identify basal cells.
Results: The optimal distance between Myosin+ and p63+ basal cells and benign panCK+ cells was identified as 25 µm in breast cancer and used – combined with deep learning-based algorithms – to exclude benign glands from the analysis. Our framework discriminated normal glands from malignant glands with an accuracy of 98.4% (95% confidence interval [CI]: 97.4 – 99.3). The approach for automated breast cancer detection improved the predictive performance of several prognosis markers significantly (each $p<0.05$) and a comparison with manually assessed data using conventional brightfield immunohistochemistry showed a high concordance for a multitude of different prognosis marker such as PR, ER, GATA3, HER2, and PD-L1 (each <0.0001).
Conclusion: The combined assessment of up to 5 markers in a prognosis score showed strong prognostic relevance ($p<0.001$) and was an independent risk factor in multivariate analysis ($p=0.005$). Thus, the data from this study show that automated breast cancer detection in combination with artificial intelligence-based analysis of multiplex fluorescence immunohistochemistry enables a rapid and reliable analysis of multiple prognostic parameters. The major advantage of this method is the analysis of malignant cells exclusively that cannot be achieved using RNA-based panel analysis.

E-PS-02-014
Androgen receptors in metastatic triple negative breast cancer
J. Boavida*, I. Pinho*, T. Barroso, V. Patel, L. Gonçalves, R. Lopes Brás, M. Esperança Martins, M. Pinho, R. Moiteiro da Cruz, R. Teixeira de Sousa, L. Correia, L. Costa
*Serviço de Anatomia Patológica, Centro Hospitalar Universitário de Lisboa Norte, Faculdade de Medicina da Universidade de Lisboa, Portugal*Department of Medical Oncology, Hospital de Santa Maria, CHULN, Portugal

Background & objectives: Triple-negative breast cancer (TNBC) expresses androgen receptors (AR) in up to 30% of cases. ARs are emerging biomarkers in metastatic TNBC (mTNBC). We aimed to evaluate the expression of ARs in mTNBC patients and correlate it with overall survival (OS).
Methods: Retrospective cohort study of mTNBC patients, with tissue sample at our Pathology Department, between 2017-2021. Demographic, clinicopathological and treatment data were gathered from records. AR expression was assessed immunohistochemically in samples prior to systemic treatment, evaluated independently by two pathologists (considered positive if ≥1% of tumour cells stained). 23 patients

fulfilled the inclusion criteria. Survival analysis used the Kaplan-Meier method.
Results: All 23 patients were women, with a median age of 56 years-old (38-88), the majority postmenopausal (n=15, 65%). Regarding tumours' characteristics, 20 patients (87%) had G3 tumours and the remaining G2. All had Ki67% > 20%. Most patients were initially treated with a curative intent (n=19, 82%) and only 4 were stage IV at diagnosis. Twelve patients (52%) had neoadjuvant chemotherapy, with pCR in 2 patients. Adjuvant chemotherapy was done in 10 patients. AR were positive in 5 patients (21%). Median OS was 6.8 months, with a median follow up time of 5.8 months. As there were only 5 patients positive for AR, the positive and negative populations weren't compared.
Conclusion: AR expression was rare in our population of metastatic patients. The low number of positive patients didn't allow for comparison of OS. This low prevalence is in line with previously reported values (approximately 30%). Patients without other treatment options should be tested for AR expression in cases where the attending oncologist considered using off-label anti-androgen medications. In this old dataset, survival of TNBC patients was dismal, with a median OS of <7 months, while recent studies show much higher survival.
J. Boavida and I. Pinho have both contributed equally to this study.

E-PS-02-015
Lymph node involvement in pure ductal carcinoma in situ is rare (DCIS): a study of 575 breast resections with pure DCIS and quantification of sampling
M. Bonert*, F. Mrair, P. Williams
*McMaster University / St. Joseph's Healthcare Hamilton, Canada

Background & objectives: Lymph node positivity with pure DCIS is noted to be 0-4.9%; however, many of these studies are older. We performed a retrospective analysis of in-house breast excisions focused on reported pure DCIS cases and quantified the tissue sampling.
Methods: All in-house breast cancer cases (2011–2020) at two institutions with a synoptic report were extracted along with the total block count per case. DCIS cases were reviewed, and "pure DCIS" cases excluded all post-neoadjuvant, and encapsulated/solid papillary carcinomas. Lymph node (LN) status was determined in the selected (DCIS) cases, based on the pN stage as reported in the synoptic.
Results: The study period included 4,292 cases with an invasive breast cancer synoptic (IBCS) and 622 with a DCIS synoptic. 575 of 622 cases remained after the exclusions. 70% (400/575) did not have any axillary LN sampling. DCIS cases that had axillary LN sampling were larger (Mean: 41.2mm, vs 23.6mm), higher grade (43% Grade 3 vs 30%), associated with comedonecrosis (69% vs 55%) and more frequently mastectomies (56% vs 15%). Only one case (of the 175 that had LN sampling) had a LN metastasis on excision. The 25%, 50% and 75% block counts were: 29, 41 and 55 for IBCS, and 26, 40 and 57 for the 575 included DCIS cases.
Conclusion: Lymph node metastases in the pure DCIS cohort examined are exceedingly rare with the local sampling practices. Sampling of breast specimens is likely a significant determinant of the diagnostic classification and should be examined in the context of resource use. The ratio between DCIS only cases to invasive breast cancer cases in conjunction with sampling metrics may be useful to compare institutional practices, assess the reproducibility of diagnostic classifications, optimize resource expenditures and improve our understanding of breast cancer.

E-PS-02-016
Primary melanoma of the breast parenchyma versus cutaneous mammary melanoma. How to diagnose to improve outcomes – case series
L. Bosoteanu*, M. Aschie, M. Boșoteanu
*Department of Dermatology, "Elias" Emergency University Hospital, Bucharest, Romania, Institute of Doctoral Studies, Doctoral School of Medicine, "Ovidius" University of Constanţa, Romania

Background & objectives: Cutaneous mammary melanoma accounts for <5% of all melanomas, while primary melanoma of the breast parenchyma (PMBP) is exceptionally rare, with <20 cases reported. This study aims to highlight the pathologist's arsenal essential to correctly distinguish between these two conditions.
Methods: In this case series, we present two patients with mammary melanoma of different tissue origins who were treated at our institution. Patient 1 was a 36-year-old female with cutaneous right mammary melanoma, while patient 2 was a 60-year-old female with melanoma of the left breast parenchyma.
Results: Patient 1 underwent surgical excision of the non-ulcerated superficial spreading melanoma with a Breslow index of 1.6 mm. Sentinel lymph node biopsy identified a tumoral deposit, thus integration in stage IIIA imposed the combined Dabrafenib-Trametinib treatment. Dermoscopy highlighted the presence of 100 typical and atypical nevi; dermatological follow-up is currently practiced quarterly.
The left upper-outer quadrantectomy sample of patient 2 microscopically displayed clusters of atypical melanocytes between the mammary glandular structures, without junctional activity. S100 and Melan-A were positive, with a Ki-67 rate of 70%. Comprehensive full-body muco-cutaneous examination unveiled no melanocytic lesions, authenticating the melanocytic lesion's primary breast origin. BRAF V600mut status imposed administration of Vemurafenib, with noteworthy efficacy.
Conclusion: In conclusion, our 2 cases highlight the challenges and polymorphism implied by the histopathological differential diagnosis between cutaneous melanoma of the breast and PMBP, as well as the importance of immunohistochemistry. Careful diagnostic consideration is pivotal in regard to therapeutic methods. Surgical excision remains the mainstay of treatment in both contexts, but the aggressive and unforeseeable biological behaviour of PMBP commonly requires the use of adjuvant treatments (immunotherapy or anti-BRAF medications).

E-PS-02-017
Invasive papillary carcinoma of the breast. A report of four cases
A. Canino*, A. Ravarino, C. Gerosa, R. Murru, J. Caschili, P. Baldussu, D. Fanni
*Department of Medical Sciences and Public Health, University of Cagliari, Italy

Background & objectives: Invasive Papillary Carcinoma (IPC) is an exceedingly rare type of breast cancer since no specific data are available. Within the last ten years, we have observed IPCs only in 4 out of 1004 invasive breast cancers in routine diagnosis.
Methods: The ages of those patients ranged between 67 and 86 years old. Samples taken from the surgical specimen were formalin-fixed, paraffin-embedded, and stained for H&E stain and the following immunohistochemistry analysis: p63, Cytokeratin 5, Cytokeratin 7, GATA-3, Oestrogen and Progesterone receptors, Her2/Neu, Ki-67 (MIB-1).
Results: Histologically, the tumours presented an invasive pattern characterized by papillae supported by fibrovascular cores, covered by epithelial cells with moderate atypia. Immunohistochemistry showed positivity for GATA 3 and Cytokeratin 7, confirming the mammary origin of the tumours. Cytokeratin 5 and p63 were negative in the papillary fronds and at the periphery of the lesion, excluding other papillary neoplasms and leading to the diagnosis of IPC. The positivity for oestrogen receptors was between 90% and 100%, while the positivity for progesterone receptors was between 95% and 5%. Her2/Neu Score was 0 in 3 cases since only one was 2+. The ki-67 index was between 15% and 35%.

Conclusion: Reported to be the 0.5% of all invasive breast carcinomas, which was consistent with the incidence we found in our series, IPC is a rare type of carcinoma. The immunophenotype was similar in all our cases except for Progesterone and Ki67, which showed high variability. Only one of the cases had lymph-node metastasis in a single lymph-node out of 30 examined, although further studies are mandatory for a better understanding of the prognosis of this histotype.

E-PS-02-018

The prognostic and predictive values of androgen receptor expression in breast cancer patients who undergone neoadjuvant chemotherapy

M.Y. Çelik*, A. Umit, H.E. Pestereli, A.M. Tatlı
*Akdeniz University Department of Pathology, Turkey

Background & objectives: The aim of this study is to determine the prevalence of androgen receptor (AR) expression status in breast cancer patients who undergo neoadjuvant chemotherapy, including all molecular subtypes of breast cancer, and to investigate its relationship with known prognostic factors.
Methods: Neoadjuvant chemotherapy (NACT) given 176 patients with luminal A (n:12), luminal B HER2 negative (n:57), luminal B HER2 positive (n:49), HER 2 positive (non-luminal) (n:25) and triple negative breast carcinoma (n:33) diagnosed at Akdeniz University Hospital were included. Histopathological parameters, NACT response and AR expression status were documented. AR expression was detected by immunohistochemically, using antibody clone AR 441.
Results: In the pre-NACT biopsies, 104 cases were AR(-) (59,1%) and 72 cases were AR(+) (40,9 %). The number cases with pathological complete response after NACT were 74 (42%). There was no statistically significant difference between the pre-NACT AR status and pathological complete response(p=0.480). When we compared the pre-NACT and post-NACT cases, there were statistically significant difference in oestrogen receptor (p=0,001), and Ki67 proliferation index (p=<0,001). In between pre-NACT AR(-) and AR(+) cases, we observed statistically significant differences in tumour size (p=0,024), histological grade (p=0,022).The mean Ki67 score of the pre-NACT AR-negative group was 50%, while the mean Ki67 score of the AR-positive group was 40% (p=0.004).
Conclusion: Although there was no statistically significant relationship between AR expression and clinicopathological parameters and survival in breast carcinoma cases with neoadjuvant chemotherapy in our study, to get more detailed information, multicentred larger series with longer observation are needed in future studies. Furthermore, given the current knowledge and literature, the relevance of AR expression in relation to clinical and pathological parameters is particularly promising in terms of new therapies to be developed.

E-PS-02-019

Axillary nodal involvement of post-radiation angiosarcoma of the breast: case report and discussion

A. Cernat-Stefan*, D. Raduta, T.G. Jaswal, A. Roşulescu, T. Georgescu
*Colentina University Hospital, Romania

Background & objectives: Post-irradiation mammary angiosarcoma (PIMA) is a high-grade vascular proliferation that develops in patients who received radiotherapy for a prior epithelial tumour of the breast. Axillary nodal involvement is exceptionally rare, with only few isolated case reports in the scientific literature.
Methods: We reviewed the case of a 67 years old female patient who presented with skin lesions and breast tumours. A history of invasive ductal carcinoma is noted. In December 2022 the patient underwent a breast biopsy, and in February 2023 a left mastectomy with lymphadenopathy was performed. All Hematoxylin and Eosin (H&E) and immunohistochemical (IHC) stained slides were reviewed.
Results: The patient had a prior history of lumpectomy with lymphadenopathy for invasive ductal carcinoma in 2007 and received polychemotherapy, hormonal therapy, and radiation. Mammography showed thickening of the left breast tegument in all quadrants and the presence of multiple nodules and an intensely opaque left axillary lymph node. IHC performed on the breast biopsy showed positivity for CD31, confirming the diagnosis of vascular proliferation. In the lymphadenectomy specimen, a nodular structure with an appearance of atypical vascular proliferation was identified, which presented lymphoid tissue in the periphery, suggestive of nodal metastasis. IHC for ERG, MYC, FLI1, CD31 and D2-40 was performed, confirming the diagnosis of PIMA with nodal involvement.
Conclusion: The particularity of the case resides in the presence of PIMA nodal metastasis. The differential diagnosis, in this case, is that of an atypical vascular lesion, also secondary to irradiation. Strong intralesional expression of MYC and peripherally located lymphatic tissue points to lymph node metastasis. However, nodal involvement is a rare event in the natural history of angiosarcomas and is not a firm indication of lymphadenectomy at this time.

E-PS-02-020

Diagnostic shift in triple negative breast cancer originating from detailed subtyping and definition of receptor status - a retrospective analysis

L. Christe*, E. Werner Rönnerman, A. Kovács, B. Linderholm, A. Valachis, T. Rau
*Institute for Tissue Medicine and Pathology, University Bern, Switzerland

Background & objectives: TNBC is a heterogenous group of tumours. Novel breast cancer subtypes as well as the thresholds for receptor status impact the definition of TNBC directly. In a retrospective cohort, the extent of this diagnostic shift was assessed quantitatively.
Methods: A previously published cohort of 366 patients diagnosed with TNBC between 2007 and 2015 and predominantly no neoadjuvant treatment was reclassified according to the WHO 2019 classification using morphology, a panel of immunohistochemistry and Her2-CISH. Tumours were evaluated for stromal tumour infiltrating lymphocytes (sTILs), tumour budding and survival analysis. Diagnostic consensus was achieved between four experienced pathologists.
Results: According to receptor status, 55 carcinomas (15.0%) were re-classified as ER positive (53) or even Her2 positive (2). Subtyping according to the current WHO classification revealed 56 apocrine carcinoma (15.3%), 9 lobular (2.5%) and 17 rare special types (4.6%). Prototypical TNBC of no special type remained in only 221 cases (60.4%). In multivariate analysis higher grading and advanced nodal status showed the expected worse prognosis. Regarding subtyping, apocrine like lobular carcinomas showed significantly better outcomes in comparison to NST subtypes, whereas rare special subtypes consisting mainly of metaplastic carcinomas appeared as unfavourable. sTILs and tumour budding demonstrated the expected outcome but did not reach statistical significance.
Conclusion: A tremendous morphology-driven diagnostic shift in TNBC was introduced with the current WHO-classification. Differences in ER assessment and the subtype of apocrine carcinoma contribute the most to this effect. The survival analysis underpins the different biological behaviour in the distinct subtypes. Interpretation and conceptualization of clinical trials and digital pathology algorithms should encounter diagnostic shift as a substantial phenomenon. Documentation according to SPIRITpath guidelines and access to digital image repositories might prepare for future adaptations with upcoming classifications.

E-PS-02-021

Outline of the implementation of a national consensus regarding the translation from guidelines to clinical practice evaluation of the Breast Cancer Biomarker HER2

N. Coimbra*, F. Schmitt, J. Magalhães, M.J. Brito, P. Borralho, S. André, R. Celestino, F. Duarte-Ramos

*Pathology Department, Portuguese Oncology Institute of Porto (IPO-Porto), Portugal

Background & objectives: Recent approval of trastuzumab deruxtecan in previously treated HER2-low advanced breast cancers introduces new challenges and needs in HER2 evaluation. Our goal is to optimize HER2 testing in clinical practice by means of a Portuguese national consensus-based guideline recommendations.
Methods: A 3-round modified Delphi exercise was conducted. The Scientific Committee (SC), composed of 6 pathologists, performed an exhaustive bibliographic search, and discussed the most relevant aspects related to the implementation of HER2-low evaluation into clinical practice. After that, the SC defined and validated the statements to be included in the Delphi questionnaire.
Results: Questionnaire is composed of 5 topics, each with several statements: (i) scientific evidence that supports clinical needs; (ii) technological capacitation; (iii) technical and analytical process and quality control; (iv) HER2 testing algorithm and interpretation; (v) structure of the anatomopathological report.
The panel of experts selected by the SC comprises pathologists and clinicians with relevant experience in breast cancer. Each expert received the Delphi questionnaire (2 rounds) and were asked to express their degree of agreement with each statement, on a 5-point Likert scale.
Data analysis and stability analysis was assessed and the percentual variation of the proportion of concordance between rounds was used as an indicator of convergence.
Conclusion: With the methodology outlined in this project, consensus is expected to be gathered regarding the following topics: (i) scientific evidence that supports clinical needs; (iii) technical and analytical process and quality control; (iv) HER2 testing algorithm and interpretation. We expect further discussion related to (v) structure of the anatomopathological report to establish a consensus.
This work had financial support of AstraZeneca Portugal.

E-PS-02-022
Spontaneous regression of breast carcinoma. Presentation of three cases with immunohistochemical study of TILs
A. Córdoba*, R. Beloqui, I. Amat, I. Fernandez, M.R. Mercado, C. Cerezo, D. Guerrero-Setas
*Hospital Universitario de Navarra, Spain

Background & objectives: Spontaneous tumour regression (SR) is defined as the partial or complete disappearance of a tumour in the absence of treatment capable of causing regression. Few isolated cases have been published yet. We present three cases of breast cancer with SR.
Methods: The studied cases are three women aged 78, 79 and 68 year-old who radiologically showed nodules of 27, 30 and 24 mm, respectively. Core needle biopsy was performed in all cases.
The tumours were infiltrating BC, grades 2 and 3 (2 cases), with luminal A (one case) and triple-negative (two cases) phenotype.
We studied TILs in the tumour bed.
Results: After diagnosis, conservative surgery with sentinel lymph node was performed with a maximum interval of 1-month. The resection specimen showed minimal residual tumour of 1.2 and 1.5 mm (30 cells) or no tumour remnants (one case). Total inclusion was performed.
In one case an intense inflammatory reaction, partly granulomatous, was observed. In another case, extensive coagulation necrosis and abundant lymphoid infiltrate was present, whereas a very dense lymphoid stroma was observed in the third case.
The TILs were composed by lymphocytes T/B = 85/15%; CD4/CD8 =30/70; and TIA-1= 40%. The population of macrophages was present as CD163+ in 30% of the infiltrate.
Sentinel lymph nodes were negative.
Conclusion: SR in breast cancer is a rare event recognized in the medical literature and remains an unexpected phenomenon. Due to the rarity of SR, case studies preclude sufficient data on its biological behaviour and clinical significance.
Possible mechanisms underlying spontaneous cancer regression include hormonal or immune system mediation, inhibition of angiogenesis, psychological factors, trauma, infection and epigenetic mechanisms.
The presence of abundant inflammatory infiltration in all three cases may suggest recruitment of the host immune system.

E-PS-02-023
Syringomatous tumour: case report
A. Das Cerci*, T. Toyran, M. Ergin, S. Zorludemir
*Cukurova University Faculty of Medicine, Department of Pathology, Adana, Turkey

Background & objectives: It is expected that the findings in study will contribute to raising awareness about the rare Syringomatous tumour, which can result in unnecessary surgical procedures due to misdiagnosis. We aim to discuss a 40-year-old female patient diagnosed with Syringomatous tumour.
Methods: The blocks of a patient who was diagnosed with malignancy in the outer centre as a result of the biopsy were brought to our hospital for consultation. Sections were taken. Stained with hematoxylin eosin and immunohistochemistry stains.
Results: Microscopically, ductular structures lined by 2 rows of epithelium and surrounded by myxoid fibrous stroma were observed, infiltrating smooth muscle bundles, around lactiferous ducts in places. Some ducts had ovoid shapes with comma-like extensions. These structures showed keratinized cysts and varying degrees of squamous metaplasia. PAS(+) secretory material was prominent in the cyst lumens. There were no significant atypia, mitoses, or necrosis. There was also no lymphovascular or perineural invasion. Cells located at the periphery showed positive staining with HMWK, CK14, P63, and CD10 on immunohistochemistry. The Ki67 proliferation index was determined as 5%.
Conclusion: First described by Rosen in 1983, Syringomatous tumour is a rare benign tumour that often mimics malignancy in clinical and histomorphological features. Less than 80 cases have been reported in the literature for this tumour. Therefore, it is important to keep in mind to avoid misdiagnosis and unnecessary surgical procedures for this rare tumour. In this study, we aim to discuss a 40-year-old female patient diagnosed with Syringomatous tumour, highlighting its significance.
Funding: Cukurova University

E-PS-02-024
Benign Müllerian inclusion in the axillary lymph node of a patient with breast carcinoma: a case report
S.K. Dursun*, T. Soylemez Akkurt
*Basaksehir Cam and Sakura City Hospital, Turkey

Background & objectives: Benign inclusions, such as capsular nevi, epithelial cysts, and heterotopic mammary glands, are common in axillary lymph nodes. Benign Müllerian inclusions are frequently seen in pelvic/para-aortic lymph-nodes but only rare reports have described involvement of lymph nodes above the diaphragm.
Methods: A 39-years old woman presented to our hospital with breast mass. On physical examination, a rigid, solid lesion was present at the superior outer quadrant. A lesion with suspicious malignancy (28x18 mm) was detected on mammography. Core biopsy was performed and the diagnosis was luminal A mammary carcinoma. Thus, the patient underwent breast-sparing surgery with sentinel lymph node (SLN) biopsy.
Results: Two SLN were submitted for frozen sections. No metastatic carcinoma was present in frozen section slide. Histopathological examination revealed invasive carcinoma with mixed ductal and lobular

features. Serial sections were applied to SLN biopsy; one was stained with AE1/AE3 while others were stained with H&E. On microscopic examination, small glands lined by monolayer of cuboidal/columnar epithelial cells were detected within the capsule and focally in the lymph node parenchyma. No atypical appearance was seen in these cells. The immunoprofile of these cells showed positive staining for AE1/AE3, Oestrogen Receptor, Pax8, and negative staining for Gata3. Morphological findings with supporting immunohistochemical results confirmed the diagnosis of benign Müllerian inclusion of SLN.
Conclusion: Benign Müllerian inclusions are most commonly seen in pelvic and para-aortic lymph nodes. Axillary lymph node involvement is extremely rare. It should be kept in mind their glandular appearance may be confused with metastasis in patients with breast carcinoma. Their histomorphological patterns and immunoprofile assist to distinguish from metastatic lesions. Especially on a small biopsy specimen and frozen sections, being aware of this entity has paramount importance during differential diagnosis and to avoid misclassification.

E-PS-02-025
Male breast carcinoma in a symptomatic breast unit, a ten year retrospective review
R. Farrell*, A. O'Shea, M. Staunton
*Department of Histopathology, Beaumont Hospital, Dublin, Ireland

Background & objectives: Male breast cancer is rare, representing 1% of all breast cancers diagnosed in Ireland between 1995 – 2019. We evaluated the histopathology of male breast specimens received from a busy symptomatic breast service.
Methods: Using our laboratory information system we retrospectively reviewed all pathology reports produced by our laboratory recorded as SNOMED T04000 breast and classified as gender: male between 01/01/2013 and 31/12/2022. The data was then corrected to remove gender misclassifications and unique patient identifiers were removed. Statistical analysis was performed with Graphpad prism version 7.0.0.
Results: We identified 192 specimens from 151 male patients, of these 44.2% (85) were small biopsies, 38% (73) benign excisions, and 15.6% (30) malignant resections. Of the 28 primary invasive breast cancers, 24 were resected. The 6 other resections were for: ductal carcinoma in situ (DCIS) (1), skin malignancies (2), and soft tissue sarcomas (3). Primary invasive breast cancers were invasive ductal carcinoma (IDC), no special type (23); IDC, papillary subtype (4), and invasive lobular carcinoma (1). All breast cancers were oestrogen receptor positive, 6 were HER2 positive. Concomitant DCIS was present in 12 cases. Tumour grade was stratified grade 1 (6), grade 2 (14), and grade 3 (8).
Conclusion: We illustrate the relative rarity of male breast cancer with on average fewer than 3 cases per year, which limits statistical interpretation. However, papillary carcinomas were seen more commonly (14.2%) among male patients than would be expected in female patients (0.5%), and invasive lobular carcinomas were rare (3%). The low number of specimens and prevalence of rarer cancer subtypes illustrates the need for further research in male breast disease.

E-PS-02-026
Computer-aided quantitative analysis as second opinion in the assessment of low HER2 IHC score in breast cancer – a pilot evaluation
Y. Glickman*, S. Zilber, Y. Arbel, Y. Sufrin, B. Benbenishti, Y. Sherman
*Applied Spectral Imaging, Israel

Background & objectives: The adoption of computer-aided quantitative assessment for the differentiation between negative and equivocal HER2 scores in breast cancer is increasing. This pilot evaluation aims at assessing the usefulness of computerized quantification as second opinion in diagnosis of low HER2 .
Methods: 19 core biopsy specimens from 14 patients were included. Two slides from each core were stained with H&E and HER2. Slides were examined by certified pathologists using conventional microscopy and digitalized images obtained on the Hamamatsu NanoZoomer S360 and reviewed on the SECTRA viewer. The specimens were further analysed using Applied Spectral Imaging's FDA-cleared HER2 quantitative scoring.
Results: Among the 14 patients included in this study, 10 had IDC, 3 ILC and one mucinous carcinoma. Following manual HER2 analysis, 8 slides were scored (0), 5 slides (1+), 3 slides (2+) and 3 slides (3+). These manual results were compared to the computerized scores obtained with the HER2 quantitative biomarker. Concordance was found in 14 out of 19 slides (11 patients). 5 slides (3 patients) were manually reported as HER2 negative (0) or (1+) while the computerized system yielded positive (2+) scoring. A second manual review of these inconsistent results was recommended in order to further confirm the diagnosis.
Conclusion: This evaluation exemplifies the potential usefulness of computer-aided scoring as a second opinion for HER2 slide assessment, especially in cases of HER2 low. This further illustrates the possible use of combined manual reading and computerized analysis as a mean to increase standardization and diagnostic confidence when reporting HER2 immunohistochemistry in breast cancer patients.

E-PS-02-027
Incidence of atypical lesions in routine breast reductions warrants assessment of the feasibility of orientation and inking each specimen
T. Gul*, M. Leader
*St James's Hospital, Ireland

Background & objectives: To assess the feasibility of orientation and inking of breast reduction specimens.
Methods: 200 cases of BRS's were analysed retrospectively for significant pathology. The age ranged from 19-84 years with a median age of 41 years. Four sections were sampled from each breast specimen. Orientation and inking of specimens were instituted after the results of our audit.
Results: Five of 200 cases (2.5%) showed a significant abnormality including 1 with atypical ductal hyperplasia, 3 with atypical lobular hyperplasia and 1 with high grade multifocal DCIS with cancerization of lobules over a span 0f 20 mms. The latter patient's specimen was not orientated or inked and prompted the use of inking in future specimens to assist patient management.
Conclusion: This study found that the procedure of orientation and inking was simple and easily performed. We recommend this should be included in guidelines to benefit further sampling, exact localization of the lesion and its excision status and patient management.

E-PS-02-028
Rare presentation of medullary thyroid carcinoma with bilateral breast metastasis: a case report
E. Gun*, O. Layth Qassid
*Basildon University Hospital, Mid and South Essex NHS Foundation Trust, Basildon, Essex, United Kingdom

Background & objectives: Medullary thyroid carcinoma (MTC) is an uncommon type of thyroid cancer that comprises only 3-5% of all thyroid cancers. We aimed to present a case with bilateral breast metastasis of MTC.
Methods: A 48-year-old female presented with a lump in her left breast. Ultrasonography revealed a 10x7 mm mobile lump in the lower outer quadrant of the left breast. Tru-cut biopsy of the lesion revealed nests and cords of tumour cells with pink amorphous material in between. The tumour was negative for ER, PR, and HER2.

Results: These findings triggered a second panel of immunostains to exclude metastasis due to the neuroendocrine morphology. The tumour was positive for CD56, and Synaptophysin and negative for GATA-3 and SOX-10. Pancytokeratin showed dot-like perinuclear staining raising the question of metastatic neuroendocrine carcinoma. The multidisciplinary team meeting discussion revealed that the patient had undergone bilateral total thyroidectomy 14 years ago, and was diagnosed with MTC.Staging computed tomography showed another mass on the contralateral breast with the same features. Additional immunostains were positive for Calcitonin and TTF-1 and negative for PAX-8. Congo red staining highlighted amyloid deposition within the tumour. The final diagnosis was a bilateral metastasis of MTC to the breast.
Conclusion: Most cases of MTC (about 75%) are sporadic while the remaining 25% have a hereditary basis. MTC most frequently metastasizes to the regional lymph nodes, liver, lungs, and bone. Metastases to the breast from extra-mammary organs are infrequent, and MTC rarely metastasizes to the breast. It is crucial to be aware of the rare metastatic lesions that could be found in the breast in order to avoid unnecessary surgical procedures and enable the appropriate management of the primary tumour.

E-PS-02-029
In hormone receptor-positive breast cancers (oestrogen receptor and/or progesterone receptor positive and HER2 negative) can the Ki-67 proliferation index in the tru-cut biopsy guide us for the neoadjuvant treatment response?
I. Guzelis*, B. Bolat Kucukzeybek, Y. Kucukzeybek
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Seventy percent of breast cancers are hormone receptor-positive group. In hormone receptor-positive breast cancer, neoadjuvant treatment has a low pathologic response rate. The question is what will be the initial treatment and if the Ki-67 proliferation index can guide us.
Methods: In this retrospective study, 62 hormone receptor positive patients with breast cancer who received neoadjuvant therapy and underwent resection were included. Ki-67 proliferation index were evaluated in initial tru-cut biopsy specimens. The cut-off point for the Ki-67 proliferation index was designated as 27.5% by receiver operating characteristic curve analysis. Clinical T was assessed according to the initial radiological tumour size.
Results: The mean value of the Ki-67 proliferation index was 37.8% ± 27.4%. Of the cases, 50 were luminal-B subtypes (81%). Before the neoadjuvant treatment, the largest radiological tumour size was 3.6 ± 1.9 centimetres. The mean tumour size in the resection specimen after neoadjuvant treatment was 1.6 ± 1.5 centimetres. Lymph node metastasis in the resection specimen was found in 28 cases (45.2%). Pathological complete response (yP0N0 or yPisN0) was seen in 8 patients (13%). Of the cases, 37 (60%) had a regression in the tumour size that would change its pT. Ki-67 proliferation index over 27.5% was seen to be associated with regression in the tumour size (p=0.02).
Conclusion: As in line with the literature pathological complete response rates after neoadjuvant treatment are low in hormone receptor-positive breast cancer cases. As we have shown 27.5% cut-off value of Ki-67 can be a useful predictive parameter for the regression in the tumour size. More data are needed to predict the response to neoadjuvant therapy in hormone receptor-positive breast cancer.

E-PS-02-030
Idiopathic granulomatous mastitis (IGM) - a diagnostic challenge
G. Hennessy*, K. Ryan, E. Houlihan, J. Mannion, B. Dunne, B. O'Connell, E. Connolly
*Ireland

Background & objectives: Idiopathic is a rare, benign, inflammatory breast disorder of unknown aetiology. Differential diagnoses include breast malignancy and granulomatous diseases. The pathological criteria for diagnosis of IGM includes granulomatous inflammation with the presence of multinucleated giant cells, fat necrosis, abscesses eosinophils.
Methods: All clinically detected cases of idiopathic granulomatous mastitis over a 5-year period (2017-2022) were identified using HIPE data.
A retrospective review was undertaken of the histological features:
1. Periductal or perilobular inflammation
2. Sheet like or well formed granulomas
3. Presence of neutrophils/eosinophils
4. Presence of necrosis
5. Special stains

Results: A new breast lump was the most common clinical presentation, 72.5% of patients. 61% of samples were biopsies of the left breast, with the remainder from the right. 19.5% were post-partum. 14.6% were current smokers. 2 patients had a history of diabetes mellitus.
All 40 samples sent for histological analysis had granulomatous inflammation present. 32 were described as in sheets, 7 well-formed, and 1 combination of both. Neutrophils were seen in 34 samples, foreign body giant cells seen in 29, histiocytes seen in all 40 samples, and necrosis was visualised in 2 samples only. A positive gram stain was reported in 2 samples, which correlated with microbiology results.
Conclusion: IGM is difficult to distinguish clinically from other inflammatory breast diseases or cancer. Clinicopathological correlation with radiology and microbiology are important, but the gold standard of diagnosis remains with histopathology.

E-PS-02-031
Breast ductal carcinoma in situ diagnosed by stereotactic vacuum-assisted biopsy has favourable pathologic features and a lower upstage rate
C. Huang*, C. Lee, C. Lin, R. Chang, P. Liao, P. Lin, Y. Lee
*Department of Pathology, National Taiwan University Hospital, Taiwan

Background & objectives: Stereotactic vacuum-assisted breast biopsy (SVAB) has a superior diagnostic accuracy than core needle biopsy (CNB) for clustered microcalcifications. We aim to compare the clinicopathological features and the upstage rate of ductal carcinoma in situ (DCIS) diagnosed by SVAB and CNB.
Methods: Data from 533 patients diagnosed with DCIS by SVAB or CNB in a single centre between 2016 and 2020 were analysed. Mammogram and ultrasound reports were retrieved. The biopsies were independently reviewed by two pathologists and evaluated by an in-house artificial intelligence (AI) system (Deep DCIS). The rates of upstaging to invasive carcinoma in subsequent wide excision specimens were compared.
Results: In patients receiving SVAB, only 17.8% showed suspicious lesions (BI-RADS 4 or 5) on breast ultrasound, contrary to those receiving CNB (96.8%). SVAB obtained a larger tissue amount with less proportion of area involved by DCIS (10.2% vs. 32.3%). Pathologists graded more cases as high-grade in CNB (48.1%) than in SVAB (37.9%). All the pathological scores evaluated by the AI system (Deep DCIS) were more severe in CNB than in SVAB, including nuclear grade (51.6 vs. 40.9), necrosis (7.9 vs. 1.1), and stromal reactivity (1.5 vs. 0.5). Oestrogen receptor positivity was higher in SVAB (85.7%) than in CNB (63.5%). SVAB shows a significantly lower upstage rate (11.4%) than CNB (66.3%).
Conclusion: SVAB is associated with less underestimation of DCIS than CNB, probably because more SVAB cases are impalpable microcalcification lesions, which tend to be less aggressive (low- to intermediate-grade and oestrogen receptor-positive). The ability of SVAB to obtain a larger quantity of tissue may also contribute to the lower subsequent upstage rate. Clinical trials are

investigating the possibility of active surveillance for the management of low-risk DCIS, and the biopsy method is a crucial factor to be considered in risk stratification.

E-PS-02-032

Comparison of two sentinel node imaging methods magtrace and scintigraphy

P. Hurník*, J. Strakos, J. Palica, Z. Vavrova, R. Ondrussek, F. Fakhouri, P. Vazan, P. Delongova, V. Zidlik, D. Ziak
*University Hospital of Ostrava, Czech Republic

Background & objectives: Imaging and excision of the sentinel lymph node is now a standard examination for the staging of breast tumours and melanomas. This examination can be performed using staining methods, scintigraphy and Magtrace.
Methods: This study compares a total of 320 patients who underwent breast cancer surgery including sentinel lymph node biopsy. In 3/21-3/22, 165 patients were screened with Tc99, and in 4/22-3/23, 155 patients were screened with an iron-based tracer (Magtrace). Primary results emphasized the number of examined nodes, the number and quality of metastases and pT status with evaluation of receptor expression.
Results: In the case of Tc99 scintigraphic examination, a total of 527 sentinel lymph nodes were examined in 165 patients with an average of 3.19 SLN per patient. Node positivity was detected in 44 SLNs (8.34%) - of which ITC in 6.8%, micrometastasis in 45.45%, macrometastasis was confirmed in 47.72%. A total of 616 nodes from 155 patients were examined using the MAGtrace method, with an average of 3.97 SLN per patient. Node positivity was detected in 59 SLN (9.57%) - of which ITC in 5.08%, micrometastasis in 40.67%, macrometastasis was confirmed in 54.23%. Of course, other statistical analyses were also carried out.
Conclusion: Magtrace is safe to use method and it has significantly increased the detection rate of positive sentinel lymph nodes in our department. It has also improved the quality of care. A significant reduction in preoperative care and a positive impact on operative time have also been reported in the literature. It has therefore helped to reduce costs and improve patient comfort when introduced.

E-PS-02-033

Metastatic uterine leiomyosarcoma presenting as a symptomatic breast lump: a case report

N. Ibišević*, A. Humackic, Z. Guzin, K. Tomic, B. Lukic, S. Vranic
*Clinical Center University of Sarajevo, Bosnia and Herzegovina

Background & objectives: Metastatic solid tumours in the breast account for ~1% of all breast malignancies. The most common metastatic tumours in the breast are hematologic malignancies, melanoma, lung, ovarian, and gastric cancers. Metastatic sarcomas, particularly symptomatic, are very rare.
Methods: We present a rare case of symptomatic metastatic uterine leiomyosarcoma to the breast. The patient had a history (six years ago) of a hysterectomy and bilateral salpingo-oophorectomy for multiple uterine fibroids, one of which was diagnosed as a symplastic leiomyoma.
Results: A 55-year-old woman clinically presented with a painless, palpable left breast mass measuring 20 mm. A core biopsy of the breast mass demonstrated a cellular spindle cell neoplasm, suggesting a smooth muscle neoplasm suspected to be malignant (B4). A wide local excision of the breast mass was performed, revealing grade 2 leiomyosarcoma. Re-review of the uterine fibroids revealed the largest one (200x130 mm) to be morphologically identical to the breast lesion. Additional diagnostic work-up revealed multiple liver and pulmonary metastases with a suspected metastatic sclerotic lesion in the L3 projection. The patient was subsequently treated with chemotherapy protocol for metastatic leiomyosarcoma (ongoing).
Conclusion: Metastatic tumours in the breast are rare, particularly symptomatic and of soft tissue origins, such as leiomyosarcoma. However, they may be more frequently seen in patients with advanced/widespread metastatic disease.

E-PS-02-034

Prognostic implications of histopathological evaluation in post-neoadjuvant chemotherapy breast cancer patients: our experience

M. Iuzzolino*, C. De Carlo, D. Gentile, A. Sagona, E. Barbieri, S. Di Maria Grimaldi, R.M. Trimboli, D. Bernardi, S. Darwish, C. Tinterri, L.M. Terracciano, B. Fernandes
*Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy; Department of Pathology, IRCCS Humanitas Research Hospital, Rozzano, Italy

Background & objectives: Breast cancer (BC) response to neoadjuvant chemotherapy (NAC) is linked to long-term outcomes. In this study, we intend to correlate post-NAC histological measures [residual tumour cellularity (RTC) and pathologic complete (pCR)/partial response (pPR)] and residual disease pattern to patient prognosis.
Methods: Consecutive BC cases undergoing NAC in our Institution between 2006 and 2020 were reviewed. We evaluated post-NAC tumour dimension, sub-type, histotype and vascular invasion. For patients with pPR, the percentage of RTC was calculated. We assessed residual disease pattern, dividing it into scattered or circumscribed. Results were correlated to disease-free survival (DFS), distant disease-free survival (DDFS), and overall survival (OS).
Results: Overall, 495 patients were analysed. The majority of patients undergoing NAC were affected by HER2-positive BC sub-type (40.4%). 148 (29.9%) achieved pCR, 347 (70.1%) had pPR, and the median RTC was 40%. Pattern of residual disease was recorded as circumscribed in 195 (56.2%) cases, scattered in 152 (43.8%) cases. At multivariable analysis, two independent factors predicting pCR were identified: BC sub-type (HER2-positive 54.7% versus triple-negative 29.8% versus luminal-like 15.5%) and vascular invasion (absence 98.0% versus presence 2.0%). We found statistically significant longer DFS, DDFS, and OS in patients with pCR and with RTC <40%; no difference was observed in terms of OS between RTC <40% and RTC ≥40% groups.
Conclusion: Patients with BC treated with NAC and subsequent surgery who achieve pCR have better long-term oncological results in terms of DFS, DDFS, and OS compared to patients with pPR. BC sub-type and vascular invasion are significantly and independently associated with pCR. Measurement of RTC in BC patients improves the prognostic information that can be obtained from the assessment of pathologic response. We are conducting further statistical studies to correlate residual disease pattern (scattered versus circumscribed) to prognosis.

E-PS-02-035

HER2 expression is sensitive to intratumoral hypoxia in HER2-low invasive breast carcinoma

P. Juhasz*, G. Mehes
*University of Debrecen, Hungary

Background & objectives: Heterogeneity of HER2 expression is common in HER2-low invasive breast carcinoma (BC). Carbonic anhydraseIX (CAIX) is upregulated in hypoxic tumour cells with an adverse prognostic effect in BC. The relation of CAIX to intratumoral HER2 and microvessel distribution was evaluated.
Methods: Altogether 60 HER2 non-amplified BC samples with 2+ HER2 status were evaluated for Her2 and CAIX expression as well as microvessel distribution using triple IHC labelling for HER2, CAIX and CD31. The extension of HER2+ and CAIX+ areas was measured in four directions and CD31 positive capillary distance was measured at 10 regions/case using the Histoquant image analysis software (3DHistech).

Results: Partial CAIX expression was found in 56.2% of BC cases with heterogenous HER2-expression. The pattern of expression was dynamically alternating with CAIX+ areas becoming virtually HER2-negative. Highest HER2-positivity was seen in the proximity of CD31+ microvessels. Gradual Her2-loss could be observed from a mean vessel distance of 85.08±15.37 µm (range 42.75 – 157.31 µm) turning in a complete HER2-negative and CAIX-positive phenotype. The transition zone appeared as double HER2+/CAIX+. CD31+ vessel-to-vessel distance was significantly higher in CAIX+ samples (mean values 80.2±22.6 vs 311.4±77.0). High intensity CAIX+ zones surrounded foci of ischemic necrosis in 4/60 cases.
Conclusion: HER2-low status is becoming important for targeted HER2-therapy. We demonstrate that intratumoral target distribution is related to tissue perfusion and adapation to hypoxia. The upregulation of CAIX highlights hypoxic tumour regions also featured by dynamic loss of HER2. The relation to the microvessel network could also be clearly established. The occurrence of CAIX indicates to a clinically significant resistance mechanism interfering with the specific effect of new-generation HER2 based therapies.

E-PS-02-037
Not all breast adenoid cystic carcinomas are created equal
M. Khmou*
*National Institute of Oncology, Morocco

Background & objectives: Breast adenoid cystic carcinoma (AdCC) is a rare salivary gland-like tumour. The solid-basaloid AdCC is rare subtype (less than 100 published cases). In opposition to classic AdCC, the solid-basaloid subtype has an aggressive clinical course, with local recurrences and metastases.
Methods: We report the case of a 78-year-old woman with a right breast mass, evolving for 2 months. Examination revealed a painless mass in the upper outer quadrant. No axillary lymphadenopathy was detected. Mammogram and ultrasound revealed a 2 cm spiculated mass with scattered microcalcifications. The lesion was excised after a negative biopsy, by lumpectomy with sentinel node dissection.
Results: Microscopically, the tumour was exclusively composed of solid nests of basaloid cells with infiltrative margins. Trabecular, tubular, or cribriform patterns were not identified.
The tumour cells had a medium to large size and displayed a high nuclear to cytoplasmic ratio with scanty cytoplasm and large, round to oval nuclei. The intervening stroma was densely hyalinized.
The typical biphasic pattern of myoepithelial-ductal differentiation as seen in the classic AdCC was not seen in this case.
Immunohistochemistry showed diffuse positivity for CD117, SOX10 and CK7 in all neoplastic cells. They lacked oestrogen receptor, progesterone receptor, human epidermal growth factor receptor-2 expression. They were also negative for Synaptophysin, chromogranin, GCDFP15 and Mammaglobin.
Conclusion: The aim of this report is to describe and to draw attention to this rare and aggressive variant of AdCC, characterized by a higher incidence of distant metastases compared with the classic AdCC. Morphological differential diagnosis of this entity is often challenging, it include solid ductal carcinoma in situ, solid papillary carcinoma, neuroendocrine tumours and invasive breast carcinoma of no special type. While minimal standardized data on therapeutic management is available, large-scale studies with long-term follow-up for patients are necessary.

E-PS-02-038
Unexpected finding in a long lasting sclerosed fibroadenoma - multiple foci of high grade invasive ductal carcinoma: a case report
A. Klevišar Ivančič*, R. Eržen Jakšič, R. Petrič, G. Gasljevic
*Institute of oncology, Slovenia

Background & objectives: Breast carcinoma (BC) arising in fibroadenoma (FA) is extremely rare; it occurs in < 0.1 % of FA specimens. High-quality ultrasonosonography (US) has a high negative predictive value. However, in the presence of suspicious US findings, histopathological correlation is mandatory.
Methods: A 53-year-old woman presented with 20-years lasting tumour, increasing in size, previously diagnosed as FA on US. Family history was BC-negative. Mammographically, it was 7cm large, well-defined. US showed small foci suggestive of necrosis. Axillary lymph nodes were unsuspicious. Two core needle biopsies showed only abundant hypocellular hyalinized stroma. Because of the tumour size and radiological-pathological discrepancy, tumourectomy was performed.
Results: Macroscopically, the excised tumour was well-defined, elastic. It weighted 95 g, measured 7x6x4 cm, was focally surrounded by a small amount of breast parenchyma. On cut surface, it was pale white with focal small softer areas. Histology showed multiple foci (at least 30) of high-grade invasive ductal carcinoma (IDC) measuring from 1-20 mm and ductal carcinoma in situ scattered within sclerosed FA. They represented approximately 70% of FA volume, mainly being limited to FA (two of them minimally infiltrated breast parenchyma). Surgical margins were tumour-free. IDC was ER/PR positive and HER-2 negative. Later on, a sentinel node was excised being negative. Patient is currently waiting for decision about further treatment.
Conclusion: In conclusion, we describe a very rare case of invasive BC arising in long lasting FA. Although clinically unsuspicious, therapeutic decision was guided by FA-size and radiologic-pathologic discrepancy. Excision of FA with histopathological examination should be performed in any of the following clinical scenario: increase in size during US follow-up, presence of suspicious findings on US examination, immobile and poorly circumscribed lesion, advanced age (> 35 years), a family history of cancer and FA greater than 2.5 cm in diameter.

E-PS-02-039
Study of CD 163 expression in breast cancer tissue
O. Kolomiiets*, R. Moskalenko
*Department of Pathology Sumy State University, Ukraine

Background & objectives: Macrophages are one leading the representatives of the tumour microenvironment is crucial in developing metastasis, prognosis, recurrence of breast cancer (BCa).
The aim. To investigate the expression of CD 163 receptors in the tissue of BCa with and without calcifications.
Methods: In the work, 60 BCa tissue samples were studied and divided into two groups. The first group included tissues of breast BCa with calcifications (30 samples), and the second group - BCa tissue without microcalcifications (30 samples). The work used an immunohistochemical study (IHC) of CD 163 expression and statistical processing of the results (Student's test).
Results: When examining a group of BCa tissue samples with calcifications, it was established that the average value of CD 163 expression was 53.21 ± 3.05. In the control group of BCa tissue without calcification, CD 163 expression was 65.57 ± 3.75 ($p<0.05$).
Conclusion: Our study shows that the expression of CD 163 receptors is higher in the tissue of BCa without calcifications compared to the tumour tissue samples of the first group. These results may indicate different mechanisms of metastasis development in the tumour tissue of BCa in the presence of calcifications.

E-PS-02-040
Heterogeneity of Her2-positive and triple negative breast cancer subtypes in primary tumour and local metastasis
K. Konyshev*, S. Sazonov
*Institute of medical cell technologies, Ural state medical university, Russia

Background & objectives: The aim of the study was to assess the stability of the biological subtype of breast cancer in regional metastasis in cases with triple negative, hormone receptor-negative Her2-positive

and hormone receptor-positive Her2-positive subtypes of the primary tumour (PT).
Methods: Surgical specimens of the PT and local metastases of 36 patients with breast cancer were studied. Immunohistochemistry (ER, PR, Her2/neu, Ki67) and SISH (HER2 gene) were used to assign the tumour to one of the surrogate biological subtypes. The frequencies of subtype changes of regional metastasis compared with PT were evaluated and then compared using Fisher exact probability test.
Results: Subtypes of PT and metastasis were concordant in 29 cases (80.6%, 95% CI 63.4-91.2%), discordance of the subtypes was observed in 7 cases (19.4%, 95% CI 8.8-36.6%) ($p<0.05$). Among 20 cases with a triple negative subtype of PT, in 1 case metastasis had another (luminal B) subtype (5%, 95% CI 0.3-26.9%). Of the 9 cases with hormone receptor-negative Her2-positive subtype of PT, in 4 cases metastasis had other (2 triple negative, 1 luminal A, 1 Luminal B) subtypes (44.4%, 59% CI 15.3-77.3%). Among 7 cases with hormone receptor-positive Her2-positive subtype of PT, in 2 cases metastasis had other (1 luminal A, 1 luminal B) subtypes (28.6%, 95% CI 5.1-69.7%).
Conclusion: The biological subtype of breast cancer with regional metastasis in most cases remains stable among the cases of the entire sample. Discordance of the subtype is most often observed in cases with a hormone receptor-negative Her2-positive subtype of the primary tumour.

E-PS-02-041
Evaluation of tonsil as tissue control for immunohistochemical demonstration of oestrogen receptor
H.L. Kristoffersen*, R. Røge, S. Nielsen
*NordiQC, Aalborg Universityhospital, Denmark

Background & objectives: The purpose of this feasibility-study was to evaluate the applicability of normal tonsillar tissue as positive tissue control in immunohistochemical staining for Oestrogen Receptor (ER). This was accomplished by comparing the analytical sensitivity in validated and selected suboptimal staining protocols.
Methods: Ten tonsils and eleven breast carcinomas (BC) with varying ER intensity were included. In addition to the validated reference immunohistochemical protocol, materials were stained using modified protocols with both reduced analytical sensitivity and with increased analytical sensitivity.
The ER expression was quantified using H-scores, and for diagnostic evaluation a cut-off at ≥10% positive neoplastic cells was used in the BCs.
Results: Using the validated reference protocol, 8/11 BCs were ER positive with a mean H-score of 81 whereas tonsillar germinal centre lymphocytes and squamous epithelial cells showed a mean H-score of 6 and 56, respectively. The protocol with increased analytical sensitivity also characterized 8/11 BCs as ER positive, mean H-score 130 and H-score of 16 and 103 in tonsillar lymphocytes and epithelial cells, respectively.
The protocol with most reduced analytical sensitivity characterized 6/11 BCs as positive, mean H-score of 31 while tonsillar germinal centre lymphocytes and epithelial cells showed H-scores of 2 and 21.
Conclusion: Tonsil was found applicable as critical positive tissue control for immunohistochemical demonstration of ER including low level ER expressing BCs. Protocols providing reduced levels of H-score in germinal centre lymphocytes and epithelial cells was associated with false negative BCs. Increased analytical sensitivity and associated increased H-scores in tonsil did not induce false positive BCs.
More studies with increased number of BCs must be performed to validate the observation and potentially combined with image analysis to elucidate H-score read-out consistency.
The project was supported by The Biomedical Laboratory Scientist Education and Research Fund in Denmark.

E-PS-02-042
Clinicopathological features of male breast cancer: a single institution experience
H. Lee*, O. Lee, S. Son, C.G. Woo
*Chungbuk National University, Republic of Korea

Background & objectives: Male breast cancer (MBC) is a rare malignancy while female breast cancer is one of the most common malignancies in Korea. Clinical and pathological characteristics of MBCs were investigated and described.
Methods: Patients of MBC were collected who visited Chungbuk National University from January 2011 to December 2022. Pathologic data were obtained including TNM stage, presence of ductal carcinoma in situ, lymphovascular or perineural invasion. Immunohistochemistry (IHC) results such as oestrogen and progesterone receptors, HER2, p53, and ki-67 index were assessed.
Results: The average age of patients was 64.5 years (range 41-89). Ten out of 13 patients underwent mastectomy, including one with distant metastasis at the time of surgery. Lymph node metastasis was found in four out of 9 who underwent axillary lymph node assessment. IHC showed that every case was positive for hormone receptors and negative for HER2. When ki-67 index was set at 14%, five (38.5%) and 8 (61.5%) were classified as luminal A- and B-like, respectively. No TP53 gene mutation was found according to p53 IHC pattern. Clinical follow-up data revealed that three (33.3%) out of 9 who had underwent curative mastectomy had recurrence and/or distant metastasis.
Conclusion: MBCs occur in elderly men and almost all have luminal A- or B- subtypes. Therefore, if an MBC showed HER-positive or triple-negative type by IHC, further studies were probably required including radiologic and genetic assessments.

E-PS-02-043
Clinicopathological characteristics and prognostic analysis of fibrotic focus in HER2-negative breast cancer
Y. Liu*, M. Yue, S. Wu
*The Fourth Hospital of Hebei Medical University, China

Background & objectives: The aim of this study is to assess the fibrotic focus (FF) with clinicopathological features and prognosis in patients with HER2-negative breast cancer, especially with HER2-low breast cancer.
Methods: We retrospectively reviewed the data of 293 patients with HER2-negative, stage I-II, invasive breast cancer of non-specific types from September 2017 to December 2018. The clinicopathological data of the patients were collected and followed up. The FF with clinicopathological features and prognosis in patients with HER2-low and with HER2 0 breast cancer was analysed.
Results: The study cohort included 178 cases (60.8%) with HER2 low and 115 cases (39.2%) with HER2 0. FF were correlated with older age, intermediate and low NHG, vascular invasion, HR positivity, HER2 low status, high Ki67 expression and low TILs. Univariate survival analysis showed that FF was significantly associated with shorter progression-free survival (PFS). Stratified analysis indicated that DFS was longer in patients without FF compared to those with FF in the HR-negative (HR=0.313, p=0.012) and HER2 low (HR=0.272, p=0.043) groups. DFS was also significantly longer in patients without FF compared to those with FF in the HR-positive (HR=0.069, p=0.002) and HER2 0 groups (HR=0.129, $p<0.001$).
Conclusion: The results indicated that patients with FF exhibited distinct biological characteristics and prognostic significance, particularly in the HR-negative and HER2 0 groups. To our knowledge, this was the first study to report this finding. This provides a rationale for accurate diagnosis and treatment of HER2-negative breast cancer.

E-PS-02-044
Tumour mutation burden and infiltrating immune cell subtypes influenced the breast cancer prognosis
Y. Liu*, J. Li, H. Liu

*The Fourth Hospital of Hebei Medical University, China

Background & objectives: Most of its issues are still undecided on the relationship between tumour mutation burden (TMB) and immune-related genes in the breast cancer. This study explores their relationship based on gene mutation and transcription data in the TCGA database.
Methods: Download and extract the somatic mutation data in the TCGA database. Cases are divided into Low-TMB and High-TMB subgroups. Differentially expressed immune-related genes were identified in different TMB subgroups, and predicted patient prognosis and gene function enrichment analysis, while comparing different TMB subgroups and invasive immune cells, different clinical pathological features.
Results: A total of 986 mutation data with breast cancer patients were obtained. Compared with Low-TMB groups, the survival period of High-TMB group was relatively longer, and the high and low expression of TMB was related to some clinical pathological characteristics. There were 337 differential expression genes between TMB subgroups. Of these genes, 7 differentially expressed immune-related genes are associated with prognosis. Among the High-TMB group, activated CD4 + memory T cells and other cells have high expression, while the expression ratio of memory B cells and other cells in the Low-TMB group is high. But these immunocytes are unrelated to the survival of the patients (P> 0.05).
Conclusion: TMB-related immunological infiltration characteristics have good predicted value for prognosis of breast cancer patients. Differentially expressed immune-related genes between TMB subgroups provide important predictive information for the survival.

E-PS-02-045
Histopathological H&E-based evaluation of HER2 status in breast cancer through a novel deep learning approach
C. Lupo*, N. Casatta, G. Gerard, G. Cervi, A. Polonia, N. Fusco, G. Curigliano, C. Eloy
*Innovation Department, Diapath SpA, Martinengo (BG), Italy

Background & objectives: Recent research introduced a new 'HER2-low' expression in breast cancer. The accurate definition of the HER2 profile is thus showing the need for more sensitive diagnostic tools to ensure that eligible patients are not deprived of effective therapies.
Methods: In computational pathology, self-supervised learning is a new paradigm for learning feature representations without fully labelled data. In particular, Vision Transformers (ViTs), which rely on self-attention mechanisms to process image data, were used as the base for the patch-wise classification of different histopathological datasets. The model aimed at the classification of HER2 biomarker expression on H&E slides of breast cancer.
Results: Through the successful project collaboration among the experts of the University of Milan, two Italian innovative companies and an excellence reference centre and through the shared knowledge of different expert teams, a model was developed. It properly defines areas interested by the presence of HER2 in WSI of breast samples on the basis of H&E slides. The ultimate goal of the project is to train the system not only to quantify HER2 expression but also to discriminate HER2 low cases on H&E WSI. The preliminary results of the model were further validated outside the training environment on real cases provided by a reference centre.
Conclusion: Preliminary results show that ViTs have great potential in the development of innovative Machine Learning systems for AI applications in Pathology. This works finally aims at providing an H&E-based algorithm that can predict HER-2 status and treatment response in breast cancer at an accuracy that may benefit clinical evaluations, especially for the identification of HER2 low-expression patients.

E-PS-02-046
Characterization of EGFR expression in low oestrogen receptor positive breast carcinoma
A. Maaoui*, Y. Houcine, S. Elfekih, S. Kamoun, S. Ayadi, M. Driss
*Pathology Department, Salah Azaiez Institute, Tunis, Tunisia

Background & objectives: EGFR (epidermal growth factor receptor) is expressed in breast cancer, particularly in the triple-negative subtype. Some low positive oestrogen receptor (ER) breast carcinomas may also express EGFR. We aim to characterize the EGFR expression in low positive ER breast carcinomas.
Methods: Patients with low ER+ breast carcinoma from 2019-2021 were identified (n=20). Low ER positive if 1 to 10% ER positivity by immunohistochemistry (IHC) was present.
An immunohistochemical study using the anti-human EGFR monoclonal antibody was performed. Interpretation was based on a scoring system identical to that of HER2neu. Cases with an overall score ≥ 1 were considered positive.
Results: The median age was 57 years (range 35-80). SBR grade III predominated (67%). The presence of tumour emboli was noted in 50% and lymph node metastases in 30% of the cases. Positive EGFR expression was noted in less than half of the cases (6 cases). EGFR seemed to be associated with high grade tumour, tumour emboli and lymph node metastases. EGFR tends to be more expressed in younger patients (≤ 50 years) without statistical significance.
The median follow-up was 400 days. Five patients were alive with disease, 4 patients died due to invasive breast carcinoma, 3 developed metastases and 3 recurrences. No evolution data were available for the other patients.
Conclusion: EGFR expression in low positive ER breast cancer has been associated with a more aggressive tumour phenotype. However, the clinical significance of EGFR expression in this subset of breast cancer is still unclear and further research is needed to fully understand its role in tumour development and progression.

E-PS-02-047
Precursor lesions and biomarker profile of mucinous breast carcinoma
F. Mengna*, Y. Zhang, L. Yang, M. Shen, F. Li, B. Wei, H. Bu, Z. Zhang
*Department of Pathology, China

Background & objectives: Mucinous carcinomas (MCs) of the breast is the most common Invasive breast carcinoma with extracellular mucin, the morphologic evolutionary pathways were not fully studied. We aim to explore the precursor lesions, clinicopathological characteristics and prognosis of MCs with different biomarkers.
Methods: A total of 245 MCs diagnosed by surgical specimens among 2014 to 2021 were included, including 163 pure mucinous carcinomas (PMCs) and 82 mixed mucinous carcinomas (MMCs). The morphology of the surrounding breast tissue adjacent to the MCs were evaluated. The follow up data were obtained and compared among PMCs and MMCs with different clinicopathological features and biomarkers expression.
Results: The median age at diagnosis was 52 years (range 20-85) and mean tumour size was 2.9 cm (range 0.5-16.0). Of all the 245 cases, DCIS were observed in 87 cases, 15 of them were high grade and coexisted with Luminal B MMCs (12/15). Mucocele-like lesion was observed in 44 cases, 68.2% of them were associated with Luminal A type A PMC. Solid papillary carcinoma was observed in 2 type B MCs and 10 MMC. Besides LN involvement and higher stage, <40 years, more micropapillary architecture and non-mucinous component (>50%), HER2-positive and coexist with high grade DCIS were significant factors for poorer prognosis.
Conclusion: MCs of breast is generally less aggressive carcinoma. Focusing on precursor lesions and high risk clinicopathologic characteristics can help provide more effective treatment for such patients. Our findings may support the concept that progression of varies IHC phenotypes of MC with specific precursor lesion is a unique evolution pathway.

E-PS-02-049

A semiquantitative study of neuroendocrine differentiation on the breast cancer subtypes

Y. Otsuki*, S. Ohtsuka, Y. Asano, T. Ikeya, Y. Ishida, S. Sezaki, H. Kobayashi
*Seirei Hamamatsu General Hospital, Japan

Background & objectives: Although breast cancers have been sometimes reported to show neuroendocrine differentiation, few reports have examined percentage of the positive cells in the tumour with neuroendocrine markers. We performed a semiquantitative study of neuroendocrine differentiation on the tumour subtypes.
Methods: Immunostaining for Synaptophysin, Chromogranin A, and INSM1 was performed on the pathological specimens. Their expression rates in the tumour cells were measured in a semiquantitative manner with three tiers of phenotypic expression on immunohistochemistry with the markers: diffuse-positive (>50% of tumour cells), focal-positive (10-50%), and weak or negative (<10%).
Results: The breast cancer subtype in this study included 127 cases of solid papillary carcinoma (SPC), 52 conventional ductal carcinoma in situ (DCIS), 41 invasive breast cancer of no special type (IBC-NST), 16 mucinous carcinoma (MUC) and 15 invasive lobular carcinoma (ILC). Number of the cases with diffuse positivity with at least one or more markers was 123 cases of SPC, 1 DCIS, 0 IBC-NST, 4 MUC, 0 ILC. And the number with focal positivity with at least one marker was 4 SPC, 5 DCIS, 1 IBC-NST, 5 MUC and 2 ILC. Weak or negative for all the markers were 0 SPC, 46 DCIS, 40 IBC-NST, 7 MUC, and 13 ILC.
Conclusion: According to our result, the phenotypic expression of SPC quite differs from those of the other subtypes. SPC typically displays diffuse neuroendocrine differentiation, IBC-NST, conventional DCIS, and ILC rarely indicate obvious neuroendocrine differentiation. It is suggested that the immunohistochemistry will help us differentiate SPC from the other subtypes of the breast tumour. And SPC may be categorized into NET because of the clear neuroendocrine differentiation that sharply contrasts with the other subtype of the breast tumours.

E-PS-02-050

Breast prognostic markers – three-year institutional experience and comparison with published benchmarks

D. Proca*, Y. Belogrivtseva, I. Mazur
*Temple University Health System, USA

Background & objectives: College of American Pathologists recommends that "for HER2 immunohistochemical (IHC) and in situ hybridization (ISH) and ER IHC tests performed on breast carcinoma that provide independent predictive information, the laboratory at least annually compares its patient results with published benchmarks."
Methods: We selected from the electronic data base all breast biopsies and lumpectomies processed between Jan 2020 and January 2023 and looked at the prognostic marker results for all breast malignant tumours. Our institution performs ER, PR, and Her-2/ Neu testing on initial biopsy or lumpectomy, and only repeats the testing on the final resection specimen, for any negative marker.
Results: 1134 total breast biopsies, lumpectomies, mastectomies were examined between 2020-2023 out of which:
- 265 were invasive ductal carcinomas
- 30 invasive lobular carcinoma
- 3 LCIS
- 93 DCIS
- 5 medullary carcinoma
- 5 mucinous carcinoma
- 53 of 305 invasive carcinomas were triple negative, corresponding to 17.37% of invasive carcinoma cases; 2/53 were medullary carcinoma, 51/53 high grade invasive ductal carcinoma
- 11/ 93 DCIS were ER negative)11.82%)
- 33/ 265 invasive ductal carcinomas were Her-2/ Neu positive by immunohistochemistry or FISH (12.45%)
- 21/ 265 ductal carcinoma had FISH performed (7.92%) for Her-2/ Neu 2/3
-1/ 30 lobular carcinomas (3.33%) was Her-2/ Neu positive.

Conclusion: It is important for each laboratory to monitor the results of breast prognostic marker testing and compare them with published benchmarks as part of quality assurance plan.
Published benchmarks are: ER-negative breast cancers (invasive and DCIS) should not exceed 30%. The proportion is somewhat lower in post vs premenopausal women (20% vs. 35%). ER-negative % is lower in well-differentiated carcinomas (<10%) and lobular, tubular, and mucinous carcinomas.
For HER2 studies, the overall proportion of HER2 positive breast cancers is 10-25%.

E-PS-02-051

Primary neuroendocrine tumour of breast: a case report of a rare neoplasm

I. Provatas*, P. Pantoula, D. Mylonaki, S. Efthymiou, A. Karakosta
*Pathology Laboratory, General Hospital of Nikaia - Piraeus "Ag. Panteleimon", Greece

Background & objectives: Breast Neuroendocrine Tumours (NETs) are uncommon, primary neuroendocrine neoplasm of the breast, requiring > 90% NET pattern, and neuroendocrine markers helpful for diagnosis. They account < 1% of primary breast cancers, occurring most commonly to women elder than 65 years.
Methods: We report a 89-year old female patient who was operated for a tumour in the left breast, following the diagnosis of NET in FNB specimen and the received mastectomy specimen measured 7x5x3 cm. On gross examination and serial sectioning, a whitish, circumscribed, solid, elastic tumour 1,7 cm was revealed, 1,7 cm in maximum diameter. Surgical margins were clear.
Results: Microscopic study of tumour showed diffuse parenchymal infiltrates from a neoplasm with a compact and atypically insular or cribriform growth pattern, composed of cells with mild cellular and nuclear atypia and polymorphism, eosinophilia and occasional granular cytoplasm, and low mitotic activity (~ 2 mitoses / 10 HPF). The immunohistochemical control of these cells revealed positivity for GATA-3, CD56, Synaptophysin and Chromogranin. In addition, global strong ER and PgR immunoexpression was observed, with negative Her2/Neu (1+). SSTR2a score was 2+ based on Volante et al scoring system and Ki-67 index was low, ranging at ~5%. Given the extent of the infiltrates, a diagnosis of well-differentiated neuroendocrine breast tumour was made.
Conclusion: Neuroendocrine tumours are a group of rare breast neoplasms. Their prognosis seems to depend on the number of mitoses and the Ki-67 index. Currently, there are no specific guidelines for their treatment, and they are graded based on existing criteria for other types of invasive breast carcinoma. Furthermore, they should not be confused with other breast neoplasms with neuroendocrine differentiation, such as mucinous type 2 carcinoma, solid papillary carcinoma, or ductal carcinoma with neuroendocrine differentiation.

E-PS-02-053

Core needle biopsy diagnosis of fibroepithelial lesions of the breast and the upgrade rate in the surgical specimen: experience of an oncology hospital

S. Reis*, N. Castelo-Branco, P. Figueiredo
*Instituto Português de Oncologia, Portugal

Background & objectives: Fibroepithelial lesions of the breast are a heterogenous group of biphasic tumours that share histological characteristics but can have a variable clinical behaviour. The aim is to study the concordance between core needle biopsy and surgical specimen diagnosis.

Methods: A retrospective analysis of 29 fibroepithelial lesions of the breast (FELB) diagnosed by core needle biopsy (CNB) who underwent surgical excision, in an oncological hospital, from 2019 to 2023. CNB were revised.
Results: Of the 29 CNB's, 26 were accurate: 16 fibroadenomas (FA), 4 cellular FELB, 3 unclassified FELB, 1 borderline phyllodes tumour (PT), 1 benign spindle cell lesion and 1 biopsy with minor changes. There was 96% of agreement with the definite histological diagnosis and 1 case was upgraded from FA to benign PT. There were 3 inaccurate CNB, all of them FELB initially diagnosed as FA. There was 100% agreement with the definite histological diagnosis: 1 benign PT and 2 borderline PT.
Conclusion: The present study suggests that FELB diagnosis in CNB has a high coherency with the histological diagnosis of surgical specimens, being the upgrade rate 3%. The intrinsic limitation of CNB and heterogeneity of FELB may explain the upgrading. The pitfalls in CNB were mainly due to core fragmentation and the cellularity of the stromal component. The CNB diagnosis accuracy of FELB and a triple multidisciplinary approach dictate the patient's clinical management.

E-PS-02-054
Morphological stability of HER-2 expression before and after breast carcinoma neoadjuvant chemotherapy
O. Reshetnikova*, L. Rudiuk, A. Musatov
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: Human epidermal growth factor receptor-2 (HER-2) protein expression level in breast cancer (BC) is a valuable prognostic marker. The evaluation of its parameters may help in personalized handling of BC diagnostics and treatment strategies.
Methods: Clinical behaviour, pathological efficacy, HER-2 protein expression were evaluated in eighty cases of BC before and after neoadjuvant chemotherapy (NAC). Nine cases after pathological complete response to NAC were excluded from further investigations. The degree of HER-2 receptor expression (DAKO, Polyclonal, 1:600) was evaluated by immunohistochemistry and in cases of equivocal expression by FISH according to ASCO/CAP guidelines.
Results: The results have shown that HER-2 receptor expression did not change after NAC in 40 cases (56.3%). An increase in HER-2 receptor expression was recorded in 19 cases (26.8%), including three residual tumours that changed to HER-2 positive status after treatment. Decreased expression levels were observed in 12 cases (16.9%) of breast cancer. There was no complete loss of HER-2 expression (0) in this study.
Conclusion: NAC changes the status of HER-2 receptors mainly towards increased expression. The obtained results show the need to study the HER-2 status of the residual tumour for an adequate selection of adjuvant therapy. The importance of further studies of the heterogeneity of HER-2 expression in personalized diagnostics and treatment of patients with BC has been discussed.

E-PS-02-055
Breast carcinoma immunophenotype features after neoadjuvant therapy
O. Reshetnikova*, L. Rudiuk, A. Musatov
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: The sensitivity of certain histological types of breast cancer (BC) to molecular targeted drugs has now been established. Neoadjuvant chemotherapy (NAC) aims to achieve a morphological response for the treatment. This investigation evaluates the BC immunophenotype changes after NAC.
Methods: Eighty women with BC underwent NAC followed by surgery. Their medical documents were studied. The grade of tumour was determined according to the Nottingham Histologic Score. IHC studies were performed on a Leica BOND MAX immunoassay using ER, PgR, HER2, and Ki67 antibodies. Nine cases after pathological complete response to NAC were excluded from further investigations.
Results: The study has shown that molecular phenotypes of the BC after prescribed NAC have changed in 29 cases (36.3%) of pathological examination. There were variable patterns of surrogate type change. In 44.8% there was a change from luminal B HER2-negative to luminal type A. Slightly less frequently, in 13.8%, triple negative changed to luminal B HER2-negative after NAC treatment. In single cases, changes between other molecular subtypes of breast cancer were observed.
Conclusion: Present investigation revealed significant differences in pathology and immunophenotype of the BC and its heterogeneous response to NAC. Various clinical behaviour and morphological features of the studied neoplasm create a challenge for managing BC patients. An analysis of the study results confirmed the need for further research in molecular heterogeneity of BC and possible responses to targeted therapy. Identifying new markers in BC for pathologic diagnostics and NAC targets should be supported.

E-PS-02-056
Variations in steroid hormone receptor status after breast carcinoma neoadjuvant chemotherapy
O. Reshetnikova*, L. Rudiuk, A. Musatov
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: Neoadjuvant chemotherapy (NAC) of the breast cancer (BC) causes alterations in clinical behaviour, morphological and immunohistochemical characteristics of the primary tumour. Changes in steroid hormone receptor expression character have an effect on disease prognosis and postoperative chemotherapy treatment guideline.
Methods: Eighty cases of BC before and after standard courses of NAC were examined. Histological examination was performed in standardized hematoxylin and eosin staining with determination of tumour's grade. IHC examination was performed on a Leica BOND MAX immunostainer using monoclonal antibodies ER, PgR. The degree of ER and PR expression was assessed using the Allred score system.
Results: Our study revealed that after neoadjuvant therapy ER and PR expression remained stable in most observations (35 cases, 49.3%, and 31 cases, 43.7%, respectively). Steroid hormone receptor conversion was detected in 22 cases (31.0%). Complete loss of ER expression discovered in 9.0% and PR - in 32.0% of observations. Combined loss of ER and PR detected in the 9.0% of tissue samples. Hormone positive status in previously negative tumours was found in 23.0% due to ER, 18.0% due to PgR; appearance of ER and PgR co-expression was noted in 9.0%.
Conclusion: The data obtained suggest the need for re-analysis of steroid hormone expression in breast tumours after neoadjuvant chemotherapy in order to correct the treatment guideline. Further investigation of hormone receptor conversion mechanisms may be incorporated into prognostic models for breast cancer and open up additional options for adjuvant therapy.

E-PS-02-057
Importance of pathological complete response after neoadjuvant therapy for breast cancer
O. Reshetnikova*, L. Rudiuk, A. Musatov, S. Korenev
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: Breast cancer has a high incidence in women. Assessment of breast tumour response to neoadjuvant chemotherapy is a key factor in the prognosis of the disease. A complete pathological response (pCR) contributes to a favourable outcome and recurrence-free survival.
Methods: Eighty cases of breast cancer (BC) after neoadjuvant chemotherapy were analysed. The tumour grade was recorded according to the Nottingham Histologic Score. Immunohistochemical (IHC) studies

of the ER, PgR, HER2, and Ki67 antibodies has been done. In each molecular type of breast cancer, the proportion of the pCR was calculated using the prognostic relevance of the residual cancer burden system.
Results: Present study revealed pathomorphology, IHC of primary and residual tumours, as well as the frequency of pCR after neoadjuvant chemotherapy. The surrogate molecular subtype of primary tumours was arranged as follows: luminal A (17.5%), luminal B, HER-2-negative (48.8%,), luminal B, HER-2-positive (12.5%), HER-2-positive (6.2%), triple negative subtype (15.0%). Complete morphologic response was reported in 9 cases, of which luminal B HER-2-negative phenotype and luminal B HER-2-positive were 33.3% each, triple negative - 22.2% and HER-2 positive phenotype - 11.2%.
Conclusion: Determination of residual tumour burden after neoadjuvant therapy provides an opportunity to predict the probability of favourable outcome of patients' treatment. Further studies to improve the methods of the evaluation the degree of the RCB after neoadjuvant chemotherapy suggested.

E-PS-02-058
Malignant adenomyoepithelioma with patterns of adenoid cystic carcinoma of the breast: a case report
G. Richter*, P. Richter, C. Uleer, T. Noesselt
*Institute of Pathology, Germany

Background & objectives: An adenomyoepithelioma (AME) is a composite tumour with a predominant and generally solid proliferation of phenotypically variable myoepthelial cells. An adenoid cystic carcinoma (ACC) is an epimyoepithelial carcinoma of low malignant potential that histologically similar to the salvary gland counterpart.
Methods: We present a case of a 68 years old Caucasian female with solid tumour of the breast. The specimens were routinely stained with hematoxylin and eosin. Moreover, Periodic acid–Schiff (PAS) were processed. Immunohistochemically stained with primary antibodies Pan-cytokeratin (Roche), cytokeratin 5/6 (Roche), cytokeratin 7 (Roche), e-cadherin (Roche), SOX 10, CD117, S100 and KI-67 (Roche).
Results: Histological examination shows a compact aggregate of tubulus with prominent myoepithelial cells and compressed lumens. In association we find a small focus of trabecular tubular pattern with spaces of variable shape, containing myxoid mucosubstances. Using Immunohistochemistry we detected a positive reaction for Pan-cytokeratin, cytokeratin 5/6, cytokeratin 7 and a negative reaction for oestrogen and progesteron receptor in the tumour cells. In accordance with the dako score we detected a Her-2 score 0 (negative). Moreover a positive reaction of the tumour cells for SOX 10 and CD117 was detected.
Conclusion: Adenomoyeptheliomas are composed of two cell components with epithelial and myoepithelial cells and have mostly a benign behaviour. But in low number one of the components or both become malignant. Most malignant alterations appear as focal lesions arising within a classic benign AME and in addition, distinctive patterns of adenoid cystic carcinoma have been observed – like the case we present.

E-PS-02-059
Immunohistochemical expression of primary breast tumours determines the metastatic organ
M.G. Rodríguez Guevara*, E. Honrado-Franco, O. Sanz-Guadarrama, J. Alzoghby-Abi-Chaker, S. Marín-Asencio, O. García-Galvis, M. López-Flores, A. López-González, L. López-González, R. Canseco Fernández, C. Martínez-Martínez, S. Sáez-Ávarez
*Complejo Asistencial Universitario de León, Spain

Background & objectives: Breast cancer often metastasizes to bones, lungs, brain, and liver in advanced stages. Gene expression of primary breast tumours in patients with metastatic disease has been correlated with tumour behaviour. Therefore, understanding these metastatic mechanisms has clinical and prognostic implications.
Methods: We present the study of 100 cases of metastatic breast cancer in one or several organs (liver, bone, brain and lung). We analysed the expression of the oestrogen receptor, progesterone receptor, Ki-67 and HER-2 in primary breast tumours, to obtain an immunohistochemical profile of metastasis to each organ and the influence of the size and lymph node involvement and survival.
Results: Triple negative tumours, metastasize more frequently to the brain 9/22 (41%) and lung 15/39 (38%) than to bone 14/58 (24%) and liver 7/24 (3%). HER-2 positive tumours (3+) are more likely to metastasize to the brain 8/22 (36%) and to the lungs 8/39 (20%) than to the bone 4/58 (7%) and the liver 4/24 (2%). Ki67 expression is greater than 10% in 80% of primary breast tumours regardless of the site of metastasis. The lowest median survival rate after metastasis is in brain (19 months) while the highest was in lung metastasis (50 months). The median survival rate after metastasis to bone and liver is 27 and 35 months, respectively.
Conclusion: We present a large study revealing the association between the immunohistochemical expression profiling patterns and organ-specific metastasis in breast carcinomas. Triple negative and HER-2 breast tumours, are more likely to metastasize to the lung and brain than to bone and liver. Metastasis to a specific organ was not influenced by tumour size or lymph node involvement. Survival varies depending on the metastasized organ.

E-PS-02-060
End-to-end deep neural network for ER, PR and Ki-67 stained WSI automatic proliferation index (PI) quantification for breast cancer tissue
Y. Salhi*, J. Rynkiewicz, C. Bossard, S. Salhi, J. Chetritt
*DiaDeep, France

Background & objectives: We develop an end-to-end pipeline based on a deep neural network for the quantification and assesfsment of nuclear biomarkers ER, PR and Ki-67 in breast adenocarcinoma stained WSI. The proliferation index as well as hotspot detection for Ki67 are proposed.
Methods: A modified U-Net network with an adequate backbone is proposed, trained and validated on 1656 images. Testing was carried on a left-out set of 701 images originating from 23 patients. The proposed algorithm allows the quantification of tumour cells, detection of hotspots and the quantification of the corresponding proliferation index and tumour expression. Performances were investigated using external datasets.
Results: In this study, the model's performance in estimating ER, PR, and Ki-67 index scores was evaluated on a left-out dataset and two external datasets (n=23, 50, 130). The model outperformed existing frameworks on the same test data for the Ki-67 (n=23) with an accuracy of 95.96%. On the external datasets, i.e. AIDPATH (n=50) and IHP Group (n=130), the model achieved an averaged accuracy score of 98.3% and 96.7%, respectively for the three biomarkers. Also, the hotspots for Ki-67 prediction were accurately inferred based on the prediction outcomes and those were compared to expert pathologists annotations. Additionally, the proposed end-to-end approach enables faster inference times compared to other available algorithms.
Conclusion: AI models for whole-slide image processing are usually task-specific and require complex processing pipelines. Unlike most algorithms that use a two-step approach to identify invasive areas and hot-spots before quantifying PI, the proposed end-to-end approach achieves this in a single step with promising results. This approach is easily adaptable to other biomarkers for prognosis and theranostics, as it doesn't require specialized intermediate models.

E-PS-02-061
HER2 spatial distribution affects neoadjuvant treatment response in breast cancer: the pisa prediction groups proposal
C. Scatena*, R. Scarpitta, L. Lacitignola, B. Fuochi, P. Cinacchi, A. Fontana, G.N. Fanelli, A.G. Naccarato

*University of Pisa, Italy

Background & objectives: Neoadjuvant therapy has become the standard of care for HER2-positive breast cancer. However, only half of the patients achieve a complete pathological response. Our study aimed to investigate the correlation between HER2 spatial distribution and treatment response.
Methods: Preoperatory biopsies from 101 HER2-positive/3+ IHC-score invasive breast cancer patients undergoing neoadjuvant chemotherapy were retrieved. Four groups of HER2 distribution (named Pisa Prediction Groups – PPG) were defined: 1 - homogeneous; 2a - big clusters; 2b - small clusters; 2c - mosaic pattern. The study was approved by the local Ethical Committee. Statistical analysis was performed using GraphPad Prism Software.
Results: Within the 64 cases of PPG 1, 75% achieved pCR; instead, among the 37 cases of the heterogeneous groups (PPGs 2a+2b+2c), only 43% achieved pCR: in detail, the pCR rate was 54% for PPG 2a, 50% for PPG 2b and 35% for PPG 2c. Interestingly, no statistically significant difference was found between PPG 1 and PPG 2a (p-value = 0.1768); instead, PPG 2c resulted different from PPG 1 (p-value = 0.0023), as well as PPGs 2c+2b from PPG 1 (p-value = 0.0022).
Conclusion: This study confirms the existence of considerable heterogeneity in the expression of HER2 protein within breast cancer. Intriguingly, the results demonstrate the need to integrate the percentage of HER2-positive cells with the assessment of their distribution within the tumour. Pattern analysis of HER2 spatial distribution could help identify breast cancer patients who will not achieve pCR. This could represent a powerful decision tool in terms of escalation treatment approaches.

E-PS-02-062
The added value of SOX10 immunohistochemistry to other breast markers in identifying Cytokeratin 5-positive triple negative breast cancers as of mammary origin
A. Sejben*, A. Voros, A. Golan, T. Zombori, G. Cserni
*University of Szeged, Hungary

Background & objectives: Triple-negative breast cancer (TNBC) represents a specific group that lacks the expression of hormone receptors and might also lack the expression other breast markers; when this occurs, proving the breast origin of a metastasis is a challenging task.
Methods: In the present study, we assessed the added value of SOX10 immunohistochemistry to known GATA3, mammaglobin (MG), GCDFP15 (growth cystic disease fluid protein 15), and NYBR1 statuses in a series of CK5-positive primary TNBCs. Tissue microarrays were made from the formalin-fixed and paraffin-embedded blocks of 120 TNBCs, and 3-4-mm-thick sections were immunostained for SOX10.
Results: In our cohort, SOX10 positivity was seen in 82/119 cases, 61, 74, 76, and 82 all of which were GATA3, MG, GCDFP15, and NY-BR-1 negative, respectively. The cut-off for a positive reaction was at least 10% of tumour cells staining. Of the SOX10 negative cases, 12 stained with at least another breast marker. Nevertheless, 25/119 (21%) cases remained negative with all markers assessed.
Conclusion: SOX10 proved to be the most commonly positive breast marker in our CK5 expressing TNBCs, but the other markers also had some additive value to SOX10.

E-PS-02-063
Examination of tumour regression grading systems in breast cancer patients who received neoadjuvant therapy
A. Sejben*, R. Kószó, Z. Kahán, G. Cserni, T. Zombori
*University of Szeged, Hungary

Background & objectives: Neoadjuvant therapy is a common form of treatment in locally advanced breast cancer (LABC) patients. Besides some guidelines for grading regression, a standardized general scheme is not yet available.
Methods: The aim of our study was to compare the prognostic impact of different regression grading systems, namely the TR/NR, Chevallier, Sataloff, Denkert-Sinn, Miller-Payne, NSABP-B18, Residual Disease in Breast and Nodes and Residual Cancer Burden (RCB) on disease-free (DFS) and overall survival (OS).
Results: Data of 746 breast cancer patients treated in neoadjuvant setting between 1999 and 2019 have been included. The DFS and OS estimates of patients with complete pathological regression and residual in situ carcinoma have been significantly more favourable than those having partial regression or no signs of regression (pDFS<0.001, pOS < 0.001). Significant differences were found between DFS estimates of classes with partial regression and without regression defined by RCB. Concerning DFS estimates, the RCB classification (p = 0.019), while regarding OS data the y-stage (p = 0.011) and the nodal status (ypN; p = 0.045) were significant prognosticators by multivariate Cox regression.
Conclusion: Regression grading systems help the evaluation of regression in LABC patients treated with neoadjuvant therapy. Of the several grading systems compared, the RCB classification makes the best distinction between the outcomes of the different classes, therefore we recommend the inclusion of RCB into the histopathological findings.

E-PS-02-064
During the COVID-19 lockdown younger breast cancer patients and those with more unfavourable prognostic parameters had the opportunity to be treated
S. Sevim*, H.K. Kahraman, E.D. Serbes, S. Dizbay Sak
*Ankara University Faculty of Medicine, Pathology Department, Turkey

Background & objectives: The COVID-19 pandemic caused by the SARS-CoV-2, has affected the routine pathology workflow, as well as many applications in medicine. In the current study, it was aimed to investigate the changes in breast pathology caused by the pandemic.
Methods: Breast specimens examined in our laboratory were divided into three groups, each for 16-month periods, as pre-COVID-19 (preCOV), lockdown period (LP), and post-COVID-19 (postCOV). Macroscopic, histopathological, immunohistochemical, molecular features, and neoadjuvant therapy status were analysed to reveal the changes in these periods. In comparative statistical analyzes of different periods in terms of clinicopathological parameters, p<0.05 was considered significant.
Results: A total of 2758 breast specimens were examined. Number of breast specimens decreased during LP (n=718), compared to preCOV (n=969) and postCOV (n=1071) (p=0.000). In LP, non-tumoral pathologies and benign tumours were decreased compared to preCOV, whereas malignancies (n=365, 56.2% vs n=406, 41.9%) were increased (p=0.000). During LP, patient age was younger (49.46 vs 51.55, p=0.004), Ki67 index was higher (p=0.04) and LVI was more frequent (p=0.031) in breast carcinomas, compared to preCOV. In postCOV, frequency of tru-cut biopsy and mammoplasty specimens and benign tumours increased. Tumour size (p=0.038) and frequency of PR positivity (p=0.027) decreased compared to LP. HER2 positivity by IHC/SISH in postCOV was higher than LP (p=0.040).
Conclusion: The COVID-19 pandemic has adversely affected breast carcinoma patients. It can be speculated that, older patients could not access to the hospital and breast physicians in the LP, due to age restrictions. Patients with unfavourable prognostic parameters like higher Ki67 and LVI were operated more in LP, probably due to the more prominent clinical symptoms/findings indirectly related to these parameters. Less essential operations such as mammoplasties and benign resections have been postponed.

E-PS-02-065
Diabetic mastopathy: two cases report and review of the literature
I. Sfiniadakis*, E. Sfiniadaki, D. Vasileiou-Dervisoglou, P. Sfiniadakis, D. Sfiniadaki, K. Sfiniadakis
*Athens Naval Hospital, Greece

Background & objectives: Diabetic mastopathy is a rare benign disease of the breast (<1% of benign breast diseases) usually in premenopausal women with insulin-dependent diabetes mellitus mainly type I but also II. A differential diagnostic problem occurs between diabetic mastopathy and malignancy.
Methods: A 34 and 37-year-old female patients with insulin-dependent DM, presented palpable lesions, both in left breast that were suspicious for malignancy. Patients underwent needle core biopsy. We examined the lesions microscopically and using immunohistochemistry. We reviewed electronic databases to identify and synthesize relevant published evidence to allow recommendations to be evidence-based wherever possible about the analysis of diabetic mastopathy.
Results: Macroscopically, lesions were whitish-coloured, ill defined, firm, scleroelastic tissue pieces. Microscopically, increased fibrosis keloidal type, periductal, perilobular and perivascular lymphocytic infiltrates and epithelioid stromal myofibroblasts were observed. Infarcts, liponecrosis, evidence of arteriitis or increased mitotic activity were not identified. No evidence of malignancy was found. The histological picture was compatible with diabetic mastopathy. A differential diagnostic problem occurs between diabetic mastopathy and malignancy mainly on imaging control. Immunohistochemistry results: positive stains: CD10, SMA, desmin, CD34 and S100 CD20, and negative stains: beta catenin, cytokeratins, p63 (useful in differential diagnosis of invasive carcinoma)
Conclusion: In conclusion, diabetic mastopathy is a rare inflammatory disorder of the breast, of unknown aetiology, (possible the result of an immune response to exogenous insulin administration, or hyperglycaemia leads to stromal matrix expansion and accumulation of glycosylation end products and a B cell inflammatory response), of benign nature, which can be differentiated from malignancy only by histological examination.

E-PS-02-066
Tubular adenoma of the breast: a report on an uncommon case
F. Sousa Vieira*, A.P. Rodrigues, D. Sá, S. Neves, G. Carrola, M.R. Correia, F.E. Costa, N.J. Lamas, J.R. Vizcaíno
*Centro Hospitalar Universitário de Santo António, Portugal

Background & objectives: Tubular adenomas of the breast are rare benign epithelial tumours that mostly occur in females of reproductive age, rarely occurring before menarche or after menopause. These neoplasms are usually described as palpable, solitary, freely mobile, well-circumscribed masses, without associated pain.
Methods: We report the case of a 13-year-old woman who had a lump in the upper inner quadrant of the left breast evolving for seven months. An ultrasound described a 57x29 mm hypoechoic homogeneous ovoid nodule. A needle biopsy was performed with a subsequently surgical excision of the lesion.
Results: The histopathological examination revealed a well-circumscribed proliferation of tubular structures of ductal type, mostly small and rounded, composed of a basal layer of myoepithelial cells and an inner layer of luminal cells, similarly to the normal mammary epithelium. There was no significant atypia, nor relevant mitotic activity, nor necrosis. The lumen of the tubular structures contained a dense amorphous eosinophilic material (highlighted with PAS) and the surrounding stroma between the different tubular structures was fibrovascular and sparse. The luminal cells were immunoreactive for EMA and ER, while the myopepitelial layer was positive for p63 and SMA. The proliferative index (%Ki-67) was very low.
Conclusion: Our patient is among the youngest ever individuals to be reported with the diagnosis of breast tubular adenoma, having symptoms beginning as early as 12 years old. Unlike in this case, they tend to occur more frequently in the breast upper-outer quadrant. They can often be misdiagnosed because of their similar clinical appearance to other, more prevalent benign tumours, such as fibroadenomas. Tubular adenomas are benign lesions without associated increased malignancy risk and, thus, surgical excision grants complete resolution.

E-PS-02-067
High-grade encapsulated papillary carcinoma (EPC) of the male breast: a rare case
G. Stanc*, E. Souka, G. Galanopoulos, V. Tselepidis, H. Trihia, C. Valavanis
*Pathology Department Metaxa Cancer Hospital, Greece

Background & objectives: Encapsulated papillary carcinoma (EPC) is a rare, breast malignancy, with clinically indolent course. It is most common in postmenopausal women. EPC of the male breast is uncommon, and accounts for up to 7.5% of all male breast cancers.
Methods: A 64-year-old male with no history of malignancy presented with a palpable cystic mass at the right breast, close to the nipple. A lumpectomy specimen 3X2, 5X1, 5cm in size was sent for gross and microscopic examination. A well circumscribed solid to cystic lesion, 1,5cm in great diameter was found. Total mastectomy and axillary sentinel lymph node excision were performed.
Results: Microscopic examination revealed an encapsulated high grade papillary carcinoma. Peripherally to it an invasive micropapillary carcinoma 0,4cm in great diameter was found.
The sentinel lymph node and the mastectomy margins were tumour free. Immunohistochemical examination revealed p63 (-) and CK14 (-) indicating the absence of myoepithelial cells at the periphery of the EPC. Both lesions displayed ER (+), PgR (+), Her-2 (-) and Ki-67 (+) in approximately 40% of the EPC neoplastic cells.
Conclusion: EPCs are usually low and intermediate grade, staged and treated as in-situ disease.
High grade EPCs have a low incidence (3% of EPC) and similar behaviour to invasive carcinoma. Therefore, they are classified and staged as high-grade invasive breast carcinomas.
In-situ and invasive disease may be focally present at the periphery of EPC and potentially unsampled at core-needle biopsy, therefore these lesions should be examined as a whole.

E-PS-02-068
Assessment of intra-laboratory Ki67 reproducibility in breast cancer using telemedicine platform
I. Telezhnikova*, G. Setdikova, A. Abduraimov, S. Khomeriki, L. Zhukova
*Loginov Moscow Clinical Research Center, Russia

Background & objectives: Interlaboratory Ki67 reproducibility is still rather low. Difficulties are especially pronounced due to the lack of standardization of the visual calculations for Ki67. The aim of this study was to evaluate intra-laboratory Ki67 reproducibility in breast cancer.
Methods: An experimental study was performed on biopsy material histological glass from 20 patients. The slides were scanned at 40x magnification by 3DHISTECH®. Slides were uploaded to the One-Cell telemedicine platform for pathology laboratories. For each slide, 4 fields of view 0.264 mm^2 were selected using markup tools. The mean deviation ± between pathologists and convergence coefficients by category were estimated.
Results: The sample were 80 fields of view. Evaluation was performed by 3 pathologists. Categories Ki67 index were distinguished (1 - less than 20%, 2 – 20% to 35%, 3 - more than 35%). Ki67 categories were defined as 1 in 8 (40%) slides, 2 in 6 (30%), and 3 in 6 (30%). The mean deviation between pathologists on the convergence coefficient was 0.89 (0.87±0.93), with a median convergence of 90%. The total absolute deviation by category was 3.5 for pathologist markup 1, 7.75 for pathologist markup 2, and 4.5 for pathologist markup 3. The

greatest variation by category between pathologists was statistically significantly difference in category 2 ($p < 0.001$).
Conclusion: Intra-laboratory Ki67 reproducibility was high. The greatest deviation was detected in the clinically significant "grey zone". The International Ki67 in Breast Cancer Working Group (IKWG) consensus is that Ki67 5% or less, or 30% or more are valid, while values 5–30% are not recommended for use in making decision about chemotherapy. The authors feel it advisable to conduct training on in-laboratory analytical validation using telemedicine platforms. Training of the visual calculations for Ki67 will improve reproducibility and accuracy.

E-PS-02-069
Adenoid cystic carcinoma of the breast: a case report special triple-negative cancer subtypes
I. Telezhnikova*, G. Setdikova
*Loginov Moscow Clinical Research Center, Russia

Background & objectives: Adenoid cystic carcinoma (ACC) of the breast is rare, accounting for less than 0.1% of all breast cancers. Unlike counterpart in the salivary gland, ACC of the breast is associated with an excellent prognosis paradoxical to its unfavourable, triple-negative profile.
Methods: We present the case of a 55-year-old woman presenting with a left breast mass identified by mammographic screening was examined at our centre. Breast ultrasound revealed a sharply marginated, hypoechoic mass. $12 \times 0.8 \times 11.2$ mm in size in the upper outer quadrant, and a core needle biopsy was performed at the mass site.
Results: The preoperative diagnosis was stage I (cT1N0M0) triple-negative breast cancer. Surgery consisted of breast segmental resection with axillary contents. Pathological examination of the excised specimen revealed a so-called adenoid cystic pattern without high-grade transformation. Note, the tumour had basaloid component ranging 10%. Immunohistochemical staining results were negative for ER, PR, HER2, were also negative for AR. The atypical epithelial cells were strongly positive for CK7, and the atypical myoepithelial cells were strongly positive for CK5/6, p63 and SMA. Ki67 labelling index was heterogeneous and focal areas elevate (25%). 12 lymph nodes were found without metastases. The patient received one course of adjuvant chemotherapy. The 3-year recurrence-free survival rate was observed.
Conclusion: Despite the triple-negative phenotype, the classic subtype ACC usually shows favourable behaviour. Regional and distant metastases are rare, and radical surgical excision is usually curative. We must search for high-grade transformation and basaloid component thorough sampling is crucial. Lymph node involvement was not present in our case. Knowing that this cancer usually presents as localized disease, can help clinicians plan the operative management of these tumours. More effective therapies for patients with special types of breast cancer require tailored treatment.

E-PS-02-070
The risk of metachronous cancers in breast cancer patients. Presentation of three rare case reports
H. Trihia*, G. Stanc, E. Souka, G. Galanopoulos, C. Valavanis, G. Vorgias
*Pathology Department Metaxa Cancer Hospital, Greece

Background & objectives: Breast cancer patients have an increased risk of developing second primaries. The risk is associated with hormonal therapy. Independent primary malignancies in the breast and cervix is a rare entity. Women with BRCA1/2-mutations have an increased risk of ovarian high-grade-serous-carcinoma.
Methods: Three postmenopausal women of 59, 69 and 56 years of age, were diagnosed with luminal A/B type, breast ductal carcinomas, grade II/II/III, received tamoxifen treatment postoperatively and subsequently developed a uterine low grade endometrial stromal sarcoma (LGESS), adenoid cystic carcinoma of the cervix and ovarian high grade serous carcinoma (HGSC) with SET features, after 12, 11 and 3 years, correspondingly.
Results: A 73-year-old woman with a history of breast cancer at 59, underwent vaginal hysterectomy, due to prolapse, where she was incidentally diagnosed with an intramural 3cm uterine tumour with histologic features of LGESS. An 80-year-old woman was diagnosed with adenoid cystic carcinoma of the cervix, after vaginal bleeding. At the age of 69, she was diagnosed with grade III, luminal B, NOS breast carcinoma. A 61-year-old woman underwent a robotic salpingo-oophorectomy of a 5,5cm ovarian mass, diagnosed as HGSC with SET features. Although there was a history of luminal A breast cancer at 56, there was not a high index of suspicion before surgery. All women have received tamoxifen treatment.
Conclusion: Women diagnosed and treated for breast cancer need to be followed up for metachronous gynaecological cancers. Uterine carcinomas and rarely sarcomas are associated with short- or long-term use of tamoxifen. The occurrence of independent primary malignancy in the breast and uterine cervix is a rare event. Metachronous adenoid cystic carcinoma has not been described before. Breast cancers in BRCA-2-mutation carriers are similar to sporadic luminal-type tumours. Cancers arising in the ovary are almost exclusively of a HGS-histotype with SET features.

E-PS-02-071
Youngest case of unusual type of carcinoma of breast in a 3 year old girl
S. Vidhale*, V. Konsam, A. Lukram, F. Ahmed, H. Thanky, N. OZA, S. Kane
*Histopia Lab, India

Background & objectives: Secretory breast carcinoma (SBC) is a rare breast cancer found in both children and adults. Although SBC usually carries a favourable prognosis, there have been reported cases of metastases. Surgery is the primary mode of management of SBC.
Methods: We report a case of a 3-year-old girl with a unilateral right breast lump suspected on Fine Needle Aspiration Cytology (FNAC) as papillary neoplasm and confirmed as primary SBC on histopathology and molecular studies.
Results: Child presented with a single retroareolar lump measuring 0.5x0.5cm, non-tender and freely mobile. FNAC smears revealed sheets and papillae of epithelial cells with extensive apocrine metaplasia. Histopathological and biomarker studies of the excision specimen revealed tumour positivity for Mammaglobin, S100, CK7, Vimentin; while negative for P63,GCDFP-15, SOX10. Molecular analysis revealed the presence of ETV6-NTRK3 fusion. Patient was reviewed at a multidisciplinary treatment planning conference, underwent lumpectomy with nodal biopsy, and ongoing long-term postoperative follow-up.
Conclusion: Considering the rarity, we report this case of secretory breast carcinoma in a three-year-old child (youngest to be reported in literature). Awareness of the cytomorphologic features and a high index of suspicion is necessary to order the right IHC panel for confirmation.

E-PS-02-072
Cytoplasmic aggregation of RPB1 predicts failure of neoadjuvant chemotherapy against invasive carcinoma of no special type
A. Voros*, B. Nagy-Miko, O. Olah-Nemeth, T. Pankotai, Z. Ujfaludy, A. Nikolenyi, G. Lazar, K. Ormandi, Z. Villanyi
*University of Szeged, Hungary

Background & objectives: Neoadjuvant chemotherapy is a common approach in treating breast cancer.
We investigated cytoplasmic aggregation of the large subunit of RNA polymerase II, RPB1 in biopsy samples taken from invasive carcinoma of no special type before chemotherapy.
Methods: Core biopsy samples were selected from patients candidating for neoadjuvant chemotherapy. Immunohistochemistry was performed to detect intracytoplasmic aggregation of RPB1 protein. For the evaluation immunofluorescent microscopy was used.
Regarding tumour regression complete, partial and non-regressive phenotypes can be distinguished. To find possible connection between RPB1 aggregation and tumour regression, statistical analysis was performed.

Results: A total of 25 patients diagnosed with invasive carcinoma of NST at the University of Szeged, were selected for this study.
Patients with tumours showing no regression in tumour size following chemotherapy had numerous cytoplasmic RPB1 aggregated foci in their first biopsy samples, compared to those who responded to the therapy with either partial or complete regression of the tumour. After investigating the samples with known regression phenotypes, we tested the use of the RPB1 cytoplasmic phenotype screen in predicting therapy outcome by categorising samples into the three possible outcome groups in a blind experiment. Out of the 13 investigated samples we have managed to categorize 10 correctly.
Conclusion: Given its predictive importance we find it urgent to report here that according to our results, the RPB1 complex has a tendency to aggregate in Epirubicin resistant tumour cells. The phenotype is easy to follow from biopsy samples immediately after diagnosing cancer. We propose that patients with cytoplasmic RPB1 foci in their biopsy samples should consider the high risk of an ineffective treatment with transcription blockers along with the time loss and chose surgery instead of neoadjuvant therapy.

E-PS-02-073
Micropapillary mucinous breast carcinoma: a rare case with unusual features, and review of the literature
L. Williams*, A. Vargiamidou
*St George's Hospital, London, United Kingdom

Background & objectives: Micropapillary mucinous carcinoma remains an under-recognised variant, characterised by a high Ki-67 index, calcifications, ER positivity, nodal metastasis and p63 expression. Controversy exists over whether these complex tumours should be classified as a primary mucinous or a primary micropapillary neoplasm.
Methods: A 59-year-old lady was presented to our university hospital with a right breast mass, revealed on imaging as a nodular density with pleomorphic calcification. Biopsy showed a grade 2 invasive carcinoma (T3, P2, M1). The tumour displayed aberrant expression of p63, had strong ER and PR positivity, and a low Ki-67 index of 6-8%. Her2 was negative (1+).
Results: Mastectomy revealed a 190mm micropapillary mucinous carcinoma, composed of morula-like aggregates with reverse polarity (confirmed on EMA staining) and frequent calcifications. 6/22 lymph nodes showed involvement, and background low-grade DCIS was present.
Micropapillary mucinous breast carcinoma is a rare breast neoplasm (<1% of breast cancers), which sits between the more indolent invasive mucinous carcinoma and more aggressive invasive micropapillary carcinoma. Literature details both genetic alterations and a behaviour which lies between the two. Molecular studies have shown it to be genetically heterogenous in terms of both copy number alterations and genetic mutations. It has therefore been hypothesised that these interesting tumours can stem from either.
Conclusion: This case of invasive micropapillary mucinous carcinoma is notable for both its unusual Ki-67 proliferation index, and its dimension of 190mm. This case is, to the best knowledge of the authors, one of the largest tumours of this type ever reported in literature.
The recognition of this variant, particularly from pure mucinous carcinoma, is of utmost importance, owing to their differing prognosis and impact on patient management. This case further highlights the heterogeneity of these rare tumours.

E-PS-02-075
Claudin expression patterns in triple-negative breast cancer
V. Zakharava*, A. Khorau, A. Portyanko
*N.N.Alexandrov National Cancer Centre of Belarus, Belarus

Background & objectives: The claudins expression is frequently dysregulated in the context of tumorigenesis, suggesting their role as biomarkers for diagnosis and prognosis.
Objective was to study the morphological features of Claudin-3,-7 expression in patients with triple-negative breast cancer (TNBC).
Methods: Biopsy material from patients with TNBC (n=91) was immunostained (IHC) with antibodies to Cytokeratin5/6, Cytokeratin14, Claudin-3 (CLDN3), Claudin-7 (CLDN7), Androgen Receptor (AR), EGFR. Digital analysis of membrane/cytoplasmic expression was performed using QuPath-0.3.2 software with calculation of Allred score for CLDN3/CLDN7.
Results: Three IHC subtypes of TNBC have been identified: Basal-like (BL, 78%), Luminal AR (LAR, 9%), mesenchymal with stem-like cells and low expression of CLDN3/CLDN7 (MSL, claudin-low – 2%) and mixed subtypes (11%). The levels and variability of CLDN3/CLDN7 expression for each IHC subtype were determined. The claudins expression had no significant differences between BL and LAR IHC subtypes, varying from 0 to 8 Allred score with a Me(CLDN3/7)=6/6 for BL subtype and Me(CLDN3/7)=6/5 for LAR subtype, respectively. At the same time, CLDN7 expression levels ≥7 were associated with a worse prognosis in breast-cancer-free survival in the BL subtype.
Conclusion: The structure of TNBC was dominated by BL and LAR subtypes with single cases was regarded as MSL claudin-low subtype. The TNBC IHC subtypes criteria we have defined and available in the literature. IHC subtypes were characterized by variable levels of claudins expression with a worse prognosis of breast-cancer-free survival with CLDN7 overexpression.
Funding: Governmental Grants 03.09 (2019-2022): To develop and implement a method of therapy for patients with triplet-negative breast cancer according to tumor subtype using chemotherapy including vincoalkoloids

E-PS-02-076
ACTL6A: May be a prognostic and predictive indicator of high proliferative activity triple-negative breast cancer
Y. Zhang*, Y. Zhou, Z. Wu, Q. Tao, F. Mengna, L. Yang, M. Shen, H. Bu, B. Wei, Z. Zhang
*Sichuan University, China

Background & objectives: Triple negative breast cancer (TNBC) with high proliferative is an aggressive subtype of breast cancer with poor tumour progression and prognosis. The purpose of this study was to explore clinicopathological features and biomarkers related to prognosis of highly proliferative TNBCs.
Methods: 192 cases of TNBCs in our institution from 2015 to 2021 were included. TNBCs were divided into high proliferative and low proliferative based on the Ki67 cut off of 50%. Using immunohistochemistry studies, AR, CD8, Forkhead box C1 (FOXC1), Doublecortin-like kinase protein 1 (DCLK1), BEN-domain containing 3 (BEND3), Actin-like 6A (ACTL6A), NK3 homeobox 1 (NKX3-1), SOX10 were evaluated in TNBCs.
Results: There were 85 cases of low proliferative TNBCs and 107 cases of high proliferative TNBCs. Compared with low proliferative TNBCs, high proliferative TNBCs had few senior patients, more Grade 3 tumour, more AR negative tumour, more FOXC1 positive tumour, and more SOX10 positive tumour. Combined with univariate and multivariate analysis, we found that tumour stage, ACTL6A high-expression, CD8 negative/low-expression were related with poorer disease-free survival (DFS) and overall survival (OS) in TNBCs. However, in high proliferative TNBCs, ACTL6A high-expression was correlated with poor OS by univariate analysis and correlated with worse DFS by univariate and multivariate analysis. Patients with ACTL6A high-expression had more lymph node metastasis and larger tumour size.
Conclusion: Patients with high proliferative TNBCs were more likely to express FOXC1 and SOX10, while patients with low proliferative TNBCs were more likely to express AR. ACTL6A, CD8 and tumour stage were associated with the prognosis of TNBC. It's worth noting that ACTL6A high-expression was associated with poor prognosis of high proliferative TNBCs. More attention should be paid to the aggressive ACTL6A high-expression tumour. ACTL6A may be used as a currently prognostic and predictive indicators of high proliferative TNBC.

Funding: Sichuan Science and Technology Program (No. 2022YFS0376).

E-PS-03 | E-Posters Cardiovascular Pathology

E-PS-03-001

Confusing myxofibrosarcoma of the left atrium, firstly diagnosed as myxoma on biopsy

A. Bdioui*, D. Belltaifa, W. Majdoub, M. Krifa, N. Missaoui, S. Hmissa
*Sahloul Hôpital of Sousse, Tunisia

Background & objectives: Primary cardiac tumours are rare, with an incidence ranging from 0.3% to 0.7%. Despite their usually benign nature, a sound pathological interpretation is crucial to identify malignancy. The diagnosis may be challenging, particulary on small biopsy.
Methods: The patient, a 32-year-old man, developed signs of dyspnea two months after COVID-19 infection. Computed tomography revealed a left atrial tumour, resection of the tumour was performed. In gross, the received specimen was cramped and of gelatinous texture.
Microscopic examination showed abundant myxoid stroma with few non atypical cells, so the diagnosis of myxoma was performed.
Results: Six months later, the patient developed left chest pain. Cardiac MRI confirmed tumour recurrence.
Meticulous microscopic examination of pathology slides revealed hypercellular area with atypical spindle cells, showing moderate atypia with hyperchromasia and mitosis figure. the stroma was myxoid and abundant.
On immunohistochemistry study, tumour cells were focally positive with SMA and CD34, and were negative for myogenic markers, MUC4, PS100 and cytokeratin. Considering the malignancy signs and the immunohistochemistry profile, the diagnosis was rectified for myxofibrosarcoma.
Conclusion: Myxoid tumour are diagnosis challenging lesion, an expanded sampling, a meticulous microscopic examination and an appropriate immunohistochemical study are crucial to avoid wrong diagnosis.

E-PS-03-002

Fatal outcome of a unique case: primary cardiac angiosarcoma with lipoblastic differentiation discovered in a young athlete – case report

A. Ciongariu*, A. Dumitru, D. Tapoi, A. Bejenariu, M. Sajin, V. Ionita, C. Badiu, M. Costache
*Department of Pathology, University Emergency Hospital Bucharest, Romania

Background & objectives: Cardiac angiosarcoma is an exceedingly rare high-grade malignancy with an aggressive clinical behaviour and rapid extension to the pericardium and mediastinum. Angiosarcomas can disclose significantly variable histomorphology, occasionally mimicking divergent lesions with mesenchymal or epithelial differentiation.
Methods: We report the case of a 21-year-old male basketball player who developed cardiac failure and was referred to the Cardiovascular Surgery Department. Further examinations identified a mediastinal tumour mass arising in the atria and infiltrating the ascending aorta and superior vena cava. Several samples from the tumour and the pericardial fluid were collected and submitted for histopathological examination.
Results: The microscopic examination revealed a malignant mesenchymal proliferation consisting of round-oval, epithelioid and spindle cells with pleomorphic nuclei and mitotic figures. Poorly formed, irregular vascular spaces were noted within the tumour proliferation. Moreover, the microscopic examination showed atypical cells with lipoblastic differentiation, exhibiting intracytoplasmic vacuoles and hyperchromatic nuclei. Upon immunohistochemical analysis, we identified strong ERG and CD31 expression within the tumour cells with endothelial phenotype, while the atypical lipoblasts showed intense S100 staining. Expression of CDK4, MDM2 and CD45 was absent in the malignant cells. Thus, the diagnosis of angiosarcoma was eventually established. The patient died a few days later due to severe complications of the condition.
Conclusion: Mediastinal tumours in young patients can be a challenging diagnosis, considering their rarity and variable morphology. The most common malignant tumours of this region are lymphomas, carcinomas and vascular lesions. Although an uncommon finding, liposarcoma of the mediastinum can also be discovered in young patients and should be considered for differential diagnosis. Microscopic and immunohistochemical studies should be performed and thorough correlation with the clinical data is recommended. Awareness of this disease is crucial in preventing misdiagnosis and improper treatment.

E-PS-03-003

Fatal case of giant cell myocarditis with near total myocardial fibrosis in a 40 year old woman

H. Goebel*, T. Tsvetkov, C. Grathwohl, A. Deppe
*Institute for Pathology, University Hospital Cologne, University of Cologne, Germany

Background & objectives: Giant cell myocarditis is a rare disease with an incidence of 0.007% and 0.051%.
Methods: We present a case of a previously healthy and sportive woman. After a bout with Covid19 the woman consulted a hospital with unclear unwellness. An highly reduced ejection fraction without sign of ischemic heart disease was found and she was admitted to the cardiothoracic centre of our hospital with suspicion of a myocarditis.
Results: Her health deteriorated rapidly leading to an inital implanation of an impella device and a myocardial biopsy showed a giant cell myocarditis. The patients condition worsened leading to ECMO and finally to the implantation of a Berlin Heart device. A second biopsy seen at our department only showed a very expanded interstitial fibrosis and hypertrophic myocytes but no active lymphocytic or giant cell infiltration. Extensive bleeding within the bronchial tree led to further desoxygenation and finally demise of the patient. At autopsy an enlarged heart with hypertrophy, fresh haemorrhage up to the alveolar spaces and very extensive fibrosis of the myocardium without presence of giant cells or other inflammation was notable.
Conclusion: An ongoing infection of Covid 19 within the lung could be excluded by pcr testing.
We present a case of a giant cell myocarditis with a very short timespan leading to a subtotal fibrosed heart with fatal insufficiency. A Covid-19-association could not be established.

E-PS-03-004

Forensic anatomo-pathological death investigation of heart transplanted victims

R.H. Henriques De Gouveia*, C. Marques, J. Barata, F. Corte Real
*Universidade da Madeira, Portugal

Background & objectives: Heart Transplantation is the final therapy for end-stage heart failure (HF), leading to morbidity/life quality improvement and to mortality reduction of irreversible HF patients. Authors aim to present how forensic anatomo-pathological study contributes to death investigation of post-heart transplantation victims.
Methods: A retrospective study of postmortem examinations performed at two branches of our National Medico-Legal Institute during a time span of 17 years, searching post-heart transplantation deaths, was done.
Results: Three cases were found: 1 female (21 years-old), 2 males (55 years-old, each); deceased suddenly, out-of-hospital, due to acute

rejection (n=2) and constrictive pericarditis (n=1) in hearts with allograft vasculopathy.
Conclusion: Forensic anatomo-pathological studies contribute to the distinction between violent versus natural death and to the detection of heart transplant outcomes, mostly in out-of-hospital deaths.

E-PS-03-005
Is it intimal sarcoma or cardiac undifferentiated pleomorphic sarcoma: a case report
S. Kaymaz*, A.M. Önenerk Men, A.B. Öz, Ş. Batur, Ç.T. Üstünışık, N. Çomunoğlu
*İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi Tıbbi Patoloji Anabilim Dalı, Turkey

Background & objectives: Recent reports claim that cardiac undifferentiated pleomorphic sarcoma (UPS) with MDM2 amplification is identical to cardiac intimal sarcoma (IS). We report a case of IS located in left ventricle and review the literature.
Methods: A 59 year old woman presented with orthopnea, dyspnea and fatigue. It was revealed that she had a 3,9 cm mass originating from mitral valve and extending into the left atrium. The patient was operated. Macroscopic examination of the mass was nonspecific. Microscopic examination revealed a hypercellular tumour infiltrating myocardium.
Results: The tumour had a nodular growth pattern and there were areas of tumour necrosis that corresponds to 5% of the tumour. The tumour was composed of spindle cells that make short fascicles within a myxoid stroma, there were also diffuse sheets and solid areas. Immunohistochemical studies showed that tumour cells stained positively with SMA, Desmin and CDK4. Also we detected MDM2 amplification with FISH analysis.
Conclusion: 5th Edition of WHO Classification of Tumours accepts provisional use of IS for tumours with undifferentiated morphology and MDM2 amplification. This change will have significant impact on the classification of cardiac sarcomas and IS is going to be the most common sarcoma of the heart. Although, current therapy options do not differ between different cardiac sarcoma types, accurate diagnosis will be essential with the emerging targeted therapies in the near future. Therefore, awareness of this entity is important for pathologists.

E-PS-03-006
Autonomic innervation in caval vein myocardial sleeves and cardiovascular death
I. Kholova*, D. Depes, A. Mennander, T. Paavonen
*Tampere University and Fimlab Laboratories, Tampere, Finland

Background & objectives: Quantitative changes in myocardial autonomic innervation may contribute to the pathogenesis of various cardiovascular diseases. Myocardial sleeves around caval veins (CVs) are highly innervated structures with heterogeneous morphological and electrophysiological characteristics. Our present analysis studied autonomic nerve density of CVs.
Methods: The study cohort consisted of 24 autopsied adult hearts (mean age 65.3±12.7 (SD) years and M:F ratio 13:11). Immunohistochemical analysis was performed using antibodies against tyrosine hydroxylase (TH, sympathetic nerve marker), choline acetyltransferase (CHAT, parasympathetic marker), and growth-associated protein 43 (GAP43).
Results: The mean density of TH-positive nerves in the superior vena cava myocardial sleeves was significantly decreased between groups with documented underlying cardiovascular vs. non-cardiovascular cause of death (mean density ± SD: 704.81±1016.41 µm2/mm2 vs. 2391.01±1841.37 µm2/mm2; P=0.008). The nerve density of GAP43-positive nerves in the superior vena cava myocardial sleeves was also significantly lower in subjects with documented underlying cardiovascular cause of death (mean density ± SD: 884.74±1240.16 µm2/mm2 vs. 2132.89±1845.89 µm2/mm2; P=0.040). No differences were found in nerve densities of TH-positive, CHAT-positive, and GAP43-positive nerves in the inferior vena cava between the groups. There was no association found in nerve densities between subjects with documented atrial fibrillation.
Conclusion: Decrease of superior vena cava myocardial sleeve sympathetic nerves may be associated with cardiovascular mortality. No difference in autonomic innervation in CVs was found between subjects with documented atrial fibrillation vs. sinus rhythm.
Funding: VTR grant, Aarne Koskelo Foundation

E-PS-03-007
Morphometric and immunohistochemical study of left ventricular cardiomyocytes' morphology during remodelling in progressing ischemic heart failure (HF)
M. Kupryte*, V. Lesauskaitė, D. Pangonytė
*Lithuanian University of Health Sciences, Institute of Cardiology, Lithuania

Background & objectives: Ischemic injury initiates cardiomyocytes' compensatory remodelling causing cellular resilience and hemodynamic function changes towards HF. Cardiomyocyte geometry and non-sarcomeric filament desmin expression analysis in different ischemic HF stages (adult heart model) is attempt to identify morphologic criteria monitoring HF progress.
Methods: Cardiomyocyte's length-diameter ratio and immunohistochemical reaction against desmin in left cardiac ventriclular segments were analysed in test groups (deceased or after heart transplantation due to ischemic injury): 1st – A, 2nd – B, 3rd – C/D stages of HF by ACC/AHA; control group – samples of patients with no cardiovascular disorders. Statistical analysis – ANOVA with post-hoc LSD tests ($p<0.05$).
Results: Mean value of cardiomyocyte length-diameter ratio was smaller in 1st group compared to control (5.137 (0.374) vs. 5.392 (0.354), p=0.015). It increased in 3rd group compared to 1st and 2nd groups (5.582 (0.448) vs. 5.137 (0.374) and 5.3 (0.245), $p<0.05$). Cardiomyocytes of 1st group had more intensive immunohistochemical reaction against desmin compared to control group ($p<0.001$), also more intensive in 3rd compared to 2nd group ($p<0.001$), and control group ($p<0.001$), whereas intensity was similar in 1st and 2nd groups (p=0.159). Positive weak correlation between changes in cardiomyocyte geometry and expression of desmin was detected (r=0.2453, p=0.012).
Conclusion: Morphofunctional changes of cardiomyocyte geometry and desmin expression during remodelling in response to ischemic injury are detected before HF, and progress in symptomatic HF, presenting morphometric and immunohistochemical diagnostic criteria to monitor myocardial disease progress at its earliest structural manifestation.

E-PS-03-008
An extensively interrogated, diagnostically challenging, fatal high grade cardiac sarcoma with intestinal and cerebral involvement in a 50 year-old man
S.H. Lai*, L.S. Punjabi, A.X.F. Chia, P.Y.K. Pang, J. Chiang
*Anatomical Pathology, Singapore General Hospital, Singapore

Background & objectives: This case illustrates the diagnostic dilemma and extensive pathological and molecular characterisation of an extremely rare primary cardiac sarcoma. Consent from the patient has been obtained for this publication.
Methods: The patient was a previously healthy 50 year-old man who presented with congestive heart failure. Transthoracic echocardiogram revealed a 4.3x3.2cm left atrial mass. Surgical resection was performed. Pathological examination showed a highly cellular, poorly differentiated sarcoma composed mainly of plump epithelioid cells with amphophilic cytoplasm and vesicular nuclei with frequent mitotic figures. In other areas, spindled morphology is seen.

Results: An Intimal Sarcoma was excluded with Undifferentiated Pleomorphic Sarcoma (UPS) being considered primarily. However, positive immunostaining for rhabdomyoblastic markers, focal glandular formation and loss of H3K27me3 suggested a Malignant Triton Tumour (MMT), although it is now known that loss of H3K27me3 staining is non-specific for nerve sheath differentiation. Sequencing did not identify EWSR1 and FUS gene rearrangements, and FISH was negative for MDM2 amplification. The final favoured diagnostic opinion was an epithelioid rhabdomyosarcoma.
Conclusion: In the two months after initial presentation, the patient suffered intestinal perforation complicated by burst abdomen as well as neurological deterioration. Neuroimaging suggested haemorrhagic metastases while pathological examination of the intestines confirmed involvement by sarcoma. The patient succumbed to the disease and complications four months following initial presentation.

E-PS-03-009
Primary cardiac synovial sarcoma: a case report
W. Majdoub*, K. Ben Lazreg, A. Baccouche, S. Mestiri, D. Benletaifa, F. Saidani, O. Belkacem, A. Bdioui, S. Hmissa
*Pathology Department Sahloul Hospital, Tunisia

Background & objectives: Synovial sarcoma is an aggressive type of soft tissue sarcoma that usually occurs in the extremities of young adults. Cardiac SS(CSS) is rare accounting less than 5% of all primary cardiac sarcomas. Herein we report another rare case of CSS.
Methods: A 27-year-old men with no medical history, presented in the department of cardiovascular surgery for a left intra-atrial mass measuring 5 cm of major axis, originating from the septum and prolapsing into the mitral valve. The patient underwent a surgical biopsy.
Results: Histological examination of the fragments showed a tumoral proliferation of diffuse pattern. Tumoral cells were large and round with distinctive cellular borders, abundant pale eosinophilic cytoplasm, and vesicular nuclei. Some cells were multinucleated. Low mitotic count (3 mitoses /10HPF) with atypical mitoses were observed. The tumour was highly vascularized with fine branching vessels. Tumoral necrosis was observed. According to immunohistochemistry staining, the tumoral cells were positive for cytokeratin, EMA, and AML. They were focally positive for desmin, PS100 and CD99. Tumoral cells were negative for H caldesmon, MDM2, CD34, MyoD1,Ber Ep4, calretinin. 60% of tumoral cells showed a nuclear expression of TLE1.Moreover, the tumoral cells were positive for the antibody SSX-SS18.
Conclusion: The mean age of the few cases reported in literature of CSS is 33.8 years with a potential predilection to occur in males. The monophasic subtype is the most described in CSS. The true poorly differentiated SS is extremely rare. In this site, differential diagnosis can be challenging. The selection of epithelial, mesothelial, myogenic, and vascular-derived specific immunohistochemistry markers may be helpful in resolving the difficulties. SSx-SS18 antibody is useful for diagnosis reflecting the presence of the translocation t(X,18).

E-PS-03-010
An unusual case of cardiac metastasis of neuroendocrine tumour
A. Pestana Lopes*, B. Martins, J. Cassis, V. Costa Sousa
*Hospital da Luz Lisboa, Portugal

Background & objectives: Intracardiac neuroendocrine tumour metastases are rare and have been estimated to occur in <5% of patients with neuroendocrine tumours. They are generally asymptomatic and detected incidentally. We, hereby, present an unusual case of cardiac metastasis of a neuroendocrine tumour.
Methods: A 52-year-old man with no significant past medical history was referred to our Institution for further evaluation of a heart murmur. The patient reported palpitations and chest discomfort. Echocardiography and magnetic resonance imaging revealed a well-circumscribed mass extending from the right ventricular free wall, measuring 29x40 millimetres in the latter. The decision was to remove the cardiac mass surgically.
Results: Histological examination of the resected mass was consistent with cardiac metastasis of well-differentiated (G2) neuroendocrine tumour, with a proliferation index Ki67 (MiB-1) estimated at 5% and mitotic rate of 3/mm2. On the immunohistochemical study, tumour cells were positive for CK (AE1/AE3), synaptophysin, chromogranin and CDX-2, making spread from a gastrointestinal primary likely. A gallium-68 DOTANOC PET/CT scan was performed, revealing a primary somatostatin-avid tumour within the terminal ileum (SUVmax of 14.45). There was also evidence of somatostatin avid metastatic disease in multiple lymph node groups, in the mesentery and in the liver (SUVmax ranging from 5.00 to 18.46, 28.51 and 17.10, respectively).
Conclusion: Our case illustrates a neuroendocrine tumour presenting as a symptomatic cardiac metastasis. While intracardiac metastases from neuroendocrine tumour are exceedingly rare, when they are present, they are generally detected incidentally and cause no symptoms. Additionally, they are frequently observed in patients with late, widespread tumours as shown in our case, based on the findings of the gallium-68 DOTANOC PET/CT scan.

E-PS-03-011
Anatomical cardiac changes in individuals with anorexia: could microcardia underlie sudden cardiac death?
J. Westaby*, M.N. Sheppard
*St George's University of London, United Kingdom

Background & objectives: Anorexia nervosa is an eating disorder characterized by low weight and food restriction. There is an increased risk of arrhythmia and premature sudden cardiac death (SCD).
We aimed to characterise anatomical cardiac changes in those with anorexia.
Methods: We identified 97 cases of anorexia with no other cause of death from 7702 cases of SCD. Anorexia was based upon a previous diagnosis or a body mass index of less than 17kg/m2 without alternate causes. Cases were age and sex matched to normal weight individuals with a BMI of 18.5-24.9kg/m2. Hearts were weighed and measured prospectively.
Results: Age was 33±16years with 58 females and 39 males in both anorexia and controls. Weight was 48±8kg and BMI was 15±2kg/m2 in anorexia compared to 65±9kg and 22±2kg/m2 in controls. There was a significantly lower heart weight in individuals with anorexia (270±98g vs 324±74g, $p<0.001$). Right atrial (44±11mm vs 39±9mm, $p=0.005$) and left atrial (44±11mm vs 39±8mm, $p=0.006$) measurements were significantly smaller in anorexia. The left ventricular cavity diameter (28±10mm vs 31±7mm, $p=0.006$) and lateral muscle wall (12±2mm vs 13±2mm, $p=0.037$) were significantly smaller in anorexia.
Conclusion: These findings raise the possibility that microcardia may underlie SCD in anorexic individuals. Genetic analysis and follow up of relatives will allow detection of genetic susceptibility to SCD or determine whether this is solely acquired. Correlation with phenotype in living patients and outcomes is required. Public health initiatives to address anorexia and good access to psychiatric healthcare may decrease SCD risk. The effect of the intervention on SCD risk is not established therefore prospective assessment is warranted.
Funding: Cardiac Risk in the Young fund the cardiovascular pathology laboratories at St George's University of London

E-PS-04 | E-Posters Cytopathology

E-PS-04-001
Drug defaulters in tubercular lymphadenitis: a cytopathological study
S. Ahuja*, A. Kumari, S. Bajaj, S. Zaheer, S. Ranga
*Department of Pathology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

Background & objectives: Although effective chemotherapy is available for tuberculosis, compliance of the patient is a major challenge. The aim of this study was to describe cytomorphological features of drug defaulters on lymph node FNAC and compare it with newly diagnosed cases.
Methods: A cross-sectional study was done for a period of 18 months in which all patients having tuberculous lymphadenitis were taken for study after taking detail history regarding previous anti-tuberculosis drug intake. Cytomorphological findings in drug defaulters were evaluated and compared with newly diagnosed cases.
Results: There were a total of 150 cases with 120 newly diagnosed and 30 drug defaulters. Splintered epithelioid cell granuloma was seen in 40% of drug defaulters while it was absent in case of newly diagnosed cases (p value< 0.0001). Well-formed epithelioid cell granuloma was most commonly seen in newly diagnosed cases (65.83%) followed by poorly formed granuloma (26.67%). Another significant finding was distribution of eosinophils were significantly high in case of drug defaulters (56.67%) (p value <0.0001).
Conclusion: Cytomorphological findings can help in identification of the drug defaulters on FNAC and thus plan further line of treatment.

E-PS-04-002
Milan System and its efficacy in salivary gland cytology
A. Uğuz, M. Aksin*, B.N. Ateş, E. Onan
*Cukurova University Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: The aims of this study is to evaluate the risk of malignancy (ROM) of ''Milan System for Reporting Salivary Gland Cytopathology (MSRSGC)" in each categories, to compare ROMs with the previous descriptive diagnoses, and to analyse the effects on management.
Methods: Our database was searched for patients who had salivary gland fine needle aspiration between 2011-2020. Each specimen was re-evaluated, and cases were reclassified according to the MSRSGC diagnostic categories. Cytopathological diagnoses were correlated with the follow-up histopathologies. ROM was calculated for each category. The overall sensitivity, spesificity, positive predictive value, negative predictive value and the diagnostic accuracy were evaluated.
Results: A total of 605 salivary gland fine needle aspiration specimens were evaluated and histologic follow-up was available for 247 specimens. The calculated ROMs for each categories was as follows: 1- 14.2%, 2- 6.2%, 3- 56.5%, 4A- 1.03%, 4B- 24.4%, 5- 26.3%, 6- 82.7%. The sensitivity, specificity, positive predictive value, and negative predictive value of the MSRSGC-based classification were 91.6%, 93.7%, 78.5% and 97.8%, respectively.
Conclusion: The present results confirm the usefullnes of the MSRSGC in clinical practice, providing prognostic information and suggestions for management strategies. In addition, it creates a common language between pathologists and the clinicians in the approach to salivary gland lesions.

E-PS-04-003
Clinicopathologic characteristics of HPV-negative/cytology-positive cervical lesions: results from a 5-year study
Y. Chun*, J.Y. Park, Y. Kim
* Korea University Guro Hospital, Republic of Korea

Background & objectives: With increasing cervical cancer screening and human papillomavirus (HPV) vaccination, the importance of HPV-independent cervical cancer is anticipated to increase. This study examined the clinicopathologic characteristics of HPV-negative/cytology-positive cervical lesions.
Methods: Over 5 years from 2017, 30,950 HPV tests were conducted using the HPV 28 Anyplex Real-time Detection kit. Of these, 25,088 cases (81%) were also tested for liquid-based cytology. Out of 1506 cases with abnormal cytology and negative HPV test results, the histological results of 52 cases with high-grade squamous intraepithelial lesion or worse (HSIL+) on cytology were reviewed.
Results: Histological examination of the 52 cases revealed that 33 cases had a diagnosis of HSIL+, including 30 cases of carcinoma and 3 cases of HSIL. The 30 cases of carcinoma included 11 cases of endometrial carcinoma, 9 cases of cervical carcinoma, 8 cases of metastatic carcinoma, 1 case of anal carcinoma, and 1 case of vulvar Paget disease. A case of carcinoma and 3 cases of HSIL were found to be HPV-positive by p16 immunostaining and HPV DNA in situ hybridization.
Conclusion: The results suggest that HPV-negative and cytology-positive cases can present with various types of cervical cancer, including HPV-independent and HPV-associated cancer, HSIL, endometrial cancer, and metastatic cancer in extrauterine organs. Also, it is important to consider the possibility of false negative HPV test results. Thus, relying solely on HPV screening may result in missing these different types of lesions, which has significant implications for the management and treatment of cervical cancer.

E-PS-04-004
Investigation of common stoma adhesive powder, paste and tapes: Identification of guar cell contamination may prevent diagnostic pitfalls
O.C. Eren*, E. Orak, S. Ilme, E. Koseoglu, E. Eren, T. Keskin, D. Ertoy Baydar, P. Fırat
*Koç University Hospital, Department of Pathology, Turkey

Background & objectives: A 75-year-old male patient with ileal conduit after radical cystectomy submitted a urostomy-bag urine sample during his annual evaluation. Cytologic examination revealed non-atypical urothelial cells, intestinal epithelial cells and vacuolated plant cells, initially mimicking an intestinal fistula.
Methods: To investigate the possibility of a contamination from urostomy adhesives, smears were made from commonly used, commercially available stoma adhesive pastes (Coloplast® and Convatec®), powder (Brava®), and hard/soft tapes (Coloplast® Alterna). Simultaneously, cell blocks were prepared and histologic sections of 3 micrometer thickness were made for hematoxylin-eosin staining. Separately, unstained sections were deparaffinized for further use in immunofluorescence.
Results: Cytologic evaluation of Coloplast® paste revealed plant cells with vacuolar cytoplasm and rigid borders, identical to what was observed in patient's sample. Sections from Coloplast® adhesive confirmed similar cells, further demonstrated to be auto-fluorescent in fluorescence microscopy. The patient was later confirmed to use the same stoma adhesive paste and was found to have no signs or symptoms suggesting an intestinal fistula. Cytopathologic examination of the remaining stoma adhesives were acellular, displaying merely inorganic material.
Conclusion: Stoma adhesives should be acknowledged as potential contaminators of urine samples, especially in circumstances where sampling is made directly from urostomy bags. Although most adhesives are devoid of organic material, Coloplast® stands out due to its plant-based component. Guar gum, found in stoma adhesives such as the latter, is characterized by auto-fluorescent, rigid-walled, vacuolar plant cells. Recognition of morphologic features may prevent pathologists misinterpreting Guar cells as contents of intestinal fistula or uncommon parasites.

E-PS-04-006
Diagnostic approach to cat scratch disease: a cross-sectional study
K. Goncalves Villarreal*, E. Oliva Dominguez, S. Gamba Torrez, I. Garcia Miranda, S. Fernandez Sole, J.D. Solano Iturri
*MD, University Hospital of Cruces, Spain

Background & objectives: Cat scratch disease (CSD) is clinically characterized by subacute painful lymphadenopathy. Histopathology is commonly nonspecific, and serology often necessary. The main objective is to describe the diagnostic approach of CSD in the Pathology Department of the University Hospital of Cruces.
Methods: Descriptive, retrospective, and cross-sectional study of 25 patients with painful lymphadenopathy diagnosed with CSD by compatible cytology and positive serology, evaluated in the Pathology Department of the University Hospital of Cruces between 1999-2020. Patients with indeterminate or negative serology were excluded. Medical records were reviewed. Qualitative data were expressed in percentages and absolute values and quantitative data as mean (range).
Results: 60% were men (n=15) with a mean age of 33 years (16-65). The location of lymphadenopathies was predominantly cervical (n=20) followed by inguinal (n=4) and axillary (n=1). Regarding cytological smears, 9 samples presented inflammatory characteristics, 4 included in their cytological spreads heterogeneous lymphohistiocytic cellularity with frequent apoptotic bodies in a context of abscess-forming necrotic material, and in the remaining 11, mononuclear cells were evident at different maturation stages embedded in a reticular network. No samples presented cytological atypia.
Conclusion: The differential diagnosis of suppurative granulomatous lymphadenitis is broad and should include CSD. The epidemiological history of contact with cats should be questioned. In the case of clinical suspicion of CSD, we recommend the systematic use of fine-needle aspiration cytology in the absence of rapid on-site evaluation and routine infectious serology.

E-PS-04-008
Audit of thyroid fine needle aspiration cytology reporting over a two-year period (2019-2020)
E. Joslin*, S. Appukutty, A. Paterson, M. O'Donovan, J. Chan, A. Duckworth, N. Patel, A. Marker
*Cambridge University Hospital, United Kingdom

Background & objectives: Calculate the proportion of thyroid fine needle aspiration (FNA) cytology and core needle biopsy (CNB) cases in each Thy and C categories compared to RCPath standards. To determine the proportion of Thy3 cases that were double-reported with MDT meeting discussion.

Methods: All consecutive thyroid FNA and CNB samples received for reporting at Addenbrooke's Hospital, Cambridge from January 2019-December 2020. The Thy and C categories were compared to RCPath standards, as well as associated malignancy rates.
Results: 401 thyroid FNA samples were received and categorised as follows: Thy1 22%, Thy1c 13%, Thy2 5%, Thy2c 6%, Thy3a 26%, Thy3f 17%, Thy4 1%, Thy5 9%, no category 1%.
88% Thy3a and 69% Thy3f samples were double reported. MDT discussion documented in 92% Thy3a, 94% Thy3f, 100% Thy4 and 92% Thy5. The subsequent histology showed the malignancy risk in each category to be Thy1 6%, Thy2 0%, Thy3a 12%, Thy3f 28%, Thy4 100% and Thy5 100%.
89 cases of thyroid core needle biopsies were received and categorised as follows: C1 3%, C2 11%, C3 68%, C4 1% and C5 17%. 100% of C5 cases were malignant on subsequent resection.
Conclusion: The use of the Thy2/Thy2C category is lower than expected; likely to reflect local clinical practice where cases which appear benign on clinical and radiological assessment, and have no symptomatic cystic component, are often not sampled. The Thy3a category is used more than expected; however, the risk of malignancy determined on subsequent histology meets RCPath standards. The lower-than-expected double reporting of Thy3 specimens as per local protocol is likely due to changing working practices secondary to the COVID-19 pandemic.

E-PS-04-009
The incidence of leptomeningeal metastasis from solid tumours on the cerebrospinal fluid smear
L. Lozneanu*, I.D. Căruntu, C. Amalinei, R. Balan, S.E. Giușcă, B. Manole, E.R. Avadanei
*U.M.F. "Grigore T. Popa" Iasi, Romania

Background & objectives: The aim of our study was to analyse the presence of tumour cells in the cerebrospinal fluid (CSF) taken from patients with clinical meningeal syndrome and pleocytosis.
Methods: We analysed 55 CSF smears from patients who presented to the Infectious Diseases Hospital in Iasi with meningeal syndrome, who underwent lumbar puncture. At the direct microscopic examination (cytobacteriological smear) they were diagnosed with pleocytosis and negative bacterioscopy. Consequently, the cytodiagnostic examination of the smears was carried out by a pathologist.
Results: We identified, in 4 cases (7.27%), the presence of atypical tumour cells with different morphology, as follows: immature hematogenous cells of the blastic type were predominant in one case, atypical cells with a morphology similar to breast cancer cells were identified in one case, which has previously diagnosed with primary breast cancer, lymphocytes with a mature appearance, but in very large numbers were seen in one case, which had history of ALL and cells with a morphology suggestive of microcellular bronchopulmonary carcinoma, were identified in another case. In the latter case, the cytological diagnosis was further on certified by imagistic investigation (CT), followed by a biopsy.
Conclusion: The routine cytological examination of the CSF obtained through lumbar punctures is inexpensive and facile to carry out in suspected cases of inflammatory meningeal diseases, as a useful tool for diagnosis of aggressive diseases.

E-PS-04-010
Ten years of experience in endoscopic ultrasound-guided fine-needle aspiration cytology in a tertiary referral hospital
V. Macarrón Aguilera*, M.M. Petrino, P. Puente López, I. de la Peña Navarro, A.M. Rodríguez-García, P. López-Ferrer
*La Paz University Hospital, Spain

Background & objectives: The endoscopic ultrasound-guided fine-needle aspiration cytology (EUS-FNAC) is a technique that involves obtaining cytological samples from lesions close to the digestive tract via endoscopy. The objective is to evaluate EUS-FNAC results from a tertiary referral centre from 2013 to 2022.
Methods: A search was made of all EUS-FNAC performed from March 2013 to December 2022, most of them executed by rapid on-site evaluation (ROSE) method. The results were subdivided according to location (pancreas, lymph node, stomach, liver, bile duct/ ampulla, duodenum, retroperitoneum, oesophagus, rectum and others). Based on the bibliography, the following variables were extracted: gender, age and cytological result.
Results: The total of EUS-FNAC performed was 988. Pancreatic lesions were 750 (75.9%) (527 solid, 182 cystic and 41 solid-cystic) with the following diagnoses: 338 positive (45,1%), 43 suspected (5.7%), 229 negative (30.5%) and 140 insufficient (18.7%). Lymph node samples were 104 (10.6%), with results of 32 positive (30.8%), 44 negative (42.3%), 7 suspected (6.7%) and 21 insufficient (20,2%). Gastric lesions were 44 (4.5%), with 24 positive (54.5%), 11 negative (25%) and 9 insufficient (20.5%) results. The remaining EUS-FNAC samples were distributed in 20 liver (2%), 19 bile duct/ampulla (1.9%), 17 duodenum (1,7%), 7 retroperitoneum (0.7%), 7 oesophagus (0.7%), 7 rectum (0.7%) and 13 others (1.3%).
Conclusion: The main sample obtained by EUS-FNAC is the pancreas, in which has been observed to have a good efficiency with 81,3% satisfactory results. The yield in the other two most frequent locations (lymph node and stomach) is similar to pancreatic samples. This reveals that EUS-FNAC is an efficient minimally invasive technique for obtaining samples of lesions accessible by digestive ultrasound.

E-PS-04-011

False positive clinical-radiological hyperprogression due to sarcoid-like granulomatosis in neoadjuvant treatment of locally advanced lung cancer

J. Martin Lopez*, P. Gil Bernabé, S. Martin Poza, G. Diaz Nuevo, G. Silvestre Egea, C. Salas Anton
*Department of Pathology. Hospital U. Puerta de Hierro, Spain

Background & objectives: Sarcoid-like granulomatous reaction is a rare effect of some drugs used in the treatment of locally advanced LC. Some patients treated with neoadjuvant immunotherapy show radiologically abnormal nodes that upon pathological evaluation are free of cancer and show non-caseating granulomas.
Methods: 67-year-old man, ex-smoker with a 7.7 cm lung mass diagnosed by bronchial biopsy of squamous cell carcinoma, stage cT4N0. He started neoadjuvant treatment with Carboplatin / Taxol plus Pembrolizumab. Radiological follow-up tests described a new ipsilateral lesion (SUVmax of 6.3) and hiliar and mediastinal lymphadenopathy. Given the suspicion of disease progression, EBUS and mediastinoscopy were performed.
Results: The EBUS-guided ROSE identified a sarcoid-type granulamatous reaction that was later confirmed by preoperative mediastinoscopy. At this time, a pulmonary lobectomy was proposed and accepted by the patient. The histopathological evaluation of the surgical specimen revealed areas of cavitation and necrosis that accounted for 60% of the neoadjuvant bed with an inflammatory reaction in the form of collagen fibrosis and a lymphocytic-type infiltrate with the presence of multinucleated giant cells with cholesterol crystals. Viable neoplastic cellularity was not observed. In the peritumoral, septal, and pleural areas, the presence of diffusely distributed granulomas of sarcoid morphology stood out. A diagnosis of complete pathological response with extensive associated sarcoid reaction was made.
Conclusion: The administration of combined chemotherapy-immunotherapy is showing clear benefits in the treatment of locally advanced lung cancer (stage III). Neoadjuvant immunotherapy can lead to the presence of paradoxical effects of disease progression in patients who develop sarcoid-like reactions. Our case exemplifies how cytological interpretation in these cases is really useful in diagnosing these reactions. Also, the histopathological study of the specimen allows the determination of the degree of pathological response, which is not always predictable on radiological studies.

E-PS-04-012

Metastatic vulvar adenocarcinoma associated with a long-standing Paget disease diagnosed by endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA): a case report of a rare entity

C. Mora*, J. Ferreira, R. Fonseca
*Serviço de Anatomia Patológica, Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisbon, Portugal

Background & objectives: Vulvar adenocarcinoma associated with Paget Disease is an uncommon occurrence (<2% of all vulvar malignancies) and distant metastasis are even rarer (only 2,5% of all cases reported). Given the rarity of this entity, diagnosis remains a challenge.
Methods: We herein report a case of a 75 year-old woman with a long-standing diagnosis (22 years) of vulvar Paget disease, who underwent multiple surgical and topic therapies, without ever having histological evidence of invasive disease. Then, because of new onset haematuria and lumbar pain she was restudied thoroughly.
Results: On evaluation, thoraco-abdomino-pelvic CT identified multiple mediastinal adenopathies and pulmonary nodules. EBUS-TBNA of a lymph node was performed. Smears were hypercellular, with tridimensional aggregates of epithelial cells with irregular nuclei and dense vacuolated cytoplasm, positive for CK7, GDCFP15, androgen receptor (AR) and ERBB2 (score 3+), and negative for CK20 and TTF1. Additional staging scans excluded a mammary origin. A new vulvar biopsy was performed, where an identical adenocarcinoma with CK7, GATA3, AR expression, and ERBB2 positivity was documented. A diagnosis of metastatic vulvar adenocarcinoma associated with Paget Disease was rendered. With rapidly evolving symptoms and "de novo" bone and liver metastasis, the patient died one month later.
Conclusion: Vulvar Paget Disease is a rare but generally indolent cutaneous neoplasm, in which relapse is common but metastases, especially distant metastases, are very rare. Due to its rarity, the cytological diagnosis of metastatic vulvar adenocarcinoma associated with Paget disease can be challenging, especially in distant locations. Nevertheless, careful clinical correlation and immunohistochemistry can help overcome this difficulty.

E-PS-04-013

Fine needle aspiration cytology of a fibrin-associated diffuse large B-cell lymphoma arising in retroperitoneal pseudocyst: a case report

K. Na*, H. Kim
*Department of Pathology, Kyung Hee University Hospital, Kyung Hee University College of Medicine, Republic of Korea

Background & objectives: Fibrin-associated diffuse large B-cell lymphoma (FA-DLBCL) is an unusual form of DLBCL associated with chronic inflammation. FA-DLBCL is frequently associated with Epstein-Barr virus (EBV) and manifests as non-mass-forming, microscopic lesions found within fibrinous material.
Methods: A 72- year-old male presented with a large retroperitoneal cyst. The mass was completely resected by a laparoscopic approach. Cystic fluid was aspirated right after surgical resection and sent to the pathology laboratory for cytological examination. The resected tissue was submitted for histological examination. Fibrinous exudate and necrotic material attached to inner cystic wall was collected for cell block preparation.
Results: Papanicolau stain for the cytological specimens showed singly dispersed large atypical cells in a necrotic background. These atypical cells possessed scant cytoplasm, hyperchromatic nuclei with irregular nuclear contours, vesicular chromatin and inconspicuous nucleoli. Frequent karyorrhexis and mitotic figures were noted. Histologically, the cystic lesion consisted of thick fibrous wall with heavy lymphoplasmacytic infiltration. The fibrinous exudate contained large atypical cells that were individually scattered or arranged in small clusters. Frequent karyorrhectic debris and mitotic figures were noted. Immunostaining revealed that the atypical lymphoid cells were positive for CD20, MUM1, and EBER-ISH but negative for CD3, Bcl-6, CD10, and HHV8.
Conclusion: FA-DLBCL is cytologically characterized by the presence of large atypical cells individually scattered in a necrotic background. They have scant cytoplasm and irregular, hyperchromatic nuclei. Karyorrhexis and mitotic figures are easily identifiable. To the best of our knowledge, this is the first case report describing the cytological features of FA-DLBCL.

E-PS-04-014

Challenges & pitfalls in rapid onsite evaluation of salivary gland lesions using Milan system for reporting salivary gland cytopathology (MSRSGC); experience from Lahore, Pakistan

E. Rehman*, A. Nawaz, M.U. Farooq, R. Saqib, K. Shehzadi, A. Hamid, A. Aftab
*Associate professor Pathology department, Ameerudin medical college/postgraduate medical institute, Lahore, Pakistan

Background & objectives: ROSE is used to achieve adequate amount of aspirated material from suspected lesion. Milan System provides standardized reporting in salivary gland cytopathology. The aim of this study is to determine the challenges faced during ROSE of salivary Gland lesions.

Methods: A prospective cross-sectional analysis of 50 cases of salivary gland lesions was conducted in a period of 6 months in histopathology department. ROSE was performed and aspirated material was spread on slides and stained with diff quik stain. Lesions were then categorized as per Milan System. The Data was entered and analysed by using SPSS version 21.
Results: A cross sectional study was conducted in histopathology laboratory with a sample size of 50 salivary gland lesions presenting in both indoor and outdoor patients. Most affected site was parotid gland followed by submandibular gland and minor salivary glands respectively. Majority of the challenges were faced in categorizing salivary gland lesions with suspicion of neoplasm on the basis of clinical and radiological data but the Milan category 'non-diagnostic' was assigned either due to lesional heterogeneity, fibrosis or necrosis resulting in non-representative sampling, aspiration of only myxoid material lacking a cellular component and various preparation artifacts during staining procedure.
Conclusion: Challenges faced during rapid onsite evaluation of salivary gland lesions can be minimized by using appropriate aspiration techniques, preservation of aspirated material for further evaluation and additional ancillary testing and provision of appropriate clinical and radiological data useful in deciding type of aspiration technique, nature and exact site of the lesion. Effective collaboration is needed between surgeon, radiologist, cytotechnicians and both resident and reporting pathologist in order to minimize wastage of time and resources and repeat testing.

E-PS-04-015
Cytohistologic correlation of gynaecologic malignancies: can peritoneal fluid cytology reliably subtype gynaecologic malignancies?
T. Sabljic*, S.K. Lou
*University Health Network, Canada

Background & objectives: Cytological examination of peritoneal fluid (PTFL) often represents the first and only pathological specimen available to guide management of gynaecological malignancies (GM). This study examines the cytohistologic concordance between subtyping of GM between PTFL and its subsequent surgical specimen (SS).
Methods: The study retrospectively identified positive PTFL specimens with a GM between 2017 and 2022. Cases where the PTFL was obtained after or concurrently with its diagnostic SS (biopsy/resection) were excluded. The diagnosis, including histotype and grading, was compared to its corresponding SS with an analysis of potential factors leading to its cytohistologic discordance.
Results: GM affected 55.8% (502/899) of malignant PTFL, of which, 22.3% (112)/15.7% (79) was the initial/only diagnostic sample, respectively. Compared to SS, when subtype was rendered/favoured (95/112, 84.8%), PTFL cytology had an accuracy of 97.9%. Factors in lack of/discordant subtyping include cytopathologist preference, specimen limitations, or discordance between morphology and immunohistochemistry. In six cases (5.4%), the PTFL diagnosis was more than or as definitive as the SpS diagnosis. In five cases (4.5%), cytology correctly identified one of the components of a mixed carcinoma/carcinosarcoma. In the six cases where the initial SS was non-diagnostic due to lack of/scanty lesional tissue or necrosis, the subsequent PTFL was diagnostic.
Conclusion: When compared to SS, diagnosis and subtyping of GM on PTFL cytology is highly accurate and sometimes, more definitive than its surgical counterpart. In some cases, subtyping is limited by extrinsic factors (e.g., specimen limitations, immunohistochemistry discordance with morphology). In other cases, cytopathologists prefer not to subtype despite classic morphologic and immunohistochemical features. This highlighted an opportunity for improvement in the diagnosis/subtyping of GM in PTFL, which may be the initial or only diagnostic specimen prior to patient treatment.

E-PS-04-016
Atypical pleural liquid cells reveal their secret
B. Suciu*, A. Maggio, C. Laurent
*Centre Hospitalier de Béziers, France

Background & objectives: Primary effusion lymphoma is a rare variant of diffuse large B-cell lymphoma which develops similarly to an effusion located inside the serous cavities. The purpose of this paper is to highlight the algorithm used to reach this difficult diagnosis.
Methods: One Papanicolaou (PAP) stained slide, two May Grunwald-Giemsa (MGG) stained slides and a cell-block, standard staining, hematoxylin and eosin, were examined. A panel of immunohistochemistry markers was ordered; the slides were stained following the standard protocol. The markers used are: CD45, CD20, CD3, CD138, Ki-67, HHV8, MUM1, ALK, EBV-LMP1, CK AE1/AE3, Ber-Ep4, CK 5/6, WT1, Calretinin, SOX10.
Results: The majority of markers came out negative: CK AE1/AE3, Ber-Ep4, CK 5/6, WT1, Calretinin, SOX10 with the exception of CD45. Ki67 80% - nuclear stain. Mesothelial tumours, carcinoma and melanoma are excluded. This did not conclude the case, so a second batch of immunohistochemistry markers was performed, with the results being quite a surprise: the cells were negative for CD20, CD3 and positive for CD138. Based on the plasmablastic morphology and the fact that the cells were CD20, CD3 negative and CD138 positive, a third round of immunostains is ordered, following a specific algorithm. The cells were HHV8, MUM1 positive and ALK, EBV-LMP1 negative. The diagnosis of primary effusion lymphoma was concluded.
Conclusion: Primary effusion lymphoma is a rare form of large B-cell lymphoma which develops in the serous cavities in patients usually infected with HIV or immunocompromised by transplants. This case was challenging because of cell morphology, but also because the aetiology of the effusion was thought to be of cardiac or renal origin. The key histological aspects are moderate to large sized plasmablastic-like cells that are negative for B-cell markers CD20, CD79a, PAX 5 and are positive for CD138, CD45, MUM1 and HHV8.

E-PS-04-017
Acantholytic squamous cell carcinoma mimicking epithelioid angiosarcoma: a diagnostic challenge by cytology
M. Taweevisit*, P. Thorner
*Department of Pathology, Thailand

Background & objectives: Squamous cell carcinoma is the most common malignancy of the head and neck region. Most cases present little diagnostic difficulty on fine needle aspiration (FNA), but unusual variants can be problematic.
Methods: The authors report a case of the acantholytic squamous cell carcinoma of the oral cavity in a 36-year-old man. Smeared slides from the FNA were fixed in 95% ethanol and stained with the Papanicolaou stain. A computerized tomographic scan demonstrated a mass of the left buccal mucosa, measuring 1.6 x 1.3 cm. Then, wide excision was carried out.
Results: The FNA showed hypercellularity. Malignant cells arranged in isolation, loosely cohesive groups and a linear configuration. Such cells were round to elongated, with vesicular nuclei and prominent nucleoli. Cells possessed occasional intracytoplasmic vacuoles, misinterpreted on FNA to be vasoformative features as seen in malignant endothelial cells. The cytologic diagnosis was "positive for malignancy, suggestive of angiosarcoma". An excision was performed and by histology, the tumour was diagnosed as acantholytic squamous cell carcinoma. The malignant cells were positive by immunostaining for AE1/AE3, p40, p63 and vimentin, but negative for CD31, CD34 and ERG. The intracytoplasmic vacuoles were PAS- and mucin-negative and negative for the above antibodies.
Conclusion: This case highlights the diagnostic challenges on cytology when malignant acantholytic squamous cells show intracytoplasmic vacuoles, and stresses how immunohistochemistry is important

for distinguishing acantholytic squamous cell carcinoma from other mimics.

E-PS-04-018

A cytohistological correlation study: cytological traits associated with cervical adenocarcinoma

M. Veras*, A. Díez Fernández, E. Revilla Sánchez, N. Alberti Masgrau, A. Pérez Campos
*Pathology Department, Hospital Universitario 12 de Octubre. Madrid, Spain

Background & objectives: The increasing incidence of cervical adenocarcinoma compared to squamous carcinoma suggests that cervical screening is inefficient at preventing it. The objective of this study is to analyse the cytological features associated with cervical adenocarcinoma and their histological correlation.
Methods: Cytology specimens from women with concurrent, histologically confirmed cervical adenocarcinomas/in situ (AIS) from 2017 to 2022, and cytology slides with a result of atypical glandular cells (ACG) from the same period and a follow-up biopsy, were reviewed retrospectively for cytologic traits associated with adenocarcinomas. Cytohistological correlation was studied. Clinical data and HPV status were also analysed.
Results: 26 cases diagnosed as cervical adenocarcinoma in biopsy were selected. Average age was 50.6 years. 65.4% (n=17) of cases with an available HPV test result were HPV-positive, all for high-risk genotypes. 19.2% (n=5) were identified cytologically as adenocarcinomas/AIS. 50% (n=13) fell into a diagnostic group that implied follow-up biopsy, that is, adenocarcinomas/AIS and high-grade lesions (HSIL/ASC-H/AGC). Also, histologically, of 128 cases of ACG, 27.34% (n=35) were high-grade lesions, and 8.59% (n=11), adenocarcinomas/AIS. Cytologic traits associated with adenocarcinomas will be reviewed.
Conclusion: A substantial proportion of cases with histologically confirmed cervical adenocarcinomas do not receive a cytological diagnosis of adenocarcinoma or other high-grade lesion that assures a histological follow-up, and consequently, diagnosis and treatment of these cases might be delayed. Most cases of AGC do not correspond with malignant or premalignant lesions. These results indicate that cytology screening is not efficient at detecting cervical adenocarcinomas, and a better definition of diagnostic criteria is needed. These findings should be consolidated in future studies.

E-PS-04-019

HPV test in cytology laboratory practice: a six-year follow-up study

D. Versa Ostojic*, D. Vrdoljak-Mozetic, S. Stemberger-Papic, M. Dinter, R. Rubesa-Mihaljevic
*Department of Pathology and Cytology, Clinical Hospital Centre Rijeka, Croatia

Background & objectives: Cervical cytology and HPV test are tools in the prevention of cervical cancer. The aim of the study was to compare the initial cytology and HPV test with the detection of HSIL+ histology and triage of ASCUS in six-year follow-up.
Methods: We analysed retrospectively the results of 1157 HPV tests (Hybrid Capture 2) and initial cytology in the detection of cervical intraepithelial neoplasia or in follow-up after excisional treatment. The results were compared with the outcome after six-year follow-up period. Negative follow-up cytology or negative histology was considered a negative outcome. HSIL+ histology was considered as a positive outcome.
Results: 473(40.9%) HPV tests were positive and 652(56.4%) had abnormal cytology (mean age 37 years, range 16-77). In the six-year follow up period 173 of 213 patients had HSIL+ histology. The false negative rate of HPV test for HSIL+ was 1.8%. HSIL+ was found in 2.5% of patients with initially negative cytology, 8.3% of ASCUS, 10.9% of LSIL, 10% of AGC, 56.5% of ASC-H, 63.5% of HSIL and in 100% of cytologically detected cancers. The HPV test showed 94.2% sensitivity, 68.4% specificity, 34% positive predictive value (PPV) and 98.5% negative predictive value (NPV). The reflex HPV test in ASCUS triage showed 86.2% sensitivity, 65.9% specificity, 18.7% PPV and 98.1% NPV.
Conclusion: The HSIL+ histology correlates with the severity of cytological diagnosis. High NPV of HPV test is shown to be a valuable tool for triaging patients with ASCUS. Although the HPV test exhibits high sensitivity and NPV, its moderate specificity and PPV suggest it should be used in conjunction with cytology. Regular screening and follow-up after treatment of HSIL are crucial for the prevention of cervical cancer

E-PS-05 | E-Posters Dermatopathology

E-PS-05-001

Contribution of direct immunofluorescence in the diagnosis of inflammatory dermatoses: a Moroccan study

G. Ablouh*, K. Znati
*Mohammed V University - Faculty of Medicine and Pharmacy of Rabat, Morocco

Background & objectives: The use of direct immunofluorescence (DIF) has enhanced the diagnosis of inflammatory skin conditions by identifying target antigens with specific antibodies on frozen biopsy samples. This study aims to investigate the diagnostic value of DIF in Morocco for Inflammatory Dermatoses.
Methods: We conducted a retrospective cohort study at the Anatomic Pathology Laboratory of Avicenna Hospital in Rabat. Our sample consisted of 30 patients who underwent a direct immunofluorescence (DIF) test in dermatology between 2015 and 2016. By analyzing patient records, we aimed to investigate the relationship between DIF findings and dermatological diagnoses.
Results: The study examined 30 patients who underwent direct immunofluorescence (DIF) testing for inflammatory dermatoses between 2015 and 2016. The final diagnoses for inflammatory dermatoses with positive DIF are as follows: four patients were diagnosed with pemphigus (including one deep and three superficial pemphigus), two patients were diagnosed with bullous pemphigoid, and two patients were diagnosed with lupus erythematosus. The study revealed a positive DIF value of 66% in pemphigus, 40% in bullous pemphigoid, and 30% in lupus erythematosus.
Conclusion: Our investigation demonstrated that the diagnostic value of DIF in inflammatory dermatoses is dependent on the type of dermatosis. The utilization of DIF in Morocco is below the international standard, indicating the necessity for more precise guidelines to increase diagnostic accuracy while minimizing costs. However, due to limited data, our study had a small sample size. Hence, a more extensive study is required to establish more robust conclusions.

E-PS-05-002

Primary cutaneous cribriform apocrine carcinoma. A case report

L. Aguirrezabal Marcotegui*, S. Fernández Ferrer, A. Tarín Nieto, J. Roselló Soria, I. Fernández de la Prieta, C. Valentí Ponsa, G. Cancho Galán, A. Nogueira Gegrorio
*Hospital Universitario de Basurto, Bilbao, Spain

Background & objectives: Primary cutaneous cribriform carcinoma (PCCC) is a rare histopathological variant of apocrine carcinoma of the skin that clinically presents as a solitary nodule located on upper and lower extremities. We present the case of a patient with PCCC.
Methods: A 78-year-old man with past medical history remarkable for hypertension, degenerative dementia and adenomectomy for benign prostatic hyperplasia, presented a nodule in the right groin of several

months of growth. Physical examination revealed a 2,2 cm firm nodule. A shave biopsy of the lesion was performed.
Results: Macroscopic examination revealed a skin-coloured nodule. Histologic study demostrated a proliferation of epithelial cells with oval nuclei, small nucleoli, and abundant granular eosinophilic cytoplasm that formed areas of ductal differentiation, acquiring a cribriform pattern. Intraluminal spaces showed variable morphology, some of them with micropapillae formation and a positive periodic acid-Schiff (PAS) staining of a decapitation secretion was observed. Immunohistochemical studies were positive for CKAE1/AE3, CK7, CK8.18, EMA, CEA, GCDFP15, AR, racemase, NKX3.1, GATA3, BerEP4, P53, CD57, PSA and HER2, with negative results for CK20, CK5/6, ER/PR, CD117, S100, P63, P40, calretinin, PAX8, CDX2, SMA, calponin, CD56, chromogranin and synaptophysin.
Conclusion: Diagnose of PCCC always requires ruling out a cutaneous metastasis of a primary prostatic, breast or colorectal adenocarcinoma. Although immunohistochemical study is useful in guiding the diagnosis, its value is limited and metastatic disease may be indistinguishable histologically and immunohistochemically from a primary PCCC.

E-PS-05-004
Chronic granulomatous periannexal dermatitis with tuberculoid leprosy morphology
S. Blasco Muñoz*, A. Ortiz González, A. Sánchez Espinosa, C.A. Capozzi, D. Pérez Parra, E. Guillén Saorín, A. Buendía Alcaraz, M.I. De la Hera Matute, S. Ortiz Reina
*Complejo Hospitalario Universitario de Cartagena, Spain

Background & objectives: A 59-year-old male Moroccan patient consulted for nail lesions. Suffered from seronegative arthritis with suspected erythema annulare centrifugum, distal sensory-motor axonal polyneuropathy and osteomyelitis with amputation of distal phalanx of the 2nd and 3rd fingers of the right hand.
Methods: The lesion was biopsied, showing epidermis with signs of atrophy and dermis with chronic perivascular inflammatory infiltrate and granulomatous reaction around the piloerector and perineural muscles with partial or total destruction of them. Cytologically, granulomata consisted of small accumulations of small epithelioid histiocytes and giant cells with few surrounding lymphocytes without atypia or necrosis.
Results: In addition to histological examination with hematoxylin-eosin, histochemical techniques are performed with the FITE technique (modified Ziehl-Neelsen staining technique that stains acid-fast bacilli, useful in the identification of mycobacterium leprae) and immunohistochemical techniques such as S100 (4C4.9), that expose peripheral nerves numerous acid-fast bacilli that occupy and partially destroy them. Leprosy (also known as Hansen's disease) is an infectious disease caused by Mycobacterium leprae and Mycobacterium lepromatosis that affects the skin and peripheral nerves, and if not treated in its early stages, can cause progressive and permanent lesions of the skin, nerves, limbs and eyes, causing paralysis and irreversible disabilities.
Conclusion: Although the incidence in Spain has been decreasing in recent years, this does not imply a decrease in its transmission, but in the awareness of the possibility of this diagnosis. As pathologists we must know the histopathological characteristics of this disease in order to understand it and keep it in mind in the differential diagnosis with other granulomatous dermatitis.

E-PS-05-005
p14 and p16 absent immunoexpression in the assessment of cutaneous familial and multiple primary melanoma – an Eastern-European cohort study
L. Bosoteanu*, E. Gheorghe, M. Aschie, G.C. Cozaru, M. Deacu, C.I. Orășanu, M. Boșoteanu
*Department of Dermatology, "Elias" Emergency University Hospital, Bucharest, Romania, Institute of Doctoral Studies, Doctoral School of Medicine, "Ovidius" University of Constanţa, Constanţa, Romania

Background & objectives: CDKN2A mutations represent a relatively common scene in the framework of melanoma, situated in direct relationship with p14 and p16 alterations. This study aims to identify the role of immunohistochemistry in establishing diagnostic particularities of familial and multiple primary melanoma.
Methods: A 5-year retrospective cross-sectional study was conducted on 23 patients with cutaneous familial or multiple primary melanomas. Tissue samples were examined by noting clinicopathological characteristics (anatomical site, melanoma subtype, Breslow index, mitotic rate, lymphovascular/perineural invasion) and BRAF status. Nuclear and/or cytoplasmic distribution of p14 and p16 expression on 4 µm-thick sections was evaluated, with focus on those with immunohistochemical negativity.
Results: 11 samples displayed lost p14/p16 immunoexpression. Exclusive p16-absent cases (n=7) were more frequently associated with distant metastases (85.71%), compared to 50% of the 4 specimens that lost p14 expression. The average Breslow value correlated with p16 and p14 loss was 6.79 mm and 5.37 mm, respectively. p16-absent specimens encompassed superficial spreading (SSM, 42.85%), nodular (42.85%) and acral melanomas (14.28%), among which 71.42% were ulcerated. The group with p14 loss totalled 2 SMMs and 2 nodular melanomas, with ulceration in 25%. p16-negative cases harboured an average mitotic rate of 5.28/mm2, versus the value of 2/mm2 in patients with absent p14. 50% of p14-negative and 42.85% of p16-negative specimens were BRAF-mutated.
Conclusion: This analysis highlights the value of p16 immunohistochemical absence as a predictor for aggressive biological behaviour and unfavourable prognosis in familial and/or multiple primary melanomas, in comparison with the loss of p14, regardless of the histopathological subtype. These discoveries are believed to initiate tailored diagnostic and therapeutic algorithms for the Eastern-European population with CDKN2A-mutated melanomas. More studies are necessary to develop specific therapies for patients with these characteristics, depending on the molecular and immunohistochemical particularities of affected proteins.
Funding: The paper was funded by Grant Competition in the Medical Field 2022, Contract no. 4/05.10.2022, registered at "Ovidius" University of Constanta under no. 15136/05.10.2022.

E-PS-05-006
The prognostic significance of skin eosinophil counts in bullous pemphigoid
Ö. Bülbül*, E. Tekin, F. Canaz, E. Yılmaz, B. Öztürk, H. Kaya Erdoğan
*Eskişehir Osmangazi University, Faculty of Medicine, Departmant of Pathology, Turkey

Background & objectives: Bullous pemphigoid is the most common vesiculobullous autoimmune disease and half of the patients show clinically peripheral eosinophilia. We aimed to analyse the relation between tissue eosinophil count and peripheral eosinophilia, mucosal involvement, disease severety and treatment response.
Methods: The skin biopsies of 77 bullous pemphigoid patients were reevaluated. Tissue eosinophil count was used to classify patients as having low (1-20 eosinophils/HPF) or high (>20 eosinophils/HPF) eosinophil counts. Other data, including peripheral blood eosinophilia, mucosal involvement, treatment response, lesion severity, and demographics, were also recorded.
Results: The mean age of patients was 75.08 years (range 36-95), and 51.9% were female. Tissue eosinophil count ranged from 1 to 167, with a mean count of 28.79. Peripheral eosinophilia was observed in 39% of patients. Peripheral eosinophilia was significantly correlated with mean tissue eosinophil count ($p<0.001$), and a negative correlation

was found between mean tissue lymphocyte and CRP (p=0.025). The high peripheral eosinophilia group had a more widespread disease (p=0.034), and cases with peripheral eosinophilia had a higher rate of complete remission (p=0.027). There were no significant differences between tissue eosinophil count and ESR, CRP, mucosal involvement, severity of lesions, and treatment response.
Conclusion: Tissue eosinophil count and peripheral eosinophilia are closely related. Peripheral eosinophilia was associated with disease severity and treatment response, while tissue eosinophil count was not correlated with clinical features. While the presence of peripheral eosinophilia was found to be inversely correlated with treatment response, the results also showed a negative correlation between tissue eosinophil count and mucosal involvement and treatment response. High comorbidity and advanced age in this patient group made disease control challenging, leading to potentially different study results.

E-PS-05-007
CD4/CD8 double positive and CD4/CD8 double negative mycosis fungoides: a preliminary study
E.K. Çagdas*, A. Okçu Heper, N. Özben, H. Şanli, B.A. Kirmizi, B.N. Akay
*Ankara University School of Medicine, Department of Pathology, Turkey

Background & objectives: In Mycosis fungoides (MF), the neoplastic lymphocytes expected to be CD4+ but they may be CD8+, double CD4-/CD8-, double CD4+/CD8+ with decreasing frequency. In this study, we aimed to analyse clinical and histopathological features of double CD4+/CD8+ and CD4-/CD8-cases.
Methods: Among total 651 MF diagnosed cases since 2005, selected 6 CD4+/CD8+ and 14 CD4-/CD8- MF cases were reexamined histopathologically, grouped as "double-positive group(DPG)" or "double-negative group(DNG)" according to CD4 and/or CD8 staining. Additional 41 CD4+ and 45 CD8+ cases were reexamined as a control group. The data evaluated with Chi-square, Kruskal-Wallis, Student's T tests in SPSS22 program.
Results: The severity of lymphocytic atypia in the double-positive group was significantly higher according to both the CD4+ (p=0.008) and CD8+ (p=0.002) groups. Loss of CD5 seen significantly less in the DPG according to both the CD4+ (p=0.000) and the CD8+ (p=0.000) groups. Both the DPG and DNGs affected significantly younger population comparing to the CD4+ group (p=0.002; p=0.000, respectively). Both in DPG and DNG either immunophenotypic conversion or similar immunophenotype was observed in consecutive biopsies. No statistically significant relation between immunophenotypic conversion with the duration of the lesions or the treatment applied were detected. No significant prognostic difference was not observed between the all DPG, DNG, CD4+, CD8+ MF groups.
Conclusion: Although epidermotropism of CD4+ atypical T lymphocytes is accepted as one of defining feature of MF which is well-known mimicry of various dermatitis and cutaneous lymphomas, CD4/CD8 double-negative and double-positive cases may cause diagnostic problems. Langerhans cells are considered as tricky component causing troubles defining immunophenotypical feature of intraepidermal cells. Besides the detected some histopathological distinct features like lymphocytic atypia, the preliminary results of study showed no significant clinical difference is present comparing to CD4+ MF and CD8+ MF.

E-PS-05-008
Palmoplantar psoriasis: a clinico-pathologic study on a series of 21 cases with emphasis on differential diagnosis
R. Caltabiano*, M. Failla, A. Palicelli, M. Zanelli, F. Sorci, G. Broggi
*Department of Medical and Surgical Sciences and Advanced Technologies "G. F. Ingrassia", Anatomic Pathology, University of Catania, Italy

Background & objectives: Palmoplantar psoriasis is a variant of psoriasis, that shares clinical and histologic features with eczema, hand dermatitis and allergic contact dermatitis. The present study aims to characterize the histologic features of palmoplantar psoriasis on a series of 21 cases.
Methods: The following morphological features and their distribution were included: parakeratosis, dilated vessels in papillary dermis, psoriasiform acanthosis with elongation of rete ridges, perivascular lymphocytic infiltrate, decrease/loss of granular layer, Munro's microabscesses, spongiform pustules of Kogoj, spongiosis and lymphocytic exocytosis.

Results: A total of 21 adult patients with histopathologically proven palmoplantar psoriasis were included. In all cases, exhibited parakeratosis and parakeratotic areas, that alternated both vertically and horizontally with orthokeratotic areas. The features we observed more frequently included: parakeratosis alternated with orthokeratotic areas, presence of congested, dilated, and tortuous vessels in the papillary dermis, and decrease/loss of the granular layer. These findings, including neutrophils in the stratum corneum, could be considered a diagnostic clue of palmoplantar psoriasis.
Conclusion: The main diagnostic clues and histologic differential diagnoses are also presented.

E-PS-05-009
Pinkus and the enigma of the skin basal cell carcinoma variants? A two-cases report
I.G. Cocuz*, R. Niculescu, A.H. Sabau, M.C. Popelea, O.S. Cotoi
*UMFST Targu Mures, Romania

Background & objectives: The fibroepithelial basal cell carcinoma (Pinkus tumour) is a non-melanocytic skin cancer type, classified by the WHO Skin tumour classification 2018 as being a variant of basal cell carcinoma. The origin of this rare tumour is still disputed.
Methods: We present two cases of Pinkus tumour from two female patients aged 53 and 68 years old who had a surgical excision of a small coloured nodule on the lumbar region. The tissue samples were sent to the Pathology Department for the histopathological diagnostic. H&E staining and immunohistochemistry (Bcl-2, CK AE1/AE3, Ki67) were performed.
Results: Microscopically, a tumour cell proliferation was observed, composed of strands of tumour cells with a basaloid aspect which were arising from the epidermis. The tumour cells were of small dimensions, and presented cito-nuclear atypia, with reduced basophilic cytoplasm and enlarged hyperchromatic nuclei. In-between the tumoral cords, a fibrous stroma was observed. No basaloid tumour cells islands were present. Immunohistochemically, the tumoral cells were positive for Bcl-2 and CK AE1/AE3. The Ki67 proliferation index was about 5-10% in the tumoral cells. The tumour was completely removed in the surgical safety limits.
Conclusion: Even though the Pinkus tumour is rare, the histopathological diagnostic should be based on the characteristic basaloid cells arranged in strands. Our two cases had a very similar aspect and based on the H&E and immunohistochemically profile, the diagnostic of Pinkus tumour was established. The origin of the tumour is still disputed between basal cell carcinoma and trichoblastoma, but in general, the complete excision of the tumour is the indicator for a good outcome of the patient.

E-PS-05-010
Are nevus remnants associated with the incidence of LMM?
E. Colon*, I. Drakensjö
*UNILABS SWEDEN, Sweden

Background & objectives: Previous studies have shown that LMM is less likely to have evidence of nevus remnants compared to other

melanomas. The aim of this study is to detect the incidence of nevus-associated LMM (NALMM) and its relationship with histopathologic aspects.
Methods: We conducted a retrospective observational study from histopathology reports of patients treated with Grenz rays (GR) Bucky, for lentigo maligna (LM) and lentigo maligna melanoma (LMM), at the dermatology department, Karolinska University hospital, Sweden, between January 1, 2004 to December 31, 2016. A total of 348 reports were reviewed for the presence of benign melanocytic nevus, with the LM/LMM
Results: Nine patients (21%) in the NALMM group had more than 50 melanocytic nevi compared to 13 patients (8%) from the control group. Twelve patients (27%) in the NALMM group had previously removed at least one dysplastic nevus (p= 0.04) and 11 patients (26%) had been diagnostic with another melanoma, of which 7 of those (64%) were also nevus-associated melanoma.
In the study group, two male patients, with facial in situ lesions with deep follicular distribution (1,6 mm and 1,7 mm), developed melanoma metastasis. One patient was treated with cryotherapy, before surgical removal, and 10 years after treatment developed a brain metastasis, with the same molecular signature as the initial LM.
Conclusion: When focusing on LMM we found discrepancies compared to previous reports. Three possible explanations for this sample variation can be due to the interpretation of these intradermal micro nevi. The first one, they are considered incidental, a collision phenomenon; the second, the micro nevi are hidden between histological cuts; and the third, they are considered an invasive part of the LMM since they can present challenges difficulty when trying to differentiate such nevi cells from melanoma.

E-PS-05-011
Three cases of cutaneous AL-amyloidoma/ primary cutaneous marginal B cell lymphoma, associated to Sjögren syndrome. Utility of fluorescence microscopy in the identification of dermal amyloid
A. Córdoba*, I. Fernandez, C. Llanos, J.I. Yanguas, C. Cerezo, M.R. Mercado, D. Guerrero-Setas
*Hospital Universitario de Navarra, Spain

Background & objectives: We hypothesize that the association between cutaneous AL-amyloidoma and Sjögren syndrome (SS) further supports the biological link between the first one and pc Marginal Zone Lymphoma. Detection of amyloid in the dermis under fluorescence microscopy (FM) might be very useful.
Methods: We report three patients with SS (two women, one man), aged 67-77 years-old. Infiltrated plaques in lumbar and leg skin were observed, being unique in two patients and multiple in the third one.
Results: Histologically, deposits of amyloid were observed in the papillary and reticular dermis, associated with a sparse perivascular infiltrate of lymphocytes and plasma cells. Congo red resulted lightly positive.
Amyloid substance gives a bright red fluorescence stained with Congo red in paraffin-embedded tissue sections examined under FM with Texas Red (TR) and double FITC/TR filters, confirming the diagnosis with high specificity.
We have observed light chain restriction in two cases, confirming the clonal nature by B rearrangement in two cases.
Conclusion: The use of FM with TR and double FITC/TR filters is useful to confirm the diagnosis of cutaneous AL-amyloidoma.
Despite the overall rarity of this disease, an association has been established with chronic autoimmune diseases, especially SS.
It might be hypothesized that in a small subset of pcMZL with extensive plasmacytic differentiation, the monotypical immunoglobulin light chains find the necessary physicochemical conditions to undergo extensive amyloidization.
SS is the autoimmune disorders associated with the highest risk of lymphoma, particularly MZL.

E-PS-05-012
Melanocytic spitzoid lesions with FISH-positive abnormalities. BRAF V600E, PRAME and BAP1 assesment
A. Córdoba*, C. Cerezo, C. Llanos, G. De Lima, M. Montes, J.I. Yanguas, D. Guerrero-Setas
*Hospital Universitario de Navarra, Spain

Background & objectives: Melanocytic spitzoid lesions are difficult to diagnose, with lack of concordance among experts. Here we evaluate the usefulness of molecular analysis (FISH and BRAF mutation) and new immunohistochemical (IHC) markers (PRAME and BAP1) for diagnosis and classification of melanocytic lesions.
Methods: The group of study consists of all spitzoid melanocytic lesions with atypia diagnosed in the period 2018-2022 in our institution (n=42 cases). FISH was performed by using the Melanoma Multiprobe set composed of RREB1 (6p25), MYB (6q23), CCND1 (11q13) and p16/CDKN2A (9p21) genes. BRAF p.V600E mutation study was analysed by qPCR and PRAME and BAP1 expression was evaluated by IHC.
Results: Abnormalities were observed in 17 (40.4%) FISH-positive cases; 3 out of 17 cases displayed two abnormalities.
p16/CDKN2A abnormalities were the most prevalent, with homozygous (11, 64.7%) or heterozygous loss (3, 17.6%).
MYB, RREB1 and CCND1 were gain in 3 (17.6%), 2 (11.7%) and 1 case (11.7%), respectively.
BRAF p.V600E mutation was observed in 9 (52.9%) of these 17 cases. 5 cases with homozygous p16 loss displayed this mutation.
PRAME was positive in 4 BRAF-mutated cases whereas the three BAP1-negative cases showed BRAF mutation.
Conclusion: - We observed that FISH-positive cases showed high incidence of BRAF mutation and PRAME expression, alterations associated to melanoma or Spitzoid melanoma.
-The integration of these diagnostic tools could help in the differential diagnosis in spitzoid melanocytic lesions which could allow to differentiate nevus (FISH-negative), melanoma (FISH-positive + PRAME-positive) and Spitz melanoma (FISH-positive + p16 loss + BRAF-positive + BAP1 negative).

E-PS-05-013
Superficial acral fibromyxoma – rare lesion or unknown entity?
S. Costache*, A. Baltan, A. Gont, A. Chefani, M. Sajin, C. D'Arrigo
*University Emergency Hospital Bucharest, Poundbury Cancer Institute, Romania

Background & objectives: Superficial acral fibromyxoma (SAF) is a rare, slow growing, benign mesenchymal tumour that was first described by Fetsch et al. in 2001. It typically occurs on the fingers and toes, particularly in the nail bed or under the nail.
Methods: We present two cases of SAF, one of a 63 year old male on second toe right foot and the other of a 62 year old female on left index. Both lesions were sampled, fixed in formalin, processed and embedded in paraffin and further studied using conventional stains and ancillary immunohistochemical (IHC) studies.
Results: Grossly both lesions have a firm, solid, grey and uniform cut surface. Histologically they consist of a large, round, well defined and non encapsulated spindle cell, deep seated dermal lesion with a small overlying grenz zone. The lesion shows a moderately cellular population of bland fibroblastic cells each surrounded by a small amount of myxoid ground substance. These cells are in close association with relatively thick collagen bundles and form randomly arranged loose fascicles with inconspicuous thin, short and curved vessels. There is no necrosis and mitoses are not a feature. IHC studies show that the component cells are diffusely CD34 positive and S100, EMA, SMA and Desmin negative.
Conclusion: SAF is usually diagnosed using IHC studies and the main differential diagnosis includes superficial angiomyxoma, myxoid neurofibroma and perineurioma. Due to its rarity and being recently described,

pathologists should be aware to include it in the differential diagnosis of fibromyxoid tumours of acral sites. There has been no report of malignant transformation, however incompletely excised SAF has a tendency to recur. An early diagnosis, along with complete resection and follow up can prevent recurrence.

E-PS-05-014

Prevalence and patterns of NTRK immunohistochemistry in Spitz lesions: a single-centre study

C. Dahlstedt-Ferreira*, F. Nogueira, I. Leskiv, M. Dias, J. Nogueira, D. Gomes Pinto
*Hospital Garcia de Orta, EPE, Portugal

Background & objectives: Diagnosing melanocytic proliferations can be challenging, which is particularly true for Spitz lesions. Various genetic alterations have been described in these, namely NTRK-fusions. This study aims to describe the prevalence of NTRK immunohistochemistry positivity and staining patterns in Spitz lesions.
Methods: We collected 48 Spitz lesions from our institution over the past five years. All cases of histologically confirmed Spitz lesions were included. NTRK immunohistochemistry was performed using the VENTANA pan-TRK(EPR17341) assay, divided into positive (threshold of ≥1% stained cells) and negative. The study is ongoing, with molecular correlation and confirmation using the IdyllaTM-Gene Fusion Assay(Biocartis) planned for the next stage.
Results: Our sample included 32 Spitz Nevi, 8 Reed Nevi, 3 AST, and 5 Spitzoid Melanomas. Five cases demonstrated pan-TRK positivity (1 Reed Nevi, 4 Spitz Nevi), with varying intensity and staining pattern. Cytoplasmic and/or membrane staining were considered positive. No AST or Spitzoid Melanoma cases showed pan-TRK positivity. The observed prevalence of NTRK immunohistochemistry positivity is consistent with published literature for Spitz lesions, 2 of the Reed Nevi showed a weaker staining pattern, with an added difficulty due to the high deposition of melanin pigment, being considered negative on immunohistochemistry and waiting for molecular studies.
Conclusion: Our study provides insight into the prevalence of NTRK immunohistochemistry positivity and staining patterns in Spitz lesions. This seems to be in line with the literature for more expensive molecular tests, supporting the role of immunohistochemistry as a surrogate marker. We identified different staining patterns in different pathologies, which could be a path of future research. Validation in larger, multicenter cohorts is warranted to confirm our findings and refine diagnostic approaches for NTRK testing in Spitz lesions.

E-PS-05-015

Subcutaneous and pulmonary nodules in a patient with systemic lupus erythematosus

F. Dolkiras*, N. Stavrinou, P. Vlachou, A. Therapontos, C. Vourlakou
*Evangelismos General Hospital, Pathology Department, Greece

Background & objectives: A 75-year-old patient with a history of systemic lupus erythematosus presented with subcutaneous nodules in the left thigh. Upon imaging, bilateral pulmonary nodules were found. Biopsies were taken from both the lung and the subcutaneous nodules.
Methods: Histopathological examination of the subcutaneous nodule revealed ischemic necrosis of the subcutaneous fat. Closer examination revealed an angiocentric processes with fibrinoid necrosis of the vessel wall. The infiltrate was transmural and polymorphous with occasional clusters of large cells. The nodule of the lung was completely necrotic with no viable cells.
Results: The large cells were positive with various B cells markers and in situ hydrization for EBV associated RNAs (EBER) was positive. A differential diagnosis between EBV-positive DLBCL, NOS, lymphomatoid granulomatosis grade 3, diffuse large B-cell lymphoma, lymphomatoid granulomatosis-type, EBV+ in the setting of immune deficiency/dysregulation (systemic lupus erythematosus under treatment with azathioprine) was raised. The EBV viral load was low, the systemic lupus erythematosus was managed with azathioprine which was halted 6 months prior to the presentation. Upon clinicopathological correlation the overall picture and the sites involved were more consistent with a diagnosis of lymphomatoid granulomatosis grade 3.
Conclusion: Lymphomatoid granulomatosis is a rare disease easily overlooked by the clinicians and the pathologists and should be in the differential diagnosis of patients presenting with pulmonary-cutaneous nodules

E-PS-05-016

Evaluating the diagnosis of mycosis fungoides: a uni-centre, multi-year approach

D. Egong*, C. Brodie, H. Ingoldsby, A. Shalaby, S. Phelan
*University of Galway, Ireland

Background & objectives: The International Society for Cutaneous Lymphomas (ISCL) describes a set of criteria for diagnosing early mycosis fungoides (MF), which is not in routine use. This study evaluates the MF diagnostic reports in University Hospital Galway (UHG) against the ISCL criteria.
Methods: Cases of cutaneous haematopoietic cell malignancies diagnosed in UHG from January 2011 to December 2022 were retrieved from the electronic health record system using the search terms: 'skin', 'lymphoma', and 'mycosis fungoides'. Clearly diagnosed MF cases were identified. The clinical, histopathological, molecular, and immunopathological features reported for these cases were compared against the ISCL diagnostic criteria and scored.
Results: 19 of the 109 retrieved cases were reported as cutaneous T-cell lymphomas. 18 were classified as MF. One case was reported as lymphomatoid papulosis; one of the MF cases was diagnosed as pagetoid reticulosis. These two reports were not scored. Within the twelve-year period, MF diagnosis ranged from 0 to 4 cases per year. 17 cases reported adequately on histopathological features, 14 on molecular, 9 on clinical and 7 on immunopathological features. Patients' age at diagnosis ranged from 27 to 84 years old. The most frequently demonstrated T-cell receptor (TCR) gene rearrangements affect V-J1+2 and D-J domains in the TCRB chain, and V1+10-J and V9+11-J domains in the TCRG chain.
Conclusion: The ISCL criteria is useful in aiding MF diagnosis. Our study reveals that clinical information, such as persistence of skin plaques and poikiloderma should be reported during specimen submission. Immunopathological reporting of CD2, CD3, CD5, and CD7 positivity should include an estimated percentage. Dermo-epidermal discordance of said markers should also be noted. The low number of MF cases diagnosed over a period of twelve years signals that a multi-centre study should be undertaken to better characterise MF patient epidemiology.

E-PS-05-017

A strange debut: antiphospolipid syndrome with extensive cutaneous necrosis and no systemic involvement

G. Escuer*, P. Puente López, R. Escudero-Tornero, T.G. Sobral-Costas, E. Sendagorta-Cudós, J.M. Busto-Leis, E. Ruiz-Bravo, M.J. Beato-Merino
*La Paz University Hospital, Spain

Background & objectives: Antiphospolipid syndrome (APS) has a wide spectrum of skin manifestations from livedo reticularis to skin ulcers. Extensive cutaneous necrosis is rare but possible. We present a case with an unusual onset: extensive skin necrosis without systemic involvement.
Methods: For this case report we searched the patient´s electronic medical records and analytics from his arrival at the emergency room as well as the medical history of a previous admission in another centre. For the literature review we searched Pubmed.

Results: A 74-year-old woman was referred to our centre due to extensive purpuric lesions centred on the lower limbs of one week of evolution that occupied 15% of the total body surface.
During admission, she presented an excellent general condition with no clinical or analytical alterations (including hepatic and renal profiles), except for a lengthening of the activated partial thromboplastin clotting time. Given the suspicion of APS, a skin biopsy and a battery of antibodies were performed.
The skin biopsy showed intravascular thrombi in small-vessels of the dermis and superficial subcutaneous tissue without associated inflammation. These findings, together with positive lupus anticoagulant antibodies, led to the diagnosis of APS.
Conclusion: APS can manifest with very diverse skin alterations, including extensive necrosis. When present, it is usually accompanied by significant damage in different organs such as the kidney, lung or brain, due to microthrombi, with subsequent severe clinical picture called catasthrophic APS. However, as in our case, APS may be limited to extensive skin necrosis with no manifestations at other levels.

E-PS-05-018
Consumption, discohesion, acantholysis and bullous changes. Malignant melanocytes ability that can affect diagnosis and prognostic parameters definition. How to manage such cases?
A. Filosa*, F. Giantomassi, G. Cazzato, C. Rubini, G. Goteri
*Polytechnic University of Marche Region, Pathological Anatomy Unit, Italy

Background & objectives: Melanoma can present a variety of histological variants, many of which are exceedingly rare. Architectural variants displaying prominent discohesion include the more recently described bullous and acantholytic-like melanomas. Acantholytic/bullous changes in malignant melanoma have been rarely reported.
Methods: We present two unique cases of malignant melanoma with varying degrees of extensive melanocytic discohesion.
Results: The present case series describe two cases of malignant melanoma with varying degrees of extensive melanocytic discohesion: the first shows acantholytic pattern mimicking pemphigus vulgaris, the second is a case of bullous melanoma. Discohesion between melanocytes and between melanocyte and keratinocyte may reflect a more aggressive behaviour of melanoma with consumption being the epiphenomenon of progression of the melanoma itself, with loss of control of the keratinocyte-melanocyte relationship. The mechanisms leading to bullous, and acantholytic-like melanoma, are not known. Apart from melanocyte discohesiveness, local trauma may play a role. Discussion is still unclear whether undiscovered antigens contributed to this pattern of discohesion between melanocytes in similar cases.
Conclusion: The histopathologist should be aware of this rare and peculiar presentation of a melanoma mostly for the implication in indicating the exact staging and prognostication of the patients. There are significant problems in estimating the Breslow index in cases such these and it is recommend subtracting the thickness of the blister to obtain a more accurate measurement.

E-PS-05-019
Fumarate hydratase deficient pilar leiomyoma: a case report
Z. Gramc*, V. Hosta, B. Hrvatin Stančič
*Department of Dermatovenereology, University Medical Centre Ljubljana, Slovenia

Background & objectives: Pilar leiomyomas (PLs) are benign dermal smooth muscle tumours. Multiple PLs are commonly inherited and can be associated with hereditary leiomyomatsis and renal cell cancer syndrome (HLRCCS). HLRCCS is a result of heterozygous mutations in the fumarate hydratase (FH) gene.
Methods: 39-year old male presented with multiple firm pink papules distributed in zosteriform pattern which he had for about two years, with new lesions appearing over time. He was otherwise healthy with no reported history of significant or hereditary diseases in the family. Clinical impression was keloid formation after herpes zoster infection. A punch biopsy was performed.
Results: Histopathological examination showed dermal tumour composed of intersecting bundles of spindle cells with eosinophilic cytoplasm and blunt-ended, elongated nuclei with perinuclear halos. Focal nuclear hyperchromasia, cytological atypia and rare mitoses were observed. Immunohistochemical studies revealed diffuse and strong immunoreactivity for smooth muscle actin, caldesmon and desmin, besides loss of FH was demonstrated. Diagnosis of FH deficient pilar leiomyoma was made. Patient was advised to undergo genetic testing. DNA mutation analysis of the FH gene was performed which detected heterozygous germline mutations in the FH gene. To our patient yearly genetic counselling and magnet resonance of abdomen were advised as well as genetic analysis for his children and siblings.
Conclusion: PLs are difficult to diagnose by clinical evaluation, but can be easily recognized and confirmed with histological examination. Recognition of FH deficient PLs can lead to diagnosis of HLRCCS, a rare genetic disorder associated with benign cutaneous and uterine leiomyomas and aggressive renal cell carcinoma. Early identification, comprehensive clinical assessments and surveillance influences patient management and can provide positive outcomes to affected individuals and their families.

E-PS-05-020
Primary cutaneous apocrine carcinoma on congenital nevus sebaceus: a case report
G. Güngör Sahin*, Y. Ozluk, M. Gulluoglu, S. Yucel, D. Yasar Aksoyler, S. Ozturk Sari
*Istanbul University, Istanbul School of Medicine, Department of Pathology, Turkey

Background & objectives: Apocrine carcinoma is rare cutaneous adnexal neoplasm with unclear histogenesis. Although commonly seen in the axilla, it may also occur on scalp. This case report outlines clinicopathological characteristics and diagnostic challenges of primary apocrine carcinoma arising in nevus sebaseus background.
Methods: A 62-year-old male patient presented with a congenital right parietotemporal mass, which had been progressively enlarging over the past decade and had developed ulceration within the most recent year. Excision was performed with a prediagnosis of squamous cell carcinoma.
Results: Gross examination revealed an irregularly circumscribed, polypoid mass with a central ulcer. Microscopically, dermal tumoral infiltration with tubular structures of varying sizes were observed. Some tubular structures showed central necrosis. Eosinophilic cytoplasmic protrusions and a decapitation sign were present in some cells. Immunohistochemistry was negative for ER, PR and D2-40, positive for AR and GATA3, focally positive for GCDFP15. p63 antibody highlighted the myoepithelial cells in the in situ component. Nevus sebaceus was observed surrounding the tumour.
Conclusion: Apocrine carcinomas have been reported to arise from benign lesions such as spiradenoma, apocrine mixed tumour, and nevus sebaceus. Metastatic breast cancer should be considered in the differential diagnosis, particularly for axillary lesions. The presence of nevus sebaceus background and in situ components facilitated the diagnosis of a primary apocrine carcinoma in our case. Meticilous microscopic and gross examination should be performed when necessary to identify the background lesion and demonstrate the in situ component.

E-PS-05-021
CRTC1::TRIMM11 cutaneous tumour: a new entity
G. Güngör Sahin*, I. Yılmaz, D. Yavuz Zor, S. Ozturk Sari
*Istanbul University, Istanbul School of Medicine, Department of Pathology, Turkey

Background & objectives: CRTC1::TRIMM11 cutaneous tumour is a new entity in the 5th edition of WHO classification. It commonly occurs in the extremities of patients of various ages. Although they are expected to behave indolently, the scarcity of cases makes this uncertain.
Methods: We present the case of a 14-year-old girl with a 1 cm exophytic nodular lesion on the shoulder that was clinically suspected to be a sweat gland tumour. The lesion was excised for pathological examination. In addition to light microscopy, immunohistochemical analysis (IHC-a), fluorescence in situ hybridization (FISH) and Next-generation sequencing (NGS) were performed.
Results: Histopathological analysis revealed a spindle-cell tumour in the dermis with a well-circumscribed border. The tumour cells had large cytoplasm without pigment, and some of them had conspicuous nucleoli. They were arranged in intersecting fascicles, with striking fibrous bundles weaving in between them. The mitotic rate was very low and atypical forms were not observed. The differential diagnoses included melanocytic tumours and dermal clear cell sarcoma. IHC-a demonstrated focal S100 and diffuse SOX10 positivity. Melan-A, HMB45, PRAME, PANTRK, and BRAF-VE1 were negative. EWSR rearrangement was investigated using a break-apart FISH probe and the results were negative. RNA sequencing using NGS revealed a CRTC1::TRIMM11 translocation.
Conclusion: Dermal tumours with a differential diagnosis of clear cell sarcoma or metastatic melanoma with SOX10 expression and negative EWSR rearrangement, should raise suspicion for CRTC1::TRIMM11 cutaneous tumour. We believe that with increased awareness of this entity, more cases will be identified, leading to the accumulation of demographic, histopathological, and clinical data.

E-PS-05-024
Bullous dermatitis artefacta secondary to aerosolized spray abuse in a child. Case report and review of histomorphological changes in factitious dermatitis
K. Kamarádová*, L. Krbal, J. Bartoňová
*Fingerland Department of Pathology University Hospital Hradec Králové, Czech Republic

Background & objectives: Dermatitis artefacta is a psychocutaneous condition with self-inflicted skin injuries addressing a psychological need. The disorder is often underdiagnosed focusing on search for an underlying somatic cause. Even in cases with clinicopathological suspicion the subsequent confirmation is often impossible.
Methods: Here we report a case of 12-year-old girl with a confirmed diagnosis of cryothermic bullous dermatitis artefacta caused by an aerolised spray abuse. The patient was examined in our institution after a three-year history of bullous lesions appearing on various areas of the body.
Results: Clinically, the lesions were nearly circular blisters filled with serous fluid, raising a suspicion of a bullous disease followed by a complex examination. Despite the initial treatment by prednisone the patient developed new lesions, some with progression to an ulcer or eschar.
Punch biopsy was performed twice with negative direct immunofluorescence. First biopsy revealed lichenoid type of dermatitis with necrotic keratinocytes. Second biopsy contained a blister with necrotic epidermis with suspicion of bullous erythema multiforme. Persistent formation of lesions without any support for a somatic cause led to a suspicion of possible self-harm which was later admitted by the patient after repeated psychiatric evaluation.
Conclusion: Although dermatitis artefacta is primarily a psychiatric disease, it can mimic true dermatosis and thus may be first seen by a dermatologist and possibly by a pathologist. Self-inflicted skin lesions have various mechanisms of injury upon which the histopathological picture is dependent often resulting in descriptive diagnosis. Main types of injury mechanisms and microscopic patterns are therefore reviewed emphasizing that dermatitis artefacta is a challenging diagnosis, but it should be considered in uncommon cases of recurrent skin lesions.
Funding: Supported by the project BBMRI-CZ LM2023033.

E-PS-05-025
Malignant blue naevus as (undiscovered) primary site of recurrent melanoma metastases?: a case report
L. Kovac*, G. Zamolo, T. Vučković, M. Belušić
*KBC Rijeka, Croatia

Background & objectives: Our aim is to present a case of a potentially malignant alteration of a blue naevus lesion and draw attention to the importance of researching this lesion, which, without proper diagnosis and therapy, can have life-threatening consequences.
Methods: A 36 year-old male presented himself to a Clinic for Maxillofacial surgery with a sudden, painless swelling in the right preauricular region, measuring 3x2 cm. A tumour mass in the right parotid gland was found. Cytology showed that it was a metastasis of melanoma. Superficial parotidectomy of the affected gland was indicated and then performed, with an orderly postoperative course.
Results: Pathohistological analysis of the removed gland confirmed the diagnosis of metastatic melanoma. A search began for the primary melanoma site, which was never found. From the anamnesis, it was learned that the patient earlier underwent surgical excision of a mole on the right side of the temporal region. The pathohistological diagnosis of the excised mole showed that it was a benign blue naevus lesion. In the following years, the patient had regular controls and examinations which revealed multiple melanoma metastases throughout his body, for which he underwent more than 20 surgical procedures. The latest findings show two melanoma metastases that were found in the patient's brain.
Conclusion: Although the blue naevus lesion is a frequent diagnosis new findings point out the potential for malignant alteration, based on the increasing number of described cases. It is necessary to deepen the research on this potentially dangerous lesion, until it is determined when, in what way and if at all blue naevus can turn malignant, which will allow diagnostics and treatment to be reevaluated and performed more precisely, bettering the survival and quality of patients' lives.

E-PS-05-026
Fibro-osseous pseudotumour of the digit, arising in the distal phalanx of the thumb in a middle aged woman, a rare dermal and soft tissue tumour, a case report and review of literature
F. Kubba*, S. Hughes, A. Owen
*Department of Histopathology, Ealing Hospital, London North West University Healthcare NHS Trust, Middlesex, United Kingdom

Background & objectives: A 56-year-old female presented with a slowly growing 13 mm ulcerated painful nodule on the pad of the right thumb, clinically thought to be a ruptured cyst It was locally excised. No recurrence was reported. No imaging was available.
Methods: Microscopy showed a dermal tumour not connected to epidermis, expressing an irregular nodular growth pattern and composed of fascicles of variably cellular, spindle-shaped cells with minimal to mild cytological atypia, focally increased mitosis, dispersed in a pale myxoid stroma and focally reminiscent of nodular fasciitis. Widespread areas of cartilage, trabeculae of osteoid formation and osteoblastic rimming were seen.
Results: Diagnosis: Fibro-osseous pseudotumour of the digit (FOPD). 21 cases were first described by Dupree et al in 1986; microscopically resembling myositis ossificans (MO) but lacking zoning. The presence of hypercellularity, mild cytological atypia and increased mitosis may be confused with parosteal or extraskeletal osteosarcoma.

The tumour involves mostly the fingers, toes, hands and can be subungual, with sizes ranging from 0.8 to 5.6 cm.
The differential diagnosis includes: extraskeletal osteosarcoma, exostosis, MO, bizarre parosteal osteochondromatous proliferation (Nora lesion).
In one study, 80% harboured USP6 rearrangements showing that FOPD belonged to the spectrum of clonal transient neoplasms including: aneurysmal bone cyst, nodular fasciitis, MO and giant cell lesion of small bones.
Conclusion: We have presented a rare case of fibro-osseous pseudotumour of the digit arising mainly in fingers and toes of young patients. Histologically it is a dermal/soft tissue tumour showing a combination of spindle cells, myxoid stroma, trabecular bone, cartilage and osteoblasts, lacking zoning and without significant atypia. Treatment is by local excision and it rarely locally recurs. It can mimic MO but it is important not to confuse it with osteosarcoma which arises in older patients. Imaging may be helpful.

E-PS-05-027

B-cell pseudolymphomatous scarring alopecia due to cutaneous discoid lupus erythematosus, a case report and review of literature

F. Kubba*, F. Teixeira, D. Schulman, K. Naresh
*Department of Histopathology, Ealing Hospital, London North West University Healthcare NHS Trust, Middlesex, United Kingdom

Background & objectives: A 76-year old female with history of osteoarthritis presented with a 2 cm crusted lesion on the vertex surrounded by and 5 cm area of scarring alopecia. Basal cell carcinoma was suspected. She underwent a surgical excision and primary closure.
Methods: Microscopy: The skin showed focal ulceration with a dense inflammatory cell infiltrate in the mid-deep dermis sparing the epidermis and involving the subcutis, forming lymphoid follicles with germinal centres. The infiltrate included small lymphocytes, plasma cells and occasional eosinophils. The edge showed a perifollicular/interfollicular lichenoid infiltrate, surrounding the isthmus and infundibulum of the hair follicles with thickened basement membrane zone.
Results: No obvious mucin deposition was seen on Alcian blue. On immunohistochemisty, the follicle centre cells expressed CD10, CD20, IgD (weak) and BCL6.
They were negative for BCL2, CyclinD1 and CD5. Ki67 was high, highlighting zonation. Plasma cells expressed MUM1 and were polytypic for light chain expression.
Our working diagnosis was a B-cell pseudolymphomatous scarring alopecia caused by cutaneous discoid lupus erythematosus (DLE). A true follicular lymphoma was excluded clinically and histopathologically.
On review of the literature, we found cases of cutaneous B-cell lymphoma arising in longstanding systemic lupus erythematosus, lupus tumidus mimicking primary cutaneous marginal zone B-cell lymphoma and cases of lichenoid cutaneous lupus erythematosus-lichen planus overlap syndrome.
Conclusion: We have presented an elderly woman who had histological features of a B-cell pseudolymphomatous scarring alopecia in the vertex with features of active DLE in the periphery. This is regarded as a complication of longstanding DLE. A punch biopsy from the active edge as well as the central ulcer also may have carried a good diagnostic yield. It is important in cases of tumours arising in longstanding DLE to exclude a true cutaneous B-cell lymphoma clinically and on histopathology.

E-PS-05-028

Lupus profundus of the scalp associated with nonscarring alopecia, skin plaques and rheumatoid arthritis in a young Afro-Caribbean man, an unusual case report necessitating a multidisciplinary team approach

F. Kubba*, A. Jay, R. Agrawal, M. Ratynska, C. Martyn-Simmons, A. Liyadipita, N. Kalavrezos, E. Calonje
*Department of Histopathology, Ealing Hospital, London North West University Healthcare NHS Trust, Middlesex, United Kingdom

Background & objectives: A 26 year old Afro-Caribbean male with recent history of rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), presented in rheumatology clinic with bilateral raised erythematous, non-itchy lumps on scalp with nonscarring alopecia and plaques on the shoulder and back.
Methods: The first two scalp punch biopsies were nondiagnostic, followed a year later by a large 4 cm x 2.5 cm deep skin excision, including the galea aponeurotica, which showed perivascular/perifollicular superficial and deep dermal/subcuticular lymphohistiocytic aggregates. Alcian blue and colloidal iron highlighted widespread mucin depostion. The epidermis showed no evidence of basal cell apoptosis, interface dermatitis or basement membrane thickening.
Results: Most of the lymphocytes in the infiltrate were T cells (CD3+); predominantly(CD4+) with less (CD8+). CD123 showed aggregates of plasmacytoid dendritic cells.
Diagnosis: Lupus profundus of the scalp associated with SLE and RA.
The superficial biopsies suggested vasculitis and the diagnosis was missed twice due to the shallow sampling. Wide excision was undertaken to exclude a tumour or lymphoma.
Lupus profundus (lupus panniculitis) of the scalp is a rare presentation of chronic cutaneous LE. It is found in 1–3% of patients with SLE and can be associated with linear, arched or annular alopecia along Blaschko's lines. It responds well to treatment with oral prednisolone and hydroxychloroquine, with intralesional triamcinolone acetonide injections.
Conclusion: We have presented a rare case of lupus profundus of the scalp, associated with nonscarring alopecia and skin plaques in the shoulder and back. The initial punch biopsies suggested vasculitis and failed to nail the diagnosis due to the superficial sampling. The patient ended up with a large excision to achieve the final diagnosis. This presentation shows the importance of multidisciplinary approach in this unusual site and supports the need of a deep incisional biopsy from the first instance.

E-PS-05-029

Acute extensive and advanced stage Marjolin's ulcer arising within a below knee amputation stump ulcer in a middle-aged man, a case report and review of literature

F. Kubba*, I. Logan, B. Gaglani, P. Baghla
*Department of Histopathology, Ealing Hospital, London North West University Healthcare NHS Trust, Middlesex, United Kingdom

Background & objectives: A 55-year-old Asian male was admitted with an infected ulcer of a right below knee amputation stump. A midtibial amputation had been performed following a traumatic injury 8 months previously. Past medical history: hypertension, non-alcoholic fatty liver disease and hyperlipidaemia.
Methods: On examination there was an extensive large fungating tumour/ulcer of the entire stump measuring 21x13cm with hypergranulating indurated margins. Multiple 1-2 cm groin lymph nodes were palpable. Features were those of a Marjolin's ulcer.
MRI scan of the right knee showed high-signal enhancement of soft tissues. CT scan chest/abdomen/pelvis showed bilateral inguinal lymphadenopathy. An above knee amputation was completed.
Results: Microscopy: Invasive moderately differentiated squamous cell carcinoma(SCC) of no special type, invading 75mm into the subcutis and fibula and consuming neurovascular bundles; stage pT4a pN0 pMx with free resection margins.
At 10 month follow-up: No evidence of locoregional recurrence or distant metastasis.

A Marjolin's ulcer is a rare and aggressive cutaneous malignancy developing within sites of previously-injured skin, scars, and chronic wounds. (French surgeon/pathologist Jean-Nicholas Marjolin). The most common malignancy is SCC. Burn scars are the most common underlying aetiology. Tumours have also been reported to arise in; traumatic wounds, osteomyelitis, venous ulcers, pressure ulcers, radiation dermatitis, stings, hidradenitis suppurativa, and inflammatory disorders. The lower extremity is most frequently affected.
Conclusion: We have described the rare case of an acute extensive 21cm Marjolin's ulcer (SCC) unusual in its development within one year of injury. In the chronic form (>1 year from injury) the average duration to malignant transformation is more than 30 years. Presentation within five years of injury, and with an exophytic formation as in this case are regarded as positive prognostic indicators. Aggressive management and close clinical follow-up is required due to the high-risk of recurrence and metastasis.

E-PS-05-030
A case report: balloon cell malignant melanoma
K. Kurt*, A. Orgen Calli
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Balloon-cell malignant melanoma (BCMM) is rare variant composed of foamy cells with abundant cytoplasm causing ballooning of cells. These features can also be seen in balloon cell nevus. Nevertheless, nuclear pleomorphism, mitoses, and lack of melanocyte maturation help differentiate BCMM.
Methods: Histomorphological features were assessed with hematoxylin-eosin sections in view of macroscopic and clinical features. Additionally, immunohistochemical stains were used during the process.
Results: A tumour excision was planned for a 49-year-old female patient who presented with 1.3 cm diameter pigmented lesion on the back, which has been present for one year. Macroscopically, a 1.3 cm diameter slightly elevated lesion with hyperpigmented was observed on the skin. Histopathologically, in the dermis, an asymmetric tumour area that forms nesting structures and also spreads as a single atypical melanocytes was observed. Tumour cells had nuclear pleomorphism and abundant clear/eosinophilic granular cytoplasm. The foamy cells in the superficial dermis extend to fatty tissue. In the intradermal component, there was mitosis and a lack of maturation of melanocytes. Immunohistochemically, HMB-45 and melan-a were positive in balloon cells.
Conclusion: BCMM is a very rare histopathological subtype of malignant melanoma challenging for pathologists. Balloon cell changes can be seen in many neoplasms, including malignant melanoma. Although there are many compelling entities in the differential diagnosis, knowing the characteristic features of BCMM will reduce the risk of misdiagnosis.

E-PS-05-031
Lymphangioma-like Kaposi sarcoma: a clinicopathological study of 2 cases
E. Kuzucular*, F. Özden
*Istanbul Medipol University, Turkey

Background & objectives: Lymphangioma-like Kaposi sarcoma (LLKS) is a rare histologic presentation of Kaposi sarcoma (KS). We report two cases with clinical and histopathological features.
Methods: In our hospital, there were 41 cases diagnosed with Kaposi Sarcoma (KS) between 2014 and 2022, two of which were in LLKS morphology. Immunohistochemically anti-human herpesvirus-8 (HHV-8), anti-CD34, and D2-40 antibodies were tested.
Results: Of the total of 41 cases of KS in skin biopsy specimens, only 2 cases showed LLKS. Both patients were male and in the advanced age group (75 and 81). Clinically, each patient presented with violaceous patches, papules, or plaques. One patient also had an actinic keratosis. All of the LLKS biopsy specimens revealed areas with characteristic light microscopic features of KS. Lymphangioma-like areas comprised ectatic, irregularly shaped vascular spaces lined by mildly atypical endothelial cells. All tumour cells showed strong and diffuse reactivity for anti-HHV-8, anti-CD34, and D2-40. KS progressed slowly in two patients with adequate follow-up.
Conclusion: Lymphangioma-like Kaposi sarcoma may cause difficulties in differential diagnosis with other vascular tumours. In these cases, definitive diagnosis relies on recognition of the distinctive clinical and histological features of KS, including a strong immunohistochemical expression of HHV-8 in lesional cells.

E-PS-05-032
BRAF mutation in primary and metastatic melanomas
L. Lozneanu*, I.D. Căruntu, C. Amalinei, R. Balan, S.E. Giușcă, A. Rusu, E.R. Avadanei
*U.M.F. "Grigore T. Popa" Iasi, Romania

Background & objectives: Our study aims to evaluate the correlation between the BRAF mutation and the stages of melanoma progression, highlighting the difference between the BRAF mutation frequency in primary versus metastatic melanomas.
Methods: 38 and 24 cases with primary melanomas and metastatic melanomas, respectively, were analysed. Tumour biopsy samples from melanoma patients were analysed, in order to determine the BRAF mutation frequency, using fully automated IdyllaTM BRAF Mutation Test (Biocartis, Mechelen, Belgium). All analyses were performed using the MedCalc statistical package.
Results: We evaluated biopsies from a number of 62 patients diagnosed with malignant melanoma, 38 of primary tumours located in the skin (35 cases - 92.10%) and in the oral mucosa (3 cases - 2.63%), and 24 presented secondary tumours with lymph node location (20 cases - 83.33%) liver (1 case - 4.16%), lung (1 case - 4.16%), parotid (1 case - 4.16%), and intestinal (1 case - 4.16%) location. BRAF mutation was present in 21 of 38 (57.89%) patients with primary melanoma and in 10 of 24 (54.16%) patients with metastatic melanoma.
Conclusion: Our results demonstrate the relationship between melanomas and BRAF mutation without differences between primary and metastatic melanomas. This feature suggests that BRAF mutation in melanoma occurs, most likely prior to metastatic disease and supports a characteristic of the initial pathological process.

E-PS-05-033
Artificial intelligence shows pathologist-level detection of sentinel node metastases of malignant melanoma
N. Neittaanmäki*, J. Siarov, D. Kumar, J. Paoli, J. Mölne
*Department of Laboratory Medicine, Institute of Biomedicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Background & objectives: Detection of nodal metastases (NM) in sentinel node biopsies (SNB) is a crucial part of melanoma staging. Benign intra-nodal nevus (INN) may be misclassified as NM. We assessed the capability of artificial intelligence (AI) in detection of these two entities.
Methods: In total 495 hematoxylin and eosin whole-slide images (WSIs) including NM and INN from 233 SNBs were collected and divided into training (288 WSIs), validation (89 WSIs) and test sets (118 WSIs). The deep learning algorithm was trained with 5956 pixelwise annotations. The test set was assessed by the AI and three blinded dermatopathologists. Immunohistochemistry served as the reference standard.
Results: The AI model showed excellent pathologist-level performance with the area under the receiver operating characteristic (AUC) of 0.965 for detection of NM. For comparison, AUC for the pathologists for NM detection varied between 0.944-0.978. For detection of INN, AUC was lower for both AI (0.781) and the pathologists (range 0.627-0.790).

There was no significant difference in the sensitivity and specificity of the AI model compared to the pathologists in detection of NM or INN.
Conclusion: To conclude, the deep learning AI model showed excellent accuracy in detection of NM. Furthermore, the algorithm showed pathologist-level performance in detection of INN. Importantly, the AI model showed potential in differentiating between these two entities on routine stained WSIs. Use of such a tool could possibly reduce the need of immunohistochemistry and assist the pathologist in assessment of SNBs.
Funding: The study was financed by grants from the Swedish state under the agreement between the Swedish government and the county councils, the ALF-agreement (Grant ALFGBG-973455) and by the Finnish Dermatopathologist Foundation.

E-PS-05-034
Cutaneous sarcoma, still a challenge in the pathological diagnosis
R. Niculescu*, I.G. Cocuz, A.H. Sabau, M.C. Popelea, O.S. Cotoi
*Mures County Clinical Hospital, Romania

Background & objectives: Cutaneous tumours with uncertain differentiation represent a group of neoplasms that due to their rarity lead to considerable diagnostic challenges. Another obstacle in the diagnosis of these tumours is the overlapping of morphological aspects with some common neoplasms (epithelial and melanocytic tumours).
Methods: This case series report documents four types of cutaneous sarcoma arising in the dermis and subcutis: epitheloid, histiocityc, pleomorphic and with clear cell, diagnosed based on the histopathological and immunohistochemical findings in our Pathology department between 2020 and 2022, all cases were with the clinical diagnosis of epidermoid carcinoma. All the samples were processed and interpreted strictly following the protocols.
Results: At the microscopic analysis on H&E stain of epithelioid, clear cell and pleomorphic sarcomas, epithelioid and spindle cells were observed, but each with characteristic aspects such as: areas of necrosis for the epithelioid sarcoma, multinucleated cells for pleomorphic sarcoma. The histiocytic sarcoma presented large and medium-sized cells, with large, irregular nuclei, with variable cytoplasm. Characteristic for all the lesions were marked cyto-nuclear atypia, a large number of mitoses with a Ki67 between 30-50%. Immunohistochemistry: S100, HMB45,SOX10,Vimentin was positive in clear cell sarcoma, CD4,S100,CD68 positive in histiocytic sarcoma, S100,EMA,CKAE1/AE3,Vimentin positive in epithelioid sarcoma, Vimentin,CD10,SMA positive in pleomorphic sarcoma. In all cases local recurrences were recorded after less than two years from the initial diagnosis.
Conclusion: Recognition of morphologic clues on HE and immunohistochemistry play a key role in the diagnosis of this types of tumours. Vimentin was the one with strong positivity in all four cases. Also for an accurate diagnosis it is required a close correlation between the clinical picture and the morphologic, immunohistochemical and molecular aspect of the tumour. One of the aspects, also observed in our case, which gives these tumours a high degree of severity is the risk of recurrence.

E-PS-05-035
Automatic detection of common malignant lesions in whole slides dermatology histopathological images
A. Nivaggioli*, N. Pozin, M. Clavel, M. Sockeel, S. Mazellier, E. Lanteri, M. Figuccio, C. Lefebvre, S. Kammerer-Jacquet, M. Battistella, V. Rouleau, S. Sockeel
*Primaa, France

Background & objectives: The vast majority of malignant lesions in dermatopathology are either Melanoma, Basal-Cell Carcinoma (BCC), or Squamous-Cell Carcinoma (SCC). Automatically detecting such lesions, which further allows for automated depths and margins measurement, could aid pathologists make faster and more precise diagnosis.
Methods: We gathered and labelled 1795 WSI containing both malignant and benign lesions and healthy tissue. We use a deep feature learning-based method to train a classifier on patches at zoom x20, to identify Melanoma, BCC, or SCC. Computer vision based methods then allow automatic measuring of lesion depth and margins.
Results: Our validation dataset contains 392 slides with one of the common malignant lesions, and 500 slides of healthy tissue or benign lesion. Our algorithm is able to detect malignant lesions with an F1 score of 0.892. If a malignant lesion is detected, we can determine the lesion type with a balanced accuracy of 0.965. At the patch level, we are able to detect a lesion with a Precision-Recall AUC of 0.946. Thank to our deep feature learning based approach, models are trained in less than an hour on a single GeForce RTX 2080 Ti GPU.
Conclusion: To our knowledge, we propose the first algorithm able to locate mentioned malignant lesions in whole slide histopathological images, while measuring depth and margins automatically. On-going developments should improve results further. Detection of benign lesions and classification of subtypes of malignant lesions are also being explored.

E-PS-05-036
Melanoma arising in a giant congenital naevus in a 16-month-old infant: a case report
W. Ouahioune*, N. Moulai, M. Guermi, Y. Taleb
*Faculty Of Medicine Of Blida, Algeria

Background & objectives: Melanoma arising in a giant congenital naevus is highly aggressive and potentially fatal tumour. Children and adults can be affected, but most melanomas appear during the first 5 years of life. The scalp and back are most commonly affected sites.
Methods: We report the case of a 16-month-old infant who consults for a 03 cm nodule developed on a scalp congenital naevus. It was an unresectable naevus of 18 cm in size. This nodule was associated with a synchronous homolateral cervical adenopathy of 02 cm in size.
Results: We received a skin resection piece measuring 12x10x1,4 cm, centred by a non-ulcerated blackish nodule of 3x2,5x1,6 cm.
Histological examination showed a well limited dermo-hypodermic nodule of a melanocytic origin, which stood out from pre-existing congenital naevus. Foci of tumour necrosis were found. The mitoses were numerous and atypia were marked.
The patient died 06 months after diagnosis.
Conclusion: The diagnosis of melanoma arising in giant congenital naevus must be made cautiously. It is imperative to eliminate a proliferative nodule in congenital naevus before confirming malignancy.

E-PS-05-037
Blastic plasmacytoid dendritic cell neoplasm on the skin: case report of a rare disease
D. Sá*, A. Coelho, J.R. Vizcaíno, F.E. Costa, F.S. Vieira, G. Carrola
*Centro Hospitalar Universitário de Santo António, Portugal

Background & objectives: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare neoplasm in which the proliferating cells derive from precursors of plasmacytoid dendritic cells. BPDCN characteristically has a predilection for cutaneous involvement and typically occurs in elderly patients.
Methods: We herein report a case of an 81-year-old man with hypertension and dyslipidaemia that resorted to a general surgery consultation with a 4-month history of erythematous skin papules on the chest, back and head. He was submitted to a skin biopsy to characterize these lesions and we received a skin ellipse measuring 1,6x1x0,8 cm presenting a violaceous epidermic surface.

Results: Histologic examination showed skin infiltrated by a neoplasia characterized by nodules of intermediate-sized cells with scant cytoplasm and vesicular and irregular nuclei sometimes with prominent nucleoli. These nodules were arranged predominantly around the adnexa, vessels, and hypodermis. There were frequent mitotic figures and extravasated red blood cells and no epidermotropism. Immunohistochemistry revealed expression of CD4, CD56, Bcl2 and CD123 in the neoplastic cells with no expression of CD20, CD3, CD2, CD5, CD7, CD8, CD10, Bcl6, MUM1, CD21, CD23, Cyclin D1, TdT, CD30, Perforin, Granzyme, TIA1, Myeloperoxidase and CD68. Chromogenic in situ hybridization (CISH) for the detection of Epstein-Barr virus-encoded RNA (EBER) was negative.
Conclusion: The diagnosis of BPDCN requires, along with morphologic features, immunohistochemistry that demonstrates CD4, CD56, CD123, CD303 and TCL1 expression, together with lack of expression of B, T, myeloid or monocytic, and NK cells. The disease usually progresses rapidly with leukemic spread and multiorgan involvement and therefore the prognosis is poor, with a median overall survival ranging from 9 to 20 months. The patient is currently alive 9 months after the diagnosis.

E-PS-05-038
From basic to the never-ending story of melanoma and its rhabdoid variant – a case report
A.H. Sabau*, I.G. Cocuz, M.C. Popelea, A.C. Tinca, O.S. Cotoi
*UMFST Targu Mures, Romania

Background & objectives: It is well known that melanoma can present a multitude of variants from a cytopathological point of view. Rhabdoid melanoma is an extremely rare variant characterized by nests of polygonal cells, with abundant cytoplasm and vesicular nuclei with prominent nucleoli.
Methods: We present the case of an 82-year-old female who presented with a nodule on her back. Surgical resection was performed, and the specimen was sent to the pathology department for histopathological diagnosis.
Results: Microscopic examination revealed an ulcerated nodule with a maximum size of 10 mm, composed of two distinct cell populations. The predominant cell population was composed rhabdoid tumour cells, polygonal in shape, with abundant eosinophilic cytoplasm and vesicular nuclei. The second population was located peripherally and was composed of epithelioid cells. 44 mitoses / 10 HPF were identified in the rhabdoid cell population. Melanic pigment was identified only in the epithelioid population. Immunohistochemistry studies showed heterogeneity, rhabdoid type cells being positive for SOX10, while the epithelioid type cells being positive for SOX10, Melan A and HMB45.
Conclusion: The histopathological appearance and the immunohistochemically profile led to the diagnosis of rhabdoid melanoma. The clue for diagnosis is based on the immunohistochemically mirror appearance, were Melan A and HMB45 are negative for the rhabdoid cell population and positive for the epithelioid one. Identifying and differentiating this type of melanoma represents a big challenge, as most of the previously reported cases described the rhabdoid type in recurrences or metastases.

E-PS-05-039
Healthy woman with active 15cm rib ulcer that does not heal: what is happening?
A. Sanz Zorrilla*, I. Sánchez Ramírez, J. Osuna Soto, S. Haro Yuste, F. Leiva-Cepas
*Hospital Universitario Reina Sofía, Spain

Background & objectives: We are used to seeing chronic wounds or torpid ulcers that do not heal in elderly patients. However, approximately 90% of these cases are usually located in extremities, we want to describe one unusual case that internists did not believe.
Methods: We present a case of a 60-year-old woman who had one of her left ribs broken by a trauma one year ago. 5 months later, she developed an ulcer in the same location, which progressively became larger. An ultrasound was performed, and it was treated as an infectious wound. A biopsy was performed to rule out Pyoderma gangrenosum.
Results: A skin punch with an irregular surface of 5mm in diameter was performed. It was studied under light microscopy, and it presented a dense, perivascular and diffuse infiltrate with infiltrative growth that was dissecting muscle and collagen bundles, with necrosis and perineural involvement. Tumour cellularity was large, irregular, pleomorphic with multiple nucleoli, and abundant mitotic figures. With immunohistochemical techniques, it was observed that they expressed: CD20+, PAX5+, CD30 (focal), EBER-, CD10-, BLC6+, MUM1- and cMYC+. The proliferative rate with ki67 was high. Abundant accompanying T cells were also observed, with involvement of the vascular wall and epidermotropism. Cells were TCRBF1 positive, and they did not express EBV (EBER) or CD30.
Conclusion: In this case, the question arose with a malignant mesenchymal neoplastic infiltration, although the definitive diagnosis was diffuse large B cell lymphoma of the germinal type, it could not be classified into any specific type because all the specific markers done were negative. A subsequent CT scan was performed, which showed retroperitoneal large lymph nodes, we have to rule out whether we are dealing with a primary skin lesion or a systemic process.

E-PS-05-040
Cutaneous Langerhans cell sarcoma of the lip: a case report of a rare entity
M. Slevin*, R. Williams
*Dorevitch Pathology, Australia

Background & objectives: Langerhans cell sarcoma is an extremely rare haematolymphoid neoplasm of dendritic lineage displaying aggressive clinical behaviour and frequent multisystem involvement. We present a case of primary cutaneous Langerhans cell sarcoma arising on the lip of a 67-year-old man.
Methods: The patient presented with what was clinically suspected to be squamous cell carcinoma of the lower lip and underwent excision. No history of myeloid neoplasia was reported.
Routinely prepared H&E stained sections of the excised tissue were examined and, after initial assessment, immunohistochemical investigations performed.
Results: Microscopically the biopsy showed a nodular superficial infiltrate with central epidermal ulceration and necrosis. Infiltrate comprised large epithelioid cells with ovoid, irregular nuclei and prominent amphophilic nucleoli extending into the deep dermis. Scattered folded nuclei with longitudinal nuclear grooves were seen. Mitotic activity, including atypical figures, was prominent.
There was an intralesional lymphoplasmacytic and eosinophilic infiltrate.
Tumour cells stained immunoreactive for CD1a, S100, CD31 and CD56. Langerin, cytokeratins, Sox-10, p40 and BRAF were negative.
Ki67 index was >80%.
This case was treated surgically and appeared completely excised initially. Local recurrence occurred 11 months later and showed similar morphological and immunohistochemical findings on re-excision.
Conclusion: In contrast to its benign counterpart, Langerhans cell sarcoma displays overt malignant cytology and ulceration and follows an aggressive clinical course. CD56 expression reportedly confers a worse prognosis. Inconsistent Langerin expression has been reported previously. Occurring primarily in adults and frequently in association with other haematological disorders, reported overall 5-year survival is less than 30%. Localised resectable cutaneous tumours have a more favourable prognosis.
Due to its rarity, pathogenesis is poorly understood, and empirical multimodality treatment response is unpredictable.

E-PS-05-041

Epidermolytic acanthoma: a case series of two cases and review of distinctive histological features

M. Slevin*, R. Williams
*Dorevitch Pathology, Australia

Background & objectives: Epidermolytic acanthoma is an uncommon and likely underdiagnosed benign acanthotic skin lesion. Two cases diagnosed at our institution are presented with photomicrographs demonstrating key features. Clinical presentation is non-specific, and diagnosis relies on familiarity with the histological features.
Methods: We present two cases of epidermolytic acanthoma. Clinically, Case A was a 3mm solitary lesion excised from the calf of a 28-year-old woman. Case B was a solitary cyst excised from the back of a 60-year-old woman.
Sections from both excised specimens were formalin fixed and routinely processed and stained with haematoxylin and eosin for histopathological examination.
Results: Microscopically, Case A consisted of a dilated cup-shaped acanthotic infundibular lesion. Case B was an invaginating corrugated epidermal hyperkeratotic epidermal lesion.
Both cases demonstrated characteristic epidermal changes of hyperkeratosis, hypergranulosis and epidermal degeneration with coarse keratohyaline granules and reticular eosinophilic material consistent with epidermolytic hyperkeratosis.
Both cases had characteristic histopathological features of epidermolytic acanthoma.
Epidermolytic hyperkeratosis is a focal feature of numerous entities and changes must occupy more than 50% of the lesion surface for a diagnosis of EA. Predominantly solitary lesions, they occur across anatomical sites with a similar distribution in both sexes, although multiple genital lesions appear to be more common in males.
Conclusion: Non-specific clinical presentation as a small asymptomatic keratotic papule means that recognising these classic histological features is few to diagnosis. Distinguishing epidermolysis from koilocytic change is crucial, especially in genital locations where multiple EAs are most common and misdiagnosis may cause harm. Epidermolytic ichthyosis, an inherited dermatosis due to mutations in keratins 1, 2, or 10 demonstrates identical lytic epidermal changes and altered keratin expression is postulated to have a role in pathogenesis of epidermolytic acanthoma.

E-PS-05-042

A rare glimpse of monkeypox histology- insights from an unusual case

F.M. Soares Nogueira*, A.E. Teles, A. Magarreiro Silva, J. Nogueira, J. Pina Alves, D. Gomes Pinto
*Hospital Garcia de Orta, EPE, Portugal

Background & objectives: Monkeypox is a zoonotic infection caused by the Monkeypox virus. Since early 2022, cases of Monkeypox have been reported in countries where the disease is not endemic. The aim of this poster is to present this rare and challenging pathology.
Methods: The methods employed in this case report encompassed patient assessment, histological analysis of biopsy specimens, digitization of histological slides, molecular testing and clinical data analysis.
Results: A 30-years-old male patient presented with multiple ulcerations with a necrotic base, along with vesicles and pustules in the genital, perianal and perioral regions, accompanied by pruritus.
An incisional skin biopsy was taken from two lesions, revealing dyskeratosis, spongiosis, and ballooning of the epidermis. In the dermis, we observed a moderate superficial and deep inflammatory infiltrate, perivascular and perianexal, consisting of lymphocytes, neutrophils and eosinophils. In one of the biopsies, there was also a focal full epidermal necrosis accompanied by rare nuclear cytopathic effect. Further testing was performed, and the diagnosis was confirmed using DNA Polymerase Chain Reaction molecular testing.
Conclusion: Monkeypox is an emerging disease that poses significant diagnostic challenges due to its clinical and histological similarities with other diseases, including other virus families such as Herpesviridae, which encompasses herpes simplex virus and varicella, as well as other members of the Poxviridae family, such as smallpox. By providing a unique insight into Monkeypox histology, this case report underscores the significance of employing molecular techniques as the optimal approach for prompt and precise diagnosis.

E-PS-05-043

A case of acquired reactive perforating collagenosis: a challenging diagnosis

A. Solombrino*, V. Dell'Anna
*Ospedale "Vito Fazzi", Lecce, Italy

Background & objectives: Reactive perforating collagenosis is a rare disease belonging to the group of perforating dermatosis. Two types are described: inherited having a childhood onset and acquired manifesting in adulthood. This report describes a case of acquired reactive perforating collagenosis (ARPC).
Methods: A 66-year old woman with a history of hypothyroidism and hypertension consulted for multiple umbilicated papules and nodules with a central keratin plug growing on her hands, arms, legs and face. The lesions developed over a period of several months, were not related to minor trauma and showed no regression after steroid treatment. Excisional biopsies were performed.
Results: Microscopic examination revealed a dense inflammatory infiltrate of lymphocytes, plasma cells and histiocytes aggregating around degenerated collagen bundles in both superficial and deep dermis, in a crater-fashion. Sparse collagen fibres were vertically oriented toward the surface and showed transepidermal penetration and elimination, mixed with neutrophils and tissue debris. In literature ARPC is typically associated to a systemic disease, especially diabetes and its complications, so the patient underwent multiple tests to exclude increased blood glucose level and kidney failure as well as infections, autoimmune and haematological disorders. In this case systemic examination was unremarkable.
Conclusion: ARPC is un uncommon dermatosis of unknown aetiology characterised by transepidermal elimination of degenerated dermal collagen. It occurs in adults in association with diabetes and renal insufficiency, but it can be linked to many other diseases, for example thyroid disorders like the case presented, and even to some malignancies. Therefore patients need clinical, biochemical, haematological and immunological workup. Currently, there is not standard therapy, but treatment options can be both topic and systemic. Management of coexisting diseases is also beneficial.

E-PS-05-044

Merkel cell carcinoma with divergent squamous differentiation: a rare case and short literature review

E. Souka*, G. Galanopoulos, G.M. Stanc, L. Karelis, K. Ntatsis, O. Tzaida
*Pathology Department Metaxa Cancer Hospital, Greece

Background & objectives: Merkel cell carcinoma (MCC), also known as primary cutaneous neuroendocrine carcinoma, is a rare aggressive cancer, affecting mainly sun-exposed skin areas of elderly and immunosuppressed patients.
Methods: A 75-year-old male with a medical history of chronic lymphocytic leukaemia (CLL) presented to the dermatology clinic with an ulcerated back skin lesion measuring 18mm which was incompletely removed and diagnosed as metatypical basal cell carcinoma. After 6

months the patient returned with relapse of a polypoid skin tumour measuring 65mm with satellite lesions. He underwent a wide excision.
Results: On gross section, the tumour was whitish, solid extending in depth up to 25mm. Microscopically, it consisted of medium sized monomorphic tumour cells with a "salt and pepper" chromatin pattern and brisk mitotic rate and cells with squamoid appearance. The neoplastic population was arranged in solid and trabecular structures with central necrosis, often with retraction artefact. The tumour cells had neuroendocrine differentiation as evidenced by their immunophenotype (CK8/18+, CK20+, CD56+, Synaptophysin+, Chromogranin-A+) and squamous differentiation in areas of p63 and CK5/6 expression. Retrospective study of the first lesion revealed similar morphology and immunophenotype with an in-situ component. The final diagnosis was MCC with divergent squamous differentiation.
Conclusion: MCC with divergent squamous differentiation is a diagnostic challenge for the general pathologist. It's a rare MCC subtype with only a few reported case studies or small case series. Recent research supports that the neuroendocrine and squamous component share genetic common profiles, while proposing the Rb-deficient subset of squamous cell carcinomas as the possible source of the divergent MCCs.
Further research is warranted to better understand the pathogenesis, clinical behaviour, and optimal treatment approaches for this rare subtype of MCC.

E-PS-05-045
Correlation between histologic subtype and location of basal cell carcinoma (BCC) in Greek population
N. Stavrinou*, S. Pantelakos, C. Vourlakou, V. Damaskou, I.G. Panayiotides
*Department of Pathology, Evaggelismos General Hospital Athens, Greece

Background & objectives: BCC is the most common type of skin cancer. Due to the high incidence of BCC in countries with high sun exposure (eg Mediterranean), the study of the correlation between histologic type and location of BCC is of particular interest.
Methods: In order to investigate the correlation between histologic subtype and location of BCC, we examined 661 BCCs. Statistical analysis was performed using IBM-SPSS. Distribution was divided into two categories: head & neck and trunk & extremities. Histology was divided into 9 categories according to W.H.O. classification. Other data, such as patient's age and gender were also taken into account.
Results: 58.1% of the patients were men; the median age of the patients was 73 ± 12.3 for men and 71 ± 12,1 for women. The most common subtype was nodular BCC (22%), most often located on the nose, which constitutes 31.4% of the total number of cases located in the head and neck area. Superficial spreading BCC arose more frequently on the back (37%). In our study, BCC in general was noted mostly between 71-80 years of age, whereas the infiltrative subtype was predominantly found in patients aged over 81 (69.2%).
Conclusion: The results of this study of a Greek population are similar to those of studies performed in other countries. In most studies, nodular BCC constitutes the most common histologic subtype, usually located in the head and neck. However, studies performed in Australia and in France showed that the most common histologic subtype is superficial spreading BCC and the distribution which was mostly noted is at the back and head and neck respectively.

E-PS-05-046
Cutaneous epithelioid angiomatous nodule (CEAN): a diagnostic pitfall
A. Syrnioti*, G. Raptou
*Department of Pathology, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece

Background & objectives: Cutaneous epithelioid angiomatous nodule (CEAN) is a rare, recently recognized, benign vascular proliferation of the skin that can pose significant diagnostic challenges due to its histological similarity with both benign and malignant vascular tumours, including epithelioid angiosarcoma, haemangioendothelioma, and haemangioma.
Methods: Here we describe a case of a CEAN, in a 24-year-old male, who presented with a solitary, 8-mm well-circumscribed, light brown nodule on the back. The nodule was excised and sent for histopathologic examination. Hematoxylin-eosin and immunohistochemical stained sections were examined.
Results: Microscopic examination revealed a well-circumscribed nodular lesion, located in the upper and mid-dermis. The lesion was composed of solid sheets of medium-sized epithelioid cells with abundant eosinophilic cytoplasm and ovoid, vesicular nuclei with conspicuous nucleoli. A small number of mitoses was focally detected, without significant nuclear atypia or pleomorphism. In the periphery of the lesion, vascular formations were also present. The overlying epidermis was ulcerated. On immunohistochemical evaluation, the lesional cells were diffusely positive for ERG, focally positive for CD34, and negative for Human herpes virus-8 (HHV-8). A moderate number of SMA-positive pericytes were also observed within the lesion. Based on these findings, the diagnosis of CEAN was established.
Conclusion: CEAN is an unusual entity that can often lead to misdiagnosis. The absence of atypical mitoses, significant nuclear atypia, necrosis, and infiltrative growth can help distinguish it from more ominous epithelioid vascular proliferative lesions and avoid unnecessary treatment.

E-PS-05-047
Primary cutaneous melanoma with rhabdomyoblastic differentiation – histopathological and immunohistochemical analysis of an extraordinarily rare malignancy
D. Tapoi*, A. Dumitru, A. Ciongariu, D. Chetroiu, S. Gradinaru, C. Alius, M. Costache
*University Emergency Hospital, Romania

Background & objectives: Melanoma is a heterogeneous disease with widely variable histopathological, immunohistochemical, and molecular features. Cutaneous melanomas can undergo divergent differentiation, displaying immunohistochemical and ultrastructural features of other cell lineages. Even though rare in primary lesions, such cases represent major diagnostic challenges.
Methods: Primary cutaneous rhabdoid melanomas are unusual entities, more commonly encountered in metastatic cases. Furthermore, true rhabdomyoblastic differentiation of primary cutaneous melanomas is extraordinarily rare, as rhabdoid melanomas usually fail to express immunohistochemical myogenic differentiation. The aim of our study is to gain further insight into this peculiar entity by evaluating histopathological and immunohistochemical characteristics as well as differential diagnosis.
Results: We report the case of a 42-year-old male with an ulcerated nodular lesion on his posterior thorax. After surgical removal, histopathological examination revealed a proliferation of neoplastic cells with a pseudo-alveolar growth pattern, ulcerating the epidermis and invading the subcutaneous tissue. The tumour cells were large, polygonal with abundant eosinophilic cytoplasm and eccentric nuclei with prominent nucleoli. Multinucleate cells were also present. The primary differential diagnoses were alveolar soft part sarcoma and rhabdomyosarcoma. Immunohistochemically, the cells were completely negative for HMB45, focally positive for desmin and myogenin and diffusely positive for vimentin, SOX10 and Prame. Based on these features, the diagnosis of primary cutaneous melanoma with rhabdomyosarcomatous differentiation was established.
Conclusion: Rhabdoid features in primary cutaneous melanomas have rarely been described. These tumours usually keep their melanocytic

profile without true rhabdomyoblastic differentiation; thus the diagnosis is easily established. Rhabdomyoblastic differentiation in primary cutaneous melanomas has been acknowledged in less than 10 cases to date. These lesions may not express melanocytic markers such as HMB45 and Melan-A. Therefore, extensive immunohistochemical analysis should be performed. PRAME is particularly useful as SOX10 is also positive in malignant peripheral nerve sheet tumours with rhabdomyosarcomatous elements.

E-PS-05-048

Verruca vulgaris overlying basal cell carcinoma: an association never described before

H. Trihia*, E. Souka, G.M. Stanc, G. Sgouros
*Pathology Department Metaxa Cancer Hospital, Greece

Background & objectives: Multiple neoplasms at the same cutaneous site, is known as multiple-skin-lesions at one site (MUSK IN A NEST). Basal cell carcinoma (BCC) presents as isolated tumour, or as collision tumours. The combination with common wart has not been described before.
Methods: A 67-year old man presented to our Dermatology Clinic for evaluation of a lesion behind his ear. He was uncertain of its duration. He reported cauterization of a lesion in the same area at the age of 12 and traumatisation during wearing of his motorcycle helmet. Physical examination revealed a 3cm raised, smooth, circumscribed, hyperkeratotic papule with solid cut surface.
Results: Histopathology confirmed three different lesions in association. An overlying common wart (CW) with hyperkeratosis, papillomatosis, hypergranulosis and columns of parakeratosis over projecting dermal papillae, corresponding to a dome-shaped papule with a keratotic and verrucous surface. There was intracorneal haemorrhage and inward bending of rete ridges at the borders of the lesion. A nearby, microscopic slightly elevated seborrheic keratosis and an underlying of the CW, 0,7cm BCC, was diagnosed. The BCC component was positive for Ker5/6, p63, p40 and BerEP4 and negative for EMA, CK20 and melanocytic markers. The final diagnosis was of a combined lesion, consisting predominantly of a verruca vulgaris, overlying a BCC, in association with the overlying epidermis.
Conclusion: Verruca vulgaris is an-HPV-induced cutaneous lesion. The relationship between BCC and co-existing conditions may be coincidental or possibly related to the development of the BCC. BCC is likely to be secondary to a koebner isomorphic or a Wolf isotopic response in an immunocompromised skin. Malignant transformation of CW into SCC and BCC has been reported. Imiquimod has been used in large lesions of superficial and nodular BCC. Our case may add to the histogenesis. Skin lesions should be fully included.

E-PS-05-049

A case series of post-herpetic Wolf's isotopic response

E.M. Vázquez Tarrio*, M. Veras, J.L. Rodríguez Peralto, M.C. Garrido Ruiz
*Hospital 12 de Octubre, Spain

Background & objectives: Wolf's isotopic response is the appearance of a new skin disease at the site of an already healed, unrelated disease, often herpes zoster. Multiple entities have been described as secondary diseases. We aim to further characterize this phenomenon.
Methods: We present a retrospective case series of patients with Wolf's isotopic response diagnosed in Hospital 12 de Octubre in the last two years, and analysed the clinical and histopathological variables (age, sex, initial and secondary lesions). A literature review was also conducted.
Results: Three cases of Wolf's isotopic response were reviewed. Two of the patients were men, with an average age of 65 years (range: 31-86 years). All the cases presented with herpes zoster as the initial disease and a non-tumoral disease as the second; Erythema multiforme in one of the cases, Lichen planus in another one and Darier disease in the third one. The diagnosis of herpes zoster was clinical, and a histologic study was performed in the second dermatosis in all cases. Time between the debut of the first and the second dermatosis was not available because there was no histological confirmation of the lesion throughout its clinical evolution.
Conclusion: Wolf's isotopic response is a rare phenomenon, and its mechanism is not clear, though it has been suggested that it may be an alteration of local skin immunity. It is important to be aware of this phenomenon, to distinguish the suspected lesions from common relapses of herpes-zoster infection and primary inflammatory dermatitis and prevent a diagnostic delay of a second and potentially aggressive disease.

E-PS-05-050

A case of Langerhans cell histiocytosis with cutaneous involvement and review of literature

M. Veras*, E.M. Vázquez Tarrio, J.L. Rodríguez Peralto, M.C. Garrido Ruiz
*Pathology Department, Hospital Universitario 12 de Octubre. Madrid, Spain

Background & objectives: Langerhans cell histiocytosis (LCH) is the most common type of histiocytosis and shows clonal proliferation of activated Langerhans cells (LC) with systemic involvement. We aim to further characterize the clinicopathological features of this entity.
Methods: We report a case of LCH with cutaneous involvement and summarize the epidemiological, clinical and histopathological features of this entity based on a review of previous literature.
Results: A 23 month-old male patient that started at the age of 3 months, with bone multifocal affection. A biopsy of the mandibular branch diagnosed a Langerhans cell histiocytosis (LCH). The patient received treatment with progression of bone lesions for the next 2 years. Then, started with systemic symptoms such as insipid diabetes, anaemia, and desquamative lesions in skin that started in the scalp and progressed. Skin and bone marrow biopsies were performed and showed infiltration of LCH. The cutaneous lesion stained for S100 and CD1a. After treatment with ARA-C, corticoids and Cladribina the patient stabilized and has maintained a non active systemic disease.
Conclusion: LCH shows a broad range of clinical manifestations and the diagnosis is based on clinical, radiological and histopathological findings. It is an uncommon condition that is more frequent in paediatric age (less than 10 years) and the suspicion would lead to an early diagnosis and treatment leads to a favourable prognosis for the patient.

E-PS-06 | E-Posters Digestive Diseases Pathology - GI

E-PS-06-001

The prognostic Impact of PD-L1, CD73, A2ar and CTLA-4 immunohistochemical expression in colorectal cancer

L. Aboelnasr*, A.G. Abdou
*Pathology Department, Menoufia University, Egypt

Background & objectives: The interactions in the tumour microenvironment are complex and dynamic, playing key roles in modulating the immune response, which impact cancer progression. This study aimed to evaluate the immunohistochemical expression of PD-L1, CD73, A2ar and CTLA-4 in colorectal cancer (CRC).
Methods: This retrospective study included 103 surgically resected human CRC tissues, 22 adenoma cases and 21 non-neoplastic specimens. Using immunostaining technique, the immunohistochemical expression levels of PD-L1, CD73, A2ar and CTLA-4 were assessed and reported as scores considering both intensity and percentage of positivity. We evaluated the intercorrelations between the 4 biomarkers,

analysed their association with clinicopathological data and survival rates.
Results: The expressions of PD-L1, CD73, A2ar and CTLA-4 in CRC were all higher than those in adenoma and non-neoplastic specimens. In cancer cells, expression levels of PD-L1, CD73 and A2ar were positively correlated. High PD-L1 expression was associated with advanced tumour stage, and low density of tumour-infiltrating lymphocytes (TILs). High CD73 expression was significantly correlated with high tumour grades, and lymph node metastasis. High A2ar expression was significantly correlated with high tumour grades. In TILs, low CTLA-4 expression was associated with advanced tumour stage and increased number of positive LNs. Multivariate Cox regression analysis showed that PD-L1 and CD73 expression were independent predictors for overall survival and recurrence-free survival, respectively.
Conclusion: The findings of this study highlight the impact of these immune checkpoint molecules as mediators of tumour progression and their potential as predictors of prognosis in CRC. These biomarkers may be used to better stratify patients with CRC with respect to prognosis and personalized treatment plans. The combination of two or more therapeutic options targeting these molecules may be a new breakthrough in CRC management.

E-PS-06-002
Colonic tubular adenoma with clear cell changes: a case report and review of literature
S. Al-Dandan*, O. Alzallal, H. Khushaim, W. AlShakweer
*King Fahad Medical City/King Fahad Hospital Hofuf, Saudi Arabia

Background & objectives: Clear cell change is rare in colorectal tubular adenomas and adenocarcinomas. To date, only eighteen cases have been reported in the English literature. We aimed to highlight this unique pathologic entity and review the previously published reports.
Methods: A 67-year-old female with a history of breast cancer, mastectomy, and hormonal therapy had a sigmoid colon polyp during a screening colonoscopy. The polyp measured 0.8 cm in maximum dimension, located 30.0 cm proximal to the anus, and was removed with a cold snare.
Results: Histopathological examination of the polyp demonstrated a tubular adenoma with low-grade dysplasia and prominent cytoplasmic clearing. The clear cytoplasm was negative for Periodic Acid-Schiff (PAS) and Mucicarmine stains. Immunohistochemically, the clear cells were positive for CK20 and CDX2 and negative for CK7, indicating their intestinal origin/lineage. The nuclear reactivity towards Beta-Catenin and p53 and the high Ki67 proliferative activity (70%) further confirmed the dysplastic nature of these clear cells. The adenomatous glands were mismatch repair (MMR) protein-proficient with a retained expression of MLH1, PMS2, MSH2, and MSH6.
Conclusion: The aetiology of clear cell change in tubular adenomas of the colorectum is poorly understood, and the pathology remains incompletely characterized. Both CD10 and CEA (monoclonal and polyclonal) showed a pattern of reactivity similar to the previously described cases in the literature. The expression of CD10 may suggest small intestinal phenotype/differentiation. The higher proliferative activity and cytoplasmic localization of CEA expression in the clear cell component of the adenoma may indicate a greater malignant potential.

E-PS-06-003
Clear cell change in colonic adenomas: a rare histopathological finding
F. Almarii*, A. Iorgescu, C. Stroescu, D. Pietrareanu, V. Herlea
*Fundeni Clinical Institute, Centre of Excellence in Translational Medicine, Fundeni, University of Medicine and Pharmacy "Carol Davila" Bucharest, Romania

Background & objectives: Clear cell change in colonic polyps is a rare finding, characterized by the presence of clear cells within the adenomatous epithelium. This morphologic alteration has been reported in various other benign and malignant tumours, less frequently in colonic adenomas.
Methods: We present the case of a 53 y.o. male diagnosed and treated in Fundeni Clinical Institute, Bucharest. The patient was previously treated for a colonic adenocarcinoma and during the control colonoscopy, another polyp was discovered at 10 cm of the anal orifice, and polypectomy was performed. Gross examination revealed a semi-pedunculated 3 × 2.5 ×1.5-cm tan polyp with friable surface.
Results: The H&E slides revealed an adenomatous polyp with tubulo-villous architecture and focal high-grade dysplasia. There were also areas with a distinct morphology, with frequent empty vacuoles, some of them subnuclear, reminiscent of the foetal variant of lung adenocarcinoma, and some areas with clarification of the whole cytoplasm. The vacuoles were negative for PAS staining.
On Immunohistochemistry the clear area showed diffuse positivity for CDX2, positive CK20 expression, intense cytoplasmic and membranous staining for CEAm and it was negative for CK7, Glypican 3 and AFP.
The final diagnosis was of a rectal adenoma with tubular architecture and focal high-grade dysplasia and the clear cell change was only shortly described.
Conclusion: Clear cell change in colonic adenomas is a rare histopathological finding that can pose diagnostic challenges. The precise clinical implications of clear cell change in colonic adenomas are not well-established, and its impact on the behaviour and malignant potential of the adenomas remains unclear. Further studies are needed to determine whether clear cell change represents a distinct histopathological subtype of colonic adenomas, with unique biological and clinical characteristics.

E-PS-06-004
Increasing incidence of colorectal serrated lesions and polyps in the Danish population 2000 - 2021
M. Andrea*, R. Karlin Jepsen, T. Plato Kuhlmann
*Department of Pathology, Herlev and Gentofte Hospital, Denmark

Background & objectives: Colorectal serrated lesions and polyps (SP) include hyperplastic polyps (HP), sessile serrated lesions -/+ dysplasia (SSL/SSL-D), and traditional serrated adenomas (TSA). 20-30% of colorectal adenocarcinomas develop from SP. We present incidence and baseline characteristics of SP in a Danish cohort.
Methods: We used The Danish Pathology Registry to include all SP in the Danish population from January 1st, 2000 to December 31st, 2021. Based on the unique Danish personal identification number and SNOMED-codes, combined with the age and sex of patients, and date of surgery, we determined the incidence of the SP subtypes, anatomical location, and changes over time.
Results: In the period 2000-2021, a total of 292 761 SP were removed from 163 949 patients: SSL: 50 702, SSL-D: 5 959, HP: 224 860, TSA: 10 293. The median age was 64.1 years [55.2-71.6] and 53.3% were male. We found a general increase of SP from 2 804 in 2000 to 25 846 in 2021. The proportion of SSL increased from 1.1% (81) in 2006 to 38% (9 891) in 2021. HP and TSA were most frequent in the rectum and the sigmoid colon, while SSL and SSL-D occurred most often in the ascending colon and the sigmoid colon, followed by the remaining parts of the right colon.
Conclusion: During the study period 2000-2021, we find an increasing number of SP, especially SSL. From 2019-2021 the number of SP seem to stabilize, while the proportion of SSL keeps rising. Essential factors most likely influencing the number of SP are the introduction of the Danish National Colorectal Cancer Screening Program in 2014 and the new WHO classification of SP in 2019. This study will form the basis for future studies on SP as an important precursor of colorectal cancer.

E-PS-06-005

Gastrointestinal tract lymphomas: a retrospective analysis

N. Arı*, S. Uyar Bozkurt, H.K. Türköz, Ç. Ataizi Çelikel
*Marmara University School of Medicine, Department of Pathology, Turkey

Background & objectives: Gastrointestinal (GI) tract is the most commonly involved site for extranodal lymphomas. This study is a retrospective analysis of GI lymphoma cases in terms of subtype, site of involvement and clinical history.
Methods: Thirty-three patients who were diagnosed as GI lymphoma either with an endoscopic biopsy or resection between 2019-2022 were included in the study. Pathology reports of these patients were analysed in terms of subtype of lymphoma and localization. Demographic data, patient history (age, sex, history of hematologic malignancies, inflammatory bowel disease (IBD)/celiac disease) and radiological findings were obtained from hospital records.
Results: B-cell lymphomas constituted 93,9%(n=31) of the patients whereas small percentage of the cases (6%,n=2) were diagnosed as T-cell lymphoma. Stomach was the most common site of involvement (57,5%,n=19). Majority of patients (63,6%,n=21) was diagnosed as diffuse large B-cell lymphoma. All 3 patients who had gastric extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) showed Helicobacter Pylori (HP) positivity. 84,8%(n=28) of the cases presented as primary GI lymphoma whereas 15,1%(n=5) of the patients were considered as secondary involvement of a non-GI lymphoma according to patient history and radiological findings. Only one patient had history of celiac disease whereas none of the patients had a known history of IBD.
Conclusion: Chronic inflammation and HP infection are well known risk factors for MALT lymphoma. Consistent with the literature, HP was seen in all 3 cases with gastric MALT lymphoma in our study. Despite the common belief that primary GI lymphomas are rarer than secondary involvement of nodal disease, our sample group consisted of mostly primary cases. This study is an important contribution to literature to achieve better understanding of GI lymphomas, as it constitutes an example for further studies in future.

E-PS-06-006

Well-differentiated papillary mesothelioma of the peritoneum: a borderline mesothelioma. Case report of uncommon tumour and literature review

R. Ayadi*, E. Braham, F. Loued, H. Ichrak, O. Ismail, A. Ayadi
*Hôpital Abderrahmane Mami, Tunisia

Background & objectives: Well-differentiated papillary mesothelioma of the peritoneum is an uncommon, benign abdominal tumour. There have been fewer than 130 cases reported in the literature today. The diagnosis of this pathology is difficult and based on histological findings.
Methods: We report the case of a 57-year old women presented with abdominal pain and vomiting. Clinical examination revealed an abdominal mass induration. Computed tomography showed a 3 larges spherical masses in the abdomen. A gastrointestinal stromal tumour was suspected. A series of biopsy specimens were done.
Results: Microscopic examination revealed multiple, uniform, coarse papillae lined by a single layer of bland, flat to cuboidal cells with no signs of atypia were recorded. This papillae were separated by scant loose to collagenous stromal septa. Chronic inflammation and haemorrhage common. Immunohistochemistry stain showed that the tumour cells were positive for calretinin and CK and negative for CD117, CD34 and chromogranine. Based on these histologic and IHC findings, the final diagnosis of Well-differentiated papillary mesothelioma of the peritoneum was considered.
Conclusion: Establishing a diagnosis of papillairy mesothelioma of the peritoneum is a challenging task, given rarity of the disease and the small number of reported cases in the literature. This tumour is known for local recurrence. It's agreed that surgery is the only effective treatment.

E-PS-06-007

Intraepithelial lymphocytosis doesn't correlate with dilated intracellular space in the oesophagus

G. Aydogan*, V. Gorgulu, P. Ergun, S. Kipcak, M. Sezak, S. Bor, B. Doganavsargil
*Ege University Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Intraepithelial lymphocytosis (IEL) and dilated intercellular space (DIS) are common in gastroesophageal reflux disease (GERD). We searched for the relationship between them in cases retrieved from Ege University Reflux Clinics database, arranged according to the LosAngeles classification and Lyon consensus.
Methods: IEL density was evaluated on hot spot areas, and the average count of 10 High-power filed (HPF) (Olympus-BX50 light microscope, 40x objective, r=0.54 mm) was noted. DIS was measured on digital images taken at 1000x, oil lens, and a total of 100 perpendicular measurements were made between the basal-lower prickle layers per patient.
Results: All cases including HCs harboured IELs and 7 cases showed eosinophil infiltration (<7/HPF). In 19 cases (13%) IEL was over the 20/HPF "lymphocytic esophagitis" threshold. The distribution of median IEL density (n/HPF) and mean DIS width (μm) according to clinical groups was as follows; Healthy control (n=12, IEL=5.50±3.53, DIS=0.93±0.22) Erosive GERD (n=74, IEL=10.00±7.07, DIS=1.25±0.25) Non-erosive GERD (n=25, IEL=9.00±8.18, DIS=0.98±0.31) Reflux hypersensitivity (n=15, IEL=7.00±9.50, DIS=0.96±0.27), Functional heartburn (n=19, IEL=8.00±8.72, DIS=1.02±0.29).
Erosive GERDs had significantly wider DIS (Anova=9.536,p<0.001) while eosinophil-positive cases showed dilatation as well (median=1.36±0.26 μm, p=0.078, Mann-Whitney U). Overall IEL count didn't significantly differ among groups (Kruskal Wallis=4.711, p=0.318) and no correlation was found between IEL and DIS (Spearman=0.081, p=0.334).
Conclusion: Despite a slightly higher IEL count in erosive cases, our results provided no solid evidence for a difference between clinical phenotypes, and no association was noted either between IELs and DIS even in lymphocytic esophagitis, in contrast with the previously shown association between eosinophilic esophagitis and DIS.

E-PS-06-008

An extraordinary case of "bi-phenotypic" gastric carcinoma: from morphology to molecular characterisation

D. Baptista*, I. Gullo, Y. Kim, B. Ylstra, F. Carneiro
*Department of Pathology, Centro Hospitalar e Universitário de São João, Porto, Portugal., Portugal

Background & objectives: Gastric carcinoma (GC) is highly heterogeneous both from morphologic and molecular standpoints. The morphological features of GC with lymphoid stroma have been associated with Epstein-Barr virus (EBV) infection. We aim to report a case of GC showing remarkable morphomolecular heterogeneity.
Methods: A 70-year-old male with a previous history of oral squamous cell carcinoma was submitted to upper endoscopy. A 3cm elevated and sessile lesion (IIa+Is by Paris classification) was found in the subcardic region. The endoscopic biopsy showed (low-grade) dysplasia of gastric phenotype. The lesion was removed by endoscopic submucosal dissection (ESD).
Results: Histopathological analysis showed GC with two juxtaposed components: GC with lymphoid stroma (GCLS) and tubulo-papillary adenocarcinoma (TPA). EBV-encoded small RNAs (EBER) in situ hybridization revealed positivity in GCLS component, while TPA was

negative. By immunohistochemistry, both components were mismatch-repair proteins (MMR) proficient. To investigate if the tumour was clonal (despite the two components) or, otherwise, a collision tumour, shallow-whole genome sequencing (sWGS) of both components was performed. Similar amplification/deletion profile was observed, pointing to a clonal origin of the two components. Since TPA showed lymphatic invasion and the endoscopic resection was incomplete (vertical margin), total gastrectomy was performed. No residual tumour or lymph node metastases (0/50) were observed.
Conclusion: The coexistence of EBV+ and EBV- components in GC has been reported only in few cases in which distinct tumour clonality (i.e.collision tumour) was observed, rather than a single tumour with distinct phenotypes. In our case, GCLS and TP components were considered clonal by sWGS, despite showing different EBV status. To our knowledge, this is the first case report of a "bi-phenotypic" GC showing a morphological switch from GCLS adenocarcinoma to TP on the basis of EBV status.

E-PS-06-009
Exploring the relationship between tumour grade, tumour size, and lymph node metastasis in colorectal carcinoma
R.A. Barna*, M. Cornianu, S. Taban, D. Lazureanu, A. Vaduva, A. Jurescu, O. Vita, A.D. Plopeanu, T. Moga, A. Plopeanu, R. Sirli
*Anapatmol Research Center, Victor Babes University of Medicine and Pharmacy, Romania

Background & objectives: Colorectal cancer ranks second in incidence and mortality in Europe and new prognostic parameters are needed despite management progress. This study aimed to investigate the relationship between tumour size, tumour grade, and the number of lymph nodes (LN) with metastases.
Methods: This study enrolled all patients diagnosed with colorectal adenocarcinoma "no other specified" at the County Hospital of Timisoara between 2021-2022. Criteria for exclusion: different histological types, multiple tumours, neoadjuvant therapy, or incomplete data. The study recorded tumour size, histological grade (high/low), and lymph node involvement. Statistical analysis was conducted using MedCalc software, including Pearson correlation test, t-test, and chi-square.
Results: This study analysed 396 cases of colorectal adenocarcinoma. The average tumour size was 50 mm and the average number of positive regional LN was 3. Compared to low-grade tumours, high-grade tumours had a significantly larger size (t-value=3.1539, p-value=0.001735), but linear regression analysis showed no significant linear relationship between tumour grade and size (p=0.9207).
High-grade tumours had a significantly (p=0.006) higher number of positive LN (38 vs 163, respectively, p=0.006) and a lower number of negative LN (14 vs 181) compared to low-grade tumours. The Pearson correlation test indicated a moderate correlation (r=0.1296, p=0.001) between tumour size and the number of LN metastases.
Conclusion: This study showed that high-grade CRC tumours have a larger size, a higher number of positive regional LN, and a lower number of negative regional LN, compared to low-grade tumours. Also, there was a moderate correlation between tumour size and the number of LN metastases.
Further studies with larger cohorts and analysis of other clinical and histopathological variables are necessary to validate these findings, which could help to predict patient prognosis based on tumour size and biopsy grade of differentiation.

E-PS-06-010
Clinical and pathological characteristics of incidental neuroendocrine tumours of the appendix: a retrospective study of 58 cases
D. Beltaifa*, W. Majdoub, A. Baccouche, S. Mestiri, O. Belkacem, L. Jaidane, F. Saidani, A. Bdioui, S. Hmissa
*Pathology Department Sahloul, Tunisia

Background & objectives: Neuroendocrine tumours encompass a diverse array of tumour pathologies, ranging from indolent, incidental tumour to poorly differentiated and aggressive carcinomas.
Our aim is to describe the clinical and pathological aspects of appendiceal neuro endocrine tumours (A-NETs).
Methods: A total of 58 cases of A-NETs were retrospectively analysed from the cancer registry of Central Tunisia spanning a 12-year period (2010-2022).
Epidemiology, clinical presentation, and histopathology features were evaluated.
Immunohistochemical confirmation was required, including neuroendocrine staining and Ki-67 proliferative index.
A-NETs were subdivided into grades G1, G2, and G3 according to the mitotic index and Ki-67expression.
Results: A female predominance was observed, with 34 females and 24 males. The mean age was 34.5 years, with a paediatric frequency of 15.5%.
A-NETs were incidentally discovered in all cases, with 88% occurring during the management of acute appendicitis and 12% detected in other pathologies. No cases of carcinoid syndrome were observed.
On macroscopy, the mean diameter was 1.88 cm, and 84.5% of A-NETs were located at the tip of the appendix.
Microscopically, A-NETs revealed typical features of well-differentiated neuroendocrine tumours.
Immunohistochemistry revealed positive staining for chromogranin A and synaptophysin in 81% and 69% of cases, respectively.
A-NETs were low or intermediate grade, with 85% of cases being Grade 1.
Conclusion: Various clinical and pathological parameters have been identified as significant prognostic factors in A-NETs. Therefore, it is crucial to include size, the presence of lymphovascular invasion, grade, and infiltration staging in the pathology report for each individual case to provide a comprehensive description and ensure optimal management.
Although the pathology features of A-NETs are well-known, studies in molecular biology are not common. Some authors have reported multiple mutations, including TP53, PTEN, SMAD4, and EGFR, in only a few cases.

E-PS-06-011
Clinicopathological study of gastrointestinal leiomyoma: about 5 cases
D. Beltaifa*, F. Saidani, O. Belkacem, T. Tlili, A. Baccouche, A. Bdioui, S. Hmissa, S. Mestiri
*Pathology Department Sahloul, Tunisia

Background & objectives: Leiomyoma is a rare benign mesenchymal tumour accounting approximately for one-third of all mesenchymal neoplasms in the gastrointestinal (GI) tract. The objective of this study is to describe the clinical and histopathological features of leiomyoma in the GI tract.
Methods: We analysed five cases of leiomyoma in the GI tract from the Cancer Registry of the Center of Tunisia between 2016 and 2022. The leiomyomas were resected from the stomach, small intestine, and colorectal regions. Immunohistochemical confirmation was required, including desmin and/or smooth muscle actin immunostaining. Staining for CD117 and DOG1 was conducted to rule out Gastrointestinal Stromal Tumours (GIST).
Results: We identified 5 patients,3 men and 2 women, with a median age of 47.5 years (range 16-65 years). The tumours were located in the gastric (40%) and colorectal regions (40%) and small intestine (20%). On gross examination, the median size was 6.4 cm (range 1-13 cm) on macroscopy. Microscopically, the tumour consisted of fascicles of

spindled cells with blunt-ended nuclei and eosinophilic cytoplasm. Although focal nuclear atypia was observed, necrosis and mitotic activity were not detected. On immunohistochemical study, all five cases were positive for SMA and desmin. The main differential diagnosis is with GIST, which may exhibit similar morphological features. However, KIT (CD117) was negative in all five cases.
Conclusion: Digestive leiomyoma is an uncommon gastrointestinal mesenchymal tumour. Given their rarity and inherent complexity, accurate diagnosis can be challenging. The combination of morphological, immunophenotypic, and molecular findings is the best strategy to confirm the diagnosis and promote the most appropriate therapeutic approach.

E-PS-06-012
Study of the associations between tumour budding in primary gastric cancer and clinico-pathological parameters
E. Benammou*, D. Bacha, I. Mallek, S. Gharbi, M. Hajri, H. Mestiri, A. Lahmar, S. Ben Slama
*Department of Pathology, Armand Trousseau Hospital-Sorbonne University, France

Background & objectives: Tumour budding (TB) is the presence of a cluster of l<5 carcinoma cells at the tumour invasion front. We aim to investigate the prognostic value of TB in gastric adenocarcinoma (ADK), which remains controversial, and its association with the usual prognostic markers.
Methods: This retrospective study, conducted at the Department of Pathology of Mongi-Slim University Hospital, includes 68 patients operated for gastric ADK over a period extending from January 2008 to December 2017. TB was classified into grade1 (0-4 buds); grade2 (5-9 buds) and grade3 (≥10 buds). Additionally, a two-grade classification was applied with low-grade (<10 buds) and high-grade (≥10 buds) TB.
Results: The sex ratio=2.57 with a mean age of 61.34 years. The ADK was papillary in 4 patients (6%), tubular in 27 patients (40%), mucinous in 6 patients (9%), poorly cohesive in 25 patients (36%) and mixed in 6 patients (9%). TB was grade 1 in 35 patients (51%), grade 2 in 12 patients (18%) and grade 3 in 21 patients (31%). It was low-grade in 69% of cases and high-grade in 31%. A significant correlation was noted between the presence of TB and poorly differentiated ADK (p=0.035), vascular emboli (p=0.006), perinervous invasion (p=0, 038), parietal infiltration (p=0.003), lymph node involvement (p=0.005), metastases (p=0.015), advanced tumour stage (p=0.014) and metastatic recurrence (p=0.033). High-grade TB was predictive of poor 5-year overall survival (p=0.007) and poor 5-year recurrence-free survival (p=0.02).
Conclusion: In gastric ADK, the standardization of TB assessment is essential in routine practice for inclusion in standardized reports to assist in the therapeutic management of patients.

E-PS-06-013
GATA3 positivity in oesophageal squamous cell carcinoma
I. Blazquez*, J. Martínez, E. Dorca, M. Gómez, M. Guerrero, M.J. Paules Villar
*Hospital Universitari de Bellvitge, Spain

Background & objectives: GATA3 is an excellent diagnostic marker for breast and urothelial carcinoma. Our study aimed to investigate the incidence of GATA3 expression in oesophageal squamous cell carcinoma (SCC) and its significance with respect to histological features, clinical parameters and overall survival.
Methods: Immunohistochemical expression of GATA3 was evaluated in 53 patients diagnosed with oesophageal SCC at our institution during 2015-2017. The percentage of GATA3-positive tumour nuclei was scored as well as staining intensity, which was rated as negative (0), weak (1+), moderate (2+) or strong. We collected clinical data and follow-up.
Results: Mean age of diagnosis was 68 years (range 51-88 years). Male predominance (n=43). Most patients exhibited advanced disease at diagnosis (39/53 stage III-IV). Median survival of 12 months. 42/53 cases were moderately differentiated (Grade 2), 6/53 poorly differentiated (G3) and 5/53 well differentiated (G1). 16/53 cases (30.19%) showed GATA3 positivity, (weak positivity 11/16; moderate 5/16). When analysing OS using Kaplan-Meyer curves, a trend towards reduced survival was noticed in GATA3+ subgroup although statistical significance was not reached (Logrank p=0.12, mean OS: 19.81 vs 20.6 months respectively). Moreover, GATA3 positivity was associated with a higher histological grade.
Conclusion: We believe that GATA3 could be a prognostic factor for overall survival; however, our data were not statistically significant as the series is limited, and studies with larger numbers of cases are needed.

E-PS-06-014
GLI-1 rearranged gastric tumour or gastroblastoma
C. Bongrain*, N. Guedj, G. Pierron, A. Sauvanet, D. Cazals-Hatem
*Beaujon Hospital, France

Background & objectives: The gastroblastoma, first described by Miettinen et al. in 2009, has been individualized in the 2019 WHO Classification as a biphasic epithelial-mesenchymal gastric tumour with MALAT1::GLI1 fusion gene. Here, we report an observation and relate it with previous similar cases.
Methods: A 28-years-old patient presented a 4 cm pyloric well-limited obstructive tumour developed in the submucosa. The resection showed an epithelioid proliferation made of regular ovoid cells arranged in nests or adenoid lobules without obvious spindle inflexion. Cytokeratin, CD56, and focally CD10 were expressed; the Ki67 proliferation index was estimated at 2%.
Results: Molecular analysis revealed an ACTB::GLI1 fusion transcript. The patient presented no recurrence after 40 months of follow-up.
To date, 20 "gastroblastomas" have been reported in the literature, 7 of them with confirmed GLI fusion transcript (MALAT1::GLI1 in six, PTCH1::GLI2 in one). Three of them presented a local recurrence and/or metastasis after a mean follow-up of 50 months [8-100], underlining the need for long-term surveillance. The novel GLI1 gene fusion partner described in our case was reported in similar tumours with predominant mesenchymal differentiation called "pericytoma with t[7;12]" or "plexiform fibromyxoma", one of them located in the jejunum, the others in soft tissue.
Conclusion: Gastroblastoma is part of the new family of GLI1-rearranged enteric mural tumours which shares a peculiar histology (biphasic differentiation), a common phenotype (variable expression of cytokeratin and CD56) and probably an indolent course. Hence, we propose that all novel tumours with GLI1 fusion gene should be collected and followed for defining the long-term behaviour of such neoplasms.

E-PS-06-015
Appendiceal actinomycosis: a case series with clinical, radiologic and histopathologic correlation
M. Bronte Anaut*, E. Carracedo Vega, J. Arredondo Montero, A.S. De Oliveira Gomes, I. Amat
*Hospital Universitario Araba, Spain

Background & objectives: Abdominal actinomycosis is an infrequent chronic infection caused by Actinomyces israelii. Appendiceal actinomycosis is a highly uncommon pathology, with isolated reports in the literature to date.
Methods: A search was made in our institution's archives and 3 patients with a diagnosis of appendiceal actinomycosis were identified.

Among the information collected we included sociodemographic and clinical data. Hematoxylin & Eosin, Silver, Grocott, Fite-ferraco and PAS stains were performed in the appendiceal samples. A review of the existing literature was carried out.
Results: We included 3 patients (2 males). The age range was 29-73 years. Clinically, one patient presented as a complicated acute appendicitis (AA), other as a non-complicated AA and the last one followed a subacute course. All patients had leukocytosis and neutrophilia. All patients had radiological studies compatible with AA. Intraoperatively, 2 of the patients presented an inflammatory plastron and other a gangrenous AA. AA was histologically confirmed in two cases. Actinomyces colonies were identified and confirmed by different stains in all cases. Two of the patients received antibiotherapy for less than 2 weeks while one patient was treated for 12 months. All patients evolved favourably and did not present recurrences.
Conclusion: Appendiceal actinomycosis is an infrequent pathology whose clinical presentation can be very variable. In our experience, 2 cases presented clinically as AA and all patients evolved favourably with surgery and empiric antibiotherapy. Future studies that characterize this entity in diagnostic, therapeutic and prognostic terms are required.

E-PS-06-016
Retrospective case series analysis of patients with inflammatory bowel disease: a laboratory experience in Northeast of Brazil
J. Carneiro Melo*, H. Neves Feitosa Filho, N. Pinheiro Rodrigues, R. Vilar Lima, A. de Carvalho Assunção, G. Ferreira Morgantetti, G. Alencar Medeiros, D. Nunes Oliveira
*Univesity of Fortaleza, Brazil

Background & objectives: Inflammatory bowel diseases (IBD) are chronic conditions characterized by inflammation of the digestive tract, including Crohn's disease and ulcerative colitis. Symptoms include abdominal pain, diarrhoea and weight loss. Aims to examine the histopathological findings in biopsy reports obtained from patients with IBD.
Methods: A retrospective and descriptive study of histopathological reports of patients with suspected inflammatory bowel disease, carried out in the Pathology laboratory, in northeastern Brazil, from January 2018 to March 2023.This study included analysis of cases of Crohn's Disease, ulcerative colitis according to the definition criteria established by the European guidelines of gastroenterology.
Results: A total of 520 histopathological reports were compatible with inflammatory bowel disease (IBD), the average age was 39,32 years and 60% (312) of the patients were women. Crohn's disease (CD) represented 60% (313) of IBDs, ulcerative colitis (UC) was responsible for 39% (203) of the cases and the diagnosis of nonspecific colitis was given in 0,7% (4) of the cases. Granulomas were seen in 15% (47) of CD and Cryptic abscess were reported in 37% (75) of the cases of UC. Low grade dysplasia was found in 1% (6) cases and a concomitant adenocarcinoma was observed in 0,3% (2) of the reports, both in CD patients.
Conclusion: Our results demonstrated that the patients were predominantly female, and CD was more prevalent than UC in this series of cases in Northeast Brazil. Accurate histopathological diagnosis, with differentiation between inflammatory bowel diseases, is important for the proper treatment and management of IBD.

E-PS-06-017
Unusual cutaneous metastases from colon adenocarcinoma
J. Carneiro Melo*, Á. Macêdo Freire, G. Carvalho de Freitas Soares, B.R. Novais Lima, S. Samuel Feitosa Machado, C. Gleidiston Lima da Silva
*Univesity of Fortaleza, Brazil

Background & objectives: Adenocarcinoma is the main histological type of colorectal cancer with increasing incidence and high morbidity and mortality. Cutaneous metastasis of this malignancy is rare, approximately 5% of cases. Report a rare case of metastasis of sigmoid adenocarcinoma in the skin.
Methods: We present the case of an 80-year-old man with a previous diagnosis of sigmoid adenocarcinoma 8 years ago, who underwent rectosigmoidectomy in 2014, progressing progressively to jaundice, recurrent hematemesis, ulcerated lesion on the right shoulder and death. At autopsy, an incisional biopsy of the lesion was performed.
Results: The microscopy showed cytoarchitectural distortion of the cutaneous tissue, large necrotic areas due to the advanced stage of the lesion and presence of sparse goblet cells. The development of cutaneous metastases in the course of visceral malignancy is an indicator of poor prognosis, they tend to occur in advanced stages of the disease and close to the site of the primary tumour, the abdominal skin being the most common region, due to contiguity or, more rarely, surgical implantation. Cutaneous metastases distant from the primary site, as presented in this case, are infrequent and the literature points out that they can be explained by haematological or lymphatic dissemination of malignant cells.
Conclusion: Cutaneous metastases from colon adenocarcinomas represent a challenge in clinical practice, since their detection requires a high degree of clinical suspicion. Early recognition and timely diagnosis are essential for the best survival rate. The reported case emphasizes that skin lesions with progressive growth or that do not heal after conventional therapy, may be the first manifestation of a new metastasis, as in the present case, or rarely be the first manifestation of advanced visceral cancer.

E-PS-06-018
Mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) of the ascending colon in a middle-aged female patient: a case report on a rare entity
G. Carrola*, A.P. Rodrigues, D. Sá, F. Sousa Vieira, J.R. Vizcaíno, N. Jorge Lamas
*Centro Hospitalar Universitário de Santo António, Portugal

Background & objectives: A mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) contains dual neuroendocrine and non-neuroendocrine components, with each component representing at least 30% of the tumour. It is an extremely rare neoplasia, scarcely reported in the colon.
Methods: We report the case of a 62-year-old female patient who came to the emergency service with an acute episode of bowel obstruction. The CT scan study revealed the presence of an ascending colon tumour with probable perforation. The patient was submitted to right hemicolectomy.
Results: Macroscopic examination revealed a 5cm vegetant tumour in the right colon, with infiltration of the muscularis propria and extension to the pericolic fat. Histological analysis revealed a MiNEN, composed of a 60% moderately differentiated adenocarcinoma component with mucinous areas and a 40% large cell neuroendocrine carcinoma component. Immunohistochemistry showed positivity for CK20, CDX2 and SATB2 on both components and for chromogranin A, synaptophysin and CD56 on the neuroendocrine component. The proliferative index was ≈60% and NGS analysis revealed a KRAS mutation. Eight out of the 16 isolated lymph nodes had metastasis. Progression of disease occurred, despite adjuvant chemotherapy, with lung and liver metastatization. The patient passed away after 7 months.
Conclusion: This case highlights the main features of the extremely rare mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN) of the colon. Some factors associated with worst prognosis are a high tumour grade, an increased number of gene mutations, and advanced-stage disease, as well as a large percentage of the neuroendocrine component. It is important to emphasize the very aggressive biological behaviour of this neoplasia, which usually portends a dismal survival, similarly to what happened with the patient.

E-PS-06-019

Digestive metastases of renal clear cell carcinoma: a series of three case reports and review of literature

A. Cernat-Stefan*, R. Ardeleanu, M. Matanie, E. Ignat, M. Filip, A. Ciocan, S. Sabo, G. Micu, A. Bastian, S. Zurac
*Colentina University Hospital, Romania

Background & objectives: Clear cell renal cell carcinoma (CCRCC) is the most common type of renal cell carcinoma. 25–30% of patients already have metastatic disease on detection most likely due to minor clinical symptoms. Rare cases of digestive metastases (DM) have been reported.
Methods: We searched the surgical pathology files of the Departments of Pathology, Colentina University Hospital for cases of DM from CCRCC reported between November 2022 and March 2023. All Hematoxylin and Eosin (H&E) and immunohistochemical (IHC) stained slides were reviewed.
Results: Three cases of DM were identified: a 58-year-old woman with gastric metastasis, a 60-year-old man with pancreatic metastases, and a 61-year-old man with cholecystic metastasis. Two of these patients had a record of primary CCRCC; the patient with cholecystic metastasis had no history of CCRCC. Gastric metastases presented endoscopically as gastric polyps. Pancreatic metastases were detected during a routine imaging check as intra-pancreatic nodular lesions, intensely iodophilic. Cholecystic metastasis had a cystic, polypoid ultrasound appearance. Histopathologically, the cases showed low-grade morphology polygonal cells with clear cytoplasm and slightly enlarged nuclei, with focal nucleoli visible at 100x magnification. The diagnosis was confirmed with immunostaining for PAX8 and CD10.
Conclusion: Although DM from CCRCC are rare, the differential diagnosis of clear cell proliferation in the gastrointestinal tract and pancreas should include CCRCC metastasis, especially in cases with history of primary renal tumour. Clinically, they might present as polypoid masses (especially gastric and cholecystic) or nodules. We presented three cases with low-grade morphology, whose main differential diagnoses were gastric xanthoma, cholecystic clear cell adenocarcinoma, and solid variant of pancreatic serous cystadenoma. PAX8 and CD10 immunostaining is useful in the differential diagnosis.

E-PS-06-020

Gastric adenosquamous carcinoma - evaluation of clinicopathological prognostic factors

E.E. Cetiner*, I.E. Cakir, A. Vergili, N. Ekinci
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Gastric adenosquamous carcinoma is a rare entity that less than 0.25% of all gastric carcinomas. Prognosis is worse than conventional gastric adenocarcinomas. They usually diagnosed at late stage. For the diagnosis squamous component should be at least 25% of tumour.
Methods: In this study, five cases diagnosed as adenosquamous carcinoma in 1875 gastrectomy operations between 2008-2022 were evaluated retrospectively. For all cases gender, age, tumour location, size, lymphovascular invasion, perineural invasion, pathological stage, prognosis and the type of metastases to lymph nodes were analysed. And those which originated from esophagogastric junction were excluded.
Results: Adenosquamous carcinomas constituted 0,26% of all gastrectomies. Among the five patients, the median age was 61,2(50-83), gender ratio was 2/3(M/F). Three tumours located distal stomach and two were proximal stomach. Median size was 6,34(3,5-10) cm. Lymphovascular invasion has been observed on all tumours and four had perineural invasion. Pathological stage of three patients was pT4 and two was pT3. Also three patients were pN3, one patient was pN1 and one patient was pN0. Mean survival time is 13,4(1-26) months. As lymph node metastasis, adenocarcinoma component was dominant in two cases, squamous was dominant in one case, and both components were observed at a similar rate in one case.
Conclusion: In conclusion, gastric adenosquamous carcinoma is a very rare tumour. Patients are usually diagnosed at late stage. The tumour has aggressive behaviour and poor prognosis. The pathogenesis is unknown but there are several hypotheses in literature. The main prognostic factor is the stage at the time of diagnosis. Also the dominant component of the tumour is a prognostically important parameter. Since this entity is rare and aggressive, adequate prognostic data could not be provided.

E-PS-06-021

A rare giant cell tumour in the gallbladder

X.F. Chen*, M. Lee, K. Sittampalam
*Department of Anatomical Pathology, Singapore General Hospital, Singapore

Background & objectives: An elderly man who presented with acute cholecystitis was found to have a gallbladder tumour measuring 2.7cm on computed tomography scan. The imaging finding was suspicious for a neoplasm. He subsequently underwent a radical cholecystectomy with liver segment 4b/5 resection.
Methods: The gross examination of the gallbladder showed a circumscribed, exophytic tumour arising from the submucosa with a tan haemorrhagic appearance. Representative sections of the tumour were submitted for microscopic examination.
Results: Histological examination of the tumour showed epithelioid to spindled mononuclear cells interspersed with many osteoclast-like multinucleated giant cells. Areas of infarction, haemorrhagic cystic degeneration, haemosiderin deposition, and osteoid-like material were observed. Scattered mitoses were seen. No epithelial dysplasia of the lining gallbladder epithelium or marked nuclear pleomorphism of the lesional cells was present. By immunohistochemistry, the lesional mononuclear cells were positive for CD163, CD68 and P63, whilst being negative for EMA, MNF116, clusterin and H3.3G34W. The multinucleated giant cells were positive for CD68. Ki67 proliferation index was 10% to 15%. The features were in keeping with a giant cell tumour despite the unusual location.
Conclusion: Herein, we reported a rare case of giant cell tumour in the gallbladder. The main differential diagnosis was an undifferentiated carcinoma with osteoclast-like giant cells. In this case, there was no marked cytological atypia, area resembling conventional carcinoma or epithelial differentiation of the lesional cells immunohistochemically to support the diagnosis of an undifferentiated carcinoma or malignancy. To our knowledge, there were only two reported cases of giant cell tumours in the gallbladder, and both pursued benign courses.

E-PS-06-023

Clear cell change in colorectal epithelial neoplasms: two case reports

S.K. Dursun*, H. Karatay, N. Dursun Kepkep
*Basaksehir Cam and Sakura City Hospital, Turkey

Background & objectives: Clear cell change in colorectal epithelial neoplasms is rarely encountered. The pathogenesis of these lesions remains unclear. It is unclarified whether it is caused by a cytoplasmic accumulation of glycogen or lipid-like material.
Methods: We report two colorectal neoplasms with clear cell change.
Case 1: 57-year-old male who presented with a 3 cm pedunculated rectal polyp in colonoscopy and the polyp was excised.
Case 2: 74-year-old female who presented with bowel obstruction and urgent surgery was decided. During operation, an ileocecal tumoral mass was detected and right hemicolectomy was performed.
Results: Histological examinations of materials:

Case 1: Focal intramucosal carcinoma, widespread clear cell change, and high-grade dysplasia arose in the base of tubulovillous adenoma were identified.
Case 2: Conventional glandular areas with extensive clear cell change and poorly differentiated areas of invasive adenocarcinoma were observed. Additionally, amphicrine-type neuroendocrine differentiation was detected, showing synaptophysin and INSM-1 positivity throughout the tumour.
Both lesions were microsatellite stable. Clear cell areas were negative with PAS, Alcian Blue, MUC2, and MUC6 and focally positive with MUC5AC stains.
Conclusion: Tumours with clear cell change can be primary to the colorectum. However, there is limited information regarding the causes and prevalence of this phenomenon. Especially on a biopsy specimen, being aware of this entity has paramount importance to avoid misdiagnosis. Histomorphological patterns and immune profile assist to exclude metastasis from other organs. Our cases are examples of extensive clear cell change in colorectal neoplasms, one of which arises on an adenoma and the other invasive carcinoma shows neuroendocrine differentiation.

E-PS-06-024
Anaplastic lymphoma of the colon: a very rare location
O. El Mnif*, A. Zehani, A. Ayari, B. Chelly, H. Azzouz, I. Chelly, K. Bellil, S. Haouet
*La Rabta pathology department Tunis, Tunisia

Background & objectives: Anaplastic lymphoma is a rare and aggressive of non-Hodgkin lymphoma. Colonic localization by anaplastic lymphoma is extremely rare, with only a few cases reported in the literature We report a case of colonic anaplastic lymphoma of a 17-year-old male.
Methods: We analysed the medical file of a 17-year-old patient with a medical history of diffuse large cell lymphoma diagnosed 6 months ago and still undergoing treatment, operated on for colocolonic intussusception following an acute abdominal presentation. A hemicolectomy was then performed highlighting a colonic mass. Representative sections of the mass were examined under H&E and immunohistochemical stains.
Results: On gross examination presence of a budding mass with a fleshy white appearance that infiltrates the subserosa.
Microscopic examination under H&E revealed a lymphoid proliferation of diffuse architecture with anaplastic large cells with abundant cytoplasm and horseshoe shaped nuclei.
The proliferation infiltrates the entire colonic wall and presents some ulceration on the surface with multiple perineural sheathing and numerous vascular emboli.
Twente lymph nodes were sampled, 17 were infiltrated.
An immunohistochemical study was performed showing that the tumour cells express focally the CD30 antibody and ALK antibody in a diffuse way. the rest of the antibodies: CD4 CD8 CD5 CD3 CD20 CD2 CD79 and CK were negative.
Conclusion: Anaplastic lymphoma of the colon is an extremely rare and aggressive neoplasm that poses diagnostic challenges. It can mimic other malignancies, such as adenocarcinoma or other high-grade lymphomas requiring careful histopathological examination and immunohistochemical staining for accurate diagnosis.

E-PS-06-025
Glomus tumour is a rare gastric mesenchymal tumour: a case report
Z. Fayed*, D. Sweed
*National Liver Institute, Menoufia University, Egypt

Background & objectives: Glomus tumours (GGTs) account for fewer than 1% of all gastrointestinal soft tissue tumours. GGT develops as a solitary, intramural nodule that radiologically mimics GIST. Lack of specific clinical, radiographic, and endoscopic findings makes the presurgical confirmation difficult.
Methods: We present a case of a 24-year-old Egyptian female who complained of a hemodynamically significant but self-limiting melena. Upper endoscopy and computed tomography revealed a mesenchymal antral mass, suggesting GIST. The patient had a distal gastrectomy with Roux-en-Y reconstruction.
Results: Macroscopically, a well-circumscribed intramural mass measuring 2.3 cm in the largest size and covered by ulcerated mucosa. The cut section was soft, brown, and had haemorrhagic areas. Microscopic examination revealed a non-capsulated intramural neoplastic growth with branching capillary-sized vessels lined by monomorphic cells organized in sheets and nests with eosinophilic cytoplasm. The tumour was expanding to the mucosa, causing ulceration but no serosal affection. There was no nuclear atypia, mitosis, or lymph vascular invasion. The tumour was totally excised. Tumour cells expressed SMA but did not express Pan CK, CD 117, chromogranin, or S100. The enhanced vascular component was highlighted by CD34.
Conclusion: A gastric glomus tumour is a rare pathologic entity with potentially benign behaviour. Despite a few reported cases, it is still missing in the differential diagnosis of a gastric intramural mass in the pre-surgical / pre-histopathology status to date. Long follow-up is recommended to exclude less like the possibility of recurrence or metastasis.

E-PS-06-026
A rare case of epidermoid cyst of the cecum
A. Firrincieli*, E. Nardi, G. Alemanno, L. Pugliese, L. Messerini
*University of Florence, Italy

Background & objectives: Cecal epidermoid cyst is a rare and benign lesion; with only 12 other cases reported in the literature. Due to its rarity, the pathogenesis remains unclear. The case of epidermoid cyst in symptomatic patient, treated by ileocecal resection, is presented.
Methods: A 28-year-old woman was admitted to hospital with abdominal pain, stable vital signs and no history of previous surgery. CT and MRI scans were performed and a large cystic mass in the anterior portion of the pelvic region was detected. Imaging techniques managed to localize the site and dimensions of the neoformation; however, they did not provide a conclusive diagnosis.
Results: The differential diagnosis was made with appendiceal mucocele, duplication cyst or endometriotic formation.
Laparoscopic right hemicolectomy was performed, and the formation was resected.
No complications occurred during surgery as the mass did not present any adhesion with the surrounding organs such as uterus, bladder, sigma, and ovaries.
The specimen was then evaluated both macroscopically and microscopically.
The macroscopic evaluation showed an irregular extraluminal cystic lesion arising from the cecal wall of 104 x 83 x 68 mm. The microscopic examination revealed a cystic wall lined by keratinized stratified squamous epithelium. No malignant findings were identified.
Thus, the histopathologic evaluation leads to the final diagnosis of epidermoid cyst.
Conclusion: Epidermoid cysts are rare benign neoformation that can be acquired or congenital. They can vary both in their clinal and instrumental presentation. The lesion can be associated with non-specific symptoms or be asymptomatic showing a wide heterogeneity both in sex distribution and age. Imaging techniques are useful for differential diagnosis with other neoplasms or abdominal masses, but the final diagnosis can be made only after the complete surgical excision of the neoformation and its histopathological examination.

E-PS-06-027

Molecular profile of dissected components of mixed neuroendocrine-non-neuroendocrine carcinomas suggest a common precursor lesion

V. Fusté Chimisana*, L. Catasús Cols, A. González, C. Fumagalli, A. Prat, D. Piñol, J. Szafranska
*Hospital de la Santa Creu i Sant Pau, Spain

Background & objectives: Mixed neuroendocrine-non-neuroendocrine carcinomas (MiNENs) are rare and complex tumours that have both neuroendocrine and non-neuroendocrine components. The origin of MiNENs is not entirely understood. We aim to provide evidence that MINENs are a single neoplastic proliferation with different phenotypic features.
Methods: Three cases of MiNENs were diagnosed in our institution from July 2021 to August 2022. The diagnosis was made upon morphology and immunohistochemical characteristics. NGS sequencing using Oncomine Focus Assay (Thermo Fisher Scientific) or TruSight R Tumour 15 (Illumina) of the two components of MINEN from colon were performed in 3 cases after manual macrodissection.
Results: Histopathologically, the neuroendocrine component was large cell poorly differentiated neuroendocrine carcinoma (NEC) in all cases. The non-neuroendocrine component (NNEC) in two cases was moderately differentiated adenocarcinoma and mucinous adenocarcinoma in the third case. The molecular profile was different in each patient, but common in both components although harbouring different proportion of allelic frequency, always higher in the NEC component. Case 1 showed mutations in BRAF (NEC 41.8% , NNEC 30.3%); and p53 (NEC 72.4%, NNEC 35.9%). Case 2 harboured KRAS mutations (NEC 58.7% , NEC 30.5%). Case 3 showed mutations in ERBB 2 (NEC 35%; NNEC 13%); BRAF (NEC 34.5%; NNEC 12%); and APC (NEC 27%; NNEC 10%).
Conclusion: The pathogenesis of MiNENs is still not clear, and different theories have been proposed to explain the biphasic morphology of these neoplasms. Our results showing the common molecular profile of the two parts of MiNENs, suggest that both neuroendocrine and non-neuroendocrine components arise from the transformation of a pluripotent stem cell that has the ability to differentiate into both phenotypes.

E-PS-06-028

Perforation as first manifestation of Enteropathy Associated T-cell Lymphoma (EATL)

L. Gallego*, F. MacSweeney
*University Hospital Waterford, Ireland

Background & objectives: EATL occurs in middle age patients with Coeliac Disease and represents less than 1% of Non-Hodgkin lymphomas. An early diagnosis and treatment of Coeliac Disease can decrease the risk of lymphoma.
Methods: The case is one of a 73 year old male with no previous enteropathy diagnosis, who underwent a bowel resection due to small bowel perforation at UHW in August 2022. Further histopathology analysis produced a diagnosis.
Results: Grossing of the specimen showed perforation associated with a fibrinous exudate, adhesions and mesenteric nodules. On microscopy, a large lymphomatous tumour mass arising from the small bowel involving mesentery and appendix was found. Loss of villous architecture and increased intra epithelial lymphocytes were noted in the background. The lymphoma was composed of medium to large cells with atypical features. Sampled lymph nodes were reactive but with no obvious involvement. Immunohistochemistry was positive for LCA, CD3, CD8 and CD30 (focal), with a Ki-67 index of 70%. Subsequent bone marrow aspirate and bone core biopsy were inconclusive and could not exclude the possibility of low volume involvement by T cell lymphoma.
Conclusion: EATL is a very rare type of Non-Hodgkin Lymphoma, which is associated to Type 2 Refractory Coeliac Disease. Staging is as per in other lymphomas, but as it is usually found as an advanced disease in laparoscopy, treatment is challenging and can combine surgery, chemotherapy, stem cell transplantation or biologic therapies. It is important to keep EATL between the differential diagnosis of GI lymphoma, and assessment of the background mucosa can provide helpful information.

E-PS-06-029

Use of deeper sections in the assessment of complete regression in rectal resection specimens

J. Gama*, S. Pessoa, I. Rodrigues, B. Sepodes, C. Courelas, A. Alves, J. Pimentel, F. Ramalhosa, J.L. Amaral, J. Madeira, V. Almeida, M.A. Cipriano
*Centro Hospitalar e Universitário, Portugal

Background & objectives: Neoadjuvant chemoradiation therapy in rectal cancer is associated with downstaging. To report tumour response to chemoradiation a modified Ryan scheme is commonly used. In this study, we sought to find whether residual tumour could be found resorting to deeper sections.
Methods: All rectal resection specimens at our institution (2015-2021) were reviewed. From these, the specimens submitted to chemoradiation therapy with complete response (Modified Ryan Scheme for tumour regression - score 0) were selected. In these cases, deeper cuts at a depth of up 30μm were requested.
Results: From a total of 425 rectal resection specimens submitted to chemoradiation therapy, 50 specimens with complete response were selected. A mean of 6.98 sections per case were studied (median:5 sections, range 2-40). Even after deeper cuts no evidence of residual tumour was found in none of the specimens.
Conclusion: In our study, the use of deeper sections in the evaluation of rectal resection specimens did not change the staging after neoadjuvant therapy, therefore showing that the tissue observed in the first cuts was indeed representative. In departments with extensive sampling of the tumour bed, one section of each block is representative.

E-PS-06-030

MUC5AC and PDX-1 are useful markers to identify colonic polyps of the serrated pathway

M. Gené Hijós*, E. Fernández, M. García, S. Roca, M.S. Martinez, E. Musulen
*Pathology Department, Hospital Universitari Joan XXIII, Tarragona, Spain

Background & objectives: Gastric metaplasia (MG) was described as the first event in the adenoma-carcinoma progression in the serrated pathway of colorectal cancer. The usefulness of MUC5AC and PDX1, markers of gastric epithelium, was investigated to properly classify conventional and serrated colorectal polyps.
Methods: A series of 229 colonic polyps were collected and characterized as follows: 74 tubular adenomas (TA), 72 serrated sessile lesions (SSL), 70 serrated sessile lesions with dysplasia (SSLD) and 13 traditional serrated adenomas (TSA). Serrated histological features and type of dysplasia were reported. MUC5AC and PDX-1 immunohistochemistry was performed in all cases and the results were statistically analysed.
Results: MUC5AC was positive in 116 (75%) of serrated polyps (66 SSL, 41 SSLD and 9 TSA) and in 12 (16%) TA (p=0.000). PDX1 was expressed in 154 (67%) of serrated polyps (64 SSL, 58 SSLD and 12 TSA) and in 38 (51%) TA (p=0.000). When we evaluated the relationship of both MUC5AC and PDX-1 expression as a function of serrated characteristics, such as the presence of serration, dilated crypts and presence of mucin, the results had statistical significance for both markers (p=0.000). In addition, the different expression of MUC5AC and PDX-1 to differentiate TA from SSLD showed high statistical significance for the two markers (p=0.000).
Conclusion: MUC5AC and PDX-1 expression is associated with serrated precursor lesions. Both markers are useful to differentiate serrated polyps from conventional when characteristic features are difficult to assess due to poor specimen orientation or fragmented resection of the lesion, even when dysplasia is present. Our results corroborated

the recent finding that GM is the first event occurring in the serrated carcinogenic pathway of colon carcinoma.

E-PS-06-031

Digestive neuroendocrine tumours with hepatic metastasis: a single centre experience

S. Gharbi*, D. Bacha, I. Mallek, E. Benammou, M. Mbarek, H. Mestiri, A. Lahmar, S. Ben Slama
*Department of Pathology, Armand Trousseau Hospital-Sorbonne University, Tunisia

Background & objectives: Patients with neuroendocrine neoplasms, develop hepatic metastases in 50-95 % of cases. Their diagnostic and therapeutic management represents a challenge, especially those with an aggressive fashion. Our study reports epidemiologic and clinicopathological features of digestive neuroendocrine hepatic metastasis.
Methods: It was a retrospective single-centre study. Cases were collected in the pathology department of the M. Slim Hospital over a period of 22 years (2000 to 2022). Clinicopathological data were collected from medical records of the surgery department of the same hospital. Tumour grades were evaluated according to the 2019 world health organization classification.
Results: Thirty-one patients with DNHM were included. Their mean age was 58 years. The sex-ratio M/F was 2. Diagnosis was performed in hepatic biopsy in the majority of cases (76,3%) and in metastasectomy specimens in 23,7% of cases. Primitive site was small intestine (n = 8), pancreas (n = 7), colon (n =4), stomach (n = 1) and in 11 patients the primary site was unknown. The majority of cases was well differentiated (grade 1 in 12 cases, grade 2 in 9 cases and grade 3 in 6 cases). Poorly differenciated carcinoma: 4 cases. Mean tumour size: 45 mm (10-65mm).
Conclusion: Although well differentiated, the rate of metatsates was high and there are cases with unknown primary site
Complete imaging, clinical, and pathological studies can help to identify the primary origin and to improve the patients' management.

E-PS-06-032

Granular cell tumour of the appendix with unusual morphologic features

C. Girleanu*, B. Murphy, J. Larkin, G. Woods
*St James's Hospital Pathology Dept., Ireland

Background & objectives: Granular cell tumour (GCT) is a rare soft tissue tumour which can occur in various sites throughout the body at any age.
We present a case of a GCT of the appendix with unusually prominent fibrous stromal bands on histology.
Methods: We described a 54-year-old male who presented with abdominal pain and bloating. A submucosal lesion at the appendiceal base was previously revealed on colonoscopy and not visualised on CT scan. A resection was performed, and the lesion was macroscopically and microscopically assessed with H&E, immunohistochemistry (IHC) and special stains being performed to reach the final diagnosis.
Results: Macroscopically a well circumscribed submucosal lesion, 12mm in size was present at the base of the appendix. Microscopically it was unencapsulated, consisting of prominent fibrous stromal bands dissecting nests of uniform cells with spindled nuclei, occasional nucleoli and abundant, eosinophilic granular cytoplasm, without significant pleomorphism, mitotic activity or necrosis.
IHC and special stains showed that the lesion was positive for S100, Inhibin and CD34, with weak, non-specific positive staining for CD1a and EMA. DPAS highlighted cytoplasmic granules. The lesion was negative for Desmin, SMA (also negative within the fibrous bands), C-kit, DOG1, AE1/AE3, Melan A and HMB45. P53 showed wild type staining and Ki-67 was manually estimated as 1-2%.
Conclusion: The features were of a benign GCT of the appendix. Clinical and endoscopic differential diagnoses included schwannoma, gastrointestinal stromal tumour (GIST), leiomyoma, inflammatory myofibroblastic tumour and also (based primarily on S100 positivity) metastatic melanoma and Langerhans cell histiocytosis, however, morphological features were not congruent with either of these.
Our case highlights an unusual morphological feature that may be seen in GCT and the importance of including them within the differential diagnosis of submucosal lesions arising in the gastrointestinal tract.

E-PS-06-033

A descriptive case series of 11 patients diagnosed with Whipple's disease

M. Gómez Tena*, J. Martínez, J. Rodriguez Pous, A. Domingo Rubio, I. BLAZQUEZ, A. De Carvalho Ovalles, E. Quirós Arape, M.J. Paules Villar
*Hospital Universitari de Bellvitge, Spain

Background & objectives: Whipple´s Disease (WD) is a rare infectious systemic illness. Its low incidence and lack of specific symptomatology makes WD a challenging and often delayed diagnosis. Before the introduction of PCR-based methods, the gold standard was histological detection of PAS-positive macrophages.
Methods: A 15-year retrospective analysis (2007-2022) identified 11 patients diagnosed with WD at our institution. We review their clinical and histological features.
Results: The mean age at diagnosis was 63 years with 7 (64%) of the patients being males. 8 had classic WD, 2 localized WD (endocarditis) and 1 isolated neurological WD. We received 21 biopsies: 14 were from duodenum, 2 from lymph node, 1 from brain, 1 from stomach, 2 from heart and 1 from subcutaneous tissue. PAS + macrophages were present in 17 samples. T. whipplei PCR was positive in 15 of 17 samples: 12 duodenal biopsies (3 with normal histology), 1 gastric biopsy, 1 endocardial biopsy and 1 brain biopsy. Two patients were diagnostic for both WD and another disease: secondary amyloidosis and *H. pylori* chronic gastritis.

Conclusion: The diagnosis of WD is based on the existence of clinical signs and symptoms compatible with the disease and in the presence of PAS+ macrophages. However, when the histologic findings are not suggestive of WD, T. whipplei PCR is a useful tool for its diagnosis.

E-PS-06-034

Double opportunistic infectious duodenitis on a immunodeficiency syndrome background: is it primary or secondary?

A. Gont*, G. Becheanu, A. Haidar
*University Emergency Hospital Bucharest, Poundbury Cancer Institute, Romania

Background & objectives: Primary or acquired immunodeficiency shows a quiescent histological impact on the gastro-intestinal mucosa. Nevertheless, it has an unexpected potential for diagnosis which leads to the proper treatment for these patients.
Methods: In the Department of Pathology from "Victor Babeș" Institute, we received for a second opinion one paraffin block containing three duodenal biopsies collected during a superior endoscopy of a patient. Following the examination of the conventional stained slides, special stains (Giemsa) and IHC studies for CMV have also been performed to confirm the diagnostic.
Results: We present the case of a 66-year-old female admitted to the Emergency Department in a critical, life-threatening condition and extremely malnourished (body mass index <18kg/m2). The attending physicians have excluded any malignancy or common infection and consideration has been given to an autoimmune aetiology. On the edge

of starting corticosteroid therapy, the case has been assigned to us. The duodenal biopsies received showed diffuse, marked inflammatory changes of chronic active duodenitis with subtotal villous atrophy. The luminal surface was covered by numerous spherical, basophilic merozoites. Despite the lack of cytomegalovirus cytopathic alterations, IHC studies for CMV have been performed and showed occasional nuclear staining in endothelial and epithelial cells.
Conclusion: Following our histopathological report of cryptosporidiosis and CMV duodenitis on a background of immunodeficiency, other tests have been performed and revealed an unknown HIV infection in this case. Immunodeficiency should always be considered as a background for gastro-intestinal opportunistic infections. Whenever we identify one pathogen we should always ponder that there may be more. Knowing and acknowledging these specific microorganism-induced histological alterations provides us the ability of identifying the systemic cause and, therefore, establishing the proper treatment for immunocompromised patients.

E-PS-06-035
Spatial transcriptome analysis and differences in immune cell infiltrate with respect to the prognostic biomarker Stroma Areactive Invasion Front Areas (SARIFA) in gastric cancer
B. Grosser*, C.M. Heyer, N.G. Reitsam, D. Vlasenko, A. Probst, M. Schlesner, B. Märkl
*Pathology, Medical Faculty Augsburg, University of Augsburg, Germany

Background & objectives: The histomorphologic prognostic biomarker Stroma AReactive Invasion Front Areas (SARIFA) is based on an interaction of tumour cells with adipocytes. The aim was to elucidate the changes in the tumour microenvironment, particularly the immune cell infiltrate, with respect to SARIFA-status.
Methods: SARIFA was classified on H&E-stained tissue sections of a local series of gastric carcinomas and in a subset of the TCGA STAD cohort. A spatially resolved transcriptome analysis in the stroma and in macrophages at the invasion front was conducted. Apart from analyzing genomic and transcriptomic data in regard to SARIFA-status the immune cell infiltrate was analysed using Spatial Deconvolution.
Results: Apart from the fact that no genomic differences were found in the TCGA STAD cohort with respect to SARIFA status, gene expression analyses again revealed upregulation of FABP4 and transcriptional regulation of white adipocyte differentiation, triglyceride metabolism, and catabolism in SARIFA-positive tumours. Spatially resolved transcriptome analysis of SARIFA-positive tumours showed increased expression of FABP4 and transcriptional regulation of white adipocyte differentiation in macrophages. The immune cell infiltrate showed no particular distribution with respect to SARIFA groups.
Conclusion: SARIFA is not driven by tumour genetics. The mechanisms underlying the interaction between tumour cells and fat cells need to be elucidated in further studies and could be a target for personalized therapies.

E-PS-06-036
Tertiary lymphoid structures before and after radiotherapy in rectal cancer (Dendritic cells – RORγt cells maintaining the immune balance)
M. Gulubova*, I. Koni, I. Maria Magdalena
*Dept. General and clinical pathology, Trakia University, Medical Faculty, Bulgaria

Background & objectives: Conventional fractioned radiotherapy delivered in small fractions for a number of weeks, kills directly tumour cells and induced tumour cell death via anti-tumour immunity and vascular damage. RT is a double-edged sword that can activate or suppress the immune response.
Methods: We investigated 18 patients operated for rectal cancer, 5 (27.8%) before RT, and 13 (72.2%) after RT. All patients have TLS. Immunohistochemistry with antibodies against DC markers: CD1c, CD141, DC-SIGN, CLEC9A, CD123, CD1a and CD83; anti-lymphocyte markers: CD8, FoxP3, IL-17, and RORγT; and anti-CD163 (M1) macrophages is used.
Results: After RT the main antigen-presenting cell (APC) types that are stimulated in TLS are CD1c+, DC-SIGN+, and CD83+ DCs. T lymphocyte subtypes IL-17 and FoxP3 are increased in TLS after RT. RORγT+ cells are statistically significantly increased after RT (67.28±7.04 v.s 39.11±5.27) ($\chi 2$=5.89, p=0.015).
Conclusion: Our results show that RT stimulates recruitment of cDC2s (CD1c+), DC-SIGN+ DCs and RORγT+ cells. The latter APC features. The quantity of CD8+ T cells is not changed. Therefore, the effective immune response in TLS is not well balanced.
Funding: NIP 7/22 "Tertiary lymphoid structures (TLS) - organization, localization and function in the tumour microenvironment"

E-PS-06-037
Immune cell content in primary Crohn's disease of the appendix compare to tuberculosis of the appendix
M. Gulubova*, C. Dimitur, Z. Georgi, P. Mariyana, H. Mehmed, I. Koni
*Dept. General and clinical pathology, Trakia University, Medical Faculty, Bulgaria

Background & objectives: Tertiary lymphoid structures develop at sites of chronic inflammation, autoimmunity and cancer. TLS lack capsule and usually develop in non-lymphoid tissue. In our opinion, Crohn's like granuloma and the tubercle itself are a kind of TLS triggered by autoimmune reaction.
Methods: Two cases are presented: case 1: A 14 years old boy operated for primary Crohn's disease of the appendix and case 2: a 22 years old women with miliary tuberculosis of the appendix operated for appendicitis. Immunohistochemistry has been performed with anti-CD3, anti-CD20, anti-CD83, anti-CD68, anti-CD21, anti-IL-17, anti-FoxP3, anti-Bcl6, anti-D2-40, and anti-CD31.
Results: In case 1 Crohn's disease TLS are situated in the muscle layer or connective tissue of the appendix. They represent lymphoid aggregates without capsule and mainly without germinal centres. CD3+ and CD20+ lymphocytes are more loosely dispersed in TLS. CD68+ macrophages are scattered in TLS periphery, where Bcl6 cells can be found. CD83+ dendritic cells are presenting in GCs and in T zone. D2-40+ lymph vessels are many in the whole TLS and are full of lymphocytes. In case 2 we find subserosal tubercles show CD3+T cells in lymphocyte clusters, CD83+ DCs in the epithelioid zone, CD83+ Langhans cells. Bcl6 cells are missing. D2-40+ form a network between epithelioid cells.
Conclusion: The immune content of Crohn's granuloma is similar to Crohn's reaction in colorectal cancer, while tubercle contains a specific immune contexture, where Langhans cells show antigen-presenting marker.
Funding: NIP 7/2020 "Hepatic monocytes/Kupffer cells, NK/NKT cells, T cells, and antigen-presenting cells in the pathogenesis of non-alcoholic steatosis, non-alcoholic steatohepatitis, and tumorigenesis"

E-PS-06-038
Gastric adenomyoma: a challenging diagnosis
S. Gurzu*, A. Kovacs, T.J. Bara, I. Jung
*George Emil Palade University of Medicine, Pharmacy, Sciences And Technology of Târgu Mureş, Romania

Background & objectives: Gastric adenomyomas are rare tumours composed of ductal-like epithelial structures and smooth muscle fibres. Only 70 cases were reported in Medline database during

1903-2023. The aim of the paper is to present a particular case of gastric adenomyoma.
Methods: A 62-year-old woman presented with a three months history of epigastric pain, nausea and lack of appetite. Abdominal CT and upper gastrointestinal endoscopy revealed a submucosal mass in the gastric antrum. Surgical removal of the lesion was decided for suspicion of a gastrointestinal stromal tumour (GIST).
Results: At macroscopic examination a 30x26x30 mm nodular mass was seen, which showed a cystic, multilocular appearance on cut section, with discharge of a transparent, serous liquid. Histology examination showed that the lesion was localized in the submucosa, consisting of multiple ductal structures, some of them cystically dilated, lined by normal-appearing columnar and cuboidal epithelium. The ducts were surrounded by interdigitating bundles of smooth muscle. The adjacent mucosa appeared normal and no exocrine or endocrine pancreatic tissue was found. Ductal epithelium showed positivity for Keratin19 and CA 19-9 and negativity for Synaptophysin, VSIG and CEA. The smooth muscle cells were reactive for SMA. A diagnosis of gastric adenomyoma was made.
Conclusion: Adenomyomas of stomach are asymptomatic or produce non-specific symptoms and can mimic a GIST. The immunoprofile suggest they could be a variant of pancreatic heterotopia without exocrine or endocrine component (Heinrich type III).

E-PS-06-040
Mycobacterial infection mimicking Crohn's disease and malignancy: a case report
Z. Hamid*, A. Arnaout
*St George's University Hospital, United Kingdom

Background & objectives: The intestinal manifestation of Mycobacterium Tuberculosis (TB) infection can mimic Crohn's disease and malignancy clinically, and histologically which is often challenging on small biopsies and even on resections.
Methods: We report a case of an ileo-caecal mass in a 35-year old Asian male who presented to the Accident and Emergency department with right sided abdominal pain and vomiting.
Results: Computerised Tomography (CT) imaging revealed an obstructing ileo-caecal valve mass. A loop ileostomy was performed, and biopsies taken reported a granulomatous moderate active chronic colitis suggestive of Crohn's disease. A repeat CT scan done a few months later showed an ileo-caecal mass suspicious of a tumour with enlarged lymph nodes. A right hemicolectomy performed showed an obstructing mass with several firm palpable mesenteric lymph nodes. The histology revealed ulceration and transmural active chronic inflammation with florid caseating and non-caseating granulomata within the bowel wall and the lymph nodes. Special stain for acid fast bacilli (Ziehl Neelsen) highlighted the organisms within the granulomatous inflammation of the lymph nodes and bowel wall.
Conclusion: The case was discussed at the multidisciplinary meeting and on review, a history of pulmonary TB was stated several years ago. This case report emphasises the importance of clinical information in handling, reporting and treating pulmonary and extra-pulmonary TB cases. TB of the intestine should always enter the differential diagnosis in particular where florid granulomata are encountered.

E-PS-06-041
Gallbladder leiomyomatosis: a rare incidental finding: a case report
S. Hidouri*, M. Hamdani, M. Walha, K. Bel Hadj Ali, Y. Maalej, A. Khabir
*Department of Pathology, Habib Bourguiba University Hospital, Medenine, Tunisia

Background & objectives: Gallbladder can hide a variety of tumours. The mesenchymal tumour is the rarest. Leiomyoma is a frequent benign mesenchymal tumour. Only a few cases of leiomyoma have been reported. Herein we report the case of discovering an incidental leiomyomatosis.
Methods: A 36-year-old female with no significant pathology, no history of uterine leiomyoma, other neoplasms or clinical evidence of immune defect. She was suffering from biliary colic accompanied by vomiting with inflammatory biological syndrome. Transabdominal ultrasonography showed a vesicular thicken-wall measuring 6mm with lithiasis. Cholecystectomy was performed.
Results: Gross examination revealed an atrophic mucosa and well-limited white nodular lesions the largest measuring 1,5cm.
Histopathological analysis revealed that the nodular aspect was composed of spindle cell proliferation with eosinophilic cytoplasm and bland cigar-shaped nuclei, without atypia or mitoses.
Immunohistochemical analysis demonstrated that the tumour cells were positive for Alpha-Smooth Muscle Actin and Desmin, but negative for CD117, CD34, anti PS100 and anti LMP1.
Conclusion: Although gallbladder leiomyomatosis still extremely rare. It is important to exclude a leiomyosarcoma, a gastrointestinal stromal tumour (GIST), an EBV infection associated to a smooth muscle tumour, which is the matter of a good immunohistochemical study.

E-PS-06-042
Schistosoma-induced appendicitis: a rare clinical entity – a case report
S. Hidouri*, M. Hamdani, S. Chahbani, M. Walha, K. Bel Hadj Ali, A. Khabir
*Department of Pathology, Habib Bourguiba University Hospital, Medenine, Tunisia

Background & objectives: Schistosomiasis is one of the most widespread parasitosis in the world, especially in Sub-Saharan Africa. Appendicitis is an unusual complication of schistosomiasis; it is still infrequently reported. Here we report a case of a Schistosomal appendicitis incidentally discovered after appendectomy.
Methods: A 29-year-old Nigerian male, with no past medical history, presented an intermittent pain in the lower right quadrant of the abdomen without fever. The leukocytes count, neutrophils eosinophils and C- reactive protein were not raised.
Results: Abdominal ultrasonography revealed a dilated appendix measuring up to 11mm in the transverse dimension. A diagnosis of acute appendicitis was made and an appendectomy was performed. Histological examination revealed an active inflammation in transmural with diffuse eosinophils and neutrophils, associated to a schistosomal colonization realizing foreign body granulomas around eggs. The final diagnosis was acute and granulomatous appendicitis associated with schistosoma eggs. Unfortunately, the patient is lost to follow-up.
Conclusion: Systematic histological examination is needed in front of all appendectomy specimens that can hide schistosomiasis infection. Even this unusual localization, intestinal schistosomiasis should be considered as a cause of acute appendicitis, especially among patients who have emigrated from or who have visited endemic areas.

E-PS-06-043
Histologic analysis of rectal biopsy samples from patients with chronic idiopathic constipation
A. Janegova*, M. Neszmeryova, R. Hustak, I. Kopecka, P. Janega
*Institute of Pathological Anatomy, Comenius University in Bratislava, Slovakia

Background & objectives: Chronic idiopathic constipation (CIC) is a common gastrointestinal disorder often causing significant disability of patients and is therapeutically hardly controllable. The pathophysiologic background of CIC is still unclear. However,

understanding the mechanisms of this disorder is crucial for effective treatment.
Methods: Morphological changes of the enteric nervous system and the interstitial cells of Cajal were evaluated by immunohistochemical staining in rectal biopsy samples from CIC patients (n=12) and compared with controls (n=4). The number of ganglion cells in the submucosa, the thickness of nerve fibres and the percentage of envelopment of myenteric ganglia by ICC was evaluated.
Results: Our study found that patients with chronic constipation showed a non-significant decrease in colonic ganglion cells in the submucosa compared to the control group. Hypertrophic nerve fibres were absent in controls but were detected in 5 out of 12 CIC samples. In addition, there was a significantly lower percentage of ICC envelopment of myenteric ganglia in samples from patients with chronic constipation compared to controls. These findings suggest that there may be morphological changes in the enteric nervous system and interstitial Cajal cells that contribute to chronic constipation, although further research is needed to confirm this hypothesis.
Conclusion: Emerging evidence suggests that abnormalities in the enteric nervous system and changes in the interstitial Cajal cells play a central role in the development of gut motility disorders. When the number of Cajal cells is reduced, pacemaker activity is impaired, and the loss of enteric ganglia and glial cells reduces nerve impulses to effector cells, leading to inefficient and uncoordinated function of the colon. Our study supports this multifactorial pathophysiology of colonic motility disorders.
Funding: APVV 20-0243 and VEGA 1/0684/21

E-PS-06-044
A rare localization of alveolar soft part sarcoma – A report of two cases
R. Jankovic*, S. Oprić, M. Denčić Fekete, M. Jovanović, M. Đuknić, J. Jevtic, L. Simic, M. Mihajlović, N. Šimšić, J. Sopta
*Institute of Pathology, Medical Faculty, University of Belgrade, Serbia

Background & objectives: Alveolar soft part sarcoma (ASPS) is a rare mesenchymal tumour typically occurring in young patients, more frequently in females. ASPS in visceral organs usually represents a metastasis from primary ASPS in skeletal muscles.
Methods: ASPS is characterized by a tumour-specific translocation which causes the fusion of the TEF3 with a ASPL gene (also known as ASPSCR1). Two patients were admitted to hospital due to symptoms of acute abdomen. Urgent surgery was performed, and tumour was detected in both cases.
Results: In first patient (female, 47 years old) ileal tumour was detected intraoperatively, while in other patient (male, 67 years old) rectal tumour with perirectal infiltration were detected. In both cases perforation within tumour were noted. Histology showed well-defined nests of pleomorphic cells separated by delicate fibrovascular septae. Beside this feature, foci of pseudoalveolar pattern were seen. Both tumours were diffusely immunopositive for TFE3 and vimentin. Other immunostainings exclude other TFE3 positive tumours – PECOMA, TFE3 positive haemangioendotheliomas and TFE3 positive renal cell carcinoma. FISH analysis was done using locus specific dual colour break-apart TFE3 (3' and 5') probe and rearrangement in the TFE3 gene was confirmed in both cases.
Conclusion: Despite the fact that ASPS is rare mesenchymal tumour in visceral organs. it should be considered as possible diagnosis, especially in cases with typical histological features and immunohistochemical profile. FISH analysis is mandatory for definitive ASPS diagnosis.

E-PS-06-045
Acute measles gastritis: a rare case report
J. Jevtic*, L. Simic, M. Đuknić, M. Korać, R. Jankovic
*Institute of Pathology, Serbia

Background & objectives: Due to availability of vaccines and timely vaccination, measles virus infections are highly unusual in developed countries, except for rare, usually imported cases from unvaccinated communities.
Methods: We report a case of a 35 years old male patient presented with fever, upper abdominal pain and vomiting with blood traces. Due to the aforementioned clinical presentation, the patient underwent upper endoscopy with biopsy sampling.
Results: Pathological analysis showed surface defects lined by fibrin and neutrophils which was consistent with acute erosive gastritis. Individual foveolae were dilated filled with apoptotic debris and neutrophils. Numerous mulberry-like multinucleated giant cells (Warthin Finkeldey) with Cowdry type A inclusions were present in foveolar and surface epithelium as well as in the stroma of lamina propria. Shortly after the endoscopy, the patient developed a rash, which raised suspicion of measles. Short anamnesis and insight into medical records showed that the patient has never been vaccinated for MMR vaccine.
Conclusion: Serological analysis was positive for measles IgM antibodies and the patient was diagnosed with measles. After a few days, with symptomatic therapy, the patient fully recovered without any complication.

E-PS-06-046
Demystifying 'hyaline angiopathy' of pulse granuloma in oral and extraoral surgical pathology- a case series of thirteen oral and five extraoral cases
R. Kanthan*, F. Sperandio
*University of Saskatchewan, Canada

Background & objectives: 'Giant cell hyaline angiopathy' described in Pulse Granuloma (PG) occurs in lesions from the beginning [mouth] and ending (colonic) of the digestive tract. The aim of this study is to demystify this 'hyaline angiopathy' that is described in these lesions.
Methods: A computer search of 135,972 consecutive surgical pathology cases with the diagnosis of 'pulse granuloma' was undertaken. The histopathological slides together with their demographic data and clinical findings were reviewed. Congo Red, Masson trichrome, Periodic Acid-Schiff (PAS), CD31, ERG, D240, and CD34 were performed on a representative formalin-fixed paraffin-embedded tissue block for each case with appropriate positive and negative controls.
Results: A total of 18 cases (thirteen oral and five extraoral) were identified. These lesions occurred in children and adults ranging from 7-83 years with a male predominance in oral cases while the extraoral cases were all females. The majority of oral PGs were associated with an inflamed odontogenic cyst or non-healing extraction socket. The extraoral cases were seen in: Appendix [3]; Peritoneum [1] and cecum [1] associated with inflammation and perforation. Congo Red was negative in all cases. The wormy 'hyaline angiopathy' expressed Masson/PAS and had no expression of the angiolymphatic markers ERG, D240 or CD31 with the latter outlining the surrounding vasculoinflammatory response of the pulse granuloma.
Conclusion: Our study supports the etiopathogenesis of oral and gastrointestinal PGs to reflect a granulomatous response triggered by the presence of certain components in legumes/seeds. The consistent positivity for Masson and PAS with total lack of vascular immunostaining within these "wormy" structures proves there is no evidence of any 'angiopathy' in these granulomas and continued usage of this term is to be strongly discouraged. We propose these "wormy" structures represent a varied fibrocollagenous tissue response dependent on the legume/seed present.

E-PS-06-047
A case of gastric adenocarcinoma with enteroblastic differentiation and carcinosarcomatous feature
Y. Kim*, Y. Chun
*National Health Insurance Service Ilsan Hospital, Republic of Korea

Background & objectives: We present a rare case of gastric adenocarcinoma with enteroblastic differentiation and massive lymph node

metastases showing carcinosarcomatous features. Our objective is to highlight the characteristic histopathological and immunohistochemical findings of this aggressive tumour.
Methods: The 83-year old woman was admitted due to acute epigastric pain. CT scan showed advanced gastric cancer with perigastric lymph node enlargement and CBD stones. The patient underwent subtotal gastrectomy with lymphadenectomy. On gross examination, a huge ulceroinfiltrative mass (9x6cm) was located in the antrum along greater curvature. The largest metastatic node measured up to 4.5cm in the diameter.
Results: On microscopic examination, the cuboidal to columnar tumour cells have clear cytoplasm, resembling foetal gut epithelium. Many multinucleated giant cells were scattered mainly at the periphery of the tumour. Multiple lymphovascular invasions were present. Metastatic nodes revealed carcinosarcomatous feature without heterologous component. On immunohistochemistry, the tumour cells were positive for AFP, glypican-3 and SALL4. Multinucleated giant cells were negative for HCG but positive for CD163. Sarcomatous area were negative for AE1/AE3, positive for vimentin and focally positive for SALL4. Serum AFP was markedly elevated even though it was measured one week after surgery.
Conclusion: Although gastric adenocarcinoma with enteroblastic differentiation is rare, pathologists should be aware of its characteristic histopathological and immunohistochemical findings due to its combination of multiple lineage of differentiation and aggressive behaviour. Our case highlights the importance of careful pathological examination and immunohistochemistry in the diagnosis.

E-PS-06-048
Primary alveolar soft part sarcoma of the stomach: a rare case report
K. Kim*, J. Ahn
*Republic of Korea

Background & objectives: Alveolar soft part sarcoma (ASPS) is a rare malignant mesenchymal tumour which commonly involves deep soft tissues of the extremities and trunk. Herein, we report a rare case of ASPS of the stomach, showing preoperative diagnostic difficulty.
Methods: The patient was a 32-year-old man who had no past history. During a screening esophagogastroduodenoscopy (EGD), a subepithelial lesion was identified in the midbody of the stomach. The following endoscopic ultrasonography and the computed tomography (CT) of the abdomen showed a 2-3cm-sized exophytic mass in the stomach, being suggestive of gastrointestinal stromal tumour. The laparoscopic wedge resection was performed.
Results: Macroscopically, a well-defined subepithelial mass with tan-to-yellow cut surface, measuring 2.5cm in size, was identified. Microscopically, the tumour consisted of large polygonal cells with round and vesicular nucleus, prominent nucleolus and abundant eosinophilic cytoplasm. It showed nested growth pattern with fibrous septa and capillary network. These nests revealed central discohesiveness. Immunohistochemically, the tumour was diffusely positive for TFE-3, focally positive for HMB45, and negative for c-kit, DOG1, SMA, desmin, H-caldesmon, CD34, S100, pancytokeratin, EMA, melan A, chromogranin A and synaptophysin. Based on these findings, it is consistent with ASPS. During two years follow-up, EGD and abdominal CT showed no evidence of disease recurrence or metastasis and no remarkable abnormal findings.
Conclusion: ASPS is a rare distinctive sarcoma, typically occurring in deep soft tissues. The current case is worthy of its rarity of primary gastric ASPS and added to the literature on ASPS of the stomach. In addition, this case emphasizes the need, even though it is unusual, for clinicians and pathologists to recognize that ASPS could be represented as a subepithelial tumour of the stomach. Long-term follow-up and further researches should be gathered to evaluate the clinical significance for gastric ASPS.

E-PS-06-050
Malignant gastrointestinal neuroectodermal tumour with SMARCA4 mutation
L. Korša*, M. Abramović, L. Kovačević, P. Jurešić, I. Veliki Dalić, Z. Marusic
*Clinical Department of Pathology and Cytology, University Hospital Centre Zagreb, Croatia

Background & objectives: Malignant gastrointestinal neuroectodermal tumour (GNET) is a rare malignant tumour which occurs mainly in the gastrointestinal (GI) tract in young and middle-aged adults. This is the first report of SMARC4 molecular alteration in a GNET.
Methods: A 54-year-old man with an uneventful previous medical history presented with ascites. Computed tomography scan of the chest and abdomen showed peritoneal carcinomatosis, thickening of the hepatic flexure and sigmoid colon, liver metastases and abdominal lymphadenopathy. Colonoscopy was not performed due to patient's poor general condition.
Results: Exploratory laparotomy revealed multiple omental nodules, peritoneal carcinomatosis and a large palpable inoperable tumour of the sigmoid colon. The tumour nodules contained solid nests of atypical epithelioid/rhabdoid tumour cells. Mitotic index was 10/mm2. Tumour cells were diffusely positive for Sox10 and MiTF, focally positive for S100, and weakly for HMB45 in few cells. Desmin, epithelial markers and melan A were negative. As the differential diagnosis included metastatic melanoma and GNET, comprehensive genomic profiling using a cancer-related gene panel confirmed an EWSR1-ATF1 fusion and the diagnosis of malignant GNET. Additionally, SMARCA4 deficiency with loss of exons 19-30 was discovered. Subsequently, there was loss of SMARCA4 expression by immunohistochemistry.
Conclusion: SMARCA4-deficient malignant neoplasms are rare, and typically present as poorly differentiated, aggressive carcinomas involving the lung, ovary, GI tract and rarely other organs. Histology is characterized by dyscohesive, rhabdoid appearing cells with eosinophilic cytoplasm, eccentric nuclei and visible nucleoli. Necrosis and mitotic activity are frequently prominent. SMARCA4-deficient malignancies of the GI tract are restricted to rare cases of undifferentiated carcinoma and to our knowledge, this is the first described case of malignant GNET with SMARCA4 deficiency.

E-PS-06-051
Collagenous gastritis: a case series and literature review
E.N. Kozan*, S. Yüksel, B. Savaş, A. Ensari
*Ankara University Medical School, Pathology Department, Turkey

Background & objectives: Collagenous gastritis (CG) is a rare disease, less than 300 cases reported so far and characterized by subepithelial deposition of collagen, variable inflammation in the mucosa. We aimed to present five cases of CG and discuss our findings with literature.
Methods: Retrospective observational study of all 5 cases diagnosed as CG based on clinical and pathological criteria, in our institution from 2010 to 2023. Clinical information was retrieved from the hospital records. All histological preparations of the cases, including histochemical trichrome stained sections, were reevaluated.
Results: Four patients in the adult age group were female, and one patient was 9 years old male. Three patients presented with iron deficiency anaemia whereas four of them had accompanying diseases including ulcerative colitis, Crohn's disease, allergic rhinitis, Sjogren's syndrome. Endoscopically, nodular appearance was observed in the gastric mucosa in 4 patients. Microscopically, CG was found to be accompanied by collagenous colitis in one case while collagenous duodenitis and colitis in another. Collagenous bands were observed in the gastric corpus and antrum mucosa in two patients while only in the gastric corpus mucosa in 3 patients. Clinical improvement was observed from PPI and iron supplementation treatment.
Conclusion: Similar to the literature; female predominance was observed and 80% of the patients had at least one autoimmune, inflammatory or rheumatological concomitant disease. Two phenotypes of CG have been

described: paediatric and adult-onset types. In paediatric-onset CG collagen deposition is generally restricted to the stomach; our paediatric patient also had no collagen deposition in duodenum or colon. CG is a rare entity; responds well to iron supplementation treatment therefore, possibility of CG should be considered in patients with persistent anaemia.

E-PS-06-052

Microsatellite instability in ampullary adenocarcinoma

V. Kropelnytskyi*, V. Shkarban, I. Romasko, I. Grygorova
*Shalimov National institute of surgery and transplantation, Ukraine

Background & objectives: Ampullary cancers make up to 6-9% of the pancreaticoduodenal zone tumours. The most frequent histology type is adenocarcinoma. Some cases are associated with microsatellite instability (MSI). The study aim is to evaluate MSI frequency in ampullary adenocarcinoma cases.
Methods: The study included 69 patients who underwent pancreatoduodenectomy for ampullary invasive adenocarcinoma during the period 2019-2022. TMA with core size 2 mm were constructed in manual mode. Immunohistochemistry for DNA mismatch repair proteins (MLH1, PMS2, MSH2, MSH6) were performed. Cases with preserved expression of all proteins were MSS. Cases with absence of expression of some proteins were considered as MSI.
Results: MSI were detected in 9 out of 69 cases (13,8%). All of them were MLH1/PMS2-defficient. Patients average age was 59.7±8.2 years for MSI cases and 61.1 ± 8.1 years for MSS cases. Intestinal type adenocarcinoma was in 5 cases (55.6%), pancreatobiliary adenocarcinoma was in 4 cases (44.4%). MSI cases more frequently have poorly differentiated morphology: 33.3% vs 14.2% in MSS cases. 2 out 5 intestinal adenocarcinoma cases have focal medullary morphology. Regional lymph nodes status for MSI cases was next: pN0 - 2 cases, pN1 – 6 cases, pN2 - 2 cases.
Conclusion: MSI frequency in ampullary adenocarcinoma according to our data is 13,8%. Which is just a little less than generally accepted MSI frequency in colorectal cancer (15%). All the MSI cases were due to MLH1/PMS2-defficiency. Further research is needed to clarify whether it is sporadic or germinal microsatellite instability. Given that MSI cases in general have specific follow-up and treatment options, it is advisable to test ampullary adenocarcinoma for microsatellite instability.

E-PS-06-053

Frequency of Her-2/neu positivity in ampullary adenocarcinoma

V. Kropelnytskyi*, V. Shkarban, I. Romasko, I. Grygorova
*Shalimov National institute of surgery and transplantation, Ukraine

Background & objectives: Her-2/neu expression is most frequently found in breast and gastric cancer cases. According to the literature some ampullary adenocarcinoma cases also could have Her-2/neu overexpression. The study aim is to evaluate Her-2/neu overexpression frequency in ampullary adenocarcinoma.
Methods: The study included 69 patients who underwent pancreatoduodenectomy for ampullary invasive adenocarcinoma during the period 2019-2022. TMA with core size 2 mm were constructed in manual mode. Immunohistochemistry for Her-2/neu was performed. Expression was assessed based on the Her-2/neu gastric cancer guideline.
Results: Her-2/neu overexpression with the expression degree 2+ and 3+ was detected in 2 out of 69 cases (2.8%). Case with 3+ expression degree has strong complete staining in 100% of tumour cells. Both were intestinal type adenocarcinoma, lymph node negative, pMMR (MSS).
Conclusion: Her-2/neu overexpression rate in ampullary adenocarcinoma according to our data is 2.8%. According to different papers this rate is from 0 to 23%. Nowadays Her-2/neu testing is not included into standard diagnostic protocol for ampullary cancer. But considering the literature data (case reports) on the HER2-directed therapy effectiveness in cases of ampullary adenocarcinoma, it is advisable to consider this diagnostic option for metastatic cases.

E-PS-06-054

Imunohistochemical study of morphologic impact of microsatellite instability (MSI) in malignant colorectal cancer (CRC) of local population

M. Kupryte*, T. Navickis, N. Cesana, L. Poškienė
*Lithuanian university of health sciences, Institute of Cardiology, Lithuania

Background & objectives: CRCs with detected MSI have distinctive morphology. Study of CRC with MSI focusing on local population-associated morphological tendencies may present clinically relevant information optimizing individualized treatment in local healthcare infrastructure. Objective - identify population-focused morphologic tendencies among CRC with MSI.
Methods: 100 cases were included in study and analysed according to parameters of CRC anatomical site, histological type, differentiation grade (G) of CRC, T and N stages of TNM classification, and MSI status (MLH1, MSH2, MSH6, and PMS2). Cases with selected CRC were classified into MSI and microsatellite-stable (MSS) groups. Statistical analysis of $\chi 2$ test was applied ($p<0.05$).
Results: Most of selected CRCs were diagnosed as infiltrative adenocarcinoma (not otherwise specified, n=81, 81%), mostly of T3 stage (n=95, 95%), N0 stage (n=93, 93%), and of G2 (n=92, 92%). 30% of selected cases (n=30) had MSI status with predominant loss of MLH1 and PMS2 expression (both – 25% of MSI-associated CRCs) and BRAF expression (74% of MSI-associated CRCs, $\chi 2=21.754$, $p=0.001$). MSI-associated CRCs were more likely to originate in ascending colon (n=11, 11%, $\chi 2=16.826$, $p=0.01$) and have G3 (n=5, 5%, $\chi 2=6.5$, $p=0.039$). No statistically significant features were detected in MSI-associated CRC group, when evaluating histological CRC type ($\chi 2=9.259$, $p=0.16$), T ($\chi 2=1.365$, $p=0.505$), and N stages ($\chi 2=2.586$, $p=0.764$) of TNM classification.
Conclusion: Immunohistochemical study of morphologic impact of MSI in local population revealed that immunohistochemically diagnosed MSI-associated CRC are more likely to loose MLH1 and PMS2 expression, originate in ascending colon, and have G3, representing worldwide tendencies of CRC morphology and its MSI status.

E-PS-06-055

Gastrointestinal stromal tumour case report series and evaluation of prognostic parameters

E. Kussever*, T. Toyran, E. Kilic Bagir, A. Acikalin
*Cukurova University, Turkey

Background & objectives: Gastrointestinal stromal tumours (GISTs) are the most common mesenchymal tumours of the gastrointestinal tract. They mostly derive from precursors of the interstitial cells of Cajal. We aimed to focused on pathological findings and prognostic parameters on GISTs.
Methods: Totally 174 patients biopsy-proven GISTs were enrolled into this study between the years of 2012-2022 retrospectively. The effects of tumour size, localization, immunohistochemical markers, gender, histologic type and risk assessment and mitotic rate on prognosis were examined. Logistic regression analysis (forward method) and chi-square test were used in this study. A value of $p<0.05$ was considered statistically significant.
Results: Patients were summarized as: the mean age was 59,34 years old, male/female ratio was 1. They were morphologically spindle cell (n:154), epithelioid (n:10) and mixed type(n:10). According to the risk assessment guideline, the risk was evaluated as no risk (n:15),very low (n:15), low (n:34), moderate (n:22) and high (n:88).There was no statistically significant relationship with gender (p:01) and tumour size (p:0.07).The prognosis was found to be better located in the GI tract than the other locations. 'No risk' and 'high risk' groups had worse prognosis. We consider that the high mortality rate in the 'no risk'

group is due to the patient's comorbidities. This study showed that proliferation index of Ki67 is directly proportional to the prognosis. An increase of 0.07 units in Ki67 increased the risk of death by 2.8%.
Conclusion: In this case series study, we wanted to emphasize the importance of parameters such as gender, risk assessment, size, localization, and proliferation index on prognosis in gastrointestinal stromal tumours.
Funding: Cukurova University

E-PS-06-056
Lymphomas with primary gastrointestinal presentation: 5 years' experience in a quaternary care centre in Southern India
A. Lakshmanan*, D. Maria George, A. Subramanyam
*Apollo Hospitals, India

Background & objectives: Lymphomas can involve the Gastrointestinal tract (GIT) either as the sole area of disease (primary) or as a secondary spread of systemic disease. GIT is the commonest site of extra nodal presentation of non-Hodgkin lymphoma (NHL).
Methods: A retrospective study from 2018 to 2022 was conducted wherein all cases of lymphoma with primary gastrointestinal presentation were retrieved. Haematoxylin and eosin-stained sections and immunostains done on all the cases were retrieved and reviewed.
Results: A total of 156 cases of lymphomas were diagnosed in GIT specimens. Stomach (n=81) was the commonest site followed by small intestine (n=40), large intestine (n=33) and oesophagus (n=2). B-cell NHLs were noted in 148 cases of which Diffuse large B cell lymphoma (DLBCL) was the commonest (102 cases) followed by high grade B cell lymphoma (14 cases), low grade marginal zone lymphoma of mucosa associated lymphoid tissue (11 cases), mantle cell lymphoma (7 cases), follicular lymphoma (4 cases) and Epstein Barr virus positive DLBCL (3 cases). 8 cases of T-cell lymphomas were noted including some rare entities. Three cases of Hodgkin lymphomas with secondary involvement of GIT were noted.
Conclusion: The distribution and incidence of various entities in our study was comparable to other Indian studies as well as few western studies. Gastrointestinal lymphomas are heterogenous with different treatment modalities. Hence, diagnosing them correctly would help in appropriate treatment.

E-PS-06-057
The prognostic value of the co-expression of Programmed Death-Ligand 1 (PD-L1) and Ki-67 in colorectal cancer: insights from a northern Portuguese patient cohort
N. Lamas*, I. Havenko, F. Sousa, S. Martins
*Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal; Anatomic Pathology Service, Pathology Department, Centro Hospitalar Universitário de Santo António (CHUdSA), Porto, Portugal

Background & objectives: Colorectal Cancer (CRC) represents a major health problem worldwide and the development of novel prognostic tools might lead to better-quality patient treatment. The co-expression PD-L1|Ki-67 has shown promising prognostic value in certain tumours, but its role in CRC is unknown.
Methods: We conducted a retrospective, observational and descriptive study involving patients with CRC undergoing curative surgery at the Hospital de Braga, Portugal, from January 1st 2005 until January 1st 2010. Tissue microarrays constructed from the primary CRC patient specimens were used to evaluate the PD-L1|Ki-67 co-expression using immunohistochemistry. The PD-L1| Ki-67 co-expression levels were then correlated with various clinical-pathological parameters.
Results: Positive co-expression of both PD-L1 and Ki-67 was observed in 35,4% of patients with CRC. PD-L1|Ki-67 co-expression was significantly associated with age at diagnosis, histological type of CRC and tumour recurrence. Positive co-expression was higher in patients without disease recurrence (44,6%) compared to those with recurrence (22,7%). A statistically significant association of marker co-expression with patient prognosis was not possible to establish, although a longer survival time was observed in patients without expression of both PD-L1 and Ki-67.
Conclusion: We demonstrated a significant association of PD-L1|Ki-67 co-expression with age at diagnosis, histological type and CRC recurrence. The double positive co-expression seems to represent a protective effect in patients without CRC recurrence. However, we could not establish a statistically significant association between PD-L1|Ki-67 co-expression with the prognosis of CRC patients. Further studies involving a larger set of patients across multiple centres worldwide may help to further clarify the relevance of PD-L1|Ki-67 co-expression in determining the prognosis of patients with CRC.

E-PS-06-058
AMACR – a marker to differentiate between primary jejunal and metastatic adenocarcinoma
A. Georgescu*, M. Sajin, T. Georgescu
*Department of Pathology, "Carol Davila" University of Medicine and Pharmacy Bucharest, Department of Pathology, Nephrology Clinical Hospital "Dr. Carol Davila", Bucharest, Romania

Background & objectives: AMACR is a marker expressed in prostatic adenocarcinoma, papillary renal cell carcinoma and ovarian clear cell carcinoma. Additionally, AMACR has been discovered to be expressed in around 81.7% of all colorectal adenocarcinomas, especially those located on the left colon.
Methods: We collected clinical, epidemiologic and pathological data regarding 10 cases of colorectal adenocarcinomas, 2 primary jejunal adenocarcinoma and one jejunal metastasis of metastasis in a patient with a known history of colon adenocarcinoma. All the cases have been stained for AMACR, CK7 and Mismatch Repair Proteins. The collected data has been analysed with SPSS software.
Results: Mean age of the patients was 58 years, males represented 69,2% of all cases and 61% came from a rural environment. Immunoreactivity for CK7 was observed in 100% of jejunal adenocarcinoma, 10% of colorectal adenocarcinoma (patchy) and it was not present in the jejunal metastasis. AMACR was however expressed in 90% of all colorectal adenocarcinomas, in none of the jejunal adenocarcinomas and it was present in the jejunal metastasis. Loss of expression for MLH1 and PMS2 was observed in 10% of all colorectal adenocarcinoma and loss of MLH1, PMS2, MSH6 and MSH2 was observed in another 10%. No correlation was observed between the loss of MMR proteins and AMACR immunoreactivity.
Conclusion: In conclusion, the combination of AMACR and CK7 can help distinguish between a primary small intestinal adenocarcinoma and a colorectal adenocarcinoma metastasis to the jejunum. The distinction between the two entities is essential, as it alters the TNM of the tumour and, subsequently, the future neoadjuvant therapy. There was no correlation observed between the immunoreactivity for AMACR and the presence of microsatellite instability. More studies, performed on a larger number of cases, are needed in order to validate this observation.

E-PS-06-059
Anal hidradenoma papilliferum, unexpected finding in haemorrhoidectomy. Case report
R.D.P. Lopez-Panqueva*, D. Ellmer, M. Rolon Cadena, J. Padron
*Fundación Santa Fe de Bogotá, Department of Pathology and Laboratory Medicine, Universidad de Los Andes, Bogotá, Colombia

Background & objectives: Hidradenoma papilliferum, an extremely rare benign neoplasm in the anal region, is typically associated with the vulva. We report an incidental case from a haemorrhoidectomy, contributing to the scant literature on this topic.

Methods: To examine haemorrhoidectomy samples and identify the rare presentation of hidradenoma papilliferum in the anal region, utilizing H&E staining and immunohistochemistry (IHC) for hormonal receptor and epithelial membrane antigen (EMA).
Results: Histopathological examination of the haemorrhoidectomy samples revealed an incidental hidradenoma papilliferum in the posterolateral right resection. The tumour appeared as a well-circumscribed, cystic-papillary lesion with benign characteristics. Cystic and papillary structures consisted of multiple stalks with vascularized fibroconnective tissue, covered by epithelium exhibiting apocrine decapitation secretion. The resection margins were tumour-free, and surrounding tissues displayed mixed haemorrhoids with congestive changes.
Immunohistochemical staining was performed on the tumour sections to confirm the diagnosis of hidradenoma papilliferum. Oestrogen receptor expression was detected in the tumour cells, confirming the diagnosis. Additionally, (EMA) staining highlighted the cellular membranes, further supporting the diagnosis of hidradenoma papilliferum.
Conclusion: This case report underscores the rare occurrence of hidradenoma papilliferum in the anal region, discovered incidentally during a haemorrhoidectomy. The diagnosis was confirmed through histopathological examination. Further studies and case reports are needed to better understand the aetiology, risk factors, and optimal management strategies for hidradenoma papilliferum in this unusual location. Clinicians should be aware of such rare presentations to facilitate accurate diagnosis and appropriate treatment.

E-PS-06-060
Use of routine special stains for gastric and oesophageal biopsies
I. Mallek*, O. Belkacem, B. Bouchabou, M. Mbarek, A. Lahmar, D. Bacha, S. Ben Slama
*Monji Slim La Marsa, Tunisia

Background & objectives: Special stains are performed systemically, in some laboratories, for the diagnosis of *H. pylori* and intestinal metaplasia (IM). The aim of this study was to evaluate the contribution of these stains in gastric and/or oesophageal biopsies.
Methods: This retrospective study included consecutive gastric and oesophageal over a six-month period. During this period, we received 209 biopsies from 139 patients. The *H. pylori* and IM were initially visualized on H&E-stained slides, In a second step, we analysed the corresponding Giemsa stained. Then, we examined the corresponding slides stained with PAS and the Alcian Blue (AB).
Results: The results of the H&E and Giemsa were concordant in 173 biopsies (82.8% of all biopsies) with kappa = 0.58: The two tests were not concordant in 36 biopsies (17,2%). IM was present in 11 H&E sections (5,3% in all biopsies sites) and absent in 198 cases (94,7%). The AB has therefore made no diagnostic gain since all negative biopsies on H&E stain were also negative on AB stain. Comparing the identification of IM on PAS and H&E stains, concordance was in 99.5% (207 biopsies).
Conclusion: Routine special stains for detection of *H. pylori* and IM are not required for most gastric and/or oesophageal biopsies. The best positive predictor is the presence of neutrophils, combined with chronic inflammation. If *H. pylori* eradication treatment has failed, then the presence of neutrophils is a sensitive marker of that failure and if organisms are not seen on H&E, then special stain or immunohistochemical stain should be performed.

E-PS-06-061
Clinicopathological features of colorectal cancer in patients younger than 40 years of age in Northern Tunisia
I. Mallek*, S. Ben Slama, B. Bouchabou, M. Mbarek, M. Hajri, H. Mestiri, A. Lahmar, D. Bacha
*Monji Slim La Marsa, Tunisia

Background & objectives: Colorectal carcinoma (CRC) in patients younger than 40 years is rare but incidence is increasing. The objective of this study was to describe demographics, clinico-pathologic and therapeutic management and to evaluate prognosis factors in this young population.
Methods: It was a retrospective study including with CRC in patients under the age of 40.
Results: 40 cases were under the age of 40 among 428 patients with CRC (9,34%) (Sex ratio M/F =0.8, average age = 33.6 years). Family history of cancer was present in 20%, and predisposing factors were present in 25% of the patients. The cancer was rectal in 55% of cases and colic in 45%. It was adenocarcinoma (not other specification) in 75% of cases with MSI-H phenotype in 17,5% of cases. The tumours were classified as stage II in 40% of cases and stage III in 47.5% of cases. The overall 5-year survival rate was 27%. Patients without Inflammatory Bowl Diseases history have significant increase in survival ($p<0.05$).
Conclusion: Young patients with colorectal cancer with predisposing factors have poorer prognosis in a population in Northern Tunisia.

E-PS-06-062
Predictive factors for histological response to neo-adjuvant treatment in rectal cancers
I. Mallek*, S. Ben Slama, B. Bouchabou, M. Mbarek, M. Hajri, H. Mestiri, A. Lahmar, D. Bacha
*Monji Slim La Marsa, Tunisia

Background & objectives: Histological response is the goal of neo-adjuvant treatment of locally advanced rectal cancer. Results of various studies focused on pathological predictive response factors are discordant. The aim of this study was to search factors of histological response to neo-adjuvant treatment.
Methods: Retrospective study involving 44 patients with locally advanced rectal adenocarcinoma who received neo-adjuvant radiotherapy or radiochemotherapy. The prognostic factors studied were clinical (age and sex), radiological (tumour size and parietal invasion) and histological (histological grade, vascular and nerve invasion) features. Complete histological response was defined by Bateman's tumour grade m-RCRG 1 and the absence of lymph node metastases.
Results: A complete histological response was observed in 25% of cases (n = 11). In multivariate analysis, age> 60 years (OR: 1.14 and p = 0.028), male sex (OR: 21 and p = 0.045) and radiological wall invasion exceeding the subserosa (OR: 11 , 5 and p = 0.008) were significantly associated with the histological response. In contrast, none of the 3 histological factors tested were correlated with this response's intensity.
Conclusion: Age, gender, and pre-therapeutic parietal invasion could be used to select «good» and «poor» responders to neo-adjuvant treatment in locally advanced rectal cancers.

E-PS-06-063
Intestinal spirochaetosis: review of cases diagnosed in a third level hospital
J. Martínez Castillón*, S. Vicente Arregui, E. Del Valle Sánchez, M.Á. Trigo Cebrián, C. Hörndler Argarate, J.L. Delgado Fernández, N. Martínez Arnau, A. Carilla Sanromán, L. Leon, L. Ollero Domenche
*Hospital Universitario Miguel Servet, Spain

Background & objectives: Intestinal spirochaetosis is a bacterial growth defined by the colonization of the apical membrane of the colorectal mucosa by spirochetes, wich generally do not become invasive. The gold standard for the diagnosis is the detection of microorganisms by histological examination.
Methods: A retrospective review was carried out, using the PAT-Win database, of the intestinal biopsies coded with the SNOMED " Spirochete", during the period from 2017 to 2023 at the Miguel Servet University Hospital in Zaragoza. Subsequently, the epidemiological

and histopathological characteristics of the cases found were analysed and compared with the findings found in the literature.
Results: 10 cases with the presence of intestinal spirochaetosis were obtained. Six of them had concomitant sexually transmitted diseases. Histologically, with hematoxylin and eosin staining, areas of fraying of the epithelial brush-like luminal border were observed in all samples. In all cases, the Warthin-Starry and Spirochete histochemical and immunohistochemical techniques were requested. In nine of them the bacteria were clearly identified by both techniques, with diffuse involvement. In eight patients, spirochetes were found not only in the superficial epithelium but also in the crypts, also identifying, and exclusively in these same cases, lymphoid aggregates in the upper third of the lamina propria.
Conclusion: It is interesting to note that our review and through histochemical and immunohistochemical techniques revealed the presence of spirochetes not only in the superficial epithelium but also within the crypts, coinciding in these cases with the presence of lymphoid aggregates. However, these findings did not have a correlation in terms of the degree and type of inflammation present in the lamina propia or in terms of the type of clinical presentation.

E-PS-06-064
Differences in immunohistochemical expression of filaggrin between proton pump inhibitor-non-responders and proton pump inhibitor-responders of eosinophilic oesophagitis
R. Maruyama*, N. Ishimura, A. Araki, M. Yuki, N. Nagano
*Izumo Tokushukai Hospital, Japan

Background & objectives: The patients with eosinophilic oesophagitis (EoE) are divided into proton pump inhibitor-non-responders (PPI-NR) and proton pump inhibitor-responders (PPI-R). Our objective was to seek the clinical usefulness of the differences of barrier protein expressions between these two groups.
Methods: Thirty PPI-NR, 45 PPI-R and 35 reflux oesophagitis patients were enrolled. After clinical information including age, gender and allergic backgrounds and histopathological findings were reviewed, immunohistochemical expressions of epidermal differential complex proteins (filaggrin, loricrin and involucrin) and desmoglein in all three groups were examined and semi-quantitatively scored. These clinical and pathological factors were statistically analysed between the three groups.
Results: There were significant differences in age and gender between EoE and RE, but no differences were observed between PPI-NR and PPI-R. Regarding allergic conditions, the prevalence of asthma was significantly higher in PPI-NR than in PPI-R. Other allergic conditions showed no differences between the three groups. Conventional histopathological findings (number of infiltrating eosinophils, basal cell hyperplasia and spongiosis) did not exhibit statistical differences between PPI-NR and PPI-R. However, immunostaining score of filaggrin in PPI-NR was significantly lower than in PPI-R, although the expressions of involucrin, loricrin and desmoglein showed no differences.
Conclusion: In the present study, we have demonstrated for the first time that the immunohistochemical expression of filaggrin in PPI-NR is significantly lower than in PPI-R. The results suggest a role of reduced filaggrin expression in the difference of effectiveness of PPI treatment between PPI-NR and PPI-R. Moreover, immunohistochemical determination of filaggrin expression in EoE patients could be informative in clinical decision of how to treat the patients.

E-PS-06-065
An exceedingly rare case of anorectal mucosal melanoma: case report
M. Matanie*, A. Birceanu, M. Florescu, A. Martiniuc, N. Copca, M. Sajin, A. Evsei
*Colentina Clinical Hospital, Romania

Background & objectives: Anorectal mucosal melanomas (AMM) are exceedingly rare, generally present at a later stage, are more aggressive and carry a worse prognosis. We report a recent and rare case of AMM.
Methods: A 77 years old patient presented to our clinic with rectal bleeding, chronic constipation, loss of appetite and a recent episode of sub occlusive colonic syndrome. On rectal examination a 2,5 cm, expansile mass and external haemorrhoids were noted. Colonoscopy revealed a fungating, circumferential, ulcerated mass and a rectal pedunculated polyp. No clinical history of cutaneous melanoma was found.
Results: Multiple biopsies were performed, and histological examination showed a solid proliferation composed of sheets of large pleomorphic cells with prominent nucleoli, amphophilic cytoplasm and large amounts of intracytoplasmic brown pigment granules which were confirmed to be melanin granules using Fontana-Masson staining. Excision of the mass and the rectal polyp revealed the same histological features. Tumour cells expressed SOX10 and S100. A diagnosis of AMM was established, and the patient underwent surgery for rectal amputation that histologically revealed a scar and residual tumoral cells in the submucosa and muscularis propria with no lymph node metastasis.
Conclusion: Mucosal melanoma typically arises in the anorectal region, the median patient age at diagnosis is 65 years and accounts for less than 1% of gastrointestinal malignancies and 1% of anorectal malignancies overall. It shows a low mutation burden, with no UV signature. As in our case, the diagnosis is made in late stages. Primary melanoma of the GI tract is an aggressive and clinically complex malignancy which remains associated with poor overall survival despite the use of multiple treatment modalities.

E-PS-06-066
Gastric adenomatoid tumour – case report and literature review
G. Miranda*, O. Pedro, J. Dos Santos, R. Machado-Neves, T. Amaro
*Unidade Local de Saúde de Matosinhos - HPH, Portugal

Background & objectives: Adenomatoid tumour is a rare benign neoplasm of mesothelial origin with predilection for the genital tract. Extragenital locations are rare and constitute a challenge in the differential diagnosis with malignant neoplasms. Description of a gastric adenomatoid tumour and literature review.
Methods: The tumour was incidentally found in a 69-year-old woman undergoing hiatal hernia repair. During the surgical procedure, a polypoid lesion was identified on the serosa of the anterior gastric wall, which had not been described by imaging methods. The lesion was sent for histopathological study.
Results: Macroscopically, a polypoid lesion measuring 7 x 6 x 3 mm with a whitish cut surface was observed. On histological examination, a neoplasm with circumferential but poorly defined boundaries was observed in a subserosal location, composed of tubules and trabeculae of varying sizes. The neoplastic cells were flattened to cuboidal with moderate and eosinophilic cytoplasm, sometimes vacuolated. No mitoses or atypia were observed. The mesothelial nature of the lesion was confirmed by immunoreactivity for AE1/AE3 cytokeratins, calretinin, and WT1.
Conclusion: Given their rarity, gastrointestinal adenomatoid tumours can represent a significant diagnostic challenge, especially in tumours with glandular and signet-ring morphology, mimicking primary or metastatic adenocarcinomas. This distinction becomes crucial in the management of the patient given the benign nature of adenomatoid tumours.

E-PS-06-067
Chronic radiation enteritis with diffuse ganglioneuromatous proliferation - a rare association presenting as subacute intestinal obstruction
S. Naresh Shah*, A. Parameswaran
*Apollo hospitals, India

Background & objectives: Chronic radiation enterocolitis can occur within days or after years in patients with history of radiation therapy for pelvic tumours. It occurs in about 20% of these patients, with obliterative arteritis causing intestinal ischemia, being the pathological process involved.
Methods: A 71year old lady, with history of radiation therapy 25 years ago for cervical carcinoma, presented with subacute intestinal obstruction. Radiological imaging revealed multiple ileal strictures with diffuse wall thickening. An emergency laparotomy was performed, and the bowel segment was sent for histopathological examination.
Results: Grossly, there were four strictures with firm white wall thickening, nodular mucosa with intervening ulceration. Histological examination showed ulceration with inflammation, hyalinised vessels with fibrointimal hyperplasia, stromal atypia and submucosal fibrosis. In addition to these findings, there was diffuse nodular transmural ganglioneuronal proliferation with Schwannian stroma. The features were suggestive of Chronic radiation enteritis with associated diffuse ganglioneuromatous proliferation. Patient had no genetic predispositions, no clinical signs/lesion of Neurofibromatosis or any such syndromes on examination.
Conclusion: We present a rare association of Chronic radiation enteritis with incidental diffuse ganglioneuromatous proliferation, probably first of a kind, the significance of which is not known. To the best of our knowledge, the presence of ganglioneuromatous proliferation has not been typically described as a part of radiation induced injury.

E-PS-06-068
Low-grade appendiceal mucinous neoplasm (LAMN) and endometriosis of the appendix in a 46-year old woman: a case report about an exceedingly rare disease association
S. Neves*, F. Sousa Vieira, D. Sá, A.P. Rodrigues, J.R. Vizcaíno, N. Jorge Lamas
*Centro Hospitalar Universitário de Santo António, Portugal

Background & objectives: Low-grade appendiceal mucinous neoplasm (LAMN) is a rare mucinous appendiceal neoplasm found in ~1% of appendectomies. Appendiceal endometriosis is only identified in <1% of patients with pelvic endometriosis. The co-existence of LAMN with appendiceal endometriosis has been scarcely reported.
Methods: We report a case of a 46-year old woman who presented with abdominal pain in the right lower quadrant. The ultrasonography and computerized tomography scan studies showed an appendiceal mucocele. The patient was submitted to right hemicolectomy.
Results: The surgical specimen comprised an ileum segment of 8 cm, cecocolic segment of 9 cm and an appendix of 10 cm, containing irregular serosa, increased caliber, lumen with abundant mucinous content and an area of rupture reaching the mesoappendix. Histological analysis showed LAMN with only acellular mucin invading the subserosa and mesoappendix, accompanied by lesions of acute appendicitis. Besides, several foci of endometriosis involving the appendix wall were present, highlighted with CD10 and ER immunohistochemistry markers. The eight lymph nodes isolated were not involved by metastasis. The molecular biology study (NGS and PCR) demonstrated a KRAS gene mutation. Cytological analysis of the peritoneal fluid did not show neoplastic cells.
Conclusion: This case highlights the exceedingly rare occurrence of LAMN in the presence of endometriosis of the appendix. A more comprehensive knowledge on cases like this is needed to optimize the surgical approach and follow-up strategy. Three months have elapsed since the surgery and the patient remains well and alive, without any signs of disease recurrence.

E-PS-06-069
Infective tumour like lesions of rectum and colon: a report of two cases
M. Odida*
*Department of Pathology, Faculty of Medicine, Gulu University, Gulu, Uganda

Background & objectives: Malignant tumours involving colon and rectum are common in many countries. There are also some infective cases which may mimic tumours. We present here two infective cases which presented clinically as tumour.
Methods: Two case reports of infective rectal and colonic lesions presenting clinically like tumours encountered during routine diagnostic histopathology.
Results: Case 1. A 49 years old female presented with pain and bleeding an indurated ulcer of colon. A provisional diagnosis of rectal carcinoma was made, and a biopsy was taken. Histological examination showed chronic inflammation with plasma cells and microgranulomas. The clue for the diagnosis was a penile ulcer biopsy from the husband which had the characteristic features of syphilis.
Case 2. A 20 years old male came with history of abdominal distension and constipation for five days. A diagnosis of intestinal obstruction secondary to intestinal tumour was made and partial colectomy done. Histological examination of the mass showed chronic granulomatous inflammation containing Schistosoma mansoni ova.
Conclusion: A number of infective lesions may present like tumours. Pathologists need to be aware of these unusual presentations.

E-PS-06-071
The molecular nodal tumour load correlates with the size of the nodal metastasis in localised colon cancer patients
B. Palomar De Lucas*, L. Alarcón, D. Mata, N. Tarazona, M. García, C. Martinez-Ciarpaglini
*Incliva, Biomedical Research Institute, Hospital Clínico Universitario de Valencia, Spain

Background & objectives: The nodal status is the major prognostic factor in colon cancer (CC). The TNM staging system includes the number of positive nodes regardless of nodal tumour load (NTL). We aimed at assessing the prognostic value of NTL in localised CC.
Methods: Patients with localized CC were prospectively selected. We isolated lymph nodes (LNs) from the fresh adipose tissue and studied each one using two methods, the histopathological H&E evaluation and PCR (RT-LAMP, OSNA). We also estimated the NTL on H&E, based on the size of the tumour and the percentage of infiltration in each node.
Results: 69 patients were included. The upstaging rate for early-stage CC patients after the analysis by OSNA was 7% (N=4). The molecular NTL significantly correlated with the pN stage ($p = 0.000$) but was not proportional to the number of affected LNs. Both the NTL and the H&E status correlated with the presence of lymphovascular invasion ($p = 0.000$) and extramural vascular invasion ($p=0.011$) however, only the NTL was significantly correlated with the presence of perineural invasion ($p= 0.005$) and the tumour budding grade ($p=0.008$). The NTL was significantly related to the size of the nodal metastasis ($p=0.0005$) and the percentage of the LN occupied by the tumour ($p=0.0005$).
Conclusion: The molecular NTL evaluation is strongly related to poor prognostic factors in patients with localized CC. Although the NTL correlated with the size of metastasis, it was not proportional to the number of affected LNs, suggesting that the NTL provides different information than the TNM staging system. The prognostic value of the NTL will be analysed in our cohort after a longer follow-up.
Funding: Project PI21/00695 financed by ISCIII and co-financed with FEDER funds

E-PS-06-072
Pathomorphological evaluation of eosinophilic oesophagitis and reflux oesophagitis
V. Pechnikova*, L. Mikhaleva, K. Maslenkina, E. Motylev, D. Atiakshin, G. Kudryavtsev, Y. Kudryavtseva, M. Gushchin, A. Konyukova, K. Midiber
*Avtsyn Research Institute of Human Morphology of Federal State Budgetary Scientific Institution "Petrovsky National Research Centre of Surgery", Russia

Background & objectives: Eosinophilic oesophagitis (EoE) is immune-mediated disease with increasing incidence, becoming the second most common inflammatory condition of oesophagus after gastro-oesophageal reflux disease. The aim of the study was to delineate histopathological features to distinguish between EoE and reflux oesophagitis (RE).
Methods: Biopsy was performed in 17 patients that fulfilled EREFS criteria for EoE (80 biopsies: 52 distal and 28 proximal) and in 10 patients with RE (41 biopsies: 30 distal and 11 proximal). Biopsy specimens were fixed in 10%-neutral buffered formalin and stained with haematoxylin and eosin and combined PASD/Alcian Blue. EoE histology scoring system (EoEHSS) was applied for histological evaluation.
Results: Male predominance was observed in both groups (11/17 and 7/10, respectively), but patients with EoE were younger [Me 32,8 (21-41) vs 52,5 (43-66) years]. EoEHSS activity (12 vs 7) and stage scores (12 vs 6,5) for EoE were almost twice as high as for RE. Peak eosinophil count reached 220 per high power view x400 for EoE [Me 65 (36-116,5)] and 12 for RE [Me 3 (3-7)]. Higher severity of intercellular space dilatation and basal cell hyperplasia favoured EoE: for both median scores were 3 compared to 1 for RE. Eosinophilic abscesses and surface layering were noticed exclusively in EoE and comprised for 58,8% and 17,6% of cases respectively.
Conclusion: Predominantly eosinophilic intraepithelial infiltration of the oesophagus is a hallmark for EoE, though various number of intraepithelial eosinophils may be revealed in other conditions including RE. For the aim of our research only RE cases with any eosinophils in oesophageal mucosa were selected. EoEHSS appeared to be a reliable tool to distinguish EoE from RE. The density of intraepithelial eosinophils, eosinophilic abscesses and surface layering were the most useful histological features for differential diagnosis between EoE and RE.

E-PS-06-073
Microinvasive ductal carcinoma arising from anogenital mammary-like glands, a case report
D. Piñol Ballús*, A. Prat, C. Fumagalli, V. Fusté Chimisana, M.P. Hernandez, J. Szafranska
*Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

Background & objectives: Background: Anogenital mammary-like glands (AGMLG) are an ectopic breast tissue found in the anogenital region of both males and females and can give rise to lesions identical to their counterparts in the native breast.
Methods: Case summary: We present a case of a 64-year-old woman, without relevant personal history, with a painless perianal mass. The endoscopy revealed a 14 mm non-encapsulated solid dermal lesion with a minor cystic component. Patient underwent surgical resection. Routine study with H&E and immunostains were performed.
Results: Discussion: Histologic examination showed the presence of anogenital mammary-like glands (AGMLG) and a malignant component resembling an "in situ" ductal carcinoma. The neoplasm displayed a solid and papillary growth pattern with foci of stromal invasion and presence of extramammary Paget disease (EMPD). Both the benign and neoplastic components were positive for CK7, CK19, GCDFP-15, oestrogen and androgen receptors and partially positive for progesterone receptors, while CK20 and CDX2 stains were negative. Myoepithelial cells (p63 positive) were present in the "in situ" component.
Conclusion: Conclusion: AGMLG are still unfamiliar entities that can be mistaken for metastatic adenocarcinomas. The "in situ" component remains the best mean to establish the origin of the lesion. The case we presented emphasizes the importance of recognizing AGMLG and their potential of malignization, which can aid in early diagnosis, appropriate management and avoid overtreatment.

E-PS-06-074
Correlations between main morphological features of gastric carcinomas
I.E. Pleşea*, A. Ciobănoiu, R.M. Plesea, R.N. Ciurea, V.T. Grigorean, V.E. Strâmbu, F. Gherghiceanu
*Doctoral School, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania, Department of Pathology, "Bagdasar-Arseni" Emergency Clinical Hospital, Bucharest, Romania

Background & objectives: Gastric carcinomas (GC) were the fifth most common malignancy and the third cause of malignancy deaths worldwide. They were heterogenous concerning phenotype, genotype, clinical and prognostic behaviour. The study aims to compare six main morphological and behavioural features of GC.
Methods: A series of 75 GCs were grossly examined and stained with Masson's trichrome, silver impregnation (Gömöri technique), and immune-stained with Smooth-Muscle Actin, CD34 and Ki67. The assessed parameters were: gross aspect (Bormann scale), tumour grade, local invasion (pT), stroma amount, vascular density (VD), and aggressiveness (Ki67 index). Each parameter was scaled individually and specifically. Results were compared using chi-square test.
Results: Gross aspect had no statistical correlation with none of the other parameters (chi-square test "p" values > 0.05).
The same situation appeared when tumour grade, local invasion, stroma account, VD and tumour aggressiveness were compared each to each.
However, "p" value of chi-square test was around 0.1 when compared tumour grade with gross aspect, local invasion, and intratumor vascular density (0,284, 0,13, and 0,134 respectively), indicating a mild tendency of correlation between the respective parameters.
Conclusion: Our data revealed no obvious trend of correlation between main morphological and behavioural features of studied gastric epithelial malignancies, excepting some correlation trend between tumour grade, on one hand, and local invasion and intratumor vascular network, on the other hand.

E-PS-06-075
Chromogranin A overexpression in the colonic mucous of patients with slow-transit constipation: clinical case series
M. Plodiienko*, S. Nikolaienko, P. Byk, I. Lieshchyshyn, T. Amalyan, S. Gychka
*Bogomolets National Medical University, Ukraine

Background & objectives: Slow transit constipation can cause serious physical and social disability. Since total colectomy may be the last treatment option, it is important to clearly identify its indications. This study focuses on the imbalance of neuroendocrine markers in the colonic mucosa.
Methods: Formalin-fixed, paraffin-embedded post-colectomy samples of sigmoid colon from 3 patients were studied with light microscopy and immunohistochemistry, IHC, (chromogranin A, synaptophysin). Levels of expression of chromogranin A and synaptophysin were estimated in myenteric plexus. Number of neuroendocrine cells in mucosa were counted in 15 HPF (0,24 mm2) for two markers separately.
Results: All patients presented with similar histological changes: focal sing of neuronal damage in myenteric plexus (red cyroplasmic inclusions, swelling of neuranal bodies); lymphoid follicular hyperplasia and increased number of lymphocytes in lamina propria. Immunohistochemically, an increase in the number of chromogranin A positive cells was defined in the crypts with a marked intensity of expression of its (206, 201, 194 positive cells/15 HPF). The expression of synaptophysin did not demonstrate this pattern in mucosal crypts. Analysis of the expression of chromogranin A and synaptophysin in myenteric plexuses demonstrated their decrease in only one of three cases.

Conclusion: The described clinical cases draw attention to the underestimated role of chromogranin A expressing cells of the colonic mucosa as a component of the pathogenesis of slow transit constipation. Further study of the pathogenesis of slow transit constipation can reduce the number of unjustified surgical interventions.

E-PS-06-076

A case of acute appendicitis as a result of actinomycosis

E. Psychogiou*, P. Tziakou, P. Megas, M. Miliou, K. Papadopoulou, A. Konstantinidou, E. Papadopoulou, D. Riga, C. Glava, I. Vamvakaris
*General Hospital of Athens Sotiria, Greece

Background & objectives: Actinomycosis is a rare, indolent, and multisystemic infection caused by Actinomyces, bacteria of the oral and intestinal flora. It affects the abdominal region and the most common presentation is a perforated appendix. Symptoms are nonspecific, which makes differential diagnosis challenging.
Methods: A 36-year-old man was admitted to our hospital with abdominal pain in the periumbilical and right lower quadrant areas. Acute appendicitis was diagnosed and appendicectomy was performed. The surgical specimen measured 6,5X1,5 cm with haemorrhagic and pseudomembranous inflammatory serosal surface.
Results: The histologic examination revealed characteristic clumps of basophilic filamentous bacteria in a vaguely rosette-like configuration surrounded by acute inflammatory cells. With higher magnification, a typical sulfur granule surrounded by neutrophils was found. Also, transmural inflammation, lymphoid hyperplasia were identified, along with mucosal ulceration and architectural distortion. At the submucosa, the outer portion of the abscess showed evidence of organization, with vascularized granulation tissue and fibrosis in addition to chronic inflammatory cell infiltration. The Actinomyces colonies were compatible with the diagnosis of appendicular actinomycosis. Microbiological exams of the patient were negative.
Conclusion: We report this case due to the rarity of this entity, highlighting the importance of considering actinomycosis in the differential diagnosis of an intrabdominal mass or unspecific, recurrent abdominal pain, especially if it has an insidious, chronic evolution. It is mostly diagnosed post-operatively by histological analysis. The combined therapy of surgery and antibiotic appears to cure more than 90% of actinomycosis, having an excellent outcome in avoiding recurrence, especially when the infection is treated in an early stage.

E-PS-06-077

A rare intestinal deposition of a common material: not everything is melanosis.

P. Puente López*, G. Escuer, C. Saus Sarrias, L. Guerra Pastrián, E. Palacios Lázaro
*La Paz University Hospital, Spain

Background & objectives: Deposits in the gastrointestinal tract are relatively frequent. They have a broad differential diagnosis and can be classified into two types: pigmented (melanosis, pseudomelanosis, brown bowel syndrome, hemochromatosis, barium granuloma, tattoo, melanoma) and non-pigmented (xanthoma, muciphages, pseudolipomatosis, infectious diseases, malakoplakia).
Methods: For this biopsy, a radiological examination of the sample was carried out and histochemistry techniques PAS and Perls were used for the histological evaluation. Mass spectrometry and scanning microscopy are also performed.
Results: 84-year-old male who underwent a colonoscopy for constipation, showing a whitish stellate area of 10mm, flat, with a normal mucosal pattern that was biopsied.
We received several fragments of large intestine mucosa in which the mucosa does not show epithelial dysplasia, what is striking is that in the lamina propria there are macrophages, with a golden pigment that is refractile but not birefringent, which are intermingled with muscle bundles.
The pigment is negative for Perls and PAS; therefore, an X-ray of the block is performed, showing radiopaque material. Mass spectrometry and scanning microscopy were performed, in which abundant deposits of barium and sulfur compatible with barium sulfate were observed.
Conclusion: A common finding in daily practice is the presence of deposits in the intestine, being more frequent the pigmented ones. The morphologic and histochemical characteristics of these materials are fundamental for their differential diagnosis.
The barium sulfate deposit presents as a refractile but not birefringent and radiopaque material. This material can cause chronic granulomatous inflammation, raising the differential diagnosis with inflammatory bowel disease.

E-PS-06-078

The adenoma-carcinoma sequence in third pathway of colonic carcinogenesis (GALT) adenocarcinomas: 3 case report and literature review

D.G. Puppa*, D. Turberg, G. Arnoux, C. Rubio
*Centre Médicale Univers. (HUG), Switzerland

Background & objectives: Little is known regarding the origin and the precursor lesion of the GALT carcinoma which despite having a favourable prognosis is not included in the current WHO classification. We report a case series covering the adenoma-carcinoma sequence in GALT neoplasia.
Methods: Three original early cases are reported with morphological, pathological staging, molecular and electron microscopy study features with follow-up. All the cases described in the litterature under the terms "dome" and "GALT" are reviewed.
Results: From our archives the following cases were selected: 1) a tubular adenoma with typical histological GALT features, 2) a tubular adenoma with malignant transformation with GALT features both in the adenomatous and in the invasive components (pT1 N0), 3) a tubular adenoma with malignant transformation and deep wall invasion showing superficially GALT features (pT3b N0).
Conclusion: A GALT differentiation can be identified not only in the adenocarcinoma but also in the pre-invasive adenoma. This variant is likely underecognized when limited to the superficial part of the tumour and shouldn't be missed. Our findings support the already proposed Third Pathway model of Colonic Carcinogenesis. The lack of adverse morphological features, synchronous metastasis and recurrences in this series as well in the literature are consistent with a low-risk histotype thus deserving to be added to the WHO classification.

E-PS-06-079

Mixed adenocarcinoma arising in Meckel's diverticulum: a case report

P. Rodrigues Veiga*, J. Fraga, A. Lapa
*Pathology Department, IPO Porto, Portugal

Background & objectives: Meckel's diverticulum (MD) represents the most common congenital malformation of the gastrointestinal tract and is caused by incomplete obliteration of the vitelline duct during intrauterine life. Malignant transformation is very rare, with carcinoid tumours being the most common.
Methods: We describe a case of a 32-year-old man that presented with a suspected Meckel's diverticulitis associated with intestinal obstruction. He was submitted to segmental enterectomy. The post-op was complicated with peritonitis and dehiscence of the anastomosis. Terminal ileum resection and terminal ileostomy were performed.
Results: The histopathological examination revealed a poorly differentiated mixed adenocarcinoma arising in a diverticulum with all layers of the small bowel compatible with MD. The tumour showed mainly tubule-papillary and poorly cohesive areas, which was invading the

subserosa and serosa in some areas, with lymphovascular and perineural invasion. There was ectopic mucosa of gastric type with foveolar epithelium. Immunohistochemically, the tumour presented epithelial cell differentiation and was negative for neuroendocrine markers. There was heterogenous loss of membranous immunopositivity of E-cadherin in the poorly cohesive areas. Two-months later, the patient presented with intestinal obstruction again and was submitted to exploratory laparotomy that revealed ascites and peritoneal carcinomatosis, compatible with peritoneal involvement.
Conclusion: MD may be asymptomatic and diagnosed incidentally or associated with complications, like intestinal obstruction. Primary malignancies of the MD are unusual. Although adenocarcinomas are exceedingly rare, they have a very poor prognosis, due to the advanced stage associated with late detection. It has been suggested an association with heterotopic tissue located within the diverticulum, like gastric mucosa, however the cause is unknown. There is no consensus on the best treatment and staging for adenocarcinomas in MD.

E-PS-06-080
In silico analysis of serrated adenocarcinoma morphology in colorectal carcinomas
Z. Sağnak Yılmaz*, M.H. Toper, S. Sarioglu
*Dokuz Eylül University, The Institute of Health Sciences, Department of Molecular Pathology, Karadeniz Technical University, Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Serrated adenocarcinoma (SAC) is a subtype of colorectal carcinoma (CRC) differentiated by serration, eosinophilic cytoplasm, vesicular nucleus, mucinous or trabecular pattern. In this pioneering study, molecular changes in the development of SAC were investigated in silico for the first time.
Methods: Data from cBioPortal for Cancer Genomics (cBioPortal) and The Cancer Genome Atlas (TCGA) were used. 181 of TCGA CRC microscopic images were examined. The cases were classified as classical adenocarcinoma and SAC. Stage, prognosis, mutation, methylation, and mRNA expression data were obtained from cBioPortal using case numbers, and the two groups were compared for each data.
Results: Classical adenocarcinomas (148 cases, 81.8%) and SACs (33 cases, 18.2%) were compared. BRAF, PIK3CA, EGFR, ERBB2, RET, MET mutations were found at a higher rate in SACs, while KRAS, NRAS, APC, TP53 mutations were found at a higher rate in the classical type, but a significant p value was obtained only for TP53 ($p=0.019$). ZNF714 DNA methylation rate were higher in the classical variant, FLOT1, SLX1B, MLLT11, PENK DNA methylation rates were higher in SACs and a significant difference was found (ZNF714 $q<0.000$, FLOT1 $q=0.0173$, SLX1B $q=0.0173$, MLLT11 $q=0.0173$, PENK $q=0.0414$, all $p<0.000$). Mean life expectancy is 56.21 months in patients with SAC and 61.79 months without SAC ($p=0.121$).
Conclusion: In this pioneering study, significant p and q values for ZNF714, FLOT1, SLX1B, MLLT11, PENK DNA methylation were determined when SACs and classical adenocarcinomas were compared. There is no comprehensive study on DNA methylation in SACs in the literature; this result is unique. A significant p value was found for the TP53 mutation, but no significant q value was found.

E-PS-06-081
RAS status by Idylla technology-what's about the invalid cases?
G. Sahraoui*, H. Douik, L. Charfi, R. Doghri, I. Nasri, D. Ghezala, K. Mrad
*Salah Azaiez Institute, Tunisia

Background & objectives: Idylla technology is an automated real time-PCR system allowing rapid molecular analysis of RAS/BRAF mutations in metastatic colorectal cancer. We evaluated the rate of "invalid cases" in a series of colorectal patients screened for KRAS mutations by the Idylla system.
Methods: 830 patients with metastatic colorectal cancer were enrolled. Sections of formalin-fixed paraffin-embedded tumour tissue were put on a Idylla Test cartridge. Results of codons 12, 13, 59, 61, 117, and 146 mutation screening are revealed directly on the console. If no mutation was found in the KRAS gene, a screening for NRAS and codon 600 BRAF gene mutations were performed.
Results: KRAS/NRAS-BRAF mutations screening showed a total of 50 invalid cases (6%) between KRAS and NRAS-BRAF testing. For the Kras test, 14 cases were screened twice: 10 among them remained invalid, 3 became "non-mutated" and one kept a G12C mutation after a second screening. For the NRAS-BRAF test, 4 samples were tested twice; all remained "Invalid". Patients' histopathological characteristics don't show any correlation with invalid cases, but we noted that 35 invalid cases were rich in tumour cells ($\geq$30%), and only 15 had unless of 20%of tumour cells; therefore,29 were the result of surgical samples and 20 were issues from biopsies.
Conclusion: Invalid cases should not be overlooked in the Idylla RAS-BRAF mutation test. Our study highlights the importance of the quality of the surgical sample or biopsy's fixing for a good quality of DNA, essential as a support for molecular diagnosis.

E-PS-06-082
A gastric follicular dendritic cell sarcoma: report of a rare incidental diagnosis
G. Sahraoui*, F. Sassi, I. Zemni, S. Chaabouni, H. Guizani, L. Charfi, R. Doghri, K. Mrad
*Salah Azaiez Institute, Tunisia

Background & objectives: Follicular dendritic cell sarcomas (FDCS) are rare tumours, typically seen in lymph nodes. The extranodal involvement is rarer. The aim of this study is to review clinicopathological features and emphasize on differential diagnosis and therapeutic modalities of this rare entity.
Methods: We report on a 36-year-old female patient with no past medical history. The patient was brought in for management of an axillary furuncle. Upon further examination, she mentioned experiencing mild difficulty in breathing but did not report any abdominal pain. Apart from having a moderate level of anaemia, her physical examination and laboratory testing did not reveal any significant findings.
Results: Abdominal ultrasonography was performed, revealing a 4 cm well-defined gastric mass. Athoraco-abdomino-pelvic CT scan was performed, showing an increase in tumour size to 9 cm with the presence of deep and retro-pancreatic lymph nodes. The mass was biopsied for histological examination. It showed a tumour composed of large, oval to spindle-shaped cells organized in sheets and interlacing fascicles. Numerous small lymphocytes coexisted with the tumour cells. Immunohistochemically, tumour cells expressed CD21 and CD23. They were negative for AE1/AE3, CD34, c-kit, DOG-1, CD20, CD30, CD10, bcl-6, CD68, S-100, D2-40, CD45, or EBER. The diagnosis of FDCS was retained. The tumour was resected by gastrectomy with extended para-aortic lymphadenectomy, with uneventful postoperative course.
Conclusion: Morphological pattern of FDCS may overlap with a broad range of potential differential diagnoses. A distinction from better known mesenchymal sarcomas, such as the gastro-intestinal stromal tumours, inflammatory myofibroblastic tumours Eptein-Barr Virus positive or interdigitating dendritic cell sarcoma must be considered. Complete surgical resection is the current gold standard of treatment.

E-PS-06-083
Incidental histopathological findings in sleeve gastrectomy specimens for weight management
E. Salmo*, A. Cotterill
*Royal Oldham Hospital, United Kingdom

Background & objectives: The routine histopathological examination of sleeve gastrectomy specimens taken as part of weight management strategy often yields pathological diagnoses, even in the absence of macroscopic pathology. We aim to identify the incidence of microscopic pathology in sleeve gastrectomy specimens.
Methods: We reviewed the histopathology reports for all sleeve gastrectomy specimens received into the Royal Oldham Hospital Cellular Pathology department within a 12 month period (2021) and recorded patient age, gender and final diagnosis.
Results: Sixty nine sleeve specimens were identified for review. 96% of patients undergoing sleeve gastrectomy procedure were female and the mean age of all patients was 42 years. Thirty seven (53.6%) showed no significant abnormality. Pathological findings were identified in thirty two (46.4%) with a range of diagnoses identified, including; Helicobacter Pylori (HP)-negative gastritis (16 [23.2%]); Reflux (10 [14.5%]); HP gastritis (3 [4.3%]); fundic gland polyp (1 [1.4%]); leiomyoma (1 [1.4%]) and gastrointestinal stromal tumour (1 [1.4%]). Of the thirty two cases with pathological diagnoses, thirty (93%) had diagnoses that would potentially require post-surgical treatment/management.
Conclusion: Given the number of treatable diagnoses identified at histopathological examination, we conclude that histopathological examination of sleeve gastrectomy specimens remains an important procedure for post-surgical treatment/management.

E-PS-06-084
The role of *H. pylori* infection and mast cells in the pathogenesis of inflammatory changes in the gastric mucosa
I. Sertakov*, V. Shishkina, A. Filin, V. Aralova
*Voronezh State Medical University, Russia

Background & objectives: Mast cells (MC) are one of the key promoters in the regulation of the cascade of inflammatory mediators and the formation of an inducible type of cytokine expression. Mast cells have a wide arsenal of biologically active substances.
Methods: Gastrobioptates of 19 patients with unknown *H. pylori* infection status were studied. IHC with antibodies to tryptase and *H. pylori* was performed. The determination of the amount of tryptase-positive MC was carried out using a planimetric analysis in the field of view. The numerical values obtained were recalculated to obtain quantitative data reflecting the density of MC distribution per mm2.
Results: *H. pylori* infection was detected in 63% of cases. The number of tryptase-positive mast cells was significantly higher in patients infected with *H. pylori*. Mast cells in the presence of *H. pylori* showed intensive degranulation. Double immunofluorescence labelling of tryptase MC and *H. pylori*: clusters of large free-lying granules around glands with a pronounced degree of *H. pylori* contamination, intensive infiltration of epithelial cells of the gastric mucosa by mast cells and their granules in patients with *H. pylori*. Activation of tryptase expression was observed (correlating with an increase in the severity of the inflammatory component of the gastric mucosa in patients with Nu pylori to a much greater extent relative to uninfected patients).
Conclusion: The role of mast cells in this process is ambiguous, it depends on many factors and features of the cellular microenvironment, the degree of damage to the mucous membrane and the duration of the inflammatory process. The polyfunctionality of tryptase makes it possible to more fully reveal the importance of mast cells in the development of both adaptive and pathological reactions during molecular morphological analysis.

E-PS-06-085
Undifferentiated oesophageal carcinoma with sarcomatoid morphology: a case report and short literature review
E. Souka*, G. Galanopoulos, G.M. Stanc, P. Bafaloukos, S. Xinogalos, O. Tzaida
*Pathology Department Metaxa Cancer Hospital, Greece

Background & objectives: Undifferentiated oesophageal carcinoma (UEC) is a very rare neoplasm. It's characterized by an expansile growth pattern of neoplastic cells organized in solid sheets, without significant glandular, squamous, or neuroendocrine differentiation, occasionally adopting a sarcomatoid or rhabdoid morphology.
Methods: A 55-year-old patient presented to the gastroenterology department with solid food dysphagia and weight loss. The endoscopy revealed a large obstructing polypoid oesophageal mass measuring 3cm. Subsequently biopsies were obtained. CT imaging showed no definite metastatic disease.
Results: Microscopically, the oesophageal mucosa was infiltrated by a high-grade neoplasm composed of highly pleomorphic cells with abundant giant and multinucleated bizarre forms diffusely arranged in a loose stroma. The epithelium was almost completely ulcerated, except of a few strands of intact non-neoplastic squamous epithelium. The immunohistochemical examination revealed the following immunophenotype: CKAE1/AE3+, CK8/18+, CK7-, p40+ few cells, Vimentin+, Chromogranin A-, Synaptophysin-, SMA-, Desmin-, c-Kit-, LCA-, CD30-, MelanA-, HMB-45-, S-100-, Ki67(MIB-1) up to 100%. The differential diagnosis included undifferentiated carcinoma, sarcoma, anaplastic lymphoma, GIST and melanoma. The final diagnosis was UEC with sarcomatoid-like morphology.
Conclusion: The prevalence of UEC ranges from 0.15% to 4.5%, likely due to lack of definite diagnostic criteria. Its' prognosis is poor, since 1-year survival rate is < 30% after esophagectomy, in comparison to >60% for stage III adenocarcinomas. Given that UEC is a very aggressive carcinoma, an accurate pathological diagnosis is of a great clinical value. UEC shares common epidemiological background with conventional adenocarcinoma, but more research is needed to elucidate its' true origin, as well as optimal treatment.

E-PS-06-086
Skin metastasis of oesophageal gastrointestinal stromal tumour. A potential pitfall
H. Trihia*, E. Souka, G.M. Stanc, P. Bafaloukos, A. Mavrogiorgis
*Pathology Department Metaxa Cancer Hospital, Greece

Background & objectives: Gastrointestinal stromal tumours (GISTs) metastasize mainly to liver and abdominal cavity. Metastases extra-abdominally occur in bone, pleura and soft tissue. Skin metastasis (SM-GIST) occurs in approximately 1% of advanced patients, with head, face and extremities been the most common sites.
Methods: A 77-year old male with history of liver echinococcosis, underwent exploratory surgery. Intra-operatively, was diagnosed with oesophageal GIST, with simultaneous bone metastases and small liver nodules seven years postoperatively. Two years later, there was progression of liver metastases. Concurrently, a recent skin nodule of 7mm of the scalp was excised. At the time of excision, medical history was not known.
Results: Histological examination revealed a spindle cell lesion in short fascicles, with occasional mitoses, located in the dermis and upper subcutaneous fat. As the medical history was not known at the time, several immunostains were used, of skin spindle tumours, as the differential diagnosis of SM-GIST is a diagnostic challenge in which the morphological differential diagnosis is broad and includes primary and metastatic tumours. After insisting for the medical history and consulting personally the patient and being informed of the GIST diagnosis, the implementation of DOG1, CD117 and CD34, established the diagnosis of SM-GIST.
Conclusion: The mean postoperative time for GIST distant metastases is 2 years. At the time of diagnosis, up to 20% have developed metastases. The mean time to SM-GIST is 4.22 years, as unlike carcinomas which sometimes initially metastasize to the skin, SM-GIST is the late manifestation of disseminated disease. Therefore, SM-GIST should always be in consideration in case of even small and easily ignored skin

nodules in asymptomatic patients, as they can indicate a widespread systemic disease and a poorer prognosis.

E-PS-06-087

Massive intestinal bleeding in a patient with AL-amyloidosis initially diagnosed as multiple vascular malformation

O. Vasyukova*, Z. Gioeva, L. Mikhaleva, R. Vandysheva, K. Midiber, N. Gutyrchik, V. Pechnikova, A. Birukov, D. Areshidze, M. Kozlova
*Avtsyn Research Institute of Human Morphology of Federal State Budgetary Scientific Institution "Petrovsky National Research Centre of Surgery", Russia

Background & objectives: Intestinal amyloidosis symptoms may mimic different digestive tract disorders which makes the diagnosis quite challenging. Objective: to present a clinical case of Al-amyloidosis in patient with recurrent intestinal bleeding, initially assessed as multiple vascular malformations of the small intestine.
Methods: 60-year-old female patient was admitted to the surgery department complaining of blood in the stool and extreme fatigue. Esophagogastroduodenoscopy did not reveal the source of bleeding. The colonoscopy results suggested that the bleeding could come from the small intestine, since there were no findings in the colon. The ileal resection and the ileo-ascending anastomosis was performed due to continuous bleeding.
Results: Pathological examination of the resected sample demonstrated multiple vascular malformations of the small intestine. The bleeding stopped after the surgical procedure, the patient's condition significantly improved, and she was discharged from the hospital for outpatient follow-up. However, 4 months later the bleeding recurred. The patient underwent gastrointestinal endoscopy which revealed mucosal haemorrhage sites and high-density tumour-like lesions in the small intestine. Lesions' biopsy results revealed AL-amyloidosis. Previous histological slides from the surgery were reviewed, and massive perivascular and interstitial amyloid deposits were found. Earlier these findings were interpreted as severe angiomatosis lesions with extensive haemorrhagic areas, leading to misdiagnosis and delayed appropriate treatment.
Conclusion: It should be kept in mind that surgical patients with massive bleeding of unknown cause from the small intestine may have amyloidosis. This disease is considered one of the causes of massive recurrent bleedings resulting from amyloid deposition within the blood vessel walls of the small intestine.
Funding: This study was supported by RSF, grant No. 23-15-00138.

E-PS-06-088

Histopathological clues for common variable immunodeficiency disorder (CVID) in a patient initially presenting with inflammatory bowel disease (IBD): case report and literature review

L. Velthof*, J. Geldof, J. Van Dorpe, T. Lobaton, A. Hoorens
*Ghent University Hospital (UZ Gent), Department of Pathology, Belgium

Background & objectives: Gastrointestinal manifestations are a major cause of morbidity in CVID and mimic IBD in 6% to 10% of patients. Diagnosis remains challenging and is often delayed, potentially resulting in life-threatening complications, hence the importance of early recognition.
Methods: We present a case of a 61-year-old man, initially diagnosed with Crohn's disease at age 33 and later found to have CVID at age 52. We reviewed all gastrointestinal biopsies and conducted an extensive literature review in search of histopathological clues that may contribute to the diagnosis of CVID when both clinical symptoms and biopsy findings are suggestive of IBD.
Results: Review of gastrointestinal biopsies and correlation with literature findings revealed histopathological features that are atypical of IBD and may indicate CVID. These features include an increase in intraepithelial lymphocytes, thickening of the subepithelial collagen layer, an increase in crypt apoptotic bodies and a relative paucity of plasma cells. However, these findings can be subtle and can easily go unnoticed if not carefully searched for. Better recognition of these histopathological indications of CVID may contribute to earlier diagnosis and treatment, thereby avoiding potentially life-threatening complications such as infections or malignancies.
Conclusion: CVID is the most common primary immunodeficiency following selective IgA deficiency and is the most important symptomatic primary immunodeficiency. Clinical manifestations are heterogenous and include infections, autoimmunity, gastrointestinal disease and malignancies. Gastrointestinal manifestations occur in up to 60% of patients and often mimic other gastrointestinal conditions such as celiac disease, Whipple's disease, microscopic colitis, graft-versus-host disease or IBD. This case report and literature review highlights histopathological clues for CVID in the gastrointestinal tract and aims to raise awareness of CVID.

E-PS-06-089

Immunohistochemical analysis of metastasis-associated protein 1 (mta-1), cyclin d1 and cd44 expression in gastric adenocarcinomas and evaluation of their relationship with clinicopathological prognostic factors

A. Vergili*, N. Ekinci
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Gastric adenocarcinoma is a common and deadly malignancy, with a poor prognosis and limited therapeutic options. In this study, we aimed to investigate MTA-1, Cyclin D1, and CD44 immunoexpressions in gastric adenocarcinomas and evaluate their relationship with clinicopathological prognostic parameters.
Methods: 80 patients who underwent radical gastrectomy and were diagnosed with gastric adenocarcinoma in our hospital in 2017 and 2018 were compiled. Immunohistochemically MTA-1, Cyclin D1 and CD44 stains were applied to appropriate tumour blocks and evaluated according to staining intensity and percentage. Immunohistochemical staining and histopathological prognostic data in those tumours were evaluated statistically and $p<0.05$ was considered statistically significant.
Results: Of the 80 patients included in the study, 54 were male and 26 were female. While 73 patients had pure adenocarcinoma, 7 had mixed carcinoma. T3 stage was the most common T stage of the patients (45%). Lymph node metastasis was observed in 66%, and distant metastasis in 2.5% of the patients. Lymphovascular invasion (LVI) was found in 70% of cases and perineural invasion (PNI) was observed in 57% of the cases. A significant correlation was found between Cyclin D1 expression and T-stage and PNI. Also, CD44 expression was correlated with N stage, LVI and PNI. Finally, a significant correlation was found between MTA-1 expression and PNI.
Conclusion: Gastric adenocarcinoma has a poor prognosis and it is the 3rd most common reason of cancer related deaths worldwide. As we found in our study, most patients present with advanced stage. Cyclin D1, CD44 and MTA-1 have pathogenetic roles in various cancers and our study showed that they are related with poor prognosis. According to our results, we think that the use of these markers in gastric carcinomas may be useful to predict prognosis and possible future treatment options.

E-PS-06-090

Vascular lesions of the gastrointestinal system: a case series of 25 patients

A. Vergili*, N. Ekinci, A. Avci
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Arteriovenous malformation, angiodysplasia, and haemangioma are used to describe vascular lesions of the

gastrointestinal tract, but there is no consensus on this issue. In this study, we aimed to evaluate those cases diagnosed in the gastrointestinal tract in our department.
Methods: 25 patients who applied to our hospital between 2010-2019 with different clinical complaints that had various diagnoses and also accompanying vascular lesions such as angiodysplasia, arteriovenous malformation, haemangioma, and Kaposi sarcoma in the gastrointestinal tract were reevaluated. 19 surgical resections, 4 colonic polypectomies, and 2 endoscopic biopsies were sent to our laboratory. All materials were reevaluated by 2 experienced pathologists.
Results: Of 25 patients, 16 were male and 9 were female. The age distribution was 19-83 (mean 58). Angiodysplasia was found to be primary in 6 of the 13 gastric resections, incidental in 3 sleeve gastrectomies, and as an accompanying lesion in 4 other malignancies. Kaposi sarcoma was diagnosed in 1 gastric biopsy. Angiodysplasia was observed in 4 hemicolectomies and 4 colon polyps. A cavernous haemangioma was found in 1 colectomy, and a haemangioma in 1 rectal biopsy. The lesions were observed as thin/thick-walled malformative vascular structures with abnormal dilatation and irregular folding in the submucosa, and also in all the organ walls including the subserosa in some cases.
Conclusion: Vascular lesions of the gastrointestinal tract, such as angiodysplasia and arteriovenous malformation, of which the true incidence is unknown, are seen in many cases presenting with gastrointestinal bleeding. They can also be seen as accompaniments in patients operated for other reasons, as in our study. Our other interesting finding is that angiodysplasia can be seen incidentally in sleeve gastrectomies. We think that increasing awareness of these lesions and evaluating all gastrointestinal materials from this perspective may increase the actual incidence.

E-PS-06-091
Appendiceal diverticulosis with inflammatory fibroid polyp and hyperplastic polyp, a rare case report
A. Vergili*, N. Ekinci, C. Tavusbay
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Appendiceal diverticulosis is a rare disease that is most commonly asymptomatic. It can accompany many benign or malignant tumours. Inflammatory fibroid polyps are benign mesenchymal lesions rarely seen in the appendix. Hyperplastic polyps are also rarely encountered in the appendix.
Methods: A 61-year-old male patient had a left hemicolectomy due to moderately differentiated adenocarcinoma located in the rectosigmoid area 5 years ago. Elective appendectomy was decided for the patient in the oncology council because of the radiological diagnosis of mucocele in the distal appendix. A 9 cm long and 0.8 cm wide appendectomy material was sent to our laboratory.
Results: Macroscopically, many diverticular structures within mucoid consistency were observed at the distal end of the appendix. In microscopic examination, formation of multiple diverticula was noted characterized by invagination of mucosa through muscularis propria. In addition, on the wall of one of these diverticula, a 2 mm diameter, submucosal, well-circumscribed lesion was incidentally observed. It was characterized by thin-walled vascular structures with spindle cell proliferation and prominent eosinophilic infiltrate. Immunohistochemically, spindle cells were positive with CD34, vimentin and fascin, and this lesion was thought to be compatible with an “inflammatory fibroid polyp”. After the total submission of the appendix, a "hyperplastic polyp" in a 2 mm focus was also found.
Conclusion: In the literature, many benign and malignant tumours and lesions accompanying appendiceal diverticulosis have been reported. For this reason, to avoid missing such lesions, new sampling for neoplastic or non-neoplastic lesions should be performed if an appendiceal diverticulum is diagnosed macroscopically or microscopically. Since the association of the appendiceal diverticulum with an appendiceal inflammatory fibroid polyp and a hyperplastic polyp has not been reported in the literature, in our opinion, our case is worth presenting.

E-PS-06-092
Expression of neuroendocrine markers in SWI/SNF deficient colorectal carcinomas.
P. Vlachou*, F. Dolkiras, N. Stavrinou, E. Spiteri, E. Athanasiou, A. Therapontos, M. Lenos
*Department of Pathology, Evaggelismos General Hospital Athens, Greece

Background & objectives: We present the case of an 87yo woman with a mass in her ascending colon. The aim of this abstract is to demonstrate that the expression of neuroendocrine markers in SWI/SNF-deficient carcinomas does not necessarily categorise them as neuroendocrine carcinomas.
Methods: A right hemicolectomy specimen was received. Upon gross examination, the tumour was of 7,9cm in greatest diameter and invaded the surrounding adipose tissue with ulceration and invasion of the adventitia. Hematoxylin/eosin staining was used in the submitted sections. Immunohistochemistry for CK8/18, synaptophysin, chromogranin A, p53, retinoblastoma, MLH1, PMS2, BRAFV600E (Ventana/ clone VE1), INI-1, SMARCA4/BRG and SMARCA2/BRM was also performed.
Results: The neoplastic cells were having a partly undifferentiated histology, with focal pleomorphism and were arranged in sheets with central coagulative necrosis. The rest of the tumour cells showed eosinophilic-rhabdoid morphology. Immunohistochemistry was noteworthy for the expression of CK8/18, diffuse and moderate expression of synaptophysin and focal-weak chromogranin A expression. Protein p53 was overexpressed consistent with a mutated pattern, retinoblastoma protein was retained. There was loss of the proteins MLH1, PMS2, while mutation specific antibody BRAFV600E (Ventana/ clone VE1) was expressed, findings consistent with a microsatellite unstable carcinoma of the colon.Nuclear expression of INI-1 and SMARCA4/BRG was retained, while nuclear expression of SMARCA2/BRM was lost, suggestive of a SWI/SNF-deficient colorectal carcinoma.
Conclusion: Based on both immunohistochemical and phenotypical characteristics the tumour was characterised as SMARCA2/ BRM deficient undifferentiated colorectal carcinoma with microsatellite instability. The pathologist should be aware of the potential expression of neuroendocrine markers in SWI/ SNF- deficient carcinomas which should not be categorised as neuroendocrine carcinomas unless they also have other neuroendocrine phenotypical characteristics.

E-PS-06-093
Early stage (T1) colorectal cancer (CRC) following endoscopic resection in screening and non-screening populations; rates of residual tumour and lymph node metastasis (LNM) following oncological resection
C. Ward*, N. Swan, N. Nolan, M. Cotter, D. Gibbons, K. Sheahan

*Saint Vincent’s University Hospital, Dublin, Ireland

Background & objectives: Oncological resection following endoscopically resected T1 CRC is considered on a case-by-case basis, given potential surgical risks and low rates of LNM (8-10%) and recurrence (3.3%). We evaluated rates of residual mural disease and LNM in screening and non-screening populations.
Methods: We analysed a database of T1 cancers diagnosed in polypectomy specimens in screening cases since 2013 and a non-screening cohort since 2018. Histopathological reports were reviewed for risk factors such as deep submucosal invasion (DSI) >1mm, lymphovascular invasion (LVI), tumour budding, grade and margin status. Rates

of oncological resection, residual disease and LNM were recorded, and corresponding risk factors evaluated.
Results: We identified 30 screening and 25 non-screening T1 CRCs in polypectomy specimens with a mean age of 65.6±2.7 years and 70.1±10.7 respectively. At least one high-risk feature was present in 80% of cases, including high tumour grade (16.4%), tumour budding (36.4%), incomplete resection (49%), lymphatic (47.3%) and venous invasion (25.4%). Twenty-six patients (47%) underwent oncological resection with screening cases more likely to be referred (53%vs40%). Residual disease was less common in screening cases (10% vs 24%), while LNM were more common (6.7% vs 0%). Tumour deposits (TDs) rates in fat were similar (6.7%vs8%). Recurrence rates were 3.6% (all were non-screening cases) with a median follow-up of 35 months (range 2-116).
Conclusion: We report low rates of LNM (3.6%), residual (16.4%) and recurrent (3.6%) disease following oncological resection in T1 CRCs. Little data is available regarding TDs, an under-recognised poor prognostic factor which we identified in an appreciable number of cases (7.3%). Screening cases were more likely to undergo surgery, possibly due to younger age as high-risk feature rates were similar. Differences in patterns of residual disease and LNM were identified in screening cases.

E-PS-06-094
Metastatic melanoma to the gallbladder- a case report
L. Williams*, A. Arnaout
*St George's Hospital, London, United Kingdom

Background & objectives: Melanoma metastasises most frequently to the skin, lung and liver, and literature reports that <5% metastasise to the gastrointestinal tract. When this occurs, the most common sites are the small bowel, colon and stomach. The gallbladder is an uncommon site.
Methods: A 75 year old lady with a 2 year history of sinonasal melanoma presented to our teaching hospital with a gallbladder lesion. Cholecystectomy was performed, revealing a 35x18x15mm lesion at the fundus and a separate 17x15x3mm lesion just proximal to the first. Both had a brown/grey cut surface and fleshy appearance.
Results: Histology revealed a malignant melanoma, characterised by sheets of atypical cells with moderate nuclear pleomorphism, prominent nucleoli and frequent mitoses. The tumour displayed areas of infarction, necrosis, and cells showed strong nuclear expression of SOX-10, with cytoplasmic Melan-A and HMB45. S100 was focal. Cystic duct node was negative for metastasis.
Conclusion: Here we report a case of sinonasal melanoma with an unusual location for metastasis. In this instance, two adjacent lesions were present. Metastatic melanoma to the gallbladder is an unusual event with poor prognosis, and controversy remains over optimal treatment. Given that these lesions are often found incidentally with few symptoms, detection is often late, and treatment of gallbladder metastasis remains a clinical difficulty.

E-PS-06-095
Enterogenous cyst causing intussusception in an adult- a case report
L. Williams*, A. Arnaout
*St George's Hospital, London, United Kingdom

Background & objectives: A 43 year old female presented to our university hospital with intussusception at the ileo-caecal valve. Emergency surgery revealed small bowel containing a cystic lesion, which was excised and sent for histology.
Methods: A 40x40x35mm small bowel specimen was received, and opening revealed a unilocular structure, comprising flattened cyst wall within the small bowel lumen. The mucosa appeared focally haemorrhagic and congested and the lesion was photographed clinically. Histology revealed a cystic structure lined by cuboidal and columnar epithelium, with smooth muscle fibres within the walls. No atypia or malignancy was present.
Results: Intussusception in an adult accounts for around 1% of bowel obstructions, with enterogenous cysts being an unusual cause for this. Most enterogenous cysts remain asymptomatic until secondary events, such as obstruction, bleeding or perforation occur. They remain an important cause to consider in such situations. The origin of these cysts remains controversial, with the most accepted explanation being that of duplication of the gut occurring due to 'pinching off of a diverticulum' during embryological development. Once detected on imaging, resection of the cyst may be indicated, however radiological surveillance may also be considered in some instances.
Conclusion: Enterogenous cysts are a rare congenital entity, which, when found in the small bowel, often involve the ileum. Most often seen in children, there are very few case reports of this presentation in adults.

E-PS-06-096
Granulomatous gastritis in a patient with sarcoidosis
B. Yeni Erdem*, G. Kat Anıl
*Kartal City Hospital, Department of Pathology, Turkey

Background & objectives: Granulomatous gastritis is a specific pattern of gastritis, characterized by the presence of granulomas in gastric mucosa. In most cases, the cause cannot be determined without clinical information. Infections, inflammatory diseases such as sarcoidosis and Crohn's disease should be investigated.
Methods: We present a 74-year-old female patient who presented with complaints of chronic dyspepsia. Upon examination, she was found to be anaemic. Upper endoscopy revealed that the gastric fundus and corpus mucous membranes were pale, while the antrum was hyperaemic and oedematous. Multiple biopsies were taken with a preliminary diagnosis of atrophic gastritis.
Results: Biopsies from the antrum revealed chronic active gastritis. Biopsies from the corpus also revealed chronic active gastritis with well-formed, non-necrotizing granulomas. Granulomas had histiocytic giant cells in the centre and no caseification. Helicobacter pylori were present on the surface. No other microorganisms were identified on histochemical stains. We signed out the case as granulomatous gastritis. Subsequently, it was discovered that the patient was diagnosed with sarcoidosis, but she was unwilling to get a treatment and she refused to be followed up. She had been suffering from a chronic cough for an extended period.
Conclusion: It is controversial if Helicobacter Pylori can cause granuloma. They are thought to be coincidental and its presence in granulomatous gastritis is not uncommon. It is therefore crucial to investigate other potential causes of gastric granulomas as they may be a significant indicator of underlying primary diseases that are yet to be detected.

E-PS-07 | E-Posters Digestive Diseases Pathology - Liver/Pancreas

E-PS-07-002
The decreasing expression of albumin mRNA in cholangiocarcinomas along the biliary tree: implications for differential diagnosis in liver lesions
E. Albertini*, S. Chillotti, D. Malvi, M. Deserti, A. Degiovanni, A. Palloni, S. Tavolari, G. Brandi, A. D'Errico, F. Vasuri

*Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Bologna, Italy., School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: The growing technologies in Albumin in situ hybridization (ISH) have changed the sensitivity and the routine application in the diagnosis of hepatic malignancies. Our aim was to assess the diagnostic accuracy of Albumin ISH with RNAscope® on different cholangiocarcinoma subtypes.
Methods: Forty-five cholangiocarcinoma (CCA) patients were retrospectively selected: 29 intrahepatic (15 small-duct and 14 large-duct subtypes), 7 peri-hilar and 9 extrahepatic. Histology was revised in all cases, and Albumin ISH was performed with the RNAscope® chromogenic detection kit, followed by a semiquantitative assessment of the percentage of positive cells on high-magnification fields.
Results: Albumin ISH gave substantial different results according to CCA localization ($p<0.001$, Kruskal-Wallis test): it was always negative in extrahepatic CCAs, only one peri-hilar case was positive, and any level of positivity was observed in 25/29 (86.2%) intrahepatic CCAs, with a mean number of positive cells of 25.5± 29.3%. In intrahepatic CCAs we noticed significant differences according to the subtype: mean cell positivity was 38.8±29.8% in small-duct and 11.4±21.9 in large-duct CCAs respectively ($p=0.003$, Mann-Whitney test). With a ROC curve we evaluated a 5% cut-off of Albumin-positive cells: 12/15 (80.0%) small-duct and 3/14 (21.4%) large-duct CCAs showed >5% positivity ($p=0.002$, chi-square test; odd-ratio 14.7).
Conclusion: Albumin mRNA detected with the past methodologies used to show a scant and irregular positivity in biliary lesions. The introduction of more sensitive techniques has changed the indications for ISH, since most intrahepatic CCAs of the small-duct subtype shows a significant number of positive cells. Albumin positivity decreases from liver periphery to the large ducts, suggesting that ISH can be helpful in the differential diagnosis between small-duct and large-duct CCAs, as well as between intrahepatic large-duct CCAs and metastases.

E-PS-07-003

Significance of more than mild portal/periportal inflammation and bile duct injury in non-alcoholic fatty liver disease (NAFLD)

D. Allende*, C. Guy, D. Kleiner, R. Gill, D. Carpenter, O. Cummings, M. Contos, M. Yeh, P. Belt, L. Wilson, C. Behling
*Cleveland Clinic GME, USA

Background & objectives: Portal inflammation (PI) in NAFLD is linked to fibrosis and 30% of cases have positive. Bile duct injury (BDI) and portal/periportal inflammation (PI/PPI) raise concerns for superimposed diseases. The study aims to determine the significance of these findings in NAFLD.
Methods: Adult liver biopsies from NAFLD cases (2017-2022) were scored included. "Moderate" (inflammation covers portal matrix) or "severe" ("moderate" and expands portal tracts) PI cases were compared to "none-mild" PI. "Moderate" (1/3-2/3 of the portal circumference) or "severe" (> 2/3 of circumference) PPI cases were "none-mild" PPI. PI, PPI, and BDI were analysed in relation to histologic and clinical data.
Results: 118/422 (28%) showed moderate/severe PI, 2/422 (0.5% of cohort) fulfilled criteria for PBC (positive AMA and BDI). Incidentally found BDI (n:20) had a lower NAS ($p=0.001$) and were less likely to have nonalcoholic steatohepatitis (NASH) ($P=0.004$). 70/422 (17%) had moderate/severe PPI. No statistically significant difference was seen between these cases and those with none/mild PPI in relation to autoantibodies (ANA, AMA, ASMA) expression, aminotransferases, NAS or diagnosis of NASH. In 33/70 (47%), ANA and/or ASMA were positive. Among patients with moderate/severe PPI, 8/70 (11% or 1.9% of the cohort) both ANA and ASMA were expressed, raising greater consideration for AIH. Moderate/severe PPI was associated with higher fibrosis stage ($p= 0.0007$).
Conclusion: Incidentally found PBC was extremely rare in our NAFLD cohort (0.5%), yet confirmatory AMA testing may be helpful if BDI is noted. Prominent PPI was noted in 17% of NAFLD cases scored with the expanded portal changes scoring system. About 11% of patients of our NAFLD cases had moderate/severe PPI and positive ANA/ASMA autoantibodies which highlights the importance of excluding AIH or drug injury in this enriched subset.
Funding: The Nonalcoholic Steatohepatitis Clinical Research Network (NASH CRN) is supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) (grants U01DK061713, U01DK061718, U01DK061728, U01DK061732, U01DK061734, U01DK061737, U01DK061738, U01DK061730, U24DK061730). Additional support is received from the National Center for Advancing Translational Sciences (NCATS) (grants UL1TR000439, UL1TR000077, UL1TR000436, UL1TR000150, UL1TR000424, UL1TR000006, UL1TR000448, UL1TR000040, UL1TR000100, UL1TR000004, UL1TR000423, UL1TR002649, UL1TR000454). This research was supported in part by the Intramural Research Program of the NIH, National Cancer Institute. The authors thank the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) for its support of the NASH CRN and this research. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

E-PS-07-004

Different kinds of embolization in advanced carcinomas: a review of literature, visual comparison and possible complications

M. Alzamora*, J. Castro, M. Hanbazazh, M. Jácome
*IPO-Porto, Portugal

Background & objectives: Trans-arterial chemoembolization (TACE) and selective internal radiation therapy (SIRT) are novel therapies for unresectable liver masses, including colorectal liver metastasis (LM). We aim to review possible complications of these therapies and provide a visual comparison of different types of beads.
Methods: We present three cases of metastatic colorectal cancer (mCCR) with LM.
Patient 1 underwent TACE with irinotecan; he died within 48 hours and an autopsy was performed.
Patient 2 underwent TACE with PVA; he was submitted to hemicolectomy and metastasectomy.
Patient 3 underwent SIRT with Yttrium-90 (Y-90); she later developed sudden epigastric pain and performed upper endoscopy with biopsies.
Results: Cause of death for patient 1 was determined as necrotizing acute pancreatitis (NAP) of embolic cause due to regurgitation of irinotecan beads. A 4cm hepatic nodule was identified and the pancreas exhibited haemorrhagic necrosis. On histology, there were numerous intravascular reddish inframillimetric microspheres occluding vessels on multiple organs.
Patient 2 presented with no complications associated with treatment. A yellow-ish intravascular material was observed throughout the liver specimen, corresponding, on histology, to a basophilic material compatible with PVA.
Patient 3 presented with treatment-associated gastritis, and histopathologic examination revealed unspecific ischemic and regenerative

changes, significant inflammatory infiltrate and occlusion of some vessels by black, opaque inframillimetric microspheres (Y-90).
Conclusion: While effective, TACE can result in serious complications, including "post-embolization syndrome", hepatic abscess, acute liver failure, and acute kidney injury. NAP is an uncommon but serious complication. SIRT is generally well tolerated, but patients may experience gastrointestinal adverse events resulting from migration or misallocation of Y-90 microspheres. Healthcare providers must monitor patients for adverse effects and be aware of potential risks. Further studies are needed to better understand these issues, including the association of different beads with adverse effects.

E-PS-07-005
Cholestatic HCV-related cryoglobulinemia, a new clinical and pathological entity: a case-control study
S. Ammendola*, A. Dalbeni, S. Romeo, F. Cattazzo, A. Tomezzoli, D. Sacerdoti
*Department of Diagnostics and Public Health, Section of Pathology, University of Verona, Italy

Background & objectives: This study aims to explore the correlation between the presence of mixed cryoglobulinaemia (MC) and plasma cells content and distribution on liver histology and its role in the development of cholestasis in patients with non-eradicated HCV-related chronic hepatitis (CHC).
Methods: CHC patients were identified through clinical records. Cholestatic parameters, HCV-RNA serum levels, HCV genotype, plasma MC levels were retrieved; plasma cells presence and distribution were assessed on Hematoxylin&Eosin stained slides and by immunohistochemistry using anti-CD38 antibody. Patients with a history of autoimmune diseases were excluded. The Mann-Whitney U or the Chi-squared tests and stepwise multivariate analysis were performed.
Results: Sixty-two participants (57.3 ± 11.1 years; males = 50%) with CHC were enrolled: 31 non-eradicated HCV+/MC+ patients matched for age, sex and HCV genotype with 31 HCV-/MC- patients. Serum cholestasis was significantly higher in MC + group ($p = 0.02$) and correlated in univariate analysis with cryoglobulinemia (OR 6.9; $p = 0.02$). At histological assessment, the number of plasma cells in one hotspot at 40X magnification was significantly higher in the MC + group ($p=0.01$) and these were more commonly found in aggregates compared to the MC- group ($p=0.05$). At multivariate analysis with genotype, HCV-RNA, steatosis, gender and age, cholestasis was only correlated to MC + ($p = 0.01$).
Conclusion: Our study identified for the first time a correlation between MC, cholestasis and an increased number of intrahepatic plasma cells in patients with non-eradicated CHC. These findings have important clinical implications since MC is the most common extrahepatic manifestation in CHC, sometimes persisting after virus eradication. Future studies are needed to understand how MC causes cholestasis and if the increase in plasma cells content can help predict the severity of liver disease after virus eradication in MC+ patients.

E-PS-07-006
Multiseptate gallbladder: case series of 6 patients and the literature review
H. Berber*, E. Ozgur, H.K. Kahraman, S. Yüksel, S. Kiremitci, B. Savaş
*Ankara University Medical School, Pathology Department, Turkey

Background & objectives: The multiseptate gallbladder (MSG) is a rare anomaly of gallbladder. So far, fifty-nine cases have been reported in literature since 1963. Herein, we share the clinical, radiological and histomorphological features of 6 cases in our archives.
Methods: Six cases of MSG were diagnosed in our clinic between 2005-2023. Symptoms, laboratory data and radiological examination of these cases were obtained from the hospital records. All histological preparations of the cases were reevaluated according to their presence of muscle fibres in septa, inflammation and additional findings. Also we conducted a literature review using the PubMed database.
Results: Among all cases, mean age was 11,91 (range:6 months-37 years). Two of them were male, 4 were female. Only one case (5 year-old male) complained of abdominal pain, while others were asymptomatic. Calculus was not detected in any of them. A 6-month-old girl had been under investigation for biliary atresia since antenatal period. Mild elevation of liver function tests was detected in this case. Septal muscle fibres were detected in most of them (n=5) as in the literature (88,9%). Mild chronic inflammation was observed in all. In the literature, mean age was 27,34 (range:15 days-70 years), most of them were adult (n=39, 66,1%), female (n=40, 67,8%) and symptomatic (n=40, 67,8%).
Conclusion: MSG is a rare biliary anomaly that can occur in children and adults. Although majority of the patients in literature present with biliary symptoms, they may be asymptomatic like most of our cases. Although malignancy hasn't been reported in MSG yet, it's been indicated that the risk of malignant transformation may increase in some associated anomalies. Most of the publications until now have been about radiological imaging, but less about histomorphological features. Further information is needed to understand this anomaly.

E-PS-07-007
Prognostic value of dihydropyrmidine dehydrogenase (DPD) expression in lymph node metastases in pancreatic ductal adenocarcinoma (PDAC)
H. Blomstrand*, F. Groth, M. Bodarve, N. Elander
*Department of Pathology, Linköping University Hospital, Department of Biomedical and Clinical Sciences, Linköping University, Sweden

Background & objectives: Previous reports have linked intratumoral expression of dihydropyrmidine dehydrogenase (DPD) with survival in resected PDAC treated with adjuvant chemotherapy. This study investigated this relationship in primary tumours and lymph node metastases (LN) from a population-based cohort of Swedish patients.
Methods: A TMA including primary tumours and lymph node metastases of 275 resected PDAC-specimens was constructed. DPD was analysed with immunohistochemistry (Abcam anti-DPD antibody, ab134922) and staining intensity scored by two observers (HB,NE). Samples were categorised into DPD-low (score 0-1) and DPD-high (score 2-3). The prognostic value of DPD and other clinicopathological parameters were analysed with univariable and multivariable Cox regression.
Results: DPD scoring was successful in 262 cases. 120 received gemcitabine and 40 other types of adjuvant chemotherapy. Between observer concordance was excellent (Kappa=0.81). In 23% the LN-score deviated from the primary tumour score (15% low-to-high, 8% high-to-low). Univariate cox regression analyses revealed impaired OS in the DPD-high group for mean (OS 15.9 vs 22.5 months, HR 1.52, p=0.008) and LN-only scores (OS 14.0 vs 19.2 months, HR 1.42, p=0.066). DPD-high patients had shorter relapse-free survival (RFS 10.8 vs 12.9 months, p=0.036). LN-DPD-high was linked with shorter OS among gemcitabine treated patients (p=0.039). In multivariable analyses, LN-score (HR 1.52, p=0.044), beside TNM-stage, LVI, and adjuvant treatment remained independent factors for OS.

Conclusion: This study reports novel data on the prognostic value of DPD staining intensity in lymph node metastases in pancreatic cancer. High expression of DPD is a negative prognostic factor and may indicate that more intense postoperative treatments and follow up programs are needed.
Funding: FORSS (grant number 941207) County of Östergötland (grant numbers 962449 and 935580)

E-PS-07-008

Hepatic inflammatory pseudotumour (HIP) as immune response adverse event (irAE) in a patient with large B Cell lymphoma treated with cancer immunotherapies (bispecific antibodies -Obinutuzumab and Glofitamab- and CAR-T).

Z. Calixto Alvarez*, M. De Uribe Viloria, A. Hidalgo Romero, J.T. Zuñiga Gaitan, Á. Serna Pareja, X. Merino, M. Riveiro Barciela, M.T. Salcedo Allende
*Vall d´Hebron Barcelona Hospital, Spain

Background & objectives: HIP is a benign lesion with various aetiologies. Due to the absence of pathognomonic findings, it's difficult differentiate it from neoplasms and histological analysis is necessary for diagnosis. We present a case of HIP as irAE associated to cancer immunotherapies.
Methods: We present a 63-year-old asymptomatic patient with refractory large B-cell lymphoma, who after receiving several immunotherapies, was diagnosed with multiples liver lesions as probable progression of the underlying disease on a follow-up CT scan. During a year, three liver biopsies of the lesions were made. Histological study with histochemical stains and immunohistochemistry, to rule out microorganisms and lymphoma, were performed.
Results: All three hepatic biopsies showed sclerosing stroma with lymphoplasmacytic and histiocytic infiltrate and multinucleated giant cell. Immunohistochemistry confirmed the presence of CD3+ and CD8+ lymphocytes, CD68+ histiocytes, IgG4- and ALK-. All these findings were consistent with HIP. The surrounding liver parenchyma demonstrated acute necroinflammatory hepatitis with abundant eosinophils. No microorgnisms were observed with PAS, methenamine silver and Ziehl-Neelsen stainings. The patient had a positive serology (IgG and IgM) for Coxiella, but PCR tests from biopsies were negative. The HIP remained stable or decreased in size when treatment was withdrawn and increased in size when immunotherapy was reintroduced, suggesting an association between cancer immunotherapies and HIP as irAE.
Conclusion: We present a case with histological confirmation of IPH as irAE associated with immunotherapies, in a disease-free patient during histological study course. Cancer immunotherapies have been associated with HIP as an uncommon irAE, that could be misdiagnosed with malignant neoplasms or infections. Because of improvement and complexity of these treatments, a multidisciplinary diagnostic approach is necessary to integrate clinical, radiological and histological findings to avoid over-treatment and identify irAE in early stages.

E-PS-07-009

Hepatic vascular tumours: a diagnostic challenge in small biopsies. The role of morphological and immunohistochemical markers in the differential diagnosis

J. Chabla Jaramillo*, T.M. Silva, C. Romagosa Perez-Portabella, A. Diazgranados Daza, A. Hidalgo Romero, X. Merino, C. Gómez Gavara, C. Dopazo, M. Caralt, S. Ramón y Cajal Agüeras, M.T. Salcedo Allende
*Hospital Universitari Vall d'Hebron, Spain

Background & objectives: Hepatic vascular tumours (haemangiomas, small vessels neoplasm (HSVN), epithelioid haemangioendothelioma and angiosarcoma) present heterogeneous histomorphology, making the diagnosis difficult in small biopsies. The purpose of this review is the comparison of the histomorphological characteristics and immunohistochemical techniques for diagnostic aid.
Methods: We reviewed 12 cases of hepatic vascular tumours from 2019 to March 2023: five cases of haemangiomas (HM), four cases of HSVN, one case of epitheloid haemangioendothelioma (EHE) and two cases of angiosarcoma (AS), in surgical specimens as well as small biopsies. The diagnosis was made taking into account hematoxylin-eosin findings, immunohistochemical study (IHC), and clinical-radiological correlation.
Results: In relation to histological findings, all cases of HM didn't show pleomorfism, multilayer growth, mitosis or necrosis; 75% of HSVN presented focal pleomorfism, without mitosis, multilayering and necrosis, similar to EHE. In contrast, AS presented marked pleomorphism, mitoses, multilayer growth and necrosis. In relation to IHC, HM had Ki67 < 3%, p53, GLUT1 and C-myc negative; HSVN had Ki67 <10%, with one case of 12% without clinical and radiological signs of malignancy after two years follow up, negative for p53, GLUT1 and c-Myc; EHE with Ki67 > 10 %, p53, GLUT1 and c-MYC negative; AS with Ki67% > 30%, p53, GLUT1 and c-Myc positive.
Conclusion: The differential diagnosis between HSVN and AS is the hardest challenge, because of the partial representation of histomorphological characteristics and the collapse artefact of these lesions in small samples. We conclude that the multilayering, presence of mitosis and necrosis are findings that can help for a certainly diagnosis of AS. The proposal of a Ki67 <10% for non-angiosarcomatous lesions is fulfilled, but less in one case. We must be cautious in small biospias due to the heterogeneity of the marker.

E-PS-07-010

Intrahepatic immune cell profile of bariatric patients with non-alcoholic fatty liver disease and associations with disease severity

L. Chen*, G. Araujo, K. Schwenger, S. Fischer, T. Jackson, A. Okrainec, J. Allard
*Sunnybrook Health Sciences Centre, University of Toronto, Canada

Background & objectives: Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease in developed countries with few therapeutic options. The pathogenesis of NAFLD is multifactorial and involves several immune-cell-mediated inflammatory processes, but the exact mechanisms causing inflammation and fibrosis remain enigmatic.
Methods: 118 morbidly obese patients who underwent bariatric surgeries were recruited and liver tissue samples were taken. Liver histology was assessed using the Brunt system: 41 patients with simple steatosis (SS), 42 patients with steatohepatitis (NASH) and 35 with unremarkable liver histology (MOC). The frequency, location and phenotype of 8 immune cell subtypes were analysed by multiplex immunofluorescence.
Results: The numbers of helper T Cells, natural Treg cells, macrophages and B Cells significantly increase as disease progresses. The number of activated macrophages increases at the early stage of the disease and decreases in the stage of severe fibrosis. In addition, patients with simple steatosis have more cytotoxic T cells and NKT cells compared to healthy controls. Patients with NASH have less NKT cells compared to patients with simple steatosis. The numbers of NK

Cells and NKT cells at portal tracts are significantly lower in the presence of fibrosis.
Conclusion: Our data provide an overview of the association between intrahepatic immune cell composition and NAFLD severity. Overall, the numbers of helper T Cells, natural Treg cells, macrophages and B Cells significantly increase as disease progresses. NK cells and NKT cells play a potential role in the regulation of hepatic fibrosis.
Funding: Canadian Liver Foundation Operating Grant

E-PS-07-011
Granular cell tumour of the distal bile duct (GCT-DBD) and gallbladder, a hidden tumour for radiologists, causing biliary obstructive symptoms. Analysis of two cases diagnosed in a university hospital during a month
M. De Uribe Viloria*, Z. Calixto Alvarez, A. Hidalgo Romero, A. Gabaldon, L. Blanco, C. Dopazo, M.T. Salcedo Allende
*La Paz University Hospital, Spain

Background & objectives: GCT are neoplasms derived from Schwann cells that can exhibit either benign or malignant behaviour. Most common locations are the oral cavity, soft tissues and gastrointestinal tract. Biliary GCTs are extremely uncommon. We present two cases diagnosed in our centre.
Methods: We present two cases both diagnosed during the month of March 2023, one of distal bile duct GCT, the other of the gallbladder, located in the neck. The diagnosis was achieved by using Hematoxilin-Eosin and immunohistochemical studies. From the clinical history we obtained clinical and radiological information. We sub-classified these lesions, according to Fanburg-Smith system, into benign and atypical.
Results: A cases of a 73 year old female with recurrent episodes of acute choledocolithiasis and cholangitis, presenting with abdominal pain, and a 43 year old female presenting with a biliary colic due to cholelithiasis. In both cases radiological studies didn't identify a mass. On gross examination of resected specimens, there was focal wall thickening. The histology revealed a tumour composed of cells resembling histiocytes, positive for CD68, NSE and s100. Necrosis and mitosis were absent. Following histological analysis. the former case was diagnosed as benign GCT–DBD. Spindle cells, vesicular nuclei with prominent nucleolus were identified in the latter warranting the diagnosis of atypical GCT of the gallbladder.
Conclusion: CGTs of the biliary tract and gallbladder are uncommon and due to their rarity they may pose a diagnostic challenge. GCT should be considered in the differential diagnosis in patients presenting as acute-on chronic cholecystitis or recurrent cholangitis, with or without imaging evidence of tumours. To date, the diagnosis and classification requires a histological examination. The optimal treatment strategy for GCTs is yet to be defined, although, to date, surgical removal with wide margins and close clinical follow-up is recommended.

E-PS-07-012
Heat shock protein 70 (HSP70), an accessible tool for differentiating biliary tract carcinomas from pancreatic adenocarcinoma?
M. De Uribe Viloria*, A. Hidalgo Romero, Z. Calixto Alvarez, I. Bilbao, M. Caralt, X. Merino, A. Gabaldon, M.T. Salcedo Allende
*La Paz University Hospital, Spain

Background & objectives: HSP70 expression has not been reported in neoplasias of the biliary tract (BT). HSP70 is a marker readily available. We aim to demonstrate its expressions in BT carcinomas and whether it may be helpful to differentiate from pancreatic carcinoma (PDAC).
Methods: We reviewed our files from 2014 to March 2023 and selected 30 cases, 10 intrahepatic invasive cholangiocarcinoma (Ih-iCC), 10 cholangiocarcinomas located in hepatic hilum and distal bile duct (HD-CC) and 10 PDACs. We examined the expressions of HSP70 by immunohistochemical staining (nuclear and cytoplasmic) in all 30 cases and stablished three degrees of positivity: focal, patched and diffuse.
Results: Our study included 30 patients (11 female, 19 male; median age 73.5). HSP70 nuclear staining was negative in 20% of Ih-iCC, 10% of HD-CC, and 50% of PDACs. Varying degrees of nuclear staining were found in 80% of Ih-iCC (Focal-10%, patched-60% and diffuse-10%), 90% of HH-DVB (Focal-20%, patched-60% and diffuse-10%), and 50% of PDACs (Focal-10%, patched-40% and diffuse-0%). Cytoplasmic staining was negative in 30% of HH-DVB, and 10% of PDACs. Varying degrees of cytoplasmic immunoreactivity were observed in 100% of Ih-iCC (Focal-30%, patched-30% and diffuse-40%), 70% of HH-DVB (Focal-0%, patched-30% and diffuse-40%), and 90% of PDACs (Focal-0%, patched-60% and diffuse-30%).
Conclusion: Our study showed varying degrees of HSP70 expression in biliary tract carcinomas and PDAC, but no clear pattern for differential diagnosis was identified. Although more studies are needed, our results suggest that HSP70 immunostaining is not a useful tool in distinguishing these two types of cancer. To date, no immunohistochemistry study has been proven to be helpful in differentiating between these two diseases. Further research is warranted to identify more reliable diagnostic markers for biliary tract carcinomas and pancreatic adenocarcinoma.

E-PS-07-013
Expression and prognostic significance of NY-ESO1 in gallbladder carcinoma
A. Demirović*, S. Ramic, A. Ibukić, S. Čiček, T. Leniček, D. Tomas
*UHC "Sestre milosrdnice", School of Dental Medicine, University of Zagreb, Croatia

Background & objectives: Gallbladder cancer (GBC) is a malignancy with high mortality. NY-ESO1 (New York Esophageal Squamous Cell Cancer 1) is one of the most immunogenic Cancer Testis Antigens (CTAs). The aim was to assess potential clinical significance of NY-ESO-1 in GBCs.
Methods: Study included 58 patients with GBC. Immunohistochemical analysis was performed on a representative paraffin block using monoclonal NY-ESO1 antibody (clone E978, Thermo Fisher Scientific). Cytoplasmic or nuclear staining of any intensity in ≥50% is considered positive. Clinicopathological data are statistically processed using statistical program StatSoft Ver, 13.5.0.17 license AHN903D046305C-NET5-B (Tulsa, USA), with a statistical significance level of $P<0.05$.
Results: The mean overall survival (OS) time was 19 ± 35.4 months, and the median OS time was 7 months. Among classic histological characteristics Spearman's correlation analysis confirmed that poorly differentiated tumours have a higher depth of infiltration ($rs=0.414$; $P=0.001$), and thus a higher clinical stage ($rs=0.533$; $P<0.001$). Expression of NY-ESO1 was recorded in 38 cases (69.1 %). COX regression analysis showed no significant difference in OS time after surgery depending on NY-ESO1 expression. Although NY-ESO1 did not show a correlation with any other observed clinicopathological parameter, relative risk of death within 12 months is slightly in favour of positive NY-ESO1 status.
Conclusion: Two thirds of GBCs in our cohort showed positive expression of NY-ESO1. NY-ESO1 has several clinical potentials such as serum NY-ESO1, vaccination and T cell receptor therapy. NY-ESO1 can serve as a predictive marker of immunotherapy as well as a serum marker in monitoring the response to the same. Patients with

NY-ESO1-positive GBC could be potential candidates for the immunotherapy. Additional research is needed in this direction due to the low frequency but high mortality of these tumours.

E-PS-07-014

Myxoid hepatocellular adenoma of the liver: a rare, diagnostically challenging case

S.K. Dursun*, Z.B. Erdem, İ. Özden, M.B. Yilmaz Ozguven, N. Dursun Kepkep
*Basaksehir Cam and Sakura City Hospital, Turkey

Background & objectives: Hepatocellular adenomas (HCAs) are benign neoplasms of the liver that are classified into four major groups in the current WHO classification. In addition to these, rare subtypes with distinct clinical behaviour such as myxoid HCAs, are believed to exist.
Methods: We report a case of 35-year-old male, presented with abdominal pain 10 years ago and was diagnosed with hepatosplenomegaly and multiple hepatic masses. Radiologic diagnosis was haemangiomas and follow-up was recommended but patient failed to attend appointments. Due to worsening sypmtoms, he presented at clinic where imaging revealed enlarged masses. Left hepatectomy was performed with differential diagnosis of epitheloid haemangioendothelioma.
Results: The liver was enlarged with 10 well-defined tumour nodules (0,3 cm to 10 cm) on the gross examination. Histomorphological evaluation of the nodules showed hepatocytes with minimal cytological & architectural atypia, forming cords on the background of the extensive myxoid stroma. Occasional peliosis-like areas, aberrant veins, and macrovesicular steatosis were also present. Thickening of hepatocyte plates, increased mitosis, or necrosis was not found. Morphological features, as well as immunohistochemistry results, were consistent with well-differentiated hepatocellular neoplasm. Molecular analysis (NGS) was also performed; HNF1a mutations were detected. Morphological findings with supporting immunohistochemical & molecular analysis results confirmed the diagnosis of "Myxoid variant HCA, HNF1A-inactivated subtype". The patient has no recurrence after 5 months of follow-up.
Conclusion: The myxoid subtype of HCA has been recently identified and it remains unclear whether it is specific to a known HCA subtype. It has distinct histomorphological features. Although it is a newly recognized subtype, recent literature has emphasized the higher risk of malignant transformation, highlighting the importance of accurate classification. Our case of a myxoid HCA, with supporting molecular analysis, highlights the need for awareness of this extremely rare variant's histomorphological features for improved treatment modalities.

E-PS-07-015

What is hidden behind focal lesions of the pancreas - our two and a half years of experience

A. Đikić Rom*, K. Eric, M. Andrejevic, M. Dimic Cumic, V. Dugalic
*Department of Pathology, Pathohistology and Medical Cytology, University Clinical Centre of Serbia, Serbia

Background & objectives: The pancreas is a complex organ that may give rise to various lesions which have significant clinical/radiological overlap with neoplastic lesions. It has been shown that 5-10% of pancreatectomies with a clinical diagnosis of pancreatic cancer, are basically non-neoplastic lesions.
Methods: Our study included 210 patients with preoperative clinically/radiologically verified focal pancreatic lesion, operated on at the Digestive Surgery Clinic, and histopathological diagnosis of the operative material was made at the Department of Pathohistology, University Clinical Centre of Serbia, in the period from January 2018 to June 2020. After the classification of the lesions, appropriate statistical analysis methods were applied.
Results: Based on morphological and immunohistochemically characteristics, the obtained samples were classified into two major categories: primary and secondary pancreatic lesions. Primary pancreatic lesions were identified in 98.1% of the total number of operated patients. These lesions were divided into five major categories, namely: 1) malignant epithelial tumours of the pancreas: 52,64%; 2) malignant epithelial tumours of the distal part of the common bile duct: 19,14%; 3) malignant epithelial tumours of the ampullary and periampullary region: 15,31%; 4) neoplastic precursor lesions of the pancreas: 7,65% and 5) pseudotumour and benign pancreatic lesions: 5,26%. Secondary (metastatic) pancreatic lesions accounted for 1.9%, and in all cases, it was about metastatic renal cell carcinoma.
Conclusion: A heterogeneous group of pancreatic pathology, which can mimic primary pancreatic neoplasms, consists of pancreatic pseudotumour lesions, small group of rare benign pancreatic tumours and secondary pancreatic lesions. The variety of pancreatic lesions presents a challenge to clinicians/radiologists, because operations are often planned only based on the results of imaging methods in combination with the clinical presentation, but without preoperative pathohistological diagnosis. Misdiagnosis of these entities as neoplastic lesions of the pancreas can lead to unnecessary and extensive operations.

E-PS-07-017

Looking beyond the obvious: non-vascular mesenchymal tumours of the adult liver

Z.B. Erdem*, S.K. Dursun, S. Bagbudar, E. Kinaci, M.B. Yilmaz Ozguven, N. Dursun Kepkep
*Basaksehir Cam and Sakura City Hospital, Turkey

Background & objectives: Vascular tumours are the most common primary mesenchymal tumours of the liver both on malignant and benign end of the spectrum. Although exceedingly rare, other mesenchymal tumours can arise in the liver which makes it difficult to differentiate.
Methods: Aim of this study is to highlight these extremely rare entities and their histopathologic differential diagnoses based on real-life cases. All liver samplings, performed due to the presence of a hepatic mass and evaluated at a single centre, between May 2020 to March 2023, were retrieved from pathology files (n=592). Primary mesenchymal tumours were evaluated according to their line of differentiation.
Results: Of all liver tumours, 24 were confirmed histomorphologically to be of mesenchymal origin(4.1 %). Of these, seven were non-vascular. The reported entities were as follows: malignant solitary fibrous tumour (n=1), inflammatory myofibroblastic tumour (n=1), rhabdomyosarcoma (n=1), leiomyosarcoma (n=2), undifferentiated embryonel sarcoma (UES)(n=2), epitheloid haemangioendothelioma (n=4), angiosarcoma (n=1), and benign vascular proliferations (haemangioma etc.)(n=12). A broad immunohistochemistry panel, and if needed, molecular diagnostics were performed to aid in accurate differential diagnosis. The patients were equally distributed between genders (F/M: 1) with a mean age of 50,6 years (20 to 89 years). All tumours were confirmed to be primary following systemic evaluation. Both of the UESs found to have arisen on the background of a mesenchymal hamartoma.
Conclusion: Vascular tumours are the most well-known mesenchymal tumours of the adult liver. Usually, benign vascular tumours are diagnosed and monitored radiologically without the need for histopathological confirmation. However, in some cases, radiological diagnosis can be misleading. While histopathological diagnosis is the gold standard and essential for proper patient management, it can be challenging due to the rarity. This study discusses tips and potential pitfalls that may be encountered in routine practice to ensure accurate diagnosis and precise patient care.

E-PS-07-018

The spectrum of Hepatocellular carcinoma precursor lesions: stemness and epithelial-mesenchymal plasticity

J. Espírito Santo*, A.F. Ladeirinha, A. Alarcão, E. Strelet, M. Reis, R. Santos, L. Carvalho
*Adult Liver Transplantation Unit, Coimbra Hospital and University Centre, Portugal

Background & objectives: Dysplastic foci (DF) may evolve to low-grade/high-grade dysplastic nodules (LGDN/HGDN) and subsequently to hepatocellular carcinoma (HCC). Hepatic progenitor cells (HPC) undergo heterogenous differentiation, displaying epithelial-mesenchymal plasticity (EMP).
Expression of HPC/mesenchymal markers was analysed in a spectrum of HCC precursor lesions.
Methods: A series of 5 regenerative nodules (RG), 8 DF, 12 LGDN and 5 HGDN was collected from 21 patients (19 were cirrhotic) undergoing liver resection/transplantation. WHO 2019 histopathological criteria, proliferation/apoptotic markers (Ki67, p53), HPC/cholangiocytic markers (CK7, CK19, EpCAM/BerEp4) and mesenchymal markers (alpha-smooth muscle actin - ASMA - and vimentin) expression were evaluated in lesional cells (Lc) and perilesional hepatocytes (Plh).
Results: Higher perilesional ductular reaction, with important HPC markers expression, was observed in DF and LGDN. RG and DF displayed relevant Lc expression of EpCAM, CK7, ASMA and vimentin, while HPC/cholangiocytic markers rose from RG to DF and mesenchymal markers expression declined. EpCAM and ASMA expression in Lc decreased from DF to LGDN to HGDN, while EpCAM expression in Plh was greater in LGDN than in DF ($p<0.05$). HGDN showed higher expression of CK7+ Plh than LGDN ($p<0.05$). Lc vimentin expression was higher in HGDN than in DF ($p<0.05$) and increased across DF, LGDN and HGDN, while LGDN showed higher Plh vimentin expression than HGDN ($p<0.05$).
Conclusion: Stemness and EMP seem to have an important role in the early steps of hepatocarcinogenesis. The applied immunohistochemical panel, following WHO advise, allowed to understand the relationship between HPC activation and EMP, determined by liver microenvironment. Further studies will help to determine different ways of targeting HPC and EMP to effectively modulate HCC development and prognosis.
Funding: ROCHE- APEF (Portuguese Association for the Study of the Liver) research grant.

E-PS-07-019

Hepatic adenomatosis with malignant transformation in a young patient with a congenital extrahepatic portosystemic shunt (Abernethy malformation)

A. Felšöová*, O. Fabián, L. Janoušek, E. Sticová
*Clinical and Transplant Pathology Centre, Institute for Clinical and Experimental Medicine, Prague, Department of Histology and Embryology, Second Faculty of Medicine, Charles University, Prague, Czech Republic

Background & objectives: Abernethy malformation (AM) is a rare congenital anomaly of the venous system characterized by presence of intrahepatic or extrahepatic porto-systemic shunts. The condition yields an increased risk for development of hepatic tumours such as hepatocellular adenoma (HCA) or carcinoma (HCC).
Methods: We report a case of hepatic adenomatosis in an 18-year-old female with AM. CT scan detected multiple hepatic tumours with morphology corresponding to HCA or focal nodular hyperplasia (FNH). Due to the progression of the size and number of the foci, the patient was indicated for a liver transplantation.
Results: In the gross findings, 12 spherical, sharply demarcated tumours were found in both lobes. Histologically, multiple HCAs were found showing cytological atypia of a various degree. In several areas, transition to well differentiated HCCs with infiltrative growth patterns were found. Immunohistochemistry of these lesions showed an aberrant nuclear positivity of beta-catenin and a diffuse cytoplasmic positivity of glutamine-synthetase. Apart from that, several foci with FNH-like morphology were detected. The surrounding hepatic parenchyma showed unevenly distributed and fibrotic portal spaces with numerous and tortuous interlobular arteries and hypoplastic interlobular veins.
Conclusion: AM is a rare vascular anomaly, the knowledge of which is important especially due to increased risk of liver tumours. We presented the case of the patient with this disease and the occurrence of multiple HCAs with beta-catenin mutation and transformation to HCC.

E-PS-07-020

Comparison between imaging and pathological findings in liver transplant recipients with hepatocellular carcinoma in the setting of chronic liver disease/cirrhosis: a retrospective study of 26 cases from 2017 to 2023

C. Gouta*, P. Panas, E. Katsiki, V. Georgopoulou, K. Gianna, E. Sinakos, G. Tsoulfas
*Department of Histopathology, Hippokration General Hospital of Thessaloniki, Greece

Background & objectives: Computed Tomography Scan and Magnetic Resonance Imaging are used in a regular basis in the follow-up of patients with chronic liver disease and cirrhosis and are essential tools for the evaluation process and placement in the liver transplant waiting list.
Methods: We conducted a retrospective study that included 26 patients with hepatocellular carcinoma who underwent liver transplantation from 2017 to 2023 in our hospital. The malignancy classification, the number of foci and the maximum diameter of the neoplasm according to the last imaging technique before transplantation were recorded and compared to the respective pathological findings in the explant.
Results: All 26 recipients (24 males and 2 females) had cirrhosis due to late-stage chronic liver disease, specifically, alcoholic/non-alcoholic fatty liver disease, primary biliary cholangiitis and chronic viral hepatitis (HBV, HCV and combined HBV/HDV). Pathological and imaging results were identical in 69,23%, 42,30% and 23,08% of the cases regarding the type of malignancy, the number of foci and the maximum diameter respectively. In 6 of the 26 cases the imaging techniques either misdiagnosed the neoplastic disease as benign or were not able to identify its type. Furthermore, both the number of foci and the maximum diameter displayed a mean deviation of no statistical significance.
Conclusion: According to our study both Computed Tomography Scan and Magnetic Resonance Imaging are equally reliable techniques for the follow-up of transplant candidates and their eligibility evaluation based on Milan Criteria. Additional factors such as the number of days between the imaging and the transplantation, the time needed for the explant fixation and the variety of methods used by the radiological laboratories involved were considered throughout the study and are extensively discussed.

E-PS-07-021

Disease patterns and entities in primary medical and tumour liver consult cases highlight challenging areas in diagnostic hepatopathology

I. Grypari*, I. Vlachos, E. Stoupi, D. Karandrea, D. Myoteri, D. Tiniakos
*Department of Pathology, Aretaieion Hospital, Medical School, National and Kapodistrian University of Athens, Greece

Background & objectives: Difficult liver pathology cases often require expert review for optimal patient care. We reviewed consult cases received in our reference centre aiming to highlight challenging areas in hepatopathology that may benefit from consultation and focused educational activities.

Methods: We included all primary liver consult cases received in our Department between October 2016 and December 2022. Data on the sender (hepatologist/pathologist/patient) and the reason for consult were collected. Initial and consult reports were screened for adequacy of clinical/laboratory/imaging information received, stains performed, final diagnosis, disease grading/staging and comment on aetiology with suggestions to the clinician, where appropriate.
Results: We retrieved 219 liver consults, 187(85.4%) submitted by hepatologists. For medical cases (n=147,67.1%), most common initial diagnoses were non-specific changes (n=37,25.2%), chronic hepatitis (n=17,11.5%), nonalcoholic steatohepatitis-NASH (n=10,6.8%). Most common consult diagnoses were vascular disease (n=22,15%), primary biliary cholangitis-PBC (n=19,12.9%), NASH (n=13,8.8%), AIH (n=12,8.2%) ($p<0.001$). Major change in initial diagnosis was noted in 73(49.6%), minor changes in 37(25.2%) and no change in 23(15.6%). For tumours (n=72,32.9%), most common initial diagnoses were hepatocellular carcinoma-HCC (n=23,31.9%), nonspecific (n=14,19.4%) or metastatic (n=6,8.3%). Most common consult diagnoses were HCC (n=36,5%), cholangiocarcinoma-CCC (n=5,6.9%) or non-tumour parenchyma (n=4,5.6%) ($p=0.033$). Major change in initial diagnosis was noted in 30(41.7%), minor changes in 24(33.3%) and no change in 15(20.8%).
Conclusion: Study of liver consult patterns provides useful information on areas of hepatopathology posing diagnostic difficulty. The majority of consult cases in our centre are submitted by hepatologists. The most common diagnostic challenges in medical cases are vascular liver disease, interpretation of hepatitic pattern of injury, and recognition of primary cholangiopathy, while in tumour cases these include classification and subtyping of hepatocellular tumours. These areas can be the subject for future continuing medical educational activities in hepatopathology.

E-PS-07-022
Reflux-associated cholecystopathy with pancreaticobiliary maljunction: a case report
G. Güngör Sahin*, M. Buyuk, N. Berker, B. Acunas, M. Gulluoglu
*Istanbul University, Istanbul School of Medicine, Department of Pathology, Turkey

Background & objectives: Pancreaticobiliary maljunction (PBM) is defined as congenital fusion of common bile duct and pancreatic duct outside the wall of duodenum and it leads to reflux-associated cholecystopathy. It occurs more often in Asian populations and may cause carcinomas of pancreaticobiliary system.
Methods: A 57 year-old woman presented with right upper quadrant abdominal pain. After clinical and radiologic examinations, she underwent cholecystectomy for gallbladder polyps.
Results: The cholecystectomy material was measured 8,5x4,7x0,4 cm. The mucosa was 0,3 cm thick and yellow coloured. No localised polypoid lesion or stone were observed. Microscopically; diffuse mucosal hyperplasia with villoglandular appearance and amyloid-like substance accumulation at the tips of papillae were detected. Intestinal metaplasia was focally observed and no inflammation was detected. These findings were consistent with reflux-associated mucosal damage resulting from PBM. Magnetic resonance cholangiopancreatography scan showed that the junction between common bile and pancreatic ducts was located 1 cm proximal to the sphincter of Oddi outside the duodenal wall, and the main hepatic and common bile ducts were dilated (12 mm and 8 mm, respectively).
Conclusion: Understanding the histopathologic characteristics of reflux-associated cholecystopathy is important as it is associated with PBM which increases the risk of neoplastic development in pancreaticobiliary tract. It is recommended to identify patients with this anomaly for prophylactic cholecystectomy and radiologic follow-up for any neoplastic development.

E-PS-07-023
A case report: concomitant lymphoplasmacytic sclerosing pancreatitis and lymphoplasmacytic sclerosing cholangitis
I. Guzelis*, A. Akder Sari, O. Gunes
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: IgG4-related sclerosing diseases can affect any organ and clinically can mimic malignant tumours. In the pancreas, it is variously termed lymphoplasmacytic sclerosing pancreatitis (LPSP) or autoimmune pancreatitis. LPSP usually responds to corticosteroids, making it important to differentiate from pancreatic ductal adenocarcinoma.
Methods: A 53-year-old woman presented with jaundice. Biochemical analysis revealed elevated AST, ALT, ALP, GGT, and bilirubinemia. On abdominal ultrasound, intrahepatic bile ducts were diffusely dilated, and a pancreatic head mass was detected. PET CT and MRCP disclosed two malignant suspicious masses which were located in the pancreatic head and main bile duct bifurcation.
Results: The patient underwent a Whipple procedure with the excision of extrahepatic bile ducts. The gross examination showed a 3 cm ill-defined mass in the pancreatic head and thickened segments of extrahepatic bile ducts. Microscopically, both lesions revealed dense lymphoplasmacytic inflammation particularly centred around neurons and ducts. Obliterative phlebitis along with periarteritis and periartheriolitis were observed. Acinar atrophy and prominent storiform-type fibrosis were present. IgG-positive plasma cells were higher than 50/HPF and IgG4/IgG percentage was 60% (>40%). The case was diagnosed as lymphoplasmacytic sclerosing pancreatitis (autoimmune pancreatitis type 1, IgG4-related pancreatitis) and lymphoplasmacytic sclerosing cholangitis.
Conclusion: Lymphoplasmacytic sclerosing pancreatitis or cholangitis might mimic carcinomas both clinically and radiologically. If untreated this disease can lead to pancreatic insufficiency, fibrosis, and other complications. Given that there is a dramatic response to corticosteroid treatment, it is important to beware of this entity.

E-PS-07-024
Immunohistochemistry in adenocarcinoma liver metastasis
M. Heritier*, T. Fenouil
*Hospices Civils de Lyon, France

Background & objectives: Adenocarcinoma liver metastasis (ALM) origin is essentially diagnosed with the expression of immunomarkers. However, we mostly know the expression pattern of these markers in primitive tumour rather than ALM. Hence, we aim to describe the expression of those in ALM.
Methods: A retrospective cohort of 231 ALM patients split into 7 origin groups were included in this study. Two pathologists, blindfolded with the origin site, went throught a semi-quantitative analysis of 18 immunomarkers (including several keratines, and "tissu-specific" markers) on each case. A preliminary statistical analysis was made, which will further be completed by clustering analysis, k-means, and combinatorial analysis.
Results: Keratines were globally well expressed in ALM from every origins, excepted for CK20, which was restrained to specific origin groups. As for tissu-specific markers, unexpected but significant expressions were found: there was a low frequency of GATA3 expression in every studied origin group, and chromogranine A in almost every group. TTF1 was expressed in some colorectal tumours (4/49). p40 was observed in certain groups (extrahepatic cholangiocarcinoma, pancreas, lung, breast and oesophago-gastric) without any previous description of it. PDX1 was weakly expressed in every group except from breast. There was a weak expression of PAX8 in some breast metastasis.

Conclusion: It seems that immunomarkers expression in ALM shows important disparities that need to be known, compared to the known patterns in primitive tumours. Here is the first analysis of a large panel including 18 immunomarkers on a significant number of ALM. The complete statistical analysis that will include clustering analysis, k-means, and combinatorial analysis should be able to identify which markers or marker combinations could be the most robust in a daily practice of ALM diagnosis.

E-PS-07-025
Solid pseudopapillary neoplasm of the pancreas – case report
M. Jikurashvili*, I. Nedkov Ivanov
*CSD-Georgia, Georgia

Background & objectives: Solid pseudopapillary neoplasm of the pancreas is a rare tumour with unclear cell of origin, affecting predominantly female individuals. It represents less than 2% of exocrine pancreatic tumours and is associated with favourable prognosis.
Methods: We report a case of a retroperitoneal mass, observed in a female individual in her 6th decade of life. The imaging showed an infiltrative tumour involving the kidney, aorta, pancreas and spleen. The management of the patient included a diagnostic biopsy followed by surgical treatment (distal pancreatectomy).
Results: H&E sections from the diagnostic biopsy revealed fibro-fatty tissues with discohesive, solid, partly pseudopapillary tumour composed of monomorphic, round, eosinophilic cells with angular and grooved nuclei and intracytoplasmic hyaline globules. Only a few mitotic figures were detected. The tumour cells were positive for CD10, S100, beta-catenin (nuclear), vimentin, CD56 and focally on Cyclin D1, NSE. E-cadherin expression was lost. Ki67 index was <5%. The post-operative sample revealed infiltrative intrapancreatic 6cm tumour with solid-cystic areas and haemorrhage without necrosis and invasion in spleen. Microscopy showed the same features described in the biopsy. In addition: foamy macrophages, cholesterol crystals and calcifications. No high-grade transformation, neural or vessel invasions were seen.
Conclusion: The overall diagnosis was a solid pseudopapillary neoplasm of the pancreas with low malignant potential. The long-term prognosis of this tumour is generally excellent for localized, metastatic and even recurrent disease after complete surgical resection.
This rare tumour may be difficult to identify in a small biopsy and immunohistochemistry plays vital role in the diagnostic process. The striking sex and age distribution with the gross features described above are also important criteria to consider.

E-PS-07-026
Unexpected pathological lesions encountered in the gall bladder: a surgical pathology review of 5,636 consecutive gall bladder surgical specimens
R. Kanthan*, S. Kanthan
*University of Saskatchewan, Canada

Background & objectives: The gall bladder, a common 'low-stakes' surgical pathology specimen received for calculous/non-calculous related inflammations, rarely has unexpected lesions that are extremely challenging for accurate diagnosis. This study aims to discuss 43 such cases encountered in our routine surgical pathology practice.
Methods: A retrospective LIS computer search of "gallbladder' surgical pathology cases for the last twenty years was undertaken. The pathological reports were reviewed and catalogued. Cases with the final diagnosis of any uncommon pathology excluding routine inflammation/cholesterol polyps/cholesterolosis were identified. These selected cases were categorized by age and sex and a detailed in-depth review of their pathological diagnosis was carried out.
Results: 352,253 cases were processed to yield 5,636 gall bladder reports. Review of these reports identified the majority of the cases to be varied degrees of acute or chronic inflammation, mostly associated with calculous disease. These lesions occurred in adults ranging from 23-83 years with a strong female predilection. Adenomyomatous hyperplasia was seen in 52 cases. Unexpected lesions encountered included Biliary Intraepithelial Neoplasia [8]: high-grade, multifocal [4] and low grade [4]; Gall bladder cancers [25] –primary [18] metastatic renal cell carcinoma [1] and secondary involvement from adjacent cancer of the hepatic flexure of the colon [6] ; Heterotopia-gastric [2], hepatic[2] and tubulopapillary neoplasms [6]: non-invasive [4] and with invasive carcinoma [2].
Conclusion: Our study highlights the rarity of uncommon pathologies in the gall bladder. It is important to be aware of these lesions as accurate histological identification is vital, as this determines the next step treatment strategies for the patient as in gall bladder cancers. The recently described tubulopapillary lesions need accurate recognition to avoid overtreatment in cases that have no 'true' invasive component. We recommend the entire gall bladder to be processed for evaluation in all cases with any unexpected pathology.

E-PS-07-027
Exploring Syndecan-1 expression profile in neuroendocrine tumours of the grastointestinal tract and pancreas
E. Koniaris*, A. Kataki, I. Angelioudaki, A. Mitrousias, A.G. Tzingounis, A. Charchanti, G. Zografos, M. Konstadoulakis, G. Kafiri
*Pathology Departmant, General Hospital of Athens 'Hippocratio', Greece

Background & objectives: Neuroendocrine neoplasms (NENs) can be developed in different sites along the gastrointestinal tract (GI) and are classified as tumours (NETs) and carcinomas (NECs). The present study is focusing on exploring the expression profile of syndecan-1 protein (SDC-1).
Methods: Study's cohort consisted of 29 NETs mean age 61.93±2.0 mean age 65.3±2.39, 20 located in pancreas (pNET) and 9 in the GI (giNEC); 20 NECs: 11 located in pancreas (pNEC) and 9 along GI (giNEC); and 7 MANEC mean age 67.56±2.62, 2 of which are in pancreas (pMANEC).
Results: SDC-1 expression was detected immunohistochemically and both percentage of positive cells and intensity were scored in lesions' as well as in normal adjacent tissue. Their multiplication score was used in statistical analysis. SDC-1 expression was both membranous and cytoplasmic in epithelial cells. A shift from membranous to cytoplasmic expression was observed from normal to lesion's stroma. SDC-1 expression wasn't detected in giNETs lesions' epithelium whereas, epithelium expression was limited to cell membrane in pNETs. In giNECs higher expression of SDC-1 was observed in cancer epithelium compared to pNECs, still without reaching a statistically significant difference. No protein expression was spotted in normal adjacent stroma. Findings were similar in MANEC.
Conclusion: The herein presented data indicate that in these rare neoplasms SDC-1 protein expression profile varied based to their site of origin. In addition, the observed shift of SDC-1 expression from the cell membrane to the cytoplasm further support that its loss of function at the cell-surface may facilitate cancer progression and the development of invasive and metastatic disease.
Funding: NeXT

E-PS-07-028
Undifferentiated carcinoma of the pancreas with osteoclast-like giant cells presenting cyto-histopathologic correlation: a case report
J. Lages dos Santos*, A. Sanches, L. Santos
*Centro Hospitalar de Vila Nova de Gaia / Espinho, Portugal

Background & objectives: Among undifferentiated pancreatic carcinomas undifferentiated carcinoma of the pancreas with accompanying osteoclast-like giant cells (UC-OGC) has been classified as an

independent identity, representing <1% of all pancreatic tumours, making the management of this disease challenging as literature is scarce.
Methods: We present the case of a 60-year-old man who presented to the emergency service with subocclusive symptoms and abdominal pain on 06/10/22, where an abdominal CT scan revealed an pancreatic nodule immediately distal to the uncinate process measuring 2.3cm. A FNA biopsy was obtained and the patient was later accepted for surgical resection and submitted to cephalic duodenopancreatectomy on 16/02/23.
Results: The biopsy revealed cells with accentuated atypia and pleomorphism and giant multinucleated osteoclast-like cells, correlating with the definitive histological exam which determined the final diagnosis as UC-OGC with a small component of ductal adenocarcinoma, with TNM staging of pT2 N0 M0.
The patient has remained stable after clinical discharge and is currently being considered for adjuvant chemotherapy as of the latest follow-up consultation on 14/04/23.
The presence of associated pancreatic ductal adenocarcinoma with UC-OCG has emerged as an important criterium for prognosis, presenting lower median overall survival than pure UC-OCG. Patients who undergo surgical resection and receive adjuvant chemotherapy also seem to present longer disease-free survival and overall survival.
Conclusion: As evidence points to pure UC-OGC presenting less aggressive tumoral behaviour than other undifferentiated carcinomas of the pancreas, careful histological characterization of the tumour is increasingly important. The differences in tumour composition may allow for new potential therapeutic targets, such as immunotherapy for PD-L1 positive UC-OCG. Due to the rarity of UC-OGC, the role of chemotherapy has not yet been standardized. As such, more thorough research will be challenging but potentially rewarding in providing further treatment options for these patients.

E-PS-07-029
Hepatic progenitor cells within a GIST liver metastasis: focusing on the role of the liver metastatic niche
J. Lobo*, J. Gama, R. Luís, D. Tiniakos, M.A. Cipriano
*Portuguese Oncology Institute Porto, Portugal

Background & objectives: Recent studies have highlighted the presence of hepatic progenitor cells (HPCs) in liver metastases, specifically of carcinomas. It is theorized that HPCs may influence homing of tumour cells to the liver.
Methods: We provide further evidence of this phenomenon, presenting a case of a gastrointestinal stromal tumour (GIST) liver metastasis with evidence of intra- and peritumoral HPCs. Clinical annotation and immunohistochemistry studies are provided, along with discussion of the available literature.
Results: A 64-year-old man presented with a gastric mass, diagnosed as a high-risk KIT-mutated GIST. The patient was treated with Imatinib, recurring five years later with a liver mass. Liver biopsy disclosed a GIST metastasis, showing a proliferation of ductular structures without cytological atypia intermingled with the tumour cells, with a K7/K19/CD56-positive immunophenotype and rare CD44 positivity. The patient underwent liver resection, and the same ductular structures were present in the tumour interior and at its periphery.
Conclusion: The ductular structures were positive for the biliary marker K7 and the HPC markers K19 and CD56, with rare cells expressing the stem cell marker CD44, paralleling previous findings in liver metastases of colorectal adenocarcinoma. HPCs may attract cancer cells, giving rise to pre-metastatic niches, and they could have a vital role in cancer growth.

E-PS-07-030
Neo-adjuvant treatment of hepatic metastases of colorectal cancer: predictive factors of histological response
I. Mallek*, S. Ben Slama, Z. Ben Romdhane, B. Bouchabou, M. Mbarek, M. Hajri, H. Mestiri, A. Lahmar, D. Bacha
*Monji Slim La Marsa, Tunisia

Background & objectives: Surgery after neoadjuvant chemotherapy (CT) improves prognosis of colorectal cancer (CRC) with liver metastases (LM). Histological response is a good prognostic factor. The aim of this study was to evaluate predictive factors of histological response of LMCRC after neo-adjuvant treatment.
Methods: Retrospective study of patients with LMCCR operated after neoadjuvant CT treatment from June 2016-June 2022. Assessment of histological response was based on the Rubbia-Brandt TRG tumour regression score. We grouped the scores into two types of response: Response Group (R) and No Response Group (NR).
Results: We studied 77 patients. Synchronous LM was present in 55% and metachronous LM in 45%. The mean time to onset of LM was 22 months. Neoadjuvant treatment included CT alone in 68% and CT with targeted therapy in 32%. Overall survival was 32 months, with a significantly greater survival in Group R (p=0.001). Predictive factors for histological response included delay in onset of LM >14 months (p=0.027), neoadjuvant treatment with CT and targeted therapy (p=0.031), and absence of lymph node metastases on LM specimens (p=0.014). In multivariate analysis, neoadjuvant treatment type (p=0.035) and absence of lymph node metastases on LM specimens (p=0.013) were independent predictive factors of histological response.
Conclusion: Predictive factors of histological response would allow to identify patients who would benefit most from neoadjuvant treatment. These are patients with LM onset of more than 14 months, treated with CT combined with targeted therapy and without lymph node metastases would be the best candidates for a neoadjuvant CT strategy followed by surgical resection.

E-PS-07-031
Comprehensive characterisation of acinar cystic transformation of the pancreas: a systematic review
P. Mattiolo*, H. Wang, A. Scarpa, C. Luchini
*Department of Diagnostics and Public Health, Section of Pathology, University and Hospital Trust of Verona, Italy

Background & objectives: Acinar cystic transformation (ACT) of the pancreas is a poorly understood pancreatic lesion. Few cases are reported, mainly as single case reports. Based on a systematic review of the literature, this study aims to comprehensively characterize this lesion.
Methods: For the systematic review, two investigators (P.M.. and C.L.) independently conducted a literature search using PubMed and SCOPUS without language restriction, from database inception until 03/31/2023. All data were extracted independently by two authors (P.M. and C.L.) and then validated by other authors (A.S. and H.W.).
Results: The main results can be summarized as follows: 1) Total number: 118 cases of ACT are reported; 2) Macroscopy: pancreatic head is the most common site (56%); ACT is more often unifocal (70%), and with multilocular structure (61%); 3) Microscopy: all cysts are lined by acinar cells without significant atypia. A not-negligible subset of cases shows ductal-like areas (18%), squamous metaplasia (8%), mucinous metaplasia (6%), and PanIN-like changes (3%); 4) Immunohistochemistry: acinar cell markers and CK7 diffusely are positive in all cases; 5) Molecular landscape: KRAS and SMO mutations have been demonstrated in two cases; 6) Clinical course: all patients are alive and free of disease after surgical resection.
Conclusion: ACT is an under-recognized entity, with specific histological and immunohistochemical characteristics. Patients with ACT have excellent prognosis after surgical resection. Recognition of this rare entity is fundamental in the differential diagnosis of cystic lesions of the pancreas. The recent report of somatic pathogenic mutations of KRAS and SMO suggests the possible neoplastic nature at least in a subset of ACTs.

E-PS-07-032

Peri-ampullary EBV-associated lymphoepithelioma-like carcinoma: a case report

E. McGrath*, K. Ryan, N. Swan, L. Clarke
*St Vincent's University Hospital, Dublin, Ireland

Background & objectives: Lymphoepithelioma-like carcinomas are rare tumours composed of undifferentiated malignant epithelial cells with characteristic lymphoid stroma that resemble non-keratinizing nasopharyngeal carcinoma, undifferentiated subtype (previously lymphoepithelioma). The majority of cases occur in the head and neck are associated with Epstein-Barr virus (EBV).
Methods: Case report: We report a case of a 50-year-old man who underwent a pancreatoduodenectomy (Whipple resection) for a primary peri-ampullary EBV-associated lymphoepithelioma-like carcinoma.
Results: An oesophagogastroduodenoscopy (OGD) revealed a tumour mass present in the peri-ampullary region of the duodenum. A biopsy showed a poorly differentiated malignant epithelioid neoplasm with lymphoid stroma that was positive for EBV by in-situ hybridisation. A pancreatoduadenectomy (Whipple resection) was carried out after neoadjuvant chemotherapy. Pathology: Macroscopically, a 24mm solid mass was present in the peri-ampullary region of the duodenum and an adjacent positive peri-pancreatic lymph node was identified. Histology showed extensive residual poorly differentiated carcinoma with lymphoid stroma extending into periduodenal soft tissue with perineural invasion. Malignant epithelial cells showed positive EBV expression by in-situ hybridisation and mismatch repair proteins (MSH-2, MSH-6, MLH-1 and PMS-2) were intact on immunohistochemistry.
Conclusion: Peri-ampullary EBV-associated lymphoepithelioma-like carcinoma is an exceedingly rare primary malignancy. To our knowledge, only one other case has been described in the literature at this site. We compare our case to the single previously reported case and review the current literature and classification of lymphoepithelioma-like carcinomas.

E-PS-07-033

GATA3 expression in pancreatic ductal adenocarcinoma: an immunohistochemical analysis of 140 cases

G. Menetlioğlu*, P. Bağcı Çulçi, E. Bozkurtlar
*Marmara University, Departmant of Pathology, Turkey

Background & objectives: This study investigates GATA3 incidence in pancreatic ductal adenocarcinoma (PDAC) and its impact on differential diagnosis, given its importance in the TGF-B signalling pathway and limited research in this area.
Methods: A total of 140 patients diagnosed with PDAC between 2012-2021 were included in the study. Microarray blocks (TMA) were created from each tumour using a 0.6 mm punch and GATA-3 immunohistochemistry was applied to these blocks. Tumours were evaluated for nuclear immunoexpression.
Results: Of the 140 patients included in the study, 66 were female and 77 were male, with a mean age of 67. GATA3 immunohistochemistry did not reveal nuclear immunoexpression in any of the cases.
Conclusion: Some studies in the literature report that GATA3 is positive in some cases of PDAC, however, in our study, GATA3 immunoexpression was not detected in any of the 140 cases. These results may limit the use of GATA3 expression in differential diagnosis due to the lack of a specific immunohistochemical marker for PDAC.

E-PS-07-034

Hepatic epithelioid haemangioendotheliomas: immunohistochemical profile and expression of CAMTA1 for its differential diagnosis

M.d.R. Mercado Gutierrez*, M.L. Gomez-Dorronsoro, B. Aguiar, I. Amat, R. Beloqui, C. Cerezo Aguirre, A. Lopez
*Navarra's Universitary Hospital, Spain

Background & objectives: Hepatic epithelioid haemangioendothelioma (HEHE) is a rare tumour that have WWTR1-CAMTA1 and YAP-TFE3 fusion gene in 90% and 5% respectively.
Our study aimed is to describe the immunohistochemical profile of HEHEs and the utility of CAMTA1 also in other digestive haemangioendotheliomas
Methods: We collected four cases diagnosed as epithelioid haemangioendotheliomas in digestive tract from 2004 to 2023 in Navarra's Universitary Hospital (Spain). One of them underwent a surgical resection. Immunohistochemistry (IHC) was performed using CAMTA1, TFE3, citoqueratin7, CD31, CD34, EGR, HepPar1 in formalin fixed paraffin embedded blocks.
Clinical data, epidemiologic features, treatment methods, and clinical courses, were reviewed through electronic medical records.
Results: Two cases were diagnosed as primary HEHE (Case1 and 2) . The others were located in spleen(Case3) and small intestine(Case4).
Case1: 73 year old male. Radiological study consistent with cholangiocarcinoma.
IHC: TFE3 positive nuclear and diffuse, CAMTA1 negative. The resected specimen showed a multifocal HEHE with portal tract and vascular involvement.
Case 2: 50 year old woman. Scan showed a unique hepatic nodule consistent with primary metastatic cervical cancer.
IHC: TFE3 negative and CAMTA1 positive.
Citoqueratin 7 and vascular markers (CD31, CD34, ERG) were strong and diffuse positive in both cases and they were negative for HepPar1.
Case 3 and 4: TFE3 negative and CAMTA1 positive.
Conclusion: Histologically, the HEHE can mimic metastatic carcinoma, angiosarcoma, hepatocellular carcinoma, and cholangiocarcinoma.
Immunohistochemical profile shows expression for vascular markers (ERG, CD 31 and CD34)
Given its epithelioid morphology, strong expression for citoqueratin 7 should be carefully assess specially in clinical and radiological finding suspicious for cholangiocarcinoma.
CAMTA1 is a helpful marker for diagnosis of hepatic HEHE as TFE3.

E-PS-07-035

Uncommon aetiology of pancreatic mass: a case report

S. Moqran*, H. Abdoulaye Biyou, F. Harmouch, R. Ben Tayab, L. Tahiri, L. Chbani
*University hospital hassan II, Morocco

Background & objectives: IgG4-related autoimmune pancreatitis (AIP) is a chronic inflammatory disease of the pancreas with a distinct histological. his diagnostic remains challenging as some features overlap with pancreatic cancer. We present a case of IgG4-related AIP mimicking pancreatic cancer.
Methods: 70-years-old male patient presented with epigastric pain, radiating to the entire abdomen with an unquantified weight loss. Magnetic resonance cholangiopancreatography (MRCP) showed a mass with 28 mm long axis, in the head of the pancreas with pancreatic duct dilatation. Thus, he is presumed to have a pancreatic neoplasm and underwent pancreatic resection without a definitive preoperative diagnosis.
Results: In terms of clinical presentation, imaging characteristics, and laboratory parameters, IgG4-related AIP can resemble pancreatic cancer. Thus, histopathological studies remain the gold standard for a definitive diagnosis, that may show a diffuse lymphoplasmacytic infiltrate with a storiform fibrosis. On immunohistochemistry, the majority of plasma cells are positive for IgG4 (>50 per high-power field [HPF]). In our case, the gross appearance was indistinguishable from a pancreatic neoplasm. The histologic diagnosis allowed us to suggest the diagnosis of IgG4-related AIP and the immunohistochemical diagnosis confirmed the diagnostic.
Conclusion: It is critical to distinguish pancreatic cancer from IgG4-related AIP due to theirs completely different prognosis and therapy.

steroid therapy is the first-line treatment that allow a reducing of risk of relapse, therefore a misdiagnosis as a malignancy leads to inappropriate surgical interventions. In this case biopsy is recommended.

E-PS-07-036

Perineural invasion score system and clinical outcomes in resected pancreatic cancer patients

F. Nozzoli*, M. Catalano, L. Messerini, G. Roviello
*University of Florence, Italy

Background & objectives: Perineural invasion (PNI), classified by its presence or absence in tumour specimen, is recognized as a poor prognostic factor in pancreatic ductal adenocarcinoma (PDAC). Herein, a histopathologic scoring system for 5 distinct measures of PNI in PDAC was developed.
Methods: Five histopathological features of PNI (diameter, number, site, sheath involvement, and mitotic figures within perineural invasion), combined in an additional total score and clinical data of PDAC patients were retrospectively analysed. PNI+ patients were stratified in two categories according to the median score value. Impact of PNI on disease free survival (DFS) and overall survival (OS) were then analysed.
Results: Forty-five patients were enrolled, of whom 34 with PNI (PNI+) and 11 without PNI (PNI-), with a PNI rate of 75.6%. The DFS was 11 months vs. not reached (NR) (p=0.258), while the OS was 19 months vs. NR (p=0.040) in PNI+ and PNI- patients, respectively. A $\geq$ 6 PNI was identified as independent predictor of worse OS vs. <6 PNI+ patients (29 vs. 11 months, p<0.001) and <6 PNI+ and PNI- patients (43 vs. 11 months, p<0.001). PNI $\geq$6 was an independent negative prognostic factor of DFS vs. <6 PNI+ and PNI- patients (13 vs. 6 months, p=0.022).
Conclusion: PNI was significantly higher in patients with exclusively systemic recurrence compared with local or local/systemic recurrence, suggesting that it may represent the determinant factor of recurrence in earlier stages of PDAC progression. We reported a PNI scoring system which stratifies surgical-treated PDAC patients in a graded manner that correlates with patients' prognosis better than the current dichotomous (presence/absence) definition. Therefore, additional measures of PNI, beyond the binary presence or absence of this finding, could further refine staging systems for PDAC.

E-PS-07-038

Effect of pancreatic ductal ligation on the development of preneoplastic and neoplastic lesions in murine models

M.E. Patriarca*, S. Sabaté Fernández, F. Real, N. Del Pozo, A.M. Andaluz Martínez, E. Berjano, F. Burdío, M. Iglesias Coma
*Hospital del Mar-Parc de Salut Mar, Spain

Background & objectives: Adding p53 mutations in a KRAS mutated murine model of pancreatic cancer accelerate tumour development. The Wirsung's duct ligation (PDL) produces atrophy in KRAS-mutated animal and decrease in pre-neoplastic lesions. We want to analyse the addition of p53 mutation.
Methods: We studied 47 KRAS mutant mice, divided into three lines depending on p53 mutational state, all with PDL procedure: Homozygous (KO), Heterozygous (HET) and Wild Type (WT).
We analysed the pre- and post-PDL changes, assessing type (Acinar-to-Ductal Metaplasia (ADM), atrophy, PanIN, Atipical flat lession (AFL) and PDAC), number and grade of lesions. We perform immunohistochemistry for p53 and p16.
Results: We identified atrophy and ADM mostly in post-PDL of WT and HET mice (47.33% and 36.58%).
We detected more PanIN in pre-PDL (WT 30 vs 1, HET 46 vs 1 and KO 25 vs 6). We have not detected any PDAC in WT, two in HET (1 pre- and 1 post-PDL) and 26 pre- and 17 post-PDL in KO.
We detected more AFLs in HET in the pre-PDL area (2) and in KO cases (4 pre- and 2 post-PDL).
In HET and WT, we found nuclear p53 (50-70%) and cytoplasmic staining (10-20%) in atrophy and in PanIN, and nuclear p16 (20-60%) and cytoplasmic staining (80-90%) in preneoplastic lesions and PDAC.
Conclusion: We have demonstrated that the three murine models with KRAS mutation and WT, HET, and KO for p53 are valid for study preneoplastic and neoplastic lesions in the pancreas.
We have found that ligation decreases premalignant and malignant lesions in the HET and KO model for p53 mutant.
We conclude that preneoplastic lesions and well-differentiated carcinomas express p16 in nucleus and cytoplasm. p53 is overexpressed in post-ligation atrophy in nuclear form, with the cytoplasmic expression remaining to be studied.

E-PS-07-039

An immunohistochemical and molecular profiling of NAFLD associated HCC

R. Pirlog*, I. Rusu, P. Chiroi, A. Nutu, L. Budisan, V. Puia, C. Braicu, I. Berindan-Neagoe, N. Al Hajjar
*Institute Curie, Saint Cloud, France

Background & objectives: Non-alcoholic fatty liver disease (NAFLD) associated hepatocellular carcinoma (HCC) can occur in NAFLD patients even in the absence of cirrhosis. NAFLD-associated HCC has a less aggressive clinical course and can be missed on routine screening, being diagnosed in advanced stages.
Methods: We included in our study a cohort of 14 NAFLD-associated HCCs diagnosed in our service. We performed a morphologic assessment on hematoxylin-eosin and trichrome stainings. Immunohistochemistry assessment was performed for β-catenin (Abcam, 17C2 clone) and p53 Abcam, DO-7 clone). We identified and analysed a 3 miRNA panel to investigate the expression difference between adjacent normal tissue (ANT) and HCC tissue.
Results: All patients included in our cohort were male with a mean age of 68,7 years, the presence of type 2 diabetes and dyslipidemia. Morphological assessment revealed a grade 1 steatosis in 10/14 patients, a grade 0 level of hepatocyte balonisation in 8/14 patients, and the presence of discrete inflammation in 7/14 patients. β-catenin expression was positive in both ANT and HCC tissue, with higher intensity in ANT samples. P53 protein showed aberrant expression in 9/14 HCC samples and a negative, non-mutated expression in all 14 ANT samples. The 3 miRNA panel showed distinct expression between ANT and HCC samples with an upregulation of miR-21-5p, miR-34a-5p, and miR-130a-3p in HCC samples.
Conclusion: Our study provides important insights regarding the morphological, immunohistochemical, and molecular characteristics of NAFLD-associated HCC. We identified in ANT and NAFLD-associated HCC samples an aberrant expression of β -catenin and an aberrant expression of p53 only in HCC cases. The 3 selected miRNAs are involved in TP53 signalling and tumour progression. They showed a distinct expression profile between ANT and HCC tissue and could be investigated as possible biomarkers for progression toward HCC in high-risk NAFLD patients.

E-PS-07-040

PD-L1 expression in gastro-entero-pancreatic neuroendocrine neoplasms and its impact on possible new therapeutic opportunities

A.D. Plopeanu*, A. Yavas, L. Haeberle, I. Esposito
*Anapatmol Research Center, Victor Babes University of Medicine and Pharmacy, Romania

Background & objectives: Gastro-entero-pancreatic neuroendocrine neoplasms (GEP-NENs) are tumours with variable clinical outcome. Immunotherapy could represent a possible treatment approach, data regarding PD-L1 expression are conflicting. We analysed PD-L1 expression in a cohort of GEP-NENs and performed correlation analysis with several clinico-morphological factors.
Methods: 74 cases of GEP-NENs diagnosed between 2015 and 2022 were included. The database consisted of 29 pancreatic, 18 ileal,

14 appendiceal, 4 gastric, 4 duodenal, 1 ampullary and 4 colorectal tumours. Representative tissue sections were stained for PD-L1 (clone 22C3, DAKO) using the Ventana Benchmark platform. PD-L1 expression was determined using the combined positive score (CPS).
Results: Cases were classified according to their morphology and graded using Ki-67 expression as follows: 41 NET G1, 27 NET G2, 1 NET G3 and 3 NEC. Out of 74 cases, 57 had <1 CPS and were considered negative, and 2 cases originating from the appendix were not classified due to major inflammation caused by acute appendicitis. In positive cases, PD-L1 CPS mean value was significantly higher in NECs compared to NET G2 and NET G1 tumours ($p<0.0001$, 9.66 vs 2.33 and 1.33, respectively). The only NET G3 case included was negative. Correlation analysis revealed no associations between PD-L1 CPS and location, stage, lymph-node metastasis, lympho-vascular or perineural invasion.
Conclusion: This study shows that higher PD-L1 CPS values are found in NECs, possibly supporting immunotherapy as a promising future therapeutic strategy. PD-L1 expression in NET G3 cases should be investigated further in larger cohorts.
Funding: Vladimir Totovici Research Grant - Project number: T0476/41987/2022/kg

E-PS-07-041
Survivin expression as a potential prognostic marker in gastro-entero-pancreatic neuroendocrine neoplasms
A.D. Plopeanu*, A. Yavas, L. Haeberle, I. Esposito
*Anapatmol Research Center, Victor Babes University of Medicine and Pharmacy, Romania

Background & objectives: Gastro-entero-pancreatic neuroendocrine neoplasms (GEP-NENs) are malignancies with variable clinical behaviour and have few therapeutic options. We explored Survivin (BIRC5) expression, an apoptosis inhibitor protein, as a potential prognostic marker in a large collective of GEP-NENs.
Methods: 64 GEP-NENs diagnosed between 2015 and 2022 were included. The database consisted of 24 pancreatic (3 liver metastasis), 19 ileal, 6 appendiceal, 5 gastric, 2 duodenal and 7 colorectal cases. Representative tissue sections were stained for Survivin and both nuclear and cytoplasmic expression were evaluated using the IRS score.
Results: Cases were classified according to morphology and graded using Ki-67 expression as follows: 33 NET G1, 19 NET G2, 4 NET G3 and 8 NEC. Survivin expression was considered positive if IRS value was ≥ 2. NET G3 and NECs had higher cytoplasmic IRS compared to NET G1 and NET G2 ($p=0.0007$, 6.5 and 3.8 vs 2.45 and 3.57, respectively). NET G1 cases showed no nuclear positivity, only 2 NET G2 cases had nuclear positivity and were both diagnosed in early stages. 3 NET G3 and 5 NEC cases showed nuclear Survivin expression. Out of 5 resection cases with nuclear Survivin expression, 3 presented lymph-node metastasis and 4 presented distant metastasis.
Conclusion: Higher cytoplasmic and nuclear Suvivin expression was directly correlated with a higher tumour grade and a more aggressive clinical behaviour in NET G3 and in NECs compared to NET G1 and NET G2 tumours. These results support the usefulness of Survivin as a prognostic marker in GEP-NEN and need to be confirmed in larger collectives.
Funding: Vladimir Totovici Research Grant - Project number: T0476/41987/2022/kg

E-PS-07-042
Epstein Barr Virus-associated post-transplant smooth muscle tumours (EBV-PTSMT) of uncertain behaviour. A short series including hepatic and multicentric tumours with literature review
Y. Rodriguez*, A. Illarramendi, A. Luzmila-Vasquez, E. Revilla, F. Cambra, C. Barcena
*Hospital Univ 12 de Octubre, Spain

Background & objectives: EBV-associated PTSMT are very rare tumours related to immunosuppression. Less than 80 cases have been reported up to this moment, and more knowledge is needed. We describe the clinico-morphological features of 2 new cases of EBV-PTSMT and literature review.
Methods: We gathered two cases of female adults. First case, was a cystic fibrosis patient who received lung transplant (LT) and second case a membranous glomerulonephritis kidney transplant (KT) recipient. In both patients ultrasound study showed hepatic incidental masses that were confirmed with CT scan, the patient with LT presented previous colonic exophytic lesions. We performed morphological and immunohistochemical study.
Results: CASE 1: LT woman 48 years-old presented 3 years after transplant, 2 ulcerated lesions in right colon and 5 incidental liver nodules. There have not been other lesions after 3 months.
CASE 2: KT woman was 44-years-old woman, transplanted 10 years before. Presented an incidental liver mass 4,3 cm size. Surgical treatment was performed with no recurrence 4 years later.
Both liver lesions were compound of interlacing fascicles of moderately differentiated spindled cells, with mixoid areas and others with high cellular density. Mitotic rate was high in inmature areas of both tumours (6-9/ 10 hpf). EBV-positive (in situ hybridization). Colonic lesions were well differentiated EBV-SMT with low mitotic activity.
Conclusion: EBV-SMT is a poorly understood entity with uncertain biological behaviour. We hypothesize that persistently high EBV viral loads, could be a risk factor for post-transplant EBV-SMT as the multicentric case was IgM seropositive with peripheral blood positive viral load. Both cases had sarcomatous features with high cellular density and mitosis but they were not related to recurrence. Literature review shows a better prognosis than conventional leiomyosarcoma. It is important to test EBV in all mesenchymal tumours arising in immunocompromised patients.
Funding: We received a grant from FUNDATION MUTUA MADRILEÑA to study liver tumours

E-PS-07-043
Unusual localisation of plasmacytoma: pancreatic presentation
Z. Sağnak Yılmaz*, I. Saygin, S. Aydin Mungan, Z. Turkmen Usta
*Dokuz Eylül University, The Institute of Health Sciences, Department of Molecular Pathology, Karadeniz Technical University, Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Plasmacytoma is a solitary tumour which consist of atypical plasma cells. It can be primary as solitary mass without bone marrow involvement or may accompany multiple myeloma. Involvement of the pancreas was reported in only 2.3% of autopsies.
Methods: The surgical specimens were formalin-fixed and paraffin embedded. The section were stained with routinary H&E.
Results: A 79-year-old male patient who was followed up with a diagnosis of low-grade B-cell lymphoma, a mass in pancreas was detected on computed tomography scans. The mass was 70 x 66 mm in diameter in the neck of the pancreas and surrounds the splenic artery. In addition, solid nodules (metastases?) are seen at the level of the ribs. Microscopically, atypical plasma cells which have an eccentrically located nucleus were seen in the pancreatic parenchyma. CD38 and CD138 were positive in the immunohistochemical study. Immunoreactivity of Trypsin was weak. However, they were negative for panCK. Ki-67 proliferation index was 80%.
Conclusion: Extramedullary plasmacytomas are mostly found in the upper respiratory tract. Pancreatic involvement is rare. In case of patients with multiple myeloma and focal or diffuse enlargement of the pancreas, plasmacytoma should be kept in mind for the differential diagnosis. Unlike pancreatic adenocarcinomas, surgical procedures are not commonly performed due to the systemic nature of the disease and

its good response to local radiotherapy. Recognizing these lesions is important as it will save patients from unnecessary surgery.

E-PS-07-044

Should we process all gallbladder specimens? An analysis of potential clues to a diagnosis of incidental carcinoma

C. Scicluna*, L. McElroy, F. Roberts, V. Gough, G. Kohnen
*Department of Histopathology, Queen Elizabeth University Hospital, United Kingdom

Background & objectives: Gallbladder cancer is rare and often first diagnosed in the cholecystectomy specimen. The aim of this study to identify any criteria that are suggestive of carcinoma to reduce processing of these specimens, which average £42,000 per year at QEUH.
Methods: Gallbladder specimen report data at QEUH between May 2012 and September 2022 was split by outcomes (benign vs malignant), and correlated to specimen structural integrity, presence of gallstones and age at surgery. Cases with clinical suspicion of cancer or with suspicious findings at macroscopic examination were excluded. Cases with outcomes of only dysplasia were considered with the benign cases.
Results: Out of 16,788 eligible reports, 16,756 had benign outcomes and 32 had malignant outcomes. The median age for benign outcomes was 50 (range 15 – 93), whereas for malignant outcomes it was 71 (range 51 – 84). Out of a total of 10,165 benign intact specimens, 8,803 had gallstones. Out of a total of 6,581 benign fragmented specimens, 5,119 had gallstones.
Results from the malignant specimens revealed that 5 specimens were intact with gallstones, 3 specimens were intact without gallstones, 15 specimens were fragmented with gallstones and 5 specimens were fragmented without gallstones. 30 of the malignant cases were of adenocarcinoma with 2 were of adenosquamous carcinoma.
Conclusion: Fragmented specimens with gallstones were more likely to harbour incidental carcinoma, however, no single feature completely predicted or excluded the presence of cancer. The lower age limit for malignancy was 51, a consideration could be made for not processing specimens from patients under the age of 45 as the likelihood of diagnosing incidental carcinoma is extremely unlikely. Therefore, a more selective approach to specimen selection would reduce yearly processing by 37% and save up to £15,500 per year.

E-PS-07-045

Combined loss of numb and p53 promotes glycogen cumulative hepatomegaly and hepatocarcinogenesis

Y. Shu*, Y. Shi
*Department of Pathology & Institute of clinical Pathology, West China Hospital, Sichuan University, Chengdu, China

Background & objectives: Hepatocyte glycogen accumulation always leads to hepatomegaly, and it has recently been reported to drive liver tumour initiation. Our previous study suggested that Numb may play an important role in glycogen metabolism, which requires further exploration.
Methods: Glycogen accumulation index and glucose metabolism related pathways were measured in liver-specific Numb deletion mice(Numb−/−) by PAS staining and RNA-seq respectively. p53 can regulate cancer glycogen metabolism, and it has a complex reciprocal regulatory mechanism with Numb. Therefore, we constructed liver-specific Numb&p53 double deletion mice to investigate the effect of Numb&p53 on glycogen accumulation induced liver cancer.
Results: RNA-seq analysis demonstrated that differential genes are significantly enriched in glucose metabolism related pathways in Numb−/− liver. PAS and HE staining revealed slight glycogen accumulation and hepatocellular hypertrophy in Numb−/− liver at 12 months. In Numb&p53−/− liver, significant hepatomegaly developed at 7 months accompanied by severe hepatocyte glycogen accumulation and hepatocyte hypertrophy. Further, tumour nodules could be observed in part of the 9-month-old Numb&p53−/− liver. After 6 months of DEN induction, tumours with a significant number and large size developed in all Numb&p53−/− mice liver but not in WT mice, which predicted that Numb and p53 double deletion could induce glycogen accumulation hepatomegaly and promote the development of HCC.
Conclusion: In this study, we demonstrated the critical role of Numb-p53 on glycogen metabolism in the liver. We found that Numb-p53 deletion cause glycogen accumulation and induces hepatomegaly, and further promote hepatocarcinogenesis.

E-PS-07-046

Porto-sinusoidal vascular disorder in patients with Turner's syndrome

E. Stoupi*, I. Grypari, S. Siasiakou, E. Stravodimou, K. Syrigos, D. Tiniakos
*Department of Pathology, Aretaieion Hospital, Medical School, National and Kapodistrian University of Athens, Greece

Background & objectives: The novel term porto-sinusoidal vascular disorder (PSVD) describes vascular liver diseases affecting the (peri) portal venules and sinusoids in the absence of cirrhosis. PSVD is frequently associated with various underlying conditions. We present two cases of PSVD in Turner's syndrome.
Methods: Case 1: An 18-year-old female with Turner's syndrome phenotype (awaiting genetic confirmation), presented with elevated aminotransferase levels and an increased platelet count without other significant clinical findings.
Case 2: A 30-year-old female with mosaic-Turner's syndrome, presented with persistently elevated serum liver enzymes without other significant clinical findings.
An adequately-sized needle liver biopsy was performed in both cases.
Results: On histology, both cases had similar morphology. The liver parenchyma showed foci of regenerative hyperplasia (reticulin stain) and mild non-zonal sinusoidal dilatation. Abnormal periportal vessels, portal venule herniation and/or slit-like portal venules were noted in few portal tracts, while rare others were hypervascularised. Masson trichrome stain highlighted mild portal fibrosis and delicate sinusoidal fibrosis. The above histological findings were consistent with PSVD. The main features of PSVD include the absence of cirrhosis documented in a liver biopsy and the detection of specific or non-specific histological findings, including those described above, with or without portal hypertension. Mild zone 3 steatosis and mild portal inflammation were additionally observed in Case 2.
Conclusion: Turner's syndrome has been linked τo various liver abnormalities but only few cases with PSVD have been described. Liver biopsy is required for PSVD diagnosis. Microcirculatory disturbances in addition to immunological dysregulation, which both occur in patients with Turner's syndrome, may be the driving force in the pathogenesis of PSVD in these cases. We highlight the importance of the assessment of vascular changes in liver biopsies from patients with known or suspected Turner's syndrome and unexplained abnormal liver function tests.

E-PS-07-047

Primary mixed adenoneuroendocrine carcinoma (MANEC) of the gallbladder and synchronous renal cell carcinoma of the right kidney. A co-existence never described before

H. Trihia*, G.M. Stanc, E. Kontis, K. Stefanidis, E. Souka, M. Paraskevaides
*Pathology Department Metaxa Cancer Hospital, Greece

Background & objectives: Mixed adenoneuroendocrine carcinomas (MANEC) rarely arise in the gallbladder (GB-MANEC). The simultaneous diagnosis of renal cell carcinoma (RCC) with a gastrointestinal malignancy, is a rare, well documented phenomenon. The coexistence of GB-MANEC and RCC, has never been described before.
Methods: A 63-year-old woman was investigated for an MRI-detected 8cm liver mass and a coexistent 3,5cm tumour of the right kidney. She

had a history of a 4-month dull (vague) epigastric pain and one episode of acute right-upper-quadrant abdominal pain. The gallbladder was radiologically unremarkable. The patient underwent liver biopsy, liver segments IVB/V/VI excision, en block with gallbladder and right nephrectomy.
Results: Liver biopsy was diagnostic of large cell neuroendocrine carcinoma (LCNC). Renal biopsy showed a Fuhrman 2, clear cell RCC. Following removal of tumours, the liver tumour mass was 8,5X7X6cm in size, centrally necrotic and was in continuity with the gallbladder. Gallbladder was 6,5X2,8X2cm, had a hard consistency in the neck area, where a 2-cm intramural gallstone was found. The mucosa was unremarkable. After fixation, there was eccentric wall thickening of 5,5X1cm, in juxtaposition with the liver mass, in liver segment V. Histologic examination revealed infiltration of the gallbladder wall by LCNC cells, admixed with pleomorphic adenocarcinoma cells, with variable areas of dysplastic epithelium in association with reactive mucosal lymphoid follicles.
Conclusion: Neuroendocrine neoplasms of the liver are metastatic from other organs. GB-MANEC is an extremely rare neoplasm, occurring in middle-aged females, incidentally found at cholecystectomy specimens. The most common symptom is vague abdominal pain and is usually associated with cholelithiasis. There are no specific symptoms and image findings. In LCNECs of the liver, in patients with symptoms or signs resembling cholecystitis, the suspicion of GB-MANEC, extending to the liver, should be raised. Simultaneous occurrence of RCC has not been described before.

E-PS-07-048
Schwannomatosis in periampullary duodenum and peripancreatic tissue mimicking malignancy, challenging case report
B. Yeni Erdem*, N. Berker, G. Unverengil, K.R. Serin, M. Buyuk
*Kartal City Hospital, Department of Pathology, Turkey

Background & objectives: Schwannomatosis is a rare disorder characterized by multiple noncutaneous, nonvestibular schwannomas, which typically affect the peripheral or spinal nerves in the absence of neurofibromatosis. Visceral involvement is infrequent. Diagnosis can be made through clinical or combined molecular and clinical criteria.
Methods: Herein, we present a case of schwannomatosis with periampullary and peripancreatic localizations, clinically mimicking malignancy in a 38-year-old male patient who presented with right upper quadrant pain.
Results: Computer tomography displayed multiple masses between the duodenum and jejunum. Upper endoscopy revealed a mass in duodenum, and the biopsy revealed spindle cell proliferation which showed diffuse S100 expression consistent with schwannoma. A pylorus-sparing pancreaticoduodenectomy was performed. Macroscopic examination revealed three separate tumoral masses in periampullary region (3.5 cm), peripancreatic tissue (3.5 cm), and mesentery of duodenum (6 cm). Tumours were nodular-shaped and multilobulated. Microscopically, tumours consisted of spindle cells arranged in fascicles alternating between cellular and loose-myxoid areas. No necrosis, mitosis, or atypia was observed. The tumour cells showed strong immunoreactivity with S100 and NSE. Immunostains for CD117, DOG1, and CD34 were negative. We rendered the diagnosis as schwannomatosis.
Conclusion: Approximately one-third of cases have anatomically localized disease with tumours limited to one side or segment, as in our case. This is defined as segmental schwannomatosis. In our case, the nodules were separate but were in close proximity. No vestibular schwannoma was detected on radiologic imaging, and our case fulfilled the clinical criteria of schwannomatosis. Neither he nor his relatives had a proven genetic syndrome. Although the disease is usually sporadic, genetic tests should be preferred to detect familial cases.

E-PS-07-049
Adult pancreatoblastoma (PB): report of a rare and challenging case diagnosed on core needle biopsy (CNB)
S. Zanella*, S. Uccella
*Department of Biomedical Sciences, Humanitas University, Milan, Italy, Pathology Service, IRCCS Humanitas Research Hospital, Milan, Italy

Background & objectives: PB is a malignant neoplasm of the pancreas, representing 25% of paediatric pancreatic. Only about 40 cases of adult PB have been reported. We present an additional case diagnosed on CNB thanks to the employment of a selected immunohistochemical panel.
Methods: A 53-year-old man presented with deep abdominal pain and jaundice. A CT scan showed a 15 cm retroperitoneal mass of questionable pancreatic origin. A CNB was performed. Microscopically, a largely necrotic proliferation of epithelial cells with large eosinophilic cytoplasm and round nucleoli with finely dispersed chromatin. An immunohistochemical panel including cytokeratins, transcription factors, acinar and neuroendocrine markers, and cancerogenesis-related markers.
Results: Immunohistochemistry was positive for CK-pool, CK19 (focal), synaptophysin, Bcl10 (focal), trypsin (focal), AFP (focal). Negative markers were chromogranin A, Islet1, TTF1, PAX8, OCT4, p63, CDX2, arginase, HepPar, NKX2.2. p53 and Rb were normally expressed; a misplaced nuclear beta-catenin staining was found. These findings were consistent with a pancreatic neoplasm with acinar and neuroendocrine differentiation. Despite typical squamoid nests were not visible, the positivity for AFP and the altered expression of beta-catenin suggested the diagnosis of PB. The revision of CT images confirmed the pancreatic pertinence of the lesion and a duodenocephalopancreatectomy was performed. On the surgical specimen, the typical morphology of PB was present. Three hepatic metastases were also resected.
Conclusion: Adult PB is histologically characterized by proliferation of epithelial cells with acinar and neuroendocrine differentiation and presence of squamoid nests. AFP expression and alteration of the APC/beta-catenin pathway are frequently present. Diagnosis on small biopsy samples is difficult, the main differential diagnoses being acinar cell carcinoma and neuroendocrine neoplasms. Recognition of a suggestive morphology and application of immunohistochemical panel including neuroendocrine and acinar markers, AFP and beta-catenin are crucial in achieving the diagnosis, prompting a correct patient management.

E-PS-08 | E-Posters Digital and Computational Pathology

E-PS-08-001
Improving PD-L1 quality control using a dynamic range cell line and Qualitopix analysis
N. 't Hart*, L. Gal, M. Grønning Nielsen, H. Høeg
*Isala, The Netherlands

Background & objectives: Immunohistochemistry (IHC) with PD-L1 is in use to predict ICI response in NSCLC patients. Inter-observer, inter- and intra-laboratory variability is, however, a known issue. To improve consistent scoring of PD-L1, IHC quality control is essential before applying artificial intelligence (AI).
Methods: To define variability of PD-L1 (1:50 22C3 laboratory developed test (LDT)) a dynamic range cell line (HistoCyte, NewCastle, UK) is repeatedly stained. Staining results were quantified using intensity scores (Qualitopix, Visiopharm, Hørsholm, DK). To illustrate relevance of a dynamic range control, alterations to the staining protocol were introduced for a NSCLC-TMA. Mean, SD and coefficient of variance (CV) were calculated.
Results: Quantification of PD-L1 expression in the cell line (n=100) showed: negative 0.00% ± 0.00 (mean ± SD), weak 9.04% ± 7.69, intermediate 96.01% ± 4.95 and strong positive 99.30% ± 0.91 cores. The CV was high in weak (85.01%) and intermediate (5.16%) cores, while it was low in negative (0.00%) and strong positive (0.92%) cores.

Despite that cell line controls are within two SDs of the mean, the NSCLC-TMA (n=40) illustrated a significant ($p < 0.05$) decrease in positive cases at 1:80 (20/25), 1:100 (17/25) and 1:150 (12/25) compared to standard 22C3 LDT. Furthermore, analysis of the dynamic range cell line revealed early detection of a faulty immunostainer.
Conclusion: IHC quality control of PD-L1 using a dynamic range cell line combined with Qualitopix analysis showed variability in stain intensity and allowed early detection of technical issues. To reduce intra-laboratory variability and ensure reliable consistent immunohistochemical assays for PD-L1, a dynamic range cell line proved to be a better control compared to the conventional tonsil. In conclusion, a dynamic range cell line combined with Qualitopix showed an improvement in identifying optimal staining for cases near or at its analytical cut-off.

E-PS-08-002
Improving breast cancer diagnosis through weakly supervised learning: promising results in malignancy detection and subtyping
A. Alexander*, C. Mayer, N. Balint Lahat, I. Barshack, S. Ben Amitay
*Sheba Medical Center, Israel

Background & objectives: The application of AI in digital pathology for breast cancer diagnosis often requires manual and time-consuming annotation. To overcome this limitation, we propose a self-supervised learning and attention-based approach with case-level annotation to detect malignancy and enable subtype classification.
Methods: We extracted tiles from 1,120 benign and malignant breast lesion slides and used them to train a self-supervised learning feature extractor with MoCo. The extracted features were fed into an attention-based deep multiple instance learning (MIL) model to detect malignancy in a weakly supervised manner. High-attention tiles selected by the MIL model were used for training subtype classification with RESNET-18.
Results: Our malignancy detection model was trained and tested on 1186 and 297 breast slides, respectively, with a balanced malignant/benign ratio. Our method achieved balanced accuracy of 0.91, AUC of 0.96 and average precision of 0.98 for the training and a balanced accuracy of 0.91, AUC of 0.96 and average precision of 0.99 for the testing. High-attention maps of 30 malignant slides were confirmed to contain tumours by a pathologist. For subtype classification, we employed a dataset of 561 slides (468 invasive ductal carcinoma, 93 invasive lobular carcinoma). We trained the classifier using 5-fold cross-validation and achieved accuracy of 0.88 and AUC of 0.91. All slides were stained with H&E.
Conclusion: Our proposed approach has demonstrated promising performance in accurate malignancy detection and subtyping of breast cancer. The utilization of a case-level annotation approach helps to mitigate the annotation burden, facilitating scalability and applicability to larger datasets. The results of the subtype classification suggest that our framework can extract meaningful tiles that represent the tumour. We plan to expand our dataset size to enhance the robustness of our subtyping approach and extend our framework to predict biomarkers and hormonal status.

E-PS-08-003
European laboratories capabilities for digital pathology and computer assisted algorithms
N. Atkey*, P.D. Ramos Cirillo, O.D. McLeod, D. Vance, A. Capece, B. Bisaro, J. Tsiampali, R. Assemat, P. Garcia, Y. Pattni
*Diaceutics PLC, United Kingdom

Background & objectives: Digital pathology (DP) is a tool for laboratories to enhance accuracy and speed of diagnosis. Adoption of DP is subject to laboratory capabilities, awareness, and regulations. We reviewed the readiness of European laboratories for DP and computer assisted algorithms (CAA).
Methods: The Diaceutics DXRX Diagnostic Network® contains real-world data from clinical laboratories worldwide. Technology capabilities from 124 European (including European Union member states France, Germany, Italy, and Spain) and UK pathology labs performing solid tumour testing were analysed, from January 2019 – August 2021, focusing on utilization of DP, whole slide image scanners (WSI) and CAA.
Results: In all five markets, DP is utilized for clinical testing in academic (33%), hospital (20%), and commercial labs (4%), while 18% of all labs use DP for research purposes and 25% do not use DP. For clinical use, DP is utilized for breast and lung cancer indications by the majority of labs (67%), and 33% of labs use DP for all solid tumour testing. Across labs with WSI platforms, Leica, Philips and Hamamatsu are the preferred choices (32%, 30%, and 20% respectively). Only 6% of all labs surveyed for CAA use it for clinical testing, 51% for research, 19% under validation, and 24% are not using CAA.
Conclusion: DP and CAA are emerging solutions to aid pathologists on precision oncology testing. Over 50% of the labs use DP for clinical diagnosis, whilst the other half do not use it or use it for research purposes. CAA can enhance diagnostic accuracy of DP but it is not yet embraced in the wider clinical setting. The number of labs using DP with integrated CAA in clinical routine remains low, with most of labs using CAA only in a research setting.

E-PS-08-004
Implementation of artificial intelligence assisted lymph node metastases detection for breast cancer
M. Balkenhol*, G. Litjens, P. Bándi, K. Grünberg, J. van der Laak
*Radboudumc, The Netherlands

Background & objectives: Breast cancer diagnostics can be supported by artificial intelligence (AI) based detection of lymph node metastases. This project aims to integrate AI into routine pathology practice, to comply with the recent EU 'in vitro diagnostic regulation' (IVDR).
Methods: In-house developed AI for detection of metastases in whole slide images (WSI) of H&E sections of sentinel lymph nodes (SN) was integrated in the clinical image management system. According to IVDR, performance evaluation was executed, including methods on scientific validity, analytical and clinical performance. A quality management system with risk analysis was developed and key performance indicators (KPI) were defined.
Results: AI was integrated using two operating thresholds for metastases detection: first processing all slides with high specificity, anticipating that the majority of SNs are negative; and second, tuning the detections of the positive slides with higher sensitivity to ensure more accurate detections. Analytical performance was tested by cutting and staining tissue blocks on various moments and scanning them multiple times, after which WSI were processed and results on detections were compared. For clinical performance a real world set-up with a fully crossed, intermodal, multireader design was used. Results on performance studies and KPIs are currently evaluated.
Conclusion: AI in pathology is rapidly developing and regulation on how to implement in clinical practice is not yet established. The recently introduced IVDR provides a framework for implementation of lab developed tests but does not specify in detail the needs for implementation of AI in clinical practice. Our project describes procedures for implementing AI in routine pathology practice under IVDR, which may serve as a blueprint for labs wanting to use in-house developed AI while complying with IVDR.

E-PS-08-005
Application of artificial intelligence in establishing uveal melanoma prognosis
A. Bdioui*, F. Hamdaoui, A. Sghaier, O. Belkacem, N. Missaoui, S. Hmissa
*Sahloul hôpital of sousse, Tunisia

Background & objectives: The mean of ten largest nucleoli in uveal melanoma is an important prognosis factor, however calculating this parameter is challenging and imprecise with usual methods. We propose an artificial intelligence automated method to evaluate correctly and easily this prognosis factor.
Methods: We chose a batch of 1280 photos, we did a training of the data then de-normalization "image processing" to finish with a display of the batch.
then we had recourse to the discriminator of a generative adversarial networks which was simply a classifier. Li distinguish the real data from those created by the generator.
Results: For image processing, we applied the, cv2.COLOR_BGR-2RGB, we have eliminated the colours of the image to leave only the levels of grey. Then we set the limits of the image, we searched for the colours within the specified limits and applied the mask then we applied the Blur to blur the image. Then we made the outline of the nucleoli. We counted the number of closed contours, which is the number of total cells. this allowed us to be able to calculate the diameter of the nucleoli and to keep only the 10 largest cells and average the sum of their diameter.
Conclusion: Automated methods using artificial intelligence are an effective and time saving tool, that can be used in histopathology for correct and precise evaluation of prognosis factors.

E-PS-08-006
Smart system for determining histological differentiation of prostate cancer biopsy using artificial intelligence techniques: from unsupervised to supervised learning
S. Bhattacharjee*, Y. Hwang, N. Cho, D. Kim, H. Kim, H. Choi
*Inje University, Republic of Korea

Background & objectives: Analysis of histological differentiation of prostate cancer biopsy can be challenging but early detection can help with treatment planning by knowing the cancer stage. We aimed to develop a smart system for diagnosing prostate cancer using artificial intelligence techniques.
Methods: Whole slide image (WSI) datasets from Yonsei University Hospital (YUH), Korea, and Radboud University Medical Center (RUMC), Netherlands, were used in this study. We performed unsupervised to supervised learning using the modified K-means clustering algorithm and newly developed deep learning (DL) model, respectively, on the internal dataset (YUH). Furthermore, the trained DL model was tested on the external dataset (RUMC).
Results: The unannotated WSIs were used for unsupervised learning to generate the labelled patch images for supervised learning. To train the model efficiently, we used the pre-trained weight of self-supervised learning. However, the DL model showed almost perfect agreement for internal data (quadratic weighted Kappa 0.872; 95%CI 0.815-0.928) and external data (quadratic weighted Kappa 0.835; 95%CI 0.766-0.904) in predicting stroma, benign, and cancer tissue components. To analyse the generalizability of our model and evaluate qualitative outputs, we compared the results with the annotated samples from YUH and RUMC. The model showed promising performance though few mispredictions were observed, this can be justified due to the use of an unsupervised technique.
Conclusion: In this study, our approach provides annotation-free prostate cancer biopsy diagnosis distinguishing between stroma, benign, and cancer. Moreover, the AI-based smart system has been applied in multiclass classification for determining histological differentiation of prostate cancer biopsy. The combination of unsupervised, self-supervised, and supervised learning can be a promising approach that could mitigate the problem of label-free data classification. In the future, we will extend this research to multi-cancer datasets and explore our approach to overcome the challenges of unsupervised learning.

Funding: This research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MIST) (Grant No. 2021R1A2C2008576), and a grant from Korea Health Technology R&D Project through the Korea Health Industry Development Institute validation (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (Grant No: HI21C0977).

E-PS-08-007
Upregulation of TIM3 and reduced expression of PD-1 on immune cell subsets in advanced prostate cancers
N. Blessin*, N.F. Debatin, E. Bady, J.H. Müller, T. Mandelkow, R. Simon, M. Lennartz, C. Bernreuther, Z. Huang, G. Sauter, T.S. Clauditz, S. Minner, E. Burandt, M. Graefen, N. Gorbokon
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: Although most prostate cancers behave in an indolent manner, a small proportion is highly aggressive. Both primary and advanced prostate cancer is widely known as a non-inflamed cancer that is characterized by a paucity of immune infiltration.
Methods: To assess the spatial interplay of more than 30 TIM3, CTLA-4, PD-1/-L1 expressing leukocyte subpopulations in 453 prostate cancers, tissue microarrays were stained with 21 antibodies using our BLEACH&STAIN multiplex fluorescence immunohistochemistry approach and analysed using a deep learning-based image analysis framework.
Results: The immune cell density of CD8+ cytotoxic T-cells, CD4+ T-helper cells, FOXP3+ regulatory T-cells, M1/ M2 macrophages, as well as CD11c+ dendritic cells increased consistently along with the Gleason grade in primary prostate cancer ($p \leq 0.034$ each). In recurrent prostate cancers under therapy, the density of FOXP3+ regulatory T-cells and M1 macrophages further increased, while the density of CD8+ cytotoxic T-cells, CD4+ T-helper cells, as well as CD11c+ dendritic cells decreased ($p \leq 0.017$ each). Although the immune checkpoint expression of TIM3 on T-cell subsets, macrophages and dendritic cells was upregulated in advanced/ recurrent tumours, the expression level of PD-1 was downregulated in all analysed T-cell subsets.
Conclusion: Although prostate cancer is a generally considered a low inflamed tumour, the degree of tumour infiltration by various immune cell subtypes increases markedly along with tumour progression and in recurrent tumours under therapy. Taken together, these data suggest that the evaluation of the spatial distribution of immune cell types along with their immune checkpoint expression can provide relevant clinical information in prostate cancer.

E-PS-08-008
HPyloriDet: a clinically deployable tool for computer-aided helicobacter pylori detection in immunohistochemically stained slides
N. Brandt*, A. Bornand, D.G. Puppa, M. Kreutzfeldt, D. Merkler, A. Janowczyk
*Department of Pathology, Division of Clinical Pathology Geneva University and University Hospitals, Switzerland

Background & objectives: *Helicobacter Pylori (HP)* is a common stomach bacteria linked to conditions including stomach cancer. Although immunohistochemical (IHC) staining of HP facilitates diagnosis, reviewing whole slide images (WSI) remains time-consuming. We investigated our computer-aided screening tool, HPyloriDet, for improving diagnostic speed/sensitivity.
Methods: HPyloriDet was developed using pathologist-annotated HP IHC WSIs (n=20). Regions of interest were identified via IHC stain deconvolution, driving the extraction of 300x300 pixel patches split into 80/20 train/test split. A DenseNet was trained to detect the presence of HP on these patches, and its performance metrics evaluated.

Clinical benefit was estimated via comparison of standard and HPyloriDet-aided diagnostic times.
Results: On extracted patches, HPyloriDet achieved an accuracy of 95%, alongside 92% sensitivity and 95% specificity. The positive predictive value was 65% while the negative predictive value reached 99%. For slides confirmed as positive, HPyloriDet reduced *Helicobacter pylori* diagnosis time by up to 80% (3 minutes) without producing false negatives. For negative slides, HPyloriDet showed a 25% (1 minute) improvement. The benefit for negative slides was more modest as they still required careful pathologist review to avoid false negative diagnoses, whereas for positive slides, correct detection alone appears sufficient. HPyloriDet is thus estimated to provide a yearly time savings of 100 hours based on a typical yearly workload of 5000 slides.
Conclusion: Standard HP detection on large IHC slides is time-consuming and our computer-aided tool HPyloriDet demonstrates preliminary evidence that this burden can be ameliorated. Preliminary findings indicate potential time-saving benefits in clinical settings, without loss of diagnostic accuracy. Future work will involve validating the time-efficiency when integrating HPyloriDet into the clinical workflow, monitoring its performance, and collecting additional data during deployment for retraining to further improve HPyloriDet's accuracy.

E-PS-08-009
Immunohistochemical evidence of mTOR C1 and C2 pathway in diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) - a digital pathology analysis
L. Comerford*, M. O'Callaghan, M. Alquier, J. McCormack, E. Lynn, O. O'Carroll, D. Murphy, R. Crowley, D. O'Toole, C. McCarthy, A. Fabre
*Histopathology department, St. Vincent's University Hospital, Dublin, Ireland

Background & objectives: Background: DIPNECH may represent a precursor to neuroendocrine tumours and is confined to the bronchial epithelium. DIPNECH is a rare disease affecting essentially women and can present with nodules on HRCT, some in association with carcinoid tumours.
Methods: Rare reports of altered signalling via the mammalian target of rapamycin (mTOR) pathway are described in neuroendocrine cell diseases.
Objective: To quantify tissue expression of specific mTOR pathway downstream proteins RPS6 and 4EBP1 on DIPNECH and control lung tissue sections using immunohistochemistry and evaluation by digital pathology.
Tissue analysed from 15 patients with a pathological diagnosis of DIPNECH, aged 26-80. Five symptomatic (cough, dyspnoea); two MEN syndrome, 4 previous breast cancer, 11 carcinoids, 2 multiple tumorlets. 7 control lung tissue without DIPNECH from lobectomies sampled away from lesions included.
Slides stained with Chromogranin, RPS6 and 4EBP1, ER and PR antibodies using Dako Autostainer48 and uploaded using Leica AperioAT2 scanner. ImageScope Pathology Slide Viewer was used to facilitate annotation of bronchioles. Image analysis of annotated areas was used to calculate (1) number of chromogranin positive cells per millimetre squared of bronchiole, (2) % chromogranin cells per bronchiole, (3) % 4EBP-1 cells per bronchiole and (4) % RPS6 cells per bronchiole, ER and PR expression.
Results: 4EBP1 is ubiquitously expressed in resident pulmonary epithelial cells and expression was observed in all cases with neuroendocrine cell hyperplasia and tumorlets. RPS6 expression varies within resident cells and is expressed in the majority of neuroendocrine cells but not as diffusely as 4EBP1. ER and PR were negative in all neuroendocrine cells.
Conclusion: Our results provide supporting evidence for the role of mTOR signalling in DIPNECH, with mTORC and C2 pathway protein expression in DIPNECH and might support the role of mTOR inhibitors in treatment of symptomatic patients.

E-PS-08-010
Validation of a quantitative image analysis algorithm for Ki67 index in breast cancer and neuroendocrine tumour
M. Cossutta*, J. Bellocq, C. Egele, A. Papine, E. B. Tatarinova, K. Socha, M. Soussaline, C. Homsy, F. Soussaline
*IMSTAR Dx, France

Background & objectives: Ki67 index evaluation in Breast Carcinoma (BC) and Neuroendocrine Tumour (NET) depends on the quality of immunohistochemistry (IHC), its interpretation by the pathologist and the spatial intratumoral heterogeneity. Our objective was to design an adapted Quantative Image Analysis (QIA) algorithm.
Methods: The evaluation used 121 slides providing from 2 external proficiency testing schemes (2021, n=55 slides; 2022, n=66 slides) conducted by the french interlaboratory comparison organization (AFAQAP), and comprising 2 different BCs and 2 different NETs. All indexes were assessed by 2 independent methods: visually by 2 expert pathologists, and by QIA using the IMSTAR PathoScan TumourMarker Ki67 algorithm.
Results: Pathologists identified 4 classes of Ki67 index for each BC and NET depending on IHC technical quality (optimal, good, borderline, insufficient): 46 Ki67 IHC slides received the "optimal technique" appreciation by the experts for each BC and NET (2021, n= 20; 2022, n= 26), with Ki67 indexes of 12-15% (2021) and 5-10% (2022) for BCs, 3-5% (2021) and 4-5% (2022) for NETs. Ki67-QIA algorithm performed an accurate evaluation of Ki67 index with a concordance ($\pm$1% outside the index classes) with the experts of 89% for BCs and 96% for NETs. This 89% for BCs results from the mixing of an heterogeneous and an homogeneous tumour (80% and 95% concordance, respectively).
Conclusion: The QIA solution was efficient to evaluate Ki67 index on technically optimal IHC slides despite multiple laboratories IHC techniques being applied, highlighting the need for quality in IHC to obtain robust digital evaluations. The objective quantification of intra-tumoral heterogeneity opens an additional challenge. Ki67-QIA algorithm allows to evaluate Ki67 index on a large number of cancer cells and to visualize and quantify Ki67 index spatial variations in tumours, enabling to identify tumour zones under or over the clinical utility thresholds.

E-PS-08-011
A complete clinically applicable lung cancer diagnostic platform based on histopathological artificial intelligence
J. Da*, N. Che, D. Zhao, Y. Zhao, S. Wang
*Dept. of Pathology, China

Background & objectives: Lung cancer is a leading cause of cancer-related deaths worldwide. We aim to establish an artificial intelligence (AI)-powered platform for lung cancer detection and subtype classification, which is crucial for precise treatment of lung cancer.
Methods: We collected 1,115 lung slides and digitized them into whole-slide images (WSIs) and randomly divided the WSIs into training, validation, and test sets. Additional WSIs for non-mucinous adenocarcinoma subtype classification were also collected. Using DeepLab v3 image segmentation model, we established pixel-level lung cancer detection and subtype classification models. Data augmentation techniques were applied for model robustness.
Results: The deep learning model achieved clinical-grade performance in lung cancer detection and main subtype classification. Based on the cancer detection model (AUC: 0.970, sensitivity: 94.1%, specificity: 94.6%), the main subtype classification model for squamous cell carcinoma, adenocarcinoma, and small cell carcinoma reached a sensitivity/specificity of: (test set) 88.6%/81.8%, 89.7%/83.1%, and 83.3%/94.3%; (surgical specimens) 87.6%/79.7%, 89.5%/80.9%, and 82.4%/75.0%; (biopsy specimens) 92.9%/85.8%, 91.7%/86.2%, and

100%/100%, respectively. The adenocarcinoma subtype classification model achieved a normalized discounted cumulative gain score of 81.8% (Top k+1). By comparing with the pathological reports, we found the model could accurately identify the cancerous areas and give pathological subtypes.
Conclusion: We have established a complete AI-powered platform for lung cancer histopathological diagnosis and subtyping based on deep learning. The platform holds great promise for cost-effective and efficient clinical applications. The clinical application of the AI-assisted platform will help pathologists relieve workloads, avoiding missed diagnoses, and producing consistent reports. AI-assisted pathology diagnosis is expected to be widely adopted in hospitals in the near future.

E-PS-08-012
Investigation of the applicability of mass spectrometry in pathological differential diagnosis
B.A. Deák*, F. Csiza, G. Horkovics-Kováts, B. Gyöngyösi
*Department of Pathology, Forensic and Insurance Medicine Semmelweis University, Hungary

Background & objectives: Metabolomics become one of the fastest growing research areas in recent years. Our aim was to investigate whether samples obtained through routine pathological processing are suitable for mass spectrometry measurements, and whether there are significant differences between different tissue types.
Methods: First we examined 10 µm thick sections of pork liver in every step during the routine pathological processing. After that we analysed ccRCC and non-tumour renal parenchyma, obtained from the Department archive. Mass spectrometry analyses were performed with REIMS mobilization technique in negative ion mode, in the 50-1200 m/z range.
Results: During processing of pork liver samples, fresh frozen sections showed a rich and highly peaked lipid profile, which was not significantly influenced by formalin fixation. During routine pathological processing, we observed signal changes, decreases, and losses in the detected lipid spectrum at every further step of dehydration. Nevertheless, measurable signal was still obtained from FFPE samples, and the remaining peaks provided assessable signals. Principal component analysis could differentiate tumour and non-tumour renal tissue in human FFPE clear cell renal cell carcinoma samples.
Conclusion: Mass spectrometry is a novel method for investigating the lipid profile of human samples. The gold standard of the method is measurement of fresh frozen samples, but formalin fixation alone does not cause significant signal reduction. Based on our preliminary results, spectra obtained through routine pathological processing may also be useful for distinguishing renal cancer and normal renal tissue.

E-PS-08-014
The development and evaluation of a novel H&E stain quantification method
C. Dunn*, D. Brettle, D. Treanor
*National Pathology Imaging Co-operative, Leeds Teaching Hospitals NHS Trust, United Kingdom; University of Leeds, United Kingdom

Background & objectives: Tissue sections are stained using histochemical stains for histopathological analysis. The staining process can introduce colour variability, yet current methods of quality control are subjective. We propose an objective method of H&E stain assessment to improve quality control in pathology.
Methods: A stain quantification method is proposed, using stain assessment slides that objectively quantify haematoxylin and eosin (H&E) stains. To validate the use of stain assessment slides, they were characterised with a range of H&E staining durations and were implemented within eight clinical laboratories across a period of two weeks to analyse variation.
Results: The stain assessment slides H&E stain response was linear with respect to increasing stain duration ($r = 0.99$). Clinical implementation of stain assessment slides quantified intra-laboratory stain variation (average = 11%) and inter-laboratory stain variation (average = 26%). The impact of stain variation on automated nuclear counts was measured with and without colour normalisation.
Conclusion: Stain assessment slides offer a quantitative method for measuring H&E staining in pathology laboratories. The results show strong linearity to H&E stain duration and the clinical utility in objectively quantifying stain variation in laboratories. This is important to improve quality control and standardisation of slides in laboratories, but also crucial for supporting the quality of digital pathology images and the growth of artificial intelligence in digital pathology.
Funding: This research is part of the National Pathology Imaging Co-operative, NPIC (project no. 104687) supported by a £50m investment from the Data to Early Diagnosis and Precision Medicine challenge, managed and delivered by UK Research and Innovation (UKRI). FFEI Ltd and Futamura Chemical UK Ltd are partners on the NPIC program, and are providing in-kind contributions to the research activities in NPIC.

E-PS-08-015
Construction of an extensive human skin dataset for artificial intelligence development
J. Frias Rose*, A. Bodén, J. Van Der Laak
*Department of Clinical Pathology, and Department of Biomedical and Clinical Sciences, Linköping University, Sweden

Background & objectives: The Bigpicture consortium consists of members from both private and public organizations. Bigpicture's main goal is to create the first European General Data Protection Regulation (GDPR) compliant platform, where quality-controlled whole slide images (WSI) and advanced AI algorithms will co-exist.
Methods: In order to help achieve the goal of 3M WSI with their associated metadata, we chose to participate as contributors to Bigpicture, since the department of clinical pathology in Region Östergötland has a digital image archive of >2 Petabytes. We developed a protocol for dataset extraction, that complies with all applicable regulations, ensuring high quality content.
Results: We were tasked with gathering WSI from skin samples. A human skin dataset was designed, mirroring daily-basis clinical cases and their WSI as our contribution to the Big picture repository. After ethical approval for using patient data for research, we selected skin cases from patients 18 years and older, from 2019-2022 including cases with only one diagnosis amongst melanoma, other melanocytic lesions, squamous cell carcinoma, basal cell carcinoma, dermatofibroma, seborrheic keratosis, actinic keratosis and scar tissue. Metadata was partly preserved (patient age, anatomical site, acquisition time, laboratory related data and diagnosis/observations). All data anonymization, conversion and extraction was automated. A dataset of 45,000 WSI with their associated metadata was compiled.
Conclusion: We succeeded in the compilation of an extensive clinically relevant dataset for Bigpicture's repository, which will be useful for research purposes and development of relevant AI-solutions. The increasing adoption of digital pathology is an enabler for the development of AI-based tools that support histopathological diagnostics. The main limiting factor when developing and implementing AI-tools is availability of data, which can be attributed to challenges with data quality, storage and regulations for patient data protection, and Bigpicture helps overcome said challenges.
Funding: IMI Funding and EFPIA in kind

E-PS-08-016
Automated quantification of stromal tumour infiltrating lymphocytes is associated with prognosis in breast cancer
M. Gonzalez Farre*, J. Gibert, P. Santiago, J. Santos, M.P. Garcia, J. Masso, B. Bellosillo Paricio, J. Albanell, B. Lloveras Rubio, I. Vázquez de las Heras, L. Comerma Blesa

*Hospital del Mar, Spain

Background & objectives: Stromal tumour infiltrating lymphocytes (sTIL) are linked to better outcomes in triple-negative and HER2-positive breast cancer (TNBC and HER2+). Specific data on the prognostic impact of plasma cells or lymphocytes within sTIL, and different cell types is still under study.
Methods: We validated a deep learning sTIL scoring model (smsTIL) based on the segmentation of various cell types in whole slide images (WSI). Focusing on HER2+ and TNBC, we assessed the concordance between sTIL visual scoring and smsTIL in 130 WSI. Furthermore, we analysed 175 WSI to correlate smsTIL and different cell types with clinical data and patient outcomes.
Results: The segmentation model classified 596510 cells. We found a high correlation between sTIL and smsTIL (R=0.76,P<2.2e-16), and a statistically significant association between smsTIL and overall survival (OS) in TNBC and HER2+ (P=0.0021, P=0.041). In TNBC, this association was also observed for lymphocytes and plasma cells separately (P=0.00069, P=0.0048). Low tumour cells and necrosis, and high 'other' cells resulted in reduced OS (P=0.039, P=0.029, P=0.04). Univariate analysis showed that smsTIL value (P=0.016), age (P=0.017), TNM status (T2: P=0.052; T3: P=0.02; T4: P=0.00024), nodal status (P=0.0023) and metastases (P=0.00019) were associated with OS. Multivariate analyses showed that smsTIL value (P=0.009), nodal status (P=0.025) and metastasis (P=0.015) were independently associated with OS.
Conclusion: We developed a deep learning algorithm to assess sTIL and confirmed that the values quantified by the pathologist and the algorithm are highly correlated, providing evidence that smsTIL can be implemented in daily routine. We demonstrated the prognostic value of smsTIL in HER2+ and TNBC, being an independent predictor of OS in TNBC. Moreover, lymphocytes and plasma cells individual quantification play an individual prognostic role in TNBC, as well as tumour cells, necrosis and 'other' cells included in the stroma.

E-PS-08-017
Unravelling the immune involvement of sentinel lymph nodes in melanoma metastasis by hyper-multiplexed imaging
T. Haran*, I. Milo, S. Deis, E. Pikarsky, L. Keren
*Department of Pathology and Department of Immunology and Cancer Research, Institute for Medical Research Israel-Canada, Hadassah Medical School - Hebrew University, Jerusalem, Israel

Background & objectives: We sought to refine our understanding of tumour-draining lymph node biology and architecture to identify characteristics predictive of future disease progression and unravel tumour-immune interactions in early phases of melanoma dissemination.
Methods: Multiplexed Ion Beam Imaging-Time of Flight (MIBI-TOF) is a novel technology that utilizes metal-labelled antibodies coupled to mass spectrometry, allowing simultaneous localization of up to 40 proteins at subcellular resolution in situ. We used this technology to examine sentinel lymph nodes from a cohort of 80 melanoma patients and identify factors other than microscopic tumour foci associated with distant metastasis.
Results: A 40-plex antibody panel was assembled to enable concurrent labelling and identification of melanoma cells and various immune cell subtypes and states. We first compared metastasis negative nodes from patients with subsequent disease progression (n = 20) with those with sustained remission (n = 28). Intriguingly, lymph nodes from patients with subsequent progression showed a distinct pro-inflammatory phenotype, characterized by the presence of active secondary lymphoid follicles, an increased proportion of Ki67-positive lymphocytes, and decreased numbers of anti-inflammatory M2-polarized CD163-positive macrophages. Conversely, evidence of T-cell exhaustion was seen in lymph nodes bearing overt metastatic disease (n = 32), with clustering of PD-1-positive CD8-positive T-cells at the periphery of tumour foci.
Conclusion: Tumour-negative sentinel lymph nodes from melanoma patients with subsequent disease progression can be distinguished from those from patients with prolonged remission. In patients who go on to develop distant metastasis, an apparently vigorous immune reaction is seen even when no tumour cells can be detected in the node. That this immune response is later overwhelmed suggests an overactive reaction followed by immune exhaustion. Identification and targeting of these patients for early immunotherapy may prevent this exhaustion and thereby disease progression.

E-PS-08-018
A novel pathological image evaluation method for prostatectomy specimens using the homology profile method
M. Ishigaki*, Y. Nomura, K. Nakane, M. Nishio, M. Watanabe, K. Uchida
*Mie University Graduate School of Medicine, Department of Medical Science, Department of Tumour Pathology, Japan

Background & objectives: The homology profile method (HPM) is a mathematical concept that analyses the connections between components. Its usefulness in detecting various cancers on pathology images has been reported.
We investigated the usefulness of HPM in cancer detection using prostatectomy specimens.
Methods: HE-stained specimens of prostatectomy performed at Mie University Hospital were scanned using Leica APERIO CS2 and then converted from svs format to jpg format. Images of 3000x3000pixel including cancerous and non-cancerous areas were arbitrarily extracted and divided into 100 images of 300x300pixel.
The diagnostic ability of cancer was examined based on the Betti number calculated from HPM for these images.
Results: The Betti number in one dimension was defined as b1, and the maximum value was defined as b1max. The Mann-Whitney U test was performed for b1max in cancerous and non-cancerous areas, and there was a significant difference between the two groups. ($p<0.05$)
The AUC from the ROC curve was 0.873 for the highest value and 0.402 for the lowest value.
The b1max contained noise in certain regions that did not depend on pathological morphology, and these were removed. After removal, the b1max was similarly significantly different between the two groups. ($p<0.05$)
The AUC was 0.944 even for the lowest value, with a specificity of 0.980 and a sensitivity of 0.800.
Conclusion: HPM was able to detect prostate cancer using currently used criteria. Unlike AI, the Betti number calculated by HPM is invariant and does not need to be relearned even if the diagnostic criteria are changed in the future. The HP method is also easy to use as a standalone system, thus avoiding the possibility of medical information leakage through the network. In the future, HPM may be used together with AI as a simple, low-risk diagnostic aid.

E-PS-08-019
Volumetric scanning achieved by collecting multiple images in Z plane for WSI image acquisition enables more accurate tumour microenvironment analysis in breast cancer cases
J. Jain*, P. Perugupalli, R. Gupta, D. Anand, V. Singh, H. Mulcahndani
*PRAMANA INC, India

Background & objectives: Tumour microenvironment plays an important role in cancer progression and treatment response prediction in breast cancer. Here we present a study of 30 breast cancer cases where tumour microenvironment analysis was done in WSI with and without capturing Z stacks.
Methods: Volumetric scanning of 30 Breast cancer cases was done using Pramana HT scanner with Z stacks (collecting multiple images in

Z plane) and without Z stacks. A deep learning based nuclei detection and classification model was built, followed by training of class-aware nearest neighbour graph to evaluate the distance, direction and proximity between different nuclei for both WSIs of cases.
Results: In several of the cases, the WSIs with Z stacks yielded more accurate distance measurement and directional vector analysis as it enables real 3-D modelling of nuclei across Z stacks. The Delta for distance measurement on best focus image vs z stack image ranges to an extent of 2.5 microns. Z stacking also increases the overall nuclei counts across layers in the range of 3-4 %, thus further improving the accurate tumour microenvironment analysis.
Conclusion: Capturing Z stacks for WSI generation enables more accurate tumour microenvironment analysis, as it allows 3D directional vector and modelling for more accurate distance analysis among different nuclei types, in addition it also increases the overall nuclei counts distributed across Z -layers. Further studies are warranted to evaluate how the distance and direction of nuclei affects the treatment response for breast and other solid tumours.

E-PS-08-020
A deep learning based tool for histological detection of malignancy In prostate core needle biopsies
R. Jialdasani*, S. Saraf, A. Khandelwal, P. Chatterjee, V. Bharani, R. Kumar, D. Kaur, B. Gogoi, B. Singh, M.A. Osama, F. Bhatt, A. Narwal, W.P.K. Teng, S. Karakaya, K.V. Santosh
*Qritive AI India Private Limited, India

Background & objectives: Diagnosing prostate adenocarcinoma on histopathology is complex and highly subjective. We have developed a deep learning-based assistive AI tool to aid practising pathologists to identify and classify malignancies using a segmentation-based output. Diagnosing prostate adenocarcinoma on histopathology is complex and highly subjective. We have developed a deep learning-based assistive AI tool to aid practising pathologists to identify and classify malignancies using a segmentation-based output.
Methods: Ten pathologists, from 8 institutions were given 150 whole slide images (WSIs) of prostate core needle biopsies obtained from multiple institutes. Review was done in two phases – without (Phase1) and with AI assist (Phase2) marking benign and malignant areas. Ground truth (GT) was established by 2 senior pathologists. A semantic segmentation algorithm producing a pixel-based segmentation was used.
Results: The WSIs were hosted over a cloud server and reported digitally. The AI agreed with GT in 148 / 150 cases, with 2 false positives. The agreement (=>8 doctors) with GT for benign cases was 34/41 and 41/41 in Phase 1 and 2, while for malignant cases, it was 105/109 and 107/109 respectively. The mean concordance for benign cases after AI assist increased by 17.07% (34 to 41) and 1.9% (105 to 107) for malignant cases. The concordance score of one of the pathologists for identifying benign cases improved by 32% using AI assist and achieved a perfect accuracy of 100%.
Conclusion: Our study demonstrates our AI based prostate cancer detection module showed a sensitivity of 100% for malignancy detection and a specificity of 95.12% in whole slide images of prostate core needle biopsies. Such AI based assistive tools have a potential to improve the concordance in independently practising pathologists while reporting complex cases like prostate needle biopsies, thus improving health equity. We intend to further refine the model to include ISUP grading and perform clinical validations with larger datasets.

E-PS-08-021
Stratipath Breast: deep learning-based risk stratification of intermediate risk breast cancers
S. Kang Lövgren*, P. Weitz, J. Ho, K. Ledesma Eriksson, B. Su, Y. Wang, S. Robertson, J. Hartman, M. Rantalainen
*Stratipath, Sweden

Background & objectives: In current clinical routine >50% of breast cancers are assigned an intermediate risk (NHG 2), with limited clinical value in treatment decisions. Stratipath Breast is the first CE-IVD marked solution for AI-based histopathology risk stratification into low- and high-risk groups.
Methods: We evaluated the prognostic performance of the predicted risk classes for 901 NHG 2 primary breast cancer patients, 204 originating from the TCGA BRCA study and 697 from a Swedish study. Prognostic performance was assessed by computing hazards ratios for recurrence with Cox proportional hazards models.
Results: In the present study the point estimate for the marginal hazards ratio between predicted low- and high-risk groups was found to be 2.2. Adjusting for clinical covariates yielded a hazards ratio of 2.1 across all patients.
Conclusion: Stratipath Breast enables risk-stratification of intermediate risk breast tumours into low- and high-risk groups, while significantly reducing costs and turn-around times compared to molecular diagnostics. Its integration into routine clinical workflows therefore has the potential to benefit both patients and healthcare providers and to expand access to precision diagnostics.

E-PS-08-022
Convolutional artificial neural network-based recognition of pancreatic adenocarcinoma by Stimulated Raman Scattering scanning microscopy in unstained tissue sections
É. Kocsmár*, K. Ócsai, Z. Mucsi, B. Barkóczi, K. Borka, A. Pesti, E. Kontsek, A. Kiss, B. Rózsa, G. Lotz
*Semmelweis University, Department of Pathology, Forensic and Insurance Medicine, Hungary

Background & objectives: Stimulated Raman Scattering (SRS) scanning microscopy allows the label-free spectral fingerprinting of lipids, proteins and water in cells and tissues, thus enabling morphological examination and analysis of chemical composition of unstained histological specimens, moreover recognition of malignancy based on this.
Methods: SRS imaging was performed on unstained sections of 49 pancreatic ductal adenocarcinomas at 2895 cm-1 and 2950 cm-1 wavelength channels. After hematoxylin-eosin staining, the cancer cell percentage and normal tissue components of the imaging site was determined. 2133 SRS images were used to train a residual convolutional artificial neural network (ResNet-101), whose cancer detection ability was tested in 2106 images.
Results: The detection rate for individual non-tumorous tissue categories (including pancreatic exocrine and endocrine tissue, nervous tissue, lymphatic tissue, adipose tissue, connective tissue, smooth muscle, inflammatory infiltrate, chronic pancreatitis and mixed non-tumorous elements) ranged from 57.7% to 100%, with the overall detection rate of non-tumorous tissue reaching 87.8%. For images with more than 30% adenocarcinoma, the cancer detection rate was 97.0%, for tumour contents between 15% and 30% it was 80.4%-91.9%, and for tumour percentages below this level it was 53.6-56.4%. Overall, the cancer detection sensitivity was 92.1%, specificity 87.8%, positive and negative predictive value 91.6% and 88.4%, respectively, using convolutional artificial neural network.
Conclusion: On deparaffinized unstained sections of formalin-fixed paraffin-embedded tissue blocks, SRS imaging combined with convolutional artificial neural network detection was able to identify the presence of adenocarcinoma with excellent results even when trained on a relatively small dataset. As the intra- and inter-institutional variability of unstained sections is much lower than that of conventional hematoxylin-eosin stained sections, their use for imaging with advanced microscopy techniques is promising.

Funding: K_22 142604 grant of the National Research, Development and Innovation Office (Hungary)

E-PS-08-024

Semantic segmentation of ductal carcinoma in situ in breast cancer histopathology whole slide images with deep learning

K. Ledesma Eriksson*, J. Ho, S. Kang Lövgren, B. Su, Y. Wang, P. Weitz, S. Robertson, J. Hartman, M. Rantalainen
*Stratipath, Sweden

Background & objectives: Detection of invasive cancer(IC) in breast cancer whole slide images (WSI) is a pre-requisite in many computational pathology methods. Due to the high interclass similarity between IC-cells and ductal carcinoma in situ(DCIS), explicit distinction between IC and DCIS regions is needed.
Methods: This study investigates deep learning methods to detect DCIS in haematoxylin and eosin stained WSIs of cancer resection specimens from 346 female primary breast cancer patients diagnosed in Sweden. Regions of DCIS and invasive cancer were annotated by a clinical pathologist. DeepLabV3+ models were trained and evaluated using 5-fold cross validation at magnifications 0.625X, 1.25X, 2.5X, 5X, 10X.
Results: At the best performing magnification of 5X, the AUC of the validation folds were 0.972, with a median slide-level sensitivity of 0.71 at a median specificity of 0.99 and a median slide-level accuracy of 0.91.
Conclusion: The study shows the possibility to detect and segment DCIS in H&E stained WSIs with reasonably high accuracy using models that operate at a single magnification level. However, due to the high interclass similarity of DCIS and invasive cancer cells, multi-resolution models considering the spatial distribution of the data has the potential to improve DCIS segmentation.

E-PS-08-025

HistoBlur: a general deep learning tool for flexible and accurate blur detection on whole slide digital pathology images

P. Liakopoulos*, L. Padayachy, M. Kreutzfeldt, S. Köfler, M. Tihy, R. Nair, M.A. Cuendet, O. Michielin, R. Langer, D. Merkler, A. Janowczyk
*Precision Oncology Center, Department of Oncology, Lausanne University Hospital, Switzerland

Background & objectives: Blur artifacts may be introduced to whole slide images (WSI) by scanners during the digitization of glass slides. Here, an open-source deep learning tool is presented that allows for rapid, precise, annotation-free detection of blurry regions in WSI.
Methods: One non-blurry skin H&E WSI at 10x was used to train a DenseNet model. Low/medium/high levels of Gaussian smoothing were applied to patches, yielding a supervised training task for blurriness identification. Medium/high blur was defined as levels at which tissue characteristics were indiscernible. For validation, n=111 slides of various tissue types (70 non-blurry, 41 blurry) had their percent blurriness computed.
Results: Despite being trained on a single H&E image, HistoBlur consistently returned higher blurriness percentages for blurry WSIs regardless of tissue type. For blurry WSIs, the median blur value was 54,95% (min=8.807%, max=100%). For non blurry WSIs, the median blur value was 0,9% (min=0%, max=15.25%). With a cutoff point of 8% blurriness, sensitivity for the detection of blurry slides was 100% and the specificity was 98,5%. The estimated computational throughput was 26mm2/s, which translates to ~30s for a typical biopsy. Preliminary results further show that due to its deep-learning backend, HistoBlur is likely to be stain/tissue agnostic, requiring only a single non-blurry representative slide of the target tissue/stain combination for training.
Conclusion: Histoblur is an open-source tool for easily training and employing a Deep Learning model for detection of blurry regions on WSI via a simple Command Line Interface. These preliminary results suggest Histoblur enables rapid identification of poor-quality slides in clinical workflows autonomously, reducing technician overhead and improving diagnostic efficiency, for any stain/scanner/organ combination. From a research perspective, the automatic detection and exclusion of blurry regions can mitigate adverse effects in building image-based biomarkers. HistoBlur is freely available (histoblur.com).

E-PS-08-026

Halo Breast AI, a deep learning workflow for clinical scoring of HER2, ER, PR & Ki67 immunohistochemistry (IHC) in breast cancer tissue

M. Lodge*, A. Graham, A. Ironside, A. Polonia, S. Reinhard, W. Solass, I. Zlobec, P. Caie
*Indica Labs, United Kingdom

Background & objectives: The assessment of ER, PR, HER2, and Ki67, although associated with observer variability, is the cornerstone of treatment stratification for invasive breast cancer. Automated biomarker quantification through HALO Breast AI aims to increase the speed and standardization of their quantification.
Methods: The algorithm was trained using 107,328 pathologist-reviewed annotations to identify and threshold DAB-positive tumour cells within automatically segmented tumour regions. Technical performance was evaluated on 60,012 pathologist-reviewed annotations from unseen cases. Clinical performance was assessed by comparing the algorithm scores across whole slide images to either a pathologist consensus score (n=80) or the clinical report (n=200) respectively from two institutes.
Results: The median image F1-score for tumour classification was 0.91, while the median image F1-score for cell-level validation was 0.96. The internal validation showed agreement between HALO Breast AI and three expert pathologists across the biomarkers: 95% for ER, 85% for PR, 85% for Ki67 and 80% for HER2. Performance on WSI obtained from an independent, external institute showed agreement between the scores obtained from HALO Breast AI and the clinical report: 96% for ER, 94% for PR, 84% for Ki67 and 84% for HER2 (91% 0/1+, 60% 2+ and 100% for 3+ scores).
Conclusion: Combined immunohistochemical assessment of HER2 status, ER, PR, and Ki67 forms part of the routine clinical prognostic and predictive pathway for invasive breast carcinomas. Pathologist scoring of IHC at the microscope is time-consuming and prone to observer variability. HALO Breast AI detects tumour regions and tumour cells within breast cancer tissue with high accuracy and clinical agreement when scoring routine diagnostic IHC. This product can support pathologists by improving workflow efficiency and standardizing results.

E-PS-08-027

Robust and generalisable classification systems for haematologic malignancies in peripheral blood and bone marrow

C. Matek*, R.M. Umer, C. Marr
*Institute of Pathology, University Hospital Erlangen, Institute of AI for Health, Helmholtz Munich, Germany

Background & objectives: Morphologic evaluation of leukocytes and their distribution in peripheral blood and bone marrow remain key steps in the diagnostic workup of haematologic malignancies. AI-based decision support algorithms have to be tested for robustness and generalizability prior to wider routine application.
Methods: We tailored state-of-the art deep-learning methods for classification support systems for both single and multiple leukocytes in patients with acute myeloid leukaemia (AML) and non-malignant controls. For single-cell classifiers, we assessed domain adaptation and domain generalization training strategies that use multi-domain data to develop more robust classification algorithms.
Results: Both single- and multi-cell classifiers attain high performance in answering clinically relevant diagnostic questions such as identifying

the presence of blast cells, or recognising morpholgic patterns of AML in peripheral blood. When trained on monocentric datasets, generalization of algorithms to data from other settings can be challenging. Availability of training data from multiple sites is key to overcoming this hurdle using adapted training strategies.
Conclusion: Deep learning-based diagnostic support algorithms for morphologic classification of haematologic samples have progressed in both diagnostic accuracy and computational efficiency in recent years. However, these systems must be evaluated for generalizability when used outside their training data domain. Key requirements for developing generalizable algorithms are availability of diverse, multi-site morphologic data at train time and using training strategies optized towards generalizability and robustness. By comparing several different methods, we show how this aim can be achieved for hematologic classification tasks.

E-PS-08-028
LymphoSight: an artificial intelligence QuPath companion application for the automated detection of tertiary lymphoid structures
K. McCombe*, S. Craig, R. Gault, J. James
*Queen's University Belfast, United Kingdom

Background & objectives: Tertiary Lymphoid Structures (TLS) are ectopic immune phenomena that occur in chronic inflammatory situations including cancer. Research suggests there are prognostic and predictive of treatment. Here we develop of a deep-learning driven, "point-and-click" application for the automated detection of TLS.
Methods: 1805 patient images across five cancer types were digitised, imported into QuPath and annotated for TLS. Images of TLS were extracted and split into training, test and independent validation sets at a 70-15-15 ratio at a patient level for model training.
The model was evaluated on the independent validation set at whole slide level based on intersection-over-union and Spearman's correlation.
Results: 310 of the 1805 patients assessed possessed a mature TLS. Of these, 47 were set aside as the validation set and were matched with TLS-negative counterparts by cancer type.
A strong correlation between predicted and expected TLS was achieved (Spearman's r=0.853, p<0.0001). In the TLS-positive patients, an average intersection-over-union (IOU) score of 0.716 was achieved, indicating good model segmentation ability.
Most false positives occurred due to gut-associated lymphoid tissue being detected as TLS in colorectal patients. Once these were manually accounted for, IOU increased to 0.762 and Spearman's correlation increased (Spearman's r=0.943, p<0.0001).
A "point-and-click" application was developed in Python to apply the model to images in QuPath projects.
Conclusion: While studies have shown that the presence of TLS can be beneficial in multiple cancer types, the task of quantifying TLS in patient samples is often time-consuming, and potentially subjective. We take advantage of developments in digital pathology and artificial intelligence to develop a model to automate this process. In addition, we have developed a point-and-click application, LymphoSight, to apply the model directly to QuPath projects in a code-free manner, which may make such a model more clinically applicable.

E-PS-08-029
Digital pathology shortens crucial steps of pathologist's decision making
Y. Molchanov*, A. Kobo-Greenhut, I. Barshack
*Institute of pathology, Sheba medical centre, Israel

Background & objectives: Digital pathology (DP) allows measurements of TAT at different stages. We tested the TAT in the pathologist's work until decisions are made,
One process of pathology can reduce TAT. Is the time between receiving H&E slide to ordering immunohistochemical staining.
Methods: Random lung biopsies were taken from a rapid diagnosis unit. H&E slide delivery to immunohistochemical stain ordering time was competed between 2018 and 2021 (before and after DP implementation).
Results: The time from when the H&E staining was delivered until immunohistochemistry staining was ordered was shorter in May-July 2021 (M=0.98 days, SD=0.89) than in May-July 2018 (M=2.49 days, SD=2.04). This improvement was statistically significant, with $t(54) = 3.59$, $p < 0.001$ (one-tail).
Conclusion: The laps time between slide delivery to release is important. After implementing DP and changes made to the work process, this time has shortened by more than 1.5 days.The time from H&E slide delivery to ordering of immunohistochemical staining been reduced by more than two times (from an average of about 2.5 days to an average of 0.98 days).

E-PS-08-030
Future-proofing histological techniques in the Glasgow Tissue Research Facility
H. Morgan*, J. Hay, J. Edwards
*University of Glasgow, United Kingdom

Background & objectives: Glasgow Tissue Research Facility (GTRF) bridges the gap between NHS Greater Glasgow and Clyde Biorepository, University and industry for tissue-based research, providing first-class automated tissue micro array (TMA) construction, digital pathology, image analysis and histology services.
Methods: Creating a pathology-pipeline to meet increasing demands for high-quality research, the GTRF combines established histological protocols with brightfield and immunofluorescent slide scanning digital pathology techniques, and pioneering AI-based image analysis using Visiopharm®. TMAs enable analysis of multi-patient samples from highly characterised cohorts within single paraffin blocks, allowing standardisation of techniques including immunohistochemistry, RNAScope and efficient analysis of expensive 'omics techniques.
Results: Collaborations have generated TMAs examining tumour and stroma-rich regions of colorectal cancer (CRC) linked with clinical and genomic data from patents within the TransSCOT trial, and from polyps of patients within the INCISE project - designed to develop a comprehensive risk stratification tool for CRC. Automation of TMA construction allows for precise block coring which may be used in DNA/RNA extraction or placed in specialised maps, for research ranging from COVID-19 studies to targeting specific tissue regions of pancreatic cancer which are subsequently used for downstream technologies such as GeoMx® and Visium®, thus allowing for highly specialised digital spatial profiling of gene and protein expression.
Conclusion: Under the governance of the NHS Greater Glasgow and Clyde Biorepository, the GTRF works with researchers to enable access archived diagnostic tissue for a broad spectrum of research areas, providing maximal preservation and use of limited and irreplaceable archival tissue samples. While the combined technologies and expertise within the GTRF and the collaborations we are involved in enables researchers to future-proof their research through adaption of ever-evolving techniques and technologies.
Funding: Cancer Research UK (Scotland Centre)

E-PS-08-031
Investigating tissue-source site-specific batch effects in H&E images for machine learning applications
P. Murchan*, P. Ó Broin, A. Baird, A. Keogh, M. Barr, O. Sheils, S. Finn
*The SFI Centre for Research Training in Genomics Data Science, Ireland

Background & objectives: ML models risk learning confounding site-specific features in histology datasets. Our aim was to assess the performance of a ML model at predicting tissue-source site (TSS) from

H&E WSIs. Furthermore, we assessed methods to help mitigate overfitting to batch effects.
Methods: WSIs from TCGA-LUAD originating from 22 separate TSSs were included in the study. Separate XGBoost models were trained to predict TSS using two sets of image features, one extracted using an Imagenet-pretrained ResNet50, and one using a ResNet50 pretrained on histology data. The effect of Boruta feature selection and ComBat batch correction for mitigating batch effects was evaluated.
Results: Image features extracted using the SSL-histology-pretrained Resnet50 (AUROC=0.902±0.005) performed better (p=0.0017) at predicting TSS than using image features extracted using ImageNet-pretrained Resnet50 (AUROC=0.857±0.029). Boruta feature selection and ComBat correction on SSL-histology image features had no impact on the performance of the model at predicting TSS (p=0.133 and p=0.255, respectively). Applied to the image features extracted with the ImageNet-pretrained ResNet50, Boruta feature selection had no impact on the performance of the model at predicting TSS (AUROC=0.839±0.026; p=0.195). However, a decrease in performance (p=6.68e-8) was observed when training the model with ComBat-corrected features extracted using an ImageNet-pretrained Resnet50 (AUROC= 0.536±0.024).
Conclusion: Image features extracted using SSL-histology-pretrained Resnet50 may contain more site-specific information than image features extracted using an ImageNet-pretrained Resnet50. Future work should assess the impact of batch correction methods on the predictability of biomarkers directly from H&E WSIs. Outputs of model interpretability methods, such as class-activation maps and attention heatmaps, reviewed by pathologists should remain as gold-standard for ensuring that machine learning models in digital pathology do not exploit confounding batch effects in H&E WSIs.
Funding: This presentation has emanated from research conducted with the financial support of Science Foundation Ireland under Grant number [18/CRT/6214]

E-PS-08-032
PD-L1 IHC 22C3 pharmDx: scoring concordance on melanoma specimens
J. Musser*, E. Olander, S. Tabuena-Frolli, E. Manna, K. Kersch, J. Christian, S. Hund
*Agilent Technologies, USA

Background & objectives: PD-L1 IHC 22C3 pharmDx is a qualitative assay used to detect PD-L1 expression in formalin-fixed, paraffin-embedded (FFPE) tissues. This study aims to establish equivalency in PD-L1 scoring on melanoma specimens between glass slides and whole slide images (WSIs).
Methods: Thirty melanoma specimens were immunostained with PD-L1 IHC 22C3 pharmDx (Code SK006) and scored using a light microscope. Digital images using Aperio Scanner were scored using ImageScope software.
Three observers scored blinded and randomized slides/images. Concordance of PD-L1 expression was analysed. A two-sided 95% confidence interval (CIs) for overall agreement (OA) was calculated using a percentile bootstrap method.
Results: Samples analysed represented the dynamic range of PD-L1 expression and included 10 (33.3%) near cutoff specimens. The data was analysed for PD-L1 binary expression status (positive/negative) based on a MEL Score cutoff of 2 (≥1%). A total of 90 comparisons were made to the reference condition (glass slides). To meet the acceptance criteria (AC), the lower bound of the two-sided 95% percentile bootstrap CI computed on OA must meet or exceed 80%. The point estimate for OA was 91.1%. The 95% CI lower-bound for OA was 86.7%, meeting the AC.
Conclusion: Digital scoring for PD-L1 expression in WSIs has been of great interest, especially in recent years. Binary PD-L1 expression status (positive/negative) concordance in melanoma specimens was achieved between glass slide and WSI scoring. These results support equivalency of PD-L1 scoring with MEL Score on both glass slides and WSIs.

E-PS-08-033
Placental angiogenesis in foetal death
E. Nardi*, E. Olivo, F. Ugolini, F. Castiglione
*Section of Anatomic Pathology, Department of Health Sciences, University of Florence, Italy

Background & objectives: Placental dysfunction is one of the causes of intrauterine foetal demise (IUFD). The role of placental angiogenesis factors hasn't been fully investigated. The aim of this study was to analyse the vascular burden through automated digital analysis in IUFD placentas.
Methods: We morphologically evaluated 37 formalin-fixed and paraffin-embedded placental tissue samples from IUFD pregnancies (of which 32 were c-kit mutated) and 16 of healthy pregnancies. Representative sections were immunohistochemically stained with anti-CD31 (clone JC70, Ventana medical system). Positive vessels area was assessed by HALO digital image software. Data were expressed as positive stained area. Statistical analysis was made with Mann-Whitney test.
Results: IUFD placentas revealed the presence of hypoxic-ischemic state characterized by predominance of dysmorphic and hypo-vascular mature intermediate villi and thrombosis of staminal vessels while such features were not observed in healthy placenta specimens. These pathological changes were particularly highlighted in IUFD placentas characterized by c-KIT gene mutation.
Digital analysis of immunohistochemical CD31 stained sections showed decreased positive stained area in IUFD placentas compared to healthy tissues ($p = 0.0002$).
Conclusion: The present study showed that IUFD placentas showed morphological and phenotypical evidence of altered and decreased angiogenesis which may conduct to an altered placental structure and vascular development possibly leading to foetal death.

E-PS-08-034
A fully automatic tumour infiltrating lymphocytes assessment tool
R. Peyret*, A. Moreau, S. Sockeel, M. Petit, S. Touioui, B. Jean Jacques, E. Lanteri, M. Sockeel, J. Adam
*Primaa, France

Background & objectives: Tumour infiltrating lymphocytes (TILs) quantification has proven a reliable prognosis factor in breast cancer. Despite efforts to standardize TILs scoring, it is subject to inter-reader variability. In this context, we propose a fully automatic tool for TILs grading on WSI.
Methods: The proposed processing pipeline includes three separate steps. The first one consists of a Deep Learning cancer localisation model. Then follows a combined segmentation of stroma and lymphocytes on cancer regions. This is performed using a convolutional backbone with two segmentation heads, that is trained through a custom multi-phase process. The final TILs score is computed from the resulting segmentations.
Results: The proposed pipeline showed state-of-the-art performance TIGER dataset with a DICE of 84.9 ± 1.0 for stroma segmentation and 84.4 ± 0.4 for TILs nuclei segmentation. To prove reliability and generalizability, the algorithm was tested on publicly available TIGER dataset and on an in-house dataset of both biopsies and surgical samples. We investigated the correlation between the final TILs scores and the pathologists scores on both datasets.
Conclusion: The resulting algorithm can be integrated into a WSI analysis pipeline and, with such performance, provide pathologists with an automatic TILs assessment tool.

E-PS-08-035
Reproducibility of serrated lesions and polyps on digital pathology, an interobserver study
C. Ravaioli*, F. Ambrosi, C. Ricci, M.E. Maracci, A.G. Corradini, D. Malvi, F. Vasuri, M.L. Tardio, R. Gafà, A. Cadioli, F. Chiarucci, A. Zangrandi, M. Camponara, D.D. Di Nanni, M. Fiorentino

*School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: Digital pathology has the potential to transform the practice of diagnostic pathology but is still an emerging field. This study evaluates interobserver agreement in the digital evaluation of serrated lesions/polyps on a computerized tool in a group of 21 pathologists.
Methods: A set of 50 routinely digitized serrated lesions/polyp lesions were reviewed by 21 pathologists belonging to 12 Italian Pathology Departments. For each case, an hematoxylin &eosin slide was evaluated according to the morphologic criteria of the WHO classification of Digestive System Tumour, and all responses were recorded. The results were statistically analysed using the Fleiss'K to assess concordance of diagnoses.
Results: The cohort included 50 patients: 23 males and 27 females, with a mean age of 68 years (range 50-89). First, the agreement in the diagnosis of serrated lesions and polyps resulted fair (0.45 Fleiss' k) among all participants. Interestingly, the agreement increased to moderate among all pathologists from the Bologna area (0.61 Fleiss' k). In particular, the kappa value resulted moderate (0.58 Fleiss' k) and substantial (0.53 Fleiss' k) in the two Bologna pathology institutes, respectively. In contrast, the agreement among the remaining 12 pathologists from other pathology departments was fair (0.42 Fleiss' k).
Conclusion: Agreement and reliability in diagnoses of serrated polyps/lesions on digital pathology were found to be higher among pathologists belonging to the same institution. The present results demonstrate the importance of working with shared criteria to be more reproducible in the diagnosis of controversial lesions.

E-PS-08-037
End-to-end pipeline for automatic grading of IHC biomarkers
C. Simmat*, N. Nerrienet, R. Peyret, M. Petit, S. Touioui, A. Chiaverini, M. Sockeel, B. Jean Jacques, S. Sockeel, E. Lanteri
*Primaa, France

Background & objectives: Immuno-histochemistry (IHC) is a staining process that highlights prognostic and predictive biomarkers. This process is tedious and time consuming. It has also proven to hold high inter-observer variability. Artificial intelligence (AI)-based systems could assist pathologists in clinical diagnosis.
Methods: Existing tools are only semi-automatic and require pathologists to select invasive carcinoma (IC) regions on IHC slides manually or by registration. We leverage a CycleGAN-based data augmentation strategy to train a model that identifies cancerous regions on IHC slides.
In those regions, we apply our automated scoring method for IHC biomarkers including Ki-67 and ER/PR based on AI methods.
Results: We show that our method consistently and precisely locates IC regions in IHC WSIs directly by comparison with pathologists ground truth annotations on a set of WSIs.
We also demonstrate the robustness of our automatic IHC grading tool with accuracy and efficiency metrics at slide-level on a multi-centric dataset.
Conclusion: In this work, we introduce an end-to-end automatic pipeline capable of * identifying IC regions directly on IHC WSIs with no need of human intervention or registration step and * performing the grading process quickly and accurately. Therefore, our method has the potential to streamline pathology laboratories workflow significantly.

E-PS-08-038
Spatial correlation between tumour microenvironment and in vivo perfusion CT parameters
H. Smits*, E. Bennink, L. Ruiter, G. Breimer, S.M. Willems, J.W. Dankbaar, M. Philippens
*University Medical Center Utrecht, The Netherlands

Background & objectives: In this study, we investigated the spatial correlation between immunohistochemistry (IHC) biomarkers Ki-67 (proliferation), HIF-1α (hypoxia), and CD45 (immune cells), and in vivo dynamic contrast enhanced (DCE-)CT parameters to test the feasibility of characterizing the tumour microenvironment with DCE-CT.
Methods: 56 whole mount tumour slides of 15 laryngeal and hypopharyngeal carcinomas were immunohistochemically stained and digitized. Heatmaps of biomarker positivity were created, registered to the in vivo maps of Ktrans (transfer constant), Ve (extravascular and extracellular space), and Vi (intravascular space), and downsampled to 3x3x3mm3. Pearson's correlation coefficient r between IHC biomarkers and DCE-CT parameters was determined for each tumour.
Results: After a Bonferroni correction for multiple testing, a significant negative correlation was found between Ki-67 and Ve (mean r=-0.15, range -0.02 to -0.32, t-test P<.001). This indicates that DCE-CT gives relevant information about the microenvironment, as it is to be expected that cell proliferation and extracellular space are negatively correlated.
Additionally, we found a significant correlation between Ki-67 and HIF-1α (mean r=0.27, range 0.06 to 0.54, P<.001). This might be attributed to continuing cell proliferation that creates temporary or mild reduction of oxygen supply within a tumour, causing upregulation of HIF-1α. No significant correlations were found between any perfusion parameters and CD45 or HIF-1α.
Conclusion: This unique study shows the technical feasibility of calculating the spatial correlation between pathological biomarker heatmaps and in vivo imaging. In vivo contrast distribution gives relevant information about tumour microenvironment characteristics.
Funding: The material used in this paper was collected in a study funded by the Dutch Cancer Society (KWF) Research Fund, project number 2011-5152. Additional funding for analysis was provided by the same society, project number 2017-10978.

E-PS-08-039
Imaging analysis of nuclear features of high-grade nonmuscle invasive urothelial carcinoma - diagnosis, staging and relapse
V. Sousa*, R. Rodrigues, M.R. Silva, M. Viseu, C. Eliseu, T. Ferreira, A.F. Ladeirinha, A. Alarcão, A.L. Alves, G. Fontinha, R. Almeida
*IAP-PM - Universidade de Coimbra, CHUC, Portugal

Background & objectives: Bladder cancer remains the sixth most prevalent cancer in man. Whole-Slide-Imaging(WSI) and image analysis techniques have demonstrated great utility in Pathology. Associations between nuclear morphometric features and histopathological type and recurrence rate were investigated on high-grade non-muscle-invasive urothelial bladder carcinoma(NMIBC).
Methods: We selected 55 patients diagnosed with NMIBC at Centro Hospitalar Universitário de Coimbra between 2014 and 2017. From each patient, a representative HE slide of the neoplasm was selected for scanning and application of an image analysis algorithm to analyse the parameters: mean nuclear size, nuclear density, mean nuclear red-green-blue (RGB) intensity and mean positive intensity.
Results: No statistically significant association was found between the morphometric parameters, mean nuclear dimension, nuclear density, mean nuclear RGB intensity, and mean positive intensity, with diagnosis, recurrence, or staging. However there seems to be an association with clinical significance, namely of the parameters mean positive intensity and mean nuclear size. In these parameters there seem to be differences between the non-invasive or intraepithelial stages (pTis and pTa), compared to cases with suburothelial connective tissue invasion (pT1). Mean nuclear size is higher and mean positive intensity is lower in invasive T1 cases.

Conclusion: Although there was no statistically significant association in the parameters analysed, an association was observed between staging and the parameters, nuclear density and positive intensity average. Nuclear size and less chromatic nuclei might be related to invasiveness.
This work sought to contribute to the knowledge and development of applications of new technologies of image analysis and artificial intelligence in Medicine, and specifically in PA and NMIBC.

E-PS-08-040
ChatGPT in pathology applications: harnessing AI language models for diagnostic decision support
S. Spasic*, D. Gonzalez
*Department of Pathology, Beo-lab, Medicover, Belgrade, Serbia

Background & objectives: ChatGPT, a popular large-scale language model, has shown potential in healthcare applications. We aim to explore its utility as an AI-assisted decision support tool in surgical pathology.
Methods: We adapted ChatGPT-4 to provide diagnostic suggestions based on histopathologic descriptions. Experiments involved listing diagnostic entities (e.g. follicular neoplasms), differentiating entities (e.g. basal cell carcinoma vs. trichoepithelioma), and generating differential diagnoses for specific histologic descriptions (e.g. follicular neoplasms with desmoplastic stroma).
Results: ChatGPT demonstrated promise in generating accurate diagnostic suggestions, though with limitations. It listed many but not all entities within a category, failed to mention CK20 for distinguishing basal cell carcinoma from trichoepithelioma, and did not provide all relevant diagnostic suggestions for the given histologic descriptions. Despite these limitations, ChatGPT offered valuable insights, indicating potential for enhancing diagnostic accuracy and efficiency in pathology.
Conclusion: ChatGPT shows promise as an AI-assisted decision support tool in pathology applications, but its limitations warrant caution. These include generating false concepts (hallucination effect), outdated training data, and inability to challenge existing biases. ChatGPT holds potential to enhance diagnostic outcomes and streamline workflow in pathology. Future research should focus on refining the model, addressing limitations, and integrating ChatGPT into clinical practice.

E-PS-08-041
Digital and mobile H&E imaging of bulk tissue in the operating room
M. Strauch*, J.P. Kolb, C. Rose, N. Merg, J. Hundt, C. Kümpers, S. Perner, S. Karpf, R. Huber
*Medical Laser Center Lübeck, Germany

Background & objectives: During surgery, frozen sections ensure the quality of the process. However, frozen section analysis can take up to 60 minutes depending on the availability of a pathologist, sample preparation time and transport delays. Meanwhile the surgery is interrupted.
Methods: We develop a mobile multiphoton microscope prototype for the operating room (OR) that uses advanced laser technology to capture H&E images without the need to freeze or section the bulk tissue sample. The tissue surface is quickly stained with H&E before being placed in the microscope. It is automatically scanned and the result is displayed in the OR or remotely.
Results: We designed the microscope to meet the operating room's requirements. We developed an H&E staining protocol that allows sample preparation and measurement in less than 15 minutes. We first investigated porcine samples and have now moved on to leftover tissue from plastic surgery to prove the concept.
Measuring tissue samples directly in the OR saves transport time and therefore reduces the waiting time for the surgeon. Once the measurement is finished, the result can be displayed on the device's monitor and on the pathologist's PC. This improves the interaction between the surgeon and pathologist; both can view the same images zoom in and out and discuss the findings together.
Conclusion: We demonstrated a microscopy technique, that is capable of obtaining digital H&E images from bulk H&E-stained tissue without the need for freezing, sectioning, or glass slide preparation. We have developed a protocol for the workflow and improved our setup to a mobile platform to allow it to be shared between different operating rooms. The images can be examined remotely by the pathologist, eliminating transport time and thus speeding up the surgery.
Funding: The project Multiphoton microscopy for section-free H&E histology is funded by the Federal Ministry for Economic Affairs and Climate Action and the European Social Fund as part of the EXIST program.

E-PS-08-042
Developing an integrative model using histopathological images and clinico-genomic data for predicting the prognosis of patients with papillary renal cell carcinoma
M.J. Tan*, S. Kee, M.A. Sy, S. Border, N. Lucarelli, A. Gupta, M. Masalunga, F.I. Ting, P. Sarder
*University of Florida, USA

Background & objectives: Overlapping histopathologic features in renal epithelial tumours require improving the criteria for evaluating papillary renal cell carcinoma (pRCC). We propose an integrative model (IM) that combines morphologic and clinico-genomic features to obtain better prognostication for pRCC.
Methods: Matched histopathological images, genomic, and clinical data (race, AJCC tumour stage, and sex) from The Cancer Genome Atlas were used. Image feature extraction was done using CellProfiler. Prognostic image features were selected using least absolute shrinkage and selection operator, and support vector machine algorithms. Weighted gene co-expression network analysis was used to determine eigengene modules.
Results: Risk groups based on prognostic features were significantly distinct ($p < 0.05$) according to Kaplan-Meier analysis and log-rank test results. Two image features and nine modules were used in Random Survival Forest models, measuring 11-, 16-, and 20-month areas under the curve (AUC) of a time-dependent receiver operating curve. The IM (AUCs: 0.86, 0.85, 0.87) outperformed models trained on eigengenes alone (0.75, 0.733, 0.785), morphological features alone (0.593, 0.523, 0.603), and clinical features alone (0.743, 0.757, 0.743). It also significantly outperformed the IM without clinical data (0.877, 0.769, and 0.811) in 16- and 20-month predictions.
Conclusion: Image granularity and Zernike shape features, along with nine eigengene modules and three clinical features, were identified as prognostic image and clinico-genomic features for patients with pRCC. Results suggest that an integrative model combining histopathological images and clinico-genomic features could improve survival prediction, especially in longer timeframes. Enrichment analysis also revealed associations with the NRF2 pathway and metabolic processes, corroborating the metabolic nature of pRCC. Therefore, the IM model shows potential applicability in clinical decision-making, particularly in personalized treatment regimens.

E-PS-08-046

Automatic detection and counting of pathological specimens with a rejection option

A. Vieira*, D. Montezuma, T. Albuquerque, L. Ribeiro, F. Rebolo, D. Oliveira, J. Monteiro, S. Gonçalves, I.M. Pinto, J. Cardoso, A. Oliveira
*Instituto Superior Técnico, INESC-ID, Portugal

Background & objectives: Pathology specimen counting aims to verify that the number of fragments on the slides remains unchanged after grossing. Since this is a manual, time-consuming procedure, our purpose was to develop an automated system to replace this manual step.
Methods: We applied a state-of-the-art object detection model to detect fragments and sets, YOLOv5, trained and evaluated on 2554 and 700 WSIs, respectively, from a labelled dataset of different pathology samples. Subsequently, we implemented several rules to improve counting performance, and added a rejection option when confidence was low.
Results: The rule to reject the automatic counting is based on dividing the number of fragments by the number of sets. If this number is not an integer (indicating an inconsistency in the number of fragments per set), a warning is given, and that sample is not classified by the model. Without rejection, the model achieves an overall accuracy of 87.9%, which increases to 92.8% if we reject 10.9% of the samples (which must be reviewed manually).
Conclusion: The obtained results are relevant because they highlight the importance of the use of a rejection option, which improves accuracy on the automated reviewed cases while still enabling the reduction of the manual workload. In future work, we will further improve the model's accuracy (by a second counting round of the rejected and misclassified fragments) and apply a threshold between 0 and 1, enabling us to fine-tune the final score, according to the desired accuracy.
Funding: This work was supported by national funds provided by Fundação para a Ciência e Tecnologia (FCT), under projects PRELUNA, PTDC/CCI-INF/4703/2021) and UIDB/50021/2020.

E-PS-08-047

Can AI teach us new features of clinical relevance in colorectal cancers?

K. von Loga*, C. Saillard, R. Dubois, O. Tchita, L. Guillou, A. Filiot, A. Fouillet, M. Sefta
*Owkin, France

Background & objectives: MSIntuit is the only CE marked AI-based MSI detection tool. The model scores known features of CRCs and highlights new characteristics that may impact prognostication and treatment decisions.
The objective is to evaluate these by a systematic pathological interpretability assessment.
Methods: The 4-step MSIntuit pipeline consists of tissue detection, tiling & normalisation, feature extraction and feature aggregation. 600 consecutive resected cases underwent the pipeline and tiles were pooled according to their assigned risk scores, clusters and heatmaps and then systematically reviewed by a pathologist for tile phenotyping, cluster analysis and spatial distribution.
Results: A total of 600 whole slide images (MSI: n=123), corresponding to 11 million 112um by 112um tiles with risk scores ranging from 0 to 1 were available for the analysis. Risk scores above 0.5 are indicative of an MSI phenotype. >15 clusters were identified and pathologically classified into 10 relevant groups and correlated with risk scores.
400 tiles most predictive of MSI (n=200) and MSS (n=200) were phenotyped and spatially located. The majority of tiles predictive of both contained tumour cells, with MSI: 70%, MSS: 60%. In the heatmap analysis, high risk tiles were also found in the surrounding normal tissue and further categorised.
Conclusion: AI adds relevant quantitative information to known features of MSI and MSS that can be used to objectively score and compare CRC cases.
AI highlights new areas of interests and features that could complement standard pathology reporting of CRC cases.
AI systematically points out and scores surrounding normal tissue which has not been taken into account in standard pathology reporting yet.

E-PS-08-048

How to get decision trees from a knowledge graph in (nephro-) pathology

C. Weis*, M. Legnar, J.H. Simoneit, S. Porubsky, Z. Popovic
*Institute of Pathology Heidelberg, Germany

Background & objectives: Having a diagnostic algorithm for all potential differential diagnoses is beyond the capability of a single pathologist. To remedy this, we test generating decision trees automatically from domain-specific knowledge (from nephropathology as a use case) stored in a knowledge graph.
Methods: Nephropathology knowledge is stored from multiple sources (textbooks, diagnostic texts) in a knowledge graph, initially based on the SnomedCT ontology. Each disease or rather diagnostic finding is represented by a node.
Eventually, different graph algorithms are tested to retrieve the path between two nodes, which should represent the diagnostic steps.
Results: Generating the nodes and edges of our knowledge graph, we learned that a) standard entity recognition tools work. However, due to many different names of one entity, a correction step is needed; and that b) the relation extraction between two entities in pathological texts fails in many cases due to the typical semantic style of such reports. Therefore, we had to develop a custom relation extraction model based on the medspaCy toolkit.
In addition, node classification approaches are used to learn relationships between diagnosis nodes and certain concept nodes. Decision trees are then extracted from these models. Currently, we test amongst other MINDWALK-tree to generate decision trees.
Conclusion: Converting a text classification task to a node classification task benefits from additional relation information stored within a knowledge graph. However, knowledge graph generation can not be done with standard tools due to the special language of pathologists.

E-PS-08-049

Conversion of a vendor-specific to a vendor-neutral quantitative biomarker digital image analysis system

K. Yao*, M. Leong, F. Chung, S. Sanati, M. Cervania, V. Kazarov, M. Venturina, M. Gayhart, M. Guindi, B. Balzer, F. Dadmanesh, R. Matter, B. Pham, T. Lee, D. Frishberg
*Cedars-Sinai Medical Center, USA

Background & objectives: Scanner vendor neutral digital image analysis for cancer biomarker can offer significant advantages over scanner vendor specific platforms. Our aim is to document our institutional experience with the conversion and to illustrate the recurring challenges with adapting digital image analysis.
Methods: We converted our Aperio System using the Aperio AT Turbo scanner to the vendor-neutral Visiopharm Oncotopix Discovery using the NanoZoomer S360 scanner for oestrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (Her2), and Ki67 image analysis. A collection of previously analysed breast cancer slides was assembled for validation followed by a post go-live analysis.

Results: We processed 83 ER, 82 PR, 78 Her2, and 83 Ki67 slides for validation. One round of algorithm calibration was performed for ER, PR, and Ki-67, while four rounds of calibration were performed for HER2. After the final calibration, the concordance between the Aperio and Visiopharm systems was 100% for ER, 100% for PR, 91% for HER2, and 100% for Ki67 cases. Review of 522 ER, 519 PR, 421 HER2, and 401 Ki67 cases post go-live shows a continuing need for fine tuning of the system to accommodate individual pathologist practice and changing management guidelines.
Conclusion: While the vendor-neutral digital image analysis allows for access to greater options for digital image analysis, there are continuing challenges for adapting digital image analysis in routine anatomic pathology workflow including quality control and pathology practice variations.

E-PS-08-050
A selection of automatic or manual cache data creation procedures of whole slide image in cloud-based digital pathology system
M. Yook*, C.K. Jung, S.H. Lee, S.K. Yoon, I.Y. Choi
*Department of Medical Informatics, College of Medicine, The Catholic University of Korea, Republic of Korea

Background & objectives: In cloud systems, store large sized data in object storage in general. This study examines the cache creation procedures of whole slide image (WSI) on cloud system from object storage to server's memory through network attached storage (NAS).
Methods: Digital pathology services delivered through online must not be designed to causes an unpleasant user experience. Therefore, this study set the limit of page loading time is below 3 seconds. The time is vary depending on a WSI file size hence measuring upper limit size for make below 3 seconds as a result.
Results: As a result of testing with 22 different sizes of WSIs, ranging from 0.83MB to 26,414.57MB, the transferred size per second ranged from a minimum of 10.38MB to a maximum of 119.57MB. Among them, exclude less than 100MB WSIs because they were always taking below 3 seconds unless it takes technical problem. The average of measured result for selected 11 WSIs were 102.17MB per second in consequences. Therefore, it needs to be less than about 300MB to be able to process in 3 seconds or less is calculated.
Conclusion: According to the test results, automatic cache creation procedure is appropriate only when the size of the WSI file to be loaded is less than about 300MB considering the user experience. However, 300 MB is a small number difficult to be founded in a typical original WSI. Therefore, it is necessary to consider reducing the size by degrading the quality or resolution of the WSI depending on the purpose of use.
Funding: This research was supported by a grant from the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI21C0940).

E-PS-09 | E-Posters Endocrine Pathology

E-PS-09-001
Interobserver reproducibility of medullary thyroid carcinoma grading system
C. Ariño-Palao*, J. Bernal-Jorquera, D. Roldán, M.G. Rosas-Hernández, I. Ruz-Caracuel
*Pathology, Ramón y Cajal University Hospital, IRYCIS, Madrid, Spain

Background & objectives: Medullary thyroid carcinoma (MTC) grading system has proven to be extremely useful to stratify patients according to their prognosis. Although simple, there is little information about pathologists intercomparison results.
Methods: Forty-one MTCs from two hospitals were collected. Two teams composed of one pathologist and one trainee blindly reviewed one representative haematoxylin-eosin slide and its associated Ki67 immunohistochemistry. We annotated necrosis, number of mitosis/2mm2, Ki67 proliferative index and grade. Cases with discordant Ki67 proliferative index were manually counted using a digital image software (QuPath). Kappa correlation index was calculated for grade.
Results: Both teams used the same criteria described in the new WHO Classification of Endocrine Tumours. Ki67 proliferative index was originally counted on a microscope. Both teams agreed on grade in 37 out of 41 cases (90%). Kappa agreement score was 0,69 for grade. In one case, discordances were due to not considering necrosis. The other three cases were very near the cut-off point of Ki67 index, with one team scoring them as high-grade and the other as low. These cases were finally counted on hot spot areas using a digital image software. After review and agreement, the case with necrosis and two cases with discrepant Ki67 index were classified high-grade.
Conclusion: MTC grading system is notably reproducible between pathologists working in different locations. Main limitations are the presence of small foci of necrosis and stablishing Ki67 proliferative index in cases very near the cut-off point. Reproducibility can be increased if Ki67 proliferative index is assessed using a digital image software.

E-PS-09-002
Paraganglioma with FUS::CREM gene fusion: a case report of an aggressive entity
M.A. Bani*, V. Suybeng, D. Vasseur, M. Faron, E. Baudin, J. Scoazec
*Department of Medical Biology and Pathology, Morphological pathology laboratory, Gustave Roussy Cancer Campus, Villejuif, France, Paris-Saclay university, Gustave Roussy Cancer Centre, Inserm US23, CNRS UMS3655, AMMICa, Villejuif, France

Background & objectives: Gene fusions are rare events in paragangliomas and usually involves UBTF::MAML3. CREB family gene fusions have been described in diverse mesenchymal neoplasms. However, paragangliomas harbouring FUS::CREM fusions have never been described. We herein describe a first case report.
Methods: We report the case of a 52-year-old man with a history of a testicular seminoma who presented with anaemia. CT-scan revealed multiple pancreatic masses with 2 lung nodules. A left pancreatectomy was performed.
Results: On microscopy, tumours appeared to be unencapsulated and infiltrating the pancreatic tissue. This tumoral proliferation had a diffuse growth with large confluent nests. Some foci of necrosis were found. Tumour cells had a basophilic to amphophilic granular cytoplasm and a vesicular nuclei and conspicuous nucleoli. Mitotic activity appeared low (1 mitosis/2mm2). Tumour cells expressed synaptophysin and chromogranin B without expression of keratins. Some small cells were highlighted by PS100. ALK(D5F4) was expressed. There was no expression of GATA3, PAX8, PHOX2B, TFE3 and SALL4. Expression of FH and SDHB was retained. RNA sequencing showed a FUS::CREM fusion and no mutation was found. The final diagnosis was paraganglioma with FUS::CREM gene fusion.
Conclusion: To the best of our knowledge, the FUS::CREM gene fusion has not been previously described in paraganglioma. This patient showed multiple pancreatic tumours with two lung metastases sustaining the aggressive behaviour of the spectrum of CREM fusion-positive neoplasms. The unexpected site and pathological diagnosis represent major pitfalls and emphasize the value of molecular testing in rare neoplasms.

E-PS-09-003
Osteoclast-like giant cell-rich anaplastic thyroid carcinoma: a diagnostic challenge
A. Borda*, N. Berger, C. Satala, Z. Reti, E. Szasz, M. Decaussin-Petrucci
*G.E. Palade UMFST Targu Mures, Romania

Background & objectives: Anaplastic thyroid carcinoma (ATC) with osteoclast-like giant cells is an exceptionally rare entity.
It can resemble other tumours with giant cell feature arising in the neck or elsewhere. Establishing the thyroid origin is crucial given prognostic and treatment implications.
Methods: We report the case of a 78 year-old female admitted to the hospital for a rapidly growing tumour mass on the left lobe of the thyroid with compressive symptoms like dysphagia, dysphonia, shortness of breath. As FNA cytology was malignant, a total thyroidectomy with lymph-node dissection was performed, and the specimen was sent to the Pathology Department.
Results: On macroscopy, the left right lobe was almost entirely replaced by a whitish tumour widely crossing the resection limit. On microscopy, the tumour was made of highly pleomorphic spindle and epitheloid cells, interspread with numerous osteocleast-like giant cells. More than 10 mitosis/mm² were counted, and no necrosis. A small contingent of tall cell variant of papillary thyroid carcinoma (TC-PTC) was noticed. No transition between ATC and TC-PTC was observed. On immunohistochemistry the anaplastic cells were negative for AE1-AE2, TTF1, PAX8, Thyroglobuline and positive for P53 and BRAF (BRAF V600 E mutation confirmed by IDYLLA technique). TC-PTC cells were positive for all markers, except P53. The osteoclast-like-cells were positive for CD68.
Conclusion: BRAF positivity, confirmed by PCR based molecular testing of the BRAF mutation is of capital importance in establishing the thyroid origin of ATC with osteoclast-like giant cells, as all other markers witnessing the follicular origin of the tumour are negative. This is an important step in order to etablish an accurate management of patients exhibiting this very aggressive and deadly cancer.
Funding: FDI project 2023 - Internationalization of higher education

E-PS-09-004

Reclassification of papillary thyroid carcinomas into differentiated high-grade thyroid carcinomas using criteria of the WHO classification of Endocrine and Neuroendocrine Tumours (5th ed.)

V. Cancer Huerva*, A. Pinedo Estalayo, B.S. Pacheco Martinez, M. Pinedo Estalayo, C. Vasquez-Dongo
*Hospital Universitari de Girona Doctor Josep Trueta, Spain

Background & objectives: High-grade follicular cell-derived non-anaplastic thyroid carcinoma arises as an entity in the latest WHO classification establishing criteria for Differentiated High-Grade Thyroid Carcinoma (DHGTC) diagnosis. We aim to identify and characterise DHGTC in our series of Papillary Thyroid Carcinomas (PTC).
Methods: Retrospective and descriptive revision of 117 thyroid surgical specimens with histopathological diagnosis of PTC from 2015 to 2019. Reclassification performed according to the latest WHO classification applying the following criteria: presence of necrosis and/or ≥5 mitosis per 10 high-power fields (2 mm²). Statistical analysis was performed using chi-squared test.
Results: 11 cases (9.4%) were reclassified as DHGTC with a mean age of 54 years (35-85y) and higher prevalence in women (8:1). Tumour size ranged from 1.4 cm to 3.9 cm. Histologically, six (5.2%) met necrosis criteria, accounting for up to 5% of the tumour, and five (4.2%) had high mitotic count. Classic PTC (8) architectural pattern was predominant followed by tall cell (1), solid-trabecular (1) and follicular (1). Seven (63%) cases presented lymphovascular invasion and nine (81%) extrathyroidal extension. Six (55%) staged as pT3 or above and five (45%) presented nodal metastasis. Within 4 years after the diagnosis, 27% DHGTC recurred without demise whereas 12.5% PTC recurred with <1% mortality.
Conclusion: In our series, DHGTC had significantly higher rates of lymphovascular invasion and extrathyroidal extension than PTC ($p<0.05$). Moreover, we found that DHGTC presented with higher tumour diagnostic stages than PTC ($p<0.05$) regardless of nodal metastasis. These findings are consistent with the need of categorisation of high-grade tumours. However, our results did not show statistical difference in recurrence or sex distribution between these groups. The tumour necrosis percentage was low, further studies can elucidate whether a cut off value is necessary.

E-PS-09-005

Papillary thyroid carcinoma presented as a hypercaptant nodule: a case report

J. Caschili*, M.L. Lai, C. Gerosa, R. Murru, P. Baldussu, A. Canino, L. Secci, P.G. Calò, D. Fanni
*Department of Medical Sciences and Public Health, University of Cagliari, Italy

Background & objectives: Hot thyroid nodules are mostly benign and rarely show a malignant nature. Here we present the case of a 45-year-old man with papillary thyroid carcinoma that presented as a hot nodule on scintigraphy.
Methods: The Fine Needle Aspiration (FNA) allowed the cytological examination of the nodule, including the immunohistochemical analysis for HBME-1 and Galectin-3 by cell block technique. Samples of the surgical specimen were formalin-fixed and paraffin-embedded to perform serial sections for H&E staining, BRAF V600E, and p53 immunohistochemical analysis.
Results: Cytology revealed thyrocytes aggregated in sheets and papillary-like fragments with voluminous and moderately pleomorphic nuclei with finely distributed chromatin, grooves and rare pseudo inclusions. Immunohistochemical analyses performed on cell blocks showed positivity for Galectin-3 and HBME-1. Thus, the patient underwent thyroidectomy. The gross specimen showed a nodule (2.6x3x1.8 cm) occupying almost the entire left lobe. Histologically the neoplasm, lacking a capsule, showed an infiltrative pattern without margin or vascular invasion. Immunohistochemical analysis revealed a positive BRAF V600E staining and focal overexpression of p53 staining.
Conclusion: Although hypercaptant thyroid nodules on scintigraphy support a benign origin of the lesion, we report the case of a papillary thyroid carcinoma presenting as a hot nodule.

E-PS-09-006

Papillary thyroid carcinoma before and during Covid-19. What has changed?

R. Catana*, S. Emoke-Andrea, D. Militaru, A. Borda
*George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mures, Romania

Background & objectives: The COVID-19 pandemic declared by the WHO on 11 March 2020, produced major changes in the healthcare systems. The aim of the study was to investigate the incidence of papillary thyroid cancer before and during Covid-19-period in a university hospital.
Methods: Patients' clinicopathological characteristics were obtained from database registries of the Department of Pathology, Emergency County Clinical Hospital, Târgu-Mureș, Romania. Papillary thyroid carcinoma (PTC) and all its histological variants were classified according to the 2017 WHO criteria. We analysed the data in a comparative way between two groups: before Covid-19 (2 years 2018-2019) and Covid-19-period (2 years 2020-2021).
Results: We observed a 45% decrease of the total thyroid surgeries: from 403 before Covid-19, to 219 in the Covid-19-period.
The distribution of the patients from the two groups according to gender (W/M ratio) was: 7,7:1 vs. 6,8:1 and the average age was: 52.33 years vs. 49.89 years.
The incidence of PTC, increased from 22.58% between 2018-2019, to 33.33% in the Covid-19-period. The conventional variant of PTC

was the most common histological form in both groups (70.32% vs. 57.53%). A total of 32.96% and 21.91% of the PTC cases in the pre-Covid-19-period and Covid-19-period, respectively, were diagnosed as microcarcinomas.
Conclusion: Social isolation, online health consultations recognized as important protections against the spread of the new virus, reduced access to investigations and to elective treatment of thyroid pathology are reflected in the decrease of the thyroid surgeries during Covid-19- period. The increased incidence of PTC in 2020-2021 could be due to a better screening of patients with thyroid pathology for surgical treatment and perhaps to the delay in diagnosis and treatment of these patients.
Funding: FDI Internationalization of higher education

E-PS-09-007
Spindle cell metaplasia in benign nodular goiter: a rare lesion mimicking neoplasia
E.E. Cetiner*, I.E. Cakir, K. Kurt, T. Cakir, A. Kahraman
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Spindle cell metaplasia of the thyroid gland is rarely reported and associated both with reactive processes and malignant neoplasms. Recognition of this entity and determination of the cellular origin has an important clinical implication for the therapy and prognosis.
Methods: In this report, we described, a rare case of benign nodular goiter with non-neoplastic spindle cell component. A 50-year-old woman was admitted to the hospital with multinodular goiter. Serum levels of fT3, fT4 and thyroid-stimulating hormone were: 4,23pg/ml (2-4,4), 1,11ng/dl (0,93-1,7) and 0,124uIU/ml (0,27-4,2) respectively. Scintigraphy confirmed the diagnosis of multiple nodules with cold areas. The patient underwent total thyroidectomy.
Results: Microscopic examination showed typical appearance of benign nodular goiter except the biggest nodule located in the left lobe. Histologically, this nodule, was composed of proliferation of spindle cells showing haphazard distribution. Spindle cells exhibited bland appearing-elongated plump nuclei with no prominent nucleoli, atypia and mitotic figures. They were intimately intermingled with various sized thyroid follicles. Characteristic features of papillary carcinoma were not seen. Capsule of the nodule was evaluated but there was no capsular or vascular invasion. Immunoreactivity with thyroglobulin, TTF1 and extremely low Ki-67 indexes proved that the spindle cell proliferation was follicular origin and non-neoplastic. CD34, calcitonin, synaptophysin, chromogranin, desmin and smooth muscle actin were all negative.
Conclusion: There are only a few cases of benign nodular goiter associated with spindle cell component in English literature. Non-neoplastic spindle cell metaplasia can occur in follicular cells of benign nodular goiter. Detailed morphologic and immunohistochemical analyses are required to achieve an accurate histopathologic diagnosis in spindle cell lesions of the thyroid.

E-PS-09-008
Mixed corticomedullary tumour: an unusual finding in an organ harvesting and literature review
R. D'amato Pascarella*, S. Uccella, M. Testa, E. Di Lauro, O. Mete, S. La Rosa
*Unit of Pathology, Dept. of Medicine and Technological Innovation, University of Insubria, Varese, Italy

Background & objectives: Mixed corticomedullary tumours (MCMTs) are extremely rare with only 29 cases described since 1969. Ours would be the 1 st case, as far as we are aware, to be incidentally discovered during organ harvesting.
Methods: Herein, we report the gross and histopathological findings of an unexpected tumour in a 77-year-old donor male, with no relevant past medical history, during organ-removal. Frozen sections underwent pathological examination and subsequently the rest of the tumour was entirely sampled, formalin-fixed and paraffin-embedded. Furthermore, a literature review on MCMTs with the related epidemiological and clinicopathological features is hereby provided.
Results: During organ-removal the pathologist on call reported a primary adrenal tumour with low malignant potential and the transplantation procedure was performed. The surgical specimen measured 6x5,5x2,5 cm and comprised a well-circumscribed, yellow to tawny-brown 3 cm-sized nodule, with focal areas of haemorrhage. Microscopically, the lesion was composed of two intimately intermingled components showing morphological and immunohistochemical features of cortical (SF1, inhibin) and medullary (chromogranin, VMAT2, GATA3, TH) cells, respectively. A MCMT was diagnosed. Neither morphological or immunohistochemical signs of malignancy were observed. In addition to ours, 28 reported cases were found in literature; no data was retrievable from one additional Japanese case-report with no English version available.
Conclusion: MCMTs are most common in females (20/29) and most patients occurred to be symptomatic (23/29). The mean age was 49,41 years and the mean tumour diameter 71,53 mm. Hypertension and Cushing Syndrome were reported in 20 and 12 cases, respectively, with 9 patients presenting both. Localization in adrenal glands was almost equal. Although MCMTs mostly have an indolent clinical behaviour, malignant potential should always be ruled out. Only four malignant MCMTs were reported, all of which with a poor prognosis.

E-PS-09-009
Thyroid hyalinising trabecular tumour: an easily misinterpreted diagnosis
O. El Mnif*, A. Zehani, H. Azzouz, B. Chelly, A. Ayari, I. Chelly, K. Bellil, S. Haouet
*La Rabta pathology department Tunis, Tunisia

Background & objectives: Thyroid hyalinizing trabecular tumour is a benign thyroid neoplasm that that could mimic multiple malignant thyroid neoplasms we present a case report of a 44-year-old female who had a total thyroidectomy for a highly suspicion of a thyroid carcinoma.
Methods: We analysed the medical file of a 44-year-old patient with no medical history, presented a suspicious thyroid nodule classified as EUTRADS 5 with clinical and laboratory euthyroidism. The patient had a thyroid cytopunction that concluded to a papillary thyroid carcinoma. A total thyroidectomy is performed with frozen section procedures. Representative sections of the specimen were examined later under H&E stains.
Results: Cytological features of the nodule were suggestive of a papillary carcinoma, including presence of monotonous, spindle-shaped cells with clear cytoplasm nuclear grooves and nuclear pseudoinclusions.
Macroscopic examination revealed a fleshy nodule measuring 2 cm in long axis and frozen section examination revealed a proliferation organized in trabeculae and in small clusters made of medium-sized cells with large nuclei sometimes presenting incisures and pseudoinclusions. The final microscopic examination showed that this proliferation was well limited without capsular invasion. It was organized in trabeculae and cords mostly with the presence of stromal amorphous material. The diagnosis of thyroid hyalinized trabecular tumour was then made.
Conclusion: HTT can be challenging to diagnose preoperatively, and it can be easily misinterpreted as other thyroid neoplasms, such as medullary thyroid carcinoma or follicular variant of papillary thyroid carcinoma.

E-PS-09-010
Immunohistochemistry a valuable tool for detecting BRAFV600E mutation: validation in papillary thyroid carcinomas
S. Emoke-Andrea*, A. Nechifor-Boila, R. Catana, A. Borda

*G.E. Palade UMFST Targu Mures, Romania

Background & objectives: BRAFV600E is the most common genetic mutation in PTC (papillary thyroid carcinoma). We performed a molecular and immunohistochemical (IHC) study to validate the IHC technique in detecting the BRAFV600E mutation, comparing it to the molecular PCR technique, considered as reference.
Methods: We stained 50 formalin-fixed PTC specimens using the monoclonal antibody anti-BRAFV600E clone VE1: 35 BRAFV600E positive and 15 BRAFV600E negative confirmed by PCR. Clinical information (age at diagnosis, sex, date of surgery) and pathological data were obtained from medical records. The sensitivity and specificity of the anti-BRAFV600E antibody were assessed.
Results: IHC of BRAFV600E showed 94.4% sensitivity and 66.7% specificity. Of 35 BRAFV600E PCR-positive PTC samples, 33 (94.3%) cases expressed the anti-BRAFV600E antibody too with cytoplasmic weak (45.5%), moderate (39.4%), and strong (15.2%) immunostaining. Of the 15 BRAFV600E PCR-negative PTCs, 66.7% (10/15) were also IHC negative. Five PCR-negative PTC showed positive immunostaining with weak (20%), moderate (60%) and strong (20%) intensity. Of these cases, 3 were observed in the Warthin-like variant and 2 in the tall cell variant.
Conclusion: BRAF IHC is a feasible and easily reproducible method. However, the presence of false positive and false negative results in our study group (similar to the data in the literature), highlights the need for caution when relying solely on one method for detecting BRAFV600E mutation. When there is a strong suspicion of the mutation being present, based on morphological criteria (certain histological variants, lymph node metastases, extrathyroid extension), using both methods would be an ideal approach.
Funding: FDI internalization of higher education

E-PS-09-011
Hypercalcemia in the debut of two parathyroid carcinomas in young patients
S. Haro Yuste*, F. Leiva-Cepas, I. Sánchez Ramírez, J. Osuna Soto, M.J. Galvez Medina, A. Sanz Zorrilla
*Hospital Universitario Reina Sofía, Spain

Background & objectives: Parathyroid carcinoma is a rare endocrine neoplasm with a poor prognosis. Two cases are presented in young patients who debuted with elevated hypercalcemia.
Methods: Calcemia showed values of 17.8 and 18.2 mg/dL (normal: 8.5-10.5 mg/dL). Cervical ultrasound showed a 4 cm cervical mass in one of the cases. In the other case, an increase in metabolic activity in the thyroid gland was identified on scintigraphy. Parathyroidectomy was performed in the first case and total thyroidectomy with cervical dissection in the second case.
Results: Histopathological findings showed in the first case the absence of a true capsule, variable cellularity, and broad bands of fibrous connective tissue extending from the peritumoral pseudocapsule; vascular invasion was also observed. In the second case, the thyroid gland was infiltrated by cell proliferation with little cell atypia, but with vascular invasion, involvement of the external thyroid capsule, and the presence of fibrous trabeculation. Both patients have a parafibromin mutation and had lymph node metastases at diagnosis. Currently, patients are asymptomatic and closely monitored.
Conclusion: Histopathologic findings rather than biochemical or clinical features predict outcome. Early and en bloc surgery, including central lymph node dissection, should be the minimal surgical approach in any patient with suspected parathyroid cancer.

E-PS-09-012
Uncommon thyroid pathology encountered in a surgical pathology review of 3,427 consecutive adult thyroid lesions
R. Kanthan*, R. Sabaratnam
*University of Saskatchewan, Canada

Background & objectives: Benign and neoplastic thyroid lesions are commonly encountered in general surgical pathology practice. The aim of this study is to raise clinical awareness of uncommon neoplastic and nonneoplastic pathological lesions of the thyroid.
Methods: Diagnosis of two unusual thyroid lesions: sclerosing mucoepidermoid carcinoma and solitary fibrous tumour prompted a 25-year review of surgical pathology cases with "thyroid" in the final diagnosis. Exclusion criteria included fine needle aspiration biopsies, and all thyroid tissue outside the thyroid gland. All cases were reviewed and categorized by age, sex and pathological diagnosis with in-depth review of uncommon lesions.
Results: 3,427 adult thyroid lesions were reviewed. They commonly occurred among 40-60 years with female predominance-2714 cases. 1896 cases~55% were benign non-neoplastic lesions with thyroiditis-352 cases~10% and Grave's disease-230 cases~7%. Neoplastic lesions accounted for 1531 cases~45% with the majority being malignant lesions-1053 cases~31%. Benign neoplastic lesions were predominantly follicular adenoma -474 cases~14%. Papillary carcinoma was the commonest malignancy-882 cases~26%, with follicular carcinoma-83 cases~2.4%, anaplastic carcinoma-17 cases~0.5%, medullary carcinoma-18 cases~0.53%, poorly differentiated thyroid carcinoma-7 cases~0.2% and malignant lymphomas-39 cases~1.14% Uncommon benign lesions included hyalinizing trabecular tumour, intrathyroidal ectopic thymus, and lymphoepithelial cyst with solid cell nests. Uncommon malignant lesions included mucoepidermoid carcinoma with/without eosinophilia, metastatic renal cell carcinoma and solitary fibrous tumour.
Conclusion: Thyroid lesions requiring surgical excision in adults occur more frequently in women. They are more likely (70%) to be benign, than malignant-30%. Papillary carcinoma is the commonest epithelial malignancy followed by follicular, malignant lymphomas, medullary, anaplastic and poorly differentiated carcinomas. Increased clinical awareness with recognition of uncommon lesions both benign and malignant as seen in this case series review is important for accurate pathological diagnosis and thus appropriate patient management.

E-PS-09-013
EBV-positive diffuse large B-cell lymphoma of the thyroid, suggesting aberrant CD3 expression
T. Kawasaki*, K. Kanemoto, H. Inoue, T. Yamazaki, M. Nakahira, Y. Ebihara, M. Kohri, K. Tsukasaki, N. Takahashi, Y. Sonoda, J. Ichikawa, K. Gotoda, M. Doi, H. Masaoka, A. Sasaki
*Department of Pathology, Saitama Medical University International Medical Center, Japan

Background & objectives: Herein, we report an exceptionally rare case with Epstein-Barr virus (EBV)- as well as aberrant CD3-positive diffuse large B-cell lymphoma (DLBCL) involving the thyroid.
Methods: The patient, a 72-year-old man, presented with a chief complaint of a neck mass that had grown rapidly in the prior three months. Anaplastic thyroid carcinoma (ATC) was clinically suspected. Fine-needle aspiration cytology of the thyroid lesion was performed three times, with the initial two attempts being nondiagnostic or unsatisfactory, while the third was suspicious for malignancy, favouring carcinoma.
Results: He underwent total thyroidectomy with lymph node dissection. Macroscopically, the thyroid tumour, measuring 89x65x39 mm, located mainly in the right lobe, was whitish, relatively well-defined and solid, accompanied by geographic necroses. Histologically, large atypical lymphoid cells showing Hodgkin/Reed-Sternberg (HRS)-like, multinuclear and/or pleomorphic forms proliferated in clusters or sporadically, with infiltration of numerous small lymphocytes and macrophages. These atypical cells extended to the anterior neck muscles as well as one of the parathyroid glands. Tumour involvement

was also found in the right III lymph nodes. Immunohistochemically, the atypical cells were positive for CD20, CD79a, CD30, PAX5, bcl-2, bcl-6, MUM-1, and EBER (ISH), while being negative for CD10, CD15 and c-myc.
Conclusion: Based on these pathological features, we diagnosed this tumour as EBV-positive DLBCL. In addition, neoplastic cells were weakly positive for CD3 and CD5, suggesting unusual expressions. It is noteworthy that, while extremely rare, EBV-positive DLBCL can occur in the thyroid and, from the diagnostic and therapeutic perspectives, differentiation from carcinoma, particularly ATC, is challenging. Therefore, it is worth considering this condition if a patient, especially one who is elderly, presents with a tumour showing rapid enlargement in the neck region.
Funding: Tomonori Kawasaki was supported by Grants-in-Aid for Scientific Research (Nos. 21K06910, 20K08131 and 23K11869) from the Japanese Ministry of Education, Culture, Sports, Science and Technology, Joint Research Support Grants based on the Comprehensive Agreement between Saitama University and Saitama Medical University (22J01 and 21J14), and the National Hospital Organization (NHO) Grant (H29-NHO-01).

E-PS-09-014
The adrenal rush: a single institute experience
A. Lakshmanan*, R. Uthayasuriyan, N. Mulchandani, S. Naresh Shah, M. Menon, A. Subramanyam
*Apollo Hospitals, India

Background & objectives: Adrenal neoplasms are uncommon and often pose diagnostic challenges. They can be primary or secondary neoplasms. The objective of this study is to analyse the frequency and distribution of various adrenal neoplasms and highlight the existence of few rare cases.
Methods: This is a retrospective study done over a period of 10 years (2011-2020) in the Department of Pathology, Apollo Hospitals, Chennai. Hematoxylin and eosin-stained sections and immunostains were reviewed and analysed.
Results: A total of 320 cases of adrenal lesions were observed during the study period. Seven cases were excluded as the material was inadequate for further immunohistochemistry studies or for a definitive diagnosis. There were 277 primary adrenal neoplasms, 36 secondary neoplasms and 12 cases of adrenal haemorrhage. Adenoma was the commonest adrenocortical neoplasm and phaeochromocytoma was the commonest adrenal medullary neoplasm. Fourteen cases of diffuse large B-cell lymphoma were also noted. A variety of benign and malignant mesenchymal neoplasms were noted in 86 cases including rare entities such as solitary fibrous tumour, Ewing sarcoma and liposarcoma. Secondary neoplasms included direct infiltration from other organ malignancies and metastatic carcinoma.
Conclusion: This study highlights a broad spectrum of adrenal neoplasms including a few rare unusual cases. Our case distribution fairly correlates with other studies in the literature. Meticulous grossing with careful histopathological evaluation supplemented by immunohistochemistry is required in arriving at the correct diagnosis of rare entities.

E-PS-09-015
Thyroid carcinoma in children, adolescents, and young adults: a retrospective evaluation on 88 cases in 10 years period
V. Macarrón Aguilera*, M.E. Brizzi, A. Carcavilla, J.C. Moreno-Navarro, M.I. Esteban-Rodríguez, R.M. Regojo-Zapata
*La Paz University Hospital, Spain

Background & objectives: Paediatric thyroid cancer is a current area of interest with few studies and has distinct features from thyroid cancer in adulthood. Our aim is to evaluate thyroidectomies performed in in our centre for the last 10 years in this population.
Methods: All thyroidectomies performed in patients under 33 years in a tertiary referral hospital between January 2013 and April 2023 were identified. Clinicopathological features were extracted from the electronic medical records, including gender, age and histological diagnoses. Cases since 2017 also included molecular studies.
Results: Of 225 thyroidectomies performed (168 women and 57 men, with a median age of 24.13 years), 88 presented a thyroid carcinoma (39,1%). Papillary carcinoma (PTC) was diagnosed in 82 cases (93,2%). Molecular studies were conducted on 47 cases, finding 26 cases (55,3%) with BRAF V600E mutation. Moreover, 5 RET rearrangements (10,6%) and 1 (2,1%) NTRK fusion gene were identified. One case (2,1%) presented a syndromic familial follicular cell-derived thyroid carcinoma (DICER1 syndrome). Minimally invasive follicular carcinoma were identified in 3 cases (3,4%). Finally, 3 cases (3,4%) of medullary carcinoma were diagnosed in prophylactic thyroidectomies performed due to a germline RET mutation.
Conclusion: In our cohort, PTC is the most common malignancy with BRAF V600E mutation in half of the cases. RET and NTRK fusions should be tested in negative BRAF V600E cases to facilitate the selection of patients for developing molecular targeted therapies. Patients with thyroid cancer predisposition syndrome should be detected for special oncological management and care. More regional and national studies are needed to better understand this pathology, and to develop diagnostic and therapeutic guidelines for this population.

E-PS-09-016
Disseminated neuroblastoma with initial presentation as a mandible mass in a child
N. Martínez Arnau*, I. Marquina Ibáñez, S. Hakim Alonso, J. Alfaro Torres, J.L. Delgado Fernández, J. Martínez Castillón, L. Ollero Domenche, A. Carilla Sanromán
*Hospital Universitario MiguelServet, Spain

Background & objectives: Neuroblastoma is a relatively common malignancy of childhood. However, when it debuts in a not typical location the diagnosis is difficult because its radiology image and symptoms suggest other kind of lesions.
Methods: We report a case of an 11-year-old child with a solid and painless lesion of 25 mm located in the right jaw branch affecting soft tissues. Clinically, seemed an inflammatory process or adenopathy and radiology suggested a mandible sarcoma.
Results: The lesion was biopsed. Several yellowish-brown fragments measuring 16 mm were received. Histological examination revealed bone fragments and skeletal muscle infiltrated by a neoplasm composed of sheets and cords of small round cells with hypercromatic nuclei and stretching artefact. Neoplastic cells expressed immunohistochemically synaptophysin, CD56, vimentin and chromogranin with negativity of CKAE1AE3, CD45, S100, CD99, CD34, actin, desmin, WT1 and FLI1. Proliferative index with Ki67 was 95%. Based on morphology and immunohistochemical profile, the lesion was diagnosed as metastasis of neuroblastoma. Given these results, further image studies were made. An adrenal mass with multiple distant metastasis was found, with neuroblastoma as a result of the biopsy.
Conclusion: Neuroblastic tumours are the third most common childhood neoplasms after leukaemias and brain tumours. Therefore, we must think of them whenever the patient is a child, no matter the starting location we have.

E-PS-09-017
Follicular cell-derived thyroid carcinoma following tyrosine kinase inhibitor treatment
S. Molés Caparrós*, A. Veliz Dominguez, J.C. Corredor-García, T. Alonso-Gordoa, B. Porrero-Guerrero, H. Pian-Arias, I. Ruz-Caracuel
*Ramón y Cajal University Hospital, Spain

Background & objectives: Thyroid carcinoma patients benefit from recently approved treatments, such as tyrosine kinase inhibitors. These are used in patients at progression but in few cases, they have been used before primary surgery. There is little data regarding histopathological effects on thyroid.
Methods: Our patient is an 89-year-old woman with a locally advanced thyroid papillary carcinoma BRAF-V600E mutated. The Multidisciplinary Team dismissed surgical treatment due to extensive invasion, and decided to start lenvatinib, a kinase inhibitor.
After three months, treatment was interrupted due to secondary effects. The CT-scan showed tumour size reduction associated with necrosis. Then, total thyroidectomy and central lymphadenectomy was performed.
Results: Thyroidectomy specimen was firm. At sections, three different areas were identifiable. One central area partially encapsulated with intermixed white and yellow tissues. Another adjacent fleshy region. And a third peripheral white firm section. At microscopy, the central area was mainly composed of loose fibrous tissue intermixed with hyalinised materials. There were scant vessels, calcifications, slight lymphoplasmacytic infiltrates and cholesterol-associated granulomatous reactions. There were isolated follicle neoplastic glands remaining in this section. The fleshy region was an area of conventional papillary carcinoma. Whereas the peripheral region was composed of papillary carcinoma with conventional morphology and an increased mitotic index (11 mitosis/2mm2), consistent with high grade follicular cell-derived thyroid carcinoma.
Conclusion: In our specimen, we identified areas suggestive of tumour regression after treatment adjacent to areas of high-grade neoplasm. We cannot discern whether this high-grade component was present before target therapy or if it was developed following therapy pressure. As pathologists, we should collect these cases to further clarify this issue and to propose a neoadjuvant response measurement system.

E-PS-09-018
Sarcoidosis and thyroid autoimmunity: a rare case of concomitant Graves' disease and thyroid sarcoidosis
P. Radia*, R. Simo, L. Collins
*Guys and St Thomas' Hospital, United Kingdom

Background & objectives: Autoimmune thyroid diseases (AITD) can be associated with other systemic or organ specific autoimmune diseases. Up to 20% of patients with sarcoidosis present with AITD. However, involvement of the thyroid gland with sarcoidosis is rare and can make management challenging.
Methods: We present the clinical and pathological findings of a patient with concomitant Graves' disease and sarcoidosis of the thyroid gland.
Results: A 46 year old woman presented with trismus and heart palpitations. Laboratory studies showed thyrotoxicosis, consistent with Graves' disease. Her medical history included fatty liver disease and sarcoid. The patient was started on carbimazole PTU and reached a suppressed TSH and T4 of 49 mIU/mL. After developed a hypersensitivity reaction, the drug had to be stopped. Although alternative anti-thyroid drugs were administered, the patient required a total thyroidectomy.
Histopathological examination of the thyroid gland showed features compatible with Graves' disease with florid non-necrotizing granulomatous inflammation. Special stains for fungal organisms and acid fast bacilli were negative. With the clinical findings, a diagnosis of Graves' disease with thyroid sarcoidosis was made.
Conclusion: Autoimmune thyroid disease is commonly seen in patients with sarcoidosis. Involvement of the thyroid gland itself with sarcoid is rare but should be considered in patients with medication unresponsive disease as it may lead to resistance of anti-thyroid drugs.

E-PS-09-019
An unusual location for a malignant epithelioid PEComa: the adrenal gland
D. Sá*, J.R. Brandão, F.S. Vieira, G. Carrola
*Centro Hospitalar Universitário de Santo António, Portugal

Background & objectives: PEComa (perivascular epithelioid cell tumour) is a mesenchymal tumour composed of perivascular epithelioid cells, and it occurs more frequently in the uterus and retroperitoneum. To our knowledge, there are fewer than ten reported cases arising in the adrenal gland.
Methods: We herein report a case of a 57-year-old woman with a 5-month history of fever, asthenia, and weight loss. During workup, a CT scan was done which revealed a right adrenal mass measuring 11cm of maximum dimension. Adrenal hormone tests were unremarkable, hence proving this was a non-secretory tumour. An adrenalectomy was then performed to characterize this lesion.
Results: We received a right adrenalectomy specimen almost totally occupied by a multinodular 13cm neoplasm, poorly delineated from the adjacent parenchyma, displaying a white cut surface and haemorrhagic areas. Histologic examination showed an infiltrative neoplasia presenting a solid or fascicular pattern and composed of epithelioid or rarely spindle cells with eosinophilic cytoplasm, elongated to ovaloid vesicular nuclei with prominent nucleoli. There were also areas of necrosis, vascular invasion, multinucleated giant cells, and a high mitotic rate with atypical mitotic figures. Immunohistochemistry revealed expression of HMB-45 and MelanA diffusely and SMA in the spindle cell component, with negativity for CAM5.2, Calretinin, Inhibin, Synaptophysin, Chromogranin, S100, SOX10, Desmin, MDM2, CAIX, PAX8 and TFE3.
Conclusion: Epithelioid PEComa can pose a diagnostic challenge as it can be difficult to distinguish from other tumours. High-risk criteria for malignancy in non-gynaecologic PEComa include having > 5 cm, a mitotic rate > 1/50 HPF, necrosis, a high nuclear grade and cellularity, vascular invasion, and an infiltrative growth pattern. If two or more features are present, as in our case, these tumours should be considered malignant. The patient currently has no evidence of recurrence or metastasis 6 months after surgery.

E-PS-09-020
Parathyroid carcinoma: a case report
A. Sifre-Ruiz*, È. Iglesias Martínez, N. Santiago-Quispe, M.M. Buda, C. Esquina, A.M. Cordovilla-Moreno, M. Bronte-Anaut
*Clinical Department Unit of Pathological Anatomy, OSI Araba, Araba University Hospital. Bioaraba Health Research Institute, Vitoria-Gasteiz, Alava, Spain

Background & objectives: Parathyroid carcinoma (PC) is a rare neoplasm, which can be either sporadic or associated with familial hyperparathyroidism related syndromes. The majority of them are functioning tumours representing <1% of primary hyperparathyroidism.
Methods: The histologic sections of a case of PC diagnosed in our centre in 2023 were reviewed. To verify the diagnosis, organ-specific staining (PTH) and vascular endothelial staining (CD31) were performed. In addition, the clinical data and personal and family history of the patient were reviewed and summed up.
Results: We report the case of a 56-year-old man diagnosed with primary hyperparathyroidism (serous calcium levels 12.6 mg/dl) with an anterior cervical node, who underwent a surgical excision. In the macroscopic study, we found a nodular and heterogeneous solid lesion that corresponded to a densely cellular capsulated tumour, composed by medium-sized eosinophilic cells arranged in solid nests, trabeculae and occasional follicles, separated by fibrous septa. The cellular population presented mild anisonucleosis, evident nucleolus and clumpy chromatin and expressed PTH. Multiple images of vascular invasion were identified, but no intratumoral necrosis was observed. After diagnosis, the patient was referred to the Genetics Department.
Conclusion: PC is a rare neoplasm that can occur at any age (mean age at time of diagnosis 51-57 years). The majority are functioning

tumours causing severe hypercalcemia and hypophosphatemia, and patients often present both renal and bone disease. Most parathyroid carcinomas are sporadic, but a genetic test is recommended due its association with hyperparathyroidism-jaw tumour syndrome (HRPT2/CDC73 gene), familial isolated hyperparathyroidism (HRPT2 gene and others) and multiple endocrine neoplasia type 1 and 2A syndromes (MEN1 and MEN2A genes).

E-PS-09-021

Morular cribiform thyroid carcinoma: two-case series

A. Sifre-Ruiz*, A. Onaindia-Pérez, È. Iglesias Martínez, N. Santiago-Quispe, M.M. Buda, C. Esquina, A.M. Cordovilla-Moreno, B. Catón-Santaren
*Clinical Department Unit of Pathological Anatomy, OSI Araba, Araba University Hospital. Bioaraba Health Research Institute, Vitoria-Gasteiz, Alava, Spain., Spain

Background & objectives: We report two cases of morular cribriform carcinoma (MCC): a twelve-year-old female (patient 1) with previous diagnosis of familial adenomatous polyposis syndrome (FAP) and a twenty-year-old one without any antecedents (patient 2). Both presented goiter with Bethesda V category nodules.
Methods: Thyroidectomy specimens were studied, including hematoxylin-eosin stains; additional inmunohistochemical stains (Ventana BenchMark ULTRA, Ventana Medical Systems, Inc., Tucson, AZ, US) and complete APC sequencing (Sanger sequencing method using MLPA technique in an ABI3130x analyzer). Clinical data, personal and family history of the patients were investigated. A descriptive analysis of the obtained data and a literature review were carried out.
Results: Macroscopically both specimens showed well-demarcated, bilateral solid nodules, corresponding microscopically to epithelial proliferations surrounded by a thick fibrous capsule, exhibiting diverse growth patterns, predominantly cribriform. Empty spaces with a striking absence of colloid were lined up by cuboidal or columnar tumour cells, with eosinophilic cytoplasm and elongated and irregular nuclei with a tendency to "crowding". Non-keratinizing squamoid morulae were also present in all sections. Immunohistochemical studies showed negativity for thyroglobulin; TTF-1 and β-catenin nuclear and cytoplasmic positivity was identified. A diagnosis of MCC was made in both cases. APC sanger sequencing was performed in patient 2 specimen, revealing a probably pathogenic variant [c.3548del, p.(Tyr1183Leufs*82)].
Conclusion: MCC is often associated with FAP (in up to 40% of the cases, precedes its diagnosis), presenting at young age with goiter. MCC has been recently catalogued as a separate entity in the 5th WHO classification of tumours of endocrine organs.
Germinal or somatic mutations, conditioning biallelic APC gene inactivation, trigger WNT/β-catenin pathway constitutive activation, which is essential for MCC pathogenesis. This tumour's peculiar morphology and characteristic immunohistochemical features, allow a prompt diagnosis enabling molecular testing for FAP syndrome screening.

E-PS-09-022

Indicators of epithelial-mesenchymal transformation in patients with papillary carcinoma of the thyroid gland and its combination with chronic autoimmune thyroiditis

I. Sorokina*, N. Filonenko, O. Kaluzhyna
*Kharkiv National Medical University, Ukraine

Background & objectives: Papillary thyroid carcinoma (PTC) is the most common form of thyroid cancer.
The aim of the work is to establish the features of epithelial-mesenchymal transformation (EMT) in patients with PTC and its combination with AIT through a complex pathomorphological study.
Methods: Histological, immunohistochemical, morphometric, and statistical methods were used in the work. The material is divided into three groups: PTC (25 cases), AIT (10 cases) and PTC on the background of chronic AIT (25 cases). We investigated pancytokeratin and keratin-7, vimentin, and E-cadherin. The percentage of cells expressing the marker in the field of view was determined, ×400.
Results: In the immunohistochemical study of thyroid tissue with PTC, it was established that pancytokeratin and keratin-7, as well as E-cadherin are expressed by the follicular epithelium of tumour structures weakly ("+"), while the expression of vimentin is evaluated as expressive ("+++"). This indicates the presence of EMT. Combination of PTC with AIT is characterized by moderate expression ("++") of all investigated markers, which indicates a relative decrease in the manifestations of EMT in this group compared to PTC.
Conclusion: In the group of PTC, there is a decrease in the expression of E-cadherin, as well as a decrease in the expression of pancytokeratin and keratin-7 with a pronounced expression of vimentin. The described changes are characteristic of EMT phenomena.
Thus, it can be assumed that the presence of AIT in a patient with PTC is a prognostically favourable circumstance for the course of the tumour process.

E-PS-09-023

Immunohistochemical detection of Sine oculis homeobox 6 (SIX6) in clinically silent pituitary neuroendocrine tumours – a pilot study

J. Soukup*, H. Faistova, L. Gerykova, P. Poczos, T. Česák, M. Kosak, D. Netuka, F. Gabalec
*University Hospital Hradec Kralove, Czech Republic

Background & objectives: Sine oculis homeobox 6 (SIX6) is a transcriptional factor expressed in pituitary gland, playing role in differentiation of gonadotroph lineage. There are however no data about SIX6 in PitNETs or other sinonasal neoplasms.
Methods: Immunoreactivity of SIX6 (polyclonal, Atlas Antibodies, 1:50) was examined in 20 non-functional PitNETs (10 gonadotroph, 5 corticotroph, and 5 Pit1-lineage) using immunoreactivity score (IRS). Normal pituitary was used as a positive on slide control. Additional data on mitotic activity, Ki67, p53 and tumour recurrence were analysed.
Results: SIX6 expression in normal pituitary tissue was heterogeneous, with strongly, weakly positive and negative cells. SIX6 immunoreactivity was detected in 18/20 (90%) PitNETs; two negative cases corresponded to Crook cell tumour and poorly differentiated Pit1+ tumour. IRS ranged from 1 to 8, with median IRS 3, and no difference was observed among the three lineages (p=0.69; Kruskal-Wallis test). Compared to strongly positive cells in normal pituitary, only moderate (6/18; 33.3%) or weak (12/18; 66.6%) immunoreactivity was observed in tumour tissue. We observed no difference in IRS among recurrent and non-recurrent tumours (p=0.78; Mann-Whitney test) and no correlation between SIX6 and Ki67 or mitotic activity.
Conclusion: Although SIX6 can be detected in non-functional PitNETs across all lineages, its immunoreactivity is usually weak and limited compared to normal pituitary tissue. This limits its use as a general marker of pituitary tumours in differential diagnosis of head and neck neoplasms.
Funding: Ministry of Health, Czech Republic, NU20-03-00360; BBMRI-CZ LM2023033; Czech Ministry of Defense MO 1012

E-PS-09-024

Expression of the transcription factor HOXB13 in the neuroendocrine tumours of the gastrointestinal tract

E. Spiteri*, N. Stavrinou, F. Dolkiras, P. Vlachou, E. Athanasiou, A. Therapontos, M. Tsoli, M. Panagaki, G. Kyriakopoulos
*Department of Pathology, Evaggelismos General Hospital Athens, Greece

Background & objectives: The HOXB13 gene encodes a transcription factor expressed in the embryonal tail bud. HOXB13 is expressed in

the cauda equina neuroendocrine tumour. We compare the expression of HOXB13 in rectal NETs with the NETs of the gastrointestinal tract.
Methods: HOXB13 immunohistochemical expression was assessed in 11 NETs (2 small bowel, 3 pancreas, 2 appendix, 2 rectum-L cell subtype and 2 rectum-EC cell subtype). The monoclonal antibody against HOXB13 (AbCam, clone EPR17371, 1:2000) was used. The intensity and proportion of positive cells of the immunohistochemical marker was estimated via the Immunoreactivity Scoring System (IRS).
Results: Complete absence of HOXB13 expression was found in the NETs of the small bowel (0/2, IRS 0), of the appendix (0/2, IRS 0) and of the pancreas (0/3, IRS 0). On the contrary, strong nuclear staining for HOXB13 in a high percentage of cells was observed in all the NETs arising from rectum, irrespective of the cell subtype (80-90%, IRS 12).
Conclusion: The transcription factor HOXB13 appears to have strong nuclear expression in the rectal NETs in comparison to the NETs of the rest of the gastrointestinal tract, making it a valuable marker when trying to assign an origin in NETs of unknown primary, taking into consideration that it is also expressed in the cauda equina NET (formerly known as paraganglioma of the cauda equina).

E-PS-09-025
Comparative immunohistochemical study of cMYC, cyclin D1 and Ki-67/MIB-1 expression in neoplastic and non-neoplastic thyroid tissues
A. Syrnioti*, E. Forozidou, A. Poutoglidis, K. Sapalidis, T. Koletsa
*Department of Pathology, School of Medicine, Aristotle University of Thessaloniki, Greece

Background & objectives: To investigate the immunohistochemical expression and the diagnostic utility of cMYC, cyclin D1, and Ki-67/MIB-1 in follicular adenomas (FAs), follicular carcinomas (FCs), poorly differentiated (PDTCs) and anaplastic thyroid carcinomas (ATCs), as well as in their corresponding adjacent, non-neoplastic tissue (NNT).
Methods: Twenty-eight cases were retrieved from the archives of our Department, 13 histologically diagnosed as FAs, 11 as FCs, and 4 as PDTCs/ATCs. Tissue microarrays with cores taken from neoplastic and adjacent NNT were constructed. Immunohistochemistry with cMYC, cyclin D1, and Ki-67/MIB-1 antibodies was performed, and the positivity was evaluated. A statistical analysis using IBM SPSS Statistics v25 followed.
Results: Nuclear cMYC positivity was observed in 4/11 FCs, and 3/4 PDTCs/ATCs, whereas cytoplasmic cMYC positivity was found in 16/24 NNTs. Globally, there were statistically significant differences between neoplasms and NNTs, with higher nuclear cMYC and cyclin D1 expression observed in neoplasms ($p=0.017$ and $p=0.001$, respectively), in contrast to cytoplasmic positivity seen solely in NNTs ($p=0.001$). Cyclin D1 positivity was noted in 11/13 FAs, 7/11 FCs, 2/4 PDTCs/ATCs, and only in one NNT. A statistically significant correlation was found between MIB1 and c-MYC nuclear positivity ($r = 0.413$, $p=0.040$). In addition, statistically significant differences regarding the biomarker expression between FA and FC versus PDTC/ATC ($p<0.001$) were noted.
Conclusion: Our findings exhibit a clear difference in the immunohistochemical expression of cMYC and cyclin D1 between different types of thyroid tumours, as well as between the neoplastic and non-neoplastic thyroid tissue. Nuclear cMYC positivity excludes the benign nature of a thyroid lesion, in contrast to cytoplasmic positivity, which supports the normal or hyperplastic nature. Although a correlation between MIB-1 and cMYC was observed, the diagnostic value of cMYC localization proves to be superior.

E-PS-09-026
Expression of somatostatin receptors in radioiodine refractory follicular cell derived thyroid carcinomas detected with [68Ga] Ga-DOTA-TOC
K. Vargas Osorio*, A. Calatayud-Cubes, E.J. Díaz-López, C. Barbarán-Corral, H. Lázare-Iglesias, U. Anido-Herranz, J.M. Cabezas-Agrícola, V. Pubul-Núñez, J.M. Cameselle-Teijeiro
*Clinical University Hospital of Santiago de Compostela, Universidad de Santiago de Compostela and Galician Healthcare Service (SERGAS), Santiago de Compostela, Spain

Background & objectives: There are still limited data regarding the immunohistochemical expression and relevance of somatostatin receptors (SSTRs) in follicular cell-derived carcinomas. We describe the clinicopathological and immunohistochemical features of three cases whose metastases were detected using [68Ga]Ga-DOTA-TOC (synthetic somatostatin analogue peptide).
Methods: We examined three cases: widely invasive oncocytic carcinoma (case 1), widely invasive follicular cell thyroid carcinoma (case 2), and minimally invasive oncocytic carcinoma (case 3), presented in 2 men and 1 woman of 41, 60 and 46 years old, respectively. Total thyroidectomy and immunohistochemical study for SSTRs (anti-somatostatin receptor-2 antibody [clone UMB1] was carried out. All patients developed metastasis.
Results: Case 1 (pT3b,N0,M1[at diagnosis]) was treated with I131, sorafenib, lenvatinib and chemotherapy. Given the tumour burden, intolerance to treatment, rise in levels of serum thyroglobulin and positivity for [68Ga]Ga-DOTA-TOC, a treatment with [177Lu]Lu-DOTATATE was administered. The patient died due to the disease 131 months after diagnosis. In case 2 (pT3,N0,M1[at diagnosis]) after 2 doses of I131 (250 mCi) the levels of thyroglobulin rose (5162ng/mL). In case 3 (pT1b, N0, M0[at diagnosis]), after 2 doses of I131 (150 mCi) the levels of thyroglobulin also rose (1635ng/mL). In both cases 2 and 3, positivity for [68Ga]GaDOTA-TOC was detected. The tumour cells in all three cases showed strong immunoreactivity for somatostatin receptor 2.
Conclusion: In radioiodine refractory metastatic lesions from follicular cell-derived thyroid carcinomas (including oncocytic carcinomas), SSTR expression can be detected either by using radiolabelled SSTR analogues or through immunohistochemical studies. In these cases, [177Lu]Lu- DOTA-TATE is an alternative treatment modality.
Funding: Supported by grant no. PI19/01316 from Instituto de Salud Carlos III (ISCIII), State Research Agency and Ministry of Science and Innovation (Spain), co-funded by the European Union

E-PS-10 | E-Posters Gynaecological Pathology

E-PS-10-001
Minimal volume, non-myoinvasive uterine serous carcinoma in an endometrial polyp, with isolated pleural metastasis, at presentation in a pre-menopausal patient
A. Abrari*, N. Ranawaka, K. Akhtar
*The Rotherham NHS Foundation Trust, United Kingdom

Background & objectives: Uterine serous carcinomas are aggressive, predilecting post-menopausal women, having bulky primary tumours with extrauterine spread at the outset. The present case illustrates that even minute, non-myo-invasive serous carcinomas are sinister, can beget distant metastases and age is no bar.
Methods: Concerted pathological evaluation of the miniscule, histologically divergent locus in the endometrial polyp, removed for abnormal uterine bleeding, and of the metastatic carcinoma detected in the pleural thickening, biopsied after imaging, following the high risk endometrial cancer diagnosis - was performed. Morphology and immunohistochemistry panels, including oestrogen receptor, vimentin, Pax8, GATA3, WT1, p53 and p16 were evaluated in both specimens.
Results: The divergent, sub-millimetric locus in the endometrial polyp was interpreted as minimal, non-myoinvasive uterine serous carcinoma. The pleural biopsy demonstrated a metastatic carcinoma, essentially a facsimile of the uterine cancer. Carcinomas from both specimens had morphology and immuno-phenotype typical of uterine serous carcinoma.

The carcinoma cells formed parodic, irregular glandular spaces populated by pleomorphic, dys-cohesive cells, with large, irregular nuclei, prominent nucleoli and eosinophilic to focally clear cytoplasm. There was luminal shedding of cells. No lympho-vascular or myometrial invasion was observed in the endometrial polyp. The background endometrium was non-atrophic.
The immuno-profiles for both carcinomas included diffuse, (mutated type) p53 positivity, p16 overexpression and concordant expression patterns for other markers.
Conclusion: This case having several instructive oddities, underpins the inherently aggressive nature of uterine serous carcinoma, notwithstanding the tumour volume or extent of involvement at the primary site.
The fact that this clinico-pathological denouement unfolded in a 43 year old pre-menopausal patient is an admonition to practicing cellular pathologists, to ratchet their index of suspicion low, for the possibility of this variant, even in patients that are much younger than those in which it is conventionally thought to occur.

E-PS-10-002
Frequency of placental histopathological lesions: a retrospective study in a tertiary hospital
L. Aguirrezabal Marcotegui*, S. Fernández Ferrer, A. Tarín Nieto, J. Roselló Soria, I. Fernández de la Prieta, C. Valentí Ponsa, G. Cancho Galán, A. Nogueira Gegrorio
*Hospital Universitario de Basurto, Bilbao, Spain

Background & objectives: The placenta is one of the most poorly understood organs and its examination often presents an intimidating task for the general pathologist. The objective of this study is to determine the frequency and type of histopathological lesions in placentas.
Methods: This retrospective systematic search included 660 placental samples received in a tertiary hospital between 2018 and 2022. Lesions were classified into the following categories: amniotic fluid infection sequence (maternal and foetal inflammatory response), maternal vascular malperfusion, foetal vascular malperfusion and other lesions. Depending on the histological findings, the placentas could be classified in more than one category.
Results: The 50,1% of the placentas did not present any significant findings. The amniotic fluid infection sequence diagnose was the most prevalent, observed in 31,5% of the placentas. The 14,4% had maternal vascular malperfusion lesions, being infarcts the 70,5% of this category. Foetal vascular malperfusion was diagnosed in the 1% of the placentas. The rest of the lesions comprised the 9,1% of diagnoses (chronic inflammatory lesions, retroplacental hematomas, chorangiosis, meconium-stained placenta and single umbilical artery among others). To be emphasized two cases os placenta accreta, one congenital leukaemia and one malaria infection.
Conclusion: Most frequent diagnoses were amniotic fluid infections and infarcts. However, in 50,1% of the placentas no histopathological lesions were found. It would be interesting to know, if the absence os lesions in half of studied placentas is due to the lack of training of general surgical pathologist, or if it is necessary to review the clinical criteria used to send placental samples for histological examination.

E-PS-10-003
Pulmonary metastasis of a TTF-1 positive endometrial endometrioid carcinoma – a case report
V. Almeida*, B. Sepodes, C. Courelas, J. Gama, V. Sousa, L. Carvalho
*Institute of Anatomical and Molecular Pathology, Faculty of Medicine of the University of Coimbra, Portugal, CIMAGO – Research Center for Environment, Genetics and Oncobiology, Faculty of Medicine, University of Coimbra, Portugal, Pathology Service, University Hospital Anatomical Pathology Coimbra, Portugal

Background & objectives: Thyroid transcription factor-1 (TTF-1) is a reliable marker for primary lung adenocarcinoma, while it is rarely expressed in endometrial carcinomas.
We report a TTF-1 positive endometrioid carcinoma (EC) of the endometrium with metastatic lung disease.
Methods: A 64 years-old non-smoker woman with a history of endometrial endometrioid carcinoma FIGO grade 3, staged as FIGO 1A, was treated with hysterectomy with lymphadenectomy and adjuvant vaginal brachytherapy. Two years later, she presented with respiratory distress, and the imaging study suggested bilateral cannonball metastases. A transthoracic biopsy directed to the largest lung nodule was performed.
Results: The lung biopsy revealed an adenocarcinoma with a predominantly solid growth pattern, and also tightly constricted microacinar structures. Tumoral cells were large cells with nuclei enlargement and atypia. On immunohistochemistry, the tumour showed strong positivity for nuclear PAX8 and cytoplasmatic vimentin; p53 had a wild-type pattern, and oestrogen receptors were negative. Nuclear TTF-1 was diffusely expressed.
We reviewed the primitive endometrial carcinoma slides and retrospectively performed a TTF-1 stain, which was also diffusively positive.
The final diagnosis was pulmonary metastasis of EC of the endometrium with aberrant TTF-1 expression.
Conclusion: Less than 10% of ECs express TTF-1, with higher rates in the G3 subset, as in this case. TTF-1 expression in EC has also been associated with a worse prognosis.
TTF-1 positive ECs metastasizing to the lung can be challenging to distinguish from primary lung adenocarcinoma. It is important to remember that TTF-1 may be immunoreactive in gynaecologic malignancies, and that the correct diagnosis frequently depends on both clinical correlation and immunostaining with multiple antibodies.

E-PS-10-004
Cotyledonoid dissecting leiomyoma of the uterus: a case report showcasing concomitant mitotically active ovarian thecoma
A. Ardelean*, G. Stefanet, M. Boros, E.M. Popescu
*Pathology Department - County Clinical Emergency Hospital Bihor, Romania

Background & objectives: Cotyledonoid dissecting leiomyoma (CDL) and mitotically active thecoma are rare variants of their otherwise common counterparts, each with their own unique clinical, paraclinical and microscopic diagnostic challenges. We aim to advance knowledge on these entities and facilitate further diagnosis.
Methods: We present a case of a 63-year-old woman with cotyledonoid dissecting leiomyoma of the uterus and concomitant mitotically active ovarian thecoma. The patient presented to our hospital due to lower abdominal pain and fecal incontinence. Clinical and paraclinical examination revealed a fibromatous uterus with compressive phenomena. The patient underwent surgery for total hysterectomy and bilateral salpingo-oophorectomy.
Results: Grossly the uterus presented with a micronodular, cauliflower and placenta-like mass that extended towards the left ovary. Microscopically it showed proliferation of short-length smooth muscle fascicles that dissected the myometrium and extended outside of the uterus. Cells were positive for oestrogen, progesterone, desmin, and SMA, negative for CD10 and with a Ki67 proliferation index lower than 5%. Microscopic examination of the ovary revealed a multilobulated thecoma with one outstanding well-circumscribed nodule showing medium to large polygonal cells with variable nuclear pleomorphism and numerous mitoses. All thecoma lobules showed positivity for Wt1, SMA, MelA and Calretinin, while being negative for MCK. Reticulin staining showed well demarcated cell borders.

Conclusion: The case we present showcases two rare disease variants that pose unique diagnostic challenges due to either their gross or microscopic appearances. To our knowledge, there are less than 100 cases of CDL reported to date and cases of mitotically active thecoma are even scarcer. Therefore, we highlight the importance of histopathology in the diagnostic procedure of surgical specimens as well as the importance of avoiding overdiagnosis of unusual aspects in such tumours.

E-PS-10-005

Prognostic significance of GATA4 in adult type granulosa cell tumour of the ovary

D. Arik*, I. Bağcı, E. Telli, T. Öge, Ö.T. Yalçın
*Eskisehir Osmangazi University, Turkey

Background & objectives: The aim of the study is to determine the expression level of GATA4 in adult type granulosa cell tumours, to determine its relationship with clinicopathological features and to reveal its effect on survival.
Methods: GATA4 expression level was determined immunohistochemically in granulosa cell tumour cases diagnosed in our department. It was investigated whether there was a significant relationship between expression level, clinicopathological parameters, recurrence and survival.
Results: GATA4 expression level was found to be higher in early stage cases. GATA4 expression level was not associated with overall survival or disease-free survival. The only consistent prognostic parameter associated with prognosis was FIGO stage.
Conclusion: GATA4 expression supports good prognostic features. Expression level does not affect survival time and is not related to other clinicopathological parameters. It is necessary to reveal the parameters that can be used to predict prognosis and recurrence. GATA4 could be a potential marker here.

E-PS-10-006

How far can a metastasis of squamous cell carcinoma of the uterine cervix spread?

S. Aviel-Ronen*, A. Dobriyan, S. Felder, E. Akerman, I. Gluck, M. Vered
*Adelson School of Medicine, Ariel University, Pathology Department, Sheba Medical Center, Tel Hashomer, Israel

Background & objectives: Cervical carcinoma commonly spreads locally and to regional lymph nodes. Here we describe an unusual case of cervical squamous cell carcinoma that at diagnosis presented with metastasis in the mandibular condyle. Tumour origin was ascertained by immunostains and molecular studies.
Methods: The medical records, imaging tests, pathological findings and molecular studies of the patient have been studied and are presented.
Results: A 55 years old female patient presented with post-coital bleeding. On gynaecological examination a 5 cm cervical mass was found, sampled and diagnosed as squamous cell carcinoma. MRI revealed local spread to the uterine isthmus, left cervical fornix and regional lymph nodes. PET-CT demonstrated an additional hypermetabolic focus in the left mandibular condyle. Despite normal and functional physical examination, an incisional condyle bone biopsy revealed squamous cell carcinoma metastasis. The carcinoma cells were positive for p16 immunostain and HPV in-situ. HPV typing was done using Master Diagnostics HPV Direct Flow CHIP on the eBRID automated system and HPV 16 and 6 were detected, confirming the cervical origin.
Conclusion: Squamous cell carcinoma of the uterine cervix might metastasize even to unusual and distant locations, such as head and neck region, without further bone spread. High index of suspicion and a thorough workup of cervical cancer patients are warranted to diagnose and treat early lesions before they become symptomatic and ensure detection of any far metastatic spread. The combination of immunostains and molecular studies is capable of determining cervical origin even in technically challenging tissues such as bone biopsies.

E-PS-10-008

Recurrent ovarian tumour with PTCH1::GLI1 fusion and loss of FOXL2 copy number: a case report of a neoplasm mimicking sex cord stromal tumour

R. Bakkar*, M. Afkhami, M. Song, R. Ali-Fehmi, H. Maluf, D. Bell, A. Malpica
*City of Hope National Cancer Center, Department of Pathology, USA

Background & objectives: GLI1-altered neoplasms encompass a rare heterogeneous group of tumours, reported in the oral cavity, soft tissue, and gastrointestinal, genitourinary and gynaecologic tracts. We report the first case of an ovarian tumour with *PTCH1::GLI1* fusion and loss of *FOXL2* copy number.
Methods: A 70-year-old female with history of unclassified right ovarian sex-cord stromal tumour (2010), initially treated with right salpingo-oophorectomy, followed by multiple pelvic recurrences treated with multiple debulking surgeries, chemotherapy, and radiotherapy. She presented in 2023 with recurrence in the liver, abdominal wall, and pelvis for cytoreduction. Grossing, routine laboratory processing, immunohistochemical studies and comprehensive next generation sequencing (NGS) were performed.
Results: The tumour masses were haemorrhagic and fleshy. Histologically, the tumour had multinodular growth, prominent vascularity, oedema and focal myxoid changes in the stroma. There was a combination of architectural patterns: nested, trabecular, solid, cystic and follicular spaces filled with eosinophilic material. The cells were epithelioid, monotonous, with eosinophilic/clear cytoplasm and small oval nuclei, with mild to moderate atypia, variable grooves, and focal vesicular chromatin, mitotically active, without necrosis. The tumour cells were diffusely positive for SF-1, and CD56, and patchy weakly positive for CD10, D2-40 and S100 while negative for SOX10, pancytokeratins, EMA, synaptophysin and chromogranin. BRG1 expression was retained. NGS detected *PTCH1::GLI1* fusion and loss of *FOXL2* copy number.
Conclusion: This case is the first reported to carry *PTCH1::GLI1* fusion and loss of *FOXL2* copy number. Some shared features with other GLI1-altered tumours may suggest commonality. Recognizing the occurrence of this entity in the gynaecologic tract is important, given the availability of targeted therapy involving the SHH-GLI1 pathway, GLI1 inhibitors, and tyrosine kinase inhibitors. Although the clinical significance of loss of *FOXL2* copy number is unclear, its presence suggests loss of function.

E-PS-10-009

Ovarian teratoid carcinosarcoma, a case report with SMARCA4 loss

R. Bakkar*, M. Afkhami, J. Cohen, R. Ali-Fehmi, L. Arvanitis, A. Malpica, D. Bell
*City of Hope National Cancer Center, Department of Pathology, USA

Background & objectives: Ovarian teratoid carcinosarcomas (TCSs), with immature neuroepithelium, with or without germ cell component, reminiscent of sinonasal tract TCSs, are extremely rare, with debatable origin- True germ cell versus pluripotential stem cell. We describe the first ovarian case with *SMARCA4* loss.
Methods: A 73 y.o. female presented with postmenopausal bleeding, 6.1 cm solid right ovarian mass by imaging and elevated CA-125, treated with total abdominal hysterectomy, bilateral salpingo-oophorectomy and debulking surgery at an outside hospital, diagnosed with ovarian carcinosarcoma with heterologous chondrosarcoma elements, FIGO IIIB. Slides were reviewed in consultation, additional immunohistochemical studies and comprehensive next generation sequencing (NGS) were performed.

Results: The tumour was heterogeneous with the following components: (1) Carcinomatous with Pax-8/ WT1 positive serous carcinoma and squamous cell carcinoma, with frequent squamous elements showing cytoplasmic clearing conferring a foetal appearance, (2) Sarcomatous, with undifferentiated spindle and pleomorphic cells with heterologous elements (chondrosarcoma and MyoD1 positive rhabdomyosarcoma), (3) Sheets and nests of undifferentiated immature neuroepithelium (EMA negative, synaptophysin, chromogranin, CD56 strong positive, neurofilament/NeuN focal positive), (4) Yolk-sac-like glandular elements with features suggestive of endodermal sinus tubules, with basal and apical vacuolation (glypican patchy positive, SALL4, AFP focal positive). NGS showed loss of *SMARCA4*, chromosome 12p amplification (with secondary amplification of several oncogenes in the same region), and *TP53* mutation.
Conclusion: The novel finding of *SMARCA4* loss in this ovarian TCS is in concordance with the *SMARCA4* inactivation recently discovered as the dominant genetic event in sinonasal TCSs. This finding points towards a somatic derivation. Some cases of gynaecological tract TCS may belong to the group of *SMARCA4*-deficient tumours. The study of additional cases is necessary to confirm the incidence of this finding.

E-PS-10-010
Intrauterine adhesions: correlations between clinical, immunohistochemical, molecular and atomic profile
R. Balan*, L. Toma, R. Socolov, N. Simionescu, D. Socolov, B. Toma, T.A. Balan, S.E. Giușcă, I.D. Căruntu
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: Intrauterine adhesions (IUA) can be asymptomatic, leading to overlooked diagnosis, or symptomatic, accompanied by menstrual abnormalities, infertility, and pelvic pain. Due to serious impairment of reproductive function, we aimed to assess the clinical, immunohistochemical, molecular, and atomic profile of IUA.
Methods: Our retrospective study included two groups of fertile aged women. The first one comprised 58 patients with IUA, treated during 2016-2022 by hysteroscopy with adhesiolysis, presenting hypo/amenorrhea, infertility, and pelvic pain. The control group involved 25 women with other pathologies hysteroscopically diagnosed. Biopsy tissue samples were histopathological and immunohistochemical examined, prepared for RNA extraction, and atomic force microscope (AFM) evaluation.
Results: The histopathological examination of the first group revealed a secretory endometrium, with stromal fibrosis and focal chronic inflammatory infiltrate. The immunohistochemical and mRNA expressions of SUSD2, CD31, NG2, PDGFR beta, CD 146 and Nestin, in the damaged endometrium and control group, were assessed. The mRNA expression levels of all six studied markers were less elevated in the damaged endometrium group versus control group. The immunohistochemical expression was higher in the first group versus control group. The atomic force microscope (AFM) evaluation revealed differences between markers. The AFM detected the morphological and topographical changes, which demonstrates the capture of measurements of various parameters in different stages of intrauterine adhesions.
Conclusion: IUA represents a challenging disease, although it is often neglected. The reserved prognosis of the disease is related to the limited therapeutic results and the complex endometrial environment. Exploring IUA through innovative techniques contributes to a deeper understanding of the pathogenic mechanisms of endometrial regeneration and repair in women with IUA. The AFM analysis of the IUA tissue compared to the normal endometrium represents the first study in the literature to date.

E-PS-10-011
Clinicopathological and immunohistochemical correlations of abdominal wall endometriosis after caesarean section
T.A. Balan*, R. Balan, I.D. Căruntu, I. Păvăleanu, L. Lozneanu, S.E. Giușcă, C. Amalinei
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: Abdominal wall endometriosis after the caesarean section (AWECS) is a rare entity, with sometimes latent development. As AWECS can mimick other entities or may undergo malignant transformation, we aim to assess the clinicopathological and immunohistochemical features of this endometriosis type.
Methods: Our retrospective study reviewed 16 cases of abdominal wall endometriosis, related to caesarean section, surgically removed and diagnosed by routine histological methods, supplemented with additional immunohistochemical techniques (ER, PR, CD10, CD45, S100), within the Pathology Department of the Clinical Hospital of Obstetrics and Gynaecology "Elena Doamna" from Iasi, Romania, for a period of 10 years (2012-2022).
Results: The clinical and ultrasound diagnosis were made on the existence of a tumour mass at the level of the post-caesarean scar, with cyclical variability in size and pain. Surgical treatment consisted of wide local excision with clear margins. The histopathological diagnosis revealed endometrial glands and/or stroma in dermis and subcutaneous tissues, accompanied by a mixed inflammatory infiltrate within or adjacent to endometriotic stroma, highlighted also by immunohistochemical assessment, CD10 revealing also possible endometrial stem cells. In our study, 4 patients (25%) presented a cutaneous endometriotic nodule, and 11 patients (75%) presented subcutaneous endometriosis. All cases presented positive immunoexpression of the studied markers. The clinico-pathological agreement for AWECS diagnosis was 68.75%.
Conclusion: AWECS should be considered in the case of a reproductive age women with a tumour mass at the level of a caesarean section scar, accompanied by cyclical pain. The histopathological examination, sometimes supported by immunohistochemical evaluation, represents the gold standard diagnosis for AWECS and for excluding a possible malignancy. An extensive panel of immunohistochemical markers could demonstrate the existence of endometrial stem cells in endometriotic foci, thus contributing to the completion of the pathogenic theories of the mechanisms involved in AWECS.

E-PS-10-012
Extensive accumulation of hemostatic agent reminants through pelvic peritoneal surfaces mimicking mucin: a diagnostic pitfall
H. Berber*, A.T. Bol Serttürk, D. Enneli, C. Cansız Ersoz
*Ankara University Medical School, Pathology Department, Turkey

Background & objectives: Oxidized regenerated cellulose(ORC) is a hemostatic agent commonly used in surgical interventions. ORC-particles remained through the peritoneal surfaces may pose a diagnostic challenge during the histopathological examination of the specimens, in case of being unawareness, as in the present case.
Methods: A 43-year-old female patient was admitted to the emergency department of our hospital, with the complaint of right lower quadrant pain. Imaging studies (abdominal ultrasound and computerized tomography) revealed a haemorrhagic cyst, 7 cm in long diameter, in the right ovary, and as the possibility of ovarian torsion can't be ruled out, the patient underwent right salpingoopherectomy.
Results: Macroscopic examination revealed multiple cysts in the ovary, with the largest haemorrhagic one, 7cm in long diameter. These were incompatible with haemorrhagic corpus luteum cyst and follicle cysts, histologically. The striking feature was the accumulation of extensive, basophilic material in the fimbria, ovarian cortex, mesovarium, along the pelvic peritoneal surfaces, reminiscent of mucin, at first glance, and dense histiocytic proliferation, some mimicking mucinophages including this material within their cytoplasm. Paler, pinky staining of this material by PAS/mucicarmine dyes removed the suspicion of mucin. Then the clinical history of the patient was questioned and learned that the patient had previously undergone cholecystectomy and ORC was used for hemostasis.

Conclusion: Widespread intraperitoneal and visceral deposition of ORS reminants, a hemostatic agent applied intraoperatively, posed a histopathological challenge in the present case, due to its mucin-like appearance. We presented this case to raise awareness of pathologists on this issue. Surgeons and radiologists should also be aware of this complication related to the use of ORS, as cases have been reported in the literature, presenting with an abdominal/pelvic mass or with an acute clinical condition.

E-PS-10-013

Incidence and evolution of carcinosarcomas in 10 years in a provincial hospital

T. Cano*, E.M. Ariza, B. Garzón, J.J. Sánchez, M.C. González, G.A. Pastrana
*Juan Ramón Jiménez University Hospital, Huelva, Spain

Background & objectives: Uterine carcinosarcoma is an aggressive biphasic high-grade tumour with a carcinomatous and sarcomatoid component. It is a rare tumour accounting for 5% of uterine malignancies. It usually occurs in elderly women. The pathological study playing a fundamental role.
Methods: The cases obtained in the last 10 years in our hospital are reviewed, obtaining diagnostic concordance data in aspiration biopsy and surgical piece, age of presentation, stage and type of sarcomatoid component (classifying it as homologous, if the sarcomatous element is native to uterine tissue, or heterologous, if the sarcoma is not native).
Results: N=11, age range from 59 to 84 years, presenting in all of them endometrioid carcinoma in its carcinomatous component and heterologous component in 7 of them (1 with osteosarcoma differentiation, 3 rhabdomyosarcomatoid , and 3 chondrosarcomatioids) in the mesenchymal component. At the macroscopic level, most were a fleshy polypoid mass with necrotic and haemorrhagic areas.
2 of the 11 cases presented metastasis at the initial diagnosis, 1 presented parametrial invasion (pT3b), 7 presented myometrial invasion >50% (pT1b) and in 1 it was <50% (pT1a).
In only 2 of the 3, there was no good diagnostic correlation in aspiration biopsy, initially being diagnosed as endometrioid carcinoma, with no evidence of sarcomatoid.
Conclusion: In summary, carcinosarcoma is a rare and aggressive tumour of the uterine body, in which the pathologist plays a crucial role for diagnosis, although the correlation in aspiration biopsy and surgical specimens is not complete, early diagnosis is still necessary to improve the patient survival. The prognosis is usually poor, in 30-40% of cases there is extrauterine involvement in the initial presentation, but in our population only 2% presented metastases at diagnosis.

E-PS-10-014

Mesonephric-like adenocarcinoma of endometrium: a wolf in sheep's clothing

T. Čeprnja*, I. Jurković, D.A. Grubišić, S. Tomić
*University Hospital of Split, Croatia

Background & objectives: Mesonephric-like adenocarcinoma of endometrium is a recently described rare entity sharing histological, immunohistochemical and molecular characteristics of mesonephric carcinomas, but lack association with mesonephric remnants or characteristic location. We present a case of this very rare subtype of endometrial adenocarcinoma.
Methods: Postmenopausal 55-year-old female presented with abnormal uterine bleeding and lower-back pain. On curretage diagnosis of serous adenocarcinoma was made, and total hysterectomy with bilateral salpingo-oophorectomy, pelvic lymphadenectomy and omentectomy was performed and a final diagnosis of endometrial adenocarcinoma with clear-cell differentiation, with unusual immunophenotype was set. Another opinion was requested, and materials were sent to our department.
Results: Histology showed a uterine carcinoma composed of round, compacted glands focally with eosinophilic material. Rare reticular and papillary structures lined by atypical cells with vesicular nuclei and solid area composed of spindled cells were also observed. Immunohistochemically, tumour cells were TTF-1, CD10 (luminal staining) and e-cadherin positive and had wild-type p53 immunoexpression. Few tumour cells were napsin positive, and p16ink was intensively positive in small part of the tumour. ER, PgR, AMACR, GATA3 and calretinin stains were negative. Additional molecular analysis showed KRAS and PIK3CA mutation.
Conclusion: Mesonephric-like adenocarcinoma of the endometrium is a recently described rare subtype of endometrial adenocarcinoma. Ability to mimic more common subtypes makes it a challenging diagnosis for gynaecologic pathologists. Although data is limited for now, it seems that mesonephric-like adenocarcinomas are high-grade carcinomas, even though they have a misleadingly low-grade morphology. The tumours have a high risk of recurrence and a high tendency for metastasis.

E-PS-10-015

Ovarian yolk sac tumour in the background of serous carcinoma – a report of a rare entity

A. Chrzan*, M. Bidziński, J. Kupryjańczyk
*Maria Sklodowska-Curie National Research Institute of Oncology (MSCNRIO), Department of Cancer Pathomorphology, Warsaw, Poland

Background & objectives: Yolk sac tumours (YST) may sometimes develop from somatic malignancies, predominantly endometrioid tumours. Herein, we report a rare case of YST arising from high grade ovarian serous carcinoma (HGSC) in a postmenopausal woman.
Methods: A 72-year-old female was referred to our hospital for the pelvic mass and slightly elevated serum CA125, HE4 and LDH. A transvaginal ultrasound revealed a 45 mm solid tumour of the left ovary. The patient underwent total hysterectomy with bilateral salpingo-oophorectomy and staging surgery. Frozen section evaluation resulted in the misdiagnosis of endometrioid carcinoma (EC).
Results: Microscopic examination revealed co-existing endometrioid-like glandular YST resembling secretory EC, solid areas with ambiguous morphology, and HGSC, which comprised 80%, 15% and 5% of the tumour, respectively. Immunohistochemically, the YST component was positive for SALL4, AFP, Glypican-3, and focally for GATA3, whereas negative for PAX8, CK7, WT1, and Napsin A. The HGSC component was positive for PAX8, WT1 and negative for YST markers. Solid areas exhibited an intermediate immunoprofile. All components showed EMA positivity and mutation-type p53 staining. Mutations in BRCA1/BRCA2 genes were not found. The serum AFP measured postoperatively was elevated (225.90 IU/ml). Therefore, a final diagnosis of ovarian YST derived from HGSC was rendered (FIGO stage IC3).
Conclusion: It is postulated that YST can arise from a carcinoma through a process of retrodifferentiation. Somatically derived YST may retain EMA expression. The presence of TP53 accumulation in both components confirms their clonal relationship. Possibly, areas with the intermediate immunoprofile reflect a transient stage from carcinoma to YST. The preexisting neoplasm can be totally or nearly totally overgrown by YST therefore thorough sampling is essential.

E-PS-10-016

SMARCB1-deficient myoepithelial carcinoma of the vulva in a pregnant woman: a rare and aggressive tumour

Y. Chun*, J.Y. Park, Y. Kim
*Korea University Guro Hospital, Republic of Korea

Background & objectives: Myoepithelioma-like tumours of the vulva are rare mesenchymal tumours that are associated with SMARCB1 loss. Vulvar myoepithelial carcinoma is even rarer. We report a case of

SMARCB1-deficient myoepithelial carcinoma of the vulva in a pregnant woman.
Methods: A 30-year-old pregnant woman presented with a vulvar mass that had been present before her pregnancy and had increased in size. The mass measured 8 x 7cm. Complete resection was performed, followed by radiation treatment. Twelve months later, the patient developed multiple lung metastases. Chemotherapy with paclitaxel and cisplatin was administered, but multiple pleural and paraaortic soft tissue metastases developed.
Results: Pathological examination of the vulvar tumour revealed a multinodular mass with an infiltrating margin. The tumour consisted of epithelioid to spindle cells growing in a reticular pattern, with myxoid or hyalinized stroma. Mitotic figures were 5 per 10 high-power fields. Immunohistochemical staining showed expression of EMA, SMA, and calponin, and loss of INI-1. ER and PR showed diffuse and focal positivity. Next-generation sequencing revealed the possibility of a heterozygous deletion of the SMARCB1 gene.
Conclusion: We report a case of SMARCB1-deficient myoepithelial carcinoma of the vulva in a pregnant woman, which exhibited an aggressive clinical course despite surgical and post-operation chemoradiation treatments. As ER and PR were positive, it is possible that the tumour grew rapidly due to pregnancy. It is challenging to differentiate between myoepithelioma-like tumours of the vulva and myoepithelial carcinomas as both tumours are SMARCB1/INI1-deficient and exhibit similar histological features. Therefore, a collective review is needed to unify the diagnostic criteria.

E-PS-10-017
Expression of Osteopontin in serous ovarian carcinoma
R. Chyzhma*, R. Moskalenko
*Sumy State University, Ukraine

Background & objectives: Ovarian cancer is one of the most common causes of death among women worldwide. One of the clinical and morphological features of ovarian tumours is calcification. To study the OPN expression in serous ovarian carcinoma with and without calcification.
Methods: We examined 30 samples of serous ovarian carcinoma with calcification and 30 samples of serous ovarian carcinoma without calcification. An immunohistochemical study was performed using an Anti-Osteopontin antibody (OPN, ab 8448, Abcam, Cambridge, Great Britain) with dilution 1:300.
Results: An immunohistochemical study of ovarian carcinoma showed the accumulation of OPN in biominerals. Protein covers the surface of the calcification, accumulating at the edges and between the lamellae. A positive cytoplasmic reaction to OPN is observed in the microenvironment cells, mainly mononuclear morphology and fibroblast-like cells. The difference between the results of an immunohistochemical study of OPN expression in groups of serous ovarian carcinoma samples with (73.34 ± 4.25 cells per 1mm2) and without calcification (26.93 ± 1.88 cells per 1mm2, $p<0.001$). This may indicate the participation of OPN in the pathological biomineralization of serous ovarian carcinoma.
Conclusion: Therefore, pathological biomineralization leads to high levels of OPN protein expression in serous ovarian carcinoma. On the other hand, samples of serous carcinoma without calcification have a lower level of these proteins.

E-PS-10-018
Development of a CD138-based histopathological semiquantitative scoring system for the diagnosis of chronic endometritis: inter-observer agreement between trained pathologists and a newly designed QuPath computational algorithm
S. De Smet*, G. Tagmouti, R. Forsyth, W. Waelput
*Universitair Ziekenhuis Brussel (UZB), Belgium

Background & objectives: It is accepted that the presence of plasma cells in the stromal endometrium is a marker for chronic endometritis. This study's objective was to develop a histopathological semiquantitative scoring system for its diagnosis, as well as assessing inter-observer agreement.
Methods: In a retrospective analysis of endometrial biopsies from 75 patients with suspected chronic endometritis, six pathologists scored the degree of inflammation using our proposed CD138-based semiquantitative scoring system. In addition, a newly developed QuPath computational algorithm was considered a seventh observer. A consensus score was determined after reviewing all cases. Inter-observer agreement was calculated using weighted kappa statistics.
Results: The CD138-based semiquantitative scoring system showed particularly good to excellent inter-observer agreement between all observers, including the computational algorithm. Weighted kappa values were ranging from 0.81 to 0.96 ($p<0.001$) in a four-tier system, and from 0.72 to 0.97 ($p<0.001$) in a two-tier system.
Conclusion: We have developed a histopathological semiquantitative scoring system for the diagnosis of chronic endometritis, with particularly good to excellent inter-observer agreement among pathologists. This scoring system has the potential to become a new standardized tool to classify the severity of inflammation in chronic endometritis. It provides an excellent tool for further studying the diagnosis of chronic endometritis, and its correlation with clinical outcomes. In addition, our computational algorithm could deliver enhanced accuracy and efficiency in the diagnosis of chronic endometritis.

E-PS-10-019
Small cell carcinoma of the ovary, hypercalcemic type (SCCOHT) in a 50 year old woman. Case report and literature review
M. De Uribe Viloria*, G. Barrios Millán, A. Berjón
*La Paz University Hospital, Spain

Background & objectives: SCCOHT is a rare and aggressive tumour mainly affecting premenopausal women. Patients usually present with advanced-stage disease. The median survival time is around nine months. Inactivating SMARCA4 mutations are thought to be the main driving molecular event.
Methods: We reviewed our files from 2013 to April 2023 retrieving a single case of SCCOHT. The diagnosis was achieved by routine stainings and immunohistochemical studies. We reviewed the histological samples and obtained clinical data such as age at diagnosis, symptomatology and radiological studies, from the clinical history.
Results: We present the case of a 50 year old female who consulted with abdominal pain. The patient showed hypercalcemia and peritoneal carcinomatosis in the CT scan. A diaphragmatic mass was biopsied showing a tumour displaying sheet-like growth, conformed by monotonous discohesive round cells with scant cytoplasm, small hyperchromatic nuclei, irregular chromatin and a brisk mitotic activity. Necrosis was present. The immunohistochemical expression of BAP1 and INI1 was preserved while it the expression of BRG1 (SMARCA4) was lost. Other immunohistochemical determinations were no specific. A diagnosis of SCCOHT was emitted. The patient died less than two months after diagnosis.
Conclusion: SCCOHT is a rare tumour, accounting for less than 1% of ovarian tumours. It poses a diagnostic and management challenge. Our case presents typical pathological and clinical findings, in spite of occurring at an older age than these tumours usually present. This case report emphasizes the importance of performing BRG1 staining on undifferentiated ovarian tumours, even if the epidemiological presentation is not typical. More studies are needed to address the challenges of this rare and deadly disease.

E-PS-10-020
Cotyledonoid dissecting leiomyoma (Sternberg tumour) - a rare and peculiar tumour
A. Dumitru*, M. Sajin, O. Munteanu, O.C. Voinea, A. Ciongariu, D. Tapoi, M. Cirstoiu

*Carol Davila University of Medicine, Romania

Background & objectives: Cotyledonoid dissecting leiomyoma is a rare benign uterine tumour whose gross and radiological appearance may raise the suspicion of malignancy The patients typically presented with menorrhagia or symptoms that were ultimately relatable to the presence of a pelvic mass.
Methods: Occasionally, benign tumours with a peculiar growth pattern may cause diagnostic confusion. These tumours are exophytic, multinodular with a placenta-like appearance, protruding over the uterine serosa. In most cases, the exophytic component is contiguous with the intramural dissecting leiomyomatous components. A fifty-six year old female was admitted to our gynaecology department with menorrhagia and undergone surgery for a pelvic mass
Results: On gross examination a fleshy polypoid tumour mass was observed with soft consistency, irregular borders which was attached to the fundus of the uterus with a large stalk. Cut surface demonstrated focal cystic degeneration and bulbous multinodularity. Adnexes were found to be grossly normal. Histological examination revealed a neoplasm consisting of spindle cell nodules with some areas of hydropic degeneration and hyalinization. Cellularity was variable through the tumour areas and nuclear atypia or mitotic activity was absent. Vascular structures with perivascular sclerotic areas were identified in the tumour stroma but vascular invasion or necrosis was not observed. Tumour cells were positive for vimentin, desmin and smooth muscle actin.
Conclusion: Cotyledonoid leiomyomas may be mistaken for placental site nodules or other types of tumours with a similar appearance. Additionally, because cotyledonoid leiomyomas are rare, they may not be immediately recognized by healthcare providers who are less familiar with this type of tumour. However, with the use of advanced imaging techniques such as ultrasound, MRI, and histopathological examination it is usually possible to distinguish cotyledonoid leiomyomas from other types of uterine tumours.

E-PS-10-021
Tumour-infiltrating immune cells as a predictive factor in advanced or metastatic leiomyosarcomas: comparison between uterine and non-uterine tumours
D. Enea*, B. Archambaud, P. Pautier, A. Leary, J. Scoazec, C. Genestie
*Department of Biopathology, Gustave-Roussy Institute, Villejuif, France

Background & objectives: We described and compared the immune microenvironment in uterine (UL) and non-uterine (NUL) leiomyosarcomas and evaluated its clinical impact in a group of patients enrolled in a randomized phase III trial comparing doxorubicin to doxorubicin+trabectedin as first-line-therapy in advanced/metastatic tumours.
Methods: The study group contained 53 UL and 63 NUL. By multiplex immunohistochemistry, we assessed the percentage of CD3+, CD20+, CD68+, and CD57+ immune cells, both in stroma and tumour. TILMs (lymphocytes + macrophages) were defined as the percentage of stromal area occupied by immune cells. p53 expression was evaluated semi-quantitatively, from 1 to 3.
Results: In both subgroups, CD68 labelled 80% of immune-cells found in contact with tumour-cells. In the stroma, CD3+ cells were more frequent (45% in NUL, 30% in UL). CD20 and CD57 stained <5% of all immune-cells.
When comparing the subgroups, high-CD3 (>27.5%) was encountered more frequently in NUL than in UL (p=0.0369). Conversely, high-CD68 (>65%) was observed mostly in UL.
Patients with high CD57 values appeared to have a better prognosis in terms of progression-free survival. Additionally, the therapy effect seemed to be more important in patients with low-p53 (30%). However, for all markers, there were no statistically significant associations with the outcomes/therapy response, regardless of group or type of treatment.
Conclusion: Several differences have been identified between UL and NUL, with regard to the tumour-infiltrating immune cells. It seems that CD3 is more expressed in NUL. High CD57 values appeared to correlate with better progression-free survival, but further investigation is needed to confirm these data. However, there is no suggestion that immune microenvironment or TILMs can be prognostic factors or predictive markers of response to therapy, be it doxorubicin alone or doxorubicin + trabectedin.

E-PS-10-022
Ureteral polypoid atypical endometriosis in a previously hysterectomised patient: a case report
I. Franin*, M. Kos, A. Demirović, D. Tomas, T. Leniček, M.S. Kirigin
*Ljudevit Jurak Department of Pathology and Cytology, Sestre milosrdnice University Hospital Centre, Zagreb, Croatia

Background & objectives: Endometriosis, according to the most recent WHO definition, is the presence of endometrial glands and stromal components outside of the uterus, whereas polypoid endometriosis is defined by exophytic growth. Endometriosis related neoplasia may occur as a result of atypical endometriosis.
Methods: An 82-year-old patient who underwent hysterectomy with salpingo-ophorectomy 20 years ago was admitted to Department of Urology, after laboratory results showed elevated creatinine. MSCT urography showed necrotic pelvic lymph node conglomerates surrounding left iliac blood vessels, causing hydronephrosis. At surgery, the tumour surrounding left ureter was found and sent for histopathological analysis.
Results: An irregular tissue sample measuring up to 8 cm in diameter was received with a 6 cm long segment of ureter. On gross examination, the tissue was multicystic with mucinous content, surrounded by some fatty tissue. Histologically, a mass of partly myxoid fibrous tissue containing cystic glands lined by one layer of columnar epithelium, and some smaller, densely packed glands with epithelium showing signs of mucinous, tubal and eosinophilic metaplasia. Immunohistochemistry epithelium showed a positive reaction to CK7, PAX8, ER, PR, CK19 and "wild type" reaction to p53. Areas with closely packed glands showed epithelial atypia. The ureter embedded into the mass showed normal structure.
Conclusion: The diagnosis was polypoid endometriosis with foci of complex endometrial hyperplasia with atypia, which is also called atypical endometriosis. The reasons for previous surgery 20 years ago are unknown (possibly endometriosis). Endometriosis can arise in the genitourinary tract, in 0.1% to 0.4% in the ureter. It is possible that the patient had endometriotic foci at the time of first surgery, and that the present condition developed during the past 20 years.

E-PS-10-023
High-grade squamous intraepithelial lesion of the cervix colonizing the endometrium: a rare case presentation
G. Galambosi*, A. Doyle, C. O'Riain, T. D'Arcy, D. O'Connor
*Coombe Hospital, Ireland

Background & objectives: Invasive squamous cell carcinoma of the cervix can extend to the endometrium and invade the myometrial wall. However, a potential diagnostic pitfall is a high grade squamous intraepithelial lesion (HSIL/CIN3) of the cervix extending into and replacing the endometrium.
Methods: We report a case of high-grade intraepithelial lesion (HSIL/CIN3) of the cervix colonizing the lower uterine segment and replacing the endometrium of a 67 year old female. The patient chart was reviewed as was the relevant histology and radiology in the preparation of this case report.

Results: A 67-year old woman attended the colposcopy clinic with a history of persistent high-risk HPV infection and repeated LLETZ (large loop excision of the transformation zone) procedures for HSIL/CIN3. In 2022 she underwent total abdominal hysterectomy as definitive treatment for residual disease of the cervix. Histological examination of the cervix revealed residual HSIL/CIN3 with extensive endocervical gland colonisation.
There was also involvement of the lower uterine segment and the endometrial cavity by strips and nests of dysplastic squamous epithelium. No true invasion was identified and following consultation with specialist colleagues, it was agreed that the lesion was best classified as in situ i.e., HSIL/CIN3 replacing the endometrium.
Conclusion: High grade squamous intraepithelial lesion (HSIL) of the cervix extending into and replacing the endometrium is a rare phenomenon, and potential diagnostic pitfall, with only occasional case reports. These lesions are best classified as in situ and do not show true evidence of invasion. Thorough sampling and microscopic examination for evidence of invasive disease is critically important in such cases.

E-PS-10-024
Uterine inflammatory myofibroblastic tumour with FN1::ROS1 gene fusion: a tumour to be known
C. Genestie*, S. Cotteret, M.A. Bani, J. Scoazec, N.I. Ben Romdhane
*Department of medical biology and pathology, Morphological pathology laboratory, Gustave Roussy Cancer Campus, Villejuif, France

Background & objectives: Most uterine inflammatory myofibroblastic tumours (IMTs) harbour ALK rearrangement. However, other gene alterations have been described. Herein, we report a case of a uterine IMT with FN1-ROS1 fusion and emphasize on the importance of extensive molecular testing in ALK-negative tumours.
Methods: A 34-year-old woman presented with menorrhagia. Endoscopic exploration found a well-circumscribed 35 mm intra-uterine lesion. The tumour was made of spindled to epithelioid cells in a myxoid stroma. A patchy expression of actin and desmin was noted. ALK was negative. Therefore, myxoid leiomyosarcoma was initially suspected. We received the specimen for second opinion, complementary immunochemistry and molecular techniques.
Results: Histologically, the tumour had suggestive morphologic features. It was made of bland spindle cells with hypercellular (fascicular/storiform) and myxoid hypocellular areas admixed with scattered lymphoplasmacytic infiltration. There was no atypia or increased mitotic figures. Tumour cells were weakly positive to actin and desmin. There was no expression of keratins, PS100, CD10, CD34 and ALK (ALK1 and D5F3 clones). No ALK-rearrangement was detected by fluorescencein situ hybridization. Interestingly, moderate and patchy cytoplasmic immunostaining for ROS1 was only noted. Targeted RNA sequencing revealed FN1-ROS1 rearrangement that fused FN1 exon 23 to ROS1 exon 34. We concluded to a IMT with a FN1::ROS1 fusion.
Conclusion: This case highlights the importance of testing for non-ALK genes in ALK-negative uterine neoplasms morphologically compatible with IMT. The absence of ALK positivity in a lesion morphologically suggestive of IMT must prompt an extensive profiling combining immunohistochemistry, fluorescence in situ hybridization and especially RNA fusion analysis. Making an accurate diagnosis is essential since such patients may benefit from targeted therapy with tyrosine kinase receptor inhibitors.

E-PS-10-025
Aggressive angiomyxoma mimicking a cervical polyp: uncommon presentation of a rare entity
T. Georgescu*, A. Georgescu, D. Cretoiu, T.G. Jaswal, M. Sajin, N. Suciu
*Department of Pathology, "Carol Davila" University of Medicine and Pharmacy Bucharest, Department of Pathology, National Institute for Mother and Child Health "Alessandrescu-Rusescu", Romania

Background & objectives: Aggressive angiomyxoma of the female genital tract is a benign, slow-growing, spindle cell neoplasm, usually encountered in perineum and vulva of reproductive age women. Cervical presentation is exceedingly rare, with only few case reports, and may pose difficult differential diagnoses.
Methods: We report the case of a 41–year-old female, who presented to our outpatient Gynaecology Department for dysuria and abdominal pain. Upon routine speculum checkup, a large polypoid mass (32/12/8 mm), tan-coloured, with wide base, apparently originating from the external cervical os. The lesion was subsequently electroresected under general anaesthesia and sent to the Pathology Department for histopathological examination.
Results: Histopathological examination revealed an incompletely excised polypoid lesion, covered by squamous epithelium and composed of bland spindle cells embedded in a loose myxoid stroma, with prominent capillary network. The differential diagnosis included a traumatized/oedematous cervical polyp, superficial angiomyxoma, deep angiomyxoma and myxoid liposarcoma. While the base of the tumour and the infiltrative character of the lesion could not be evaluated, immunohistochemical stains proved unequivocal. The lesion was diffusely positive for SMA, Desmin, CD34 and hormonal receptors (ER, PR), with a low Ki67 proliferation rate, confirming the diagnosis of aggressive angiomyxoma. The patient underwent a second intervention for complete excision and shows no signs of recurrence at 8-month follow-up.
Conclusion: In conclusion, aggressive angiomyxoma of the cervix, although benign, is an extremely rare entity, with important clinical outcome due to its prognosis and evolution. Aggressive angiomyxoma of the lower female genital tract should be entirely excised in order to minimize the recurrence rate. Although no distant metastases have been reported, local infiltrative character and characteristic immunohistochemical profile distinguishes aggressive/deep angiomyxoma from a superficial angiomyxoma or from a traumatized/ulcerated cervical polyp.

E-PS-10-026
Mesonephric-like adenocarcinoma of the ovary - an underdiagnosed entity
T. Georgescu*, A. Georgescu, A. Cernat-Stefan, M. Sajin, N. Suciu
*Department of Pathology, "Carol Davila" University of Medicine and Pharmacy Bucharest, Department of Pathology, National Institute for Mother and Child Health "Alessandrescu-Rusescu", Romania

Background & objectives: Mesonephric adenocarcinoma is a rare aggressive tumour affecting the uterine cervix or corpus. In the cervix, it develops from mesonephric remnants, which may be present deep in the cervical wall and is composed of well-differentiated glands featuring eosinophilic intraluminal secretions.
Methods: A 56-years-old female presented to our Gynaecological Department with abdominal pain. Ultrasound examination revealed a 12/8,5/7 cm solid left adnexal mass with variable echogenic areas. During surgery, the tan-grey tumour with multiple areas of necrosis was diagnosed as well-differentiated adenocarcinoma NOS on frozen section. Paraffin-embedded sections were supplemented by additional immunohistochemical stains in order to establish the final diagnosis.
Results: Histopathological examination revealed a solid proliferation of well-differentiated glandular structures with clear or pale-eosinophilic cytoplasm, elongated nuclei and intraluminal secretory material. The overall aspect was that of a well-differentiated endometrioid neoplasm without squamous differentiation and with rather frequent areas of necrosis. The tumour was diffusely positive for CK7, showed “wild-type” pattern of staining for p53 and was negative for hormone receptors as well as WT1 and p16. Additional stains showed diffuse positivity for PAX8, GATA3 and TTF1. Moreover, CD10 showed apical membranous positivity in most tumour cells and Ki67

proliferation index was 80% within hot spots. The final diagnosis was mesonephric-like adenocarcinoma of the ovary.
Conclusion: Mesonephric-like adenocarcinoma is an extremely rare occurrence in the ovary (<1% of all ovarian adenocarcinomas) and should always be considered when dealing with a well-differentiated adenocarcinoma with endometrioid morphology, which is negative for ER and PR. Additionally, clinical and imaging correlations are required in order to exclude a metastasis from the uterus, cervix or even other organs.

E-PS-10-027
An unusual synchronous tumour of the uterus: leiomyosarcoma and endometrium adenocarcinoma
F. Gundogdu*, A. Usubutun
*Hacettepe University Department of Pathology, Turkey

Background & objectives: Synchronous endometrium adenocarcinoma and other gynaecologic system tumours are rarely seen. The most common combination is endometrium and ovary adenocarcinomas. Here, we present a scarce example of synchronous leiomyosarcoma and endometrium adenocarcinoma, which can be mixed up with carcinosarcoma.
Methods: The clinical and pathological findings of the case were evaluated. A 76-year-old female was admitted to the hospital due to postmenaouposal bleeding. In the abdominal MRG, a 10x8.5 cm in diameter mass in the uterine corpus and polypoid lesions in the endometrium were seen. The patient underwent a hysterectomy and bilateral salphingoooferectomy.
Results: Macroscopically, an 11 cm-sized nodular lesion in the corpus, and a 2 cm-sized polypoid lesion in the endometrium were seen. Microscopically, a sarcomatous lesion that shows intersecting fascicular growth pattern, necrosis, increased nuclear atypia, and mitotic activity was seen spatially distinct with a well-differentiated endometrium adenocarcinoma. Immunohistochemically, the sarcomatous lesion was positive with Desmin and H-caldesmon while it was negative with PAX8 and Pan-Keratin. p53 staining pattern was "wild" type in both. So, based on these findings the diagnosis of synchronous leiomyosarcoma and endometrium adenocarcinoma was made. Endometrial adenocarcinoma showed loss of expression with the mismatch repair proteins (MMRs), MLH1, and PMS2, despite the preserved expression in the leiomyosarcoma.
Conclusion: Leiomyosarcoma and endometrium adenocarcinoma can be seen synchronously although there are only two other cases reported. Differentiating this tumour from the carcinosarcoma is really important since the patient management and outcome are different. The loss of expression of MMRs in only endometrium adenocarcinoma can be thought of as a result of epigenetic changes rather than genetic syndromes.

E-PS-10-028
Uterine tumour resembling ovarian sex-cord tumour: a diagnostic challenge
I. Hurmuz*, D. Anderco, B. Nataras, R. Barna, M. Bacila, I. Bacila, A. Dema
*Anapatmol Research Center, Victor Babes University of Medicine and Pharmacy Timisoara, Romania

Background & objectives: Uterine tumour resembling ovarian sex-cord tumour (UTROSCT) is a rare mesenchymal tumour of the uterus with uncertain biological potential. We present the clinical and pathological features of a case of UTROSCT which represented a challenge for both pathologist and gynaecologist.
Methods: A 42-years-old woman was admitted to the hospital for abnormal vaginal bleeding. A vaginal ultrasonography revealed a nodular uterine mass. Suspecting uterine leiomyoma, a hysterectomy was performed, and the tumour was diagnosed in another pathology department as low-grade endometrial stromal sarcoma. The case was sent to our department for re-evaluation. Additional slides from the paraffin blocks were immunohistochemically (IHC) stained.
Results: The gross examination of the resection specimen revealed a poorly delineated intramural nodular mass, 5/6cm, with firm consistency and yellowish colour. The microscopic examination of the tissue fragments from the described nodule showed cord, nests, trabeculae, tubules of epithelioid-looking cells with scant cytoplasm and bland nuclei, rare mitoses. Based on the morphological re-evaluation of the HE stained slides and on the IHC profile of the tumour which showed diffuse positive reaction for CKAE1/AE3, ER, PR, CD99, extended reactivity for calretinin, focal staining for CD56 and Melan A, Ki67 LI <2% and lack of reactivity for CD10, the diagnosis of UTROSCT was established.
Conclusion: UTROSCT is a very rare mesenchymal neoplasm. To our knowledge, this is the first case diagnosed in our department in the last 30 years. The correct diagnosis and management of patients with these tumours requires familiarization of the pathologist and gynaecologist with this unusual tumour and additional IHC evaluation of the lesion.

E-PS-10-029
COX2 expression in serous carcinomas of fallopian tubes
N. Hyriavenko*, K. Sikora, Y. Lyndina, R. Chyzhma, D. Tsepochko, D. Ohiienko, M. Lyndin, A. Romaniuk
*Sumy State University, Ukraine

Background & objectives: Cyclooxygenase-2 (COX2) is expressed in many types of malignant tumours and can indicate the treatment prognosis. We aimed to evaluate the expression of COX2 in serous carcinomas of fallopian tubes and its correlation with the main clinical and morphological signs.
Methods: We examined 32 samples of serous fallopian tube carcinomas. Polyclonal anti-COX2 and rabbit monoclonal Ki-67 antibodies performed an immunohistochemical assay.
Results: It was established that the expression of COX2 of varying intensity was noted in fallopian tube tumours. We detected that patients with serous fallopian tube carcinomas with COX2 had a more aggressive tumour phenotype. It depended on the degree of tumour malignancy, proliferative activity index, and lymphogenic metastasis ($p<0.05$). We found no relationship between the expression of COX2 and the clinical stage of the disease.
Conclusion: Therefore, COX2 is an independent prognostic factor in serous fallopian tube carcinomas and requires further research.

E-PS-10-030
Changes of protein sialylation in the endometrium during the hormonal cycle of women
P. Janega*, T. Kuracinova, M. Cebova, A. Janegova
*Institute of Pathological Anatomy, Comenius University in Bratislava, Medirex Group Academy, n.p.o., Nitra, Slovakia

Background & objectives: Hormonal changes can affect surface glycoconjugates in the endometrium. This study focused on examining glycoconjugate sialylation in endometrial and stromal cells during different phases of endometrium cycle, which is crucial for understanding how these changes are involved in tumour development.
Methods: This study analysed endometrial tissue samples from 100 fertile women who underwent therapeutic curettage for reasons such as infertility and irregular cycles, including those with hypersecretion endometrial changes. The samples were analysed using lectin fluorescent histochemistry with sialic acid-specific lectins and evaluated quantitatively through histomorphometry image processing methods.
Results: The endometrium mostly contains alpha-2,6 linked sialic acid. However, hormonal changes can cause significant changes in sialic

acid expression, resulting in reduced alpha-2,6 sialylation of cytoplasmic and luminal membrane bounded glycoconjugates during the early secretory phase and increased levels during the late secretory phase. In contrast, alpha-2,3 sialylation significantly increases during the early secretory phase and decreases during the late secretory phase. The study found no significant changes in stromal cell positivity during the different phases of the menstrual cycle.
Conclusion: These findings indicate that hormonal changes during the menstrual cycle can impact the sialylation patterns in endometrial and stromal cells. The discovery of a predominant presence of alpha-2,6 linked sialic acid in the endometrium and the dynamics of glycosylation is intriguing. Previous studies have linked alpha-2,6 sialylation to an increased cell adhesion to mesothelium, which may be implicated in endometriosis and metastatic processes. These glycoconjugates could potentially serve as therapeutic target, warranting further research.
Funding: BIOMEDIRES II. phase, 313011W428

E-PS-10-031
Complete hydatidiform mole with lung metastasis and coexisting alive foetus: unexpected twin pregnancy mimicking placenta accreta
H. Jung*
*Ilsan CHA medical centre, Republic of Korea

Background & objectives: Twin pregnancy with a complete hydatidiform mole and coexisting foetus (CHMCF) is an exceedingly rare condition with the incidence about one of 20,000–100,000 pregnancies. CHMCF can be detected by prenatal ultrasonography and elevated maternal serum human chorionic gonadotropin (HCG) level.
Methods: Herein, we report a case of CHMCF which was incidentally diagnosed through pathologic examination without preoperative knowledge. 41-year-old women, transferred as preterm labour, delivered a female baby by caesarean section at 28+5 weeks. Clinically, the surgeon suspected placenta accreta on surgical field, and the placental specimen was sent to pathology department.
Results: On gross examination, partial vesicular lesions were identified separately from the normal-looking placental tissue. Microscopic examination demonstrated two distinct areas of villi: 1) hydropic large villi with peripheral trophoblastic hyperplasia and cistern formation, 2) relatively small normal villi. Areas of hydropic villi had massive necrotic changes and in the viable portion, P57 immunohistochemical staining was negative for stromal cells and cytotrophoblasts. Pathologic diagnosis was CHMCF and regarding the fact that placenta accreta was originally suspected, invasive hydatidiform mole was not ruled out. After radiologic work-up, metastatic lung lesions were detected, and methotrexate was administered by six cycles every two weeks interval.
Conclusion: The last HCG level was 0.2 mIU/mL at five months after delivery and follow-up imaging confirmed no evidence of recurrence or metastasis. The preterm baby had respiratory distress syndrome but improved and was discharged with 2260gm weight after two months care of neonatal intensive care unit.
In this study, we describe the clinicopathological features of unexpected CHMCF case accompanied by extrauterine metastasis and emphasize the meticulous pathologic examination.

E-PS-10-032
Vaginal endocervicosis: a case report and the review of the literature
B. Karabulut*, G. Bilir Dilek
*Ankara Etimesgut State Hospital, Turkey

Background & objectives: Endocervicosis is an uncommon form of müllerianosis. While it has been described at several locations, mostly bladder, there are three reports about vaginal endocervicosis. As it's rarity and possible relationship of malignancy, our case will supply information to the literature.
Methods: A 41-year-old multiparous woman having a history of perineal laceration went under surgery for repair. Gynaecologist observed a 1,5 cm diameter mass in the right inferior part of vagina. No history of pelvic operation. Histologically, there were mucinous glands which lined a single layer of endocervical type cells. There was not any atypia, mitotic activity, and epithelial layer on surface.
Results: Vaginal endocervicosis is the presence of benign glands lined by mucin-secreting endocervical-type epithelium in deep stroma of vagina. Implantation, and metaplastic theories are the most acceptable theories which explain the aetiology of endocervicosis. Implantation theory suggests that a history pelvic operation can be the cause of endocervicosis. Metaplastic theory is the transformation of the previously existing müllerian tissue into tubal, endometrial, or endocervical epithelium with metaplasia. Endocervicosis can also occur because of dysfunctions of genes that encode positional information during organogenesis. Although endocervicosis is described as a nonneoplastic lesion, there're case reports that show its association with malignancy.
Conclusion: Vagina is one of the rarest locations of endocervicosis can be seen. Initially, endocervicosis was concerned as a nonneoplastic lesion, two of three published vaginal endocervicosis cases have malignant transformation. Therefore, endocervicosis holds the possibly of malignant transformation. Even though it is an uncommon lesion in vagina, due to the possible malignancy risk endocervicosis becomes important entity.

E-PS-10-033
Pilomatrix-like high grade endometrioid carcinoma of the ovary – extra-ovarian disease at diagnosis but with positive short term oncologic outcomes
S. Khan*, J. Xu, P. Weisman, A. Karnezis, K.J. Park, A. Hodgson
*University of Toronto, Canada

Background & objectives: Pilomatrix-like high grade endometrial endometrioid carcinomas have been recently described and recent literature has also documented an identical neoplastic phenomenon occurring in the ovary. Herein, we present the clinicopathologic details of 2 cases of this apparently rare ovarian tumour.
Methods: Cases that fit the following criteria were identified from the files of the authors: a) primary ovarian high-grade tumour (+/- adjacent/associated low grade endometrioid component) composed of solid nests of basaloid cells with associated geographic necrosis and ghost cells, b) lack of PAX8/hormone receptor expression, and c) evidence of nuclear/cytoplasmic β-catenin expression and positivity for CDX2.
Results: The patients were 51 (patient 1) and 60 (patient 2) years of age at diagnosis and both presented with abdominal pain with subsequent radiological identification of left-sided adnexal masses (as well as lymphadenopathy and peritoneal thickening in patient 1). Both patients underwent upfront surgical resection, and the final FIGO 2018 stage was IIIA1(i) and IIA, respectively; both were subsequently treated with 6 cycles of paclitaxel/carboplatin chemotherapy. Patient 1 also had an endometrial-confined FIGO grade 1 endometrioid adenocarcinoma while patient 2 had atypical endometriosis identified in the contralateral ovary. Patient 1 is alive without disease at 15 months and patient 2 passed away 39 months after diagnosis due to COVID-19-related pneumonia.
Conclusion: Pilomatrix-like high grade endometrioid carcinomas of the ovary morphologically and immunohistochemically resemble their counterpart in the endometrium. An identifiable low-grade component may not be evident, possibly causing diagnostic confusion. These tumours may be under-recognized but are likely quite rare. Identification of additional cases and longer follow up periods will yield further information regarding their overall clinical behaviour; here, neither tumour caused patient death.

E-PS-10-034
Uterine tumour resembling ovarian sex-cord tumour: a rare and challenging entity
M. Khmou*

*National Institute of Oncology, Morocco

Background & objectives: Uterine tumour resembling ovarian sex-cord tumour (UTROSCT) is a rare tumour characterized by morphological patterns resembling those in ovarian sex-cord tumours, without an endometrial stroma component. Diagnosis of UTROSCT can be challenging, in order rule out other common uterine lesions.
Methods: We report the case of a 65-year-old post-menopausal female that presented with irregular uterine bleeding and pelvic pain. Ultrasonography and MRI revealed a heterogenous mass measuring 4,8x4cm, located in the lumen and infiltrating partially the uterine wall. An endometroid carcinoma was suggested in front of the clinical and radiological presentation and the patient underwent non conservative hysterectomy with bilateral annexectomy.
Results: Macroscopic examination revealed a whitish, polypoid intracavitary mass. Microscopic analysis showed a proliferation of tumour cells organized in sheets, cords and trabeculae. Neoplastic cells were small, round with a scant eosinophilic cytoplasm and nuclei with minimal atypia. This neoplasm seemed to infiltrate less than 50% of the myometrial thickness.
Immunohistochemically, the tumour cells showed focal positive staining for Alpha-inhibin, CD10 and Melan A, a diffuse positive staining for calretinin, desmin and CK AE1/AE3, while cyclin D1, Synaptophysin and WT1 were all negative. Given all those morphological and immunohistochemical criteria, the diagnosis of UTROSCT was confirmed. The patient did not receive any adjuvant therapy, with no evidence of recurrence during follow-up.
Conclusion: Although rare, it is essential to considered UTROSCT in the differential diagnosis of uterine neoplasms, such as endometrial stromal tumours with sex cord-like elements, epithelioid leiomyosarcoma, adenosarcoma, sertoliform endometrioid carcinoma, corded and hyalinized endometrioid carcinoma, and mesonephric-like adenocarcinoma. Those tumours mostly harbour different molecular abnormalities with different prognoses.

E-PS-10-035
Myometrial myxoidosis; a rare case report
E. Kilic Bagir*, Ö. Yaprak, T. Toyran, D. Gümürdülü
*Department of Pathology, Faculty of Medicine, Cukurova University, Adana, Turkey

Background & objectives: Myometrial myxoidosis is an entity that has been described in recent years with case reports. It is a terminology that describes of non-neoplastic extracellular mucin deposition in the myometrial wall. Myxoid changes can also be seen other mesenchymal tumours.
Methods: A 28-year-old patient with complaints of abdominal swelling, abnormal uterine bleeding and menstrual irregularity; On USG, the uterus was severely enlarged and heterogeneous. Based on the radiological and physical examination findings, the patient is primarily diagnosed with leiomyoma and adenomyosis. After the control smear and endometrial biopsy were normal, the patient underwent hysterectomy and bilateral salpingectomy.
Results: In macroscopic examination of the resection specimen; uterus was 23x20x12 cm and myometrium was diffusely thickened, average thickness was 7 cm. Widespread myxoid changes were observed between the muscle fibres without forming a mass in the myometrium. hypocellular myxoid areas dissecting the smooth muscle bundles in a uterine section. Alcian blue pH 2.5 and mucicarmine stains were diffusely positive in the interstitial myxoid of the myometrium whereas a Periodic acid–Schiff (without diastase) stain was negative. immunohistochemically CD34,CD10 were focal positive and negative for desmin, S100, ALK, H-caldesmon. As a result of immunohistochemical and microscopic findings, the case was diagnosed as myometrial myxomatosis.
Conclusion: Myxoid changes in the uterus have been described in several neoplastic conditions such as leiomyomas, leiomyosarcomas, adenosarcomas, malignant peripheral nerve sheath tumours and endometrial stromal sarcomas. It has been reported that patients with myometrial myxomatosis have systemic diseases such as SLE and NF-1, which may contribute to the pathogenesis. Since it has an important place in the differential diagnosis of myxoid neoplasms of the uterus, the presence of this entity should not be forgotten by pathologists.

E-PS-10-036
Copy number does not differ in HER2 amplified endometrial cancer to breast cancer
M. Kinloch*, H. Li
*University of Saskatchewan, Canada

Background & objectives: HER2 amplification exists in Endometrial Cancer (EC) and Breast Cancer (BC). However, the mechanism of amplification [LH1]differs, and no quantitative comparisons have been reported. We aim to investigate if differences exist in HER2 Copy Number between EC and BC.
Methods: HER2 CNV was [LH1]quantified via in-situ hybridization (ISH). Each ISH was scored by 2 independent reviewers. HER2 was considered amplified if the average number of HER2 copies per cell exceeded 4.0 and the ratio of HER2 to Chr17 exceeded 2.0. HER2 copy number and ratio was compared between EC and breast cancer.
Results: We reviewed 55 EC and 242 BC cases. The average HER2 copy number of all cases was 3.09 for EnCa and 2.87 for breast cancer ($p = 0.21$). Of these, 20% (11; 7 HER2 IHC 3+, 4 HER2 2+) EC and 8.3% (20; all HER2 2+) BC were HER2 amplified. In the HER2 amplified population, the average HER2 copy number was 6.21 vs. 6.83 for EC and BC ($p = 0.22$). The HER2/Chr17 ratio for EC and BC was 3.27 and 3.09 respectively ($p = 0.33$). The Human Protein Atlas HER2 mRNA expression data showed HER2 expression of 25.2 nTPM vs 56.0 nTPM for EC and BC respectively.
Conclusion: We show, at the DNA level, there is no significant difference in HER2 copy number in amplified EC and BC. This study does not consider differences in HER2 at gene expression levels that may exist downstream of DNA, which may be important in EC where factors such as TP53 have been shown to affect HER2 expression. Looking ahead to refining companion diagnostics, it may be more accurate to measure EC HER2 mRNA to better correlate with response to anti-HER2 therapy.

E-PS-10-037
Incidence and clinicopathological features of mismatch repair deficient (MMR-d) endometrioid type endometrial adenocarcinomas: a tertiary single-centre data from Turkey
K. Kurt*, A. Orgen Calli, A. Akder Sari
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Mismatch repair immunohistochemistry (MMR-IHC) is suggested for all newly diagnosed endometrioid-type endometrial adenocarcinomas (EECs). This study aims to evaluate the incidence of MMR-deficient (MMR-d) endometrial carcinomas and clinicopathological features.
Methods: A total of 30 cases diagnosed as pure EECs of the uterus between February 2020 – March 2023 were included in the study. All cases were stained immunohistochemically for MLH1, MSH2, PMS2, and MSH6. All the data were recorded from the database including MMR-IHC results.
Results: The mean age of patients was 61 years (min35-max74). MMR-d tumours constituted 37% (n=11/30) of all ECs. Loss of MLH1 and PMS2 proteins was the most common, compromising %73 (n=8) of MMR-d cases. There were 2 MSH6-deficient cases (18%) and one case had a loss of three proteins (9%), MLH2, PMS2, and MSH6. No MSH2-deficient case was present. No statistically significant relationships were found between any of the clinicopathological parameters and the MMR status of tumours. However, the rate of grade 1 tumours

was approximately twice as high in MMR-intact (n=12/19, %63,2) than in the MMR-d cases (n=4/11, 36,6%).
Conclusion: According to our single-centre data in the Turkish population, the ratio of MMR-d cases among EECs seems to be in line with the literature. There were no statistically significant clinicopathological differences in MMR-d and MMR-intact tumours. The number of patients in our study is small, we believe that once reflex testing is implemented in all centres in Turkey, more accurate data will be available. In our clinic, this is a preliminary study of incidence and statistics of MMR-d endometrioid-type adenocarcinomas.

E-PS-10-038
Immunohistochemical expression of CD47 and its potential role in endometrial carcinoma
M. Lambropoulou*, V. Papadatou, S. Polychronidou, S. Tologkos, C. Alexiadi, T. Deftereou, T. Alexiadis, C. Nikolaidou, V. Lampropoulou, G. Tripsianis
*Histology-Embryology Lab., Medical Department, Democritus University of Thrace, Alexadroupolis, Greece

Background & objectives: CD47 is a transmembrane protein expressed in various cells, that binds with SIRPa ligand of macrophages workings as a "don't eat me" signal. CD47 is overexpressed in many malignancies. We aimed to evaluate its correlation with endometrial carcinoma.
Methods: Forty-two (42) paraffin-embedded endometrial tissues were studied. Thirty-two (32) of them were endometrial cancer samples (study group) and the other 10 (control group) came from total hysterectomies without malignancies. CD47 expression was studied via indirect immunohistochemistry using a monoclonal anti-CD47 antibody. The expression was then statistically correlated with variant clinicohistopathological parameters.
Results: Our results showed that CD47 expression was more positive in patients' tissues compared to controls' ($p<0.001$). The association of CD47 expression with clinicopathological parameters revealed that higher CD47 expression was associated with ages older than 60 ($p<0.001$), invasive carcinomas ($p<0.001$), moderate or poor differentiation ($p<0.001$) and advanced stages ($p<0.001$). Patients with moderate or high CD47 expression were more likely to die of cancer compared to those with negative or low CD47 expression (94.4% vs 0%, $p<0.001$). Multivariate logistic regression analysis revealed that higher age ($p=0.049$) and invasive carcinomas ($p=0.009$) remained the two independent determinants for moderate or high CD47 expression in women with endometrial carcinoma.
Conclusion: Our research demonstrated a clear correlation between the overexpression of CD47 in endometrial malignancies and worse clinical and histological parameters.
Our results indicate that CD47 overexpression can provide the tumour with resistance to phagocytosis. However, more studies are needed to establish these results, as CD47 seems a useful prognostic factor as well as a predictive therapeutic target for patients with endometrial carcinoma.

E-PS-10-039
Pure uterine lipoma – case report of a rare benign entity presenting as a fast-growing tumour
Ž. Ledinek*, B. Ninković Krstonošić, T. Bujas
*Department of Pathology, University Medical Centre Maribor, Slovenia

Background & objectives: Pure uterine lipoma is a rare subtype of the lipomatous tumours of the uterus that include lipofibroma, angiomyolipoma, liposarcoma and others. There are few reported cases, all occurring in postmenopausal women presenting with abdominal mass, abdominal pain, or postmenopausal bleeding.
Methods: We present a case of a 74-years old woman with a fast-growing tumour of the uterine corpus which recently increased in size. Due to the patient's medical history of postmenopausal bleeding and her family history of cancer, laparoscopically assisted vaginal hysterectomy with bilateral adnexectomy was performed. Only gynaecologic ultrasound but no other imaging was done preoperatively.
Results: Gross examination of hysterectomy specimen revealed submucosal, well circumscribed, completely encapsulated mass of fatty tissue without solid areas, measuring 6,4 cm in its greatest dimension. Microscopically the tumour was composed of islands of mature adipocytes intersected by thin fibrous septa with no elements of atypia. No additional immunohistochemical methods were necessary to define the lesion as a pure uterine lipoma. Histological examination of the uterine corpus also showed atrophic endometrium with foci of endometrial glandular hyperplasia without atypia.
Conclusion: Pure uterine lipomas are extremely rare with an estimated incidence of 0,2–0,03% and this is the first documented case in Slovenian population. Little is known of their origin and tumorigenesis. Since they are benign and can be diagnosed on an MRI or CT scan, it is important to consider conservative management for women with no significant symptoms to prevent unnecessary surgery. They can coexist with other, also malignant conditions or cause alarming symptoms, and are therefore often surgically removed anyways.

E-PS-10-040
Metastatic low-grade endometrial stromal sarcoma initially presenting as a shoulder lump
W. Lee*, Y.M. Lee
*Dankook university college of medicine, Republic of Korea

Background & objectives: Low-grade endometrial stromal sarcoma is a relatively indolent sarcoma. It is characterized by frequent, late and slow-growing tumour recurrences. The tumour relapse is common in the pelvis, followed by abdomen, vagina, lung, liver, heart and bone.
Methods: A 79-year-old female patient was transferred from an outside clinic for a management of a recurrent shoulder lump. Six months ago, the patient underwent an excision of a shoulder lump at the outside clinic that has been recurred recently. The patient's past medical history was unremarkable except for a gastrectomy due to early gastric cancer 20 years ago.
Results: MR shoulder revealed a 5 cm-sized lobulated mass at the subcutaneous tissue of right shoulder. The patient underwent a wide re-excision of the mass. Macroscopically, a multinodular fish-flesh soft mass was noted at the subcutis and dermis. Microscopically, the mass showed a sheet of monotonous short-spindle cells with scant cytoplasm and frequent mitotic figures. The vasculature was distinctive and comprised of thin arteriole-sized vessels. Immunohistochemically, tumour cells were diffusely and strongly positive for vimentin, CD10, WT-1 and caldesmon, and they were weakly positive for progesterone receptor (PR) and oestrogen receptor (ER). A diagnosis of metastatic low-grade endometrial stromal sarcoma was made.
Conclusion: In conclusion, we reports a rare case of metastatic low-grade endometrial stromal sarcoma that initially presented as a solitary shoulder lump without a previous history of intrauterine tumour.

E-PS-10-041
Features of COX2 expression in endometrial carcinomas
M. Lyndin*, O. Kravtsova, K. Sikora, Y. Bova, Y. Sikora, Y. Lyndina, N. Hyriavenko, A. Romaniuk
*Sumy State University, Ukraine

Background & objectives: Uterine corpus cancer is a highly prevalent gynaecologic malignancy, with endometrial cancers (EC) accounting for approximately 90% of cases. The prognosis of EC is determined by the histological type of carcinoma, the qualitative characteristics of the neoplastic cells and stroma.
Methods: The investigation was conducted on 50 cases of EC, including 30 cases of endometrioid endometrial carcinomas (EEC), 10

cases of serous endometrial carcinomas (SEC), and 10 cases of clear-cell endometrial carcinomas (CCEC). The expression of COX2 was detected by immunohistochemistry using rabbit polyclonal anti-COX2 antibodies from Diagnostic Biosystems (Pleasanton, CA, USA).
Results: The EC tissue exhibited variable membranous-cytoplasmic expression of COX2, which did not differ significantly between its histological types (p=0.15). It is important to note that high-grade EC showed only moderate to strong expression of COX2, which differed significantly from low-grade EC where expression varied from weak to moderate to strong (p=0.0054). In grade 1 EEC, COX2 was mainly localized in the apical part of the cytoplasm. In EEC tissue with solid growth and grade 3 nuclear atypia, as well as in SEC and CCEC tumour cells, COX2 was detected around the perimeter of the cytoplasm and membrane.
Conclusion: The levels of COX2 in EC tissue are higher compared to the normal endometrium, and this elevation depends on the histological features and differentiation of the tumour. This can serve as an indicator of neoplastic transformation of endometrial cells and the progression of carcinomas. The availability of selective COX2 inhibitors and preliminary data on their effectiveness in some carcinomas suggest that it may be a promising adjunct in the treatment of EC.

E-PS-10-042
Features of ER and COX2 expression in endometrial polyps
Y. Lyndina*, N. Tsyndrenko, N. Hyriavenko, K. Sikora, O. Romaniuk, Y. Sikora, M. Lyndin, A. Romaniuk
*Sumy State University, Ukraine

Background & objectives: Endometrial polyps (EPs) are a variant manifestation of endometrial hyperplastic processes that can progress to endometrial cancer. The rate of malignancy depends on the morphological characteristics (presence or absence of nuclear atypia) and immunohistochemical features of the endometrial epithelium.
Methods: The research was conducted on samples of EPs obtained after surgical treatment (hysteroresectoscopy) at the Sumy Regional Clinical Oncology Dispensary (Sumy, Ukraine). The expression of proteins was detected using immunohistochemistry with rabbit polyclonal anti-COX2 antibodies from Diagnostic Biosystems and rabbit monoclonal antibodies against ER (clone SP1). Data processing was performed using SPSS Statistics 29.0 for Windows.
Results: The expression of ER and COX2 was detected in all of the studied samples. The glandular EPs showed strong expression of ER in 86% and median expression in 14%. In glandular-fibrous EPs, ER expression was strong in 72% and median in 28%. COX2 expression was mainly found in the apical part of the cytoplasm of the prismatic epithelium. We did not find a statistically difference in the expression of COX2 and ER between the two groups of tissues (p>0.05). However, their expression significantly exceeded the indicators of intact endometrial tissue. A direct correlation was found between the expression of COX2 and ER in the epithelium of the endometrial glands (p<0.05).
Conclusion: The tissue of endometrial polyps is characterized by variability in the expression of ER and COX2. The direct correlation between ER and COX2 in the endometrial epithelium may indicate their synergistic involvement in the initiation and progression of endometrial hyperplastic processes and possible involvement in subsequent tumour transformation. The results of immunohistochemical studies of ER and COX2 expression can serve as criteria for a differentiated approach in choosing treatment strategies.

E-PS-10-043
Immunohistochemical evaluation of microsatellite instability in endometrial cancers and its relationship with clinicopathological variables
B. Malkoc*, B. Dogan Gun
*Ardahan State Hospital Pathology Division, Turkey

Background & objectives: Endometrial cancer is the most common invasive cancer of the female genital tract. In this study, we aimed to analyse the microsatellite instability of the endometrial cancer materials, by applying immunohistochemistry method and their relationship with clinicopathologic features are investigated.
Methods: Tumour materials of 140 patients who were diagnosed with endometrial cancer were included in the study of which were all total abdominal hysterectomy materials extracted between 2016 and 2021 in Zonguldak city. We chose to use the immunohistochemical evaluation of MMR genes, which is also the most cost-effective method for this study and we're experienced in colon cancers before.
Results: 73,6% were found to be MSS and %26,4% were found to be MSI. A significant statistical relationship was found between FIGO grade and the comparison between the MSI and MSS groups (p=0,03). A significant difference in the MSI group(48.6%), and the MSS group(29,1%) was related to the MSI condition. There was no significant statistical relationship between TILs score and MSI and MSS status (p=0,928). However, in the group of where TILs score was 1 or more, the rate of MSI was greater. Even though, this finding doesn't carry a statistical significance, a strong clinical relationship could be proven with more detailed survival analysis on larger patient groups in future studies.
Conclusion: According to the findings in our study, there is a significant statistical relationship between the FIGO grade and MSI status (p=0,03). We believe that using the most practical and easily accessible immunohistochemistry method to analyse the MMR gene expressions in those patients who were diagnosed with endometrial cancer, could become one of the current protocols for the diagnosis and treatment of the cancer and the post-operative management of the patients in gynaecological oncology daily practice.

E-PS-10-044
Confocal microscopy in the initial evaluation of vulva biopsies. Preliminary results
L. Marimón*, S. Lopez-Prades, C. Marti, C. Miralles, L. Sisuashvili, A. Saco, M. Del Pino, N. Carreras, P. Fuste, A. Torne, J. Ordi, N. Rakislova
*Hospital Clínic, Barcelona, Spain

Background & objectives: Ex-vivo fusion confocal microscopy (FuCM) provides haematoxylin and eosin-like digital images from fresh tissue specimens minutes after sampling without wasting material. The aim of this study was to assess the usefulness of this technique in the evaluation of vulvar biopsies.
Methods: Prospective study including 35 vulvar biopsies, which were processed immediately after sampling (10", 70º alcohol and 20" acridine orange) and scanned using a VivaScope 2500-G4 device. After scanning, the specimens were routinely processed for conventional microscopy. FuCM images were evaluated by a pathologist. This diagnosis was compared with the diagnosis of the routinely processed biopsies blindly evaluated by another pathologist.
Results: The final diagnoses were inflammatory diseases (12 biopsies); melanocytic nevus (1); condyloma acuminata (5); high-grade squamous intraepithelial lesion/vulvar intraepithelial neoplasia (HSIL/VIN, 12) and squamous cell carcinoma (5). The agreement between FuCM and final diagnosis was complete in 24/35 biopsies (69%: 9/12 inflammatory diseases; 0/5 condylomas; 0/1 nevus; 10/12 HSIL/VIN and 5/5 carcinomas). FuCM mistakes were due to technical problems (difficult orientation with absence of epithelium in the FuCM image, 3 cases) and misdiagnosis due to limited experience (3 cases), or absence of immunohistochemical support (5 cases). The accuracy of FuCM evaluation increased from 9/17 (53%) in the first set of biopsies to 15/18 (83%) in the second set (p=0.07).
Conclusion: FuCM is a promising tool that allows providing histological information a few minutes after sampling without altering the tissue

for eventual immunohistochemical and/or molecular analyses. The technique can be useful for clinical and research purposes. However, a period of adaptation to the method is required to allow technicians and pathologists to become familiar with the method to reach an adequate diagnostic accuracy. After this training period, the agreement between FuCM and conventional microscopy diagnoses may be as high as 83%.

E-PS-10-045

Uterine cervix blue nevus: a 10 years study from a spanish hospital

S.J. Marín Asensio*, O. García-Galvis, M.G. Rodríguez Guevara, J. Alzoghby-Abi-Chaker, C.J. Martinez Martinez, S. Sáez-Álvarez
*Complejo Asistencial Universitario de León, Spain

Background & objectives: The gynaecological mucosal blue nevus is a rare lesion, usually referred as analogous of the cutaneous blue nevus. Usually is an incidental diagnosis and has been described as a benign macular or papular lesion with a characteristic dark-blue pigmentation.
Methods: We reviewed our institution diagnosis on cervical specimens since 2013, including conization and hysterectomies, showing 5 cases of CBN. The average age of the patients was 54, the most frequent surgical intervention was hysterectomy (4/5) and in every one of our cases the diagnosis was an incidental finding.
Results: Microscopically we could see dendritic or spindle cells with elongated nuclei and cytoplasms with intense melanin pigmentation, immersed in a stroma with variable desmoplasia. The lesions were mainly in the superficial endocervical channel, subendothelial.
No mitosis or atypia were observed.
Conclusion: CBN is a rare entity that offers no special diagnosis difficulty, but we should be aware of it in case of a pigmented lesion that appears on cervical channel or exocervix. The diagnosis is usually done on HE stains alone but ancillary techniques such as Perls or S100 or others melanocytic markers would be helpful in some cases.

E-PS-10-046

A case of unilateral ovarian splenosis seen after domestic abuse

L.D. Micoogullari*, A. Orgen Calli
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Ectopic splenic tissue seen throughout the body may represent a case of accessory spleen, splenosis or splenogonadal fusion. In this case, a solitary ovarian mass in a 42-year-old female diagnosed as ovarian splenosis is presented.
Methods: Intraoperative consultation was requested for a bilateral salpingo-oopherectomy specimen. Gross examination revealed a left adnexial specimen consisted of a hydropic tuba and an ovary of 8x4x3 cm in size. Cut-surface of the ovary showed a well-demarcated, solid mass with hemorrhagia. Paraffin-embedded tissue sections of this specimen were evaluated for the histopathological characteristics. Demographic, clinical, and imaging data were collected.
Results: A 42-year-old female admitted to emergency service with pain at the bilateral iliac regions. She underwent left hemicolectomy and splenectomy due to domestic abuse -stabbing incidence- 4 years ago. To rule-out any abdominal emergencies computed tomography (CT) was obtained. CT revealed a solitary mass with both cystic and solid components at the left ovary. Intraoperative consultation was requested for the left ovarian mass since it's nature could not be cleared out. Histopathological examination showed typical red and white pulp with lymphatic follicles and penicillary arterioles consistent with splenic tissue. Due to the history of splenectomy and the location of lesion diagnosis of "unilateral ovarian splenosis" was rendered.
Conclusion: Ovarian splenosis usually presents as a component of extensive pelvic splenosis. Thus, a solitary ovarian splenosis may mimic an abdominal or ovarian tumour. In our case, the localization and the previous history of being stabbed and undergoing splenectomy could explain auto-transplantation of splenic cells. To conclude, solitary ovarian splenosis is a rare lesion which can cause diagnostic problems. In the literature, apart from our case, there are only 8 cases of ovarian splenosis reported.

E-PS-10-047

Immunohistochemical evaluation of microsatellite instability in random selected endometrial biopsies

K. Mikus Kuracinova*, V. Mihál, V. Poorova, P. Janega, M. Sekerešová
*Institute of Pathological Anatomy, Medical faculty, Comenius University, Slovakia

Background & objectives: In our retrospective study, we immunohistochemically analysed the expression of MMR proteins in randomly selected endometrial biopsies. Immunohistochemistry is a useful and simple form of testing for Lynch syndrome, a widely available method, unlike genetic testing for germline mutations.
Methods: We evaluated biopsy material taken from curettage or uterine resections with the histological results of endometrioid intraepithelial neoplasia or endometrial cancer followed by immunohistochemical staining for MMR gene protein expression. Immunohistochemically positive staining is defined as the clear nuclear expression and loss of protein expression is the complete absence of nuclear staining in tumour cells.
Results: In our series, we evaluate biopsy material from 46 patients consisting of curettage (16 samples) or uterine resections (30 samples). Based on the diagnostic criteria and immunohistochemical evaluation, our analysis showed a loss of one or more MMR proteins was present in 24% of cases, so in 10 patients. Loss of MLH1 expression was predominant (in 17 % of cases), and MSH2 and PMS2 expression was absent in 13 % of all cases. According to our findings, the prevalence of Lynch syndrome is relatively high, although we acknowledge that it would need a larger statistical sample.
Conclusion: Immunohistochemistry can be performed to detect MMR proteins with the same accuracy on curettage or hysterectomy biopsy samples in use to screen Lynch syndrome and is increasingly used to screen patients with suspected Lynch syndrome. We assume, that routine immunohistochemical testing of each uterine biopsy for MMR proteins may be the gold standard, as in colorectal cancer, and it can lead to earlier detection of patients with Lynch syndrome and identification of genetic mutations.
Funding: (BIOMEDIRES – II. phase, ITMS: 313011W428)

E-PS-10-048

Non-syndromic sex cord tumour with annular tubules: two cases of a rare entity

C. Mora*, F. Cunha
*Serviço de Anatomia Patológica, Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisbon, Portugal

Background & objectives: Sex Cord Tumour with Annular Tubules (SCTAT) is a rare type of ovarian tumour. Although associated with Peutz-Jegher Syndrome in a third of cases, non-syndromic cases should be suspected when unilateral, and usually has an excellent prognosis after surgical resection.
Methods: Herein, we report the clinicopathological features of two cases of sex cord tumours with annular tubules, non-related to Peutz-Jeghers syndrome, along with a brief review of the literature. Case 1 refers to a 31-year old woman with a right adnexal mass, and case 2 to a 34-year old with a left ovary mass, both presenting with abdominal pain.
Results: An anexectomy was performed after scans demonstrated unilateral ovary-confined disease, along with lymphadenectomy in the second case. Grossly, tumours were 15cm and 28cm, with yellow solid and cystic areas, intact capsule, and fallopian tube was unaltered. Microscopically, they were composed of rounded nests with complex tubules, encircling a hyaline material, without calcifications. The cells had round nuclei with

an antipodal distribution, pale cytoplasm and expressed calretinin, WT1, inhibin and CD56. There was no cytological atypia. No lymph node metastasis were identified. Neither had Peutz-Jeghers manifestations, and genetic study, when performed, was unremarkable. Both patients are alive and disease-free for 3 years and 6 months, respectively.
Conclusion: SCTAT is a rare low-grade malignancy often found incidentally or presenting with unspecific abdominal pain. Awareness for this entity in female population without Peutz-Jeghers syndrome , along with the recognition of its morphological and immunophenotypical features, are essential to confirm the diagnosis. As in syndromic cases, an excellent prognosis is described.

E-PS-10-049
Lymphovascular invasion plays a pivotal role in Endometrial cancer prognosis
E. O'regan*, Z. Greally, P. Lewitowicz, O. Adamczyk-Gruszka, A. Horecka-Lewitowicz
*Collegium Medicum Jan Kochanowski, Kielce, Poland

Background & objectives: The morbidity and mortality associated with endometrial cancer (EC) has increased in past decades despite diagnostic progress. We aim to analyse a vast panel of genes on their potential involvement in the genesis of endometrial cancer in the Polish Population.
Methods: A total of one hundred and three white female patients with confirmed EC were enrolled in the study. To align tumour staging each patient case was re-diagnosed according to the Eight Edition of the TNM Classification and the recent ESMO Clinical practice guidelines for diagnosis, Treatment and follow-up. All participants underwent surgical treatment without previous radio-chemotherapy to conduct a credible comparative analysis.
Results: LVI had the strongest impact on OS. With regards to a correlation between LVI and targeted gene panel the mutations are as follows. PTEN 49%,PIK3CA 35%,KRAS 25%, TP53%, FGFR-2 14%, CTNNB1 12%, FBXW7 9%, ATM 1%, ALK1% and APC1%. Lymphovascular invasion was more commonly observed in TP53 mutated tumours (R=0.3138,p=0.009). This was most often seen with EMT.
The opposite results were seen in FGFR-2 mutation.
Our results unanimously confirm, that the EMT features are useful for prediction but only LVI reached the predictive validity in the multivariant Cox model. The approach to explain the LVI mechanism led us to TP53 pathway, However the FGFR2 mutation in this field is unclear.
Conclusion: Our Study confirmed EMT would be a reliable biomarker for the prediction of EC outcomes. FGFR-2 mutation could contribute to EMT and indirectly worsen it.FGFR-2 plays an important role in cancer progress even if via epithelial-mesenchymal transition. It seems that the original TCGA rules should be replaced with new ones. Future plans are for a control group and analysis of POLE gene. This involved long-term observation use of modern genetic testing methods. Our Results show other driving mutations to compare with the recommended panel.

E-PS-10-050
Malignant transformation of mature cystic teratoma into strumal carcinoid - a rare case report
N. Oza*, V. Salunke, S. Vidhale, H. D'Souza, S. Kane
*HISTOPIA LAB, India

Background & objectives: Malignant transformation of mature cystic teratoma (MCT) is an infrequent, often asymptomatic event with a risk of transformation between 0.17– 2%. Ovarian carcinoids comprise approximately 0.1% of primary ovarian tumours. It's an admixture of struma ovarii with a carcinoid component.
Methods: We report a case of a 34-year-old female patient with an incidentally detected right adnexal mass on scan who was subjected to excision with a frozen section. This was further followed by a total hysterectomy with bilateral pelvic nodal dissection and omentectomy. The lesional ovarian tissue was further characterized with immunohistochemical markers.
Results: The well-encapsulated right adnexal lesion measured 9x6x2 cm which on opening showed a multiloculated cyst and focal brown nodule measuring 1 cm. The frozen section revealed ovarian parenchyma involved by malignant neoplasm and struma ovarii. Paraffin sections revealed mature cystic teratoma with a predominance of Struma Ovarii with infiltrative tumour cells arranged in nests, cords, and trabeculae patterns. By immunohistochemistry, infiltrative tumour expressed positivity for Synaptophysin, Chromogranin, and Cytokeratin; while benign thyroid tissue showed positivity for PAX8, TTF-1, and TG. Sections from the cystic component showed features of mature cystic teratoma. No other immature elements/ other malignant components were seen. Malignant transformation of mature teratoma into Strumal carcinoid was offered.
Conclusion: In view of FIGO stage IA disease, surgical resection was sufficient as treatment. The patient is being followed up every three months and is so far disease free. Thereby, despite the rarity of this lesion, the frozen section should be emphasized, and extensive sampling of ovarian solid-cystic tumours should be of utmost priority even in a benign condition such as a mature cystic teratoma, in order to exclude malignancy.

E-PS-10-051
Vulvar solitary fibrous tumour: a case report
J. Pimentel*, J. Gama, J.L. Amaral, A. Alves, C. Courelas, R. Almeida, M.A. Cipriano
*Pathology Department, Coimbra Hospital and University Centre (CHUC), Portugal

Background & objectives: Solitary fibrous tumour is a rare fibroblastic tumour, characterized by prominent staghorn vasculature and STAT6 and CD34 immunoexpression. It has been uncommonly described in female genital tract, most frequently in the vulva, where less than 40 cases have been described.
Methods: N/A
Results: We present the case of a 22-year-old female who underwent surgical removal of a 6 cm left labia mass. Histological examination showed a well-delimited, encapsulated, multinodular, and heterogeneous lesion, centred in the superficial dermis. It was composed of hypercellular and hypocellular myxoid areas with diffusely distributed thin-wall staghorn vessels throughout the lesion. The neoplastic cells had oval to irregular nuclei with finely granular chromatin, occasional nucleoli, and pale eosinophilic cytoplasm. In the more cellular areas, mitotic figures were identifiable, with 5 mitoses per 10 high-power fields. Immunohistochemistry techniques showed diffuse positivity for STAT6 and CD34. The patient was lost in the follow-up period.
Conclusion: Solitary fibrous tumours can develop in multiple locations, but are rare neoplasms in the female genital tract. It is characterized by a haphazardly distributed population of spindle cells and a staghorn vasculature pattern. STAT6 expression is an important diagnostic tool. Though a rare entity, this diagnosis must be kept in mind while dealing with spindled cell neoplasms of the lower female genital tract.

E-PS-10-052
Whole exome sequencing in relapsing and non-relapsing low-grade early-stage endometrial carcinomas
I. Ruz-Caracuel*, Á. López-Janeiro, M.E. Brizzi, V. Heredia-Soto, A. Berjón, L. Yébenes, A. Redondo, M. Mendiola, A. Peláez-García, D. Hardisson
*Pathology, Ramón y Cajal University Hospital, IRYCIS, Madrid, Spain

Background & objectives: Low grade, early-stage endometrial carcinomas are the major proportion of uterine carcinomas and altogether have an excellent prognosis. However, some patients experience

relapses. We search for genomic differences between relapsing and non-relapsing carcinomas using whole exome sequencing (WES).
Methods: Twelve carcinomas were analysed by WES, half from patients with relapse. DNA was extracted from formalin-fixed paraffin-embedded blocks. Capture was done using xGen Exome Research Panel. After alignment, variant calling and filtering was performed using VarSome Clinical v10.2. Tumour mutational burden (TMB) was calculated and KEGG cancer pathways were screened to perform an overrepresentation analysis (ORA).
Results: TMB was increased in patients with mismatch repair deficiency. One tumour had nearly double the TMB of the second highest and was found to have a pathogenic POLE mutation. Most recurrent mutated genes were PTEN (9 mutations in six patients) and ARID1A (5 mutations in four patients). ORA showed that PI3K-Akt signalling pathway accumulated the highest number of pathogenic mutations, followed by FoxO signalling, which was the most frequently mutated pathway among non-relapsing patients. Members from the Ras signalling pathway were the most recurrently mutated among relapsing patients. It was also the most differentially mutated pathway between relapsing and non-relapsing patients, followed by Wnt signalling and Hippo signalling pathway.
Conclusion: PTEN is a tumour suppressor gene that is frequently mutated in low grade, early-stage endometrial carcinomas. In these subgroups, Ras signalling pathway and CTNNB1 mutations are potential markers for identifying patients at higher risk of relapse.
Funding: This research was funded by the Instituto de Salud Carlos III (ISCIII) (PI17/01723 and PI21/00920), cofinanced by the European Development Regional Fund 'A way to achieve Europe' (FEDER).

E-PS-10-053
Confocal microscopy in the evaluation of uterine transplantation biopsies
A. Saco*, N. Rakislova, L. Marimón, N. Carreras, E. Barnadas, L. Sisuashvili, M. Rius, B. Diaz-Feijoo, F. Carmona, J. Ordi
*Hospital Clínic, Barcelona, Spain

Background & objectives: Control of rejection after uterine transplantation includes protocolized biopsies, which require urgent evaluation. Confocal microscopy (CM) allows providing histological diagnoses a few minutes after sampling. We aimed at assessing the accuracy of CM in the interpretation of transplantation biopsies.
Methods: Seventeen cervical biopsies from two uterine transplantation recipients were evaluated using CM (VivaScope 2500-G4) immediately after sampling. Following routine histological processing all biopsies underwent a second evaluation by an independent pathologist (final diagnosis, FD). The Brännström criteria were used in both evaluations. Discordances were classified as "major" or "minor" depending on the impact on management. The interobserver agreement was evaluated.
Results: The FD were: 11 no rejection, two borderline changes, one grade 1 rejection, three insufficient. Additionally, five biopsies showed a low grade squamous intraepithelial lesion (LSIL). The inter-observer agreement was complete in 82% of the biopsies (13 samples). Three of the discordances were classified as major discrepancies (two cases diagnosed as rejection, one borderline and one grade1 by CM, that were negative in the FD; one negative biopsy with CM diagnosed as borderline rejection in the FD) and one showed a minor discrepancy. LSIL was successfully diagnosed in all cases. Three out of the four (75%) discrepancies were detected in the first weeks after CM implementation.
Conclusion: Confocal microscopy has a good concordance with the conventional microscopy evaluation and can be successfully used in the assessment of control cervical biopsies from uterine transplantation recipients. The technique allows providing a diagnosis a few minutes after sampling and is an adequate option for biopsies requiring urgent evaluation, such as uterine transplantation biopsies. Nevertheless, an adaptation and learning process is recommended before relying on confocal microscopy results to avoid under or overtreatment of rejection.

E-PS-10-054
About a rare case of cervical localisation of uterine tumour resembling an ovarian sex cord tumour
G. Sahraoui*, F. Sassi, F. Ltaief, R. Doghri, A. Amara, L. Charfi, K. Mrad
*Salah Azaiez Institute, Tunisia

Background & objectives: Uterine tumour resembling an ovarian sex cord tumour (UTROSCT) is a rare histological type of endometrial stromal and related tumours according to the latest WHO classification of female genital tumours. Here, we report the third case of a cervical UTROSCT.
Methods: A 19-year-old woman presented with a history of lower abdominal pain and irregular menstrual cycles. Gynaecological examination revealed a firm mass in the cervical region. The vulva, urethra and vagina were normal. Computed tomography was performed showing a 30 mm mass arising from the cervix. A cervical lumpectomy was performed.
Results: Microscopically, the tumour exhibited nested and trabecular patterns. Tumour cells ahd abundant cytoplasm, ovoid and spindle-shaped nuclei with fine chromatin. Mitoses were <1/10 HPF. A delicate vascular network of small capillaries was observed. Immunohistochemically, the tumour cells were positive for Calretinin, AE1/AE3, Desmin, progesterone receptors, SMA and h-caldesmon, while being negative for CD10, WT1, Myo D1, HMB45, ALK, EMA, and Inhibine. Based on these observations, the diagnosis of cervical UTROSCT was made. No metastasis was detected in the omentum or lymph nodes, and the tumour was classified as stage IB according to the International Federation of Gynaecology and Obstetrics tumour staging system. The patient had an uneventful recovery after surgery.
Conclusion: This case highlights the clinical presentation, diagnostic evaluation, and management of a cervical UTROSCT in a young patient, providing significant insights into this rare condition. Early recognition and prompt surgical intervention are essential to achieve favourable outcomes.

E-PS-10-055
A rare case of superficial myofibroblastoma of the lower genital tract
E. Souka*, G. Stanc, G. Galanopoulos, C. Iavazzo, H. Trihia
*Pathology Department Metaxa Cancer Hospital, Greece

Background & objectives: Superficial myofibroblastoma of the lower female genital tract (SMFGT) is a benign mesenchymal neoplasm increasingly recognized in the vagina and less often the cervix or vulva.
We present a rare case of cervical SMFGT and short review of the literature.
Methods: A 51-year-old female with a past medical history of breast cancer and tamoxifen therapy, presented with metrorrhagia. On gynaecologic examination there was a well-circumscribed submucosal mass of the cervix, clinically consistent with a cervical fibroid. The patient underwent excisional biopsy of the mass.
On gross examination the mass was submucosal, circumscribed, solid, white-tan, 3.4 cm in greatest diameter.
Results: Microscopic examination revealed a well-circumscribed, non-encapsulated hypocellular tumour. The neoplasm was composed of bland spindle cells with vaguely fascicular growth and interspersed thick collagen bundles or lacelike pattern, in a loose oedematous stroma. There was minimal mitotic activity or necrosis. Immunohistochemical examination revealed a Desmin(+), Calponin(+), SMA(-), CD34(+), BCL-2(+), CD99(+), ER(+), phenotype.

The morphological and immunohistochemical findings were consistent with SMFGT, in association with prior tamoxifen treatment.
Conclusion: SMGT is usually located at the vulva, vagina, or cervix. It's a benign tumour and very rarely recurs after complete surgical excision.
SMFGT originates from pluripotent primitive cells but is commonly related with tamoxifen treatment.
It should be included in the differential diagnosis of more common mesenchymal cervical tumours.

E-PS-10-056
HPV-independent adenocarcinoma of the uterine endocervix of endometrioid type: a case report on a rare entity
F. Sousa Vieira*, A.P. Rodrigues, D. Sá, S. Neves, G. Carrola, J.R. Vizcaíno, N.J. Lamas
*Centro Hospitalar Universitário de Santo António, Portugal

Background & objectives: Endocervical adenocarcinoma is a malignant epithelial neoplasm arising in the cervix whose incidence has increased, especially in developed countries, accounting for up to 25% of cervical tumours. Nearly 10-15% of cases are HPV-independent.
Methods: Here, we report the case of a 74-year-old woman diagnosed with HSIL in gynaecological screening, who underwent cervical conization, having HSIL-positive surgical margins. For this reason, the patient was subsequently submitted to total hysterectomy with bilateral adnexectomy.
Results: No relevant macroscopic findings were found, but the histological analysis revealed an endocervical neoplasm forming tubular glands, in many areas replacing the cells of pre-existing endocervical glands; alternating with areas of confluent growth and with features suggestive of stromal invasion. Neoplastic cells showed high nucleus-to-cytoplasmic ratio, cytological atypia, increased mitotic activity and apoptotic bodies were identified. The neoplastic cells were immunoreactive for PAX-8, CK7, ER and PR. p16 showed a "patchy" staining, while p53 had "wild-type" expression and MMR proteins expression was preserved. The proliferative index (%Ki-67) was nearly 30-40%. Adenocarcinoma was not identified in the lower uterine segment, nor in other endometrial areas, which were fully submitted and analysed.
Conclusion: A diagnosis of primary endocervical adenocarcinoma, HPV-independent, of endometrioid type, in a background of adenocarcinoma in situ of endometrioid type was performed. This is an exceedingly rare case, which represents less than 1% of primary endocervical adenocarcinomas. This diagnosis can only be established after exclusion of endocervical extension of primary endometrial adenocarcinoma, HPV- dependent adenocarcinoma or mesonephric carcinoma. The patient remains well and without evidence of disease recurrence one year after surgery.

E-PS-10-057
Perivascular epithelioid cell tumour of broad ligament of uncertain malignant potential - a cases report
G. Stanc*, E. Souka, C. Iavazzo, O. Tzaida, C. Valavanis, H. Trihia
*Pathology Department Metaxa Cancer Hospital, Greece

Background & objectives: Perivascular epithelioid cell tumours (PEComas) are mesenchymal neoplasms composed of cells which express both melanocytic and myogenic markers. PEComas of the female genital tract account ≈25% of all PEComas in all body sites.
Methods: A 37-year-old female was referred to our hospital with an incidentally found large mass of the left broad ligament. Surgical excision was performed and a circumscribed tumour 5X4X2cm in dimensions was sent to the Pathology Department. On gross examination the tumour showed a tan to white cut surface. No areas of necrosis were recognized.
Results: The microscopic examination revealed a high cellular epithelioid neoplasm, with diffuse and nested pattern. The neoplastic cells showed abundant eosinophilic cytoplasm with mild to moderate nuclear atypia. The mitotic activity was low to absent – up to 2-3 mitoses/ 50HPF, with atypical forms. No necrosis, multinucleated giant cells or vascular invasion were present. Stromal hyalinization was recognized focally.
Immunohistochemical examination was positive for Melan A, MITF, Vimentin, ER, HHF-35, SMA and Ki-67 was positive in 5% of tumour cells. Negative immunostaining was observed for CD10, CKAE1/AE3, CK 8/18 and S-100.
A final diagnosis of perivascular epithelioid cell tumour of uncertain malignant potential was made.
Conclusion: Prognosis is favourable in the majority of PEComas and surgery is considered the first line of therapy.
A small percentage of these tumours showed recurrence years after original diagnosis and long-term surveillance is recommended.
Chemotherapy and radiation may be administered in patients with metastatic or recurrent disease. The mTOR inhibitors have shown variable results especially in the neoplasms with TFE3 fusions.

E-PS-10-058
Primary vulvar adenocarcinoma of intestinal type: report of two cases showing molecular similarity with colorectal adenocarcinoma
S. Stolnicu*, A. Palicelli, T. Maloberti, D. de Biase, A. De Leo, M. Lindh, K. Stenström Bohlin, C. Mateoiu
*Department of Pathology, UMFST Gh E Palade of Targu Mures, Romania

Background & objectives: Vulvar adenocarcinoma of intestinal type (VAIt) is uncommon. In an attempt to clarify the aetiology, clinicopathologic spectrum of this neoplasm and to inspire additional research into their biology, two more cases of VAIt are reported, including immunohistochemical and molecular analysis.
Methods: Two VAIt cases were identified and stained for immunohistochemical markers. After DNA extraction using DNA isolation, I kit on a Magnapure LC instrument (Roche Molecular, Mannheim, Germany), amplification was performed in 15 separate real-time Polymerase chain reactions, one for each of the 14 Human Papillomavirus types and one for beta-globin. Targeted Next-generation DNA sequencing was used to assess somatic mutations.
Results: Two patients of 63 years old each presented with an exophytic vulvar mass. At microscopic examination, a primary adenocarcinoma resembling a colorectal cancer, was identified in both cases. The infiltrative area displayed a glandular architecture, with glands of variable size and shape, lined by columnar to cuboidal cells with large nuclei and coarse chromatin; goblet cells were present. Based on microscopic and immunohistochemical analysis both tumours were diagnosed as HPV-independent VAIt FIGO stage 1. Both cases harboured pathogenic somatic mutation of TP53 (Case 1: p.Arg248Gln; Case 2: p.Gly266Glu). In addition, case 1 displayed pathogenic somatic mutation of KRAS (p.Gly12Asp) and case 2 showed DPYD variant (p.Glu412=/HapB3[AP1]).
Conclusion: VAIt is a rare HPV-independent tumour harbouring TP53, KRAS and DPYD mutations similar to colorectal adenocarcinomas which might indicate an increased risk for lymph node and distant metastases but also that they might be resistant to chemotherapy and might respond to anti-epidermal growth factor receptor (EGFR) antibody therapy.

E-PS-10-059
Ovarian gynandroblastoma of unusually large size in a 44-year-old woman: a case report with immunohistochemical analysis
A. Sykaras*, N. Stavrinou, F. Dolkiras, E. Spiteri, C. Magkou
*Department of Pathology, Evangelismos General Hospital, Athens, Greece

Background & objectives: Ovarian Gynandroblastoma (GAB) is an extremely rare sex cord stromal tumour consisting of both male and female components. The male element is Sertoli/Sertoli-Leydig cell

tumour (SCT-SLCT) whereas the female component consists of either juvenile or adult granulosa cell tumour (JCCT-AGCT).
Methods: A 44-year-old woman visited our hospital's emergency room due to acute abdominal pain. The patient had a well-known history of menstrual disturbances. Abdominal-pelvic Computerized Tomography scan revealed a large solid and partly cystic mass in the pelvic cavity. Due to its size and the possibility of malignancy, the patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy.
Results: The left ovary was replaced by a 38x29x15 cm partly cystic tumour. Microscopically, the tumour consisted of AGCT and SCT areas. The AGCT component was manifesting solid, alveolar, pseudopapillary and nodular growth patterns, within rich fibrous stroma, as well as Call-Exner bodies. On the other hand, the SCT component was well-differentiated consisting of tubules of clear cells with basally located nuclei. Immunohistochemically, the tumour cells of both components were positive for inhibin, calretinin, and CD56. CK8/18 was also expressed by both components, although in a dot-like manner in AGCT cells. EMA and CK7 were negative. Based on morphological and immunohistochemical features the diagnosis of a gynandroblastoma was established.
Conclusion: The present case of GAB has some atypical features. The patient is older than the average GAB patient, the neoplasm is extremely large and its histologic profile represents a relatively uncommon combination of well-differentiated SCT with AGCT. Pathologists should be aware of the atypical presentations of GAB and rely on morphological criteria. Immunohistochemical analysis can be used to confirm the sex cord stromal nature of the tumour to establish a confident diagnosis.

E-PS-10-060
Unlocking the key to surviving endometrioid carcinoma: a single-centre retrospective analysis
A.E. Teles*, F.M. Soares Nogueira, A.S. Carralas Antunes, P. Sequeira, D. Gomes Pinto
*Hospital Garcia de Orta, EPE, Portugal

Background & objectives: This study aims to assess the impact of histological parameters on patient outcomes in cases of endometrioid or mixed carcinoma with intraoperative consultation (IOC) in a single-centre setting, focusing on endometrial invasion.
Methods: We included all patients who underwent IOC for endometrial lesions at Hospital Garcia de Orta, Portugal between 2015 and 2022. Data were obtained from pathology reports and clinical files. We assessed the impact of histological criteria, including endometrial invasion, lymphadenectomy status, number of positive lymph nodes, staging, and grade, on overall survival (OS), using Kaplan-Meier curves and Mantel-Cox tests.
Results: Of the initial 85 patients, 70 remained after excluding those without endometrioid or mixed carcinoma diagnoses. The mean age was 68 years. In total, 5 patients died and 5 had recurrence or metastasis. There was a significant association ($p < 0.0001$) between locally advanced tumours (pT2 and pT3) and those with higher histological grades (G2 and G3) with reduced survival rates. Invasion ≥50% of the myometrium was associated with a higher rate of local metastases (p= 0,0026). None of the patients who died had positive lymph nodes. There was no relation between endometrial invasion and lymphadenectomy with overall survival. Lymphadenectomy status was not associated with surgical complications in our series.
Conclusion: Our analysis found that high pathological staging and histological grade are significantly associated with reduced OS in these patients. IOC enabled lymphadenectomy in patients with a higher local stage, sparing those with early malignancies. It is interesting that we did not find a correlation between lymph node metastases and OS, although that may be attributable to the small size of the series. Our findings highlight the importance of IOC, accurate staging and grading in determining both patients' prognosis and management.

E-PS-10-061
A rare encounter: anastomosing haemangioma and the ovary – case report
A.E. Teles*, F.M. Soares Nogueira, C. Dahlstedt Ferreira, P. Sequeira, D. Gomes Pinto
*Hospital Garcia de Orta, EPE, Portugal

Background & objectives: Anastomosing haemangioma of the ovary (AHO) is a rare vascular tumour that can be challenging to diagnose and can mimic other ovarian neoplasms. The purpose of this case report is to describe the histopathological features of this benign tumour.
Methods: We present a case report of a 69 years-old woman, asymptomatic, who had a history of breast cancer and had been taking tamoxifen for three months. During a pelvic ultrasound, a cystic mass was detected in her right ovary, later confirmed by MRI. As a result, she underwent a total hysterectomy with bilateral adnexectomy with subsequent pathological analysis.
Results: On gross dissection, the right ovary weighted 70g and measured 6,3x5,0x3,0cm. In section, the lesion presented a predominant cyst measuring 6,0cm, with a smooth internal wall and haemorrhagic content. The wall showed a whitish nodular area with 1,1cm which was histologically characterized by a complex network of anastomosing thin-walled vessels, layered by endothelial cells with no atypia, that form irregular channels and clefts within a fibrous stroma, without necrosis. Immunohistochemical staining for CD31 and CD34 was positive. Around this vascular lesion, there were hypertrophied stromal cell strongly immunoreactive for inhibin and calretinin. The final diagnosis was AHO associated with hyperthecosis. The remaining ovary showed a seromucinous cystadenoma with ovarian endometriosis.
Conclusion: AHO can be present without any specific symptoms or imaging features, which requires an accurate histopathologic diagnosis and must include immunohistochemical staining for vascular markers. Surgical resection is the treatment of choice, with excellent long-term prognosis. Our case report highlights the importance of considering AHO as a differential diagnosis for ovarian tumours (such as angiosarcoma or epithelial ovarian tumours with vascular differentiation), especially in older women, and emphasizes the need for close follow-up in asymptomatic patients.

E-PS-10-062
Recurrent extra-gastrointestinal stromal tumours (EGISTs) of the posterior vagina wall with liver metastasis - a cases report
C. Valavanis*, E. Souka, E. Kontis, G. Stanc
*Molecular Pathology Unit Metaxa Cancer Hospital, Greece

Background & objectives: Extra-gastrointestinal stromal tumours (EGISTs) are rare GISTs occurred outside the GI tract. Vaginal tumours account ≈1% of all gynaecological cases and are especially leiomyomas. Vaginal GISTs are extremely rare and are considered tumours originated from rectovaginal septum.
Methods: A 54-year-old female presented for vaginal bleeding. CT imaging revealed a vaginal mass and a tumour in the liver. Fragments from the vaginal tumour 4X3,5X1,2cm in dimensions were sent for examination along with a liver tumour 5,3X4,5X4,3cm in dimensions after left hepatectomy. Diagnosis of low-grade GIST from posterior vagina wall has been made 5 months ago with no treatment.
Results: Microscopic examination of both tumours (vaginal and hepatic) revealed a high-grade gastro-intestinal stromal tumour, with spindle and epithelioid cells morphology and moderate nuclear atypia.
Both tumours have high mitotic activity – 15-20 mitoses / 5mm2, no necrosis and immunohistochemically displayed DOG-1 (+), C-KIT (+), CD34 (+) and Ki-67 positivity in 30-40% of the neoplastic cells. Based on the clinical information recurrent high-grade EGIST of the vagina with metastasis in the liver was made. Genetic analysis showed c-kit mutations. Postoperative adjuvant therapy was followed.

Conclusion: Primary EGISTs are very rare and occur in the retroperitoneum, mesentery, omentum, liver, pancreas, spleen, pleura, pelvis, rectovaginal septum and vagina, with morphological and immunophetotypical features similar to GISTs. EGIST of posterior vaginal wall with liver metastasis is extremely rare. EGIST lymph node metastasis is rare, so lymph node dissection is not recommended. Postoperative adjuvant therapy (Imatinib, chemotherapy, radiotherapy) should be administered and close follow-up is recommended.

E-PS-10-063

Riluzole: a neuroprotective drug with possible antineoplastic activity in ovarian cancer?

C. Villa*, E. Duranti, C. Venturin, M. Cadamuro, M. Lavitrano
*Department of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy

Background & objectives: The glutamate release inhibitor riluzole (RIL) has been shown to reduce the course of amyotrophic lateral sclerosis. Recent research demonstrated that RIL can exert antitumor properties, but no studies have explored its effects on ovarian cancer.
Methods: OVCAR5 and OVCAR8 cell lines were treated with different concentrations of RIL (25-1000 μM) for 48 hours. MTT and wound healing assays were performed to investigate the effects of RIL on cell viability and migration, respectively. The expression of proteins linked to these molecular pathways was evaluated by Western blot analysis.
Results: No differences in cell viability were found for both cell types after RIL treatment at different concentrations (25, 50, 100, 200, 400, 700 and 1000 μM) for 48 hours. As a result, no changes in cleaved caspase-3 levels were observed. Conversely, wound healing assays revealed that 48h treatment with RIL (50 or 100 μM) significantly reduces cell motility of both OVCAR5 and OVCAR8 to untreated controls ($p < 0.05$). The migration of both cell lines was reduced by more than 30% when compared to the untreated groups.
Conclusion: Our preliminary findings suggested that RIL has no effect on cell viability but can significantly slow migration capacity in in the ovarian cancer cell lines OVCAR5 and OVCAR8. However, a more extended research is required to validate our conclusions and to further investigate the molecular targets of RIL and its underlying antitumor mechanisms in ovarian cancer.

E-PS-10-064

Luteinized thecoma associated with sclerosing peritonitis in a 13-year-old female: a case report

M.N. Villca Huayta*, B. López Martinez- Bernal, A. Van Der Biezen, C. Vieru, M.L. Abascal Camacho, M. Cebollero Presmanes
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Luteinized thecoma with sclerosing peritonitis (LTSP) is an extremely rare lesion. The age range of patients is broad with most cases occurring in the third decade. We describe a case with a view to improving its knowledge and therapeutic management.
Methods: We are reporting a case of unilateral ovarian luteinized thecoma with sclerosing peritonitis. A 13-year-old female with abdominal pain that on CT scan showed an abdominal mass dependent on the right ovary, images of micronodular peritoneal dissemination, ascites and bilateral pleural effusion. She had elevated serum tumour marker CA-125 (253 U/ml). Pathological history of absence crisis in treatment with ethosuximide.
Results: A right adnexectomy was performed. Macroscopy showed a large solid tumour with geographic pattern. Histology revealed a spindle cell neoplasm with rounded nuclei, arranged in an anarchic pattern. Alternating hypo- and hypercellular areas, the latter with cells with enlarged nuclei, occasional nucleoli and up to 7 mitoses/HPF. After 2 weeks, due to clinical worsening of the patient, omentectomy and biopsy of the intestinal serosa were performed. Microscopy showed extensives areas of sclerosing fibrosis and fibroblasts with oval isomorphous nuclei without atypia or evident proliferative activity. Immunohistochemical stains were positive for PR, Calretinin, and negative for Desmin, Inhibin, CD34, CKAE/AE3, ER, SMA, C-kit in ovarian. Sclerosing peritonitis was positive for Calretinin and negative for PR, Inhibin.
Conclusion: Usually, LTSP presents in the third decade and is bilateral in 84-90% but few cases have been reported between the ages of 12-17 years and one of them with a history of treatment with ethosuximide. The appropriate treatment is unclear but surgery is one of the main therapeutic measures. Our patient received high-dose corticosteroids as first line, then gonapeptyl for 7 months and is currently on maintenance tamoxifen without signs of relapsed until the time of this study.

E-PS-10-065

The significance of histological and immunohistochemical studies in the diagnosis of chronic endometritis in infertility

Z. Zhalimbetova*, B. Ibraimov
*Corporative fund University Medical Center, Kazakhstan

Background & objectives: To determine the diagnostic significance of endometrial biopsy in establishing the cause of infertility.
Methods: 30 women diagnosed with infertility were examined. With the help of endometrial biopsy, histological, immunohistochemical studies of the endometrium were carried out.
Results: According to the results of the study, it was found that in 20 women, the expression of ER and PR receptors in the glands corresponded to the morphological picture, and in the stromal component, the expression of ER and PR were reduced; 8 patients had severe chronic endometritis, 3 patients had moderate chronic endometritis, 3 patients had mild chronic endometritis, and it was also found that endometrial pathology was noted in 11 patients. So, glandular, glandular-fibrous polyps in 7 women, and glandular endometrial hyperplasia - in 4.
Conclusion: The immunohistochemical method of research is highly specific and highly sensitive and allows to reliably identify the types of the inflammatory process, also chronic endometritis is one of the leading causes of infertility, violation of the endometrial receptor apparatus, are detected in almost all patients with chronic endometritis. The analysis of the data obtained allows us to conclude that the use of a comprehensive study in women with infertility is a necessary condition at the stage of preparation for IVF.

E-PS-10-066

Ganglioglioma arising from ovarian mature cystic teratoma: report of a rare case

Z. Zhao*, P.Y. Tang, S.H. Chew
*Department of Anatomical Pathology, Singapore General Hospital, Singapore

Background & objectives: Somatic neoplasms occasionally arise in ovarian teratomas, however, central nervous system (CNS)-type neuroepithelial tumours are rare, mostly glial neoplasms and embryonal tumours. Here we present a rare case of ganglioglioma arising from ovarian mature cystic teratoma of a 30-year-old female.
Methods: Our patient underwent ovarian cystectomy for an incidentally found 6.8 cm dermoid cyst. Microscopically, components from all three germ layers were identified. Focal glioneuronal tissue showed increased glial cellularity with mild cytologic atypia and rare accompanying perivascular lymphoid aggregates. There were intermixed, dispersed dysmorphic neurons, with cytomegaly, perimembranous aggregation of Nissl substance and occasional binucleation. Hardly any mitoses were seen.
Results: In this case, increased cellularity in the glial tissue at low power raised the possibility of a low-grade glial neoplasm, such as astrocytoma, or reactive gliosis. However, dysmorphic neurons identified at higher power suggested a glioneuronal tumour instead. The diagnosis of ganglioglioma

arising in ovarian mature cystic teratoma was rendered, supported by immunohistochemistry, highlighting GFAP-positive glial component with coarse processes and NeuN-positive neurons. CD34, BRAF and IDH1 immunostains were negative in the neoplastic cells. Additionally, in view of the presence of reactive lymphoid infiltrate in the glial tissue, teratoma associated anti-NMDAR encephalitis might be considered. However, this is a clinical diagnosis and our patient did not have neurological symptoms.
Conclusion: Ganglioglioma of CNS is a low-grade indolent tumour. However, considering its rarity in the ovary, the behaviour and prognosis is difficult to determine and our patient is under close follow-up. To our knowledge, this case represents the second report of ganglioglioma arising in ovarian teratoma.

E-PS-11 | E-Posters Haematopathology

E-PS-11-001
Differential diagnosis in a rare spleen mass: inflammatory pseudotumour (inflammatory myofibroblastic tumour) versus inflammatory pseudotumour like dendritic cell sarcoma
B. Altuntaş Keskin*, A.S. Demiröz, T. Elverdi, H. Aki
*Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Pathology Department, Turkey

Background & objectives: Lesions that cause a spleen mass are usually haemangioma, lymphoma, and angiosarcomas. Inflammatory pseudotumor is one of the rarely encountered lesions in the spleen. Dendritic cell sarcomas are much rarer. Both lesions are problematic in radiological and histological differential diagnosis.
Methods: We present a rare case of a 70-year-old male patient admitted to the emergency department with mucosal bleeding and a spleen mass. On imaging, no hepatomegaly, lymphadenomegaly was detected. Total splenectomy was performed. The differential diagnosis included granulomatous lesions, angiosarcoma, sclerosing angiomatoid nodular transformation, splenic hamartoma, inflammatory pseudotumor (IPT) and inflammatory pseudotumor like dendritic cell sarcoma.
Results: Histopathological examination revealed a well-delimited, off-white elastic mass, consisting of spindle cells intertwined with inflammatory cells (histiocytes, lymphocytes, plasma cells, multi-nucleated giant cells). There was no necrosis. Dystrophic calcification was rarely present. No microorganisms were monitored with EZN or PAS dyes. Immunohistochemically, infiltration usually consists of positive cells for Vimentin, CD68, SMA, CD31, and negative cells for CD23, CD30, CD34, S100, ALK, CD1a, CD8, and also lymphocytes showing various B and T cell markers were abundant. Unlike inflammatory pseudotumor observed in other regions, EBER positivity can be seen in IPT of the spleen and inflammatory pseudotumor like dendritic cell Sarcoma.
Conclusion: The rarity of these lesions and the difficulty in distinguishing them from other tumours of aggressive character require a multidisciplinary approach to ensure accurate diagnosis and optimal management. Although it is difficult to make a differential diagnosis in these two entities, both lesions are diagnosed and treated with surgery. Close follow-up is recommended especially for IPT-DCS because of the risk of local recurrence and metastasis. Our patient has been followed up without recurrence for 16 months after surgery.

E-PS-11-002
Atypical monomorphic epitheliotropic intestinal T-cell lymphoma with brain invasion: a case report
A. Arackal*, C. Murga-Zamalloa
*Department of Pathology, University of Illinois at Chicago, USA

Background & objectives: Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) is a rare, incidental primary intestinal T-cell lymphoma. Poor prognosis and high mortality rate are due to delayed diagnosis and lack of targeted therapy. Distinctive histopathological features have been described to have prognostic implication.
Methods: A 66-year-old Cantonese-speaking male presented with abdominal pain. Further clinical investigation prompted an emergent partial ileectomy for small bowel perforation. Microscopically, pleomorphic atypical lymphocytes effaced the intestinal architecture. Positivity for CD3, CD8, CD56, c-MYC, TCR gamma/delta, and TIA-1, with aberrant loss of CD5 supported MEITL. CHOP regimen was initiated. Brain parenchymal lesions were eventually identified and biopsied, confirming metastatic MEITL.
Results: MEITL represents less than 5% of gastrointestinal tract lymphomas and is predominantly seen in South American and Asian countries. Other T-cell neoplastic proliferations, such as Enteropathy-associated T-cell lymphoma (EATL), should be excluded. Histologically, MEITL is characterized by epitheliotropism, with monomorphic atypical T-cell lymphocytes that express CD56, CD8, and TCR gamma/delta. Recently, an atypical variant has been described and is characterized by pleomorphic morphology, increased frequency of c-MYC amplification, and lower overall survival rates. Extradigestive/extranodal involvement is commonly detected in the lung or liver, and extension of MEITL into the brain parenchyma is rarely reported.
Conclusion: In summary, MEITL is a primary intestinal T-cell lymphoma with an aggressive clinical course and is rarely identified in North America. Recognition of variant morphological presentations is critical to establish the diagnosis, allowing for prompt and aggressive chemotherapy. Further studies can better quantify the prognostic implications of immunohistochemical and molecular characteristics for MEITL.

E-PS-11-003
Necrotising lymphadenitis (Kikuchi disease) (NEL) may be induced by endoplasmic reticulum stress
S. Asano*, K. Yamazaki, H. Yuko, S. Kawana, H. Sato, M. Kashimura, H. Naito, Y. Sogame, K. Shikano
*Iwaki City Medical Center, Japan

Background & objectives: We examined immunohistochemical analysis and electron microscope of NEL in detail and found aggregates (tubuloreticular structure) within the expanded ER, as well as concentric changes of the ER, which led us to further investigate ER stress in more detail.
Methods: Data from 70 NELs were collected between 1989 and 2016. Lymph node samples were fixed in 2.5%-glutaraldehyde for electron microscopy (EM). For immunohistochemical analysis (IHC), formalin-fixed paraffin-embedded tissue sections were performed using an automated staining machine; anti-GRP78 and anti-CHOP antibodies were used to examine ER stress and ER stress responses.
Results: Tubular structures (TRS) were often observed within the expanded endoplasmic reticulum within microvessels, lymphocytes, and plasmacytoid dendritic cells, and SARC bodies were also observed. Strongly GRP78-positive cells, an endoplasmic reticulum chaperone molecule, and CHOP-positive cells, a pre-apoptotic factor, were also frequently observed in the focal areas.
Conclusion: TRSs in the endoplasmic reticulum are unfolded proteins (UPs), which induce ER stress that leads to activation of stress sensors and massive mobilization of the chaperone molecule GRP78. However, when ER stress is strong and lasts longer, CHOP-positive cells appear and induce apoptosis, suggesting that apoptosis in this disease is induced by ER stress.

E-PS-11-004
Castleman disease: multicentre case series from Turkey
M. Ayyildiz Mercan*, E. Mercan Demirtaş, B. Altuntaş Keskin, A.Y. Altay, A.S. Demiröz, G. Yegen, H. Aki, F. Öz Puyan
*Trakya University Medical Faculty, Pathology Department, Turkey

Background & objectives: Castleman disease (CD) is a rare lymphoproliferative disorder divided into subtypes with different aetiologies,

clinical presentation, histological features, classified as unicentric or multicentric according to the involved lymph nodes. We aimed to evaluate the epidemiological and histopathological features of CD's.
Methods: We included patients with a diagnosis of CD between 2001 and 2023. Patients' demographic information, clinical histories, laboratory and imaging studies' findings were collected retrospectively. The 146 cases were re-classified from 3 tertiary consulting centres in Türkiye according to the 5th WHO classification criteria.
Results: A total of 146 patients (80 male and 66 female) from 3 centres with a diagnosis of UCD (n= 101) or MCD (n= 45) were included in the study. The mean age was 43.5 (1 to 83 years). The most common site of involvement was the cervical region (%22.6). Histopathologically, 84 cases (%83.1) revealed hyaline vascular subtype, 15 cases (%14.8) were plasmacytic subtype. 2 cases were mixed subtype among UCD cases. Human immunodeficiency virus (HIV) positivity was detected in 5 patients. Polyclonal plasma cell infiltration was present in 38% of cases on which have taken bone marrow biopsy. 5 cases had POEMS syndrome and 1 case had TAFRO syndrome.
Conclusion: Castleman disease is a heterogeneous lymphoproliferative disease and requires a multidisciplinary approach. Classification should be made with detailed clinical, laboratory radiological and histopathological examination. Besides HIV status, Human herpes virus 8 (HHV8) positivity, presence of systemic symptoms, blood levels, renal function tests, organomegaly status, presence of oedema or effusions, fever and other laboratory studies are needed for the correct diagnosis of CD.

E-PS-11-006
The need to set up a biobank dedicated to lymphoid malignancies: experience of a single centre (Laboratory of Clinical and Experimental Pathology, University Côte d'Azur, Nice, France)
C. Bontoux*, A. Marcovich, S. Goffinet, F. Pesce, V. Tanga, D. Bohly, M. Salah, J. Benzaquen, C. Marquette, S. Lassalle, E. Long-Mira, V. Hofman, L. Xerri, M. Ilié, P. Hofman
*Laboratory of Clinical and Experimental Pathology, Hospital-Integrated Biobank (BB- 0033-00025), Pasteur Hospital, IRCAN Team 4, Inserm U1081, CNRS 7284, FHU OncoAge, Université Côte d'Azur, Nice, France

Background & objectives: Many therapies are under investigation to improve the management of lymphoma. To identify new biomarkers, high quality and clinically annotated biological material is required. We have formed a lymphoma biobank and outlined our strategy for sustaining this collection.
Methods: We listed available biological material (tissues specimens and matched-additional biological resources) and associated clinical data of patients with lymphoma diagnosed between 2005 and 2022, according to the 2022 WHO classification, in the Laboratory of Clinical and Experimental Pathology, University Côte d'Azur, Nice, France. Selected cases were then retrospectively included as a new collection within the Côte d'Azur Biobank (BB-0033-00025).
Results: 2150 samples from 363 cases (351 patients) were selected, collected, annotated, registered and then stored in the biobank. Median cold ischemia was 20 minutes [IQR:15-25] and median tumour content was 70% [range:1 to 100]. Male/female ratio was 1.3. Median age at diagnosis was 58 years [IQR:43-71]. 30% of patients were dead at time of retrospectively inclusion. Main types of lymphoma were classical Hodgkin lymphoma (26%), diffuse large B-cell lymphoma (17%) and extra-nodal marginal zone lymphoma of MALT tissue (11%). Main sites of lymphoma were mediastinum (36%), lymph node (23%) and Waldeyer's ring (14%). Age at diagnosis >60, male, stages III-IV and T-cell lymphoma subtype were associated with shorter survival.
Conclusion: The Côte d'Azur Biobank holds certifications in both ISO 9001 and ISO 20387, enabling comprehensive lymphoma sample characterization for research purposes. Its objective is to supply high quality and varied materials to any research facility that proposes translational research projects related to lymphoma. The resulting data would facilitate the identification of new biomarkers, ultimately improving survival in lymphoid malignancies.

E-PS-11-007
Medullary eosinophilia, a clue to reconsider the diagnosis of lymphoma
M.M. Buda*, V. Moreno Nieto, È. Iglesias Martinez, A. Sifre Ruiz, A. Onaindia Perez
*Clinical Department Unit of Pathological Anatomy, OSI Araba, Araba University Hospital. Bioaraba Health Research Institute, Vitoria-Gasteiz, Alava, Spain

Background & objectives: Myeloid sarcoma (MS) is a rare entity consisting of a tumour mass composed of mature or immature myeloid blasts that occurs at any extramedullary site. We report the case of a 65-year-old man with MS involving the shoulder.
Methods: We reviewed the patient's medical history which showed a 3-month history of pain in the left arm. Imaging tests revealed a large soft tissue mass in the left shoulder with the complete occupation of the axilla, encompassing the vascular-nervous structures and infiltrating the perihumeral musculature. A biopsy of the tumour was performed with the consequent histological analysis.
Results: The biopsy of the lesion showed infiltration by a medium-large lymphoid population with an irregular nucleus and occasional nucleoli. The cells showed CD4, CD25, CD43, Tia-1 and Granzyme expression. A diagnosis of Peripheral T cell lymphoma NOS was made. Afterward, we received a bone marrow (MO) biopsy. It was hypercellular with eosinophils and signs of multiline dysplasia, making the diagnosis of unclassifiable myelodysplastic/myeloproliferative neoplasm. Given the findings of the BM biopsy and the polyclonality of the TCR Gamma rearrangement, we reviewed the first biopsy by performing additional techniques. The lesion was positive for myeloperoxidase, lysozyme and CD68. All in all, a final diagnosis of MS was made.
Conclusion: MS could be the first manifestation of acute myeloid leukaemia, myeloproliferative neoplasm, or myelodysplastic syndrome or it could manifest at relapse. That's why reaching the final diagnosis of MS can be challenging, especially in the absence of BM involvement. Moreover, histologically it can be misdiagnosed as malignant lymphoma, as occurred in our case. To avoid this error, the most sensitive markers for MS are CD43 and lysozyme. In addition, myeloperoxidase is expressed in up to 96% of cases.

E-PS-11-009
Clinical overlapping of idiopathic multicentric Castleman disease-NOS and indolent symptoms despite a large intrapulmonary mass and complete pleural effusion
J.O. Cázares Lara*, O.E. Falcón Antonio, M.K. Suaste Luna, L.M. Soberanes Contreras, M.J. Ballesteros Alfaro, E.A. Alamo Capula, E. Carrillo Maravilla, D. Montante Montes de Oca
*Salvador Zubiran, Mexico

Background & objectives: 42-year-old woman with dyspnea and infrascapular pain. Thoracic CT- scan unveiled a heterogeneous and calcified middle-mediastinum lesion, with 2,700 cc of exudate. In laboratories only polyclonal hypergammaglobulinemia. Enhancement on the lesion plus cervical and mediastinal lymph node on PET-CT scan.
Methods: The resection of mediastinal mass (8.7x5.5x6cm) confirmed a Castleman disease principally hyaline vascular but with plasmacytic traits, 4 of 21 positive ganglions, negative for LANA1 reactive. During the entire follow-up, she didn't have fever, oedema, polyneuropathy, organomegaly, endocrinopathy, or skin changes. The only trait of inflammation was thrombocytosis (Ptl 677) 6 months after the beginning of symptoms.

Results: Castleman disease (CD) is classified into Unicentric CD (UCD) or Multicentric CD (MCD) depending on lymphadenopathy and systemic symptoms. The infection status of Human herpesvirus type 8 defines the aetiology.
Our patient has an iMCD TAFRO-NOS (Not Otherwise Specified), sub-divided in iMCD-idiopathic plasmacytic lymphadenopathy (iMCD-IPL) or iMCD-non IPL, being the latter the one that resemble more to our patient.
Following this subclassification, our patient still shares clinical and pathological features between both groups of iMCD-NOS, with significant thrombocytosis, elevated serum IgG levels and indolent clinical course as is expected in IPL, but also pleural effusion, as well as increased vascularity in the architectural pattern that defines it as iMCD non-IPL.
Conclusion: Nishikori et al mentioned "there aren´t studies to validate whether or not IPL has distinct clinicopathologic features compared to other iMCD-NOS", for that reason we present our patienet with iMCD-nonIPL that overlaped clinical traits and matched with the term "oligocentric" or "regional" CD, with multiple enlarged nodes in adjacent regions and indolent clinical evolution. To conclude the subtlety of the presentation contrast with the large mass, multiple ganglionic areas affected, as well as a large pleural exudate.

E-PS-11-011
Artificial intelligence for classifying leukocyte in the peripheral blood: reliable subclassification into 11 types with deep learning algorithm
T. Costa*, Y. Usami, M. Iwaya, H. Aguierre, K. Tanaka
*Shinshu University Graduate School of Medicine, Science and Technology, Japan

Background & objectives: Classifying Leukocyte an important task in the medical routine, which is commonly done with automatic machine's help, but even the latest machines must be checked by experts. This work aims to improve classification accuracy by using deep learning.
Methods: YOLOv7, a new deep learning architecture was used in this study to classify 1779 blood cells images obtained by the CELLAVISION DM96 into 11 types of neutrophils (band and segmented), lymphocyte, monocyte, basophil, eosinophil, lymphocyte variant, metamyelocyte, myelocyte, thrombocyte, and erythroblast. To detect the abnormal situation more carefully, detailed classification was chosen instead of the typical five types of Leukocytes.
Results: We evaluated the simple classification method, where images were classified one time for the neural network with one set of trained weights, and the cascade method, where images were classified in two phases, using two sets of trained weights. Experimental results verified that the cascade method resulted in an accuracy of 96.4% and an F1-score of 98.1%, while the simple method presented an accuracy of 87.4% and an F1-score of 93.28%. Compared with the classification results by CELLAVISION DM96, an F1-score of 89.71% and an accuracy of 81.33% for the same evaluation database, classified by professionals, we could improve 15.07% of accuracy and 8.39% of F1-score by the cascade approach.
Conclusion: We found that our method achieved excellent performance which suggests the possibility of clinical implementation. Even though the classification by the neural network still presented errors, the rate was quite small and was considered irrelevant by the experts. The proposed method was considered reliable to the point that the reclassification by experts of the images after the classification by the machines is no longer necessary, which contributed to reducing the time consumed in the haematology laboratory.

E-PS-11-012
Diagnostic utility of digital pathology in the classification and recognition of gastrointestinal non-Hodgkin large B-cell lymphomas – a retrospective-observational study of 15 cases
M. Cristian*, M. Aschie, A. Mitroi, A.A. Nicolau, N. Dobrin, I. Poinareanu, G. Baltatescu
*Center for Research and Development of the Morphological and Genetic Studies of Malignant Pathology - CEDMOG, "Ovidius" University of Constanta, Romania; Department of Clinical Pathology, "Sf. Apostol Andrei" Emergency County Hospital, Constanta, Romania

Background & objectives: Using the example of cases of gastrointestinal malignant non-Hodgkin large B-cell lymphomas, we want to show that improved visualization and analysis by using digital pathology contribute to the convergence of these complementary diagnostic modalities of lymphomas.
Methods: We have conducted a retrospective study of 50 paraffin-embedded tissues of large B-cell lymphomas diagnosed at the Pathology Department of the Emergency County Clinical Hospital of Constanța and Sacele County Hospital of Brasov, Romania, between 2012 and 2021. All slides were digitized at 40X using the Huron LE120TM 4000XT scanner, Huron Viewer Software, and analysed with the QuPath Software platform.
Results: The expression profile of immunohistochemical markers established the diagnosis of non-Hodgkin large B-cell lymphomas, with a high nuclear proliferation marker in most cases. Six patients were female, and nine were male, with ages ranging from 32 to 86 (mean age: 56 years old). Two tumour specimens were sampled from the oropharyngeal region, five were from the stomach, five were from the small intestine, and three were sampled from the large bowel. Corroborating these findings, the most often type of lymphoma is DLBCL, NOS and the most often localization in the GI tract is the stomach and the small intestine.
Conclusion: The routine histopathological evaluation was assessed by two experienced pathologists with good collaboration, but the automatic identification was more objective and reproducible. In hematopathology, the distinction between various types of NHL using digital microscopy is highly needed to classify images sharing numerous morphological features and provide a specifically dedicated tool for accurately diagnosing different types of lymphoma. Also, digital pathology is essential to the continuous quality improvement of medical education.

E-PS-11-013
Diffuse large B cell lymphoma CD5-positive arising in an immune deficiency and immune dysregulation setting: A case report and review of the literature
M. Cristian*, M. Aschie, R. Baz, A. Stoica, M. Ghinea, M. Deacu, M. Boșoteanu, A. Mitroi, N. Dobrin, I.E. Iordache, G. Baltatescu
*Center for Research and Development of the Morphological and Genetic Studies of Malignant Pathology - CEDMOG, "Ovidius" University of Constanta, Romania; Department of Clinical Pathology, "Sf. Apostol Andrei" Emergency County Hospital, Constanta, Romania

Background & objectives: In the era of antiretroviral therapy, lymphoma is the primary cause of cancer-related death among HIV-infected people. The current report presents the clinicopathological features, diagnostic approach, and clinical outcomes of this HIV-related CD5-positive DLBCL.
Methods: We present a case of a 30-year-old male patient with a medical history of HIV-positive serology and antiviral treatment, presenting with diffuse abdominal pain and symptoms related to obstruction or perforation, followed by exploratory laparotomy and surgical resection of the small intestine with other areas of involvement. The surgical specimen was morphologically evaluated and immunohistochemically stained.
Results: Histopathological examination revealed a diffuse neoplastic proliferation of large B lymphocytes within the small intestine, lacking features of other defined types of large B cell lymphoma. The CD5-positive DLBCL subtype was diagnosed after immunostaining with twelve monoclonal antibodies (CD3, CD5, CD10, CD20, CD23, CD30, CD68,

Cyclin D1, MUM1, Bcl2, Bcl6, and Ki-67). The expression profile of immunohistochemical markers (CD10, Bcl6, and MUM1) established the cell of origin of this case of DLBCL by using the Hans algorithm.
Conclusion: The current report highlights the importance of early diagnosis of CD5-positive DLBCL because of its poor prognosis and calls attention to the critical importance of identifying immunodeficiencies because doing so affects the types of treatments available. Although cell-of-origin helps predict outcomes, the germinal centre B cell-like and activated-B cell-like subtypes remain heterogeneous, with better and worse prognostic subsets within each group.

E-PS-11-014

Expression of PIM1 and MYD88 in diffuse large B-cell non-Hodgkin's lymphomas –10 years of experience and 50 cases

M. Cristian*, M. Aschie, A. Mitroi, M. Deacu, A.A. Nicolau, G. Baltatescu, N. Dobrin, E. Matei, C.S. Branzan, I. Poinareanu
*Center for Research and Development of the Morphological and Genetic Studies of Malignant Pathology - CEDMOG, "Ovidius" University of Constanta, Romania; Department of Clinical Pathology, "Sf. Apostol Andrei" Emergency County Hospital, Constanta, Romania

Background & objectives: Oncogenically active MYD88 mutations are found in one-third of ABC-DLBCLs and PIM1 has been found in over 50% of DLBCLs. We aimed to determine the level of MYD88 andPIM1 expression, and their associations with clinicopathological parameters in DLBCLs.
Methods: This retrospective study included 50 cases of DLBCL diagnosed at the Pathology Department of the Emergency County Hospital of Constanţa and Sacele County Hospital of Brasov between 2012 and 2021. MYD88 and PIM1 protein expression was evaluated by immunohistochemistry (IHC) using two different scoring systems and was assessed by two experienced pathologists with good collaboration.
Results: Diffuse large B-cell lymphomas interest both sexes equally (1:1). Non-Hodgkin's diffuse large B-cell lymphoma, NOS is the most common type of lymphoma in the studied group of patients (80%), with an alignment of the results obtained with the data provided by the WHO 2022. IHC analysis was performed using monoclonal antibodies against MYD88 and PIM1. MYD88 mutation more frequently affects female adults and an increased incidence of PIM1 has been observed in older men. In the cohort analysed in this research, diffuse large B-cell lymphomas exhibit a high frequency of PIM1 mutation (50%), as shown by the IHC method, compared to the presence of MYD88 mutation (16%).
Conclusion: In conclusion, our preliminary data suggests that the immunohistochemical expression of PIM1 and MYD88 in our DLBCL cohort may improve the diagnosis and prognosis of DLBCL patients. The presence of the mutation, together with its protein overexpression, could also be used as a prognostic marker in advanced-stage DLBCLs.
Funding: This study was funded by "Grants competition in bio-medical field 2021", Contract no. 5/21/10.2021, registered by "Ovidius" University of Constanta with no. 14453/21.10.2021 and supported by the Institute of Doctoral Studies, School of Medicine, "Ovidius" University of Constanta.

E-PS-11-015

A diagnostic challenge: castleman disease - plasma cell variant with monotypic lambda light chain plasmacytic proliferation

A. Cutitaru*, D. Ferariu, I.D. Căruntu
*"Grigore T. Popa" University of Medicine and Pharmacy of Iasi, Romania

Background & objectives: Castleman disease (CD) represents a heterogeneous group of nonclonal lymphoproliferative disorders including 4 histological subtypes with clinical diversity. Pathogenic mechanisms involve immune dysregulation, IL-6 having a critical role. CD is regarded as an orphan disease, with global incidence still unknown.
Methods: We report a case of a 62 year-old male patient, admitted in Oro-Maxillo-Facial Surgery Department – "Sf. Spiridon" Clinical Emergency County Hospital of Iasi to investigate a rapidly progressing large mass developed in the left submandibular region. Clinical and imaging exams revealed a multicentric lymph node involvement (submandibular and laterocervical). Subsequently, excision of affected lymph nodes was performed by surgeons.
Results: Macroscopically, one sample (6/4/2 cm) presented a nodular structure (3/2.5/2 cm), red-brown on cut section; another sample (2.5/1.6/1.2 cm) included two nodular structures. In both samples, histopathology showed three lymph nodes with partially preserved histoarchitecture: free subcapsular sinuses; normal or hyperplastic follicles (displaying marked germinal centres surrounded by small lymphocytes, hyalinization and penetrating arterioles – typical for CD); highly vascularized interfollicular and medullary areas, occupied by mature, monomorphic plasma cell aggregates with large, hyperchromatic nuclei, lacking brisk mitotic activity. Immunohistochemistry revealed: CD20+ and CD3+ in lymphoid follicles, with predominant mantle zone CD3+; CD21+ in follicular dendritic cells; HHV8-; kappa/lambda chain+ in plasma cells, with lambda chain restriction indicating monotypic proliferation.
Conclusion: The pathologic spectrum of CD includes hyaline vascular, plasma cell (PC), mixed, and HHV-8 subtypes. Histology corroborated with immunophenotype supports the final diagnosis of multicentric CD – PC variant with monotypic lambda light chain plasmacytic proliferation. In PC variant, proliferation is typically polyclonal; rarely can be monotypic, predominantly lambda light chain restricted (IgG/ IgA). The case report is valuable considering the presence of monotypic lambda chains, in an HIV-negative patient, without other clinical manifestations (i.e., POEMS syndrome), with favourable outcome.

E-PS-11-016

Intraparenchymal low grade B-cell lymphoma of the CNS: a case series and literature review

M.T. Dawid de Vera*, F.J. Díaz de la Pinta, F.J. Díaz-Crespo, M. Conde Ferreirós, D. Morillo Giles, S.M. Rodríguez-Pinilla
*Hospital Universitario Virgen de la Victoria, Spain

Background & objectives: Low grade B-cell lymphomas of the central nervous system (CNS) are infrequent entities, most commonly extranodal marginal zone B-cell lymphoma (MZBCL-CNS). We present a series of cases of intraparenchymal low grade B-cell lymphomas of the CNS and a literature review.
Methods: Our series consisted of 2 men and a woman, with a mean age of 65 years. One patient suffered an outbreak of multiple sclerosis 20 years ago. All of them presented with headache and neurological focality. Imaging tests showed a subcortical white matter lesion of the frontal lobe (2 cases) and cerebellum. A biopsy was taken on suspicion of lymphoma.
Results: Case 1 shows intraparenchymal aggregates of plasma cells with light chain restriction and few small CD20+ lymphocytes in a perivascular arrangement. Case 2 exhibits an intraparenchymatous infiltrate of small lymphocytes with CD20 and BCL2 expression without plasmacytic differentiation. Case 3 shows a diffuse small cleaved nuclei lymphoid infiltrate with occasional large cells expressing CD20, CD10, BCL6 and BCL2. All cases have low-moderate proliferative index with absence of MYD88 gene mutation. The final diagnosis is MZBCL-CNS (cases 1 and 2) and primary cerebellar follicular lymphoma (FL) (case 3). Systemic involvement was ruled out. Two patients received radiotherapy or chemotherapy and remain stable after diagnosis. The remaining patient died of other causes.
Conclusion: Primary MZBCL of the CNS commonly affects the dura mater, while exclusively intraparenchymatous location has been exceptionally described, with only 11 cases reported so far. Secondary involvement by a systemic process should always be ruled out before making this diagnosis. The mean age at onset is 56 years, with main frontal lobe involvement. Complete remission is achieved in 40% of

cases after treatment. To the best of our knowledge, there are no previous reports on primary cerebral FL.

E-PS-11-017

Splenic Epstein–Barr virus associated leiomyoma: histological and immunohistochemical analysis of a single case in a university hospital

M. De Uribe Viloria*, I. Voinescu, G. Escuer, E.M. Fernandez, G. Olmedilla Arregui
*La Paz University Hospital, Spain

Background & objectives: Splenic Epstein–Barr Virus associated leiomyoma (EBVAL) is a rare entity associated with immunodeficiency. It is frequently found in the liver, though it can affect any organ and can occur at different sites synchronously or metachronously. No metastasis have been reported.
Methods: We reviewed our files from 2010 to April 2023 finding a single case of EBVAL. The diagnosis was achieved by using Hematoxilin-Eosine and immunohistochemical studies. We present the case of an 18 year old female with a history of renal transplant, presenting with two splenic masses found in a routine follow up.
Results: With the clinical suspicion of Lymphoma, an splenectomy was performed. Both lesions showed intersecting fascicles of bland monotonous spindle cells with indistinct borders, eosinophilic cytoplasm and elongated nucleus with tapered ends and without atypia. It showed positivity for SMA, calponin and EBER, and was negative for CD117, CD30, CD3, CD79a, CD21, CD23, oestrogen and progesterone receptors. The expression of fumarate hydratase and INI1 was preserved. The proliferation index (Ki 67) was close to 3%. Some areas presented dystrophic calcification. No necrosis or mitosis were identified.
Conclusion: EBVAL is an exceptionally rare entity and due to its rarity it may pose a diagnostic challenge. The oncogenesis of smooth muscle tumours in immunosuppressed patients remains to be elucidated, though Epstein Barr virus (EBV) infection seems to play a central role. It is important to report the presence of mitosis, necrosis and atypia, since EBV associated Smooth muscle tumours display a wide spectrum of histologic differentiation from benign, borderline, to malignant morphologic features.

E-PS-11-018

Erdheim Chester disease. Histological, immunohistochemical and molecular analysis of a single case in a universitary hospital

M. De Uribe Viloria*, M.M. Petrino, E.M. Fernandez, G. Olmedilla Arregui
*La Paz University Hospital, Spain

Background & objectives: Erdheim-Chester disease (ECD) is rare form of non-Langerhans cells histiocytosis with multi-organ involvement. Activating mutations of the MAPK pathway are found in most patients, mainly the BRAFV600E activating mutation (>50%). We present a case diagnosed in our centre.
Methods: We reviewed our files from 2010 to April 2023 and found just a single case of ECD. The diagnosis was achieved using routine staining, immunohistochemical and molecular studies. Age at diagnosis, symptomatology and radiological studies were obtained from the clinical history.
Results: A 55 year old male presented with vomiting, asthenia and oedema in the lower extremities. A CT scan revealed an irregular symmetric infiltration of the bilateral perirenal and posterior pararenal spaces (hairy kidney sign) and mesentery, with concomitant involvement of the pericardium. Blastic endomedular lesions were identified in both iliac crests. A biopsy of the retroperitoneal infiltrate was taken. Pathological analysis revealed an inflammatory infiltrate formed by foamy histiocytes with immunoreactivity for CD68, Factor XIII, BRAF and CD163. ALK-6, s100, CD1a and Langerin/CD207 were negative. BRAFV600E was mutated in molecular studies. Marked clinical and radiological improvement was achieved after Vemurafenib treatment. Verrucous keratosis Vemurafenib related appeared later on.
Conclusion: ECD is a rare, multisystem and idiopathic disorder. Activating mutations of the MAPK and PI3KCA pathway have been related to ECD. Due to its clinical heterogeneity the diagnosis may be challenging. It should be place in the list of differential diagnosis regarding retroperitoneal processes around major vascular structures, ureters, and perinephric space. This case report emphasizes the importance of correctly diagnosing this entity and performing molecular studies since prognosis is widely improved with the use of novel targeted therapies.

E-PS-11-019

Extracavitary primary effusion lymphoma (EC-PEL) of the central nervous system: an evolving entity with diagnostic difficulties

O.C. Eren*, O.M. Akay, O. Dogan
*Koç University Hospital, Department of Pathology, Turkey

Background & objectives: With its rarity and unconventional presentation, extracavitary primary effusion lymphoma (EC-PEL) of the central nervous system (CNS) poses diagnostic difficulty for both clinicians and pathologists. To increase awareness and discuss diagnostic approach, we present a case of EC-PEL of CNS.
Methods: A 62-year-old HIV(+) HBV(+) male presented with recent-onset headache and difficulty speaking. He had a 10-year-history of Burkitt lymphoma in complete remission. MRI revealed multiple lesions in cerebral hemispheres and scans revealed no systemic involvement. Stereotactic biopsy revealed infiltrative cells with immunoblastic/paraimmunoblastic morphology. Paraffin blocks from prior biopsy suggesting Burkitt lymphoma were retrieved and both were evaluated morphologically and immunohistochemically.
Results: Neoplastic cells were CD45(+), CD20/PAX5/CD79a(-), CD10/Bcl-6(-), CD38/138(+), MUM-1/EMA(+); suggesting terminal B-cell differentiation. CD30, ALK, CD3, CD2, Bcl-2, CD23, IgM/G/D/A/κ/λ were all negative. Expression of c-myc was diffuse (90%) and strong, with high Ki67-index (90%). Cells were positive with EBER(+) HHV-8 LANA(+) and a diagnosis of EC-PEL was made. Re-evaluation of previous biopsy approved presence of CD20(+), Bcl-6(+), c-myc(+, >95%), EBER(+), HHV-8(-) neoplastic cells with high Ki67-index (>95%), confirming Burkitt lymphoma as the initial diagnosis.
Conclusion: EC-PEL should be considered in an infiltration of EBV(+)/HHV-8(+) cells of high grade immunoblastic/paraimmunoblastic morphology in immunocompromised individuals. Systemic screening should be done to exclude classic PEL (with cavitary involvement) and large B-cell lymphomas secondarily involving the CNS. With limited cases described in literature, EC-PEL necessitates further emphasis for both pathologists and clinicians. Appropriate initial diagnosis, ensuing molecular workup and further clinicopathologic follow-up may culminate in upcoming tumour classification systems generating a distinct approach for this entity with unique properties.

E-PS-11-021

Primary cardiac lymphoma as a pathological expression of acute myocardial infarction

M.J. Gálvez*, F. Leiva-Cepas, A. Sanz Zorrilla, J. Osuna Soto, S. Haro Yuste, I. Sánchez Ramírez
*Hospital Universitario Reina Sofía, Spain

Background & objectives: Cardiac involvement in disseminated lymphomas is frequent: 25% in autopsy series, but primary or localized cardiac lymphoma is exceptional.
Methods: We present the case of a man in the sixth decade of life without toxic habits or cardiovascular risk factors who attended the emergency department due to typical chest pain with EKG changes.

Echocardiography reveals asymmetric hypertrophic cardiomyopathy that on MRI implies biventricular involvement. Biopsy is performed by cardiac catheterization.
Results: Tissue fragments are received where infiltration by a low-grade B lymphoma (monomorphic proliferation) is observed, suggestive of extranodal marginal zone lymphoma (MALT) with an immunophenotype: CD20+, CD3-, CD43-, CD5-, BCL6-, CD10-, CD23-, CYCLIN D1- and low proliferative index. In bone marrow there was no infiltration by lymphoma. Currently, after CHOP chemotherapy, he presents a good evolution with complete remission.
Conclusion: Primary lymphoma is an infrequent tumour. It usually has a torpid evolution, sometimes fatal with rapid evolution. Histopathological diagnosis is essential to guide the choice of targeted treatment.

E-PS-11-022
A comparative study of Ki67 evaluation in mantle cell lymphoma: human vs. artificial intelligence
J. García-Gómez*, A. Castillo, P. Osorio, L. Hernández, M. Jimeno, S. Roca, A. Sánchez, J.L. Mate, G. Tapia Melendo
*HOSPITAL U. GERMANS TRIAS I PUJOL, Spain

Background & objectives: Mantle cell lymphoma (MCL) is an aggressive B cell non-Hodgkin lymphoma. The Ki67 index is a powerful prognostic biomarker for this lymphoma subtype. Here, we study the reproducibility in Ki67 evaluation between observers and compare with artificial intelligence (AI) evaluation.
Methods: Ki67 percentage was evaluated in 44 MCL cases by four pathologists by "eyeballing" in 5% increments, and using two AI programs (ClinicalViewer-3DHistech & QuPath). The same selected areas, avoiding residual germinal centres, proliferating T-cells and hot-spots were analysed in both approaches. A cut-off point of 30% was used to classify high/low proliferation cases. Statistics analysis was performed with R package.
Results: The concordance between all four pathologists was excellent (ICC=0,91) when Ki67 was studied as a continuous variable. Moreover, the concordance between pathologists and AI programs was high for QuPath (CCC=0,93) but moderate with ClinicalViewer (CCC=0,65).
However, the agreement between observers was lower when cases where analysed in a dichotomized way applying the recommended cut-off point of 30% (concordance 77,27%), and higher between observers and AI programs (pathologists vs. QuPath: concordance 88,63%; pathologists vs. CinicalViewer: concordance 84,09%).
The discrepant cases between observers were mostly near the cut-off point, thus explaining the low concordance in the dichotomized study, whereas the discrepant cases between pathologists and AI programs where randomly distributed.
Conclusion: Our results indicate that there is an excellent agreement between pathologists in evaluating Ki67 by "eyeballing" as a continuous variable, and it becomes lower when dichotomized using the 30% cut-off.
The correlation between pathologist and AI programs was moderate or high, mainly depending on the program used. Importantly, the evaluation requires selection of the area of interest by a pathologist, in order to avoid hot-spots, residual germinal centres or proliferating T-cells.

E-PS-11-023
Histiocytic/dendritic cell neoplasms following therapy for haematolymphoid tumours - transdifferentiation or sui generis?
V.M. Godkhindi*, V. Bhat K, A.M. Venkatagiri, V. Mv, S. Mailankody
*Department of Pathology, Kasturba Medical College, Manipal, Manipal Academy of Higher Education(MAHE), Manipal, Karnataka, India

Background & objectives: A subset of histiocytic/dendritic cell neoplasms are known to be associated with or follow preceding lymphoma/leukaemia therapy with similar molecular signatures, thus evincing the transdifferentiation hypothesis; however, they also carry additional novel genetic alterations in the histiocytic/dendritic cell lineage.
Methods: A series of 3 cases of secondary clonal histiocytic/dendritic cell neoplasms of varied histomorphology & immunophenotype occurring post-therapy for preceding haematolymphoid neoplasms have been discussed.
Results: Case 1:17/male, T-ALL on maintenance therapy, complains of generalised lymphadenopathy. Nodal biopsy revealed atypical histiocytes, immunopositive for CD68, CD163, CD4, Ki67 10%. Treated with 2 cycles of CHOP chemotherapy followed by trametinib, succumbed to progressive disease.
Case 2:13/male, B-ALL on maintenance therapy, complains of swelling over right distal femur. Biopsy revealed Blastic plasmacytoid dendritic cell neoplasm, immunopositive for CD4, CD56, CD123, BRAFp. V600E, Ki67 60%. 2 cycles of ICE chemotherapy followed by resection and 2 cycles adjuvant chemotherapy. Patient well.
Case 3: 48/male, MDS-h, low blasts on therapy, imaging revealed lytic lesion in left proximal tibia. Biopsy revealed high-grade histiocytic sarcoma marking with CD68, CD163, CD4, S100, Ki67 60%. Lost to follow-up.
Conclusion: Histiocytic/dendritic cell neoplasms arising in the setting of preceding cytotoxic therapy for haematolymphoid neoplasms are extremely rare. The 5th edition of the WHO classification of tumours of haematolymphoid tumours envisions an enhanced grouping framework with the introduction of a newly segregated category of Secondary myeloid neoplasms; post cytotoxic therapy. Along the same lines, we propose the decoupling of histiocytic/dendritic cell neoplasms arising post-therapy from the general framework of histiocytic/dendritic cell neoplasms into a unique subgroup, thus facilitating focused research.

E-PS-11-024
Rare primary extranodal lymphoma of the genitourinary tract in a human immunodeficiency virus positive young woman
E. Horvath*, E. Lázár, O. Cotoi, S. Turdean, G. Molnár, J. Köpeczi
*Department of Pathology, Faculty of Medicine, George Emil Palade University of Medicine, Pharmacy, Science, and Technology of Targu Mureş, Romania

Background & objectives: Plasmablastic Lymphoma of HIV-positive patients may be the initial manifestation or a complication of immunodeficiency with an aggressive clinical course. Typically presents as a mass in the oral cavity and/or gastro-intestinal tract, but >1% of PBL cases include other localizations.
Methods: Because lymphomas with plasmablastic differentiation may lead to diagnostic dilemmas, we reported a PBL of genitourinary tract, which show all the characteristic features helping establishment of the diagnosis. A 25-year-old woman, without relevant previous anamnesis presented in emergency service with acute urinary retention. MRI and ultrasound examination revealed tumoral involvement of the bladder, vagina, uterus and bilateral adnexa.
Results: Histopathological examination of solid fragments obtained by transurethral resection showed large areas of coagulative necrosis, rich in apoptotic nuclear debris and nests of tumour cells with frequent mitotic figures and tingible body macrophages, resulting in a 'starry-sky' appearance. Detailed immunophenotypic analysis confirmed the origin of terminally differentiated plasma cells, which were CD138, MUM1, and kappa chain positive. B cell markers such as CD20 and PAX5 were not expressed. As immunophenotypic aberrances, CD10 and CD56 were also detected. HIV immunodeficiency was confirmed by immune serology and viral load analysis. Based on primary pelvic localization, after high-dose chemotherapy bilateral adnexectomy was performed. The histological examination of ovaries resulted in the same diagnosis.
Conclusion: Because patients with HIV-associated PBL have been reported to respond better to chemotherapy compared to HIV negative PBL subjects, identification of HIV infection is important the in those diagnosed de novo with PBL.

E-PS-11-025

A case of acute monoblastic leukaemia in adult patient

P. Kasparova*, K. Rudolf, A. Sykorova
*The Fingerland Department of Pathology, Charles University, Faculty of Medicine in Hradec Králové and University Hospital Hradec Králové, Czech Republic

Background & objectives: Acute monoblastic/monocytic leukaemia is one of the most common subtypes of Acute Myeloid Leukaemia (AML) in children. Patients with AMoL often exhibit hyperleukocytosis, disseminated intravascular coagulation, and extramedullary involvement, particularly in the skin, gingiva, and central nervous system (CNS).
Methods: We report a case of adult patient (62 years old) presenting with ascites and clinical suspicion of acute pancreatitis. Than the diffuse infiltration of stomach wall was found, suspected of poorly cohesive type of gastric carcinoma. The biopsy was done, and the leukemic infiltration was found. Afterward the diagnosis of AMol was set from the trephine biopsy specimen.
Results: During the diagnostic process cytology was done at first, from the ascites, with finding of population of histiocytic cells, but due to the clinical data it was interpreted as reactive, „cleaning" reaction to pancreatitis. When the biopsy from the stomach mucosa was examinated with the finding of leukemic infiltration of monocytic/monoblastic type, the cytologic report was revised to leukemic infiltration. Because of the finding of extramedullary leukemic infiltration, the bone marrow examination was suggested. In the trephine biopsy specimen massive leukemic infiltration was found as well.
Conclusion: Our case represents quite typical problems of diagnostic process of AMoL in adult patients – due to other more typical diagnosis and causes of the effusions could be the right diagnosis missed for some time. But although AMoL is more typical for children, we can find in adult patients as well, with rather common extramedullary infiltration and especially malignant effusions. That´s why we should have the possibility of AMoL in the differential diagnostic scheme in adult patients as well.

E-PS-11-026

A rare case of jejunal plasmacytoma presenting with small bowel stricture

C. Kwon*, K. Davidson, M. Rahilly
*NHS Lothian, United Kingdom

Background & objectives: The gastrointestinal tract is a rare site for extramedullary plasmacytoma (EMP), an uncommon tumour. We present an unusual case of a solitary jejunal plasmacytoma in a 33-year-old male who presented with subacute jejunal obstruction, and discuss the clinical implications.
Methods: In addition to the patient's notes, the literature was reviewed utilising Google Scholar, Pubmed and WHO Blue Books references.
Results: A 33 year-old man presented with intermittent abdominal pain and vomiting. CT scanning demonstrated a jejunal obstruction with local mesenteric lymphadenopathy. The strictured jejunum was resected at laparotomy. Histopathology showed a 16mm submucosal nodule at the stricture.
The nodule was composed of solid sheets of CD138 positive lambda light chain restricted mature appearing plasma cells. The cells were negative for Cyclin D1, CD56, pan-cytokeratins and neuroendocrine markers. Local nodes were negative for tumour.
Para-protein, serum free light chain ratio and a skeletal survey were negative. Bone marrow aspirate and trephine were negative for plasma cell neoplasia. The features were interpreted as a plasma cell neoplasm based in the jejunal wall.
Conclusion: EMP is a localised monoclonal plasma cell neoplasm that is rarely found in the jejunum[1]. We discuss EMP of the jejunum and the differential diagnosis of localised marginal zone lymphoma with extreme plasmacytic differentiation. The patient is well and awaits radical radiotherapy.

E-PS-11-027

Immunomorphological characteristics of diffuse large B-cell lymphomas - a quaternary care centre experience

A. Lakshmanan*, N. Mulchandani, A. Ravichandran, A. Subramanyam
*Apollo Hospitals, India

Background & objectives: Diffuse large B-cell lymphomas (DLBCL) are the commonest aggressive B-cell non-Hodgkin Lymphomas worldwide. Their subclassification is challenging due to overlapping histopathological, immunophenotypical and genetic characteristics. This is reflected by the WHO classification of DLBCL into many variants and specific entities.
Methods: All cases of DLBCL that were diagnosed during the period of 2017-2019 were retrieved and analysed. Immunohistochemistry (IHC) was done on all the cases. The cell of origin (COO) subtyping was done using Hans algorithm. A cut-off of 40% for C -MYC and 50% for BCL2 and BCL6 has been applied to assess the expressor pattern.
Results: A total of 395 cases of DLBCL were diagnosed over the study period. The mean age at diagnosis was 57.2 years (12-95 years). A male predominance was noted with a male to female ratio of 2:1. Nearly half of the cases had primary extra nodal presentation. The mean proliferation index as assessed by Ki67 was 74%. The morphology had predominant centroblastic features (72.9%) followed by anaplastic (15.7%) and immunoblastic features (6.3%). 5.1% of the cases had blastoid morphology. They were predominantly non-germinal centre B cell type (55%). The double expressor and triple expressor phenotypes were seen in 11.4% and 17.2% cases respectively. Isolated c-MYC expression was noted in 6.6% cases.
Conclusion: DLBCL is a heterogeneous disease with numerous entities. Molecular studies play a substantial role in diagnosing few of these specific entities as well as in prognostication. Although there are no strict recommendations in how to choose cases for FISH analysis or other molecular studies, morphological and IHC findings are invaluable to assess various prognostic factors such as COO determination and expressor patterns especially in resource limited countries.

E-PS-11-028

Comparison of the expression of regulatory T cells transcription factor FOXP3 and PD1 in the tumour microenvironment of EBV+ and EBV- diffuse large B-cell lymphoma NOS

N. Moulai*, R. Bennoui, M. Guermi, W. Ouahioune
*Faculty of Medicine of Blida, Algeria

Background & objectives: There is little information about the possible role of Tregs in EBV + DLBCL NOS. We aim to determine the contribution of the immunomodulator microenvironment and its relationship with the immune checkpoints, by the expression of Foxp3, and PD-1.
Methods: We evaluated the expression of FOXP3 (236A/E 7) using an H-Score and PD1 (NAT 105) by immunohistochemistry in 78 EBV-DLBCL including 67 with ABC and 11 GCB and 13 EBV+DLBCL ABC phenotype. We compared their expression on the microenvironment (ME).
Results: The Mann-Whitney test showed no significant difference for FOXP3 (p=0.06) between the two groups. Our results showed a significant difference. The PD1 expression in the microenvironment of EBV+ DLBCL and EBV- DLBCL was significantly different p=<0.0001. Pearson's test showed a significant correlation between PD-1 expression and FOXP3 (r=0.56, p=<0.0001) with linear regression. Our results showed a significant difference between the two groups EBV(+)-DLBCL and

EBV(-)-DLBCL on the response to R-CHOP treatment (p=0.01) and survival rate between the two groups. Log Rank (Mantel-Cox) p=0.0001.
Conclusion: We suggest that regulation of EBV-induced immunosuppression by inhibiting PD-1 and its ligands may improve immunotherapy outcomes.

E-PS-11-029
Expression of IL-6 in Epstein–Barr virus-positive diffuse large B-cell lymphoma, a potential targeted therapy and cell signalling
N. Moulai*, R. Bennoui, M. Guermi, W. Ouahioune
*Faculty of Medicine of Blida, Algeria

Background & objectives: Epstein–Barr virus-positive (EBV +) diffuse large B-cell lymphoma not otherwise specified (DLBCL NOS) is an aggressive clinicopathological entity associated with a poor prognosis. The IL-6/JAK/STAT3 signalling pathway is aberrantly hyperactivated in patients with haematopoietic malignancies or solid tumours.
Methods: We evaluated the expression of IL-6 (10C12) using an H-score, STAT3 Thyr705 (13-7) with 40% of cut-off, and NF-κB P50 (polyclonal) by immunohistochemistry in 78 EBV-DLBCL including 67 with ABC and 11 GCB and 13 EBV+DLBCL ABC phenotype. We compared the expression on the microenvironment (ME) and lymphoid tumour cells.
Results: In our study, a significant difference in IL-6 expression was found between the EBV+DLBCL and EBV-DLBCL p=0.002. However, its expression was noted mainly by lymphoid tumour cells and ME in the EBV+ DLBCL and only by the ME of the EBV-DLBCL. The Pearson test showed a significant correlation between the expression of IL-6 and STAT3 (r=0.368, p=<0.000) and between the expression of IL-6 and NF-κB P 50 (r=0.272, p=0.009).
Conclusion: We suggest that the IL-6 signalling pathway has a key role in the lymphomagenesis of EBV+ DLBCL. IL-6 expression by lymphoid tumour cells and ME cells would activate the transcription factors STAT3 and NF-κB P50. This leads to new therapy perspectives.

E-PS-11-030
Gastrointestinal follicular lymphoma: comprehensive clinicopathological review of 22 cases and diagnosis classification
K. Na*, C.H. Oh, H. Kim, S. Do
*Department of Pathology, Kyung Hee University Hospital, Kyung Hee University College of Medicine, Republic of Korea

Background & objectives: Duodenal type follicular lymphoma (DFL) and classic follicular lymphoma (CFL) are important differential diagnosis of gastrointestinal follicular lymphoma (GIFL). This study describes an integrated diagnostic process of GIFL and identifies useful features for the differential diagnosis.
Methods: We thoroughly reviewed clinicopathological features of 22 patients with GIFL, providing long follow up data and lymph node (LN) status. Following WHO classification, the cases were classified into DFL or CFL. Some undetermined cases were initially classified as GIFL, not otherwise specified (NOS) and their diagnosis was further classified with integration of overall clinicopathological features.
Results: Thirteen cases in duodenum showing grade 1 histological feature and the absence of LN involvement were classified as DFL. Five cases in non-duodenal location showing either grade 3 histological feature or LN involvement were classified as CFL. Endoscopic finding of CFL was overt mass forming lesion, in contrast to tiny nodules observed in DFL. CD21 expression in neoplastic follicles of DFL was predominantly or completely peripheral, whereas that those in CFL was strong and homogeneous. Four cases of GIFL, NOS were further categorized into 3 CFL of duodenum, stomach and colon, and 1 colonic DFL. Of these 4 cases, LN involvement was detected in CFL of duodenum and colon.
Conclusion: Our study supports that clinicopathological features of DFL are largely different from CFL. Routine LN evaluation may not be mandatory for patients with typical case of DFL. In cases of GIFL showing unusual features for DFL, the possibility of GI involvement of CFL should be considered and the presence of LN involvement should be carefully evaluated. In addition to endoscopic findings and histopathological features, CD21 expression pattern can assist in the differential diagnosis between DFL and CFL.
Funding: This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT and Future Planning (2020R1G1A1003692).

E-PS-11-031
MiR-125b and miR-155b and their relationship with MYC, BCL2 and TP53 in diffuse large B-cell lymphoma
E. Neves Filho*, S. Zancheta, S.H. Rabenhorst
*LABGEM, Brazil

Background & objectives: Tumoral microRNAs, such as miR-125b and miR-155b, are important gene expression regulators with complex pathogenetic mechanisms. However, their role in DLBCL, especially when other biomarkers and cell-of-origin classification are considered, are still to be elucidated.
Methods: In a series of 139 DLBCL cases considering germinal centre (GC) versus nonGC subtypes according to Hans algorithm, we investigated miR-125b and miR-155b expression by in situ hibridization and their association with some immunophenotypic presentations, including MYC, BCL2 and TP53 expression by immunohistochemistry and MYC, BCL2 and BCL6 translocation status by FISH.
Results: miR-125b was detected in 58.5% and miR-155b in only 24.4% of the studied cases. In the nGC patients, miR-125b detection was positively correlated to the Ki-67 index (p= 0.035). Considering the GC subgroup, besides a miR-125b association to Ki-67>70% (p= 0.043), the percentage of miR-125b positive cells was also correlated to either MYC and MYC/BCL2 double expression (p= 0.047 and p= 0.049, respectively). No associations were observed between miR-125b and the studied chromosomic rearrangements, nor between miR-155b and any of these parameters.
Conclusion: In conclusion, miR-125b is associated to high proliferation index independently on cell-of-origin subtypes and a pathway involving miR-125b and MYC seems to be a GC characteristic.
Funding: This work was supported by the Fundação Cearense de Apoio ao Desenvolvimento Científico e Tecnológico (FUNCAP) [PPSUS 2017].

E-PS-11-032
Gastric mastocytosis: an underdiagnosed and rare entity
N. Oza*, V. Anandaswamy, S. Gujral, F. Ahmed, S. Kane
*HISTOPIA LAB, India

Background & objectives: Mastocytosis is rare heterogeneous group of neoplastic mast cell disorders. The disease is divided into pure cutaneous and systemic disease with over 90% cases exhibiting D816V KIT mutation. Gastric mastocytosis poses a challenging diagnosis and represents major cause of morbidity.
Methods: An elderly male with clinical suspicion of lymphoproliferative disorder presented with abdominal pain and vomiting. Imaging revealed circumferential thickening of gastric and D1/D2 wall; while endoscopy revealed oedematous hyperemic gastric and D1 mucosa. Histopathologic evaluation of gastric biopsy revealed mast cell neoplasm which was further confirmed by Sanger sequencing and serum tryptase levels.
Results: A gastric biopsy of 67-year-old male with oedematous gastric mucosa on endoscopy revealed antral type of gastric mucosa with lamina propria showing mast cells arranged in sheets. These show round to ovoid nuclei with vesicular chromatin and pale eosinophilic cytoplasm. By Immunohistochemistry, the mast cells showed diffuse positivity for

LCA, C-KIT, CD25, and CD43; while negative for synaptophysin, CK, CD2, CD3, CD4, CD20, DOG-1, MPO, and CD123. Sanger sequencing confirmed D816V KIT mutation. The patient then revealed itchy macular lesions over the axillary region. Bone marrow biopsy revealed approximately 8-10 % mast cells confirmed by CKIT. Serum tryptase levels were elevated (72.9µg/l). Treatment with midostaurin demonstrated good response so far.
Conclusion: Systemic mastocytosis (SM) is a disease with a heterogeneous presentation and gastric involvement is frequently affected with rather vague and nonspecific clinical manifestations, making the diagnosis of gastric mastocytosis particularly difficult. Histologically, systemic mastocytosis can be easily confused with other conditions such as inflammatory bowel disease or eosinophilic colitis. The differential diagnosis is easily resolved with appropriate immunohistochemical stains and molecular study. Thereby, high index of suspicion is essential to correctly recognize this rare entity and improve quality of life.

E-PS-11-033
Fibrin-associated diffuse large B-cell lymphoma (FA-DLBCL) in a renal cyst
C. Padrão*, J. Derman, P. Gaulard, M. Mamodaly, E. Poullot
*Hospital Prof. Dr. Fernando Fonseca, Portugal

Background & objectives: An incidental suspect renal cyst (Bosniak IV) was discovered in a 72 years-old man in the context of follow-up from prostate cancer operated in July 2022. He underwent surgical removal of the cyst in December 2022.
Methods: Macroscopically the lesion measured 7 x 6.5 x 6 cm. It was a well-defined, encapsulated nodular lesion. In section it was composed of a fibrous dense capsule, and a multiloculated cavitary with a gelatinous and liquid yellowish citric content. The cavitary lesion was totally included after one first microscopic evaluation that did not show any neoplastic evidence.
Results: On histopathology, the capsule was fibrous and did not show any epithelial lining, with some lymphoid infiltrate and lymphoid follicles. In a small percentage of the slides in the subcapsular area, there were clusters of medium to large atypical lymphoid cells with abundant clear cytoplasm and a voluminous nucleus, often with a prominent central nucleolus. Numerous figures of mitosis and apoptosis were observed. The content of the cavity was composed of fibrin with some atypical cells detected within.
Immunohistochemistry showed that the neoplastic cells were CD20+, PAX5+, CD5-, CD10-, Bcl6+, MUM1+, Bcl2+, cMYC-, CD30+(>80%), EBV+(latency type-3 profile), HHV8-, ALK1-, p53 wildtype. The proliferation index (Ki67) was high (80-90%).
Conclusion: These findings are consistent with the diagnosis of Fibrin-associated diffuse large B-cell lymphoma in a renal pseudo-cyst.
Fibrin-associated diffuse large B-cell lymphoma was previously considered a subtype of diffuse large B-cell lymphoma associated with chronic inflammation (DLBCL-CI) but is now recognised as an entity in the WHO Classification of Haematolymphoid Tumours 5th edition and ICC classification. Pathologists should be aware of this entity and differentiate it from conventional DLBCL and DLBCL-CI to avoid overtreatment since it has a better prognosis.

E-PS-11-034
Granulomatous slack skin with lung and oesophagus involvement? A case report and molecular analysis
F. Pereira*, G. Esteves, J. Costa Rosa, J. Cabeçadas, M. Cravo, I. Barbosa, A. Robson
*Hospital Professor Doutor Fernando Fonseca, Portugal

Background & objectives: Granulomatous slack skin (GSS) is a rare subtype of mycosis fungoides (MF), and few cases have been known to spread to the blood, lymph nodes, or viscera. We present a case with early dissemination to the lung.
Methods: A 27-year-old female, previously healthy, presented with vulvar and intergluteal firm oedema and groin-skin hardening, associated with scattered disseminated scaly patches for one year, without pain or pruritus. She also complained of mild fatigue and breathlessness on moderate exertion. There were no B symptoms. The patient underwent blood tests, skin biopsies and computed tomography (CT) scan.
Results: The skin biopsy showed a mildly atypical T-cell lymphoid infiltrate involving the dermis/hypodermis, with focal epidermotropism, associated with a granulomatous infiltrate dominated by multinucleated giant cells. Elastophagocytosis was seen. The CT scan revealed bilateral ground-glass lung nodular opacities. Positron Emission Tomography showed increased signal in skin and subcutis around buttocks, inguinal and mediastinal lymph nodes, and lobes of the lungs. The lung biopsy confirmed a dense T-cell infiltrate with numerous multinucleated giant cells. Subsequently, oesophageal involvement was also observed following biopsy. Molecular analyses demonstrated identical T-cell clones in the skin and lung. After six cycles of chemotherapy/localized external radiotherapy, the patient had stable lung disease and a partial skin response.
Conclusion: A preferred diagnosis of GSS with systemic spread was made based on clinical/histological/molecular findings, after considering granulomatous MF and peripheral T-cell lymphoma, NOS. This case highlights the frequent diagnostic difficulty in distinguishing GSS from an inflammatory granulomatous dermatitis. Pulmonary and oesophagus involvement is rare in GSS and the simultaneous presentation of characteristic skin GSS with systemic disease poses an additional classification challenge.

E-PS-11-035
Primary follicular lymphoma limited to the endometrium in a 55-year-old woman
Z. Prouzová*, M. Kalinová, M. Mrhalová
*Department of Pathology, 3rd Faculty of Medicine, Charles University and University Hospital Královské Vinohrady, Department of Pathology, 1st Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic

Background & objectives: A 55-year-old woman with no history of malignancy was indicated for hysterectomy for significant postmenopausal bleeding.
Methods: The material from the hysterectomy was processed in a standard way, formalin fixed and paraffin embedded tissue blocks were used for standard histological examination. Further immunohistochemical evaluations were used for detailed investigations of the process and, moreover, fluorescent in situ hybridisation (FISH) was added.
Results: The endometrium was atrophic, infiltrated by the nodular lymphoid infiltrate composed of medium-sized centrocytoid cells with minimal admixture of large centroblasts. Immunohistochemical examination revealed a CD20 positive B-lymphocyte population with co-expression of CD10 and BCL2 markers. FISH revealed characteristic abberation t(14;18) and, thus, confirmed the diagnosis of follicular lymphoma.
Conclusion: The patient underwent a detailed haematological examination and since she did not show signs of generalization of the disease, a "watch and wait" approach was chosen for the patient. She has now been relapse-free for 4 years.
Primary lymphomas of the female genital tract are rare (0.2-1.1% of all extranodal lymphomas), moreover follicular lymphomas are unique, especially when they are not generalized. Treatment depends on the extent of the underlying disease, in our case, hysterectomy was a curative therapeutic procedure.

E-PS-11-036
Grading of myelofibrosis post-polycythemia vera and post- essential thrombocythemia
G. Sahraoui*, N. Kouki, R. Doghri, N. Boujelbene, I. Abbes, L. Charfi, K. Mrad
*Salah Azaiez Institute, Tunisia

Background & objectives: Polycythemia vera (PV) and essential thrombocythemia (ET) are among the most common chronic

myeloproliferative disorders. Myelofibrosis (MF) is a recognized complication that occurs rarely in ET. We aimed to determine its frequency in ET and PV in a Tunisian population.
Methods: All patients diagnosed with PV or ET between March 1999 and March 2023 were recruited from the database of the pathology department of Salah Azaiz Institute. Clinicopathological data were retrieved from pathological reports. MF grading was assessed according to The European consensus on grading bone marrow fibrosis.
Results: We included 211 patients diagnosed with ET (151 cases) and with PV (60 cases). Fifteen patients (7,1%) developed MF: 8 cases post-ET and 7 cases post-PV. The median age of patients that developed MF was 57 years, with a sex ratio of 1,5. Grade 2 and Grade 3 post-ET MF were seen in 4 cases respectively (1,9%). Grade 2 post-PV MF was assessed in 4 cases (1,9%) and Grade 3 post-PV MF in 3 cases (1,4%). Bone marrow hypercellularity was recorded in 7 cases with post-ET MF and in 4 cases with post-PV MF.
Conclusion: Bone marrow histopathology is an essential tool in chronic myeloproliferative disorders. The finding of MF must arise the diagnosis of primary myelofibrosis, which is the main differential diagnosis of complicated ET. In these difficult cases, a multidisciplinary study is determining in the diagnostic workup.

E-PS-11-037
ALK positive large B cell lymphoma: clinicopathological study of 37 cases from a tertiary cancer centre in India
U. Sakhadeo*, M. Ranade, S. Epari, L. Nayak, B. Bagal, H. Jain, M. Sengar, C. Dhamne, N. Moulik, G. Narula, S. Banavali, T. Shet
*Tata Memorial Centre, Homi Bhabha National Institute, India

Background & objectives: Anaplastic lymphoma kinase–positive large B-cell lymphoma (ALK+ LBCL) is rare and shows characteristic plasmablastic/immunoblastic morphology with ALK expression. The objective of this study is to examine the clinicopathologic features of ALK+ LBCL to ensure its accurate diagnosis.
Methods: We retrospectively reviewed the electronic medical records and archival material for the clinico-pathological details of 37 cases of ALK+LBCL, diagnosed at our institute between 2012 and 2022.
Results: The age range was 11-73 years (mean 34.97 years, median 35 years). Male preponderance was noted with M:F of 3.63:1. Immune status was available in 27 patients and all were immunocompetent. 50% of the patients showed B symptoms and/or advanced stage disease. Majority (62%) of patients had both nodal and extranodal disease. 6.9% had isolated extranodal disease. 89.2% cases showed diffuse pattern while nodular and sinusoidal was noted in rest. Majority showed plasmablastic morphology. CD138/MUM1/OCT2/BOB1 were variably positive in all cases, indicating plasmablastic/B cell differentiation. Cytoplasmic granular expression of ALK was present in all cases. CD30 showed focal weak staining in 50% cases. Median survival was 13 months.
Conclusion: To the best of our knowledge this is the largest single institution study of ALK+ LBCL, which is a rare, aggressive B-cell lymphoma with characteristic clinical-morphologic-immunophenotypic profile and unfavourable outcome. ALK+ LBCL is an important differential diagnosis of plasmablastic/immunoblastic morphologies, particularly in cases with immunocompetent adults and non expression of mature B cell markers.

E-PS-11-038
T-Cell lymphomas in solid organ transplantation: review of this rare entity in a tertiary hospital
E.P. Sánchez López*, P. Pérez-Montero, G. Olmedilla Arregui, E. García Fernández
*La Paz University Hospital, Spain

Background & objectives: Outside the context of inborn errors of immunity (IEI), T-cell lymphomas in the setting of immune deficiency/dysregulation (IDD) are extremely rare and most often are EBV-negative. Our objective is to review the post-transplant associated T-cell lymphomas diagnosed in our centre.
Methods: We searched cases diagnosed as post-transplant lymphoproliferative disorder (PTLD) in the last 10 years and reviewed the histology, immunohistochemistry slides and molecular studies of T-cell lymphomas. We revised the medical records: gender, type and cause of transplant, age at transplantation, immunosuppressive treatment, time to diagnosis of lymphoma and vital status.
Results: We found 41 cases of post-transplant associated lymphoproliferative disorders (LPD), of which 5 were T-cell lymphomas (12%), 14 B-cell lymphomas, 9 polymorphic lymphoproliferative disorders and 13 hyperplasias. Among the T-cell lymphomas, 4 cases were peripheral T-cell lymphomas (PTCL), NOS and 1 case anaplastic large cell lymphoma (ALCL), ALK-negative. Two cases were males and 3 females. Three of the transplants were renal, 1 hepatointestinal and 1 intestinal, which later became multivisceral. The ages at transplant ranged from 1 year to 51, and the time from transplant to diagnosis of lymphoma ranged from 3 months to 34 years. All cases were EBV-negative. Two patients died during follow-up and 3 patients are alive.
Conclusion: Our results show that T-cell lymphomas are rare and most of them are EBV-negative in this clinical setting. This data correlates with the previous published literature. Interestingly, we found one rare case of ALCL, ALK-negative. The time to diagnosis of lymphoma was variable, although in cases of renal transplantation it took more than 10 years, suggesting perhaps a longer latency time for the onset of T-cell lymphoma in this context.

E-PS-11-039
Expression of CD30 in primary central nervous system lymphoma
H. Sartelet*, E. Aboud, L. Taillandier, J. Broseus, P. Feugier
*Chru nancy, France

Background & objectives: Primary central nervous system lymphoma (PCNSL) is an aggressive lymphoma with poor prognosis. The expression of CD30 is known to be a potential target therapeutic biomarker. The aim of the study is to evaluate CD30 expression in PCNSL.
Methods: We present a retrospective and unicentric study of 91 adult patients initially diagnosed and treated between January 2011 and December 2019 at the University Hospital of Nancy for PCNSL. We excluded the patients with systemic relapse or meningeal involvement or with EBV related disease. The antibodies used were against CD79a, CD20, CD10, CD3, CD5, BCL6, MUM1, CD30, and Ki67.
Results: Among the 91 patients, the repartition of gender is nearly equal with a low predominance of male (51.6%) and the median age at diagnosis is 67.8 years. The average of follow-up is less than 2 years (22 months). It is observed more non-GC PCNSL than GC subtype (75 vs 16). 14% of PCNSL (13/91) express CD30. Their median survival is 27 months (cd30+) versus 7 months for CD30 negative PCNSL but the difference is not significant. The PCNSL CD30+ are significantly more non-GC lymphoma (12/13, $p=0.01$) and the expression of CD30 is significantly negatively correlated with those of CD10 and Bcl-6 ($p<0.01$).
Conclusion: The presence of CD30 found in 14% of PCNSL may be useful to enlarge the therapeutic panel proposed to patients after relapse or refractory disease.

E-PS-11-040
Not every bearded man is your grandfather. Crystal storing histiocytosis: a case report and literature review
S.N. Sayir*, E.D. Serbes, S. Yüksel, G. Kaygusuz
*Ankara University, Faculty of Medicine, Turkey

Background & objectives: Crystal storing histiocytosis (CSH) is a rare entity characterized by the accumulation of immunoglobulin crystals (especially kappa light-chains) in the cytoplasm of histiocytes

which is taken by phagocytosis that is mostly seen in plasma cell neoplasms or lymphoproliferative disorders.
Methods: A 43-year-old man presented with a mass on his right shoulder. Imaging showed widespread lytic bone lesions. The results of serum protein electrophoresis were not yet known. Excisional biopsy of the mass was sent to our lab with the question of malignancy.
Results: Microscopically, the mass revealed a diffuse neoplastic growth in corticomedullary area, consisting of atypical cells with plasmacytoid morphology. Cells had rounded nuclei, coarse chromatin and large eosinophilic cytoplasm. Additionally, homogeneous eosinophilic material containing cells were noted among the tumour cells which was suspicious of amyloid deposition. Immunohistochemically, the neoplastic cells were CD38 and CD56 positive, and Ki67 proliferation index was 30%. Eosinophilic material containing cells were strongly stained with Kappa and CD68. Lambda was broadly negative with the exception of only a few plasma cells. Histochemically, gentian violet and congored staining were not compatible with amyloid. With these findings, the case was accepted as CSH accompanying plasma cell malignancy.
Conclusion: CSH is an uncommon entity seen mostly in lymphoproliferative disorders and plasma cell neoplasms but it can also be seen throughout the body (spleen, lymph nodes, bone marrow, kidney, gastrointestinal tract, central nervous system, skin, kidney etc) in different circumstances. CSH is important to recognize as it may associated with increased mortality and worse prognosis. Recognition of this entity by pathologists and knowing that it may be mistaken with amyloid may help its differential diagnosis.

E-PS-11-041
Hodgkin's lymphoma with bone marrow involvement – study of immune escape markers
T. Shet*, R. Johal, S. Epari, U. Sakhadeo
*Tata Memorial Hospital, India

Background & objectives: A small proportion of Hodgkin's lymphoma (HL) present with hematologic symptoms of marrow involvement requiring a bone marrow biopsy. With immunotherapy being used in Hodgkin lymphoma understanding immune escape markers will help treat these patients better.
Methods: We evaluated Immune escape markers in 7 cases of primary bone HL(BHL) and 17 primary bone marrow presentation of HL(PMBHL) with 56 staging marrows involved by Hodgkin lymphoma (SBMHL). Stains for beta2 microglobulin, MHC class I, HLA class II and PD-L1 (Roche, SP142, monoclonal) were evaluated in Hodgkin / Reed Sternberg (HRS) cells and background in the three subsets.
Results: MHC I correlated significantly with B2 microglobulin In HRS cells whereby 25/32 (78.1%) tumours with downregulated MHC I also had reduced B2 microglobulin. HLA II expression in HRS cells was negative or lost in 24 cases (44.6%). Expressions of beta2 microglobulin, MHC class I and HLA class II were significantly negative in BHL as compared to SBMHL or PBMHL. More cases of PBMHL appear to be positive for MHC-I and beta2 microglobulin as compared to SBMHL. PDL1 (SP142) was positive in 50/65(62.5%) samples. EBV was not associated with PD-L1. Univariate analysis revealed that tumours with > 90% HLA II expression in HRS cells showed favourable prognosis.
Conclusion: Besides HLA II expression, complete response on PET scan and histological pattern were significant for both overall survival (OS) and disease free survival (DFS) while in addition EBV negativity was adverse for OS. Patient with diffuse sclerotic pattern and nodular fibrohistiocytic pattern of marrow involvement had poorer survival. A unique pattern of Immune escape markers was seen in BHL, PMBHL and SBMHL and knowledge of these markers could help understand options for immunotherapy in these patients.
Funding: Intramural funding from Tata Memorial Hospital

E-PS-11-042
Smouldering systemic mastocytosis with the development of striking osteosclerosis
S. Stojnev*, M. Krstic, A. Ristic Petrovic, I. Conic, I. Petkovic, B. Lilic, M. Jevtic, M. Vucic
*University Clinical Centre Nis, Medical Faculty University Nis, Serbia

Background & objectives: Mastocytosis is a rare disorder caused by the clonal proliferation of neoplastic mast cells and their accumulation in tissues. In systemic mastocytosis, various organs can be affected, including the skeletal system. Bone involvement usually leads to osteoporosis and pathological fractures.
Methods: We present a case of a sixty-year-old male patient with macular skin rash, episodes of hypotension, and organomegaly who was diagnosed with systemic mastocytosis (SM) based on bone marrow (BM) biopsy findings. The patient was closely monitored and treated with H1-antagonists for 18 months. Clinical progression ensued, but BM examination showed no signs of associated myeloid or lymphoid neoplasm.
Results: The initial diagnostic BM biopsy revealed remarkable histologic alterations: myeloid spaces were occupied by dense, granuloma-like aggregates of spindled and ovoid mast cells with paratrabecular and perivascular distribution. Neoplastic mast cells comprised more than 50% of total cellularity and showed typical immunophenotype with positive immunohistochemical expression of CD117, CD25, and CD30. Somatic point mutation of KIT D816V was confirmed. After the patient started to deteriorate clinically and developed leukocytosis and elevation of serum alkaline phosphatase, a novel BM biopsy was obtained. Examination revealed mast cell infiltration associated with prominent, diffuse osteosclerosis. Expanded bony trabeculae caused stenosis and subtotal obliteration of marrow spaces.
Conclusion: SM represents a major diagnostic challenge since the release of mast cell mediators causes a myriad of manifestations. Skeletal involvement is rare and underlined by the interaction of mast cells with bone remodelling but prominent osteosclerosis is rare. Sclerotic lesions of the bone, especially in the axial skeleton, can lead to misdiagnosis of metastatic cancer of Paget's disease. This case depicts an unusual evolution of SM and highlights the importance of including SM in diagnostic protocols of sclerotic bone lesions.

E-PS-11-043
Plasmablastic lymphoma: multicentre case series from Turkey
C.S. Sucubulak*, B. Altuntaş Keskin, E. Mercan Demirtaş, A.Y. Altay, M. Ayyildiz Mercan, A.S. Demiröz, G. Yegen, H. Aki, F. Öz Puyan
*İstanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Pathology Department, Turkey

Background & objectives: Plasmablastic lymphoma(PBL) is a rare lymphoma that is mostly found in HIV-infected patients and infiltrates mostly oral cavity. Different extranodal site involvement can also be encountered. We have limited sources of PBL in the literature because of its rare nature.
Methods: We retrospectively reviewed 32 PBL cases from 3 tertiary consulting centres in Turkey (n=32). The cases were evaluated by their clinical findings, associated viral exposure (HIV and EBV), immunohistochemistry, histology, and site of involvement.
Results: The mean age of the patients was 59 (range=22-85). 23 patients were male, and 9 were female. 16 patients presented with nodal disease, 20 of them had extranodal involvement. Extranodal infiltration sites were stomach, gingiva, nasopharynx, maxilla, femur, epidural cavity, soft tissue, and hypophysis. HIV status of 9 patients were known and 3 of them were positive. Our immunohistochemistry results showed CD20(-)(26/30), CD138/CD38(+)(15/17), MUM1(+)

(26/28), CD79a(-)(12/22), EBER and/or EBV-LMP1(+)(11/15). 16 patients' ki-67 levels were 80% and over (range=50-100%). 15 out of 17 patients had no bone marrow infiltration. One of the patients had a previous history of diffuse large B-cell lymphoma, and one patient had a previous history of Burkitt lymphoma.
Conclusion: PBL is a rare lymphoma type with a worse prognosis and the main challenge with PBL is considering it as a differential diagnosis. After evaluating the general status of the patient, it is important to focus on the immune-suppression history of the patient. Then immunohistochemistry and morphological features help pathologists to give the correct diagnoses. Lastly, plasmablastic lymphoma diagnosis should be kept in mind in HIV(-) immunopotent patients with extraordinary infiltration sites.

E-PS-11-044
Angiosarcoma of the liver and spleen with thrombocytopenia and haemolytic anaemia (Kasabach–Merritt Syndrome)
A. Therapontos*, N. Stavrinou, E. Athanasiou, E. Spiteri, P. Vlachou, F. Dolkiras, T. Georgiadi, A. Antonopoulou, G. Kyriakopoulos
*Department of Pathology, Evaggelismos General Hospital Athens, Greece

Background & objectives: Kasabach–Merritt syndrome is characterized by thrombocytopenia secondary to the entrapment and platelet consumption by the vascular spaces of a vascular neoplasm (benign or malignant). We describe a case with severe thrombocytopenia and haemolytic anaemia in a patient with liver-spleen angiosarcoma.
Methods: A 64-year woman presents with marked swelling of the liver and spleen with thrombocytopenia (100.000 platelets) and anaemia (21 hematocrit) in the context of Coombs-negative haemolytic anaemia. The clinical differential diagnosis included haematological disease (lymphoma). Fine needle biopsy with transoesophageal ultrasound was performed.
Results: The neoplasm was characterized by large anaplastic nuclei isolated or in aggregates with abundant eosinophilic cytoplasm with presence of sufficient hemosiderin. The extended immunohistochemical analysis was negative for markers of haematological, epithelial, neuroendocrine, melanocytic, histiocytic and hepatocellular differentiation while it exhibited strong positivity for vascular differentiation markers such as CD31, ERG, Fli-1 και Factor VIII establishing the diagnosis of angiosarcoma with proliferation index ki-67 30%. Thrombocytopenia and Coombs-negative haemolytic anaemia were interpreted within the context of Kasabach–Merritt syndrome.
Conclusion: Angiosarcoma of the liver and spleen can cause thrombocytopenia due to platelet consumption and Coombs-negative microangiopathic haemolytic anaemia within the context of Kasabach–Merritt syndrome

E-PS-11-045
Amyloid accumulation in bone marrow: clinicopathological features in systemic amyloidosis
C. Utku*, D. Demir, B. Sarsik Kumbaraci, N. Ozsan, F. Keklik Karadag, M. Yetisken, M. Hekimgil, S. Sen
*Department of Pathology, Ege University Faculty of Medicine, Izmir, Turkey

Background & objectives: Amyloidosis is characterized by amyloid accumulation in various tissues, leading to dysfunction. The aim is to evaluate the amyloid accumulation in BM interstitium, vascular, peri-cortical soft-tissue besides bone-trabeculae and cartilage by semi-quantitatively and determine the possible correlations among clinicopathological features.
Methods: The study analysed 213 BM biopsies performed on 157 patients in our department between 2014-2019. The diagnosis was established with Congo-red under polarized-light by at least two pathologists. Some slides were examined under fluorescence-filter; also, tioflavinT/tioflavinS stains were evaluated with isotiosiyanat-filter. Amyloidosis type, involvement of other organs, plasma cell percentage, clonality, and repeated biopsies according to progression were analysed retrospectively.
Results: The male-to-female ratio was 1.24:1, and the mean age was 61.89. Most of the patients had vascular amyloid depositions in BM. The most commonly involved other organs were the kidney, myocardium, and gastrointestinal tract, respectively, and five patients had manifestations in multiple sites. AA amyloidosis was observed in 19 patients.
Of the patients, 44 presented without myeloma, 60 had simultaneous myeloma, and 14 had a previous myeloma history. In 39 patients, myeloma developed after amyloidosis within 8.5 months. The most commonly accompanying diseases were myeloma with lambda and, according to immunoglobulin (IG) depositions IGG (55.8%), IGA (21.1%), and light-chain (17.9%), respectively. Immunohistochemically, CD56 positivity was identified in 25.3% of myelomas.
Conclusion: The prognosis depends on various factors, such as the underlying cause, the extent of amyloid deposition, and other comorbidities. In this condition, amyloid deposits interfere with the normal functioning of the BM. Amyloid accumulation can be seen in non-AL amyloidosis types on the BM biopsies. It is essential to perform a BM biopsy to diagnose and manage systemic amyloidosis. The biopsy can help determine the type and extent of amyloid deposition in the body, which can guide treatment decisions.

E-PS-11-046
Low-grade nodal B cell lymphoma co-expressing CD5 and CD10 but not CD23 or cyclin D1: a case report with diagnostic challenge
K. Win*, S. Chuang
*Department of Pathology, Chi-Mei Medical Center, Taiwan

Background & objectives: Co-expression of CD5 and CD10 is unusual in B-cell lymphomas. Either the biologic basic or clinical significance for such co-expression is unclear. Yet, this rare event may complicate the interpretation of lymphoma immunophenotyping. We present one such challenging case.
Methods: A 63 year-old male patient without a significant past history presented to our hospital with palpable neck mass bilaterally. There is no fever or other clinical symptoms. Blood count showed anaemia and leukocytosis with normal platelets and lymphocytosis (abnormal lymphocyte 33.0%). Neck computed tomography (CT) revealed bilateral cervical, axillary and superior mediastinal lymphadenopathies. Right cervical lymphadenectomy was performed for diagnosis.
Results: Flow cytometry showed a distinct B-cell population expressing lambda immunoglobulin light chain, with CD5+/CD10+/CD19+/CD20+/CD23-/CD43- phenotypes, raising possibility of mantle cell lymphoma. Histologically, effacement of nodal architecture by diffuse and nodular patterns was seen. The diffuse areas contain small atypical lymphocytes with slightly irregular nuclear contours and pale cytoplasm. The nodular areas are composed of small and large lymphocytes without polarity. Immunohistochemical study showed the small atypical lymphocytes are B-cells expressing CD5, CD10, CD20, bcl-2, IgM, MNDA, but not CD3, CD23, bcl-6, IgD, SOX11, or cyclin-D1. The Ki-67 labelling index is low. Bone marrow and blood involvements are present. Abdominal CT showed multiple abdominal and pelvic lymphadenopathies together with a splenomegaly.
Conclusion: We present a rare case of a low-grade nodal B cell lymphoma expressing both CD5 and CD10 but not CD23 or cyclin D-1, and which also manifests splenomegaly, bone marrow and blood involvement with the same immunophenotypic profiles. These elements taken together suggest secondary nodal involvement by splenic marginal zone lymphoma (SMZL). Dual expression of CD5 and CD10 is extremely unusual, and can lead to misdiagnosis. Detailed clinical information and a comprehensive immunophenotyping are paramount for the diagnosis.

E-PS-11-047

Clinical and pathological features that predict double-hit lymphoma: a systematic review and meta-analysis

K. Wong*, E. Lee*, H.C.J. Yang, E. Soilleux
*Department of Pathology, University of Cambridge, United Kingdom

Background & objectives: Differentiating double-hit lymphoma (DHL) from other high-grade B-cell lymphomas (HGBCL) is crucial, as DHL patients require more intensive treatment. We aimed to identify clinicopathological, morphological and immunohistochemical features predicting DHL, as alternatives to more expensive and inaccessible fluorescence in-situ hybridisation.
Methods: We conducted a PRISMA systematic review and meta-analysis on 27 studies comparing the clinicopathological features between double-hit and non-double-hit HGBCL patients using four databases. Data on study characteristics, patient demographics, and clinicopathological, morphological and cytogenetic features of the lymphomas were extracted and risk ratios were calculated between DHL and HGBCL, and between MYC/BCL2-rearranged and MYC/BCL6-rearranged DHL.
Results: Our literature search yielded 771 DHL and 1551 HGBCL patients. DHL patients were more likely than HGBCL patients to have higher Ann Arbor stage and IPI score, elevated lactate dehydrogenase, bone marrow involvement, GCB immunophenotype (RR 1.2723, p=0.0361) and MYC immunohistochemical expression (RR=1.1106, p=0.0272); extranodal disease and B symptoms were more common in DHL, albeit not at a level reaching statistical significance. Furthermore, MYC/BCL6-rearranged compared to MYC/BCL2-rearranged DHL patients were more likely to present with extranodal disease and central nervous system involvement and to show BCL2 immunopositivity (RR 0.4062, p=0.0251); MYC immunopositivity was slightly more common in MYC/BCL6-rearranged lymphoma although this did not reach statistical significance.
Conclusion: Our meta-analysis has identified MYC immunohistochemical expression and GCB immunophenotype as histopathological features that strongly predict DHL. Our results support their inclusion in selection criteria for stratifying potential DHL for confirmation with FISH, an important finding as there is no consensus on which histopathological features should be included. Investigations with larger sample sizes and establishment of detection thresholds will be essential to determine whether further immunohistochemical or immunophenotypic markers, such as BCL2 immunopositivity, can potentially expand the selection criteria.

E-PS-11-048

Megakaryocyte size in myeloproliferative neoplasms and myelodysplastic syndromes measured with digital pathology

J.T. Zuñiga Gaitan*, C.E. Haro Haro, Z. Calixto Alvarez, J. Chabla Jaramillo, S. Ramón y Cajal Agüeras, J. Castellvi Vives
*Vall D' Hebron University Hospital, Spain

Background & objectives: Megakaryocytes size and number are frequently used as a morphological criterion for the diagnosis of Myeloproliferative Neoplasms (MPN) and Myelodysplastic Syndromes (MDS) in bone marrow biopsies. However, there are no objective standardized measures. Digital evaluation of megakaryocytes was performed.
Methods: We selected 45 consecutive cases of MPN (15 ET, 15 PV, 15 PMF), 15 MDS and 15 normal bone marrow biopsies for lymphoma staging. The slides were scanned for primary diagnosis, and the size of 20 megakaryocytes was measured in a 2 mm2 area. Additionally, the number of megakaryocytes and the number and size of aggregates were also quantified.
Results: The size of megakaryocytes was 11.7-53.8 µm (average 26.4 µm) in normal bone marrow and 10.8-94 µm (average 41.1 µm) in ET, 17.2-122.4 µm (average 49.5 µm) in PV, 14-92.4 µm (average 44.4 µm) in PMF and 11-53 µm (average 25.1 µm) in MDS. The differences between normal, MPN and MDS were statistically significant ($p<0.001$). The number of megakaryocytes was not different within MPN, but the number of aggregates was higher in PV (p=0.009) and higher in size for PMF (p=0.005). Between normal and MDS, the number of megakaryocyte per area was higher in MDS (p=0.049) but there were no differences in their average sizes.
Conclusion: It is well known that BRC-ABL negative MPN have larger megakaryocytes. In our study, sizes above 40 µm were found to be the best cut-off to suggest a MPN, but none for MDS. However, no differences in the size between the various MPN studied were found. On the other hand, the number of megakaryocytes per area was no different between MPN and MDS, but there were statistically significant when compared to MDS and normal bone marrow.

E-PS-12 | E-Posters Head and Neck Pathology

E-PS-12-001

Can recurrences be predicted with the histopathological changes observed in Schnederian Papillomas?

Y. Adali*, S. Ekmekci, N. Akcan, Ü. Küçük
*Izmir University of Economics Faculty of Medicine, Turkey

Background & objectives: Inverted, exophytic, and oncocytic subtypes of Schnederian papillomas are prone to recurrence and carry the risk of malignant transformation. In this study, it is aimed to examine the predictive value of histopathological findings for recurrence.
Methods: 57 schnederian papilloma cases diagnosed in a training and research hospital between 2011-2023 January were included in the study. All slides of the cases were re-evaluated in terms of metaplasia, dysplasia, lymphoid aggregates, inflammation, and stromal features. The relationship between papilloma subtype, location, demographic characteristics, histopathological findings and recurrence was evaluated statistically.
Results: Twenty (27.8%) of the cases were female and 37 (51.4) were male. 49 (68.1%) were inverted papillomas, 4 (5.6%) were exophytic papillomas and 4 (5.6%) were oncocytic papillomas. 11 (15.3%) cases had recurrence, 32 (44.4%) had squamous metaplasia, and 9 (12.5%) had concomitant dysplasia. Eight of the dysplasias were low grade and 1 high grade. Squamous cell carcinoma development was observed on the inverted papilloma in 1 case. Although there is no significant relationship between diagnosis and recurrence, all cases with recurrence are inverted papillomas. Although not statistically significant, squamous metaplasia was noted in 8 (72.7%) of 11 cases with recurrence. No significant correlation was observed between recurrence and dysplasia.
Conclusion: The most important risk factor for recurrence is inadequate surgery. Although molecular alterations that predict recurrence have been reported in sinonasal papillomas, detection of these alterations is not routinely performed. It is thought that the identification of predictive factors that can be easily evaluated by light microscopy will facilitate patient follow-up. Although statistical significance was not found with histopathological findings and recurrence in this study, the remarkable increase in numbers indicates that significance can be detected in large case series.

E-PS-12-003

Central mucoepidermoid carcinoma arising in glandular odontogenic cyst: a rare case report

F. Al Hinai*, H. Al Kindi, Z. Al Hajri, M. Al Saadi
*Oman Medical Specialty Board, Oman

Background & objectives: Central Mucoepidermoid Carcinoma (CMC) is a rare subtype of mucoepidermoid carcinoma, which can arise from Glandular Odontogenic Cyst (GOC). This paper reported a CMC arising in GOC, focusing on the main histological and molecular features of this tumour.

Methods: A 58-year-old man presented with a history of mandibular cyst for 2 years. The first biopsy showed inflammatory odontogenic cyst. He was treated by marsupialization. After 6 months, he had recurrent symptoms, and the size of the lesion had increased. Computed Tomography scan showed expansile lytic mandibular lesion with focal cortical defect. The lesion was excised and sent for histopathology.
Results: Histology showed a cystic lesion lined by mucin cell-rich mixed epithelial aggregate containing basal cells and squamoid cells. They showed sharp delineation to the subepithelial fibrous stoma which contained variable degree of chronic inflammatory infiltrates. The other fragments showed a multicystic lesion composed of haphazard admixture of monomorphic epidermoid cells, intermediate cells and focally prominent mucinous (goblet) cells in a fibrous stroma. Focal area with a predominance of clear cells was seen. No high-grade nuclear features were seen. The diagnosis of a predominantly cystic low-grade CMC developing from a pre-existing GOC was made. Fluorescence In Situ Hybridization (FISH) testing showed MAML2 translocation which confirmed the diagnosis.
Conclusion: Cystic low-grade CMC shares common features with the GOC. Careful histological examination and – in some cases – molecular tests are required for the definite diagnosis. Rare forms of CMC can develop from GOC. However, the nature of the pre-existing lesion – whether it is a GOC or a genuine bland looking mucoepidermoid carcinoma– carries no prognostic significance.

E-PS-12-004
Ameloblastoma featuring plexiform granular cell odontogenic tumour: an under-recognized entity
R. AlRasheed*, R. AlShagroud
*King Saud University, Saudi Arabia

Background & objectives: Plexiform granular cell odontogenic tumour (PGCOT) has been initially described as plexiform strands composed of granular cells. Few cases of ameloblastoma featuring PGCOT have been previously reported. Herein, we report additional case of ameloblastoma with granular cells in plexiform architecture.
Methods: 31-year-old male presented to the clinic with a 4-month history of a swelling of the right posterior mandible. The patient indicated that the mass was painless and was associated with a yellowish discharge. Radiographic examination showed a multilocular radiolucent lesion with scalloped borders. Incisional biopsy of the mass was performed.
Results: Grossly, the received specimen consisted mainly of multiple soft tissue fragments that were firm in consistency. Histopathological examination revealed long thin anastomosing cords and strands of closely packed, large, epithelial cells with granular eosinophilic cytoplasm in a collagenized connective tissue stroma. These strands and cords occupied almost the entire specimen and consisted of a parallel arrangement of tall cylindrical cells with the nucleus exhibiting hyperchromasia and palisading, reverse polarization, occasional basilar cytoplasmic vacuolation, and intranuclear inclusion. In addition, the tumour showed formation of neoplastic follicles demonstrating similar nuclear features as the strands within the peripheral layers while the centre of the follicles exhibited "stellate reticulum-like" structure.
Conclusion: The presentation of ameloblastoma as PGCOT has been only rarely reported in the literature. Typically, the granular cells in ameloblastoma are present focally and limited to the area within the neoplastic islands. Interestingly, the presented case showed granular changes within the cells forming the plexiform strands and cords mimicking other neoplasms and posing a diagnostic challenge. It is important for pathologists to recognize this entity in order to avoid misdiagnosis and consequently provide patients with the proper management.

E-PS-12-005
Intratumour molecular heterogeneity in mucosal melanoma of the head and neck region
M.V. Altavilla*, D. de Biase, C. Ricci, B. Corti, E. Pasquini, L. Presutti, A.M. Baietti, L. Amorosa, T. Balbi, C. Baldovini, F. Ambrosi, M. Grillini, A. D'Errico, M. Fiorentino, M.P. Foschini
*Pathology Unit, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy; School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna, Italy

Background & objectives: Mucosal melanoma of the head and neck (MM-H&N) is a rare but aggressive histotype, with limited data on its genetic landscape. We tested a series of MM-H&N to evaluate the intratumor molecular heterogeneity (IMH) among samples from the same patients.
Methods: 39 histological samples of MM-H&N obtained from 24 patients (2003-2023) were collected and reviewed to confirm its primary nature and exclude metastases. The cases were analysed with a multi-gene NGS panel (covering 28 genes involved in the pathogenesis of melanoma), and patients with sequential samples (excision of the primary tumour and excision of residual tumour) were compared to investigate IMH.
Results: In 35 histological samples (22 patients) the obtained material was suitable for NGS analysis. The most commonly detected mutations involved RAS (KRAS and NRAS) (5/35, 14.3%), TP53 (3/35, 8.6%), and KIT (3/35, 8.6%) genes; by contrast, BRAF (p.Asn581Ile), IDH1, and GNA11 mutations were detected in only 1 sample (2.9%), and 17 samples (48.6%) resulted wild-type (wt). In 9 patients with multiple/sequential samples and at least two suitable for NGS analysis, 5 (55.6%) showed IMH, as follows: patient #1 (KRAS and TP53), patient #6 (NRAS and EIF1AX), patient #11 (GNA11, NRAS, and wt), patient #21 (BRAF and wt), patient #24 (KIT and wt).
Conclusion: Our study confirms that the most commonly involved mutated genes in MM-H&N are RAS (KRAS and NRAS), with a higher frequency of wt cases compared to the cutaneous counterpart. Furthermore, we showed that more than half of patients with multiple/sequential samples showed IMH. This data increases our knowledge of the genetic landscape of MM-H&N and underlines how the NGS analysis of multiple/sequential samples could be required to better stratify the prognosis of these patients and plan the best therapeutic approach.

E-PS-12-006
Adenoid cystic carcinoma ex-pleomorphic adenoma: a case report
J.L. Amaral*, J. Pimentel, A. Alves, C. Courelas, L. Carvalho
*Pathology Department, Coimbra Hospital and University Centre (CHUC), Portugal

Background & objectives: Carcinoma ex pleomorphic adenoma (CXPA) is rare and occurs in 1.5 to 13.8% of pleomorphic adenomas, most commonly in parotid/major salivary glands. The most frequent malignant components are salivary duct carcinoma and adenocarcinoma NOS, followed by epithelial myoepithelial/myoepithelial carcinoma.
Methods: We present a case of adenoid cystic carcinoma arising in previous pleomorphic adenoma.
Results: A 75-year-old woman presented with paresthesia in left preauricular area. A hypodense mass with 26 x 17 mm was detected in a cervical CT scan, in left parapharingeal area, without a cleavage plane with adjacent muscular and bone structures. A first biopsy showed pleomorphic adenoma component, predominantly with cells of myoepithelial phenotype (CK5/6, calponin and p40 positives). Considering the aggressive behaviour of the tumour, a second biopsy was made that confirmed pleomorphic adenoma and showed three areas with a cribriform pattern and heterogeneous expression for CD117, suggesting adenoid cystic carcinoma arising in a previous pleomorphic adenoma. The patient has been proposed for treatment with radiotherapy which is yet to start.
Conclusion: Carcinoma ex pleomorphic adenoma can pose a diagnostic challenge, therefore, it must be kept in mind, given the impact it has on patient prognosis. Furthermore, this case raises the importance of articulation of clinical and imagiological information with histopathological patterns in order to make a precise diagnosis.

E-PS-12-007

Sinonasal non-intestinal type adenocarcinoma with clear cell features: a morphologic and immunohistochemical study

G. Arcovito*, I. Dallan, A. Franchi
*University of Pisa, Italy

Background & objectives: Occasionally, sinonasal non-intestinal-type adenocarcinomas (non-ITAC) present with clear cell morphology, including cases that may closely mimic renal cell carcinoma. The aim of our study is to perform a histologic and immunohistochemical analysis of sinonasal clear cell non-ITACs.
Methods: We searched our institutional files for sinonasal non-ITAC and we selected those presenting clear cell morphology. All available histologic slides and formalin fixed paraffin embedded tissue blocks were retrieved. The immunohistochemical panel applied to all cases included pancytokeratin, cytokeratin 7, S100, calponin, smooth muscle actin (SMA), P40, carbonic anhydrase IX (CAIX), PAX8 and RCC.
Results: Three cases were identified. The patients were 2 females and 1 male of 44, 80 and 63 years, respectively. All lesions were in the nasal cavities and were surgically treated. Two patients experienced local recurrence at 40 and 67 months. Histologically, all lesions were formed by a uniform population of epithelioid cells with clear cytoplasm organized in small nests separated by thin fibrous septa. In addition, 2 tumours presented areas with papillae lined by cuboidal or cylindrical cells with pale eosinophilic cytoplasm. All cases were positive for pancytokeratin, cytokeratin 7 and P40; 2 cases were positive for S100, while calponin was focally expressed. SMA, CAIX, PAX8 and RCC were negative.
Conclusion: We report a subset of sinonasal non-ITAC with clear cell features that appear to differ from the so-called sinonasal renal cell–like adenocarcinomas for their histologic and immunohistochemical profiles, including absence of CAIX expression. Our results, including S100 and P40 positivity and focal calponin expression, suggest a putative myoepithelial differentiation in these tumours.
Funding: This study was partly supported by funds from Tuscany Health Service (ADAPTA project) to AF

E-PS-12-008

Primary head and neck paraganglioma cell culture expresses markers of cancer and mesenchymal stem cells

I. Bakhtogarimov*, M. Fedorova, A. Kobelyatskaya, A. Ayupova, V. Pavlov, A. Kudruavtseva, A. Snezhkina
*EIMB RAS, Russia

Background & objectives: Head and neck paragangliomas (HNPGLs) are highly hereditary neuroendocrine tumours that poorly investigated due to their rarity. At present, there is no commercially available HNPGL cell culture, due to the complexity of neuroendocrine tumour cell cultivation.
Methods: Primary cell culture was derived from patients with HNPGL and subjected to immortalization through the expression of human TERT (hTERT). After selection, cell culture was categorized by single cell expression profiles using 10X Genomics. Single cell sequencing was performed on Illumina NextSeq 2000 System. Bioinformatics analysis was carried out using Cell Ranger. t-SNE method was used for clustering and visualization.
Results: Cell types of HNPGL culture were annotated based on single-cell RNA-Seq data using cCATCH toolkit. Expression of cluster marker genes were matched with CellMatch reference database that includes 353 cell types and 686 related subtypes associated with 184 tissue types. We found that 55% and 35% of studied cells expressed markers of cancer and mesenchymal stem cells, respectively. As an alternative, we used PollenGliaData RNA-Seq dataset and revealed that almost all cells (91%) also showed expression of radial glia markers. Analysis of cell cycle phase was done with Seurat; the majority of cultivated cells were in G1-pahse (53%), followed by S-phase (28%), and G2M-phase (19%).
Conclusion: We could conclude that primary HNPGL cell culture is characterized by expression profiles close to cancer and mesenchymal stem cells. This is to agree with the evolution origin of paraganglia from multipotent mesenchymal stem cell. Extension of G1-phase could be associated with transition from undifferentiated phenotype of cells to differentiated one.
This work was financially supported by a grant from the Russian Science Foundation (no. 21-14-00353) and performed using the equipment of the EIMB RAS "Genome" centre (http://www.eimb.ru/rus/ckp/ccu_genome_c.php).

E-PS-12-009

An infrequent case of odontogenic myxoma of the maxilla in a 28-year-old female

M. Barbesier*, L. Christe, S. Sancho, S. Berezowska
*Institute of Pathology, Lausanne University Hospital (CHUV) and University of Lausanne, Lausanne, Laboratoire Promed, Marly, Switzerland

Background & objectives: Odontogenic myxoma (OM) is an uncommon benign odontogenic neoplasm of the jawbone. The diagnosis of this entity poses a challenge because its clinical and radiological manifestations are non-specific and often lead to confusion with other benign and malignant neoplasms.
Methods: A 2 cm osteolytic lesion of the maxilla was discovered radiographically in 28-year-old women who presented with painless jaw swelling. Microscopically, the tumour consisted of a hypocellular proliferation of bland spindled to stellate cells set in myxoid stroma, without islands of odontogenic epithelium. The diagnosis on biopsy was followed by a surgical excision with tumour free margins.
Results: Histomorphology allowed the diagnosis of an odontogenic myxoma on biopsy. OM of the jaw is a rare benign, but locally aggressive odontogenic neoplasm, mainly affecting younger adults, with marked female predilection. The mandible is more frequently affected than the maxilla. It comprises 0,5% of all bone tumours and 3-6% of odontogenic tumours. These tumours originate from the primitive mesenchymal portion of the developing tooth. Because of its slow growth, OM is often asymptomatic. However, OM is associated with a high recurrence rate ranging from 10% to 43% (mean 25%). Thus, surgical excision is the treatment of choice, but without agreement on surgical margins.
Conclusion: OM is diagnosed according to H&E histomorphology. Due to the unspecific nature of the clinical and radiological presentation, histology plays a major part in the diagnosing OM, especially to exclude the others differentials diagnoses, and particularly the malignant neoplasms that could be initially suspected by the locally aggressive behaviour of these tumours. Moreover, histological diagnosis allows adequate surgical management of the patient, in order to reduce the known risk of tumour recurrence.

E-PS-12-010

Laryngeal spindle cell carcinoma: a diagnostic challenge. Review of cases from the last 23 years in a tertiary hospital

G. Barrios Millán*, E. Ruiz-Bravo
*Hospital Universitario La Paz, Spain

Background & objectives: Spindle cell carcinoma (SCC) of the head and neck represents a diagnostic challenge due to its overlap, both morphological and immunohistochemical, with other benign and malignant entities. Our objective is to review the histopathology of the cases diagnosed in our centre.
Methods: A retrospective review of the cases diagnosed as SCC in our hospital from 2000 to 2023 was carried out. The histopathological

and immunohistochemical data, along with the clinical history of the patients, were analysed. Clinical evolution was reviewed as well.
Results: We have found 10 cases, all of them in men, with a mean age of 71. Of the 10 cases, two were outpatient clinics where the preparations were returned. The remaining 8 microscopically presented mostly ulcerated surface epithelium. In 4 cases the tumour presented epithelial differentiation in hematoxylin-eosin. One case presented epithelial differentiation only IHC for CK AE1/AE3. The remaining 3 did not present epithelial differentiation both by morphology and by IHC, but the patients had a history of SCC in the same location. One case presented mesenchymal differentiation to high-grade chondrosarcoma, the rest the sarcomatoid component was composed of spindle cells arranged in sheets and intertwined bundles.
Conclusion: SCC is a tumour in which differential diagnosis includes entities like sarcomas, melanoma, fibromatoses, and leiomyoma, to name a few. When dealing with these biopsies, we must first consider whether we are dealing with benign or malignant entities and request a directed IHC panel that includes epithelial, melanocyte, and muscle markers, always keeping in mind that they may not express them. In the end, be aware that a spindle cell tumour in this location is SCC unless proven otherwise.

E-PS-12-011
An aggressive sinonasal tumour with neuroepithelial differentiation: olfactory carcinoma
M. Bundele*, L. Rooper
*Tan Tock Seng Hospital, Singapore

Background & objectives: 55-year-old Chinese male presented with right nasal cavity mass. MRI showed intracranial extension with involvement of cribriform plate raising possibility of olfactory neuroblastoma. He had a previous history of undifferentiated nasopharyngeal carcinoma, treated with chemoradiation 7 years before.
Methods: Histology showed high grade infiltrative tumour featuring neuroectodermal component in nested/ lobulated/ solid architecture within vascular stroma and prominent rosettes with intermixed well-formed glands.
Tumour was diffusely positive for cytokeratin AE1/3 with focal staining for synaptophysin and chromogranin and CD56. CK7 was focally positive. INI1 was retained. CK20, CDX2, TTF1, p40, CD99, WT1, FLI1, SOX10, S100 and HMB45 were negative.
Results: Further in situ hybridization for EBV encoded RNA was negative.
The tumour recurred in less than a month and showed mainly solid (blastomatous) component on histology.
Blastomatous and rossettoid areas raised the differentials of other small round blue cell tumours such as neuroendocrine tumours including neuroendocrine carcinoma, olfactory neuroblastoma, primitive neuroectodermal tumour, INI-1 deficient carcinoma and teratocarcinosarcoma, however overall morphology and immunostaining excluded these differentials. No stromal or foetal elements that define teratocarcinosarcoma were seen. A metastatic poorly differentiated adenocarcinoma was also excluded.
Post recurrence resection, patient developed orbital apex syndrome, developed dural metastasis, underwent chemotherapy but finally succumbed to disease within 10 months of the initial diagnosis.
Conclusion: We present a case of aggressive sinonasal tumour with a neuroepithelial phenotype involving cribriform plate. The term 'Olfactory carcinoma' has been prominently used in previous literature for tumours with similar morphology. The progenitor stem cell-Olfactory basal cell with potential for differentiating into multiple lineage is believed to be precursor cell.
Further clinicopathologic and molecular analysis of these tumours with neuroepithelial phenotype should be considered to better define them, to facilitate more complete understanding of their classification, pathogenesis, and treatment.

E-PS-12-012
Recidivant chordoma of the clivus with progression to dedifferentiated subtype: a case report on a rare entity
G. Carrola*, A.P. Rodrigues, D. Sá, F. Sousa Vieira, J.R. Brandão
*Centro Hospitalar Universitário de Santo António, Portugal

Background & objectives: Dedifferentiated chordoma is a very rare entity, representing the least common subtype of chordomas and also the most aggressive. Our aim is to review a case initially diagnosed with a conventional chordoma that progressed to the dedifferentiated subtype during follow-up.
Methods: We reviewed the history of an 84-year-old female patient with a previous diagnosis of conventional chordoma located at the skull base. The patient was submitted to surgical treatment and adjuvant stereotactic radiotherapy. Nevertheless, several recurrences occurred, so multiple re-excisions were necessary during a five-year period. Histopathological and immunohistochemical investigation of these specimens was conducted.
Results: Histological examination of the first recurrence showed a multinodular neoplasm composed of typical physaliferous cells set in a myxoid stroma and a 7mm focus of undifferentiated spindle cells with high mitotic rate. Immunohistochemistry demonstrated normal positivity for CAM5.2, vimentin, S100, CD99, INI1 and negativity for, calponin, SMA, p63, and GFAP. The undifferentiated component showed loss for all immune stains. Proliferative index (Ki-67) in hotspot areas was 5% in the conventional subtype and 30-40% in the sarcomatous component. We signed out as recidivant dedifferentiated chordoma. After the second re-intervention, analysis showed similar histopathological features, this time with a greater undifferentiated component, with high mitotic rate and focal necrosis.
Conclusion: Dedifferentiated chordoma is extremely rare, having few cases reported in literature. It represents the most aggressive subtype of chordomas and treatment is challenging. Total excision with free margins is still the gold standard, combined with adjuvant radiotherapy. Recurrence, with the need for reintervention, and progression to a higher volume of the dedifferentiated component can lead to less favourable outcomes. Overall, poor prognosis and poor quality of life is expected, particularly in old females with skull base involvement.

E-PS-12-013
Methodology for fluorescence signal analysis in head and neck cancer surgical specimen after indocyanine green intravenous injection: MAGNOLIA project
O. Casiraghi*, G. Marguerit, P. Khneisser, N.I. Ben Romdhane, I. Breuskin, S. Temam, P. Gorphe, M. Abbaci
*Gustave Roussy, Université Paris-Saclay, France

Background & objectives: Fluorescence guided surgery for tumour tissue resection or lymph node identification is described mainly with Indocyanine Green (ICG). We are conducting a clinical trial after ICG injection for intraoperative control of surgical margins in head and neck cancers.
Methods: For now, five patients diagnosed with squamous cell carcinoma and indication for oral surgery (T1-T2) were included (5/60). They received ICG at 0.2 mg/kg , 45 min prior tumour incision. After fixation, the pathologist sectioned the surgical specimen every 3mm. Fluorescence signal from each tissue section was recorded according to standardized conditions with Spectrum hand-held Near-Infra-red (NIR) fluorescence camera.
Results: We developed a methodology based on tiles technique approach and threshold values, to analyse fluorescence signal in each tissue section containing or not cancer tissue. The data were correlated with final histology to measure intensity and distribution of fluorescence signal according to tissue histology. This strategy made it possible to determine the percentage of false negatives, false positives, true negatives and true positives within regions of interest of 4mm2 in each sections, and to evaluate the global concordance rate for each patient.

The results show that for all tested thresholds, the limit of consideration of the technique, set at 72% by protocol statistical methodology, was not only achieved but exceeded.
Conclusion: A standardized method has been built to quantify and measure the distribution of the fluorescence signal in an entire surgical specimen. The quantification analysis strategy includes: the creation of a quantification tiles matrix, the normalization of the intensity values in the tumour and non-tumour zones, and the integration of detection thresholds to extract fluorescence signals from tumour areas. The surgeon's choice to privilege the sensitivity or specificity will guide the selection of the fluorescence threshold for the MAGNOLIA project.

E-PS-12-014
Precursor lesions of odontogenic carcinomas: case report of an intraosseous mucoepidermoid carcinoma developed on a dentigerous cyst
J. Castro*, J. Azevedo, M. Alzamora, A. Varelas, J. Costa, C. Meireles, T. Bacelar, M. Jácome
*IPO-Porto, Portugal

Background & objectives: Odontogenic carcinomas are rare neoplasms but comprise a wide variety of different entities. Although these tumours are known to be related to the dental lamina, they are often diagnosed in advanced stages when precursor lesions are not evident.
Methods: We present a case report of a 74-year-old man with intraosseous mucoepidermoid carcinoma associated with an odontogenic cyst. Imaging, histological and molecular studies were consistent with the diagnosis.
In this case, there was evidence of malignant transformation of a dentigerous cyst, suggesting a primary origin. We reviewed the current literature about these possible precursor lessions of odontogenic carcinomas.
Results: The patient was referred due to a 6.8 cm, solid and multiloculated mass, centred in the body and left ramus of the mandible, involving an unerupted third molar. Histology showed a low-grade mucoepidermoid carcinoma, with areas of clear cells, developed on a dentigerous cyst. FISH analysis detected CRTC3-MAML2 fusion transcript, excluding primary intraosseous squamous cell carcinoma and clear cell odontogenic carcinoma.
These tumours and others, such as ameloblastic carcinoma and ghost cell odontogenic carcinoma, can originate from the epithelium of odontogenic cysts or the primitive rests of the dental lamina. Mucoepidermoid carcinoma may also have its origin in ectopic salivary gland tissue or the lining of the maxillary sinus.
Conclusion: Precursor lesions of odontogenic carcinomas are scarcely described in the literature and even less documented with images. This case provides histological evidence of an intraosseous mucoepidermoid carcinoma arising from a dentigerous cyst.
This finding suggests that other odontogenic carcinomas may share the same origin. However, developmental odontogenic cysts have their own distinct histogenesis. The dental lamina and ectomesenchyma may also play a role in the development of such lesions.

E-PS-12-016
Sinonasal meningioma: a case report
D. Ceyran*, T. Çiftçi, K. Başak
*Kartal Dr. Lütfi Kırdar Hospital, Turkey

Background & objectives: Extracranial meningiomas are quite rare in the sinonasal region. Four different mechanisms have been proposed for the development of extracranial meningiomas. One of these mechanisms is the extension of an intracranial meningioma into the nasal cavity by causing bone resorption.
Methods: A 62-year-old female patient presented to our hospital with a 3-month history of nasal discharge. The patient had a history of surgery for olfactory groove meningioma 17 years ago, but the tumour could not be totally excised due to its location. A biopsy was recommended due to the presence of a mass in the right nasal cavity on physical examination.
Results: Microscopically, a development characterized by oval-rounded, uniform-nucleus, wide, eosinophilic cytoplasm meningothelial cells forming a syncytial pattern starting from the nasal mucosa epithelium is observed. In a few foci, meningothelial cells form whirlpool-like structures and a few psammoma-like microcalcifications are notable. Tumour cellularity is moderately elevated, and mitosis, necrosis, and small cell components are not observed. Immunohistochemical examination revealed that the tumour cells were EMA, PR positive and Ki67 was seen in the most intense area at 5-6%. Based on these findings, the tumour lesion was evaluated as meningothelial meningioma, grade 1, and it was concluded that the previously existing olfactory groove meningioma had spread to the right nasal cavity.
Conclusion: In the patient, the meningothelial meningioma in the right nasal cavity is a secondary lesion that developed due to the extension of the intracranial (olfactory groove) meningioma to the right nasal cavity 17 years ago. While meningiomas are generally benign tumours, the presence of optic nerve involvement, subtotal surgical resection, advanced age, and a Ki67 proliferation index of over 4% (5-6%) in our case can explain the clinically aggressive behaviour of the tumour despite its histomorphological Grade 1 status.

E-PS-12-017
The possible prognostic role of Mena in oral squamous cell carcinoma
R. Chiciudean*, L. Banias, Z. Kovacs, I. Jung, D. Bereczki-Temistocle, S. Gurzu
*Department of Pathology, Clinical County Emergency Hospital of Târgu Mureș, Romania

Background & objectives: The prognostic role of HPV status in oral squamous cell carcinoma (OSCC) was hypothesized to be related to the actin cytoskeleton. This paper aimed to assess the possible connection between HPV status and Mena, an actin cytoskeleton remodelling marker.
Methods: This retrospective cohort analysis was conducted on 43 patients diagnosed with OSCC at the Department of Pathology of the Clinical County Emergency Hospital of Târgu Mureș, Romania. The HPV status was assessed through DNA-HPV testing. Mena expression was detected immunohistochemically, and the cytoplasm positivity was assessed in the tumour cells.
Results: Of the 43 examined cases, 18 tumours were HPV positive and 16 of them were Mena positive, compared with only 14 of the 25 HPV-negative tumours ($p<0.0001$). Mena was not expressed in normal oral tissue, but its expression increased in parallel with tumour de-differentiation ($p=0.03$): 8 of the 13 well-differentiated SCCs expressed Mena; in the moderately differentiated category, 12 out of 16 were positive whereas in 10 of the 14 poorly differentiated SCCs the tumour cells were marked by the examined protein. Regarding localization, tumours of the tongue and lips exhibited higher Mena upregulation compared to the floor of the mouth and maxillary sinus ($p<0.0001$).
Conclusion: In OSCC, Mena upregulation seems to increase with tumour de-differentiation and the presence of HPV mutations. Further studies are needed to further elucidate the role of the HPV mutation in relation to cytoskeleton modulation and the particularities in HPV-associated OSCC. Shaping molecular profiles of HPV-associated OSCC and establishing the role of the actin cytoskeleton can establish the basis for the development of new therapeutic tools for the personalized therapeutic approach.

E-PS-12-018
A simple case of a Warthin tumour or maybe more?
F. Dolkiras*, N. Stavrinou, E. Spiteri, E. Athanasiou, C. Vourlakou
*Department of Pathology, Evangelismos General Hospital, Athens, Greece

Background & objectives: A 76years old woman presented with a painless cervical mass measuring 3cm in greatest diameter. Biopsy of the mass was performed.

Methods: Histopathological examination of the mass was consistent with a Warthin tumour. Closer examination of the lymphoid stroma was significant for the presence of atypical hyperchromatic cells with ample clear cytoplasm arranged in sheets alongside the presence of numerous eosinophils and prominent proliferation of high endothelial venules with follicular dendritic cells.
Results: The clear cells expressed T cell markers (CD3, CD5 and CD4) with the expression of T follicular helper markers: PD1, BCL6, CD10 and CXCL13. CD23 and CD21 positive clusters of follicular dendritic cells were noted in close proximity to the T cells and away from the B cell areas. In situ hybridization for EBV encoded RNAs was focally positive in scattered B cells whilst kappa and lamba were polyclonal.
Conclusion: A diagnosis of Warthin tumour with involvement of the lymphoid stroma by a T-follicular helper (TFH) cell lymphoma, angioimmunoblastic-type was rendered. The pathologist should pay attention to both the lymphoid stroma and the epithelium when dealing with Warthin tumours as they can rarely be involved by lymphomas or carcinomas.

E-PS-12-019
Lymphoepithelial cyst of the thyroid gland in the background of lymphocytic thyroiditis
A. Faur*, D.C. Lazar, L.A. Ghenciu
*"V. Babes" University of Medicine and Pharmacy, Romania

Background & objectives: Lymphoepithelial cysts of the thyroid gland are relatively rare lesions of the head and neck region with only a few cases described in the current literature. We present a case report of branchial cleft-like lymphoepithelial cyst in a thyroid gland.
Methods: A 41-year-old female presented to the Surgery Department of City Hospital Timisoara with a nodular goiter. A resection of the thyroid gland and regional lymph nodes was performed.
Results: Macroscopically the thyroid was 5/5/1.5 cm with a cystic area in the right thyroid lobe of 2.5/1.2/1.1 cm. Microscopic examination revealed a cystic lesion with an epithelial lining represented by stratified squamous epithelium. Dense lymphoid tissue was present beneath the lining epithelium with lymphoid follicles and reactive germinal centres. In the rest of thyroid gland parenchyma there were present areas with extensive lymphocytic infiltrate with germinal centre formation and small follicles with oncocytes. The resected lymph nodes showed nonspecific findings with features like follicular hyperplasia and increased number of histiocytes.
Conclusion: Lymphoepithelial cysts have been postulated to originate from the derivatives of the embryonic ultimobranchial body and were originally reported in 1989. Less than 40 cases were published and only a few were associated with Hashimoto thyroiditis. The differential diagnosis in our case has to be made with Hurtle cells neoplasms, lithium intake, lymphoma thyroglossal duct cyst and Warthin-like thyroid papillary carcinoma.

E-PS-12-020
Hyalinizing trabecular tumour in a patient with oncocytic adenoma, lymphocytic thyroiditis and papillary carcinoma of the thyroid gland
A. Faur*, C.V. Gurban, L.A. Ghenciu, D.C. Lazar
*"V. Babes" University of Medicine and Pharmacy, Romania

Background & objectives: Hyalinizing trabecular tumour (HTT) comprises less than 1% of the thyroid neoplasms. We present the histopathological and immunohistochemical findings in a case of HHT of a patient who also presented with multifocal papillary carcinoma, oncocytic adenoma and lymphocytic thyroiditis.
Methods: A 65-year-old female presented to the Surgery Department of City Hospital Timisoara and a nodular goiter diagnosis was made by the clinician and a thyroidectomy was performed.
Results: Macroscopically in the right lobe of thyroid gland two nodular areas with dimensions between 0.2-1.3 were described but also another two tan-coloured areas with diameters between 0.6-2 cm were identified. The microscopic examination revealed that the two smaller areas had the features of a multifocal thyroid papillary carcinoma. From the two tan coloured areas one had aspects suggestive for an thyroid lesion of HHT and the other one of an oncocytic adenoma. An immunohistochemical analysis with MBME-1, CD56 and TTF-1 antibodies was performed. The final diagnosis was of multifocal papillary thyroid carcinoma with associated lesion of HHT, oncocytic adenoma in a background of lymphocytic thyroiditis (Hashimoto) and nodular goiter.
Conclusion: Thyroid lesions are a heterogenous group of entities including rare and challenging tumours.

E-PS-12-021
Medullary thyroid carcinoma, pigmented epithelioid melanocytoma and pleomorphic adenoma with lymph-node metastases in the same patient - inherited cancer syndrome or coincidence?
D.A. Grubišić*, T. Čeprnja, N. Kunac, K. Vilović
*University Hospital of Split, Croatia

Background & objectives: We present the patient with medullary thyroid carcinoma, pigmented epithelioid melanocytoma and histologically benign pleomorphic adenoma with lymph-node metastases (MPA). Thyroid cancer and melanoma can be part of Cowden syndrome. MPA is controversial entity with benign histology, but malignant behaviour.
Methods: In 2014, after the surgery, the patient was diagnosed with medullary carcinoma of the right thyroid lobe and pleomorphic adenoma of the right submandibular gland. No remaining tumour tissue was found in the extended surgery. In 2020, after the skin excision in the right infraorbital area, the patient was diagnosed with pigmented epithelioid melanocytoma.
Results: USG examination in August 2021, showed, in the upper third of the right side of the neck, inhomogeneous hypoechoic nodule. Cytological puncture raised the suspicion of metastasis of medullary thyroid cancer. In 2021, the neck discection of region I-V was performed. PHD diagnostic showed three lymph nodes in region II filled with tumour tissue composed of clusters of uniform myoepithelial cells with some epithelial cells or tubular structures lined with epithelial and myoepithelial cells surrounded by myxoid or chondromyxoid stroma, without polymorphism, necrosis and mitosis. Fewer smaller nodules in region I and II of the same histological composition were found. Described changes correspond to the recurrence of a pleomorphic adenoma.
Conclusion: By searching the literature, these tumours cannot fit together into any hereditary form of tumour syndromes. Further research in terms of next generation sequencing or other genetic analysis would be preferred solution. Almost all tumour inherited syndromes are rare and cause variety of symptoms. It is important to make patients and doctors aware of the existence of these conditions in order to detect a greater number of such patients through timely diagnosis and thus prevent the further development of cancers.

E-PS-12-022
Evaluation of miR- 21 and PDCD4 expression in liquid biopsies of oral dysplasia and oral squamous cell carcinoma patients
S.E. Gultekin*, L. Bozdag, L. Acik, N. Mollaoglu, E. Ersoy, O. Bayir, M.H. Korkmaz
*Gazi University Faculty of Dentistry, Turkey

Background & objectives: Liquid biopsy plays a pivotal role in non-invasive detection of cancer at the early stages of the disease. We aimed to determine miR -21 and PDCD4 expression levels in saliva and blood samples of oral dysplasia and oral cancer patients.
Methods: The study was carried out in blood and saliva samples, obtained from oral dysplasia (OD) (n:15) oral squamous cell carcinoma

(OSCC) (n:15) patients, and healthy individuals as control (n:15). The demographic data and clinical parameters of the patients were recorded. Determination of miR- 21 and PDCD4 expressions was done by using RT-qPCR and ELISA.
Results: The results of the study showed higher miR-21 levels in both blood and saliva samples of OSCC patients compared to controls ($p<0.05$), while PDCD4 expression was lower in the OSCC group ($p<0.05$). In the oral dysplasia group, the miR-21 level was found to be higher than controls and PDCD4 expression was also lower ($p<0.05$).
Conclusion: The PDCD4 and miR-21 displayed inverse expression status in both OSCC and oral dysplasia patients which may have potential as biomarkers in liquid biopsies.

E-PS-12-023
An unusual case of neurofibromatosis 1 syndrome
F. Gundogdu*, F. Soylemezoglu, Y. Atay, E. Eroglu, O. Kuscu
*Hacettepe University Department of Pathology, Turkey

Background & objectives: In neurofibromatosis 1 (NF1) syndrome neurofibromas and malignant peripheral nerve sheath tumours (MPST) are seen more commonly, unlike other unusual findings like hamartomas of the retinal pigment epithelium (RPE). Here, we present an unusual spectrum of NF1 syndrome.
Methods: The clinical and pathological findings of the case were evaluated. The 9-year-old patient had been following with the diagnosis of NF1 with multiple cafe-au-lait macules, neurofibromas, and pilocytic astrocytoma. Tumour excision and enucleation surgery were performed on the patient, who was found to have a giant mass extending to the right orbital area in the follow-up.
Results: Macroscopically a 16 cm-sized, multinodular tumour was seen. Histologically, the tumour consisted of a major hypercellular spindle neoplasm showing marbled appearance, geographic necrosis, and increased mitosis adjacent to a multinodular, hypocellular, wavy spindle-cell neoplasm with interspersed collagen bundles. The hypocellular component was diffusely positive for S100 while the hypercellular tumour was only focally positive for S100 and showed loss of H3K27me2 expression. The diagnosis of MPNST arising from plexiform neurofibroma was made. Macroscopic examination of enucleation revealed a haemorrhagic globe. Microscopically, a hamartomatous lesion that was composed of disorganized glial tissue and proliferated RPE intermixed with prominent vasculature was seen. The diagnosis of combined hamartoma of RPE was made.
Conclusion: NF1 is an autosomal dominant genetic syndrome that can be present with cutaneous and extracutaneous findings in various frequencies. Patients tend to have MPNSTs arising from neurofibromas at an early age. The combined hamartoma of RPE which is a benign lesion is one of the less common extracutaneous findings that can be a part of NF1 syndrome.

E-PS-12-024
Laryngeal spindle cell squamous cell carcinoma: report of three cases
S.E. Horoz*, I.T. Ceran, M.F. Tekin, O.C. Eren, N. Enver, L. Cinel
*Marmara University, Department of Pathology, Turkey

Background & objectives: Laryngeal spindle cell squamous cell carcinoma(SCSCC) is an epithelial malignancy that has undergone epithelial-mesenchymal transition. It is usually affecting elderly men. Less than 1% of all laryngeal malignancies is SCSCC. It is presented due to frequent misdiagnosis as sarcoma.
Methods: One of three patient is woman. Ages of cases are 77, 77 and 88. One patient has a history of smoking and the other has radiotherapy. All of them present with variable durations of hoarseness. Laryngoscopy reveals polypoid masses located in the glottis in all cases. Excisional biopsy was performed in 2 cases, punch biopsy was performed in 1 case.
Results: Histologically, in three cases, wide ulceration, focal dysplasia and in two cases squamous carcinoma in situ were observed in the surface epithelium. There was pleomorphic undifferentiated spindle cell proliferation in one case. In the other case, a nodular fasciitis-like histology was observed. The third case was resembled well differentiated leiomyosarcoma. Immunohistochemistry staining was observed as p40, p63 negative but SATB2 and p53 positive in all cases. PANCK was negative in two cases and focally positive in one case. In the leiomyosarcoma-like case, H-caldesmon and desmin were negative, while SMA was focally positive. With genetic analysis, USP6 translocation was not observed in the nodular fasciitis-like case.
Conclusion: The diagnostic value of immunohistochemistry is limited for SCSCC, especially in small biopsies. SATB2 may be helpful because 60 % of SCSCC is positive. In differential diagnosis, laryngeal sarcomas are often confused with SCSCC, but they are extremely rare and located deeper, not superficial mucosal lesions. The diagnosis of laryngeal SCSCC is based on the presence of a polypoid lesion with histologically undifferentiated spindle and/or pleomorphic cells and usually associated with surface squamous dysplasia and/or invasive SCC.

E-PS-12-025
A comparative study of the human dental tissue decalcification efficiency using various decalcifying agents
P. Hurník*, V. Skopelidou, J. Stembirek, J. Vaculova, L. Izakovicova-Holla, A. Konecna, P. Porizka, M. Buchtova
*University Hospital of Ostrava, Czech Republic

Background & objectives: Decalcification is an important step in the processing of histopathological samples of hard tissues, particularly human teeth due to their high inorganic content. In this study, five different decalcification agents were evaluated for their effectiveness.
Methods: During the study, 54 freshly extracted human teeth were processed. The following descaling agents were used: 5%nitric acid, 8%formic acid, decalcifier DC1, Microdecfast, and Lowy solution. The decalcified teeth were then routinely processed, sectioned, and stained. Corresponding samples were histologically evaluated (tissue morphology and staining characteristics). Furthermore, a spectrophotometric examination of 4-6 randomly selected samples from each group was performed.
Results: The study's findings revealed that using 5% nitric acid resulted in the quickest decalcification of dental tissue. In this group, the shortest sample decalcification time was 19hours and the longest was 312hours. The microscopic histological quality of the prepared samples was also satisfactory. Using Lowy's solution, on the other hand, resulted in the slowest decalcification. The process took a long time, and some teeth could not be processed properly in this solution even after two months of the study. Surprisingly, the results of the spectrophotometric analysis revealed that DC1 (combination of formic acid and formaldehyde) is the best decalcifying agent. The average decalcification time, however, was longer, averaging 20 weeks.
Conclusion: High-quality preparation of human teeth samples is extremely difficult, as is determining the correct procedure and identifying the best decalcification agent. It was found that 5% nitric acid appears to be the most effective decalcification agent (considering time and sample quality) for processing human dental tissue in routine histopathology practice. However, if time is not an issue, the most appropriate reagent according to the spectrophotometric examination is DC1, which ensures significant decalcification quality.
Funding: This research was supported by the Ministry of Health (NU20-06-00189/2020) and by MH CZ—DRO (FNOs/2021)

E-PS-12-026
p53 immunostaining can aid in accurate interpretation of p16 staining in the classification of head and neck squamous cell carcinomas
J. Huvila*, P. Pakkanen, A. Silvoniemi, K. Aro, L. Bäck, H. Irjala, L. Aaltonen, J. Hagström, J. Laine, H. Minn

*Department of Pathology, University of Turku and Turku University Hospital, Finland

Background & objectives: Our aim was to study the immunohistochemical (IHC) staining patterns of p53 in head and heck squamous cell carcinomas (HNSCC) and compare p53 IHC staining patterns to *TP53* mutation status and p16 IHC staining.
Methods: We stained 31 HNSCCs (22 oropharynx, six larynx/hypopharynx, three other sites) by IHC for p53 and p16, and performed next-generation sequencing (FoundationOne©CDx) on all cases. p53 IHC patterns were assessed as described in SCCs: wildtype, and abnormal patterns: overexpression, null and cytoplasmic staining. p53 wildtype staining patterns in p16+ tumours were assessed separately. p53 IHC was compared to *TP53* status.
Results: Of the 31 tumours, 18 showed abnormal p53 expression (11 parabasal/diffuse overexpression, seven null) and had a *TP53* mutation. 10 tumours showed p16 positivity without TP53 mutations. Of the remaining cases, two were p53 wildtype but had a *TP53* mutation (one p16 positive, one p16 negative) and one was p53 wildtype and p16 negative. One p53 overexpressing tumour showed p16 positivity and was originally assigned as p16 positive. Of the ten p16 positive cases nine showed p53 wildtype IHC staining patterns described in HPV-associated SCCs; four showed single positive cells i.e. "null-like" pattern or single positive clusters and five showed basal sparing pattern of which two had only scattered positivity.
Conclusion: There is excellent correlation between p53 abnormal IHC staining and the presence of a *TP53* mutation. Although p53 abnormal pattern and p16 positivity are almost mutually exclusive, mutations in *TP53* can occasionally be associated with p16 positivity and lead to misclassification as p16 positive HNSCC. p16 positivity is often associated with wildtype p53 patterns that can mimic abnormal p53 staining. In conclusion, performing p16 and p53 together improves the accurate interpretation of both stainings.

E-PS-12-029
Primary PNET/Ewing's sarcoma of trachea in an adolescent girl – case report
M. Jikurashvili*, R. Davitashvili
*CSD-Georgia, Georgia

Background & objectives: PNET/Ewing's sarcoma is a malignant small round blue cell tumour found mostly in bone and soft tissue of the extremities and the axial skeleton. The involvement of the trachea has rarely been reported.
Methods: We present a case of a 12 year old female patient who presented with a stridor and pneumonia signs. Bronchoscopy revealed intraluminal movable polypoid round mass attached to the wall of trachea clinically thought to be an adenoma. The mass was excised en toto and delivered for routine pathologic examination at our laboratory.
Results: H&E sections showed a wall of trachea with a tumour composed of atypical small round blue cells infiltrated within a myxoid stroma having a focal necrosis. One could easily notice pseudovascular/pseudocystic spaces too. Mitotic figures were numerous. Surface epithelium was focally ulcerated but not connected to the tumour. Immunohistochemistry revealed positive CD99, NSE, CD56 and Vimentin positivity. Mitotic index of Ki67 was around 30%. Other markers like S100, desmin, sma, p63, synaptophysin, chromogranin A, TTF1, CD34, CKs, CD45, OCT3/4 were negative. The results obtained were consistent with the diagnosis of PNET. The recommendation to confirm the pathology with further molecular studies was given. FISH analysis reported EWSR1-FLI1 fusion.
Conclusion: Ewing sarcoma of the trachea is a rare entity, especially in the paediatric age group. The diagnostic challenge lies in differentiating it from other location-specific tumours. Extensive immunostaining and FISH confirm the diagnosis. The therapeutic approach requires a combination of surgical resection, followed by chemotherapy and radiotherapy to achieve disease-free survival. Presently newer modalities of targeted immunotherapy against EWSR1-FLI1 chimeric fusion transcript are being explored.

E-PS-12-030
PDL1 and p16 immunohistochemical expression in oral squamous cell carcinoma
J. Kini*, N. Prasad, H. Kini
*Kasturba Medical College, Mangalore, Manipal Academy of Higher education, Manipal, India

Background & objectives: Programmed cell death ligand 1 (PD-L1) is an immune checkpoint molecule that weakens the host response against tumours. The aim of this study was to evaluate PDL-1 and p16 expression by immunohistochemistry in oral squamous cell carcinoma (OSCC)
Methods: A retrospective study was conducted including all resected specimens of OSCC received in the Pathology department over a three year period. Clinical and morphological features were correlated with immunohistochemical expression of PD-L1 and p16. PD-L1 staining was quantified by percentage of tumour positive cells and PD-L1 positive inflammatory cells assessed by tumour proportion score (TPS) and combined positive score (CPS).
Results: Of a total of 101 resected cases of OSCC, paraffin blocks with tumour were available for 94 cases. p16 expression was seen in 5.3% of the cases. Increased expression of PD-L1 was found in 38.3% cases. The tumour proportion score (TPS) (p value= 0.019) and combined positive score (CPS) (p value=0.009) were significantly associated with PDL1 staining intensity. Nearly one third of well, moderately and poorly differentiated OSCC were positive for PDL-1. Marked lymphocytic response was present in 53% of the positive PDL1 cases. A highly significant association was seen between CPS, TPS and lymphovascular invasion (p value = 0.005) and TPS with perineural invasion (p value = 0.030).
Conclusion: PD-L1 expression was seen in nearly two- fifths of the cases of OSCC. There was no significant association between PD-L1 and p16 expression. Intensity of p16 expression was significantly associated with tumour thickness, nodal status and eosinophilic host response. Perineural and lymphovascular invasion were seen to be significantly associated with PDL1 expression, indicating an aggressive nature of these tumours.

E-PS-12-031
A case of renal cell–like sinonasal adenocarcinoma: rare entity
A. Kret*, M. Pankhania, A. Al-Omari
*Histopathology Department, Sheffield Teaching Hospitals NHS Trust, United Kingdom

Background & objectives: A 84-year-old male presented with epistaxis. He was found to have a mass primarily in the left sinonasal cavity with radiological evidence of infiltration into the anterior skull base.
Methods: The lesional tissue was excised in piecemeal. Histological assessment demonstrated nasal mucosa largely infiltrated by a neoplasm showing a predominant clear cell morphology arranged in cohesive lobules and sheets. The lesional cells were monomorphous and cuboidal in nature, lacking mitotic activity, necrosis, lympho-vascular and perineural invasion.
Results: Immunohistochemistry demonstrated expression of AE1/3, SOX10, CK7, Vimentin, PAS positive and diastase resistant. The CK20, p63, TTF1, Synaptophysin, S100, CD10, AMACR, DOG1, RCC, PAX8, SMA, CD56, HMB45, and TFE3 were not expressed. The diagnosis of Renal cell–like sinonasal adenocarcinoma (RCLSA) was made. RCLSA is a rare entity and it is one of the variants of non-intestinal type sinonasal adenocarcinoma which arises in nasal cavity, paranasal sinuses and nasopharynx.

Conclusion: This low-grade malignancy is characterised by neoplastic gland formation with monomorphic lesional cells displaying clear to eosinophilic cytoplasm. The histological features of RCLSA are not specific to this entity, thus, one is required to exclude primary and metastatic tumours which have a similar morphology. Surgical resection is the treatment of choice. The overall prognosis is favourable, with low recurrence rate and no reported metastasis. This is the first case to report the immunohistochemical results of CD56 and TFE3.

E-PS-12-032

Head and neck follicular dendritic cell sarcoma - report of five cases

A. Lakshmanan*, A. Subramanyam
*Apollo Hospitals, India

Background & objectives: Follicular dendritic cells (FDC) are accessory cells which play a major role in antigen presentation. FDC sarcomas (FDCS) are very rare and have been in reported in many sites. FDCS is often misdiagnosed due to lack of awareness about this entity.
Methods: We retrieved cases of follicular dendritic cell sarcoma reported in the head and neck region for a period of 10 years and reviewed. Haematoxylin and eosin-stained sections and immunostains were reviewed and analysed. Clinical data were obtained from electronic medical records.
Results: We had 5 cases of follicular dendritic cell sarcomas arising in the head and neck region. Three were nodal and two cases were extra nodal in location. The patients age ranged from 34 – 46 years. There were 3 males and 2 females. Two cases had multiple recurrences. Surgery was the main stay of treatment with three of them received adjuvant chemotherapy and radiotherapy. They showed varied morphology with spindle, epithelioid and pleomorphic appearances.
Conclusion: FDCS are rare neoplasms with intermediate prognosis. They have varied histomorphological patterns and are often misdiagnosed, as four cases in our series were initially misdiagnosed as different neoplasms. Hence, awareness about these rare neoplasms and including them as a differential under neoplasms with spindled, epithelioid, and pleomorphic morphology would prevent misdiagnosing these entities.

E-PS-12-033

An unusual site for extramedullary (extraosseous) plasmacytoma: nasopharynx - case report

D. Lazureanu*, M. Cornianu, A. Jurescu, R. Cornea, A. Vaduva, A. Dema
*University of Medicine and Pharmacy Victor Babes Timisoara, Romania

Background & objectives: As specialists in head and neck pathology are aware, the incidence of nasopharyngeal plasmocytoma has a wide range, from 1% to 16% accordingly to different references. By all means its rarity uncover some challenges for histopathological diagnosis to be accurate.
Methods: The biopsy from a left-sided nasopharyngeal tumour mass of a 69 years-old male was routinely processed, paraffin-embedded and H&E stained. Ancillary test were needed: immunohistochemistry using a panel of antibodies (EMA, light chains, LCA, S100, CKs, synaptophysin, S100) in conjunction with imagistic investigation.
Results: Endoscopic examination, magnetic resonance imaging (MRI) and tomography show a cauliflower mass (19 mm maximum diameter) starting from the nasopharynx and reaching the inferior left choanal process, without a cleavage plan.
As a result of biopsy, the mass was characterized by high cellular density with eosinophilic cytoplasm and an eccentric nucleus. Neoplastic cells were positive for EMA and Kappa light chain, negative for all the rest. Also magnetic resonance imaging and computed-tomography excluded any other lesions or multiple myeloma-related tissue organ damage.
Conclusion: Although nasopharyngeal plasmacytomas are rare, their histopathological recognition and the assurance through interdisciplinary consultations that the monoclonal proliferation of plasma cells is only with this localization, allows the optimal therapeutic conduct: radiotherapy.

E-PS-12-035

Sino-nasal tract adenoid cystic carcinoma: a clinico-pathological study of 21 cases

A. Maaoui*, I. Mallek, S. Kamoun, N. Ben Othmen, Y. Houcine, K. Hamza, S. Elfekih, I. Bettaieb, A. Goucha, Y. Chaabene, S. Ferchichi, N. Aloui, A. Methnani, S. Dhambri, M. Driss
*Pathology Department, Salah Azaiez Institute, Tunis, Tunisia

Background & objectives: Adenoid cystic carcinoma (ACC) is the second most common malignancy and the most common salivary gland-type tumour of the sinonasal tract. The aim of this study is to describe the clinico-pathological features of ACC series in Tunisian patients.
Methods: A retrospective and descriptive study of 21 patients with ACC of sinonasal tract from 2003 to 2022, retrieved from the files of Pathology department of Salah Azaiez Institute. We reviewed the patients' demographics (gender, age), the anatomic site, growth pattern, pleomorphism; bone, neural and lymphovascular invasion.
Results: Twenty-one cases of ACC included 12 females and 9 males aged 28-84 years (mean 59,5). The tumours involved nasal cavity in 6 cases, the maxillary sinus in 14 cases and a combination of nasal cavity and paranasal sinuses in 1 case. Histologically, the tumour was composed of a variable growth pattern; predominantly cribriform (n=8), solid (n=2), tubular (n=2) and a combination of patterns in 9 cases.
Pleomorphism was mild in most cases (n=11), moderate (n=7) and sever (n=3). These tumours showed bone invasion in 6 patients and neural invasion in 5 cases. Only one case of lymphovascular invasion was seen.
Conclusion: ACC, while rare, represent the most common carcinoma of sinonasal tract. The diagnosis is essentially made on H&E stained slide. It is crucial to differentiate the ACC from the multiphenotypic sinonasal carcinoma, as the clinical features and management are distinctive. The immunohistochemistry of p16 followed by high-risk HPV testing may help in the differential diagnosis.

E-PS-12-036

Oropharyngeal squamous cell carcinoma: prevalence of Human papillomavirus infection

A. Maaoui*, S. Kamoun, Y. Houcine, K. Hamza, N. Ben Othmen, S. Elfekih, I. Bettaieb, A. Goucha, S. Mhalli, F. Ammous, C. Hmaied, M. Dhaha, S. Kedous, M. Driss
*Pathology Department, Salah Azaiez Institute, Tunis, Tunisia

Background & objectives: Human papillomavirus (HPV) infection represents a risk factor for oropharyngeal squamous cell carcinoma (OPSCC).
We aim to evaluate the prevalence of HPV infection in OPSCC by immunohistochemical study of p16 and the association between HPV status, epidemiological and anatomical-clinical factors.
Methods: We conducted a retrospective study of 43 cases of OPSCC collected between January 2008 and December 2021 in the immune-histo-cytology department of the Salah Azaiez Institute.
The criterion of judgement of p16 positivity in the immunohistochemical study was a moderate to intense nuclear and cytoplasmic staining of at least 70% of the tumour cells according to the international recommendations.
Results: We included 43 cases. The median age of the patients was 63 years with a sex ratio of 2.9.
Alcohol and tobacco intoxication was noticed in 44% of cases (n=19). Tumour size ranged from 7 to 80 mm with a mean size of 37 mm. Palpable cervical adenopathy was noticed in 54% of cases.

Among our cases, 23% expressed p16 (n=10) and 77% were p16 negative (n=33). No significant association was found between p16 positivity and the following parameters: age, sex, smoking, alcohol intoxication, tumour localization, tumour size, clinical tumour stage T, clinical lymph node stage, degree of differentiation and degree of keratinization.
Conclusion: Our results confirm that we are one of the countries with a low rate of HPV infection and that alcohol and tobacco intoxication remains the primary risk factor for CEIOP in Tunisia. We recommend to systematically include the p16 status in our anatomo-pathological reports of OPSCC.

E-PS-12-037
Mandibular chondrosarcoma: a report of four cases
W. Majdoub*, K. Ben Lazreg, S. Mestiri, Z. Lajmi, O. Belkacem, D. Benletaifa, A. Bdioui, S. Hmissa
*Pathology Department Sahloul Hospital, Tunisia

Background & objectives: Chondrosarcoma is the second most common primary malignant bone tumour, occurring in the pelvis and ribs in the 4th decade. The localization inface's bones and more particularly the mandible is extremely rare. We report four cases of mandibular chondrosarcoma (MCHS).
Methods: It's a retrospective study of 4 patients diagnosed with MCHS, listed in the Cancer Registry of Center Tunisia during a period of 15 years between 2006 and 2021. These tumours were diagnosed on biopsy or on hemimandibulectomy specimen.
Results: The mean age was 57 years with extremes of 25 and 83 years. There were two males and two females. Two cases were diagnosed on biopsy and two cases on a hemi-mandibulectomy specimen. For tumours diagnosed on surgical specimen, the tumour size was 4.5 and 6 cm. Grade I chondrosarcoma was diagnosed in one case, two cases were consistent with grade II, and one case was a mesenchymal chondrosarcoma. Excision was complete in mesenchymal chondrosarcoma case and incomplete in patient with chondrosarcoma grade II.
Conclusion: The most frequent locations of chondrosarcomas developed in the head and neck are the larynx, the maxillary bone, and the nasal region. Mandibular localization is extremely rare. Preoperative diagnosis is difficult because of the rarity of the lesion and the non-specific symptoms. The most common histological type is conventional chondrosarcoma, most of them are grade I and II. Grade III is rarely described. The main prognostic factors are the quality of excision, the TNM stage and the grade.

E-PS-12-038
Post-traumatic proliferative activity of the nasal epithelial cells under experimental injury and repair therapy conditions
A. Malysheva*, O. Reshetnikova, I. Berest, O. Teleshova, E. Burgelo
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: The morphological integrity of the nasal mucosa is the important protective barrier of the upper respiratory tract from exogenous airborne pathological agents. The research aimed to study the epithelial proliferative activity features after experimental nasal injury and repair therapy.
Methods: Histological and immunohistochemical(Ki-67) studies of the rats' nasal mucosa' tissue samples in 160 cases of the post-traumatic experimental rhinitis were carried out. The proliferating epithelial cells were determined on the 2nd, 5th, 10th, 14th, 21st, 30th, 42nd, 60th day after injury under various repair therapy conditions. Eighty animals(G2) had the 0.25% sodium deoxyribonucleate solution added to the standard anti-inflammatory treatment(G1).
Results: The proportion of proliferating cells on the second day of the experiment were not statistically significant in both groups. On the 10th day in group No. 2 there was an increase in the number of proliferating cells up to 6.9; 6.2/7.9% (G1-5.4; 5.2/5.8%; $p^{\wedge}0.05$). The maximum increase was recorded in G2 on days 14-21: 7.5; 7.2/7.9% versus 6.6; 6.4/7.3%; $p^{\wedge}0.05$ in G1. By the 30th day, a gradual decrease in the number of proliferating cells was noted, but a statistically significant difference in the groups persisted even by the 42nd day. By the 60th day, the number of proliferating cells in the experimental groups had no statistically significant differences ($p^{\wedge}0.05$).
Conclusion: The recent COVID-19 pandemic has highlighted the need to study the dynamics of structural adaptation of the human respiratory system in response to pathogens. The analysis of the conducted studies showed an increase in the proliferative activity of the epithelial cells of the nasal mucosa during the experimental use of the reparant. The data obtained are discussed in terms of the dynamic interaction between the mechanisms of damage and restoration of the integrity of epithelial tissues.

E-PS-12-039
Merkel cell carcinoma in maxillary sinus. Case report and literature review
J.S. Marrero Afonso*, I.J. Expósito Afonso, L. Martínez Blanco, K.M. Gallardo Rodríguez, S. Carrión Marrero, A.J. Nazco Deroy, F.A. García Machado
*Spain

Background & objectives: Merkel cell carcinoma (MCC) is a rare skin cancer with a tendency to affect regional lymph nodes. Because of nonspecific radiological findings, its wide differential diagnosis in head and neck area, rarity and clinicopathological characteristics could justify its presentation.
Methods: A 72 years-old female non-smoker patient with metabolic syndrome and a treated MCC in 2016. She presented a mild oppressive holocraneal cephalea with nasal congestion. A CT (august 2022) revealed a 5 cm heterogeneous lesion centred in the left maxillary sinus with extension to bone and soft tissue, highly suspicious of a primary malignancy. Therefore, an incisional biopsy was planned.
Results: Gross examination revealed multiple red-whitish tissue fragments with moderate consistency. Microscopically, it was formed by necro-haemorrhagic material and few groups of small round blue cells with scant cytoplasm and big nuclei with dispersed chromatin. An initial panel of immunohistochemistry (IHQ) revealed positivity to CK20, chromogranin A and synaptophysin. Absence of other lesions in radiological images compelled to amplify IHQ panel: positivity to CKAE1/AE3, CAM 5.2, CD56, SATB2 and negativity to S100, calretinin, EBV was demonstrated. A final diagnosis of Merkel cell carcinoma was made, the patient underwent systemic treatment with avelumab and a partial response to treatment was obtained.
Conclusion: Although Merkel cell carcinoma is rare in non-cutaneous head and neck area, correlation with clinical history is important. Furthermore, it should be taken into account in differential diagnosis to exclude other mimickers: carcinomas such as neuroendocrine carcinoma (CK20+, EBV- and SATB2+), sinonasal undifferentiated carcinoma and squamous cell carcinoma, olfactory neuroblastoma, melanoma, sarcomas, lymphomas and others.

E-PS-12-040
Acquired encephalocele mimicking a glomus tumour. Case report and literature review
J.S. Marrero Afonso*, I.J. Expósito Afonso, L. Martínez Blanco
*Spain

Background & objectives: Encaphalocele is the result of the herniation of brain tissue through an osseous defect. It is related to traumatisms, previous surgery, congenital defects and complicated otitis media. Its rarity and clinicopathological characteristics could justify its presentation.
Methods: We report a 57 years-old female non-smoker patient in follow-up because of mixed bilateral hipoacusia and repeated otitis

media. An exploratory tympanotomy was planned and revealed a tumoral lesion adhered to hypotympanum, ossicular chain and incudostapedial joint with free clear serous liquid in cavity, highly suspicious of glomus tumour. Lesion was partially excised and morphologic description was performed.
Results: Gross examination revealed multiple red-whitish tissue fragments with moderate consistency. Microscopically, it was formed by nervous tissue without significant morphological alterations with some associated singled-lined glandular structures without atypia and surrounded by loose stroma with mild chronic inflammatory cell infiltrate. Immunohistochemistry revealed strong positivity to GFAP. Findings propose differential diagnosis between acquired encephalocele and middle ear neuroglial heterotopia, which are differentiated by connection or not with the brain. However, presence of glandular structures suggests the former because it is considered a metaplastic change, but radiological is still needed. A later CT revealed a 6 mm solution of continuity in the posterior region of tegmen tympani, therefore surgical reparation was planned.
Conclusion: Given the rarity of acquired encephalocele, few large series exist in the literature, and optimal surgical management remains controversial, but it is recommended to decrease the incidence of meningitis. Pathological examination of specimens is still important and impacts directly in patient care.

E-PS-12-041
Extramedullary plasmacytoma in nasopharynx. Case report and literature review
J.S. Marrero Afonso*, S. Carrión Marrero, K.M. Gallardo Rodríguez, C. Febles Pérez
*Spain

Background & objectives: Extramedullary plasmacytoma represents a rare entity among the plasma cell neoplasms which are treated with radiation alone. Because of nonspecific radiological findings, its wide differential diagnosis in head and neck area, rarity and clinicopathological characteristics could justify its presentation.
Methods: We report a 52 years-old male non-smoker patient who presented a 2 years history of intermittent epistaxis in left nasal fossa. A CT showed mucosal enhancement in nasopharynx and nasal fibroscopy revealed hematic material rests which were adhered to middle turbinate, highly suspicious of haemangioma. Therefore, an incisional biopsy was planned, and morphologic description was performed.
Results: Gross examination revealed multiple reddish tissue fragments with moderate consistency. Microscopically, there was haemorrhagic material and a proliferation of plasmacytoid cells with homogenous eosinophilic cytoplasm, peripherally placed hyperchromatic nuclei, sometimes with conspicuous nucleoli and irregular contour. Immunohistochemistry revealed positivity to CD138, CD20, EMA and cyclin D1 with negativity to vascular markers, CK AE1/AE3, S100, CD45, CD3, CD5, CD79a, CD56, MUM1, BCL2, EBV, HHV8 without monotypic expression of light chains. A provisional diagnosis of plasma cell neoplasm was made. Patient had no clinical suggestive of multiple myeloma or bone marrow infiltration. Therefore, a final diagnosis of extramedullary plasmacytoma was made and the patient underwent radiotherapy (40Gy) with complete response to treatment.
Conclusion: Extramedullary plasmacytoma is an infrequent entity that should be taken into account in differential diagnosis of head and neck region that includes carcinoma, melanoma and other lymphomas. Pathological examination of specimens is still important and impacts directly in patient care.

E-PS-12-042
Nasopharyngeal hairy polyp in a male adult: a case report
N. Menezes*, A. Lança Neto, M. Mendes Las Casas Moreira, F. Fernandes Guimarães, C. Issa De Azevedo
*Laboratório Dairton Miranda, Faculdade de Ciências Médicas de Minas Gerais, Brazil

Background & objectives: Hairy polyp is a benign polypoid lesion usually located in the nasopharynx. This report intends to describe a rare lesion that might be unknown to surgical pathologists in general and highlight the possibility of management issues by the pathologists.
Methods: We describe a case of a 58-year-old male who has presented intermittent and purulent otorrhea since infancy. The patient was referred to an otorhinolaryngologist to investigate the cause of these symptoms. A sinonasal videoendoscopy and a videolaryngoscopy incidentally identified a polypoid mass in the left region of his nasopharynx compatible with squamous cell papilloma or carcinoma which was biopsied later.
Results: The gross analysis of the specimen demonstrated a polypoid whitish tissue fragment measuring 0,6x0,4x0,3cm with an irregular surface. Microscopically it showed a polyp covered by an ectodermal layer characterized by keratinizing squamous epithelium with underlying associated adnexal structures, including hair follicles and sebaceous units. There was also a combination of mesodermal tissue including adipose tissue and skeletal muscle. The primary histological analysis initially raised the possibility of any error during the analytical phase (identification of the block, embedding, cutting, identification of the slide). A detailed check excluded an error and then the diagnosis of hairy polyp was rendered after a search in Head and Neck WHO Blue Book.
Conclusion: Surgical excision is the best therapeutic procedure and is curative in the majority of cases. Hairy polyps are important differential diagnosis in neonate patients presenting with upper airway obstruction, but they can also be rarely found in adults. In these cases, appropriate knowledge about these malformations guides the management. The histological findings of mature and typical mesodermal and ectodermal tissues forming a polypoid lesion in the nasopharynx defines the diagnosis of hairy polyps and guides the patient's prognosis and follow-up.

E-PS-12-043
Sclerosing odontogenic carcinoma - a case report of a rare lesion
K. Moutasim*, R. Webb
*University Hospital Southampton, United Kingdom

Background & objectives: A 34 year old man was referred by his doctor to the oral and maxillofacial surgery department complaining of discomfort over 3/52 in the upper right quadrant. A radiolucent lesion was noted in association with the UR4 tooth.
Methods: OPG imaging showed a well-defined cystic lesion that had caused resorption of the upper right 4 tooth roots. A CT scan showed a radiolucent 2.5cm lesion in the right maxilla, which had displaced the alveolus in the premolar region. Excision biopsy was performed.
Results: Histological feature showed an epithelial tumour composed of bland strands and cords of epithelial cells within a densely slcerotic stroma. There were foci of perineural invasion.
The differential diagnosis included sclerosing odontogenic carcinoma, as well as muco-epidermoid carcinoma, odontogenic fibroma, hyalinising clear cell carcinoma or squamous odotongenic tumour.
There was no evidence of keratinisation and no intracytoplasmic mucin was seen on PAS staining. There was no EWSR1 gene rearrangement on genomic studies. There was no amyloid on Congo Red staining. The epithelial cells were positive with CK19 immunohistochemistry. Taken together, the features were interpreted as those of a sclerosing odontogenic carcinoma (SOC).
Conclusion: SOC is a rare odontogenic carcinoma, comprising thin cords of epithelial cells in a slcerotic stroma with often striking perineural invasion.
The patient is under follow-up and two years later, remains well with no evidence of recurrent or metastatic disease on imaging.

E-PS-12-044

Sarcoma mimicking an epithelial malignancy in the head and neck: a cytomorphological diagnostic challenge

M. Munonyara*, A. Sandison
*Guy's and St Thomas' Hospitals NHS Foundation Trust, United Kingdom

Background & objectives: Spindle cell/sclerosing rhabdomyosarcoma (SRMS) is a rare sarcoma in adults with a predilection for the head & neck. We present a case of a buccal SRMS mimicking epithelial malignancy clinically and on FNA cytology.
Methods: A 24-year-old man presented with a 3/52 history of left facial swelling and pain. A 3cm fluctuant swelling was present in the oral cavity and FNAC was performed. The cytology showed clusters of irregular, hyperchromatic, basaloid neoplastic cells, some arranged in a luminal formation with stroma. Based on the location and cytomorphology, the initial diagnosis was primary salivary gland neoplasm.
Results: Staging CT scan revealed a 5cm lobulated buccal tumour extending into the deep buccal space and eroding the dorsal wall of the ipsilateral maxillary antrum. A core biopsy sent for histology showed small round and spindled tumour cells arranged in a pseudo- micro alveolar pattern within hyalinised stroma. Occasional mitotic figures were present but no necrosis. On immunohistochemistry the tumour expressed desmin, myogenin and MyoD1. FOX01 gene rearrangement was not detected on FISH. The histological diagnosis was SRMS.
Conclusion: SRMS is rare and challenging to diagnose on cytology and histology. Clinically and histologically they can mimic epithelial tumours including basaloid cell neoplasms and myoepithelial tumours. Routinely, FNAC is the first diagnostic test when assessing head and neck lesions. Therefore, awareness of SRMS presenting in this location is imperative as it mimics epithelial malignancy. Sarcoma, such as SRMS should be considered in the differential diagnosis of a head and neck lesion showing aggressive radiological features and rapid onset of symptoms.

E-PS-12-046

Human papillomavirus (HPV)-related multiphenotypic sinonasal carcinoma: analysis of three cases with uncommon HPV subtypes

J.H. Nam*, Y. Choi
*Chonnam National University Hospital, Republic of Korea

Background & objectives: Human papillomavirus (HPV)-related multiphenotypic sinonasal carcinoma (HMSC) is a newly emerged tumour restricted to the sinonasal tract and associated with high-risk HPV. We describe a pathologic features of HMSC and draw attention to the uncommon HPV subtypes in given cases.
Methods: We described 3 HMSC cases diagnosed at our hospital. We will describe the epidemiology and unique pathologic features, discuss its distinction from other tumours including adenoid cystic carcinoma and squamous cell carcinoma. Immunohistochemical stains for p16, c-kit, p63, and SOX-10 were performed along with HPV DNA test in all 3 cases using PANA RealTyper™ HPV Kit (PANAGENE Inc., South Korea).
Results: All cases were from men aged 60 to 86 years (mean, 75), and all tumours were larger than 3cm in size (mean, 4cm). Histologically, solid nests of basaloid cells and cribriform pattern were the main characteristics. Every case demonstrated atypia of surface squamous epithelial layer, morphologically similar to the squamous cell carcinoma in situ. All 3 cases showed strong, diffuse positivity for p16, and it is noteworthy that positive results were also obtained in the surface squamous epithelial layer, including the lesion showing the atypical change. As a result of the HPV DNA test, all three cases had different high-risk HPV subtypes (18, 56, and 82, respectively).
Conclusion: Majority of HMSC cases published are from the west, and HPV subtype testing confirmed that HPV type 33 was the most common subtype. These results may suggest the possibility that the dominant HPV subtypes of HMSC in East Asia are different from those in the West. Still, an accurate interpretation is difficult due to the limited number of cases.

E-PS-12-047

The first reported case of intraparotid ganglioneuroma masquerading as a malignancy

B. Othman*
*Charles University, Czech Republic

Background & objectives: Ganglioneuromas (GNs) are slow-growing, benign tumours arising from Schwann cells and ganglion cells. The incidence of GNs is extremely rare, especially in the head and neck. We herein describe the first reported case of intraparotid ganglioneuroma masquerading as a malignancy.
Methods: We report a 42-year-old female presented with a parotid mass. The case was diagnosed mainly based on morphology.
Results: The excised lesion revealed two intermingled cell populations with variably trabecular or pseudoglandular architecture: large, rounded cells with an abundant, finely granular eosinophilic cytoplasm, and fasciculated cells with an elongated cytoplasm featuring fine fibrillar extensions. No mitosis or tumour necrosis was observed. Perineural entrapment, areas of colliding neuronal components, and granular gangliocytes were conspicuous. Immunohistochemical staining for S100, synaptophysin, and chromogranin A were positive. Nonetheless, no immunoreactivity for cytokeratins (CK5/6, CK7, AE1/AE3), epithelial membrane antigen, HMB45, Melan A, CD30, calponin, SSTR2A, DOG-1,TTF-1, CD117, and p40 was detected. The lesion was excised after nerve dissection to preserve the motor nerve fibres; the frozen section revealed margins to be free from neoplasms.
Conclusion: We emphasize the possibility of the development of ganglioneuroma inside the parotid gland. Caution should be taken to avoid diagnosing this benign lesion as a metastatic malignancy (e.g. neuroblastoma) or requesting unnecessary aggressive treatment (e.g., postoperative chemotherapy and radiotherapy).

E-PS-12-048

Insights into investigating the pathogenesis of salivary carcinoma ex adenomas with taxonomical implications

B. Othman*
*Charles University, Czech Republic

Background & objectives: Carcinomatous transformations are common atop (monomorphic) basal cell, canalicular, and/or pleomorphic adenomas. Nonetheless, the prognostic value of a newly developing malignancy is variable. This study underpins the literature for outlining malignant transformations with reference to morphologic changes.
Methods: After mining the published literature for all salivary carcinomas arising in benign lesions from 2014 to 2022, we annotated each carcinoma for the marker(s) used and the level of evidence attained for diagnosing each published case. Questionable diagnoses were discarded.
Results: The term 'salivary carcinoma ex mixed adenoma (CXMA)' is proposed as a generic term that clusters, at least, 63 malignant subtypes. Each subtype could reveal one or many mutations drivers that pertain either to a known molecular profile of the malignant component or molecularly unlabled malignancy developing secondary to a preexistence mixed adenoma.
Conclusion: Coining new designations for known pathologic entities featuring unreported morphological variations without significant change in clinical behaviour is as beguiling as considering all salivary gland malignancies either low-grade or high-grade. With using the umbrella term CXMA, either mesenchymalizing, reprogramming, transdifferentiating or, with lineage plasticity, to encompass all mixed

adenomas that develop malignancies. This typology could prove useful at the clinical level, without compromising the accuracy of the pathological diagnosis.

E-PS-12-049

Chondromesenchymal hamartoma and DICER-1 mutation: a case report and literature review

A. Prat*, L. López, M.C. Campos, D. Piñol, J.R. Gras, M. Casasayas, J. Szafranska
*Hospital de la Santa Creu i Sant Pau, Spain

Background & objectives: Nasal Chondromesenchymal Hamartoma (NCMH) is a rare benign lesion of sinusoidal tract, predominantly affecting children and young adults, associated with DICER1 mutation. Our aim is to describe NCHM and its association with DICER1 syndrome.
Methods: We present a case of an isolated nasal mass in a 22-year-old women with anosmia and hyposmia, without relevant personal or family history. Clinical exploration revealed polypoid lesion, measuring 50x40x10mm extending from cribiform plate to nostril. The patient underwent endoscopic sinonasal resection surgery. Routine studies with H&E and immuno-stains were performed.
Results: Microscopically, the case is described as a polypoid lesion containing variable-size cystic spaces filled with mucoid acellular material, lined by pseudostratified ciliated epithelium, respiratory-type. Cysts were admixed with nodules of cartilage variably in size, shape and contour with myxo-hyaline loose stroma, formed by spindle cells without atypia in a background of mixed inflammatory cells. Morphological characteristics confirmed NCHM and DICER1 immunostain turned out positive. Patient went through genetics consultation to exclude DICER1 germline mutation, which resulted negative.
Conclusion: DICER1 mutation carriers have a predisposition for development of various tumours, most commonly pleuropulmonary blastoma, thyroid, kidney and ovary cancers. The presence of NCMH in young patients, which is rare tumour not included in current WHO classification, can be associated with DICER1 germline or somatic mutations, are frequently overlooked by pathologists. Hence, genetical studies should be performed in those cases to exclude it.

E-PS-12-050

Case report: Epithelial-myoepithelial carcinoma in the nasal cavity- a diagnostic pitfall in frozen section evaluation

T. Rattay*, J. Knolle, C. Taege, A. Haak, J. Lautermann
*Krankenhaus Martha-Maria Halle-Dölau, Institut für Pathologie, Germany

Background & objectives: Epithelial-myoepithelial carcinoma (EMC) is a rare low to intermediate grade malignant salivary gland tumour mostly occurring in the major salivary glands. A less common site of appearance are the seromucinous glands of the sinonasal tract.
Methods: A 69-year-old male patient presented with progressive pressure pain on the left cheek and left eye. Endoscopic examination showed a polypoid mass in the left nasal cavity. CT and MRI further revealed an expansive mass with bone destruction of adjacent structures: the medial nasal concha, the medial wall of the maxillary sinus and of the left orbita.
Results: Before tumour excision a biopsy was taken. Frozen section showed an invasive papillary epithelial lesion without nuclear atypia, suspicious for inverted papilloma. On paraffin embedded tissue sections this diagnosis was initially confirmed. Complete excision of the tumour was performed. Shortly afterwards the tumour recurred locally. Histology now showed an invasive biphasic tumour with tubular and cribriform growth pattern composed of luminal ductal and outer myoepithelial cells. Immunohistochemically the luminal cells were strongly positive for CK8/18 and CD117 while the myoepithelial cells stained positive for smooth muscle actin and P63. Molecular analysis was performed and revealed a loss of PTEN. A diagnostic HRAS mutation was not detected.
Conclusion: Although the occurrence of EMC in the nasal cavity is extremely rare, pathologists must consider it. Diagnosis is based on the biphasic architecture and the immunophenotype. Especially histological variants can be challenging to diagnose. HRAS mutations can help to rule out EMC mimics. Sometimes only reconsidering the chosen analytical approach as much as peer review leads to the correct diagnosis.

E-PS-12-051

Pharyngolaryngeal amyloidosis. Five years experience in a single institution

M.G. Rodríguez Guevara*, C.J. Martinez Martinez, S. Fernández Cascón, J. Alzoghby-Abi-Chaker, O. García-Galvis, S. Marín-Asencio, E. Honrado-Franco, S. Sáez-Ávarez
*Complejo Asistencial Universitario de León, Spain

Background & objectives: Head and neck amyloidosis is rare, being the laryngeal the most common location. However, this last area represents less than 1% of all benign lesions of the larynx, and it is usually manifests as a form of localized amyloidosis.
Methods: Since 2018 until 2022 (included), a retrospective analysis of diagnosed cases of laryngeal amyloidosis have been performed in our centre. Based on this, a systematic search was carried out in the specialized database (PatWin), considering all diagnoses with laryngeal amyloidosis. The clinical and morphological data were collected and analysed.
Results: We have identified 2 patients with Laryngeal and 1 patient with Pharyngeal Amyloidosis, which correspond to two men and one woman between the third and fourth decade of their life. Recurrent dysphonia was a common symptom for all consulted patients after continuous vocal effort. In the first case, the cervical CT revealed a small smooth lesion in the right posterior pharyngeal wall, in the other 2 cases a thickening of the soft tissues with isolated calcifications was observed. The pathology study revealed a subepithelial deposit of acellular, eosinophilic, and amorphous material, which stains with Congo red and offers apple-green birefringence, as well as immunoreactivity with P amyloid.
Conclusion: Laryngeal amyloidosis is a rare entity that clinically manifests in a very non-specific manner and can be confused with other entities such as vocal cord polyps, lipoid proteinosis, among others, which are negative for Congo Red. It usually presents locally in this area, although it can occur in association with a systemic disease (multiple myeloma, neuroendocrine tumour, small cell carcinoma, etc.), or as an initial manifestation of it. For this reason, multidisciplinary management of these patients is necessary.

E-PS-12-052

Pleomorphic adenoma of the parotid gland with canalicular adenoma-like morphology: a recently recognized distinct subtype

F. Rosa*, M. Rito, J.A. Ortiz-Rey, C. Martins, I. Fonseca
*Instituto Português de Oncologia de Lisboa Francisco Gentil, Portugal

Background & objectives: Pleomorphic Adenoma (PA) derives its name from the significant cytomorphological and architectural diversity it can display. Notably, a specific tumour may only have a single pattern. Most PAs harbour gene fusions involving PLAG1 (>50%) or HMGA2 (10-15%) genes.
Methods: We present a case of a PA of the parotid with a prominent canalicular adenoma (CA)-like pattern, similar to the characteristic minor salivary gland CA and creating a diagnostic dilemma. The case was investigated by FISH using a break-apart probe for HMGA2 gene. Review of the literature was performed.

Results: A 53-year-old woman presented with a parotid gland mass. A category IVB neoplasm was reported by FNAC. The patient was submitted to superficial parotidectomy.
The tumour was well-circumscribed and encapsulated. It was composed of monotonous cells arranged in anastomosing trabeculae, with acinar and microcystic spaces. Beading of tumour cells, characteristically described in CAs, was observed. The background stroma was loose with oedematous-haemorrhagic areas. No conventional PA component was identified. FISH analysis revealed HMGA2 rearrangement, supporting PA diagnosis.
A recent study described a series of PA with CA-like morphology with recurrent HMAG2 fusion, supporting that they are distinct from CA of minor salivary glands and a "monomorphic variant" of PA.
Conclusion: PAs have a wide morphological spectrum that encompasses monomorphic tumours. PAs with a CA-like morphology are a diagnostic challenge, especially when no conventional PA component is present. Knowledge of this distinct variant and, in this setting, genetic testing for HMGA2, gene is of great value. This case increases the awareness of this atypical presentation, helping to avoid diagnostic difficulties.

E-PS-12-053
Collision tumour of sclerosing microcystic adenocarcinoma and squamous cell carcinoma of the tongue: an exceptional case report
O. Sahin*, M.H. Karabulut, Y.K. Duymaz, I.E. Zemheri
*University of Health Sciences, Umraniye Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Sclerosing microcystic adenocarcinoma (SMA) is a rare type of malignant tumour arising in the head and neck mucosa, resembling microcystic adnexal carcinoma (MAC). Here, we report a unique case of simultaneous co-occurrence of SMA and squamous cell carcinoma (SCC).
Methods: A 64-year-old male with a one-year history of a solid lesion on the right side of the tongue presented to the clinic. Clinical examination and magnetic resonance imaging (MRI) revealed a heterogeneously contrasted lesion with irregular contours. The lesion had also invaded the left genioglossus muscle. Tru-cut biopsy was performed. Subsequently, the patient underwent hemiglossectomy.
Results: Tru-cut biopsy revealed MAC. Upon evaluation of the resected specimen, gross examination disclosed ulcero-infiltrative tumoral lesions. Histological examination revealed that the tumour was comprised of 75% poorly differentiated SCC and 25% SMA. The SMA segment formed tubules within the dense fibrous stroma and exhibited deep infiltration. Two types of cell populations were observed: luminal cells, which showed bland nuclear morphology and expressed cytokeratin 7 (CK7) and carcinoembryonic antigen (CEA), and myoepithelial cells, which expressed P63 and P40. Both cell populations were negative for SOX10 and CD117. The Ki67 proliferation index was 5% in SMA and 40% in SCC. Perineural invasion was present in both SMA and SCC.
Conclusion: SMA is a new entity included in the 5th edition of the World Health Organization (WHO) classification of Head and Neck Tumours, and a rare type of malignant tumour should be differentiated from MAC. This case report presents a novel contribution to the literature by documenting the coexistence of SMA and another tumour, a finding that has not been previously reported.

E-PS-12-054
Low-grade nasopharyngeal papillary adenocarcinoma with breast metastasis: a unique case report
O. Sahin*, M.H. Karabulut, S. Cetin, Y.K. Duymaz, I.E. Zemheri
*University of Health Sciences, Umraniye Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Low-grade nasopharyngeal papillary adenocarcinoma (LGNPPA) is rare indolent tumour that originates from nasopharyngeal surface epithelium. It has favourable prognosis, with no previously reported cases of metastasis. In this report, we document the first instance of metastatic LGNPPA in the literature.
Methods: A 41-year-old female patient presented with a nasopharyngeal mass and was evaluated at an external facility for carcinoma of unknown primary origin. Upon the biopsy, the patient was inaccurately diagnosed with papillary thyroid carcinoma, which subsequently led to the initiation of chemotherapy treatment. The patient was then referred to our centre for verification of the histopathological diagnosis.
Results: Clinical and radiological examinations revealed a mass in the nasopharynx, causing destruction to the skull base. Microscopically, adenocarcinoma with a papillary configuration invading the bone tissue was observed. Immunohistochemical staining was positive for TTF1, cytokeratin, and EMA and negative for thyroglobulin and PAX8. During follow-up, a suspicious lesion in the breast was detected on positron emission tomography (PET-CT), prompting magnetic resonance imaging (MRI). A subsequent tru-cut biopsy revealed adenocarcinoma with a papillary and tubular pattern. Histopathological and immunohistochemical findings confirmed the presence of metastatic LGNPPA.
Conclusion: In this unique case report, we underscored the importance of LGNPPA in the differential diagnosis of nasopharyngeal tumours, highlighting the challenges in differentiating LGNPPA from papillary thyroid carcinoma (PTC) owing to overlapping morphological and immunohistochemical features. This report presents the first documented instance of LGNPPA metastasis. Future research should focus on elucidating the molecular and genetic characteristics of LGNPPA and its metastatic potential, which may ultimately reshape our perception of the behaviour of what is known as an "indolent tumour."

E-PS-12-055
Two paediatric immature teratoma cases located in the head and neck region
K. Simsek*, A. Yavuz, G. Karaguzel, N. Yaprak Barıt, I.E. Gurer
*Akdeniz University Department of Pathology, Turkey

Background & objectives: Teratomas with immature tissues and with various quantities of mature tissues are referred to as immature teratomas. Midline localization is where extragonadal teratoma frequently manifests itself. We present two paediatric immature teratoma cases located in the head and neck region.
Methods: Pathological examination was performed by routine hematoxylin-eosin and for the immunohistochemical staining Pan CK, CD56, synaptophysin, GFAP and Ki67 immunohistochemical markers were used. Patients' AFP and Beta-Hcg levels were measured as of biochemical markers. MRI was used as radiologic imaging.
Results: Case 1
A 9-day-old female newborn was admitted with dyspnea and stridor. Physical examination showed a mass on the cervical region. The patient was operated and histopathological examination revealed teratoma morphology which contains three germ layers. In three low-power fields, an immature teratoma component was seen that comprises primitive neuroectodermal cells.
Case 2
A female newborn presented with dyspnea, cleft palate and parapharyngeal mass. After the resection of this mass, histopathological findings were compatible with immature teratoma.
During the follow-up both of the patients, they did not experience any recurrence or metastasis in 3 and 24 months, respectively. The patients' AFP levels were within the normal range during these periods.
Conclusion: In paediatrics, teratomas are the most prevalent histologic type of germ cell tumours. There are two types of teratomas; mature and immature type. Histopathological examination of immature

teratoma shows immature tissues mixed with ectodermal and endodermal tissues of varying maturation. Head and neck localization is uncommon for teratomas. The majority of newborns with cervical or oral-pharyngeal teratomas have an apparent mass and an airway obstruction. Treatment requires chemotherapy and has to be further investigated for the effects on relapses.

E-PS-12-056

Myoepithelial carcinoma: a case report and short review of the literature

E. Souka*, G. Galanopoulos, G.M. Stanc, P. Bafaloukos, G. Sgouros, O. Tzaida
*Pathology Department Metaxa Cancer Hospital, Greece

Background & objectives: Myoepithelial carcinoma (MC) is a rare myoepithelial cell tumour usually of the parotid, but also submandibular and minor salivary glands. It accounts for < 1% of all salivary gland malignancies, arising de novo or ex-pleomorphic adenoma (MC ex-PA).
Methods: A 67-year-old male presented to the dermatology clinic with an aggravated tumour of the submandibular area. He underwent radical excision. On gross sectioning the tumour was protruding, multinodular, whitish, with focally microcystic configuration measuring 6.5cm.
Results: Microscopically, the tumour was multinodular extending to the subcutis with pushing borders. The neoplasm was epithelioid, with areas of distinct clear cell morphology, indicative of myoepithelial differentiation. The tumour cells were arranged in solid, trabecular, and cord-like pattern with myxoid, myxochondroid and focally osseous metaplastic stroma. There was a mild mitotic activity. There was no apparent necrosis, nor remnants of salivary gland or elements of pleomorphic adenoma. The neoplastic cells had a CKAE1/AE3+, CK903+, p63+, SOX10+, GFAP+, S100+ focally, SMA+ focally, CK7-, CK5/6-, HMB45- immunophenotype. Ki67 (MIB-1) was up to 3%. The tumour was signed out as myoepithelial carcinoma.
Conclusion: Because of the rarity of MC there is no standard treatment guideline. Surgical resection is the main approach. In recent literature local recurrence rates 23–50 % have been reported with 25 % chance of distant metastasis. Currently, there is not a widely accepted grading system with a reproducible correlation to the prognosis. Even so presence of tumour necrosis is considered by some as a high-grade feature. Patients with high-grade histopathologic markers could be good candidates for adjuvant radiotherapy.

E-PS-12-057

BRAF p.V600E-mutated papillary-cystic neoplasm of the middle ear: Expanding the spectrum of the sialadenoma papilliferum family tumours

O. Stanowska*, C. Götting, M. Caversaccio, A. Agaimy, S. Weder
*Institute for Tissue Medicine and Pathology, University of Bern, Switzerland

Background & objectives: Papillary-cystic neoplasms of the head and neck are a heterogenous group of rare and poorly classifiable epithelial tumours. Recently, many of them were redefined as homologous neoplasms of exocrine glands.
We present a case of BRAF p.V600E-mutated middle-ear papillary-cystic lesion.
Methods: 41-year-old, previously healthy female presented with left-sided otalgia, continuous hearing loss, otorrhea and tinnitus for over a year. MRI revealed tumour of the middle ear with extension to auditory tube and external auditory meatus. The patient underwent microscopic endoscopic radical tumour excision. FFPE tissue was used for H&E and immunostaining as well as for targeted Next Generation Sequencing.
Results: Histology demonstrated a surface squamous inverted papilloma-like component with a deeper bilayered glandular component showing papillary growth of cytologically bland monomorphic columnar cells with eosinophilic/oncocytoid cytoplasm and apical snouts. Microabscess-like microcystic formations with epithelial and neutrophil aggregates were present in the epithelium. Immunostains showed delimiting p63 positive basal layer around the CK7 positive glandular elements. S100 was positive in the spindle cell stromal component, PAX8 faint diffuse positive in the epithelium. SOX10, TTF1, CA-9, Chromogranin, Synaptophysin were negative. The case demonstrated BRAF p.V600E mutation and was classified as a benign papillary neoplasm - middle ear analog to the sialadenoma papilliferum family tumours. Follow up of 11 months revealed no recurrence.
Conclusion: Papillary tumours of the middle ear represent a heterogeneous group of distinct neoplasms characterized by a prominent papillary-cystic pattern. The appropriate interpretation of histological findings and genetic alterations are necessary for their diagnosis. Exophytic squamous, combined with papillary-cystic ductal proliferation, evidence of the dual population of the papillae (CK7 in the ductal, p63 in the basal component), as well as presence of BRAFV600E mutation, allowed to classify the tumour as a middle ear analog to the sialadenoma papilliferum family tumours.

E-PS-12-058

Ectopic olfactory neuroblastoma (ONB) of the sellar region: report of a rare case and review of the literature

M. Testa*, S. Uccella, R. D'amato Pascarella, S. La Rosa
*Università degli Studi dell'Insubri, Italy

Background & objectives: ONB is a non-epithelial neoplasm of the upper nasal cavities showing neuroendocrine differentiation. Anecdotic ectopic cases have been reported. We present a case of ONB of the sella, initially misdiagnosed as PitNET. The diagnostic importance of transcription factors (TFs) expression is highlighted.
Methods: A 46-year-old man presented with progressively worsening visual symptoms for 7 years, with bitemporal inferior quadrantopia and scotomas. Magnetic Resonance Imaging (MRI) revealed a 41x24x37 mm sellar mass, incorporating the right carotid syphon. The patient underwent endoscopic endonasal trans-sphenoid surgery and the removed mass was sent to our Pathology Department. The specimen was entirely sampled, formalin fixed and paraffin embedded.
Results: Microscopically, nests and rosettes of monotonous cells with round nuclei and scant cytoplasm were observed, showing immunoreactivity for Chromogranin A and Synaptophysin, and questionable reactivity for ACTH (absent at a later review). Immunostains for αHCG, PRL, GH, FSH, LH were negative. The Ki67 proliferation index was 5%. The original diagnosis formulated in 2016 was pituitary adenoma with ACTH immunoreactivity. Seven years later we reviewed the case and performed additional immunohistochemical studies. Tumour cells were negative for pituitary TFs (Pit1, TPIT, SF1 and GATA3) and CK8/18, but positive for SSTR2A (3+), SATB2 and OLIG2; S100 and GFAP highlighted positive sustentacular cells. A final diagnosis of ectopic ONB was rendered.
Conclusion: ONB is a rare neoplasm. Ectopic cases have been reported in maxillary sinus, ethmoidal bulla and sinus, lacrimal sac, nasopharynx, pterygopalatine fossa. Only 7 cases of sellar ectopic ONBs have been reported in literature so far. In our case, tTFs proved to be reliable tools for the differential diagnosis. TFs must be included in the immunohistochemical panel for the diagnostic management of all sellar region lesions as they are essential for PitNETs classification and to rule out potential mimickers.

E-PS-12-059

Agnostic and potential agnostic biomarkers and their relationship with prognosis in squamous cell carcinomas of the larynx: in silico evaluation

M.H. Toper*, A. Tan, S. Sarioglu
*Dokuz Eylul University, Turkey

Background & objectives: Agnostic biomarkers are predictive and independent from histological type and site. In this study, the status of agnostic and potential agnostic markers in laryngeal squamous cell carcinomas were analysed by in silico analysis method.
Methods: In this study, cBioPortal for Cancer Genomics database providing open access bioinformatics service was used. The genes most frequently mutated and showing copy number changes were examined. Additionally, the mutation status of agnostic markers (microsatellite markers, tumour mutation load, NTRK, BRAF, RET) and potential agnostic markers (KRAS, HER2, PIK3CA, NRG1, FGFR, MET) and also the relationship with prognosis was determined.
Results: The first three genes that mutated most frequently were TP53 (87.4%), LRP1B (29.7%), NSD1 (28.8%), while the first three genes with copy number changes were P3H2 (36.2%), CDKN2A (35.3%), TP63. (35.3%). Mutation rates of agnostic markers were MLH1 (0.9%), MSH2 (0.9%), MSH6 (1.8%), PMS2 (0.9%), NTRK3 (4.5%), BRAF (2.7%), and RET (5.4%). The rate of tumours with a tumour mutation-load $\geq$10 was 34.3%, and there were more mutations in twelve genes in this group ($p<0.001$). Methylation was detected in more genes in cases with tumour mutation load <10 ($p<0.05$). Mutation rates in potential agnostic markers were PIK3CA (19.8%), ALK (2.7%), MET (1.8%), EGFR (0.9%), FGFR2 (0.9%) and FGFR4 (% 0.9).
Conclusion: Tumour mutation burden and PIK3CA may be important agnostic markers in laryngeal squamous cell carcinomas, while the other agnostic and potential agnostic biomarker positivity is rare.

E-PS-12-060
Determining clinically relevant histopathological parameters of the invasive margin in head and neck squamous cell carcinomas
S. Tzorakoleftheraki*, T. Koletsa, K. Markou, S. Chrisafi, E. Daskalaki, E. Sgouramali, P. Hytiroglou, V. Kotoula
*Department of Pathology, School of Medicine, Aristotle University of Thessaloniki, Greece

Background & objectives: To investigate the patterns and prognostic impact of histological parameters along the invasive margin (IM) in head and neck squamous cell carcinomas (HNSCCs).
Methods: We examined the IM of 83 HNSCCs (73.5% laryngohypopharyngeal; 21.7% oral cavity; 4.8% oropharyngeal). We recorded the following histologic parameters: percentage of keratinization and mature cells; cellular atypia and pleomorphism; worst pattern of invasion (WPOI); lymphocytic host response (LHR) and presence of perineural invasion (PNI). We evaluated the association of these parameters with patient overall survival (OS).
Results: Most HNSCCs (67/83; 80.7%) were devoid of keratinization in the IM. Twenty-seven (32.5%) HNSCCs revealed >51% mature cells. The vast majority presented moderate to severe pleomorphism and atypia (65/83; 78.3% and 75/83; 90.4%, respectively). WPOI showed heterogeneity in a considerable number of tumours (33/83; 39.8%). Large neoplastic islands were predominant (35/83; 42.2%), followed by small groups and finger-like infiltration. Pushing borders and satellites were infrequent. Different patterns of LHR were equally distributed among HNSCCs. Nine (10.8%) HNSCCs presented PNI, 2 of which invaded nerves >1mm. Dense LHR was beneficial for patient outcome ($p<0.0001$), while PNI adversely affected OS ($p=0.0160$).
Conclusion: The evaluation of the IM in HNSCCs is important for determining patient prognosis. Even though WPOI was not associated with patient outcome, LHR density and PNI proved to be significant prognosticators. These parameters are easily and cost-effectively examined on H&E. Their assessment may be incorporated in daily practice, in order to provide further clinically relevant information in histology reports.

E-PS-12-061
Report of rare malignant tumour of the larynx: spindle cell squamous cell carcinoma (SCSCC) with heterologous component of malignant chondroid differentiation
E. Vouza*, M. Theodorakopoulou, E. Boltetzou
*General Hospital of Athens "ELPIS", Greece

Background & objectives: SCSCC represents less than 1% of laryngeal cancers. It's consisting of spindle cells that are epithelial in nature, and/or component of squamous epithelium with dysplasia, carcinoma in situ with or without infiltration. In 7% of cases, heterologous elements are observed.
Methods: We report a case of a 66-year-old-man, with long smoking history, that presented dysphonia and dyspnea the last two months. During a laryngoscopy an exophytic polypoid tumour of the glottis was revealed and biopsies were taken and sent to pathology department. We received a biopsy-material of whitish/grey colour, which entirely submitted to microscopic examination.
Results: The microscopy revealed tumour segments consist from hyperchromatic spindle cells and high pleomorphic cells within a myxoid or chondromyxoid stroma. There were also seen areas of heterologous malignant chondroid differentiation.
Though most of the biopsies were ulcerated, adjacent to invasive component, a focally preserved surface squamous epithelium, was also found. The epithelium showed features of carcinoma in situ.
Immunohistochemically, the spindle-cell component of the tumour was strongly positive for vimentin, weakly positive for cytokeratin AE1/AE3 and S100, focal positive for p63, CK5/6, SMA and negative for EMA, Melan-A, CK7 and CK20.
All the above findings supported diagnosis of spindle squamous cell carcinoma.
Conclusion: Spindle cell squamous carcinoma is a rare malignancy that poses diagnostic and therapeutic challenges.
The spindle cell component usually represents the largest part of the tumour and constitutes a diagnostic challenge given morphologic overlap with fibrosarcoma, leiomyosarcoma, malignant melanoma and inflammatory myofibroblastic tumour. The presence of epithelial component in the biopsy samples is essential for correct diagnosis.
SCSCC is more aggressive than squamous carcinoma, with highly recurrence and tendency towards lymphatic metastasis. A wide local excision is recommended.

E-PS-12-062
Expression of MMPs in assessing the effectiveness of therapy in patients with chronic generalised periodontitis
V. Zakharava*, L. Kazeko, J. Benesh
*N.N.Alexandrov National Cancer Centre of Belarus, Belarus

Background & objectives: The study of the expression of matrix metalloproteinases is important for understanding the pathogenesis of periodontitis and for the opportune treatment selection.
Objective was to study the levels of metalloproteinases expression before the therapy and at intervals of 1,3,6,9,12 months.
Methods: Gingival biopsy from patients with chronic periodontitis (n=18) was immunostained (IHC) with metalloproteinases -1,-2,-8,-9,-14. Image analysis of cytoplasmic expression was performed using AperioImageScopev12.4.0. Therapy included gingival curettage with insertion of an antiseptic pledget containing hemostatic sponge with tricalcium phosphate, eugenol and iodoform in periodontal pockets; NSAIDs were used in case of suppuration.
Results: A wave-like dynamics of the MMPs levels during the course of periodontitis treatment was revealed. At initially low levels of MMPs at the disease manifestation: a tendency to an increase of MMP1 expression levels by 6 and 12 months of observation was found. At initially high levels of MMPs expression: a progressive decrease in MMP2 and MMP9 expression by 6 and 12 months of follow-up, a decrease in MMP8 expression by 3 month with minimal levels during follow-up, a decrease of MMP14 expression by 6 month with a subsequent increase by 12 month was found.

Conclusion: The dynamics of the levels of MMP2, MMP8 and MMP9 expression suggests the effectiveness of the new protocol, also as compared to the standard therapy. At the same time, wave-like dynamics of MMP1 and MMP14 expression correlated with clinical signs of relapse and indicated their role in the progression of inflammation and destruction of periodontal tissues with insignificant response to the applied therapy.

E-PS-13 | E-Posters History of Pathology

E-PS-13-001

NGS evaluation of an ovarian neoplasm of a 19th century natural mummy from Goriano Valli, Central Italy

C. Bellevicine*, F. Pepe, C. De Luca, C. Mercurio, A. Avitabile, M. Traversari, L. Ventura
*Università Federico II Department of Public Health, Italy

Background & objectives: The body of an anonymous female dating back to 19th century was found among the natural mummies in the friary of "San Giorgio degli Osservanti" in Goriano Valli, L'Aquila, central Italy. A paleoradiologic, paleopathologic and molecular study was undertaken.
Methods: Autopsy study performed by posterior approach and CT were performed. Samples of the organs were rehydrated using Sandison solution, fixed in formalin, and embedded in paraffin to obtain sections stained with H&E. DNA was extracted and its quantity (6.63 ng/μL) and quality (DIN=1.3) was evaluated by Genomic DNA ScreenTape assay. Oncomin BRCA Assay GX on NGS platform (Thermofisher) was performed.
Results: The body (stature: 166+/-4 cm; weight: 4,050 g) belonged to a 43–50 years old woman affected by severe periodontitis, lung anthracosis, diffuse pleural adhesions related to pleuritis, abdominal distension, and perivescical phleboliths. CT examination showed a large cribrous mass in the right iliac fossa and pelvis. Histology showed a cystic-solid architecture, possibly related to an ovarian neoplasm. NGS analysis revealed a BRCA2 Variant of Uncertain Significance (VUS) (c.7093C>T, p.His2365Tyr), whose Mutant Allelic Fraction (MAF) was 21.8%. Secondary level analysis by using Golden Helix Genome Browser v.2.0.7 (Bozeman, MT, USA) also confirmed BRCA2 VUS.
Conclusion: BRCA VUS identifies ovarian cancer patients- related molecular alterations from database consultant. Although the VUS are associated with ovarian neoplasms, their pathogenetic role is uncertain. However, the identification of this alteration strengthen the hypotesis of the neoplastic nature of the ovarian mass.

E-PS-13-002

The national specialty exam in Spain; pathology questions related to images

M.J. Gálvez*, F. Leiva-Cepas, I. Sánchez Ramírez, S. Haro Yuste, J. Osuna Soto, A. Sanz Zorrilla
*Hospital Universitario Reina Sofía, Spain

Background & objectives: Access to specialized medical training in Spain is carried out through a national and multidisciplinary test-type exam (MIR). The objective of this work is to analyse the questions directly related to Pathology specialty, evaluating their weight in the MIR exam.
Methods: Questions from the exams officially published by the Ministry of Health in the last 12 years (2010-2022) have been analysed. They have been grouped by year, according to whether they are associated with an image or not. Difficulty and discrimination indices were calculated. They were analysed according to values of indices and grouped by year, blocks and types of question.
Results: 16 questions with images (2015-2022) and 26 without images have been asked. The questions with images have dealt with nephropathology, chronic inflammation, digestive system and a miscellany. The questions without images are more varied and oscillate between molecular pathology and general pathology. Two questions were canceled in the period analysed. The questions in the exam are not grouped by blocks, and some of them are used as reserve questions.
Conclusion: Pathology is a specialty whose representation in the MIR exam varies annually. There are no complete blocks of questions in Pathology. The introduction of images to the exam has kept the number of questions stable.

E-PS-13-003

Revival of teaching anatomy, histology and pathology in Gdansk, Poland, after WWII

J. Gulczynski*, A. Szarszewski, M. Michalski, E. Izycka-Swieszewska
*Medical University of Gdansk, Poland

Background & objectives: After WW II Doctors Academy was established in Gdansk in 1945. It used the premises of Medizinische Akademie in Danzig, created before the war by the Nazis. Majorority of new Professors came from University of Stefan Batory in Vilnius.
Methods: We analysed available articles and papers presenting three most important scientists in anatomy, pathology and histology with embryology – professors Michał Reicher (1888-1973), Wilhelm Czarnocki (1886-1963) and Stanisław Hiller (1891-1965), their work, teaching and research, but also how their students remembered them. Those students became later our teachers and passed the strive for development upon next generations.
Results: Those Professors were invited to a new place, with short dark chapter of Nazi medicine, asked to create new medical academy with full scope of specialties to educate new generations of medicals. Hiller graduated from Jagiellonian University, with Rockefeller Foundation scholarship studied at Yale and Cornell Universities, to become the Head of Histology and Embryology Department in Vilnius. Reicher studied anthropology and medicine, after scholarship in Carnegie Institute returned to Warsaw University in 1915, became the Head of Anatomy Department, in 1920 nominated position in Vilnius. Czarnocki graduated from Jagiellonian University, worked in Pathology Department at Warsaw University. Due to war outbreak never reached Vilnius, settled in Gdansk in 1945.
Conclusion: Doctors Academy in Gdansk was founded in 1945, changed its name to Medical Academy in 1950. With ones of the best available teachers it quickly became one of the most important in Poland, releasing generations of new doctors and pharmacists. All of the mentioned above professors had strong impact on following generations. Their manuals are in many aspects timeless and sometimes actual. Students should remember those researchers, not just the nameplates in our University lecture rooms they enter nowadays.

E-PS-13-004

Forgotten war of the 20th century - Prof. Rudolf Weigl (1884-1957) and his fight against typhus

J. Gulczynski*, M. Chodyna, M. Michalski, E. Izycka-Swieszewska
*Medical University of Gdansk, Poland

Background & objectives: Rudolf Weigl was Polish biologist and creator of the first effective vaccine against typhus. The aim is to recall research and history of fighting this epidemic by creating method of obtaining a vaccine from lice, carriers of the disease-causing microorganism.
Methods: We used biographical articles describing the life of Prof. Rudolf Weigl; literature and demographic and epidemiological data in the area of Poland from the period between the First and Second World War. We also analysed scientific articles by Rudolf Weigl describing his research and methods that resulted in obtaining the effective vaccine.

Results: This poster presents the epidemiological realities prevailing in Poland and the rest of Europe, the history of Professor Weigl's achievements. In particular focuses on the methodology of developing a vaccine, taking into account the innovative use of lice as a source of infectious material for inducing active immunity. The impact of research and its final effect on human life during the Second World War is discussed, as well as the lack of recognition of the importance of Weigl's achievements and condemning him to oblivion, despite saving thousands of human lives and significantly contributing to the development of epidemiology and the production of vaccines.
Conclusion: Rudolf Weigl and his life's work do not deserve to be overlooked or forgotten in the history of medicine and academic consciousness. Weigl undertook the difficult task of fighting an epidemic that was a real threat to the population all over Europe. As a pandemic in Silesia typhus was analysed even by Rudolph Virchow. Weigel managed to create an effective solution that contributed to protecting people against typhoid fever on a large scale.

E-PS-13-005
Teaching anatomy and pathology and first autopsies in Atheneum Gedanense in Gdansk – starting from 16th century
J. Gulczynski*, P. Paluchowski, M. Chodyna, E. Izycka-Swieszewska
*Medical University of Gdansk, Poland

Background & objectives: Atheneum Gedanense established in 1558 was not a University, nevertheless the level of teaching medicine including anatomy was so high that its alumni were accepted for final years of medical training at best universities in Europe.
Methods: We analysed available articles and sources presenting the most prominent researchers of that time, Joachim Oelhaf (1570-1630), Laurentius Eichstaedt (1596-1660) and Johann Adam Kulmus (1689-1745), their work and how great impact on development of anatomy and pathology they had, in Gdansk, but also other countries.
Results: This poster presents the anatomists, lecturers and professors of medicine, City Physicians, but also professors teaching at Atheneum Gedanense from the turn of 16th until 18th century. Joachim Oelhaf performed first public autopsy of foetus with multiple malformations (first recorded case of Limb Body Wall Complex) with printed report quoted later by Caspar Bauhin. Laurentius Eichstaedt also performed autopsy on foetus monstrosus just a few decades later. Johann Adam Kulmus published thorough and detailed autopsy report with high quality engravings after dissecting conjoined twins. But he is more fampus for Tabulae Anatomicae, translated to several languages including Japanese. He is considered as a father of modern Japanese medicine.
Conclusion: Gdansk had a very strong political and economic position starting from 15th century. In 1558 Academic Gymnasium was founded and City Hall saw to have the best teachers. Promising students were given the scholarships to travel all over Europe to learn at best Universities. Usually after return to Gdansk, they became professors for new generations of students and gave foundation for development of science, including medicine, anatomy but in the end also pathology.

E-PS-13-006
Parasitosis & zoonosis: an alert from the past!
R.H. Henriques De Gouveia*, T. Ferreira, V. Sousa, I. Furtado, L. Carvalho
*Universidade da Madeira, Portugal

Background & objectives: Health Politics and Medical Preventive/Therapeutic Measures in developing countries were predominantly focused on Oncological, Cardiovascular and Degenerative Diseases. Covid-19 pandemics and Monkeypox outbreaks shifted the focus towards Infectious Diseases. Authors intend to share educational tools from an Historical Pathology Museum.
Methods: To reach the goal, a search for Parasitosis / Zoonosis specimens was performed inside the collection of the XIXth century, UNESCO's World Heritage Anatomical Pathology Museum – Medical Faculty, Coimbra University. It is a museum, that houses thousands of objects of various natures [books, photographs, scientific equipment, anatomo-pathological specimens in glass containers with fixative liquid and artificial (clay, wax) models].
Results: Twenty-seven (n=27) specimens were found. Twenty-four (n=24) were biological, preserved in fixative liquid and the other 3 samples were wax models. They include mites, tapeworms and roundworms, affecting multiple tissues and organs: skin, soft tissues, heart, liver, bowel, kidney, eye, and unknown location. The biological samples were procured during surgical procedures and autopsies. The artificial models were acquired in Paris, handcrafted by French professional modeler, and represent the pathological lesions / entities and anatomical structures in accurate three-dimensions; since they were executed facing the real victims/samples or copied from an original model.
Conclusion: The study of the XIXth and XXth centuries' specimens give an Historical perspective of infectious diseases / parasitosis / zoonosis in the old times, allowing to use knowledge and experience from the past to prevent new unexpected pathological events – epidemics/pandemics. Anatomical-Pathology Museums provide priceless and unique channels to teach young medical generations, especially in what concerns apparently overcome diseases.

E-PS-13-007
Questionnaire portrait of the Russian pathologist, bacteriologist, scientist and educator, Doctor of Medicine, Professor of Pathological Anatomy and Bacteriology Sergei Semyonovich (Simeonovich) Abramov (14.09.1875-21.08.1951)
A. Zubritsky*
*Russia

Background & objectives: This work has the aim to collect and systematize the biographical data on S.S.Abramov in accordance with the questionnaire I have developed. Born in Nakhichevan-on-Don of the Russian Empire in the family of an official of Armenian origin.
Methods: Graduated from Moscow University with a doctor's degree with honours (1899). Dissertation defense on the topic "Materials for the study of the jaundice pathogenesis. About liver changes in various types of jaundice" (1905). On a business trip abroad, he completed work on studying the influence of the environment's reaction on the phenomenon of complement fixation.
Results: In 1906 he was elected a privatdozent of Moscow University in the Pathology Department; he worked at the Moscow General Military Hospital (1912-18), etc. His scientific interests included general pathology, pathological anatomy, bacteriology, and problems of immunity. Since the consequences of the civil war in Russia made further scientific work almost impossible, he emigrates. He happened to work at the Pathology Institute of Berlin University, Sofia University, where he founded the first Department of General Pathology and Pathological Anatomy and at the Russian Faculty of the Paris University.
Conclusion: He entered the history of pathology with the eponym "Abramov-Fiedler's myocarditis". It is believed that he described dilated cardiomyopathy before Fiedler described myocarditis. After 1945 he left for the USA from 1945 to 1951 his fate remains unknown. He died in the small town of Hathown (USA) at the age of 75.

E-PS-13-008
Questionnaire portrait of the well-known Russian scientist-pathologist, honoured scientist of the RSFSR, Doctor of Medical Sciences, Professor Ya.L.Rapoport (19.11.1898-17.03.1996)
A. Zubritsky*
*Russia

Background & objectives: This work has aim to collect and systematize biographical data om Ya.L.Papoport in accordance with

questionnaire developed by me. Born in Simpheropol in family of teacher of Russian language and literature. Graduated from Medical Faculty of 2nd Moscow University.
Methods: Work in various positions at 2nd Moscow Medical Institute; defense of doctoral dissertation on topic "The role of nonspecific allergies in the occurrence and localization of respiratory tuberculosis", awarded by People's Commissariat of Health; service in Red Army: chief pathologist on various fronts; after severe brain confusion and fracture of right shoulder, he was demobilized (1944).
Results: Head of Laboratory of Pathological Anatomy of Institute of Normal and Pathological Morphology in Moscow, etc. after refusing the offer, in cooperation with Moscow State Security authorities, He was relieved of his post as hotbed of "Virchowianism"; arrest, charges of participating in terrorist Jewish organization of "killer doctors" investigation terminated, released from custody with full rehabilitation (1953). Head of Pathomorphology Laboratory at the A.N.Bakulev Institute of Cardiovascular Surgery; he left the institute at age of 80 and was engaged in viewing histopreparations at home until almost 95 years old; described allergic myocarditis and obtained experimental model of myocarditis when various antigens were injected into body.
Conclusion: Proposed etiopathogenetic classification of myocarditis; formulated the concept of "resuscitation pathology" and singled out "resuscitation traumatology" from it; pointed to effectiveness of transvasal heart biopsy for diagnosis of myocarditis. Research interests: Infectious, cardiovascular pathology, etc. Author of more than 200 scientific papers. Motto: "Catch a moment of luck." "The pathologist holds in his hands not only corpses, but also fate of living person". Hobbies: Photography, theater, music. Died in Moscow at age of 98 and was buried at Golovinsky cemetery.

E-PS-13-009
Professor Aron Iudovich Zelensky - Russian pathologist, scientist and educator (11.06.1912-19.03.1983)
A. Zubritsky*
*Russia

Background & objectives: This work has the aim to collect and systematize the biographical data on A.I.Zelensky in accordance with the questionnaire I have developed. Born in Kansk, Krasnoyarsk Krai in family of an employee. Graduated from the Khabarovsk Medical Institute (1936).
Methods: As a 4th year student, he was trusted to conduct practical classes at Pathology Department; PhD thesis defense on topic "Renal vein thrombosis in amyloid-lipoid nephrosis" (1945); doctoral - on topic "Acute venous stasis of kidneys and its role in pathogenesis of renal syndrome in haemorrhagic nephrosis-nephritis" (1969). Assistant, Associate Professor, Head, Pathology Department, etc. Chief Pathologist of Khabarovsk region.
Results: contributed to organization of biopsy and sectional work in Far East; the founder of original concept of renal syndrome of haemorrhagic nephroso-nephritis, and modelling of clinical and morphological syndromes of haemorrhagic fever with renal syndrome in the experiment allowed to justify a more effective pathogenetic therapy of this severe disease; under his leadership, 3 doctoral and 20 candidate dissertations were completed and defended; awarded medals "For the Victory over Germany", "For Labor Valor", "For Valiant Labor in the Great Patriotic War of 1941-1945", etc. Scientific interests: The problem of renal pathology, issues of teaching, training and improvement of the pathoanatomical service in city and region. Author of 57 scientific papers.
Conclusion: Member of the CPSU, Board of the All-Union Scientific Society of Pathologists, Chairman of the Regional Society of Pathologists. Distinctive feature: General erudition, great pedagogical skills and deep professional knowledge, an amazing ability to combine the rigor and exactingness of the head with the care and attention of an older comrade and friend. He died at the age of 70 from acute recurrent myocardial infarction. His name is included in the University's Book of Honor.

E-PS-14 | E-Posters Infectious Diseases Pathology

E-PS-14-002
Placental malaria in a patient with sickle trait haemoglobin: an infrequent finding
I. Fernández*, S. Fernández, A. Tarín, J. Rosselló, L. Aguirrezabal, C. Valentí, G. Cancho, A. Nogueira
*Hospital Universitario de Basurto, Bilbao, Spain

Background & objectives: Malaria is the most prevalent vector-borne disease in the world, but it was eradicated in Spain. Meanwhile, sickle cell trait protects carriers against severe malaria. We report a case of placental malaria in a patient with sickle trait haemoglobin.
Methods: We present a case of a 27-year-old woman from Guinea on her 38 week of pregnancy, who is admitted to the hospital with premature rupture of membranes. Although she referred normal prenatal care, laboratory data revealed anaemia, thrombocytopenia and leukopenia. After a caesarean delivery, a healthy female child was born, and the placenta was submitted for histopathological and microbiological examination.
Results: Histopathological study of the placenta showed presence of hemozoin; a dark-brown pigment, product of haemoglobin digestion, that accumulates inside maternal intervillous monocytes and infected red blood cells. As a consequence, there was perivillous fibrin deposition and also syncytial knot formation. Furthermore, occasional structures suggestive of parasites could be observed inside some red blood cells, and hemozoin pigment deposit in fibrin and stroma was concordant with chronic infection. Finally, occasional erythrocytes with anomalous morphology were found within intervillous space. This is likely to be due to a sickle trait haemoglobin, which was revealed later in blood analyses performed on the mother.
Conclusion: Malaria in pregnancy is diagnosed when Plasmodium parasites are found either in maternal peripheral blood or in the placenta. In our country, this circumstance is almost exclusive to immigrant pregnant women. Therefore, in these cases it is important to bear in mind the possibility of this parasitic infection, since the histopathological changes in the placenta may provide a definitive diagnosis. Additionally, even though sickle cell trait confers some resistance to malaria, it does not completely protect against the infection.

E-PS-14-003
Leukocytoclastic vasculitis after exposure to COVID-19 vaccine: report case
F. Figueiredo*, S. Maria Macêdo, H. Neves Feitosa Filho, C.E. Maia Rodrigues, D. Coelho de Sá, D. Nunes Oliveira, J. Carneiro Melo, A.V. Pinto de Lima
*Universidade de Fortaleza, Brazil

Background & objectives: Leukocytoclastic vasculitis is an inflammation that affects dermal capillaries and venules. This condition may be idiopathic or related to infections, malignancies, autoimmune disorders, or medications. This work aims to describe a case of leukocytoclastic vasculitis possibly consequent to SARS-CoV-2 vaccination.
Methods: Case presentation based on summarization of patients clinical history, image findings, laboratorial exam, cytology and skin biopsy.
Results: A 51-year-old patient received Pfizer SARSCoV immunization. He also referred the appearance of erythematous lesions, which extended to the lower limbs in less than 1 month after the vaccine and a month and a half later he developed bilateral ankle pain and swelling.

On physical examination, she had purpuric macular and papular spots, in addition to large confluent plaques on both lower limb. Laboratorial exams showed mild leukocytosis (13,600/mm3) without deviation and CRP of 0.90 mg/L. A biopsy of an irregular fragment of skin on the right lower limb was performed, which showed infiltration inflammation compatible with leukocytoclastic vasculitis.
Conclusion: In view of the condition, the patient was started on prednisone at a daily dose of 60 mg in the morning for 10 days, with progressive weaning after this period. This report suggests the possibility that the COVID-19 vaccine has the potential to induce factors for leukocytoclastic vasculitis.

E-PS-14-004
Features of cerebral injury in papillomavirus infection in HIV-positive patients
V. Gargin*, A. Bondarenko, D. Katsapov, O. Bondarenko, M. Lytvynenko, T. Bocharova, R. Nazaryan
*Kharkiv National Medical University, Ukraine

Background & objectives: Multifocal leukoencephalopathy (MLP) is often observed in HIV-infected individuals. The aim of our work was to identify the features of brain injury in patients with polyomavirus infection with the background of HIV infection of the IV clinical stage.
Methods: For the morphological study, sectional material (brain) of HIV-positive patients with PML and lifetime detection of JCV and BKV in the cerebrospinal fluid was used with instrumental signs of PML. T. gondii was detected in 28.6% of cases, EBV in 42.9% of cases, JCV was detected in 14.3% of cases, and BKV was detected in 14.3% of cases.
Results: Vasculitis of the microvasculature with the formation of fibrin thrombi has been revealed. There is a perivascular accumulation of cells of inflammatory origin, cerebral oedema, and the appearance of microcalcifications. 2-3 mm zones of demyelinated lesions have been revealed with a tendency to merge. Dystrophic changes and demyelination are more developed in the deep areas of the white matter. Small areas of demyelination are observed predominantly in the juxtacortical/subcortical white matter and in cortical areas of the brain. Most demyelinating lesions are present locally at the corticomedullary junction, and demyelinating lesions extend into deeper layers of the white matter and are seen in relatively limited areas.
Conclusion: The presence of multiple foci in the brain substance, according to neuroimaging methods, may be due to the presence of a number of etiological factors, namely: JCV, BKV, EBV, T. gondii, and C. neoformans, which requires obligatory laboratory confirmation. Morphological changes in the brain in PML caused by JCV and BKV are characterized by zones of demyelinated lesions 2-3 mm in size with a tendency to confluent, with dystrophic changes mainly in the juxtacortical/subcortical white matter.

E-PS-14-005
A case of generalised accumulation of histiocytes - histiocytic neoplasms or result of immunosuppression?
D.A. Grubišić*, T. Čeprnja, N. Kunac, K. Vilović
*University Hospital of Split, Croatia

Background & objectives: Histiocytic disorders and neoplasms are rare and may have overlapping features. We present a patient diagnosed with a generalized accumulation of histiocytes after a duodenal biopsy, bone marrow biopsy and dissection of enlarged lymph nodes in the axillary region.
Methods: The hypotrophic patient presented herself to the Emergency Medicine Service because of weakness and fever. The patient had nausea, vomiting and periumbilical and epigastric pain with band-like spreading. Duodenoscopy revealed an oedematous, mildly hyperaemic mucosa of the bulb and post-bulbar villi that were reduced, so the clinician suspected coeliac disease. Later, lymph node dissection and bone marrow biopsy were performed.
Results: Histologically, duodenal mucosa was with blunted, expanded villi and lamina propria was massively infiltrated by macrophages and focally by granulocytes. Lymph nodes had extremely enlarged sinuses, which were filled with both epithelioid and spindle-shaped histiocytes, without necrosis. The histological picture was not specific so Rosai-Dorfman's disease, Whiple's disease, and mycobacterial infection were considered as differential diagnoses. Also, the bone marrow was more cellular and haematopoiesis was suppressed by abundant infiltration with histiocytes. Histochemical Ziehl-Neelson staining showed acid-resistant bacteria within the cytoplasm of histiocytes. Since infection with Mycobacterium avium complex occurs almost exclusively in immunocompromised patients, patient undergoes serological testing for HIV. The patient was serological ELISA HIV Ag/At positive.
Conclusion: Mycobacterium avium complex is an aerobic opportunistic bacterium that usually causes small bowel disease only in immunosuppressed (CD4+<100/mm3) patients, usually as part of a disseminated infection with general symptoms (fever, weight loss, thrombocytopenia, enlarged lymph nodes, hepatosplenomegaly, diarrhoea, malabsorption). Morphologic features along with immunophenotype and pattern of involvement should be taken together with clinical and radiographic findings to establish a unique diagnosis. The described case shows how the non-tumour pathohistological diagnosis can lead to an appropriate clinical diagnosis.

E-PS-14-006
Proliferation of smooth muscle cells in the arterial walls of the lungs of the newborn and of the placenta in a case of early neonatal death in a woman who suffered from COVID-19 during pregnancy
S. Gychka*, T. Savchuk, S. Nikolaienko, Y. Suzuki
*Bogomolets National Medical University, Ukraine

Background & objectives: COVID-19 is associated with increased neonatal and maternal morbidity and mortality. Numerous studies demonstrated remodelling of placental arteries in parturients who had COVID-19 during pregnancy. The effects of COVID-19 on the intrauterine development of foetal vessels are not completely understood.
Methods: We described vascular changes in a case of early neonatal death in the lung tissues of the newborn and in the placenta of a woman who suffered COVID-19 at 25th week of pregnancy (PCR confirmed). Placenta and post-mortem lung tissues of the newborn were studied with light microscopy and immunohistochemistry (alpha-smooth muscle actin) and morphometry.
Results: Morphometry analysis included arterial wall thickness and arterial lumen ratio (lumen area/artery area). For newborn lung arteries of 30-50μm diameter, the average wall thickness was 8,34 μm (SD 2,29 μm). Average thickness of the arterial walls of the placenta was 18,06 μm (SD 2,88). Average lumen area index of newborn lung arterial walls was 20,84% (SD 6,1%).
Median lumen area index of placental arteries was 14,98% (SD 7,15%). These indicators coincide with the data of our previous studies showing the changes in the walls of the pulmonary vessels in adult patients who died of COVID-19 as well as the thickening of the walls of placental vessels.
Conclusion: Infection with SARS-CoV-2 leads to systemic damage to the vascular system. COVID-19 during pregnancy can be accompanied by remodelling of both placental arteries and foetal pulmonary arteries. These events may be responsible for the mortality of newborns whose mothers had COVID-19 during pregnancy.

E-PS-14-007

SARS-CoV-2 spike glycoprotein and nucleocapsid protein expression in cerebral vessels of COVID-19 patients with microcirculatory disorders

S. Gychka*, S. Nikolaienko, V. Vasylyk, M.S.A. Tuffaha, Y. Suzuki
*Bogomolets National Medical University, Ukraine

Background & objectives: In case of severe COVID-19, various forms of cerebral blood circulatory disorders may develop including stroke. This study describes clinical case series of patients died of COVID-19 aiming to demonstrate the connection between the viral load and brain microcirculation disorders.
Methods: Formalin-fixed, paraffin-embedded post-mortem brain tissue samples of five COVID-19 patients were studied with light microscopy, Masson's trichrome stain and immunohistochemistry (Spike glycoprotein, Nucleocapsid protein).
Results: All autopsy cases have shown similar morphological changes in the brain tissue microcirculation: impaired capillary permeability due to severe oedema of endotheliocytes, signs of blood stasis, sludge phenomenon, and the formation of microthrombi. A significant number of capillaries contained only plasma without blood cells. Pronounced perivascular oedema and small perivascular haemorrhages were detected. In two autopsy cases, high expression of SARS-CoV-2 spike glycoprotein and nucleocapsid protein was detected in the brain vessels. Such changes were accompanied by the presence of microthrombi in the microcirculatory vessels (1-2 in 10HPF). The frequency of the detection of microthrombi in cases of low SARS-CoV-2 marker expression was low.
Conclusion: In this clinical case series, we have shown the high expression of SARS-CoV-2 spike glycoprotein and nucleocapsid proteins in cerebral vessels of patients with the severe brain microcirculation disorders and the formation of microthrombi.
Funding: Funded by NIH (R21AG73919)

E-PS-14-008

Pneumocystis jiroveci pneumonia in COVID-19 & HIV co-infected patients

A. Malysheva*, O. Reshetnikova, A. Ermakov, T. Shapovalova
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: Pneumocystis jiroveci pneumonia (PJP) is the opportunistic infection, which is commonly associated with human immunodeficiency virus (HIV) infection. The aim of present study was to evaluate morphological features of PJP in COVID-19-related deaths of HIV infected individuals.
Methods: Post-mortem examinations were performed on five cadavers with PJP in HIV& COVID-19 co-infected individuals (one female and four male bodies 30-47 y.o.). Medical histories, laboratory data and clinical peculiarities of these patients were studied. Macroscopic pictures of lungs and other organs, as well as histological features of their tissue samples at the magnifications x10, x20, x40 were recorded at the autopsy protocols.
Results: Autopsies revealed that the lung was the most frequent organ involved by HIV& COVID-19 co-infection-associated pathologies leading to death. All cases were represented with gross picture of diffuse bilateral pneumonias. Histological examination has shown alveolar spaces in lungs were filled with amorphous, foamy, eosinophilic, mostly acellular fibrinous exudate. Inflammatory reaction with fibrin exudate, hyaline membranes formation was a common histological pattern in our material. In some areas, there were signs of organization of exudate in the alveoli and the development of fibrosis. The interstitial inflammation was accompanied with the sclerotic features in the lungs septas' interstitium. Widespread microangiopathy, with focal thrombosis of the vessels discovered in all lung parenchyma samples.
Conclusion: Studying an autopsy material using a collection of lung and other internal organs tissues is essential to increase knowledge of a COVID-19 clinical manifestations worsened by compromised immune function. Pathological examination is an important instrument to better understanding of the PJP's role in thanatogenesis, particularly when the knowledge of disorders in COVID-19 & HIV co-infected individuals is restricted and the influence on the healthcare system is significant. Future studies is needed to understand the pathogenesis of combined infection's severe course.

E-PS-14-009

Coagulopathy as a contributor to the lethal outcome to COVID-19 & HIV infection comorbidities

A. Malysheva*, O. Reshetnikova, A. Ermakov, L. Rudiuk
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: Thrombotic complications are the common cause of increased morbidity and mortality in patients with COVID-19. The aim of present study was to evaluate the role of the coagulopathy in lethal cases' thanatogenesis in SARS-CoV-2 & HIV co-infected individuals.
Methods: Medical records, blood tests information and autopsy findings were studied in ten lethal cases the COVID-19 & HIV infection comorbidities. Naked eye examinations of the internal organs of five male and five female corpses were followed with the histological studies their tissue samples collection. Microscopy of H&E stained slides performed at x10, x20, x40. Clinical-morphological analysis carried out.
Results: Haematological changes noted in most lethal cases of COVID-19 & HIV infection comorbidities. Thrombocytopenia was recorded in half of the individuals, and in 20% of cases it was severe. Elevated plasma D-dimer levels and decreased prothrombin Index were common findings. Post-mortem examinations revealed multiple haemorrhages, severe damages to various internal organs, especially to the respiratory system. The alveoli were filled with oedematous fluid; hyaline membranes were found in 80% of lung histological slides. The development of acute respiratory distress syndrome against this background caused the death of many patients. The presence of chronic hepatitis was noted in 40% of patients with an outcome in cirrhosis in a third of individuals.
Conclusion: An analysis of the data obtained showed that the respiratory pathology characteristic of COVID-19 is exacerbated by the presence of liver damage, usually noticeable in patients with HIV infection. A decreased level of blood platelets in combination with coagulopathy contributes to the development of a widespread haemorrhagic syndrome. The data obtained are discussed in the aspect of thanatogenesis of the COVID-19 & HIV infection lethal cases.

E-PS-14-010

Clinical and morphological comparisons in lethal cases of co-infection with SARS-CoV-2 and HIV

A. Malysheva*, O. Reshetnikova, A. Ermakov, T. Shapovalova
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: In recent years SARS-CoV-2 pandemic resulted in a global public health emergency. High morbidity and mortality is one of the major concerns.
Clinical-pathological features of the SARS-CoV-2 infection' fatal cases in patients co-infected with HIV evaluated in the study.
Methods: Full pathological post-mortem examinations were performed in ten fatal cases of SARS-CoV-2 and HIV co-infection, including five males and five female's bodies. Gross pictures of the internal organs

were studied and their tissue samples were taken for histological examinations. Microscopy of H&E stained slides performed at x10, x20, x40. Autopsy protocols were recorded. Demographic data and clinical peculiarities were noted.
Results: Present investigation revealed that majority of deaths were recorded in 43-54 group (70%).The second age group with frequent fatal outcomes ranged 28- 38 years (30%).The respiratory system was the most frequent one involved by SARS-CoV-2 and HIV co-infection diseases leading to death. Interstitial pneumonia, tracheitis with epiglottitis features revealed in all cases and were complicated by acute respiratory distress syndrome in 60 % of patients. Autopsy investigation also discovered HIV-induced pathological changes, including pneumocystis infection, candidiasis, chronic meningitis, chronic hepatitis, chronic pancreatitis, chronic nephritis and malignant lymphoma. The main histological peculiarities were in lungs as alveolar damage, vascular involvement accompanied with local and systemic tissue damages in the internal organs.
Conclusion: A pandemic of SARS-CoV-2 is still an urgent problem of modern medicine. Accession of HIV infection is an additional risk factor for severe disease course with a high probability of the patient's death. Autopsy studies make it possible to find out in detail the entire spectrum of pathological changes observed in a combination of two infections, as well as taking into account damage caused by concomitant diseases. Investigation of these lesions will have a positive impact on the health care system.

E-PS-14-011
Retrospective histopathological classification of 348 skin biopsies from patients with suspected leprosy from Fortaleza, Northeast Brazil 2018-2023
D. Nunes Oliveira*, G. Ferreira Morgantetti, G. Alencar Medeiros, J. Carneiro Melo, V. Queirós Calheiros Campelo Maia, H. Neves Feitosa Filho, M.C. Rocha Muniz, A. de Carvalho Assunção, M. Macêdo Militão Mendonça, A.V. Pinto de Lima, F. Figueiredo
*University of Fortaleza, Brazil

Background & objectives: Leprosy is a chronic disease caused by Mycobacterium leprae that affects the skin, peripheral nerves and mucous membranes. Our objective was to analyse the histopathological findings in biopsy reports obtained from patients with suspected leprosy.
Methods: This was a retrospective, descriptive study of biopsy reports from patients with suspected leprosy, carried out in a pathology laboratory, in northeastern Brazil, from January 2018 to March 2023. The variables age, sex, and histopathological subtype were analysed. Also, a correlation with the WHO classification of the cases was established.
Results: A total of 361 cases were obtained, in 175 (48.4%) the histology showed chronic dermatitis, but in the other 186 (51.5%) cases the histopathological diagnosis of leprosy was made, with a mean age of 40.3 years with 99 (53.2%) men. 127 (68.2%) used Ziehl, 44 (34.6%) positive and 83 (65.4%) negative; 83 (44.6%) Fite, with 57 (68.7% of these 83 reports) negative and 26 (31.3% of these 83 reports) positive; 103 (55.3%) .140 (75.2%) were paucibacillary, 18 (9.6%) undetermined, 97 (52.1%) tuberculoid and 25 (13.4%) borderline tuberculoid. In addition, 46 (24.8%) were multibacillary, 6 (3.2%) borderline borderline, 8 (4.3%) borderline lepromatous and 32 (17.2%) lepromatous.
Conclusion: Histopathological reports of biopsies from patients with suspected leprosy found that, in just under half of the patients, histology failed to confirm the presence of the leprosy bacillus. However, in the other cases, the histopathological diagnosis of leprosy could be confirmed, with the majority of patients having paucibacillary leprosy. Accurate histopathological diagnosis is crucial for the proper management of leprosy.

E-PS-14-012
Histological and immunohistochemical characteristics of lung tissue from deceased patients in early convalescent phase of viral pneumonia caused by a SARS-CoV-2
V. Pechnikova*, L. Mikhaleva, A. Kontorshchikov, D. Atiakshin, G. Kudryavtsev, Y. Kudryavtseva, R. Vandysheva, Z. Gioeva, L. Kakturskiy
*Avtsyn Research Institute of Human Morphology of Federal State Budgetary Scientific Institution "Petrovsky National Research Centre of Surgery", Russia

Background & objectives: The aim of the study was to analyse clinical and pathological data of the deceased patients, who had previously had viral pneumonia caused by SARS-CoV-2 during early convalescent phase.
Methods: The clinical, laboratory and pathological data of 9 deceased patients were analysed. Clinical diagnosis was established in period of 12-46 days, period from clinical recovery to death averaged from 2 up to 30 days. Histological slides were stained with H&E, Martius Scarlet Blue and Van Gieson's stain. Immunohistochemical (IHC) staining was performed with antibodies to SARS-CoV-2 S-protein and CK5.
Results: H&E staining revealed hyaline membranes in the alveoli, bronchial and alveolar epithelial desquamation. We observed granulocytes, erythrocytes, siderophages, giant cells and fibrin filaments in the lumen of the alveoli and bronchioles. Foci of bone tissue were found in the cartilaginous plates. Martius Scarlet Blue stain confirmed the presence of hyaline membranes, mixed and hyaline thrombi in the lumen of the branches of the pulmonary arteries. Van Gieson's stain revealed foci of collagen fibre growth, fibrosis of the alveolar septa. Metaplasia of the bronchial and alveolar epithelium was confirmed by IHC reaction (CK5). No intracellular viral particles were detected during the IHC reaction to the SARS-CoV-2 S-protein.
Conclusion: Despite the absence of a clinical features of viral pneumonia in patients and a negative PCR test result, we found diffuse alveolar damage (DAD) features microscopically in the lungs. In all cases microscopic changes correspond to the exudative-proliferative phase of DAD. Sanogenesis was complete, which was confirmed by a negative IHC reaction with a SARS-CoV-2 S protein. There was no confirmation of "Long Covid" development, since the microscopic picture corresponded to the exudative-proliferative phase of DAD.

E-PS-14-013
The role of cell death in the pathogenesis of rabies virus-infected mice isolated from insectivorous bats
I.S. Santos Katz*, G. Hering Motta, L.P. Guimarães, E. Raniero Fernandes, S. Dos Ramos Silva, F. Guedes, O. Garcia Ribeiro
*Pasteur Institute, Brazil

Background & objectives: Rabies is a viral zoonotic infectious disease that affects mammals. *Rabies virus* (RABV) from insectivorous bats activates the inflammatory response and cell death by distinct mechanisms. Here we characterized the molecules related to cell death in RABV-infected mice.
Methods: Brain tissues from mice infected with CVS-31, Myotis nigricans and Eptesicus furinalis were subjected to an H&E histopathology study and immunohistochemistry assay. Double-stained with anti-NeuN or anti-GFAP, and molecules related to cell death (Anti-Caspase-3 or Anti-iNOS or Anti-TNF-α) were evaluated. Differences in the distribution of astrocytes or neurons expressing cell death molecules between groups were analysed using the Kruskal-Wallis test.

Results: Histopathological examination in the CNS of mice infected with *Eptesicus furinalis* (EPBRV), *Myotis nigricans* (MNBRV) and positive control (CVS-31) were characterized by non-suppurative meningoencephalomyelitis with lymphocytic perivascular cuffing, neuronal necrosis, neuronophagia, neuropil vacuolation, presence of microglial nodules and Purkinje cells depopulation, which could be associated with higher levels of cell death-related molecules. The production of TNF-α, iNOS and Caspase-3 by neurons and astrocytes were significantly ($p<0.05$) higher in EPBRV than in MNBRV and positive control, mainly in the hippocampus and cortex.
Conclusion: Greater expression of molecules correlated with cell death in EPBRV-infected mice may trigger the extension of neuronal damage and be related to the various symptoms observed in the infection, such as tremors and paralysis. Our results also provide important insights into understanding the biological characteristics and interaction of RABV isolated from insectivorous bats with the host. They may help advance new therapies, epidemiological surveillance, and the implementation of a better rabies control strategy, particularly in developing countries.
Funding: This work was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP –Process No. 2017/08215-7) and Instituto Pasteur/São Paulo/Brazil (Process No. IP02/17).

E-PS-15 | E-Posters Molecular Pathology

E-PS-15-001
Unravelling the sarcoma puzzle: insights from next generation sequencing on diagnosis and treatment in 100 cases

B.K. Aktas*, P. Bulutay, I. Kulac, C. Aydin Mericoz
*Koç University, School of Medicine, Department of Pathology, Turkey

Background & objectives: The molecular characterization of sarcomas has become essential for accurate diagnosis and treatment. This study highlights the advantages and limitations of RNA-based next generation sequencing (NGS) in over 100 sarcoma cases, emphasizing its diagnostic and therapeutic impact.
Methods: We reviewed the Koç University Department of Pathology Laboratory Information System for all sarcoma cases sequenced between 2019 and 2023, including 100 consecutive cases (128 studies) using four commercial targeted panels: ArcherDx Sarcoma Panel, ArcherDx CTL Panel, ArcherDx FusionPlex Solid Tumour Panel, and ArcherDx VariantPlex Solid Tumour Panel, in respective numbers and percentages (72%, 31%, 16%, 5%).
Results: Reliable sequencing studies were conducted for 90 (90%) cases, while 10 (10%) failed quality tests. Pathogenic alterations were identified in 61 (61%) cases. The most common alterations were EWSR1 fusions, with FLI1 being the most frequent partner. NGS results significantly altered the initial diagnosis in 19 cases (19%) and confirmed it in 24 (24%) cases. Notably, NGS clarified diagnoses for eight cases initially diagnosed as malignant small round cell tumours: five had EWSR1-FLI1 fusion (Ewing sarcoma), and three had CIC-DUX4 fusion (CIC-rearranged sarcoma). We also identified targetable alterations such as NTRK fusion (n=2) and KIT mutation (n=3).
Conclusion: Targeted NGS panels prove to be reliable and informative, enabling pathologists to confirm and refine diagnoses while serving as valuable prognostic and predictive tools. Importantly, NGS-guided diagnosis changes led to treatment modifications, emphasizing the need for integrating molecular test results with morphological and clinical findings to ensure accurate diagnosis and treatment planning.

E-PS-15-002
Increase in expression of exosomal long non-coding RNA H19 in the blood of patients with castration-resistant prostate cancer is associated with the development of docetaxel resistance

I. Bakhtogarimov*, E. Pudova, A. Kobelyatskaya, I. Katunina, M. Fedorova, A. Snezhkina, G. Krasnov, A. Kudruavtseva
*EIMB RAS, Russia

Background & objectives: Profiling of circulating lncRNA is a promising direction for the new predictive markers search. The aim of the study is to identify lncRNAs potentially associated with disease progression in the dynamics of treatment of patients with castration-resistant prostate cancer (CRPC).
Methods: The study included 11 patients with CRPC treated with docetaxel, from which libraries were prepared and RNA-Seq was performed on the Illumina platform. Differential expression analysis was performed between docetaxel response and onset of progression samples using the edgeR package in the R statistical environment. Statistical analysis of results between time periods for each patient was performed in paired mode.
Results: According to the bioinformatic analysis results of the obtained RNA-Seq data, a statistically significant increase in differential expression of H19 was detected in the group with the beginning of progression of CRPC on the background of docetaxel therapy by 5.93 times (LogFC = 2.57; p-value QLF test = 0.002). Spearman rank correlation analysis also showed a statistically significant correlation between H19 expression and the period of progression onset in patients (rs = 0.43; p-value = 0.04).
Conclusion: Thus, based on the study, it was shown that an increased level of H19 expression is statistically significantly associated with the development of resistance to docetaxel and can be considered as a potential predictive marker in CRPC.
This research was financially supported by the Russian Science Foundation, grant 22-24-01093.

E-PS-15-003
MET immunohistochemistry reflex testing in non-small cell lung carcinoma. A real world prospective study in a single centre (LPCE, Nice, France)

C. Bontoux*, V. Hofman, M. Abboute, S. Goffinet, E. Long-Mira, S. Lassalle, M. Ilié, P. Hofman
*Laboratory of Clinical and Experimental Pathology, Hospital-Integrated Biobank (BB- 0033-00025), Pasteur Hospital, IRCAN Team 4, Inserm U1081, CNRS 7284, FHU OncoAge, Université Côte d'Azur, Nice, France

Background & objectives: Development of new MET inhibitors have recently shown promising efficacy for MET-dysregulated non-small cell lung cancer (NSCLC) in clinical trials, in particular in NSCLC with MET overexpression. However, MET IHC reflex testing is not currently recommended in international guidelines.
Methods: We evaluated prospectively MET expression (SP44 clone) as a reflex testing in 429 NSCLC consecutively diagnosed in biopsies, cytological or surgical samples between January 2022 and January 2023. MET+ was defined by an H-score greater than or equal to 150 of tumour membrane staining and MET high as tumour having strong (3+) staining of ≥50% tumour cells.
Results: Whatever sample types the MET H-score and the MET intensity was significantly correlated with the histological subtype, being superior in adenocarcinoma than in squamous cell carcinoma. MET H-score ≥150 was observed in 55% of surgical specimens, in 38% of biopsy and in 32% samples. 48% of all samples showed a MET high expression.

Conclusion: Systematic screening for the MET expression status using SP44 IHC showed discrepancy results according to the histological and the sample types.

E-PS-15-004

EGFR assessment using next generation sequencing (NGS) as a reflex testing on surgically resected non-squamous non-small cell lung carcinoma (NS-NSCLC)

C. Bontoux*, S. Goffinet, V. Hofman, F. Pezzuto, F. Calabrese, M. Ilié, P. Hofman
*Laboratory of Clinical and Experimental Pathology, Hospital-Integrated Biobank (BB- 0033-00025), Pasteur Hospital, IRCAN Team 4, Inserm U1081, CNRS 7284, FHU OncoAge, Université Côte d'Azur, Nice, France

Background & objectives: EGFR status assessment is mandatory in early-stage NS-NSCLC. Whether RT-PCR versus NGS should be used as reflex testing is still controversial. Co-occuring mutations, notably TP53 mutations, could have an impact on tumour behaviour and on adjuvant therapeutic strategies.
Methods: EGFR mutations were assessed using DNA and RNA NGS (Oncomine Precision Assay genes panel) in 720 stage IA-IIIA surgically resected NS-NSCLC. PD-L1 expression was evaluated in all tumours.
Results: EGFR mutations were detected in 11.5% tumours. A common non-compound EGFR mutation (L858R or del19) was observed in 75% of these latter cases. 55% of the global series has a co-occuring mutation, including a TP53 mutation, mostly in exons 7 and 8. EGFRmut/TP53 mut tumours were significantly associated with higher PD-L1 expression compared to EGFRmut/TP53 wt tumours.
Conclusion: Genomic alterations should be systematically evaluated using an NGS reflex testing in surgically resected NS-NSCLC, since future adjuvant therapeutic decision making may also take into account the presence of compound EGFR mutations as well as co-occuring mutations specially in TP53.

E-PS-15-005

ALK protein expression and ALK mutations in neuroblastic tumours correlate with poor differentiation

R. Bruinsma*, M. Fiocco, K. Langenberg, G. Tytgat, M. van Noesel, M. Wijnen, A. van der Steeg, R. de Krijger
*Princess Máxima Center for paediatric oncology, The Netherlands

Background & objectives: The anaplastic lymphoma kinase (ALK) gene has been identified as major oncogene for neuroblastic tumours (NBT). This study aimed to correlate the morphology of NBT, with genetic aberrations, immunohistochemical and mRNA expression of ALK.
Methods: Diagnostic tumour samples were available from 182 patients. These patients were divided into two categories based on the international neuroblastoma pathology classification: undifferentiated and poorly differentiated neuroblastoma (n=134) versus differentiated neuroblastoma, ganglioneuroblastoma and ganglioneuroma (n=48 patients). ALK protein expression was scored following immunohistochemistry, while whole transcriptome sequencing yielded ALK mRNA expression levels.
Results: ALK protein expression was categorized into three categories: negative (n=99), weak (n=30) and moderate/strong (n=37). The NBT were more often classified as undifferentiated or poorly differentiated in tumour samples that were ALK positive (negative versus weak OR 1.170, 95% CI (0.449-3.048)) (negative versus moderate/strong OR 2.279, 95% CI (0.803-6.471)). ALK amplification was only present in three NBT. ALK mutations (n=22) were more often seen in NBL that were undifferentiated or poorly differentiated (OR 2.056, 95% CI (0.576-7.341)). There was no correlation between the diagnosis category and mRNA expression level of ALK (OR 1.005, 95% CI (0.998-1.012)).
Conclusion: Both ALK protein expression and ALK mutations are associated with poor differentiation degree in NBT, whereas mRNA expression levels are not.

E-PS-15-006

Profiling spatial interactions of cancer-associated fibroblast subtypes in the wider tumour microenvironment of muscle invasive bladder cancer using multiplex immunofluorescence

A. Burley*, T. Silveira, T. Lund, A. Melcher, N. James, A. Wilkins
*Institute of Cancer Research, United Kingdom

Background & objectives: Cancer-associated fibroblasts (CAFs) are a heterogenous population with reported pro-tumour, and some anti-tumour functions. In muscle invasive bladder cancer (MIBC), CAF-enrichment is associated with inferior survival outcomes following immunotherapy, surgery and chemotherapy. Yet, little is known about radiotherapy outcomes.
Methods: Antibodies were optimised for immunohistochemistry and validated for single-plex immunofluorescence (IF) using the Opal system (Akoya). Staining order and antibody:opal pairings were considered in the final multiplex design. Slides were stained using the Leica Bond autostainer, IF images were acquired using the Vectra Polaris (Akoya) and unmixed with inForm (Akoya).
Results: The following antigens were selected for use in the multiplex panel; aSMA (Abcam, 1A4), FAP (Abcam, EPR20021), PDGFRa (Abcam, EPR22059-270), PDPN (Biolegend, D2-40), CD8 (Dako, C8/144B), panCK (Dako, AE1/AE3). The CAF markers selected reflect independent and co-expressing stromal populations. We found antigen stability was variable, and observed antigen degradation and enhancement, as such the panel and staining order was tailored accordingly.
Quantification of the resulting images facilitates comparison with clinical data and helps to address our hypothesis that CAF enrichment in MIBC is associated with inferior survival outcomes and correlates with poor responses to radiotherapy.
Conclusion: Transcriptomic/single cell studies of CAFs are limited due to difficulties distinguishing the origin of stromal signatures from bulk transcriptomic data, plus the spatial complexity of the tumour is lost. To overcome this, we have developed a novel CAF-specific mIF panel that offers an exciting and unique opportunity to explore the expression of multiple CAF markers in combination, their spatial arrangement, and their relationship with cytotoxic CD8+ T cells in the translational setting for MIBC patients treated with radiotherapy and beyond.

E-PS-15-007

Real world evidence of RET fusion testing and prevalence in non-small cell lung cancer

B. Cajiao Garcia*, V.D. de Jager, C. Kuijpers, A.J. van der Wekken, S.M. Willems, L.C. van Kempen, E. Schuuring
*Department of pathology and medical biology, University of Groningen, University Medical Center Groningen, The Netherlands

Background & objectives: Molecular analysis is key to identify treatment options for non-small cell lung cancer (NSCLC) patients. Inhibitors for *RET* fusion-driven NSCLC have been approved. The objective of this study was to determine the national testing rate and incidence in the Netherlands.
Methods: Clinical and pathology data from patients with stage IV non-squamous NSCLC diagnosed in 2017 and 2019 were collected from the Netherlands Cancer Registry (NCR) and linked to histopathology data collected in the Netherlands national registry of pathology reports (PALGA). *RET* fusion test rate, test type, timing of the test and test results were retrieved from these reports.

Results: In 2017, 23% (825/3,652) of all NSCLC patients were tested for *RET* fusions, which increased to 32% (1,211/ 3,830) in 2019. This test was commonly performed sequentially in patients with wild-type *EGFR* and wild-type *KRAS*: 76% in 2017 and 55% in 2019. *RET* fusion testing was not performed for 759 (52%) patients in 2017 and 596 (37%) patients in 2019 despite being *EGFR* and *KRAS* wild-type. DNA FISH was the most frequently used test in 2017 (86%) and 2019 (48%), while RNA-based NGS increased from 6% in 2017 to 27% in 2019. The prevalence of a *RET* fusion was 2.4% (20/825) in 2017 and 1.2%(15/1,211) in 2019.
Conclusion: The observed prevalence for a *RET* fusion in stage IV non-squamous NSCLC decreased from 2.4% in 2017 to 1.3% in 2019. This decrease may be a consequence of a change in test methodology from DNA-based FISH assays to RNA-based gene fusion transcript analysis. Furthermore, the data indicates that in 2019, 37% of patients were not tested for *RET* fusions despite a lack of driver mutations.
Funding: This work was supported by Lilly, Roche, MSD, Astrazeneca and Pfizer. The funders had no role in the design of the study, in the collection, analysis, or interpretation of data, in the writing of the abstract (All fees transferred to UMCG account)

E-PS-15-008
Unravelling leukemic landscapes: cerebrospinal fluid-derived next generation sequencing analysis provides comprehensive diagnostic, therapeutic and prognostic perceptions
O.C. Eren*, I. Kulac, T. Akan, O. Dogan, C. Aydin Mericoz
*Koç University Hospital, Department of Pathology, Turkey

Background & objectives: Cerebrospinal fluid (CSF) occasionally harbours the sole site of haematolymphoid malignancy recurrence. Our study emphasizes the value of Next Generation Sequencing (NGS) on CSF samples, especially in isolated central nervous system relapses, for crucial theranostic insights.
Methods: Case 1: An 11-year-old male with B-cell precursor acute lymphoblastic leukaemia in remission exhibited numerous CSF blasts, while synchronous bone marrow biopsy and aspirate were unremarkable. Case 2: A 50-year-old male experienced CSF-confirmed recurrence a year after localized myeloid sarcoma diagnosis and treatment. An NGS study using an RNA-based panel was performed on both CSF samples.
Results: Case 1: NGS revealed ETV6-RUNX1 fusion, IKZF1 exon skipping deletion (exons 1-8), and PTPN11 point mutation (p.1472C>T; p.P491L). The patient had another CSF-based relapse one year post-chemotherapy. Case 2: NGS identified CBFB-MYH11 fusion and NRAS mutation (c.35G>A; p.G12D). The patient underwent allogeneic stem cell transplantation (allo-SCT) and has been in clinicopathologic remission for 12 months.
Conclusion: IKZF1 deletion co-occurrence (case 1) may explain multiple relapses in a tumour with otherwise favourable prognosis due to ETV6-RUNX1 fusion. CBFB-MYH11 fusion (case 2) provides valuable insight, indicating intrabdominal prevalence among myeloid sarcomas and predicting complete remission with aggressive therapy, supporting allo-SCT. NGS on CSF should be considered for clinicopathological necessity as it enables evaluation of genetic transformations in hematopoietic tumours with sufficient CSF blast counts.

E-PS-15-009
Robust validation and implementation of the C2i genomics whole-genome sequencing minimal residual disease assay for ultrasensitive ctDNA detection in liquid biopsy
A. Erental*, T. Katz-Ezov, R. Tzabari, R. Campbell, U. Alon, D. Afterman, B. Oklander, A. Zviran, D. Hershkovitz
*Tel-Aviv Medical Center, Israel

Background & objectives: Accurate ctDNA detection is vital for MRD monitoring in solid tumours. Our goal was to implement and validate the highly sensitive C2i Genomics WGS MRD assay at Ichilov Medical Center's Pathology Lab, utilizing patient-specific tumour signatures and sophisticated analytical techniques.
Methods: Validation process included WGS of tumour tissue and germline peripheral blood mononuclear cells (PBMCs) for patient-specific signature identification and ctDNA WGS from blood samples for MRD detection. We sequenced 8 formalin-fixed paraffin-embedded (FFPE) samples, 12 reference plasma samples (6 healthy donors, 6 cancer patients), and 15 contrived reference plasma samples with varying ctDNA dilution rates.
Results: Our validation demonstrated 100% sensitivity and specificity on MRD positive and negative reference samples. The concordance in quantitative values of MRD, in terms of tumour fraction, was very high across dilutions spanning the aforementioned orders of magnitude. Mainly, a significant correlation (p-value < 0.01) of tumour fraction values among analytical samples processed at C2i Genomics and Ichilov was observed, indicating successful implementation and strong concordance with the reference lab. The established LLOD of 10e-4 matches that of the reference lab, with no ctDNA detection in control samples. The results indicate high reproducibility and robustness between sequencing labs.
Conclusion: The validated C2i Genomics WGS MRD assay offers ultrasensitive ctDNA detection in liquid biopsies, enabling effective MRD monitoring in solid tumours, and providing valuable insights into disease progression and treatment response. The robust performance of this assay supports its application in clinical trials and routine clinical practice worldwide.

E-PS-15-010
Implementation of the SOPHiA DDM™ homologous recombination deficiency (HRD) solution to detect HRD in ovarian cancer tumours
A. Erental*, A. Kaplan, C. Wizeman, R. Tzabari, L. Ifat, A. Mager, Y. Inbaram, D. Hershkovitz
*Tel-Aviv Medical Center, Israel

Background & objectives: Homologous recombination deficiency (HRD) is present in approximately 48% of ovarian cancer tumours. Some causes of HRD are well established, like BRCA1 and BRCA2 mutations, while others remain unknown. Here we describe the implementation SOPHiA HRD Solution in our Lab.
Methods: A set of 20 pre-characterized clinical samples in which the HRD status was determined in Myriad was used. DNA was extracted, libraries were prepared and sequenced. The validation process includes 13 samples that according to Myriad results expected to be BRCA positive & HRD positive samples, 4 BRCA negative & HRD positive samples and 3 BRCA negative & HRD negative.
Results: Analysis of the validation cohort showed complete concordance with the Myriad results. At the time of writing the abstract, 32 clinical samples were received in the lab. Analysis showed that 3 samples were BRCA positive and HRD positive (9.3%), 4 were HRD positive BRCA negative (12.5%), 17 were HRD and BRCA negative (53.1%), 4 samples were BRCA negative and HRD status could not be determined (12.5%) and 4 samples failed (12.5%). Turnaround time for diagnosis was 14.5 ± 7.5.
Conclusion: SOPHiA HRD Solution combined the detections of HRR gene mutation and the Genomic Integrity Index in a single assay. In light of the validation results, it is suitable for clinical performance locally. There is a growing tendency worldwide to perform tests locally rather than outsourcing. This shortens TAT times and optimizes the process. Determining HRD status for ovarian cancer patients can help provide information regarding the potential benefit for PARP inhibitor therapy and bring help treatment decisions.

E-PS-15-011

Long non-coding RNA NEAT1 cannot be used as a diagnostic and prognostic biomarker in patients with locally advanced rectal cancer

K. Eric*, J. Rosic, M. Miladinov, S. Dragicevic, G. Barisic, V. Markovic, K. Zeljic
*Department of Pathology, Pathohistology and Medical Cytology, University Clinical Centre of Serbia, Serbia

Background & objectives: The NEAT1 (Nuclear Paraspeckle Assembly Transcript 1) gene encodes a long non-coding RNA that is deregulated in carcinomas of the gastrointestinal tract. Diagnostic and predictive potential of NEAT1 was investigated in patients with locally advanced rectal cancer.
Methods: The study group consisted of 19 patients with rectal cancer treated with neoadjuvant chemoradiotherapy (nCRT). RNA was isolated with TRIzol reagent from samples of rectal cancer and noncancerous tissue before and after nCRT. The relative expression level of NEAT1 normalised to GAPDH was determined by qRT-PCR method.
Results: Expression of NEAT1 did not differ between rectal cancer and noncancerous tissue before nCRT (p=0.953) and cancer and noncancerous tissue after nCRT (p=0.210). There was no difference in NEAT1 expression between tumour tissue before and after nCRT (p=0.079). NEAT1 was significantly higher in noncancerous tissue before than after nCRT (p=0.005). Therapy responders (TRG1, TRG2) and non-responders (TRG3, TRG4) did not differ in NEAT1 levels in tumour tissue before (p=0.790) and after nCRT (p=0.352). NEAT1 expression in rectal cancer tissue before nCRT cannot be used as a biomarker to distinguish responders from non-responders (AUC=0.559, 95%CI=0-1, p=0.790). Demographic and clinicopathological characteristics were not associated with NEAT1 expression in rectal cancer tissue.
Conclusion: The obtained results suggest that the long noncoding RNA NEAT1 cannot be considered as a biomarker with diagnostic potential or for predicting response to nCRT in patients with rectal cancer. Validation of the current results in a larger group of patients with locally advanced rectal cancer is warranted.
Funding: This work was supported by the Strategic Project of the Serbian Academy of Sciences and Arts Molecular basis of response to chemioradiotherapy in rectal cancer - MOHERATEKA, F-69

E-PS-15-012

Stability of testing of microsatellite instability

J. Fairley*, S. Deans
*GenQA, United Kingdom

Background & objectives: Microsatellite instability testing (MSI) is important in determining the potential hereditary nature of colorectal cancer and recently has been expanded to be a biomarker for immune checkpoint inhibitors. This testing needs to be of high quality therefore EQA is important.
Methods: GenQA has provided external quality assessment (EQA) for MSI testing for over ten years both as a standalone EQA and as part of the colorectal cancer testing EQA . Participants test formalin-fixed paraffin-embedded tissue and are expected to report their results in their usual format and interpret in the context of the clinical scenario supplied.
Results: The standard of MSI testing has been high with an average error rate of less than 2%. The 2022 EQAs error rates were higher at 10% and 15% respectively. For the MSI EQA the errors seemed to be technique related. For the colorectal cancer EQA this was due to an unusual subtle signal patterns which highlighted the limitations of testing without matched germline DNA.
Assessment of BRAF variants and MLH1 promoter methylation testing was introduced in 2016 to reflect routine testing strategies for the identification of Lynch syndrome. BRAF variant testing has been accurate, however, errors have been reported by laboratories for MLH1 promoter methylation.
Conclusion: The provision of EQA for MSI testing has shown improvements in the quality of testing and interpretation of results by participating laboratories. Issues have been observed when more challenging tests and samples are introduced such as MLH1 promoter methylation testing demonstrating the need for further education and EQA in this evolving field of molecular pathology.

E-PS-15-013

Epigenetic analysis of surrogate markers in consensus molecular subtypes of colon cancer

D. Guerrero-Setas*, I. Fernández De Los Reyes, I. Monreal-Santesteban, L. Alonso, B. Fernández-Marlasca, P. Azcue, J. Suarez, M. Gómez-Dorronsoro
*Hospital Universitario de Navarra, Spain

Background & objectives: Consensus Molecular Subtypes (CMS) of colon cancer (CC) are obtained by surrogate immunohistochemical expression of CDX2, FRMD6, HTR2B and ZEB1. Aberrant methylation contributes to tumour progression. The objective was to study the aberrant methylation of the surrogate genes in CC.
Methods: 144 stage II (55.6%) and III (44.4%) tumours were classified into CMSs with the primary antibodies against mismatch repair proteins-MMR and proteins of the surrogate panel.
CDX2, FRMD6 and ZEB1 methylation levels were analysed by bisulfite pyrosequencing after bisulfite modification of DNA and PCR with specific primers designed for this study. It was not possible to design primers for HTR2B.
Results: Tumours were classified into CMS1, CMS2/CMS3 and CMS4 in 18 (12.5%), 117 (81.3%) and 9 patients (6.3%), respectively. CDX2 and ZEB1 were hypermethylated in 32.8% and 32.6% of the cases and FRMD6 hypomethylated in 50.9% of the patients. These alterations were more frequent in tumoral than in normal tissue.
FRMD6 and ZEB1 IHC expression were not associated with any of the variables tested. Nevertheless, CC cases with absent/low CDX2 expression were associated with CDX2 hypermethylation and were preferentially of mesenchymal type, MMR-defective, stage III, less differentiated and right colon-sided CC tumours (p=0.044, p<0.005, p=0.024, p=0.006, p=0.093, respectively).
Conclusion: We describe for the first time the epigenetic abnormalities of two surrogate markers used for CMS classification, i.e. ZEB1 hypermethylation and FRMD6 hypomethylation. We also demonstrate that ZEB1 and CDX2 hypermethylation are associated with CMS1 subtype. CDX2 hypermethylation is clearly associated with less CDX2 expression and bad prognostic variables.

E-PS-15-014

Usefulness of an extense Next Generation Sequencing panel in endometrial cancer

D. Guerrero-Setas*, T. Zudaire, I. Fernández De Los Reyes, Y. Laplaza, P. Fernández, M.C. Caballero, B. Fernández-Marlasca, E. Gochi, M. Gómez, J.C. Muruzabal, R. Guarch
*Hospital Universitario de Navarra, Spain

Background & objectives: The study of POLE, TP53 and MMR genes by molecular and immunohistochemical techniques are essential for the molecular classification of endometrial cancer (EC). We analyse whether the use of Next-Generation-Sequencing (NGS) gives added value to EC diagnosis.
Methods: Targeted DNA/RNA-based NGS was conducted to identify pathogenic/likely pathogenic/uncertain variants in 32 endometrioid and clear-cell EC. DNA/RNA were extracted from macrodissected areas. Library preparation was carried out using a 161-gene panel with

automatic workflow to annotate the somatic variants (SNVs, indels, copy number variations and fusions). IHC for MMR and p53 proteins was also performed in all the cases.
Results: All the cases were not pathogenic for MMR and not-mutated for p53. All the cases were evaluable for NGS; we detect allelic variants in POLE and TP53 genes in 29.0% and 41.0% of the cases, respectively. CNVs and additional SNVs in crucial genes (PIK3CA, PTEN, among other) were present in 76.5% of the tumours analysed. We also detect TP53 mutations in patched p53-positive cases ($p<0.05$).
Conclusion: NGS gives added value to gene-to-gene/protein-to-protein analysis because it allows the detection of extra variants of possible clinical value. NGS also allows to detect unexpected TP53 mutations in those cases with patched TP53-positive expression.

E-PS-15-015
Comparison of diagnostic coverage of RET fusion partners by various RNA-based assays
M. Gupta*, A. Mota, I. Simon, J. Cazier
*Eli Lilly, United Kingdom

Background & objectives: *RET* fusions are actionable in non-small cell lung cancer (NSCLC) and papillary thyroid cancer (PTC). Design of different gene-panels affects their sensitivity to detect these fusions. We compared different RNA panel designs and their ability to detect *RET* fusion partners.
Methods: We performed in silico comparison of RNA-based next-generation sequencing (NGS) panels and PCR based assays against a catalogue of known *RET* gene fusion partners. The panels included TSO500, Archer FusionPlex (Lung and Pan-solid tumour), Oncomine assays (Focus, Precision, Comprehensive, Comprehensive Plus and Dx Target Test) and PCR based assays from Biocartis and AmoyDx.
Results: The results show a descriptive analysis of the specific *RET*-fusions and their partners that can be detected in NSCLC, PTC and other tumour types by each of the panels described above. Only a couple of fusion partners constitute the significant majority of *RET*-fusions. Therefore, we also present the proportion of known fusions that each technology can detect (i.e. sensitivity by design).
Conclusion: This analysis determines the ability of different RNA-based panels to detect different *RET* fusions and their partners. These findings may provide clinical laboratories with additional information on the limitations of each assay for different tumour types.
Funding: This project was funded by Eli Lilly.

E-PS-15-016
Feasibility and impact of retrospective testing for RET fusions and other actionable biomarkers not previously tested in non-small cell lung cancer cases: an experience from England
M. Gupta*, J. Bradbury, H. Sanna, S. Forrest, S. Taylor, C. Felix, F. Carter, C. Escriu, S. Brown, D. Bury, J. Gosney, M. Powari, M. Evans
*Eli Lilly, United Kingdom

Background & objectives: Non-availability of biomarker testing in advanced/metastatic non-small cell lung cancer (mNSCLC) limits access to targeted treatments for many patients. Here, impact of sponsored retrospective testing for biomarkers not previously tested was explored, including identification of new patients for treatment.
Methods: Gene-fusions were tested for RET, NTRK1/2/3 and METex14 skipping where patients were alive at the time of analysis and had sufficient quality and quantity of archived tissue available. Cases with previously identified actionable biomarkers were excluded. All testing was performed on Idylla GeneFusion Assay at five participating centres and, where needed, reconfirmed by next-generation sequencing (NGS) as per local protocols.
Results: Of the 423 cases tested to date, Idylla assay was successful in 405 (95.7%). The testing identified 15 new biomarker positive cases, including 3 for RET and 12 for METex14. Confirmation through NGS is in progress for one and could not be completed in three others because of different reasons. Two patients have already received a targeted treatment. Importantly, this project enabled two centres to establish prospective testing for all routine cases. Additionally, one centre took the opportunity to test the blocks pulled out from the archives for KRAS in parallel. Fifteen KRAS positive cases were identified, including 8 with the actionable G12C mutation.
Conclusion: This feasibility study identified new patients for targeted treatments that would have been missed otherwise and emphasises the need for timely broad testing of genomic drivers in mNSCLC . It also increased awareness of biomarkers and local testing pathways among the healthcare staff, and motivated one centre to evaluate two different testing pathways. The project also catalysed dialogue between the oncologists, pathologists and laboratory staff, and the experience helped establish prospective testing at two centres.
Funding: The project was sponsored by Eli Lilly and Company

E-PS-15-017
Implementation of a multidisciplinary molecular tumourboard (MTB)
L. Häberle*, S. Labuhn, M. Schlensog, W. Goering, K. Horny, S. Redler, I. Esposito
*Institute of Pathology, University Hospital Duesseldorf, Germany

Background & objectives: With high-throughput sequencing becoming more and more readily available and precision medicine on the rise, molecular tumour boards (MTBs) represent a pivotal tool in translating molecular findings into patient management.
Methods: In July 2022, a multidisciplinary MTB was implemented at our university hospital, including cancer patients in last-line or near-last-line therapy, patients with rare cancers, and patients with initial cancer diagnosis at 50 years or younger. Next generation sequencing (NGS)-based molecular diagnostics is performed for all tumours. All cases are systematically documented and followed-up.
Results: Between July 2022 and April 2023, 57 case presentations (56 individual patients) were documented at 19 online MTB conferences. Most cases were gastrointestinal cancers including hepatopancreaticobiliary cancers (43%), followed by urological (21%) and gynaecological (18%) cancers. Possible targets for therapy were detected in 55% of cases. Off-label therapies were recommended in 36%, inclusion into therapy studies in 18%, and EMA-approved therapies in 16% of cases.
Conclusion: MTBs are a useful tool to guide therapy of cancer patients and facilitate access to therapy studies and off-label therapies. Follow-up data will be collected to evaluate adherence to MTB recommendations and patient outcomes.

E-PS-15-018
Squamous cell carcinoma of the lung with microsatellite instability in a patient with Lynch syndrome: a case report
E. Haddad*, B. Bottet, P. Thiebaut, S. Morin, H. Dreyfus, E. Vanier, C. Vincent, H. Sobol, F. Marguet, J. Baste, F. Guisier, J. Sabourin, N. Piton
*CHU Rouen, France

Background & objectives: A 68 year old man with a history of colorectal cancer at age 36 (with recurrence at age 56) and a family history of cancers. A germline pathogenic mutation of MLH1 confirmed the Lynch syndrome.
Methods: In 2022, as part of the follow-up of his colon cancer, a CT-scan was performed, retrieving a nodule of the right lung. A biopsy revealed a squamous cell carcinoma, that has been surgically treated. IHC showed a loss of MLH1 and PMS2 expression in tumour cells.

MSI was confirmed by PCR amplification of tumour microsatellites, with comparison of normal tissue.
Results: Lynch syndrome is due to constitutional mutations impairing the mismatch repair system, which result in tumour microsatellite instability. Patients with this condition are at a high risk of developing colorectal, uterine, ovarian, stomach, small bowel, pancreatic, kidney and brain cancers. However, the risk of lung cancer is considered the same as in the general population. In the literature, 3 cases of lung dMMR adenocarcinoma in patients with Lynch syndrome, including a Muir-Torr syndrome.
In our patient, we rulled out the hypothesis of the lung metastasis of an urothelial carcinoma, which belongs to the spectrum of Lynch syndrome, by the microscopic appearance of the tumour and the lack of GATA3 expression.
Conclusion: dMMR status is a strong predictive biomarker for the efficacy of immune checkpoint inhibitors. Interestingly, a recent study reported a durable response to toripalimab in a dMMR squamous cell cancer of the lung. This must lead us to discuss immunotherapy in case of recurrence of this squamous cell carcinoma of the lung in our patient.
We report here the first case of a dMMR squamous cell carcinoma of the lung in a patient with Lynch syndrome.

E-PS-15-019
Whole-exome sequencing of brain metastases and paired primary tumours of small cell lung carcinoma – preliminary results
K. Heß*, F. Kellers, A. Kuenstner, N. Reimer, S. Fliedner, H. Busch, L. Bastian, C. Röcken, B. Konukiewitz
*University Medical Center Schleswig-Holstein, Campus Kiel, Department of Pathology, Kiel, Germany

Background & objectives: The process of brain metastasis of small cell lung cancer (SCLC) is poorly understood. The project aimed to compare the brain metastases of SCLC and their primary tumours using Whole Exome Sequencing (WES).
Methods: WES was performed on formalin-fixed, paraffin-embedded tissue from 11 patients, including paired primaries and brain metastases from 5 patients. DNA was analysed using high-throughput sequencing on an Illumina sequencer. Data processing was performed with the "MIRACUM-Pipe" workflow and the OncoKB cancer gene list system. Cancer-relevant mutations were identified after comparison with the COSMIC database.
Results: The most frequently observed genetic aberrations were nonsense mutations, missense mutations, or deletions of TP53 (n=9; 82%) and RB1 (n=7; 64%). Alterations in the Notch signalling pathway were detected in the primary tumours and also in the brain metastases by mutations in NCOR1, CREBBP, and NOTCH1. In contrast, KDM5A mutations have only been detected in the primary tumours. Furthermore, VEGFR1 and RNF213 mutations were identified as angiogenesis-regulating genes, and AFND and ABL2 as modulators of cell-cell contacts and extracellular matrix. Besides VEGFR1 (n=2; 18%), BRCA2 (n=4; 36%) could be identified as a possible therapeutic target in primary tumours and brain metastases.
Conclusion: In the comparative analyses between SCLC and brain metastases, gene mutations considered driver genes (TP53 and RB1) of neuroendocrine carcinoma were detected, as well as gene mutations associated with angiogenesis, tumour growth, and invasion that presumably contribute to the process of metastasis. In addition, our results suggest potential therapeutic options for a subset of SCLC metastases, especially with regard to VEGFR1 and BRCA2/PARP inhibitors.
Funding: The author Katharina Hess received funding from "Familie Mehdorn foundation".

E-PS-15-020
Homologous recombination deficiency analysis by panel NGS in 148 penile squamous cell carcinoma samples
J. Hojný*, M. Kendall Bártů, E. Krkavcová, R. Michálková, J. Hrudka
*Department of Pathology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Czech Republic

Background & objectives: Penile squamous cell carcinoma (pSCC) is rare tumour with limited understanding of its genomic background. We investigated the potential of homologous recombination deficiency (HRD) as a prognostic and/or predictive marker in pSCC, considering its recent success in various cancer types.
Methods: We analysed a cohort of 148 histologically confirmed invasive pSCC cases. A panel of 359 gene-targets (1.16 Mbp) was used for capture NGS. The data were bioinformatically processed with CLC Genomics Workbench software, and the HRD score was calculated as the sum of "Loss of Heterozygosity," "Large-scale State Transitions," and "Telomeric Allelic Imbalance" events and compared to optimized HGSC cut-offs.
Results: The overall results of HRD analysis showed high scores compared to the cut-offs optimized for HRD-high HGSC samples, especially in low-quality samples. Out of 148 pSCC samples, 36 were evaluated as HRD-high, of which 26 had limited quality and/or coverage. Therefore, 58/148 samples with coverage <400x were discarded, and the HRD score was recalculated. The final results showed an average pSCC HRD score of 51 (median = 51; minimum = 20; maximum = 80). Out of the final 90 samples, 10 were evaluated as HRD-high (11%; HRD>=65), 63 as HRD-intermediate (70%; HRD>42 and <65), and 17 as HRD-low (19%; HRD<=42).
Conclusion: Our HRD analysis of pSCC revealed relatively high levels of HRD score with potential treatment implications for 11% of patients, compared to standardized HGSC calculation. However, further correlation with molecular profiles and histopathological pSCC subtypes is needed to fully evaluate the prognostic and/or predictive value of HRD status in pSCC (currently in progress). Additionally, the observed limitations of small NGS panels combined with low-quality samples in HRD calculation should be considered in future NGS studies.
Funding: This work was supported by the Ministry of Health, Czech Republic (MH CZ AZV NU21J-03-00019 and DRO-VFN 64165)

E-PS-15-021
Revolution in pathology, no more formalin fixation! Reduced DNA deterioration in five years in nonfixed tissues processed with supercritical CO2 compared to formalin fixation
M. Hoogland*, N. van der Horst, A. Knol, M. Niemantsverdriet
*Isala, The Netherlands

Background & objectives: Toxic, DNA damaging formaldehyde was banned, except in the medical sector where it is routinely used during pathological analysis. The objective was to compare long term effect on DNA quality of formalin fixation to processing tissues using non-toxic supercritical CO2.
Methods: Fresh human tissues were collected and split in 2018. Of each tissue, one sample was processed using conventional method (FFPE, Formalin Fixed Paraffin Embedded). The second sample freshly processed in non-toxic supercritical CO2 (NFPE, Non Fixed Paraffin Embedded). As pilot, five years after storage in the archive, of four selected tissues DNA parameters were compared between FFPE and NFPE processing.
Results: In a 4-tissue pilot experiment (lung, kidney, mamma and liver), five years after embedding in paraffin and archive storage; DNA parameters of NFPE samples were typically better compared to

matching FFPE samples. The DNA yield per mm2 tissue of 3/4 tissues was higher for NFPE than FFPE and the 4th was only marginally lower. The ladder PCR for NFPE samples was better than FFPE for all 4 tissues, the NGS library generation capacity per ng DNA was higher for NFPE than FFPE for all 4 tissues and the mean read length in NGS was higher for all 4 NFPE samples compared to the FFPE samples with the same tissue.

Conclusion: Formalin is toxic and carcinogenic because it can bind to DNA, leading to mutations that cause cancer, making it a very undesirable compound to work with. In DNA analysis for diagnostic purposes formalin also is a nuisance because it progressively damages DNA over time, leading to fragmentation and sequencing artefacts mimicking mutations. Using supercritical CO2 and paraffin embedding, without toxic formalin fixation may result in remarkable 5-year conservation of DNA quality, resulting in superior molecular parameters compared to FFPE material.

E-PS-15-022

Lack of correlation of MET and PD-L1 expression in non-small cell lung cancer challenges anti-PD-1/PD-L1 and anti-MET therapeutic strategies, per a comparative study of matched biopsies and surgical resection samples

M. Ilié*, V. Hofman, C. Bontoux, S. Goffinet, J. Benzaquen, J. Boutros, S. Lassalle, E. Long-Mira, A. Gómez-Caro, C. Cohen, J. Berthet, C. Marquette, P. Hofman
*CHU Nice LPCE, Pavillon J, France

Background & objectives: Companion diagnostics for the treatment of advanced non-small cell lung carcinoma (aNSCLC) patients include MET expression and PD-L1 tumour proportion score (TPS). To determine the correlation rate between them, we examined matched biopsies and surgically resected specimens from NSCLC patients.

Methods: This retrospective analysis assessed the prevalence and correlation between MET expression (SP44 clone) and the PD-L1 TPS (22C3 clone) by immunohistochemistry together with molecular alterations determined by targeted next-generation sequencing in matched lung biopsy and surgically lung resected specimens from 70 patients with NSCLC.

Results: The study discovered a significant correlation between the MET H-score in surgical samples and matched biopsies (P-value<0.0001), as well as between the PD-L1 TPS in paired biopsies and surgical samples (P-value<0.0001). However, there was no significant correlation found between the MET H-score or expression subgroups and the PD-L1 TPS in both types of paired samples (P-value=0.47 and P-value=0.90). In addition, the MET H-score was significantly higher in adenocarcinoma compared to squamous cell carcinoma (P-value<0.0001). A mutational analysis indicated that the MET H-score was significantly higher in NSCLC cases with targetable molecular alterations (P-value=0.0095), particularly MET amplifications, while no significant correlation was found for the PD-L1 TPS.

Conclusion: Our study found no significant correlation between PD-L1 and MET expression in samples from NSCLC patients, highlighting the importance of personalized treatment strategies based on individual expression profiles. These findings provide valuable insight into the development of effective immunotherapy and targeted therapy for NSCLC patients.

E-PS-15-023

Creation of contrived plasma samples with RNA variants to use as liquid biopsy reference material

M. Jasti*, S. Hernandez, M.D. Chen, K. Bramlett, A. Luchetti
*THERMO FISHER SCIENTIFIC, USA

Background & objectives: Creating RNA variant containing contrived plasma is challenging due to high concentration of ribonucleases in plasma that degrade exogenous RNA. Current study reports three proprietary methods for creating contrived plasma with RNA variants, to be applied for liquid biopsy studies.

Methods: The proprietary methods used for creation of contrived plasma samples with RNA variants include three different procedures for introducing the RNA variants into healthy donor plasma. Different RNA variants such as fusions and splicing variants were used for spike in to plasma pool. Following the spike in, nucleic acid was isolated from plasma and sequenced to detect the variants.

Results: To evaluate the methods used, nucleic acid from plasma pool with RNA variants spiked in was isolated using a GenexusTM Cell-Free Total Nucleic Acid Purification Kit and GenexusTM Purification System. The isolated nucleic acid was sequenced on an Ion TorrentTM sequencing platform using an AmpliSeqTM HD target amplification assay to detect the presence of variants. Feasibility data for all these proprietary methods showed that exogenously spiked in RNA variants are stabilized by the methods used and increased recovery rates. In addition, varying the ratio of exogenous RNA variant inputs to healthy donor plasma shows a linear recovery trend indicating a good correlation between input amount and recovery.

Conclusion: This study demonstrates the successful creation of contrived plasma samples with RNA variants that mimic the biological complexity of human blood samples, which can be used in liquid biopsy tests. The use of both surrogate and contrived samples can foster innovation, when real variant positive samples are difficult to obtain.

E-PS-15-024

The Pathology Genomics Imaging Collection: progress on the collaboration between Genomics England and the National Pathology Imaging Cooperative

C. Jennings*, M. Humphries, C. Colquhoun, D. Kaye, G. Stankeviciute, C. Chen, G. Chan, B. Selinsek, R. Chabra, L. Valis, D. Bansal, P. Arumugam, D. Westhead, D. Treanor
*Leeds Teaching Hospitals NHS Trust and National Pathology Imaging Cooperative, Leeds UK, Genomics England, Queen Mary University of London, University of Leeds, United Kingdom

Background & objectives: Datasets containing whole slide images and molecular data have shown potential to advance diagnostic, prognostic and predictive understanding of cancer through multimodal deep-learning. Addressing the scarcity of multimodal datasets is a priority and should be informed by understanding data requirements.

Methods: A collaboration between Genomics England and the National Pathology Imaging Cooperative will enhance pathology assets of the cancer arm of The 100,000 Genome Project with approximately 250,000 whole slide images and 15,000 COSD compliant, .XML format structured pathology reports. These will accessible with genomic, radiological and clinical data in the new multimodal platform of the Genomics England Trusted Research Environment.

Results: Over 70,000 images from 18 contributing NHS sites have been scanned at the National Pathology Imaging Cooperative Scanning facility, generating 100 terabytes of image data so far.

Additionally, the results of user discovery research; including expert interviews, a survey of prospective users and focussed user interviews, have been used to inform the data curation, tooling, and architecture decisions in developing the multimodal research environment.

Conclusion: As this work nears completion, we share our experiences and lessons learnt for the multimodal research community. We also present the dataset and describe the architecture that has been developed within the Genomics England Research Environment to enable its use alongside the other modes of data available for its participants.

Funding: National Pathology Imaging Co-operative, NPIC (project no. 104687), is supported by a £50m investment from the Data to Early Diagnosis and Precision Medicine challenge, managed and delivered by UK Research and Innovation (UKRI).

E-PS-15-025

CCND1 but not DOG1 is associated with an aggressive phenotype of urothelial bladder cancer

M. Kluth*, A. Frericks, H. Plage, M. Lennartz, N. Blessin, M. Slojewski, T. Ecke, S. Koch, R. Simon, G. Sauter, T. Klatte, T. Schlomm, D. Horst, H. Zecha, K. Jansen
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: DOG1 and CCND1 are jointly localized on 11q13.3, a frequently amplified region in different tumours. Both genes are potential candidates for the management of targeted tumour therapies. The prognostic role of DOG1 and CCND1 alterations are unknown in bladder cancer.
Methods: DOG1 expression was analysed by immunohistochemistry and CCND1 amplification by fluorescence in situ hybridization on tissue microarrays containing more than 2,700 urothelial bladder carcinomas, including 636 patients that underwent radical cystectomy for muscle-invasive disease.
Results: CCND1 amplification occurred in 15.5% of the 1,880 analyzable carcinomas. Amplification rate increased from pTa G2 low (2.4%) to pTa G2 high (16.5%), and pTa G3 (27.8%; $p<0.0001$). It was 18.9% in muscle-invasive pT2-pT4 carcinomas. Amplification was unrelated to phenotype and prognosis. DOG1 positivity occurred in 27.0% of 2,515 analyzable carcinomas, including 4.1% with strong staining.DOG1 positivity was more frequent in pTa (36.2%) than in pT2-4 carcinomas (22.8%; $p<0.0001$) but unrelated to phenotype and prognosis in pTa and pT2-4 carcinomas. Strong DOG1 immunostaining was linked to CCND1 amplification ($p<0.0001$). Tumours with strong DOG1 positivity had CCND1 amplification in 45.0% while only 12.2% of amplified cases showed strong DOG1 staining.
Conclusion: CCND1 is amplified in about 20% of invasive urothelial bladder cancers and results in high level DOG1 expression in about 50% of cases. CCND1 amplification correlates with a higher grade in pTa tumours. Neither CCND1 amplification nor DOG1 expression are related to patient prognosis.

E-PS-15-026

Tumour mutation burden analysis in solid tumours

Y.B. Kök*, S. Erdamar Çetin, M.C. Yakıcıer, A. Erşen Danyeli, F. Tokat, Ü. İnce
*Acıbadem Mehmet Ali Aydınlar University, Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Tumour mutation burden (TMB) is a measure of the somatic mutations in tumour genome. The prognostic role of TMB in solid tumours is debated. This is the first study in Turkey to document TMB in solid tumours with clinicopathologic characteristics.
Methods: DNA and RNA was isolated from FFPE tumour tissues; then comprehensive genomic profiling (Trusight Oncology 500assay) of more than 500 genes whose mutations are known to participate in carcinogenesis were searched for including insertions, deletions, single nucleotide variations, amplifications, fusions or alternative splicing, using NOVASEQ 6000 SYSTEM, ILLUMINA platform and PERIANDX software. Threshold for TMB-high was accepted as >10mutation/megabase.
Results: Of 142 patients, mean age:56,3(1-87) and female/male:73/69, with solid tumours evaluated for TMB, 45(31,7%) were found to have high TMB. In TMB-high patients, mean age was 60,6 and female/male ratio was 17/28. The most common site in TMB-high group was lung(n=22; 67% of total lung cancers), followed by colon(n=6), uterus (n=4) and ovary(n=4), stomach(n=3), skin(n=1; 11% of total melanocytic lesions), adrenal gland(n=1), mediastinum(n=1), breast(n=1), bladder(n=1), gallbladder(n=1). Microsatellite instability was found in 5 cases (3,5% of total) in TMB-high group(11%) whereas there was none in TMB-low group. There was not any correlation between TMB level and age, gender and PD-L1 expression.
Conclusion: This is a preliminary study on TMB analysis of solid tumours. Similar to the literature, TMB levels varies across different tumour types. In our study, highest levels were seen in non-small cell lung cancer, probably due to heavy smoking habbit in our country. On the other hand, melanocytic skin tumours showed lower TMB levels in our series compared to other studies. Considering its importance for immunotherapy, standardization of TMB is getting more important.

E-PS-15-027

Homologous recombination deficiency analysis in solid tumours

Y.B. Kök*, S. Erdamar Çetin, A. Erşen Danyeli, F. Tokat, M.C. Yakıcıer, Ü. İnce
*Acıbadem Mehmet Ali Aydınlar University, Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Homologous recombination deficiency (HRD) is a type of DNA repair deficiency, which may give rise to malignancies with increased sensitivity to platinum-based chemotherapy and PARP inhibitors. In this preliminary study, we analysed of HRD status for various solid tumours.
Methods: This is a retrospective study of solid tumours for which HRD panel studies were requested by the clinic. DNA was isolated from FFPE tumour tissues, then NGS scanning for variations in genes ATM, BARD1, BRCA1/2, BRIP1, CDK12, CHEK1/2, FANCL, PALB2, PPP2R2A, RAD51B/C/D, RAD54L, TP53 was performed using MiSeq SEQUENCING SYSTEM, ILLUMINA platform and SOPHiA-DDM-V-5.10.12.1 software.
Results: HRD was analysed in 74 patients with malignant solid tumours. Mean age was 60,7 (39-78) and male/female ratio was 24/50. Tumours of various origins included ovary(n=28), prostate(n=17), pancreatobiliary system(n=7), breast(n=5), endometrium(n=3), colon(n=3), peritoneum(n=2), oesophagus (n=1), fallopian tube(n=1), while 7 carcinomas were of unknown origin. 54 cases showed at least 1 pathogenic variation in the panel: TP53(n=40), BRCA1(n=10), ATM(n=5), CHEK2(n=4), BRCA2(n=3), RAD51(n=2), BARD1(n=2), PALB2(n=1), CDK12(n=1). 29 (39%) cases showed mutations only for TP53. In 25 (34%) cases evaluated as HRD (excluding TP53-only cases), rates according to organ distribution were as follows: Ovary:39%(n=11), prostate:53%(n=9), pancreatobiliary system:29%(n=2), endometrium:33%(n=1), unknown origin:29%(n=2). Three of these HRD cases (relatively 12%) showed mutations in two different HRD-genes.
Conclusion: The HRD rates shown in tumours are reported in a wide range in the literature, and our results (34%) also fell within this range. While pioneering studies in HRD-targeted therapies centred around ovary and breast, it has become recognized day by day in other organs, such as prostate and pancreas. In addition, the focus on searching for BRCA mutations is giving way to multi-gene panels containing genes that have been shown or predicted to contribute to therapy implications.

E-PS-15-028

Different miRNA involvement in rectal neuroendocrine tumours showing either common mutation or high mitotic index: a pilot study

M.J. Kwon*, S.Y. Kang, H.S. Kang, H.Y. Park, N.Y. Kim, M. Hong
*Hallym University Sacred Heart Hospital, Republic of Korea

Background & objectives: Neuroendocrine tumours (NETs) are uncommon, heterogeneous groups of neoplasms with malignant potential. They need to determine the frequency of clinically and pathologically relevant mutations and miRNA expressions in rectal NETs to identify morphologic profiles related to prognosis and behaviour.

Methods: Twenty-four rectal NETs that were endoscopically resected were enrolled. To evaluate the miRNA expression profile relevant to common genetic mutations in rectal NETs, we used next-generation sequencing and the NanoString nCounter miRNA Expression assay. KEGG pathway analysis predicted the possible target signalling pathway correlated with dysregulated miRNAs.
Results: 19 rectal NETs (79.2%) showed more than 1 mutation in the 24 cancer-related genes (TP53 [29.2%], FBXW7 [20.8%], CDKN2A [16.7%], PTEN [16.7%]). 7 miRNAs (hsa-miR-769-5p, hsa-miR-221-3p, hsa-miR-34a-5p, hsa-miR-181c-5p, hsa-miR-1246, hsa-miR-324-5p, hsa-miR-361-3p) were down-regulated in the tumours harbouring FBWX7 mutation ($p<0.0001$). Hierarchical clustering of miRNA expression profiles separated the tumour group with a high mitotic index from the mutated group. Among these down-regulated miRNAs, using the KEGG pathway, hsa-miR-769-5p was correlated with extracellular matrix-receptor interaction and lysine degradation (FDR<0.05). Among clinicopathological factors, the up-regulated hsa-miR-3934-5p was linked with increased mitotic count (FDR<0.05). No changes in miRNAs expressions involved in tumour size >1 cm, lymphovascular invasion, and Ki-67 index could be identified.
Conclusion: In conclusion, using miRNA expression profiling, we have identified different miRNA signatures involved in either FBXW7 mutation or high mitotic index in rectal NETs, which may play an essential role in tumour behaviours.
Funding: the National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIT) (No. 2022R1F1A1065335)

E-PS-15-030
Evaluation of the expression of 148A and 192 mirRNA association with postoperative complications in patients undergoing liver transplant at Fundación Santa Fe de Bogotá
R.D.P. Lopez-Panqueva*, D.M. Grajales Urrego, P.C. Trujillo Morales, H.A. Gonzalez, R.E. Andrade Perez, M.L. Tapias, A. Vera Torres
*Fundación Santa Fe de Bogotá, Department of Pathology and Laboratory Medicine, Universidad de Los Andes, Bogotá, Colombia

Background & objectives: Post-transplant complications include acute rejection and recurrence of the underlying disease. MicroRNAs are proposed as specific and sensitive biomarkers for early detection of liver damage. Our objective was to evaluate the association between miRNAs expression and the occurrence of complications.
Methods: The expression of miRNAs 148a and 192 was evaluated in relation to the appearance of complications in 38 patients undergoing liver transplantation, through a nested case-control study. Serum plasma samples were taken from the patients before and after the transplant, RNA extraction and rt-qPCR were subsequently performed, clinical history data were collected, and retrospective statistical analysis was performed.
Results: The appearance of complications such as acute cellular rejection and recurrence of post-transplant hepatic steatosis was associated with overexpression of miRNAs 148a and 192 in blood ($p<0.0001$). Gender was a statistically significant variable, since men had fewer post-transplant complications than women ($p=0.004$).History of smoking, obesity and blood group did not have a statistically significant relationship with respect to the risk of post-transplant complications. History of non-alcoholic hepatic steatosis ($p=0.002$), diagnosis of hepatocellular carcinoma as a complication of hepatic steatosis ($p=0.0032$), and a high MELD score ($p=0.023$); were associated with an increase in miRNAs 148a and 192, as well as post-transplant complications.
Conclusion: Circulating miRNAs have emerged as promising highly specific and sensitive diagnostic and prognostic biomarkers for the non-invasive detection of diseases, due to their capacity for gene regulation at the post-transcriptional level, in different pathologies. Our study was able to show that they are sensitive predictors of complications after liver transplantation; so in the future they could be more reliable markers to predict the risk of complications in these patients.

E-PS-15-031
Mechanisms of resistance to EGFR tyrosine kinase inhibitor therapy in lung adenocarcinomas
M. Mihálffy*, E. Tóth, L. Báthory-Fülöp
*National Institute of Oncology, Hungary

Background & objectives: EGFR mutations in non-small cell lung carcinomas (NSCLCs) represent potential targets for treatment using tyrosine kinase inhibitors. Our aim was to identify and analyse the various types of resistance mechanisms (including the most common T790M) that influence the therapeutic response.
Methods: We screened plasma (circulating tumour DNA) and thoracic fluid samples, cytology smears, cell blocks, biopsy and resection specimens from patients with lung adenocarcinoma who received first or second-generation TKI treatment. For the T790M mutation we used EGFR monogenic testing (COBAS EGFR and EGFR AmoyDx kit). For diagnosing other types of resistance, we employed multigenic NGS (IonTorrent S5, Oncomine Focus Assay).
Results: We detected the T790M mutation in approximately 50% of cases where we could identify the original EGFR mutation, but the detection rate depended on the type of sample used. The rest of cases showed a variety of different changes, including individual EGFR, KRAS, CDK4, FGFR, MET, HER2 amplification, PIK3CA mutation, MET 14 exon skipping or a group with the presence of several concurrent genomic alterations as well. So some of the identified resistance mechanisms were eligible for different targeted therapy. We also distinguished a case where histological transformation into squamous cell carcinoma phenotype took place.
Conclusion: NSCLCs with mutated EGFR account for approximately 12% (11% in our cohort) of all lung cancers in Europe. While treatment with TKIs is often effective, the emergence of resistance mechanisms poses a therapeutic challenge. The identification of the commonly occurring T790M mutation or any other targetable resistance mechanism is of paramount importance, since the information aids the selection of the most appropriate therapy for the patient. Nevertheless, the simultaneous presence of other resistance mechanisms or non-T790M resistance requires further investigation.

E-PS-15-032
Novel NTRK2 gene rearrangement in CNS neoplasia: pitfall or new finding?
D. Morotti*, E. Antelmi, A.C. Bettini, E. Costi, G. Ghirardi, M. Iascone, S. Intagliata, C. Lucca, R. Merli, M. Motta, R. Muni, G. Pezzetti, E. Rigoli, M. Sicignano, A. Gianatti
*Department of Pathology, Papa Giovanni XXIII Hospital, Bergamo, Italy

Background & objectives: Neurotrophic tyrosine receptor kinase (NTRK 1/2/3) gene fusions are rare but present across multiple tumour types and their frequencies can vary by cancer type. Testing is essential to identify patients who may benefit from target therapy.
Methods: Two high grade glioma patients were tested with a DNA-based NGS custom panel detecting NTRKs gene rearrangements. Pan-TRK IHC and a FISH test with a break- apart probe for NTRK2 gene were performed. Moreover, we ran a PCR with designed primers followed by Sanger sequencing and, finally, the IdyllaTM GeneFusion Assay was applied to test the chimeric transcript.
Results: A novel gene fusion PHLPP1(5')-NTRK2(3') was found in two cases by NGS DNA sequencing with allelic frequencies of 15,4% and 30,4% respectively. QC parameters and coverage were suitable.

Pan-TRK immunohistochemistry was positive in both cases but ineffective in ruling out ectopics from endogenous gene expression. FISH test analyses were negative for NTRK2 breakage, while PCR results confirmed the presence of a rearrangement. Sanger sequencing confirmed the breakpoint on the NTRK2 gene but not the PHLPP1 one due to the high homology of the analysed trait with other genomic regions. RT-PCR of mRNA analyses revealed a consistent expression imbalance between 3' and 5' of NTRK2 gene.
Conclusion: Pan-TRK antibody is a good screening tool to detect NTRKs gene rearrangements in many tumours but not in the CNS, being TRK receptors usually expressed in nervous tissues. A DNA-NGS custom panel based on hybrid capture enrichment is efficient to detect rearrangements but new gene involvement needs an additional workload. RNA analysis by real-time PCR confirmed the loss of NTRK2 transcript amount caused by translocation. A RNA-NGS panel based on targeted RNA enrichment could identify actively transcribed new chimeric fusions.

E-PS-15-033
Placenta molecular characteristics in intrauterine feotal demise
E. Nardi*, I. Seidita, I. Abati, C. Donati, F. Castiglione, C. Serena, F. Mecacci, F. Petraglia
*Section of Anatomic Pathology, Department of Health Sciences, University of Florence, Italy

Background & objectives: Placenta may have a central role for explaining foetal death as intrauterine foetal demise (IUFD) has been correlated with an impaired secretion of some placental factors. The aim of this study was to investigate molecular mechanism involved in idiopathic IUFD.
Methods: Ten cases of singleton pregnancy ended in IUFD were selected, excluding pregnancies complicated by foetal anomalies and diseases that might affect placentation. Ten placentas collected from healthy singleton term pregnancies served as controls.
Histopathological examination of the selected samples was made, and RNA was extracted. The quantification of mRNA expression levels was performed using real-time polymerase chain reaction.
Results: No significant difference in maternal and foetal sex distribution between the two groups whereas gestational age and birth weight were significantly lower in the cases compared to the group control. The histological examination of the placentas ended in IUFD can be classified in vascular malperfusion or placental dysfunction. The control placentas did not show any pathological changes.
Using real-time PCR, difference in placental mRNA expression of different proteins were observed: IL-6 (P= 0.0495) and VEGFR2 (P= 0.0305) resulted more expressed in samples of IUFD compared to control, while activin A (P= 0.0098), ABCB1 (P= 0.0450) and ABCG2 (P= 0.0232) expression was lower in IUFD.
Conclusion: The present study showed that placenta from pregnancies with IUFD have an increase in inflammatory factors (IL-6 and S1P) as well as a decrease in the expression of growth factors (activin A) and molecules implicated in trophoblast migration and invasion. This could explain an inflammatory state and growth defect underlying the process that leads to IUFD.

E-PS-15-034
Molecular analysis of non-small cell lung carcinomas in the National Institute of Oncology, Hungary
K. Nemeth*, E. Tóth, L. Báthory-Fülöp
*National Institute of Oncology, Hungary

Background & objectives: In the treatment of non-small cell lung carcinomas several new targeted agents have become available in recent years, and the benefits of targeted therapy have led to the need for detailed molecular pathology testing in lung adenocarcinomas.
Methods: We performed Oncomine™ focus assay on Ion-Torrent S5 (NGS) platform.The classification of detected variants and the therapeutic relevance of pathogenic variants was evaluated using Ion Reporter™. In cases not suitable for sequencing, COBAS tests were used. Parallel ALK (Ventana ALK D5F3 CDx Assay), ROS1 (Cell Signaling D4D6) and PD-L1 immunohistochemistry (DAKO 22C3 PharmDx kit) were also performed.
Results: 1412 adenocarcinoma and 474 squamous cell carcinoma samples included 1049 biopsies, 367 cytological samples and 470 surgical resection specimens were investigated.
37% of adenocarcinoma cases were suitable for sequencing. Histological features, specimens' types and molecular results were analysed. 554 cases (39%) of adenocarcinomas showed KRAS mutations. 160 of 1412 tumours (11%) were EGFR mutant. We found ALK and ROS1 fusion in 21 and 5 cases.
Regarding PD-L1 expression, Tumour Proportion Score (TPS) were negative in 26,2%, 48,5% showed 1-49% TPS and 25,3% were more than or equal to 50% of the 423 squamous cell carcinoma. The distribution was nearly equal in the 1088 adenocarcinoma cases, 33,4%, 35,1% and 31,5%, respectively.
Conclusion: In our laboratory, KRAS mutation was more common compared to the literature's data, and we found fewer ALK and ROS1 fusions which is probably associated with higher incidence of smoking in Hungary. A significant proportion of small biopsy and cytology samples were suitable for sequencing.
PD-L1 positivity (TPS>1%) was higher among squamous cell carcinomas compared to adenocarcinomas. Our results show a good correlation with the literature, which is an important indicator of the quality of the lab's work.

E-PS-15-035
A combined digital and molecular approach to precision oncology: the lung and breast cancer use cases
F. Pagni*, D. Seminati, G. Cazzaniga, V.L. L'Imperio
*University Milan Bicocca Department of Medicine and Surgery, Italy

Background & objectives: The use of molecular tests has grown rapidly in recent years as they have been shown to provide more accurate and detailed information about the genetic characteristics of the tumour, leading to more effective treatment options.
Methods: In order to assess the impact of molecular testing on a pathology department, data for BC and NSCLC was extracted from the LIS over the year period from 2020 to 2022. The number and percentage of tests were estimated from data extracted and estimation of costs was performed based on the currently recognized reimbursement from the National Health System.
Results: Increased use of Gene Expression Profiling, performed on 4,54% of BC cases in 2022, and Next Generation Sequencing, performed on 42% NSCLC cases in 2022, led to higher average institution costs per patient (54% and 140% rise, respectively). This shift to molecular testing has reduced single gene testing in NSCLC, causing a 58% drop in RT-PCR and 50% decrease in IHC predictive tests.
Conclusion: The paradigm shift in the assessment of BC and NSCLC cases due to the introduction of molecular tests changed the landscape of pathology departments from an organization and economic point of view. The integration of different data sources thanks to digital pathology and LIS dashboards allowed us to track the dynamic changes of this precision oncology transition.

E-PS-15-036

Histopathological and molecular spectrum of KRAS- mutant non-small cell lung carcinoma (NSCLC): Indian tertiary cancer centre experience

T. Pai*, S. Dash, M. Gurav, P. Gogte, N. Karnik, P. Shah, R. Kumar, A.K. Singh, O. Shetty
*Department of Pathology, Tata Memorial Hospital, Parel, India

Background & objectives: KRAS mutant NSCLC indicate an overall poorer survival compared to KRAS wild-type tumours. The approval of direct KRAS G12C inhibitor, sotorasib, mandates the need to identify these mutations. We present the spectrum of KRAS mutations among the Indian NSCLC patients.
Methods: This is a retrospective analysis of NSCLC subjected to NGS on FFPE tumour samples between 2019 to 2022 using Ampliseq Focus and Sophia Solid Tumour Plus Solution. The data analysis was performed using Base space software for Ampliseq Panel and Sophia DDM platform for STS Plus. The analysis and interpretations were done as per the AMP and CAP guidelines.
Results: KRAS mutations were seen in 59 cases. Age range: 23-89 years. 16 (27%) were female patients. Majority cases were histologically adenocarcinoma, (88%), one each of SCC and NSCLC, NOS, with the rest were poorly differentiated carcinoma. Mucinous histology was noted in 7 cases. Most common KRAS mutations were G12C & G12D (n=19 each, 32%) & G12V (n=12, 20%). Others: Q61H (n=4), G12A (n=3), and one each of G12R and K117N. Concurrent mutations were seen in 44%, most commonly with p53 mutations (69%). PDL1 (SP263 Ventana clone) was negative in 23 cases (39%), while was ≥50% in 12 cases (20%). EGFR and CDK4 gene amplifications were seen in 1 case each.
Conclusion: The present study unravels the diverse spectrum of KRAS mutations seen in Indian population, with G12C & G12D being the most common mutant variants. Histologically adenocarcinoma is the most common histological subtype, followed by cases exhibiting poorly differentiated/ undifferentiated/ sarcomatoid morphology. With the novel KRAS inhibitors, it is important to ascertain the exact mutant variant to determine the eligibility to the targeted therapy.

E-PS-15-037

VHL pathogenic variants in a series of Russian patients with clinical signs of von Hippel-Lindau disease

G. Raskin*, G. Yanus, E. Suspitsin, Y. Gorgul, S. Aleksakhina, E. Imyanitov
*Dr. Berezin Medical Insitute, Russia

Background & objectives: von Hippel-Lindau disease is a hereditary tumour syndrome, caused by VHL mutations, and presenting with renal cysts and clear cell kidney cancer, hemangioblastomas, pheochromocytomas, etc.

Methods: The study included 19 unrelated Russian patients (age range: 16-56 years, mean: 35,3 years). Clear cell renal cancer was diagnosed in 14/19 (74%) subjects, hemangioblastomas were identified in 5/19 (26%) cases, pheochromocytomas were found in 4/19 (21%) individuals. VHL (NM_000551) coding sequence was analysed by HRM/Sanger sequencing. Large gene rearrangements (LGRs) involving VHL were assessed by droplet digital PCR.
Results: VHL PVs were identified in 6/19 (32%) patients. There were 4 known pathogenic/likely pathogenic nucleotid substitutions (c.463+2T>G, c.491A>G (p.Gln164Arg), c.499C>T (p.Arg167Trp), c.641G>T (p.Ter214Leuext*) and a deletion of exons 1-2. A novel c.632_636del (p.Met211Argfs*) variant was found in a family involving 3 generations of affected subjects. This variant is located close to the stop codon and does not lead to a nonsense-mediated RNA decay, however, clinical data indicated at potential pathogenicity of this allele. Known variant of unknown significance c.364G>A (p.Ala122Thr) was identified in a 16-years-old proband with pheochromocytoma. His mother was also a carrier of this variant but showed neither signs of VHL-related disorders herself, nor significant family history.
Conclusion: We have not identified recurrent pathogenic variants in our small case series of Russian patients, which is in line with a rarity of founder effects for this disease. Frame-shift mutations located close to the VHL stop-codon may still render a pathogenicity.
Funding: Russian Science Foundation, grant 22-45-08004

E-PS-15-038

Lung cancer and precision medicine: sample profile, morphological control, and results detected by NGS

R. Silva*, R. Pinto, L. Cirnes, F. Schmitt
*IPATIMUP – Institute of Molecular Pathology and Immunology of Porto University, Porto, Portugal

Background & objectives: The accuracy of the molecular diagnosis is dependent on the pathological assessment of the tumour samples. This step is particularly relevant in central laboratories that receive material from several hospitals. To examine the profile of lung cancer samples and results detected byNGS.
Methods: We analyse the characteristics of tumour samples and the data resulting from NGS analysis of lung cancers, studied from April to November of 2022. The cases were analysed in order to verify the percentage of malignant nuclei (PMN), made by a pathologist (in internship) and technician, and the correlation between the morphological assessment of PMN, and the allelic fraction (AF) detected.
Results: From 1501 lung cancers, 66.7% (1001 cases) presented at least one alteration. The estimated average of PMN present in the samples was 36%. Samples with estimated tumour content <30% corresponded to 42.3%. The allele frequency was collected for 879 of the 1001 cases. In 70.8% of the cases, we observed an expected relation between PMN and AF of the mutated genes by NGS. No correlation was observed in 29.2%, with a low PMN compared to the AF (more than 90%). The specific detected genetic anomalies showed clinical actionability of molecular targets in 86.4% of cases. The genes more frequently mutated were KRAS (38.7%), EGFR (30.4%), MET (5.8%), BRAF (5.5%), and HER2 (3.3%).
Conclusion: Our study showed that, in non-centrally collected lung cancer tissues, small samples with limited tumour cell content corresponded to almost half of the cases. We observed a good agreement between the estimation of PMN and the AF. The discrepancies—underestimation—can be explained by multiple hits in some of the genes tested. The morphological control with dedicated molecular pathology that evaluates the feasible material before proceeding to any molecular test ensures the accuracy of the analysis by NGS.

E-PS-15-039

Ultra-fast NGS in lung cancer with HER2 mutation (ERBB2): Is the detected allele frequency the same when compared to the fast-NGS assay?

R. Silva*, L. Cirnes, F. Schmitt
*IPATIMUP – Institute of Molecular Pathology and Immunology of Porto University, Porto, Portugal

Background & objectives: Molecular diagnosis of lung cancer is a constantly evolving field. The implementation of Ultra-fast NGS platform in the detection of actionable mutations is being analysed and adjusted. Our objective was to analyse the allelic fraction detected by fast and ultra-fast NGS technologies.

Methods: We compared the data resulting from fast (Ion S5) and ultra-fast NGS (Genexus) in the evaluation of non-small cell lung carcinoma (NSCLC) with HER2 (ERBB2) mutations identified for both platforms. The cases were analysed in order to verify a correlation between the morphological assessment of the percentage of tumour cells (PTC) and the allelic fraction detected by each of the methods.
Results: The study was performed on a sample of 29 NSCLC, with 75.8% primary lung cancer and 93% FFPE tissue block material. The estimated average tumour cell content (PTC) of the sample used in both tests was 41.7%. Small samples with limited estimated tumour cell content (30%) corresponded to 38% of the cases. On the ultra-fast NGS platform, we observed a correlativity of 55% between PTC and AF for the detected variant. For fast-NGS, in 65.5%, there was a correlation between PTC and the allelic fraction (AF) detected. In the discordant group, the ultra-fast NGS analysis showed a greater AF detected compared to the fast method (3.6-10.1 points higher).
Conclusion: The development of ultra-fast NGS tests has been implemented to expand molecular assays. Our study showed that in the majority of the cases there is a good agreement between the estimation of PTC and the AF for a rare mutation in lung cancer, detected by the ultra-fast and fast-NGS platforms. The greater agreement observed in the fast-NGS method can be explained by the need for adjustments in the emergent method's workflow in order to enable its use in clinical practice.

E-PS-15-040
PIK3CA hotspot mutations in circulating tumour cells in breast cancer
G. Smagulova*, S. Yessentayeva, G. Kalmursayeva, A. Tulepbayeva, S. Kaus
*Diagnostic laboratory, Gamma Lab, Kazakhstan

Background & objectives: BC in terms of incidence ranks first among oncology diseases in women in Kazakhstan. Of these, more than 70% are women under the 60. PIK3CA mutations are often found in hormone-dependent,HER2-negative types of BC and can used for CTC identify.
Methods: In total, 48 samples of BC were studied. 30 patients with luminal type A and B after therapy, 18 patients before therapy. Total 6 ml peripheral blood were used for LB. CTCs were isolated in a density gradient followed by morphological and molecular identification. DNA extraction kit for ctDNA and primary tumour DNA analysis was used. PIK3CA test kit real-timePCRkit was used.
Results: PIK3CA tests performed for 48 patients with BC on primary tumour. Activating mutations in the PIK3CA gene were found in 20/48(41%) of cases in hormone-dependent and HER2-negative breast cancer. 16(80%) of which were due to E542K and E545K mutations. Liquid biopsy was performed for 7cases with PIK3CA positive primary tumour . PIK3CA positive CTC were found in all 5/7 cases BC with progression after hormone therapy. For that patients plasma ctDNA analysis also were PIK3CA positive. In 2/7 cases of oestrogen- and PIK3CA positive primary patients, PIK3CA-positive CTCs and cell free DNA were not detected. Primary patients underwent IHC testing for oestrogen, progesterone, Her2neu, and Ki67 concomitantly with PIC3CA tests.
Conclusion: During CTC isolating in density gradient PIk3CA-positive DNA concentration in the Mononuclear cells fraction is less than in the cell free DNA fraction.
Since targeted therapy with a selective inhibitor of the alpha isoforms of PIK3 is recommended for patients with mutated PIK3CA gene, it is advisable to include this genetic testing in the domestic Protocol for the diagnosis and treatment of breast cancer to determine the status of the PIK3CA gene simultaneously with the detection of the tumour immunophenotype.

E-PS-15-041
EML4-ALK fusion variants and NTRK1 fusion in lung adenocarcinoma – case report
V. Sousa*, A. Alarcão, A.F. Ladeirinha, M.R. Silva, T. Ferreira, C. Eliseu, M. Viseu, V. Almeida, R. Almeida, G. Fontinha, A.L. Alves, L. Carvalho
*IAP-PM - Universidade de Coimbra, CHUC, Portugal

Background & objectives: According to published data, lung cancer continues to increase every year. It is important to study the new data obtained through the use of technologies that allows us to have greater knowledge of the changes that occur on these tumours.
Methods: Authors present a case of a woman diagnosed with a lung adenocarcinoma. Mutation research was performed by next-generation sequencing (Genexus, Oncomine Precision Assay Panel, Thermo Fisher Plataform). Manual macrodissection was performed and nucleic acid extraction was carried out with the MagMAX FFPE DNA/RNA Ultra Kit.
Results: Several molecular alterations were detected. We found three different EML4-ALK fusion gene (EML4-ALK.E6aA20.AB374361.1; EML4-ALK.E6bA20.AB374362.1; EML4ALK.E6ins18A20.1), and one TPM3-NTRK1 fusion gene. ALK and NTRK1 gene fusion are associated with response with tyrosine kinase inhibitor therapy anti ALK and NTRK1 respectively.
According to the last Non-small Cell Lung Cancer NCCN Guidelines, the presence of fusions in the ALK gene are associated with response to Lorlatinib and the presence of fusions in the NTRK1 gene are associated with response to Larotrectinib. There are ongoing clinical trials for each of the fusions in these two genes, but no ongoing clinical trials were found where the two fusions, EML4-ALK and TPM3-NTRK1, were present simultaneously.
Conclusion: Patient started Brigatinib therapy for ALK rearrangement in August 2022. Molecular Tumour Board are important in complex molecular cases in order to identify the best therapeutic or clinical trials available.
Studies show that the "short" and "long" forms of ALK fusions leads to differential responses to ALK TKIs, demonstrating that "shorter " variants are associated with poor outcomes. It is important to understand the meaning of the various variants of mergers and to study the meaning of concomitant mergers.

E-PS-15-042
Complex MET gene alterations in a lung adenocarcinoma – case report
V. Sousa*, A. Alarcão, A.F. Ladeirinha, M.R. Silva, T. Ferreira, C. Eliseu, M. Viseu, V. Almeida, R. Almeida, G. Fontinha, A.L. Alves, L. Carvalho
*IAP-PM - Universidade de Coimbra, CHUC, Portugal

Background & objectives: MET mutations and/or amplifications are primary oncogenic drivers, in lung cancer with amplification being mechanisms linked anti-EGFR/ALK therapies resistance. Among MET mutations METex14 skipping is one the most frequent. A broad range of molecular alterations lead to METex14 skipping.
Methods: Authors present the case of a woman with lung solid adenocarcinoma. Mutation analysis was made by NGS (Genexus, Oncomine Precision Assay Panel, Thermo Fisher Plataform). Macrodissection was performed and nucleic acid extraction was carried out with the MagMAX FFPE DNA/RNA Ultra Kit. For MET gene the Oncomine Precision Assay Panel search: DNA Hotspots (SNVs/Indels), CNVs (polysomy/amplification), inter-genetic and intra-genetic fusions.
Results: MET-MET.M13M15.1 variant was identified, which corresponds to MET exon 14 skipping. Two other mutations were also identified, c.3082+1G>A;p.? (47,5%) and c.3082+1_3082+2insA;p.? (25,8%), not knowing which protein

is formed. MET gene amplification (copy number: 4.45) was also identified.
According to NCCN Guidelines MET exon 14 skipping mutation is associated with response with MET TKIs. Classification in high-level MET amplification is evolving and may differ according to the assay used for testing. According to the same Guidelines, for results obtained by NGS, a copy number greater than 10 is consistent with the classification of high-level MET amplification.
Conclusion: Patient started systemic chemotherapy in February with Carboplatin and Pemetrexed, and since March with Pemetrexed.
The emergence of complex cases is more and more frequent, with the use of more advanced and informative technologies. It becomes essential to have multidisciplinary therapeutic decision meetings, where the mutations found can be discussed with information on the general condition of the patient and with the drugs/clinical trials in progress.

E-PS-15-043
MET exon 14 skipping and EML4-ALK fusion in a NSCLC metastatic case – case report
V. Sousa*, A. Alarcão, A.F. Ladeirinha, M.R. Silva, T. Ferreira, C. Eliseu, M. Viseu, V. Almeida, R. Almeida, G. Fontinha, A.L. Alves, L. Carvalho
*IAP-PM - Universidade de Coimbra, CHUC, Portugal

Background & objectives: Gene alterations are increasingly found in bronchopulmonary carcinomas using NGS for researching therapeutic targets.
Fusions in ALK, RET and MET genes has been very successful targets for therapies in lung adenocarcinomas. Mutations have been found whose meaning is unknown.
Methods: We present a case of a woman with a right intracranial temporal brain NSCLC metastasis. It was performed mutation research by next-generation sequencing (Genexus, Oncomine Precision Assay Panel, Thermo Fisher Plataform). Manual macrodissection was performed and nucleic acid extraction was carried out with the MagMAX FFPE DNA/RNA Ultra Kit.
Results: Several alterations have been detected. The MET-MET. M13M15.1 variant was identified which corresponds to MET exon 14 skipping. In the ALK gene, the following alterations were identified: Fusion with the partner being the gene EML4 (EML4-ALK.E13A20) and ALK expression imbalance. In the RET gene, the nonsense mutation c.2689C>T;p.(Arg897*) was identified. According to the NSCLC NCCN Guidelines, MET exon 14 skipping is associated with response with MET TKIs. ALK gene fusion is associated with response to ALK tyrosine kinase inhibitor therapy. There is no reference to the ALK expression imbalance. The mutation c.2689C>T;p.(Arg897*) in the RET gene lacks relevant evidence in public data sources included in relevant therapies: EMA, ESMO, NCCN.
Conclusion: The patient started Brigatinib therapy for ALK rearrangement in October 2022. No other therapy was registered prior to the study. The patient is clinically well with a good Performance Status (PS=0).
We are increasingly finding concomitant actionable mutations for therapy, making it important to understand how we should proceed in terms of therapy to promote a better patient response, and Molecular Tumour Board might be of great importance in these cases.

E-PS-15-044
MYB gene rearrangement in adenoid cystic carcinoma: a multi institutional study from Turkey
M.H. Toper*, L. Cinel, F. Bir, K. Başak, Ö. Saraydaroğlu, A. Uğuz, İ.H. Özbudak, A. Tan, S. Altınay, Ü. Han, Ü. Küçük, D. Etit, F. Çakalağaoğlu, A.N. İhvan, S. Sarioglu
*Dokuz Eylul University, Turkey

Background & objectives: Adenoid cystic carcinoma (ACC) is a common salivary gland malignancy and many ACCs have been reported to have MYB rearrangement. This study aims to analyse the frequency of MYC rearrangement in the region and its relationship with clinical/pathological parameters.
Methods: 122 ACC cases were selected retrospectively from thirteen institutions between 2008-2022. If available, clinical and pathological characteristics of cases including age, gender, tumour size, stage, grade, lymphovascular/perineural invasion were obtained from the original reports. FISH analysis for MYB gene rearrangement was carried out and >10% of cells with break-apart signals were accepted as the threshold for a positive result.
Results: The study comprised cases aged 22–86 years (median 55 years) and 66% of cases were female. 36% cases were located at major salivary glands, while rest of tumours were at other sites of head and neck, mostly minor salivary glands. Tumour size ranged from 5 to 80 mm.
FISH analysis of MYB gene was found 77 cases (63.1%). MYB FISH status was not significantly associated with other parameters, including gender, age, tumour stage and grade, lymphovascular or perineural invasion, and lymph node or distant metastasis. MYB status also were not associated with statistically significant differences in overall survival (p=0.8).
Conclusion: These findings suggest that rearrangement involving MYB is a frequent event in ACC and does not seem to have association with survival and pathological parameters. The identification of this significant molecular alteration may demonstrate that it can be used for differential diagnosis in routine clinical practice and also might be target of specific therapy in molecularly-defined patient subgroups in future clinical studies.

E-PS-15-045
MAML2 gene rearrangement in mucoepidermoid carcinoma: a multi institutional study from Turkey
M.H. Toper*, F. Bir, Ö. Saraydaroğlu, L. Cinel, K. Başak, A. Uğuz, S. Altınay, Ü. Han, A.N. İhvan, İ.H. Özbudak, A. Tan, Ü. Küçük, D. Etit, F. Döger, S. Sarioglu
*Dokuz Eylul University, Turkey

Background & objectives: Mucoepidermoid carcinoma (MEC) is a common salivary gland malignancy. A major subset of MECs have been reported to have a specific MAML2-NFIB gene rearrangement. This study aims to analyse the frequency of MAML2 rearrangement and its relationship with clinical/pathological parameters.
Methods: 119 MEC cases were selected retrospectively from thirteen institutions between 2007-2022. If available, clinical and pathological characteristics of cases including age, gender, tumour size, stage, grade, lymphovascular/perineural invasion were obtained from the pathology reports. FISH analysis for MAML2 gene rearrangement was carried out and >10% of cells with break-apart signals were accepted as the threshold for a positive result.
Results: The study sample comprised aged 8–92 years (median 48 years) and 55% of cases were female. 60% cases were located at major salivary glands, and rest of cases were at other sites of head and neck. Tumour size ranged from 5 to 105 mm.
FISH analysis of MAML2 gene was found 74 case (62.2%). MAML2 positive result was significantly associated with better overall survival, absence of lymphovascular invasion and absence of distant metastasis (p<0.05). MAML2 FISH status was not significantly associated with other parameters, including gender, age, tumour stage and grade, perineural invasion, and lymph node metastasis.
Conclusion: These findings suggest that MAML2 rearrangement is a frequent event in MEC and does seem to have association with favourable clinical outcome and absence of lymphovascular invasion

and distant metastatis in univariate analysis. Although, a high frequency of mutation was observed in high grade tumours, statistical significance was not found.
The identification of this significant alteration may demonstrate that it can be used for differential diagnosis in routine practice and also might be biomarker for favourable overall survival of MECs.

E-PS-15-046

Development and validation of assays for testing EGFR amplification in tissues, based on gene copies, RNA and protein expression

S. Tsuriel*, V. Hannes, D. Hershkovitz
*Tel Aviv Sourasky medical centre, Israel

Background & objectives: EGFR amplification is leading to uncontrolled cell growth and tumour proliferation; it can be used as a biomarker for treatment based on EGFR inhibition. Still it's unclear what the best marker for EGFR amplification and how to measure it accurately.
Methods: The aim of this study was to develop and validate a protocol for measuring EGFR gene copy, RNA, and protein expression. A multiplexed digital PCR-based method was developed and validated to detect EGFR gene copy number amplification. Immunohistochemistry was used to assess the protein levels, and qPCR was used to measure EGFR gene expression.
Results: A total of 123 clinical FFPE tissue samples from various tumours were collected. The digital PCR-based assay was validated against samples with a known amplification status and found to have 100% agreement. Five different protocols were compared to optimize the immunohistochemistry EGFR labelling. Samples that showed gene copy amplification had high RNA and protein expression, while samples with high RNA also showed high protein levels. However, samples with high EGFR protein levels did not necessarily have a high gene copy number.
Conclusion: Efficient and useful methods for measuring EGFR amplification in its various forms have been developed. These methods can be easily applied in many pathology laboratories. However, to determine the best way to test EGFR for adjusting treatment and whether the measurement of one form of EGFR is sufficient or more is needed, it must be compared to the clinical results of the new EGFR inhibitors.

E-PS-15-047

Implementation of the 2021 WHO Classification of Tumours of the Central Nervous System and molecular assessment of diffuse gliomas in a Belgian cohort

L.C. van Kempen*, M. Ahmed, A. Sieben, B. Verbraeken, T. Menovsky, M. Rasschaert, P. Meijnders, P. Cras, M. Lammens
*Department of pathology, University of Antwerp, University Hospital Antwerp, Edegem, Belgium, Department of pathology and medical biology, University of Groningen, University Medical Center Groningen, The Netherlands

Background & objectives: The implementation of the 2021 WHO CNS tumour classification has introduced molecular analyses as an ancillary diagnostic test. The objective of this study was to investigate how often a molecular result contributed to the final diagnosis of diffuse glioma.
Methods: All cases with a diagnosis of IDH1/2-wild type diffuse glioma were included (n=148). The time span for inclusion was limited to the period between November 1st, 2021 (the implementation of the 2021 WHO CNS our centre) until March 31st. Molecular testing on the DNA and RNA levels was a requirement for inclusion.
Results: A TERT promotor mutation was observed in 117/148 cases (79%), a rate comparable with the literature. An isolated TERT mutation was observed in 12/148 (8%) of the cases. Morphological diffuse glioma grade 2 or 3 was upgraded to glioblastoma based on molecular alterations alone in 17/148 cases (i.e. molecular GBM, 11%). Sixteen of these 17 cases showed a TERT promotor mutation, 7 cases showed an EGFR amplification, and 6 cases showed both alterations.
At the RNA level, different gene fusion transcripts were detected: EGFR, FGFR3, PTRRZ, MET and ROS1.
Only one case of IDH1/2-wild type low-grade diffuse glioma did not contain a molecular alterations.
Conclusion: Implementation of molecular diagnostics for CNS tumours according to the current WHO guideline resulted in upgrading of IDH-wild type diffuse glioma, (grade 2 or 3) to IDH-wild glioblastoma, (grade 4) in 11% of cases based on the molecular results only. This has a considerable impact on the treatment trajectory for these patients. An isolated TERT promotor mutation was seen in 8% of all cases, which may also have prognostic consequences. Furthermore, molecular results pointed towards potential targeted therapy options.

E-PS-15-049

Mitochondrial genome variants associated with pathogenesis of colorectal cancer

O. Vasyukova*, N. Shakhpazyan, N. Sadykhov, V. Pechnikova, L. Mikhaleva
*Avtsyn Research Institute of Human Morphology of Federal State Budgetary Scientific Institution "Petrovsky National Research Centre of Surgery", Russia

Background & objectives: Mitochondria contribute to colorectal cancer (CRC) pathogenesis. Identified mitochondrial genome variants (MGVs) are hypothesized to be associated with the inflammatory response and the innate immunity regulation in CRC. The study aimed to evaluate MGVs heteroplasmy changes in tumour tissue.
Methods: We examined 12 patients (59-70 years old, 5 females, 7 males) with stage pT2T0N0 CRC (adenocarcinoma of the colon or sigmoid colon). Quantitative PCR was used to analyse heteroplasmy of MGVs m.652delG, m.1555A>G, m.3336T>C, m.3256C>T, m.5178C>A, m.12315G>A, m.13513G>A, m.14459G>A, m.14846G>A, and m.15059G>A in tumour and healthy colon tissue. Nonparametric statistical methods were employed for comparisons, using the U-test.
Results: It was revealed that MGVs m.14459G>A and m.15059G>A in genes MT-ND6 and MT-CYTB, respectively, exhibited a higher level of heteroplasmy in tumour tissue compared to healthy tissue from the same patient ($p<0.05$). Other variants did not demonstrate significant increases or decreases in heteroplasmy levels in tissues. No significant associations were found between heteroplasmy levels and age, gender, or disease stage. Since the tumour tissue analysed comprised tumour cells and the microenvironment, including immune cells, the study results do not pinpoint the specific cells in the pathological tissue where MGV accumulation occurred. Nevertheless, the findings suggest that changes in MGV heteroplasmy may play a role in CRC pathogenesis.
Conclusion: Observed differences in MGV heteroplasmy may be associated with altered cellular processes within tumour microenvironment, including cancer and immune cells. These changes could impact energy metabolism, apoptosis, or inflammation regulation, contributing to CRC pathogenesis. The discovered MGVs might play a role in modulating tumour cell behaviour or interactions with the surrounding microenvironment. Further research is needed to elucidate the underlying mechanisms, identify the specific cellular processes affected by MGV heteroplasmy differences, and determine their potential therapeutic implications in colorectal cancer.
Funding: Research was supported by RSF, grant № 23-25-00196

E-PS-15-050

Implementation of a Next Generation Sequencing (NGS) service for cfTNA analysis to facilitate driver mutation reporting in blood

R. Werner*, R. Crosbie, M. Dorney, J. McCarthy, C.K. Hand, L. Burke
*Pathology Department, Cork University Hospital, Cork, Ireland, Department of Pathology, School of Medicine, University College Cork, Cork, Ireland, Ireland

Background & objectives: The establishment of a cfTNA (cell-free-Total Nucleic Acid) NGS service integrated within an ISO15189-accredited clinical diagnostic NGS laboratory in a designated tertiary cancer centre. This is an emerging clinical tool with rapidly expanding utility as cost reduces and sensitivity/specificity improve.
Methods: Validation was performed on the Genexus™ utilising Oncomine™, a targeted NGS panel on cfTNA extracted from plasma. Oncomine Reporter™ software was used to report on variants, and fusions across >42 key genes. Plasma verification samples with known driver mutations in matched tissue biopsies were utilised. Assessment criteria included sensitivity, specificity, limit of detection, reproducibility, and the establishment of performance metrics.
Results: Performance metrics and quality parameters established. Sensitivity between plasma and tissue of >83%, Sensitivity between plasma and plasma NGS or cfDNA orthogonal methods of 100%. Variant specificity of 100% across all methods.
TNA extraction and purification was optimised on the Genexus Purification Instrument and sequencing performance established with an accepted LOD of 1.2% when depth of coverage of >22,000 was reached. Allelic frequency of NSCLC tier I variants did detect as low as 0.6%.
Stability of plasma samples from EDTA blood tubes established with >90% of the verification samples in prolonged storage at -80°C for >12 months. Turnaround times (TAT) of cfTNA results to Oncologists reduced by >50% to date.
Conclusion: Successful implementation and clinical validation of a fully automated novel cfTNA NGS workflow was achieved. Optimisation of Oncomine Reporter software to streamline NGS on cfTNA without in-house bioinformatics expertise.
The average TAT from reference laboratories with expertise in sequencing cfTNA are typically >3 weeks; prolonged TAT for biomarker analysis can adversely affect patient outcomes. Significant reduction in TAT of cfTNA NGS results has not yet been achieved in any diagnostic pathology laboratory in Ireland.

E-PS-15-051

Spectrum of mutations in homologous recombination repair genes in metastatic hormone-sensitive prostate cancer

V. Zakharava*, D. Balshakova, M. Smal, R. Goncharova, A. Muradkhanau, Y. Poddubny, A. Rolevich, S. Krasny
*N.N.Alexandrov National Cancer Centre of Belarus, Belarus

Background & objectives: Mutations in homologous recombination repair genes increase the risk of prostate cancer, as well associated with poor prognosis and response to systemic therapy.
Objective was to study germline mutations in DNA repair genes in metastatic hormone-sensitive prostate cancer (mHSPC).
Methods: Genetic study of mHSPC patient specimens (n=40) was performed using high-throughput targeted sequencing platforms and included the detection of mutations in the BRCA1, BRCA2, ATM, CHEK2 and PALB2 genes. ISUP Grade varied from 2 to 5, with predominant of GG4-27.5% and GG5-41.25%. Multiple and solitary metastases were observed in 96.1% and 3.9% of patients; regional lymph node involvement in 70%.
Results: In group of patients with mHSPC twenty-four mutations (10 in introns, 14 in exons) were found. The frequency of germinal mutations in patients was: BRCA1-12.8%, BRCA2-35.9%, ATM-12.8%, of which pathogenic variants were 5.1%. The identified variants included: 2 pathogenic mutations, 4 of indeterminate clinical significance, and 18 benign/probably benign. Analysis of polymorphic variants of BRCA2, BRCA1, and ATM revealed 23 single-nucleotide substitutions (13 missense and 10 synonymous variants). Two mutations (5.1%, including 1 pathogenic variant) were detected in the CHEK2 gene, five mutations (12.8%, including 2 pathogenic variant) in the PALB2 gene, and one mutation in the AR gene (2.6%).
Conclusion: The frequency and spectrum of mutations in the BRCA1, BRCA2, ATM, CHEK2 and PALB2 genes using high-throughput targeted sequencing in patients with mHSPC were shown. The pathogenic frameshift deletion c.4035del, which is causal in breast and ovarian cancer, was detected. A rare in the population single nucleotide substitution rs28897688 was found in 5.13% of patients with mHSPC, which may indicate its risk significance for mHSPC.

E-PS-16 | E-Posters Nephropathology

E-PS-16-001

Membranous nephropathy associated with monoclonal gammopathies: case series

M.L. Abascal Camacho*, C. Vieru, Y. Gómez Navarro, Ú. Verdalles Guzman, T. Bada Bosch, J.C. De la flor, F. Arias, M. Goicoechea Diezhandino., F.J. Díaz Crespo
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Membranous glomerulonephritis (MGN) is a common cause of nephrotic syndrome, characterized by subepithelial polyclonal immune-complexes deposits along glomerular basement membrane. MGN pattern with or without monoclonal deposits associated to monoclonal gammopathies is a rare entity with few cases reported.
Methods: A retrospective analysis was perform on renal biopsy samples received between 2019-2023, identified 4 cases of MGN, 3 with monotypic deposits. Light microcopy, immunochemistry-immunofluorescence and electron microscopy were performed. The average age of diagnosis was 62 years, with female predominance. Two patients had a lymphoproliferative disorder (Marginal zone lymphoma (LMZ) and LLC-B)), and two monoclonal gammopathy of renal significance (MGRS).
Results: Patients with lymphoma demonstrated a mean serum creatinine of 1,45mg/dl, proteinuria 4g/24h and Kappa/lambda ratio 19. Conversely, MGRS cases had mean serum creatinine 1,21mg/dl, proteinuria 2,16g/24h, Kappa/lambda. Renal biopsies showed diffuse thickening of capillary walls and silver positive "spikes" without evidence of endocapillary proliferation or crescents. One case showed infiltration of LM (40%) and LLC patient showed scattered interstitial monotypic plasma cells. Immunofluorescence revealed IgG and C3 granular deposits in capillary wall in 100% cases C1q++ in 2 cases and IgM+++ in one. 75% of cases presented light-chain restriction (3 kappa/1 lambda). PLA2R was negative in serum and by immunochemistry. Electron microscopy evidenced amorphus subepithelial electron-dense deposits in all cases.
Conclusion: MGN pattern associated to monoclonal gammopathies is an extremely rare and heterogenous group. All cases with monotypic deposits coincide with monoclonal component and sowed remission after clone-targeted therapy. IgG-subclass staining could be useful to clarify the light chain restriction. Despite not being recognized as a histological pattern within monoclonal gammpopathies, it may be worthwhile consider it. The diagnosis of this entity require careful evaluation of renal biopsy specimens using a combination of light microscopy, immunofluorescence and electron microscopy.

E-PS-16-002

Cellular variant of focal glomerulosclerosis: a single centre experience

M.L. Abascal Camacho*, Y. Gómez Navarro, C. Vieru, M.T. Mora Mora, Ú. Verdalles Guzman, F. Arias, F.J. Díaz Crespo
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Focal segmental glomeruloesclerosis (FSGS) is a heterogenous entity with 5 histologyc patterns based on columbia FSGS Clasiffication: not otherwise specified (NOS), collapsing, tip, perihilar, and cellular variants. The cellular subtype is the lest frequent, accounting for only 3% of cases
Methods: We performed a retrospective study of renal biopsies, between 2018-2023, obtaining 5 cases of cellular FSGS. The inclusion criteria was the presence of at least one glomerulus with segmental expansion of the glomerular tuft with endocapillary hypercellularity occluding luminas and the exclusion of collapsing and tip variants. Mean age of diagnosis was 64 years with male predominance.
Results: Medical history was diverse, 2 cases had hypertension,1 fibrilloid arteropathy and 1 toxic substance abuse. The mean serum creatine was 1,19mg/dl, proteinuria 8,3gr/24h, eGFR 60ml/min and serum albumin 2,34g/dl. Microhematuria was present in 75%. Light microscopy revealed mean 8% sclerosed glomeruli and 25% segmental endocapillary proliferation and sclerosis, and the cellularity was composed of histiocytes in 100% and neutrophils in 75% of cases. The remaining glomeruli showed endocapillary hypercellularity (out of segmental lesions) in 75% of cases with a mean of 50% affected. The interstitium showed minimal lymphocytic infiltration, fibrosis and tubular atrophy. Inmunofluorescence examination was negative. Electron microscopy revealed extensive foot process effacement, without deposit in 100% of cases.
Conclusion: Our study, although based on a small number of cases, indicates a higher incidence in adult males with nephrotic syndrome. Microscopy findings highlights the presence of proliferative endocapillary lesions in glomeruli not affected by segmental sclerosis. Renal biopsy plays a crucial role in accurate diagnosis for early detection and management. Further research is needed in order to understand the underlying pathology mechanisms and develop effective treatment strategies, as some cases progress to kidney failure.

E-PS-16-003

Cristal storing light chain histiocytosis: case report

M.L. Abascal Camacho*, T. Bada Bosch, M. Fernandez Nieto, F. Arias, Y. Gómez Navarro, F.J. Menarguez Palanca
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Crystal-storing histiocytosis (CSH) is a rare entity within monoclonal gammapopathies of renal significance (MGUS) characterized by histiocyte infiltration containing light chain crystals. We present a case diagnosed by renal and skin biopsy with CSH.
Methods: A 71-year-old woman was diagnosed with IgG-kappa MGUS in 2011. Later, she developed purpuric lesions and acute kidney failure (AKF) with persistent low C4, IgG-K serum and urine monoclonal component. She was clinically diagnosed of ANCA-negative vasculitis and received immunosuppressive treatment based on Cyclophosphamyde and Rituximab. In 2022, she experienced new onset AKF and purpuric lesions. A biopsy was performed.
Results: Light microscopy showed global mesangial proliferation along with endocapillary hipercelullarity composed by monocytes and neutrophils. Additionally, it was presented focal and segmental dilation of capillary loops with obstruction by histiocytes (CD68+) containing eosinophilic cytoplasmic inclusions, with angulated appearance in some sections. Immunofluorescence showed Kappa positivity restriction (3+) on intracytoplasmic deposits. Electron microscopy revealed capillary lumens occupied by histiocytes with markedly electron-dense inclusions of varying sizes, amorphous and some crystalline with angulated appearance corresponding to intracytoplasmic crystals. Skin biopsy revealed overlapping features in dermal capillaries with presence of fibrin thrombi tactoids (CD61+). Bone marrow biopsy was performed, showing polyclonal plasmacytosis of 15% without histiocytes.
Conclusion: HAC is a rare entity, which usually occurs around 60 in men. It is unclear whether crystal formation occurs within plasma cells and is digested by histiocytes or if crystals form in histiocytes due to a failure in light chain degradation. HAC is a systemic disorder affecting multiple organs, being renal involvement typically interstitial rather than glomerular, with a poor vital prognosis, most diagnosed on autopsies. Treatment targets with bortezomib and autologous hematopoietic cell transplantation achieve remission in some cases.

E-PS-16-004

Anti-oxidant and anti-inflammatory effects of montelukast in preventing Iohexol-induced contrast-induced nephropathy in rats

E. Baris*, O. Simsek, C. Ural, C. Incir, S. Aydemir, M. Gumustekin, Z. Cavdar, O. Yilmaz, S. Ozbal, M.A. Arici
*İzmir University of Economics, Faculty of Medicine, Department of Medical Pharmacology; Izmir, Turkey

Background & objectives: Pathophysiology of contrast-induced nephropathy (CIN) includes reactive oxygen species (ROS) generation, inflammation and apoptosis. In this study, the prophylactic effect of Montelukast (M) with antioxidant, anti-inflammatory and anti-apoptotic properties was investigated in rats with CIN.
Methods: Rats randomized into four groups: 1.Control (C), 2.CIN (iohexol; 3 g iodine/kg), 3.M (10 mg/kg), 4.M+CIN. Rats were sacrificed on the 7th day. Kidney injury was evaluated histologically. Serum kidney injury molecule-1 (KIM-1), urea, serum and urine creatinine levels were measured. Tumour Necrosis Factor-α (TNF)-α, Nuclear Factor-κB (NF-κB), KIM-1 mRNA expressions, ROS levels, active caspase-3 were analysed in the kidney.
Results: Serum and urine creatinine levels slightly increased in the CIN group compared to the C ($p>0.05$). Renal tubular damage increased in the CIN group compared to the C ($p<0.01$). Increased mononuclear cell infiltration (MNC) in the CIN decreased in M+CIN. TNF-α, NF-κB, KIM-1 mRNA expressions and ROS levels increased in CIN group compared to the C ($p<0.001$ and $p<0.05$). TNF-α, NF-κB, KIM-1 mRNA expressions and ROS levels decreased in the M+CIN group compared to the CIN ($p<0.001$ and $p<0.001$). Active caspase-3 immunostaining score of CIN increased compared to the C ($p<0.01$) whereas decreased in the M ($p<0.05$) group compared to CIN group.
Conclusion: Montelukast pretreatment produced antioxidant, anti-inflammatory effects in the CIN group. This study demonstrated montelukast pretreatment decreased renal tubular injury and MNC infiltration in kidneys via downregulating TNF-α, NF-κB, KIM-1 mRNA expressions along with ROS levels. These pre-clinical findings might contribute the pathophysiology of CIN and development of the montelukasts' repurposing strategies for preventing CIN.
Funding: This study supported by Dokuz Eylul University (Project number:2019.KB.SAG.068).

E-PS-16-005

Predictive value of activity and chronicity indices in lupus nephritis

I.D. Căruntu*, T. Azoicai, E.R. Avadanei, M. Onofriescu, A. Covic, S.E. Giușcă
*"Grigore T. Popa" University of Medicine and Pharmacy, Romania

Background & objectives: Renal damage in lupus nephritis (LN) consists in different glomerular and interstitial lesions that delineate diagnostic criteria for classification. Our study focuses on the activity

and chronicity indices in LN as valuable tools for assessing aggressiveness and predicting disease course.
Methods: The study group comprised 53 renal biopsies diagnosed as LN by light and immunofluorescence microscopy. The distribution in LN classes and the assessment of activity index (AI) and chronicity index (CI) were performed using the revised ISN/RPS classification including the modified NIH semiquantitative scoring system. Main clinico-biological characteristics were extracted from the patient records. Data were statistically analysed.
Results: Histologically, LN cases were classified as class II - 2 cases, class III - 4 cases, class IV - 19 cases, class V - 22 cases, class VI - 6 cases. We registered a noticeable increase of active status from classes II-III to class IV, followed by a small increase in class V and a strong decrease in class VI, and a significant increase in chronic status from classes II-V to class VI. Analysis of ROC and AUC for AI and CI predictive value in relation to clinico-biological parameters showed a good prediction for a GFR <30 ml/min on patient's appointment, provided by CI (AUC 0.763, $p = 0.008$).
Conclusion: The modified NIH semiquantitative scoring system for AI and CI allows, through new cut-offs for the glomerular and tubulointerstitial lesion – assigned scores of 0 to 3, an accurate evaluation of severity degree. In our study, AI and CI showed great variability between diagnostic classes and within the same class. Our work added valuable results in the evaluation of active and chronic indices in LN – that still require further refinement to improve interobserver reproducibility and to validate prognostic value.

E-PS-16-006
Congenital nephrotic syndrome: a case series
A. Demir*, K. Erdogan, G. Gonlusen, B. Atmış, A. Karabay Bayazıt
*Çukurova University, Pathology Department, Turkey

Background & objectives: Congenital nephrotic syndrome (CNS) is characterized by massive proteinuria, hypoalbuminemia and oedema. We present a case series of CNS.
Methods: Five CNS cases were enrolled into this study. The patients' clinical datas were collected from medical records. Renal biopsies were evaluated with routine examination, immunoflourescent and electron microscopy.
Results: First case was 20-day male that's renal biopsy was composed of 1/20 cresent formation and mesengial cellularity without immune deposits. Diffuse enhancement of foot process of podocyte and microvilli formation were found ultrastructurally. Second case was 3 month female. Renal biopsy showed diffuse mesengial cellularity and interstitial inflammation without immune deposits. Third case was 22 day male presenting with polyhydramnios and a history of in utero ex sibling. Renal biopsy was composed of mesengial cellularity, microcystic areas and inflammatory cells. Fourth case was 1 month male presenting with proteinuria. His renal biopsy was consistent with minimal lesion disease ultrastructurally. Fifth case was a 6 month old male that's renal biopsy revealed diffuse mesengial sclerosis.
Conclusion: CNS has a risk to develop end stage kidney disease. Albeit this progression, CNS patients under dialysis have good outcomes rather other kidney diseases in the infancy.

E-PS-16-007
Clinicopathological significance of monotypic light-chain deposition in IgA nephropathy
C.A. Gomez Gonzalez*, B. Sarsik Kumbaraci, B. Yaman, D. Demir, Z. Akcali, G. Asci, S. Sen
*Department of Pathology, Ege University Faculty of Medicine, Turkey

Background & objectives: IgA nephropathy (IgAN) is characterized by the deposition of IgA within the mesangium and can also have light-chain deposition kappa/ lambda in a polytypic or monotypic (mIgAN) profile, with or without bone marrow alterations, conferring different scenarios of clinical outcomes.
Methods: Between 2017-2021 retrospectively, renal biopsies with fresh tissue for immunofluorescence assessment were evaluated, and 164 cases with IgA deposition were included. For each case, light-chain and IgA staining were evaluated, and divided into five groups: lambda monotype, lambda predominant, polytype, kappa monotype, and kappa predominant. Histopathologic findings according to Oxford classification were described. In mIgAN cases, bone marrow biopsies were also evaluated.
Results: In our series 65% were male, the mean age was 44 ±14 years old, and the follow-up time was 38±21 months. The prevalence of mIgAN and pIgAN was 49%(lambda/kappa=72/8) and 43%(n=70) respectively. In two cases lambda predominance was detected. At the histopathological findings, in mIgAN, endocapillary proliferation was statistically significant(p=0,02). Within mIgAN cases, two cases had diagnoses of myeloma. In the first case, the initial kidney biopsy had weak IgA deposition, and two years later in a bone marrow biopsy myeloma was detected. Seven years follow-up in kidney biopsy "kappa mIgA" deposition was detected. In the second case three years after the bone marrow biopsy, in the kidney biopsy "lambda mIgA" deposition was detected.
Conclusion: At the evaluation of IgA deposition, the light-chain co-deposition might correspond to a different entity within IgAN, noticing that mIgAN had an association with hematologic malignancies. Therefore, adequate approach and classification are mandatory for optimal treatment and surveillance of the patients.

E-PS-16-008
Significance of C4d and Jones stain in renal amyloidosis
C.A. Gomez Gonzalez*, A. Celtik, M. Yetisken, B. Sarsik Kumbaraci, H. Toz, S. Sen
*Department of Pathology, Ege University Faculty of Medicine, Turkey

Background & objectives: Amyloidosis refers to the abnormal deposition of fibrillary proteins within the tissues leading to organ failure. Kidney compromise is usually seen in systemic amyloidosis, grouped into AA, AL, and non-AA-non-AL type amyloidosis. Congo red stain is the gold standard, silver-Jones stain can be positive.
Methods: Kidney biopsies performed between 2014 and 2022 at Ege University's hospital were retrospectively evaluated. Cases with diagnosis of systemic amyloidosis were included, and grouped into AA, AL and non-AA-non-AL types. For each case distribution of amyloid deposition at hematoxylin-eosin was recorded and compared with histochemistry techniques (congo red and methenamine silver Jones staining) and immunohistochemistry (C4d).
Results: A total of 196 kidney biopsies with a diagnosis of systemic amyloidosis were evaluated. AA, AL, and non-AA-non-AL type cases were 122, 47, and 27 respectively. We observed amyloid deposition within the glomeruli, mesangium, basement membrane, and vascular structures. Positive silver staining among amyloid deposits for each group was 24,54% (AA), 76,92% (AL), and 57,89% (non-AA-non-AL). Amyloid deposits in all the groups, in cases where C4d staining was available, had positive results.
Conclusion: Congo red staining with evaluation under polarized light is the gold standard for the diagnosis of amyloidosis. In kidney biopsies congo red staining can be faint and hard to be evaluated. Silver staining usually highlights alterations on glomerular basement membrane,being negative for amyloid. We detected positive silver staining as well as positive C4d staining among amyloid deposition within the glomeruli, mesangium and basal membranes setting a challenge for differential diagnosis with membranous glomerulonephritis and fibrillary glomerulonephritis when congo red is unavailable.

E-PS-16-009

Clinicopathological evaluation of 124 biopsy-proven lupus nephritis

E. Kussever*, G. Gonlusen, K. Erdogan, B. Atmış, B. Kaya, A. Karabay Bayazıt, S. Paydas
*Cukurova University, Turkey

Background & objectives: Lupus nephritis (LN) is a common cause of kidney injury in systemic lupus erythematosus. We aimed to focused on pathological findings on LN.
Methods: Totally 38 paediatric and 86 adult biopsy-proven LN were enrolled into this study. Paediatric and adult forms were evaluated comparatively. The histopathological examination was based on 2003 International Society of Nephrology/Renal Pathology Society system.
Results: Paediatric patients data: the mean age was 11.5,male/female ratio was 0.4.Morphological classifications were divided into Class I(n:5),Class II(n:11),Class III(n:5),Class IV(n:15),Class V(n: 2).The mean activity scores were 2,5.6,8.5 and 1; chronicity scores were 0.09,0,0.78,1 according to Class II,III,IV and V respectively. The ultrastructural features were allowed Class II to Class III(n:1); Class III to Class III+Class V(n:1).Adult patients data: the mean age was 37, male/female ratio was 0,2.Morphological classifications were divided into Class I(n:1),Class II(n:8),Class III(n:19),Class IV(n:51),Class V(n:7). The mean activity scores were 1,2.2,6.2,10.7,1.5; chronicity scores were 0.8,0.7,2.2,0.5 according to Class II,III,IV and V respectively. The ultrastructural features were allowed Class II to Class IV(n:1); Class III to Class III+Class V(n:2); Class IV to Class IV+V(n:3).
Conclusion: Paediatric patients were summarized as: the mean age was 11,5 years old, male/female ratio was 0.4.Morphological classifications were divided into Class I(n: 5), Class II(n: 11), Class III(n: 5), Class IV(n:15), Class V(n: 2). The mean activity scores were 2, 5.6, 8.5 and 1 according to Class II, III, IV and V respectively. Chronicity scores were 0.09, 0, 0.78, 1 according to Class II,III,IV,V respectively. The ultrastructural features were allowed Class II to Class III (n:1); Class III to Class III+Class V(n:1).
Funding: Çukurova University

E-PS-16-010

T-cell-mediated cellular rejection and antibody-mediated rejection in HLA-DSA-negative kidney transplant recipients

J. Osuna Soto*, F. Leiva-Cepas, I. Sánchez Ramírez, A. Sanz Zorrilla, M.J. Galvez Medina, S. Haro Yuste
*Hospital Universitario Reina Sofía, Spain

Background & objectives: Banff 2021 categorized the previously "suspicious" Antibody Mediated Rejection (ABMR) without circulating HLA Donor Specific Antibodies (DSA) in Kidney Transplant (Ktx) biopsies. Recent series describe absent HLA DSA (DSANeg-ABMR) up to 60% of ABMR histologies.
Methods: To evaluate presentation and outcomes of biopsy-proven ABMRs (bpABMR) in patients with and without HLA-DSA Abs in solid-organ transplant (SOT) recipients. Single centre descriptive study of SOT patients (31KTx, 3 multiorgan) with ABMR under contemporary BANFF criteria between Feb 2014–Feb 2023 compared by HLA-DSA status. 34 total bpABMR were included.
Results: 57,1% were DSANeg-ABMR. In this group, 55% were males, mean age of 41.8±12.6 vs 51.8±13.3 (p=0.04). 6 had preTx DSAs that vanished post-KTx and 5 developed them after the index biopsy. 47.1 % were first kidney allografts. 78,3% DSANeg-ABMR patients vs 41.7% (p=0.05) had received antibody-induction. 41.2% of DSANeg-ABMR vs 8.3% had acute TCMR ("Mixed Rejection") (p=0.06). There were no differences in creatinine (Cr) pre-biopsy nor the 1st month postrasplant (1.87±0.73 vs 1.82±1.17mg/dl). ABMR appeared earlier in DSANeg-ABMR (median 276 vs 2487days, -p=0.04-). Survival analysis showed no significant differences between groups and 53% of allografts were lost at the second year.
Conclusion: In our series, 57,1% of SOTs with ABMR had no circulating anti-HLA DSAs and as all ABMRs were diagnosed as per indication biopsy, this outcomes appeared earlier during follow up than in those with mensurable HLA-DSAs. The DSANeg-ABMR group showed a clear trend to present as a Mixed Rejection. Both groups entail a poor prognosis with a 53% renal survival after two years.

E-PS-16-011

Stress biomarkers: from serum to tissue

K. Palamaris*, A. Gkivalou, I. Theochari, E. Theodoropoulou, H. Gakiopoulou, P. Papazafiri, G. Chrousos, A. Charonis
*First Department of Pathology, National and Kapodistrian University of Athens School of Medicine, Athens, Greece

Background & objectives: The biological fingerprint of stress is under intensive current investigation. Stress-biomarkers like DDX6, β2-microglobulin and FKBP5 have been isolated in the serum of stressed patients. We comparatively investigated for the first time their histological expression in stressed and normal renal tissues.
Methods: The study included 5 normal renal tissues derived from nephrectomy specimens and renal tissues from 15 patients (7 with hypertension without diabetes and 8 with diabetes without hypertension) as hypertension and diabetes constitute distinct well known stressor stimuli and their appearance is significantly influenced by the stress. Immunohistochemistry was performed with polyclonal antibodies against DDX6, β2-microglobulin and FKBP5.
Results: In normal renal tissues no significant expression of DDX6 protein was observed. In contrast, hypertensive and diabetic kidneys showed significant increase in DDX6 expression in tubular epithelial cells, mainly in distal tubules. In normal kidneys, β2-microglobulin demonstrated diffuse immunohistochemical granular cytoplasmic expression in tubular epithelial cells, mainly proximal, and in glomeruli along the basement membranes of the capillaries. In hypertensive and diabetic kidneys there was decreased expression of β2-microglobulin in both compartments. As far as FKBP5 is concerned, its expression in normal tissues was mostly faint and cytoplasmic in some tubular cells. In contrast, in pathologic tissues a nuclear expression in tubular cells was observed.
Conclusion: Although a limited number of samples were examined, quantitative differences and differential patterns of expression of each protein between normal and pathological tissues, seem to exist. This is a first attempt to establish a link between serum stress-biomarkers and tissue pathology of stressed organs. The ultimate goal would be the discovery of molecular stress-algorithms with organ and/or tissue specificity in order to predict the appearance of stress, to quantify it, and to discover targeted therapies in the context of precision-medicine.

E-PS-16-012

Chronic kidney graft neprhopathy. Prognostic histopathological variables?

I. Sánchez Ramírez*, F. Leiva-Cepas, M.J. Galvez Medina, J. Osuna Soto, S. Haro Yuste, A. Sanz Zorrilla
*Hospital Universitario Reina Sofía, Spain

Background & objectives: The aim of our work was to perform an histopathological analysis of a cohort of cases presenting interstitial fibrosis (IF) and tubular atrophy (TA) after renal transplantation to clarify the mechanism underlying the development and prognostic significance of FI/TA.

Methods: FI/TA was diagnosed in 50 renal allograft biopsy specimens (BS) obtained fron 85 renal transplant recipients under follow-up in our department in the last 5 years (2018- 2023). The biopsies were digitized for visualization.
Results: FI/TA was diagnosed at a mean of 33.5 months after transplant. Among the 85 patients with FI/TA, 29 (44%) had history of acute rejection. Among the 85 BS with IF/TA, FI/TA was grade I in 53, II in 29, and III in 3. Arteriosclerosis of medium-sized arteries was observed in 73 BS (86%). The 85 patients were then classified according to general histopathological characteristics: FI/TA alone (15 BS; 18%), FI/TA+ medullary injury (30 BS; 32%), and FI/TA + rejection (32 BS; 36%). Renal allograft loss occurred in two of the patients (4%). Of the remaining patients with functioning grafts, deterioration of allograft function after biopsies occurred in 22 patients (26%).
Conclusion: The results of our study suggest that rejection contributes to FI/TA in 20-30% of cases, medullary injury in 30-40% of cases, and non-specific injury in 20% of cases. FI/TA significantly contributes to impaired renal allograft function.

E-PS-16-013
Sarcoidosis and COVID-19: is there a link?
E. Theodoropoulou*, E. Chelioti, K. Palamaris, G. Christofilidis, M. Kaniadaki, A. Stofas, M. Papadaki, H. Gakiopoulou
*Nephrology Department, Tzaneio General Hospital of Pireaus, Greece

Background & objectives: COVID-19 and sarcoidosis share common pathophysiologic mechanisms including dysregulation of renin-angiotensin-system, exacerbation of immune responses involving increased cytokine levels, and cell-death pathways. Although the causal association is not well established, case reports depict time-association and interaction between these two diseases.
Methods: A 50-year-old male presented with malaise, anorexia, and cough starting one month ago as well as vomiting in the last few days. Two months ago, he suffered from mild to moderate COVID-19 with fever and dry cough without hypoxemia and normal X-ray. The symptoms lasted for about a week. He received no special treatment. He was not vaccinated against Sars-COVID-19.
Results: At presentation, painless brownish symmetrical plaques were noted in both knees. Initial work-up was significant for creatinine (11.2mg/dL), urea (228mg/dL) and calcium (13.8mg/dL). PTH was low at 21pg/mL. Urine sediment was inactive and proteinuria minimal (448mg/24h). Central hypothyroidism was noted with low TSH/T4/T3. Renal ultrasound demonstrated increased kidney volume bilaterally and multiple hyperechoic depositions scattered throughout the renal parenchyma. Chest-CT-scan showed nodular lung lesions, bilateral hilar lymphadenopathy and multiple enlarged mediastinal lymph nodes. Brain-CT-scan showed heterogeneity of the pituitary gland. Serum-Angiotensin-Converting-Enzyme (SACE) was high at 130Units/L. A kidney biopsy was performed revealing non-caseating granulomatous interstitial nephritis accompanied by severe acute tubular injury and nephrocalcinosis. Clinicopathologic correlation suggested the diagnosis of sarcoidosis.
Conclusion: Haemodialysis was started, and 3 boluses of methylprednisolone were administered followed by 1mg/kg prednisolone. Eleven haemodialysis sessions were totally performed. Urine output gradually increased, and values of creatinine, urea and calcium subsequently decreased to normal levels. Three months later, SACE had been normalized at 45Units/L. Chest-CT-scan showed no evidence of pulmonary lesions or lymphadenopathy. Our case represents a rare case of sarcoidosis with multi-organ involvement (lung, lymph-nodes, skin, kidney and pituitary gland) following and probably triggered by COVID-19 infection.

E-PS-16-014
Cryoglobulinemic vasculitis in a patient with HCV infection and IgMk paraproteinemia
E. Theodoropoulou*, E. Chelioti, G. Christofilidis, K. Palamaris, M. Kaniadaki, M. Papadaki, A. Stofas, H. Gakiopoulou
*Nephrology Department, Tzaneio General Hospital of Pireaus, Greece

Background & objectives: Several glomerular diseases have been associated with HCV infection including mixed cryoglobulinemia syndrome (MCS) which is a systemic vasculitis.
Methods: A 51-year-old female diagnosed with mild ulcerative colitis one month earlier, presented with weakness, leg oedema, palpable purpura in lower legs, anaemia, pericardial effusion and reduced ejection fraction, peripheral neuropathy, pulmonary fibrosis, ground glass opacities, impaired renal function with reduced urine output, glomerular haematuria and proteinuria (3,1gr/day). Complement was low and rheumatoid factor was positive. A renal biopsy was performed.
Results: Renal biopsy showed glomerulonephritis with membranoproliferative-pattern and endocapillary hyaline thrombi with hypermicroscopic features suggestive of cryoglobulines. Immunofluorescence showed IgG/IgM/ C3/ C1q and both light chains κ and λ.
Type II cryoglobulins (monoclonal IgM and polyclonal IgG) were positive. Serum and urine immunofixation revealed monoclonal IgMκ. Further evaluation revealed HCV positivity, genotype 4, with liver fibrosis grade-3 albeit with normal liver function tests. The work-up for non-Hodgkin lymphoma or lymphoproliferative disease was negative.
The patient initially received high dose methylprednisolone and haemodialysis treatments. After the biopsy result, she underwent 6 plasmapheresis treatments and started direct-acting-antivirals/DAAs (elbasvir-grazoprevir) and rituximab. Gradually, kidney function improved and all manifestations of MCS subsided.
Conclusion: MCS diagnosis should be raised in any patient who presents with one or more of the following clinical features: palpable purpura, skin ulcers, arthralgias and/or arthritis, peripheral neuropathy, and/or microscopic haematuria or proteinuria with or without chronic kidney disease. The index of suspicion for MCS should be raised further if these occur in the setting of viral infection (eg, HCV, HBV, or HIV), connective tissue disease (systemic lupus erythematosus, Sjögren syndrome, or rheumatoid arthritis), or lymphoproliferative disorder.

E-PS-16-015
Prognostic value of histological parameters in acute tubulointerstitial nephritis (ATIN)
C. Vieru*, M.L. Abascal Camacho, P. Nuñez Ramos, Y. Gómez Navarro, M. Goicoechea Diezhandino., M.R. Melero Martin, T. Bada Bosch, I.G. Arenas Moncaleano, J.C. De la flor, Ú. Verdalles Guzman, J.M. Lara Martínez, F. Arias, F.J. Díaz Crespo
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: ATIN is a varied aetiology and increasing incidence entity and it is a frequent cause of acute kidney injury (AKI). Renal biopsy is not always used to diagnose it and scarce histological studies of prognostic value are available.
Methods: We searched the pathology archives of our department between 2017 and 2023. We retrospectively analysed sociodemographic (age and sex), clinical (biopsy date, microhaematuria, leukocyturia, renal function at diagnosis, AKI, acute dialysis, protein/creatinine, 24h proteinuria, renal recovery) and histological data (number of glomeruli and inflammatory infiltrate percentage, distribution and components, tubulitis degree, tubular destruction and acute tubular necrosis).
Results: 34 cases were retrospectively studied, 20 males (58.8%) and 14 females (41.2%) with mean age of 62,15 +/- years. All patients received standard corticotherapy. Patients were divided into two groups based

on tubulitis score [<!--=5 leukocytes (67.6%) and -->5 leukocytes per tubular cross section (32.4%)] and cortical inflammatory infiltrate [<!--=25% (44.1%) and -->25% (55.9%)]. Mean follow-up time was 19.8 months. Renal recovery based on serum creatinine reduction levels, was 76.25%, consistent with the literature. The analysis of tubule-interstitial parameters compared with renal recovery rate, showed that patients with >5 inflammatory cells/tubular cross section and/or >25% interstitial inflammatory infiltrate and/or tubular destruction, significantly improved renal function (p=0.027, 0.05 and 0.041, respectively).
Conclusion: The histological parameters analysed as tubulitis score, cortical inflammatory infiltrate percentage and tubular destruction demonstrated an independent and statistically significant association with renal recovery, without association to other variables such as acute tubular necrosis or additional glomerular pathology. These results highlight the importance of renal biopsy in ATIN to stablish a histological activity index, nevertheless future studies with larger sample sizes will be necessary to evaluate the reproducibility of these results.

E-PS-16-016
Morphology and clinical presentation of small vessel vasculitides involving the kidney
M. Životic*, G. Nikolić, A. Mioljević, P. Ratković, R. Naumović, A. Kezić, M. Radović, D. Paripović, G. Miloševski Lomić, N. Stajić, J. Putnik, D. Dunđerović, S. Radojević Škodrić
*Institute of Pathology, Serbia

Background & objectives: Pauci-immune small vessels vasculitides in kidney, could be divided into ANCA associated vasculitides (AAV) and non-ANCA associated vasculitides (NAAV). Our aim was to compare clinical and pathohistological characteristics of small vessel vasculitides in kidneys of patients with AAV and NAAV.
Methods: We performed a retrospective analysis of kidney biopsies, diagnosed between 2000-2020, at Institute for Pathology Faculty of Medicine University of Belgrade. Overall, 157 kidney biopsies with pauci-immune small vessels vasulitides were examined (79 patients with AAV and 78 patients with NAAV). Clinical data collected from medical records, and pathohistological parameters were examined and compared between the AAV and NAAV patients.
Results: ANCA positive patients were significantly older (55.5±17.6 years) than ANCA negative (45±18.1 years) patients (p<0.001), and they also had significantly higher frequency of glomeruli involved by crescent formations (≈40%) compared to patients with non-ANCA vasculitides (≈30%), p=0.012. Moreover, ANCA positive patients had higher frequency of chronic lesions such as interstitial fibrosis, tubular atrophy and glomerular sclerosis. Laboratory parameters were high in both groups, without significant difference. Clinically assessed BVAS score was similar in both investigated groups and did not show any significant difference.
Conclusion: Patients with ANCA positive renal vasculitis are significantly older and have higher frequency of chronic glomerular and tubulointerstitial lesion, while laboratory and clinical parameters are not significantly different between ANCA positive and ANCA negative patients.
Funding: The study was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia.

E-PS-16-017
Oxford classification (MEST-C score) - IgA nephropathy and Henoch Schoenlein pupura: similarity and difference?
M. Životic*, G. Nikolić, A. Mioljević, V. Brković, A. Janković, S. Radojević Škodrić
*Institute of Pathology, Serbia

Background & objectives: We conducted a retrospective study, in order to assess potential clinical and morphological differences (assessed by MEST-C score), between IgA nephropathy (IgAN) and Henoch Schoenlein purpura (HSP).
Methods: The study included patients with IgAN (n=67) and HSP (n=28) diagnosed at the Institute of Pathology, Medical Faculty, Belgrade, Serbia. Clinical patient's data (gender, age, haematuria, proteinuria and disease duration before biopsy) and pathohistological MEST-C score were analysed and compared between IgAN and HSP.
Results: Patients diagnosed with IgAN were significantly older (33±17.9 years) than those with HSP (15±10.3 years). Higher serum creatinine values were observed in HSP (356.5±1071.1 μmol/l) compared to IgAN (117.4±73.6 μmol/l). The majority of patients with IgAN and all patients with HSP had diffuse glomerular mesangial hypercellularity. Endocapillary hypercellularity is observed in 6/67 IgAN and in 13/28 HSP patients. Segmental glomerular sclerosis was detected in more than a half of IgAN cases, while only a quarter of HSP exhibited these changes. Tubular atrophy and interstitial fibrosis were not observed in HSP, while 13/67 patients with IgAN had this lesion. Crescents formations were detected in 3 HSP and 15 IgAN patients.
Conclusion: Active glomerular lesions are characteristics of HSP, while chronic parameters are frequently observed in IgAN patients who are generally older than HSP group.
Funding: This work was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia.

E-PS-17 | E-Posters Neuropathology

E-PS-17-001
Bithalamic diffuse midline glioma H3K27-altered harbouring concomitant EGFR and HIST1H3B mutation: a case report
M.L. Abascal Camacho*, C. Vieru, A.J. Van der Biezen, M.N. Villca Huayta, E. Carceller Ortega, C. Garrido Ortega, F.J. Díaz Crespo, F. Arias
*Hospital General Universitario Gregorio Marañón, Spain

Background & objectives: Concomitant EGFR and H3mutations in diffuse midline glioma H3K27altered are extremely rare, with only 5 cases reported in the literature to date. We present a new case to expand our understanding of this pathology.
Methods: A 4year-old boy, presented with tremor in the upper extremities. Magnetic resonance imaging (MRI) revealed a diffuse supratentorial tumour, centred in the midline with bitalamic involvement and right hemispheric extension. The mass was hypointense on T1 and isointense to hyperintense on fluid-attenuated inversion recovery images. The patient underwent stereotactic biopsy.
Results: Histopathological evaluation revealed a diffuse glial neoplasm with high cellularity. Tumour cells displayed oval morphology, with hyperchromatic, irregular nuclei and sparse mitotic activity. Microvascular proliferation and necrosis were absent. Immunohistochemistry revealed strong nuclear immunoreactivity with H3K27M and P53, with complete loss of H3K27me3 in tumour cells. Ki67 index was approximately 20%. Next-generation sequencing detected mutations in HIST1H3-H3K27 (c.83A>T, p.Lys28met), EGFR (c.1793G>T, pGly598Val) and TP53 (c.524G>A, pAr175His). MGMT promoter methylation was not present. DNA methylation analysis classified this tumour as a paediatric-type diffuse high-grade glioma-H3K27 altered, subtype EGFR altered. The patient received radiotherapy, chemotherapy, and immunotherapy treatment (Erlotinib) with poor response. Currently, the patient is receiving palliative care.
Conclusion: DMG-H3K27 altered are characterized by the loss of H2K27me3. The WHO classification of 2021 recognizes four subtypes based on molecular alterations. The concurrent presence of H3K27 and EGFR mutations, leads to the loss H3K27me3, potentially resulting in the recognition of a fifth DMG-H3K27 altered subtype in the future. These tumours are extremely rare with limited treatment

options and poor prognosis. Further research is required for a better understanding of the underlying pathophysiology to implement targeted molecular therapy.

E-PS-17-002

Stearoyl-CoA desaturase 1 overexpression in temozolomide-resistant glioblastoma cell line associates with an epigenetic modification

S.M. Alqahtani*, A. Alkhanjaf, A.M. Assiri, A. Abusharib, A. Ibrahim, E. Elagab, A. Shediwah, S. Talballah, S. Samer
*Najran University, Saudi Arabia

Background & objectives: SCD1 is a key rate-limiting enzyme for lipogenesis. Overexpression of SCD1 has been reported to promote tumorigenesis. Temozolomide (TMZ) is used as a treatment for glioblastoma patients, however, resistance to TMZ is one of the major clinical challenges.
Methods: The U87 glioblastoma cell line was treated with 120 μM of TMZ for four months after testing different concentrations to develop U87-resistant cells (U87-RC). The non-tumour normal human astrocytes (NNHA) cell line was used as another control. For studying methylation status, genomic DNA was extracted, and methylation was carried out using a OneStep qMethyl Kit according to the manufacturer's protocol.
Results: There was a significant upregulation of SCD-1 mRNA and protein levels in both U87 and U87-RC, compared to NNHA. Interestingly, there was a significant increase in the expression of SCD1 at the mRNA levels in U87-RC, Compared to U87. Although the mRNA and protein levels of SCD1 in U87 were significantly higher than those of NNHA and up to a greater extent during starvation on 2% of foetal bovine serum (FBS), there was no change in the level of methylation with or without starvation (10% FBS). However, the levels of methylation of SCD1 were suppressed significantly in U87-RC.
Conclusion: The results conclude that the upregulation of SCD-1 mRNA and protein levels in U87-RC and UR87 are regulated by different biological processes. In addition to that, the association between the increased expression levels of SCD1 and methylation suppression in U87-RC may have a role in TMZ resistance. Finally, further studies are needed to reveal detailed relation between SCD1 overexpression and TMZ resistance in astrocytic tumours.
Funding: Charity Department at PentaM Co.

E-PS-17-003

Extraspinal soft tissue sacrococcygeal myxopapillary ependymoma. Report of a case

E. Athanasiou*, E. Michalopoulou-Manoloutsiou, M. bobos, D. Hatzibougias
*MicroDiagnostics, Private cyto/histopathology/molecular lab, Greece

Background & objectives: Primary extraspinal soft tissue myxopapillary ependymoma (MPE) is an exceptionally rare lesion that is mainly located in the subcutaneous sacrococcygeal region. We report a case of a 33-year-old man presenting with a slow growing painful mass on sacrococcygeal region.
Methods: Grossly, the tumour had yellowish cut surface, measured 3*2.8*1.8 cm. Microscopically, it was a cellular lesion, containing ovoid cells with only minimal nuclear variation and mitotic activity. There was microcystic areas with cuboidal cells arranged around pools of basophilic myxoid material and also radially around fibrovascular cores with intervening myxoid material. The tumour cells expressed CD99, CD56, S100, GFAP and, focalCKAE1/AE3.
Results: The final diagnosis was soft tissue MPE. Subsequently, the patient underwent a wide local surgical resection that confirmed complete removal of the tumour.
Conclusion: Extraspinal MPE probably arise from extramedullary ependymal rests representing remnants of the coccygeal medullary vestige. The differential diagnosis includes sacrococcygeal teratoma, neurogenic tumour, soft tissue sarcoma, and metastatic carcinoma, and in sacrum and coccyx, tumours such as chordoma and chondrosarcoma. Immunopositivity of the tumour cells with GFAP helps in confirming the diagnosis of MPE. The treatment of choice is gross total resection. This treatment makes possible a cure without the need for adjuvant therapy.

E-PS-17-004

Primary EBV-negative CNS T cell lymphoma in a patient with B cell chronic lymphocytic leukaemia: a case report

L. Cardisciani*, M.E. Maracci, L. Di Sciascio, M. Martinoni, C. Tonon, R. Liguori, P.L. Zinzani, E. Sabattini, S. Asioli
*School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: Peripheral T-cell lymphoma accounts for 2–4% of primary Central Nervous System (CNS) lymphomas, usually present as single mass and involved sites include the frontal and temporal lobes, cerebellum, pituitary gland and (rarely) the leptomeninges.
Methods: A 57-years-old male patient with a diagnosis of Chronic Lymphatic Leukaemia (CLL) developed persistent headache, fever and seizures. Head-CT and brain-MRI revealed multiple oedematous lesions with contrast enhancement. A stereotaxic biopsy was performed after dexamethasone. 18FDG-PET-CT and CSF analysis were unremarkable, marrow biopsy confirmed mild B-CLL infiltration (<10%). Meanwhile the symptoms worsened and oedema and lesions increased at the MRI.
Results: The biopsy showed extensive necrosis and macrophages, with sparse lymphocytes showing prominent angiocentricity, cytologic atypia, medium/large size and moderate nuclear pleomorphism. The phenotype showed T-cell origin (CD3+, CD2+), Tia-1 positivity, high Ki67 and defective expression of CD5, CD7, CD4, CD8; TdT, CD30, ALKc and CD56 were negative. EBV-encoded small RNAs were not detected at in-situ hybridization. Clonal T-cell Receptor Gamma genes rearrangement was detected. Diagnosis was consistent with peripheral T/NK cell lymphoma, better classified as Not Otherwise Specified. The patient was treated with methotrexate, cytarabine and thiotepa but ultimately died 3 months later.
Conclusion: The present case fulfils the criteria of primary CNS T/NK cell lymphoma with extensive necrosis and angiocentric growth-pattern. The latter features and the cytotoxic double-negative phenotype, in the context of a likely BCLL-related immune-deficiency, could suggest a nasal-type subtype. However, the evidence of T-Cell-Receptor rearrangement, absence of EBV integration, CD56 and CD30 negativity favoured a final diagnosis of a NOS subtype. The clinical course of this case was rapidly progressive with very poor prognosis with no effective available treatment protocols.

E-PS-17-005

A possible diagnostic pitfall in tumours of pineal gland region in adults: poorly differentiated primary glial tumour with primitive neuroectodermal differentiation

T. Čeprnja*, K. Žarković, I. Brnadić, I. Lukić, D.A. Grubišić, A. Jakovčević
*University Hospital of Split, Croatia

Background & objectives: Pineal region tumours are rare neoplasms, most of which originate from pineal gland parenchyma. Pineal region gliomas arising from glial stroma of pineal gland are even more uncommon. We present a case of malignant glioma arising in pineal region.

Methods: A 61-year-old female patient with history of breast cancer presented herself to an outside facility after experiencing periods of confusion, intense headaches and generalized epileptic seizures. MRI was performed, which described a tumour originating from pineal gland, with radiomorphological characteristics of pineoblastoma. Patient was admitted to our hospital, and two craniotomies were performed with aim of maximal tumour reduction.
Results: Two samples of tumour tissue were separately admitted for histological examination, both consisting of small tissue fragments. Examination of both samples showed a highly cellular tumour composed of small, blue, round cells with scant eosinophilic cytoplasms, and with numerous mitoses and apoptotic bodies. No necrosis was observed, and microvascular proliferation was seen focally. Immunohistochemicaly, tumour cells were GFAP negative, NSE and synaptophysine positive. No mutations of IDH1 or ATRX were observed, and Ki67 proliferation index was around 40%. On further testing Olig2 staining was positive. Diagnosis of primary high grade glial tumour with primitive neuroectodermal differentiation was set, and samples were sent for molecular analysis, which later confirmed the diagnosis.
Conclusion: While most cases of pineoblastoma, a WHO grade 4 tumour arising from pineal parenchyma, are described in children and young adults, some cases were reported in older population. As cases of primary glial tumours of this region are very rare, radiomorphological characteristics of high-grade glial tumours can easily be mistaken for pineoblastoma. Similarly, on histological examination, poorly differentiated tumours with loss of GFAP expression and neuroectodermal differentiation, could easily be misdiagnosed as pineoblastomas if not taken into consideration.

E-PS-17-006
Cerebral amyloid angiopathy and neurodegenerative pathologies: beyond Alzheimer's disease
A. Chaachou Charradi*, I. Burgueño García, M. Riba Barroso, S. Ramón y Cajal Agüeras, A. Rábano Gutiérrez, E. Martínez Sáez
*Vall d'Hebron University Hospital, Spain

Background & objectives: Cerebral amyloid angiopathy (CAA) is the main cause of intracerebral haemorrhage in normotensive elderly. Its association with Alzheimer's disease (AD) is known, as they share abnormal deposits of Amyloid-β protein. However, we consider interesting to elucidate its frequency outside AD.
Methods: We present a cohort of 362 brain donors from two Spanish brain banks, including 71 control patients (absence of clinical diagnosis of dementia), 203 AD cases (including early-onset (EOAD)) and 59 other neurodegenerative diseases (ND) (Lewy body disease (LBD), amyotrophic lateral sclerosis (ALS), tauopathies). Clinicopathological data were collected, and the presence of CAA pathology was evaluated.
Results: As expected, there was a significant correlation between CAA and AD (88,2% prevalence of CAA within the group). However, CAA was also found in a non-negligible percentage of LBD (57,7%), control cases (31%) and ALS/TDP-43 (26,7%).
Conversely, the tauopathies group showed the lowest percentage of CAA (15,8%). Interestingly, there were no statistically significant differences in CAA affectation between early and late-onset AD, although the percentage is notably higher in EOAD (98%).
Regarding the age at exitus, groups were homogeneous and no significant differences were found between them, being the highest mean age in the AD group (84,26 years) and the lowest mean age in the ALS/TDP-43 group (61,13 years).
Conclusion: In summary, we should keep in mind that, outside AD, CAA can be present, particularly in LBD and even in asymptomatic patients.
This is an important finding, as CAA is a major cause of morbidity and mortality, and significant progress has been made in the development of targeted therapies against Amyloid-β protein.
Improved knowledge of CAA in non-AD ND could extend these treatments to other NDs, as the above mentioned.

E-PS-17-007
Secondary diffuse large B-cell lymphoma of the CNS: a case report
J.L. Delgado Fernández*, I. Marquina Ibáñez, J. Alfaro Torres, S. Hakim Alonso, J.M. Lazaro Maisanava, N. Martínez Arnau, J. Martínez Castillón, L. Leon, J. Medrano Ruiz, A. Carilla Sanromán
*Hospital U. Miguel Servet, Spain

Background & objectives: Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin's lymphoma. Central nervous system (CNS) metastasis of DLBCL are uncommon, ranging from 2% to 25%, and result in an extremely guarded prognosis.
Methods: We report a case of a 67-year-old man previously diagnosed with colonic DLBCL treated with chemotherapy and in complete remission for 3 years that presented with language and memoire impairment. An MRI was performed, showing a lesion in the left temporal lobe. The patient underwent surgery, performing a left temporal lobe craniotomy with a biopsy/removal of the lesion.
Results: Macroscopically, several whitish cylindrical fragments between 0,5 and 0,9 cm in maximum diameter were received. Histologic study revealed neuroglial tissue infiltrated by loose cells of lymphoid habit. These cells were large, with irregular nuclei and tended to gather around vessels in Virchow-Robin spaces with perivascular cuffs. The cells expressed CD20, CD79a, BCL6, CD10 and MUM1 (focally), with a proliferative index of 70% and were negative for BCl2, CD30 and EMA. Given the clinical history and these histologic and inmunohistochemistry findings, a diagnosis of metastatic DLBCL was made.
Conclusion: Metastatic involvement of the CNS by a lymphoproliferative process is uncommon. In those cases, specifically DLBCL, previous history and CD10 are indispensable for differentiate this CNS relapse from a primary CNS-DLBCL.

E-PS-17-008
OPN overexpression in psammomatous meningiomas
A. Denysenko*, R. Moskalenko
*Sumy State University, Ukraine

Background & objectives: Meningiomas are the most common primary tumours of the central nervous system. Their calcification is controversial and can both facilitate and complicate diagnosis and treatment. The work aims to study OPN expression in meningiomas tissue with and without calcification.
Methods: The study group included 30 samples of psammomatous meningiomas (group I) and 30 samples of meningiomas (meningothelial, fibroblastic) without any signs of biomineralization (group II). We use histological and immunohistochemical methods. We use the anti-OPN antibody (Thermo Fisher Scientific, PA5-34579, dilution 1:300), followed by DAB detection substrate and counterstained with Mayer's hematoxylin.
Results: We can conclude that OPN expression increased in meningiomas with calcifications (137,19±12,97 cells per 1 mm2) in comparison to those without them (57,47±9,34 cells per 1 mm2, $p<0.001$, Student test). Also, we can observe OPN mainly localized in the tissue around the calcifications.
Conclusion: We observe a significant difference in OPN expression in the group of meningiomas with calcifications compared to those without signs of biomineralization. Overexpression of OPN in meningiomas with calcification tissue may be a promising diagnostic marker.

E-PS-17-009

Spindle cell oncocytoma and granular cell tumour of the pituitary gland: report of three cases

O. El Mnif*, F. Sassi, A. Zehani, A. Ayari, B. Chelly, H. Azzouz, I. Chelly, K. Bellil, S. Haouet
*La Rabta pathology department Tunis, Tunisia

Background & objectives: The 2021 WHO classification of the central nervous system's tumour recognizes distinct low- grade neoplasm grade I of the sellar region:Pituicytomas, granular cell tumours (GCT) and spindle cell oncocytoma (SCO).We present 2 cases of SCOs and one case of GCT.
Methods: Gross materials were fixed with 10% buffered formalin. Hematoxylin and eosin (H&E) sections of 4-5 microns were obtained. The cases (n=3) were analysed according to their histopathological, radiological and clinical features. S-100 protein and thyroid transcription factor 1 (TTF-1) were performed immunohistochemically. Two of the three cases were female and one male. The mean age was 53.6 years (range: 45-60).
Results: Clinical findings at presentation included decreased visual acuity with left facial paralysis, headaches, and vertigo. Brain MRI showed an intra- and suprasellar expansive process with destruction of the dorsum sellae and floor, globular solid mass located in the suprasellar region and a mass with enhancement in the sella. The three patients underwent resection.
Grossly, the tumour was yellow and soft in two cases. Neuropathological analysis showed a proliferation of large ovoid and spindle cells in nests with abundant eosinophilic cytoplasmic granules with no mitosis and no necrosis. Immunohistochemistry in all cases showed positivity for S100 and thyroid transcription factor 1 (TTF-1). All the patients had no recurrence after total resection.
Conclusion: SCO and GCT are rare tumours. These tumours manifest in patients aged 40 to 60 years and affect both genders equally. They can mimic adenoma, Rathke's cleft cyst or present with endocrine disturbances. The best treatment is surgical removal. The primary obstacle to complete resection is the strong attachment of the tumour to nearby normal structures which necessitates adjuvant radiotherapy.

E-PS-17-010

Immunohistochemical expression of MUC-4 in different subtypes of meningioma: descriptive study of all cases diagnosed in our hospital over a two-year period

I. Fernández*, J.C. López, A. Tarín, J. Rosselló, L. Aguirrezabal, L. Ortega, S. Fernández
*Hospital Universitario de Basurto, Bilbao, Spain

Background & objectives: Meningiomas are the most common primary tumours of the central nervous system. However, current immunohistochemical markers for the diagnosis lack specificity and sensitivity. Several recent studies have proved that MUC-4, a membrane-associated mucin, is also expressed in these tumours.
Methods: Immunohistochemistry with MUC-4 was performed in every meningioma diagnosed over two years (2021-2022) in the Pathology Department of our hospital, with a total of 44 cases. Afterwards, MUC-4 expression was evaluated, and positive staining was classified in three groups based on intensity and extension of the staining (diffuse, patchy or focal). Meningioma subtypes were also taken into account.
Results: Most meningiomas (77%) showed positive MUC-4 expression. Meningothelial meningioma was the most frequently diagnosed subtype, representing 80% of the cases; and most of them had a positive MUC-4 expression with either diffuse (34%), patchy (23%) or focal (20%) staining. All angiomatous, psammomatous and atypical meningiomas showed positive MUC-4 expression, with variable intensity and extension of the staining. However, fibrous meningiomas were MUC-4 negative in most cases (66%), with only one case showing focal positivity. Regarding clinical data, the age of the included patients was above 50 years in 82% of the cases; and both male and female population were similarly represented, being a 48% and 52% of the cases, respectively.
Conclusion: This study shows that MUC-4 is frequently expressed in meningiomas, despite some differences in the staining pattern; with the exception of fibrous meningioma subtype, which is often MUC-4 negative. This suggests that this marker could be used in the diagnosis of meningiomas, but it might not be helpful in some cases. This study has some limitations because of the small number of cases. Nonetheless, the results are concordant with the findings of other previous studies on this matter.

E-PS-17-011

Morphological and immunophenotypic features of gliosarcoma

M.J. Gil-Belmonte*, G. Urreta-Juárez, B. Agredano-Ávila, M.d.M. Berenguel-Ibáñez, F.J. Velasco-Albendea
*UGC Anatomía Patológica, Hospital Universitario Torrecárdenas, Spain

Background & objectives: The fifth edition of the WHO Classification for CNS Tumours gives IDH-wildtype glioblastoma its unique place among adult-type diffuse gliomas while recognizing its classical histological heterogeneity. This work aims to highlight the main morphological and immunophenotypic features of gliosarcoma.
Methods: Two female patients in their seventies and eighties were diagnosed with a growing mass confined to the right and left temporal lobes, respectively. After surgical excision, well-defined elastic lesions were remitted for their analysis. Hematoxylin-eosin staining supported by immunohistochemical techniques for IDH-1, ATRX, p53, proliferative Ki67 index, vimentin, CK AE1/AE3, INI-1, and staining for reticular fibres were performed.
Results: Hematoxylin-eosin sections showed, in both cases, a presumably glial-derived neoplasm with alternating areas exhibiting mesenchymal differentiation. Tumours were composed of morphologically variable, atypical, and pleomorphic cellularity. Prominent microvascular proliferation, increased mitotic activity, and extensive necrosis were observed. Immunohistochemical study revealed negativity for IDH-1 [R132H], retained ATRX, p53 heterogeneous positivity, and a high Ki67 (35%) index. GFAP stained positive in the glial component, while vimentin showed diffuse positivity for both glial and sarcomatous elements. Reticulin staining demonstrated dense bundles of reticular fibres in the sarcomatous regions. INI-1 evidenced a nuclear-retained staining pattern, while CK AE1/AE3 tested negative. An integrated diagnosis of glioblastoma, IDH-wildtype, grade 4, gliosarcoma subtype was then released.
Conclusion: Sarcomatous metaplasia can be found in some CNS neoplasms, especially in the setting of de novo or recurrent glioblastoma IDH-wildtype. Gliosarcomas constitute a rare glioblastoma variant, accounting for 2% of glioblastomas. The demonstration of a dual morphological and immunohistochemical phenotype with biphasic glial and sarcomatous elements allows the designation of gliosarcoma, a distinct glioblastoma IDH-wildtype subtype. Thus, their histological and immunohistochemical peculiarities should be carefully regarded for an adequate differential diagnosis.

E-PS-17-012

Isocytrate dehidrogenase 1 and 2 (IDH1and IDH2) mutations in brain gliomas – association with tumour grade and patients age

D. Jasar*, K. Kubelka - Sabit, V. Filipovski, E. Stojkoska
*Department of Histopathology and Cytology, Clinical Hospital Acibadem/Sistina, Skopje, Faculty od Medical Sciences, University "Goce Delcev" – Stip, North Macedonia

Background & objectives: Isocytrate Dehidrogenase 1 and 2 (IDH1and IDH2) mutations are frequent findings in gliomas. The

aim of this retrospective study was to determine association between IDH1/2 mutations and the glioma grade with the patients' age.
Methods: Samples from 184 brain glioma patients surgically treated in the period from January 2017 to December 2022 have been re-evaluated. All the patients were histologically and immunohistochemically analysed to determine the type and grade of the tumour according the 2016 CNS WHO guidelines. The samples were further subdivided for IDH1 and IDH2 mutations according molecular analyses report.
Results: No mutations were detected in grade I gliomas (n=13) while in grade II samples (n=31) mutations were observed in 14 cases (45%). Among grade III gliomas (n=58), mutations were found in 32 cases (55%) and in the group of grade IV gliomas only 7 cases were positive (8.5%). Patients with grade I and II gliomas were much younger (range 23-54, mean 39) compared with higher grade gliomas (range 49-72, mean 61, $p<0.05$).
Conclusion: In our study group the majority of IDH1 and IDH2 mutant brain gliomas are more associated with higher tumour grade, possibly with tumour progression from grade II to grade III affecting older patients.

E-PS-17-013
Change in macrophage subtypes ratio is a risk factor for intracranial aneurysm rupture: results of an extended study
M. Koblizek*, M. Hundza Stratilova, A. Hejcl, A. Steklacova, V. Benes, J. Zamecnik
*Department of Pathology and Molecular Medicine, 2nd Faculty of Medicine, Charles University, Motol University Hospital, Prague, Czech Republic

Background & objectives: Prediction of intracranial aneurysm (IA) rupture is complicated as the underlying processes are not well understood. Our team previously presented importance of inflammatory infiltration in this process; however, further extension of studied cases was needed to get more robust data.
Methods: Walls of both ruptured and unruptured intracranial aneurysms were neurosurgically resected, formol fixed and paraffin embedded. Each sample was routinely stained and immunohistochemical studies of CD45R0, HLA-DR and CD163 were performed to identify all leukocytes, M1 and M2 macrophages, respectively. Positive cells were counted in two hot-spots with area 0,314 mm2. Statistical significance was calculated using Mann-Whitney test.
Results: Totally 56 IAs (ruptured n = 20, unruptured n = 36) from 55 individuals (38 females, 17 males) were collected. Morphological changes of the vessel wall such as fibrosis and destruction of elastic membranes were observed both in ruptured and unruptured IAs. Quantity of all inflammatory elements was significantly higher in the specimens of ruptured IAs ($p < 0.001$). The M2:M1 ratio was low in the unruptured aneurysms. The ruptured aneurysms showed increased M2:M1 ratio to > 1 and the difference between ratios in ruptured and unruptured IAs was statistically significant ($p < 0.001$).
Conclusion: This study shows that there is significant increase in quantity of macrophages and increase of M2:M1 ratio in ruptured intracranial aneurysms. We presume that these changes had to precede the rupture as the most of the patients with the aneurysm rupture were surgically treated shortly after clinical presentation.
Funding: Supported by grant NU22-08-00124.

E-PS-17-014
Primary central nervous system GFAP-negative pleomorphic tumour with histiocytic differentiation?
O. Kuczkiewicz-Siemion*, M. Zdzienicki, P. Rutkowski, K. Seliga, A. Tysarowski, A. Szumera-Ciećkiewicz
*Department of Pathology, Maria Sklodowska-Curie National Research Institute of Oncology Warsaw, Poland

Background & objectives: The BRAF mutation is characteristic of specific subtypes of brain tumours as well as tumours of histiocytic origin. We describe a case of a 43-old male with a BRAF-positive brain tumour located in the lateral sulcus area.
Methods: The tumour was under observation from October 2021, when the patient presented with an epileptic seizure. In January 2023, the patient was qualified for the tumour excision and sent for histopathological evaluation. The follow-up in March 2023 revealed tumour progression.
Results: The histopathological examination showed a tumour composed of large pleomorphic epithelioid to rhabdoid cells with abundant eosinophilic cytoplasm, sometimes multinucleated, with scattered mitotic activity and focal necrosis. No microvascular proliferation was present. Additionally, the inflammatory and histiocytic background was prominent, with neutrophilic emperipolesis manifesting throughout the tumour area. By immunohistochemical evaluation the pleomorphic cells were: BRAF(+),S100(+),CD163(+),CD68(+/-)focally,GFAP(-),synaptophysin (-),IDH1R132H(-),olig2(-),ATRX(+),PR(-),EMA(-),ALK1(-),CD30 (-),CD15(-),CD3(-),CD20(-),CD23(-),CD117(-),MPO(-),Langerin(-), CD1a(-), SOX-10(-),HMB-45(-),MelanA(-),CD34(-),CKPan (-),SMA(-),desmin(-),MyoD1(-),Myogenin(-),Lysozym(-),EBER(IHS) (-),Ki-67(+)10%. The tumour exhibited an abundant underlying reticulin network, enclosing individual or small groups of neoplastic cells. The preliminary diagnosis of histiocytic sarcoma was established. The tumour tissue was sent for extended NGS analysis.
Conclusion: The principal differential diagnosis included histiocytic sarcoma, pleomorphic xanthoastrocytoma and Rosai-Dorfman disease. However, none of the diagnostic criteria was fully met. The clinical course of the disease is relatively slow, and the mitotic index is low. Additionally, an interesting finding was neutrophils emperipolesis demonstrated throughout the tumour.

E-PS-17-015
Alk-positive histiocytosis of the cavernous sinus and sellar region in an elderly woman
M.E. Maracci*, L. Cardisciani, C. Ravaioli, E. Sabattini, M. Zoli, D. Mazzatenta, S. Asioli
*School of Anatomic Pathology, Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

Background & objectives: alk-positive histiocytosis (ah) is a histiocytic neoplasm first reported by chan jk et al. with multisystem or single-organ involvement and common favourable outcome. the histiocytic cells show mild cytologic atypia, positivity for histyocyte-associated markers, alk protein, and alk gene rearrangement.
Methods: a 70-year-old female with a unremarkable personal history developed acromegalic features. in the suspicion of a somatotroph pitnet/adenoma she underwent mri that revealed a right cavernous sinus mass with infra-laterosellar extension, that was resected.
Results: a diffuse cohesive polygonal cell proliferation with finely granular, mildly eosinophilic cytoplasm, without nuclear atypia was observed with scattered adenohypophyseal cells. mitoses and ki67-index were low. neoplastic cells showed positive cd68 and alk, patchy staining for s-100, negative cd1a, braf-v600e, gfap, ttf-1, pituitary transcription factors, gh, chromogranin-a, brachyury, cytokeratin cam 5.2. ini-1 was preserved. a diagnosis of alk-positive histiocytosis was rendered.
Conclusion: we first report the case of a ah in the cavernous sinus in an elderly female with acromegalic features. The association of adenohypophyseal hypersecretion syndromes with ah has never been reported. Possible mechanisms explaining this association might be gh-hypersecretion induced by histiocytic cells, induction of local proliferative signals on the adjacent adenohypophyseal-neurosecretory cells or the presence of a metachronous pitnet/adenoma. in our case, no

neuroendocrine cell proliferation was detected, so we might primarily suppose that alk positive histyocytes induced gh-hypersecretion.

E-PS-17-016

Primary melanoma of the brain: a case report of an extremely rare tumour

I. Provatas*, P. Pantoula, E. Ventouri, D. Glarelis, M. Karagianni
*Pathology Laboratory, General Hospital of Nikaia - Piraeus "Ag. Panteleimon", Greece

Background & objectives: Melanoma of the brain is an extremely rare neoplasm, with most cases reported in the fourth and fifth decade. It has predilection for spinal cord or posterior fossa and it may appear with cord compression symptoms or mass effects.
Methods: We report case of a 51 year-old female, with mass effect and without history of cutaneous, ophthalmic or mucosal melanocytic lesions, who was operated for a tumour located in the brainstem. Multiple segments of a dark brown, solid, elastic and partially friable tumour were received, 4 cm in maximum diameter.
Results: On microscopic examination, the tumour segments consisted of compact aggregations and nests of homogenous, epithelioid or spindle-shaped cells, with high nuclear atypia, eosinophilic and focally amphiphilic or clear cytoplasm, with medium-sized vesicular nuclei and apparent nucleoli, in a relatively sclerotic stroma. 14 mitoses / 10 HPF were counted and there were focal extracellular melanin depositions, many melanophage aggregations and extended necroses. The immunohistochemical control of the neoplasm revealed strong expression of S-100, HMB-45, MART-1 and negativity for EMA, GFAP, CKAE1/AE3. Cell proliferation rate was very high, ~ 85%.
Conclusion: Melanocytes are found normally in small numbers in the leptomeninges, but they are most frequently met over the anterior / lateral cord, brainstem, base of brain. They may give rise to rare primary central nerve system melanocytic tumours, such as diffuse melanocytosis, melanocytoma and malignant melanoma. The diagnosis of primary melanoma is challenging, because of the morphological similarities with metastatic melanoma. In this occasion, it very important to exclude clinically other primary sites, especially skin, eyes or mucosae.

E-PS-17-017

Myeloid sarcoma of the brain and spinal cord: three case reports

S. Yilmaz Erozbek*, N. Yeldir, A. Çakır
*Department of Pathology, Istanbul Medipol University, Turkey

Background & objectives: Myeloid sarcoma (MS) is an extramedullary mass composed of myeloblasts, can occur at any age, can develop in skin, lymph nodes, bone-soft tissue, gastrointestinal tract but central nervous system is rare. Patients have concurrent or existing myeloid neoplasia.MS sometimes develops de-novo.
Methods: We present 3 cases of myeloid sarcoma located in the central nervous system (two spinal, one brain).
Results: Two patients were female. The ages of the patients were 3, 7 and 65 years. One patient had Down syndrome and was diagnosed with acute myeloid leukaemia (AML) and her mass was paraventricular. The masses in the other two regions were cervical and thoracic extradural localized. Histopathological, blastoid cells with prominent nucleolus and high mitotic activity was observed. Although the blastoid cell morphology varied from case to case, immature, monocytoid and plasmacytoid appearance were noted. Immunohistochemical expression differed in each tumour; CD33, MPO, CD34, CD117, CD68, lysozyme, CD45 positivity were observed. FLT-3 mutated AML was detected in the bone marrow of the case whose mass was in cervical spinal.
Conclusion: MS are masses formed by myeloblasts with different morphological features. It shows abnormalities in cytogenetics and complications like AML. Although the differential diagnosis varies according to its localization, it includes carcinoma, melanoma, lymphomas, plasmacytoid dendritic cell sarcoma, histiocytic sarcoma. These tumours especially kept in mind in de-novo MS. It should not be forgotten that MS can be seen in any localization at any age, and patients should be investigated for myeloid neoplasms.

E-PS-17-018

Proposed to consider so called "low-grade astrocytoma, IDH-wildtype" as a tumour with a similar prognosis to glioblastoma, IDH-wildtype – Providing more simplified guidance for treatment to clinical departments

C. Yoo*, U. Cho, S.H. Yang
*The Catholic University of Korea, St. Vincent Hospital, Republic of Korea

Background & objectives: Glioma, IDH-mutant is a completely different disease from glioma, IDH-wildtype. Therefore, it was assumed that "low-grade astrocytoma, IDH-wildtype (LAIDHW)" is more like a glioblastoma, IDH-wildtype (GBIDHW). In this study, we looked at whether LAIDHW showed a similar prognosis to GBIDHW.
Methods: We collected 85 cases of adult gliomas diagnosed from 2000 to 2018 in this institute. We reclassified the study cases according to the 2020 WHO. We were going to see how much LAIDHW was among them, and analysed whether there was a difference in survival time between low grade (grade 2) astrocytoma, IDH-mutant (LAIDHM), LAIDHW and GBIDHW using Log-Rank test.
Results: Among them were 47 (55.3%) cases GBIDHW and 25 (29.4%) cases astrocytoma, IDH-mutant including 14 (16.5%), 5 (5.8%) and 6 (7.1%) cases of grade 2, 3 and 4, respectively. Cases included in this group were previously diagnosed IDH-mutant anaplastic astrocytoma and glioblastoma. The other 13 (15.3%) cases were identified as LAIDHW. Therefore, it can be seen that LAIDHW which presents diagnostic difficulties accounts for a considerable amount. There were definite survival differences between LAIDHM and GBIDHW ($p=0.01$) as is well known. The survival curve between LAIDHM and LAIDHW showed a tendency to differ in survival but statistically insignificant ($p=0.15$). The survival difference between LAIDHW and GBIDHW was not found ($p=0.42$).
Conclusion: We expected to see the survival difference between LAIDHW and LAIDHM. Unfortunately, there was no statistical significance, just a trend. The low number of cases is thought to be the reason for the weak statistics. It was difficult to see that there was a difference in survival period between LAIDHW and GBIDHW. We think statistical evidence will emerge as we add to the number of cases in the future, and we can safely include LAIDHW into the group of GBIDHW.

E-PS-18 | E-Posters Ophthalmic Pathology

E-PS-18-001

Primary CNS lymphoma – ocular variant: clinical and pathological features and treatment outcomes

H. Fadlelseed*, M. Rhatigan, M. Treacy, C. Murphy, S. Kennedy, D. Kilmartin
*Department of Pathology, St Vincent's University Hospital, Dublin, Ireland

Background & objectives: Ocular lymphoma is a subtype of primary CNS lymphoma (PCNSL). Cytological analysis of vitreous fluid is the gold standard in diagnosis. MYD88 L265p mutation and IL10: IL6 >1 are useful tools for diagnosis. Chemotherapy is the mainstay of treatment.
Methods: Retrospective review of medical records and pathology specimens of 169 patients with suspected ocular lymphoma over an 11-year period in a tertiary hospital was carried out. Clinical

data was gathered including patient's gender, age at disease onset, medical history, clinical findings, laboratory investigations, mode of diagnosis, therapeutic regime, recurrence rate and ocular and overall outcome.
Results: A total of six patients had cytology confirmed PCNSL-O. All were diagnosed by pars plana vitrectomy. The average age was 72 years with a range from 58- 82 years old. Three patients were male and three were female. Four patients had bilateral ocular disease and two had unilateral. All patients were treated with chemotherapy and one had brain radiotherapy. MYD88 mutation was confirmed in three patients. IL-10: IL-6 ratio was >1 in the vitreous fluid of three cases which strongly assists the diagnosis of PCNSL -O. All patients are alive, four are disease free, one had CNS relapse and one is on first- line local chemotherapy treatment.
Conclusion: This case series demonstrated excellent treatment outcomes with all six patients alive at the time of the study. Both local radiotherapy and chemotherapy achieved good ocular control. The high ratio of IL-10: IL-6 in the vitreous fluid strongly assists the diagnosis of PCNSL -O. MYD88 L265P mutation is a valuable diagnostic and promising tool; particularly in cases where limited vitreous material makes cytological evaluation challenging. However, molecular and interleukins results should be interpreted within the clinical and cytological context.

E-PS-18-003
Primary malignant melanomas of the uvea - a case report series
E. Lampri*, I. Tragani, S. Sotiriou, P. Zafeiropoulos, D. Dimou, I. Parthymos, C. Kalogeropoulos
*Department of Pathology, University Hospital of Ioannina, Greece

Background & objectives: Uveal melanoma (UM) is the most frequent primary intraocular malignancy, however it represents a relatively rare neoplasm. A case series of UM of the past decade is derived from the archive of the Pathology Department of University Hospital of Ioannina.
Methods: Nine cases of melanoma on specimens of orbital enucleation were included. Fixation, gross examination and sampling, in addition to Grading and Staging, were processed according to up-to-date version of the College of American Pathologists' "Protocol for the Examination of Specimens From Patients With Uveal Melanoma" on time of diagnosis. Microscopic evaluation involved standard hematoxylin-eosin staining and application of immunohistochemical markers.
Results: Interestingly, seven out of nine patients were males with affection of the left eye (78%), while the mean age of diagnosis was 66 years (ranged 42-82). All tumours concerned choroidal melanomas of medium to large size, with R0 excision, and two arised from pre-existing nevi. Six cases had mixed-cell histologic type and three cases had spindle-cell histologic type, whereas none qualified as an epithelioid-cell melanoma. Scleral involvement was found in five cases, one of which with extrascleral extension, and ciliary body was involved in three cases. Optic nerve invasion and vascular emboli were observed in only one case each (11% each). Pathologic Stage ranged between pT2a and pT3c.
Conclusion: UM is a slow growing tumour with a high tendency to metastasize, particularly to the liver, even years after surgery. Metastases are associated with limited overall survival, hence detection and treatment of small lesions are essential for optimal patient care. Pathologists' role in providing information about Grading and Staging is crucial, guiding treatment and follow-up surveillance. Our findings support prior literature regarding UM, except of high prevalence of left laterality, and hopefully will contribute to further understanding of this disease.

E-PS-19 | E-Posters Paediatric and Perinatal Pathology

E-PS-19-001
Ovarian central-type PNET of medulloepithelioma subtype in a young female
S. Al-Dandan*, N. AlHawashim, M. Elhassan, H. Fatani
*King Fahad Medical City/King Fahad Hospital Hofuf, Saudi Arabia

Background & objectives: Primary primitive neuroectodermal tumour (PNET) of the ovary is a rare neoplasm. Medulloepithelioma is a subtype of central PNET and a highly malignant embryonal tumour. There are only 13 cases described up to date in the English literature.
Methods: A 16-year-old female patient presented with a right adnexal mass and ascites. The enhanced abdominopelvic CT scan revealed a large heterogeneously enhancing right ovarian mass associated with peritoneal and omental nodularity. The patient underwent right salpingo-oophorectomy and remained in remission for ten months until she developed peritoneal deposits. The patient eventually developed pancytopenia and pneumonia and died.
Results: Histopathological examination of the salpingo-oophorectomy specimen revealed minor teratomatous growth with mature and immature elements. The bulk of the tumour was composed of primitive neuroectodermal tissue with variable morphologic patterns. There were anastomosing cords and loops of pseudostratified neuroepithelial cells in addition to papillary and tubular formations. The trabeculae focally encircled loose and pale vitreous-like mesenchymal tissue. Anaplastic features (nuclear gigantism and atypical mitoses) were evident. The apical surface was Alcian Blue-positive, while the basement membrane was PAS-positive. Tumour cells were reactive to PAX8 immunostain, indicating differentiation towards the ocular ciliary body. Next-generation sequencing showed a pathogenic variant in the TP3 gene and no amplification of C19MC.
Conclusion: Ovarian medulloepitheliomas are best viewed as monophasic teratomas due to their exclusive or almost exclusive neuroectodermal composition. Despite aggressive therapy, the tumour disseminated and proved fatal within two years. The anaplasia and TP3 gene pathogenic variant may explain, in whole or part, the poor clinical outcome. The proper classification of medulloepithelioma remains unclear, and treatment protocols are yet to be established.

E-PS-19-002
A fatal case of DiGeorge syndrome and tetralogy of fallot in a newborn: an autopsy report and histopathologic insights
S. Andrei Dan*, M. Boroș
*Spitalul Clinic Judetean de Urgenta Oradea, Romania

Background & objectives: DiGeorge syndrome, a congenital disorder resulting from a microdeletion at 22q11.2, is characterized by a hypoplastic/absent thymus, cardiac malformations, including tetralogy of Fallot, and parathyroid hypoplasia. This case report aims to compare the antenatal diagnosis with autopsy and histopathologic findings.
Methods: Antenatal diagnosis was made using genetic testing and imaging techniques, revealing thymus agenesis, corpus callosum agenesis and the tetralogy of Fallot. Postmortem examination was performed using standard techniques. Gross and microscopic examination was done on representative tissue samples. The autopsy findings were analysed and correlated with the antenatal diagnosis to evaluate the accuracy of prenatal diagnosis in DiGeorge syndrome.
Results: The autopsy findings revealed craniofacial dysmorphism, hydrocephalus, as well as thymus hypoplasia, corpus callosum agenesis, hydronephrosis and hydroureter secondary to uretero-vesical stenosis, tight pulmonary stenosis, ventricular septal defect, overriding aorta, and right ventricular hypertrophy, confirming DiGeorge syndrome with tetralogy of Fallot and other anomalies. Following microscopic

examination, the foetus presented with diffuse pulmonary lymphangiomatosis and foci of extramedullary hematopoiesis in the liver. The bladder muscular wall showed hypertrophy and denuded urothelium. Overall, the autopsy findings confirmed the antenatal diagnosis of DiGeorge syndrome with tetralogy of Fallot and revealed several other malformations.
Conclusion: This case report highlights the challenges in accurately diagnosing and managing complex congenital anomalies such as DiGeorge syndrome and tetralogy of Fallot. Despite antenatal diagnosis, the patient's clinical course was complicated by multiple systemic abnormalities, resulting in cardiorespiratory arrest and death. Autopsy findings revealed thymus hypoplasia, not agenesia, and other extensive malformations affecting various organs that were not diagnosed antenatally. This case emphasizes the importance of early and comprehensive evaluation of foetal anomalies in order to improve patient outcome.

E-PS-19-004
An unusual location of a synovialosarcoma in a child, a case report
A. Bdioui*, L. Jaidane, S. Mestiri, A. Baccouche, O. Belkacem, S. Hmissa
*Sahloul Hôpital of Sousse, Tunisia

Background & objectives: Malignant cardiac tumours are rare, especially in a paediatric age. It is dominated by the rhabdomyosarcoma, synovialosarcoma is exceptional. We report a case of a 12-year-old child, for which a cardiac synovialosarcoma was discovered.
Methods: We report a case of a 12 year old boy, without significant pathological history, who presents to the emergency room in a state of cardiogenic choc. He was admitted to the intensive care unit. A cardiac echography highlighted an intra cavitary mass.
Results: The material brought back was friable yellowish, mimicking a mass of 10 cm. it showed, microscopically, a hypercellular malignant tumoral proliferation infiltrating the ventricular muscle. This proliferation was arranged in storiform pattern composed with monomorphic ovoid cells. The atypia was slight. The figures of mitosis were numerous. The stroma, richly vascularized, showed a haemangiopericidal appearance. On immunohistochemistry the tumour cells were positive for TLE and focally for CD99. However, they were negative for EMA, AML, Desmin, CD34, Erg and for Myod1.
Conclusion: However, this entity is rare, it is not exceptional. The sites of predilection are the pericardium followed by the left ventricle. Although the recruitment of cardiac surgical specimens is frequent in our department, only one case of ventricular synovialosarcoma has been identified in recent years.

E-PS-19-005
Misleading presentation of an inflammatory myofibroblastic tumour of maxillary sinus, a report of a paediatric case
A. Bdioui*, K. Bilazreg, A. Baccouche, O. Belkacem, S. Mestiri, S. Hmissa
*Sahloul Hôpital of Sousse, Tunisia

Background & objectives: Inflammatory myofibroblastic tumour (IMT) is a rare neoplasia, occurring primarily in the viscera of children and young adults. The head and neck region is relatively less commonly involved. Herein we report another rare case of maxillary sinus' IMT.
Methods: A 13-year-old patient with recurrent nasal inflammatory pseudoplyposis, presented in the department of maxillo facial surgery for tumour of right maxillary sinus with epistaxis. He underwent a surgical biopsy.
We received whitish and haemorrhagic small specimen, whose size varies between 0.4 and 3 cm.
Results: Histologically, the specimen was boarded by respiratory epithelium, lining a lamina propria with abundant lymphocytic and plasmacytic infiltrate. Within this infiltrate, we found scattered cells with abundant amphophilic cytoplasm containing an enlarged nuclei and a distinct nucleoli. There were no necrosis and no mitotic activity. The first suspected diagnosis was Hodgkin lymphoma and rhabdomyosarcoma, considering the age of the patient and the location of the tumour, therefore, the tumours cells were negatives for CD15,CD30, Myogenin and MyoD1.
The case was then presented to a paediatric pathology expert, IMT was evocated, the expression of ALK1 and the morphological features were in line with this diagnosis.
Conclusion: IMTs affecting the nasal cavity and paranasal sinuses are rarely described in the english literature. Unlike our case, the cases of IMT in nasal cavity and paranasal sinuses described in the literature can arise in patients of all ages more commonly in adults. The most frequently affected site is the maxillary sinus. Some IMT have large histiocytoid cells resembling ganglion cells or Reed-Sternberg cells of Hodgkin lymphoma. The presence of these cells is related to poorer clinical outcomes.

E-PS-19-006
Rare simultaneous appearance of maternal neuroendocrine carcinoma and giant placental chorangioma in a preterm male pregnancy
D.P. Burlacu*, A. Burlacu, B. Szabo, T. Mezei
*Department of Pathology of Emergency Clinical Hospital of Targu-Mures, Romania

Background & objectives: Giant placental chorangioma (GPC) is a rare indolent vascular tumour greater than 5 cm, affecting 1 in 10.000 female pregnancies. We report the case of a GPC occurring in a preterm male pregnancy complicated with congestive heart failure.
Methods: A normotensive, nondiabetic 30-week primigravida was admitted to our hospital complaining of severe abdominal pain. Medical history revealed an advanced-stage rectal neuroendocrine carcinoma. Ultrasonography showed a morphologically normal foetus, except for cardiomegaly. A well-vascularized placental tumour with arterio-venous shunts was also discovered. A C-section was performed, and a 1500 g premature male foetus with congestive heart failure was delivered.
Results: A 16x14x2.5 cm placenta weighing 577 g with a tan, fleshy tumour near the umbilical cord measuring 13.5x11.5 x 6.5 cm, weighing 412 g, was submitted to our Pathology Department. Microscopically, the tumour was unencapsulated but well-circumscribed, with a lobular architecture mainly composed of congested vascular capillaries and thin-walled vessels. Immunohistochemistry revealed CD31-positive endothelial cells lining the vessels. Cytokeratin 18 focal positivity suggested a chorionic plate and anchoring villi origin of the vessels. No mitotic figures nor significant cytological atypia were encountered. Given the dimensions and weight of the tumour, a diagnosis of giant placental chorangioma (GPC) was rendered.
Conclusion: GPC is a rare and challenging condition. Typically, it occurs in hypertensive or diabetic primigravidas with female foetuses. GPC in a preterm male pregnancy complicated with foetal congestive heart failure highlights the importance of timely antenatal diagnosis and appropriate management to prevent possible complications in order to provide a favourable perinatal outcome. To our best knowledge, this is the first case reporting the existence of a maternal neuroendocrine carcinoma associated with a benign placental tumour.

E-PS-19-007
Human herpesvirus 6 associated encephalitis with fulminant brain oedema in a 5-month-old child: a case report
J. Carneiro Melo*, Á. Macêdo Freire, G. Carvalho de Freitas Soares, B.R. Novais Lima, S. Samuel Feitosa Machado, R. Beserra Landim, C. Gleidiston Lima da Silva
*Univesity of Fortaleza, Brazil

Background & objectives: Human Herpes Virus 6 (HHV-6)'s infections occur mainly during childhood, causing a variety of clinical

manifestations, usually with a benign course. The aim of this paper is to report a case of HHV-6 encephalitis with fulminant cerebral oedema.
Methods: This is an autopsy case of a 5-month-old child who had pneumonia, requiring hospitalization. After the resolution of the condition, he was discharged in good general condition without alterations in the physical examination. 2 days later, he got cough, runny nose and irritability in the 24 hours before his death.
Results: At the autopsy examination, the brain had a soft consistency, with significant oedema, mainly in the grey matter and small foci of subarachnoid haemorrhage. CSF was collected and sent for laboratory analysis, in which HHV-6 was detected by means of PCR in the cerebrospinal fluid (CSF). Histopathological analysis of the brain tissue showed diffuse and intense cerebral oedema, in addition to lymphocytic inflammatory infiltrate in the meninges.
Conclusion: HHV-6 is an uncommon cause of central nervous system infection, primarily affecting immunocompromised patients. In other reports, the febrile syndrome is frequent, associated with irritability or seizures, in addition to imaging findings compatible with diffuse cerebral oedema and CRP detected in the CSF. Although HHV-6 is a rare cause of encephalitis in children, it is important to consider it as a differential diagnosis in the presence of cerebral oedema, as HHV-6 can be lethal, even in immunocompetent children.

E-PS-19-008
Waardenburg anophthalmia syndrome: case report and a review of the literature
A.B. Çetinkaya*, M.B. Bereketoğlu, B.N. Ateş, S. Büyükkurt, S. Tuğ Bozdoğan, K. Erdogan
*Department of Pathology, Faculty of Medicine, Cukurova University, Adana, Turkey

Background & objectives: Waardenburg anophthalmia syndrome (WAS) is a rare autosomal recessive genetic disorder that is caused by *SMOC1* gene mutation. Present case is an autopsy case of genetically proven WAS.
Methods: Approximately 300,000 SNP markers were examined by SNP arrays with Human Cyto SNP-12 DNA Analysis Bead Chip v2.1 kit (Illumina, San Diego, California, USA). Blue Fuse Multi Software and Genome Studio Data Analysis Software v.2011.1 assisted to analyse that were based on the reference human genome (hg19/GRCh37) and interpreted according to ISCA and ACMG guidelines.
Results: The presenting case was a male foetus. The gestational age was 24 weeks, proven by second trimester ultrasound measurement. Physical examination showed microcephaly, agenesis of the 5th toe of both feet, tibial bowing, rocker bottom feet, left eye anophthalmia and right eye severe microphtalmia, antevert nose, microretrognathia, low set ears. The thoracal, and abdominal cavity examination revealed agenesis of right hemidiaphragm and horseshoe kidney. On radiographic examination, limb abnormalities such as hypoplastic and bowing tibia and fibula, hip dislocation and cleft vertebra were detected. SNP arrays showed, 203 kb homozygous deletion containing the entire *SMOC1* gene as well as heterozygous 203 kb deletion in parents.
Conclusion: This is the first case that the homozygous *SMOC1* whole gene deletion was observed in the literature. Hemidiaphragm agenesis is the other unique finding that was not reported yet.
In conclusion, Waardenburg Anophtalmia syndrome is a rare disorder that should be kept in mind in patients with anophthalmia and limb abnormalities.

E-PS-19-009
Recurrent respiratory papillomatosis: a case of lung transplantation as a therapeutic option
A. Chaachou Charradi*, I. Sansano Valero, J. Camacho Soriano, M. Garrido Pontnou, C.E. Haro Haro, A. Navarro Jiménez
*Vall d'Hebron University Hospital, Spain

Background & objectives: Recurrent respiratory papillomatosis (RRP) is a benign entity of the aerodigestive tract caused by human papillomavirus (HPV), mainly affecting children and young adults. Papillomas appear as exophytic nodules, mostly laryngeal, but occasionally in the nasopharynx, tracheobronchial tree and lung parenchyma.
Methods: We reviewed the case of a 13-year-old patient transplanted bipulmonary due to chronic respiratory failure secondary to laryngeal papillomatosis with pulmonary dissemination.
Results: Our patients was diagnosed at 3 months age, as the majority of infections occur at birth, during passage through the birth canal of infected mothers.
Upon histopathological study of the lung explants, we identified a multifocal proliferation of lesions composed of nested squamous cells with fibrovascular axis. These cells showed minimal atypia with prominent nucleoli, poorly demarcated eosinophilic cytoplasm and few mitotic figures. Its growth pattern was expansive, and no areas of invasion were identified.
A polymerase chain reaction (PCR) test was performed on this tissue, yielding a positive result for HPV serotype 11, which, together with HPV-6, is responsible for most cases of RRP.
Conclusion: Despite being a generally benign entity, RRP can present serious complications, especially with the pulmonary parenchyma involvement, even reaching malignant transformation.
Its clinical manifestations are mainly respiratory and can end in respiratory failure as in our case.
Currently, no curative treatment has been developed and surgery remains the mainstay of treatment. Although bipulmonary transplantation is not described in the literature as a therapeutic option in RRP with lower airway involvement, we present the first case with good evolution so far.

E-PS-19-010
Sex cord-stromal ovarian: a 10-year experience with paediatric ovarian tumours in a surgical pathology department from a tertiary Portuguese hospital
C. Courelas*, A. Alves, J. Gama, J. Pimentel, V. Almeida, A. Lai, R. Almeida
*Pathology Department, Coimbra Hospital and University Centre (CHUC), Portugal

Background & objectives: Paediatric ovarian tumours are rare. Sex cord-stromal tumours (SCST) are even rarer, and diagnosis is challenging due to their heterogeneous histologic features. This study aims to describe 10 years of experience diagnosing these tumours in a Portuguese Surgical Pathology Department.
Methods: We collected histopathological data from all paediatric ovarian tumours diagnosed in girls younger than 18-year-old, from 2012 to 2022, by the Surgical Pathology Department from Coimbra Hospital and University Centre. SCST were further analysed according to malignant potential, treatment, and follow-up information.
Results: In the 10 years, 82 ovarian paediatric tumours were diagnosed: 58,5% Germ cell tumours, 31.7% Epithelial tumours and 9.8% SCST. Over this period, the distribution was uneven - 2019/2020 showed a sharp decrease in cases, with a slow recovery since 2021. Age distribution ranged between 2-18 years old, mean 14 ± 3.89 - 50% 15 years or older.
Relating to SCST the sample included: fibroma (2/8), sclerosing stromal tumour (2/8), granulosa cell tumour (3/8) and Sertoli-Leydig cell tumour (1/8). Besides surgery, two patients were eligible for neoadjuvant chemotherapy. Currently, we have follow-up information on 6 patients, all disease-free, with no recurrence or progression history.
Conclusion: In our department, about eight cases per year of paediatric ovarian tumours were diagnosed, with a marked decrease in the pandemic years. Germ cell tumours were the most frequent (58,5%).

In our sample, 9,8% were SCST, 2/8 were eligible for neoadjuvant treatment. Currently, all are alive, disease-free, and without recurrence or progression reported. Our data do not show significant differences from those reported in literature. A large sample is needed because of the rarity of these neoplasms.

E-PS-19-011

Investigating the presence of microplastics and additives on complicated pregnancy: a study of human amniotic fluids and placentas

P. Delongová*, P. Hurník, J. Škarda, J. Halfar, K. Čabanova, K. Vávra, R. Špaček, O. Šimetka
*Institute of Pathology and Molecular Genetics, University Hospital of Ostrava, Czech Republic

Background & objectives: Recently it was demonstrated by numerous studies that microplastics are almost ubiquitous in various environments. Thus, exposure of pregnant women to microplastics poses a possible risk to the unborn child.
Methods: All women involved in this study had physiological, singleton pregnancies complicated with preterm prelabour rupture of membranes (PPROM). 20 samples of amniotic fluid and placenta from 10 patients were analysed for the presence of microplastics and plastic additives by Fourier transform infrared spectroscopy - attenuated total reflectance (FTIR–ATR) after alkaline digestion with KOH.
Results: 9 of 10 patients were found to have microplastics or additives in amniotic fluid, placenta, or both. The most represented materials were Chlorinated Polyethylene (CPE) and Calcium zinc PVC Stabilizer.
Conclusion: This study presents the first evidence of the simultaneous presence of microplastics and additives in amniotic fluid and placentas.
Funding: 16/RVO-FNOs/2021

E-PS-19-014

Two true knots in umbilical cord: a report of two cases with different pathological findings and clinical implications

C. Gouta*, S. Angelidou, D. Dalakoura, E. Demertzidou, E. Hanioti, M. Paida, E. Ralli, E. Sakellariou, A. Kougioumtzidou, A. Sotiriadis
*Department of Histopathology, Hippokration General Hospital of Thessaloniki, Greece

Background & objectives: The incidence of a single true knot in umbilical cord ranges from 0,3 to 2% of all pregnancies. We report two cases of two true umbilical knots with completely different histopathological findings and clinical presentation.
Methods: Case 1: A 30-year-old woman presented at the emergency department due to reduced foetal movements at 33w+3d of gestation. Intrauterine foetal demise was verified and a caesarean section was performed. Case 2: A 27-year-old woman was referred to our hospital with polyhydramnios at 35w+6d of gestation. After amniocentesis, a nonreactive NST was observed and led to an emergency caesarean section.
Results: Case1: Macroscopic examination revealed the existence of two simple, tight true umbilical knots. The umbilical cord appeared hyper-coiled and exceeded in length the 90th percentile for the gestational age. Microscopically, the diagnosis of acute, sub-acute and chronic foetal vascular malperfusion was established and attributed to the umbilical cord obstruction. Case 2: Macroscopic examination showed the existence of two simple, loose true knots in umbilical cord. Additionally, a single umbilical artery was observed. Microscopic examination of the placental disc displayed no specific lesions but rather findings compatible with early adaptation to acute hypoxia. The two true umbilical knots were therefore considered to be an incidental finding.
Conclusion: While the existence of a single true knot is encountered in the everyday practice, the occurrence of more than one umbilical knot is quite rare. To our knowledge, the exact prevalence of two true knots in general population has not been documented and only a short number of cases have been reported. Our case report contributes to the literature presenting two rare cases of two true umbilical knots with diverse predisposing factors, varying macroscopic and microscopic findings and clinical outcomes.

E-PS-19-015

Vulvar botryoid variant of embryonal rhabdomyosarcoma in a 5 months old girl

B. Malkoc*, B. Dogan Gun, E. Kaymaz, F. Kutlu, N. Yuksek, D. Bilgili, B.H. Guvenc
*Ardahan State Hospital Pathology Division, Turkey

Background & objectives: Rhabdomyosarcoma (RMS) originates from primary mesenchymal cells that show skeletal muscle differentiation, being the third most common extracranial malignant solid tumour in children and adolescents. Genitourinary location compromise 20% of the primary site, but vulvar location is exceptional.
Methods: We report a 5 months old girl presenting with vulvar mass in gross appearance of "grape bunches", initially recognized as small polypoid lesion during newborn period. Abdominal MR showed 4.5x2.6x2 cm sized, lobulated and well-demarcated vulvar lesion neighbouring left of urethral meatus. The resident mass was finally removed totally, successfully saving the urethral meatus, following initial incisional biopsy and chemotherapy.
Results: Histopathologic evaluation of incisional biopsy material revealed focally ulcerated squamous epithelium, neighbouring hypercellular rhabdomyoblastic groups, as described cambium layer which is specific for Botryoid variant of Embryonal RMS. These atypical cells had narrow cytoplasm, contained oval or spindle shaped hyperchromatic nuclei, no necrosis, significant mitotic activity and pleomorphism. Occasionally some of them had broad cytoplasm and rhabdoid morphology, the nucleus was located peripherally.
Following successful chemotherapy and fertility-preserving surgery, pathologic evaluation showed cytodifferentiation due to chemotherapy and contained numerous maturating rhabdomyoblasts. Ki-67 proliferation index was 2-3% and proximal surgical border was free of tumour. Currently the patient is in 2 years clinical follow-up without any complaints and progression.
Conclusion: The Paediatric Oncology Group (POG) has declared the assessment of malignancy based on the histological type, presence and amount of the necrosis and mitotic activity. The recurrence rate of vaginal and cervical embryonal RMS is high (70%) in some case series. Thus, all types of RMS must be considered as high-grade sarcomas. New multidrug chemotherapy regimens with or without radiation therapy used in combination with less radical fertility-preserving surgery is promising in treatment with good results.

E-PS-19-016

Management of an infected vesico-urachal diverticulum in a 12-year-old male

B. Malkoc*, F. Kutlu, B.H. Guvenc, F. Sezer
*Ardahan State Hospital Pathology Division, Turkey

Background & objectives: The urachus is an embryonic remnant of the apical portion of the primitive bladder dome and changes into fibrous band during descendance into the pelvis. Vesico-urachal diverticulum is the rarest form of an incomplete obliteration and early diagnosis is important.
Methods: We report a 12-year-old male, complaining of generalized abdominal pain, with no umbilical discharge, diagnosed as infected urachal cyst under ultrasound. A vesico-urachal diverticulum as a focal outpouching at the vesical dome with a narrow opening was confirmed under VCUG and cystoscopic evaluation. The connection between the umbilicus was divided and the mass was totally resected through a Pfannenstiel incision.

Results: Pathological evaluation confirmed a three-layered, non-atypical, 35 x 34 mm sized vesico-urachal diverticulum, with a narrow (5 mm) opening. The inner layer was lined with urothelial epithelium, the middle layer composed of connective tissue including intense chronic inflammation, and the outer muscular layer in continuity with the detrusor muscle. There were no dysplastic enteric or mucinous (signet ring type) cells inside connective tissue or muscular layer. Bladder diverticula on the other hand, are protrusions of the bladder urothelium and mucosa via muscle fibres of the muscularis propria; which results in a thin-walled structure connected to the bladder lumen and poorly empties during micturition.
Conclusion: Case reports advocate surgical intervention as the optimal treatment in patients with vesico-urachal diverticulum manifesting as acute abdominal pain, containing calculus or colic-urachal fistulas, and spontaneous rupture, since urachal anomalies usually do not disappear spontaneously. Timely differential diagnosis in such cases is important, since dysplastic forms as primary urachal carcinoma require early optimal management.

E-PS-19-017
Exceptional association of chromosomal abnormalities: trisomy 15 associated with X triploidy
I. Mallek*, Y. Elaribi, L. Jaidane, H. Abassi, A. Lahmar, S. Hizem, L. Ben Jemaa, H. Jilani, D. Bacha, S. Ben Slama
*Monji Slim La Marsa, Tunisia

Background & objectives: Trisomy 15 is a rare and its association with X triploidy is exceptional. The definitive diagnosis is made according karyotyping resultats. Foetopathological examination confirms morphological anomalies. The aim of this report was to describe an extremely rare chromosomal abnormalities association.
Methods: We report a case of a 29-week-old foetus with trisomy 15 associated with X triploidy.
Results: A morphological ultrasound of a 41-year-old woman, revealed severe and harmonious growth retardation, agenesis of the nasal bones, and clenched hands. Amniocentesis was performed at 26 weeks of gestation and FISH analysis revealed X triploidy. Karyotyping confirmed the X triploidy and revealed also trisomy 15. Therapeutic termination of pregnancy was performed at 29 weeks of gestation. Foetopathological examination showed a female foetus (23-24 weeks of gestation). Malformations included facial dysmorphia with a long neck, a flat forehead, a slightly flared nose, hypertelorism, and retrognathism. The limbs were elongated with clenched hands and thorax was bulging. On organ dissection, no visceral anomalies or brain abnormalities were found.
Conclusion: The cases of trisomy 15 described in the literature are relatively rare. A few were viable at birth. However, skeletal and cardiac malformations, as well as obesity and its metabolic complications put the functional and vital prognosis at stake. Most of these patients rarely reach adolescence. Currently medical progress can extend their life expectancy. But the mental deficiency is constant.

E-PS-19-018
Foetal vascular malperfusion and I-cell disease – a report of 3 cases
S. McGrath*, E. Mooney
*National Maternity Hospital, Ireland

Background & objectives: I-cell disease (Mucolipidosis type II) is a lysosomal storage disorder. Vacuolated placental trophoblasts in I-cell disease are well described. We noted foetal vascular malperfusion in a placenta with I-cell disease and reviewed other cases to examine this association.
Methods: We reviewed placental pathology at a single site to identify all cases in which features of I-cell disease were seen histologically, and a diagnosis of I-cell disease was made in the neonate. This search yielded three suitable cases for review.
Results: All three cases demonstrated classic trophoblast vacuolation, and in one of these cases, the placental findings prompted the neonatal diagnosis. In the preterm case, approximately 30% of the villi were normal in appearance. High grade foetal vascular malperfusion was present in all 3 cases, assessed using the Amsterdam Criteria. No cause of foetal vascular malperfusion was inferred from the cord in any of these cases. Cords were normal or hypocoiled, with central or paracentral insertion. Stem vessel narrowing was seen in all 3 cases.
Conclusion: These cases suggest an association between foetal vascular malperfusion and I-cell disease, which has not been previously described. Cardiovascular disease is a well-recognised feature of I-cell disease, and the finding of foetal vascular malperfusion may presage the identification of cardiovascular abnormalities.

E-PS-19-019
Cases of infantile form of marble disease in the territory of Chuvashia
V. Mironov*, E. Ignatyeva, S. Lezhenina, E. Guryanova, E. Makarova, E. Sapozhnikova, A. Grigoryeva
*Chuvash State University by I.N.Ulianov, Russia

Background & objectives: The paper presents autopsy data on cases of infantile osteopetrosis, caused by a genetic mutation and having specific pathomorphological manifestations. In a retrospective study of 729 pathoanatomical protocols of children's autopsies, we identified 11 cases of the infantile form.
Methods: In a retrospective study of 729 pathoanatomical autopsy protocols for children, 11 cases were identified, of which in 7 cases the diagnosis of marble disease, the infantile form was genetically confirmed. Repeated histological examination of children's organs was performed as follows: bone marrow after additional decalcification was stained according to Romanovsky Giemsa; internal organs by staining with hematoxylin-eosin and Kason.
Results: In most cases, craniostenosis, secondary external non-occlusive hydrocephalus prevailed; atrophy of the optic nerves; flask-shaped thickening of both ends of the ribs, and distal femurs; the medullary canal of the proximal epiphysis of the tibia was not observed in 3 cases, it was completely filled with bone tissue and calcifications; in the bone marrow of the sternum and thigh, there was a decrease in cellularity with a predominance of the reduction of the megacarocyte germ; widespread foci of extramedullary haematopoiesis in the liver; multiple stigmas of dysembryogenesis. In 95% of lethal cases, pulmonary hypoplasia with focal pneumosclerosis was also noted; in all cases, there were manifestations of a secondary immunodeficiency.
Conclusion: The fatal complication in all cases was secondary bronchopneumonia and leukomalacia. In all cases with intravital molecular genetic testing, a mutation was detected - c.807+5g>a in the TCIRG1 gene in a heterozygous state, encoding an osteoclast-specific α3 isoform of one of the subunits of the transmembrane vacuolar ATP-dependent proton pump. An extremely unfavourable combination of this pathology is the underdevelopment of the lung parenchyma with foci of pneumosclerosis.

E-PS-19-020
Sectional observation of a child with a rare case of chromosomal pathology: mosaic variant of trisomy 8 pairs of chromosomes
V. Mironov*, E. Ignatyeva, S. Lezhenina, E. Guryanova, A. Polkovnikov, A. Sapozhnikova, M. Sapozhnikov
*Chuvash State University by I.N.Ulianov, Russia

Background & objectives: Varkani syndrome or trisomy 8 mosaicism is a chromosomal abnormality with an incidence of 1:25,000 to

1:50,000 cases. The purpose of the work is to demonstrate a multi-stage approach to making a pathoanatomical diagnosis.
Methods: We have studied a sectional case of pathoanatomical autopsy of an 8-month-old child with a chromosomal abnormality, which included the stage of autopsy with an assessment of organometric and morphometric parameters, microscopic and histochemical studies of organs with additional staining of the PAS reaction.
Results: Pathologically, the child revealed: agenesis of the corpus callosum, internal non-occlusive hydrocephalus; perimembranous ventricular septal defect (1cm); bilateral ureterohydronephrosis and cryptorchidism; bilateral aplasia of the patella (confirmed x-ray); clinodactyly 2 fingers; deformed phalanx and nail plate of 2 fingers of the right foot; synostosis of the spinous processes C2-C3. Stigmas of dysembryogenesis: sunken nose bridge, snub nose, symmetrical orbital hypertelorism, short palpebral fissures, thick lips, gothic palate, short and wide folded neck, dysplastic large low-lying auricles, transverse palm furrow. On the part of the pancreas, hypoplasia of the islets of Langerhans (2-3 in each lobule) was revealed, the number of PAS-positive cells was reduced.
Conclusion: in the biochemical analysis of cadaveric blood, the content of glycohemoglobin was 5.9%; determination of glucose - the result is negative, acetone at a concentration of 30.5 mg / ml.The mos 47, XY, +8 karyotype was cytogenetically identified. The complications of the disease include: oedema and swelling of the substance of the brain, pronounced metabolic disorders in the form of uncorrectable hyperglycemia, decompensated metabolic acidosis and multiple organ failure. A post-mortem comprehensive approach is needed to clarify this pathology.

E-PS-19-021
Comprehensive assessment of thanatogenetically significant changes in the heart in miscarriages at a period of 15-21 weeks of gestation
V. Mironov*, E. Ignatyeva, S. Lezhenina, E. Guryanova, E. Shamitova
*Chuvash State University by I.N.Ulianov, Russia

Background & objectives: We analysed the dynamics of macrometric parameters and pathomorphological changes in the vegetative ganglia of the heart, contractile and conductive myocardium of foetuses at 15-22 weeks of gestation under the influence of various intrauterine factors.
Methods: The protocols of autopsies of miscarriages with a single method of morphometric analysis of the 121 hearts were retrospectively studied at 15-22 weeks of gestation. First the perimeters of large vessels and outlets, foetal circulatory communications, the mass and volume ofthe heart with separate weighing ofits chambers, the ventricular index were measured. Microscopy of preparations stained with hematoxylin-eosin was performed.
Results: The main causative factors leading to intrauterine foetal death are identified: congenital malformations, intrauterine infection and intrauterine foetal hypoxia. In 50% of cases, intrauterine growth retardation was detected. Weight and hemodynamically significant macrometric parameters of the heart directly depend on the gestational age of the foetus (CI=98%, $p<0.01$). The calculation of the volume of the heart in the foetus is more informative than its size, and in combination with its assessment and the mass of the heart, it serves as strong evidence in ascertaining thanatogenetically significant manifestations of heart failure in the foetus.
Conclusion: Thus, the dynamics of macrometric parameters and pathomorphological changes in the autonomic ganglia, contractile and conductive cardiomyocytes in miscarriages with a gestation period of 15 to 22 weeks are directly dependent on the gestational age and do not have specificity to the nature of the impact of antenatal factors (intrauterine hypoxia, intrauterine infection and congenital developmental anomalies). The noted macrometric indicators make it necessary to revise the existing standards for autopsy studies in foetuses.

E-PS-19-022
Total anomalous pulmonary venous return: two unusual perinatal autopsy cases of a rare diagnosis
C. Mora*, J. Vaz Silva, A. Costa Braga
*Serviço de Anatomia Patológica, Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisbon, Portugal

Background & objectives: Total anomalous pulmonary venous return (TAPVR) accounts for 2% of congenital cardiac anomalies, where pulmonary veins communicate into systemic venous circulation rather than left atrium. Prenatal diagnosis is often missed, with a high mortality in the first year of life.
Methods: We describe two unusual presentations of this entity, with a brief literature review. A 19 day-old term newborn (case 1), presented with cyanosis and severe pulmonary hypertension, and a 3 day-old term newborn (case 2), with a diagnosis of an obstructive TAPVR, whom a stent was placed after birth. After multiple episodes of hemodynamic instability, both newborns deceased.
Results: Regarding the autopsies, in case 1, the pulmonary veins converged into a common descending vertical vein, anterior to the abdominal aorta, which crossed the diaphragm, and drained into the portal vein - infracardiac TAPVR- associated with interatrial defect (ostium secundum type) and a patent ductus arteriosus. Case 2 showed a retroatrial common confluence with a stent, communicating with the innominate vein - obstructive supracardiac TAPVR. The case 1 also had syndactyly of the 5th/6th fingers of the right foot. No facial dysmorphic features were identified. Histopathological examination showed hypoxic-ischemic alterations in both cases and a bronchopneumonia and osmotic tubulopathy in case 2.
Conclusion: Performing an autopsy with meticulous inspection of cardiac vascular connections, pulmonary and systemic circulations, allows more discoveries and a better understanding of TAPVR, resulting in earlier diagnosis and surgical intervention. Despite the improvement of the overall prognosis, our cases had conditions associated with poor outcome which contributed to their demise. We highlight the importance of acknowledgment of this rare entity, as clinical recognition is challenging, and it can be mistaken for respiratory diseases or sudden infant death.

E-PS-19-023
Diffuse multifocal chorangiomatosis: a rare case of placental pathology
O. Pedro*, G. Miranda, M. Honavar, R. Machado-Neves, T. Amaro
*Unidade Local de Saúde de Matosinhos - HPH, Portugal

Background & objectives: To report a case of diffuse multifocal chorangiomatosis, presented in a 27-year-old woman with a history of Type 1 Diabetes and autoimmune thyroiditis presented with a 32+4 weeks gestation and foetal growth restriction with umbilical cord flow abnormalities.
Methods: Six days after the admittance, a caesarean section was performed due to late decelerations in foetal cardiotocography. The delivery was uneventful, with a live female newborn weighing 1350g and Apgar scores of 6/9/9. The newborn was admitted to the neonatal intensive care unit, and both the mother and newborn's hospitalizations were uneventful.
Results: Gross decription: The placenta weighed 237.9 grams with brownish and partially translucent membranes, with marginal insertion. The umbilical cord measured 180 mm in length, with paracentral insertion and hyper-spiralization. The parenchyma showed several compact nodular areas, whitish, yellowish, and reddish, dispersed and occupying 40% to 50% of the placental parenchyma.
Microscopy: There where several nodules of variable size, scattered throughout the placental parenchyma with proliferation of small capillaries with a circumferential layer of pericytes, and occasional

trophoblastic hyperplasia - features consistent with diffuse multifocal chorangiomatosis. Occasional sclerotic, avascular, and oedematous villi were noted.
Conclusion: Chorangiomas have an incidence rate between 0.5% and 1%, and the diffuse multifocal form is even rarer (0.23%). This condition is associated with preeclampsia, twin gestation, intrauterine growth restriction, congenital malformations, and avascular villi, suggesting that this process may represent an abnormal response to hypoxia in very immature placentas.

E-PS-19-024
Melanotic neuroectodermal tumour of infancy: report of three cases
F. Rosa*, M.M. Lemos, R. Cabrera
*Instituto Português de Oncologia de Lisboa Francisco Gentil, Portugal

Background & objectives: Melanotic neuroectodermal tumour of infancy (MNTI) is a rare biphasic tumour of neuroectodermal origin, which typically occurs in the head and neck of young infants, with a slight male predilection. It has the potential to behave aggressively, recur and metastasize.
Methods: We describe three cases of MNTI that were referred to our institution for treatment, two of them from developing countries, that illustrate the clinicopathological features, management and outcomes of this entity, with a review of the literature.
Results: Case 1 refers to a 6-month-old boy with a recurrent 4 cm maxillary mass. Case 2 is a 7-month-old boy with a 4,5 cm paratesticular mass, and case 3 regards a 4-month-old boy with a 10 cm orbital mass. Microscopically, the tumours were comprised of small neuroblast-like cells and larger melanin-producing epithelial cells in a fibrocollagenous stroma. In the first two cases, complete surgical excision was achieved, via total maxillectomy and radical orchiectomy, respectively. At the age of two years, the patients were free of disease. In case 3 the lesion was unresectable and neoadjuvant chemotherapy was initiated, but the patient died from septic complications.
Conclusion: These cases illustrate the classical clinicopathological features of MNTI and its possible outcomes. When completely resected, the patients were discharged from follow-up with no evidence of disease. However, in the case with the larger skull inoperable lesion, the tumour resulted in the patient's death. Early diagnosis and adequate resection, sometimes not available in developing countries, are key for an effective management, preventing recurrences and death.

E-PS-19-025
Situs inversus totalis in combination with cardiomyopathy in the foetus: a case report
I. Sertakov*, D. Tsimbalist, N. Alekseeva, A. Kvaratskheliya, A. Abasov, A. Filin
*Voronezh State Medical University, Russia

Background & objectives: Situs inversus totalis is a rare anomaly in the position of viscera, characterized by their mirrored inversion. The objectives of the study are studying the specificities of the location of viscera and analysis of the causes and frequency of anomalies.
Methods: Patient U. 28 years old, admitted to the hospital with a gestation period of 35 weeks, one foetus. In the first trimester she suffered from ARVI.
Results: During ultrasound examination in a specialized centre situs viscerum inversus has been identified in foetus:
In addition there were revealed a non-compact left ventricle of the heart, dilated cardiomyopathy, total failure of atrioventricular valves.
The Genotek laboratory links the wrong position of organs with mutations of 41 genes. The patient had the cardiomyopathy with a mirror arrangement of organs, so we can assume the presence of a mutation in the ACTC1 gene.
Conclusion: Situs inversus of internal organs can be diagnosed by ultrasound examination during prenatal period. The anomaly can be caused by the mutations in the genes responsible for the development of left-right asymmetry. There is a linkage between the position of the abdominal viscera and the heart's position.

E-PS-19-026
Clinicopathological evaluation of infantile fibrosarcoma: case series from a tertiary cancer centre
D. Sharma*, M. Ramadwar, P. Panjwani, S. Qureshi, G. Chinnaswamy, M. Prasad, A. Baheti, V. Patil
*Tata Memorial Hospital, Homi Bhabha National Institute, India

Background & objectives: Infantile fibrosarcoma (IFS) is a rare malignant fibroblastic (rarely metastasizing) tumour commonly occurring in infancy. It is characterized by alterations leading to oncogenic activation of tyrosine kinase signalling.
We aimed to characterize clinicopathological features of IFS cases at our centre.
Methods: Retrospective analysis of 14 patients diagnosed with IFS in our department was performed over 7 years. Clinical and demographic details, including treatment and follow-up information of patients, were gathered from the electronic medical records of our hospital. Available pathological data, including histological, immunohistochemical, and molecular characteristics were reviewed. Fluorescence in-situ hybridization (FISH) for NTRK1/2/3 alterations was performed in 4 cases.
Results: All 14 patients were diagnosed within their first quinquennium (median age: 4 months). Three were congenital and 9 were diagnosed in infancy. Male to female ratio was 3.67:1. Microscopically, cellular tumours with monomorphic spindled cells and numerous mitoses were the most consistent finding. Pan-TRK immunohistochemistry (IHC) was diffusely positive in 4 of 4 cases with differential antigen localisation. FISH for NTRK gene rearrangement was positive in 3 of 4 cases.
Six patients received neoadjuvant chemotherapy. Twelve patients underwent surgery. Adjuvant chemotherapy/radiotherapy was given to 4 patients. One patient developed bilateral lung metastases. All patients were alive with no evidence of disease at the last follow-up (range 1 to 44 months).
Conclusion: IFS is a rare and frequently misdiagnosed malignant tumour that portends an overall good prognosis. Diagnosis is generally based on the age of onset, clinical presentation, histologic features, and/or driver molecular aberrations. Lack of NTRK alterations by IHC/FISH does not rule out a diagnosis of IFS. Neoadjuvant therapy with NTRK inhibitors is purported to alter the prognosis and surgical management of patients with advanced or inoperable diseases. Awareness of the classic morphology and localization patterns of pan-TRK IHC is essential.

E-PS-19-027
Placental foetal vascular malperfusion in congenital diaphragmatic hernia
J. Stanek*
*Division of Pathology, Cincinnati Children's Hospital, USA

Background & objectives: Congenital diaphragmatic hernia (CDH) is a severe, potentially treatable foetal malformation. The in-utero or intrapartum treatment success can be impacted by poor placental function which has not been studied yet. This analysis aims to analyse placental pathology results in CDH.
Methods: Frequencies of 24 independent clinical and 48 placental variables were statistically compared. Slides from 103 CDH placentas (Group 1), and from 133 clinical umbilical cord (UC) compromise/anatomical UC abnormalities placentas, but without CDH

(Group 2), stained with hematoxylin/eosin and CD 34 immunostain were reviewed, the latter for clustered distal villi with endothelial fragmentation of recent foetal vascular malperfusion (FVM).
Results: Caesarean delivery and ex utero intrapartum treatment were more common in Group 1, but Group 2 showed more statistically significantly increased other clinical phenotypes. Frequencies of large vessel (foetal vascular thrombi, stem vessel obliteration, intramural fibrin deposition) and distal villous FVM (clustered endothelial fragmentation by CD34 immunostaining, stromal vascular karyorrhexis, avascular, or mineralized villi) were not different between the groups, but low grade distal villous FVM was statistically significantly more common in Group 1 than in Group 2 (39% vs. 24%), while high grade distal villous FVM in Group 2 than Group 1 (18% vs. 6%), respectively. Recent distal segmental FVM by endothelial fragmentation was similarly frequent in both groups.
Conclusion: Large vessel and distal villous FVM in both CDH and UC compression were overall qualitatively and quantitatively similar, but several times more common than in general population. However, CDH placentas showed more frequent low grade distal villous FVM and less frequent high grade distal villous FVM than those seen in UC compromise. FVM of CDH may be therefore caused by similar pathomechanism as that of UC compromise, with resulting impaired placental foetal blood outflow, but less severe.

E-PS-19-028
Chronic histiocytic intervillositis with maternal cushing disease: a case report
H.S. Toru*, D. Durna, C.Y. Sanhal, N. Yılmaz
*Akdeniz University, Turkey

Background & objectives: The pathological examination of the placenta is generally not of interest compared to other surgical pathology branches. However, a good understanding of placental pathologies can provide good obstetric care and evaluation in terms of recurrence risk in subsequent pregnancies.
Methods: Chronic histiocytic intervillositis (CHI) is a pregnancy disorder characterized by infiltration of maternal macrophages into the intervillous space of the human placenta, often with accompanying perivillous fibrin deposition. We want to highlight this interesting case to encourage further research on CHI.
Results: C/S surgery was planned at 38 weeks for a 40-year-old female patient who was followed up for Cushing's disease, who underwent IVF treatment. As a result of the endocrinology consultations, an operation order was obtained with the "steroid umbrella" protocol. No signs of IUGR were found in the antenatal follow-ups. No abnormal findings were detected in Doppler artery indices and biophysical profiles. According to these data, it was reported with the diagnosis of Chronic histiocytic intervillositis
Conclusion: Chronic intervillositis do not have a current standardized determination and there are few studies on this entity. Most important point is high rates of recurrence. Differential diagnosis and misdiagnose is an important pathologic challenge. CHI diagnosis is made microscopically by histology of the placental tissues. The diagnosis can also be made by examing histology of chorionic villous sampling in the first trimester.

E-PS-19-029
Gaucher Disease involment of mediastinal lymph node case report
M.L. Yamac*, E. Kilic Bagir, T. Toyran, A. Das Cerci, M. Ergin, D. Gümürdülü
*Cukurova University, Turkey

Background & objectives: Gaucher disease is a lysosomal storage disease characterized by a genetic autosomal recessive transmission because of the gene encoding glucocerebrosidase enzyme defect. And affects multi-organs such as RES, pulmonary. Lymph node infiltration is common manifestation but has limited reports.
Methods: here in we report a 11-year-old female presented at the age of 13 months with anaemia, thrombocytopenia and hepatosplenomegaly clinical symptoms, bone marrow biopsy, enzyme assay and gene mutations confirmed Gaucher disease type 3. Patient had been receiving enzyme replacement therapy for 9 years. Cervical and mediastinal multiple lymphadenopathies detected from abdominal/ thoracal CT and MRI.
Results: Biopsy had done from mediastinal lymph node with suspicion of lymphoma or tuberculosis. Mediastinal lymph node biopsy showed that lymph node structure completely effaced by a diffuse Gaucher cells infiltration of lymphoid tissue at the big area. Gaucher histiocytes had with finely fibrillar, wrinkled paper-like cytoplasm and eccentric nuclei. They were positively stained with PAS and iron by histochemical method. No microorganisms or malignant changes were detected.
Conclusion: In Gaucher Disease there are limited case reports about mediastinal and mesenteric lymph nodes. In this case enzyme replacement therapy had shown limited efficacy for the presentation and treatment of lymph node involvement. The relation between enzyme replacement therapy and lymphadenopathy development is unclear. We presented a rare finding in Gaucher Disease and we think that more studies should be done for treatment and clinical manifestations in such cases with systemic lymph and organ involvement.
Funding: Cukurova University

E-PS-20 | E-Posters Pathology in Favour of Developing Countries

E-PS-20-002
Is the histological type of tumour or molecular profiling of a tumour more relevant for the choice of therapy; a case report of AFP-producing carcinoma with an unknown primary location
N. Bilalovic*, F. Erkan Akay, G. Berić Jozić
*Department of Clinical Pathology & Cytology, Clinical Center, University of Sarajevo, Bosnia and Herzegovina

Background & objectives: Background & Objective: We present clinicopathological features and survival outcomes of primary alpha-fetoprotein (AFP)-producing carcinoma with an unknown primary location that responded significantly to immune checkpoint inhibitor (ICHI) atezolizumab.
Methods: Case: A 42-year-old female patient was admitted to the hospital with symptoms of headache, transient dysphagia, constipation, and bloating. Her FDG-PET scan revealed hypermetabolic masses in the left temporal lobe (29x24mm), in the left upper lobe of the lung, and two nodules in the left adrenal gland.
Results: The patient underwent surgery after being diagnosed with adenocarcinoma, due to morphological findings, at a minor pathology department. As the specimens arrived at our centre, the diagnosis was revised to AFP-producing tumours with an unclear primary tumour site. Her immunohistochemical markers displayed positivity for Arginase 1, HepPar 1, Glypican 3 and AFP, which is characteristic of hepatocellular carcinoma. Hence, she received chemotherapy as first-line treatment, but the tumour was resistant. Her AFP levels, which was 220 ng/mL at the beginning of therapy, surged to 13917 ng/mL (the normal range is 0–40 ng/mL), and she developed new metastases.
Conclusion: Given the limited number of AFP-producing tumours, it is challenging to identify precise therapy choices through extensive clinical trials. Moreover, recent research has revealed that PD-L1 negative tumours with high TMB (defined as 16–20 Muts/Mb) respond favourably to ICHI. On that account, this paper's objective is to portray how PD-L1, PD-1, and TMB might be possible biomarkers for malignancies with high AFP levels, perhaps elucidating viable treatment strategies.

E-PS-20-003

A case series of patients with NTRK fusion from the Federation of Bosnia and Herzegovina

N. Bilalovic*, F. Erkan Akay, L. Pilav
*Department of Clinical Pathology & Cytology, Clinical Center, University of Sarajevo, Bosnia and Herzegovina

Background & objectives: Multiple novel drugs developed for precision medicine have demonstrated outstanding efficacy in neoplastic patients with unique molecular targets. Detecting patients with a neutrophilic tropomyosin receptor kinase (NTRK) fusion has become clinically significant, especially with the discovery of TRK inhibitor treatment.
Methods: In this case series, during the years 2021 and 2022, 60 patients were tested for NTRK fusion, with three displaying moderate expression and two expressing strong cytoplasmic positivity. This study aimed to determine the nationwide landscape of NTRK/TRK testing in the Federation BH and the usage of pan-TRK immunohistochemistry (IHC) as a preselection tool to detect NTRK fusions.
Results: A total of 2 fusions involving NTRK were identified in tumours. One of the two patients was a 44-year-old male patient diagnosed with an infantile fibrosarcoma (IFS)-like tumour with an ETV6-NTRK fusion who presented with a painful and palpable mass in the proximal adductor region of the right hip. The other patient was a 15-year-old male with juvenile NTRK-rearranged SPN who presented with a mass on his right knee underwent surgery at first. But after 4 months, the mass recurred in the inguinal region, hence he was put on lacrotrectinib treatment for 8 cycles, displayed an outstanding response, and has been in remission since.
Conclusion: Our goal is to raise awareness, especially in developing countries, of NTRK fusion testing, which may lead to the expansion of actionable target treatments and the advancement of precision medicine and testing modalities

E-PS-20-004

Mirror mirror on the wall, who is the fairest of us all; lessons learned from audits of histopathology laboratories; an auditor's perspective from Lahore, Pakistan

F. Rehman*, A. Iqbal, M.U. Farooq, Z. Zafar, S. Yar, A. Hamid
*Associate professor Pathology department, Ameerudin medical college/postgraduate medical institute, Lahore, Pakistan

Background & objectives: In order to comply with international standards and ensure quality assurance, participation in external audits plays an essential role. Laboratories in Pakistan seek accreditation from Pakistan national accreditation council (PNAC, a local accreditation body) or College of American Pathologists (CAP).
Methods: Audits were conducted in terms of different phases of routine testing including pre-analytical, analytical and post-analytical phases. Histopathology laboratories from both governmental and non-governmental institutions were included in the study. A structured checklist was used as per ISO 15189 requirements for medical laboratory accreditation. Auditor then inspected compliance with various parameters of the checklist.
Results: Some of the non-governmental histopathology laboratories have been accredited by College of American pathologists. Only 6.25% of laboratories from governmental institutions applied for accreditation and future surveillance. Histopathology laboratories were participating in both diagnostic and technical modules of proficiency testing programs offered by international accreditation bodies including CAP & RCPATH Australasia. Challenges faced by governmental institution's laboratories were mainly inappropriate fund allocation for quality assurance & accreditation, lack of human resources and delay in routine purchase of reagents & consumables. Maximum errors were observed in preanalytical phase of testing due to non-compliance with specimen submission guidelines and lack of relevant information on requisition forms.
Conclusion: Quality assurance and improving customer satisfaction is the main goal of any histopathology laboratory. Medical laboratories should be encouraged to comply with regular scheduled audits. Timely reporting, participation in proficiency testing, adherence to international guidelines and reporting protocols, effective monitoring of turnaround time and collaboration with physicians and paramedics will help in continuous improvement in histopathology laboratory services. The organizations play a crucial role by provision of technical support and allocating appropriate funding and human resources especially in governmental institutes.

E-PS-20-005

Role of multidisciplinary team meetings in reshaping histopathology laboratory image: physician's perspective

F. Rehman*, Z. Rashid, M.U. Farooq, F.N. Alam, A. Hamid
*Associate professor Pathology department, Ameerudin medical college/postgraduate medical institute, Lahore, Pakistan

Background & objectives: Multidisciplinary team meetings involve healthcare professionals from different disciplines; working together to evaluate and manage patients with complex medical diseases. The pivotal role of a histopathologist in MDT's is of providing important diagnostic clues essential in deciding patient's management.
Methods: A cross-sectional study involving 323 physicians was conducted at a tertiary care hospital in Lahore, Pakistan. A self-designed structured questionnaire covering various aspects of histopathologist role in MDTs was prepared after extensive literature search. The physicians from different departments of hospital were questioned regarding various aspects of histopathologist's participation in MDTs. Data was entered and analysed using SPSS version 21.
Results: Physicians from various disciplines mainly surgery and allied departments (including plastic surgery, otolaryngology, neurosurgery, orthopaedics, paediatric surgery) and medicine and allied departments participated in the survey. The main advantages of MDTs was coordination between physicians and diagnosticians in making an appropriate decision regarding patient therapeutic management, prognosis and follow up. The main hurdles in these collaborative meetings were lack of coordination, delayed access to complete clinical information, abrupt changes in duty rosters of both residents and practicing physicians, insufficient histopathology reports due to additional testing or rework and lack of adherence to management guidelines and reporting protocols and checklist.
Conclusion: Histopathologists play a critical role in MDTs by providing expert opinions on patient's laboratory results, essential in provision of an accurate diagnosis and effective management decisions. they also serve in bridging the gap between physician's perception of laboratory services and the efforts put by histopathologist in justifying their results.

E-PS-20-006

Acquisition of histotechnical knowledge in surgical pathology training programs, a necessity or a need? A cross sectional multi-institutional study from Pakistan

F. Rehman*, H. Salahuddin, R. Basharat, S. Anwar, A. Hamid, M.U. Farooq
*Associate professor Pathology department, Ameerudin medical college/postgraduate medical institute, Lahore, Pakistan

Background & objectives: Acquiring the histotechnical knowledge regarding general and advanced histotechniques is an integral part of surgical pathology training programs in Pakistan. This is important for optimal performance of professional duties and management of troubleshooting in daily sign outs.
Methods: This cross sectional prospective study was conducted over a period of six months. Self-generated questionnaire was shared with the supervisors of surgical pathology training programs working in local

medical institutes. In the questionnaire, the amount of histotechnical knowledge acquired during training period of residents was evaluated. The domains where our institutes failed to meet the international guidelines were highlighted.
Results: Majority of our institutes lacked the appropriate training of residents regarding routine and advanced histotechniques. The main factors being lack of any scheduled rotation on different stations, non-availability of ancillary testing in various institutes or lack of interest at the end of both supervisor and residents. In some institutes the technical staff itself wasn't competent enough to provide effective training of histotechniques to the residents. Learning histotechniques in developing countries like ours is important due to the facts that histopathologists in different private and particularly in governmental institutions usually have the additional tasks of laboratory management, supervision of technical staff and monitoring various quality indicators in addition to routine reporting.
Conclusion: It is vital for histopathology residents to learn the know how of basic core and advanced histotechniques performed in histopathology laboratory. Our study helped in highlighting a gap in the histopathology residency programs, running in majority of the private and governmental institutes of our country. The reasons behind this pitfall, identified in this study can be promising to uplift the training standards of histopathology residents and thus maintaining their good standard practices as future consultants and laboratory supervisors.

E-PS-21 | E-Posters Pulmonary Pathology

E-PS-21-001
Pulmonary adenofibroma: study of 10 cases of a rare lung lesion

A. Álvarez-Muñoz*, J. Machuca-Aguado, E. Rodríguez-Zarco, S. Umbría-Jiménez, A. García-Escudero, M.A. Idoate Gastearena
*Virgen Macarena University Hospital, Seville, Spain

Background & objectives: Pulmonary adenofibroma (PA) is a rare lung tumour not included in the last the WHO classification of lung tumours. Ours is the second largest serie. This study aims to increase the knowledge of this entity describing clinicopathological and molecular features.
Methods: Retrospective observational clinicopathological study of a serie of 10 cases of pulmonary adenofibromas in the period 2002-2022. Clinicopathological features were described and immunohistochemical and molecular analysis was performed, evaluated by three independent pathologists. Immunohistochemical techniques were performed using the following antibodies: CD34, STAT6, BCL2, CD99, TTF1, ER, PR, S100 and SMA. In addition, NATB2-STAT6 gene fusion was performed by FISH.
Results: Patients ranged in age from 41 to 75 years (mean 60.1) and 70% were male. Most of the patients were diagnosed on routine imaging.
The most frequent location was the right lower lobe (40%), (mean size 1.4 cm). No patient recurrence or death due to the lesion was observed.
All the cases showed a biphasic histologic pattern with a glandular epithelial component and a stromal spindle cell component. In none of these components were evident histologic signs of malignancy.
Immunohistochemistry showed diffuse stromal positivity in all cases for BCL2, 9 for CD34 and 6 for STAT6. Strong TTF1 staining was observed in the epithelial component in all cases.
Conclusion: We report the clinicopathologic features of a new serie of PA, a rare neoplasm. The nature of this lesion has not been clarified: hamartomatous origin versus neoplastic stromal proliferation.
In this sense, some studies report NATB2-STAT6 translocation in PA, similar to solitary fibrous tumour (SFT). The positive immunostaining for STAT6 and CD34 in most of our cases may suggest that at least some of the PA are indeed intrapulmonary SFT with an entrapped epithelial component.

E-PS-21-002
Endobronchial lipoma, an extremely rare benign tumour involving the lung

R. Ayadi*, E. Braham, F. Loued, H. Ichrak, O. Ismail, A. Ayadi
*Hôpital Abderrahmane Mami, Tunisia

Background & objectives: Endobronchial lipomas are extremely rare benign tumours and account for only 0.1% of all benign tumours of the lung. Their clinical presentation mimics obstructive lung diseases or malignancy because of their obstructive character, leading to a delay in diagnosis.
Methods: We report a retrospective study of 6 cases of endobronchial lipoma diagnosed at our department of pathology.
Results: There were 5 male and 1 female patients, aged between 69 and 72 years with a mean of 71 years. cough and dyspnea were the most commonly reported symptom. In all cases, bronchoscopy revealed well-defined submucosal endobronchial lesions and the clinical impression was that of a benign neoplasm. Histologic diagnosis was obtained by endobronchial biopsy in 4 cases and thoracoscopic lobectomy in 2 cases. All lesions showed similar morphology: mature adipose tissue predominated. Examination of all sections did not reveal any areas of cellular atypia or mitoses. Typical features of pulmonary hamartoma were not identified.
Conclusion: Endo bronchial lipoma is an extremely rare benign lesion of the respiratory tract which may lead to obstructive complications if unresected. It should be distinguished from fat-rich pulmonary hamartomas. All endobronchial lipomatous tumours in the present series behaved in a benign manner.

E-PS-21-003
The coexistence of pulmonary hydatid cyst and aspergillosis: an incidental finding

R. Ayadi*, B. Emna, H. Ichrak, L. Farah, O. Ismail, A. Ayadi
*Hôpital Abderrahmane Mami, Tunisia

Background & objectives: The co-existence of hydatid cyst with aspergillosis is extremely rare. There are only a few case reports in the literature on the concomitant of pulmonary hydatid cyst and aspergillosis.
The aim was to describe clinocopathological characteristics of this entity.
Methods: We report a retrospective study of 8 cases of co-infection of pulmonary hydatid cyst and aspergillosis diagnosed at our department of pathology between 2004 and 2022.
Results: There were 5 male and 3 female patients, aged between 19 and 81 years with a mean of 41,57 years. This diagnosis was established by surgical resection in all cases. All lesions showed similar morphology: laminated membrane of hydatid cyst and infiltration of its wall with septate fungal hyphae with acute angle branching, consistent with aspergillosis. These fungal hyphae were positive with PAS and Grocotts methenamine silver.
Conclusion: The co-existence of hydatid cyst and aspergillosis is uncommon and the radiological diagnosis may not be helpful in detecting the fungal co-infection. The diagnosis is confirmed by histological examination.

E-PS-21-004
Sclerosing pneumocytoma of the lung: a case report

E. Aydemir*, G.G. Geçmen
*University of Health Sciences, Umraniye Training and Research Hospital, Department of Pathology, Istanbul, Turkey

Background & objectives: Pulmonary sclerosing pneumocytoma (PSP) is a rare benign tumour. It particularly affects middle-aged

women. PSP occurs in the peripheral parenchyma of the lung and can affect any lobe. Clinically, most patients are asymptomatic. Rarely, non-specific respiratory symptoms can be seen.
Methods: A 48-year-old female presented in our hospital, who had a lung solid nodular lesion incidentally found by a chest X-ray. Pet/CT scan resulted as "A well-circumscribed slightly hypermetabolic mass lesion of approximately 3x2.6cm in diameter located in the lower lobe of the right lung". Clinically thought of as lung cancer, the mass was excised and sent for histopathological examination.
Results: We observed an infiltrative proliferation in replace of the lung parenchyma in microscopic examination. The proliferation consisted of two types of cells: cuboidal "surface cells" resembling type 2 pneumocytes and polygonal "round cells" with eosinophilic cytoplasm. We saw that surface cells lined papillary structures while round cells formed solid islands. Additionally, we noted a sclerotic stroma. An immunohistochemical panel consisting of markers was applied, and both cell types were positive for Epithelial Membrane Antigen(EMA) and Thyroid Transcription Factor-1(TTF-1). Napsin, AE1/3, and CK7 were positive in surface cells and negative in round cells. And 3% of tumour cells were positive for Ki67. No necrosis, frequent mitoses and marked pleomorphism were observed.
Conclusion: The differential diagnosis of pulmonary sclerosing pneumocytoma includes benign lesions as well as malignant neoplasms such as primary carcinoma of the lung, metastatic carcinoma, carcinoid tumour. The different treatment options for these tumours emphasize the importance of making an accurate diagnosis. And since PSP can be confused radiologically and microscopically with a malignant neoplasm, this case has been presented.

E-PS-21-005
Extended SARS-CoV-2 pneumonia complicated by cytomegalovirus and aspergillus infection
P. Babal*, L. Krivosikova, T. Kuracinova, P. Martanovic, P. Janega
*Institute of Pathological Anatomy, Medical faculty of the Comenius University in Bratislava, Slovakia

Background & objectives: Infection by SARS-CoV-2 affects predominantly the respiratory system causing an acute disease in the majority of cases. Many patients develop lasting symptomatology of the long COVID.
Methods: Clinical course: We report a patient with bronchial asthma who presented with initiating COVID pneumonia, was hospitalized and received oxygen therapy for two weeks. Successively, he developed interstitial lung fibrosis. Two months later the patient died with signs of rapid worsening dyspnea.
Results: At autopsy, even after more than 2 months, the SARS-CoV-2 virus still could be detected with immunohistochemistry in scattered alveolar epithelial cells of lungs, although the tests from the nasopharynx were negative. In addition to that, there was diffuse distribution of alveolar epithelia with large nuclear inclusions immunohistochemically positive for cytomegalovirus and multiple foci of necrosis with Aspergillus hyphae.
Conclusion: Immune dysregulation induced by COVID-19 and corticoid therapy administered to the patient created conditions favourable for extended persistence of the SARS-CoV-2 infection in lungs complicated by fatal combination of cytomegalovirus and Aspergillus infection.
Funding: BIOVID-19, ITMS: 313011AVG3, co-financed by the European Regional Development Fund

E-PS-21-007
Cross sectional study of metastases to the lung on 5,867 lung core biopsy specimens
M. Bonert*, C. Finley, A. Naqvi
*McMaster University / St. Joseph's Healthcare Hamilton, Canada

Background & objectives: Lung metastases are a common pulmonary pathology specimen. This work examines metastases/possible metastases (MPM) through the lens of lung core specimens only. Prior work on the data set examined TTF1 negative lung adenocarcinomas (TNLA) and identified 50 specimens.
Methods: All lung core biopsies cases accessioned 2011-2020 were retrieved from a regional centre. Specimens were classified by location, diagnosis, diagnostic category (benign/ suspicious/ malignant) with a hierarchical free text string-matching algorithm (HFTSMA) that was previously validated. The MPM assessment of the TNLA cases was evaluated. All MPM reports were reviewed by a pathologist.
Results: The cohort had 5,867 specimens from 4,973 patients. 3,226/5,867 were malignant and 600/3,226 were MPM per HFTSMA. 19/50 TNLAs were identified as MPM by HFTSMA. 459/600 specimens were classified as MPM on pathologist report review. Primaries by frequency were colorectal cancer (CRC) 82, breast 42, melanoma 37, kidney 31, gynaecologic 26, soft tissue 21, prostate 19, gastrointestinal not CRC 17, urothelial 17, miscellaneous 14, unknown/possible metastasis (UPM) 153. The UPMs were subclassified in five hierarchical groups: squamous cell carcinoma (33/153), CK7+/TTF-1 negative tumours (50/153), CK5+ tumours (8/153), CK20+ tumours (18/153), and unclassified (44/153). More lesions were on the right (235) than left (189); however, this was not statistically significant.
Conclusion: The HFTSMA assisted categorization facilitated the analysis; however, it was not sufficiently accurate without pathologist review. The classification of the 50 TNLA cases suggests MPM cases are missing, and work remains. Approximately 4-5% of malignancies (153/3,226) were unclassified in relation to primary site. Clinical information is required to differentiate MPMs from primary tumours; however, this is most often not provided. Standardized history and pathologic reporting would be desirable and could facilitate work that provides further insight into the MPM-primary interface.

E-PS-21-008
Primary salivary gland-type carcinomas of the respiratory tract: a case series review from an oncology institute
A. Coutada*, J. Azevedo, N. Coimbra
*Department of Pathology, Portuguese Oncology Institute of Porto / Porto Comprehensive Cancer Center Raquel Seruca, Portugal

Background & objectives: Primary salivary gland-like carcinomas (PSGCs) of the respiratory tract are rare neoplasms that occur primarily in the central airways and apparently originate from the submucosal glands. Herein, we describe a single institution experience regarding this type of tumours.
Methods: We conducted a retrospective analysis of all PSGCs of the respiratory tract diagnosed at our Institution between 1995 and 2022. Evaluation of clinicopathologic features, such as age at diagnosis, localization and number and local of metastases were assessed. Both biopsy and surgical specimen results, including histomorphology, tumour grade, immunohistochemistry and genetic results were also included.
Results: In total we identified 14 cases: 9 mucoepidermoid carcinomas (MECs) and 5 adenoid-cystic carcinomas (ACCs). Median age was lower in MECs (54.4 years vs 60.6 years), with male predominance in MECs and female in ACCs. Lobectomy was the main surgical treatment. The majority of tumours were localized in central region. Most MECs were low-grade. Genetic analysis showed 2 MECs with MAML2 rearrangement and 1 ACC with MYB rearrangement. Follow-up (median, 39.4 months) revealed invasion of adjacent structures (2 ACCs), lymph node metastases (1 MEC) and local and distant metastases (2 MACs; 1 ACC). Median overall-survival was 43.9 months for MECs and 31.6 months for ACCs.
Conclusion: Diagnosing PSGCs of the respiratory tract can be challenging due to their rarity and diverse morphology. Molecular testing

for gene fusions can be useful in confirming the diagnosis but given the similarity to their counterparts in the salivary glands, exclusion of secondary involvement by clinical and radiology findings is mandatory. Although our results are limited by the small number of cases included, they are similar to those described in the literature.

E-PS-21-009

Distinct RET rearrangements in an unusual case of intratumoral metastases of a papillary thyroid carcinoma in a primary lung adenocarcinoma

A. Coutada*, J. Azevedo, A. Lapa, C. Escudeiro, N. Coimbra
*Department of Pathology, Portuguese Oncology Institute of Porto / Porto Comprehensive Cancer Center Raquel Seruca, Portugal

Background & objectives: Uncommon phenomenon known as tumour-to-tumour-metastasis (TTM) occurs when a metastasis from one primary-tumour deposits within another primary-tumour. Lung is a typical site for TTM. Herein, we describe a case of lung adenocarcinoma with metastases of papillary thyroid carcinoma.
Methods: A 61-year-old woman was diagnosed with a classic papillary carcinoma of the thyroid in 1999. Almost 20 years later, during the follow-up presented multiple lung nodules detected by thoracic computed tomography. Lung biopsy was performed on the largest nodule with 19mm. The patient later underwent a left lobectomy. Both biopsy and surgical specimen underwent histopathological examination, immunohistochemistry and molecular tests.
Results: Histological examination of the biopsy showed an adenocarcinoma with acinar, papillary and lepidic pattern, that stained for CK7 and TTF-1. Additionally, there were areas of papillary architecture with nuclear features such as pseudoinclusions and grooves, that stained for CK7 and TTF-1, but also for PAX-8 and thyroglobulin. Histological examination of the surgical specimen confirmed the presence of a primary lung adenocarcinoma with multiple intratumoral metastases of papillary thyroid carcinoma and also involvement of the adjacent parenchyma. Molecular analysis revealed RET rearrangements in both neoplasms: lung adenocarcinoma presented a KIF5B-RET fusion gene, while metastases of the papillary thyroid carcinoma showed a CCDC6-RET fusion gene.
Conclusion: TTM diagnosis can be challenging since it requires a high level of suspicion/clinical correlation and careful examination of the tumours' histological features. There is no evidence that the occurrence of RET fusion genes in both tumours results from genetic susceptibility in this patient. Although the partners are different, the presence of these RET fusion genes might be considered a therapeutic target for both lung adenocarcinoma and papillary thyroid carcinoma.

E-PS-21-010

Pulmonary silico-tuberculosis mimicking metastatic carcinoma – a case report

L. D'Sa*, F. Pezzuto, F. Lunardi, F. Scalvenzi, M. Tinè, G. Comacchio, C. Giraudo, F. Calabrese
*Addenbrooke's Hosital, Cambridge, United Kingdom

Background & objectives: Silicosis caused by inhalation/deposition of free silica particles is characterized by pulmonary inflammation/fibrosis. Among the clinical disorders associated with silicosis, tuberculosis is by far the most prominent. The diagnosis is challenging especially in patients with a previous neoplasia.
Methods: A 66-year-old male non-smoker, originally from North Africa, reported a dry cough and significant weight loss. He was a foundry worker. He had a medical history of bladder carcinoma associated with schistosomiasis. CT and PET/CT showed bilateral multiple hypermetabolic lung nodules, some with cavitation. The patient underwent surgical resection of the largest nodule, highly suspicious of lung metastasis.
Results: Surgical resection showed well-circumscribed small nodules. The histological examination revealed multiple nodular formations mainly localized in subpleural and peribronchial sites. Several lesions showed characteristic features of silicotic nodules with a central zone of cellular hyalinized collagen with a whorled appearance and a peripheral zone of dust-laden macrophages. Polarized light microscopy showed bright white crystals of varying sizes. There were adjacent well-formed granulomas some with central caseous necrosis. Microdissection of the largest necrotising granuloma was performed for molecular investigation of mycobacteria. Real time polymerase chain reaction, performed for the identification and quantification of the DNA of Mycobacterium tuberculosis complex, was positive. The final diagnosis was pulmonary silico-tuberculosis.
Conclusion: Silico-tuberculosis is often encountered in patients with a history of silica exposure in tuberculosis endemic areas. This case serves as a reminder to never underestimate patient occupational exposure and geographic origin. A careful histological diagnosis and molecular investigation are mandatory to approach difficult cases especially for patients with a prior cancer history and clinical/ radiological features suggestive of tumour recurrence/metastasis.

E-PS-21-011

Immunohistochemistry as an adjunct to molecular testing in difficult cases: using phenotype to ascertain the relevance of genotypic variants

U. Oedema*, K. Krishnamurthy, D. Goldstein
*Montefiore Medical Center, USA

Background & objectives: Novel variants are being identified in lung adenocarcinomas by next generation sequencing (NGS) with increasing frequency. Predictive analysis and literature are often limited, complicating interpretation. Herein, we investigate whether immunohistochemistry (IHC) can clarify the nature of some of these variants.
Methods: Primary lung adenocarcinoma cases with ambiguous variants were identified. Formalin-fixed, paraffin-embedded tissue sections marked by a pathologist, were manually micro-dissected for tumour DNA, which was amplified using Ion AmpliSeqTM Cancer Hotspot Panel v2 multiplex PCR primer set. Sequencing was performed on an Ion Torrent PGM™ NGS. β-catenin and p53 immunohistochemical staining was performed using the Dako Autostainer systems (Agilent Technologies).
Results: Three lung adenocarcinoma cases, two resections and one cytology, were selected. APC c.3949G>C, p.E1317Q variant was identified in two cases while a TP53 splice donor variant c.559+1G>A was identified in the third case, at variant allele fractions (VAFs) congruent with the estimated tumour content. Two of the cases had concomitant driver mutations in KRAS at similar VAFs. The NGS run met all quality control criteria. Corresponding immunostains for β-catenin showed cytoplasmic staining (wild-type) in both cases with APC variants, while P53 showed heterogenous (wild-type) staining pattern in the isolated case with TP53 variant. In the light of the above findings, these variants were interpreted to be likely benign.
Conclusion: APC p.E1317Q has been reported a possible pathogenic driver in a subset of lung adenocarcinomas. TP53 splice donor variant is well-described in adenocarcinomas. Wild-type β-catenin and P53 IHC staining provides some evidence of maintained WNT and p53 pathway homeostasis and may help identify these as incidental variants resulting from genomic instability in tumour cells. This case series exemplifies the role of IHC as an adjunct to NGS by ascertaining the phenotype in tumour cells, aiding variant classification in difficult cases.

E-PS-21-012

Epithelioid haemangioendothelioma of the thorax

L. Farah*, R. Ayadi, H. Ichrak, B. Emna, O. Ismail, A. Ayadi, S. Hamza
*CHU Abderrahmen mami Tunisia, Tunisia

Background & objectives: Epithelioid haemangioendothelioma (EHE) is an extremely rare malignant vascular neoplasm. Thoracic EHE involves not only the lungs but also the pleurae, the bones and the mediastinum.
The aim of this study is to discuss clinical-pathological characteristics of this tumour.
Methods: We report a retrospective study of 8 cases of EHE diagnosed at our department of pathology between 2004 and 2022.
Results: There were 3 female and 5 male patients, aged between 38 and 80 years with a mean of 40,5. The diagnosis was made on surgical resection (n=5), mediastinoscopic biopsy (n=2) and liver biopsy (n=1). The histological examination showed nodules with increased cellularity at the periphery and an abundant hypocellular, eosinophilic sclerotic centre. It is composed of infiltrative cords and nests of epithelioid cells within a myxohyaline stroma. Tumour cells have a glassy eosinophilic cytoplasm, uniform ovoid nuclei and inconspicuous nucleoli. Intra-cytoplasmic vacuoles containing erythrocytes were observed. Some cases were associated with necrosis and mitotic figures (high risk factors). Immunohistochemistry revealed diffuse positivity with CD34 and CK negative cells.
Conclusion: Establishing a diagnosis of EHE is a challenging task, given the rarity of the disease and the large spectrum of symptoms.

E-PS-21-013

Pulmonary tuberculosis associated with lung cancer: report of an institutional experience in Northern Tunisia

L. Farah*, R. Ayadi, B. Emna, O. Khouildi, A. Ayadi, S. Hamza, H. Ichrak
*CHU Abderrahmen mami Tunisia, Tunisia

Background & objectives: The simultaneous occurrence of pulmonary tuberculosis and lung cancer has been reported in various case series. But this association is still controversial. The objective of this study is to report our experience in case of coexistence of the two diseases.
Methods: We performed a retrospective study involving 65 cases of combined pulmonary tuberculosis and lung cancer diagnosed at our department between 2004 and 2022.
Results: There were 61 male and 4 female patients, aged between 43 and 80 years, with a mean of 52, 5. In all cases, tuberculosis was an incident finding, simultaneous to the diagnosis of cancer. Adenocarcinoma was the most common histological type (65%), followed by Squamous carcinoma (28%), Neuroendocrine carcinoma (5%) and finally Adenosquamous carcinoma and Lymphoepithelioma-like carcinoma in 1% each. Most of our patients were diagnosed with advanced lung cancer stage IIIA (n=17), followed by Stage IIB (n= 14), Stage IA (n = 13), Stage IIA (n= 4), Stage IB (n = 3) and finally stage IIIB (n= 1).
Conclusion: If a coexistence between tuberculosis and lung cancer is possible, the phenomenon remains too rare to sustain the theory of « tumour in the scar ». Nevertheless, this emphasizes the importance of LC screening in pulmonary tuberculosis patients even after the infection is treated.

E-PS-21-014

Pulmonary sclerosing pneumocytoma: a histological diagnostic challenge

L. Farah*, R. Ayadi, B. Emna, O. Khouildi, H. Ichrak, A. Ayadi, S. Hamza
*CHU Abderrahmen mami Tunisia, Tunisia

Background & objectives: Sclerosing pneumocytoma is an uncommon benign pulmonary tumour, derived from primitive respiratory epithelium. This neoplasm represents a diagnostic challenge with adenocarcinoma and carcinoid tumours. The aim of this study is to present clinical-pathological characteristics of these tumours with literature review.
Methods: We report a retrospective study involving 3 cases of Sclerosing pneumocytoma diagnosed at our department of pathology between 2004 and 2022.
Results: There were 3 women ranged in age from 32 to 59, with a mean of 54. the tumour presented with multiple formations in two patients, and as a solitary nodule in one patient. The tumour size ranged from 0,1 to 7,5 cm. Histological examination showed solid and papillary architecture with sclerotic stroma. Papillae were lined with two types of cells: cuboidal and round cells. Surface cells are cuboidal, resembling type II pneumocytes. Round cells are polygonal with abundant eosinophilic cytoplasm, oval nuclei, even chromatin and indistinct nucleoli. Immunohistochemical findings revealed positive staining in both cell types for cytokeratin and TTF1. But only round cells expressed positivity for EMA.
Conclusion: Sclerosing pneumocytoma is a rare pulmonary tumour. Pathologists should always keep this entity in mind, since its broad spectrum of differential diagnosis makes it a diagnostic pitfall.

E-PS-21-015

Utility of bronchoscopic small biopsy samples - experience of one centre in two-year period

S. Glumac*, R. Janković, M. Stjepanović, S. Popević, J. Varda, V. Valčić, M. Jovanović
*Institute for Pathology, Medical Faculty, University of Belgrade, Serbia

Background & objectives: Increasing incidence of lung disease worldwide warrants reevaluation and improvement of diagnostic procedures with optimal celerity and certainty. This study aims to analyse bioptates acquired through small lung biopsies as a form of evaluating them as a diagnostic method.
Methods: Pathological reports assessed in this cross-sectional study are from biopsy samples procured at the Pulmonology Clinic of the University Clinical Centre of Serbia, and processed and reviewed at the Institute for Pathology, Medical Faculty, University of Belgrade, during 2021. and 2022.
Results: In two year period a total of 1038 reports were reviewed; cytological samples of pleural effusions were excluded. Non-neoplastic pathological conditions were 275 reports, of which sarcoidosis is the most common diagnosed (61/275). Various neoplastic disorders were present in 764 reports. As for primary malignant neoplasms of lung a squamous cell carcinoma was the most common diagnosed (226/764), 222 as adenocarcinoma, 72 as NSCLC NOS, 110 as small cell carcinoma. and 60 metastatic tumours. The average patient age at the time of diagnosis was approximately 67. With the exception of secondary neoplasms, all neoplasms were more prevalent in the male population.
Conclusion: Small lung biopsies are a significant part of the diagnostic algorithm and monitoring of both non-neoplastic and neoplastic diseases of the lungs, trachea and bronchi. The significance rises by the fact that over two thirds of lung cancers are diagnosed in advanced clinical stage and by small biopsy, as well as that the procured tissue is to be used for future predictive immunohistochemical and molecular testing.

E-PS-21-017

The utopia study: ultrafast next-generation sequencing testing in patients with non-small cell lung carcinomas

S. Hernandez Prieto*, E. Conde, M. Alonso, M. Veras Lista, A. Illarramendi, D. Curto, M. Herrera, H. Bote, J. Baena, J. Zugazagoitia, L. Paz-Ares, F. Lopez-Rios
*Pathology Department, Hospital Universitario 12 de Octubre. Research Institute Hospital 12 de Octubre (i+12). Madrid, Spain

Background & objectives: Although comprehensive genomic profiling is now standard of care for non-small cell lung carcinomas

(NSCLC), several clinical practice gaps still remain. We hypothesized that we could sign-out the report of a large next-generation sequencing (NGS) panel in three working days.
Methods: A prospective cohort of early and advanced NSCLC diagnosed at Hospital 12 de Octubre were considered. At the tumour board, four patients per week were included in the ultrafast workflow. We performed a large NGS panel (Oncomine Comprehensive Assay v3, Thermo Fisher) for screening of mutations, copy number variations and fusions in 161 genes, using a fully automated workflow.
Results: Comprehensive genomic profiling using NGS was performed successfully on all 44 patients in less than 3 working days. The material available for all tumours had been formalin-fixed and paraffin embedded. The majority of the samples analyzed were core-needle biopsies (57%). The pathological characteristics of the tumours were as follows: 36 (82%) adenocarcinomas, four (9%) NSCLC not otherwise specified, two large cell neuroendrocrine carcinomas (4,5%) and two (4,5%) sarcomatoid carcinomas. Seventeen (38,6%) patients had actionable findings: 8 (18%) EGFR mutations, 3 (7%) MET exon 14 skipping mutations, 2 (4,5%) ALK fusions, 2 (4,5%) BRAF mutations, 1 (2,3%) KRAS G12C mutation, and 1 (2,3%) RET fusion.
Conclusion: We have successfully implemented a fully automated ultrafast NGS workflow using a large panel with a turnaround time of three working days. Our proposal can easily be adapted to different size laboratories and clinical scenarios, but it requires very effective communication with the team at the clinical and molecular tumour board.
Funding: This study was supported by Oncomine Clinical Research Grant Program of Thermo Fisher Scientific. We also thank Instituto de Salud Carlos III (Fondos FEDER and Plan Estatal I+D+I 2013–2016 [PI14-01176, PI17-01001] and 2021-2023 [PI22-01700]), Fundacion Mutua Madrileña (AP18051-2022) and Comunidad de Madrid iLUNG Program [B2017-BMD-3884, S2022-BMD-7437].

E-PS-21-018
Pleuropulmonary blastoma: an aggressive intrathoracic neoplasm and review of literature
H. Ichrak*, R. Ayadi, B. Emna, L. Farah, S. Hamza, O. Ismail, A. Ayadi
*CHU abderrahmen Mami Tunisia, Tunisia
Background & objectives: Pleuropulmonary blastoma are uncommon and very aggressive tumours that account for less than 0.5% of primary lung tumours. It originates from foetal lung tissue and it is typically characterized by a biphasic pattern of an epithelial and a mesenchymal component.
Methods: We report a retrospective study of 5 cases of pleuropulmonary blastoma diagnosed at our department of pathology between 2004 and 2022.
Results: There were 4 male and 1 female patients, aged between 6 and 61 years, with a mean age of 42. This diagnosis was established by surgical resection (n=4) and transparietal biopsy (n=1). On gross examination, tumours were described as poorly circumscribed, whitish or yellowish-white mass, with necrosis or haemorrhagic changes. Microscopically, the lesion appears as a biphasic malignant tumoral proliferation, partially necrotic, made up of an entangled epithelial carcinomatous contingent and a mesenchymal contingent of the embryonic type. The immunohistochemical study shows expression of epithelial markers and of synaptophysin by the carcinomatous contingent (n=2). Immature mesenchymal contingent is positive for vimentin and smooth muscle actin (n=5).
Conclusion: Pleuropulmonary blastoma is an infrequent and aggressive malignancy. It is associated with a high incidence of recurrence and carries a poor prognosis.

E-PS-21-019
Broncholithiasis: diagnosing a rare respiratory entity
H. Ichrak*, R. Ayadi, B. Emna, L. Farah, S. Hamza, O. Ismail, A. Ayadi
*CHU abderrahmen Mami Tunisia, Tunisia
Background & objectives: Broncholithiasis is a rare lesion, defined as the presence of calcified materials in the tracheobronchial tree. Their clinical presentation mimics obstructive lung diseases or malignancy, leading to a delay in diagnosis. Therefore, making precise diagnosis may be challenging.
Methods: We report a retrospective study of 16 cases of Broncholithiasis diagnosed at our department of pathology between 2004 and 2022.
Results: There were 9 male and 7 female patients, aged between 15 and 72 years, with a mean of 43. A past history of pulmonary tuberculosis was found in 2 cases. Thoracic CT scan was performed in all patients and showed parenchymal calcification in six cases. The diagnosis was made on surgical resection (n = 14), transparietal biopsy (n = 1), and spontaneously expelled particles (n=1). The histological examination revealed similar morphology: calcified material filling the bronchial lumen It associates lesions suggestive of endobronchial aspergillosis (n=1), amyloid deposits (n=1), a bronchogenic cyst (n=1), bronchial dilation (n=11), and non-specific lesions (n=2). The outcome was satisfactory in all cases.
Conclusion: The rarity of broncholithiasis and the difficulty of a pathological diagnosis make it difficult to study which may lead to obstructive complications if unresected. This entity should be considered in the differential diagnosis of some patients with bronchial obstruction.

E-PS-21-020
In-situ protein expression analysis of Seizure Protein-6 (SEZ6)
A. Jungbluth*, E. Hernandez, P. Ruh, N. Choudhury, N. Rekhtman, D. Frosina, M. Baine
*Memorial Sloan Kettering Cancer Center, USA

Background & objectives: SEZ6 plays an important role in developing and adult nervous system; it is also found in a high percentage of small cell lung carcinomas (SCLCs). We identified suitable IHC reagents and studied SEZ6 expression in a wide variety of tumours.
Methods: Only a few anti-human SEZ6 antibodies are available, three were obtained commercially. Rabbit pAb (LS-B16535; LSBio), mAb SC17.14 (Creative Biolabs) and mAb 14E5 (Abcam). Appropriate immunohistochemical protocols were developed for the use on FFPE material on Leica Bond-3 automated stainer. After specificity analysis, SEZ6 expression was analysed in panels of normal tissues and a wide variety of tumours.
Results: Rabbit pAb LS-B16535 did not render staining compatible with the presence of SEZ6 and was not further pursued; mAbs, SC17.14 and 14E5 demonstrated staining specific for SEZ6 and were used for expression analyses. Interestingly, 14E5, a rat mAb showed a more intense and consistent immunostaining compared to murine SC17.14, a subclone of mAb SC17 employed in a therapeutic anti-SEZ6 antibody-drug conjugate (ADC). SEZ6 immunostaining was most intense and homogeneous in oligodendroglioma, medullary thyroid carcinoma, and SCLC, but was also present in pheochromocytoma, neuroblastoma, neuroendocrine tumours of the GIT and pancreas and ganglioneuroblastoma; NSCLCs and carcinomas of various other primary sites, melanomas and several haematological neoplasms were all negative.
Conclusion: SEZ6 is best detected in IHC using mAb 14E5, rendering intense and consistent immunostaining without any background reactivity. MAb SC17.14, subclone of therapeutically employed mAb SC17, displayed less optimal staining. Besides SCLCs, SEZ6 was present in all tested neuroendocrine and neurological tumours albeit displaying variable homogeneity. SEZ6 is not expressed in any other tumours or tumour entity. Besides SCLC, SEZ6 appears to be a potential therapeutic target for most tumours of neural/neuroendocrine lineage and is best detected by mAb 14E5.

E-PS-21-021

Insights into synchronous squamous non-small cell lung cancer genomics – a case viewpoint into the broader literature

M.M. Köteles*, G. Olteanu
*Emergency County Hospital Bihor, Romania

Background & objectives: The most common synchronous primary lung carcinoma (SPLC) is, statistically, squamous cell carcinoma (SCC). Here we report a case of SPLC SCC that was molecularly dissected and used as a viewpoint for a review of the literature.
Methods: A 77-year-old female patient presented to our hospital with two lung tumours in the right upper lobe (RUL), she underwent lobectomy with pathological diagnosis and staging of both tumours. Next, for both tumours' next-generation sequencing (NGS) from the corresponding formalin-fixed paraffin-embedded (FFPEs) tissue blocks was performed with COSMIC variant ID calling. The results were used for a literature review viewpoint.
Results: Both tumours, diagnosed as NSCLC nonkeratinizing squamous cell carcinoma, had pathological stages of pT1cN0R0 and pT2aN0R0. The pT1c tumour exhibited NGS-detected EGFR (COSM18419), BRAF (COSM449) missense mutations, and several p53 gene nonsense and missense mutations alongside KIT (COSM12708) and VHL missense mutations (COSM14387). In contrast, the pT2a tumour displayed different genomic alterations, including PTEN (COSM23657), PIK3CA (COSM163484), RB1, and FLT3 (COSM28047) missense mutations. P53 nonsense and missense alterations also occurred but with differing amino acid level changes. Notably, previous SCC literature emphasizes TP53, PIK3CA, and FGFR1 as frequent findings, differing from the tumours described here.
Conclusion: NGS profiling may be useful for establishing the relationship between tumours, with a significant role in the differential diagnosis between intrapulmonary metastasis and synchronous primary lung cancer. For this case, our findings showed different molecular profiles with only one relevant similarity, the same missense SMARCB1 genomic alteration, with akin allele frequency and identical amino acid change, supporting the anticipated diagnostic of synchronous tumours.

E-PS-21-022

SMARCA4-deficient lung adenocarcinoma—case report

A. Lapa*, N. Coimbra, A. Coutada, P. Rodrigues Veiga
*IPO-Porto, Portugal

Background & objectives: SMARCA4-deficient lung adenocarcinoma is rare, usually poorly differentiated and typically affects young male smokers. It usually presents as a TTF1-negative tumour with preponderant solid pattern and aggressive behaviour, leading to short survival rates.
Methods: A 41-year-old ex-smoker male was evaluated due to 1-month long persistent pain, located at the right hemithorax. The patient had a medical history of a right-sided pneumothorax that was conservatively treated. TC-scans showed a 4,3x3,3cm pulmonary lesion, with extensive pleural contact, but no clear evidence of bone involvement. An extensive surgical resection was performed.
Results: The histopathological examination showed a poorly- differentiated adenocarcinoma, with solid and acinar patterns and loss of SMARCA4 expression. Spreading through airspaces, lymph-vascular permeation and invasion of parietal pleura and thoracic wall were present. PD-L1 expression was between 5 and 10% and expression of cytokeratin was diffuse. Genetic testing showed no mutations in EGFR, ALK, ROS1, KRAS, BRAF, MET or RET genes, but two mutations in TP53 gene were found. Genetic testing for SMARCA4 is still pending. Less than two months after surgery, local relapse with metastatic multifocal pleural disease was found, leading to a new staging of T4N0M1. The patient is currently undergoing palliative treatment.
Conclusion: Testing for loss of expression of SMARCA4 is recommended in poorly-differentiated thoracic tumours given the dismal prognosis and limited therapeutic solutions of the entities harbouring this alteration. Debate is still ongoing if SMARCA4-deficient adenocarcinoma should be considered a separate entity. Nevertheless, although both lose the expression of SMARCA4, it should be distinguished from SMARCA4-deficient undifferentiated tumours. Additional genetic testing beyond the recommended for NSCLC, including members of the SWI/SNF complex, might be considered until final entity definition is achieved.

E-PS-21-023

Late presentation: a case of tuberous sclerosis complex associated lymphangioleiomyomatosis

A. Lazim*, A. Arriola, M. Mollaee
*Temple University Hospital, USA

Background & objectives: Lymphangioleiomyomatosis (LAM) is a rare cystic lung disease, may occur sporadically or with tuberous sclerosis complex (TSC). It is characterized by a proliferation of abnormal smooth muscle in the pulmonary interstitial spaces leading to cystic destruction, respiratory failure, pneumothorax.
Methods: LAM is the most common lung manifestation of TSC and can be seen in both males and females. Sporadic LAM occurs mostly in young reproductive-aged females. Here we report a 35-year-old Spanish female with TSC, and medical history significant for intellectual disability, seizures, blindness, ash leaf spots, and retinal hamartoma.
Results: She had subependymal giant cell astrocytoma status post resection with a 9 cm fat containing cystic mass of the kidney likely angiomyolipoma on MRI, who presented with severe shortness of breath and cough. High-resolution computed tomographic imaging of the chest revealed numerous bilateral cysts and multiple sub centimetre nodules. She underwent right upper and middle lobe wedge surgery with bullectomy and pleurodesis. Histological examination revealed cysts with subtle abnormal smooth muscle proliferation in the cysts' wall and multifocal micronodular pneumocyte hyperplasia. Immunohistochemical stains showed positivity for SMA and HMB-45 in the abnormal smooth muscle areas confirming the LAM diagnosis.
Conclusion: LAM has been underreported and should be included in the differential diagnosis in any young female with respiratory dysfunction, pneumothorax, or pleural effusion. In patients with TSC, early screening and regular follow-up of organs including lung should be considered to establish diagnosis of LAM to minimize subsequent complications and associated morbidity and mortality.

E-PS-21-024

Thymic high grade neuroendocrine neoplasm with carcinoid morphology: rare occurrence

A. Lazim*, A. Arriola, M. Mollaee
*Temple University Hospital, USA

Background & objectives: High grade neuroendocrine carcinoma of the thymus are extremely rare. WHO classifications of pulmonary/thymic neuroendocrine tumours (TNETs) classify these tumours into low and high grade. A subset of TNETs identified have low grade morphological features and high mitotic counts.
Methods: We report a rare case of a 59-year-old woman who presented with progressively enlarging anterior mediastinal mass. The imaging study revealed 7.5 cm mass abutting the distal SVC, anterior and lateral wall of the right atrium. Following neoadjuvant chemotherapy, the thymic mass was resected en block with adhesed pericardium and portion of the lung.
Results: On histology, the tumour lacked characteristic features of large cell neuroendocrine carcinoma (LCNEC) such as peripheral palisading, prominent nucleoli. There were 18 mitotic figures per10 HPF, extensive necrosis, and direct invasion into adjacent parietal pericardium and lung parenchyma. Ki-67 was 35%, further supporting the notion that this is a high-grade tumour. This case is a rare occurrence and has

been well described in various organ systems under several names, most recently, "high-grade neuroendocrine carcinoma with carcinoid morphology". No consensus on the best term for this tumour in the pulmonary pathology literature. It remains listed as a variant of LCNEC in the current WHO classification for lung and thymic tumours.
Conclusion: The clinical experience with this rare tumour is obviously limited in the literature, but data suggests that it may be more closely related to atypical carcinoid tumours rather than LCNEC (at least from a molecular genetic standpoint). Clinically, there is data suggesting that it may not be as highly aggressive as conventional LCNEC, but it should be noted that this patient's tumour has clearly declared itself as a "bad actor" showing aggressive behaviour and hence should be treated accordingly.

E-PS-21-025
Multiple lung tumours with identical morphology. Synchronous primaries or intrapulmonary metastasis?
A. Lazim*, A. Arriola, M. Mollaee
*Temple University Hospital, USA

Background & objectives: The incidence of synchronous multiple primary lung cancers (SMPLC) have been increasing with an estimate of 2%. Tumours with identical morphology remains a challenge to be classified.
Methods: Distinguishing SMPLC from a primary tumour with intrapulmonary metastasis is very important for the clinical management as the response of different tumours to therapy is different. Here we report a case of an 84-year-old female found to have two discrete, synchronous lung masses bilaterally on imaging studies.
Results: The patient underwent wedge resection and segmentectomy of the tumours within 4 months interval. The 1.9 cm right upper lobe showed invasive adenocarcinoma, acinar predominant with focal visceral pleural invasion. PD- L1 reported strong expression (70%). No mutation was identified on targeted next generation sequencing (NGS). The opposite side wedge resection for the second tumour was performed 4 months after. The 1.7 cm left upper lobe tumour showed invasive adenocarcinoma, acinar predominant. The tumour had no expression of PD- L1 and NGS analysis demonstrated only TP53 mutation.
Conclusion: Following institutional multidisciplinary discussion, based on different molecular genetic characteristics, the decision was made to treat the patient's tumours as synchronous multiple primary lung cancers rather than intrapulmonary metastasis. In clinical practice, it is difficult to distinguish synchronous multiple primary lung cancers from intrapulmonary metastasis especially when the tumours have identical morphology. Hence, advancement of biomarker testing, and next generation sequencing and application of these tools combined with histopathological analysis will improve the clinical management and outcome of these patients significantly.

E-PS-21-026
Adenomyomatous Pulmonary Hamartoma with mucinous differentiation: avoiding subclassifications
J.d.B. Machuca Aguado*, A. Álvarez-Muñoz, E. Rodríguez-Zarco, S. Umbría-Jiménez, J.J. Rios Martin, A. García-Escudero
*Virgen Macarena University Hospital, Seville, Spain

Background & objectives: Recently, a rare variant of pulmonary hamartoma has been described, characterised by a leiomyomatous stroma and glandular structures of different types.
Rossi et al. published 6 cases in 2021 involving mucinous epithelium and found 5 additional cases in the literature.
Methods: Retrospective observational clinicopathological study of a series of 3 cases of pulmonary adenomyomatous hamartoma. Clinicopathological features were described and immunohistochemical analysis was performed, evaluated by three independent pathologists.
Results: We described the morphological features of a biphasic lesion with a stromal component consisting of smooth muscle tissue and a glandular component. We identified three types of glands: several small glands covered by cells with round nuclei and scarce cytoplasm; branching epithelial clefts; and a third type covered by an epithelium with a broad mucinous cytoplasm, with mucoid content. This last type was only present in two of the cases, and they did not express TTF1 nor did it present p63 expression because it lacked a row of basal cells, unlike the first two types of glands. With Ki67, we observed a low proliferation index in all components.
Conclusion: Unlike many of the cases published, the glandular component of our patients was not exclusively mucinous. Therefore, we believe that these lesions should be included in the same category. We propose a broader generic term for all these lesions to avoid confusion in the terminology by overly extensive subclassifications. The term "adenomyomatous pulmonary hamartoma" seems appropriate, specifying, when appropriate, mucinous differentiation. The biphasic appearance and the mucinous glands may result in diagnostic problems if pathologists are unaware of this entity.

E-PS-21-027
Mass-forming pulmonary crystal-storing histiocytosis with mediastinal lymph node involvement: a case report and literature review
E. McGrath*, G. Heuston, R. Shatwan
*St Vincent's University Hospital, Dublin, Ireland

Background & objectives: Crystal-storing histiocytosis is an extremely rare manifestation of underlying lymphoproliferative disorders that presents as an accumulation of histiocytes with abnormal intra-lysosomal deposition of immunoglobulin light chains as crystals of unknown aetiology. Deposition can occur in a number or organ systems.
Methods: Case report: we report a case of a 58-year-old male who underwent surgical resection of multiple pulmonary nodules of crystal-storing histiocytosis with mediastinal lymph node involvement and with no associated lymphoproliferative disorder.
Results: After presenting with multiple episodes of shortness of breath, a CT scan showed mediastinal lymphadenopathy with slowly enlarging right upper lobe nodules and ground glass opacities, one of which showed low grade PET positivity. An elective right upper lobectomy and lymph node dissection were carried out. Histology showed multiple well-formed nodules of crystal storing histiocytosis which were positive for CD68 and kappa and lambda light chains on immunohistochemistry. Other markers including AE1/3, CD1a, desmin, myo-D1, HMB45 and S100 were negative. The patient was not found to have any lymphoproliferative disorder after extensive haematological work up.
Conclusion: We report a case of nodular pulmonary crystal-storing histiocytosis involving the right upper lobe and ipsilateral hilar lymph nodes in a patient with no history of lymphoproliferative disorder. The main differential diagnosis for mass-forming crystal storing histiocytosis is pulmonary malignancy and this may cause diagnostic challenges on both imaging and histology. It is therefore an important, albeit extremely rare differential diagnosis to consider.

E-PS-21-028
A rare case of NSCLC with TTF1 and p40 coexpression - a new subtype to consider?
O.F. Mülkem*, E. Tekin, M.C. Sivrikoz
*Eskişehir Osmangazi University, Faculty of Medicine, Department of Pathology, Turkey

Background & objectives: Lung cancer is currently the leading cause of cancer-related deaths worldwide. The treatment of lung cancer has been determined by the histological classification and stage. The coexpression of TTF1 and p40 within the same tumour cells is an exceedingly rare.

Methods: We present a rare case of non-small cell lung carcinoma (NSCLC) with an uncommon histopathological subtype and occurring at a relatively young age in this study. A 37-year-old female with a two-month persistent cough presented to the hospital. Imaging revealed a 40x35 mm mass in the right lung's lower lobe. The resected specimen exhibited squamous and adenoid areas with intracytoplasmic mucin.
Results: Immunohistochemistry revealed positive expression of TTF1, p40, CK7, and Napsin A in all cells, ruling out the diagnoses of adenosquamous carcinoma and primary pulmonary mucoepidermoid carcinoma. Based on the literature search, the case was classified as "NSCLC, showing biphenotypic features," and was found to be PD-L1 positive. Visceral pleural invasion and six metastatic lymph nodes were also identified, resulting in a stage 2A diagnosis. Next-generation sequencing detected somatic mutations in the FGFR3 and RB1 genes. The patient received four cycles of navelbine-cisplatin chemotherapy and is currently under observation for 15 months without medication. No signs of recurrence or metastasis have been detected in the latest control tomography.
Conclusion: The significance of coexpression of TTF-1 and p40 in NSCLC cells remains unclear. To date, only 19 cases have been reported, which frequently present with advanced age at presentation. In most cases, TP53 gene mutation and FGFR1 amplification have been observed. However, our case differs from others reported in the literature due to its early onset and somatic mutations in FGFR3 and RB1 genes.

E-PS-21-029
Seromucinous hamartoma mimicking lung cancer: case report
F. Mundim*, R. Grande, M. Engelman, G. Engelman, P. Mundim, N. Sousa, E. Berti, M.C. Oliveira, G.H. Junqueira, G. Mendonça, A. Silva
*UNIFENAS, Brazil

Background & objectives: The patient is a 63-year-old man with previous surgery for colorectal adenocarcinoma without loss of DNA repair gene protein expression. CT scan of the chest reveals a vegetating lesion in the left main bronchus, suspicious for a lung tumour.
Methods: Resection of the bronchial tumour was performed by endoscopy and the sample was sent for histopathological analysis.
Results: Under microscopy, tumour tissue is composed of epithelial and mesenchymal components. The epithelial components are primarily seromucous acini similar to the salivary glands and the glands lining the respiratory epithelium. The mesenchymal components are consistent fibrous stroma, free of fat, smooth muscle and cartilage component, without cellular atypias. Immunohistochemistry was focally positive for epithelial membrane antigen (EMA) and tumour suppressor gene TP53 - p53, positive for cytokeratin CK7, and positive for less than 1% of Ki-67 cells of interest. Diagnosis confirmed by immunohistochemical study: Seromucinous hamartoma.
Conclusion: Seromucinous hamartoma that occurs in the lung is very rare and has unique clinicopathological features that need to be differentiated from other benign and malignant lung tumours, which can mimic lung cancer.

E-PS-21-030
Primary adenoid cystic carcinoma of the lung: a case report
M. Muñoz Martín*, M.L. Vazquez, S. Simón Alonso, M.C. Soriano Rodriguez, V. Sotelo Peña
*Hospital Universitario Virgen de la Luz, Spain

Background & objectives: Primary adenoid cystic carcinoma of the lung (ACC) is a low-grade malignant epithelial neoplasm, originates in trachea and bronchial system, without association with cigarette smoking and represents 0.04-0.2% of all lung cancers, therefore clinicopathological behaviour is poorly understood nowadays.
Methods: We have reviewed 50 cases per year of primary lung carcinoma during the last twenty years, which only one was diagnosed as a ACC (1/1000). We present one case of ACC, and analyse its evolution and characteristics in relation to features described up to now in the context of this entity.
Results: The patient was a 42-year-old man, former smoker, and with recurrent pneumonia for one year. Fiberoptic bronchoscopy described an infiltrating lesion in traqueal carina. Endobronchial resection of the lesion was performed.
Histologically, the tumour presented a cribriform pattern, pseudocystic spaces containing basement membrane-like material, lined by a luminal cuboidal line of cells and a peripheral myoepithelial cells. Immunohistochemistry: positive for Vimentin, smooth muscle actin, S100 and p63. Five years later, he presented an unresectable recurrence of lesion, receiving radiotherapy and several lines of chemotherapy depending on the evolution of size of lesion. Currently, the patient is still alive and on active maintenance treatment with pemetrexed with stabilization of disease.
Conclusion: ACC has a prolonged clinical course, with high recurrence trend. The stage at diagnosis, positive margins, and solid pattern are indicators of a poor prognosis. Studies should have a long follow-up due to low frequency and long survival of this type of tumours, as in the case of our patient.

E-PS-21-031
Thoracic SMARCA4-deficient undifferentiated tumour with anaplastic lymphoma kinase (ALK) rearrangement - a case report
J.H. Nam*, Y. Choi
*Chonnam National University Hospital, Republic of Korea

Background & objectives: Thoracic SMARCA4-deficient undifferentiated tumour (SMARCA4-DUT) is a recently identified high-grade malignancy. It is characterized by inactivating mutations of SMARCA4, gene encoding the ATPase subunit of the SWI/SNF chromatin remodelling complexes. We report the case of thoracic SMARCA4-DUT with ALK rearrangement.
Methods: A 59 years old male visited the hospital complaining of 1-month history of chest pain. He was 30-pack year Ex-smoker and had no comorbidity. Chest radiograph and computed tomography showed a 13 x 7.8 cm sized heterogenously enhancing mass involving right middle lobe and extending to adjacent lobes. He was performed lobectomy with stage IIIA (pT4N0M0) malignancy.
Results: The resected specimen showed a poorly differentiated malignant neoplasm, characterized by sheets of epithelioid cells with moderate amounts of eosinophilic cytoplasm, atypical vesicular nuclei and focal necrosis. Some of the cells have rhabdoid morphology. Immunohistochemistry showed that the neoplastic cells were entirely negative for SMARCA4, indicating loss of the product of this gene in the SWI/SNF complex. There was positive in situ hybridization for ALK gene, and next generation sequencing revealed the ALK rearrangements with intergenic-breakpoints. The patient had been received an adjuvant chemotherapy to prevent postoperative recurrence. But, about 2.8 cm sized mass, near operation stump site, was shown. At present, three cycles of ALK-tyrosine kinase inhibitor are being treated.
Conclusion: Our case highlights the significance of ALK rearrangement identification in the quest for the precise therapeutic potential of thoracic SMARCA4-DUT. Given the rarity of this condition and the lack of relevant literature, further studies are still needed.

E-PS-21-032
Blastomatoid pulmonary carcinosarcoma - a case report and literature review
J.H. Nam*, Y. Choi
*Chonnam National University Hospital, Republic of Korea

Background & objectives: Blastomatoid pulmonary carcinosarcoma is one of the rarest histologic types of carcinosarcoma of the lung.

Pulmonary carcinosarcoma is a biphasic tumour with an unfavourable prognosis. The differential diagnosis includes pulmonary blastoma and is often challenging.
Methods: We here describe a case of blastomatoid pulmonary carcinosarcoma in a 68-year-old patient, who underwent surgical lobectomy of left upper lobe. The tumour size was 60x58x40mm. Histopathological examination revealed immature glandular epithelium resembling high-grade foetal adenocarcinoma expressing epithelial markers and membranous beta-catenin, and blastomatoid spindle cells with rhabdomyosarcoma differentiation.
Results: The tumour was composed of areas of glandular differentiation and immature spindle cell areas with a sharp border between both. The tumour exhibited an extensive necrosis (about 70% of tumour). The epithelial component, accounting for 75% of the viable tumour, showed a branching immature gland composed of columnar cells with palisading elliptic nuclei with subnuclear vacuoles. The epithelial cells have a focal an immunoreactivity for glypican-3 and SALL4, but, not in CK7 and TTF-1. Staining for beta-catenin demonstrated a membranous expression. The spindle cells expressed desmin and myogenin indicating rhabdomyosarcoma-like differentiation. A STX-SS18 fusion protein was not detected. Next generation sequencing showed no EGER, KRAS, ALK, ROS1, and CTNBB1 mutation.
Conclusion: The diagnosis of the blastomatoid variant of pulmonary carcinosarcoma was established and the tumour was finally staged at pT3, pN0 (0/15), pMX. Currently the patient is doing well and there is no evidence of tumour relapse 30 months after the resection. The presence of high-grade foetal adenocarcinoma without TTF-1 expression and absent nuclear expression of beta-catenin in a biphasic lung tumour in adult patient favour the diagnosis of blastomatoid pulmonary carcinosarcoma.

E-PS-21-033
Pulmonary histoplasmosis mimicking metastatic lung cancer: a case report
D. Nunes Oliveira*, P. Vianna Caldas Ribeiro, R. Vilar Lima, H. Neves Feitosa Filho, D. Vianna dos Santos, J. Carneiro Melo, F. Rocha Fernades Távora, I. Santos Costa
*University of Fortaleza, Brazil

Background & objectives: Infection with the thermal dimorphic fungus Histoplasma capsulatum (Hc), when found in the form of pulmonary nodules, can become indistinguishable from malignant disease on imaging examinations. Here we report a case of Hc with initial presentation of multiple pulmonary nodules.
Methods: Report a case of a 53-year-old man living whose diagnosis of histoplasmosis was delayed since the findings had been initially misinterpreted as pulmonary malignancy.
Results: Male patient, 53 years old, presented with high fever, sporadic dry cough, weight loss of approximately 6 kg in 15 days. Initial results, including serologies and histopathological study of a lung biopsy guided by computed tomography, which found multiple pulmonary nodules associated with hilar lymph node enlargement, were inconclusive and negative. Although there was clinical improvement, the tomographic changes persisted. This led to a second biopsy by thoracotomy, which confirmed the diagnosis of fungal infection by Histoplasma capsulatum together with the positivity of new serologies.
Conclusion: This case highlights the need to consider Histoplasma capsulatum, a fungus, as a potential cause of pulmonary nodules since its imaging appearance can mimic that of malignant disease. A 53-year-old male patient presented with symptoms and conflicting initial test results, but a thoracotomy biopsy confirmed the diagnosis of Histoplasma capsulatum infection. The case underscores the importance of a comprehensive evaluation and a high degree of suspicion when trying to differentiate between infectious diseases and cancer in patients with pulmonary nodules.

E-PS-21-034
Analysis of asbestos body count in the lungs of female patients with malignant pleural mesothelioma who underwent extrapleural pneumonectomy
K. Okabe*, H. Kinoshita, N. Furukawa, H. Komatsu
*Bell Land General Hospital, Japan

Background & objectives: Malignant pleural mesothelioma (MPM) is well known as very poor prognosis and related to asbestos inhalation. This study analysed the asbestos body count in the lungs of female patients with MPM who underwent extrapleural pneumonectomy (EPP).
Methods: Among 60 consecutive EPP cases for MPM from 2006 to 2019, eleven patients of female MPM were reviewed. Asbestos body quantification involved the digestion of 1-4 grams of lung tissue in bleach employing a modified Smith and Naylor method (Am J Clin Pathol 1972; 58:250-254). In addition, age, MPM type, affected side, cause of asbestos exposure, and prognosis were investigated.
Results: The median age at EPP was 60 (46 - 68) years old. The epithelioid type was 9, and the biphasic type was 2. Right side was 7, and left side was 4. Four patients had occupational asbestos exposure in asbestos factory, casting factory, and architect office. Four patients were judged as environmental asbestos exposure. However, asbestos exposure was unknown in three patients. The prognosis was greatly improved, and 5-year survival rate and median survival time of nine female patients with epithelioid MPM were 67% and 70 months, respectively. The median asbestos body count in one gram of dried lung was 4027 (range: lower than the detection limit - 443571).
Conclusion: Relationship between asbestos and female MPM was reconfirmed. The median asbestos body count in one gram of dried lung of female MPM was 4027. The asbestos body counts of occupational exposure were 443571, 51073, 7169, and lower than the detection limit. The asbestos body counts of environmental exposure were 5911, 4027, 2340, and 265. Although the dried lung of MPM were investigated, the asbestos body counts of 36% were less than 1,000/g, and those of 45% were more than 5,000/g.

E-PS-21-035
Ambivalent aspects of TNF-α in relation with proinflammatory cytokines in patients with COPD
D. Pasarica*, F. Toparceanu, M. Gheorghiu, L. Ichim, M. Serban
*"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Background & objectives: Cytokines are important in responses to COPD. We investigated the dynamics of cytokines IL-8, IL-6 and TNF-α in the serum of patients with COPD to understand the behaviour of TNF-α in relation to the stages of the disease.
Methods: 20 patients (4 women and 16 men) with COPD (mean age 61.0±14.19 years), smokers for more than 20 years were recruited for our study. 10 patients were classified as having GOLD stage II, 10 patients as having GOLD stage III. Serum sample was evaluated by ELISA kit. Pearson correlation coefficient (r) was calculated.
Results: The percentage of circulating neutrophils was 64±5,19% in GOLD II(FEV174-55%) and 73±1.69% in GOLD III(FEV154-35%). IL-8 correlated positively with TNF-α (r=0.539 p=0.05) and IL-6 (r=0.554 p=0.02) in patients with GOLD II. On the contrary IL-8 correlated positively with IL-6 (r=0.777 p=0.05) but not with TNF-α in patients with GOLD III.These suggest that IL-8 and IL-6 can modulate the action of TNF-α towards apoptosis through the TNFRI receptor involving JNK on neutrophils infiltrating in GOLD II. In COLD III the lack of correlation between IL-8 and TNF-α but the presence of a positive correlation between IL-8 and IL-6 suggests that apoptosis by TNF-α is reduced explaining the neutrophilia in GOLD III.

Conclusion: In conclusion our results suggest that the local microenvironment (IL-8, IL-6) modulate the dual behaviour of TNF-α in GOLD. A high concentration of IL-8 and IL-6 uncorrelated with TNF-α is an aggravating factor in COPD.

E-PS-21-036

Feasibility and utility of transbronchial cryobiopsy in lung cancer

V. Pasini*, S. Tomassetti, C.E. Comin
*Università degli Studi di Firenze, Italy

Background & objectives: Transbronchial lung cryobiopsy (TBLC) is an innovative procedure. Currently there are few data regarding its use in neoplastic lung disease, especially in mediastinal lymph node staging. We evaluated the usefulness of TBLC for lung cancer diagnosis and predictive biomarkers analysis.
Methods: Thirty-seven patients with lung and mediastinal lesions were included. Forty-two tumour specimens obtained by TBLC were compared to those obtained by other techniques, in particular EBUS-TBNA (7 cases) and trans-bronchial lung biopsy (TBLB, 10 cases). All specimens were formalin-fixed, paraffin-embedded, and hematoxylin-eosin stained. Samples included 33 peripheral lesions, 7 central lesions and 2 mediastinal lymph nodes.
Results: Lung parenchyma was well preserved in all TBLC samples. TBLC was found to be diagnostic in 33 (78.5%) cases; TBLB was diagnostic in 4 (40%) cases; clot-core samples from EBUS-TBNA were diagnostic in 4 (57%) cases. The case cohort included 13 adenocarcinomas, 8 squamous cell carcinomas, 3 small cell lung cancers, 4 Langerhans cell histiocytosis, 1 undifferentiated carcinoma, 1 myoepithelioma, 1 sclerosing pneumocytoma and 2 secondary tumours. The success rate of TBLC for PD-L1 evaluation was 100%. The success rate of TBLC specimens for DNA and RNA next-generation sequencing (NGS) was 93.3%.
Conclusion: Few studies have analysed the utility of this procedure in lung cancer. Our study demonstrated that TBLC might be a feasible approach for diagnosis and staging of lung cancer. Compared to EBUS-TBNA and TBLB, TBLC seems to provide more adequate samples for diagnosis and molecular analysis. Since tissue quality and quantity are still the most important issues in the therapeutic management of patients with lung cancer, we suggest that TBLC could represent a feasible alternative procedure in clinically selected cases.

E-PS-21-037

Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH); a case report and review of the literature

D. Proca*, M. Hussain, M. Jabbar, M. Mollaee, D. Zenezan
*Temple University Health System, USA

Background & objectives: Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a rare, under-diagnosed pulmonary benign disorder with numerous lesions that can progress to malignancy in 10% of cases. Histologically, it manifests as a proliferation of bland neuroendocrine (NE) cells around bronchial walls.
Methods: We report a case of DIPNECH that was incidentally diagnosed in an explanted lung from a 65 yo female with end stage lung disease due to COPD. Her clinical history includes a 40- pack year smoking history. Imaging before the transplant showed mild narrowing of the bronchi in the expiratory phase, focal thickening of bronchial walls and severe emphysema.
Results: The explanted lung weighed 496 g and measured 20.5 x 10.0 x 1.2 cm. Sections revealed severe emphysema with subpleural bullae and anthracosis.
Histologically, more than 10 aggregates and micronodules of NE cells were seen in all three lobes of the explanted right lung; the clusters measured up to 1.5 mm in greatest dimension and didn't infiltrate through the basement membrane of the airways. The aggregates reacted positive with AE1/AE3, Chromogranin and Synaptophysin. Given the widespread nature of NE proliferation, a diagnosis of DIPNECH was made after correlation with radiological studies. The challenge in this case was the rarity of the diagnosis and nonspecific symptoms overlapping with those of COPD.
Conclusion: Our case is unique because the diagnosis was made in an explanted lung with end stage COPD. The definitive diagnosis is based on histopathologic examination, correlated with radiologic confirmation of the widespread nature of the lesions. Increased awareness of this preneoplastic disease is important due to its late diagnosis and its propensity to evolve to invasive neuroendocrine tumours. The importance of this diagnosis is that the patient has to be followed up for progression of DIPNECH in the contralateral lung.

E-PS-21-038

Endobronchial case of Langerhans cell histiocytosis (eosinophylic granuloma)

E. Psychogiou*, P. Tziakou, P. Megas, M. Miliou, K. Papadopoulou, A. Konstantinidou, E. Papadopoulou, D. Riga, C. Glava, I. Vamvakaris
*General Hospital of Athens Sotiria, Greece

Background & objectives: Eosinophilic granuloma is a form of Langerhans cell histiocytosis that can involve lung and bone. It is primarily an interstitial disease, although epithelial destruction may lead to alveolar involvement, characterized by an abnormal proliferation of histiocytes mixed with inflammatory cells.
Methods: A 45-year-old man with free medical history was admitted to our hospital complaining of irritant cough. Fibreoptic bronchoscopy discovered a well-circumscribed polypoid mass, measuring 0,5 cm, protruding into trachea and biopsy was performed.
Results: Histopathological sections revealed a polypoid lesion covered with stratified squamous epithelium with subepithelial presence of lymphocytes, eosinophils, fibroblasts, histiocytes and larger cells with prominent nucleus and cytoplasmic groove. The immunohistochemical analysis showed positivity to SMA, S-100, CD68, LCA, CD1a and Langerin while the stains Chromogranine, KLMW, p40, CD56 and CK19 were negative. Both histological findings and immunohistochemical results concluded to Langerhans' cell histiocytosis.
Conclusion: Pulmonary histiocytosis X is a form of Langerhans' cell histiocytosis and it is characterized by an abnormal proliferation of Langerhans' cells, which seem to serve as accessory cells for a lung immuno-pathologic response. It is observed exclusively in smokers. Histopathologic confirmation remains the most definitive way to establish the precise diagnosis. The clinical course is uncertain and varies from complete or partial regression to progression until the end-stage lung. Treatment consists of corticosteroids, but cessation of smoking should be encouraged.

E-PS-21-039

Pulmonary sclerosing pneumocytoma mimicking neuroendocrine tumour

E. Psychogiou*, P. Tziakou, P. Megas, M. Miliou, K. Papadopoulou, A. Konstantinidou, E. Papadopoulou, D. Riga, C. Glava, I. Vamvakaris
*General Hospital of Athens Sotiria, Greece

Background & objectives: Sclerosing pneumocytoma is a rare benign pulmonary tumour composed of a dual population of surface cells resembling type II pneumocytes and round cells. It is typically solitary and peripheral and the patients are asymptomatic, with the tumour often discovered incidentally.
Methods: A 39-year-old woman was admitted to our hospital after MSCT scan demonstrated a 2,3X1,4cm solid mass on her left lower

lobe. Both MSCT and intraoperative consultation pointed out the D/D between NET and other benign lesion, so lobectomy was decided.
Results: The tumour was well circumscribed, nonencapsulated, with a cut surface tan-yellow to grey. Histopathological sections revealed a solid and a papillary pattern. The neoplastic cells were medium sized, with oval nuclei and distinct nucleoli, with abundant eosinophilic cytoplasm. The mitotic activity was low (Ki67 5%) and there was absence of necrosis. The intermediate stroma was sclerotic with haemorrhage and chronic inflammation. The pleura were free of neoplastic invasion. Both the neoplastic cells were immunohistochemically positive to TTF-1, CD56, CK18, Napsin A, while the papillary component was CK7(+) and ER(+) and the solid component was ER/PR(+). All lymph nodes were disease-free and the surround parenchyma showed areas of emphysema and atelectasis.
Conclusion: Sclerosing pneumocytoma can present as solid tumour with biphasic pattern and is challenging to distinguish from adenocarcinoma or carcinoid tumour on frozen sections. It was usually seen in the fifth-decade female, which was possibly attributed to the presence of progesterone receptors. Possible malignant characteristics with lymph node metastasis or local recurrence have been documented. Sublobectomy, segmentectomy and wedge resection, tended to be preferred for peripheral small-sized tumour, while lobectomy could prevent potential metastasis and recurrence which would worse long-term prognosis.

E-PS-21-040
Endobronchial lipoma: an incidental finding during bronchoscopy
E. Psychogiou*, P. Tziakou, P. Megas, M. Miliou, K. Papadopoulou, A. Konstantinidou, E. Papadopoulou, D. Riga, C. Glava, I. Vamvakaris
*General Hospital of Athens Sotiria, Greece

Background & objectives: Endobronchial lipoma is a rare benign neoplasm accounting for only 0.1%–0.4% of all bronchial tumours and is composed exclusively of mature fat. It is difficult to differentiate benign from their malignant counterparts, as their symptoms and complications are alike.
Methods: A 66-year-old man was admitted to our hospital complaining of irritant cough. Chest radiography showed atelectasis of the right lung and MSCT scan demonstrated a mass on right upper lobe. During fibreoptic bronchoscopy, a well-circumscribed polypoid mass, measuring 0,4X0,2 cm, protruding into trachea was incidentally found and was successfully excised.
Results: The biopsy specimen was a well circumscribed tumour with a uniform glistening yellow surface. Histopathological sections revealed bronchial tissue covered by benign epithelium, benign seromucinous glands and mature adipose tissue. No malignant cells were seen. There was absence of cartilage, myxoid matrix, entrapped bronchial epithelium, or other mesenchymal components. The presence of fat attenuation narrows down the differential diagnosis to the following: pure endobronchial lipoma, which demonstrates homogeneous fat attenuation; fibrolipomatous tumour, which contains soft tissue attenuation with islands of fat; and hamartoma, which has fat density alternating with calcific foci and other mesenchymal components. The tumour was pathologically confirmed as endobronchial lipoma.
Conclusion: This case suggests that an endobronchial lipoma can present as incidental finding. Patients are middle aged with a strong male predominance. Clinically, these patients most often present with cough and symptoms of chest infection. CT examination is highly specific and sensitive for the detection of fat. Endoscopic resection is usually the first line of treatment, as it is both diagnostic and curative. Recurrence of endobronchial lipoma is exceedingly rare after complete surgical resection.

E-PS-21-041
Semi-automated microscopic evaluation of mesothelin and immune landscapepredicts survival after surgical resection of malignant mesothelioma
A. Qualiotto*, C. Machado Baldavira, M. Balancin, A. Ab'Saber, T. Takagaki, V.L. Capelozzi
*Laboratory of Genomic and Histomorphometry, Department of Pathology, University of Sao Paulo Medical School, Brazil

Background & objectives: Anti-mesothelin and anti-PD-L1 emerged as promising drugs to inhibiting the invasion of malignant mesothelioma (MM) and restoring the immune landscape. Thus, we sought to study the relationships between mesothelin and the immune landscape in MM.
Methods: We examined mesothelin, immune cells (CD4, CD8, CD68, CD20), and PD-L1 markers in tumour tissues from 82 patients with MM. All our patients were stage III/IV, and 50.6% of patients had been exposed to asbestos. We used immunohistochemistry and quantitative digital analysis (QuPath software) to evaluate the amount of tumour staining for mesothelin, immune cells, and PD-L1.
Results: Our results showed that high mesothelin expression was associated with male (P=0,013) and sarcomatoid histotype (P<0.01). High CD4 expression was associated with not asbestos exposure and alive patients (P<0.01, for both). High CD8 expression was correlated with epithelioids histotype, while high PD-L1 expression was associated with women (P=0.03, for both). When combined the expressions CD4 and CD8, the increased expression this combination was associated with no asbestos exposure and alive patients (P<0.01, for both). Multivariate Cox model analysis, controlled for asbestos, histological type, and PD-L1 expression, demonstrated that quantitative staining of the tumour for mesothelin and CD4 added prognostic information (P=0.001 and P=0.016, respectively).
Conclusion: Tumour staining for mesothelin, CD4, and PD-L1 in resected MM of the pleura are strongly related to survival. Patients with staining for mesothelin >23.96%, and PD-L1 >0.58% in their tumours, after 40 months of follow-up comprise a subset with a high hazard of dying of MM, while patients with CD4 >0.7% in their tumour presented better survival. These findings suggest that those markers may be an appropriate target for prospective studies of adjuvant immunobiological agents combined with immune checkpoint proteins.

E-PS-21-042
Increased epithelial-mesenchymal transition transdifferentiation proteins increasesextracellular matrix proteins in invasive non-small cell lung carcinomas
C. Machado Baldavira, A. Qualiotto*, M.L. Fernezlian, S. Fernezlian, A.P. Pereira Velosa, W. Rosolia Teodoro, A. Ab'Saber, T. Takagaki, V.L. Capelozzi
*Laboratory of Genomic and Histomorphometry, Department of Pathology, University of Sao Paulo Medical School, Brazil

Background & objectives: In NSCLC, invasion is defined as tumoral infiltration into stroma, be enhanced by the epithelial-mesenchymal transition (EMT) process. We hypothesize that the density of extracellular matrix (ECM) proteins and expression levels of EMT-proteins may correlate with clinicopathologic variables and outcomes.
Methods: We analysed the protein expression of the EMT indicators E-cadherin, B-catenin, and SPARC as well as of the putative ECM indicators fibrillin, elastin, heparan sulfate (HS), chondroitin sulfate (CS), collagen types (Col) I, III, IV, and V in both intratumoral stroma and carcinoma cells in a cohort of NSCLC (n=81) by immunohistochemistry quantification by digital analysis (QuPath software).
Results: We observed a significant moderated correlation between fibrillin vs SPARC, elastin vs SC, HS vs SPARC, E-cadherin vs β-catenin, and E-cadherin vs Col III. Lower fibrillin was associated with

male gender, higher pT, and pN categories, and adjuvant chemotherapy. Lower elastin was associated with tobacco consumers, SqCC and LCC histology, and early disease. Col I correlated positively with the pT category; Col III, CS, and E-cadherin were both associated with age. In multivariate analysis, high SPARC and relapse were found to be a prognostic factor for decreased progression-free survival (P=0.03) when controlled for male gender, SqCC histology, tumour size, and Col III.
Conclusion: Because up-regulation is frequently observed in the stromal and epithelial tumour compartment, EMT-ECM indicator proteins may be integrated into progression models of NSCLC, eventually allowing the selection of patients who can benefit from targeted therapies.

E-PS-21-043
Endobronchial solitary fibrous tumour: a perfect mimic of carcinoid
E. Ramalhosa*, F. Pezzuto, F. Francesco, G. Canu, E. Faccioli, C. Giraudo, F. Calabrese
*Centro Hospitalar e Universitário de Coimbra, Portugal

Background & objectives: Solitary fibrous tumours (SFTs) are rare mesenchymal neoplasms (less than 2% of all soft tissue tumour) commonly arising in the thoracic cavity. However, they may occur at any site, including the lung parenchyma, pericardium, and, rarely, the bronchus.
Methods: A 49-year-old woman presented to the pulmonary unit with progressive chronic cough. She was a non-smoker with history of allergy to plants, fruits and drugs. Due to progressive obstructive dysfunction an explorative bronchoscopy was performed revealing an intrabronchial mass of the left superior bronchi. Somatostatin Receptor-Based PET/CT showed high affinity to somatostatin receptors rising the main diagnosis of carcinoid tumour.
Results: The patient underwent pulmonary segmentectomy and an intramucosal well circumscribed polypoid lesion of 19 mm was detected. Pathological examination revealed a low-grade mesenchymal spindle cell neoplasm arranged in sheets and storiform pattern without necrosis. The tumour cells had mild atypia with low mitotic index (1 mitosis/mm2). The lymph nodes and margins were negative. The immunohistochemical analysis was positive for STAT6, and negative for S-100, MDM2, cytokeratin, chromogranin A,and synaptophysin. The proliferation index (Ki-67) was 5%. Based on the histopathological and immunohistochemical findings the diagnosis of a bronchial SFT was made. The patient became asymptomatic after lesion's excision, and during the 6-month follow-up there were no recurrences.
Conclusion: Endobronchial SFT are unusual. To the best of our knowledge only five cases have been reported in the literature. Carcinoid is the main mimicker sharing clinical and radiological characteristics. Considering the location and the features at imaging mucoepidermoid carcinoma, endobronchial pleomorphic adenoma, hamartoma or leiomyoma and, last but not least, metastases should be considered among the differential diagnoses. This report highlights the importance of careful histological and immunohistochemical evaluation for an accurate diagnosis and appropriate risk stratification of this lesion.

E-PS-21-044
SMARCA4 deficiency in poorly differentiated/ undifferentiated non-small cell lung carcinoma
G. Raskin*, A. Fedorova, M. Mukhina, R. Orlova, M. Kleshev
*Dr. Berezin Medical Insitute, Russia

Background & objectives: SMARCA4-deficient lung tumours are highly aggressive malignancies without mutations in EGFR, ROS1, or ALK genes. The aim of the study was to evaluate the frequency of SMARCA4-deficient tumours in patients with poorly differentiated and/or undifferentiated non-small cell lung carcinomas (NSCLCs).
Methods: 133 cases of poorly differentiated NSCLCs were studied immunohistochemically using the anti-BRG1 (SMARCA4) and anti-SMARCA2/BRM (Abcam) antibodies. The expression of TTF1 (Leica), p63 (Agilent) was also investigated. Specimens considered SMARCA4 and/or SMARCA2-deficient if negative reaction observed in tumour cells, while stromal cells showed positive nuclear staining. EGFR, BRAF, ROS and ALK mutations were analysed retrospectively in such cases.
Results: 26 cases (19,5%) of NSCLCs were identified as SMARCA4-deficient. There were 21 men and 5 women with average age 61.3±1.9. In 20 SMARCA4-deficient tumours, a negative TTF1 or p63 reaction was detected. In addition, 14 of 20 tumours showed a combined loss of both markers. SMARCA2 expression was studied in 24 SMARCA4-deficient tumours. Complete loss of both markers was found in 5 cases (20,8%), and a focal attenuation of SMARCA2 expression was noted in 3 cases (12,3%). The rest 16 tumours were SMARCA2 -positive. EGFR, BRAF, ROS and ALK mutations were not detected in any of the cases.
Conclusion: According to our investigation SMARCA4-deficient tumours occurred in 20% of poorly differentiated NSCLCs. Predominantly these tumours were TTF1/p63 negative and often demonstrated loss of SMARCA2 expression (33%). As SMARCA4-deficient tumours respond poorly to standard therapy in comparison with other poorly differentiated and/or undifferentiated lung tumours, further study with an assessment of prognostic and predictive value of these markers is recommended.

E-PS-21-045
The combination of PDL-1 expression and TIL levels as predictors of response to immunotherapy in non-small cell lung carcinoma
R. Rendón García*, J.d.B. Machuca Aguado, M.L. Bernal Sanchez, F.J. Rubio Garrido, J.J. Rios Martin, M.A. Idoate Gastearena
*Virgen Macarena University Hospital, Seville, Spain

Background & objectives: Immunotherapy has been a revolution in the treatment of non-small cell lung carcinoma (NSCLC). However, its high cost and limited availability highlights the needing of prognostic and predictors biomarkers, being the tumour infiltrating lymphocytes (TILs) a possibility.
Methods: This is a retrospective observational clinicopathological study of a series of 29 patients with NCLSC treated with immunotherapy. They had a median follow up to 40 months. The level of PDL1 expression was determined immunohistochemically. The number of stromal and intraepithelial CD8+ TILs were assessed by two observers and cut-off points were established according to the Donnen classification.
Results: The relationship between PDL-1 and overall survival was statistically significant (r= 0,341; p= 0.03).When patients were divided in 4 subgroups according to PDL-1, high (>50%) or low (<50%) expression, and intraepithelial TILs, high (>25%) or low (<25%) level, those in the high-PDL-1 and high-TILs-CD8+ subgroup were associated with the highest overall survival (p=0.047).
Conclusion: We consider that the quantification of PDL-1 and CD8+ TILs could be adequate biomarkers to perform a clinical approach to patients. These biomarkers can be predictors of immunotherapy response and prognostic of survival, being of better prognosis those patients with elevated levels of both parameters.

E-PS-21-046
A comparison of pulmonary placental transmogrification with immature placenta
L. Rothenbächer*, J. Knolle, M. Krüger, W. Schütte, E. Gradhand
*Krankenhaus Martha Maria Halle Dölau, Institut für Pathologie, Germany

Background & objectives: Pulmonary placental transmogrification (PPT) represents an extremely rare benign lesion of the lung and histomorphologically, it resembles immature placental villi. We compare

the histological findings and iimmunohistochemical expression of the PPT with immature placenta.
Methods: Histological H+E- and immunohistologically stained sections of a pulmonary placental transmogrification of a 40 year old former smoker and an immature placenta of the 12th week of pregnancy of a 39 year old woman are compared.
Results: Histologically, the PPT show a cavernous placental-ilike neoplasia without atypia or atypical mitoses. Pre-existing pneumocytes express TTF-1. The epithelium expresses AE1/AE3. Vascular structures express CD31 and CD34. Lymphangioma-like structures express D2-40. Scattered single CD117 positive mast cells are seen. The stroma cells are moderately CD10-positive but positive for Actin and with negativity for Desmin. Ki67 marks 1% oft he lesional cells. Isolated Progesterone and PAX8 positive cells with negativity for Oestrogen are seen. Immunohistochemistry of immature placenta shows a similar result. Though, TTF-1, Progesterone, PAX 8 are not expressed. However, Desmin, BetaHCG and PLAP are positive in placental tissue, which were not expressed in PPT.
Conclusion: Pulmonary placental transmogrification and immature placenta are very similar histomorphologically. Even though, the immature placenta of the 12th week of gestation shows villi with a double-row trophoblast epithelium; in the PPT, the epithelium is delicately single-rowed and the villi-like structures are more rounded. Immunohistochemically, they show some similar expression pattern. Nevertheless, there significant differences in immunohistochemical expression with BetaHCG and PLAP negativity in PPT.

E-PS-21-047
Next generation sequencing in non-small cell lung carcinoma: two-year institution experience
S. Sáez-Álvarez*, M.G. Rodríguez-Guevara, C. Diez-Tascón, S. Medina-Valdivieso, C. Martínez-Martínez, B.I. Tavara-Silva, S. Marín-Asencio, L. López-López
*Complejo Asistencial Universitario de León, Spain

Background & objectives: Multigene analysis by Next Generation Sequencing is recommended by ESMO in patients presenting with advanced non-squamous Non-Small Cell Lung Carcinoma (NSCLC). The present work aims to describe the NGS results obtained in our institution for NSCLC in a two-year period.
Methods: Tumour samples obtained from consecutive patients diagnosed during 2021 and 2022 underwent targeted NGS analysis using a 52 genes panel (Oncomine Focus Assay, ThermoFisher), including DNA variants, copy number variants (CNV) and gene fusions. Data was processed using Microsoft Excel and IBM SPSS.
Results: 297 samples of NSCLC from 287 patients underwent NGS during this period. Most patients were males with an average age of 68.3 years. Active/former smokers accounted for 63%. Most samples were biopsies (63.3%), the rest corresponding to cytology and Fine-Needle Aspiration.
Molecular alterations were found in up to 72% patients, with EGFR and KRAS being the most frequently altered genes. EGFR mutations were identified in 14.5% tumours (45.7% deletion exon19; 28.6% p.L858R). KRAS mutations accounted for 35% (41,2% p.G12C). Translocations showed lower frequency (3% ALK; 1.3% ROS1; 1.7% RET). Other single nucleotide variants (SNV) were also present (5.1% BRAF; 6.7% PIK3CA). MET exon14 skipping was identified in 5 tumours (2.7%).
Conclusion: NGS is a sensitive and specific technique to identify molecular alterations affecting predictive biomarkers of NSCLC. Biopsy and cytology samples are both eligible for NGS. A large percentage of NSCLC harbour molecular alterations with clinical and/or therapeutic value. Alterations in biomarkers found this work are similar to those described in other studies performed in our country.

E-PS-21-048
A peculiar case of endometrioid type adenocarcinoma of lung
C. Stamou*, K. Iliadis, M. Sotiropoulou
*Department of Pathology, Hygeia Hospital, Athens, Greece

Background & objectives: Adenocarcinoma with endometrioid type morphology of lung is rare and is usually seen in the context of primary foetal adenocarcinoma or metastatic disease from gynaecological adenocarcinoma. We present a case of a 47y.o. woman without history of myllerian endometrioid adenocarcinoma.
Methods: A right lower lobectomy specimen was received, in multiple sectioning of which two compact and whitish nodules of 2.6 cm and 1.4 cm in maximum diameter were found.
Results: The histological examination of both nodules revealed well demarcated neoplastic lesions composed of glandular either tubular formations lined by pseudostratified epithelium of cylindrical cells with eosinophilic cytoplasm, ovoid to elongated nuclei, coarse chromatin and incospicuous nucleoli. There were also focal back-to-back and cribriform configurations, numerous morules and rare squamous metaplasia. Moreover, tiny nodules of immature chondroid tissue were present. Upon immunohistochemical control, neoplastic cells were positive for Pax8, ER, PgR, CK7 and AE1/AE3, with membranous expression of β-catenin stain and wild-type staining pattern of p53. Further immunohistochemical control with TTF1, AFP and Vimentin was negative, while morules were positive for CD10.
Conclusion: A diagnosis of low grade endometrioid type adenocarcinoma was made, probably of myllerian origin. We also stated the probabilities of primary lung endometrioid adenocarcinoma arising in lung endometriosis and of low grade foetal adenocarcinoma/pulmonary blastoma. Radiological examination revealed no mass in uterus and ovaries, however a total hysterectomy with bilateral salpingo-oopherectomy was decised, after multiple sectioning and examining of which no neoplastic areas were detected. Next generation sequencing of multiple genes from lung nodules revealed mutations in CTNNB1, PTEN and PIK3CA genes.

E-PS-21-049
Lung Epithelioid Hemangioendothelioma (EHE) with YAP-1-TFE3 fusion: diagnostic approach in endobronchial biopsy
N. Stavrinou*, F. Dolkiras, E. Spiteri, E. Athanasiou, E. Papagianni
*Department of Pathology, Evaggelismos General Hospital Athens, Greece

Background & objectives: Epithelioid haemangioendothelioma of the thorax is a malignant vascular neoplasm, usually intraparenchymal, less often pleural, rarely mediastinal. It affects mostly young people. Patients often present with metastatic disease; therefore its prognosis seems to be worse than the soft tissue counterpart.
Methods: A 37-year-old man, smoker, presented with haemoptysis due to a large mass in the hilum of the right lung. An endobronchial biopsy was performed and sent for pathologic evaluation. The tissue sample was fixed in 10% neutral buffered formalin, processed and embedded in paraffin.
Results: Microscopically, bronchial mucosa was infiltrated by an epithelioid malignant neoplasm consisting of relatively uniform tumour cells of plasmacytoid or rhabdoid morphology, with moderate nuclear atypia, mostly arranged in a solid pattern around vessels or forming rudimentary vascular spaces. Mitotic activity was estimated at 6/50HPF. Spindle cell morphology and necrosis were absent. Immunohistochemically, tumour cells were positive for vascular markers (CD31, D2-40, FVIII, ERG, Fli-1) as well as TFE3, Vimentin, CD56, and CD163. Cytokeratins, neuroendocrine, melanocytic, and lymphocytic markers were negative. In situ hybridization for YAP1-TFE3 fusion was also performed. Ki67 was estimated at 35%.

Conclusion: On the basis of morphological, immunohistochemical, and molecular findings, the diagnosis of EHE with YAP-1-TFE3 fusion was established. Due to its aggressiveness, EHE's diagnostic approach in the limited tissue of endobronchial biopsy is crucial. Immunohistochemical markers and molecular techniques may be helpful.

E-PS-21-050

Inflammatory fibroblastic tumour (IMT) of the right lung - a case report

C. Valavanis*, E. Souka, E. Fergadis, N. Baltagiannis, G. Stanc
*Molecular Pathology Unit Metaxa Cancer Hospital, Greece

Background & objectives: IMT of the lung represents an extremely rare type of inflammatory pseudo-tumour. It is most common in children and young individuals, mostly in first and second decades. IMT are extremely rare in adults and comprise <1% of adult lung tumours.
Methods: A 49-year-old female presented with cough and dyspnea. Chest CTscan showed solitary, circumscribed lobulated lesion on the lower right lobe. FNB of the lung was performed and the diagnosis of inflammatory fibroblastic tumour was made followed by right lobe pneumonectomy On gross examination a circumscribed yellow lobulated tumour, 1,5cm in great diameter was found.
Results: Microscopic examination revealed a neoplasm with spindle cells, without nuclear atypia and no mitotic figures. The cells are seen as interlacing fascicles among a polymorphous inflammatory infiltrate consisting of mature plasma cells and small lymphocytes. Immunochemistry displayed Vimentin (+), Calponin (+), Desmin (+), ALK (+) and Ki-67 positivity in 1-5% of the tumour cells. Negative were CKAE1/AE3, CK7, TTF-1, Napsin A and GATA-3. The diagnosis of inflammatory fibroblastic tumour of the lung was made.
Conclusion: IMT of the lung are rare, with incidence <1% of all lung tumours.
IMTs show typically benign clinical behaviour. Malignant evolution has been described including recurrent (2-25% of cases) and metastatic disease (<5% of cases).
Clinical symptomatology of pulmonary IMTs is various and nonspecific. In approximately 70% of the cases, the disease is discovered incidentally on imaging exams requested for other reasons.
The diagnosis of IMT is difficult to establish, and histologic examination is always required.

E-PS-21-051

Tissue culture for organ-on-chip approaches to study interactions between non-small cell lung cancer tumours and proximal lymph nodes

I. Vamvakaris*, K. Potaris, K. Tsilingiri, C. Karakostas, G. Zachou, M. Chliara, I. Zergioti, A. Klinakis
*SOTIRIA, Greece

Background & objectives: Metastasis to the lymph nodes is often the first step before distal tumours are established. In this work, we are optimizing a microfluidic organ-on-chip to examine the interaction between precision-cut tumour slices and immune cells.
Methods: In this work, standard tissue culture techniques are coupled with advanced microfluidic circuit optimization. Potential interaction between cancer cells and immune cells are assessed in both traditional transwell culture settings (vertical movement of cancer cells) as well as on a novel organ-on-chip platform connected to a microfluidic circuit which provides fresh media throughout the culture (horizontal movement of cancer cells).
Results: We have set up co-culture conditions which promote viability of both tissue types (tumour and lymph node) for up to 5 days. Tissue viability is assessed with haematoxylin and eosin staining, while cell viability is assessed via flow cytometry. Slices remain in good condition throughout the experiment on both transwells and microfluidic chips. We have so far observed only vertical movement of cancer cells for two out of eight samples tested. Initial evaluations indicate that cell migration is increased in the presence of lymph node slices or immune cell suspensions. We have retrospectively confirmed that highly migrating cells came from tumours of metastatic patients, undiagnosed at the time of surgery.
Conclusion: We are optimizing a state-of-the-art organ-on-chip set up to observe migration of metastasizing cancer cells in real time. To this end, we have determined optimal co-culture conditions guaranteeing viability of tissue slices for up to 5 days. We have shown that a media flow of 2μL per minute on a microfluidic chip is sufficient to maintain tissues in good condition. Molecular analyses will be performed on sorted metastasizing cells to highlight genetic and functional differences between metastatic and non-metastatic clones.

E-PS-21-052

Generation of a predictive xenograft platform of patients with bronchial neuroendocrine tumours in zebrafish

I. Vamvakaris*, G. Evangelou, A. Bianchi, G. Lolas, L.D. Jensen, K. Syrigos
*SOTIRIA, Greece

Background & objectives: Neuroendocrine tumours of the lung constitute a wide spectrum of neoplasms. At one extreme are the bronchial carcinoids with an excellent prognosis, at the other are the poorly differentiated carcinomas, with a poor prognosis regardless of the therapeutic combination.
Methods: A key barrier to improving treatment efficacy and patient survival is the lack of predictive biomarkers for most treatment regimens. Preclinical platforms, such as patient derived xenografts (PDX) models, which aim to predict the efficacy of drugs in each individual patient before the actual administration of drugs, are under development.
Results: In zebrafish tumour xenografts (ZTX) models, patients' cancer cells are labelled with red fluorescent dyes and implanted into the subcutaneous tissue located between the skin (epidermis) and the yellow epithelial membrane, known as the periperitoneal space. In the present study, we first constructed NENs xenografts in zebrafish using patient-derived tumour biopsies. The main advantage of zebrafish is the non-invasive in vivo imaging of cancer progression as well as the limited time required to monitor these responses, which in most cases ranges from 3–6 days compared to several weeks in mouse models.
Conclusion: The specific objectives of the ZTX zebrafish model are as a drug screening platform and to examine the optimal sequencing of available therapies as well as to provide evidence on the feasibility and accuracy of the proposed preclinical platform for the personalized treatment of bronchial NETs.

E-PS-21-053

Comparative analysis of a new IHC assay for PD-L1 expression in non-small cell lung carcinomas

D. Wang*, S. Nielsen, M.K. Stensballe, A. Saxena, V.M. Calero, J. LaMar, R. DeCamillis
*Sakura Finetek USA, USA

Background & objectives: Program death ligand-1 (PD-L1) IHC expression is used to select patients with non-small cell lung carcinoma (NSCLC) for immunotherapy. This study is to determine analytical concordance between PD-L1 IHC 22C3 pharmDx and PD-L1 IHC Assay (clone RM320) in NSCLC.
Methods: 104 human formalin-fixed paraffin-embedded (FFPE) NSCLC cases from three microarrays were analysed by the two IHC

methods. Evaluation of PD-L1 IHC was performed by a pathologist and certified external reviewer using the Tumour Proportion Score (TPS) based on the official recommended scoring guidelines and related cut-off levels at 1% and 50% used to stratify patients for immunotherapy with pembrolizumab (KEYTRUDA®).
Results: Using the PD-L1 IHC 22C3 pharmDx as a benchmark, 57.6% of the NSCLC cases (n=60) were classified as TPS-negative (<1%), 24.0% as TPS Low (≥1-49%, n=25) and 18.3% as TPS High (≥50%, n=19). An overall analytical concordance of 92% between the two methods was observed. The PD-L1 IHC Assay developed using clone RM320 on the Tissue-Tek Genie® Advanced Staining System showed a positive predictive accuracy of 81.5% and 100% for TPS 1% and 50%, respectively and a corresponding negative predictive accuracy of 98.3% and 96.6%.
Conclusion: Based on this initial study, high accuracy and analytical concordance for PD-L1 expression were found using the presently applied cut-off values and guidelines for TPS in NSCLC. More studies with validated positive PD-L1 expression levels in NSCLC cases are required to further evaluate the potential usability of the PD-L1 IHC assay developed on the Tissue-Tek Genie® Advanced Staining System for stratification of patients for immunotherapy with pembrolizumab (KEYTRUDA®) treatment.

E-PS-21-054
Assessment of HER2 immunohistochemistry scoring by pathologists with or without specific HER2-low training
A. Wróbel*, M. Vandenberghe, M. Scott, F. Jones, T. Matsuo, A. Boothman, J. Whiteley, C. Barker
*AstraZeneca R&D, Poland

Background & objectives: Proven benefit of trastuzumab deruxtecan in HER2-positive and HER2-low (immunohistochemistry [IHC] 1+, IHC 2+/in situ hybridization–negative) metastatic breast cancer means accurate identification of HER2-low tumours is now clinically important. We compared central versus real-world HER2 IHC scoring, including HER2-low.
Methods: Consensus scores for 500 archival FFPE breast cancer samples, stained with the Ventana PATHWAY anti-HER2 (4B5) assay, were generated by three pathologists trained for HER2-low scoring. Inter-pathologist concordance was assessed by Fleiss Kappa across all IHC categories and including HER2-low cut-off (IHC 0 vs ≥ IHC 1+). Real-world HER2 IHC scores from 3 CAP/CLIA clinical labs were compared with consensus.
Results: Substantial agreement was observed between three pathologists trained in HER2-low across all HER2 scores (κ=0.70 by Fleiss Kappa) and for the HER2-low cut-off (i.e., the boundary between IHC 0 vs IHC 1/2/3+), (κ=0.80). Overall, historical real-world pathologist scoring performance evidenced moderate agreement (κ=0.60) to trained pathologist consensus across all scores and substantial agreement for the HER2-low cut-off (κ=0.71).
Conclusion: This study was performed prior to approval of trastuzumab deruxtecan for treatment of HER2-low metastatic breast cancer patients. The substantial agreement between pathologists trained in HER2-low gives confidence in the ability to robustly categorise above and below the HER2-low cut-off for samples stained with the Ventana 4B5 assay. Higher agreement between trained pathologists versus historical real-world pathologist scoring indicate education and training will improve accuracy of HER2 scoring, including at the IHC 0/IHC 1+ boundary.
Funding: This work was funded by AstraZeneca in accordance with Good Publication Practice (GPP) guidelines (http://www.ismpp.org/gpp-2022). In March 2019, AstraZeneca entered into a global development and commercialization collaboration agreement with Daiichi Sankyo for trastuzumab deruxtecan (T-DXd; DS-8201).

E-PS-22 | E-Posters Soft Tissue and Bone Pathology

E-PS-22-001
A rare case: a 15 year-old-female patient presenting with multiple vascular tumours and enchondromas: Maffucci syndrome
S. Aker*, F.M. Dogukan, S. Toy, A.K. Ganiyusufoglu
*Basaksehir Cam&Sakura City Hospital, Turkey

Background & objectives: Maffucci syndrome (MS) is a rare phenomenon with less than 200 cases have been reported so far. It is characterized by multiple enchondromas and benign vascular cutaneous tumours. About 50% of patients harbour a lifetime risk of malignancy.
Methods: A 15-year-old female presented with nodular masses on her trunk and lower extremities since the age of 8 years.
Results: Magnetic resonance imaging (MRI) revealed multiple vascular tumours consistent with arteriovenous malformations on her lower extremities. In addition, several enchondromatous tumours were detected on her left scapula, right 4th and 9th ribs, left 6th and 7th ribs, left proximal femur and left pubic ramus. On histopathological examination, histomorphologic features of the biopsy material sampled from the vascular tumour were compatible with an arteriovenous malformation. On the other hand, biopsy sample from the left scapular tumour displayed a cellular cartilaginous proliferation with occasional binucleations and focal enchondral ossification which was diagnosed as enchondroma. In molecular study performed for a potential IDH mutation, results were invalid for both tumours.
Conclusion: In conclusion, MS was proposed as the ultimate diagnosis considering the age, and multiple vascular and enchondromatous tumours of the patient. Maffucci and Ollier syndromes constitute a spectrum of diseases with multiple enchondromatous tumours in both and accompanying vascular malformations in the former. They are characterized by post-zygotic somatic mutations in IDH1/IDH2 genes. MS must be noted since it may cause considerable morbidity and mortality through the formation of multiple benign or occasionally malignant neoplasms.

E-PS-22-002
An analysis of giant cell-rich lesions of bone with emphasis on the role of p63 expression as a diagnostic biomarker for giant cell tumour of bone
S. Al Shehhi*, H. Al Kindi, M. George
*Oman medical specialty board, Oman

Background & objectives: Objectives: This study aimed to analyse giant cell-rich lesions of bone and determine whether p63 can be used as a biomarker to discriminate giant cell tumours of bone from other giant cell-rich lesions.
Methods: A retrospective cross-sectional diagnostic accuracy study of all patients at any age who were diagnosed with giant cell rich lesions on bone biopsy in Khoula Hospital from 2009 to 2021. The sample size was 128 cases. P63 expression was evaluated using immunohistochemistry. Data were analysed using MedCalc software 19.1.6 and IBM SPSS Statistics version 28.0.
Results: Among the sample size, 45% male and 55% female with a mean age of 23 years have giant cell-rich lesions. Lesions were frequent in the femur and tibia. Immunohistochemical analysis showed a p63 nuclear expression in 92.3% of giant cell tumours of bone, 42.3% of aneurysmal bone cysts, 100% of chondromyxoid fibromas, 13.6% of non-ossifying fibromas, 66.7% of brown tumour of hyperparathyroidism, 75% of chondroblastoma, 25% of giant cell reparative granuloma, and 0% of metaphyseal fibrous defect. The sensitivity and negative predictive value (NPV) of p63 immunohistochemistry of giant cell tumour of bone were 92.31% and 92.0%, respectively. The specificity and positive predictive value (PPV) were 60.53% and 61.54%, respectively.

Conclusion: P63 is a helpful marker for diagnosing giant cell tumours of bone due to its high sensitivity. However, it cannot be recommended as the single definitive test for making this diagnosis. The results need to be carefully interpreted in conjunction with other diagnostic methods such as imaging studies.

E-PS-22-003

Dedifferentiated liposarcoma in a spindle cell rhabdomyosarcoma: a rare and complex case

E. Almarii*, A. Procop, T. Radaschin, C. Vasilescu, V. Herlea
*Fundeni Clinical Institute, Centre of Excellence in Translational Medicine, Fundeni, University of Medicine and Pharmacy "Carol Davila" Bucharest, Romania

Background & objectives: Dedifferentiated liposarcoma(DDLPS) and spindle cell rhabdomyosarcoma(SCRMS) are rare subtypes of soft tissue sarcomas, each with their own unique histopathological and molecular characteristics. Association of the two has rarely been described, making the diagnosis and management of these cases particularly challenging.
Methods: We present the case of a 63 years old female diagnosed and treated in Fundeni Clinical Institute. She was diagnosed with retroperitoneal liposarcoma in May2022 and while pursuing chemotherapy, the radiologic team described a 13.6 cm tumour in the left infrarenal compartment and surgical approach was proposed. We received a large whitish grey tumour, with cystic, myxoid and necrotic areas.
Results: The tumour consisted of a well-differentiated liposarcoma component (WDLS) juxtaposed with a non-lipogenic, high-grade sarcomatous component, characterized by round and elongated, spindle-shaped tumour cells with eosinophilic cytoplasm and peripherally placed pleomorphic nuclei, arranged in a fascicular or storiform pattern, with a prominent vascularization, necrosis, frequent mitoses and vascular invasion.
On immunohistochemistry, the cells were diffusely positive for MDM2, CD99 and MyoD1, were focally positive for smooth muscle actin and were negative for S100 and AE1/AE3.
This case was signed out as a dedifferentiated liposarcoma with a spinde cell rhabdomyosarcomatous transformation, grade 3 FNCLCC, with vascular invasion, located in the retroperitoneum.
Conclusion: Dedifferentiated liposarcoma in a spindle cell rhabdomyosarcoma represents a rare and complex presentation of soft tissue sarcoma, posing significant challenges in diagnosis and management. The accurate identification of both components within the same tumour is crucial for determining the appropriate treatment strategy and predicting prognosis. Further research is needed to better understand the molecular mechanisms underlying the co-occurrence of DDLPS and SCRMS and to identify potential therapeutic targets for this rare and aggressive form of sarcoma.

E-PS-22-004

Histopathological and clinical features of pelvic chondrosarcomas

B. Altuntaş Keskin*, S.A. Arsoy, A.M. Onenerk Men, M.K. Ozsahin, H.F. Dincbas, C. Comunoglu, N. Çomunoğlu
*Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty, Pathology Department, Turkey

Background & objectives: Pelvic chondrosarcomas are primarily treated with surgery with wide margins. These tumours show frequent local recurrence and distant metastasis. We aimed to present histopathological features and clinical outcomes of our case series of pelvic chondrosarcomas.
Methods: A total of 60 pelvic chondrosarcoma cases diagnosed between 1998-2022 in three hospitals (Istanbul Cerrahpaşa University, M. Sabancı Baltalimanı Hosp. and Prof. Dr C. Taşçıoğlu Ş. Hosp.) were retrospectively analysed. Clinical and histopathological features were examined.
Results: Thirty-nine cases were male and 21 were female. Mean age at the diagnosis was 52,6 (ranging between 18-91). Thirty-nine cases were located at iliac bone, 1 at ischium, 5 at acetabulum and 9 at sacrum. In 23 patients, local recurrence occurred. In 3 patients, metastasis was detected. Twenty-eight patients died of disease. Twenty-three cases were grade 1 and 37 cases were grade 2 or 3.
Conclusion: Pelvic chondrosarcomas are mostly high grade highly malignant tumours having poor prognosis with high recurrence and mortality rates, and they are difficult to treat.

E-PS-22-005

A case report of a 25 year old woman with a known history of biphasic synovial sarcoma and a late recurrence in the retroperitoneal space

E. Baliou*, M. Christidis, E. Bairamidis, D. Nikolakopoulos, M. Pandazi
*417 Army Equity Fund Hospital of Athens, Greece

Background & objectives: Synovial sarcoma is a rare malignant soft tissue tumour of unknown histologic origin usually affecting the extremities, can also involve mediastinum and viscera. Synovial sarcoma can occur in any age. More than half of patients are teenagers and young adults.
Methods: A 25 year old female patient with a history of known synovial sarcoma involving the kidney presented to our hospital with symptoms of abdominal pain and hypoalbuminemia. Imaging diagnosis revealed a mass occupying the retroperitoneal space and extending to the diaphragm. Upon surgical resection, the mass weighing of 2365 gr and 30x20x5,5 in dimensions, having a soft and gelatinous consistency,
Results: Microscopic examination revealed a biphasic tumour of mesenchymal origin with an epithelial and a spindle cell component in varying proportions. The epithelial component was consisted of cystic areas lined by epithelial cells and the sarcomatous component was composed primarily of monotonous, relatively small spindle cells arranged in dense or vague fascicles, showing severe nuclear atypia and high mitotic activity (15 mitosis/10 HPFs).Few areas exhibiting hypercellularity whereas areas of necrosis were present in the poor differentiated part of the tumour. Mast cells were abundant. Immunohistochemistry showed strong positivity of tumour cells for TLE-1, Bcl-2,EMA and CD99 while cells of the epithelial component were positive for AE1/AE3 and Cam5.2
Conclusion: Biphasic synovial sarcoma has a variable prognosis. Favourable and unfavourable histological features are described precisely. Most distant recurrences occur within a few year but late recurrences can develod as well. Poorly differentiated tumours show aggressive behaviour with metastasis most commonly in lung and bones. In our case, the initial diagnosis of synovial sarcoma was made in 2011 with a late recurrence and the involvement of the right mediastinum by 2017.By 2018, our patient showed distant metastases with a poor outcome.

E-PS-22-006

Clinicopathologic spectrum of myxoid tumours: a diagnostic challenge and helpful ancillary studies

Y. Belogrivtseva*, A. Tushir, K. Khouri, D. Proca
*Temple University Hospital, USA

Background & objectives: Myxoid tumours of the soft tissue show significant variability in their biological behaviour. They include benign tumours, ones that tend to recur locally, and malignant tumours. Broad morphological overlap within this group presents diagnostic difficulties for the pathologist.

Methods: Herein, we have accrued four cases of myxoid tumours of soft tissue. Imaging findings were documented. Morphology was assessed through light microscopic evaluation with hematoxylin and eosin–stained sections. Immunohistochemical stains and molecular studies were performed and also analysed. This review illuminates the various aspects related to the differential diagnostic workup of these challenging entities provided in Table 1 (see poster).
Results: Case #1. Intramuscular myxoma.
-Collagen-poor myxoid stroma with monomorphic fusiform fibroblast-like cells, scant vasculature
-Positive for vimentin, CD34
Case #2. Atypical myxoid spindle cell tumour.
-Pronounced myxoid stroma
-Vacuolated atypical cells admixed with bland spindle cells
-Curved delicate vasculature
-Positive for vimentin, CD34
-FISH for MDM2 amplification and for EWSR1 translocation are negative.
Case #3. Myxofibrosarcoma.
-Highly myxoid background
-Fibroblast-like, pleomorphic cells
-Prominent, communicating vessels surrounded by dense tumour cell aggregate
-Positive for vimentin, S100
Case#4. Undifferentiated pleomorphic sarcoma.
-Focally myxoid collagenous stroma
-Cells with marked pleomorphism
-Prominent thick-walled blood vessels and focal haemorrhage
-Positive for vimentin, desmin (focally), CD34 (weakly)
-2.4 muts/Mb; ARID1A, FGFR1; RPSAP52::HMGA2, multiple genomic alterations
Conclusion: The biological behaviour of myxoid tumours varies from entirely harmless to highly aggressive. Pathologists encounter challenges frequently, as the diagnosis of malignancy frequently is not based on conventional malignancy criteria but is defined by the entity itself (e.g. low-grade fibromyxoid sarcoma). While tumour morphology remains the basis of diagnostic pathology, the continuous developments within the fields of immunohistochemistry and molecular cytogenetics also serve as an additional tool, allowing the development of new diagnostic criteria and hence facilitating an accurate diagnosis.

E-PS-22-007
Hemosiderotic fibrolipomatous tumour, a diagnostic challenge
M.M. Buda*, È. Iglesias Martinez, A. Sifre Ruiz, N. Santiago Quispe, C. Esquina Rodriguez, B. Caton Santaren
*Clinical Department Unit of Pathological Anatomy, OSI Araba, Araba University Hospital; Bioaraba Health Research Institute, Vitoria-Gasteiz, Alava, Spain

Background & objectives: Hemosiderotic fibrolipomatous tumour (HFT) was first described as a reactive process. It's locally aggressive with potential sarcomatous transformation. HFT is more common in middle-aged women, and up to 80% occur on the foot or ankle dorsum.
Methods: We report the case of a 51-year-old man who presented a 2.5 cm mass on the back of his right foot. Given the clinical suspicion of lipoma, surgical excision of the lesion was performed. Afterward, light microscopy, immunohistochemistry (IHQ), and molecular pathology studies were made. A literature revision was also carried out.
Results: Histologic examination revealed an infiltrating tumour consisting of lobules of mature adipose tissue interspersed with a spindle cell proliferation which formed fascicles of variable cell density. This cell population showed focal nuclear atypia. The lesion presented thin-walled vessels accompanied by a mixed inflammatory infiltrate with macrophages and mast cells. The stroma alternated myxoid and collagen-rich areas. The tumour included hemosiderin which was identified by the PERLS technique. With IHQ studies, expression of CD34 was seen. The tumour was negative for smooth muscle actin, desmin, calponin, and S-100. Ki-67 was 2% and molecular pathology did not reveal deletion of the RB1 gene. Thus, HFT diagnostic was made.
Conclusion: HFT is a rare entity and it could be confused with an atypical spindle cell/pleomorphic lipomatous tumour, but, as in our case, HFT does not show deletion of the RB1 gene. HFT also shows similar morphologic features to Pleomorphic Hyalinizing Angiectatic Tumour. The latter would present more ectatic vessels with organized thrombi and perivascular deposition of amorphous eosinophilic material. Finally, it must be distinguished from Myxoinflammatory Fibroblastic Sarcoma, which shows characteristic Reed-Sternberg-like cells, not seen in our case.

E-PS-22-008
Desmoplastic fibroma of bone: a series of five cases
Y. Cakir*, B. Bambul Sığırcı, E. Hacıhasanoğlu, Y.B. Kök, G. Başdemir, K. Behzatoğlu
*Dokuz Eylül University, The Institute of Health Sciences, Department of Molecular Pathology, Turkey

Background & objectives: Desmoplastic fibroma of bone (DFB) is a rare tumour resembling an extra-abdominal desmoid tumour. Due to its rarity and similarities to other bone lesions, it can pose diagnostic problems. We present five DFB and discuss clinicopathologic features and differential diagnosis.
Methods: Five cases were diagnosed as DFB in 13 years period in our department. The clinical findings of the patients were recorded, and the slides were re-evaluated.
Results: The mean age was 26,4 (3-73), 60% were male. All patients presented with pain and swelling. Wide resection was performed in all cases. Tumours were from different anatomical sites including mandibula (2), proximal fibula, proximal tibia, proximal humerus. Microscopically, all cases were characterized by a mild to moderately cellular fibrocollagenous stromal tissue matrix devoid of cellular pleomorphism, nuclear hyperchromasia, mitosis. Immunohistochemically, SMA was positive at varying rates in 3 cases whereas MUC4, SATB2, S100, CD34, desmin were negative. Ki-67 proliferation index was 1-2%. Two cases had been diagnosed as low-grade fibrosarcoma and fibrous dysplasia on tru-cut biopsies at other institutes. In follow up, local recurrence was detected in one case.
Conclusion: DFB is a rare tumour with local recurrence risk. Clinically, radiographically, and histopathologically, DFB has many features that overlap other bone lesions, such as periosteal desmoid tumours, fibrous dysplasia, non-ossifying fibromas, odontogenic fibromas, and low-grade fibrosarcomas. Therefore, a multidisciplinary approach is required.

E-PS-22-009
Angiomatoid fibrous histiocytoma - case series with detailed morphological and immunohistochemical features
G.H. CAVUS*, A.M. Önenerk Men, S. Çetinkaya, R. Tanrıtanır, H.K. Türköz, N. Çomunoğlu
*Istanbul University-Cerrahpasa, Cerrahpasa Medical School, Turkey

Background & objectives: Angiomatoid fibrous histiocytoma (AFH) is in the group of tumours with uncertain differentiation with over 90% EWSR1 rearrangement, a wide morphological spectrum, no specific immunohistochemical markers. In this series, we compared the histomorphological, immunohistochemical and molecular features of the cases.
Methods: In this multicenter study, 13 cases diagnosed with AFH were re-examined and their epidemiological features as well as microscopic and immunohistochemical features were analysed in detail. In addition, EWSR1 rearrangement was studied by FISH method in some cases.

Further, the clinical course of the patients was compared with all the findings.
Results: Characteristic histological and immunohistochemical features were observed in all cases in our series. EWSR1 rearrangement was found to be positive in 7 of 9 cases studied. Mild atypical cells were observed in only 1 of 13 cases in our series, and no prognostic difference was found between this case and the others. Three cases showed pseudovascular spaces in the nodules and a fibrous capsule with inflammatory cells, particularly prominent secondary follicles in some areas, which raised suspicion of metastasis. At the time of diagnosis, metastasis to the lung was found in 1 of 2 cases located in the lower extremity, and lymph node metastasis was found in the other case.
Conclusion: As distinct from the literature, lung metastasis was detected for the first time in our series. The diagnosis of angiomatoid fibrous histiocytoma is difficult due to its rarity, pattern diversity, and the absence of a specific immunohistochemical marker. Although the risk of metastasis and death rates are low, correct diagnosis is extremely important. Recently identified gene fusions are the most important diagnostic indicators for a definitive diagnosis.

E-PS-22-010
Molecular identification of an intra-thoracic BCOR-rearranged sarcoma with novel BCOR-CLGN gene fusion
Y.C. Chang Chien*, K. Madarász, S.L. Csoma, J.A. Mótyán, H. Huang, A. Mokánszki, G. Mehes
*University of Debrecen Clinical Center Institute of Pathology, Hungary

Background & objectives: BCOR-rearranged sarcomas (BRS) are a heterogeneous entity previously classified as "atypical Ewing" sarcomas with histopathological similarities which make diagnosis challenging. The most common aberrations are CCNB3 fusion and BCOR ITD. Various new fusion partners have been reported, further increase its complexity.
Methods: We present a case of intra-thoracic tumour from a 52-year-old female patient with clinical impression of metastatic carcinoma from endometrium. Morphological evaluation was performed, followed by immunohistochemistry (IHC) studies, fluorescence in situ hybridization (FISH), next generation sequencing (NGS) and Sanger sequencing. In silico protein analysis was also carried out to demonstrate the 3D structure of the chimeric protein.
Results: A 52-year-old female patient with history of endometrioid adenosarcoma (grade 2) revealed a right-side chest wall tumour during follow up with costal and pleural invasion. The tumour cells showed typical small, round-spindle morphology resembled Ewing sarcoma with positivity for CD99(diffuse to patchy), INSM1, NKX2.2, TLE1, SATB2 and BCOR by IHC. Further molecular analysis identified BCOR gene translocation by FISH. BCOR (exon 15) and CLGN (exon 9) gene fusion was found by NGS and confirmed by Sanger sequencing. In silico protein analysis showed the protein product of the BCOR-CLGN is composed of full-length BCOR protein and N-terminal signal sequence of calmegin (protein product of CLGN gene) was missing, which hampered the intracellular translocation.
Conclusion: We report the first case of BRS with a novel CLGN fusion which shared morphological and immunophenotypical similarities with other fusion variants, which contribute to the continued expanding molecular subtype of BRS. Molecular ancillary tests, such as NGS and confirmatory Sanger sequencing, serve as powerful tools to discover these rare variants. In addition, the in silico analysis of the BCOR-CLGN fusion protein is an appropriate approach to better understand the pathogenesis by evaluating the fusion protein's characteristics.

E-PS-22-011
Rare tumour with uncommon clinical behaviour: relapsed intramuscular angioma of the elbow
A. Ciongariu*, A. Dumitru, M. Sajin, A. Marin, M. Costache
*Department of Pathology, University Emergency Hospital Bucharest, Romania

Background & objectives: Intramuscular angioma is an exceptionally rare neoplasm arising in skeletal muscle. It typically affects young patients and frequently develops in the upper extremities. Although considered a benign tumour, incomplete surgical resection followed by relapse may lead to a difficult diagnosis.
Methods: We present the case of a 28-year-old male who developed a large, rapidly growing, soft tissue tumour of the upper limb and underwent surgical excision, followed by relapse. Considering the aggressive clinical behaviour of his lesion, a malignant proliferation was suspected. Surgery was carried out and a frozen section was performed during the procedure, suggesting the diagnosis of intramuscular angioma.
Results: Microscopic examination revealed a benign tumour proliferation consisting of endothelial cells lacking atypia and mitotic figures, forming variable-sized vascular spaces, with occasional plexiform architecture. The lesion was poorly defined and displayed vascular structures and chords dissecting the adjacent striated skeletal muscle fibres. Upon immunohistochemical analysis, we identified strong ERG, CD31 and CD34 expression within the tumour cells. Ki 67 proliferation marker was expressed within 1% of tumour cells. Expression of S-100, HHV8 and MDM2 was absent in the proliferated elements. The diagnosis of intramuscular angioma was confirmed. However, the tumour proliferation extended close to the surgical resection margins and thorough correlations with the surgical and clinical data were recommended.
Conclusion: Intramuscular angioma can be a challenging diagnosis, considering the peculiar permeative growth pattern and unusual clinical behaviour of this proliferation. Management of this entity requires increased attention during microscopic examination and should be completed by immunohistochemical analysis. We also emphasize the importance of adequate examination of the surgical resection margins, to prevent relapses and inappropriate treatment. As a result, knowledge and awareness in the matter of this condition is crucial in order to avoid misdiagnosis, especially considering its rarity.

E-PS-22-012
Epithelioid neoplasm with EWSR1/FUS-CREB fusions and predilection for mesothelial-lined cavities: case report
A.P. Diazgranados Daza*, T.M. Silva, G. Tapia Melendo, J. Chabla Jaramillo, J. Garcia Gomez, S. Ramón y Cajal Agüeras, C. Romagosa Perez-Portabella
*Hospital Vall D'Hebron, Spain

Background & objectives: Recently a case series describing a group of tumours with predilection for mesothelial-lined cavities showing epithelioid morphology has been reported; co-expression of citokeratines/WT1, negativeness of calretinine and EWSR1/FUS-CREB fusion genes presence. We report a case of this potential novel entity.
Methods: We report a case of a 43-year-old male patient admitted to the hospital for fever and anaemia. The CT scan showed a solid mediastinal subcarinal and right hilar mass (65x45mm). The patient underwent a thoracoscopy for pleural and mediastinic mass biopsy. We analyse the histological sections, carry out immunohistochemistry and molecular analysis by next-generation sequencing (NGS) "Archer FusionPlex Expanded Sarcoma".
Results: The histopathology examination revealed a fibrous-looking tissue with myxoid degeneration and cystic changes, infiltrated by a proliferation of monotonous small/epithelioid cells arranged in nests, trabeculae and cords-like. Tumour cells show round nuclei, sometimes

hyperchromatic and rejected to the periphery, small nucleoli and scant eosinophilic/clear cytoplasm. One mitosis per 1.7 mm² and no necrosis were observed. The immunohistochemical profile demonstrated neoplastic cells with positivity for CAM5.2, CKAE1/AE3 and WT1 (nuclear), BAP1 (no loss of expression), SMARCA4 (no loss of expression). Negative markers: CK5/6, calretinine, D2-40, p40, CD5, PAX8, Claudin4 and SALL4. The NGS molecular study result was EWSR1(8)- ATF1(4) fusion gene.
Conclusion: Pathologists should be aware that EWSR1/FUS-CREB family fusions could be present in malignant epithelioid neoplasms with predilection for mesothelial-lined cavities. Until now did not correspond to any known tumour category, suggesting a novel entity with distinctive microscopic features, despite of it can share morphological features with tumours harbouring EWSR1/FUS-CREB fusions like Angiomatoid Fibrous Histiocytoma (AFH) and Epithelioid mesothelioma (EM). Further research is needed to clarify if these tumours are part of a spectrum along with EWSR1 rearranged EM and/or AFH.

E-PS-22-013
Sclerosing epithelioid fibrosarcoma (SEF) with YAP1/KMT2A rearrangement: case report and systematic review of the literature
L. Dore*, M. Iuzzolino, L. Samà, L. Ruspi, L.M. Terracciano, A. Bonometti, F.C.M. Cananzi, S.L. Renne
*Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milan, Italy, Department of Pathology, IRCCS Humanitas Research Hospital, Rozzano, Milan, Italy

Background & objectives: SEF is a rare sarcoma characterized by MUC4 positivity and EWSR1-CREB3L1 fusion. However, a subset lacks MUC4-expression and EWSR1-CREB3L1-rearrangement and is instead characterized by YAP1/KMT2A rearrangement. We here report a YAP1/KMT2A-rearranged-SEF case and perform a systematic review of the literature.
Methods: We identified a MUC4 negative SEF and performed a Targeted RNAseq. Systematic review of the literature was performed using the PRISMA guidelines. We systematically searched the literature for molecularly confirmed YAP1/KMT2A rearranged SEF cases. We recorded the clinical data (sex, age, site, depth, follow-up), the histological data (mitotic count, necrosis) and MUC4 positivity.
Results: 4/51 identified publications met the inclusion/exclusion-criteria accounting for 33 cases. We reported the 34th. Median age was 43.5 (interquartile range, IQR: 31.25–55.50) years; 19/34 (56%) of cases were female. Median tumour size was 3.2 (IQR:2.5–6.12) cm; 11/19 (65%) had a deep location; lower limb was affected in 11/19 (58%) cases. Median mitotic count (/10HPF) was 5 (IQR:2–9); necrosis was present in 4/9 (44%) of cases; MUC4 was never expressed (in 19 tested-cases). Survival analysis showed for distant metastasis (12 cases, 5 events) a mean survival of 12 months (CI95%:11–NA); for overall survival (14 cases, 5 events) the median survival was 80 months (CI95%:24–NA).
Conclusion: Less than 40 cases of YAP1/KMT2A-rearranged-SEF have been reported. Similarly to typical SEF, they arise in middle aged adults with equal sex distribution. They occur more often in the lower limb, not infrequently (35% of cases) in the subcutaneous fat. One out of three patients will die because of the disease. Recognition of these cases is therefore important for correct patient management.

E-PS-22-014
Unusual presentation of Kaposi sarcoma: a case report of a lymph node localisation
O. El Mnif*, A. Zehani, B. Chelly, A. Ayari, H. Azzouz, I. Chelly, K. Bellil, S. Haouet
*La Rabta pathology department Tunis, Tunisia

Background & objectives: Kaposi sarcoma is a malignant vascular tumour that occurs typically as a cutaneous or mucosal lesions related mostly to HIV infection However other locations may occur although rarely have been described. We report a lymph node location of Kaposi sarcoma.
Methods: We analysed the medical file of a 47-year-old patient with a personal history of HIV infection who presented for about 6 months multiple cervical adenopathies, fluctuating fever and fatigue without any cutaneous lesions. Representative sections of the cervical mass were examined under H&E and immunohistochemical stains.
Results: Initially the suspected diagnosis was lymphoma or lymphatic tuberculosis in view of the endemic situation and medical history of the patient, a cervical adenomectomy was therefore performed the initial microscopic examination with routine hematoxylin and eosin staining was not at all suggestive of Kaposi's sarcoma. It showed a lymph node parenchyma of globally preserved architecture containing lymphoid follicles with reactive germinal centres associated with sinus dilatation.
An immunohistochemical study was performed using the HHV8 antibody showing an increased positivity of endothelial cells of the vascular structures in the peri-ganglionic tissue, which concluded to a lymph node localization of a kaposi sarcoma.
Conclusion: Lymph node localization of KS is a rare form of the disease that poses diagnostic challenges. It can mimic other tuberculous infection or malignant neoplasms, such as lymphoma. Therefore, a high index of suspicion for KS should be maintained in patients with HIV infection or other risk factors for KS who present with unusual nodal masses.

E-PS-22-017
Solitary fibrous tumour of the spinal canal - a clinically challenging case
J. Ichikawa*, H. Imada, T. Kawasaki, M. Higashi
*Department of Orthopedic Surgery, University of Yamanashi, Japan

Background & objectives: Solitary fibrous tumour could occur almost anywhere, with the prototype being located in the pleura. Here, we report an unusual clinical course of spinal solitary fibrous tumour.
Methods: A 55-year-old man complained of pain in his right back and the side of chest four years ago. An MRI revealed a spinal tumour at T6-7 and he was referred to our hospital. The back pain improved but four years later, he started to develop weakness in his left leg, which gradually spread to both legs, resulting in difficulty walking.
Results: An MRI showed that the T6-7 tumour had grown. It was clinically suspected of meningioma and surgical removal of fragmented pieces of the tumour. The histological examination revealed that the tumour was composed of uniformly spindle-shaped tumour cells with haphazard distribution and occasional ectatic vessels. Differential diagnosis of meningioma, Schwannoma and solitary fibrous tumour was suggested. Immunohistochemically the tumour cells were positive for CD34 and STAT6 while negative for S100 protein. These findings were consistent with solitary fibrous tumour. His symptoms were relieved after surgery and no recurrence has been confirmed to date.
Conclusion: While solitary fibrous tumours can occur in various locations, they are rare in the spinal canal. Pathological findings are rather straightforward, but clinical and radiological findings are challenging to diagnose. Our case will expand the knowledge about the clinical presentation of spinal solitary fibrous tumour.

E-PS-22-018
Vertebral ochronosis - a rare, histologically confirmed case
J. Ichikawa*, H. Imada, T. Kawasaki, M. Higashi
*Department of Orthopedic Surgery, University of Yamanashi, Japan

Background & objectives: Vertebral ochronosis is a rare disease commonly associated with alkaptonuria and it is not common to have a chance of histological evaluation. Herein we report a case of vertebral ochronosis verified histologically.

Methods: A 66-year-old man had complained bilateral knee pain which was diagnosed as osteoarthritis and treated conservatively for ten years. One month prior to surgery, he had buckling and bilateral leg numbness. He had a rupture of Achilles tendon and urolithiasis.
Results: Physical exam revealed a black pigmentation in the conjunctiva, posterior auricle and lip. The urine was coloured black and urine homogentisic acid was increased. Radiology revealed osteoporosis with vertebral disc narrowing. Based on the imaging finding, his symptom was supposed to be due to the instability at T10/11 level and surgery was performed for posterior decompression and posterior fixation of kyphosis. Vertebral bone was sampled for histological evaluation. Histologically, brown pigment was deposited in the bone fragments, which was coloured by methylene blue stain. Molecular study revealed homogentisic acid oxidase mutation.
Conclusion: Ochronosis is caused by the accumulation of a homogentisic acid in connective tissue, and the endogenous type is called alkaptonuaria, which is an autosomal recessive disease. Histological examination of vertebral ochronosis is rare and our case will reinforce the understanding of ochronosis.

E-PS-22-019
Clear cell sarcoma of the knee - an unusual presentation masquerading benign bursitis
J. Ichikawa*, T. Kawasaki, H. Imada, S. Kanno, T. Torigoe, Y. Yazawa
*Department of Orthopedic Surgery, University of Yamanashi, Japan

Background & objectives: Clear cell sarcoma is a rare soft tissue sarcoma with melanocytic differentiation. It usually forms a well-demarcated, expansile mass, however, pericystic growth is uncommon. Herein, we report an unusual presentation of clear cell sarcoma mimicking bursitis.
Methods: A 63-year-old woman had presented with left knee pain that worsened after turning over. Conservative therapy failed to improve her symptoms. An magnetic resonance imaging revealed a clinically intra-articular lesion and the tumour surrounded the joint of the left knee. It was low on MRI T1-weight imaging. Focal invasion of the posterior side of the femur was also observed.
Results: Because the tumour was found to be malignant upon biopsy, it was surgically resected. Gross examination of the resected specimen showed peri-capsular/peri-articular extension of the whitish tumour with focal intramedullary invasion of the femur. Histologically, the tumour cells had round nuclei with prominent nucleoli. While most of the synovial cells were intact, focal intra-articular extension was seen. Immunohistochemical analysis revealed positivity for MITF, HMB45, SOX10, and S100 protein. Fluorescence in situ hybridization demonstrated breakapart signals of EWSR1, consistent with clear cell sarcoma.
Conclusion: Our case highlights the unique extension of clear cell sarcoma, which can be clinically challenging to diagnose and may masquerade as benign synovitis or tenosynovial giant cell tumour, diffuse type. The current case also expands the variation of clear cell sarcoma extension, emphasizing the importance of careful consideration of differential diagnoses in patients with atypical presentation of this rare malignancy.

E-PS-22-020
Spinal metastasis of well-differentiated liposarcoma component in retroperitoneal dedifferentiated liposarcoma treated by minimally invasive surgery
J. Ichikawa*, T. Kawasaki, H. Imada, S. Kanno, T. Ohba, H. Haro
*Department of Orthopedic Surgery, University of Yamanashi, Japan

Background & objectives: Generally, well-differentiated liposarcoma (WDL) has the potential to become a dedifferentiated liposarcoma (DDL) but lacks metastatic potential. We present a rare case of spinal metastasis of a WDL component in retroperitoneal DDL treated by Minimally Invasive Surgery (MIS).
Methods: A 65-year-old woman presented with low back pain and left sciatica. Magnetic Resonance Imaging showed a mass with high signal intensity on both T1 and T2-weighted images in L1. She had undergone resection of retroperitoneal DDL previously, with two recurrences, but had no metastasis except to L1. Therefore, we diagnosed L1 metastasis of the WDL component in DDL.
Results: Therefore, we diagnosed the vertebral tumour as metastasis of the WDL component of DDL, and planned surgery to achieve symptomatic improvement. Tumour curettage and laminectomy followed by percutaneous pedicle screw fixation with CT navigation were performed. Histological examination in the primary retroperitoneal lesion showed mixed well-differentiated and dedifferentiated liposarcoma. Lipoblasts containing hyperchromatic nuclei were apparent in the well-differentiated area. On the other hand, there was a well-differentiated component in the spinal metastasis lesion. Positive immunohistochemical staining for MDM2 and CDK4 confirmed dedifferentiated liposarcoma. She could walk with neither pain nor palsy. However, the retroperitoneal mass enlarged and she died 1.5 years after surgery.
Conclusion: We have described an extremely rare case of spinal metastasis of a well-differentiated liposarcoma component of retroperitoneal dedifferentiated liposarcoma. The clinical behaviour of WDL differed markedly between the extremities and retroperitoneum, as reflected by dedifferentiation and the high recurrence rate. Although surgical indications for metastasis are of course restricted, considering the slow growth of DDL and relatively long survival, MIS including percutaneous pedicle screw fixation is a promising tool.

E-PS-22-021
Atypical spindle cell/pleomorphic lipomatous tumour masquerading as a myxoid tumour
J. Ichikawa*, T. Kawasaki, H. Imada, S. Kanno, N. Taniguchi, T. Ashizawa, H. Haro
*Department of Orthopedic Surgery, University of Yamanashi, Japan

Background & objectives: Atypical spindle cell/pleomorphic lipomatous tumours (ASPLT) can now be categorized and immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) are essential for accurate diagnosis. Herein, we report a case with ASPLT masquerading as a myxoid tumour.
Methods: A 64-year-old man presented with a mass on his right buttock. Magnetic resonance imaging (MRI) revealed a low signal on T1-weighted images with a few high signals suggesting the presence of intratumoral fat and a high signal on T2 short tau inversion recovery images suggesting the presence of myxoid components. Taken together, the imaging findings suggested myxoid liposarcoma.
Results: Needle biopsy findings suggested myxoma, because there were few atypical spindle cells. Collectively, the preoperative findings indicated intramuscular myxoma. Marginal resection was thus performed. Macroscopically, the tumour consisted of mainly myxoid components with little fat tissue. Histopathologically, the tumour had an ill-defined border and most of the tumour cells were bland and short-spindled with a myxoid matrix, with some showing cytological atypia and pleomorphism. IHC indicated the tumour to be positive for CD34 and negative for retinoblastoma. FISH showed no amplification of MDM2 and no rearrangement of FUS or EWSR1. The final diagnosis was ASPLT. One year after surgery, the patient remains free of recurrence.
Conclusion: We have described an atypical case of ASPLT and difficulties with differential diagnosis of this tumour. Pathological findings and molecular confirmation including IHC and FISH are more useful than imaging for ASPLT because MRI findings are heterogeneous. Although wide resection is recommended, some cases, such as our case, have an inconclusive preoperative diagnosis. Since ASPLT is a benign tumour that does not metastasize, careful, long-term follow-up may benefit patients more than additional surgery.

E-PS-22-022

CD16 (FcRIII) expression might play a pivotal role in neurofibroma progression as a tumour-associated immune cell

K. Kim*, M. Yeo, K. Suh, D. Kang, J.E. Choi
*Chungnam National University, Republic of Korea

Background & objectives: Neurofibroma (NF) is a benign tumour in the peripheral nervous system, but it can infiltrate around structures and cause functional impairment and disfigurement. We hypothesized that inflammation is relevant to tumour progression with infiltrative growth in NF.
Methods: We evaluated the expressions of CD16, CD68, and SOX-10 in the 45 cases of neurogenic tumours (neurofibromas (NFs), n=24; atypical NFs, n=6; atypical neurofibromatous neoplasms of uncertain biologic potential (ANNUBP), n=9; malignant peripheral nerve sheath tumour (MPNST), n=3; neuroma, n=3).
Results: CD16 expression increases along with CD68 positivity in the tumour microenvironment (TME) of the atypical NFs and ANNUBPs. In the atypical NFs and ANNUBPs, CD16 increased more than in the NFs (P=0.006 and P=0.005, respectively), in contrast to depleting CD16 expression in the MNPSTs than ANNUBPs (P=0.002). The quantitative variables were compared using the Kruskal-Wallis H test and Benferroni Correction Method.
Conclusion: Increased expression of CD16 was detected in the NFs but decreased with malignant progression. The CD16 overexpression with CD68 positivity in the atypical NFs and ANNUBPs potentially reflects that the TME immune modulation could be associated with the NF progression. Further studies should be explored therapeutic approaches for targeting the mechanism of CD16 associated with an immunomodulatory role in accelerating NF growth.

E-PS-22-023

Intramuscular nodular fasciitis with MYH9-USP6 fusion: a case report

B. Konuk*, I. Tosun
*University of Health Sciences, Umraniye Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Nodular fasciitis is a benign myofibroblastic neoplasm. it is mostly located in the upper extremity, head/neck, trunk. About 20 percent of cases have a history of trauma. It can be confused with malignant mesenchymal tumours due to rapid divisions and various morphological features.
Methods: A 50 year old male patient presented with a painful mass at the level of the 8th rib on the right. After the evaluation, the mass was excised together with the attached rib. Macroscopically, a firm beige lesion with irregular borders was seen invading the muscle. Surgical margins were intact.
Results: In microscopic examination, the tumour was composed of short, intersecting fascicles of myofibroblastic cells in a loose myxoid matrix. Presence of mixed inflammatory infiltrate tissue culture appearance and frequently extravasated erythrocytes were remarkable. No significant cellular atypia, atypical mitosis, or necrosis were observed. Fibroblastic benign and malignant neoplasms such as nodular fasciitis, fibromatosis, benign fibrous histiocytoma, infantile fibrosarcoma, fibromyxoid sarcoma, dermatofibrosarcoma protuberans were considered in the differential diagnosis. Sma positive, cd34,s100 negative, desmin focal positive was evaluated in immunohistochemical studies. Fusion between MYH9 gene exon 1 and USP6 gene exon 6 was detected by NGS method. This supported the diagnosis of nodular fasciitis. No recurrence was observed in the 1-year follow-up.
Conclusion: Nodular fasciitis is considered as reactive lesion due to its self-limiting nature, post-traumatic formation and non-recurrency. However, recent studies have identified the USP6 mutation, revealing that nodular fasciitis represents a clonal neoplastic proliferation. Hence, it can mimic malignant mesenchymal tumours, It is important to rule out other differential diagnosis and avoid over-treatment. We aimed to present our case because of its infrequent intramuscular localization within a case with no history of trauma. Also, MYH9:USP6 fusion which supports the diagnosis, detected in this case by using NGS analysis.

E-PS-22-024

Primary epithelioid rhabdomyosarocma of gastrointestinal tract

O. Kuczkiewicz-Siemion*, M. Lenarcik, M. Wągrodzki, B. Gierej, A. Mróz, A. Szumera-Ciećkiewicz
*Department of Pathology, Maria Sklodowska-Curie National Research Institute of Oncology Warsaw, Poland

Background & objectives: Rhabdomyosarcomas are classified according to WHO 2020 into embryonal, alveolar, pleomorphic and spindle cell/sclerosing types. Recently a morphologically exceptional variant called "epithelioid RMS" was identified. Here we present a case report of primary epithelioid RMS of gastrointestinal tract.
Methods: A 69-year-old female was admitted for consultation on a tumour 5.3 cm in diameter located in the proximal jejunum; the perforation and ulceration of the intestinal wall were described. The patient was previously treated for metastatic lung squamous cell carcinoma.
Results: In the initial evaluation of the biopsy material, lymphoma suspicion was described. Microscopically, the tumour was composed of a solid infiltrate of poorly differentiated, small cells with high mitotic activity (12 mitoses/10HPF), no necrosis, with numerous lymphoid cells in the background. The immunohistochemical analysis showed: Desmin(+), Myogenin(+/-) in scattered cells, MyoD1(-), CKAE1/AE3(-/+), EMA(-/+), Ki67(+) w 90% of cells; cancer [EA(-), p63(-), p40(-), Chromogranin A(-), Synaptophysin(-)], melanoma [S100(-), SOX10(-)], lymphoma [CD20(-), PAX5(-), CD3(-), CD30(-), ALK1(-), CD43(-), CD23(-), CD5(-), BCL6(-), CyclinD1(-), CD31(-), CD33(-), CD34(-), EBER-ISH(-), CD68(-), CD163(-)], other sarcomas [CD117(-), DOG1(-), SMA(-), Caldesmon(-), Calretynin(-)] were excluded and epithelioid rhabdomyosarcoma was diagnosed.
Conclusion: Epithelioid RMS are rare, localized mainly in soft tissues (our case is second for the gastrointestinal tract), affecting elders and clinically aggressive tumours. The diagnosis is challenging because of carcinoma, melanoma, and lymphoma mimicry. Crucial for correct classification is the high expression of desmin, with variable MyoD1/Myogenin positivity; remarkably, in some cases, cytokeratins could be aberrantly seen. The immunohistochemical stains still remain an essential step of diagnosis; further molecular analysis is needed for a better understanding of epithelioid RMS pathogenesis.

E-PS-22-025

Chondrosarcoma of the ribs: a report of 6 cases

W. Majdoub*, K. Ben Lazreg, S. Mestiri, D. Benletaifa, A. Bdioui, O. Belkacem, L. Jaidane, M. Krifa, S. Hmissa
*Pathology Department Sahloul Hospital, Tunisia

Background & objectives: Chondrosarcoma is the second most common sarcoma of bone, arising in the pelvis or long bones. It is rare for chondrosarcoma to arise in the rib. We aim to provide a clinicopathological description of chondrosarcoma of the ribs (CSR).
Methods: we conduct a retrospective study of 6 patients diagnosed with CSR listed in the Cancer Registry of Center Tunisia during a period of 16 years from 2006 to 2022. All cases were diagnosed on surgical resection specimen.
Results: There were 4 males and 2 females. The mean age was 45 ans with extremes of 19 and 67 ans. In four cases the tumour was localized on fourth, fifth and sixth ribs and in two cases the tenth rib was involved. Median size was 11 cm and ranged from 4 to 23 cm. A radical excision with widely negative microscopic margins was performed in

all cases. Five cases were consistent with conventional CSR grade I in three cases and grade II in two cases. In a case the diagnosis of dedifferentiated CSR was made. This patient underwent chemoradiotherapy, but he died 2 years later. Five patients have no recurrence.
Conclusion: Conventional chondrosarcoma is the most common variant of CSR. Histologic grading is challenging and is subject to high rates of interobserver variability. Tumour grades are predictor for local recurrence, systemic metastasis, and survival. The decision of whether to perform reconstruction is based on lesion location and defect size. Access to chest wall reconstruction forms a barrier to patient compliance. The prognosis of chondrosarcoma varies widely and is based on tumour grade, stage and subtype.

E-PS-22-026
Activation of PIK3/mTOR pathway in a case of spindle cell adamantinoma with dedifferentiation
S. Mangray*, S. Chen, T. Scharschmidt, A. Shenoy, B. Setty, L. Biederman, M. Conces, V. Prasad, C. Cottrell
*Nationwide Children's Hospital, USA

Background & objectives: There is limited data on the comprehensive genomic profile (CGP) of spindle cell adamantinoma (SpAda). Herein we report the CGP in a SpAda with focal dedifferentiation arising in the soft tissue and tibia of an 18-year-old young man.
Methods: The morphologic and immunohistochemical features of the tumour are reviewed. The genomic workup performed on a paired germline (blood sample) and snap-frozen tumour, and included germline and somatic variants, copy number (CN) variations, structural variation (SV), DNA methylation (DNAmet) sarcoma classification, and transcriptomic outlier (TO) analyses.
Results: The resected 2.7 x 1.6 tumour was centred in the soft tissue but focally involved the tibial cortex and medulla. Histologically, there was a cellular spindle cell proliferation in short fascicles with focal pleomorphic cells. The peak mitotic rate was 30/10 HPFs and focal necrosis was noted. No epithelial component was present. The tumour was diffusely positive with pan keratin and p63, while S-100, CD99, EMA, desmin, and NKX2.2 were negative.
Genomic profiling revealed: NF2 somatic alteration [NM_000268.3 (NF2) :c.146dupT:p.Leu49fs]; hyperdiploidy; enhanced oncogene expression (MET Log2 fold change 6.1, PIK3R1 4.8, and EGFR 4.8) by TO analysis; chromosome 22 copy number loss (NF2); DNAmet score of 0.3 (no match); and no SV.
Conclusion: The morphologic features, immunohistochemical profile, and CGP are consistent with a SpAda with focal dedifferentiation. The CGP demonstrated overexpression of MET, EGFR, and PIK3R1 in this tumour suggesting activation of the PI3K/mTOR signalling pathway through multiple receptor tyrosine kinases.
Although the standard management for recurrent disease in adamantinomas is surgery, the genomic findings described suggest a potential role for the use of tyrosine kinase inhibitors should there be advanced progression of disease.

E-PS-22-027
Case report: uncommon case of epithelioid angiosarcoma post endovascular aortic repair
I. Mergeanu*, A. Birceanu, A. Procop
*University Emergency Hospital Bucharest, Poundbury Cancer Institute, Romania

Background & objectives: Epithelioid angiosarcoma is a rare entity, moreover so when it arises post endovascular aortic repair, following descending aortic aneurysm. The latest literature reviews cite no more than 15 cases reported up to date of such occurrences.
Methods: Our Department of Pathology received a biopsy specimen from a pelvic mass which had been fixed with 10% buffered formalin and processed by conventional histopathological methods, using paraffin embedding, sectioning and Haematoxylin–Eosin (HE) staining. Afterwards, the sections were deparaffinized and prepared for immunohistochemical staining, using the following markers: AE1/AE3, S100, desmin, SATB2, CD99, SS18-SSX, CD31, NKX2.2, ERG and FLI1.
Results: We report the case of a 68-year-old female patient with previous history of descending aorta aneurysm, that had undergone endovascular aortic repair with a synthetic graft. Three years later, the patient presented with pelvic mass extending towards the right thigh, invading the quadriceps and the femur. The biopsy revealed sheets of malignant, pleomorphic, epithelioid cells, focally exhibiting vasoformative pattern. Immunohistochemical studies showed that the tumour cells were AE1/AE3 (-), S100 (-), desmin (-), SATB2 (-), CD99 (+), CD31 (+), SS18-SSX (-), NKX2.2 (-), ERG (+) and FLI1 (+), therefore confirming the diagnosis of post-EVAR epithelioid angiosarcoma.
Conclusion: Epithelioid angiosarcomas are highly aggressive malignant entities with rapid evolution. According to literature, the period of time from the procedure and until the appearance of the tumour is relatively short. This warrants a very prompt diagnosis, in order to ensure maximum chances in overall survival, but more often than not this proves to be a tall order. The spectrum of differential diagnoses is wide; therefore, an accurate past medical history is of paramount importance to enunciate a diagnostic algorithm.

E-PS-22-028
Osteosarcoma arising from an osteochondroma in a patient with multiple hereditary exostoses
L.D. Micoogullari*, A. Avci, E. Ozmen
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Multiple hereditary exostoses (MHE) is an autosomal dominant skeletal disorder with a rare incidence. MHE presents with painless and slow-growing multiple osteochondromas. In this case, we report an osteosarcoma arising from an osteochondroma in a 28-year-old male patient with MHE.
Methods: A spinal mass specimen from L3 vertebrae consisting of multiple nodular pieces of bony tissue, measuring in total of 17x15x3 cm, was decalcified and then sampled. Paraffin-embedded tissue sections of this specimen were evaluated for the histopathological characteristics. Demographic, clinical, and imaging data were collected.
Results: A 28-year-old male patient admitted to our hospital with the complaint of back pain and loss of sensation in the lower extremities. His examination showed multiple bony exostoses throughout his body. He mentioned that he has MHE syndrome. He noticed that the lesion in his lumbar region has rapidly grown. Computed tomography revealed a mass with 10 cm thickness at the level of L3 vertebrae. Histopathological examination revealed a characteristic fibrous cartilaginous cap covering a lace-like osteoid tumour with irregular trabeculae. Tumour cells showed marked nuclear atypia, pleomorphism and frequent mitoses including atypical mitoses. Diagnosis of "osteosarcoma arising from an osteochondroma" was made.
Conclusion: MHE, also known as diaphyseal aclasis or familial osteochondromatosis, has heterogenous genetical characteristics which are shown to be depending on two genes: exostosin-1 (EXT-1) gene located at 8q24 and exostosin-2 (EXT-2) gene located at 11p11–p12. Malignant transformation of osteochondromas is a rare entity to encounter. When malignant transformation occurs, the majority of cases show transformation to chondrosarcomas. In English-language literature, apart from our case, there are only 13 cases that report malignant transformation of MHE to osteosarcoma.

E-PS-22-029

Discrimination of bone and cartilage by speed-of-sound

K. Miura*, T. Iwashita
*Department of Regenerative and Infectious Pathology, Hamamatsu University School of Med, Japan

Background & objectives: Scanning acoustic microscopy can assess tissue elasticity because more rigid tissues show higher speed-of-sound (SOS). Bones show variable stiffness in growing ossification, fracture recovery stages, and osteogenic neoplasia. This study evaluates bone and cartilage stiffness to understand the pathological state.
Methods: Unstained flat decalcified sections in 10 μm thickness were scanned to plot SOS values of each area on the screen in serial colours. Special resolution was 4.7 μm. Finished SOS images were compared with LM images to analyse the relationship between stiffness and histological structure. Adult mouse and human specimens' cartilages, osteoids, and mineralized bones were compared in various conditions.
Results: Virtual SOS images made by plotting SOS values on each location of the section corresponded well to their palpable stiffness and LM images. SOS values (mean ± SD) of cartilages, osteoid, and bones presented 1524.2±35.8, 1632.4 ± 48.6, 1794.4 ± 81.1 m/s, respectively. Bone formation from membranes and cartilage were visualized by alteration of SOS values in developing bones, fracture callus, and various bone tumours. Lamellar bones consisting of thick collagen bundles showed multilayer sheets with high SOS values, while woven bones presented a reticulated structure with lower SOS values. Colour images of SOS were changeable to adopt the SOS range within the region of interest.
Conclusion: SOS images are comparable with LM ones and correspond well to bone and cartilage stiffness to discriminate these states. Numerical values of SOS are relative to bone or cartilage structures to reveal bone formation, fracture recovery, and the metabolic state in sections. SOS images determined woven or lamellar bones. Because unstained sections are free from stain bias and obtained SOS data are objective, SAM can be a scientific tool to evaluate regenerative, metabolic, and neoplastic diseases of orthopaedics.

E-PS-22-030

Aneurysmal bone cyst-like myositis ossificans of the digit - a rare occurrence

S. Naresh Shah*
*Apollo hospitals, India

Background & objectives: Myositis Ossificans is a self-limited reactive process of heterotopic bone formation in soft tissue, which usually follows a trauma. Secondary Aneurysmal bone cyst in soft tissue lesions, a rare occurrence, is believed to be a change associated with hematoma formation.
Methods: A 45 year old man presented with swelling in his left ring finger, of one month duration (only history provided at the time) to histopathology department at Apollo hospitals, India. We received an excision biopsy with clinical diagnosis of "osteoma" from remote centre. Radiologically, only roentogram was done which was suggestive of Nora's lesion. No fluid filled spaces were appreciated.
Results: The specimen was received in fragments. Histologically, there were zonation phenomena with spindled myofibroblasts in the centre, surrounded by immature woven bone and mature bone in the periphery. In the centre of the lesion cystic blood-filled spaces with septae and surrounding multinucleated giant cells were seen. On persistent perusal, a history of trauma to the finger was obtained. Hence, a diagnosis of ABC-like MO was made.
Conclusion: This is a rare case of ABC-like MO presenting at an unusual site (finger), with only two other such cases in the literature to the best of our knowledge. The history of trauma favoured a diagnosis of ABC-like MO rather than MO-like ABC. USP6 rearrangement by FISH is seen in both ABC and MO and may not help in differentiating between the two entities.

E-PS-22-031

Malignant peripheral nerve sheath tumour with perineural differentiation (malignant perineurioma)

E. Pérez Béliz*, L.I. Rojo-Alvarez, I. Abdulkader Nallib, J.M. Cameselle-Teijeiro, M. Piso Neira, F.J. Caneiro Gómez
*Clinical University Hospital of Santiago de Compostela, Universidad de Santiago de Compostela and Galician Healthcare Service (SERGAS), Santiago de Compostela, Spain

Background & objectives: Malignant peripheral nerve sheath tumour (MPNST) with perineural differentiation, is a spindle cell sarcoma with positivity for EMA, claudin-1 or GLUT-1, that arises in adults, in extremities or trunk. Here we describe one case illustrating the diagnostic difficulties encountered.
Methods: Histopathological, immunohistochemical and FISH analysis of one case presented in a man of 58 years of age with an axillary mass, adjacent to the brachial plexus, and ipsilateral shoulder pain.
Results: First, a needle biopsy was performed, showing a malignant spindle cell neoplasm with scattered pleomorphic cells, necrosis and myxoid stroma. The preliminary immunohistochemical analysis was inconclusive, and a diagnosis of undifferentiated pleomorphic sarcoma was made. The patient received radiotherapy, chemotherapy, and ulterior radical surgery. The tumour consisted of a 16 centimetres multilobular myxoid mass, with an histological appearance similar to the first biopsy. Tumour cells showed positivity for CD34, EMA, GLUT-1, cytokeratins and focal SMA, and were negative for desmin and MUC4. FISH analysis for FUS showed absence of rearrangements. Hence, a diagnosis of malignant perineurioma was proposed.
Conclusion: Malignant perineurioma is an infrequent, neglected variant of MPNST. Given its undifferentiated pleomorphic appearance, such diagnosis can become a challenge, particularly in needle biopsies. Differential diagnosis must include conventional MPNST and low grade fibromyxoid sarcoma, therefore the relevance of MUC4 staining and FUS rearrangements analysis. Positivity for EMA and CD34, alongside GLUT-1 or claudin-1, should raise suspicion for this tumour. Awareness of this entity, proper sampling, and a standardized immunohistochemical panel will lead to an accurate diagnosis of malignant perineurioma.

E-PS-22-032

Primary pleuropulmonary synovial sarcoma: a case report with review of the literature

D. Proca*, D. Zenezan, J. Yin
*Temple University Health System, USA

Background & objectives: Primary pleuropulmonary synovial sarcoma (PPSS) is a rare malignant tumour, accounting for 0.1% to 0.5% of all primary lung malignancies. PPSS is associated with a characteristic t(X;18) (p11.2; q11.2) chromosomal translocation.
Methods: Our patient is a 24-year-old female who was previously healthy and active. She presented with two weeks of posterior left chest wall pain, dyspnea, and neuralgia of left upper arm. A heterogeneous pleuropulmonary mass in the left lower hemithorax was discovered on Chest CT scan; it measured 10.5 x 8.7 x 8.0 cm and had associated pleural effusion.
Results: Biopsy of the mass showed high cellular fascicles of monomorphic spindle cells with infrequent mitoses and hemangiopericytic vascular pattern. The neoplastic cells were reactive for TLE-1 (indicative of synovial sarcoma), vimentin and bcl-2, with focal, non-specific weak staining with desmin, calponin, and CD99. A ki-67 proliferative index was approximately 15%. The tumour was negative for AE1/AE3, CK5/6, CK7, CK20, CK19, EMA, STAT6, myogenin, S100, SOX 10,

Calretinin, WT-1, D2-40, DOG-1, c-kit, SMA. B-catenin and Myo-D1 showed non-specific cytoplasmic staining. The diagnosis of monophasic synovial sarcoma was confirmed by FISH for SS18 rearrangement (10% of tumour cells).
Conclusion: Translocation-related sarcoma should be considered in the differential of a cellular monomorphic spindle cell tumour. Although pleura/lung is a rare site of synovial sarcoma, PPSS is part of the differential diagnosis for lung/pleural masses. A broad immunohistochemical panel is necessary to rule out other spindled lesions, such as solitary fibrous tumour, spindled rhabdomyosarcoma, spindled mesothelioma, desmoid tumour, leiomyosarcoma, sarcomatous carcinoma, and spindled MM. FISH analysis is the gold diagnostic tool in confirming t(X;18) and the diagnosis of PPSS.

E-PS-22-033
Beckwith-Weidemann syndrome and rhabdomyosarcoma: review of the literature and a novel case of MyoD1 spindle cell/sclerosing rhabdomyosarcoma
G. Raghuram*, M. Madni, H. Mugalaasi, A. Haider, T. McCulloch
*Nottingham University Hospitals NHS, United Kingdom

Background & objectives: Beckwith-Weidemann syndrome (BWS) is a genetic disorder caused by imprinting defects at the chromosome 11p15.5 region. Alveolar and embryonal rhabdomyosarcomas (RMS) are associated with BWS. We describe the first occurrence of MYOD1 spindle cell/sclerosing RMS in a child with BWS.
Methods: In this case, an 11 year old male patient with known BWS presented with a 4 week history of pain around the left mandible. The biopsy showed cords and trabeculae of small blue cells with scant cytoplasm separated by cords of dense hyalinised stroma. Next generation sequencing was performed and revealed a mutation in MYOD1 (Exons 1-3 p.(Leu122Arg) variant).
Results: At least three sub-groups within the overall spindle cell/sclerosing RMS category have been described, one of which is MYOD1-mutant spindle cell/sclerosing RMS. These appear to be associated with more aggressive behaviour. In addition, within our case, mutations in PIK3CA and CDKN2A were noted.
A review of the literature revealed ten cases of RMS in BWS patients. Of these, five were reported as alveolar RMS, three as embryonal and two as RMS not otherwise stated. However, in previous studies genetic confirmation of subtype has not been achieved and alveolar RMS when associated with BWS have lacked their characteristic translocation; t(2,13) or t(1,13), that generate the PAX3-FKHR or PAX7-FKHR fusion proteins.
Conclusion: Spindle cell/sclerosing RMS is a recently described distinct entity that accounts for approximately 5-10% of RMS. Given our understanding of RMS is constantly changing, this case adds new information to our knowledge of not only RMS, but also to the association between BWS and RMS. This may open new avenues of research including possible treatment. Here, our patient was discussed at the regional paediatric multidisciplinary team meeting and responded well after initial treatment with ifosfamide, vincristine and actinomycin (IVA) chemotherapy.

E-PS-22-034
Desmoplastic small round cell tumour in a palatine tonsil: a unique case report
L.I. Rojo-Alvarez*, E. Pérez Béliz, F.J. Caneiro Gómez, I. Abdulkader Nallib, J.M. Cameselle-Teijeiro
*Clinical University Hospital of Santiago de Compostela, Universidad de Santiago de Compostela and Galician Healthcare Service (SERGAS), Santiago de Compostela, Spain

Background & objectives: Desmoplastic small round cell tumour (DSRCT) is a rare malignant mesenchymal neoplasm that primarily affects male children and young adults, usually located intra-abdominally. We describe a case of a 13-year-old-girl with a DSRCT in the left palatine tonsil.
Methods: The fragments of the tonsillectomy specimen formalin-fixed and paraffin embedded showed small round tumour cells associated with prominent desmoplastic stroma. Immunohistochemical (IHC) studies, fluorescent in-situ hybridization (FISH) analysis using the EWSR1 gene break-apart probe, as well as RNA-seq using Next-Generation Sequencing (NGS) analysis were performed. MRI and 18F-FDGPET-TC provided monitoring the response to treatment and excluded residual disease.
Results: The patient, a 13-year-old girl, presented with left ear pain owing to ipsilateral tonsillitis. Histological examination showed clusters and confluent sheets of small neoplastic round blue cells within a desmoplastic stroma with prominent vascularity. The immunohistochemical examination showed positivity for CK8/18, neuron-specific enolase, vimentin, desmin (paranuclear dot pattern), WT-1 (carboxy-terminal antibody) and CD99. FISH showed EWSR1 rearrangements and NGS analysis confirmed the EWS-WT1 fusion gene. Considering the set of findings, the polyphenotypic immunohistochemical pattern along with the presence of EWSR1 and WT1 rearrangements, a diagnosis of DSRCT was made, excluding other morphologically similar entities such as extraskeletal ewing sarcoma, rhabdomyosarcoma, neuroblastoma and poorly differentiated neuroendocrine carcinoma.
Conclusion: To the best of our knowledge, this is the first reported case of a DSRCT occurring primarily in a palatine tonsil. Physicians must be aware of the possibility of this rare location and also that this rare neoplasm can occur in very unusual locations.

E-PS-22-035
Phosphaturic mesenchymal tumour: series of three cases in a tertiary hospital
L.I. Rojo-Alvarez*, E. Pérez Béliz, F.J. Caneiro Gómez, I. Abdulkader Nallib, J.M. Cameselle-Teijeiro
*Clinical University Hospital of Santiago de Compostela, Universidad de Santiago de Compostela and Galician Healthcare Service (SERGAS), Santiago de Compostela, Spain

Background & objectives: Phosphaturic mesenchymal tumour (PMT) is a rare neoplasia that occurs in bone and soft tissue and is associated with overproduction of fibroblast growth factor (FGF-23) that decreases phosphate reabsorption causing tumour-induced osteomalacia (TIO). Here we describe 3 cases.
Methods: PMTs were diagnosed in two women and a man of 57, 69 and 71 years of age (2010-2023). Two cases showed hypophosphatemia, hyperphosphaturia, high FGF-23 serum levels, osteolytic lesions and a femoral fracture. PMT in the third case was located in a finger, without biochemical alterations. Biopsy and resection material was evaluated by routine staining and immunohistochemical analysis.
Results: The PMTs showed similar appearances: a neoplastic proliferation of ovoid to spindle cells with bland nuclei, embedded in a hyalinized eosinophilic matrix enriched by well-developed vascularity with hemangiopericytoma-like areas, chondromyxoid and osteoid foci as well as typical grungy calcifications. Clusters of osteoclasts and mature adipose tissue were also present. Immunohistochemical analysis showed positivity for CD56, ERG, SATB2 and SSTR-2. The third case was considered a "non-phosphaturic variant" of PMT. After resection, the first case recurred, while the second case normalized biochemical and clinical symptoms in the following three months. In the third case, the amputation of the distal half phalanx of the hand with free margins was curative.
Conclusion: Our case series demonstrate that histological features along with an appropriate immunohistochemical profile lead to a reliable diagnosis of PMT, especially when combine with the biochemical and clinical data of TIO. Furthermore, the more accessible anatomical

location of the tumour in the third case permitted an earlier diagnosis despite the absence of biochemical alterations.

E-PS-22-036
Infantile fibrosarcoma with ETV6-NTRK3 fusion: a rare case report
O. Sahin*, I. Tosun, G. Unverengil, I.E. Zemheri
*University of Health Sciences, Umraniye Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Infantile fibrosarcoma (IFS) is a rare malignant fibroblastic tumour that typically presents in the first 1 year of life. ETV6-NTRK3 fusion is present in the majority of cases. IFS is a locally aggressive tumour; recurrence and metastasis are rarely seen.
Methods: We present a case of 3 months old baby girl with a rapidly enlarging right axillary mass. On clinical examination, contrast-enhanced magnetic resonance imaging (MRI) revealed a 36x26 mm densely contrasted solid mass lesion in the posteromedial aspect of the proximal humerus. Tru-cut biopsy was performed, followed by total excision.
Results: Tru-cut biopsy revealed a tumoral lesion consisting of spindle cells arranged in crossed fibres. There were haemorrhages, but no necrosis. The mitotic activity was 8/mm2. Immunohistochemically, negative immunostaining for S100, CD34, Desmin, Myogenin, and MyoD1 was observed. Ki67 proliferation index was 80%. The tru-cut biopsy is diagnosed as "malignant spindle cell mesenchymal tumour." In the excised specimen, a partially encapsulated nodular mass with a firm consistency was observed on gross examination. Microscopically, the neoplasm was highly cellular and was composed of spindled to immature-round cells. Necrosis and calcification were observed. Mitotic activity was 14/mm2. Molecular analysis revealed ETV6-NTRK3 fusion-positivity.
Conclusion: Infantile fibrosarcoma is a rare neoplasm resembling other paediatric mesenchymal neoplasms. Despite having features similar to those of adult fibrosarcoma, IFS is a completely different entity with better clinical outcomes and molecular features. In most cases, ETV6-NTRK3 fusion is detected as a result of chromosomal translocation, t(12:15). This translocation has also been detected in cellular congenital mesoblastic nephroma and secretory carcinomas of the breast and salivary glands. Histomorphologic findings and clinical history will help reach the correct diagnosis.

E-PS-22-038
Endometriosis of sciatic nerve: case report
L. Simic*, J. Jevtic, G. Djuricic, M. Popovic Vukovic, J. Sopta
*Institute of Pathology, Serbia

Background & objectives: Endometriosis is defined as the occurrence of endometriotic tissue outside the uterus. The most affected areas are the pelvic peritoneum, ovaries, and recto-vaginal septum. Nearly 5–10% of women in their reproductive years develop endometriosis.
Methods: We present a case of a 26 years old women, which was examined because the continuous back and leg pain with severe exacerbation before and during menstruation. MRI showed diffuse thickness of left sciatic nerve with focally presented cystic formation. They decided to do biopsy.
Results: Grossly tissue were fragmented, soft, greyish to reddish with small pseudocystic structures. Microscopically, on H&E examination among fields of fibrous and neural tissue, there were parts with glandular formations lined by columnar epithelium, surrounded with hypercellular stromal layer which resemble endometrial stroma. Immunohistochemical analyses (CK AE1/AE3+, CK7+ in glands, CD10+, PAX8+ in stroma, Oestrogen+, Progesterone+ in both glands and stroma) correlated with morphological characteristics proved diagnosis of sciatic nerve endometriosis. In addition, patient mentioned confirmed cystic formation on her last gynaecological US examination, but since now she has never been diagnosed endometriosis.
Conclusion: Endometriosis rarely involves major nerves, so affection of sciatic nerve is very rare condition. Mostly it is caused by direct extension of deeply infiltrative recto-vaginal disease, but in a minority of cases it can be isolated form, without any apparent signs of pelvic endometriosis. Since severe clinical presentation, and possible destruction of the nerve, endometriosis of sciatic nerve must be always considered when it comes to possible cause of unexplained pelvic nerve pain.

E-PS-22-039
Rhabdomyosarcoma in the oral cavity of a paediatric patient: a rare case
B. Simsek*, E. Atik Doğan, D. Gürsoy Kuzuluk, M. Cemaloğlu
*Hatay Mustafa Kemal University, Turkey

Background & objectives: Rhabdomyosarcoma(RMS) is a rare,rapidly growing,aggressive malignant neoplasm mainly affecting children and adolescents. We present a case of rhabdomyosarcoma detected in the hard palate of a 6-year-old boy who presented to the clinic with a complaint of swelling on the cheek.
Methods: 3 punch biopsy materials taken from the hard palate were sent to our pathology laboratory with clinical prediagnoses of sarcoma, acinic cell carcinoma and maxillary sinus tumour. In the light of histopathological findings Small Round Cell Tumours, Neuroendocrine Tumour, Plasma Cell Neoplasia and Malignant Melanoma were included in the differential diagnosis. A large immunohistochemical panel covering all differential diagnoses was applied.
Results: Histopathological examination showed a tumoral lesion formed by cells with narrow eosinophilic cytoplasm, hyperchromatic round-oval nuclei, arranged in the form of islands and cords with crush artifact in the fibrocollagenized stroma with occasional myxoid changes. Cells with eccentric or spindle nuclei were also noted infrequently. No rosette formation was observed.
Immunohistochemical examination revealed that the tumour cells were positive for myogenin, desmin and vimentin. The Ki67 proliferation index was ~80-90% per HPF.
As a result of the histopathological and immunohistochemical examination, the patient was diagnosed with embryonal RMS. There is no paediatric oncology unit in our hospital, so the patient was referred to another centre for oncological evaluation and treatment.
Conclusion: The patient was classified as intermediate risk group according to the Europen paediatric Soft tissue sarcoma Study Group (EpSSG) in the referred centre. Embryonal RMS has being treated via vincristine, actinomycin D, cyclophosphamide and irinotecan.
A pathological diagnosis for RMS is necessary because a specific diagnosis cannot be made based on clinical findings alone.
In conclusion, the current case was found worth presenting as a rare diagnosis in the literature.

E-PS-22-040
Secondary malignancy in Li-Fraumeni syndrome patient
J. Tuziak*, P. Wiśniewski, H. Koseła-Paterczyk, P. Rutkowski, K. Seliga, A. Tysarowski, A. Szumera-Ciećkiewicz
*Maria Sklodowska-Curie National Research Institute of Oncology Warsaw, Poland

Background & objectives: Li-Fraumeni syndrome (LFS) is a rare, autosomal dominant genetic disease with high penetrance characterised by germline TP53 mutations. Females with LFS and before age 30 have a nearly 90% and 25% lifetime risk of developing breast cancer and sarcoma, respectively.
Methods: A 29-year-old female was admitted for consultation on a chest tumour. Five years earlier, she was diagnosed with breast cancer (luminal type, pT4b N(sn)1a) and underwent mastectomy with

chemotherapy and radiotherapy. The patient remained without recurrence or progression until the tumour mass of soft tissues in the post-radiotherapy field was identified.
Results: The biopsy material revealed epithelioid cells, with high cytological atypia and mitotic activity (26 mitoses/10HPF), without necrosis. The immunohistochemical profile of neoplastic cells showed: Vimentin(+), EMA(-/+), CD34(-/+), ERG(-), CKAE1/AE3(-), ER(-), PGR(-), HER2(-), GATA3(-), PAX8(-), S100(-), SOX10(-), HMB45(-), SMA(-), Desmin(-), LCA/CD45(-), CD30(-), INI1(+), CD163(-). The molecular analysis with the NGS extended sarcoma panel (53 gene fusions and 14 gene mutations) was negative. We compared the primary breast cancer image with the current neoplasm and excluded recurrence; the undifferentiated sarcoma high-grade, G3 as a second malignancy was diagnosed. Additionally, the genetic predisposition test (blood) revealed a TP53 germline mutation.
Conclusion: Breast cancer in young women should trigger testing its association with the inheritance of a pathogenic variant in one of the breast cancer susceptibility genes. The LFS patients require special care i.e., favouring the mastectomy rather than lumpectomy to avoid adjuvant radiotherapy and subsequent risk of radiation-induced second primary malignancies, dose-adjusted careful consideration of radiation when indicated post-mastectomy. The diagnostic challenge includes differential diagnosis between breast cancer and sarcoma, possibly secondary and/or radiotherapy-induced malignancies.

E-PS-22-041
Myxoid angiomatoid fibrous histiocytoma with EWSR1-CREM fusion: a case report
J. Tuziak*, M. Wągrodzki
*Maria Sklodowska-Curie National Research Institute of Oncology Warsaw, Poland

Background & objectives: Angiomatoid fibrous histiocytoma (AFH) is a rare mesenchymal tumour. It harbours EWSR1-CREB1 or EWSR1-ATF1 gene fusion. Hereby we present the first case of myxoid AFH of soft tissue with CREM fusion.
Methods: A 56-year old woman presented with a mass located between her left humerus and clavicle. The tumour was evaluated on MRI. First a fine needle biopsy then resection of the mass after neoadjuvant therapy was conducted. Tumour was assessed using extensive immunohistochemistry panel and molecular studies - Next Generation Sequencing (NGS).
Results: Gross sectioning revealed tan, solid soft tissue tumour with bloody spaces, measuring 4,8 x 5,8 x 4,5 cm with destruction of the clavicle.
On H&E slides there was a lobulated neoplasm with epithelioid, dyscohesive cells exhibiting eosinophilic cytoplasm with nuclear pseudoinclusions. The presence of multinucleated giant cells was also noted. Part of the tumour showed nested architecture. Tumour stroma was predominantly chondro-myxoid. The neoplastic cells exhibited: membranous CD99 (MIC2), and retained INI1 (MRQ27) nuclear staining with focal EMA (E29) and podoplanin (D2-40) expression. NGS CREM[3]-EWSR1[13] fusion was detected.
Conclusion: Our tumour shows striking resemblance to previously described intracranial myxoid AFH-like tumour occurring in central nervous system.
To the best of our knowledge, it is the first tumour with this rearrangement in soft tissue. Since CREM gene belongs to the CREB family transcriptor factors along with ATF1 and regarding the presence of EWSR1-CREM fusion in classic AFH, the myxoid tumours with EWSR1-CREM fusion should be regarded as myxoid variant of AFH both in central nervous system and in soft tissues.

E-PS-22-042
Giant dedifferentiated liposarcoma of the omentum with rhabdomyosarcomatous differentiation - a rare case
C. Valavanis*, E. Souka, G. Stanc
*Molecular Pathology Unit Metaxa Cancer Hospital, Greece

Background & objectives: Liposarcoma is the most common soft tissue sarcoma and accounts ≈20% of all mesenchymal malignancies. Primary tumours of the omentum are very rare. The incidence is not known, and the information is available in the literature only from case reports.
Methods: A 55-year-old man presented with abdominal pain, nausea, weight loss and gastric haemorrhage. CTscan showed a large mass 19X16X12cm in dimensions, which causes pressure to the stomach from outside, in touch with the liver, gallbladder, anterior surface of the stomach and duodenum.
Partial gastrectomy for duodenal ulcer has been performed in 1993. A distal partial gastrectomy and omentomy was made.
Results: Microscopic examination revealed morphology of well differentiated liposarcoma. The neoplasm was characterised by cells with high-grade atypia, focally by the presence of multinuclear bizarre cells or signet-ring lipoblasts. Foci of pleomorphic liposarcoma and rhabdomyosarcomatous differentiation were present. The mitotic activity was high, 23mitoses/10HPF. Cystic degeneration of the tumour and necrosis were seen.
Immunochemistry showed positivity for S-100, CD34, CDK4, MDM2, SMA, Desmin and Vimentin. Negative were CD117, HMB45, Melan A, CK7, CK19, CK8/18, CK20, MUC2 and MUC5AC.
The diagnosis of high-grade dedifferentiated liposarcoma with pleomorphic component and rhabdomyosarcomatous differentiation was made.
Conclusion: The main therapy for omental liposarcoma is surgical removal. The type of gastrectomy depends on the location of the tumour. Lymph node dissection may be unnecessary.
Clear guidelines for chemotherapy and radiotherapy in patients with omental liposarcoma does not exist in the literature.
In high-grade liposarcomas, adjuvant therapy may be considered because of a high local recurrence rate (70-90%).

E-PS-22-043
Dedifferentiated leiomyosarcoma with heterologous osteosarcoma component in the thigh: case report and review of literature
M. Zaryouhi*, R. Ben Tayab, L. Chbani
*Hassan II hospital University, Morocco

Background & objectives: The terminology dedifferentiated leiomyosarcoma refers to a tumour characterized morphologically by an abrupt transition from a classical leiomyosarcoma to a high-grade sarcoma, not expressing muscle markers.
The aim of this report is to explain the histological features of dedifferentiated leiomyosarcoma.
Methods: We are reporting a case of 43-year-old woman who, after three surgeries, chemotherapy, and radiation therapy on a previously diagnosed pleomorphic leiomyosarcoma grade 3 of the French Federation of Comprehensive Cancer Centers (FNCLCC) grading system, had a local recurrence made of a subcutaneous permeation nodule on the posterior compartment of the left thigh.
Results: Histomorphologic features of this nodule revealed a biphasic pattern. The first one is made of atypical spindle cells arranged in short fascicles, focally pleomorphic with an ovoid hyperchromatic nucleus and eosinophilic cytoplasm typical of a leiomyosarcoma. The second component has a distinctive osteoid laid down by malignant cells.

The diagnosis was supported by positive immunoreactivity for smooth muscle actin and in areas with leiomyosarcomatous appearance, whereas the osteosarcomatous component was negative.
A FISH study was performed as well to rule out the main differential diagnosis that is dedifferentiated liposarcoma with heterologous smooth muscle and osteochondroblastic differentiation, and it came back negative (no amplification of MDM2 gene).
Conclusion: Dedifferentiated leiomyosarcoma is a very rare disease with poor outcome. It is a diagnosis of exclusion that require knowledge, patience, and time. Extensive sampling and FISH study are strongly recommended in diagnosis approach.

E-PS-23 | E-Posters Thymic and Mediastinal Pathology

E-PS-23-001
Thoracic SMARCA4-deficient undificient tumour

A. Demir*, E. Kilic Bagir, D. Gümürdülü
*Çukurova University, Pathology Department, Turkey

Background & objectives: Thoracic SMARCA4-deficient undifferentiated tumour was described in the final who 2021 classification, that exhibits an undifferentiated and rhabdoid phenotype and defiency of SMARCA4, an important member of the BAF chromatin remodelling complex.
Methods: We present 61 years old man had been smoking 50 pack/year, who applied to the hospital with the complaints of back pain and shortness of breath.
CT imaging revealed 8x6x5 cm solid irregular left bronchial mass involvement mediastinal involvement areas. In Frozen section, the patient is diagnosed with non-small cell carcinoma and left pneumectomy lymph node dissection is performed.
Results: 17x15x8 cm pneumectomy material was examined, a centrally located 8x6x5 cm solid lesion was observed, invading the pleura, at a distance of 3 cm from the bronchial surgical margin.
Microscopic examination of the mass a poorly differentiated with eosinophilic cytoplasm, vesicular nuclei, prominent nucleoli and plasmocytoid appearance tumour cells and large areas with necrosis was observed. İmmunohistochemically tumour cells were CD34 focal positive, SALL4 focal positive, keratin focal positive and SMARCA4 negative (loss).
Conclusion: smarca4-deficient tumours are rare, aggressive tumours with undifferentiated morphology. It should be considered in male patients with a history of smoking at a young age. The differential diagnosis includes lymphoma, NUT carcinoma, germ cell tumour, neuroendocrine carcinoma, large cell carcinoma, melanoma, as well as various types of sarcoma such as CIC rearranged sarcoma, malignant rhabdoid tumour, epithelioid sarcoma. Clinical correlation is imperative, as SMARCA4-UTs with a similar phenotype can metastasize to the thorax from external sites (uterus, ovary, stomach, kidney, pancreas).

E-PS-23-002
A single-institution experience of primary mediastinal large B-cell lymphoma: a report of 88 cases

L. Farah*, R. Ayadi, H. Ichrak, B. Emna, O. Khouildi, A. Ayadi, S. Hamza
*CHU Abderrahmen mami Tunisia, Tunisia

Background & objectives: Primary mediastinal large B-cell lymphoma (PMBCL) is a rare large B-cell neoplasm, characterized by a rapidly increasing anterior mediastinal mass, causing compression of the surrounding tissues.
The aim of this study is to describe its clinical-pathological and immunohistochemical features.
Methods: This retrospective study included all patients with a pathologically confirmed diagnosis of PMBCL treated at our department of pathology between 2004 and 2022.
Results: There were 54 female and 34 male patients, aging between 15 and 87 years with a mean of 39,5. The diagnosis was made on surgical biopsy (n=55), lymph node biopsy (n=16), transparietal biopsy (n=13), bronchial biopsy (n=3) and surgical resection (n=1). The histological examination revealed diffuse sheets of lymphomatous tumour cells intermixed with a moderate inflammatory infiltrate. This proliferation is dissociated by a rather extensive and dense fibrosis. Tumour cells are large, with abundant clear cytoplasm, round to oval nuclei, irregular contours and conspicuous nucleoli. Immunohistochemistry revealed diffuse positivity with CD20 in all cases, focal positivity for CD30 (n=15) and CD3 but negative stain with CD15 and CK.
Conclusion: The pathological diagnosis of PMBCL remains challenging because of features that may overlap with other types of lymphoma (Hodgkin and non-Hodgkin). However, recognition and diagnosis are crucial for the initiation of optimal treatment.

E-PS-23-003
Pseudotumoral mediastinal amyloidosis: a histological surprise!

L. Farah*, R. Ayadi, B. Emna, O. Khouildi, A. Ayadi, S. Hamza, H. Ichrak
*CHU Abderrahmen mami Tunisia, Tunisia

Background & objectives: Amyloidosis is an ubiquitous deposition of extracellular abnormal proteins. An isolated mediastinal location is unusual and typically raises concern for underlying malignancy.
The aim is to describe the clinical-pathological findings and discuss the differential diagnosis of this disease.
Methods: We report a retrospective study concerning 12 cases of mediastinal amyloidosis diagnosed at our department of pathology between 2004 and 2022.
Results: There were 11 male and 1 female patients, aged between 16 and 78 years, with a mean of 46 years. The diagnosis was made on mediastinoscopic biopsy (n = 8), surgical resection (n= 2) and lymph node biopsy (n= 2). The histological examination revealed extracellular deposits of amorphous eosinophilic material often surrounded by foreign-body type of multinucleated giant cells. The material was Congo-red stain positive and showed the characteristic apple-green birefringence when examined by polarizing microscopy. Immunohistochemistry stain showed that the amyloid was composed of lambda light chains in most cases.
Conclusion: Despite its rare occurrence in the mediastinum, Amylodosis should be considered as a differential diagnosis when facing a mediastinal mass.

E-PS-23-004
Lipofibroadenoma of the thymus in a patient with myasthenia gravis; a case report

E. Hijazi*, M. Al-Hussaini
*Islamic Hospital, Jordan

Background & objectives: Lipofibriadenoma (LFA) of the thymus is a rare, benign thymic tumour, with different manifestations, with only 6 reported cases so far.
We report a case of LFA in a 39 year old man diagnosed with myasthenia gravis.
Methods: Our patient is a 39 year old male, who is diagnosed as myasthenia gravis, and presented with myasthenia crises. Radiology study showed a well-defined, partially- calcified lesion in the anterior mediastinum, measuring 2.3 cm in maximum dimension.
The patient underwent thymectomy with complete excision of the mass and surrounding fatty tissue.
Results: Histological study revealed a well-circumscribed lesion, showing fibrotic and hyalinized stroma, with narrow strands lined by bland -looking epithelial cells in between, resembling fibroadenoma of the breast, as well as foci of mature adipose tissue and aggregates

of lymphocytes. Immunohistochemical stains showed positive staining for ck19 in the epithelial cells, with CD 20 and CD 3 positive B and T lymphocytes respectively, the former forming small follicles, mostly representing follicular hyperplasia. The adjacent fatty tissue showed scattered aggregates of residual thymic tissue, including Hassall corpuscles and lymphocytes with follicular hyperplasia.
Conclusion: Lipofibroadenoma of the thymus is a rare tumour with different manifestations. Our patient is diagnosed with myasthenia gravis and showed thymic LAF with adjacent follicular hyperplasia.

E-PS-23-005
Thymolipoma, a rare mediastinal tumour: pathological study of 6 cases
H. Ichrak*, R. Ayadi, B. Emna, L. Farah, S. Hamza, O. Khouildi, A. Ayadi
*CHU abderrahmen Mami Tunisia, Tunisia

Background & objectives: Thymolipoma is an extremely benign tumour of the anterior mediastinum and accounts for only 2- 9% % of all tumours of the thymus. When symptomatic, they present with non-specific compressive symptoms such as chest pain and dyspnea.
Methods: We report a retrospective study of 6 cases of thymolipoma diagnosed at our department of pathology between 2004 and 2022.
Results: There were 3 male and 3 female patients, aged between 24 and 48 years, with a mean age of 40. All patients underwent a surgical resection. On gross examination, tumours' size ranged between 7,5 and 23 cm with a mean of 18,5 cm. They were described as fairly well-circumscribed, soft, yellowish, fatty and lobulated tumours with focal solid areas. Microscopically, all lesions showed similar morphology: mature adipose tissue admixed with areas containing remnants of thymic tissue and limited by a thin peripheral fibrous capsule. Examination of all sections did not reveal any areas of cellular atypia or mitoses. The clinicaloutcome was satisfactory in all cases.
Conclusion: Thymolipomas are rare tumours but should be considered in the differential diagnosis of mediastinal anterior lesions. They pose a significant challenge due to their unclear histogenesis and atypical clinical presentation. Complete surgical resection is recommended in all thymolipomas with favourable survival rates.

E-PS-23-006
The 2021 WHO Classification of tumours of the thymic neuroendocrine neoplasms
H. Ichrak*, R. Ayedi, B. Emna, L. Farah, S. Hamza, O. Ismail, A. Ayadi
*CHU abderrahmen Mami Tunisia, Tunisia

Background & objectives: Thymic neuroendocrine neoplasms are uncommon tumours. They were recently classified by the World Health Organization into four histological entities: low-grade carcinoid tumours, intermediate grade carcinoid tumours, and high-grade neuroendocrine carcinomas including large cell neuroendocrine carcinomas and small cell carcinomas.
Methods: We report a retrospective study of 8 cases of thymic neuroendocrine neoplasms diagnosed at our department of pathology between 2004 and 2022.
Results: There were 4 male and 4 female patients, aged between 32 and 64 years with a mean age of 49. The diagnostic was made on surgical resection (n=5) and transparietal biopsy (n=3). An intraoperative frozen section was performed (n=7) showed a malignant tumour process (n=4), non-small cell carcinoma (n=2) and malignancy that may be consistent with non-Hodgkin's lymphoma or thymic carcinoma (n=1). The histological examination revealed, intermediate grade carcinoid tumours (n=6) and high-grade neuroendocrine carcinomas (n=2). Immunohistochemically, the tumour cells were positive for synaptophysine (n=8), chromogranine (n=8), NCAM (n=6), EMA (n=3) and pancytokeratin (n=1). However, they were negative for muscle actin, PS100, CD5 and TTF1.
Conclusion: The rarity of thymic neuroendocrine neoplasms and the difficulty of pathological diagnosis make it a difficult malignancy to study. Their main differential diagnosis are extension or metastases of their bronchopulmonary counterparts. As there are no known differentiating morphological or immunohistochemical features, the distinction relies heavily on clinical and radiological assessment.

E-PS-23-007
Lymphohistiocytoid variant of malignant mesothelioma of the pleura: a case report and diagnostic approach
I. Provatas*, P. Pantoula, N. Tsibidis, E. Ventouri, A. Karakosta
*Pathology Laboratory, General Hospital of Nikaia - Piraeus "Ag. Panteleimon", Greece

Background & objectives: Diffuse mesothelioma is a malignant, aggressive mesothelial neoplasm, with a total survival time up to 27 months. The lymphohistiocytic variety is a rare type of mesothelioma and very few cases are described internationally.
Methods: A 75-year-old man, with no history of exposure to asbestos or other predisposing factors, comes to our Hospital with breathing difficulties, cough and weight loss. Chest X-ray and CT scan show localized pleural thickening, visceral and parietal pleural nodules bilaterally, and bilateral pleural effusion, the cytology of which suggested mesothelioma. The patient underwent decortication.
Results: All the received tissue portions concerned strongly sclerotized parts of pleura, within which abundant histiocytic cells were observed, with severe cellular and nuclear atypia, focally with a large eosinophilic nucleus. Binuclear - polynuclear forms and atypical mitoses coexist, on a substrate including many lymphocytes and few plasma cells. Immunohistochemically, Vimentin, CD68 and focal CKAE1/AE3 expression was observed, whereas the lymphocytic substrate expressed CD8, CD3 and focally CD20. Ki-67 index was highly elevated. The differential diagnosis included undifferentiated pleomorphic sarcoma, sarcomatoid carcinoma, melanoma, anaplastic lymphoma, thymoma, and sarcomatoid mesothelioma. The consideration of all the above data led to the diagnosis of the lymphohistiocytic type of diffuse mesothelioma.
Conclusion: Diffuse Mesothelioma is a malignant neoplasm, closely related to exposure to asbestos as well as to mutations in the BAP-1, MSH-3, BRCA-2 etc. genes. The lymphohistiocytic type of Diffuse Mesothelioma is associated with a dense lymphocytic infiltrate. The overt T-cytotoxic lymphocytic infiltrate seen in this type of mesothelioma appears to correlate with an initially good clinical course. Therefore, a regulation of the lymphocytic immune response could be a field of study to improve the treatment of mesothelioma.

E-PS-23-008
Mediastinal clear cell sarcoma: a challenging diagnosis of a rare tumour
I. Provatas*, P. Pantoula, N. Tsibidis, V. Solomou, M. Karagianni
*Pathology Laboratory, General Hospital of Nikaia - Piraeus "Ag. Panteleimon", Greece

Background & objectives: Clear cell sarcoma (CCS) is an uncommon soft tissue sarcoma with melanocytic features, occurring mostly to young adults, without gender predilection. Most of them arise in the distal extremities and they are very rarely located in the mediastinum.
Methods: We report a case of a 52 year-old male with Trisomy 21, operated for a tumour located in the lower left thoracic wall. We received multiple segments of a white-creamed and partially dark brown, solid, elastic tumour, 5,8 cm in maximum diameter,

accompanied by small segments of muscle and adipose tissue, without history of cutaneous or mucosal melanocytic lesions.
Results: On microscopic examination, the tumour segments consisted of compact aggregations and nests of homogenous, epithelioid or spindle-shaped cells, with high nuclear atypia, eosinophilic and focally amphiphilic or clear cytoplasm, with medium-sized vesicular nuclei and apparent nucleoli, in a relatively sclerotic stroma. 23 mitoses / 10 HPF were counted and there were focal extracellular melanin depositions and necroses. Also, tumour cells were infiltrating between muscle fibres and fat cells. The immunohistochemical control of the neoplasm revealed strong expression of S-100, HMB-45, MART-1 and negativity for cytokeratins, WT-1, Calretinin, TTF-1, Synaptophysin, Chromogranin, NSE and BRAFV600E. Also, fluorescence in situ hybridization was positive for EWSR1 gene translocation.
Conclusion: Clear cell sarcomas are mesenchymal tumours, classified as tumour of uncertain differentiation in WHO 2020, which occur very rarely in the mediastinum. The diagnosis of these type of sarcomas is challenging, because of the morphological similarities with melanoma. In our case, the lack of previous cutaneous or mucosal melanocytic lesions and the positivity of fluorescence in situ hybridization for EWSR1 gene translocation, lead us to the diagnosis of this type of sarcoma.

E-PS-23-009
A case of thoracic SMARCA4-deficient undifferentiated tumour
E. Psychogiou*, P. Tziakou, P. Megas, M. Miliou, K. Papadopoulou, A. Konstantinidou, E. Papadopoulou, D. Riga, C. Glava, I. Vamvakaris
*General Hospital of Athens Sotiria, Greece

Background & objectives: Thoracic SMARCA4-deficient undifferentiated tumours are aggressive neoplasms that most commonly occur in the mediastinum of male smokers. SMARCA4 is considered a tumour suppressor gene, both the loss of protein expression as well as protein upregulation have been associated with neoplasia.
Methods: A 54-year-old man with free medical history was admitted to our hospital after the diagnosis of a mediastinal mass at CT scan. Biopsy was performed by thoracic surgeons for the determination of the nature of the tumour.
Results: Histopathologically, the tumour had a solid architecture pattern, comprising of medium-sized and larger cells, with dark-coloured round to oval nuclei, prominent nucleoli and basophilic cytoplasm, mild pleomorphism, extensive necrosis and very high mitotic activity. Plenty of lymphocytes were observed. Based on morphologic features and location of the mass the differential diagnosis includes non-small cell carcinoma, sarcoma, malignant melanoma, lymphoma, and malignant mesothelioma. Immunohistochemistry study demonstrated positive expression of RB and KLMW, while there was negative expression of TTF-1, P40, CD56, CK7, CD30, PLAP, S-100, NUT and loss of SMARCA4. This immunoprofile in association with the location of the mass supports a diagnosis of SMARCA4-UT.
Conclusion: SMARCA4-UT, formerly called "SMARCA4-deficient thoracic sarcoma" are very aggressive tumours and are characterized by a poorly differentiated morphology with at least a subset of these tumours exhibiting focal rhabdoid features. While the immunophenotype can vary, in general these tumours show no or only focal keratin expression. Loss of expression of BRG1 is the hallmark of these tumours. The diagnosis of these tumours is important as preclinical and early clinical trials using enhancer of zeste homolog (EZH2) inhibitors are promising.

E-PS-23-010
Glomus tumour of the trachea: a rare finding
N. Stavrinou*, F. Dolkiras, P. Vlachou, A. Therapontos, M. Lenos
*Department of Pathology, Evaggelismos General Hospital Athens, Greece

Background & objectives: Glomus Tumour is a neoplasm which usually arises on superficial and rarely on deep locations. Its cells resemble modified smooth muscle cells of the normal glomus body. Few cases of glomus tumour arising on the tracheobronchial tree have been reported.
Methods: We report a case of a 75-year-old man who presented with dyspnea. A tracheal mass was recognized during bronchoscopy and surgery was performed. The specimen received by the pathology department was a tracheal segment consisting of 3 cartilaginous rings, with an identifiable luminal exophytic mass measuring 1,8 cm.
Results: Microscopic evaluation of the tumour revealed a neoplasm consisting of uniform eosinophilic cuboidal cells arranged mostly in nests. Fibrovascular septa and foci of haemorrhage were also identified. Mitoses were rare (1/50HPF), and necrosis was not observed.
Immunohistochemical analysis was positive for SMA and h-caldesmon, whereas AE1/AE3, CK 8-18, CK7, p40, Synaptophysin, Chromogranin, CD34, CD31, TFE3, MelanA, HMB45 were negative.
Conclusion: Glomus tumours are classified into three histopathologic categories (benign, tumours of uncertain malignant potential, malignant tumours) according to strict histopathologic criteria (deep location, size > 2cm, mitotic rate >5/50 HPF, marked nuclear atypia). The vast majority is associated with a benign biologic behaviour. However, in the current case due to its deep location the lesion was diagnosed as "Glomus tumour of uncertain malignant potential". Due to their rare occurrence, follow up guidelines for tracheobronchial glomus tumours are not well established.

E-PS-23-011
Ectopic cervical thymus in a patient with oral squamous cell carcinoma: a diagnostic pitfall
D. Tapoi*, A. Dumitru, A. Ciongariu, I.A. Dandu Colceriu, D. Dumitrescu, V. Ionita, C.C. Badiu, M. Costache
*University Emergency Hospital, Romania

Background & objectives: Ectopic cervical thymus is a relatively frequent finding in children and is the result of an incomplete migration of the thymic tissue during embryogenesis. However, remnants of thymic tissue are a rare and usually incidental encounter during adulthood.
Methods: We present the case of a 55-year-old woman who presented to hospital for an exophytic, ulcerative palatine tumour. Upon physical examination, several enlarged lymph nodes were discovered in the cervical region, which were excised along with the tumour. The aim of our study is to gain further insight into tumours of the head and neck and discuss unusual differential diagnoses.
Results: Upon histopathological examination, the palatine tumour was diagnosed as an invasive keratinizing squamous cell carcinoma extending into the chorion of the mucosa. The lateral cervical lymph nodes showed only reactive changes for the most part, but one of them exhibited nests of squamous cells with keratinization phenomena. This finding prompted further immunohistochemical testing. p63 was positive in the squamous nests and in scattered epithelial cells, and p16 was negative throughout the tissue. The lymphocytes were positive for CD1a but negative for CD20. Thus, the diagnosis of ectopic thymic tissue was established instead of a squamous cell carcinoma metastasis in a lymph node.
Conclusion: Ectopic thymic tissue is a rare finding and is usually not included in the differential diagnosis of neck tumours, especially in adulthood. Furthermore, it is usually easily diagnosed solely on histopathological features. However, given the context of regional or adjacent squamous cell carcinomas, it should be taken into consideration and ancillary testing should be performed to establish a certain designation for any lesion with a morphology that bears the hallmarks of squamous differentiation.

E-PS-24 | E-Posters Uropathology

E-PS-24-001

Does mean nucleolar volume have prognostic significance in seminomas?

Y. Adali*, V. Şen, B. Tuna, O. Bozkurt, K. Yörükoğlu
*Izmir University of Economics Faculty of Medicine, Turkey

Background & objectives: Seminomas consists of large, tumour cells which contain one or two prominent nucleoli. In this study, it was aimed to examine the impact of the mean nucleolar volume (MnV) on prognosis in seminomas, which has prognostic importance in various tumours.
Methods: 54 cases diagnosed as pure seminoma were included in the study. The section of tumour was photographed at 400X magnification and digitally enlarged. The length of the nucleoli was measured using a transparent direction finder and ruler at a total magnification of 1200x. For each case,15 cells were counted and MnV was calculated stereologically. Clinical data were compared with MnV.
Results: The mean tumour diameters were 59.2±31.4, and 33 (61.1%) of the cases were pT1, 8 (14.8%) pT2, and 13 (24.1%) pT3. The MnV of the cases was calculated as 2471.8±1072.3 μm³. MnV was found to be increased as the tumour diameter increased (p= 0.000). No statistically significant correlation was observed between the pT stages and MnV (p= 0.762). 9 (16.7%) cases showed biomarker recurrence, 4(7.4%) cases had metastasis and the mean disease-free survival was 6.4±4.1 years. The MnV of the cases with metastasis was 2712.3±1763.0 μm³, and without metastasis 2452.5±1023.8 μm³; revealing no statistical significance (p= 0.645). It was observed that higher MnV was related with better survival (p= 0.000).
Conclusion: The present study revealed a relationship between MnV and tumour diameter. As MnV increases, the increase in survival seems to be inverse to the relationship with tumour diameter. However, in cases known to be manifested mostly with a painless mass, it can be thought that the increase in tumour size as MnV increases, leads to an association with a rise in the probability of early diagnosis and therefore a better survival.

E-PS-24-003

PTEN and ERG status and relationship in a prostate cancer cohort from Jordanian Arab population

S. Al Bashir*, M. Alorjani, I. Matalka, M. Matalka, K. Kheirallah
*Jordan University of Science and Technology, Jordan

Background & objectives: ETS-related gene (ERG) gene rearrangements and phosphatase tensin homologue (PTEN) deletions are ones of the most common genetic aberrations occurring in prostate cancer (PCa). However, their relations and patterns of expression in PCa in Jordanian population are not well studied.
Methods: We retrieved 108 PCa specimens from the archives of the King Abdullah University Hospital, spanning a period from 2005 to 2022. These cases included 48 biopsies, 37 prostatectomies (RP) and 33 (TURP). PTEN and ERG expression status were assessed by immunohistochemistry and correlated with other clinicopathologic parameters (patient age, preoperative PSA, Gleason Score (GS)/ Grade group(GG) , and biochemical recurrence.
Results: PTEN loss of any degree was observed in 45.3 % of the prostate cancer cases. ERG was expressed in 85% of the cases. There was an increased loss of PTEN expression with increasing the severity of the PCa (GS6 (GG1) to GS9-10 (GG5)). PTEN loss prostate cancer cases were less likely to be ERG Negative (9%). 36% of the total samples were PTEN loss and ERG positive cases and this was not statically significant.
Conclusion: In this first study to address the question of PTEN loss and ERG status in a predominantly Jordanian Arab population, we documented that PTEN loss are associated with more aggressive prostate cancers with higher Gleason scores/ Grades. PTEN loss prostate cancer cases were less likely to be ERG Negative. These findings support a rationale of screening for these biomarkers for prognostic purposes and molecular subtyping of the disease.

E-PS-24-004

Sporadic renal hemangioblastoma: a rare benign vascular renal tumour

A. Al-Zakwani*, M. Al-Riyami
*Oman medical speciality board, Oman

Background & objectives: Hemangioblastoma is a benign vascular tumour that is typically arise in the cerebellum. Renal hemangioblastoma cases are seldom seen and usually accompany VHL disease. It shows histological morphology features similar to its cerebellar counterpart.
Methods: N/A
Results: Background: Hemangioblastoma is a benign vascular tumour that is typically arise in the cerebellum. Renal hemangioblastoma cases are seldom seen and usually accompany VHL disease. It shows histological morphology features similar to its cerebellar counterpart and it is frequently misdiagnosed as various malignancies such as renal cell carcinoma (RCC), epithelioid angiomyolipoma and epithelioid hemangiopericytoma. Immunohistochemistry is crucial to differentiate it from the other malignant renal neoplasms. Objective: This case report describes one case of sporadic renal hemangioblastoma happened in a 72-year-old male, presenting with vague right flank abdominal pain. The radiological findings were suggestive of renal cell carcinoma.
Conclusion: 0

E-PS-24-005

The prevalence of SPOP gene mutations in prostate cancer: a retrospective cohort study

M. Alorjani*, S. Al Bashir, M. Al Zoubi
*Jordan University of Science and Technology, Jordan

Background & objectives: Speckle-type POZ (SPOP) gene mutations were reported in primary human prostate cancer (PCa). Isocitrate dehydrogenase-1 (IDH1) oncogene mutation was found in only 1% of PCa. This study aimed to investigate prevalence of SPOP and IDH1 mutations in PCa in Jordan.
Methods: One hundred formalin-fixed paraffin-embedded tissue samples were collected from Jordanian patients diagnosed with prostate adenocarcinoma. The obtained specimens were subjected to genomic DNA extraction, PCR amplification and direct sequencing of exons 4, 5, 6 and 7 for the SPOP gene and exon 6 for the IDH1 gene.
Results: The SPOP gene mutations were found in 17 % of PCa cases, while no mutation was detected in the screened exon 6 of the IDH1 gene.
Conclusion: The current study confirmed the presence of a high frequency of SPOP gene mutations in prostate cancer in the Jordanian Arab population; reported in four exons in 17 % of the studied PCa patients, consistent with findings of previous reports from other populations. Most of these mutations were found in exon 7 representing the hotspot exon in PCa cases. On the other hand, no tested sample showed the presence of IDH1 mutation in the screened exon 6 of the gene.
Funding: This research was funded by the Deanship of Scientific Research and Graduate Studies at Yarmouk University (grant number 12/2020)

E-PS-24-006

A rare presentation of relapsed multiple myeloma: ureteric plasmacytoma

A. Alves*, C. Courelas, J.L. Amaral, J. Pimentel, R. Almeida, M.A. Cipriano
*Pathology Department, Coimbra Hospital and University Centre (CHUC), Portugal

Background & objectives: Multiple myeloma (MM) and plasmacytoma are clonal plasma cell neoplasias, the former affecting the bone marrow, with serum/urine elevation of monoclonal immunoglobulin and end-organ damage and the latter being solitary lesions, isolated or in the context of relapsed MM.
Methods: Male patient in his 70's, with history of multiple myeloma (in remission), Diabetes Mellitus II, dyslipidemia and chronic renal disease, presented to the emergency room with dysuria and pollakiuria. The ultrasound study revealed hydronephrosis and a left ureteric wall thickening on its middle third, with 5cm length, confirmed by abdominopelvic CT-scan. The patient underwent a left nephroureterectomy.
Results: In macroscopic study, the ureter had a whitish firm nodular mass at its middle third, causing a reduction of the ureteric lumen and an upstream dilation, where the diameter was of 2,2cm.
Histologically, the tumour was composed of sheets of small cells with small, eccentric, hyperchromatic nuclei and basophilic cytoplasm, with occasional multinucleated cells.
The neoplastic cells showed immunopositivity to CD138 and were negative to CD45, Cam5.2, AE1/AE3, P63, E-Cadherin, Melan-A and pS100. In situ hybridization revealed lambda chain restriction.
This patient did not show any other concurrent lesions and the bone marrow aspiration and immunophenotyping were normal.
An extramedullary plasmacytoma diagnosis was rendered.
Conclusion: Extramedullary plasmacytomas, solitary or in the context of MM, are infrequent and generally located in the upper airway, with genitourinary involvement being rare. In the ureter, they can cause obstruction, leading to pollakiuria/anuria that can be the presentation symptom.
In this case, because there was no bone marrow involvement nor any other lesions, no adjuvant therapy was performed.
At last follow-up, one year after surgery, the patient remained in remission.

E-PS-24-007

The effect of COVID-19 pandemic on renal cell carcinomas' staging and grading at diagnosis: a tertiary centre perspective

A. Alves*, G. Fontinha, J. Gama, J. Madeira, S. Bárbara, R. Almeida, M.A. Cipriano
*Pathology Department, Coimbra Hospital and University Centre (CHUC), Portugal

Background & objectives: COVID-19 was a hard test for healthcare institutions, having to manage Sars-CoV2 infections while maintaining daily practice. We intended to evaluate if the pandemic and its challenges had any impact on renal cell carcinomas (RCC)' stage at presentation.
Methods: We selected all renal cell tumours diagnosed at our institution between 2019-2022 (n=311) and compared their clinical and pathological features, highlighting the pTNM stage at diagnosis in pre-pandemic (2019), pandemic (2020-2021) and post-pandemic (2022) periods.
Results: Our sample comprised clear cell RCC (43,9%), chromophobe RCC (22,3%), papillary RCC (19,7%), clear cell papillary RCC (7,2%) and other rarer subtypes of RCC (5,6%).
The patients were mainly males (70,8%), with a mean age of 65 years. In 34,2% of cases ISUP grade was not applicable, but when it was, the majority were ISUP 2 (51,2%), followed by ISUP 3 (34,3%). Regarding staging, 50,5% were pT1a at presentation.
When comparing RCC's pTNM stage at diagnosis, there were no differences with statistical significance between pre-pandemic, pandemic and post-pandemic times (ANOVA test, p=0,585). ISUP grade, when applicable, had statistical significant differences (ANOVA test, p=0,013; Linear regression test, coefficient beta<0,024).
Conclusion: Although the common perception that healthcare institutions, when facing COVID-19 challenges, have not given a proper response to daily practice issues, that does not seem to have interfered with the well-timed diagnosis of RCC at our institution, as the stage at diagnosis of these entities on pandemic and post-pandemic periods was similar to the stage on pre-pandemic era. However, there were statistical differences regarding ISUP grade among these periods.

E-PS-24-008

Battling multiple fronts: metachronous triple urogenital cancers and prostate BCGitis in one patient

R.A. Barna*, L. Daminescu, V. Dema, M. Iacob, D. Herman, B. Nataras, A. Dema
*Anapatmol Research Center, Victor Babes University of Medicine and Pharmacy, Romania

Background & objectives: Renal cell carcinoma (RCC) patients have a higher risk of a second urogenital malignancy. While urinary bladder and prostate cancer often coexist, occasionally with Bacillus Calmette-Guérin (BCG) therapy-associated granulomatous inflammation, diagnosing three urogenital tumours in a single patient is exceptional.
Methods: A 67-year-old man was incidentally diagnosed on CT with a renal tumour. A year later, the patient had macroscopic haematuria caused by a bladder tumour, treated by transurethral resection (TURBT) and BCG instillations. A year after that, a PSA level of 5.06 ng/ml, enlarged prostate, and an "indeterminate" lesion detected by multiparametric MRI required needle biopsy, followed by radical prostatectomy.
Results: Radical nephrectomy grossly unveiled a 42x35x30 mm orange, solid tumour, with cystic and haemorrhagic areas. Microscopy demonstrated a clear cell RCC, WHO/ISUP grade 2, infiltrating the renal sinus fat.
Histologically, TURBT showed a non-muscle invasive bladder cancer – papillary urothelial carcinoma with focal areas of high-grade component and squamous differentiation.
Gross examination of the radical prostatectomy was non-specific. Microscopic results of the needle-biopsy and resection specimen correlated. The "indeterminate" lesion was a chronic granulomatous inflammation in the right lobe, with eosinophilic, amorphous necrosis, Langhans giant cells, epithelioid macrophages, lymphocytes, and fibrosis. The left lobe presented an acinar adenocarcinoma, Gleason score 3+3=6 (Grade group 1), with tertiary pattern 4 (<5%).
Conclusion: The association of these triple malignant cancers can be caused by genetic (e.g. Lynch syndrome-associated upper urinary tract urothelial cancers) and epigenetic modifications, carcinogenic exposure, therapy for one of the tumours, or may be unrelated. A thorough investigation will be conducted.
Granulomatous prostatitis following BCG instillation can mimic prostate cancer on imaging tests. Prolonged elevated PSA level in these patients should prompt additional evaluation. Histopathological examination remains the definitive method for establishing a diagnosis.

E-PS-24-009

HER2 expression in bladder invasive urothelial carcinoma, a study of 60 cases

A. Bdioui*, K. Ben Lazreg, N. Kalaii, Z. Lajmi, W. Majdoub, S. Hmissa
*Sahloul hôpital of sousse, Tunisia

Background & objectives: Bladder urothelial carcinoma (UCB) is common, prognosis of invasive forms is poor; identification of therapeutic targets could improve the prognosis.

Our purpose is to study the frequency of HER2 overexpression in UCB and its correlation with histo- prognosis parameters.
Methods: We performed a cross-sectional and analytic study, enrolling all patients diagnosed with UCB on surgical specimen during two years. Immunohistochemistry (IHC) expression was tested by an HER2 antibody and scored according to Hoffman score. In situ hybridization technique (CISH) was performed for cases with IHC2+ score. HER2 overexpression was defined by a score IHC3+ or a score IHC2+ and CISH+.
Results: We enrolled in this study 60 patients, with a median age of 67.5 years. A masculine predominance was observed. Patients were divided to four groups according to their HER2 status: 80% were scored IHC 0, 8% were scored IHC1+, 12% were scored IHC3+ and only one case was scored IHC2+.The result of CISH for the case of IHC2+ was negative. Therefore, the HER2 overexpression was observed in 12% of all cases. In our study we didn't founf any association between HER2 overexpression and bad prognosis parameters: the grade, the tumour staging, vascular and neural invasion, tumour Budding.
Conclusion: There is no guidelines for HER2 testing in UCB. In consequence the prevalence of HER2 expression in UC is not well defined. It depends on preanalytical conditions, IHC techniques and the score employed. In concordance with our results, HER2+ prevalence ranged from 6.7% to 37.5% with a weighted average of 13%. Unlike our results, studies found an association between Her2 overexpression with the grade and stage of local infiltration (pT). Studies on a larger scale are needed to verify our results.

E-PS-24-010
A case of xanthogranulomatous pyelonephritis mimicking renal neoplasia with clinical and histopathological features
H. Berber*, D. Enneli
*Ankara University Medical School, Pathology Department, Turkey

Background & objectives: Xanthogranulomatous pyelonephritis (XGP) is a rare, severe form of chronic pyelonephritis, usually associated with infection and nephrolithiasis. Herein, we present a case of XGP, strongly mimicked renal malignancy with its clinical, radiological, histopathological features, to draw attention to this diagnostic trap.
Methods: A 56-year-old female patient was taken into evaluation due to fever and elevated serum acute phase reactants. Bacterial growth (E.coli, E.faecium) was detected in the urine culture. Computerized tomography revealed a mass lesion(8x7cm), in the upper-pole of the left kidney, extending to the perirenal adipose tissue. The patient underwent left radical nephrectomy with a preliminary radiological diagnosis of renal cell carcinoma.
Results: Gross examination of the nephrectomy specimen revealed an irregularly circumscribed nodular mass, infiltrating perirenal adipose tissue. It was 5.5 cm in long diameter and had yellow-white cut surface with centrally necrotic, haemorrhagic areas. Microscopically, the renal parenchyma was infiltrated by intense granulomatous inflammation, composed of neutrophils, plasma cells, lymphocytes, xanthomatous histiocytes and multinucleated giant cells. The lesion extended into perirenal adipose tissue. These xanthomatous cells had foamy cytoplasm, mimicking clear cells of renal cell carcinoma.
Conclusion: XGP is a rare and agressive form of pyelonephritis, that can be usually confused with renal neoplasias, clinically, radiologically and even macroscopically. As correct preoperative diagnosis is frequently not possible, patients with XGP usually undergo radical nephrectomy and the accurate diagnosis could frequently be made after the histopathological examination of nephrectomy specimen. Pathologists should be aware of this entity which can be a good mimicker of renal neoplasia and consider it in the differential diagnosis of renal masses.

E-PS-24-011
Cancer prevalence, grade and number of transurethral resections of prostate specimens 2006-2020
M. Bonert*, N. Nikzad, P. Major, B. Shayegan, I. El-Shinnawy
*McMaster University / St. Joseph's Healthcare Hamilton, Canada

Background & objectives: Changes in serum PSA screening resulted in a decrease of prostate biopsies, negative biopsies and grade group 1 cancers. However, trends in cancer and grade in transurethral resections of prostate specimens (TURPs) have not been well studied.
Methods: All in house TURPs at two centres within a regional laboratory accessioned 2006-2020 were retrieved. The diagnosis and cancer grade (if applicable) were extracted by a validated hierarchical free text string matching algorithm (HFTSMA).
Results: The cohort had 3,790 TURPs. 522 had prostate cancer and of these 27 could not be graded. To assess the HFTSMA, randomly selected specimens were reviewed (200 correct/200) and results were compared to cancer synoptic data (230 correct/232); these confirmed a classification error rate of <1%. Volume varied from 134 to 338 specimens/year. A local volume minimum was seen in 2012 and a relative volume decrease in 2020. The number of specimens with low-grade (grade group (GG) 1/2) cancer (270 cases, range: 9 to 35 cases/year) tracked the number of specimens. High-grade (GG3/4/5) cancers (225 cases, range: 8 to 21 cases/year) increased transiently after the 2012 case volume local minimum.
Conclusion: The lower TURP procedure volumes in 2011-2013 likely led to the decreased number of low-grade cancers in 2012 and the relative surplus of high-grade cancers in 2013-2014. The modest 2020 procedure volume decrease is probably explained by the COVID-19 pandemic. The association between the number of TURPs and prostate cancer on TURP may allow inferences about prostate cancer prevalence and behaviour in large cohorts.

E-PS-24-012
Large nested urothelial carcinoma: clinicopathological study on 12 transurethral resection materials
Y. Cakir*, B. Bambul Sığırcı, E. Hacıhasanoğlu, Y.B. Kök, Y. Sağlıcan, K. Behzatoğlu
*Dokuz Eylül University, The Institute of Health Sciences, Department of Molecular Pathology, Turkey

Background & objectives: Large nested urothelial carcinoma (LNUC) is a rare variant of urothelial carcinoma revealing inverted growth pattern, bland cytological features and generally presenting with muscular invasion. In study presents 12 LNUC cases that cause diagnostic difficulties in transurethral resection (TUR) materials.
Methods: Haematoxylin&eosin-stained slides of bladder TUR materials submitted to our department in 2017-2023 were re-examined. 12 cases were diagnosed with LNUC.
Results: 10 cases were male (83,3%). The mean age was 57,7. The average tumour size was 4,4 cm. Non-invasive urothelial carcinoma component was present in all cases. Five and seven cases were pT1, pT2 respectively. Histopathologically, tumours showed invasion of lamina propria or muscularis propria as large nests with inverted proliferation. The tumour cells had bland cytological features and the non-invasive urothelial carcinoma (UC) component almost always showed low grade morphology. Tumour-stroma interface was irregular, and fibrous stromal reaction and/or stromal lymphoid infiltration was present. Most tumours revealed tumoral budding described as small nests in the stromal interface of medium-large nests.
Conclusion: Diagnostic problems can be experienced at LNUC because of their bland features and unclear invasion criteria compared to conventional UC. Tumours with an inverted growth pattern, irregularity at the stroma-tumour interface, and budding in TUR materials should be evaluated in detail for invasion.

E-PS-24-013

Bilateral gonadoblastoma in a nine-year-old patient with ambiguous genitalia: a case presentation

M.Y. Çelik*, S.B. Yolburun, G.Ö. Elpek, C.I. Bassorgun, B. Ünal
*Akdeniz University Department of Pathology, Turkey

Background & objectives: Most patients with gonadoblastoma present as neonates with ambiguous genitalia in the setting of a disorder of sexual development. Because of the rarity of bilateral gonadoblastoma, we present a nine-year-old patient with bilateral gonadolastoma appear on streak gonads.
Methods: A 11-days-old patient presented to paediatric endocrinology clinic with ambiguous genitalia. Laboratory data showed that total testosterone and 11- deoxycortisol was high. Chromosomal analysis reported as 46XY. hCG stimulation test resulted with increase in the ratio of testosterone to DHT after hCG administration. After 9 years, USG scan showed that right testis was 9*7*3 mm and left testis was 10*8*2.5 mm.
Results: Bilateral gonadectomy was carried out by paediatric surgeons. The encapsulated, soft, whitish grey, shiny materials was examined carefully. After total sampling, we observed round nests and cords composed of germ cells, small sex cord cells, and globoid deposits of hyaline basement membrane material in both gonadal materials. The germ cells that had large nuclei, prominent nucleoli and pale cytoplasm scattered between the sex cord cells that showed angulated nuclei with basement membrane material was seen microscopically. A few mitosis were observed in some germ cells without atypia and necrosis. Germ cells were stained with PLAP, CD 117 while the stromal cells expressed inhibin, WT1.
Conclusion: Given the potential for gonadoblastoma to transform into an invasive germ cell tumour, gonadectomy is recommended. On microscopic view, nested to corded arrangement of germ cells and sex cord cells with deposits of basement membrane material are essential diagnostic criterias whether immunohistochemical markers for germ cells and sex cord stromal cells applied or not. Also gonadoblastoma should be differentiated from sertoli cell nodules colonized by GCNIS, sex cord stromal tumour with entrapped germ cells for exact diagnosis in prepubertal cases.

E-PS-24-014

Paraganglioma of urinary bladder: report of 4 cases

E.E. Cetiner*, F. Çakalağaoğlu, F.H. Dilek, A. Akder Sari
*Izmir Katip Celebi University, Ataturk Training and Research Hospital, Department of Pathology, Turkey

Background & objectives: Paragangliomas are extra-adrenal pheochromocytomas. Paraganglioma of urinary bladder is very rare. They are rarely malignant. Typical symptoms are catecholamine secretion associated such as micturition periods. However, it may be asymptomatic and can be diagnosed incidentally.
Methods: This is a retrospective study that includes four bladder paraganglioma cases diagnosed between the years 2008-2022 in our hospital.
Results: All cases were female. Median age was 46,5 (between 34-57) years old. Three patient was diagnosed incidentally, and one presented with incontinence and abdominal pain. Median size of tumours was 3,3 (between 2,8-4) cm. All patients were diagnosed by transurethral resection one of which afterward underwent partial cystectomy. All tumours were positive for synaptophysin, chromogranin and GATA3. Pankeratin was negative. Succinate Dehydrogenase B(SDHB) was available in only one case which was intact. Proliferative index was low. Zellballen growth pattern which is typical for paragangliomas was either not present or not prominent. Follow up of two patients for six and twelve months were free of recurrence.
Conclusion: Paraganglioma of urinary bladder is very rare. Features which might serve as clues for paraganglioma diagnosis such as typical clinical symptoms and characteristic Zellballen pattern are not always present, and the tumour cells express GATA3 which may mimic urothelial carcinoma. Therefore, awareness of this entity is upmost important to avoid misdiagnoses.

E-PS-24-015

Traditional serrated adenoma of the bladder: a rare case originating from urachal diverticulum

A. Chikha*, F. Skenderi
*Clinical Center of University of Sarajevo, Department of Pathology, Bosnia and Herzegovina

Background & objectives: A 61-year- old female patient was hospitalized due to haematuria. CT urography revealed polypoid tumour in the area of highly suspicious urachal diverticulum. During cystourethroscopy, tumour were detected at the bladder dome and was partially removed by transurethral resection.
Methods: Pathological examination revealed a complex villiform growth pattern with slit-like serrations and ectopic crypts. The tumour was lined by intestinal type epithelium, with cells exhibiting eosinophilic cytoplasm and pseudostratified elongated nuclei. Immunohistochemical analysis demonstrated positivity for CK7, CDX2, CD20 (partial), Ki-67 and beta-catenin in the ectopic crypts and at basis of the crypts, where displayed cytoplasmic and membranous positivity.
Results: The epithelium showed mostly low-grade dysplasia, with focal high-grade dysplasia. These findings were consistent with a traditional serrated adenoma, an infrequent type of colonic serrated polyp that typically observed in the distal colon and accounts for less than 1% of colonic polyps. The adjacent mucosa of bladder exhibited signs of intestinal metaplasia. After transurethral resection and diagnosis of traditional serrated adenoma, residual tumour was resected by partial cystectomy.
Conclusion: To date, only few cases of extra-gastrointestinal traditional serrated adenoma has been previously reported. Our case verifies the rare occurrence of this type of adenoma in the bladder that may originate from intestinal metaplasia and in our case more likely from urachal diverticulum.

E-PS-24-016

Grading of T1a clear cell renal cell carcinoma based on nodule size, tumour necrosis, and ISUP grade

C. Choi*, M. Noh, S.S. Kim, E.C. Hwang
*Chonnam National University Medical School, Republic of Korea

Background & objectives: Although majority of T1a clear cell renal cell carcinomas (T1a-CRCC) reveal very good prognosis, a few cases show catastrophic prognosis. The purpose of this study is to stratify T1a-CRCC into prognostically accurate subgroups.
Methods: T1a-CCRCC surgically treated and diagnosed in the pathology departments of CNUH and CNUHH between 2004 and 2019 were selected. They were 614 nodules from 611 patients. Multivariable logistic regression analysis was performed to find the factors associated with cancer specific survival (CSS). They were graded based on nodule size, tumour necrosis, and ISUP grade.
Results: Grading of T1a-CRCC based on nodule size, tumour necrosis, and ISUP grade was a better predictor of CSS (c-index 0.798) than that based on ISUP grade only (c-index 0.685). Group A (nodule $\leq$1.5 cm, without necrosis, and any ISUP grade) was 89 cases, group B (nodule 1.5-4.0 cm, without necrosis, ISUP grade 1 or 2) 416, and group C (nodule 1.5-4.0 cm, with necrosis and ISUP grade 2-4, or without necrosis and ISUP grade 3-4) 109. With a median follow-up of 69.8 months, 10-year CSS rate of group A was 100%. That of group B and C was 99.0% and 95.5%, respectively.
Conclusion: We suggest a grading of T1a-CRCC based on nodule size, tumour necrosis, and ISUP grade.

E-PS-24-017

Peroxidasine overexpression in intratumoral vessels and in proximal tubular cells adjacent to clear cell renal cell carcinomas (CCRCC): a case series

A.R. Coelho*, R. Silva, I. Alencastre, J. Reis Almeida, I. Brandão, J.P. Oliveira
*Centro Hospitalar Universitário de São João, Porto, Portugal

Background & objectives: Peroxidasine (PXDN) is an extracellular matrix protein with peroxidase activity important in the development of fibrosis. Its role in cancer is still not well established. We aimed to characterise PXDN expression in a series of oncocytoma and CCRCC.
Methods: Ten cases of oncocytoma and twelve cases of CCRCC were retrieved from our hospital files between 2021 and 2022. Their clinicopathological features and follow-up were reviewed. PXDN expression was analysed by immunohistochemistry in tumour and in non-neoplastic adjacent parenchyma (< 1cm), using a defined score established for intensity and extent of expression. Statistical analysis was performed using SPSS Statistics.
Results: Both tumour types showed an expression of PXDN in >50% of tumoral cells with high intensity. However, the expression in intratumoral vessels showed a higher extent (p=0.030) and intensity (p<0.001) in CCRCC versus oncocytoma. The expression of PXDN in proximal tubular cells was more intense in non-neoplastic parenchyma adjacent to CCRCC (high intensity in 83,3% of cases) versus oncocytoma (p=0.030). PXDN expression in distal tubules was similar in both groups, with a high intensity of expression. No relation between PXDN expression and grade or stage was found. There were no evidence of metastasis nor tumour related deaths.
Conclusion: The literature suggests that in cancer, PXDN might be important for proliferation and invasion. Our results showed a significantly different pattern of expression in PXDN between CCRCC and oncocytoma, namely in intratumoral vessels and in proximal tubular cells of non-neoplastic adjacent parenchyma. Therefore, we hypothesise a potential role of PXDN in the angiogenesis of CCRCC and a potential paracrine effect in non-neoplastic parenchyma. Further studies need to be performed to confirm these findings and explore their significance.

E-PS-24-018

Utility of GCDFP15 as a marker of seminal epithelium in prostate biopsies

M. Conde Ferreirós*, M.d.l.Á. Betancor Santos, M.J. Acuña Martínez, L.M. Liste Tizón, S. Abdulkader Sande, P. Mendez Pena, M.P. San Miguel Fraile, M.T. Dawid de Vera, J. González-Carreró Fojón, J.A. Ortiz-Rey
*Hospital Álvaro Cunqueiro, Spain

Background & objectives: The incidental presence of seminal vesicle epithelium in prostate needle biopsies may occasionally be misinterpreted as malignant because of architectural and cytologic features. We have analysed the utility of GCDFP15 as an immunohistochemical marker to confirm seminal epithelium.
Methods: 22 prostate needle biopsies from 19 patients which incidentally contained seminal vesicle epithelium, 20 seminal vesicle sections coming from prostatectomy surgical specimens and three TMAs constructed from 75 cases of prostatic adenocarcinoma Gleason≥8 were immunostained. Monoclonal antibodies anti GCDFP (Gross Cystic Disease Fluid Protein)-15 and PAX8 (as a positive control of seminal epithelium) and a multimer-based detection method were used.
Results: GCDFP15 cytoplasmic immunoreactivity was intense in the 20 seminal vesicle surgical specimens, as well as in the seminal epithelium of the 22 prostate needle biopsies that contained it with focal or diffuse staining. GCDFP15 was expressed in 3 of the 75 samples of prostatic adenocarcinoma included in the TMAs: one intraductal carcinoma and two foci of normal prostatic epithelium. Sensitivity of GCDFP15 as a marker of seminal epithelium was 100% and specificity was 96%. PAX8 was positive, intense and diffusely, in all cases of seminal epithelium (20 samples of surgical specimens and 22 biopsies) being negative in benign or malignant prostate epithelium, with sensitivity and specificity=100%.
Conclusion: The strong immunohistochemical expression of GCDFP15 aids to the identification of seminal vesicle epithelium in prostate biopsies. It is a sensitive marker but not completely specific (96%): GCDFP15 can be rarely positive in normal prostate epithelium and intraductal carcinoma of the prostate. The use of additional markers, like PAX8, could be advisable to confirm accurately seminal epithelium. A possible application of our findings is that seminal vesicle tissue can serve as a positive control for the immunohistochemical staining of GCDFP15.

E-PS-24-019

The reticulin pattern in renal neoplasias, the old new tool for differential diagnosis – a histochemical evaluation

M. de Brito Pereira*, A.S. Carralas Antunes, M.E. Vitorino, K. Amaral Freitas, P. Fernandes, J. Palla Garcia, R. Ilgenfritz
*CUF Descobertas Hospital, Portugal

Background & objectives: Among the most frequent renal neoplastic entities, heterogeneity is expected and morphological overlap is common. (1) Even with immunohistochemistry and other complementary evaluation, the diagnosis can be difficult. This study aims to evaluate reticulin stain as a diagnostic tool.
Methods: We evaluated the reticulin pattern in 47 cases of the most common renal neoplasms [clear cell renal cell carcinoma (RCC) – 11 cases, papillary RCC – 13 cases, oncocytoma - 11 and chromophobe RCC – 12 cases].
Each case was randomly selected in two different institutions, one fragment was chosen and the reticulin staining was performed by automated methods.
Results: Among the clear cell renal cell carcinomas, a single cell pattern of staining in the periphery/fibrous areas was the most common finding (10/11), among groups of cells, it varied from complete to incomplete bridging depending on morphologic patterns.
In papillary carcinomas, 1-layer staining pattern in each side of the papillary pole, without any staining in micropapillary structures was observed (13/13), with occasional peri-macrophage staining. In 3 cases with reverse polarity, additional weak luminal staining was present.
Regarding oncocytomas, a complete bridging pattern (1/2-layered) with irregular groups was observed, without perivascular reinforcement (11/11).
Chromophobes presented perivascular reinforcement in rectilinear vessels, with incomplete to absent bridging in solid areas (12/12).
Conclusion: In this study, significant differences in the reticulin pattern of each entity were observed. Although different morphologic patterns added some variation between cases, certain findings were common among almost all cases of the same entity.
Further studies, with a higher sample and more entities, should be considered in order to support the use of reticulin as a diagnostic tool similar to its use in hepatic pathology (2) and sex cord stromal tumours (3).
Funding: Partial funding by Roche Portugal

E-PS-24-020

A rare disease series of 3 cases in testis: Mesothelioma

M. Dicleli*, G. Türkcü, S. Özekinci
*Cizre State Hospital, Turkey

Background & objectives: Mesothelioma of tunica vaginalis testis (TVT) is a very rare and it has a poor prognosis. Mesotheliomas of

the TVT are often clinically mistaken with benign entities, which can result in delayed diagnosis. We will present a 3-case mesothelioma series.
Methods: Histopathological findings and immunohistochemistry were used for diagnosis. For immunohistochemical markers 4µm thick sections were taken from the blocks. Sectioned slides were kept in an oven at 65°C for 30 minutes, deparaffinized and tissues were adhered to the slides. The primary antibodies used in the study were in ready-to-use form and were automatically studied in the Ventana BenchMark Ultra device.
Results: In our study, we examined three cases aged 60, 35 and 54 years, 2 of whom were known to have asbestos exposure, with complaints of mass in their testicles. Their hormone levels were normal in the laboratory. Histopathologically, it was observed that the tumour consisted of epithelioid-like cells with large, hyperchromatic nuclei, eosinophilic cytoplasm, some of which formed tubular, glandular or adenomatoid structures, some of which made nests. Immunohistochemically, the tumours were PAN-CK, calretinin, CK5/6, WT1 positive, SALL4, PLAP, CD117, MELAN A and inhibin negative. The cases were diagnosed as malignant mesothelioma based on clinical information, asbestos exposure history, histopathological and immunohistochemical findings.
Conclusion: Paratesticular mesothelioma is a rare tumour with nonspecific symptoms, clinical and radiological findings. There are a number of histological presentations to be aware of and pitfalls to be avoided, and caution should be exercised in the differential diagnosis. It is common in middled-aged older men with asbestos exposure. Histologically, it is often observed in epithelioid morphology. The cases will be presented with literature information because it is rarely seen in the paratesticular area.

E-PS-24-021
Periampullary metastasis of renal cell carcinoma: a case report and review of the literature
A. Dutta*, S.S. Nayak, V. Pradeep
*Homi Bhabha Cancer Hospital and Research Centre, Visakhapatnam, India

Background & objectives: Renal cell carcinoma (RCC) has potential to metastasize to almost any site and this may occur many years following nephrectomy. The most common metastatic sites are lung, bone and liver. Periampullary metastasis of RCC is an extremely uncommon clinical scenario.
Methods: A 49-year-old woman presented with fatigue, shortness of breath on exertion and melena of two months' duration. She had undergone right nephrectomy for clear cell RCC 2 years ago. CECT scan showed an enhancing 4.6 x 4.2 cm periampullary lesion and two other lesions in body of pancreas. CT guided biopsy was done from the periampullary lesion.
Results: Histological examination showed tissue cores infiltrated by a tumour arranged in sheets with interspersed thin walled blood vessels. The tumour cells were polygonal, had abundant amount of clear cytoplasm with well-defined cell border and round to oval, hyperchromatic nuclei. On immunohistochemistry, the tumour was diffusely positive for cytokeratin (AE1/AE3), PAX8 and focally positive for CD10. Final diagnosis was metastatic clear cell RCC. Thereafter, the patient was treated with palliative intent and started on sunitinib. The patient developed brain metastasis a month later and was offered whole brain radiotherapy. The patient eventually died after a month.
Conclusion: Metastatic involvement of the periampullary region and other unusual sites should be suspected in any patient with a history of RCC. Optimal management is challenging because of high risk of relapse following treatment, leaving such cases with a very poor prognosis.

E-PS-24-022
Sarcomatoid urothelial carcinoma on ureteral urothelial carcinoma in situ: a case report
C. Esquina*, È. Iglesias Martínez, N. Santiago-Quispe, M.M. Buda, A. Sifre-Ruiz, A.M. Cordovilla-Moreno, M.J. De-Diego-Rivas
*Clinical Department Unit of Pathological Anatomy, OSI Araba, Araba University Hospital; Bioaraba Health Research Institute, Vitoria-Gasteiz, Alava, Spain

Background & objectives: Sarcomatoid urothelial carcinoma represents 0.3% of urinary epithelial tumours. This is one of the most aggressive neoplasms of the urinary tract, developing in elderly patients and smokers. They are variants with possible heterologous differentiation with a more aggressive behaviour.
Methods: We report a 61-year-old man with a history of pT1 uretheral carcinoma with tumour–like mass adhered to the psoas. Intraoperative biopsy was performed with a positive result for carcinoma. Right nephroureterectomy was carried out with subsequent pathological study and literature review.
Results: Gross examination of surgical specimen revealed marked thickening of the ureteral wall and the renal pelvis. The histopathological study showed an urothelial carcinoma in situ and an infiltrating tumour with extension to the periureteral adipose tissue. This consisted of an atypical proliferation of spindle and epithelioid cells with extensive necrosis that was immunohistochemically positive for CKAE1/AE3, p63, vimentin and focally for GATA-3. Was negative for S-100, desmin, CD45 and actine. The proliferative index Ki-67 was 90%. A definitive diagnosis of sarcomatoid urothelial carcinoma was made.
Conclusion: Urothelial carcinoma exhibits multiple histological subtypes, including the sarcomatoid variant, characterized by areas indistinguishable from sarcoma. The differential diagnosis includes other entities, such as rhabdomyosarcoma, pleomorphic sarcoma and leiomyosarcoma. The presence of conventional urothelial carcinoma, as occurred in our case, and the compatible immunohistochemical study supports this diagnosis. In any case, even if there is a loss of expression of urothelial markers, priority should be given to histopathological findings after an exhaustive study.

E-PS-24-023
Primary testicular lymphoma: a clinical, morphological and immunohistochemical characterisation of a long multicentre series
B. Garzón*, J.d.B. Machuca Aguado, T. Cano, E. Montijano, G.A. Pastrana, Á. Gutiérrez
*Juan Ramón Jiménez University Hospital, Huelva, Spain

Background & objectives: Primary testicular lymphoma represents 1-2% of extranodal non-Hodgkin lymphomas, with diffuse large B-cell lymphoma (LBDC) being the most common histological subtype. Our objective is to make a clinical-pathological correlation of the diagnosed cases, comparing them with the literature.
Methods: The series includes 25 cases, from three hospitals, diagnosed between 2005 and 2022 in orchiectomy specimens. Clinical data (age, laterality, stage, and follow-up) were collected. An immunohistochemical study was carried out with CD20, CD79a, CD3, CD5, CD43, CD10, BCL2, BCL6, MUM-1, cyclin D1, granzyme B, C-MYC and Ki67.
Results: All the patients debuted with a testicular whitish mass sized 7 to 10 cm that occupied the testicular parenchyma.
N=25, age range from 35 to 89 years. 23 cases were diagnosed as DLBCL (8 germinal-centre immunophenotype, and 15 with activated immunophenotype, following Hans algorithm).
At diagnosis, 9 were in stage I-II, 14 in stage III-IV and 2 unknown cases. 5 patients suffered CNS or testis relapse after treatment (all LGDLB). Survival at 5 years was 35%, being 75% in neoplasms limited to the testis at diagnosis, versus 17% in cases of disseminated disease at diagnosis. 36% (9/25) patients died from lymphoma. Of the rest, 24% (6/25) are in complete remission.

Conclusion: We corroborate that, in our series of cases, the most frequent histological subtype of primary testicular lymphoma is DLBCL, and within this, the activated immunophenotype, according to the literature reviewed. Early diagnosis and prophylaxis in the CNS is important for its prognosis.

E-PS-24-025

Renal collision tumour composed of oncocytoma and clear cell renal cell carcinoma: case report and review of literature

J.M. Gutiérrez Herrera*, H. Olauson, D. Chatzianastasiou, F. Jansson, D. Krantz
*Karolinska University Hospital, Sweden

Background & objectives: Collision tumours are rare and occur when two distinct neoplasms coexist together. Only limited data on their prognosis, immunohistochemical- and mutational profile is available. We characterized these features in a case of a renal collision tumour and reviewed the literature.
Methods: Upon morphologic evaluation, both tumour types were further characterized immunohistochemically and with a broad next-generation sequencing (NGS) cancer panel. For literature review, PubMed and Web of Science databases for renal collision tumours composed of oncocytoma and RCC were searched. Data collection was focused on morphologic characteristics, tumour stage, immunohistochemical profile and genetical aberrations.
Results: We report an 83-year-old man with a left renal mass. Histological evaluation revealed a pT3a kidney tumour consisting of a sarcomatoid clear cell renal cell carcinoma (sCCRCC) and oncocytoma. The tumour components bore distinct, characteristic immunohistochemical profiles for their respective morphology. NGS analysis disclosed a PTEN mutation in the sCCRCC component, which was not present in the oncocytoma area. During follow-up, bilateral lung metastases were detected, which prompted radiotherapy and immunotherapy. To date, only two collision tumours composed of CCRCC and oncocytoma have been reported. To our knowledge, this is the first report of a PTEN mutation carrying, and immunohistochemically bona fide, collision tumour of CCRCC and oncocytoma.
Conclusion: This report reveals an extremely rare renal collision tumour, with the novel finding of the CCRCC component to carry a PTEN mutation. Both components displayed their essential immunohistochemical characteristics, which somewhat differs from the previously reported case. Yet, this entity is diagnostically challenging and is important for pathologists to be aware of. Further studies are needed to determine the best treatment path for these tumours.

E-PS-24-026

Bladder cancer in patients with spinal cord injury or neural tube defects: a retrospective study

A. Hidalgo Romero*, Z. Calixto Alvarez, A. Diazgranados Daza, J. Chabla Jaramillo, I.M. de Torres Ramirez, S. Ramón y Cajal Agüeras, F. Lozano Palacio, M.E. Semidey Raven
*Vall d´Hebron Barcelona Hospital, Spain

Background & objectives: Spinal cord injury (SCI) or neural tube defects (NTD) patients have increased risk of developing bladder cancer, with high grade/aggressive tumours and high mortality rate. Our aim is to describe morphological and outcome characteristics associated with this patient population.
Methods: A cohort of 10 cases of bladder carcinomas were selected with SCI/NTD from pathology files between 2007-2023. In each case, histomorphological features were collected, such as histological type, grade, carcinoma in situ presence, lymphovascular invasion and TNM stage. Clinical features such as age, gender, smoking habit, latent period, disease-free and overall survivals were included. Comparison between variables was done.
Results: A series of 10 SCI/NTD patients were selected with bladder carcinoma. The median age was 39 years (SD9,43). Nine patients (90%) were women. Four (40%) had smoke habit associated. Seven (70%) had congenital medullary injury and three (30%) had acquired injury: post-traumatic (2) and infectious (1). Latent period was >30y in six (60%) patients, 10-30y in two (20%) and <10 years in one (10%) patient. Histological subtypes were reported as squamous (80%) and adenocarcinoma (20%), high grade (100%) and infiltrative: >pT2 (90%), pT1 (10%). Three (30%) had lymph node metastasis and lymphovascular invasion. Seven (70%) died in <1 year, two (20%) are alive after 10 years and 2 months, respectively.
Conclusion: Bladder cancer in patients with SCI/NTD are high risk tumours that appear at an earlier age with advanced stage and poor outcome. Specific risk factors include indwelling catheters, urinary tract infections, bladder stones, and smoking history. Surveillance programs and early detection may require more invasive follow-up due to the atypical aggressiveness and lack of specificity of symptoms. Further research is needed to identify more reliable understanding of the disease in order to improve the outcome of these patients.

E-PS-24-027

Mixed epithelial and stromal tumour: an exceptional tumour of seminal vesicle: a case report

S. Hidouri*, M. Hamdani, M. Walha, C. Abdelhedi, K. Bouraoui, K. Bel Hadj Ali, A. Khabir
*Department of Pathology, Habib Bourguiba University Hospital, Medenine, Tunisia

Background & objectives: Seminal vesicle (SV) is an uncommon primary site for neoplasic-disease. The mixed epithelial and stromal tumour (MEST) of SV is extremely rare. Only a few cases have been reported. Here we report a case of a seminal vesicle MEST.
Methods: N/A
Results: A 38-year-old male, consulted for lower urinary-tract symptoms. On physical examination, he had a palpable prostate at digital rectal exam. Abdominal and pelvic MRI reported a huge heterogeneous mass of the SV. The patient carried on a surgical resection. Macroscopically, the mass measured 15cm in largest dimension, containing multi-locular cysts, including gelatinous substance. The histological examination revealed two distinctive components. The glandular one is lined by cubo-columnar cells, with focal nuclear pseudo-stratification without atypia. The stromal component is myxoid and paucicellular. The diagnosis of MEST was then made.
The patient's postoperative recovery was uneventful, he was alive and without evidence of diseases recurrence 4 months after the surgery.
Conclusion: MEST of seminal vesicle is a rare entity. Patient's long-term-follow-up with radiological exploration is recommended after tumour removal to control the possibility of recurrence. These neoplasms have been described under various names such as cystadenoma, but the distinction between them remains a subject of debate, that is why more histological details are needed to better characterize and study them in the future.

E-PS-24-028

Assessment of the prognostic role of PDL-1 in prostate cancer versus benign prostate hyperplasia

C. Ionescu*, M. Aschie, G.C. Cozaru, A. Mitroi, G.I. Baltatescu, A.A. Nicolau, N. Dobrin, S. Topliceanu, M. Enciu
*CEDMOG "Ovidius" University of Constanta / "Sf. Apostol Andrei" Emergency County Hospital of Constanta, Romania

Background & objectives: PD-L1 is a type-I transmembrane glycoprotein which correlates with a poor prognosis. Therefore, we aimed to determine the expression of PDL-1 in biopsies of human prostate

cancer (PCa) patients of different Gleason scores compared to benign prostate hyperplasia (BPH).
Methods: PDL-1 expression was evaluated immunohistochemically using SP142C-terminal Recombinant Anti-PD-L1 monoclonal antibodies (Abcam). Marker expression was determined to be positive for moderate or severe immunolabeling in at least 1% or 10% of neoplastic cells or associated immune cells. We then established the relationship between marker expression and available clinical and pathological parameters: patient age, Gleason score, prognostic group grade, tumour stage.
Results: PDL-1 expression was higher in the PCa group compared to cases diagnosed with BPH. Also, the PDL-1 expression was correlated with the Gleason score, but not with the other parametrically evaluated ones.
Conclusion: The value of PDL-1 is strongly expressed in prostate cancers, unlike non-tumour prostate lesions and correlates with the Gleason Score, which highlights a potential independent prognostic role in prostate cancer, with a role in the therapeutic management of patients.

E-PS-24-029
Neoplastic transformation of prostatic tissue is accompanied by alteration in protein sialylation
A. Janegova*, P. Babal, P. Janega
*Institute of Pathological Anatomy, Comenius University in Bratislava, Slovakia

Background & objectives: Prostate cancer is a common malignancy in men, there is no reliable screening test for early detection. Altered sialylation is often seen in cancerous tissues, including prostate tissue. This study investigates changes in sialic acid expression in prostatic adenocarcinoma.
Methods: The study analysed tissue samples from 120 patients with benign prostatic hyperplasia and prostatic adenocarcinoma of various Gleason scores (ISUP Grade Group 1-5) using lectin fluorescent histochemistry to evaluate sialic acid expression. Quantitative changes were analysed through morphometric analysis, using sialic acid-specific lectins, specific for alpha-2,3 linkage Maackia amurensis leukoagglutinin and alpha-2.6 linkage Sambucus nigra agglutinin.
Results: In prostatic tissue, the majority of sialic acid positivity is attributed to alpha-2,6 linkage. However, neoplastic transformation results in a significant decrease of alpha-2,6 sialylation in affected glands, which is more pronounced in adenocarcinomas with higher Gleason scores. Conversely, no significant changes were observed in alpha-2,3 sialylated glycoconjugates. There were no significant changes observed in the expression of sialic acid in stromal cells.
Conclusion: Alterations in sialic acid expression are linked to the development of malignancies, which can affect the behaviour of neoplastic cells such as their survival, invasiveness, and metastatic potential. The evaluation of changes in sialic acid expression in prostatic tissue can provide insights into the malignant potential of prostate cancer, one of the most common malignancies in men. Understanding these changes is crucial for the development of new diagnostic and therapeutic strategies.
Funding: APVV 20-0243 and VEGA 1/0684/21

E-PS-24-030
Primary poorly differentiated carcinoma in seminal vesicle
Y. Jang*
*Ewha Womans University Medical Cent, Republic of Korea

Background & objectives: Primary seminal vesicle carcinoma is an extremely rare and poor prognostic tumour. Here, we reported a poorly differentiated carcinoma of the primary seminal vesicle.
Methods: Here, we present a case of a 63-years-old man with intermittent haematuria. A Magnetic Resonance Imaging (MRI) scan revealed lobulated mass of the right seminal vesicle (3.8cm). The serum prostate specific antigen (PSA) and serum cancer antigen 125 (CA125) level were within the normal range(PSA, 0.11 ng/mL; CA125, 6.3 ng/mL)
Results: Radical prostatectomy was performed. Microscopically, the right seminal vesicle showed poorly differentiated invasive carcinoma with solid pattern and extensive necrosis. Immunohistochemically, the tumour was positive for high molecular weight cytokeratin, cytokeratin 7 and cancer antigen 125 and negative for cytokeratin 20, prostate specific antigen and NKX3.1. After operation, he received additional radiotherapy. Currently, he is well with no signs of recurrence at 20 months after operation.
Conclusion: The seminal vesicle carcinoma is very rare, and only a few have poorly differentiated, with poor prognosis. We share its microscopic characteristics and immunohistochemical staining of rare case.

E-PS-24-032
MALT/extranodal marginal zone lymphoma of urinary bladder
E. Koniaris*, M. Sevastiadou, A. Aktselis, G. Kafiri
*Pathology Departmant, General Hospital of Athens 'Hippocratio', Greece

Background & objectives: Extranodal marginal zone (EMZ) lymphoma of urinary bladder/MALT, is an extremely rare entity in the urinary bladder, affecting females, representing less than 0,2 % off all malignant urinary bladder neoplasma and about 60 cases have been reported in the literature.
Methods: An 84-year-old patient admitted to our hospital with cystitis and haematuria and transurethral cystoscopy was performed. Endoscopically, a broad-based elevation of the cystic wall was observed and resection of the tumour was performed and send for biopsy in our department. Macroscopically, the tissue had brownish hue, fibroelastic consistency and measured 3,5X3X0,8 cm.
Results: Microscopically, the tissue specimens were almost completely infiltrated by monomorphic, small and medium sized B lymphocytes, which were CD20 positive. The Lymphocytes had irregular nuclei, many with nucleolus and scanty cytoplasm. The neoplastic cells had a diffuse and/or partly nodular growth pattern, with scattered, reactive collonized lymphoid follicles and presence of atrophic germinal centres. On immunohistochemical (IHC) examination with cytokeratin AE1/AE3, we recognized lymphoepithelial lesions within the neoplastic cells. The lesion infiltrated the part of the muscular wall of the urinary bladder that was also resected. Other IHC findings included positivity of bcl2, ki67 (40-45%) and MUM-1 (30-35%). CD10, bcl6, CD3. PSA, CD5, CD23, were evaluated as negative.
Conclusion: EMZ lymphomas of the urinary bladder are extremely rare low grade extranodal B-cell lymphomas, with excellent general prognosis, mainly affecting female patients and have been strongly associated with recurrent episodes of infectious cystitis (like E. coli). There are plenty of treatment modalities including: a) observation based on risk factors (age, grade, etc), b) surgical resection (complete excision or biopsy), c) radiation, alone or following biopsy, d) chemotherapy, in systemic cases and e) targeted antibody therapy, with rituximab (anti-CD20 antibody).

E-PS-24-033
Prolaris kit cell-cycle risk scores are reproducible across external molecular and pathology laboratories
M. Kornilov*, V. Kuhl, W. Clegg, B. Mabey, J. Lehmann-Che, J. Champ, R. Fattouh, K. Boissinot, F. Moinfar, S. Ratzel, S. Delee, J. Doedt, R. Kronenwett
*Myriad International, Germany

Background & objectives: The Prolaris test predicts the risk of prostate cancer aggressiveness. The Prolaris kit was developed and validated to be used as a decentralized solution. Here, we assessed the Prolaris kit cell-cycle progression score (CCP) reproducibility across three different laboratory sites.

Methods: At each site, operators isolated RNA from 50 FFPE samples, performed RT-qPCR, and determined the CCP Score using the Prolaris Biopsy Report Generator. Each sample was analysed once at each site. After an outlier analysis, overall reproducibility was estimated using a random intercepts mixed model using restricted maximum likelihood and was then decomposed using variance component estimates from previous work.
Results: In total, 43 samples were used for statistical analysis. Using CCP Scores for each sample from all three sites, outlier analysis did not identify any scores that fell outside of 4 MAD (mean absolute deviation). Variance decomposition using these samples, along with previously calculated variance component estimates, demonstrated a site-to-site variability of 0.115 CCP Score units (CCPsu). As acceptance criterion, a standard deviation of at most 0.31 CCPsu was defined as it leads to a clinically relevant absolute shift of disease-specific mortality risk at the active surveillance threshold of less than 1%. The overall standard deviation for the Prolaris test was 0.184 CCPsu, which fulfilled the defined acceptance criterion.
Conclusion: The variance in CCP Scores across the three external sites was within the acceptable range, indicating that Prolaris kit results are reliable and reproducible when performed locally by trained laboratory staff.

E-PS-24-034
Malignant Leydig cell tumour with MDM2 amplification - a case series
O. Kuczkiewicz-Siemion*, M. Wągrodzki, A. Chrzan, J.K. Wolski, B. Puton, K. Olszewska, M. Grabowska-Kierył, M. Prochorec-Sobieszek
*Department of Pathology, Maria Sklodowska-Curie National Research Institute of Oncology Warsaw, Poland

Background & objectives: Malignant cases constitute 5-10% Leydig cell tumours (LCTs) and so far the only objective features of aggressiveness are metastases. Colecchia et al. indicated the role of MDM2 amplification as a marker of metastatic potential, describing three LCTs with this alteration.
Methods: Cases of metastatic LCTs diagnosed in a single Cancer Center in Poland between January 2015 and March 2023 were included. Three cases fulfilled the inclusion criteria. Those cases were tested for MDM2 amplification by both immunohistochemistry (IHC) and fluorescence in-situ hybridisation (FISH) as well as assigned the Leydig cell tumour Scaled Score (LeSS).
Results: We present a case series of three male patients aged from 44 to 68 years diagnosed with metastatic LCTs. Patients presented metastases to lymph nodes or distant sites such as lungs or liver with different time intervals from initial diagnosis. All analysed cases demonstrated MDM2 amplification confirmed by IHC and FISH analyses. In one case the calculated LeSS indicated a low-risk class of metastatic behaviour. The follow-up duration ranged from 9 months to 6 years.
Conclusion: LCTs occurring with delayed metastasis could potentially benefit from early retroperitoneal lymphadenectomy. As effective treatment options are lacking, retroperitoneal lymphadenectomy at short notice may be beneficial for patients with high-risk tumours. While microscopic evaluation of LCTs is not sufficient to predict metastatic behaviour, therefore the status of MDM2 amplifications seems to be a promising new prognostic marker.

E-PS-24-035
Renal Cell Carcinoma with Tubulocystic Morphology, A Great mimicker of Tubulocystic Renal Cell Carcinoma
A. Lazim*, A. Arriola, M. Mollaee
*Temple University Hospital, USA

Background & objectives: Tubulocystic renal cell carcinoma is a rare variant of renal cell carcinoma (RCC), new entity in the WHO classification of renal tumours. Morphologically, characterized by a pure tubulocystic morphology, a pattern that may be also seen in other renal neoplasms.
Methods: However, recent studies have identified distinct genomic features of this tumour that can aid in distinguishing it from other RCC. We present a case of a 64-year-old male who presented with abdominal pain and found to have an incidental 7.4 cm left upper pole renal cystic mass on imaging studies. Subsequently, he underwent a partial nephrectomy.
Results: Microscopically, the well circumscribed unencapsulated tumour was composed of tubules and cysts, lined by cuboidal, columnar, flat, hobnail cells with eosinophilic cytoplasm, occasional large nuclei and prominent nucleoli. The tumour cells were positive for CD10, vimentin, PAX8, AE1/AE3, CAM5.2, AMACR, FH (retained), SDHB (retained), CK7 (focal), negative for CAIX, and TFE3. The preliminary diagnosis was reported as renal cell carcinoma, unclassified. Molecular testing was requested for cytogenetic microarray analysis (CMA) and RNA fusion for definite classification of the tumour. Results revealed alterations of chromosome 1, which was not consistent with the reported genomic profile of tubulocystic RCC. Hence, a diagnosis of renal cell carcinoma WHO/ISUP grade 3 was rendered.
Conclusion: This case demonstrated that a definitive diagnosis of tubulocystic RCC can be challenging by morphology and stains alone, as the tubulocystic pattern can be seen in a variety of other renal neoplasms. Definitive diagnosis of tubulocystic RCC can be challenging if based on morphology and stains alone. The presence of a pure tubulocystic architecture combined with the use of molecular testing to identify distinct genomic features, help distinguish tubulocystic RCC from its mimickers, as seen in other renal neoplasms.

E-PS-24-037
Gleason grading on a set of 1,903 tumours with known clinical follow-up data allows objectively measuring the quality of Gleason grading and comparing the impact of different grading attitudes
M. Lennartz*, F. Büscheck, D. Hoeflmayer, S. Kind, S. Minner, M.C. Tsourlakis, N. Gorbokon, M. Freytag, C. Wittmer, K. Möller, C. Bernreuther, N. Blessin, M. Graefen, T. Schlomm, G. Sauter
*University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: In prostate cancer Gleason grading system is the strongest prognostic parameter with high impact for determining patient treatment. However, Gleason grading is subject to substantial interobserver variability, even between specialized pathologists.
Methods: To objectively assess the quality of the Gleason scoring of individual pathologists, images of 1,903 H&E stained prostate cancer samples measuring 0.6 mm in diameter were collected. To evaluate the utility of our "Gleasonaut" approach, 11 different pathologists were invited to assign Gleason scores to each of these images and these data were then compared to clinical follow-up data.
Results: A comparison of the Gleason scoring of our 11 pathologist identifies substantial differences. A complete agreement of all pathologists was only achieved in 5.4% for Gleason 3+3, in 1.9% for Gleason 3+4, and in 0.1% for Gleason 4+3. An agreement of at least 2/3 of the pathologists was reached in only 25.1% for Gleason 3+3, 23.0% for Gleason 3+4, and 2.9% for Gleason 4+3. The availability of follow-up data enabled head-to-head comparisons of the prognostic impact of individual grading attitudes. For tumours initially graded as 3+3=6, 21 of 110 comparisons resulted in significant differences. For tumours initially graded as 3+4=7, 85 of 110 comparisons resulted in significant differences.
Conclusion: Our "Gleasonaut" is highly useful to objectively measure the quality of Gleason grading and to compare the impact of different grading attitudes. The particularly high rate of clinically relevant interobserver variability in Gleason 3+4 carcinomas is obviously driven by substantial prognostic differences between Gleason 3+4 tumours with very high or low fraction of Gleason 4. Image databases with

associated outcome data represent an ideal source for developing AI systems that can better predict cancer aggressiveness than the Gleason score.

E-PS-24-038

Clinical and pathological correlation in Erdheim Chester disease - a case report

A. Georgescu*, T. Georgescu, S. Barbu, L. Petrescu, F. Pop
*Department of Pathology, "Carol Davila" University of Medicine and Pharmacy Bucharest, Department of Pathology, Nephrology Clinical Hospital "Dr. Carol Davila", Bucharest, Romania

Background & objectives: Erdheim-Chester disease is a histiocytic proliferation, which was first described in 1930, but which was only recently recognized as being a neoplasm. Accurate diagnosis requires a characteristic radiological aspect, which is supported by the perinephric soft tissue biopsy.
Methods: We report the case of a 47–year-old male, who presented to the Nephrology department with altered kidney function of unknown aetiology. Upon CT, a circumferential thickening of the perinephric fat, suggestive for the "hair kidney sign" was observed. Subsequently a PET-CT revealed symmetrical osteosclerosis of long bones and a perinephric biopsy was performed in order to establish the diagnosis.
Results: Four core needle biopsies were received in the Pathology Department of the Nephrology Clinical Hospital "Dr. Carol Davila" Bucharest, three of which revealed an infiltration of the soft tissue with foamy macrophages and discrete histiocytes. Additionally, a mixed inflammatory infiltrate composed of lymphocytes and plasma cells, embedded in a fibrotic stroma was noticed. Immunohistochemical stains were performed and revealed that the histiocytic infiltrate was diffusely positive for CD68, CD163 and FXIIIa. No immunoreactivity towards CD1a was observed. The proliferation index was extremely low, of approximately 2%. BRAFV600E stain revealed diffuse strong cytoplasmic positivity of the proliferated histiocytes, and further molecular tests have confirmed the presence of the mutation.
Conclusion: In conclusion, Erdheim-Chester disease requires a specific imagistic and pathological finding in order to be accurately diagnosed. Rarely, Erdheim-Chester disease can present with renal dysfunction secondary to ureteral compression, although more commonly the skin lesions and the haematological affliction usually precipitate the recognition of this rare multisystemic disease. Our case highlights the importance of accurately recognizing the characteristic findings, which will consequently result in a multidisciplinary therapeutic approach. A favourable outcome can be achieved after BRAF or MEK inhibitors.

E-PS-24-039

Solitary fibrous tumours of the genitourinary tract – report of two cases in rare locations

J. Lobo*, M.A. Morini, B. Zein-Sabatto, S. Harada, V. Dal Zotto, C. Magi-Galluzzi
*Portuguese Oncology Institute Porto, Portugal

Background & objectives: Solitary fibrous tumours (SFT) arising in the genitourinary (GU) tract are rare. Differential diagnosis with other more common spindle cell tumours is challenging, especially in the context of small biopsies.
Methods: We report two cases of SFT of the GU tract (involving seminal vesicle and spermatic cord), including morphology, immunophenotype and molecular analysis.
Results: Case #1 corresponded to a 40-year-old male presenting with haematospermia. Imaging revealed a 2 cm seminal vesicle nodule. Case #2 corresponded to a 48-year-old male presenting with scrotal enlargement. Imaging revealed a 9 cm mass arising from the spermatic cord. Both cases showed a bland spindle cell proliferation with alternating cellularity, collagen deposition and thin-walled branching vessels. No necrosis, high mitotic index or pleomorphism were seen. Both cases were diffusely positive for STAT6/CD34. The seminal vesicle SFT was originally diagnosed in a pre-surgical biopsy; NGS confirmed NAB2-STAT6 fusion. MDM2 FISH was negative on the spermatic cord tumour excluding liposarcoma. Patients are alive without disease at 6 months/14 years after diagnosis.
Conclusion: SFT should be included in the differential of spindle cell lesions of the GU tract. STAT6 IHC (strong nuclear expression) is a good surrogate marker for the NAB2-STAT6 fusion characteristic of SFT. While most tumours are indolent, 10-30% behave aggressively; outcome can be predicted based on available risk stratification models combining size and histopathological features (pleomorphism, mitotic index, necrosis).

E-PS-24-040

Primary renal Ewing sarcoma: report of two cases, including one with an exceedingly rare EWSR1-ETV4 fusion

J. Lobo*, R. Ahmed, B. Zein-Sabatto, T. Winokur, S. Wei, S. Harada, C. Magi-Galluzzi
*Portuguese Oncology Institute Porto, Portugal

Background & objectives: Ewing sarcoma (ES) of the kidney is exceedingly rare, with approximately 300 cases described in literature, the majority as case reports. Current challenges include differential diagnosis with other small blue round cell tumours with implications for treatment/prognosis.
Methods: We report two cases of primary renal ES, including immunophenotype and molecular analysis.
Results: Two female patients, aged 28/32 years, presented with abdominal complaints. Each nephrectomy specimen revealed a 15cm mass with necrosis, extending into perinephric fat, renal sinus/vein, and involving the adrenal gland in one case. Tumour cells were small and ovoid/spindled. The differential diagnosis included Wilms tumour, desmoplastic small round cell tumour, rhabdomyosarcoma, synovial sarcoma, lymphoma, melanoma and neuroendocrine carcinoma as well as recently described ES variants. A panel of immunohistochemical markers, including pancytokeratins, PAX8, WT1, muscle/melanocytic markers and CD45 was performed; both tumours were only positive for CD99, FLI1 and synaptophysin. EWSR1-FLI1 fusion was detected (by FISH and RT-qPCR) in one case and EWSR1-ETV4 fusion (by NGS) in the other.
Conclusion: Accurate diagnosis of ES is important to select appropriate chemotherapy regimen. Molecular testing is critical to confirm the diagnosis. While approximately 90-95% of ES show a EWSR1-FLI1 fusion, EWSR1-ETV4 fusion has been described in rare isolated case reports, none primary in the kidney. ES with unusual fusion partners may have a predilection for extraskeletal sites. Additional studies are needed to assess the potential prognostic value of ETV4 gene partner.

E-PS-24-041

Cystic trophoblastic tumour of the testis: report of two cases and utility of miR-371a-3p testing

J. Lobo*, N. Tavares, D. Barros-Silva, A. Rosinha, A. Morais, C. Jerónimo, Â. Rodrigues, R. Henrique
*Portuguese Oncology Institute Porto, Portugal

Background & objectives: Cystic trophoblastic tumour (CTT) of the testis is an infrequent and under-recognized entity, often focal and admixed with mature teratoma in post-chemotherapy retroperitoneal lymph-node dissection (pcRPLND) specimens. Its pathogenesis is still poorly understood.
Methods: We report two cases of CTT, one in the context of pcRPLND and the other in a post-chemotherapy primary testicular tumour. We provide histopathological description, immunohistochemistry study and clinicopathological annotation. Additionally, we submitted the CTT component to miR-371a-3p RT-qPCR testing, comparing with

results obtained in a cohort of testicular germ cell tumours (TGCTs) representative of all histological subtypes.
Results: Both specimens showed predominantly teratoma, with focal variably sized cysts, lined by large, eosinophilic, squamoid-appearing cells, with frequent vacuolization, corresponding to CTT. Fibrinoid change was common, and no necrosis, marked pleomorphism or mitotic figures were seen. There were areas of transition between (glandular) mature teratoma and CTT in cystic spaces. Tumours were positive for CK8/18, with multifocal positivity for GATA-3, and positivity for HCG in scattered cells only. Alpha-inhibin, OCT3/4 and p63 were negative. Patients are alive with stable disease at two years of follow-up. MiR-371a-3p levels in CTT were undetectable, as well as in additional teratoma cases, while being elevated in seminomas, embryonal carcinomas, yolk sac tumours and choriocarcinomas.
Conclusion: Recognition of CTT is important, avoiding the pitfall of diagnosing choriocarcinoma foci, which would dictate a much poorer prognosis and lead to unnecessary systemic treatments. CTT behaves similarly to teratoma. The finding of transitions between mature teratoma and CTT, as well as the negativity for miR-371a-3p (a universal biomarker of TGCTs, being negative only in teratoma) in CTT support a maturation phenomenon towards teratoma. This is the first report of miR-371a-3p testing in CTT.
Funding: The authors would like to acknowledge the support of 'Bolsa de Investigação Médica LPCC/Lions – Cancro Infantil' 2022 and PI27 – Financiamento Base GEBC.

E-PS-24-042
Fumarate hydratase-deficient renal cell carcinoma, a diagnostic pitfall in the renal tumours classification
A. Loghin*, M. Decaussin-Petrucci, C. Chibelean, M.C. Popelea, A. Raicea, A. Borda
*G.E. Palade UMFST Targu Mures, Romania

Background & objectives: Fumarate hydratase deficient renal cell carcinoma (FH-deficient RCC) is a RCC characterized by variable morphologic aspects and germline mutation in the FH gene.
Methods: We present the case of a 65 years-old men admitted to the Urology Department, where a left nephrectomy was performed for a of 130 mm renal tumour. The specimen was sent to the Pathology Department.
Results: The macroscopy revealed a tumour with solid and cystic architecture, with a fibrous capsule, extended in the perirenal adipous tissue. Microscopically, we observed multiple admixed morphological patterns: papillary, tubulo-cystic and cribriform. The tumour cells had eosinophilic cytoplasm, large nuclei, focally with eosinophilic macronucleoli. Also, in some cells, intracytoplasmatic vacuoles were present. These findings were not characteristic for any common type of RCC. In immunohistochemistry tumour cells were positive for PAX8, focally for AMACR, negative for CD10, CK7, TFE3, CK20, CD117, with preservation of SDHB expression and loss of FH expression. The morphological aspect and the immnohistochemical profile lead to a diagnostic of a FH-deficient RCC.
Conclusion: The recognition of FH-deficient RCC is important because of its very aggressive behaviour and also because of the association with Hereditary Leiomyomatosis and Renal Cell Cancer Syndrome. Therefore FH immunohistochemical expression must be determined in all cases of renal tumours without a classic morphological aspect and immunohistochemical profile.
Funding: FDI internalization of higher education

E-PS-24-043
TFE3-rearranged renal cell carcinoma: a case report
W. Majdoub*, K. Ben Lazreg, A. Baccouche, A. Bdioui, O. Belkacem, D. Benletaifa, F. Saidani, S. Hmissa
*Pathology Department Sahloul Hospital, Tunisia

Background & objectives: Transcription factorE3-rearranged renal cell carcinomas (TFE3-RCCs) harbour gene fusions involving TFE3. This RCCs account for 40% of paediatric RCCs and 1.6-4% of adult RCCs. Herein we report another rare case report.
Methods: A 15-year-old adolescent presented with right lumbar pain and haematuria. The diagnosis of right renal tumour was made by radiologic examinations. The patient underwent a nephrectomy.
Results: At macroscopic examination, the tumour was medio-renal measuring 7x6cm. It was white yellowish with haemorrhagic aspects and infiltrated focally the renal capsule without infiltration of the renal vein. Microscopically, the tumour had heterogenous aspects: papillary and diffuse pattern. Tumoral cells were large epithelioid with clear or focally eosinophilic cytoplasm. Multiples psammomatous bodies were observed. There was no rhabdoid or sarcomatous component. On immunohistochemistry stains, tumoral cells were diffusely positive for CD10 and AMACR and focally positive for HMB45 and EMA. Immunostains for Vimentin, ck7 and MelanA were negative. Strong and diffuse nuclear staining for TFE3 was observed.
Conclusion: TFE3-RCCs have heterogeneous morphological and immunohistochemical profile. Cases presenting at a younger age or cases with atypical morphology are suspected to be a TFE3-RCC.TFE3 IHC antibody have a high predictive value for detecting TFE3 rearrangement. Paediatric patients with TFE-RCCS have a better prognosis than adults.

E-PS-24-044
Clinical and morphological characteristics of bladder cancer
A. Malysheva*, O. Reshetnikova, O. Teleshova, O. Zinchenko, M. Malich, I. Sinenko
*Immanuel Kant Baltic Federal University, Russia

Background & objectives: Bladder cancer (BC) is a severe disabling disease that requires careful differential diagnosis. The aim of the present study was a statistical analysis of the prevalence of bladder cancer, assessment of its histological variants and stages of the process.
Methods: The study was conducted in the Department of Pathology, Luhansk Regional Oncology Center. A total of 307 cases with suspected bladder tumours were analysed. The results of histological examinations of the tumour, as well as the frequency of various cancer types in different age group of patients were considered.
Results: The bladder tissue samples were obtained during the transurethral resection of the tumour in 79.1% of cases and in 20.9% of cases a diagnostic biopsy was performed. Patients were divided into several age groups: up to 55 years (61 cases), 55-64 years (107 cases), 65-74 years (109 cases) and over 75 years (30 cases). BC was more common in men (82.4%) than in women (17.6%). The highest incidence rate was in the 65-74 y.o. age group (35.5%). Moderately differentiated urothelial carcinoma was a leading histological variant of the BC. The predominant BC stage at the time of the pathology diagnostics was a T1 with the invasion into the submucosal layer.
Conclusion: BC is associated with an important health care problem due to the morbidity and mortality associated with disease. The challenge is to control neoplasia based on pathomorphology and morphogenesis of the tumour growth. Based on the data obtained, the need for further comprehensive clinical and morphological studies is discussed, taking into account information about BC histopathology, socioeconomic factors, detailed information the treatment, its side effects and causes of death.

E-PS-24-045
Sarcomatoid chromophobe renal cell carcinoma: a case report
S.J. Marín Asensio*, A. Cuesta Díaz de Rada, O. García-Galvis, M.G. Rodríguez Guevara, J. Alzoghby-Abi-Chaker, C.J. Martinez Martinez, A.R. Gonzalez Medina, A. Farres Rabanal, F. Izquierdo García
*Complejo Asistencial Universitario de León, Spain

Background & objectives: Chromophobe renal cell carcinoma (CRCC) is the third most common type of renal cell carcicnoma (RCC)

characterized by a relatively good prognosis. Any type of RCC can undergo sarcomatoid differentiation, being most common in clear cell renal cell carcinomas (CCRCC).
Methods: We present a 75 year old male with severe loss of weight in the last 2 months who shows radiologically a 16 centimetres heterogeneous tumour on the left kidney. In macroscopy the tumour shows an irregular aspect, 15 centimetres in its maximum axis, with yellowish colour that invades the adjacent perirenal fat tissue.
Results: Histological examination shows a biphasic tumour formed on one hand by uniform nests of big cells with clear cytoplasm, perinuclear halo and very low or inexistent mitotic activity. The other component, which is the majority of the tumour, is formed by irregular spindle cells distributed in a stream or framework pattern with nuclear pleomorphism and high mitotic activity.
There is necrosis associated in 40% of the mass.
Both areas show common positive inmunostaining for CD117, CK7 and CKAE1/AE3.
Conclusion: Chromophobe renal cell carcinomas are tumours who have a very good prognosis.
We report an unusual CRCC with sarcomatoid transformation which greatly decreases survival.
The common positive stainings supports the possibility that both areas have the same origin.
Three months after the diagnosis the patient presents radiological distant metastases and overall worsening.

E-PS-24-046
Aquaporins expression in renal cell carcinomas: diagnostic and potential prognostic implications
S. Marletta*, A. Caliò, F. Comper, F.M. Martelli, L. Stefanizzi, L. Marcolini, M. Brunelli, G. Martignoni
*Department of Diagnostic and Public Health, Section of Pathology, University of Verona, Department of Pathology, Pederzoli Hospital, Peschiera del Garda, Italy

Background & objectives: The ongoing evolution of renal cell carcinoma classification advocates for the identification of novel diagnostic and predictive markers. Aquaporins (AQPs) are a class of channels physiologically regulating cellular water flow, whose role in renal neoplasms has not been studied yet.
Methods: In the present study, we sought to evaluate in a wide series of renal neoplasms the diagnostic and prognostic value of the immunohistochemical expression of the aquaporins molecules AQP-1, AQP-2, and AQP-3. Three-hundred fifty cases were retrieved, including both common and much rarer entities, according to the recently released 2022 WHO classification, and fourteen tissue microarrays (TMAs) were built.
Results: While all major types of renal cell neoplasm failed to express AQP-3, immunolabeling for AQP-1, normally found in proximal renal tubules, was mainly observed in clear cell (101/102, 99%) and papillary renal cell carcinoma (27/41, 66%). Conversely, all chromophobe renal cell carcinomas (55/55, 100%) and oncocytomas (92/92, 100%) expressed AQP-2, physiologically found in distal renal tubules. Regarding rarer histotypes, both fumarate hydratase-deficient and succinate dehydrogenase-deficient renal cell carcinomas were only immunolabeled for AQP-2. Concerning prognostic variables, the coexpression of AQP-1 and AQP-2 significantly correlated with a high nucleolar grade (G3-G4) in both clear cell ($p < 0.04$) and papillary renal cell carcinomas ($p < 0.02$).
Conclusion: In this study we have demonstrated that AQP-1 and AQP-2 can be added in a diagnostic panel as an additional tool to distinguish clear cell/papillary renal cell carcinoma from oncocytoma/chromophobe renal cell carcinoma, and fumarate hydratase-deficient (just labelling for AQP-2) from papillary renal cell carcinomas (usually staining for both), which represent their main differential diagnosis. Furthermore, higher AQP-1 and AQP-2 expression in clear cell and papillary tumours showing aggressive nucleolar features (G3-G4) suggests a possible prognostic role.

E-PS-24-047
PD-L1 expression in two molecular subtypes of muscle invasive urothelial bladder carcinoma
S. Mašic*, S. Trifunović, V. Vrbić, M. Knežević, R. Terlević, B. Krušlin, M. Ulamec
*Clinical Department of Pathology and Cytology, University Hospital Center Sestre milosrdnice, Zagreb, Croatia

Background & objectives: Muscle invasive urothelial bladder carcinoma (MIBC) represents aggressive neoplasm with high mortality. Two main MIBC molecular subtypes with diverse molecular signature are familiar. Recently, immunotherapy with immune checkpoint inhibitors and PD-L1 expression level as potential response predictor was introduced.
Methods: Forty FFPI tissue samples of patients with MIBC were stained for HE and immunohistochemistry. GATA-3 and CK5/6 expression was used to roughly determine molecular subtype (basal or luminal). PD-L1 expression (SP 142) was interpreted as the percentage of positive peri- and intratumoral staining of tumour microenvironment immune cells and correlated with molecular subtype. Results were considered statistically significant when $p<0.05$.
Results: Cases showing CK5/6 positive and GATA-3 negative reaction were classified as basal subtype, while CK 5/6 negative and GATA-3 positive as luminal subtype. PD- L1 positive expression was observed in 28 samples based on cutoff value of 1%. Statistically significant positive correlation was determined between PD-L1 expression and basal subtype, while negative correlation was established between PD-L1 and the luminal subtype.
Conclusion: Results of our study demonstrated possible immunohistochemistry algorithm in molecular subtype assessment, as well as correlation of PD-L1 expression with basal immunophenotype, which could suggest patients' positive response to anti- PD- L1 immunotherapy and more successful management of this group of patients.
However, to confirm the connection between basal molecular subtype and PD-L1 expression, we believe further research and molecular analysis should be conducted on larger patient cohort.

E-PS-24-048
A rare localisation for intravascular papillary endothelial hyperplasia (Masson's tumour)
A.S. Mavuş*, S.G. Barut
*Haseki Education and Research Hospital, Turkey

Background & objectives: Intravascular papillary endothelial hyperplasia (Masson's tumour) is a vascular proliferation that considered as a benign and non-neoplastic proliferation. Herein, we represent our rare case of Masson's tumour in spermatocele cyst wall in an 76 years-old male patient.
Methods: The patient underwent operation for scrotal swelling with preoperative diagnosis of spermatocele. The operational material is 8x7x5.5 tan- brown cystic flat tissue. Hematoxylin- Eosin slides were mostly consist of hyalinized fibrous cystic tissue surrounded by the mesothelial layer and adipose tissue. In one slide, we saw papillary proliferation within and at the borders of an empty space inside cyst wall.
Results: On higher magnification the cells were monotonous, with round and small nuclei. We didn't notice any atypia or mitotic figures. Benign and malignant mesothelial proliferation and vascular lesions were in our differential diagnosis. We ordered some immunohistochemical stains for differential diagnosis. None of the mesothelial markers (CK5/6, Calretinin) were positive in our case and all the

vascular markers (CD31,CD34,FLİ-1) were positive. Pancytokeratin and HHV-8 was also negative. These finding were consistent with vascular origin not mesothelial or epithelial. With low ki67 and negative HHV-8 supported benign proliferation. Papillary projections are not expected in haemangiomas so we rendered the diagnosis of Masson's tumour.
Conclusion: With combination of ancillary study and morphological findings we rendered the diagnosis of Masson's tumour. Masson's tumour is mostly localised in head and neck region and we couldn't find any case of Masson's tumour in spermatocele wall reported up-to-date.

E-PS-24-049
A rare site of metastasis of lung adenocarcinoma: kidney
A.S. Mavuş*, A. Tarlacı
*Haseki Education and Research Hospital, Turkey

Background & objectives: Lung adenocarcinomas (ACA) are known to metastasize frequently. Most common site of metastasis are bone, brain, adrenal and liver. Kidney is a rare site of metastasis for lung ACA. Herein, we represent our case of renal metastasis from lung origin.
Methods: Our patient was 53-year-old man who was diagnosed stage 3 lung ACA and received chemotherapy. 1,5 year after the diagnosis patient developed renal metastasis. Gross material was left nephroureterectomy with 15,5x 8,5x 6,5 cm dimensions. When opened, there was centrally necrotic, solid dirty white-tan mass with 3,5 x 3 x 2 cm dimensions in the lower pole of kidney.
Results: On Hematoxyline- Eosine stained slides, we saw highly haphazardly arranged, solid tumoral areas and large necrotic areas on low power. Tumour cells were highly pleomorphic with hyperchromatic nuclei. There were lots of mitotic figures and frequent lymphovascular invasion. Histopathologically, our case ha necrotic areas which may be as a result of neoadjuvant chemotherapy. On ancillary study, TTF-1 (nuclear), napsin-A (cytoplasmic), cytokeratin-7 were positive and markers for renal primary (PAX-2, PAX-8 , RCComa, CD10, vimentin) and urothelial and squamous cell carcinoma (p63, uroplakin) were negative. Histopathological and ancillary findings combined with patients' history we made the diagnosis of "metastatic adenocarcinoma consistent with patient's known lung primary."
Conclusion: Although renal metastases from non-small cell lung cancer (NSCLC) are frequent at postmortem examination, clinically recognized isolated metastasis to the kidney from NSCLC is very rare. Due to rarity, renal metastasis of lung ACAs cause major problem in diagnosis especially in absence of clinical history. Primary RCCs, other primary kidney tumours (like collecting duct carcinomas), and metastatic carcinomas (like urothelial carcinomas and ACAs from other primary) are other differential diagnosis.

E-PS-24-050
TFE3 translocation renal cell carcinoma: A case report
M.R. Meléndez Gispert*, C. Ariño-Palao, N. Cadavid-Fernández, A. Tenelanda-Santillán, E. Moreno Moreno, S. Molés Caparrós, A. Sáiz González
*Ramón y Cajal University Hospital, Spain

Background & objectives: TFE3 translocation renal cell carcinoma(TFE3-tRCC) is a rare and aggressive tumour, which is more frequent in young adults. It is characterized by translocations involving TFE3. Diagnosis is achieved with histopathological and immunohistochemical findings or TFE break-apart fluorescent in situ hybridization(FISH).
Methods: We present a case of a 37-year-old male without previous medical history who consulted for pain in left lumbar area, haematuria and weight loss in the last 2 months. A CT scan showed a renal mass in the left kidney with invasion of both the renal vein and the inferior vena cava. Left radical nephrectomy and cava thrombectomy were performed.
Results: The microscopic study showed a high grade tumour with predominance of clear cells with abundant cytoplasm, pleomorphic and sarcomatoid areas, extensive necrosis and a minor component of papillary type carcinoma. The tumour infiltrated renal parenchyma, renal sinus fat, perirenal fat and renal vein as well as an adenopathic conglomerate of the hilium with extranodal extension (stage pT3bN1 AJCC 8th ed, 2017). Immunohistochemistry (IHC) showed intense nuclear positivity for TFE-3. The diagnosis was therefore TFE3-tRCC. The patient started adjuvant therapy, but he died four months later.
Conclusion: In TFE3-tRCC the clinical behaviour is aggressive and the response to targeted therapy and immune checkpoint inhibitors is low. Because of the morphological overlap with more common renal cell carcinomas, we are probably misdiagnosing this entity. We should always keep in mind the particular morphology of this entity and always perform TFE3 in our IHC panel in order to diagnose this carcinoma earlier for a better prognosis.

E-PS-24-051
Strong PD-L1 expression in high grade inflammatory prostate
A. Mollova- Kyosebekirova*, M. Koleva, D. Dikov
*Department of General and Clinical Pathology, University Hospital "Sveti Georgi", Plovdiv, Bulgaria

Background & objectives: Chronic inflammation (CI) is associated with the most frequent socially important prostate diseases: prostatitis, benign prostatic hyperplasia (BPH), and prostate adenocarcinoma (PCa). We examined the programmed death-ligand 1 (PD-L1) expression in benign prostatic tissue in inflammatory microenvironment of these diseases.
Methods: We studied the PD-L1 expression in 144 prostatic surgical and autopsy specimens with various types of CI:nonspecific histologic prostatitis (HP), granulomatous prostatitis (GP), and reactive lymphoid infiltrates in the vicinity of BPH and PCa. HP was scored in low and high grade (LG,HG) accordingto the severity of inflammation. The control group included autopsy prostates of medico-legal cases of young men.
Results: It was established a strong PD-L1 immunoreactivity in the epithelium of ductal lympho- epithelial lesions (LEL) in prostates with HG HP and fully positivity in the foci of localised granulomatous inflammation in GP. The lack of positivity of the marker was showed in the control group of prostates.
Conclusion: The study presents the first attempt to examine the PD-L1 expression in inflammatory human prostate. The results of this study proving strong expression of PD-L1 in the epithelium of ductal LEL in prostate HG HP and in the granulomas in GP. The unregulated expression of PD-L1 during HG prostatic inflammation prevent tissue injury and consequently lead to peripheral prostatic immune tolerance and inflammatory microenvironment in prostatitis, BPH and PCa.

E-PS-24-052
Is the cribiform pattern in the prostate cell biopsy already indicative of a poor prognosis?
G. Moreno Abenza*, F. Gómez Pálomo, J.L. Ruiz Cerdá, D. Ramos Soler
*Hospital universitario y politécnico La Fe, Spain

Background & objectives: It is known that the cribriform pattern in a radical prostatectomy specimen confers a poor prognosis, but in cylinder biopsy this prognosis is controversial. We are going to evaluate cribriform pattern in the cylinder biopsy of intermediate-risk patients.
Methods: Prospective cohort study carried out in 271 patients. Quantification of global, small and large cribriform pattern was performed

by two pathologists, independently. The cut-off points established were <5% vs > 5%. We used univariate analysis with Kaplan Meier curves and Long Rank test to determine association between cribiform pattern and time to recurrence. Then, a Cox regression was performed.
Results: 30.6% of patients presented recurrence. In the univariate analysis, the percentage of cribriform pattern greater than 5% was significantly associated with time to recurrence (p= 0.02). The large cribriform pattern was significantly associated with recurrence (p= 0.02) but not the small cribriform pattern (p= 0.155) with cut-off values of <3% vs > 3. The Cox model showed that more than 5% cribriform pattern on biopsy carries a significantly increased risk of recurrence (HR = 1.8, 95% CI: 1.1-3.18, p = 0.02), regardless of other pathological findings of posterior radical prostatectomy (ISUP grade group 2 vs ISUP 3, R- vs R+, % tumour < 10% vs > 10%).
Conclusion: The presence in the biopsy of a percentage of cribriform pattern greater than 5 provides predictive information for biochemical recurrence and is independent of other surgical pathological findings in radical prostatectomy performed later. These association may lead to a change in the follow-up and treatment of patients with intermediate-risk prostatic acinar adenocarcinoma (ISUP grade 2 and 3).

E-PS-24-053
Primary renal mesenchymal neoplasms - a retrospective analysis over a 8 year period from a tertiary care centre in South India
S. Naresh Shah*, S. Kar, M. Menon
*Apollo hospitals, India

Background & objectives: Primary renal mesenchymal tumours although rare, can be of varied morphology and subtypes. They present as renal masses and are often misdiagnosed as carcinomas, clinically and radiologically.
Methods: We retrospectively analysed the renal tumours received in the histopathology laboratory at Apollo hospitals, Chennai, India, from 2012 to 2020 and herein describe their frequency, incidence and demographical features. Histopathological examination was done in all cases, with confirmation by immunohistochemistry and molecular studies when required.
Results: Out of 2050 renal tumours, 67 (3.2%) cases of mesenchymal renal tumours were identified. Of these 51(76.1%) cases were benign, 14(23.8%) cases were malignant, and 2(0.1%) cases were unclassifiable. There was female (64%) preponderance over males (36%). Angiomyolipoma (43, 65.8%) constituted the major bulk of these tumours, followed by leiomyosarcomas (5, 7.5%), Ewing sarcoma (4,5.9%), Leiomyomas (3, 4.4%) and benign vascular tumours (3,4.4%). Two cases of synovial sarcoma(2.9%) were present. One case each of Schwannoma(1.5%), solitary fibrous tumour(1.5%), angiomyoadenomatous tumour (1.5%) and sarcoma with heterologous elements (1.5%) was documented.
Conclusion: Mesenchymal renal tumours cover a wide spectrum of benign and malignant tumours. Here we emphasize the role of histopathological examination, in conjunct with immunohistochemistry and molecular studies, which remains the gold standard for diagnosing these tumours. Some of these tumours have an aggressive course, present at end stage and may require multidisciplinary patient management modalities.

E-PS-24-054
Aberrant CK7/CK20/HMWK expression in prostatic adenocarcinoma with unusual urothelial-like morphology: a case series
N.J. Nguyen*, C. Sherman, T.H. van der Kwast, M.R.D. Downes
*University of Toronto, Canada

Background & objectives: Prostatic adenocarcinoma typically expresses markers of prostatic lineage while lacking CK7, CK20 and high molecular weight keratin (HMWK). Occasionally prostate cancers have unusual morphology which requires immunohistochemistry (IHC) to determine lineage. We report here a series of CK7/CK20/HMWK-positive prostatic adenocarcinoma.
Methods: We describe 11 cases of prostatic adenocarcinoma with unusual IHC expression and urothelial-like morphology, seen between 2018 and 2023 at two Toronto academic centres. We collected patient age, prior androgen deprivation therapy (ADT), tumour site, histomorphology, Grade group (GG), and results of IHC, including prostatic, urothelial and neuroendocrine markers.
Results: Patients' age ranged from 41 to 85 years (median 80). The tumour sites were: prostate (n=6), bladder (n=2), liver metastases (n=2), and lung metastasis (n=1). Six cases had prior ADT. The GG were: GG3 (n=1), GG5 (n=7); metastases were not graded. Nine cases had diffuse urothelial-like morphology, and two cases had focal urothelial morphology. CK7 (n=10) was strong/diffuse in seven cases, and weak/focal in one case. CK20 and HMWK showed patchy/moderate positivity in 3/6 and 4/7 cases, respectively. Eight cases expressed at least one prostate-specific marker. 6/9 cases had focal to diffuse positivity for neuroendocrine markers. Molecular testing (n=6) showed one TMPRSS2:ERG fusion (lung) and one ATM deletion (bladder).
Conclusion: This case series illustrates a cohort of high grade and/or metastatic prostatic adenocarcinomas with distinctive urothelial-like morphology and aberrant immunoprofiles (expression of CK7/CK20/HMWK) that initially suggest urothelial origin, a potential diagnostic pitfall with significant clinical consequences. This highlights the importance of (1) clinical history and (2) utilization of broad IHC panels, as 6/11 cases had prior ADT and 8/11 had expression of at least one marker of prostatic lineage, to aid in determining the correct diagnosis.

E-PS-24-055
Nephrogenic metaplasia: a pitfall on frozen section of urethral strictures
A. Oberc*, C. Sherman, M.R.D. Downes
*University of Toronto, Canada

Background & objectives: Urethral strictures (US) are a common cause of urinary obstruction which can be treated with surgical resection. Frozen sections are rare and pose a diagnostic challenge to pathologists due to the presence of benign lesions such as nephrogenic metaplasia (NM).
Methods: We retrospectively examined all cases of US resections submitted to pathology at our institution from 2012 to 2022 (n=258). Final pathology reports were searched to identify cases with dysplasia, carcinoma, or NM. When available, frozen section (FS) reports were also examined and compared to the final report, and additional clinical history and microscopic images were collected for cases with NM.
Results: NM was identified in the final report of 3.8% (10/258) of US resections. Dysplasia was identified within US in a single patient who underwent two separate resections, and squamous cell carcinoma (SCC) was found in one case. Intraoperative FS was requested in 3.4% of all cases (9/258). In two of these cases, an initial diagnosis of SCC was favoured by the intraoperative pathologist, however when reviewed with a genitourinary pathologist the diagnosis was changed to "reactive process" with a final diagnosis of NM. NM can be challenging on FS due to variable architectural patterns, eosinophilic cytoplasm and surrounding inflammation and additional reactive changes.
Conclusion: While US are relatively common, their assessment by intraoperative FS is rare and pathologists may lack familiarity with the variable morphology of benign entities such as NM that can be seen on FS resulting in their misinterpretation. Here we present two cases of NM that were initially misclassified as SCC to highlight this potential diagnostic pitfall at FS and the value of a second opinion prior to definitive FS diagnosis of malignancy.

E-PS-24-056

Low-grade oncocytic tumour of the kidney: report of two cases

K. Palamaris*, A. Stofas, A. Patereli, D. Goutas, N. Katsoulas, A. Georgiou, H. Gakiopoulou, P. Korkolopoulou
*First Department of Pathology, National and Kapodistrian University of Athens School of Medicine, Greece

Background & objectives: Low-grade Oncocytic Tumour (LOT) of kidney is a newly renal tumour entity that carries good prognosis as compared with other renal cell neoplasms, shows oncocytic cell-like morphology and is characterized by a CK7-positive/CD117-negative immunoprofile.
Methods: We report 2 cases of LOT of a 64-year-old male with a history of polycystic kidney disease/chronic renal failure with a tumour in his left kidney and of a 75-year-old male with a tumour in his left kidney. Grossly, both tumours were well circumscribed, with solid brown cut surface, measuring 6 and 3,1 cm in the greatest dimension respectively.
Results: On microscopy, both tumours showed a predominantly solid and nested growth pattern. The tumour cells had abundant eosinophilic cytoplasm, with bland low-grade nuclei. Necrosis was not observed. On immunohistochemistry, the tumour cells were strongly and diffusely positive for CK7, while being negative for CD117. PAX8, CK7 and CK8/18 were also positive in both neoplasms, while all tumour cells were negative for Vimentin, CD10 και CAIX. Based on these features, a diagnosis of low-grade oncocytic tumour of kidney was given.
Conclusion: Low-grade oncocytic tumour of the kidney is a new category in the family of renal cell tumours that should be distinguished from other renal epithelial cell tumours showing eosinophilic cytoplasm, as the former is an indolent neoplasm and carries good prognosis.

E-PS-24-057

Renal oncocytomas: morphological and immunophenotypical variability in central scar

M. Pané-Foix*, D. Fernández-Calvo, A. Domingo Rubio, N. Espejo-Herrera, E. Condom, M.R. Taco, M. Gomà Gallego, M.Á. López, A. Vidal
*Pathology Department - Hospital Universitari de Bellvitge, Spain

Background & objectives: Renal oncocytomas (RO) usually present areas of scarring. Cellular groups adjacent/enclosed within often exhibit a different morphology from the rest of the tumour. The aim of this work is to verify these morphological changes and to characterize its immunophenotype.
Methods: Cases of RO diagnosed between 2016-2022 (N=103) were reviewed and those in which an area of central scar was observed (N=20) were selected. The presence of morphological changes in cell groups encompassed in the scar was verified and an immunohistochemical panel was applied: CK7, Vimentin, Racemasa (AMACR), Carbonic Anhydrase IX (CAIX), Napsin, CD117.
Results: Twenty cases that contained, at least focally, areas of tubular morphology within the fibrous scar were identified. These areas, unlike the rest of the tumour, showed a different morphology characterised by tubular or cord-like architectural patterns, cells with ovoid or spindle-shaped nuclei, clear cytoplasm, and absence of typical oncocytic features. Immunohistochemically they displayed intense positivity for CK7 (in 20/20 cases) and Vimentin (20/20 cases) and tended to lose CD117 expression (negative in 19/20 cases); weaker and more irregular positivity for AMACR (19/20 cases) and Napsin (19/20 cases). CAIX was variably and focally positive (9/20 cases).
Conclusion: Scar areas in RO usually encompass cellular groups with morphology and immunohistochemical profile different from the rest of the tumour. These features could be tentatively interpreted as adaptive changes to hypoxia and/or, considering positivity for AMACR and Napsin A, as a form of nephrogenic metaplasia. It is important to know its existence to avoid, especially in limited samples, confusing OR with other histological types or collision tumours.

E-PS-24-058

Differential diagnostics of urothelial lesions via immunohistochemical method

V. Pechnikova*, L. Mikhaleva, O. Vasyukova, A. Konyukova, K. Maslenkina, A. Birukov, K. Midiber, R. Vandysheva, Z. Gioeva, L. Kakturskiy
*Avtsyn Research Institute of Human Morphology of Federal State Budgetary Scientific Institution "Petrovsky National Research Centre of Surgery", Russia

Background & objectives: To develop a panel of immunohistochemical (IHC) antibodies to simplify the differential diagnosis between urothelial lesions (reactive atypia of bladder vs. urothelial dysplasia).
Methods: The material of the study (histological slides) was obtained from patients with urothelial lesions: 10 cases with verified reactive bladder atypia and 10 cases with urothelial dysplasia. IHC staining was performed using CK7, CK20, Ki-67, p53, CD44, Bcl-2, HER2, Uroplakin III, FGFR3, PTEN and GATA3 antibodies. IHC scoring was completed using the HistoScore (HScore) method.
Results: The study revealed significant differences in HScore values between the two study groups for CK20 ($p=0.021$), p53 ($p=0.018$), Bcl-2 ($p=0.025$), GATA3 ($p<0.001$), HER2 ($p<0.001$) and Uroplakin III ($p<0.001$). Expression of CK20, Bcl-2, GATA3, HER2, and Uroplakin III is significantly more pronounced in the reactive atypia group; on the contrary, dysplasia is characterized by a pronounced reaction with the p53 marker.
Conclusion: The resulting IHC panel of antibodies (CK20, p53, Bcl-2, GATA3, HER2, and Uroplakin III) will improve the differential diagnosis of inflammatory and precancerous lesions for pathologists

E-PS-24-059

Plasmacytoid variant of invasive urothelial bladder carcinoma: a case report

T. Pikivača*, A. Zenko Sever, A. El-Saleh, A. Lukač
*Clinical Department of Pathology and Cytology, University Hospital Centre Zagreb, Croatia

Background & objectives: Plasmacytoid urothelial carcinoma of the urinary bladder is a rare and an aggressive variant of high-grade urothelial carcinoma. It is characterized by somatic mutations of CDH1 leading to frequent loss of E-cadherin expression.
Methods: A 56-year-old man was diagnosed with invasive urothelial carcinoma (pT2) after he underwent transurethral resection of the urinary bladder tumour. The radiological staging of the disease did not show any signs of an extended disease. After neoadjuvant chemotherapy, radical cystectomy with bilateral pelvic lymphadenectomy and resection of the distal portion of the ureters was performed.
Results: Grossly, there was poorly circumscribed thickened area near the trigonum and at the ostia of the ureters. Histologically, the tumour was composed of discohesive plasmacytoid tumour cell aggregates, cords and individual cells, some of which resembled signet-ring cells. The tumour infiltrated the full thickness of the bladder wall, surrounding fatty tissue, seminal vesicles, prostate, prostatic urethra, lymphovascular spaces and the resection margin of the distal portion of the left ureter. There were metastasis in multiple regional lymph nodes. Immunohistochemically, tumour cells were diffusely CD138 positive with the loss of membranous E-cadherin expression. The patient was sent for re-staging, followed by a decision on further treatment.
Conclusion: Awareness of plasmacytoid urothelial carcinoma´s unique morphology and immunohistochemical profile is important to avoid a potential misdiagnosis from its mimics. The discohesive tumour cells can spread extensively along tissue planes and peritoneal surfaces. Compared with conventional urothelial carcinoma, plasmacytoid urothelial carcinomas have a greater chance for higher-stage disease, surgical margin positivity and metastasis at presentation. It is important to make accurate distinction especially on the initial transurethral resection specimens because of the therapeutic and prognostic implications.

E-PS-24-060

Immunohistochemical assessment of PD-L1, Trop2, HER2 as potential targets for renal collecting duct carcinomas therapy, an ancillary study of the BEVABEL GETUG/AFU 024 trial

R. Pirlog*, J. Fontugne, M. Nourieh, C. Krucker, S. Oudard, C. Thibault, Y. Allory
*Institute Curie, Saint Cloud, France

Background & objectives: Renal collecting duct carcinomas (CDC) are an aggressive type of cancer with poor survival. Standard chemotherapy, i.e. platinum agents and gemcitabine, is of limited efficacy. We aimed to investigate the immunohistochemical expression of potential new targets in CDC.
Methods: We included 20 CDC surgical specimens from patients of the prospective BEVABEL trial (NCT02363751). After pathological review, immunohistochemical staining was performed for the following potential predictive biomarkers: HER2 (clone A0485), Trop2 (clone AF650); PD-L1 (clone 22C3). RNA was extracted from from FFPE tumour sections for 3'RNA sequencing.
Results: Immunohistochemical staining was completely negative on tumour cell membranes for both HER2 and Trop2 proteins in all 20 cases, which was consistent with the low mRNA expression of *ERBB2* and *TACSTD2* genes. PD-L1 protein expression evaluated by tumour positivity score (TPS) and combined positivity score (CPS) was high in 4 cases (TPS ≥10%, CPS > 10), low in 6 cases (TPS <10%, CPS < 10) and negative in 10 cases. There was a positive correlation between CD274 mRNA expression and PD-L1 TPS (r=0.60) and CPS (r=0.62) scores, CD274 and CD8A (r=0.51) and CD4 (r=0.55) mRNA gene expression.
Conclusion: HER2 and Trop2 were not expressed on CDC cell membranes, not supporting the use of related antibody-drug conjugates. Nectin4, another possible target, is currently under study. High CPS and TPS PD-L1 was seen in 20% of cases, suggesting a possible benefit of immunotherapy for this subgroup of CDC. Despite an improved morphological definition, CDC remains a heterogeneous tumour group, and further studies integrating immune and tumour cell characteristics for identifying possible therapeutic targets are required.

E-PS-24-061

E-Cadherin expression in different variants of prostate adenocarcinoma

R.M. Plesea*, M. Șerbănescu, F. Giuroiu, R.N. Ciurea, F. Gherghiceanu, I.E. Pleșea
*Department of Cell and Molecular Biology, University of Medicine and Pharmacy of Craiova, Romania

Background & objectives: The study aims to compare the expression of E-Cadherin (ECHAD), one of the main cell adhesion molecules related to epithelial malignancies evolution in the classic form (P_ADK) and the ductal form (D_ADK) of prostate carcinoma (PC) according to Gleason system.
Methods: A series of 435 areas of P_ADK and 90 areas of D_ADK with different Gleason's system patterns were stained with ECHAD. Images were evaluated through a computational algorithm designed by the authors. The location of ECHAD expression was stratified as follows: E1=Membrane only, E2=Membrane+Cytoplasm, E3=Cytoplasm only. Results were compared using chi-square test.
Results: ECHAD expression site evolved differently in the two variants of prostate adenocarcinoma.
In P_ADK, ECHAD had a dominant E1 expression in well-differentiated (WD) areas and evolved towards a predominant E3 expression in poorly differentiated (PD) areas, with a chi-square test p value < 0.0001. In D_ADK, in turn, ECHAD had different types of expression in the four main types of Gleason patterns (chi-square test p value = 0.022) but with an oscillating trend of expression, with obviously dominant E1 expression in the most PD areas (Gleason pattern 5), followed by moderately (Gleason pattern 3) and WD areas (Gleason pattern 2) and predominant E3 expression only in Gleason pattern 4 areas.
Conclusion: The degree of intercellular adhesion, expressed by the ECHAD presence on cell membrane, has different profiles in the main morphological variants of PC. Thus, whereas in classic forms of PC it correlates with lower degrees of differentiation of epithelial malignant proliferation, in ductal adenocarcinoma this correlation is not present, not being statistically validated.

E-PS-24-062

Unusual extragonadal presentation of testicular germ cell tumours

E. Poon*, K. Trpkov, T. Cheng, A. Yilmaz
*University of Calgary, Canada

Background & objectives: Diagnosis of primary testicular germ cell tumour (TGCT) presenting initially with extragonadal metastasis can be challenging. We reviewed our institutional files to identify cases with unusual extragonadal presentations where testis primary was clinically unsuspected.
Methods: 9 patients were identified from our testicular cancer database with 1236 cases over a 20-year period. We documented the clinical and pathologic findings to emphasize the impact and challenge of accurate diagnosis in these unusual clinical settings.
Results: Initial presentation (8/9) included gastrointestinal discomfort(x4), leg swelling/DVT(x3), neck mass(x1); psychiatric disorder/seizures(x1). Extragonadal sites included duodenum(x3), pelvis(x2), thoracic spine(x1), neck node(x1) and abdominal mass(x1). Diagnosis of GCT was established by a biopsy of the extragonadal mass in 6/9 patients and was clinically suspected in 3/9. Testicular primary was confirmed in all cases. Median age was 39 years (range 20-79 years); 3/9 patients were >65 years. Mean tumour size in testis was 1.7 cm (range 0.6-3.5 cm). Treatment included chemotherapy (8/9) and orchiectomy (5/9) which showed seminoma with regression in 3/5 cases, burned-out tumour in 2/5. Two patients died of disease, 7/9 were disease-free.
Conclusion: Diagnosis of TGCT should be included in the differential of extragonadal neoplasms and in patients with a disseminated metastatic disease of unknown primary. Pathologists play a crucial role in the accurate diagnosis and the proper management of a potentially curable disease. Regression related changes at the primary site were a common finding and may have contributed to a clinically unsuspected testicular primary.

E-PS-24-063

Urothelial carcinoma with trophoblastic differentiation – a case report

M.C. Popelea*, D. Porav, A. Loghin
*Pathology Department of Mures County Clinical Hospital, Romania

Background & objectives: Urothelial carcinoma (UC) is a very heterogenous tumour, with a diversity of morphological appearances. Up to 25% of urothelial carcinoma display squamous or glandular differentiation. UC with trophoblastic differentiation is very rare and is associated with a poor prognostic.
Methods: A 64-year-old patient presented in August 2022 at the Urology Department with gross haematuria. A CT-scan revealed a tumour in the bladder, and cystoscopy revealed a multifocal tumour infiltrating the prostatic urethra. TURV was performed and the specimen was sent to our Pathology Department.
Results: Microscopically, we observed a tumour consisting of nests, sheets and trabeculae of tumour cells with a urothelial appearance. The cells presented cyto-nuclear atypia, marked pleomorphism and numerous atypical mitoses. We identified several cells with monstrous nuclei and multinucleated cells with eosinophilic cytoplasm, with an appearance of syncytiotrophoblasts. In immunohistochemistry, tumour cells were diffusely positive for GATA3, CK34βE12 and p63 and syncytiotrophoblastic-like cells were focally positive for β-hCG. The tumour was pT2 pathologic stage, with extensive areas of necrosis. The

morphological aspect and the immnohistochemical profile led to a diagnostic of a UC with trophoblastic differentiation.
Conclusion: UC with trophoblastic differentiation is associated with high-grade UC, poor response to chemo- and radiotherapy, and a worse prognostic than the conventional variant. It is also related with a high risk of recurrence, progression, and death of patients. Therefore, the morphological recognition of this category of UC is important, in order to ensure an individualized therapeutic strategy and the best possible clinical outcome of the patient.

E-PS-24-064
PIN-like carcinoma of the prostate, an incidental finding on a TURP – a case report
M.C. Popelea*, C. Chibelean, I.G. Cocuz, A. Loghin
*Pathology Department of Mures County Clinical Hospital, Romania

Background & objectives: Prostatic intraepithelial neoplasia (PIN)-like carcinoma is an uncommon subtype of prostatic acinar adenocarcinoma, composed of large glands lined by malignant pseudostratified columnar epithelium. Herein, we report a case of a patient clinically diagnosed with prostatic adenoma.
Methods: A 59-year-old patient known with bladder lithiasis since 2016 and benign prostate hyperplasia diagnosed in 2019, presented in January 2023 at the Urology Department with urinary symptoms. The total serum prostate-specific antigen (PSA) was 1,61 ng/ml. Transurethral resection of prostate (TURP) was performed, and the specimen was sent to our Pathology Department for histopathological diagnosis.
Results: Microscopically, the prostatic tissue showed glandular and stromal hyperplasia. On only one fragment a tumoral proliferation was revealed, measuring about 5 mm and consisting of glands of various shapes and sizes, some of them dilated, with intraluminal papillary projections, without a fibrovascular core. The glands were lined by cuboidal or pseudostratified epithelium, with enlarged, elongated nuclei and prominent nucleoli. Immunohistochemically, the tumoral glands were positive for AMACR and negative for p63, highlighting the absence of basal cells. The differential diagnosis was ductal adenocarcinoma and HG-PIN, but both were excluded by the morphology and the immunohistochemical stains. A diagnosis of PIN-like adenocarcinoma was established, Gleason score 3+3=6, grade group 1.
Conclusion: PIN-like carcinoma of the prostate is a relatively new entity, being reclassified as a subtype of acinar prostate carcinoma rather than ductal adenocarcinoma in the 5th edition of the WHO Blue Book. This lesion represents a challenge for pathologists, being particularly important to avoid under or over-diagnosis for optimal treatment and outcome of the patient. In our case, the tumour was identified incidentally, emphasizing once again that a low PSA level does not completely exclude the existence of cancer.

E-PS-24-065
Post immunotherapy nephrectomy specimens - a series of three cases
O.B. Popescu*, E.M. Fernandez, P. González Peramato
*Hospital Universitario de Guadalajara, Spain

Background & objectives: The incidence of kidney cancer has increased. The stage at diagnosis determines treatment options and influences survival. About 15% of cases have disseminated disease without surgical therapeutic option. Immunotherapy treatment is used for patients with advanced metastatic renal cancer.
Methods: We report three cases of radical nephrectomy post neoadjuvant immunotherapy with surgeries performed between 2022 and 2023. All patients were male, mean age 63.3 years (55-67) diagnosed with clear renal cell carcinoma on biopsy. They had distant metastases in lungs, bones and soft tissues and underwent radical nephrectomy after a period of immunotherapy ranging from eight months to one year.
Results: All radical nephrectomy specimens were received in formaldehyde. Before sampling the margins, photographs were taken, and samples were weighed and measured. The mean tumour size was 8.16 cm (7.5-9). Two of the tumours were in the middle zone of the kidney and one in the upper pole. Macroscopically, whitish and firm areas were observed. The tumours were extensively sampled. On microscopic examination, areas of viable residual tumour cells were found ranging from 10% to 30%. Areas of regression showed accumulation of macrophages, fibrosis, inflammatory infiltrate and calcification. The pathologic stages were ypT1a, ypT2a and ypT3a with free margins.
Conclusion: Gross examination and extensive sampling of these specimens is very important. Treatment with immunotherapy produces changes that can be identified macroscopically and histologically and can sometimes be challenging. Adequate sampling provides an adequate result of the percentage of viable residual tumour and evaluation of complete/partial response to treatment. To our knowledge, there are no guidelines on how to sample and report these specimens and as post neoadjuvant immunotherapy treatment is increasingly used there is a need for them.

E-PS-24-066
An audit of the information provided to pathologists on bladder tumour location in transurethral resection of bladder tumour (TURBT) specimens
S. Prendergast*, N. Mayer
*Cork University Hospital, Ireland

Background & objectives: We audited how often tumour location was included in the clinical details accompanying TURBT specimens. A tumour's anatomical location may have staging implications for patients and facilitates tumour identification and sampling in subsequent cystectomy specimens, particularly in the neoadjuvant context.
Methods: TURBTs received in our department between January 1st 2021 and January 1st 2022 were searched for using appropriate SNOMED codes. Inclusion or omission of the tumour's location in the clinical details was recorded in Microsoft Excel. The urology team were surveyed using an online questionnaire to assess if they routinely included this information and were aware of its value.
Results: The standard to be met was that the clinical details should always provide this information. Of 168 TURBTs received, the majority (n=95, 57%) did not state the resected bladder tumour's location on the request form, although this was routinely recorded in the clinical notes. Of these, 17 (18%) had muscle invasive cancer, prompting consideration of cystectomy. The urology team were consulted regarding our initiative to improve provision of this information. A sticker showing a schematic of the bladder was designed and made available in urology theatres. When affixed to specimen request forms, it allows the precise location(s) of a bladder tumour to be marked or drawn out by clinicians.
Conclusion: The provision of details of tumour location with TURBT specimens was inadequate. To implement change, we designed and produced a sticker to be routinely affixed to specimen request forms to capture this information. This will direct block taking for any subsequent cystectomy specimens, particularly in the neoadjuvant setting, leading to optimum diagnoses for patients and reduced block numbers and associated costs. The success of this initiative will be evaluated in a subsequent re-audit to close the audit cycle.

E-PS-24-067
Thyroid-like follicular carcinoma of the kidney, a rare histologic subtype of renal cell carcinoma: a case report
A. Raicea*, A. Loghin, C. Chibelean, T. Csilip, A. Borda
*Pathology Department of Mures County Clinical Hospital, Romania

Background & objectives: Thyroid-like follicular carcinoma of the kidney is a very rare subtype of renal cell carcinoma with histological features similar to those of well-differentiated thyroid follicular neoplasms and is associated with a low malignant potential.
Methods: We report the case of a 57 years-old woman admitted to the hospital during her regular clinical follow-up. An incidentaloma of

the left kidney was found through ultrasonography exam. Following further clinical and paraclinical examinations, a partial nephrectomy was performed. The specimen was sent to the Pathology Department.
Results: Gross examination was specific. A well-circumscribed tumour, with a tan-brown appearance, measuring 2.5 cm (mean size range: 2.8 cm) was identified. Microscopically, the tumour was surrounded by a fibrous capsule and presented a follicular architecture composed of micro and macrofollicles with a "colloid-like" appearance. The cells had amphophilic cytoplasm, with round nuclei and uniform chromatin. Unobtrusive nucleoli, classified as ISUP/WHO grade 2 were observed. Focci of haemorrhage were present. On immunohistochemistry, tumour cells expressed PAX 8, CK 7, CK19, and were negative for TTF-1, CD10 and AMACR, proving their renal origin and excluding a metastatic thyroid carcinoma. The final diagnosis was Thyroid-like follicular carcinoma of the kidney, stage pT1a.
Conclusion: Thyroid-like follicular renal cell carcinoma is a distinct histological subtype of renal cell carcinoma with only a few cases described in the literature (<50). This case illustrates the heterogeneity of this rare renal tumour in terms of morphology and immunophenotype. The tumour shares morphological similarities with primary thyroid follicular carcinoma, but immunohistochemistry is mandatory for establishing a correct diagnosis.

E-PS-24-068
Expression of programmed death ligand -1 and mismatch repair status in renal cell carcinomas
M. Rao*, P. Elhence, A. Nalwa, G.R. Choudhary
*Department of Pathology & Lab Medicine, AIIMS, Jodhpur, India

Background & objectives: Programmed death ligand -1 (PD-L1) is a co-regulatory molecule which suppresses the local immunity. Mismatch repair (MMR) deficiency has been implicated in the pathogenesis of many malignancies and has been reported to influence response to anti PD-L1 targeted therapy.
Methods: Expression of PD-L1 and MLH1, MSH2, MSH6 and PMS2 was assessed by immunohistochemistry (IHC) on 60 resected cases of renal cell carcinomas (RCCs).
Results: Mismatch repair deficiency was noted in 6 cases (10% of the cases), of which five cases showed isolated loss of MLH-1, and one case showed combined loss of MSH2 and MSH6. PD-L1 expression was noted in 12 cases (20%). No significant relation was seen between MMR status and PD-L1 expression in RCCs.
Conclusion: Approximately one fifth of RCC cases express PD-L1. However, mismatch repair deficiency is noted in only 10% of RCCs. More studies on a larger sample size are required to study relation between MMR status and PD-L1 expression in RCCs.
Funding: Institutional Intramural Research Grant

E-PS-24-069
Prostatic cystadenocarcinoma presenting as large pelvic cystic lesions – report of two cases
F. Rosa*, J. Ferreira, F. Santos
*Instituto Português de Oncologia de Lisboa Francisco Gentil, Portugal

Background & objectives: Prostatic cystadenocarcinomas (PC) are exceedingly rare tumours mostly presenting as large pelvic cystic lesions (PCL). Imaging studies often fail to determine their anatomic origin and biopsies are frequently non-diagnostic, rendering pre-operative diagnosis exceptionally challenging.
Methods: We describe two cases of PC presenting as massive PCL without unequivocal continuity with the prostatic gland, according to pre-operative imaging studies and intra-operative findings. The literature was reviewed.
Results: Case 1 refers to a 78-year-old man presenting with a 15,5 cm multilocular PCL. Case 2 refers to a 70-year-old man with a 21,5 cm unilocular PCL. Both had elevated serum PSA and prostatic lesions classified as PiRADS 5 and 4. In case 1, fine-needle aspiration was performed, and the cystic fluid revealed high PSA levels. In case 2, no biopsy or aspiration were performed. Radiologically and intra-operatively, unequivocal prostatic origin was not established. Both PCL were excised without radical prostatectomy. Morphologically, tumours had thick fibrous walls with intracystic papillary formations composed of ductal adenocarcinoma. Neoplastic cells were immunoreactive for PSA and NKX3.1 and negative for p63 and 34βE12.
Conclusion: PC may present as multilocular or unilocular PCL, sometimes lacking unequivocal continuity with the prostate. Association with a suspicious prostatic lesion or known prostatic adenocarcinoma, elevated serum PSA levels and elevated PSA in the cystic fluid may raise concern for this diagnosis. Accounting for the lack of a well-defined histologic spectrum of cystic prostatic lesions, this report raises awareness for this rare and pre-operatively challenging diagnosis.

E-PS-24-070
A recently described entity: papillary renal neoplasm with reverse polarity
D. Sá*, F.S. Vieira, S. Neves, F.E. Costa, J.R. Vizcaíno
*Centro Hospitalar Universitário de Santo António, Portugal

Background & objectives: Papillary renal neoplasm with reverse polarity (PRNRP) was first described in 2019 by Al-Obaidy KI et al. They reported eighteen cases of a distinct subset of papillary renal tumours composed of cells with eosinophilic cytoplasm and apically located nuclei.
Methods: We herein report a case of an 81-year-old man who was submitted to a renal ultrasound due to lower urinary tract symptoms. The ultrasound and subsequent CT scan revealed a renal nodule in the lower pole of the kidney measuring 1,8 cm and 1,6 cm, respectively. To remove this lesion, a partial nephrectomy was performed.
Results: We received a partial nephrectomy specimen almost totally occupied by a tumour measuring 2,4 cm in greatest dimension, well delineated from the adjacent parenchyma and with a solid and tan cut surface. Histologic examination showed a well delineated neoplasia composed of papillae with thin fibrovascular cores covered by cuboidal to columnar cells with granular eosinophilic cytoplasm and apically located and regular nuclei without conspicuous nucleoli (grade 1 WHO/ISUP). Some oedematous papillae were also seen. Immunohistochemistry revealed expression of CK7 and GATA3 in the neoplastic cell with negativity for AMACR. Idylla® PCR molecular testing revealed a KRAS missense mutation involving c.35G>T resulting in p.G12V.
Conclusion: Papillary renal neoplasm with reverse polarity is described in the WHO classification of tumour as a distinct pattern of papillary renal cell carcinoma. However, these tumours typically have a small size, low pathological stage and an indolent behaviour with no recurrences, metastasis, and disease-related deaths. Furthermore, KRAS mutations are frequent as opposed to 7, 17 and Y chromosomal anomalies, which are rare. For these reasons, recent studies suggest that this tumour should be separated from the papillary renal cell carcinoma.

E-PS-24-071
Renal myopericytoma – report of a very rare case and review of the literature
D. Sá*, G. Carrola, F.S. Vieira, F.E. Costa, J.R. Vizcaíno
*Centro Hospitalar Universitário de Santo António, Portugal

Background & objectives: Myopericytoma is a distinctive perivascular myoid neoplasm. It typically occurs in the skin and soft tissues and is extremely rare in visceral organs, with only 12 cases previously reported in the kidney, to our knowledge.
Methods: We herein report a case of a 69-year-old woman with sarcoidosis that presented with fever of unknown origin. She was submitted to a CT scan that revealed a renal mass in the middle third of the left kidney measuring 2,8cm suggestive of a renal cell carcinoma. To remove this lesion, a partial nephrectomy was performed.

Results: We received a partial nephrectomy specimen almost totally occupied by a tumour measuring 2,5 cm in greatest dimension, well delineated from the adjacent parenchyma, with a solid and brown cut surface. Histologic examination showed a well delineated, non-capsulated neoplasia composed of small to intermediate size vessels surrounded by a concentric proliferation of spindle to ovaloid cells with eosinophilic cytoplasm, elongated to ovaloid regular nuclei without nucleoli. The intervening stroma was oedematous or collagenous. There were no areas of necrosis or atypical mitotic figures. Immunohistochemistry revealed expression of SMA, Collagen type IV, Bcl-2 and CD34 (focal and weak) in the neoplastic cells with negativity for Desmin, HMB-45, Melan-A and STAT6.
Conclusion: Myopericytomas are characterized by a perivascular concentrical proliferation of spindle or ovaloid cells. Typically, these cells express SMA and h-caldesmon and, more rarely, CD34 and desmin on immunohistochemical staining. Some studies also report positivity for Collagen type IV and Bcl2. Tumours located in the kidney tend to be larger than peripheral tumours (5.6cm vs < 2cm). The prognosis of these lesions is excellent with no cases of recurrences or metastasis with the longest follow-up time being 66 months.

E-PS-24-072
A rare subtype of urothelial carcinoma: lymphepithelioma-like carcinoma
D. Sá*, S. Neves, F.S. Vieira, A. Duarte, F.E. Costa, J.R. Vizcaíno
*Centro Hospitalar Universitário de Santo António, Portugal

Background & objectives: In the urinary tract, lymphoepithelioma-like carcinoma (LELC) typically arises in the urinary bladder. It was first reported by Zuckerberg et al in 1991, and it is uncommon with a reported incidence between 0.4 and 1.3% of all bladder carcinomas.
Methods: We herein report a case of an 83-year-old man that went to the emergency department with a three-day history of haematuria. He was submitted to a bladder ultrasound which revealed a 3cm polypoid lesion on the anterior wall. Urinary cytology was suspicious for high grade urothelial carcinoma. The patient was then submitted to a transurethral resection of the lesion.
Results: We received a transurethral resection specimen that weighted 1g and was composed of six fragments. Histologic examination showed fragments of bladder wall infiltrated by a neoplasia characterized by sheets of cells with eosinophilic cytoplasm and round nuclei with prominent eosinophilic nucleoli admixed on an inflammatory background, imparting a syncytial appearance. The tumour was confined to the lamina propria of the mucosa, not invading the muscularis propria. Immunohistochemistry revealed expression of CKAE1/AE3, CK7, p63 and GATA3 in the epithelial cells and CD45 in the inflammatory cells. Chromogenic in situ hybridization (CISH) for the detection of Epstein-Barr virus-encoded RNA (EBER) was negative.
Conclusion: Amin et al. proposed the division of these tumours based on the percentage of LELC pattern with pure, predominant, and mixed types composed of, respectively, 100%, ≥ 50% and < 50% of the tumour with LELC pattern. Some authors report a more favourable prognosis and better response to systemic chemotherapy when pure or predominant. Others have found no differences between LELC and conventional urothelial carcinoma. CISH-EBER has been reported to be consistently negative in different series in these tumours.

E-PS-24-073
Intertubular growth of testicular seminoma; a distinct clinical and pathological entity
E. Salmo*
*Royal Oldham Hospital, United Kingdom

Background & objectives: Intertubular growth of seminoma is a rare entity but present a distinct subset of such tumours. It does not usually present or detected as a mass and may be discovered during work-up for testicular related problems.
Methods: No distinct tumour is grossly apparent in most of these cases. Microscopic examination usually shows the tumour cells to infiltrate between the seminiferous tubules forming no solid lesion. Evidence suggests that this type of seminomas represent a more aggressive seminoma variant.
Results: A 42-year-old man presented with a testicular lesion and clinically suspected to have left testicular cancer. A testis weighing 36.2 grams received at the pathology laboratory showing vague yellow nodule measuring 10mm in diameter which appeared to be limited to the testis.
Microscopy showed a diffuse tumour composed of thin trabeculae and cords of tumour cells showing the typical H&E appearance of a seminoma. The tumour cells were positive for OCT3/4, CD117 and PLAP. There microscopic tumour size measured 20mm in maximum diameter, greater than the documented macroscopic size of 10mm due to the diffuse nature of most of the tumour. The tumour staged as pT1.
Conclusion: A diagnosis of seminoma with intertubular growth was entertained.
Seminomas may present exclusively with intertubular growth with altered echogenicity seen on ultrasound examination in such cases and may feel firm at palpation. It is important to identify this sub-type of seminomas as such tumour appeared to be associated with worse prognosis that the typical pattern of seminomas. In addition, this sub-type of seminomas are associated with prominent lymphocytic infiltrate admixed with the tumour cells making their identification difficult and challenging.

E-PS-24-074
Prognostic significance of inactivated Forkhead Box O1 (FOXO1) in non-muscle-invasive bladder cancer
M.M. Savas*, F. Gürsoy, F.Y. Suçeken, I.E. Zemheri
*SBÜ Ümraniye EA Hastanesi, Turkey

Background & objectives: FOXO1, a transcription factor, promote apoptosis which is known as a tumour suppressor in several types of malignancies including bladder cancer. The present study aimed to determine the alteration of expression of pFOXO1 in patients with bladder cancer.
Methods: 112 consecutive patients who underwent at least two recurrent bladder biopsies in our hospital between 2008 and 2022 were included. The first and the last biopsies of the patients who had recurrence and progression were evaluated in terms of change in pFOXO1 staining, clinicopathological features and prognosis. The Immunoreactivity scoring system (IRS) was used to evaluate nuclear pFOXO1 staining.
Results: At a median follow-up of 43 months, 49 (43.7%) of the 112 patients had shown tumour progression while 63 (56.3%) of those had not. When comparing the last biopsy with the first biopsy, decreased pFOXO1 nuclear staining was associated with progression while increased pFOXO1 nuclear staining was not (p=0.039). On the other hand, in 28 patients (25%) histologic grade was found to be increased, unchanged in 70 of those (62.5%) while decreased in 14 (12.5%). In terms of the last biopsies, significant associations were found between pFOXO1 positivity and pT stage (P<0.001); histologic grade (p=0,023); lenfovascular invasion (p=0,001); lymph node-positivity (p=0,002) and distant metastasis (p=0,002).
Conclusion: Multivariate Cox model showed that pFOXO1 lowness was an independent predictor for prognosis (β=-1,493, P=0.002). In conclusion, staining of pFOXO1 was significantly decreased with higher histological grade, advanced clinical stage and lymph node metastasis in patients with bladder cancer. Thus, pFOXO1 staining may serve as a new prognostic marker for bladder cancer.
Funding: Health Sciences University Umraniye Education and Training Hospital

E-PS-24-075

Immunohistochemical analysis of EGFR, HER2/NEU, ERK and phosphorylated ERK expression in prostatic adenocarcinoma with clinicopathological correlation

A. Shalaby*, H. Mahmoud, S. Al Sinawi, S.A. Saad El-Din
*Oman

Background & objectives: The alterations of EGFR, HER2/neu and RAS/RAF/MEK/ERK signalling are important in carcinogenesis. Their activation in prostate cancer is not fully addressed. we aimed to assess expression of EGFR, HER2-neu, and ERK) in prostatic adenocarcinomas and to correlate with the clinicopathological parameters.
Methods: Immunohistochemistry using tissue microarrays was done for EGFR, HER2/neu, inactive, and phosphor-ERK was performed on tissues from 166 patients. Markers expression and correlation with the clinicopathologic parameters were analysed statistically.
Results: Expression of EGFR, HER2 neu, phosphorylated and inactive ERK was seen in 8.4%, 1.4%, 78.2%, and 83.4% respectively whether low (patchy) or high expression (diffuse). No significant correlations were found between patient criteria and expression of the four studied markers. The negative expression of inactive ERK and EGFR was significantly correlated to the high tumour stage with p values 0.03 and 0.01 respectively.
Conclusion: EGFR and HER2neu may play a limited role in prostatic adenocarcinoma in view of their expression in a small number of cases. The expression of inactive ERK and phosphorylated ERK was appreciated in most cases. Thus, we suggest that EGFR inhibitors may have a limited role in the treatment of castrate-resistant prostate cancer patients, but MEK/ERK inhibitors may be more promising as a targeted therapy, further molecular studies are needed to investigate the exact mechanism and significance of their expression.

E-PS-24-076

Renal cell carcinoma, unclassifed (high grade oncocytic) with MSH6 mutation - a case report

R. Shi*, C.Y. Chow, T.K.Y. Tay, L.Y. Khor
*Singapore General Hospital, Department of Anatomical Pathology, Singapore

Background & objectives: Renal cell carcinoma (RCC), unclassified represents a group of RCC cannot be classified into any established subtypes. They have heterogenous pathological features and usually aggressive clinical course.
Methods: Herein, we report a case of 78 year old male, presented as an incidental finding of a 12cm left kidney tumour during the work-up of loss of weight.
Results: On the histology of radical nephrectomy specimen, the tumour showed exclusive high grade oncocytic morphology with extensive extra-renal extension. The next generation sequencing revealed no known molecularly defined RCC related gene mutation, but a single nucleotide variation of MSH6 gene. The immunohistochemistry staining showed possible subclonal staining patter of MSH6 protein. The patient has been referred to subsequent genetic counselling to rule out Lynch Syndrome.
Conclusion: As MSH6 gene mutation has not been well reported in RCC, unclassified. Our case may contribute a new insight into this group of tumour.

E-PS-24-078

A case report: cystadenoma of the rete testis

S. Stifter-Vretenar*, E.B. Hansen
*Aarhus University Hospital, Denmark

Background & objectives: A finding of cystadenoma in the rete testis is presented. This rare entity can represent a diagnostic pitfall in small testicular cystic lesions since there are far more common conditions such as epididymal cysts, tubular ectasy, or rete hyperplasia.
Methods: A 69 old man was admitted to the urology clinic with a painless mass symptom in the left scrotal region. The sonography evaluation revealed a complex partially extra-testicular overall mediastinum located mass measuring 2.5x3 cm. Clinically was process diagnosed as a multicystic spermatocele. Consequently, was the patient subjected to a left-sided orchidectomy, and the specimen was submitted for pathohistological evaluation.
Results: Pathologic examination revealed a macroscopically inconspicuous collapsed, multiseptated cystic process consistent with a predominantly rete testis origin. Some of the peripherally extra-testicular located cystic spaces had small accumulations of spermatids with a small proportion of venous space appearing congested. The lesion mostly comprised thin-walled fibrous stroma-derivated septated empty cystic space with bland cubic cell epithelial lining and occasional small foci of proliferating, budding, and tufting cells with minimal atypia. The lesion was immunohistochemically AE1/3 and EMA positive. A proliferation rate Ki67 determined was low.
Microscopic appearance and localization of the lesion supported with immunohistochemical analysis (IHC) confirmed the diagnosis of cystadenoma together with a small spermatocele laying peripheral to tumour.
Conclusion: The rete testis cystadenoma is a rare finding. The importance of noting it is in gaining additional information on tumour developmental biology. Furthermore, since benign tumours of the rete testis are rare entities, they can be easily overlooked and misdiagnosed when presented in an initial stage. Therefore, we think this entity is of merit for presentation and should draw our attention since it is one of the differential diagnoses of the multicystic process of the testis and scrotal region.

E-PS-24-079

Diagnostic role and prognostic impact of PSAP immunohistochemistry: a tissue microarray study on 31,358 cancer tissues from 127 different tumour types

L. Tribian*, M. Lennartz, N. Blessin, S. Kind, F. Viehweger, C. Hube-Magg, A. Menz, R. Uhlig, E. Burandt, G. Sauter, R. Simon, M. Kluth, S. Steurer, T.S. Clauditz, C. Bernreuther
*Institute of Pathology, University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: Prostatic specific acid phosphatase (PSAP) protein is produced in prostate epithelial cells and it is used as an immunohistochemical marker for prostate cancer. However, studies have reported PSAP expression to occur in various other tumour entities as well.
Methods: To assess the level of specificity of PSAP expression for prostate cancer and to evaluate the prognostic impact of reduced PSAP expression in prostate cancer, 14,137 tumour samples from 127 different tumour (sub)types, 17,747 prostate cancers, and 8 samples each of 76 different normal tissue types were analysed by immunohistochemistry in a tissue microarray format (TMA).
Results: In prostate cancer, PSAP staining was seen in 100% of Gleason 3+3, 95.5% Gleason 4+4, 93.8% recurrent prostate cancer under androgen deprivation therapy, 91.0% Gleason 5+5 and 31.2% small cell neuroendocrine prostate cancer. Reduced PSAP staining was strongly linked to high pT stage, high Gleason grade, lymph node metastasis, early PSA-recurrence ($p<0.0001$ each),high androgen receptor expression and TMPRSS2:ERG fusions. In multivariate analyses, low

PSAP expression was able to predict PSA recurrence independent of pre- and postoperative prognostic markers in ERG negative cancers. In extra-prostatic cancers, PSAP immunostaining was only seen in 3 of 94 (3.2%) neuroendocrine tumours of the pancreas and in 1 of 129 (0.8%) diffuse type gastric adenocarcinomas.
Conclusion: A positive PSAP immunostaining is highly specific for prostate cancer and reduced PSAP expression is associated with an aggressive prostate cancer phenotype. The independent association of reduced PSAP expression with poor prognosis in ERG negative prostate cancer makes PSAP measurement a candidate marker for prognostic multiparameter panels for prostate cancer.

E-PS-24-080
Tuberous sclerosis - associated chromophobe renal cell carcinoma – a rare case report of a family
C. Valavanis*, E. Souka, N. Skouteris, G. Papageorgiou, N. Charalampakis, G. Stanc
*Molecular Pathology Unit Metaxa Cancer Hospital, Greece

Background & objectives: Tuberous sclerosis complex (TSC) is a genetic disorder characterized by intellectual disability, epilepsy, facial angiofibromas and tumour formation in multiple organs, including the kidney. Renal cell carcinoma occurs in 2%–4% of patients with TSC.
Methods: A case of two sisters, 38-year-old and 36-year-old, respectively, diagnosed with eosinophilic chromophobe renal cell carcinoma, in a randomized control with no systemic manifestations. Both sisters and mother had c.170G>A/p.(Arg57His) mutation in the TSC2 gene in heterozygocity. The father has no TSC2 mutations.
On gross examination both tumours were brown, well circumscribed and solid, measuring 6,5X5X4cm and 8,5X6X5,5cm in dimensions.
Results: Microscopic examination revealed neoplastic cell population of medium sized cells with eosinophilic cytoplasm (> 80% of the cells), perinuclear halo, round nuclei with small rare conspicuous nucleoli. In some areas the nuclei have irregular nuclear membrane, folded or raisinoid. No mitotic figures or necrosis were recognized.
Immunochemistry displayed positivity for CK7, CK8/18, E-cadherin, EMA and CD117. Negative were Vimentin, RCC, CAIX, CD10, HMB45, Melan A, AMACR and PAX-8.
In our case the mutation TSC2 gene in heterozygosity was currently considered to be VUS.
The diagnosis of Chromophobe Renal Cell Carcinoma of eosinophilic variant was made.
Conclusion: The TSC-associated renal cell carcinoma has been recognized for many decades. Based on the bibliography (case series) they tend to occur more often in young females, are multiple or bilateral, with indolent course. Metastases have been reported.
Hybrid Oncocytic / Chromophobe Renal Cell Carcinoma are commonly described in patients with Birt-Hogg Dubé syndrome.

E-PS-24-081
Evaluation of the rates of histological subtypes of urothelial carcinoma (UC) and divergent differentiation on trans-urethral tesection of bladder tumour (TURBT) specimens
C. Ward*, N. Swan
*Saint Vincent's University Hospital, Dublin, Ireland

Background & objectives: The updated WHO Classification of Tumours highlights the prognostic significance of histological subtypes and divergent differentiation of UC. Identification may alter clinical management significantly, while it is suggested they are under-reported. We aimed to assess rates in a tertiary hospital.
Methods: We reviewed histopathology reports of all malignant TURBT cases over a one-year period (August 2020-August 2021). Patients with confirmed UC were included and the rates/types of divergent differentiation and/or histological subtypes were recorded. Clinicopathological data regarding grade (WHO 1973 and WHO 2004), detrusor involvement, stage, carcinoma in situ were also recorded and assessed for report completeness as per RCPath recommendations.
Results: We identified 131 malignant cases on TURBT specimens over the study period. Cases of pure squamous cell carcinoma (2/131) and adenocarcinoma (1/131) without a urothelial component were excluded. Of 128 UCs there were eight cases of divergent differentiation (6.25%) comprised of squamous cell carcinoma (5/8) and small cell carcinoma (3/8). Four histological subtypes were identified (3.13%) including clear cell (2/4), lymphoepithelioma-like (1/4) and micropapillary (1/4). Report completeness was 84.4% with carcinoma in situ the predominant omitted factor (18/128).
Conclusion: Histological subtypes and divergent differentiation in UC are diverse and often subtle. Recognition is crucial given significant implications for treatment and prognostication as outlined in the recent WHO 5th edition. Rates are reported to range from 16-25%, however there is marked heterogeneity across studies. We report rates of 9.38%, suggesting that they are under-reported. Important clinicopathological factors were omitted in 15.6% of reports. These findings highlight the increasing complexity of subspecialties in histopathology and the potential role for standardized reporting.

E-PS-24-084
Metanephric adenofibroma: case report
V. Zakharava*, P. Kisialeu
*N.N.Alexandrov National Cancer Centre of Belarus, Belarus

Background & objectives: Metanephric adenofibroma (MAF) is a rare tumour with a favourable prognosis from metanephric tumour family wich may include the morphologic features between benign pure metanephric stromal tumour and pure metanephric adenoma.
Objective was to study the immunomorphological features of MAF.
Methods: Morphological examination and immunohistochemistry of MAF was performed: CK7, WT1, CD57, Desmin, S100, SMA, CD34, Inhibinα, ER, PR, Ki67. An 18-year-old man presented with a 30*17*27 mm solitary tumour of a lower pole of the left kidney with heterogeneous structure and multiple calcifications, irregular contour extending beyond the renal capsule. Subsequently, laparoscopic resection of the kidney was performed.
Results: Histologically, this was a well-defined tumour with focally irregular margin. The stromal component was prevalent (˜85%) and was composed from fibrous bland spindle and stellate cell tissue with variable size of tubules (small to cystic, CK7+, CD57+/-, WT1-, CD10+/-, Inhibinα-) and a perifocal inflammatory response. The mesenchymal component showed immunoreactivity for CD34 and PR and was negative for SMA, Desmin, Inhibinα, ER, and Ki67 (~1%). The epithelial component was composed of primitive tubules with bland cytology and multiple psammoma bodies. The adenomatous component showed nuclear positivity for WT1 (~90% tubular cells) and PR, cytoplasmic/membrane expression of CD57 and focally CK7, negative staining for CD10, Inhibinα, ER, no mitotic activity (Ki67˂1%).
Conclusion: We report the case of metanephric adenofibroma of the kidney in 18-year-old man, histologically and immunohistochemically presented as a biphasic tumour with a predominance of metanephric stromal tumour component (CD34+ and PR+) and a focal component identical to metanephric adenoma (WT1+, CD57+, focally CK7+ and PR+). Intratumoral angiodysplasia and concentric cuffing of entrapped

tubules ("onion skinning") were absent. The patient was no recurrences during the 8 months of postoperative follow-up.

E-PS-24-085
Molecular classification of urothelial carcinomas of the bladder: study of the north-east population of Morocco
M. Zaryouhi*, A. Douida, H. El Fatemi
*Hassan II hospital University, Morocco

Background & objectives: Molecular classification of bladder carcinoma is an ongoing area of focus in modern oncology. Subtyping is important because it predicts patient outcomes. Our study aims to establish a molecular classification of bladder carcinoma and correlate it with classical histoprognosis factors.
Methods: We included in this retrospective study covering the period from 2012 to 2019 patients with urothelial bladder carcinoma that infiltrate the chorion (pT1 at least). Lesions were classified according to the WHO 2004 classification. Stage, grade, molecular subtypes, recurrence, and survival were studied.
Results: The cohort comprised of 243 patients with a mean age of 62 years. The histological type was urothelial carcinoma, and it infiltrates the muscle in 51%. The most frequent tumour stage is pT1 followed by pT2. An immunohistochemical study was performed in 82 patients for molecular classification according to the approach reported by the MD Anderson group. 39.2% of the cases were classified as Basal subtype, 27.3% of the cases as Luminal subtype and 21.5% of the cases as p53-positive subtype, 12% of the cases were not classified. At the end of this classification, correlations between molecular subtype and histoprognosis factors have been established.
Conclusion: Molecular subtypes of urothelial carcinoma of the bladder have been associated with distinct prognoses and responses to therapies in retrospective studies. If validated, molecular profiling could be integrated into the clinical management of this cancer. Nevertheless, histology will keep an important place to allow a rapid diagnosis at lower costs, but a comparison of the two aspects, molecular and histological, will be essential. Ideally, both classifications should probably be used.

E-PS-25 | E-Posters Other Topics

E-PS-25-001
HEG1 expression in mesothelial tumours
M. Dicleli*, A. Keleş
*Cizre State Hospital, Turkey

Background & objectives: Sialylated protein HEG homolog 1(HEG1), is a mucin-like membrane protein found on mesothelioma. It can detect even sarcomatoid and desmoplastic mesothelioma. We evaluated HEG1 in mesothelial and nonmesothelial tumours to understand the importance of HEG1 expression in determining mesothelial origin.
Methods: Our study included 69 cases of pleura, peritoneum and testis diagnosed with 64 mesothelioma, 3 well-differentiated mesothelial tumour, 2 atypical mesothelial proliferation Also, 25 non-mesothelial (various organ carcinoma metastases, sarcoma and other tumours) tumours were included. Staining scores were calculated for IHC by adding the number of categories for the staining intensity and the staining extension.
Results: HEG1 expression was observed in 68 of 69 mesothelial cases. Although HEG1 expression was observed in most of mesotheliomas, lower scores of HEG1 expression were observed in sarcomatoid mesotheliomas (p=0,043).
Higher scores of HEG1 expression were observed in low-grade epithelioid mesotheliomas than in high-grade epithelioid mesotheliomas (p=0,049).
None of the non-mesothelial tumours (3 pulmonary adenocarcinoma, 3 squamous cell carcinoma, 2 papillary thyroid carcinoma, 2 renal cell carcinoma, 1 large cell carcinoma, 2 colorectal carcinoma, 3 breast carcinoma, 1 urothelial carcinoma, 2 ovarian serous carcinoma 1 sarcomatoid carcinoma, 1 large cell neuroendocrine carcinoma, 1 malignant melanoma, 1 myxoinflammatory fibroblastic sarcoma, 1 solitary fibrous tumour, 1 Ewing sarcoma) HEG1 expression was not observed.
Conclusion: In all of our cases with surface epithelium, the surface epithelium was immunoreactive with HEG1.
HEG1 was observed with higher scores in epithelioid mesotheliomas compared to sarcomatoid mesotheliomas and in low-grade epithelioid mesotheliomas compared to high-grade ones.
While HEG1 was positive in mesothelial tumours, it was negative in all non-mesothelial tumours.
HEG1 was observed with high sensitivity and specificity in mesotheliomas.
HEG1 may be a useful marker to distinguish between mesothelial and non-mesothelial tumours, to show mesothelial origin.

E-PS-25-003
Reducing errors and lost samples in the AP lab through implementing preprocessor scanning
S. Gable*
*Cardiff and Vale University UHB, United Kingdom

Background & objectives: Procedures exist in every histology laboratory to protect samples in the diagnostic process, however, errors still occur. Cardiff and Vale University Health Board implemented a new system to ensure positive identification and tracking of samples and reduce/eliminate sample loss.
Methods: CVUHB conducted an observational study with a new system and workflow that enables pre-processor scanning of histology cassettes in tissue processor baskets. This system reduced manual tasks that are prone to human error, while enabling accurate and definitive monitoring of processing schedules, reagents used, times, and user activities to enhance the traceability of samples throughout the laboratory until final archiving.
Results: Introducing the new workflow at CVUHB from October 2022 to January 2023 resulted in a reduction in time associated with reconciling lost/misplaced samples in the lab workflow. This reduction went from as long as three days to as short as a couple of hours (nearly 82% reduction). All misplaced samples were properly recognized and corrected within 2.5 hours as a consequence of the new system workflow and tracking database. There were 96 potential touch points (prone to error) eliminated in the preprocessing workflow. Time associated with scanning cassettes and baskets was reduced by 91%. These improvements created a more efficient laboratory workflow, reduced stress, and enhanced turnaround times.
Conclusion: Introducing preprocessor sample scanning to the histology lab delivers several advantages beyond sample tracking and patient safety. As cancer incidence rates grow, sample tracking is important to provide a necessary level of patient safety. It also contributes to consistently high sample quality and more efficient laboratory workflows with fewer human errors. This is essential considering the shortage of qualified personnel to support laboratory procedures. The new workflow was more effective at sample tracking and reconciliation than the prior manual workflow.

E-PS-25-004
Use of virtual microscopy in university teaching of pathological anatomy: comparative study with optical microscopy
S. Gharbi*, D. Bacha, I. Mallek, E. Benammou, M. Hajri, H. Mestiri, A. Lahmar, S. Ben Slama
*Department of Pathology, Armand Trousseau Hospital-Sorbonne University, Tunisia

Background & objectives: Interest in virtual microscopy (VM) as a means of simulation learning in pathological anatomy is growing. The objective of our work was to compare the learning by MV to that by MO, in terms of skill acquisition and student satisfaction levels.

Methods: Prospective study, in which ten histological slides were exposed in OM for 21students and in VM for 24students.Thechoice of learning method was made by draw. An evaluation of the acquisition of knowledge was carried-out using multiple-choice questions. An assessment of the degree of satisfaction with the learning method used was based on a questionnaire. Mann-Whitney nonparametric-test was thus used to compare the means between groups.
Results: Regarding the acquisition of knowledge, the scores varied from 8 to 15, with a median of 13/15, for each of the 2 groups. There was no significant difference between the means obtained for each group (respectively 12.67 +/- 0.48 for the OM and 12.75 +/- 0.391 for the MV, $p = 0.935$). Regarding the degree of satisfaction, a statistically significant difference was noted between the 2 groups for each of the 6 items tested. The overall convenience score was significantly better for the VM ($p = 0.001$), whereas for the overall IM score there was no significant difference between the 2 groups ($p = 0.297$).
Conclusion: The performance of the VM is comparable to that of the OM. Taking into consideration its best convenience, VM could serve as an alternative tool to OM in teaching general pathology to students, although it does not fully satisfy their IM.

E-PS-25-005
Revolution in pathology, no more formalin fixation!
M. Hoogland*, A.M. Eshuis, P. van Smeerdijk, J. van der Starre- Gaal
*Isala, The Netherlands

Background & objectives: Formaldehyde is banned, except in medical sector. In 2012 supercritical CO2 in tissue processing was discovered. Validation was performed on formalin-fixed tissues.
We examined morphology and some of the most widely used markers on tissues, freshly processed in supercritical CO2.
Methods: Fresh human tissues were collected and split. One sample processed using conventional methods (FFPE, Formalin Fixed Paraffin Embedded). The second sample freshly processed in non-toxic supercritical CO2 (NFPE, Non Fixed Paraffin Embedded). HE staining was performed and a tissue library was built. Ten widely used histochemical and ten immunohistochemical markers were selected to validate on NFPE tissues.
Results: Six histological markers (Elastica von Giesson, Giemsa, Masson Goldner, PAS, PAS-diastase and Schmorl) needed no adaptations to the standard protocol. Three histological markers (Alcian blue, Azan and Hale's iron) needed small changes to the standard protocol. One histological marker, reticulin, needs a formalin dip to result in a near perfect staining pattern.
Five immunohistochemical markers (cytokeratin AE1/AE3, CDX2, e-cadherin, CD20 and SOX10) needed no adaptations the standard protocol. For three immunohistochemical markers (TTF1, P63, CD3), small changes to the standard protocol were needed. For two markers, (CD68 and PAX-8) all adaptations did result in a more or less usable but not completely specific staining pattern, however not always specific.
Conclusion: Diagnostic tissue processing without formalin is possible, reliable and safe with the use of supercritical CO2. A future with hardly any, or no formaline at all. Nine out of ten tested histochemical markers and eight out of ten immunohistochemical markers perform near perfect on formalin free, processed tissues. One marker, Reticulin, still needs a small amount of formalin in the process to perform well. Two immunohistochemical markers were less perfect, application of another antibody, other epitope might solve this.

E-PS-25-006
Revolution in pathology, no more formalin fixation! Supercritical CO2 tissue processing for immunofluorescence with improved morphology
M. Hoogland*, J. van der Starre- Gaal, N. van der Horst
*Isala, The Netherlands

Background & objectives: Formaldehyde is banned, except in medical sector. In 2012 supercritical CO2 in tissue processing was discovered. Validation was performed on formalin-fixed tissues.
We examined morphology and specificity of immunofluorescence (IF) on tissues, freshly processed in supercritical CO2.
Methods: Appropriate fresh human tissues were collected and split. One sample processed using conventional freezing method (frozen section). The second sample freshly processed in TISPA II tissue processor (NFPE, Non Fixed Paraffin Embedded). HE staining was performed and a tissue library was built. Conventional IF (IgA, IgG, IgM, C3c, C1q, kappa and lambda) were validated on the NFPE tissues.
Results: Several tissues were collected known for their autofluorescence properties for one or more of the tested markers, as well as tonsil tissue, widely used as positive control.
In the HE slides, morphology was markedly superior in the NFPE tissues compared to the frozen slides. IgA, IgG, IgM, kappa, lambda, C3c and C1q all performed as expected, on the NFPE tissues, with minor changes to the conventional protocol (Ventana Benchmark Ultra). Background staining in kappa and lambda improved with a prolonged washing in physiological salt after deparaffination.
Conclusion: Immunofluoresence is usually performed on frozen tissues (used in primary kidney disease and bullous skin disease diagnostics), with a highly specific staining pattern, but with loss of morphology due to freezing artifacts. In the NFPE tissues, both morphology and a highly specific staining pattern are combined.
Diagnostic tissue processing without formalin is possible, reliable and safe with the use of supercritical CO2. A future with hardly any, or no formalin at all.

E-PS-25-007
Carcinoembryonic antigen (CEA) expression in human tumours: a tissue microarray study on 15,413 tumours
K. Jansen*, L. Kornfeld, M. Lennartz, N. Blessin, S. Dwertmann Rico, S. Kind, V. Reiswich, A.M. Luebke, C. Hube-Magg, F. Büscheck, A. Menz, R. Uhlig, G. Sauter, R. Simon, C. Bernreuther
*Department of General, Visceral and Thoracic Surgery, University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: Carcinoembryonic antigen (CEA; CEACAM5) is a cell surface glycoprotein which constitutes an attractive therapeutic target and serum CEA is used for cancer monitoring. CEA is overexpressed in various cancers, but the reported prevalence data vary considerably for many tumour types.
Methods: To comprehensively determine CEA expression in normal and neoplastic tissues, a tissue microarray containing 15,413 samples from 120 different tumour types and subtypes as well as 76 different normal tissue types were analysed by immunohistochemistry.
Results: CEA positivity occurred in 65 of 120 tumour categories including 49 entities with at least one strongly positive case. CEA positivity was most common in colorectal carcinomas (98.7%), other gastrointestinal adenocarcinomas (61.1%-80.3%), medullary carcinomas of the thyroid (96.3%), pulmonary adenocarcinoma (73.7%), mucinous carcinomas of the ovary (79.8%) and the breast (43.2%), squamous cell carcinomas of various sites (30.2%-69.1%), and small cell carcinomas of the lung (64.3%), the urinary bladder (38.9%), and the prostate (50.0%). High CEA expression was linked to high grade ($p<0.0001$) and invasive growth ($p<0.0001$) in urothelial carcinoma. Reduced CEA expression was associated with mismatch repair deficiency ($p<0.0001$) but not with pT and pN stage in colorectal cancer.
Conclusion: In summary, CEA is abundantly expressed in a broad range of epithelial neoplasms. Our data thus identify various tumour entities where CEA positive cancers might best benefit from CEA serum monitoring and anti-CEA therapies.

E-PS-25-008

The opinion of pathology resident physicians on their training as specialists in Spain

F. Leiva-Cepas*, A. Sanz Zorrilla, M.J. Galvez Medina, I. Sánchez Ramírez, S. Haro Yuste, J. Osuna Soto
*University Hospital Reina Sofia, Spain

Background & objectives: The objective of this study is to know the opinion of the residents about the role of their residence tutor, to analyse the characteristics more focused on teaching and to identify the needs that the residents demand from their tutors.
Methods: A cross-sectional study was carried out through a questionnaire addressed to residents in their first-fourth year of specialization. The survey consisted of 24 items and a "Google Form" was used for the survey, with several options for each Likert-type question. The survey was disseminated through different media and through the Spanish Society of Pathological Anatomy.
Results: The survey was disseminated for 12 months, in the period of time prior to the incorporation of the new first-year residents (September 2020). The total sample consisted of 186 answers per multiple choice question and 92 answers in the open question of free response. Of the 186 responses, 21 corresponded to first-year specialists and 12 to second-year specialists. 153 residents of the 4 years of training responded, 35.01% of the total (437 places offered in the last 4 years). This sample is considered representative with a correlation factor of 0.91 according to the regression line between the surveys received and the number of MIR by autonomous community.
Conclusion: Among the different hospitals, there was heterogeneity in the training, the positive evaluation of the tutors and their temporary involvement. Resident physicians consider that little research and case studies are done during training.

E-PS-25-009

Steroidogenic acute regulatory (StAR) protein is a useful marker for sex-cord-stroma tumours and normal/neoplastic adrenocortical tissue

M. Lennartz*, D. Amirzada, N. Blessin, C. Fraune, N. Gorbokon, C. Hube-Magg, T. Krech, A. Hinsch, E. Burandt, G. Sauter, R. Simon, M. Kluth, F. Jacobsen, C. Bernreuther, S. Steurer
*University Medical Center Hamburg-Eppendorf, Germany

Background & objectives: Steroidogenic acute regulatory (StAR) protein is a mitochondrial transport protein with a critical regulatory role for steroid hormone production. As its expression is limited to few normal tissues, the immunohistochemical analysis of StAR was proposed to be diagnostically useful.
Methods: To comprehensively evaluate the diagnostic utility of immunohistochemical StAR expression analysis, a tissue microarray containing 19,202 samples from 152 different tumour types and subtypes and 608 samples of 76 different normal tissue types was analysed by immunohistochemistry (IHC). Melan-A "cross-reactive" data were available from a previous study for comparison.
Results: StAR immunostaining occurred in 198 (1.2%) of the 17,135 analyzable tumours. StAR expression was observed in 27 of 152 tumour categories, 9 of which included at least one strongly positive case. The highest rate of StAR positivity occurred in Leydig cell tumours of the testis and the ovary (100%), steroid cell tumours of the ovary (100%), adrenocortical carcinomas (93%) and adenomas (87%), Sertoli-Leydig cell tumours (67%) and granulosa cell tumours of the ovary (56%) as well as in seminomas (7%). As compared to Melan A, StAR was more often positive in adrenocortical neoplasms and in Leydig cell tumours while StAR (but not Melan-A) was negative in Sertoli cell tumours.
Conclusion: Our data provide a complete overview on the patterns of StAR immunostaining in human tumours and suggest a diagnostic utility of StAR immunohistochemistry for supporting a diagnosis of Leydig cell tumours or of normal or neoplastic adrenocortical tissue. In contrast to Melan A, StAR appears to be more sensitive for these tumours while StAR is always negative in malignant melanoma, a frequent source of adrenal metastasis.

E-PS-25-010

Dielectric permittivity analysis of human tissues

S. Lopez-Prades*, M. Torrecilla, M. Rus-Villena, A. Muñoz, M.T. Rodrigo, I. Archilla, A. Diaz, J.M. O'Callaghan, M. Cuatrecasas
*Hospital Clinic, Barcelona, Spain

Background & objectives: Dielectric permittivity (DP) characterizes the interaction of tissues when exposed to an external electric field. Tissues with different cellular composition will provide different DP values. We aim to determine DP values in healthy human tissues to create a database.
Methods: Prospective observational study of all types of healthy human tissues. Fresh tissue samples are placed in a Teflon® base placed on a scale to ensure optimal pressure (1g) of the coaxial probe for real time DP measurement. After DP measurement, we select the measured area, and conventional FFPE process is performed. H&E slides are reviewed and annotated for any changes.
Results: We analysed 110 healthy tissues from 27 patients, obtained from surgical specimens or autopsies of less than 12 hours: 6 CNS, 1 thyroid, 13 lung, 12 spleen, 15 liver, 7 kidney, 13 salivary gland, 15 fat, 13 skeletal muscle, 14 heart, and 1 tongue. The semi-logarithmic DP graphs showed different patterns depending on the type of tissue. Fat DP values were the most characteristic, showing an almost linear curve, with DP values between 0 and 5, way below other tissue measures. Of notice, histologically visible intrahepatic and intramuscular fat could be predicted by DP measurements, which were lower than permittivity from other liver and muscle samples.
Conclusion: There are differences in dielectric permittivity between different types of healthy human tissues. The DP analysis allows the identification of certain alterations, such as the presence of intrahepatic or intramuscular fat. A DP database of healthy tissues will provide the basis for future applications and could help in the discrimination between healthy and tumoral tissues, among other pathologies.

E-PS-26 | E-Posters One-Day Molecular Diagnostics Pathology Symposium

E-PS-26-001

Platelets–lymphocytes network biomarkers in haematological malignancies by flow cytometry methods

E. Matei*, A. Chisoi, A. Mitroi, M. Aschie, M. Cristian, E. Gheorghe, N. Dobrin, M. Manea
*1 Center for Research and Development of the Morphological and Genetic Studies of Malignant Pathology, "Ovidius" University of Constanţa, Romania

Background & objectives: Acute myeloblastic leukaemia (AML) is characterized by the clonal proliferation of malignant hematopoietic precursor cells in the hematogenous marrow, and non-Hodgkin lymphomas represent malignancies characterized by a monoclonal proliferation of B-cell (BCL) or rarely T-cell.

Methods: Characterization of patients subgroups (AML, age ≤/> 65 years- S1, S2; low BCL- Ann Arbor I-II tumoral stages-S1, high stage BCL- Ann Arbor III-IV tumoral stages-S2; match control healthy patients-C1; C2), CD4+, CD3+ T lymphocytes, platelet membrane glycoproteins (CD42b, CD61), and platelets derived microparticles (CD61-PMP) biomarkers from blood samples were performed by flow cytometry methods.
Results: An intravascular platelets activation in AML patients was observed by increased CD61-PMP expressions than controls (S1-63.97±0.88 vs. C1-34.96±0.82; S2-72.11±0.32 vs. C2-29.26±1.23; p<0.01). CD4+ and CD3+ lymphocytes biomarkers presented differences in AML patients (S1-71.32±1.09 vs. C1-67.05±0.76; S2-64.94 ±0.88 vs. C2-59.92 ±1.33; S1-76.53 ±0.73 vs. C1-71.78±0.91; S2-69.17 ±0.35 vs. C2-58.53 ±1.80; p<0.01). Platelet activation in low-stage BCL patients manifests increased expressions of CD61, CD42 b glycoproteins, and CD4+ lymphocytes reported to controls (S1-51.99±2.65 vs. C1-33.35±2.84; S1-60.74±3.62 vs. C1-48.66±0.76; p<0.01; S1-71.26±1.32 vs. C1-66.92±0.72, p< 0.05). High-stage BCL had lower values for CD-biomarkers reported to controls (CD61-S2-17.61±1.16 vs. C2-28.87±2.09; CD4+-S2-59.45±1.33 vs. C2-67.00±0.94; CD42b-S2-16.60±1.24 vs. C2-49.65±0.65; CD3+-S2-49.29±8.36 vs C2-72.02±1.76; CD 61 PMP-S2-9.30±0.60 vs. C2-35.16±0.81; p<0.01).
Conclusion: Platelet–leukocyte interactions in AML and BCL patients may prove to be a useful tool in different diseases, as biomarkers by flow cytometry. Platelet microparticles show promise as a diagnostic biomarker for diseases and potentially as a delivery system for therapeutics.

E-PS-26-002
Biological mechanisms involved in the prostatic tumorigenesis by flow cytometry methods
E. Matei*, M. Aschie, A. Mitroi, M. Deacu, G.I. Baltatescu, A.A. Nicolau, L.A. Tuta, I.C. Iorga, M. Enciu
*1 Center for Research and Development of the Morphological and Genetic Studies of Malignant Pathology, "Ovidius" University of Constanţa, Romania

Background & objectives: Prostate intratumoral heterogeneity, driven by epithelial-mesenchymal plasticity, contributes to the limited treatment response and therefore is necessary to use the biomarkers to improve patient prognostic survival.
Methods: Characterization of patients groups (prostate adenocarcinoma –PCa; benign prostatic hyperplasia-BPH; controls for experimental groups using non-malignant adjacent tissue samples recovered from patients with PCa or BPH (controls, C), and biological mechanisms studies as cell cycle, cell proliferation by adhesion glycoproteins, and cell apoptosis involved in the evolution of the prostate tumour process were performed by flow cytometry methods.
Results: Proliferative activity (S-phase) revealed lower values of prostate adenocarcinoma (PCa) and benign prostatic hyperplasia (BPH) reported at non-malignant adjacent cell samples (PCa-4.32±4.91; BPH-2.35±1.37 vs. C-10.23±0.43, p<0.01). 68% of BPH cases and 88% of patients with PCa had aneuploidy. Increased values of cell proliferation (CD34+CD61+) were observed in prostate adenocarcinoma and hyperplasia cases reported to non-malignant adjacent cell samples (PCa-28.79±10.14; BPH-40.65±11.88 vs. C-16.15±2.58, p<0.05). CD42b+ cell population with a role in cell adhesion and metastasis had an increased value in PCa cases (38.39±11.23) reported to controls (C-26.24±0.62, p<0.01). The intratumoral expression of CD34 showed an increased pattern of PCa tissue samples reported to controls (PCa-26.12±6.84 vs. C-1.50±0.70, p<0.01).
Conclusion: Flow cytometric analysis of cell cycle, apoptosis, and cell proliferation by adhesion glycoproteins, recommend as efficient methods in diagnostic and therapeutic targets for adenocarcinoma and hyperplasia prostate patients and should be explored in the future for others maligned affections.