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ABSTRACTS

ESP Abstracts 2012

Free Papers

Monday, 10 September 2012, 17.00–19.00, Congress Hall
OFP-01 Oral Free Paper Session Breast Pathology I

OFP-01-001

A study of Sperm-associated Antigen 5 (SPAG5) in predicting response to Anthracycline (ATC)/Platinum Chemotherapies (CT) in breast (BC) & Ovarian Cancers (OVC)

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Objective: SPAG5 plays an essential role in cell cycle progression. In this study the molecular and clinicopathological functions of SPAG5 was investigated.
Method: A series of 171 BC was evaluated for SPAG5 gene copy number (using aCGH) and mRNA expression (using GEA). The expression of SPAG5 protein was evaluated in BC and OCV cell line and in 1650 primary BC. The association between SPAG5 and response to CT was investigated in three independent datasets: 350 ER- BC treated with adjuvant ATC-CT, 250 BC treated with neo-adjuvant (NEO-A)-ATC-CT, and 200 primary OVC treated with cisplatinum.
Results: 5 % of BC showed amplification of SPAG5 locus at 17q11.2. SPAG5 mRNA expression displayed a significant correlation with its copy number. In BC, SPAG5+ was associated with aggressive phenotypes ($p<0.0001$) and poor survivals ($p<0.0001$). Anthracyclin CT had a positive impact on clinical outcome of SPAG5+ BC ($p<0.0001$). SPAG5+ BC received NEO-A-ATC based CT achieved 38 % pathological complete response (pCR) and SPAG5 protien expression was confirmed as an independent predictor for pCR ($p=0.001$). Similarly, SPAG5- OVCs were resistant to platinum ($p<0.001$) and independently associated with poor survival ($p<0.001$).
Conclusion: SPAG5 is an important novel gene implicated in the survival of BC & OVC cells and its protein expression is an independent predictor for CT.

OFP-01-002

Intraoperative evaluation of breast cancer sentinel lymph node metastasis with an automated molecular detection method as an alternative to standard pathological evaluation

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Objective: One-step nucleic acid amplification assay (OSNA) from Sysmex® is an automated system to detect sentinel lymph node (SLN) metastasis in breast cancer patients. This assay is based on the detection of cytokeratin 19 mRNA amplification by reverse-transcription loop-mediated isothermal amplification. Traditionally intraoperative evaluation of SLN is accomplished by cytology and/or frozen section, accounting for heavy workload to pathology department. The objective of this study is to compare the OSNA assay with our standard processing for intraoperative SLN evaluation.
Method: 82 SLN from 45 patients with CK19+ and invasive primary carcinomas where simultaneously evaluated by cytology and/or frozen section and by OSNA assay. Results where compared with gold-standard definitive H&E evaluation (serially sectioned at 150 μm intervals).
Results: The sensitivity and specificity of OSNA assay was 92.3 % and 98.2 %, respectively with a positive predictive value (PPV) and a negative predictive value (NPV) of 96 %. For standard intraoperative evaluation, specificity was 100 % and sensitivity was 73.0 %.

Conclusion: OSNA assay showed similar specificity and higher sensitivity than standard pathologic examination. These findings suggest it can be used as an accurate tool for intraoperative evaluation of SLNs metastasis and possibly contribute to reducing the need for re-intervention for axillary lymph node dissection.

OFP-01-003

Topoisomerase 2A expression as a predictive marker of chemotherapy efficacy in breast cancer patients

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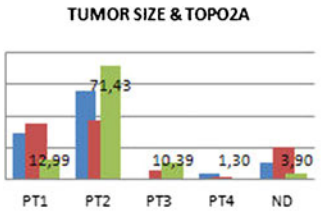
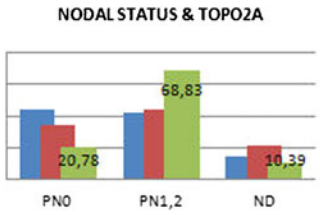
Objective: Antracycline-based chemotherapy represents a standard of care in breast cancer patients especially who overexpress HER-2. Topoisomerase 2A has been considered a molecular target for antracyclines and its co-amplification with HER-2 genes has been proposed. In our study we investigated if Topoisomerase 2A overexpression can be used as a molecular marker on predicting response to antracycline-based chemotherapy.

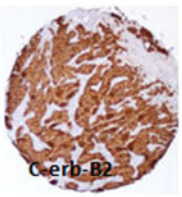
Method: Breast cancers tissues from 40 patients underwent to antracycline-based neoadiuvantchemotherapy and 267 treated with adiuvant therapy were collected into 4 Tissues microarrays, and classified according to pathological stage, ER, PR, HER-2 and TOPO2A status. The expression of topoisomerase 2A has been correlated to response to chemotherapy.

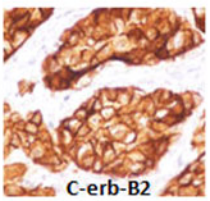
Results: Our results show that TOPO2A expression is significantly higher in neoplasms with larger size, nodal metastasis, scant ER end PR receptors, and amplification of HER-2 gene ($p<0,00$, *T*-test). Cancers in witch high level of TOPO2A has been found exhibit a better clinical response to treatment with anthracycline ($p<0,0000$, *T*-test). Therefore TOPO2A expression could be considered both as predictive and prognostic marker.

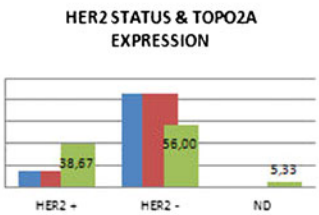
Conclusion: The employment of TOPO2A as a predictive marker in clinical practice may be useful for the medical therapy of non-endocrine-responsive patients candidate to undergo treatment based on anthracycline, that is no free from adverse effects as cardiomyopathy and leukemia.

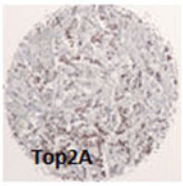


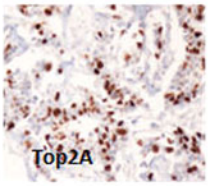


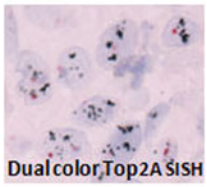


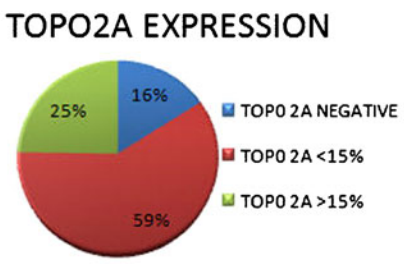












Statistical analysis T-test	Topo 2A negative vs topo2A <15%	Topo 2A <15% vs Topo 2A >15%
variabile	*P value*	*P value*
T	0,0100	0,4157
N	0,0000	0,0001
c-erbB2	0,0000	0,0001
HER2	0,0018	0,0000
Clinical response to therapy	0,0001	0,0035
Hormonal status	0,0018	0,0028

OFP-01-004

Stem cells in triple negative breast cancer and associated in situ lesions

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Objective: Triple negative breast cancer (TNBC) (negative for expression of estrogen and progesterone receptors (ER, PR) and HER2/neu protein) represent a subtype of breast cancer associated with poor prognosis and highly aggresive behaviour. Genetic characterization of stem cell (CD 44,....) in this type of carcinoma might provide important data concerning origin and evolution. Data of the literature focused specifically on TNBC but, despite the interest shown to stem cells recently, there are no data concerning the genetic characterization of stem cells in the context of cell biology of TNBC as compared with associated DCIS.
Method: We investigated, through immunohistochemistry, the expression and distribution of several stem cell/related antigens, exploring the association of TNBC with DCIS and comparing the presence of stem cells in the invasive and in the in situ component.
Results: The multiplicity of parameters to be detected for characterising stem cells and of the diagnostic materials that are available would prevent a straightforward approach and a sequential combination will have to be planned.
Conclusion: Optimization of detection, identification and characterisation of tumourigenic breast cancer stem cells might permit further identification of targeted treatment.

OFP-01-005

Over- and undergrading of Breast Cancer on core biopsies in comparison to surgical specimens

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Objective: To evaluate the relevance of histological grading (HG) based on core biopsies (CB) for clinical decision making in breast cancer (BC) we evaluated the concordance with HG from surgical specimen (SSP) and the reasons for under- or overgrading.
Method: CB and related SSP of 398 BCs were prospectively graded according to the Nottingham grading system (SSP: 65 G1, 162 G2 and 171 G3). CB/SSP agreement rates and positive predictive values (PPV) of CB based HG were calculated. Rates of over- and underestimation of glandular differentiation (GD), nuclear pleomorphism (NP) and mitotic activity (MA) were calculated.
Results: CB/SSP agreement rates came out with 95 % for G1, 73 % for G2, and 56 % for G3. The PPVs of CB based HG were 56 % for G1, 61 % for G2 and 100 % for G3. The overgrading and undergrading rates on CB were 1 % and 37 %, respectively. Main causes for undergrading in CB were underestimated MA (40 %) and a combination of underestimated NP and MA (32 %).
Conclusion: Whereas overgrading on CB is an exception, undergrading derives largely from underestimation of proliferation. Agreement of HG between CB and SSP ranges from almost perfect for G1, moderate for G2 to slight for G3 tumours.

OFP-01-006

Comparative histopathology of mammary alterations in women and dog

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Objective: Companion animals such as dogs share the same environment with people. Mammary tumours are the most prevalent spontaneous neoplasia in intact bitches. More animal models are needed for human mammary tumour research. Our objective was to describe equivalent non-neoplastic and neoplastic mammary gland alterations in woman and dog.
Method: Formalin-fixed, paraffin-embedded archived human and canine mammary gland tissue samples. Epidemiological data were collected and analyzed from human (n=1935) and canine (n=161) patients for the years 2003–2005. Histological comparison was performed with HE-stained tissue sections and immunohistochemistry. Applied antibodies included CK5/6, ERα, PR, Ki67, Her2, p63, SMA, E-cadherin and calponin.
Results: Several comparable benign and malignant mammary gland alterations were identified, consisting of lobular, tubular and ductal as well as mesenchymal of origin. Most of these have not been described previously. The epidemiological results show also shared characteristics.
Conclusion: Although there are canine specific lesions there also exist equivalent entities. Our results indicate the female canine as a suitable model for translational research.

OFP-01-007

St. Gallen intrinsic subtyping of breast cancer: Influence of proliferation assessment methods

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Objective: The St. Gallen Conference 2011 strongly recommends intrinsic subtyping of breast cancer (BC) for therapeutic

decisions. We analyzed the influence of different proliferation assessment methods on the BC subtype distribution.
Method: Intrinsic subtyping was performed according to the St. Gallen criteria on 225 BCs. Proliferation was assessed by Mitotic Activity Index (MAI) (area: 1,59 mm², cut-off ≥10) and by several variants of Ki67-Labeling-Index counting any nuclear staining of (1) 100 tumor cells within the hot spot (Ki67-100), (2) 1020 tumor cells in 3 HPF in the tumor periphery, including the hot spot (Ki67-1020periphery), and (3) 1020 tumor cells in 3 HPF, including hot spot, cold spot and an intermediate area (Ki67-1020spectrum) using the recommended cut-off of <14 %.
Results: Of 225 carcinomas, 10 % were Triple-negative, 2 % Her2+, 6 % Luminal B Her2+, and 9 % Special Type. The rates of Luminal A vs. Luminal B-Her2neg BCs after different proliferation assessment methods were: MAI 49 % vs. 24 %; Ki67-1020spectrum: 34 % vs. 39 %, Ki67-1020 periphery: 24 % vs. 49 % and Ki67-100: 10 % vs. 63 %.
Conclusion: Subtyping of Luminal A and Luminal B Her2-neg BCs according to St. Gallen 2011 is highly influenced by the method of proliferation assessment used. Its biological relevance seems to be not unequivocal.

OFP-01-008

The utility of cytological smears allied to the OSNA method for intraoperative analysis of sentinel lymph-node metastasis in breast cancer patients

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*Loures, Portugal

Objective: One-Step-Nucleic-Acid-Amplification (OSNA) is a recently introduced PCR method to evaluate intraoperative sentinel lymph-node metastasis in breast cancer. It assesses the whole lymph-node in a 20-minutes protocol. Many studies have reported it to be more sensitive than frozen section and/or cytology. Yet, it is more expensive and takes longer to perform.
Method: Between 2010 and 2012 at CHLC, we have performed the intraoperative analysis of sentinel lymph-node using both OSNA and cytological smears in a group of patients.
Results: 35 lymph-node evaluations were done. 16 cases were OSNA positive (5 micrometastasis and 11 macrometastasis). Of those, 11 were also positive for tumor cells on cytological smears. 19 cases were negative by both methods and 5 cases were detected by OSNA but not on cytological smears. Importantly, all macrometastasis diagnosed by cytology were confirmed by OSNA. Of notice, in this series, 69 % of the positive cases detected by OSNA were also detected by cytological smears.
Conclusion: Like previously reported, OSNA showed a greater sensibility than cytology to diagnose sentinel node metastasis. However, the majority of metastasis can be detected by cytological smears alone. Our results suggest that a less expensive and faster cytological analysis should precede OSNA, and if positive, the latter method could be disregarded.

Tuesday, 11 September 2012, 17.00–19.00, Forum Hall
OFP-02 Oral Free Paper Session Breast Pathology II

OFP-02-001

Intraductal concentration of HER2-ECD and CA15-3 in early breast cancers

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Objective: Tumor markers may be concentrated intraductally in early breast cancers.
Method: To test this hypothesis, HER2-ECD and CA15-3 of the needle washout fluid from 29 benign lesions, 26 DCIS, and 95 invasive carcinomas of the breast were measured using chemiluminescence. The measuring limit for HER2-ECD (0.5 ng/ml) and that for CA 15-3 (4 U/ml) were used as the cutoff values, respectively.
Results: The proportion of patients with any biomarker elevation was 6.9 % in cases of benign lesions, 46.2 % in DCIS, and 15.8 % in invasive carcinomas. Thus, biomarker elevation was most frequent in DCIS, followed by invasive carcinomas ($P<0.01$). HER2-ECD values over 6 ng/ml or CA 15-3 values over 25 U/ml were s een exclusively in DCIS or invasive ductal carcinomas with an extensive intraductal component, supporting the hypothesis.
Conclusion: Our approach may be useful to identify a subset of breast cancer patients who are suitable for intraductal molecular targeted therapy.

OFP-02-002

Biological significance of proliferation and HER2 over-expression in luminal/oestrogen receptor-positive breast cancer

D. Jerjees*, A. Green, A. Benhasouna, A. Alshareeda, R. Abduljabbar, F. Barros, C. Nolan, I. Ellis, E. Rakha
*University of Nottingham, Dept. of Oncology, United Kingdom

Objective: In this study, we have compared the biological significance of proliferation; assessed using Ki67 labelling index (Ki67-LI), with respect to HER2 expression in oestrogen receptor positive (ER+) breast cancer to assess the impact on growth fraction and biological characteristics of luminal breast cancer.
Method: 1562 well-characterised ER + breast cancers were assessed for expression of a large panel of biomarkers (no=30).
Results: 53 % of the cases showed high Ki67-LI (>13 %) and 12 % showed HER2 over-expression and both were positively associated with younger age, higher tumour grade, lymph node stage and shorter outcome. Both markers were associated with up-regulation of ER-coactivators (CD71, CARM1, PI3KCA&TK1), P-cadherin, p53 and with lower levels of ER expression and down-regulation of ER-related genes (PgR,

AR&GATA3) and BRCA1. Neither of the two markers was associated with expression of basal-associated cytokeratins. High Ki67-LI was associated with down-regulation of luminal enriched markers including luminal cytokeratins, MUC1, GCDFP-15, FHIT, and transcription and differentiation ER-related genes (FOXA1 and TFF3). In contrast, HER2 expression was associated with up-regulation of luminal cytokeratins, GCDFP-15, FHIT and E-cadherin.
Conclusion: Unlike high Ki67-LI, HER2 overexpression is not associated with the down-regulation of luminal enriched genes. Increased growth fraction in ER + tumours may be driven by different mechanisms in HER2+&HER2- disease.

OFP-02-003
Loss of Drosha expression is associated with poor survival in breast cancer patients
S. Khoshnaw*, T. Abdel-Fatah, C. Nolan, Z. Hodi, E. Rakha, D. Macmillan, I. Ellis, A. Green
*University of Nottingham, Breast Cancer Pathology, United Kingdom

Objective: Drosha is a protein that plays a key role in the biogenesis of microRNAs which are well known to be deranged in human breast cancer. The purpose of this study was to investigate the hypothesis that Drosha is significant in the development and progression of breast cancer and has clinical relevance as a potential predictive and prognostic target.
Method: We have examined Drosha protein expression, using microarray and immunohistochemistry, in a well-characterised series of unselected invasive breast cancer patients (n=750) with long-term follow-up and documented expression characteristics for a large range of biomarkers of known relevance in breast cancer. Furthermore, a smaller cohort of selected breast cancer cases (n=24) was also investigated for differential Drosha protein expression in distinct stages of tumour progression, including in situ (DCIS), invasive and metastatic components.
Results: Drosha cytoplasmic and nuclear expression was lost with cancer progression, and was associated with loss of BRCA1 expression. Multivariate statistical analyses showed that Drosha cytoplasmic expression was an independent predictor of breast cancer specific survival, tumour recurrence and metastases.
Conclusion: Drosha cytoplasmic expression in breast cancer is an independent predictor of patient outcome, tumour recurrence and metastasis. These observations imply that alterations in mechanisms of miRNA regulation can influence tumour behaviour.

OFP-02-004
Prognostic impact of proliferation markers Ki-67, PHH3 and mitotic count in breast carcinomas
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*Haukeland University Hospital, The Gade Institute, Bergen, Norway

Objective: Determination of proliferation in breast carcinomas is highly prognostic and can have treatment implications. However, there is no consensus on issues such as counting area or cut-off values. Our aim was to examine and compare Ki-67 counts in various tumor areas, the novel mitosis marker PHH3, and standard mitotic count.
Method: We examined a nested case–control series (n= 190) as part of the population-based Norwegian Breast Cancer Screening Program. Mitotic count (mitosis per mm2) was assessed on H&E-sections. The percentage of Ki-67 positive nuclei among 500 tumor cells was recorded for both hot-spots (HS; highest proliferation) and cold-spots (CS; lowest proliferation). PHH3 counts (per mm2) were evaluated by immunohistochemistry.
Results: The upper quartiles for Ki-67-HS, Ki-67-CS, PHH3 and mitotic count consistently showed the strongest associations with known unfavorable tumor features (high histologic grade, ER negativity, HER2 positivity, CK5/6+, P-cadherin+). Univariate survival analysis showed comparable prognostic strength of Ki-67-HS, PHH3 count and mitotic count. In multivariate analysis, mitotic count was the strongest prognostic factor among these.
Conclusion: By upper quartile, Ki-67-HS, PHH3 and mitotic count all showed strong associations with various tumor features. In multivariate survival analysis, mitotic count was the strongest proliferation marker.

OFP-02-005
Comparison of Ki67 labelling index of five antibodies in breast cancer and their prediction capacity of disease-free survival
J. Kulka*, A. Kovács, L. Madaras, R. Keszthelyi, Á. Meczker, A. Voigt, R. Hajós, G. Szekeres, M. Szász
*Semmelweis University, 2nd Dept. of Pathology, Budapest, Hungary

Objective: Ki67 LI is a good marker of breast cancer prognosis. We aimed at comparison of performance of 5 Ki67 antibodies.
Method: 283 breast cancer cases were retrieved. Immunohistochemical staining for 5 Ki67 clones (30-9, B56, MIB1, polyclonal, SP6) performed in TMA-s in automated immunostainer. Evaluation performed on digital slides utilizing linear 0–10 frequency score.
Results: Average scores: SP6:3.791, 30-9:3.397, poly:3.054, MIB1:2.395, B56:2.342. Antibodies correlated with the expression of MIB1 (correlation coefficients shown): B56:0.841, 30-9:0.812, SP6:0.784, poly: 0.755. Each clone was able to split prognostic subgroups at 15 % threshold (HRs and 95 % CIs shown): B56:2.750 (1.827–4.138), 30–9:2.291 (1.694–3.099), poly:2.187 (1.560–3.066), MIB1:2.160 (1.499–3.111), SP6:1.629 (1.206–2.203). Cohen's Kappa coefficient was

calculated between MIB1 and other antibodies: 30-9:0.602, B56:0.621, poly:0.665, SP6:0.485, representing moderate (30-9 and SP6) and substantial (B56 and poly) agreement.

Conclusion: Each tested Ki67 clone is suitable for predicting DFS. The clones display different staining frequencies. Grant support: TÁMOP-4.2.2/B-10/1-2010-0013. MKOT-GSK-2010

OFP-02-006

Elemental composition of breast microcalvification: Comparative study in benign and malignant lesions

M. Scimeca*, E. Bonanno, C. Pistolese, F. Dellagatta, L. G. Spagnoli

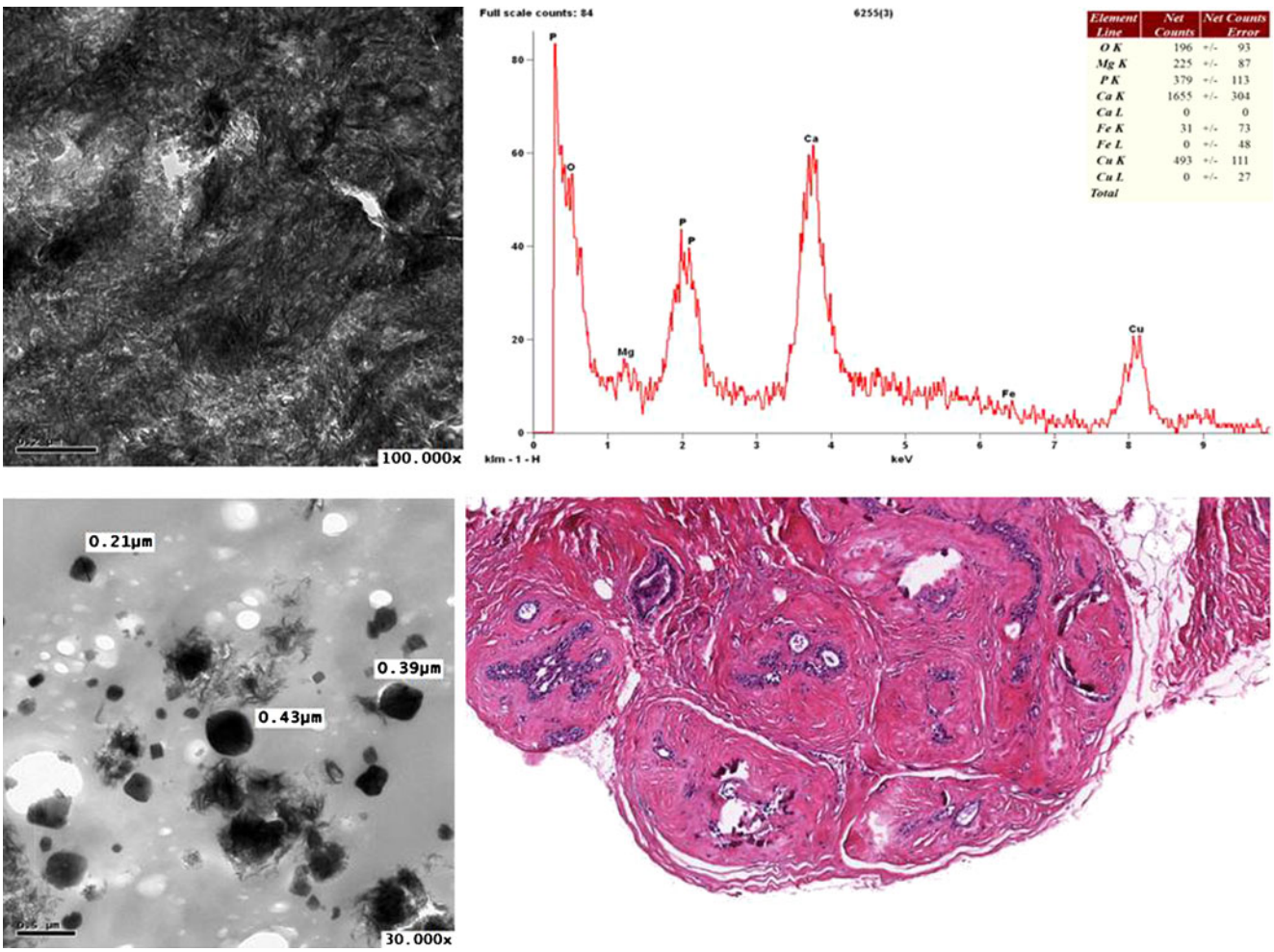
*University Tor Vergata di Roma, Dipr. di Biopathologia, Rome, Italy

Objective: Pattern and density properties of mammary calcifications are used to screen by imaging breast cancer without reference to their elemental composition.

Method: In order to characterize microcalcification composition related to pathology and mammography we utilized ultrastructural microanalysis, to analyze the elemental composition of microcalcifications in 30 mammary biopsies. Microcalcifications were taken from tissue sections and processed for the electron microscopy and microanalysis.

Results: The elemental composition of the microcalcifications of the analyzed tissues demonstrated calcium oxalate in 16 %, hydroxyapatite in 38 % and Mg-substituted hydroxyapatite (Mg-HA) in 46 % of cases. Noteworthy, hydroxyapatite resulted to be present in the 50 % of hyperplasia, in the 33 % of fibrosis and in the 17 % of carcinomas whereas Mg-HA mainly correlated with the ductal in situ carcinoma, 86 %. The density of mammographic Mg-HA is greater than hydroxyapatite and calcium oxalate one.

Conclusion: Our data suggest a strong correlation between Mg-HA and the ductal in situ carcinoma. The ability of these calcifications to sequester interstitial magnesium determines a local magnesium deficiency which could favor the carcinogenesis and/or tumor progression mechanisms. Further studies to correlate mammographic density to the Mg-HA, could improve the discrimination of calcification associated to malignant mammary lesions.



OFP-02-007

Connexin 26 and 46 expression improves prediction of neoadjuvant chemotherapy in breast cancer

I. Teleki*, T. Krenacs, A. M. Szasz, J. Kulka, C. Leo, B. Papassotiropoulos, C. Riemenschnitter, H. Moch, Z. Varga
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Objective: In breast cancer, classification systems are used to assess pathological response to neoadjuvant chemotherapy. Biomarkers are still needed to better predict the efficiency of primary systemic therapy. Dysregulation of connexin (Cx) channels (gap junctions) is involved in carcinogenesis and tumor progression.
Method: We have correlated Cx expression and the pathological response in neoadjuvant treated breast cancers. Fifteen of the 21 human Cx isotypes were pre-screened. Cx26, Cx32, Cx43 and Cx46 were found widespread and tested in tissue microarrays of 96 breast cancers prior to and after neoadjuvant chemotherapy. Pathological response was characterized according to the EWGBSP, CPS-EG, Miller-Payne, Sataloff, and NSABP classification systems.
Results: Only the CPS-EG classification had prognostic relevance by score 1–2 cases presenting better overall survival (p=0.015) than those scoring 3–5. Cx43 levels pre-chemo correlated with hormone receptor status pre- and post-chemo and had inverse correlation with HER2 levels pre-chemo. Reduced Cx26 expression (<5 %) post-chemo correlated with better overall survival (p=0.011). Moderate or higher Cx46 expression (>20 %) pre-and post-chemo was also associated with better survival in the EWGBSP TR2b (ppre=0.006), Sataloff TB (ppre=0.005; ppost=0, 029) and Miller-Payne G3 (ppre=0.002; ppost=0.012) subgroups.
Conclusion: Classifications combined with testing for Cx46 and Cx26 expression can improve prediction of neoadjuvant chemotherapy in breast cancer.

OFP-02-008

Atypical vascular lesions after radiation therapy for breast cancer: A clinicopathologic study and outcomes of 24 cases

H. Gobbi*, C. Fraga-Guedes, M. Mastropasqua, M. Kneubil, E. Botteri, G. Viale
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Objective: We assessed clinicopathologic features and outcomes of 24 cases of atypical vascular lesions (AVL) in patients submitted to radiation therapy for breast carcinoma.
Method: Data from all patients were retrieved from the files of the European Institute of Oncology (EIO), Milan. Histopathological review of all cases was carried out.
Results: All patients were women (median age: 58 year, range: 36–81 year). Median lesion size was 0.5 cm (range: 0.3 to 1.1 cm). Median latency interval from radiation to AVL diagnosis was 49 months (range: 17 to 124 months). 62.5 % of cases presented as an erythematous unique papule confined to superficial/middermis with proliferation of thin-walled, vascular channels, lined by a single layer of bland endothelial cells. No prominent nucleoli, mitoses or blood lakes were seen. Patches of chronic inflammatory infiltrate accompanied all AVL. One patient (4.2 %) developed local recurrence, and two patients (8.3 %) developed angiosarcoma in the previous biopsy site, 19 and 89 months later. Margin involvement was associated to unfavorable outcome.
Conclusion: Our data suggest that post-radiation AVL and angiosarcoma may represent a spectrum of the same disease process. The development of local recurrence and subsequent angiosarcoma indicate that AVL must be completely excised, with free surgical margins, and patients must be accompanied by clinical exams and imaging.

Monday, 10 September 2012, 17.00–19.00, North Hall
OFP-03 Oral Free Paper Session Digestive Diseases Pathology I

OFP-03-001

Gastric dysplasia: Immunophenotypic classification and expression of CDX2 and ALDH1

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Objective: Gastric dysplasia is classified as gastric/foveolar and intestinal/adenomatous according to morphological (architectural and cytologic) features. The immunophenotypic classification of dysplasia, based on the expression of mucins and CD10, recognizes three major types: gastric (MUC5AC and/or MUC6); intestinal (MUC2 and/or CD10); hybrid (gastric and intestinal markers). CDX2 is a transcription factor responsible for early intestinal differentiation. ALDH1 is recognized as a stem cell marker in several organs.
Method: Nineteen cases of dysplasia were classified as gastric/foveolar (n=8) or intestinal/adenomatous (n=11) and graded as low-grade (n=9) and high-grade (n=10). Immunophenotypic classification showed gastric (n=5; 26 %), intestinal (n=6; 32 %) and hybrid (n=8; 42 %) phenotypes.
Results: Cases classified by morphology as gastric/foveolar-type displayed gastric (50 %) or intestinal (50 %) immunophenotype, whereas intestinal/adenomatous-type cases displayed gastric (9 %), intestinal (55 %) or hybrid (36 %) immunophenotype (p=0.023). High-grade dysplasia was identified in cases with gastric (80 %), intestinal (17 %) and hybrid (63 %) immunophenotype (p=0.085). CDX2 expression was significantly lower (p=0.044) in gastric

(60 %) than in intestinal and hybrid immunophenotypes (100 %). ALDH1 expression was displayed only in gastric (80 %) and hybrid (50 %) immunophenotypes (p=0.023).
Conclusion: Gastric dysplasia is heterogeneous and morphology is insufficient to elucidate cell differentiation. High-grade dysplasia, decreased CDX2 expression and high ALDH1 expression are associated with gastric immunophenotype.

OFP-03-002

Tumor budding in pancreatic cancer: Are we missing important prognostic information?

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Objective: Tumor budding is defined as single tumor cells or small cell clusters at the invasive front of gastrointestinal (including colorectal, gastric and ampullary) carcinomas and is linked to adverse prognosis. To date it has not been reported in pancreatic ductal adenocarcinomas (PDACs). We assessed the presence and prognostic importance of tumor budding in PDAC.
Method: Whole-tissue sections of 120 PDACs with full clinico-pathological and follow-up information were stained with pancytokeratin. Tumor budding was assessed in 10 high-power fields (HPFs) by two pathologists and considered high-grade (HG) when an average of >10 buds was counted. Measurements were correlated to the patient and tumor characteristics.
Results: Inter-observer agreement was strong (ICC=0,72). HG-budding was found in 70.3 % of cases and was linked to advanced pT-stage (p=0.0463), lymphatic invasion (p=0.0192) and decreased disease-free and overall survival (p<0,0001 and p=0,0005). There was no association with pN, pM, R-stage or vascular invasion. In multivariate analysis the prognostic effect of HG-budding was independent of lymphatic invasion, pN and R-stage [p<0,0001, HR (95 % CI)=3,65(2,1-6,4)].
Conclusion: Tumor budding occurs frequently in pancreatic cancer, is an indicator of worse outcome and adds independent prognostic information. Routine use of tumor budding would help to better stratify patients into prognostic subgroups.

OFP-03-003

Epstein-Barr virus and p53 in the development of gastric cancer

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Objective: Epstein-Barr virus (EBV) is associated with a subset of gastric cancers (GC). In this study, the prevalence of EBV and its presence in the development of GC were assessed.
Method: EBV was evaluated in GC by tissue microarrays using in situ hybridization for EBER (n=610). Non-tumorous, dysplasia, intramucosal and invasive carcinomas and metastasis of EBV positive GC were analyzed (n=22). p53 expressen was evaluated in EBV positive and a subset of 84 EBV negative GC.
Results: 4.9 % of gastric cancers were positive for EBER. All invasive cancers showed diffuse EBER positivity and only 2 lymph nodes revealed a focal loss of EBER. In 13 GC with foci of atypia/low grade dysplasia, no or only focal EBER positivity was observed. p53 was overexpressed in 24 of 84 EBV negative but not in EBV positive GC (28.6 % vs. 0 %; p=0.007).
Conclusion: EBV is diffusely expressed in invasive GC and only occasionally lost in metastasis. In low grade dysplasia, however, EBV is often focal or missing, indicating that EBV infection may be associated with progression from low grade dysplasia to invasive cancer and this progression is p53 independent.

OFP-03-004

P2X7R attenuates colitis associated carcinogenesis

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Objective: It is now well established that patients with inflammatory bowel disease presented a higher risk to develop a colon cancer. Our previous works characterized the link that exists between bacterial infection and inflammation and highlighted the role of the microenvironment on the onset of chronic inflammation. Here, we wished to understand the role of inflammasome, a complex of proteins that is activated by microbial motifs and the purinergic receptor P2X7 and involved in the maturation of IL-1β.
Method: We treated P2X7R knockout mice to induce acute colitis (3 % DSS) or colitis associated colon cancer (AOM and DSS).
Results: We showed that P2X7R KO mice are more resistant than wild type mice to a DSS-induced colitis. Further, we demonstrated that P2X7R KO mice are highly susceptible to inflammation driven colon tumorigenesis. In addition, we showed that tumors from P2X7R KO contained more neutrophils (CD11b+/Ly6G+cells) and less macrophage (CD11b+/Ly6G–) than tumors obtained from WT mice.
Conclusion: We will present results on the characterization of the pro tumoral tumor associated neutrophils and the molecular mechanisms that are linked to the presence of such immune cells.

OFP-03-005

IEL counts and distribution in normal duodenum, non-GSE IELosis and GSE: Do we need a cut-off?

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Objective: Intraepithelial lymphocytosis (IELosis) is a characteristic feature of gluten-sensitive enteropathy (GSE), though, the cut-off is still debatable. We aimed to evaluate the number and distribution of IELs in normal duodenum, and in non-GSE IELosis and GSE.
Method: The study group comprised of a spectrum of normal duodenal biopsies (n=31), non-GSE IELosis (n=30), Type 1 (n=22) and Type 3 (n=21) serologically diagnosed GSE cases. The number of IELs/100 enterocytes and distribution on H&E and CD3-immunostained sections, were assessed for each group. Chi square test was used for statistics.
Results: IELs increased significantly through the spectrum (15,81–21,55 in normal, 25,73–40,37 in non-GSE, 37,05–54,00 in Type 1, 67,86–85,10 in Type 3) on H&E and CD3, respectively (p<0,001). IEL counts ≥20 on H&E and ≥25 on CD3 had a sensitivity of 95,35 % and 100 %, and a spesificity of 40,98 % and 32,79 %, respectively, for GSE. IEL distribution was diffuse in Type 1 (95,5 %), Type 3 (100 %) but focal in non-GSE (80 %) (p<0,001).
Conclusion: The current cut-off for IEL counts seems to be sensitive for IELosis, though, not specific for GSE and needs to be accompanied by the diffuse distribution of IELs.

OFP-03-006

Geographic analysis of the protein expression of metastasis suppressor gene RKIP and its clinical relevance in colorectal cancer

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Objective: Loss of Raf-1 Kinase Inhibitor Protein (RKIP) expression has been implicated in disease progression in several tumor types. The aim of this study was to evaluate RKIP expression in colorectal cancer stratified by histological "zones" and to determine the zone responsible for its clinical relevance.
Method: Immunohistochemical expression of RKIP was assessed in 100 colorectal cancers using whole tissue sections. Four different areas were evaluated using 10 high-power-fields (HPFs) each: normal mucosa, tumor center, invasion front and tumor buds. The average expression for each zone was assessed for its clinical relevance.
Results: Expression of RKIP was diffuse in normal mucosa and progressively lost towards the tumor center and front (26 %, 15 % and 8 % RKIP-positivity, respectively; p<0.0001). Only 3 % of tumor buds were RKIP-positive. RKIP loss in the tumor center only corresponded to more frequent lymph node positivity (p=0.0766), distant metastases (p=0.0243), lymphatic invasion (p=0.0533) and more advanced TNM stage (p=0.0278). RKIP loss was highly prognostic (HR (95 % CI): 0.45 (0.2–0.9); p=0.0288) independently of TNM and therapy.
Conclusion: The clinical relevance of RKIP is restricted to the tumor center where it acts as an independent prognostic factor. Its absence in tumor buds provides further evidence to support their hypothesized metastatic potential.

OFP-03-007

Outcomes of neoadjuvant chemoradiation for rectal carcinoma

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Neoadjuvant radiation and chemoradiation is currently the treatment of choise for patients with locally or advanced carcinoma of the rectum. Patients treated with neoadjuvant chemoradiatheraphy with good clinical response and tumor regression present a controversial management dilemma. To assess the effects of chemoradiation on tumor regression and disease free survival, consecutive series of 27 patients receiving neoadjuvant chemotheraphy or chemoradiation and a control series of 32 patients without pretreatment were studied. The overall survivals and disease free survivals were compared in terms of variables such as tumor regression grade, stromal response in tumor bed, state of lymph node metastasis, and the localization of the tumor in between patients treated with chemoradiation and the control group. Neoadjuvant treatment is one of the treatment modalities in rectal carcinomas. We want to present our experience between 2005 and 2011 in our institution. Key words: Rectal carcinoma, neoadjuvant treatment, pathologic complete response

OFP-03-008

Identification of Tissue Microvascular Invasion Biomarkers in Hepatocellular Carcinomas by MALDI Imaging Mass Spectrometry

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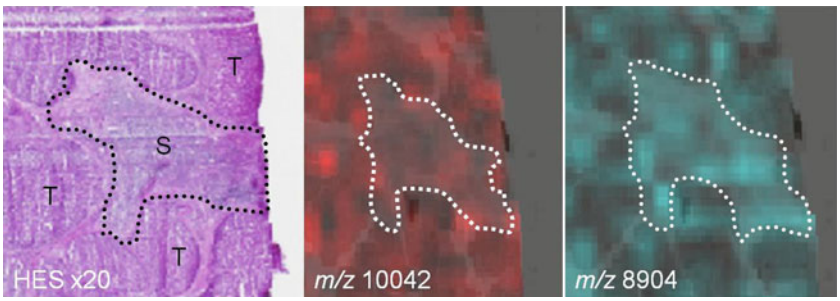
Objective: Microvascular invasion (mVI), a major predictive factor of tumoral recurrence and mortality in patients with hepatocellular carcinoma (HCC), is only detectable on pathological examination. So far, there is no reliable tool to identify mVI prior to surgical procedures. MALDI Imaging Mass Spectrometry (IMS) represents a new analytical tool to provide the relative abundance and distribution of the whole

proteins expressed in a tissue section. The aim of this study was to compare, using MALDI IMS, the tissue proteome of HCC without and with mVI in order to identify surrogate biomarkers of mVI.
Method: A total of 56 HCC samples obtained from surgical specimens, for which frozen samples were available, were retrospectively collected. Two groups of tumors were defined (26 HCC without mVI; 30 HCC with mVI) and were analysed by MALDI IMS. A statistical comparative analysis of acquired mass spectra was then performed in order to identify protein peaks differentially expressed between the two groups.
Results: 30 protein peaks were differentially expressed between the two groups, all overexpressed in HCC with mVI. Protein characterization of some of these peaks is in progress.
Conclusion: These results highlight the potential of MALDI IMS to uncover new biomarkers in liver carcinogenesis. The identification of mVI biomarkers would be helpful in the therapeutic strategy of patients with HCC.



OFP-03-009
A histopathological scoring system can predict the recurrence of hepatocellular carcinoma in liver transplant patients treated with transarterial chemoembolization
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Objective: Aim of this study is to define the histopathological features predictive of hepatocellular carcinoma (HCC) recurrence in patients treated with orthotopic liver transplantation (OLT) after tumoral transarterial chemoembolization (TACE), in order to establish a predictive "score" applicable by pathologists for recipient risk stratification.
Method: We retrospectively enrolled 110 patients (276 total neoplastic or necrotic nodules) who received TACE for HCC downstaging before OLT. The following data were collected: number of neoplastic/necrotic nodules, microscopic thrombosis, the residual neoplastic tissue (RNT), and dysplastic nodules. Sizes, percentage of necrosis, Edmondson's grade, clear cell features were also collected for each nodule.
Results: Median follow-up was 1230 days: 14 (13 %) HCC recurrence cases were recorded. Statistically RNT (best cut-off 3 cm3, P=0.032), the total nodule number (best cut-off ≥ 3, P=0.001), and the neoplastic thrombosis (P=0.011) were the only variables predictive of HCC recurrence. Scoring 1+ each parameter, recipients with 0 (n=43) had 0 % recurrence rate; recipients with 1+/2+ (n=49) had 12 %; recipients with 3+ (n=18) had 44 % recurrence rate (P<0.001).
Conclusion: We were able to stratify OLT recipients with TACE-treated HCC in 3 risk groups based only on histopathological analysis.

OFP-03-010
Discovery of a new histopronostic factor in rectal adenocarcinoma treated by radiochemotherapy followed by surgical resection
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Objective: Neoadjuvant radiochemotherapy (RCT) followed by surgical resection became the treatment for locally advanced rectal cancer. Pathological diagnosis is important for the prediction of prognosis and adjuvant treatment. Study aim was to identify histopronostic factors in a consecutive series of patients treated by RCT and surgery.
Method: 113 patients were included, follow-up, tumor morphologic pattern and Modified Rectal Cancer Regression Grade (m-RCRG) were assessed. Univariate and multivariate analysis were used to assess predictors of disease-free survival (DFS).
Results: 5-years DFS was 58 %. In univariate analysis, ypT, budding, calcifications, circumferential margin, node involvement, invaded margin, vascular emboles and perineural involvement were pronostic factors (p<0.05). In multivariate analysis, presence of calcification in tumor bed (p=0.027) and small circumferential margin (p=0.037) were the only two independent factor of worse DFS. mRCRG was not correlated

to DFS. Among the 50 mRCRG1 tumor, DFS was significantly better in patient with ypT0 than in other ypT stages (p=0.003).
Conclusion: Presence of calcification in tumor bed is a new major histopronostic factor described for the first time in rectal cancer. Our results raised the question of whether ypT stage or histological tumor regression is more important in the prediction of patient prognosis.

Tuesday, 11 September 2012, 17.00–19.00, Club D
OFP-04 Oral Free Paper Session Digestive Diseases Pathology II

OFP-04-001
Histological grading: A prognostic factor for stage I colorectal cancer?
V. Barresi*, L. Reggiani Bonetti, G. Branca, C. Di Gregorio, M. Ponz de Leon, G. Tuccari
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Objective: The most widely used system for histological grading of colorectal cancer (CRC) is based on the degree of gland formation, despite significant interobserver variability and low prognostic value. Herein we analyzed the prognostic significance of a grading system based on the presence of poorly differentiated clusters in stage I CRC.
Method: Poorly differentiated cancer clusters were assessed by two independent pathologists in stage I CRC characterized or not by disease progression. Tumors with <5, 5 to 9, and >10 clusters were classified as G1, G2, and G3, respectively. The prognostic value on disease-free survival and the association with other clinicopathologic characteristics of the conventional and novel grading systems were analyzed.
Results: K statistics for inter-observer variability in the assessment of histological grade based on poorly differentiated custers was 0.728 (good). High histological grade assessed with the novel system, but not with the traditional one, represented a negative significant prognostic factor for disease-free survival and it was significantly associated with venous invasion, lymphatic invasion, budding, invasive growth and nodal micrometastases.
Conclusion: We suggest that a tumor grading system based on the number of poorly differentiated clusters has a stronger power to stratify stage I CRC patients by prognostic outcome than conventional grading.

OFP-04-003
Cytokeratin 7: A marker for BRAF mutated colorectal carcinomas?
S. Gurzu*, Z. Szentirmay, I. Jung
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Objective: Cytokeratin20+/Cytokeratin7− (CK) is used as the characteristic immunophenotype of colorectal carcinomas (CRC). Some new studies suggested that aberrant pattern CK20/CK7 can be identified in colorectal cancer with microsatellite instability (MSI). Our aim was to establish which factors may determine changing in this immunophenotype.
Method: In 70 CRC, randomly selected, we performed immunohistochemical stains with CK20 and CK7 and analyzed the microsatellite status and BRAF mutations with real time PCR.
Results: From the 70 CRC, 15 were MSI and 55 MSS (microsatellite stable) cases. 90 % of MSS cases diffusely expressed CK20 without CK7 expression. From the 15 MSI cases, 6 presented BRAF mutations. In MSI cases with BRAF mutations, CK20 was focally expressed or negative and CK7 was diffusely expressed.
Conclusion: Cytokeratin7 positivity may be used to select BRAF mutated MSI colorectal carcinomas. Both CK7 and CK20 should be used for differential diagnosis of colorectal cancer.

OFP-04-004
Intratumoral budding in preoperative biopsies predicts local and distant metastasis in colorectal cancer patients
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Objective: In 2011, the term "intratumoral budding, ITB" was used to describe the presence of tumor buds within the main tumor body and was correlated to worse clinical outcome in colorectal cancer patients. Here, we further elucidate the potential clinical role of ITB in pre-operative biopsies using pan-cytokeratin stained tissues and a quantitative scoring system.
Method: 139 pre-operative biopsies from patients with colorectal cancer underwent immunohistochemistry for pan-cytokeratin (AE1/AE3). ITB were counted in the area of densest budding (40×) and classified as high-grade when >10 buds/HPF were observed based on receiver operating characteristic (ROC) curve analysis.
Results: High-grade ITB occurred in 26.6 % of cases and was associated with right-sided tumor location (p= 0.0356), more advanced pT (p=0.0198) and pN (p< 0.0001) classifications, distant metastasis (p=0.0164), higher tumor grade (p=0.0037) and lymphatic invasion (p=0.0445). The specificity and positive predictive value for lymph node metastasis was 86.7 % and 75.6 %, respectively. Disease-free survival was significantly worse in patients with high-grade ITB (5-year survival=25 %) in comparison to patients with low-grade ITB (5-year survival= 55 %) (p=0.0157).
Conclusion: The assessment of ITB in pre-operative biopsies is predictive of local and distant metastasis in corresponding resections and should be considered in daily management of colorectal cancer patients.

OFP-04-005

Alpha-methylacyl-CoA (AMACR) in gastric cancer - Correlation with clinicopathological data and disease free survival

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Objective: Diagnostic and prognostic significance of alpha-methylacyl-CoA (AMACR) has been established in many human cancers. Its correlation with clinical and pathological data in gastric cancer has not been fully elucidated and its impact on surveillance has not been studied thus far.
Method: We analyzed consecutive gastric cancer cases in terms of AMACR immunohistochemical expression and clinical/pathological characteristics and followed patients' postoperative history.
Results: AMACR was expressed in 94/164 gastric cancers (57.3 %). We did not find correlation between AMACR expression and gender, age, location, histological type, pTN staging, vascular and nerve sheaths invasion. Overall disease-free survival tended to be worse in AMACR positive patients (p=0.062), and in adenocarcinoma subgroup it was significantly shorter (p=0.021).
Conclusion: AMACR expression might represent promising adverse prognostic factor in gastric cancer, particularly in adenocarcinoma histological type.

OFP-04-006

Development of a rabbit monoclonal antibody for determining hENT1 status and predicting response to gemcitabine in pancreatic ductal adenocarcinoma

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Objective: Human equilibrative nucleoside transporter 1 (hENT1) is the primary membrane channel through which gemcitabine (Gem) enters pancreatic tumor cells, and patients whose tumors have low expression of hENT1 may derive little benefit from Gem therapy.
Method: An analytically validated rabbit monoclonal antibody immunohistochemistry (IHC) in vitro diagnostic (IVD) for assessing the degree of hENT1 expression in pancreatic adenocarcinoma using an automated IHC platform has been developed.
Results: Using primary tumor samples (n=201) from a randomized controlled clinical adjuvant trial (RTOG 97-04), we developed and verified a hENT1 scoring methodology and cut-off for identifying patients least likely to benefit from Gem (hENT1-low). The distribution of hENT1 expression was similar between these samples and an independent set of 130 pancreatic adenocarcinoma specimens from the AIO-PK0104 study of which 77 were confirmed metastatic biopsies. Overall, using this cut-off, approximately two thirds of pancreatic tumors displayed low-hENT1 expression across the different data sets.
Conclusion: A robust hENT1 IHC IVD has been developed using a rabbit monoclonal antibody and identifies two thirds of primary and metastatic PDAC cases as having low expression of hENT1.

OFP-04-007

Hypoxia activates pancreatic stellate cells: Development of an organotypic culture model of thick slices of normal human pancreas

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Objective: Pancreatic stellate cells (PSC) promote oncogenesis by modulating cell proliferation. Aim- To evaluate the early activation of PSC in case of hypoxia in normal human pancreas.
Method: An organotypic culture model of thick sections of human pancreas has been developed and validated. Slices of pancreas (300 μm) were prepared from surgical specimens and cultured in hyperoxia conditions. Half of the samples underwent an initial phase of culture in normoxia (21 % O2) to reproduce hypoxia. The total duration of culture was 72 h. Cell viability, hypoxia, apoptosis and activation were monitored.
Results: 30 sections per specimen were cultured. Analysis was performed at baseline, 24 h, 48 h and 72 h. Morphological analysis showed gradual appearance of ductal/acinar dedifferentiation. At 72 h, foci of necrosis were identified. Hypoxia was confirmed by the expression of HIF1 and CA9 at 48 h (10 % and 50 % of labeled cells). Apoptosis was limited, acinar cells expressed caspase 3 at 48 and 72 h. Analysis of proliferation using Ki67 index showed significant activation of PSC at 48 h (×5/baseline) and at 72 h (×6/baseline). Activation of PSC was confirmed by smooth muscle actin immunochemistry.
Conclusion: Organotypic culture of normal human pancreas is possible with optimized cell viability at 72 h. Hypoxia-induced activation of PSC occurs very early.

OFP-04-008

Intraductal Papillary Neoplasms of the bile duct (IPN): Stepwise progression to invasive carcinoma comprises alterations of KRAS, p53, p16, ß-catenin, HER2, EGFR and smad4

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Objective: IPN are still poorly characterized precursor lesions of bile duct adenocarcinoma. We present a multicenter study with focus on morphology, subtyping and prognosis and provide a detailed molecular analysis in the stepwise progression from low-grade to high-grade lesions and invasive carcinoma.
Method: Fourty-five patients with biliary IPN were included into the cohort, twenty-two patients with conventional adenocarcinoma of the bile duct served as control cohort. Subtyping was performed based on histomorphology and expression profile of mucins and cdx2 expression. Furthermore, low grade lesions (n=14), high-grade lesions (n=38) and invasive components (n=13) of IPN as well as conventional bile duct adenocarcinomas (n=22) were investigated individually for alterations of common oncogenic pathways using immunohistochemistry, real-time polymerase chain-reaction and direct sequencing.
Results: IPN are mainly detected at preinvasive stage (71 %), pancreato-biliary and intestinal type are the most common subtypes (36 and 29 %, respectively). Detailed molecular analysis showed that p53 overexpression, k-ras mutation, loss of heterozygosity of p16 locus and nuclear ß-catenin expression are early events and loss of smad4 and overexpression of EGFR and HER2 are later events in the tumor progression of IPN.
Conclusion: Stepwise alterations of common oncogenic pathways are required for progression of biliary IPN from non-invasive precursors to invasive carcinoma.

OFP-04-009

Influence of BRAF mutations and RAC1b/RAC1 mRNA ratio or protein expression on outcome in patients with metastatic Colorectal Cancer (mCRC) treated with first-line chemotherapy

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*Hospital Clinic, Barcelona, Spain

Objective: Metastatic colorectal cancer (mCRC) patients with BRAF mutation V600E present poor overall survival (OS). RAC1b, a RAC1 spliced variant, is overexpressed in CRC and impairs apoptosis by activation of nuclear-factor-KB. We evaluated if RAC1b was an independent prognostic factor in mCRC.
Method: We examined BRAF (V600E) mutational status, RAC1b by immunohistochemistry, RAC1b/RAC1 expression ratio by mRNA RT-PCR, and mismatch repair (MRR) deficiency by microsatellite instability (MSI) analysis, in 186 mCRC patients treated in first-line therapy with FOLFOX or CAPOX from three Spanish institutions. We assessed whether these biomarkers were independently predictive of progression free survival (PFS) or OS.
Results: 7 % CRC had BRAF mutations, 5 % MSI-H, 20 % high RAC1b/RAC1 ratio, and 25 % RAC1b protein overexpression. Five of 11 CRC (46 %) with BRAF mutations had high RAC1b/RAC1 ratio/protein vs 25/144 (18 %) without BRAF mutation (p=0.036). All BRAF mutated or RAC1b/RAC1 high were MSS. Low RAC1b/RAC1 ratio and BRAF WT had higher response rate (68 % vs 43 %; p= 0.035). Multivariate regression analysis identified ECOG PS as a significant variable for PFS and LDH levels, PS and high RAC1b/RAC1 ratio for OS.
Conclusion: High RAC1b/RAC1 expression ratio or immunoexpression constitutes a marker of poor OS and a potential marker of acquired chemo-resistance in mCRC treated with oxaliplatin-based therapy.

Monday, 10 September 2012, 17.00–19.00, Terrace 1
OFP-05 Oral Free Paper Session Endocrine Pathology

OFP-05-001

Morphological and biochemical atypism of papillary thyroid cancer

T. Pavlova*, I. Pavlov, D. Kolesnicov, L. Pavlova, I. Goncharov, I. Bashuk
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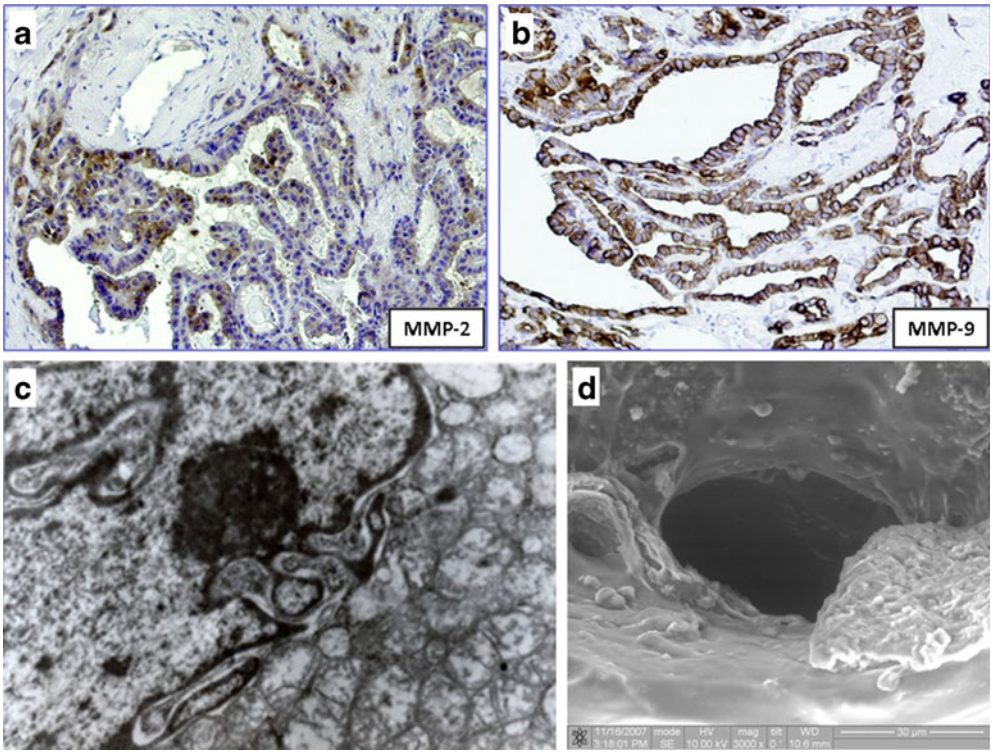
Objective: Annually more than 120.000 new cases of papillary thyroid cancer, that is 1 % of malignant tumors, are registered all over the world.
Method: There are clinical and morphological methods: immunohistochemistry (MMP-2, MMP-9, TIMP-1, TIMP-2), light, transmission, electron, probe and scanning microscopy with the trace element analysis. It was studied 1541 cases of thyroid cancer since.
Results: At the papillary thyroid cancer progression matrix metalloprotease and specific tissue inhibitors of metalloprotease (TIMP-2) increased in the cytoplasm of tumor cells, but the concentration of TIMP-1 decreased. Tumors with low degree of ultrastructural differentiation were presented by cells with electron-dense dark cytoplasm and cells with poor cytoplasm organelles and differently formed nucleus with numerous deep invaginations. High level of some matrix metalloproteaseexpression (MMP-9) and low level of TIMP expression (TIMP-1) were observed in current cases more (45 % and 58 % respectively), than at more differential papillary thyroid cancer (23 % and 37 %). At performance of atomic force microscopy it was shown that connection between cells had become weak at the decreasing of malignancy degree. It was revealed the significant increasing of oxygen, magnium, potassium, calcium in tumor nodes.
Conclusion: Conducted comlex morpho-chemistry analysis display diagnostic patterns of papillary thyroid cancer.



OFP-05-002

Benign Thyroid Nodules with Papillary Hyperplasia (BTN-PH): A retrospective cytological study of 48 cases with surgical follow-up

M. Pusztaszeri*, J. Krane, E. Cibas, W. Faquin
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Objective: Cytological features of BTN-PH, sometimes interpreted as papillary carcinoma (PC) on fine-needle aspiration biopsies (FNAB), have not been studied extensively.
Method: Available material from 48 BTN-PH was reviewed retrospectively and compared with 15 PCs.
Results: FNAB diagnoses were: non-diagnostic (n=1), benign (n=18), AUS/FLUS (n=10), suspicious for follicular neoplasm (n=4), suspicious for malignancy (S-PC) (n=13), and malignant (P-PC) (n=2). The extent of papillary hyperplasia on histology was higher in S-PC/P-PC diagnostic categories (50 %; P=0.019; range: 5–90 %). On cytology, papillary structures, present in 53 % of BPN-PH cases, were more frequent and numerous in the S-PC/P-PC group (89 %; P= 0.0093). Focal nuclear atypia was seen in all S-PC/P-PC cases, including rare grooves (87.5 %), enlargement/crowding (75 %), chromatin clearing/rare pseudoinclusions (25 %), but were less than in PCs (P<0.0001). Nuclei were smaller in BTN-PH than in PCs (mean diameter/range (μm): 8.2/6-12 vs 14.2/7-26; P=0.0001). All BTN-PH tested (n=9) were immunonegative for HBME-1, galectin-3, and keratin-19.
Conclusion: BTN-PH diagnosed as S-PC/P-PC often show papillary structures and focal nuclear features of PC but they are significantly less than in classical PCs, stressing the need to apply strict criteria for PC diagnosis.

OFP-05-003

Genetic alterations in glucagon cell adenomatosis

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Objective: Glucagon cell adenomatosis (GCA) was recently recognized by us as a multifocal neoplastic disease of the endocrine pancreas unrelated to MEN1. Multiple micro- and a few macrotumors are found on the background of a hyperplasia of glucagon cells. The disease may cause unspecific abdominal symptoms and only rarely a glucagonoma syndrome. Recently a mutation in the glucagon receptor (GCGR) gene was described in one GCA patient.
Method: The extracted DNA of five patients with GCA was sequenced and the GCGR gene analyzed for mutations.
Results: Sequencing of the GCGR gene revealed germline mutations in three out of five patients. One patient shows

two different heterozygous point mutations in the hyperplastic alpha cells as well as in the non-tumorous tissue leading to two premature stop codons. One patient harbors a homozygous stop mutation. The third patient shows two homozygous missense mutations of the GCGR gene that most likely also led to a dysfunction of the GCGR. In the two other patients no germ line mutations of the GCGR gene were detected. These variants were not identified in healthy subjects.

Conclusion: The finding of germ line and somatic "loss of function" mutations of the GCGR gene in three of five patients with GCA suggests that a change in the signalling function of the GCGR may cause glucagon cell adenomatosis via glucagon cell hyperplasia.

OFP-05-004

TIMP-1 expression and hypoxia in papillary thyroid carcinoma: Relationship to BRAFV600E mutation and clinical behavior

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Objective: BRAFV600E causes up-regulation of TIMP-1, promoting cell invasion in papillary thyroid carcinoma (PTC). HIF-1α is regulated by hypoxia but also by BRAFV600Emediated signaling pathway in PTC. We assessed the impact on clinical behavior in PTC of TIMP-1, HIF-1α and the hypoxia-inducible CAIX and CAXII.

Method: The protein expression was assessed by Western blot in two cell lines, TPC-1/BRAFWT and BCPAP/BRAFV600E. TMA-immunohistochemistry analysis was used to study protein expression in 114 PTC samples. BRAF status was analyzed by pyrosequencing. Data were correlated with clinicopathological variables of patients.

Results: Higher expression of all proteins was detected in BCPAP exposed to hypoxia. TIMP-1 expression displayed 87 % sensitivity and 83 % specificity for identifying BRAF mutation ($P<0.001$), and was associated with pT-stage ($P=0.001$), pN-stage ($P=0.02$), and multifocality ($P=0.03$). HIF-1α expression was correlated to pT-stage ($P=0.05$). CAIX expression was related to pN-stage ($P=0.02$), and both CAIX ($P=0.004$) and CAXII ($P=0.05$) were highly associated with vascular invasion.

Conclusion: TIMP-1 protein expression is reliable surrogate of BRAF mutated status in PTC. TIMP-1 and hypoxia-regulated proteins have potential for future use as predictors of the malignant change in PTC, and warrant further investigation as new therapeutic targets for the treatment of highly aggressive form of PTC.

OFP-05-005

A microRNA profile signature can distinguish hereditary medullary thyroid carcinoma (HMTC) from sporadic MTC (SMTC)

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Objective: MTC are usually aggressive tumours which account for 3–5 % of all thyroid carcinomas. Most of MTC are sporadic, the remaining tumours are due to hereditary forms with germline activating mutations of the RET proto-oncogene. The aim of this study was to assess the microRNA profiling expression in both sporadic and hereditary forms of MTC.

Method: A total of 40 frozen MTC from patients with well-documented clinico-pathological parameters were used for microarray analyses (14 HMTC and 26 SMTC) using Human MicroRNA Mircoarray Kit version 2 (Agilent Technologies). After identification of a set of miRNA of interest, validation was done using qPCR.

Results: When comparing HMTC harbouring germinal RET mutation with SMTC, seven miRNA were significantly deregulated (miR-96, −10a, −376c, −15a, −7–2*, −106b, −132). The most highly discriminative miRNA in tumoral samples (>3 fold change) identify miR-375, −129-3p, −136, −376c and −451. Moreover, 5 miRNA could segregate MTC with good prognosis and better clinical outcome (miR-137, −144, −224, −144 and −224).

Conclusion: A specific microRNA signature in HMTC can be identified. Moreover, detection of microRNAs in tissue samples might be of interest for improved clinical management and treatment of patients with MTC.

OFP-05-006

Focus on the follicular variant of papillary thyroid carcinoma: Combination of the immunohistochemical markers CK19, HBME1 and TPO is associated with histopathological diagnosis, better than molecular markers

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Objective: The follicular variant (FVPTC) is the major variant of papillary thyroid carcinoma (PTC), ranging from 9 % to 22 % of all PTC. It remains however a problematic entity. Some consider that the encapsulated FVPTC (enFVPTC) have an excellent prognosis like follicular adenomas (FA); others showed that enFVPTCs had potential for hematogenous spread like follicular carcinoma. Its place in the spectrum

of well-differentiated thyroid follicular lesions (WDTFL) is discussed. Our objective was to assess the immunohistochemical and molecular profiles of WDTFL with a focus on FVPTC.
Method: 190 WDTFL (66 PTC, 29 FVPTC, 95 FA) were tested for CK19, HBME1 and TPO expression by immunohistochemistry. Pyrosequencing analysis of BRAF, KRAS, NRAS, HRAS mutations was performed on paraffin-embedded samples.
Results: We identified an immunohistochemical profile HBME1+ and/or CK19+/TPO + associated to FVPTC whereas FA were frequently HBME1-/CK19-/TPO + (kappa=0.73). This association was not reinforced by molecular analysis. Our highly sensitive pyrosequencing method detected NRAS mutation in 28 % FVPTC and 9 % FA. NRAS mutation was significantly associated with TPO expression by multivariate analysis (p=0.01).
Conclusion: We identify an original combination of immunohistochemical markers associated to the diagnosis of FVPTC. NRAS mutation correlates with TPO expression meaning with achieved follicular differentiation. FVPTC appears thereby as an individual entity among WDTFL.

OFP-05-007

Prognostic role of CXCR4 and BRAF V600E analysis in poorly differentiated and anaplastic thyroid carcinomas

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Objective: Poorly differentiated (PDC) and anaplastic thyroid carcinomas (ATC) represent aggressive thyroid cancers both sharing controversial pathogenesis and poor prognostic outlook. CXCR4 is a chemokine inducing cell adhesion associated with tumour progression and nodal spread in WDC. The aim of this study is to compare CXCR4 expression and BRAF mutational analysis in the groups of PDC/ATC respect to WDC.
Method: The study include the surgical specimens of 23 WDC, 23 PDC and 9 ATC on which immunohistochemistry for CXCR4 and mutational analysis for BRAF V600E were carried out.
Results: CXCR4 resulted negative in all PDC/ATC cases and positive in 79 % WDC. A BRAF wild-type was present in all PDC/ATC cases whereas WDC showed a BRAF mutation in 75 % of cases. CXCR4 and BRAF analysis show a significant correlation (p<0.001) in WDC compared with PDC/ATC. CXCR4 predicts nodal involvement (p< 0.002) in WDC, while its absence in PDC/ATC is linked with haematogenous metastases in 54 % of cases.
Conclusion: CXCR4 is important in predicting nodal metastases in WDC whereas its absence is an unfavourable prognostic marker in PDC/ATC. BRAF V600E mutation in WDC predicts a more aggressive behaviour whereas it is constantly absent in PDC/ATC.

Tuesday, 11 September 2012, 17.00–19.00, Terrace 1
OFP-06 Oral Free Paper Session Gynaecological Pathology

OFP-06-001

Human Papilloma Virus (HPV) in patients with cervical pathology compared with general population. A study of 6375 cytology samples in 3 years

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Objective: HPV prevalence and genotypes in correlation with cytological findings in patients with cervical pathology, compared with general population data from the Cervical Cancer screening program in Castilla y León.
Method: We compile 6375 cytological studies made in our Pathology Service, from years 2009, 2010 and 2011. Every sample was taken by liquid-based cytology and a Papanicolaou smear was performed in addition to a HPV testing with the system CLART® HPV2.
Results: We obtained 76,8 % of normal cytological studies, while in general population there are 97 %. The prevalence for high risk viruses was 25.6 %, 3.7 % for intermediate risk and 4.8 % for low risk, while in general population it is of 4 %, 1.2 % and 1.5 % respectively.
Conclusion: The most frequent cytological lesion in our compilation was LSIL (17.6 %) while in general population it is ASCUS (0.8 %). The most prevalent genotype was 16 (9.7 %) while in general population it is placed under low and intermediate risk genotypes. It is important to study women under 35 when they have symptomatology since 60 % of them are positive for HPV (being 45.7 % for high risk HPV) and 45 % have cytological abnormalities.

OFP-06-002

Histological and immunohistochemical characterization of squamous differentiation (SD) in endometrial endometrioid adenocarcinomas (EEASD)

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Objective: SD occurs in≈20 % of endometrial endometrioid adenocarcinomas (EEA), and displays intra/extraglandular, morular (M)/squamoid (S) phenotype which raise diagnostic controversies.
Method: Evaluation of morular, squamoid, and mixed phenotype, p63, CDX2, 34βE12, ER, PR, p53

immunohistochemistry, grade (G), and FIGO stage of EEASD with >10 % SD of Centro Hospitalar S. João (2000–2011) hysterectomies.
Results: 31 EEASD (17 % of EEA) were identified, with 4.4 cm mean size, 65 years mean age, in multiparous (77 %), post-menopausal (81 %) and obese (52 %) women; 67 % EEASD were FIGO stage I, 35 % with vascular invasion (VI); G1(55 %), G2 (32 %), and G3 (13 %). SD: M (29 %), S (52 %), and mixed (19 %); M significantly associates with lower grade and S phenotype with higher grade. M significantly associates with greater extension of CDX2 expression whereas S phenotype associates with p63 extent; 34BE12 was common in well differentiated/keratinized areas of S; and ER, PR and p53 absent/scarce in SD. Overall mean survival: 97 months (CI 95 % 85.3–109.6), and 84 % 5-year survival rate. In univariate analysis: stage and VI were prognostic, but only stage in multivariate analysis.
Conclusion: SD characterization, including p63, CDX2 and 34βE12 immunohistochemistry, may assist differential diagnosis of EEASD, namely with solid patterns and other EEA, and influence treatment option decisions.

OFP-06-003
Liquid-based cytology-new possibilities in the diagnosis of cervical lesions
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Objective: The aim of this study was to analyze the correlation between p16-INK4a and Ki-67 immunoexpression in cervical cytologic samples and human papillomavirus (HPV) detection by polymerase chain reaction (PCR) from the same sample.
Method: Liquid-based cytology (LBC)- cervical cytology samples, prepared and stained by Papanicolaou method (B & D TriPath), were analyzed using Bethesda cytologic classification. A second slide, prepared from the same sample, was immunostained for p16INK4a and Ki-67 using CINtec PLUSCytology Kit (mtm laboratory, Germany). Residual material was used for 14 HR HPV DNA detection by the PCR based cobas test (Roche Molecular Systems).
Results: A total of 50 Pap tests with the following cytologic diagnoses: 6 NILM, 31 ASCUS,5 LSIL, 8 HSIL. Expression of p16INK4a and Ki-67 was detected in all smears with HSIL (8/8) and LSIL (5/5), while in ASCUS – only in 3 of 31. In contrast to HR HPV DNA detected in 7 of 8 HSIL, in 4 of 5 LSIL, in 3 of 31 ASCUS, in 3 of 6 NILM.
Conclusion: We noticed a good correlation between the expression of p16INK4a, Ki-67 and the cobas test results in liquid-based cytology with atypical cells of cervix.

OFP-06-004
Atypical epithelial inclusion in a para-aortic lymph node in a young woman with chlamydia salpingitis
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Objective: Mullerian derivatives often are responsible for epithelial inclusions in the abdominal lymph nodes. It is rare, however, for the epithelial cells to present with cellular atypism.
Results: Case Report: A 24-year old diabetic woman underwent laparotomy under the presumptive diagnosis of ovarian cancer because of elevated levels of CA 125 and CA19-9 and mild FDG uptake of the bilateral uterine adnexa and para-aortic lymph nodes. No gross tumor was found at laparotomy and right salpingectomy with excisional biopsy of the para-aortic lymph node was performed. Pathologic examination revealed acute salpingitis with marked endosalpingiosis involving the peritoneum. The para-aortic lymph node bore several clusters of glandular epithelium showing cellular atypism and a few mitoses. Immunohistochemistry revealed p53 positive cells along with increased MIB-1 reactivity (13 %). The peritoneal glands involved in endosalpingiosis also exhibited p53 immunoreactivity. The patient remains free of symptoms 3 years after the operation with normalized values of the tumour markers and persistent FDG uptake in her ovaries.
Conclusion: It is possible to assume that the epithelial inclusions of the lymph node associated with atypical endosalpingiosis per se might give rise to primary abdominal and pelvic malignancies without involvement of the female genital tract proper.

OFP-06-005
Geometric relations in histologic sections predict the outcome of CIN 1 lesions
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Objective: Cervical Intraepithelial Neoplasias (CIN) are precancerous lesions, which may regress or progress to a higher grade. The analysis of the histologic architecture in neoplasms may reveal information about the pathophysiology, The aim of our study was to investigate whether an analysis of the geometric relations in CIN 1 lesions could help to predict their evolution.
Method: 74 patients with a biopsy-proven diagnosis of CIN 1 were submitted to a second biopsy during follow-up. In routine paraffin sections of the first biopsy, the hematoxylin stained nuclei were interactively marked and their geometric relations (syntactic structure) analyzed by Delaunay triangulation. The prognostic relevance was calculated with the help of Cox regressions.
Results: 19 CIN 1 lesions regressed, 29 patients maintained their diagnosis in the second biopsy and 26 women had

progressed to CIN 2 or 3. The maximum angle of the Delaunay triangels was an important prognostic factor: Cases with large values had an increased probability to progress whereas CIN 1 lesions with smaller ones were prone to regress.
Conclusion: In CIN 1 lesions discrete alterations of the tumor architecture indicate different evolutions and can be used for prognostication. Financial Support: CNPq, FAPESP.

OFP-06-007
Prognostic and Pathogenetic Relevance of Stem Cell Factors for Serous Ovarian Carcinomas
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Objective: Tumor stem cells and reexpression of stem cell factors are thought to contribute to therapy resistance and recurrent disease. Therefore, we performed a comparative analysis of stem cell markers in serous ovarian carcinomas.
Method: 155 ovarian serous carcinomas (147 high-grade, 8 low-grade) were analyzed by immunohistochemistry in a tissue microarray for SOX2, Nanog and Oct4 as well as ALDH1 and proliferation marker Ki67. A double immunostaining experiment compared the percentage of Ki67-positive cells in the ALDH1-positive and -negative cell fractions case by case. The effect on overall and disease-free survival was analyzed (Kaplan-Meier).
Results: Regarding SOX2 we confirmed the association with poorly differentiated tumors and improved recurrence-free survival (median survival 27 months vs. 21 months, $p=0.041$). Oct4 or Nanog were not detected. We observed a correlation between ALDH1 and Ki67, indicating a role of ALDH1 in cell proliferation. However, double staining showed, that ALDH1 is mostly expressed in the in the non-proliferating cell fraction.
Conclusion: Stem cell factors show divergent association with tumor characteristics like poor differentiation or survival (SOX2) and resting populations in proliferating tumors (ALDH1). These findings suggest that stem cell factors in serous ovarian tumors do not reflect a unique stem cell phenotype.

OFP-06-008
Estrogen receptor a loss in endometrial carcinoma is associated with epithelial-to-mesenchymal transition and a potential for PI3Kinase inhibition
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Objective: We hypothesized that ERα loss, associated with poor prognosis in endometrial carcinomas, is reflected in transcriptional signatures representing a molecular basis for tumor phenotype and targets for new therapy.
Method: Endometrial carcinoma samples were analyzed in a primary investigation cohort ($n=76$) and three independent validation cohorts ($n=155/286/111$). Biomarkers were assessed by IHC, DNA oligonucleotide microarray, qPCR, SNP array and sequencing.
Results: ERα loss was correlated to poor prognosis. Activation of genes involved in Wnt-, Sonic hedgehog- and TGF-β signaling was highly associated with loss of ERα ($p<0.001$). An association between receptor loss and activation of EMT was validated in three independent data sets. Transcription factors cross-linking with TGF-β were activated in the ERα negative tumors in an EMT promoting way. Furthermore, drug signatures for PI3Kinase- and mTOR inhibitors were highly significantly associated with the signature for ERα loss. PIK3CA amplification, a PI3K activation score and Stathmin were associated with ERα loss (all $p<0.02$).
Conclusion: ERα loss in endometrial cancer is associated with epithelial-to-mesenchymal transition. Inhibitors of the PI3Kinase-AKT- mTOR signaling pathway as well as EMT inhibitors are supported as promising drugs to be tested in clinical trials in metastatic ERα negative endometrial carcinomas.

Tuesday, 11 September 2012, 17.00–19.00, North Hall
OFP-07 Oral Free Paper Session Haematopathology

OFP-07-001
Comparison of prognostic markers in acute myeloid leukemia
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Objective: In acute myeloid leukemia (AML), several cytogenetic and molecular features are independent prognostic factors. In other malignant diseases descriptors of nuclear chromatin texture have been found to be of prognostic relevance. The aim was to analyze in AML patients the relations between molecular features, morphometric characteristics and methylation pattern in AML and survival.
Method: AML patients without cases of promyelocytic leukemia entered the study. Mutations of FLT3 and NPM1 and the methylation status of CDKN2B, > CDKN2A, CDKN1C, and ESR were recorded. MGG-stained bone marrow blasts were digitalized and studied by computerized texture analysis. The prognostic relevance of molecular and nuclear was studied by Cox regressions.
Results: We studied 87 cases of AML. Blast nuclei of AML without maturation showed higher entropy, contrast, energy and diagonal moment and lower second angular moment. In

the multivariate Cox regression the FLT3-ITD mutation (p= 0.001) was an independent poor prognostic factor, whereas the goodness-of-fit of the Minkowski fractal dimension an independent favorable prognosticator (p=0.025). The karyotype had no influence on survival.
Conclusion: FLT3-ITD and chromatin fractal characteristics were more important as prognostic factors for overall survival than karyotype and gene methylation status. Financial Support: FAPESP and CNPq.

OFP-07-002

Incidence of preclinical manifestations of mantle cell lymphoma and mantle cell lymphoma in situ in reactive lymphoid tissues

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Objective: The prevalence of Cyclin D1 (CyD1) positive B-cells with mantle cell lymphoma (MCL) phenotype in the mantle zones of reactive lymph nodes ("in situ" MCL/MCLIS). and related minimal MCL infiltrates in reactive lymphoid tissues of healthy individuals and in MCL patients are unknown.
Method: All 1.292 reactive lymph nodes from unselected consecutive surgical specimens of 131 patients without a history of lymphoma obtained over a 3 months´ period were stained for CyD1. Additionally, all morphologically reactive lymph nodes and extranodal lymphoid infiltrates of MCL patients from 2000 to 2011 were studied. Samples predating the lymphoma diagnosis for at least 2 months were available from 37/423 (8.7 %) patients.
Results: A MCLIS was not identified. However, in four MCL patients, an early manifestation of MCL with mantle zone growth pattern was detected retrospectively, antedating the lymphoma diagnosis for 3–86 months. In six MCL patients, only small groups of CyD1 positive cells in morphologically reactive extranodal infiltrates were detected more than 2 months before the diagnosis of MCL (range 3–59 months).
Conclusion: MCL "in situ" is an extremely rare phenomenon in morphologically reactive lymph nodes. In MCL patients, however, immunohistochemically detectable infiltrates of MCL cells antedating the lymphoma diagnosis were found in a significant proportion of cases (10/37=27 %).

OFP-07-003

E2F-1's relationship with tumor growth in Hodgkin's lymphoma is regulated by p53 status

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Objective: E2F-1 is a member of the E2F family group of transcriptional factors that play a major role in cell cycle progression and arrest, as well as in apoptosis. In different tumors E2F1 can demonstrate opposing roles, acting either as an oncogene or as a tumor suppressor gene.
Method: We have previously established E2F-1's immunohistochemical expression in Hodgkin lymphoma (HL) and its correlation with p53 expression, although no relationship with either proliferation or apoptosis was demonstrated. A further investigation in a larger series of 100 cases of primary HL with the addition of new apoptotic techniques and the use of p21 expression as an indicator of p53 functional status was undertaken.
Results: Following stratification of our cases based on p53 functionality, E2F-1 was inversely correlated with the proliferation marker TopoIIa. Independently of p53, high levels of E2F-1 expression showed a linear trend with apoptosis and an inverse trend with proliferation (borderline p value in both cases).
Conclusion: Both E2F-1 and p53 activity is upregulated in HL, however it seems that p53 status is a major regulator of the relationship between E2F-1 expression and tumor growth. Alternatively, E2F-1 may use p53-independent pathways to induce apoptosis.

OFP-07-004

EBV replication in tumor samples of Post-transplant Lymphoproliferative Disorders (PTLD) is associated with aggressive clinical course

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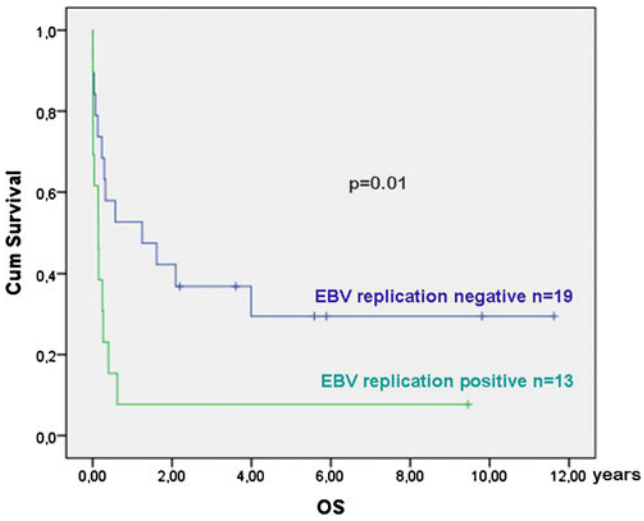
Objective: PTLD represent a spectrum of usually EBV-driven lymphoplasmacytic proliferations in the settings of immunodeficiency associated with allograft. EBV infects cells in latent or lytic forms. Although viral oncogenes are expressed in latency programs, lytic EBV replication is required to develop lymphomas in mouse models. The role of intratumoral EBV replication in PTLD has never been addressed before.
Method: A series of 35 PTLD was reviewed and EBV latency genes were explored in all cases and included EBER1-2, LMP1 and EBNA2. Moreover, two early lytic genes involved in EBV replication, BZLF1/ZEBRA and EAD11 were also analyzed. All clinical and pathological data were collected.
Results: The median age was 50 years (27–77) with a male predominance (26 M: 9 F). EBV infection was observed in 28 cases (80 %). EBV replication was observed in 40 % of the cases. These were more likely to be polymorphic PTLD with latency III in the context of stem cell transplantation. Moreover these cases had atypical clinical presentations such as brain involvement or disseminated disease with aggressive behavior (OS: 11 months vs. 48 months).
Conclusion: EBV replication occurs in tumor cells of PTLD-patients associated with poor outcome and may be

used to select high-risk patients that may benefit of antiviral therapies.



OFP-07-005

Peripheral T cell lymphoma, not otherwise specified, follicular variant with classical Hodgkin-Reed-Sternberg like cells

V. Tabanelli*, E. Sabattini, C. A. Sagramoso-Sacchetti, C. Agostinelli, P. P. Piccaloluga, F. Bacci, A. Gazzola, S. Righi, S. A. Pileri
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Objective: We present the case of a peripheral T cell lymphoma-NOS, follicular variant (PTCL-NOS fv), morphologically resembling the "lymphocyte predominance Hodgkin's lymphoma" subvariant but with a classical Hodgkin's phenotype in the HRS-like cells, occurring in a 69-year-old man first treated as a HL with rapid relapse.
Method: Formalin-fixed paraffin-embedded tissue. Histology: H&E and Giemsa. Immunohistochemistry performed with RealDetection Kit (DAKO). In situ hybridization for EBV with PNA detection kit (DAKO); TCR/IgH/IgL genes rearrangement performed according to Biomed2 protocol.
Results: Histologically, the lymph-node architecture was substituted by vague nodules made of small/medium and few larger mononuclear lymphocytes, admixed with a minor component of HRS-like cells. The phenotype of the former component was: CD3+/CD4+/CD8−/CD2+/CD5+−/CD7−/CD20−/Pax5−/CD30−+/CD15−/PD1+/CD10+/CXCL13−+/Bcl6+/IRF4−+/ki67 60 %. The phenotype of HRS-like cells was: CD30+/CD15−/CD20−/PAX5+/IRF4+/CD4−/CD8−/CD2−/CD5−/CD7−/PD1−/CD10−/CXCL13−/Bcl6−/Ki67+; HRS-like cells were surrounded by neoplastic T cells. EBER was negative in HRS-like and neoplastic T-cells. TCR, but not IgH/Igk, was monoclonally rearranged.
Conclusion: To our knowledge cases of PTCL-NOS fv with HRS-like cells provided with classical phenotype posing the differential diagnosis between composite lymphoma or HL features in PTCL-fv has never been previously reported.

OFP-07-006

Mantle Cell Lymphoma Prognostic Index and proliferative activity are strong prognostic markers in clinical practice: A retrospective study on 235 patients of the Czech Lymphoma Study Group

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Objective: Prognostic factors of mantle cell lymphoma (MCL) are searched as outcome and therapy are heterogeneous and largely unsatisfactory. A new MCL prognostic index (MIPI) has a strong significance in academic studies on selected types of patients, yet it has not been tested in an unselected population. The aim is to test suitability of MIPI for clinical practice in an unselected series.
Method: 235 patients, their FFPE specimens, diagnosed as MCL between 1996 and 2008, followed-up till April 2012. Proliferative activity assessed using Ki-67 immunostaining. MIPI and biological-MIPI were calculated, Kaplan-Meier survival curves and log-rank test were used for statistical analysis.
Results: Median survival (MS) of all patients was 48 months, median progression free survival (MPFS) 22 months. With a cutoff 30 %, cases were divided according to low and high proliferation, with MS 63 and 21 months, (P<0,0001), MPFS 27 and 15 months, (P<0,0001). MIPI distinguished cases with low, intermediate, and high risk, showing MS 101, 58, 24 months, (P<0,0001); MPFS 43, 25, 16 months (P< 0,0001). Biological MIPI distinguished 2 groups, with MS 94 and 24 months (P<0,0001), MPFS 41 and 16 months, (P<0,0001).
Conclusion: This large study with a long follow-up confirms that MIPI, proliferative activity, and biological-MIPI are robust prognostic factors suitable for clinical practice.

OFP-07-007

Immunohistochemistry combined with fluorescent in situ hybridization helps to differentiate CD20+/CD5+ diffuse large B cell lymphoma from blastoid variants of mantle cell lymphoma

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Objective: Diffuse large B-cell lymphoma (DLBCL) and blastoid variants of mantle cell lymphoma (bMCL) may

share common morphological and phenotypical features. In routine praxis, their differential diagnosis might represent a challenge requiring a specific work-up of immunohistochemical (IHC) and fluorescent in situ hybridization (FISH) analyses.
Method: Paraffin sections from 17 CD20+/CD5+ blastic B-NHL were examined for cyclin-D1, CD10, bcl-6 and MUM-1 IHC expression together with FISH method using probes for CCND1 rearrangement and/or IGH/CCND1 translocation. The final diagnosis was established according to the criteria of WHO classification.
Results: 11/17 cases were diagnosed as bMCL showing cyclin-D1 positivity and CCND1 rearrangement, other analysed IHC markers were negative. Five of these cases were polyploid. 6/17 cases were diagnosed as CD5+ DLBCL in spite of coexpression of cyclin-D1 in 2 of them, as they showed various CD10, bcl-6 and MUM-1 expressions and missed CCND1 gene rearrangement.
Conclusion: Cyclin-D1 positivity may appear in other than MCL lymphomas due to changes at transcriptional or post-transcriptional level. In spite of overlaping phenotypes, FISH analysis of CCND1 represents an effective tool to increase the diagnostic accuracy to distinguish CD5+ DLBCL from bMCL. Supported by VEGA grant Nr. 1/0378/12 and projects CEPRII (IMTS: 26220120036) and MDCC (IMTS: 26220220113) co-financed by EU sources.

OFP-07-008

Still's Disease associated lymphadenopathy: Report of two cases resembling malignant lymphoma with review of possible morphological findings

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Objective: Still's disease (or systemic onset juvenile idiopathic arthritis, SOJIA) is a systemic inflammatory disorder characterized by fever, rash, and arthritis. It has a peak of incidence in early childhood with rare occurence in adulthood (adult-onset Still's disease, AODS). Several other symptoms as hepatosplenomegaly, leukocytosis and lymphadenopathy may be associated possibly mimicking malignant lymphoma.
Method: We present two cases of Still's disease associated lymphadenopathy in a child and in an adult simulating morphologically peripheral T-cell lymphoma and classical Hodgkin lymphoma respectively.
Results: Histological, immunohistochemical and molecular examination revealed non-neoplastic lymphadenopathy with atypical paracortical T-cell hyperplasia with immunoblastic reaction in the former and burnt-out histiocytic pattern in the latter, both falling into a broad spectrum of reactive lymph node changes associated with Still's disease.
Conclusion: The lymph node lesions in Still's disease can be histologically divided into four major categories: 1) simple atypical paracortical hyperplasia, 2) burnt-out histiocytic pattern, 3) exuberant immunoblastic reaction in paracortical hyperplasia and 4) follicular hyperplasia. The second and the third pattern may closely resemble malignant lymphoma. Extended and careful clinical examination with relevant laboratory findings and possible complex histochemical and molecular analysis are necesarry to rule out the suspition of lymphoma. Supported by the project (Ministry of Health, Czech Republic) for conceptual development of research organization 00064203 (University Hospital Motol, Prague, Czech Republic).

OFP-07-009

Intravascular large B-cell lymphona: A rare type of lymphona frequently undiagnosed until autopsy

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Objective: Intravascular large B-cell lymphoma (IVLBCL) is a rare form of diffuse large B-cell lymphoma characterized by exclusive or preferential intravascular growth. IVLBCL often goes clinically unrecognized. We report three clinically unsuspected cases of classic variant IVLBCL.
Method: Cases diagnosed as IVLBCL were collected from the pathology files of Germans Trias i Pujol Hospital. The diagnosis was reviewed in agreement with WHO 2008 criteria and immunophenotypic and clinical data were gathered.
Results: A 71-year-old male and an 87 year-old-male showed neurological symptoms leading to progressive deterioration and death. A 79-year-old female presented with fever of unknown origin and died 2 days after admission. At autopsy there were no gross findings suggestive of a neoplastic process in any instance. Histologic study showed intravascular large B cells with vesicular nuclei involving predominantly the central nervous system in the first two cases and the adrenal glands, liver, and spleen in the third case.
Conclusion: The three cases of aggressive, advanced-stage lymphoma herein described illustrate how the clinical diagnosis of IVLBCL remains elusive due to its low frequency and variegated clinical presentation and how the pathologic diagnosis of IVLBCL continues to be highly dependent on autopsy examination.

OFP-07-010

Post-Transplant Lymphoproliferative Disorders (PTLD) after renal transplantation in the Republic of Ireland: A 20 year review

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Objective: The World Health Organisation (WHO) currently recognises four categories of PTLD, which are lymphoid/plasmacytic proliferations occurring due to immunosuppression after organ transplantation. The aim of this study was to examine the clinicopathologic characteristics of PTLD occurring after renal transplantation in the Republic of Ireland.
Method: The National Renal Transplant Registry from 1991 to 2000 (inclusive) was cross referenced with the National Cancer Registry to identify renal transplant recipients who had developed PTLD up to the present day. Review of Pathology and chart review was conducted for each case.
Results: Of 2,441 patients (2,667 allografts), 34 cases of PTLD were identified, with pathology review possible in 33 cases. There were 26 (79 %) Monomorphic PTLD (23 Diffuse Large B Cell {DLBCL}, 1 Anaplastic Large Cell, 1 Burkitts-like, 1 Myeloma], 3 Hodgkin-type PTLD, 1 (3 %) Polymorphic PTLD and 1 (3 %) early lesion. In addition, there was 1 Mantle cell lymphoma and 1 Lymphomatoid Granulomatosis. The annual incidence of PTLD was estimated as 0.2 % (95 % CI 0.14–0.28). Median time to diagnosis was 8.7 years (Range 2 to 19.2 years).
Conclusion: Similar to other studies, Monomorphic PTLD is the most common type, with DLBCL representing the majority of cases. Of interest, early onset PTLD was very uncommon in this study.

Monday, 10 September 2012, 17.00–19.00, Forum Hall
OFP-08 Oral Free Paper Session Head and Neck Pathology

OFP-08-001

Human papilloma virus associated oropharyngeal carcinoma is strongly correlated with cancer of unknown primary

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Objective: Human papillomavirus (HPV) associated oropharyngeal carcinoma has been identified as a distinct entity within squamous cell carcinoma of the head and neck and is preponderantly restricted to palatinal tonsils and base of tongue. These two primary locations have for long - and HPV-associated carcinomas have recently - been associated with the clinical situation of cancer of unknown primary (CUP).
Method: To investigate the relationship between HPV and CUP in detail, we studied 26 consecutive patients who initially presented as CUP and were finally diagnosed with carcinomas of these two locations.
Results: Twenty-one carcinomas (81 %) proved to be positive for high-risk HPV (p16 and polymerase chain reaction). They were frequently very small (smallest: 0.3 cm; 6 cases: ≤ 0.6 cm; on average 0.9 cm) and located in a deep, submucosal position.
Conclusion: This demonstrates an overrepresentation of HPV-associated carcinoma in patients who were initially diagnosed with CUP, supporting a strong causal relationship between HPV-association and CUP. The frequent manifestation as CUP presumably is caused by the unusual predisposition for small size and submucosal location, combined with frequent and early lymphatic metastization. In order not to miss these small, clinically occult carcinomas, consequent interdisciplinary cooperation and meticulous histological work-up is mandatory.

OFP-08-002

Methylthioadenosine phosphorylase inactivation depends on gene deletion in laryngeal squamous cell carcinoma

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Objective: Methylthioadenosine phosphorylase is an essential enzyme for the methionine and adenosine salvage pathway in normal cells, frequently inactivated in many different human cancers. The MTAP status could be important for tumor cell sensitivity to adjuvant chemotherapy. To date there are no reports on MTAP status in laryngeal carcinoma.
Method: A series of 31 laryngeal squamous cell carcinomas was investigated for MTAP mRNA expression through reverse transcription and quantitative PCR (qPCR) as well as for MTAP gene deletion and/or promoter hypermethylation through qPCR and methylation-specific PCR respectively.
Results: Low MTAP mRNA expression was found in 32 % of cases, associated with MTAP gene deletion in 70 % ($p < 0.001$) but not to MTAP promoter hypermethylation, indicating that in this tumors gene deletion is the main mechanism of MTAP inactivation. Neither low mRNA expression nor gene deletion was associated with any of the clinicopathologic parameters investigated.
Conclusion: Given the significance of MTAP status for cell sensitivity to different chemotherapeutic regimes, our results suggest that determination of MTAP inactivation could be useful for adjuvant therapy selection in laryngeal squamous cell carcinomas.

OFP-08-003

ERCC1, p16 and ki-67 immunohistochemical expression as predictive and prognostic markers in head and neck squamous cell carcinoma treated with platin-based induction chemotherapy

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Objective: ECC1 enzyme has been associated with resistance to platinum-based chemotherapy. The purpose of this study was to evaluate the role of ERCC1 expression with p16 and Ki-67 as predictive and prognostic markers in the response to platin-based induction chemotherapy in patients with head and neck carcinoma (HNSCC).
Method: 208 patients treated from 2000 to 2006 by an induction chemotherapy regimen for HNSCC were included retrospectively. We assessed response to treatment, progression-free survival (PFS) and overall survival (OS).
Results: 68 % and 81.5 % of HNSCC showed low expression of 8 F1 and FL297 ERCC1. No correlation was found between the two clones (p=0.1). In the 129 patients treated with cisplatin-5FU chemotherapy, a low expression of 8 F1 ERCC1 was associated with a better response (p=0.027). Over expression of p16, (34.5 % of cancers of the oropharynx) was correlated with a better OS (p=0.0007) and a better PFS (p=0.01).
Conclusion: These results suggest that ERCC1 expression might be a useful predictive marker of HNSCC in patients treated by cisplatin-based chemotherapy. The 8 F1 ERCC1 clone appears to be the best for immunohistochemistry. Our study confirms the prognostic value of the over expression of p16 in carcinoma of the oropharynx.

OFP-08-004

The prognostic value of proportion of tumor in layringeal squamous cell carcinoma

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Objective: Tumor-stroma ratio or proportion of tumor (PT) has been presented as a prognostic factor in colorectal and breast adenocarcinomas, but there is no information about squamous cell carcinomas (SCC) and laryngeal carcinomas in particular.
Method: Eighty-five laryngeal carcinoma cases were included in this series. Five digital images of the tumor sections were obtained (H&Ex20). Percentage of epithelial tumor component was determined by software allowing the pathologist's selection of tiny areas as carcinomatous and stromal region for statistical analysis as a prognostic marker.
Results: Median follow up was 48 months (range 3–194). The mean PT was (48,63+18,18). There was no difference for PT when tumor grade and stage were considered. Although statistically insignificant, the mean PT was the lowest (37,46+12,49) for subglottic carcinomas and cases with perinodal invasion (44,72+20,23), and highest in pN0 cases (50,05+17,34) but there was no statistical significance. The over all and disease free survival analysis did not reveal significance for PT. Only pathological stage was an independent factor for over all survival (p=0,08).
Conclusion: Although there might be an association with adverse prognostic factors and low TP, the findings in this series does not support PT as a prognostic marker in laryngeal carcinomas.

OFP-08-005

Tumoral microvasculature in ameloblastoma subtypes

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Objective: Angiogenesis is essential for tumoral growth and progression. The ameloblastoma is a benign but locally-invasive odontogenic neoplasm with distinct behavioural characteristics of its subsets. Whether angiogenesis contributes to a more aggressive course in these variants remains unclear. The aim here was to determine and compare the tumoral microvasculature in different ameloblastoma subtypes and to speculate on their significance.
Method: Immunohistochemical staining for 4 vascular markers (CD31, CD34, CD105 and VEGF) was performed on archival tissues of 40 cases solid/multicystic (SMA), 20 unicystic (UA), 3 desmoplastic (DA) and 14 recurrent ameloblastoma (RA). Mean microvessel density (MVD) at the tumour advancing front and centres were obtained.
Results: VEGF was heterogeneously expressed in the tumoral epithelium in all ameloblastoma subtypes. Protein localization was membranous/cytoplasmic. Mean MVD was slightly higher in SMA compared to UA but the difference was not significant (P>0.05). Mean MVDs were not significantly different between primary and recurrent ameloblastoma; and between tumoral centre and advancing front of each subtype (P>0.05).
Conclusion: Although ameloblastoma subtypes are distinctive in their clinicopathologic presentations and behaviour, their tumoral microvasculature is not different. This suggests that angiogenesis is not a major factor influencing the progression of these ameloblastoma subsets.

OFP-08-006

An immunohistochemical study of E-Cadherin and snail expression in laryngeal squamous cell carcinoma

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Objective: Snail 1 and 2 (Slug) are zinc-finger transcription factors, repressing the E-Cadherin in epithelial tumors. Published data in Head and Neck Squamous Cell Carcinoma show either inverse relationship or unrelated co-expression, but E-Cadherin reduction/loss and Snail overexpression seem to confer an aggressive phenotype.

Method: Thirty cases of laryngeal squamous cell carcinomas (LSCCs) (gradeI: 11, gradeII: 8, gradeIII: 11) and one large cell neuroendocrine carcinoma (NEC) were studied using double staining immunohistochemical method for E-Cadherin (mAb-DAB) and SNAIL + SLUG (pAb–AP). The colocalization of both molecules was assessed and the expression was compared to the adjacent normal or dysplastic epithelium and the histological grade.
Results: Normal squamous and dysplastic epithelium show strong nuclear Snail expression and complete E-Cadherin membranous positivity. Reduction/loss of Snail with or without E-Cadherin membranous expression is observed in 14/30 (47 %) LSCCs with a tendency for inverse relationship with E-Cadherin at the invasive front. 16/30 (53 %) LSCCs strongly express nuclear SNAIL, without absolute relationship to the reduction/loss of E-Cadherin, with a tendency for SNAIL negativity in grade II (75 %). The NEC is nuclear SNAIL negative but cytoplasmic positive.
Conclusion: SNAIL and E-Cadherin may be retained, reduced or lost in LSCCs, without a definite inverse relationship. These immunophenotypic combinations need further investigation.

OFP-08-007

Non-sebaceous lymphadenoma of salivary glands: Proposed development from intraparotid lymph nodes and risk of misdiagnosis

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Objective: Non-sebaceous lymphadenoma (NSLA) is a recently described, rare benign salivary tumour composed of lymphoid and epithelial components, definitionally lacking sebaceous differentiation.
Method: Nine cases of NSLA were immunohistochemically stained for CK5/6, CK7, CK14, CK18, p63, and Ki67.
Results: All tumours (6 males, 3 females, mean age 50 years) were located in the parotid gland and showed intimate intermingling of lymphoid tissue with islands of epithelium with a wide spectrum of histological differentiation. The immunohistochemical profiles mirrored the epithelial differentiation; tumours with basaloid or lymphoepithelial differentiation strongly expressed CK5/6, CK14, p63, while tumours with ductal differentiation showed strong positivity for CK18/CK7 and CK5/6/CK14/p63 in luminal and basal cell layers, respectively. A hilus structure with salivary inclusions or D2-40 (podoplanin) positive marginal sinus were identifiable in 4 and 9 of the cases, respectively, confirming origin within intra-/periparotid lymph nodes. Six cases were initially misdiagnosed as other benign (n=4) or malignant (n=2) tumours.
Conclusion: Our study provides strong evidence that NSLA belongs to the group of salivary tumours that pathogenetically develop from embryonic salivary inclusions in intra-/periparotid lymph nodes. Knowledge of the wide histological spectrum of this rare tumour is important in order to avoid misdiagnosis.

OFP-08-009

CRTC1/MAML2 fusion transcript in central mucoepidermoid carcinoma of mandible: Diagnostic/Histogenetic implications

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Objective: MEC typically arises from major/minor salivary glands. Intraosseous salivary carcinomas are extremely rare (2–3 % of all MECs reported). The t(11; 19) and its CRTC1/MAML1 fusion transcript have been identified in MEC at different sites and are associated with development of a subset of these tumors. We report 9 examples of central MEC of the mandible, including a case with a history of primary retromolar MEC.
Method: RT-PCR and DNA sequencing analyses used to study microdissected components of 9 central MEC and 1 noncentral MEC. Of the central MEC tumors, 5 arose from ectopic salivary rests; others appeared to be of glandular odontogenic origins.
Results: We identified CRTC1/MAML1 in 5 central MEC arising from ectopic salivary rests. This fusion transcript was not detected in non-central MEC or in another 4 central MEC arising from a glandular odontogenic etiology.
Conclusion: Central MEC can manifest the fusion transcript in a subset of central MEC originating from ectopic salivary rests, and may have diagnostic/histogenetic roles in the future analysis of this entity, given the absence of the fusion transcript in MEC with glandular odontogenic precursors. Since the initial clinical and radiological diagnosis in three central low-grade MECs was a benign odontogenic cyst, our findings support a future role for the fusion analysis in initial diagnostic efforts.

OFP-08-010

Salivary duct carcinoma: Morphological and immunohistochemical study of 15 cases

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Objective: An evaluation of morphological and imunohistochemical features of salivary duct carcinoma (SDC).
Method: 15 cases SDC were retrieved from tumor archives collected at Belarusian Cancer Centre from 2002 to 2011 years. Immunohistochemistry, FISH.
Results: A man to women ratio was 10:5; median age 61,5 years (average 35–85). Tumors arose in the parotid

(n=13), submandibular (n=2) glands. SDC developed from pleomorphic adenoma (n=3) or de novo (n=12), there were foci of ductal carcinoma in situ (n=4), sialodochodysplasia (n=4) and Pagetoid spread (n=1) additionally to usual features of SDC. As well, tumors demonstrated acinic cell carcinoma-like (n=2) and micropapillary growth patterns (n=1), oncocytic (n=4), clear cells (n=3), apocrine (n=1) and mucinous (n=1) changes. Immunohistochemically, tumors were characterized by AR-expression (n=9), Her2/neu overexpression (n=7), of them score 2+ in 2 cases. CK8 and S-100 positivity, STAT5 negativity was detected in one case with acinic cell carcinoma-like pattern. Foci of SDC in situ were highlighted by CK14 and calponin. Amplification of c-erb2-gene was found in 1 case, ETV6/NTRK3 gene was not identified in acinic cell carcinoma-like SDC.
Conclusion: Salivary duct carcinoma, like breast cancer, is characterized by wide variability of morphological patterns and immunohistochemical features reflecting possible molecular heterogeneity, which need further investigation.

Sunday, 9 September 2012, 17.00–19.00, Meeting Hall V
OFP-09 Oral Free Paper Session IT in Pathology

OFP-09-001
Quantification of protein expression in immunohistochemical sections using a newly launched image analysis software
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Objective: Quantification of protein expression based on immunohistochemistry (IHC) is an important step for translational research and clinical routine. However, routinely used eyeballing scoring systems are time-consuming and subject to significant intra- and interobserver variability. Aim of our study was to explore, whether an image analysis software proves sufficient as an alternative tool to assess protein expression.
Method: 630 prostate cancer specimens were stained with one nucleus specific marker (i.e., ERG), one cytoplasmic specific marker (i.e., SLC45A3), and one marker expressed in both compartments (i.e., TMPRSS2). A pathologist visually quantified all stainings, applying a four-step scoring system. For digital quantification, an image analysis software (Tissue Studio v.2.1) obtained a continuous spectrum of staining intensity.
Results: For each of the three antibodies we found a strong correlation of the eyeballing protein expression score and the score of the image analysis software (correlation coefficient of 0.94, 0.92, and 0.90 for ERG, SLC45A3, and TMPRSS2, respectively, $p<0.01$).
Conclusion: Our data suggest that Tissue Studio is a powerful tool for the quantification of protein expression in IHC stainings. Further, since the digital analysis is precise, it might help to overcome intra- and interobserver variability and increase objectivity of IHC based protein assessment.

OFP-09-002
Is quality of histological and cytological slides a palatable issue?: The TASTE project
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Objective: The TASTE (technological platform and repository of high quality images and slides) project aims at developing a novel tele-pathology system by means of modern ICTs (Information and Communication Technology) and is addressed to technicians and doctors.
Method: Histological and cytological preparations are the basis for pathological diagnosis performed in daily practice throughout Europe in a number of several millions per year and correctness and reproducibility of such diagnosis are heavily dependent on the technical quality. Yet, quality is variable in different places and countries, related to school level, technicians' dedication, standard of apparatuses and reagents. Variation in technical quality of the preparations prevents their open circulation at European level and precludes optimal diagnosis.
Results: The TASTE project tackles these problems by building-up an ICT environment TASTE System where professionals from different countries will submit, via Web, "virtual slides" of their own preparations to a panel of internationally recognized experts who will give comments and suggestions on the quality of the preparation.
Conclusion: The present approach (unprecedented at world level) will fuel a Web-based community, aimed to a levelling and improvement of histopathological and cytopathological preparations, thus leading to an innovative training and more reproducible diagnosis, a basic requisite for disease treatment.

OFP-09-003
Hypertext Atlases of Pathology
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Objective: Hypertext Atlases of Pathology are available on the web (http://atlases.muni.cz) since 1998 with 25000 of registered users. The atlases contain more than 9000 images.
Method: A new virtual microscope interface will be presented. The interface is based on jpeg2000 compression that enables fast access to stored images and reduces disk usage

of the whole atlases. Virtual microscope positions can be stored in the memory and users can navigate quickly back and forward similarly to web pages. All these features are available through any web browser without need to install any additional software.
Results: In addition to the current atlases (Dermatopathology, Fetopathology, Pathology of the Newborn and Bone Marrow), an interdisciplinary Atlas of Pathology for pregraduate students of Medicine is under development. It will contain full size annotated virtual slides. The Atlases are free of charge, but registration is required. In order to ease the access, the Atlases are connected to 15 national academic identity federations. The members of institutions connected to identity federations can use theirs home credentials without revealing them to the Atlases.
Conclusion: The atlases can serve not only to the students as a source of information, but they can be used by teachers as a source of teaching material.

OFP-09-004
Proving experiment of international virtual slide telepathology, Japan-Vietnam and Japan-China trial
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Objective: The communications between Asian countries are growing. In the field of medical information and technologies, the necessity of communication is also required. In this work, as communication of pathology field, we tried to prove that international remote pathology diagnosis is possible using virtual microscopy (VS) telepathology.
Method: We put VS scanner and server to 1) our Hospital, Tokyo, Japan, 2) Cho-Rai Hospital, Ho-Chi-Minh city, Vietnam, and 3) Chinese Rehabilitation Research Center, Beijing, China. Pathologists go and look the VS through leased optical line circuit and make diagnosis. Discussion was made through teleconference system.
Results: The VS image maintained adequate quality for pathology diagnosis even looked cross-border. The diagnoses matched well between hospitals. The response of VS viewer was also good this time. When we use too much band width to the Teleconference system or we sent too many data in the background, the response deteriorate, and was not good enough for diagnosis.
Conclusion: It was confirmed that the international VS telepathology diagnosis is now reached to a stage of actual use at least when connected by leased optical line circuit.

OFP-09-005
Challenges and solutions in the setup of a findings database for a large scale tissue collection
R. Reihs*, H. Müller, S. Sauer, K. Zatloukal
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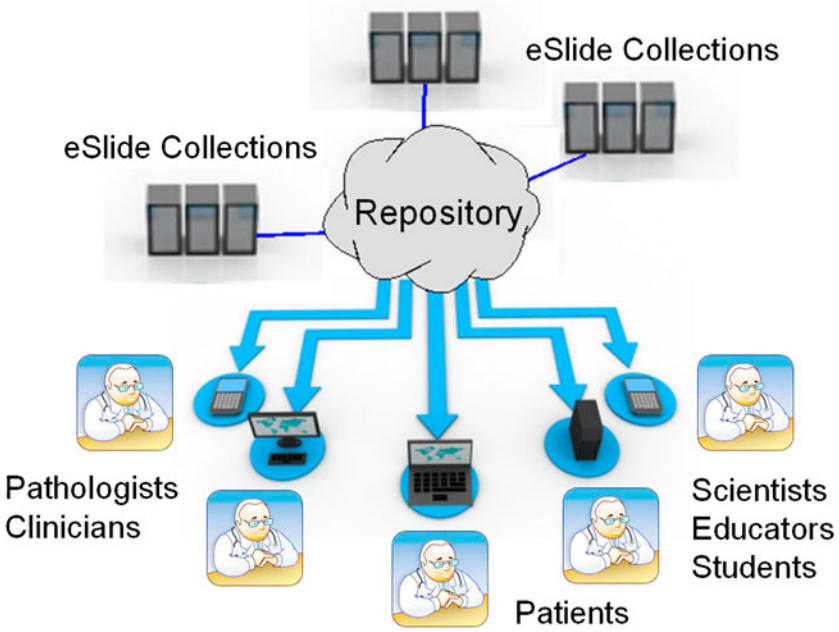
Objective: Many medical centres have acquired through the last years huge data collections of great relevance for biomedical research. In order to utilize this knowledge it is necessary to analyse this records in a structured way. In our use case the starting point were approximately 1.4 million pathological findings of a non-selected patient group.
Method: We developed software tools for the classification of medical records using a phonetic a multi-level spell correction module and an ontology term extraction and decision tree text classification system. With the help of a visual editor a comprehensive decision tree (4174 nodes) was set-up by a team of bioinformaticians and medical experts.
Results: With our tool set we achieved in the ICD-10 classification a F-Score of 89,7 % (precession 83,2 % and recall 97,5 %) For the interpretation of the classification results we developed visualization tools and applied the whole software suite at several test cases, e.g. the analysis of a colon data-set with 216.000 findings over 28 years.
Conclusion: We developed an automatic classification and visualization system and applied the results in a series of research projects. The software suite is currently used in several research projects and can be easily adjusted to specific phrases used in different institutions and languages.

OFP-09-006
An image repository for decision support
O. Eichhorn*
*Aperio, Vista, USA

Objective: Pathology is a visual field, and pathologists make decisions based on visual information. An online repository of easily searched, well-categorized pathology images can be of immense use to pathologists, scientists, educators, and students.
Method: Individuals and institutions all over the world have accumulated collections with thousands of slides representing a huge variety of pathologies. Some collections are digitized and available online, while others remain libraries of glass slides, with a variety of formats for case information and other metadata. Working with collectors to publish their slides and aggregating them together can yield an amazing decision support resource.
Results: Long-term archival storage is a key issue for organizations adopting ePathology. A cloud-based repository can provide an inexpensive and scalable solution. ePathology is increasingly used for remote consultations. Cases managed by online consultation networks can be de-identified and contributed to a common repository, increasing the value of the decision support tool while providing a long-term archive.
Conclusion: This talk will present concepts for an Image Repository for Decision Support, and discuss technical and

business considerations for making it a reality, including ways to curate image metadata, organizational principles and search tools, relationships with users and contributors, access methods, and security and privacy considerations.



OFP-09-007

Perfect diagnostic accuracy using pathomorphological diagnosis spectra constructed with the help of whole slide imaging

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Objective: Pathomorphological diagnosis (PD) is important for estimation of clinical trials and new medical equipment such as elastography. However, interpretation of pathomorphological findings is often subjective, and pathology publications show only a limited number of photographs. Because pathomorphological changes occur in succession, we attempted to construct PD spectra to improve PD accuracy.
Method: PD spectra are defined as the series of pathomorphological images arranged in the order of disease progression or cell cycle procession. The images from the whole slide imaging (WSI) server were arranged in order in Power Point files at a fixed magnification, and 4 PD spectra were constructed: chronic hepatitis staging, nuclear grading of hepatocellular carcinoma, nuclear grading of breast cancer, and Ki-67 labelling index (LI). The numbering of all images in the PD spectra corresponded with that of the WSI images so that the whole slides could be viewed alongside. Next, these tools were tried out by 6 people.
Results: These tools brought on perfect accuracy with regard to staging and grading, and very high precision of Ki-67 LI for breast cancer.
Conclusion: PD spectra are valuable not only for PD but also as learning tools and have a worldwide applicability for measuring PD online.

OFP-09-008

Color correction of immunohistochemistry stained tissue section images by histogram transfer according to control tissues

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Objective: For semiquantitative and quantitative analysis, previous normalization attempts of images of tissue sections are not satisfactory. In this study we evaluated, if color correction can be achieved by histogram transfer depending upon control tissue image (CTI) differences.
Method: Images from colon and placenta sections stained by anti-CD34 were used as CTI and/or sample tissue images (STI). Thirty-four but one (standard stained slide with images sCTI and sSTI), was stained for different durations and dilutions than the standard

procedures. Digital images taken by a CCD camera connected to a light microscope without normalization was stored at a computer. Software was prepared in order to find the histogram difference between two CTIs and transfer the difference to the STI for achieving a corrected STI (corSTI). sSTI (one image) and STI and corSTI (34 images each) were semiquantitatively scored by two observers in blind fashion and the STI and corSTI scores were compared with sSTI score.

Results: The wKappa was 0,59 for two observers. The STI semiquantitative score was same as the sSTI in 23,5 % of the STI but this was 76,35 % for corSTI.

Conclusion: It seems histogram transfer depending upon CTIs may be a valuable tool for color correction of tissue section images.

Sunday, 9 September 2012, 14.15 - 16.15, Terrace 1
OFP-10 Oral Free Paper Session Molecular Pathology I

OFP-10-001

Prognostic significance of circulating melanoma cells detection using the CellSearch® System in patients with Metastatic Melanoma

D. Giacchero*, E. Long, M. Ilie, E. Selva, J.-P. Lacour, P. Hofman, P. Bahadoran
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Objective: There is a crucial need for identification of markers to choose the best treatment schedule and monitor the effectiveness of treatment in metastatic melanoma (MM). The detection of circulating tumor cells (CTC) correlates with prognosis in different cancer subtypes. CTC can be detected by direct and indirect methods such as cytopathological approach, RT-PCR or immunomagnetic separation using the CellSearch (CS) method.

Method: From June 2011 to December 2011, blood was drawn from 27 patients with MM and 10 controls patients and processed into 72 h by the CS method. The primary end-point was the overall survival (OS) of MM patients.

Results: Enumeration of at least 1 CMC was effective in 61.5 % of patients with MM (n=16) and in 20 % of controls patients (n=2). Nine patients (35 %) had ≥ 2CMC. None of the controls patients had more than one CMC. Mean OS time was 5.6 months among patients with MM and <2 CMC (n=8) and mean OS time was 1.7 months among patients with MM and CMC ≥2 (n=26) (p=0.002).

Conclusion: Our results demonstrate that detection of CMC correlates with OS in melanoma. Thus, CMC monitoring should be developed to ensure the best treatment follow-up for patients with MM.

OFP-10-002

Significance of Circulating Tumor Cells (CTCs) detection using the CellSearch system in patients with locally advanced Head and Neck Squamous Cell Carcinoma (HNSCC)

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Objective: The significance of CTCs in patients with HNSCC is debated currently. We evaluated the potential detection of CTCs using the CellSearch (CS) Assay TM (Veridex, NJ, USA) in HNSCC patients and to identify the clinical factors predictive of the presence of CTCs in this population.

Method: Forty-nine patients with locally advanced HNSCC were included. The presence and number of CTCs were determined using the CS system in all patients prior to the initiation of therapy, in 21 patients 3 months after treatment, and in 10 healthy individuals.

Results: The CS system was able to detect the presence of CTCs in 8 of 49 patients (16 %) before therapy and in 4 of 21 disease-free patients (19 %) after therapy. No CTC was found in the control group. When considering the presence of CTCs before or after therapy, the presence of CTCs was statistically associated with patients' age (p=0.04; t-test) and N-stage (p=0.02; Fisher's exact test).

Conclusion: CTCs are identified in a relatively low proportion of patients with locally advanced HNSCC and correlated with initial lymph node involvement. CTC detection could be a future useful prognostic tool to adapt the treatment intensity in HNSCC patients.

OFP-10-003

The diagnostic utility in identifications of an aneuploid chromosomal (Ch.) pattern by using Urovysion™: A Fluorescence in Situ Hybridization (FISH) commercial test, to improve the efficacy of cytology in peritoneal effusions

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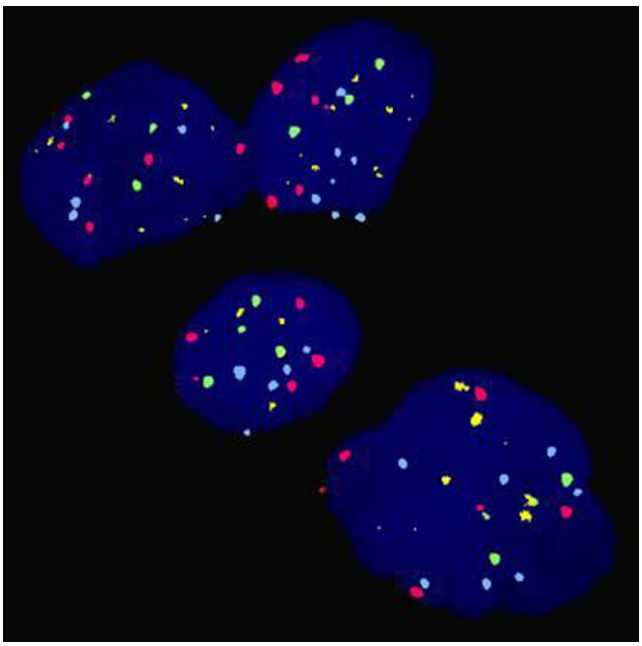
Objective: The challenge in diagnosis of effusion is in differentiation of reactive and neoplastic mesothelial or metastatic cells and identification of primary neoplasia. The difficulties in this differential diagnosis derived from the low sensitivity (~ 50 %) and specificity of effusion cytology. By identification of tumor associated aneuploidy FISH could enhance the cytodiagnostic yield in effusions.

Method: We used Urovysion™ (Abbott), a FISH commercial kit, designed for identifications of Ch. 3, 7, 17 polisomy and 9p21 loss in urothelial tumors. It has been applied to

detect chromosomal aneuploidies as a marker of malignancy in 64 effusions with or without known source primary tumors. Also was evaluated reproducibility of molecular alterations with primary tumors and any their specific aneuploidies.
Results: FISH positivity was observed in 44 (69 %) of cases, whereas 31 were positive at cytology (48 %). Overall results of cytology and FISH together rised to 75 %.
Conclusion: Urovysion™ test could be an useful tool to distinguish malignant cells in inconclusive effusions cytology but it doesn't seem to be used to provide definitive indications about primary neoplasia.



OFP-10-004
Loss of imprinting of isulin-like growth factor 2 (IGF2) in colon carcinomas leads to the cell cycle genes activation -hints to intense proliferation
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Objective: The insulin-like growth factor 2 (IGF2) gene is regulated by imprinting in normal tissues. The loss of imprinting (LOI) results in the bi-allelic expression of IGF2. Its increased activity has been associated with many cancers including colorectal cancer (CRC). To investigate the significance of IGF2 in CRC, normal tissue and tumor biopsies from 400 patients were analyzed and correlated with clinical outcome and the KRAS and PIK3 status.
Method: The IGF2 820 G/A gene polymorphism and imprinting status were examined by restriction fragment length polymorphism of DNA derived from normal tissues and tumors then of RNA from heterozygous cases. IGF2 protein analysis as well as an RNA microarray were performed.
Results: 41 % of the analysed cases were heterozygous. LOI was detectable in both normal tissues and tumors in 60 % of cases. Tumors with LOI had significantly higher IGF2 protein levels. Gene expression analysis revealed significance of cell cycle progression and mitosis genes in LOI.
Conclusion: IGF2 LOI is a common and early change in patients with CRC and in normal tissues, provides possibly a preneoplastic change. However increased IGF2 protein levels as well as a different cell cycle specific gene expression profile were detected in tumors with LOI. Future studies must be performed to find out, whether such subsets of tumors differ in their response to chemotherapy or alternative therapies.

OFP-10-005
Detection of EZH2 and CD79B mutations in B-cell Non-Hodgkin lymphomas utilizing cytological preparations for high-throughput sequencing
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Objective: Novel high-throughput technologies has revealed numerous genomic abnormalities in B-cell non-Hodgkin lymphomas (NHL). This study aimed to detect point mutations involving EZH2 and CD79B in a population of B-cell NHL by applying a multiplex mutation assay to minimal residual material from needle aspirates, and to determine the evolution of their mutational status overtime using all sorts of available samples from these patients.
Method: DNA was extracted from residual cytological material stored on FTA® Cards as well as from archived cytological and histological specimens. The presence of point mutations was investigated by a specifically developed assay utilizing MassARRAY spectrometry and confirmed by direct sequencing.
Results: All 121 samples from 80 B-cell NHL cases were successfully analyzed. Mutations in EZH2 (Y641) and CD79B (Y196) were detected in 13.2 % and 8 % of the samples, respectively. Mutational status varied in one third of the positive cases, with either gain or loss of mutations over the course of time.
Conclusion: Minimal material from lymph node fine needle biopsy is a reliable source for high-throughput multiplex analysis for the detection of point mutation involving EZH2 and CD79B. Whenever possible, the most recent sample should be tested to verify the current status of the disease.

OFP-10-006

MicroRNA expression profile identifies a distinct molecular signature between MYC translocation-positive and negative Burkitt Lymphoma cases

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Objective: The molecular hallmark of Burkitt Lymphoma (BL) is a dysregulation of MYC oncogene, due to one of the three translocations leading to IG-MYC fusion. However, about 10 % of BL cases lack an identifiable MYC rearrangement, although no significant difference of MYC expression among cases has been observed. Additional mechanisms alternative to translocations were explored by microRNA profiling.
Method: Ten MYC translocation-positive and ten MYC translocation-negative formalin-fixed and paraffin-embedded BL specimens were used for this study. For microRNA and gene expression profile, the samples were hybridized on the miRCURY™ LNA Array and the Illumina DASL whole genome Assay, respectively.
Results: Our results identified a panel of four microRNAs which are differentially expressed between the two groups. Importantly, these microRNAs control relevant biological processes, such as the angiogenesis, apoptosis and cell proliferation, according to Gene Ontology categories. Furthermore, the impact of microRNA dysregulation on the gene expression pattern identified genes which more likely are regulated by the selected microRNA.
Conclusion: Using this approach, we showed a clear-cut microRNA and gene signature between MYC translocation-positive and negative BLs. The identification of specific altered microRNAs may represent an alternative molecular mechanism leading to MYC over-expression in the absence of genetic alteration in cancer.

OFP-10-007

Droplet Digital PCR: A highly sensitive assay for B-Raf, K-Ras and EGFR mutation detection

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Objective: Droplet Digital™ PCR (ddPCR™) enables the absolute quantitation of nucleic acids in a sample. Horizon Discovery's patented gene editing technology enables it to manufacture reference material that is genetically defined and validated for the allelic frequency of the mutation. These reference standards were used to test the sensitivity of Bio-Rad's QX100™ Droplet Digital™ PCR platform.
Method: A panel of defined genomic DNA allelic standards and formalin fixed paraffin embedded (FFPE) cell line samples were used in this study. This panel covered EGFR (G719S, T790M, L858R and L861Q), K-Ras (codon 12) and B-Raf (V600E and V600K) mutations containing allelic frequencies between 0.05 % and 50 %. Droplet Digital™ PCR was performed using mutation specific TaqMan custom SNP assays.
Results: There was a strong correlation between the predicted and actual allelic frequencies even down to 0.05 %. The allelic frequency called by the ddPCR™ platform was highly reproducible between experiments particularly in the 1–50 % dilution range.
Conclusion: This study has demonstrated that the Droplet Digital™ PCR QX100™ platform can detect allelic frequencies down to at least 0.05 % using genomic DNA purified from cell lines and down to at least 3.5 % using genomic DNA extracted from FFPE cell lines.

OFP-10-008

Chromothripsis and focal copy number alterations determine poor outcome in malignant melanoma

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Objective: Genetic changes during tumorigenesis are usually acquired sequentially. However, a recent study showed that in 2–3 % of all cancers a single catastrophic event, termed chromothripsis, can lead to massive genomic rearrangements confined to one or a few chromosomes.
Method: In order to explore whether the degree of genomic instability and chromothripsis would influence prognosis in cancer, we applied high-resolution array comparative genomic hybridization to 20 malignant melanomas (MM) that were, despite comparable conventional clinical and pathological parameters, defined by a profoundly different clinical course.
Results: We observed a striking association between both number and structure of chromosomal aberrations and outcome. MM associated with good prognosis showed only few chromosomal imbalances (average 1.6 alterations per case), predominantly presented as whole chromosome or chromosome arm gains and losses. MM with poor prognosis harbored significantly more chromosomal aberrations (13.9 per case; $p=0.008$). These aberrations were mostly focal events, which culminated in two cases in a pattern consistent with chromothripsis.
Conclusion: Here, we describe for the first time the phenomenon of chromothripsis in primary MM and reveal a link between focal copy number alterations and chromothripsis with poor outcome in MM patients ($p=0.0002$), providing a genetic approach to predict outcome in histopathologically indistinguishable MM.

OFP-10-009

Targeting endometrial stromal sarcoma: Histone deacetylase and PI3K/Akt/mTOR signaling

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Objective: Endometrial stromal sarcoma (ESS) is a gynecological malignancy with few therapeutic options. Up-regulated histone deacetylase (HDAC) 2 was observed in ESS patients. The HDAC inhibitor SAHA reduced ESS cell growth by inhibiting mTOR. The PI3K/Akt/mTOR signaling cascade, vital to cancer growth is a critical target in cancer therapy. This study aimed at investigating if HDACs interact with the PI3K signaling in ESS pathogenesis and thus might serve as targets for ESS therapy.
Method: Tissue microarrays were used to determine HDAC expression in ESS specimens. Western blots revealed protein expression levels of HDACs and PI3K related molecules in two independent ESS and one control cell lines (ESS-1, MES-SA and HESC).
Results: Elevated HDAC1 and 2 levels were found in ESS tissues and cell lines. Increased cell growth and Akt/mTOR cascade hyperactivation were detected in ESS cells. SAHA reduced growth of all cells, and induced cell death in ESS cells. SAHA reduced phosphorylated 4EBP1 in all cells, but only inhibited activation of Akt and p70S6k in ESS-1 cells.
Conclusion: HDACs are linked to PI3K signaling during ESS pathogenesis. SAHA reduced cell growth via inhibiting PI3K/Akt/mTOR components suggesting that a combination of SAHA with PI3K inhibitors might be effective in treating ESS.

OFP-10-010

Usefulness of linking biobanking field and animal model: High successful rate of human primary Non-small Cell Lung Carcinoma (NSCLC) xenografts in a model system separated by distance and time

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Objective: With the ongoing need to improve therapy for NSCLC, there has been an increasing interest in the development of reliable preclinical models to test novel therapeutics. The aim of this study was to evaluate the rate of establishment of patient-derived NSCLC xenografts in the context of a long-distance research network.
Method: Fresh surgically resected NSCLC specimens were addressed from the human biobank hospital (Nice) to the animal facilities (Sanofi, Vitry-sur-Seine). Shipment was performed in AQIX medium at room temperature. Within 24 h post surgery, tumour fragments (~63 mm3) were subcutaneously implanted in female SCID mice. The growing tumours were passaged in new mice (≤10 passages). The xenografts were histologically checked to eliminate human or murine lymphoma.
Results: Overall, 98 NSCLC samples were implanted leading to 32 (33 %) NSCLC xenografts. The rate of tumour growth was higher in non-adenocarcinoma specimens (23/45; 51 %): 20/38 (53 %) for squamous cell carcinoma, 2/4 (50 %) for large cell carcinoma, and 1/3 (33 %) for pleomorphic carcinoma, when compared to adenocarcinoma samples (8/51; 16 %).
Conclusion: We report a high successful rate of xenotransplantation established from patient-derived NSCLC tissues. Our biobanking model system, regardless to extended time and distance, provides a stable and reliable animal model in human lung cancer research.

Monday, 10 September 2012, 14.15 - 16.15, North Hall
OFP-11 Oral Free Paper Session Molecular Pathology II

OFP-11-001

Macrophages recruitment with different roles at different stages of tumor growth

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Objective: We tried to interpret "the job" of MF in different stages of tumor growth by monitoring the dynamics of their distribution.
Method: On a rat model of experimental tumorigenesis using BP6 fibrosarcoma cells injected intraperitoneally, we performed a semiquantitative analysis of the recruitment of MF in the tumor compartment (microenvironment) as well as in peripheral blood.
Results: We observed a slow increase of MF count in the initial phase of tumor growth followed by a slow decrease in the late phase within the tumor compartment. Simultaneously peripheral blood showed constant increase throughout the experiment resulting in typical leukocytosis accompanying developed tumors.
Conclusion: Increased MF in the initial phase could reflect their enrollment to "prepare a suitable microenvironment for tumor seeding". Their decrease began after the tumor size was macroscopic, thus it was time for them to carry out a "different job". In the mean time their amount in peripheral blood started becoming significant, this is also the time when tumor - host interactions reach a systemic level. In futher experiments we will attempt to verify our assumption: When the tumor flourish in the host organism, it uses informed, transformed and recruited macrophages for growth

and building construction of the tumor, and for communication with distant organs on a regulatory level.

OFP-11-002

WWTR1 and CYR61 are early markers of Barrett's esophagus malignant progression

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Objective: Barrett's esophagus (BE) is the major risk factor for esophageal adenocarcinoma (EA). BE has a low risk of progression to EA, being imperative to identify markers to stratify the risk. Our aim was to look for potential early biomarkers of BE malignant progression.
Method: Three available microarray datasets were analyzed with R Statistical Computing software complemented with Bioconductor. Biomarker prioritization included: 1) Expression Barcode 2.0; 2) filtering using differential expression analysis. Candidate genes were validated by qRT-PCR on RNA from paraffin embedded samples (RNA-PES) of BE patients with high-grade dysplasia/ADC diagnosed during surveillance and of their index endoscopy dysplasia-free samples. As controls, we used samples from BE patients who have not progressed.
Results: Under conservative criteria, we identified 19 up-regulated genes that distinguish EA-progressed from non-progressed BE samples. A second filter, followed by qRT-PCR validation, trimmed the candidates to 2 markers (WWTR1 and CYR61). qRT-PCR on time-series RNA-PES of EA-progressed and EA-free BE samples showed these genes are up-regulated years before the development of EA as compared to patients who did not developed EA.
Conclusion: WWTR1 and CYR61 were identified as early risk markers for BE neoplastic progression and may have a potential role in BE risk stratification.

OFP-11-003

Combined microRNA in situ hybridization and immunohistochemical detection of protein markers

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Objective: MicroRNAs are small noncoding RNAs that constitute a novel group of biomarkers with exciting functions in cell differentiation, proliferation and apoptosis by mediating degradation or destabilization of target mRNAs. miR-21 is highly prevalent in malignancies. Previous reports on miR-21 in situ hybridization (ISH) in colon and breast cancer identified expression in the stromal cell population that was related to recurrence and cell proliferation (Nielsen et al., Clin Exp Metastasis 2011, 28:27; Rask et al., APMIS 2011, 119:663). Here, we present a histological assay platform that allows parallel localization of microRNAs and protein markers.
Method: Routinely processed paraffin embedded breast cancer samples were analyzed. MicroRNA ISH probes were detected with fluorescent tyramine reagents and primary antibodies with compatible immunofluorescence. The reagents were introduced on a semi-automated platform, HistoFlex, which has a precise temperature control unit and utilizes continuous liquid flow.
Results: By combination of miR-21 ISH and PDCD4 immunofluorescence we found differential expression in many but not all miR-21 positive cells. Using the HistoFlex, the double fluorescence assay was reduced from 7 to 2 h without loss of sensitivity and specificity.
Conclusion: A 3-fold faster assay platform was developed and our in vivo findings support the assumption that PDCD4 is a target of miR-21.

OFP-11-004

The TNF-superfamily members APRIL and BAFF and their receptors (BAFFR, BCMA, TACI) are differentially expressed in tumors and normal tissues and exert specific effects related to cell fate and differentiation

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Objective: Classically, tumor immune-related microenvironment was synonym of inflammatory cell infiltrate. Recently, the detection of synthesis and secretion of immune mediators by tumor cells highlighted TNF-superfamily (TNFSF) members as key counterparts of cell fate-related signals. Here, we assayed the synthesis-expression-function of a subset of TNFSF ligands and receptors (BAFF, APRIL, BAFFR, BCMA, TACI) in normal epithelial tissues and tumors and resident adult mesenchymal stem cells.
Method: Tissues (breast, CNS, kidney, skin, adipose tissue) have been assayed by means of immunohistochemistry and Real-Time PCR. Cell models were used for signaling, transcriptomics and functional assays.
Results: All tumors expressed this TNF-SF subset. BAFFR is absent, while its specific ligand BAFF is ubiquitously expressed; contrairewise, APRIL, BCMA and TACI are expressed in tissue-specific manner. APRIL relays on tumor evolution/grade and is involved in tumor proliferation/differentiation/apoptosis signaling through NFκB-related, or a novel pathway, implicating JNK/FOXO3A/GADD45, triggering transcriptional events.
Conclusion: Autocrine/paracrine effects of APRIL and its receptors BCMA and TACI in normal/tumoral parenchyme and the recruitment/attraction of immune-related cells could orchestrate tissue response, regulating cell fate, differentiation,

inflammation, tissue remodeling and cancer, with potential tailored-therapy application.

OFP-11-005

Mutations of cKit and PDGFRa genes in GIST patients diagnosed within the centralized diagnostic program in Slovakia in the years 2004–2008

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Objective: Mutation analysis of KIT and PDGFRA genes is currently used in gastrointestinal stromal tumors (GIST) as an important step in diagnostic protocol.
Method: DNA samples obtained from parafin-embedded biopsy material of 278 GIST patients diagnosed in 2004–2011 were screened for mutations in exons 9, 11, 13 and 17 of KIT and 12, 14 and 18 of PDGFRA. Results were tested for associations with clinical parameters of the tumor.
Results: Causal mutations (according to in silico analysis with PolyPhen-2 predictor) were identified in 83.8 % of patients, most frequently in KIT exon 11 (62.95 %). The KIT exon 9, PDGRFA exons 18 and 12, KIT exon 13, PDGFRA exon 14 and KIT exon 17 mutations appeared with frequencies 8.3 %, 7.6 %, 2.5 %, 1.4 %, 1.1 % and 0.0 % resp. Genotype-phenotype correlation analysis revealed statistically significant association between intestinal localization of tumors and presence of KIT exon 9 p.503-504_dup2 mutation and gastric localization of tumors and presence of PDGFRA exon 18 p. D842V mutation.
Conclusion: Centralized and standardized GIST diagnosis offers clinically and prognostically relevant informations and is necessary for the indication of appropriate targeted therapy of GIST patients. Supported by projects CEPR II (IMTS 26220120036) and MBCC (IMTS 26220220113) at CU JFM co-financed by EU and by grant Novartis Slovakia.

OFP-11-006

Frequency of mutations of the Cystic Fibrosis Transmembrane Regulator (CFTR) gene in a cohort of consecutive patients candidate for assisted reproductive techniques

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Objective: An association between cystic fibrosis transmembrane regulator (CFTR) gene mutations and infertility may occur. This study investigated the frequency of mutations in the CFTR gene, of a group of consecutive patients candidate for assisted reproductive techniques with the aim of identify subjects carriers of the most severe ones.
Method: We screened 11208 healthy subjects (5943 females and 5265 males) for 56 CFTR gene mutations and IVS8-poliT polymorphism utilizing the CFTR INNO-LiPA Amplification kit including both general and Italian regional strips.
Results: CFTR mutations were detected in 6.2 % of the patients, a percentage similar to that reported in the general population. The most common mutation was ΔF508/N observed in 0.9 % of patients. No difference in the gender distribution was evidenced. In the large group of patients analyzed 87.7 % were wt, 11.8 % carrier of one mutation, and interestingly 0.5 % compound heterozygous.
Conclusion: Our data support the relevance of an accurate determination of mutations in the CFTR gene in order to inform the couple of their carrier risk and the possibility on having affected child. Moreover our findings highlight the potential of genetic screening as a tool to identify possible compound heterozygous subjects without CF-like symptoms.

OFP-11-007

Still room for improvement: An update of the ESP KRAS EQA scheme

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Objective: A patient's response to cancer treatment can depend on their biomarker status. Therefore it is important that laboratories perform their biomarker tests well. In 2009 an international external quality assessment scheme for KRAS mutation analysis on FFPE slides was set-up.
Method: This scheme was run for 3 years by the coordination center, a medical and technical expert and scheme organizers under the umbrella of ESP. Participants received 10 samples. Genotype results were analyzed and labs with good performance were listed on the ESP website. Written reports of 2011 were evaluated in detail.
Results: In 2011, 79 % of participants identified all samples correctly. Results seemed to improve over the years from 9.49/10 to 9.62/10. Genotype results from laboratories that participated for 3 years appeared to improve overtime, although this couldn't be statistically proven. In the reports some important elements weren't always present. For example, the patient's name was only present in 80 %, correct HGVS nomenclature in 90 % and interpretation of results in less than 40 %.
Conclusion: KRAS-EQA probably facilitates improvement of laboratory testing. The quality of reports of KRAS tests needs to be improved. A guideline for reporting molecular pathological results would be a good instrument for both participants and assessors.

OFP-11-008

Comparative analysis of MIR-155 and MIR-21 expression in MSI and MSS Colorectal cancers complicating Inflammatoty Bowel Diseases (IBS)

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Objective: Microsatellite instability (MSI) due to mismatch repair (MMR) deficiency is reported in a fraction of colorectal cancers (CRCs) (5–10 %) complicating IBDs (IBD-CRCs). Our recent findings argued for the existence of yet unknown mechanisms underlying MMR-deficiency in IBD-CRCs, different from those involved in sporadic and hereditary MSI CRCs. Here we hypothesized that over-expression of miR-155 and miR-21, two inflammation-related miRNAs that target core MMR proteins, could constitute a mechanism underlying MMR deficiency in IBD-CRCs.
Method: We compared the expression of both miRs in IBD-CRCs and non-IBD hereditary or sporadic CRCs using non-neoplastic IBD and healthy mucosa samples as controls.
Results: Overall, miR-155 and miR-21 were significantly over-expressed in both non-neoplastic and neoplastic mucosa of IBD patients as compared to healthy controls. MiR-155 alone was preferentially expressed in MSI vs. MSS IBD-CRCs. In contrast, miR-155 was poorly deregulated in non-neoplastic and neoplastic tissues of non-IBD MSI or MSS CRCs.
Conclusion: miR-155, alone or synergistically with miR-21, may favor the emergence of MSI IBD-CCRs. Since its deregulation was not limited to neoplastic tissues but extends to non-neoplastic normal mucosa as well, the hypothesis of a miR-155 field defect promoting MMR deficiency and yet MSI-driven transformation can be proposed.

OFP-11-009

PI3K, AKT and PTEN expression in enucleated Brazilian uveal melanoma cases using tissue microarray

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Objective: In the world literature, little has been published on the molecular pathways in primary uveal melanoma or subsequent development of metastases. The PI3K pathway has been implicated in regulation of apoptosis, cell cycle regulation, transcription and translation.
Method: We used immunohistochemistry with TMA to investigate expression of PI3K, AKT and Phos- AKT, and PT in over 200 formalin fixed paraffin embedded blocks of uveal melanoma from the A.C. Camargo Hospital, São Paulo, Brazil from 1988 to 2005. FISH was performed for PTEN copy numbers.
Results: In this study, neither immunohistochemistry nor FISH results showed a statistically significant difference between the primary tumors and the tumors which metastasized. Statistical analysis of all tumors together (TMA) revealed only one molecular marker (PTEN), which gave results close to statistical significance.
Conclusion: This is the first large study of Brazilian patients for PI3K, PTEN AKT expression by Immunohistochemistry and PTEN using FISH. Expression values for molecular markers chosen did not reach statistical significance, although PTEN values were close. Use of FISH to distinguish metastatic from non metastatic cases also came close to statistical significance. These results suggest that the expression of PTEN in uveal melanoma may be a good topic to investigate further.

Tuesday, 11 September 2012, 17.00–19.00, Panorama Hall
OFP-12 Oral Free Paper Session Nephropathology

OFP-12-001

Molecular signatures of chronic rejection of renal allografts

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Objective: Chronic antibody-mediated (CAMR) and chronic T-cell-mediated rejection (CTCMR) represent predominant reason for late graft dysfunction. Both categories share similar morphological features. We ask the question whether there are differences between CAMR and CTCMR on the molecular level.
Method: Graft biopsies (>3 M) were performed and evaluated according to the Banff classification. Biopsy specimens with CAMR (n=13), CTCMR (n=9) and from protocol biopsies with normal histology (n=10) were stabilized in the RNA-later. Using the Taqman Low Density Array, the intrarenal expressions of 378 genes relating to immune response (B-cell activation, T-cell activation, chemokines, growth factors, immune regulators and apoptosis) were analyzed.
Results: Both categories of chronic rejection were associated with up-regulation of many genes in comparison with the control group: chemokines (CCL4, CCL5, CXCL9, CXCL10, CXCL11), growth factor TGFB1, MHC class II (HLA-DMA, HLA-DMB, HLA-DR, UBD), and in T-cell dependent mechanisms (CD3, CD86, LAG3), including cytotoxic T-cell associated transcripts (GBP1, GZMK). In hierarchical clustering, CAMR and CTCMR gene expression profiles were similar.
Conclusion: Chronic rejection very probably involves prolonged cooperation of innate immunity and allospecific

immune response. Our study showed that CTCMR and CAMR do not differ on the molecular basis.

OFP-12-002

Podocyte loss and glomerulosclerosis in inducible mouse model of podocin mutation-related Nephrotic Syndrome

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Objective: Mutations in NPHS2 gene, encoding podocyte specific protein podocin, cause hereditary nephrotic syndrome. Knock-in mice carrying the R140Q mutation, murine analogue of the most common human mutation R138Q, show developmental arrest of podocytes and renal failure at neonatal age. The aim of this study was to quantify renal histopathological changes in mice with postnatally induced R140Q hemizygosity.

Method: C57BL/6 mice with Nphs2Flox/R140Q, Cre + genotype were injected with Tamoxifen for 5 days to induce hemizygosity for R140Q-mutant podocin. Tissue samples were collected at defined intervals after induction. Renal morphology was evaluated by quantitative histology, immunohistochemistry and electron microscopy.

Results: Animals developed proteinuria within 1 week that progressed into renal failure and advanced uremia at week 12–16. The number of podocytes per glomerulus started decreasing at week 2 (42±19 vs. 98±31, $p=0.05$), whereas glomerular sclerosis index increased from week 4 (1.5±0.15 vs. 0.25±0.08, $p<0.00001$). Interstitial changes included fibrosis (up to 20 % of section area in end stage renal disease), tubular atrophy and dilatation.

Conclusion: Our results implicate that the expression of mutated podocin in induced R140Q-podocin mice leads to podocyte loss that precedes interstitial damage and glomerulosclerosis. Quantification of histological changes will enable better evaluation of the efficacy of different pharmacological approaches directed to improvement of podocyte viability and attenuation of glomerulosclerosis.

OFP-12-003

Heavy chain deposition disease in kidney biopsies

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Objective: Heavy chain deposition disease (HCDD) is a rare and not yet fully explored monoclonal immunoglobulin-related disorder.

Method: We studied the histopathology in 4 kidney biopsy cases of HCDD, representing a 0.07 % prevalence among 5481 native kidney biopsies.

Results: HCDD was diagnosed in kidney biopsies of 4 women (mean age 73.0 years). Light microscopy showed diffuse nodular glomerulosclerosis (4/4), associated with mesangial proliferation (3/4) and capillary aneurysms (4/4). Immunofluorescence showed abundant mesangial deposits and ribbon-like deposits along glomerular, capsular, tubular and vascular basement membranes, positive for heavy chain IgG3 (3/4) and IgG1 (1/4), with deleted gamma CH1 domain (4/4). Complement C3 and C1q stained positive in all cases. By electron microscopy, punctate and powdery electron-dense deposits were found on the same locations.

Conclusion: Immunofluorescence examination of kidney biopsies, including testing for immunoglobulin heavy and light chains, is crucial for diagnosis of HCDD. Our study confirmed that HCDD is peculiar among monoclonal immunoglobulin deposition diseases not only because of its rarity but also because of uniform histomorphologic pattern of nodular glomerulosclerosis with pronounced capillary aneurysms and significant proliferation due to complement activation. Deletion of the heavy chain CH1 domain and its significance in the pathogenesis has to be emphasized.

OFP-12-004

Two cases of ANCA associated vasculitis with geographical necroses in the kidney tissue

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Objective: ANCA associated vasculitides (AAV) are rare systemic autoimmune diseases affecting small to medium-sized blood vessels. In kidney biopsy samples, AAV usually demonstrate pauci-immune necrotizing crescentic glomerulonephritis (GN).

Method: Among 198 cases of AAV evaluated at IKEM during 10 years, 2 had a very unusual pattern of renal involvement.

Results: The first patient had been treated for recurrent otitis media with unilateral hearing loss. He also suffered from artralgias and hematuria. An ultrasound study revealed a tumor-like mass in his kidney. During exploratory surgery, the lesion appeared to be infiltrative and a nephrectomy was performed. The second patient presented a granulomatous inflammation in a scar. A month later she developed multiple kidney and spleen "abscesses" with negative hemoculture, and underwent a nephrectomy with splenectomy. In both cases, the final pathological diagnosis was necrotizing granulomatous vasculitis of small and medium-sized vessels, with large geographical necroses of kidney tissue simultaneously with necrotizing crescentic GN. Tests for ANCA antibodies were positive. No microbial pathogens including mycobacteria were detected.

Conclusion: This extremely rare renal presentation of AAV can mimic other granulomatous inflammation or tumor lesions, which can be misleading and cause a diagnostic delay.

OFP-12-006

Murine IgA nephropathy induced by O-glycosylated IgA rheumatoid factor

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Objective: IgA nephropathy is known to be associated with structural aberrations of O-linked glycans in the IgA1 hinge region. We explored the nephritogenic potential of two different monoclonal IgA anti-IgG2a rheumatoid factors (RF) in relation to the possible presence of O-linked glycans in their hinge regions.
Method: 6–19 or 46–42 IgA hybridoma was implanted into BALB/c mice, and serum levels of RF and renal lesions were assessed. The oligosaccharide profiles of both IgA RFs were analyzed by the MALDI linear-TOF MS.
Results: In parallel to increases in serum levels of IgA RF, mice implanted with 6–19 IgA, but not 46–42 IgA, hybridoma developed acute glomerular lesions within 2–3 weeks. They were characterized by mesangial expansion with mesangial cell proliferation and IgA deposits accompanied by IgG2a and C3 deposition. The analysis of oligosaccharide structures revealed the presence of highly galactosylated O-linked glycans in the hinge region of 6–19 IgA, but not 46–42 IgA.
Conclusion: Glomerular lesions resembling human IgA nephropathy were induced by 6–19 IgA anti-IgG2a RF, which is highly O-glycosylated in its hinge region. This experimental model could provide a useful tool to better define the immunopathological mechanisms critically involved in the development of himan IgA nephropathy.

OFP-12-007

Pathology of resolving polyomavirus nephropathy

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Objective: Polyomavirus nephropathy (PVN) is a common complication after renal transplantation. Virus control is achieved by a reduction of immunosuppression allowing an effective T cell-mediated antiviral immune response. The morphology of resolving PVN has not been investigated.
Method: 101 protocol biopsies of 34 patients with PV viremia treated by reduction of immunosuppression only were included and scored according to Banff criteria. The extent of interstitial inflammation was estimated as % of cortex. The number of tubular cross sections with SV40+ cells per mm of biopsy length was counted. Findings were grouped as pre-, increasing, decreasing, and post-viremia.
Results: During the phase of decreasing viremia, we found a significant increase in the tubulitis score, the extent of tubules with intraepithelial lymphocytes, and interstitial inflammation ($p<0.001$). These, to a lower extent, persisted after virus clearance. The number of SV40+ tubules correlated with the virus load in the serum, but SV40 immunohistochemistry was frequently negative (33/55 cases), especially if viremia was below 106 geq/ml.
Conclusion: Resolving PVN is characterized by a self-limiting acute interstitial nephritis. Our findings are important because the diagnosis of interstitial rejection depends on the same morphological criteria. Therefore, acute interstitial rejection cannot be diagnosed with certainty during PV viremia.

OFP-12-008

Neural cell adhesion molecule and fibroblast growth factor receptor positive interstitial cells increase in interstitial fibrosis in different renal diseases

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Objective: NCAM + cells with dendritic morphology are rarely present in normal renal interstitium. The aim of this study was to evaluate presence of NCAM + cells in kidney biopsies of different renal diseases with and without interstitial fibrosis (IF). Further immunophenotyping of NCAM + renal interstitial cells was performed.
Method: 97 kidney biopsies, after routine diagnosis, were stained applying antibodies against NCAM clone123C3.D5 or cloneEric1. For double immunofluorescence, antibodies against NCAM cloneEP2567Y and FGFR1, alpha5beta1 integrin, alphaSMA, cadherin9, cadherin11 were used. By RPCR, different NCAM isoforms (120,140,180) were detected using specific primers in 11 renal tissues with and without IF.
Results: NCAM + interstitial cells were identified in 48 cases: 69 % lupus nephritis, 64 % focal segmental glomerulosclerosis, 64 % IgA nephropathy, 55 % membranoproliferative glomerulonephritis, 50 % membranous glomerulonephritis. NCAM + cells coexpressed FGFR1 and alpha5beta1 integrin, and were increased in IF. NCAM + cells did not coexpress alphaSMA, cadherin9 and cadherin11, although they were closely colocalised. All normal renal tissues tested for RPCR showed presence of all NCAM isoforms, however NCAM180 lacked in some tissues with IF.
Conclusion: NCAM + renal interstitial cells coexpress FGFR1 and alpha5beta1 integrin and are increased in renal diseases with IF, mostly in diffuse proliferative lupus

nephritis. In contrast to normal kidneys, in renal tissue with IF NCAM180 is present in a lesser extent.

OFP-12-009

Reproducibility for C4d immunohistochemistry in renal allografts: Results from the Banff Trial

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Objective: Detection of C4d is crucial for diagnosing antibody mediated rejection, yet formal reproducibility studies are limited.

Method: We conducted an international multi-center trial to assess the reproducibility for C4d immunohistochemistry on paraffin-sections. A tissue microarray (TMA) was constructed comprising 44 kidney allograft specimens representing negative, focal, and diffuse C4d positive cases. Participants stained the TMA slides, evaluated their stains and entered their scores online. Stained slides were returned for centralized panel scoring. Weighted kappa statistics were used to determine reproducibility.

Results: Inter-institutional reproducibility, i.e. the product from variability between observers and staining methods was low (mean kappa 0.17). Inter-observer reproducibility was fair (kappa 0.39), while inter-laboratory reproducibility was moderate (kappa 0.49). Inter-observer reproducibility could be significantly improved by omitting the Banff C4d grading schema and only considering +/− calls (kappa 0.60). Scoring only C4d+/− inter-laboratory reproducibility improved considerably (kappa 0.78). Higher dilutions of the primary antibody were associated with worse reproducibility. Fixation <1 h or fixation in ethanol had significant negative impact on inter-laboratory reproducibility.

Conclusion: C4d results reported from paraffin section are highly variable between institutions. Simplification of the grading schema would improve reproducibility between observers. Technical reproducibility between laboratories is acceptable but could further be improved by standardizing protocols.

OFP-12-010

Heparanase in diabetic nephropathy: Mode of action and therapeutic implications

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Objective: Heparanase is a predominant mammalian enzyme that cleaves heparan sulfate, the key polysaccharide found in the basement membranes and at cell surface. Heparanase is overexpressed in the diabetic kidney; however, its role and mode of action in diabetic kidney disease remains largely unclear.

Method: Applying heparanase-null mice we found that deletion of the heparanase gene protects diabetic mice from diabetic nephropathy (DN). Recombinant heparanase enzyme and a specific heparanase inhibitor (SST0001) were used to explore its mode of action in several in vivo and in vitro models.

Results: There is essential involvement of heparanase in the pathogenesis of DN. Deleting the heparanase gene protects diabetic mice from DN and administration of specific heparanase inhibitor decreases the extent of albuminuria. In vitro, heparanase enhances macrophage activation by diabetic milieu components, and thus increases the kidney-damaging properties of macrophages.

Conclusion: Our results validate the role of heparanase in DN and reveal the mechanism of heparanase action emphasizing its function in coupling chronic inflammation, macrophage activation and diabetic kidney injury. These findings will help in developing effective strategies to disrupt the heparanase-driven sequence of events in diabetic kidney disease, and in designing novel therapeutic interventions in DN.

Sunday, 9 September 2012, 17.00–19.00, Terrace 1
OFP-13 Oral Free Paper Session Neuropathology

OFP-13-001

Microvascular angiogenesis occurs in a subset of only the arteriovenous types of vascular malformations and is more abundant in men than in women

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Objective: Episodic volume expansion may complicate the very slow growth pattern of congenital vascular malformations. We investigated the role of microvascular angiogenesis in this process of sudden growth.

Method: 100 resection specimens of symptomatic vascular malformations were screened for presence and extent of sheets or clusters immature microvessels, interpreted as microvascular angiogenesis. Microvessel density (MVD), mast cell density (MCD) and Ki67 labelling index of endothelial cells (EC) were assessed immunohistochemically and quantified. Extent of angiogenesis was correlated with the type of vascular malformation and clinical characteristics.

Results: Of 107 cases, 71 were arteriovenous malformations (AVM), 21 were venous (VM), and 8 were lymphatic (LM). Microvascular angiogenesis was observed in 30 % of all vascular malformations, of which 94 % appeared to be AVM. MVD, MCD and Ki67 labelling indexes of EC were

significantly higher in immature vessel areas. Moreover, in affected patients these angiogenic responses were far more extensive (in terms of area involvement) in men than in women ($p<0.05$).
Conclusion: Microvascular angiogenesis appears a specific feature of the arteriovenous type of vascular malformations, and is much more extensive in men than in women. We suggest that these microvascular responses may contribute to onset of symptoms due to a mass forming effect.

OFP-13-002

The impact of ventricular assist device prior to transplantation on acute cellular rejection and antibody-mediated rejection in cardiac allografts with due consideration of seasonal behaviour: A prospective study

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Objective: This study evaluated the impact of bridge-to-transplant ventricular assist device support on development of acute cellular (ACR) and antibody-mediated rejection (AMR) with due consideration of seasonal behaviour in cardiac allografts.
Method: We studied 263 consecutive right ventricular endomyocardial biopsies (EMB) between 01/2011 and 03/2012 prospectively. Paraffin-embedded sections were evaluated for acute cellular rejection, endothelial cell swelling and capillary deposition of C4d, C3d and IgA/M/G. The effects of VAD ($n=101$) on ACR and AMR, classified according to the ISHLT, were studied for seasonal effects and compared to results of EMB harvested from patients without VAD support ($n=162$).
Results: Our results did not reveal significant differences between the two groups in any given parameter. A positive correlation was found for endothelial cell swelling and capillary C4d deposition; the data failed to show a correlation between C4d and C3d deposition or C3d deposition and endothelial swelling. Complement and immunoglobulin depositions seemed to be more pronounced but without statistical significance in autumn and winter.
Conclusion: Our results demonstrate only statistically insignificantly more pronounced capillary complement deposition in autumn and winter. The use of VAD did not predict development of AMR or ACR. The C3d staining does not add to the pathological diagnosis of AMR.

OFP-13-003

Relevant changes of the molecular profile in the recurrence of glioblastomas with respect to the correspondent primary tumors

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Objective: In the literature, there is not enough information about changes of relevant molecular parameters in the recurrent glioblastoma.
Method: The study included a total of 11 grade IV astrocytomas (OMS) and their correspondent recurrences in a series of patients treated by 5-ALA guided surgery. All patients received similar treatment. A comparative histologic and molecular study which included LOH of PTEN region, EGFR amplification SISH, methylation of MGMT by MSP-PCR and sequencing of EGFR variant III mutation on representative tumor samples was obtained.
Results: The recurrences appeared adjacent to surgical cavity in seven cases. The mean time between the diagnosis of primary and the recurrence was 500 days (215–1670). The primary glioblastomas showed LOH10q23 in 82 % of cases, hypermethylation of MGMT in 50 %, EGFR amplification in 45 % and EGFRvIII in 37 %. In five cases (45 %) the molecular profile of the recurrences was different to the primaries and most of them (80 %) in the group of vaccines treated glioblastomas. The molecular profile change included one to several of the studied parameters. In one case all of the molecular parameters had changed.
Conclusion: The molecular profile change of the recurrences of glioblastomas in respect to the primaries is a frequent event that could be due to the selection of tumor cells due to both heterogeneity and treatment effect.

OFP-13-004

The proliferative activity of the border of glioblastoma defined in vivo by 5-aminolevulinic fluorescence is a relevant independent prognostic marker in glioblastomas

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Objective: There is not literature reference on the prognostic significance of the proliferative activity in the border of tumor. A large series of patients with glioblastomas operated by fluorescence guided surgery with uniform treatment and enough follow-up have been studied.
Method: A total of 207 samples of different fluorescence quality from 67 glioblastomas, 44 primaries and 23 recurrences, were studied. For each tumor, the maximum value of Ki-67 was determined by a semiquantitative counting by two observers and by an autoanalyzer. These values were compared with relevant oncologic parameters.
Results: The results of Ki67 according both counting methods were concordant. The Ki67max values of red (center), pink (intermediate) and blue (border) fluorescence samples obtained by quantitative analysis were 28 % 11 % and 6 %. In the Cox regression analysis for overall survival, the Ki67 value was an independent prognostic factor, stronger than

other relevant clinical parameters studied (p=0.002). In the Kaplan-Meier for a Ki67 cut-off of 5 %, the median overall survival was 25.1 months against 13.0 months (p=0.023). For the patients with recurrent glioblastomas the overall survival according to Ki67 values was also significant (p=0.017).
Conclusion: The evaluation of the proliferative activity by Ki-67 in the border of tumor defined by 5-ala fluorescence is a relevant independent prognostic marker of primary and recurrent glioblastomas.

OFP-13-005
Prognostic value of estrogen receptor expression measured by IHC in brain metastases of breast carcinoma
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Objective: According to the levels of estrogen receptor (ER) expression, primary breast carcinoma (BC) cases are divided into two groups: ER-positive and ER-negative (Godhirsch et al. 2011). In metastatic BC, and especially in brain metastases (BM) of BC, the role of ER expression is not clearly defined. Aim: Investigate ER expression levels in brain metastases of BC and evaluate its prognostic significance.
Method: Surgically obtained tumor specimens from sixty BC female patients (median age 52, ranges 29–73) with BM BC were stained with antibodies to ER (DAKO). IHC expression was evaluated according to the semi-quantitative method. Survival was estimated by means of Kaplan-Meyer curves. Statistical analysis was performed using STAITISTICA 8.0 software.
Results: ER expression was detected in 52 % of patients (31/60), and 48 % (29/60) were ER-negative. Median time period between primary diagnosis and BM development was significantly (p<0.05) longer in ER-positive group compared to ER-negative group (48 and 23 months, respectively). Recurrent BM developed in both groups with a similar frequency (32 % and 34 %, respectively). General survival was significantly (p=0,026) higher in ER-positive patients compared to that of ER-negative group.
Conclusion: ER expression is considered to be an important prognostic factor for development of BMBC. Nevertheless, further studies involving more patients with BMBC are required.

OFP-13-006
Dopamine and alpha synuclein interplay in neurodegeneration: A rat animal model
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Objective: A spontaneous autosomal recessive rat model for neurodegeneration was developed in our laboratory. These rats demonstrate progressive increases in alpha synuclein (α-syn) in the brain mesencephalon followed by loss of dopaminergic terminals in the basal ganglia and motor impairments.
Method: Histology, immunohistochemistry, transmission electron microscopy were used for morphological analyses. For α-syn assessment real-time PCR and western blot were used. Dopamine measurements were performed by ion mobility mass spectral (IMMS).
Results: The severity of pathology is directly related to the overexpression of α-syn and parallel decrease in dopamine (DA) level in the striatum (ST) of affected rats. The neurodegeneration in this model is characterized by the presence of perikarya and neurites Lewis bodies (LB) and diffuse marked accumulation of perikaryal α-syn in the substantia nigra (SN), brain stem, and striatum along with neuronal loss. Light and ultrastructural analyses revealed that the process of neuronal degeneration is a "dying back" type. The disease process is accompanied by gliosis and release of inflammatory cytokines.
Conclusion: Decrease dopamine and overexpression of α-syn in the brain mesencephalon may provide a naturally occurring animal model for Parkinson's disease and other synucleinopathies that reproduces significant pathological, neurochemical, and behavioral features of the human disease.

Sunday, 9 September 2012, 14.15 - 16.15, Meeting Hall V
OFP-14 Oral Free Paper Session Other Topics I

OFP-14-002
Proliferation indices of PHH3/MART1 double stains are strong independent predictors of clinical outcome in primary cutaneous melanoma
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Objective: The mitotic index in thin primary melanomas replaced Clark level in the 2009 staging system of the AJCC. However, the recommended quantification of proliferation by hot spots on HE stains is criticized. An alternative may be the immunohistochemical proliferation marker phosphohistone H3 (PHH3) visualizing all mitotic cells. And, when combined with the melanocytic marker MART1, PHH3 insures quantification of proliferating melanocytes, only.
Method: 153 primary melanomas with a median follow-up of 12 years for patients with event-free melanoma were included. PHH3/MART1 stains were performed by an indirect sequential immunoenzymatic technique. The number of

PHH3/MART1 positive cells was counted in a fixed 1-mm2 frame in the dermal area with the highest concentration of positive cells (hot spots).
Results: In multivariate analysis, PHH3 in hot spots was a strong independent prognostic marker for recurrent disease (HR=3.7, 95 % CI, 1.4 to 9.6; *P*=.008) and melanoma-specific death (HR=3.4, 95 % CI, 1.3 to 9.0; *P*=.013), when corrected for primary tumor thickness and ulceration.
Conclusion: Cellular proliferation is an independent prognostic marker in primary cutaneous melanoma. However, accurate quantification is crucial for correct clinical staging. For this purpose, proliferation indices of the novel PHH3/MART1 double stains seem very promising.

OFP-14-003
Matrix metalloproteinases underexpression in melanoma with regression
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Objective: Melanoma regression results as a complex interaction between tumor and host immune response; it has debatable prognostic significance but promising anti-cancer vaccine strategies were proposed based on immune-mediated destruction of tumor cells from regression areas. Alterations of matrix metalloproteinases (MMP) expression may be involved in tumor regression.
Method: We analyzed 35 cases of superficial spreading melanomas (22 cases with regression – 6 segmentary regression (SR), 8 partial regression (PR) and 8 segmentary&-partial regression (SPR); 13 cases with no regression ((NR); we investigated MMP1, MMP2, MMP3, MMP11 and MMP13 immunohistochemical expression in both NR cases and nonregressed&regressed component in melanoma with regression.
Results: MMP1 presented significantly lower expression in nonregressed component in both SPR and SR + SPR groups versus NR (*P*=0.041 and *P*=0.050); similar results were recorded in PRvsNR cases for MMP11 (*P*=0.037); all the other MMPs had similar expression in nonregressed component (irrespective of regression type) and NR. Nonregressed versus regressed component analysis in the same tumor identified overexpression of MMP3, MMP11 and MMP13 in nonregressed component (*P*<0.05).
Conclusion: Regression in melanoma is correlated with diminishing expression of MMP3, MMP11 and MMP13 in regressed component; certain types of regression associate MMP1 and MMP11 underexpression in nonregressed tumor. Acknowledgments: project partially supported by Postdoctoral Program POSDRU/89/1.5/S/60746

OFP-14-004
New morphological feature of Reinke's edema
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Objective: Some of the more common benign vocal fold lesions are polyps, nodules and polypoid corditis (Reinke's edema). The majority of vocal fold pathology develops in the mucosal layer of the vocal fold, precisely in Reinkes space. Basic science and clinical research over past decades has led to advances in our understanding of benign laryngeal lesions. The aim of our study was compared contact telescopy findings with histological analyzes in a patients with Reinke's edema.
Method: The our study included 80 consecutive patients with clinical diagnosis of Reinke's edema. Videoassisted contact telescopy was performed in all cases under general anesthesia and mucosa was stained by methylene blue. Tissue biopsies were taken from areas exhibiting visible pathological changes and sent to routine histopathology and immunohistochemical analyses. We analyzed expression of pancytokeratin antibodies, vimentin and CD 34.
Results: In the all case of Reinke's edema, contact telescopic scans showed a change of direction or a disappearance of regular distribution and morphology of blood vessels (irregular shapes, positions, and patterns, apparently running in random directions) in vocal fold mucosa. Marked pathological changes were noted by contact telescopic scans, confirmed with histopathology analyses.
Conclusion: Contact telescopy is a useful additional diagnostic tool regarding Reinke's edema.

OFP-14-005
Volunteering in Malawi: A snapshot of surgical pathology in sub-Saharan Africa
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Objective: The breadth of material found in surgical pathology services in African countries significantly differs from the common spectrum of "the West". We report our experience in the pathology departments of Blantyre and Lilongwe, Malawi.
Method: During a six-week period 405 cases were processed (378 histology, 27 cytology).
Results: The vast majority of cases showed significant pathological findings (n=369; 91.1 %): 175 (47.4 %) were non-tumoral conditions and 39 (10.6 %) benign tumors or tumor like lesions. The large group of malignancies (n=140; 37.9 %) comprised 11 pediatric tumors (e.g. rhabdomyosarcoma, small blue round cell tumors), and 129 adult tumors. Amongst women (n=76), squamous cell carcinomas (SCC) of the cervix uteri predominated (n=25; 32.9 %), followed by breast carcinomas (n=12; 15.8 %), and esophageal SCC (n=9; 11.8 %). Males (n=53) most often showed SCC of the esophagus (n=9; 17.0 %), and SCC of the urinary bladder (n=7; 13.2 %). Lymphomas (n=7) and Kaposi's sarcomas (n=6) were less frequent.
Conclusion: Providing pathology service in a low resource country may be handicapped by lack of personal, inadequate material resources, or insufficient infrastructure. Rotating volunteers offer a bridge for capacity building of both personnel and the local medical service; in addition, the volunteer's horizons are broaden professionally and personally.

OFP-14-006

Comparative analysis of antinuclear antibodies by indirect immunofluorescence and immunoblot tests

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Objective: Antinuclear antibodies (ANA) are routinely tested by indirect immunofluorescence (IF) and immunoblot. In this paper we aim to retrospectively analyze results of both methods.
Method: On two cohort groups: A (a total of 5518 samples), and B (a total of 2615 samples) we performed IF on commercially obtained Hep-2 cell, and immunoblot on (strips Euroline).
Results: IF revealed at least 14 different morphological patterns of ANA staining, which we grouped into 5 easily distinguished categories: speckled nuclear fluorescence, homogenous nucleoplasmic fluorescence, multiple nuclear dots, nucleoli staining, and scattered nucleoplasmic dots. We compared these groups according to frequency, type of antibody and correlation with immunoblot resuts.
Conclusion: We summed the characteristics of each IF category, and noticed that both cohorts revealed 7.4 % and 6 %, respectively of sera, which did not show positive IF at an acceptable dilution (only by 1:10) or were fully negative in IF test, but were clearly positive in immunoblot test. This was especially alarming with anti-Scl-70 antibodies, which could be barely recognized in IF test, but were clearly present in 53 of 407 positive stained strips (cohort A) and/or 14 out of 156 positive stained strips (cohort B).

OFP-14-007

Macrophages and their subtypes in tumorigenesis and growth

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Objective: It has been established that Macrophages (MF) play a basic role in the tumor microenvironment. Still, the definition of the function of MF with relation to tumors is still vague, mainly when MF are observed acting occasionally as pro tumor and elsewhere as anti tumor.
Method: In this paper we attempt to sum up the accumulating observations of MF function with respect to the microenvironment and the tumor entity.
Results: Through the different stages of tumorigenesis and growth, macrophages are engaged in various signaling cascades that tame them to perform a certain function in a given microenvironment. This makes MF a multi-program cell with unique adaptivity. We assume that without the macrophages tumors cannot progress.
Conclusion: The available MF subtype analysis is still inadequate and doesn't bear into account the dynamics of tumorigenesis and growth. Our presented MF schemes provide an insight on the tumor microenvironment with respect to stage. A complex view on the signaling cascades affecting MF is needed to formulate a novel classification of MF based on their programming. This consequently can be the basis of the development of "anti-MF therapy" or on a larger scale "anti-tumor microenvironment therapy".

OFP-14-008

Needle aspiration in the diagnosis of metastatic bone disease

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Objective: There is an increasing number of bone needle aspirations. To evaluate the accuracy of this technique in the diagnosis of metastatic carcinoma we performed this study.
Method: Retrospective series of patients with needle study of bone lesions, either by cytology (FNA) or biopsy (Core) that were diagnosed as metastatic bone disease, between 2003 and 2011.
Results: The study included 167 CT-guided needle specimens (156 patients). Bone needle aspiration biopsy showed metastatic carcinoma in 153 aspirates (92 %). In 83.76 % of FNA we made the diagnosis of Metastasis: 40.8 % without specific site of origin & 59.2 % Specific site. On the other hand, in 94.25 % of Core we made the diagnosis of Metastasis: 14.6 % without specific origin & 85.4 % with specific site. Thus, the primary tumors were identified in 115 cases (68.9 %), with the aid of Immunohistochemistry (CK7 and CK20). In 2003 there were just 4 Core within the total number of 27 aspirates, but in 2011 there were 20 Core over a total number of 26.
Conclusion: In patients with metastasis to bone, the needle biopsy is a very effective technique. The best results obtained in Core diagnosis can explain the upraising number of such procedures over the last 10 years.

OFP-14-009
Lodox X-ray is an invaluable asset in autopsy procedures
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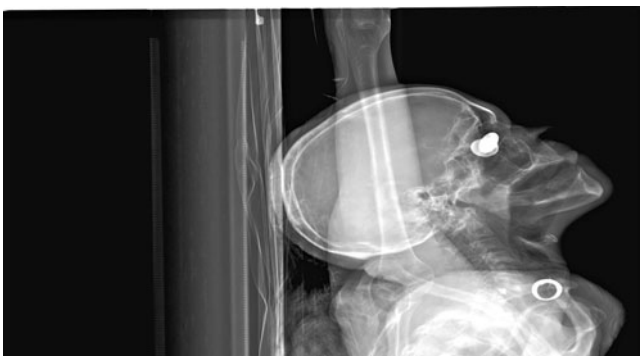
Objective: The field of autopsy performance has faced numerous challenges internationally. Minimal background information on the deceased, various religious and personal objections regarding cutting a deceased body as well as health hazards face the pathologist regularly. Lodox X-ray is a huge help for the pathologist.
Method: Lodox X-ray (low dose X-ray) using the Statscan has proven invaluable in busy forensic pathology laboratories in Cape Town, South Africa. The digitally captured radiology images render a wealth of clear, recognizable, easily documented and user friendly images for use in diagnosis and court evidence.
Results: The use of the Statscan has revolutionized the process of forensic autopsy procedures in Cape Town, South Africa. The radiology images obtained in an unusually user friendly and time efficient way have improved efficacy, efficiency, accuracy and pro-active occupational health safety in our forensic laboratories.
Conclusion: Lodox X-ray is a proven invaluable special investigation in forensic, and also academic, autopsy examination procedures.



Sunday, 9 September 2012, 17.00–19.00, Club D
OFP-15 Oral Free Paper Session Other Topics II

OFP-15-001
Whole exome sequencing identifies potential therapeutic targets for castration resistant prostate cancer
R. Menon*, M. Deng, D. Boehm, F. Fend, S. Biskup, S. Perner
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Objective: Castration resistant prostate cancer (CR-PCa) is the most aggressive form of prostate cancer (PCa) posing a significant therapeutic challenge. Our aim was to perform whole exome-sequencing on 5 CR-PCa/normal paired formalin fixed paraffin embedded (FFPE) samples using the SOLiD4 next generation sequencing platform (NGS). We identified two promising genes- YWHAZ and PTK2, that could serve as novel potential therapeutic drug targets in PCa.
Method: Genomic DNA was sequenced from 5 CR-PCa/normal paired FFPE samples. A set of amplified/deleted genes were validated using fluorescence in-situ hybridization (FISH) assays using a PCa progression cohort consisting of 138 cases for localized PCa, 105 patients with primary PCa and corresponding LN metastasis, and 39 samples for CRPCa.
Results: Exome-sequencing identified regions of deletions/amplifications, including NKX3.1, PTEN, CMYC and AR genes, known to play a role in PCa. We identified several amplified genes as druggable targets such as PTK2 and YWHAZ. For YWHAZ we identified 3.5 % amplification in localized PCa, 24.2 % amplification in LN metastasis and 45.5 % amplification in CRPCa. For PTK2 we 4 % amplification for localized PCa and 34 % for both LN metastasis and CR-PCa.

Conclusion: This is the first study to use exome-sequencing approaches on FFPE CR-PCa to understand the biology of disease and its plausible treatment options.

OFP-15-002

A study of d-Np63 (p40) expression in tumours of stratified epithelium

D. Nonaka*

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Objective: p63 can be expressed by a minority of adenocarcinomas. ΔNp63 (p40), isoform of p63, has recently been reported as more specific in lung squamous cell carcinoma (SCC) than p63, and it appears to be a more reliable marker for SCC. There is no comprehensive study on p40 expression in tumours of different histotypes.
Method: 460 tumours of various hisotypes were studied, including tumours of stratified epithelium such as SCC (84 cases) of the skin, head/neck, lung, cervix, and oesophagus, urothelial carcinomas (18), cutaneous basal cell carcinomas (5), thymomas (20) and thymic carcinomas (5), adenocarcinomas (210) from multiple organs, germ cell tumours (25), brain tumours (17), lymphomas (14), and sarcomas (12). p40 immunostains were performed on tissue microarrays and staining extent was evaluated as focal (1–50 %) and diffuse (50–100 %).
Results: All but one tumours of stratified epithelium diffusely expressed p40. The negative case represents spindle cell SCC. Other tumours except for basal/squamous component of two teratomas, one breast metaplastic carcinoma, and squamous component of 5 adenosquamous carcinomas were all negative for p40.
Conclusion: p40 is specific in tumours of stratified epithelium and its sensitivity appears comparable to p63. p40 can serve as a marker for tumours of stratified epithelium.

OFP-15-003

Glyoxal fixation: 10-years' experience of formaldehyde substitute fixative for diagnostic surgical pathology

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Objective: Although formaldehyde is the standard fixative used in routine histopathology, it is not considered an "ideal" fixative. Formaldehyde presents carcinogenic properties, a slow fixation and produces cross-links with proteins and nucleic acids. Formaldehyde-free fixatives are commercially available.
Method: From 2002 to 2012 we used Glyo-Fixx (Thermo Scientific, US), a glyoxal-based fixative, as formaldehyde substitute, analysing 54314 surgical pathology specimens and 205 autopsies. All samples were processed and stained routinely. Moreover we performed immunohistochemistry by an automated immunostainer and special stains with standard techniques, where needed. In tumoral cases we fixed 1 cm3 sample in neutral buffered formalin and compared the results with Gyo-Fixx fixation.
Results: Glyo-Fixx fixation needed less hours than formaldehyde and not harden the tissues. On gross examination of the adipose tissue, lymph nodes were easily found, due to a more marked whitish appearance. Morphologically we have not found differences between formalin and Glyo-Fixx, except for the eosinophils degranulation. Special stains resulted similar to those with formaldehyde fixations. Almost all antibodies not required pretreatment, but needed adjusts in the standardized protocol for formaldehyde.
Conclusion: Our experience demonstrated Glyo-Fixx is a good non-toxic alternative to formaldehyde in routine pathology, capable to preserve morphology and protein integrity of the tissues.

OFP-15-004

Liposarcoma with solitary fibrous tumor-like dedifferentiated areas: Clues on differential diagnosis

M. Aizpurua*

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Objective: Well-differentiated liposarcoma (WDLS) can undergo dedifferentiation to nonlipogenic sarcomas. Solitary fibrous tumour (SFT) characteristics have not been highlighted as a pattern of dedifferentiated liposarcoma (DLS). However, this does occur and could be the cause of diagnostic pitfalls in atypical locations or partial tumoral resections. The aim of this comparative study is to demonstrate that some DLS's may show morphologic features resembling SFT's, and furthermore to describe the clue features supporting differential diagnosis.
Method: Study comprised 11 WDLS-DLS and 12 SFT (4 malignant). Histological features were systematically reviewed, and CD34/CD99/S100/BCL2 immunostains and MDM2 FISH-analysis were evaluated in all cases.
Results: There are many overlapping characteristics between DLS and SFT (Table 1). Significant differences between both tumor types were observed in lipoblast-like cells (lpc); mature adipocitic cells within tumor (mac); stromal bands surrounding adipose tissue with atypical cells (sac); patternless (pa); keloidal-collagen (kcm) and haemangiopericytoid-pattern (hp). Diagnostic accuracy of different features is shown in table 2.

Conclusion: The dedifferentiated component in some liposarcomas may resemble SFT. In the DLS/SFT differential diagnosis, immunohistochemistry may be confusing. Presence of WDLS areas is the main diagnostic clue and MDM2 FISH amplification is successful in distinguishing DLS from SFT.

FEATURE	DLS	SFT	p
Sclerosing collagen matrix	9/11	10/12	1
Keloidal collagen matrix	6/11	11/12	0.52
Storiform-pattern	3/11	3/12	1
Hemangiopericytoid vascular pattern	4/11	10/12	0.31
Patternless	8/11	11/12	0.76
Alternating hyper/hypocellular areas	10/11	10/12	1
CD99 reactivity	10/11	10/12	1
CD34 reactivity	9/11	12/12	0.77
BCL2 reactivity	10/11	11/12	1
S100 reactivity	5/11	0/12	0.05

Table 1

%	SENSITIVITY	SPECIFICITY	PPV	NPV
LPC+MAC+SAC	100	92	92	100
PA+KCM+HP	75	91	90	77
MDM2	100	100	100	100
IHQ (CD99+CD34+BCL2)	75	33	60	50

Table 2

OFP-15-006

Osteoblastoma and diagnostics pitfalls

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Objective: Osteoblastoma is a rare benign osteoblastic tumor with a potential for local bone destruction and aggressiveness. The most common site of osteoblastoma is the vertebral column particularly the posterior elements and the sacrum.

Method: In this study we present nine cases of osteoblastoma and the principal differential diagnosis.

Results: On a period of 10 years, nine cases of osteoblastoma had been diagnosed including seven males and two females. The age of those patients ranged from 5 to 29 year old. The tumor was localized in the spine in five of the nine cases and the other ones in the long bones. The radiological diagnosis of osteoblastoma was made in just two cases. The diagnosis was made by histology in eight cases. All our patients had been treated with curettage. On the nine patients, just one of them had developed two successive recurrences.

Conclusion: Osteoblastoma is a rare benign tumor which is rarely diagnosed by radiology alone. The pathologist should always suspect an osteoblastoma in front of a vertebral localization of any tumor.

OFP-15-007

Congenital hepatic fibrosis. Radiology – Pathology correlation

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Objective: Congenital hepatic fibrosis (CHF) is a developmental disorder of the portobiliary system. Clinical findings usually include enlarged liver, well-preserved hepatocellular function and portal hypertension. CHF is frequently associated with hepatorenal fibrocystic disease.
Method: A 29-year-old woman was referred to our hospital for further evaluation of hepatomegaly, and portal hypertension was found. Laboratory tests were all negative. MRI identified hepatosplenomegaly with hypertrophic left medial segment, high uptake nodular areas and homogeneous boundary liver. Needle biopsy was performed.
Results: The biopsy demonstrated slight portal fibrosis and fibrous septa with proliferation of numerous biliary ducts, some of them containing inspissated bile. It was also noticeable the few number of portal vein branches. There was no inflammation or hepatocyte necrosis. Therefore, our diagnosis was congenital hepatic fibrosis. We correlated these results with radiology. Magnetic resonance cholangiopancreatography showed peripherally dilated biliary intrahepatic branches contrasting with preserved caliber of main intrahepatic branches. These findings were also diagnostic for CHF.
Conclusion: The low prevalence of CHF makes it hard to think about this entity in patients with portal hypertension and normal laboratory findings. The histological differential diagnosis must be done mainly with cirrhosis, but also with idiopathic portal hypertension and, in small biopsies, with biliary hamartoma.

OFP-15-008

Digestive lymphomas in the Central Tunisia: Epidemiological and anatomoclinical study of 97 cases

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*Farhet Hached Hospital, Dept. of Pathology, Sousse, Tunisia

Objective: Digestive tract lymphoma is the main extranodal type lymphoma worldwide, digestive tract counting about 35.4 % of extranodal lymphomas in the Centre of Tunisia. The aim of this study was to describe the epidemiological status and the anatomo-clinical features of digestive tract lymphomas in the Centre of Tunisia.
Method: All digestive tract lymphoma cases diagnosed in the Pathology Department, Farhet Hached Hospital, Sousse during a 15-year period were analyzed.
Results: A total of 97 cases of digestive tract lymphoma were reported (64 males, 33 females) with a sex-ratio of 2.0. The patient age ranged between 6 and 82 years with a median age of 48 years. Stomach location was the most frequent with 80 % of cases followed by intestine (15 %) and colon (5 %). Among the 97 digestive tract lymphomas, 48 % were of Marginal zone type (MALT) and 47 % were large B-cell lymphoma. According to the Ann Arbor staging system, 85 % of patients were diagnosed at stage I and II.
Conclusion: Lymphomas of the digestive tract are still frequent in the Centre of Tunisia. The Malt Type lymphoma is main reported histological type. The association with the Helicobacter pylori should be considered.

OFP-15-009

Collecting duct carcinoma in the west of ireland: A rare experience

A. Shalaby*, C. E. Connolly
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Objective: Collecting duct carcinoma is a rare renal neoplasm arising from the epithelium of Bellini's ducts in the distal part of the nephron.
Method: We describe our experience of this entity in University Hospital Galway with a series of four cases diagnosed between 2003 and 2011.
Results: Three patients aged between 35 and 62 years presented with either lymph node or bone metastases without evident abdominal mass. In each case the biopsy from the metastatic lesion showed adenocarcinoma with an immunohistochemical profile suggestive of renal origin and a renal mass was subsequently confirmed by radiology. The fourth patient was an 81 year old male who presented with haematuria. Abdominal CT scan revealed a 5.6 cm mass in the right kidney extending into the renal vein. Biopsy of the renal mass in all cases confirmed adenocarcinoma with a tubular pattern with positive cytokeratin and Vimentin staining and CD10 negative staining. One patient was treated with nephrectomy with post-neoadjuvant chemotherapy and died 25 months after surgery. The other three patients died few months after their diagnosis.
Conclusion: Collecting duct carcinoma is a rare renal neoplasm that can be difficult to diagnose on core biopsies, however, it can be identified based on radiological findings, gross, microscopic, histochemical and immunohistochemical features.

Monday, 10 September 2012, 17.00–19.00, Panorama Hall
OFP-16 Oral Free Paper Session Perinatal and Paediatric Pathology

OFP-16-001

Tissue factor expression is upregulated in primary and metastatic tissue samples of Wilms Tumor

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Objective: Wilms Tumors (WT) is the most frequent renal tumor of children. Genetic alterations have been suggested

as associated factors but the exact pathogenesis of WT is not fully characterized. Tissue factor (TF) is a glycoprotein which happens to be a key receptor for factor VII/VIIa and a primary initiator of coagulation. TF has also been associated with angiogenesis. Recent evidence pointed out an important role for TF in cancer progression and metastasis.
Method: In the present investigation the differential expression of TF in WT was assessed by real-time PCR of RNA retrieved from paraffin sections using microdissection.
Results: Different histological components of WT were analysed. The results revealed that TF was upregulated in blastema and epithelial components as compared to non-neoplastic tissue (14.38 and 16.02-fold respectively, $P<0.001$). Stroma and non-neoplastic tissue presented low levels of TF expression. TF expression in WT metastatic lesions was also significantly upregulated as compared to non-metastatic WT. Microvessel density was positively correlated with TF expression ($r=0.721$).
Conclusion: As described in other tumors, TF seems to play a significant role in the behavior of WT. Further investigations are warranted to better understand the pathways by which TF exerts its effects on tumor progression and its potential as a target for therapy.

OFP-16-002

Histopathological markers as clinical indicators of early liver transplantation in biliary atresia

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*Faculdade de Medicina da USP, Disciplina Cirurgia Pediátrica, São Paulo, Brazil

Objective: Biliary atresia (BA) is the most common neonatal cholestatic disorder and the prime indication for liver transplantation (LTx) in children. Histopathological markers in liver biopsies emerge promise as indicator of early LTx in patients with BA.
Method: Ductular proliferation, ductal plate malformations and type I, III, IV and V collagen deposition were evaluated on Kasai portoenterostomy (KPE) and liver transplantation (LTx) biopsies from 36 children with BA. Formalin fixed and paraffin embedded liver biopsies were stained with hematoxylin-eosin, picrosirius-polarization and immunofluorescence methods. There were analyzed liver histoarchitecture, biliary ductus and collagen deposition in hepatic compartments. Pathologic findings were graded according to a 5-point semi-quantitative severity-based scoring system. Impact of these markers was tested on LTx time (<2 year and >2 year).
Results: Median age of KPE was 12 weeks (range 6–20) and of LTx was 27 months (range 6–120). In KPE liver biopsies, ductular proliferation, ductal plate malformations and collagen deposition were increased but these parameters presented no association with clinical evolution for early LTx. Furthermore, collagen V prominent deposition was found along of hepatic sinusoids and type I, III and IV were more frequent in portal compartment.
Conclusion: These results suggest that histopathological parameters evaluation presented may not determine early LTx in biliary atresia.

OFP-16-003

The role of Hofbauer cells on villous vasculature in early fetal losses

E. Özer*, Y. Arman Karakaya
*Dokuz Eylul University, Dept. of Pathology, Izmir, Turkey

Objective: The aim of this retrospective study is investigate the role of Hofbauer cells in early fetal losses.
Method: The slides obtained from archieval blocks of missed abortion (MA, $n=15$) and blighted ovum (BO, $n=15$) cases and unwanted pregnancies materials (control group, $n=15$) were stained by immunuhistochemical methods using CD68 and CD31 antibody to label Hofbauer cells and endotelial cells, respectively.
Results: The mean number of vilous Hofbauer cells was found to be significantly higher in both BO and MA in contrast to the control group ($p=0.005$ and $p<<0.001$, respectively). However it was not significantly different between BO and MA ($P=0.04$). Chalkey method revealed no statisticaly significant difference in the control group in comparison with MA and BO in ($P=0.29$, $P=0.09$, respectively). Higher microvessel scorring were found in MA in contrast to BO and the control group ($p=0.003$ and $p=0.003$, respectively). However, there was no difference between the control group and BO ($p=0.54$).
Conclusion: We think that Hofbauer cells may be of biological importance in early fetal losses and play a role on defective vasculature formation in MA.

OFP-16-004

Placental VEGF and its receptors expression patterns in preeclampsia

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*V.I. Kulakov Scientific Center, Dept. of Pathology, Moscow, Russia

Objective: Placental angiogenesis anomalies play an important role in some complications of pregnancy development, including preeclampsia (PE). VEGF and its receptors – one of the key placental angiogenic factor. Aim: to evaluate patterns of VEGF and its receptors (VEGFRs 1, 2 and 3) expression in placentas from PE complicated pregnancies.
Method: We performed complex morphological and immunohistochemical study of 9 term placentas from mild preeclampsia (mPE) cases (1st group), 6 term placentas from

severe preeclampsia (sPE) cases (2nd group) and 10 term placentas from uncomplicated pregnancies (control group).
Results: We revealed significantly increased syncitial VEGF expression levels in preeclamptic placentas terminal villi and these changes were much prominent in sPE. We also detected insignificantly increased endothelial VEGF expression levels in preeclamptic placentas terminal villi. VEGFR-1 syncitial expression levels in sPE terminal villi were significantly higher in compare to the mPE and control groups. VEGFR-2 endothelial and syncitial expression levels were significantly lower in both PE groups terminal villi and these changes were much prominent in mPE. Patterns of VEGFR-3 expression in preeclamptic and control groups were multidirectional.
Conclusion: Revealed patterns of VEGF and its receptors expression point on altered placental angiogenesis in PE and reflect different degree of such alteration in mild and severe PE.

OFP-16-005

Placental VEGF and it receptors expression in diabetic pregnancies: Clinical and morphological correlations

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Objective: Chorionic villi vascularity disturbances, caused by abnormal expression of angiogenic factors could correlate with maternal and fetal complications in diabetic pregnancies.
Method: Aim: to evaluate the patterns of VEGF receptors (VEGFR1, VEGFR2 and VEGFR3) expression in placentas from gestational diabetes (GD) and type 1 diabetes (D1) pregnancies and correlation between them and some clinical parameters in newborn (placental weight (PW), newborn weight (NW), placental/newborn weight index (PNWI),1st day of life blood glucose test results (1BGTR)). 29 term placentas from D1 (n=16) and GD (n=20) and 12 term placentas from normal pregnancy (control group) were studied.
Results: In both D1 and GD group we revealed significantly higher level of VEGFR1 (p=0.0001), VEGFR2 (p=0.001) and VEGFR3 (p=0.01) endothelial expression in terminal villi. Difference in VEGFR1 expression among D1 and GD groups was also significant (p=0.0009) as difference in its expression between D1 and control group (p=0.002). Among clinical parameters we only revealed significant increase in 1BGTR in diabetic groups (p=0.03) with marked difference between D1 and control group (p= 0.002). We revealed multidirectional correlation between VEGF and VEGFR2 expression and NW in D1 and GD groups.
Conclusion: Revealed changes reflect placental angiogenesis disturbances influence on intrauterine fetal development.

OFP-16-006

Microvillus inclusion disease (MVID) is a disorder of defective intracellular trafficking and disrupted epithelial cell polarity

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Objective: MVID is a congenital enteropathy characterized by loss of microvilli and formation of microvillus inclusions (MI) in enterocytes. MVID is caused by mutations in the MYO5B gene, coding for the Myosin Vb (M5B) motor protein involved in intracellular transport and maintenance of epithelial cell polarity. We examined the effects of loss of M5B in enterocytes of MVID patient and in a CaCo-2 cell model.
Method: The expression and localization of cell membrane transporters (CD36, Na/K ATPase) and various cell organelle markers : endosomal Rab GTPases [Rab5,7,8,9,11]; early (EEA1) and late endosome (LAMP2), and Golgi (Giantin)) were analyzed using multilabel immunofloures-cence and confocal microscopy of a duodenal biopsy from MVID patient and in CaCo-2 cells following M5B si RNA knock-down (Hum Mut 31:1-8,2010).
Results: Depletion of M5B in both enterocytes and CaCo-2 cells resulted in disruption of epithelial cell polarity with loss of apical microvilli, formation of MI; mislocalization of transporters as well as aggregation of epitopes for different Rab GTP ases, early and late endosomes.
Conclusion: M5B plays a critical role in polarized organization of enterocytes in MVID - a disorder characterized by defective intracellular trafficking and altered endosomal sorting. CaCo-2 cells provide an excellent model to study the pathogenesis of MVID.

OFP-16-007

Beta-catenin expression and mutational analysis of CTNNB1 gene in pediatic Adrenocortical Tumors (ACT)

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Objective: ACT have an unpredictable clinical behaviour, and no liable histological or molecular parameters are available to predict outcome. The activation of WNT/β-catenin pathway, involved in tumor growth and progression in adult ACT has been explored only in Brasilian pediatric ACT. The aim of this study is the investigation of the possible prognostic role of β-catenin accumulation and/or CTNNB1 (β-catenin gene) mutations also in Italian pediatric ACT.

Method: β-catenin immunostaining and mutational analysis of CTNNB1 gene at exons 3 and 5, when possible, were carried on a series of 19 ACT (7 malignant and 12 benign, according to Wieneke classification), from patients enrolled in the Italian Pediatric Rare Tumor (TREP) Study.
Results: Immunostaining for β-catenin showed membrane/cytoplasmic staining in 9 cases, 5 benign and 4 malignant, and nuclear staining in 1 malignant. No mutations of CTNNB1 gene were found in the 8 tumors analyzed.
Conclusion: CTNNB1 gene mutations do not appear to be involved in pathogenesis of pediatric ACT. The accumulation of protein might be related to different mechanisms. Its presence in the majority of malignant ACT suggests a possible role in tumor progression.

OFP-16-008

Neuroblastoma presenting like a Wilms' Tumor with thrombus in inferior vena cava: A case series

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Objective: Neuroblastomas and Wilms' tumors are frequent pediatric solid tumors. The first is frequently detected in the adrenal gland and the second develops in the kidneys. The extension through the vena cava and the lung metastases are frequent in Wilms' tumors and are rarely in neuroblastoma. We present the cases of three children with abdominal tumors with thrombus in the inferior vena cava and pulmonary metastases were discovered yet demonstrated a stage 4 neuroblastoma.
Method: The three male patients were between 23 and 48 months old. They presented an abdominal mass, near the superior pole of the kidney. Thrombus of the vena cava was evoked on imaging studies in all cases and pulmonary metastases were always found. Catecholamine metabolites were present in the first case and negative in the two others. Two out of three patients had a radical nephrectomy.
Results: The pathological analysis always found a neuroblastoma poorly differentiated or undifferentiated without MYCN amplification and confirmed the tumoral thrombus in the second case. The evolution of the two first patients was unfavorable and the third is alive.
Conclusion: Invasion of the inferior vena cava and pulmonary metastases in children with neuroblastoma is uncommon and can modify the surgical management.

OFP-16-009

EpCAM - A marker for Tufting enteropathy (TE) and a useful tool in the differential diagnosis of congenital enteropathies

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*Division of Cell Biology, Medical University Innsbruck, Austria

Objective: Congenital enteropathies (CE) are characterized by villous atrophy and disruption of apical microvilli in duodenal enterocytes. TE is characterized by focal eptithelial tufts and mutations in the EpCAM gene, coding for epithelial cell adhesion molecule, important for cell-cell contacts. Microvillus inclusion disease (MVID), shows loss of apical microvilli and formation of intracytoplasmatic microvillus inclusions. MVID is caused by mutations in the MYO5B gene, important for intracellular transport and organization of epithelial cell polarity. In this study, we identified a new EpCAM mutation in a patient with TE and used anti-EpCAM antibody as a marker for the diagnosis of TE and distinction from MVID.
Method: We used Immunohistochemistry (IHC) with monoclonal EpCAM antibody (mouse monoclonal AB for EpCAM, NCL ESA/Leica Microsystems) on routinely processed duodenal biopsies from patients with TE, MVID and age matched controls. Immunostaining for E-Cadherin served as reference.
Results: EpCAM expression was completely absent in the biopsy from TE patient homozygous for a novel EpCAM mutation (c227 C>G, Ser 76X). E-Cadherin showed normal expression and distribution pattern in the enterocytes. In MVID, expression and distribution pattern was comparable to controls for both EpCAM and E-Cadherin.
Conclusion: Loss of EpCAM is specific and a sensitive marker for confirmation of TE. EpCAM antibody is useful in the differential diagnosis of CE.

Monday, 10 September 2012, 08.30 - 12.00, Club D
OFP-17 Oral Free Paper Session Pulmonary Pathology I

OFP-17-001

Rapid on site evaluation of bronchoscopy specimens for EGFR mutation analysis. A retrospective study of 354 consecutive bronchoscopies

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Objective: In pulmonary adenocarcinoma EGFR mutation analysis has become an important part of the diagnostic work-up. Frequently the tissue of bronchoscopies is of limited diagnostic value. The aim of the present study was to evaluate the impact of ROSE on brochoscopy specimens with regard to EGFR mutation.
Method: ROSE was used for adequacy of the specimen and for separating adenocarcinomas and carcinomas NOS from other neoplasms in the lung. If it was not possible to retrieve material for histology, cytology and cellblock were made. If adenocarcinoma or carcinoma NOS was suspected in ROSE, further two biopsies or two cell blocks were

obtained. EGFR mutation analysis was performed by PCR (Light Cycler 480; EGFR RGQ PCR Kit; Qiagen).
Results: Malignancy was diagnosed in 93 of 354 cases by histology or on cytology with and without cell blocks. Adenocarcinomas (n=30) and carcinomas NOS (n=9), SCC (n=26), SCLC (n=13), and rare tumors (n=15) were diagnosed, respectively. Among the group of adenocarcinomas and carcinomas NOS (n=39), EGFR mutation analysis was performed in 29 (74,3 %) cases and showed mutations in 3 (10,3 %) and "wild type" in 26 (89,7 %) tumors. No material was left in 10 (25,6 %) cases.
Conclusion: ROSE supports bronchoscopic procedures to retrieve adequate specimens for tumor diagnosis and subsequent EGFR mutation analysis.

OFP-17-002
FGFR1 amplification in metastatic squamous cell carcinoma of the head and neck: A potential target for a rational therapy?
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Objective: Patients with Fibroblast growth factor receptor 1 (FGFR1) amplified squamous cell lung cancers (L-SCC) are treated in phase I clinical trials using small molecule inhibitors (SMI). SCC of the lung share common molecular alterations with squamous cell head and neck cancers (HN-SCC). Aim of our study is to assess if HN-SCCs also harbor FGFR1 amplifications. Furthermore, we aim to inhibit cell proliferation of FGFR1 amplified HN-SCC cell lines using a SMI.
Method: The cohort consists of 227 patients suffering from HN-SCC, 97 of these suffering from metastatic disease. Primary tumors and metastatic tumors were assessed for FGFR1 copy number status using fluorescence in-situ hybridization (FISH). We tested cell lines for FGFR1 amplification status and inhibited these with SMIs.
Results: 16 % of primary HN-SCC displayed FGFR1 amplifications. Of interest, almost all metastatic tumor samples revealed a FGFR1 amplification if the corresponding primary tumor harbored the amplification. The cell lines HN and SCC-25 harboured FGFR1 amplifications. HN cell proliferation was inhibitable with small molecule inhibitors.
Conclusion: FGFR1 amplification frequently occurs in primary and metastatic HN-SCC and proves as a potential target for small molecule therapy. Cell growth of FGFR1 amplified cell lines is inhibitable with SMIs. Further functional studies are needed for further validation.

OFP-17-003
The antioxidant components in the pequi (Caryocar Brasiliense Camb) oil fruit diminish the oxidative stress status and the DNA damage in experimental lung cancer
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*Universidade de São Paulo, Dept. of Pathology, Brazil

Objective: The pulp of pequi has high levels of antioxidants properties.
Method: Eighteen male BALB/c mice divided: 14 animals received by gavage 0,5 μL/mg/day of pequi oil (Control + CBCoil=4) during 75 days. After 15 days, 10 of these mices received two doses of 1,5 g/kg intraperitoneal of urethane (Urethane + CBC oil=10). The other 4 animals were only submitted to two doses of 1,5 g/kg intraperitoneal of urethane (Urethane group=4). After 75 days, groups were sacrificed. Antioxidant activity was evaluated in the lung tissues by TBARS (Thiobarbituric acid-reactive substances), CAT (catalase) and SOD (superoxido dismutase) test. DNA damage was estimated by comet test.
Results: The lung parenchyma from Urethane groups without oil and with oil showed neoplasic formations induced by the chemical carcinogenesis in contrast with Control + CBC oil group. The results of TBARS test showed a significant decrease of lipid peroxidation in the Urethane + CBC oil, than Urethane group. The CAT and SOD test didn't show a significant difference. Comet assay showed a significant decrease of DNA damage in Urethane + CBC oil when compared with Urethane group.
Conclusion: The antioxidant components in the pequi oil diminish the oxidative stress status and DNA damage in chemical carcinogenesis, suggesting that this type of strategies may have a greater impact in lung cancer treatment.
Financial Support: FAPESP.

OFP-17-004
An algorithm for gene mutation analysis in lung cancer
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Objective: Somatic alterations of K-RAS, EGFR and ALK which are increasingly requested in order to predict response to personalized therapies in lung cancer are mutually exclusive and are represented in over 50 % of lung adenocarcinomas. The approach to be followed for planning analyses is not standardized in the literature.
Method: We have studied by molecular methods (PCR-RFLP for K-RAS, direct sequencing for EGFR and FISH

for ALK) 185 formalin fixed, paraffin embedded cases of lung adenocarcinomas of different subtypes.
Results: Based on rational, biological and economic considerations we started with K-RAS analysis by PCR-RFLP, which showed mutations in 38 cases (37 with mutation on codon 12 and one case with mutation on codon 13), The 147 residual cases were all analyzed for EGFR mutations. FISH for ALK translocation followed in EGFR- wild cases.
Conclusion: The analysis for K-RAS mutations allows to select the significant percentage (approximately 25 % of adenocarcinomas) when EGFR mutation analysis by direct sequencing can be postponed. K-RAS and EGFR wild cases will then undergo FISH analysis for ALK translocation. ACKNOWLEDGEMENTS Study conducted with the support of the following project: Project PERSOTHER - SMIS-CSNR: 549/12.024; With the support of Sectoral Operational Programme "INCREASE OF ECONOMIC COMPETITIVENESS" Priority Axis 2: Research, Technological Development and Innovation for Competitiveness.

OFP-17-005

Gene mutation analysis in adenosquamous carcinomas of the lung

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Objective: Adenosquamous carcinomas of the lung constitute a rare and aggressive variant of lung cancers. The pressing interest in evaluating the mutational status in lung carcinomas for predicting responsiveness to targeted therapies is presently focused on adenocarcinomas (of different sub-types), which makes preliminary histological typing a crucial step in order to select cases to be genetically analyzed. Hence the interest in deciding if adenosquamous carcinomas should be included among adenocarcinomas or, viceversa, if they should be interpreted as a variant of squamous cancers and excluded from the process of gene analysis.
Method: We have thus collected, from our two Institutions a large number (45 cases) of cancers showing the histological definition of adenosquamous carcinomas according to the WHO criteria and performed gene analysis for k-RAS (codons 12, 13) and EGFR (codons 18, 19 and 21) mutations. The detection of rearrangements of the ALK gene by FISH was also performed.
Results: The results indicate that k-RAS and, specifically, EGFR mutations are detectable in a fraction of these tumors.
Conclusion: In conclusion, adenosquamous carcinomas should not be denied the chance of genetic analysis eventually leading to a targeted therapy. Acknowledgement Project PERSOTHER - SMIS-CSNR: 549/12.024 Romania.

OFP-17-006

Pathology of the lung progenitor cells and their niches in idiopathic interstitial pneumonias and lung sarcoidosis

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Objective: The aim of the study was to investigate the morphological and the molecular-biological changes of the lung progenitor cells and their niches in idiopathic interstitial pneumonias (IPF) and lung sarcoidosis (LS).
Method: We performed an immunohistochemical study on open lung biopsies from 250 patients (usual IPF – 87, desqvamative interstitial pneumonia-37, nonspecific IPF – 42, Cryptogenic IPF – 20, LS – 32, control – 34 patients). Immunochemistry was done on step paraffin sections with monoclonal and polyclonal antibodies: Apo-Cas, PCNA, CK 5-7, 18, 19, TNF-α, TGF-β, PDGF, FGF, IGF II, CD 34, MMP 1, 2, 7, 9, TIMP 4, CD 68, SMA, EMA.
Results: Deep injury of Clara cells together with pneumocytes II and their nishes were found in usual IPF, SK with prominent IPF and desqvamative interstitial pneumonia. Myofibroblast proliferation, neoangiogenesis, adenomatosis and fibrosis with high production of TNF-α, TGF-β, PDGF, FGF, IGF II, CD 34, MMP 1, 2, 7, 9, TIMP 4 accompanied proliferation of these epithelial cells. While in other variants of IPF pathological changes were localized in the interstitium, vessels and basal bronchiolar epithelial cells.
Conclusion: Localization of injury and inflammation in progenitor cells niches results in pathologic reparation, sclerosis and precancer lesions.

OFP-17-007

A small immunohistochemical panel allows for accurate diagnosis of primary and metastatic lung cancer in biopsy specimens

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Objective: Precise subclassification of lung cancer, mostly performed in biopsy or fine needle-aspiration specimens, is required for appropriate therapy. Moreover, distinction between primary and metastatic carcinoma is critical. Thus, the role of immunohistochemistry (IHC) has been emphasized, although an optimal IHC diagnostic algorithm has not been firmly established. Herein, we evaluated the performance of the IHC panel used at our institution in subclassification of lung cancer and identification of metastatic carcinoma.
Method: Cases of non-neuroendocrine lung carcinoma, diagnosed from March 2011 to April 2012 were selected. IHC

was performed for CK7, CK20, TTF-1 and p63. Resection specimens were compared with the respective biopsy.
Results: Of 184 cases analysed, 73 (39.7 %) were diagnosed as lung adenocarcinoma, 59 (32.1 %) as epidermoid carcinoma, 22 (12 %) as other forms of NSCLC, and 17 (9.2 %) as metastasis. Importantly, 26 % of primary lung adenocarcinomas were initially suspected to be metastasis. In 26 cases submitted to surgical resection, 22 (84.6 %) were correctly diagnosed in the biopsy, revealing a substantial agreement (κ-value=0,757).
Conclusion: Our IHC panel allows for reliable subclassification of lung carcinomas in most cases and is decisive for appropriate diagnosis in patients suspected of lung metastasis, which is critical issue in a cancer institute.

OFP-17-008

Rationale for treatment of metastatic squamous cell carcinoma of the lung using FGFR1 Inhibitors

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Objective: We previously identified amplified fibroblast growth factor 1 (FGFR1) as a therapeutic target for small molecule inhibitor (SMI) therapy in squamous cell lung cancer (L-SCC), resulting in currently running clinical trials treating patients with stage III disease. As most patients present with metastatic stage of disease, we attempt to demonstrate FGFR1 amplification in lymph node metastases of amplified primary tumors. Our study aims to give a rational to include these patients in a targeted SMI therapy.
Method: We assessed 75 formalin-fixed paraffin-embedded (FFPE) primary L-SCC samples. 46 samples were primary tumours with corresponding FFPE lymph node metastasis. The biotin-labelled FGFR1 target probe (8p11.23 to 8p11.22) was used to determine the FGFR1 amplification status performing fluorescence in situ hybridization (FISH).
Results: Of 39 assessable metastatic L-SCC, 7 samples displayed FGFR1 amplification (18 %). All of these primary tumors also harbored FGFR1 amplification in their lymph node metastasis. Non-amplified tumors never displayed FGFR1 amplification in corresponding metastases.
Conclusion: We found FGFR1 amplification not only in primary L-SCC, but also in corresponding lymph node metastasis, suggesting that this genetic aberration is a clonal event in tumor genesis. Our study provides data indicating new therapeutic possibilities for patients suffering not only primary, but also metastatic FGFR1 amplified SCC lung cancer disease.

OFP-17-009

KRAS mutation spectrum in 485 primary lung adenocarcinoma from a French Caucasian population: Correlation with smoker status, histological subtypes, pathological staging and clinical behaviour

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Objective: Lung cancer patients with mutant KRAS tumours fail to benefit from adjuvant chemotherapy, and their disease does not respond to EGFR inhibitors. There is a dire need for therapies specifically for patients with KRAS mutant NSCLC, which may depend on KRAS oncogene substitutions.
Method: 485 lung adenocarcinoma French Caucasian patients were tested for KRAS mutation hot spots in codons 12, 13 and 61 by pyrosequencing. PCR amplification was performed using the corresponding Therascreen® Pyro kits (KRAS Pyro® kit, Qiagen, Hilden, Germany). Spectrum of KRAS mutations were correlated with main clinico-pathological parameters.
Results: 195/485 (40 %) of tumours were KRAS mutated. KRAS mutation was a G to T transversion in 80 % of the smoker NSCLC population and a G to A transition in 98 % of the non smoker NSCLC population. Mutations were noted at codon 12 (90 %), codon 13 (8 %) and codon 61 (2 %). A KRAS mutation was a negative prognostic factor with a hazard ratio for death of 1.38 (95 % confidence interval, 1.16–1.63). A mucinous histological subtype was observed in more than 75 % of KRAS mutated tumours.
Conclusion: KRAS oncogene substitution must be accurately determined in primary lung adenocarcinoma for correlation with tumour behaviour and clinico-pathological parameters.

OFP-17-010

Plasma miR-155, miR-152, miR-20a, miR-223, miR-126 and miR-199a expression as a novel prognostic signature of resectable Non-small Cell Lung Carcinoma (NSCLC)

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Objective: There is an urgent need for diagnosis of NSCLC at its early-stages and for improving the survival rate of patients. MicroRNAs, small non-coding RNAs, are frequently deregulated in NSCLC. This study aimed to explore plasma microRNAs for diagnostic value, and evaluated the correlation between expression profiles of plasma microRNAs and disease-free survival (DFS) in NSCLC patients.
Method: We selected eighteen most frequently expressed microRNAs in NSCLC. Total plasma RNA including microRNAs was isolated and reverse-transcribed into cDNAs. The level of microRNAs was determined by quantitative real-time RT-PCR in 42 resectable NSCLC patients

and 10 matched cancer-free individuals. The correlation between the expression of microRNAs in plasma and patient DFS were examined by log-rank and Cox analysis.
Results: Expression levels of miR-320,−296,−145,−199a, −191,−223,−24,−152,−126, and let-7f in the plasma of NSCLC including stage-I patients were significantly higher compared with controls ($P<0.0001$). The combination of these microRNAs yielded 87 % sensitivity and 90 % specificity (AUC=0.934) in discriminating NSCLC patients from controls. The levels of miR-155, −152, −20a, −223, −126 and miR-199a were significantly associated with DFS ($P<0.05$).
Conclusion: Our results suggest that high expression of 6-plasma miRNAs signature would provide potential non-invasive blood-based biomarker for the prognosis of NSCLC.

Monday, 10 September 2012, 14.15 - 16.15, Terrace 1
OFP-18 Oral Free Paper Session Pulmonary Pathology II

OFP-18-001
Dynamic responses of carbonic anhydrase isoforms IX and XII during tumour reoxygenation: Contribution to an aggressive phenotype and discrimination of clinical outcome in Non-small Cell Lung Cancer (NSCLC)
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Objective: Intratumoral disorganized neo-vasculature induces oxygen fluctuations which contribute to tumour growth and metastatic potential. Although the activation by hypoxia of the carbonic anhydrases CAIX and CAXII is well known, responses of these proteins under reoxygenation remain to be elucidated.
Method: In this study we evaluated the effects of hypoxia-reoxygenation on CAIX and CAXII expression and cell proliferation in A549 and H1975 lung adenocarcinoma cell lines. We further investigated by immunohistochemistry on tissue microarray the value of the combined expression of these proteins to predict outcome in 552 NSCLC patients.
Results: CAIX expression was maintained at high level after reoxygenation in contrast of the rapid CAXII down-regulation, whereas the cell proliferation rate was significantly increased. Survival analyses showed that high CAIX/low CAXII was associated with high cumulative incidence of relapse and with poor overall survival of NSCLC patients ($P<0.05$).
Conclusion: Our results provide insight into understanding dynamic responses of CAIX and CAXII expression under tumour cells reoxygenation and demonstrate a critical role for reoxygenation on CAIX and CAXII levels that may select for aggressive lung cancer phenotype. These findings suggest that CAIX and CAXII play selective roles in tumour progression and emphasize their significant prognostic and potential therapeutic value.

OFP-18-002
ALK-gene rearrangement: A comparative analysis on Circulating Tumour Cells (CTCs) and tumour tissue from lung adenocarcinoma patients
M. Ilie*, E. Long, C. Butori, V. Hofman, C. Coelle, V. Mauro, K. Zahaf, C.-H. Marquette, J. Mouroux, P. Paterlini-Bréchot, P. Hofman
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Objective: Until now the ALK status in CTCs isolated from lung cancer patients has not been characterised. We assessed the ALK status in CTCs detected in lung cancer patients and correlated the results to the ALK status defined in the corresponding tumour tissue.
Method: 87 lung adenocarcinoma patients showing CTCs isolated using the Isolation by Size of Epithelial Tumour cell method were screened for their ALK status both in tumour samples and in CTCs. ALK break-apart fluorescence in situ hybridisation (FISH) and immunochemistry using an anti-ALK antibody were done on CTCs and compared with results obtained on corresponding tissue specimens.
Results: 5 patients showed ALK-gene rearrangement and strong ALK protein expression in CTCs and corresponding tumour samples. Negative results were found for 82 patients in CTCs and corresponding tumour samples.
Conclusion: We demonstrate that the ALK status can be determined in CTCs from lung cancer patients both by immunocytochemistry and FISH analysis. A strong correlation was found for the ALK status obtained from corresponding tissue specimens. These results favour non-invasive, ALK-gene status pre-screening on a routine basis on CTCs isolated form lung cancer patients and open new avenues for real-time monitoring for adapted targeted therapy.

OFP-18-003
Detection of EGFR mutations and EML4-ALK rearrangements in lung adenocarcinomas using archived cytological slides
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Objective: While the molecular analysis of EGFR and ALK in archival lung cancer tissues is relatively well established, the acceptability of genetic investigation of cytological material in clinical routine remains a subject of debate.

Method: Islets of malignant cells were visually located on the archived cytological slides, lysed in situ by the drop of SDS-containing buffer, and subjected to the standard DNA and RNA extraction. Examination of paraffin-embedded tissue blocks from the same patients was done in parallel.
Results: 75 cytological/histological lung adenocarcionoma sample pairs underwent the analysis for EGFR mutation. 2 cytological and 1 morphological samples failed to produce DNA. Concordance for the wild-type and mutation status was observed in 53/72 and 14/72 informative pairs, respectively; 1 pair was non-interpretable; 3 and 1 pairs had mutation only in the cytological or histological material, respectively. RNA extraction followed by RT-PCR analysis for the EML4-ALK translocation was done for the 51 pair; failures were observed for 3 cytological and 8 histological samples. 34/40 informative pairs were concordant for the norm, 3 contained identical translocations, and 2 were non-interpretable. 1 pair demonstrated ALK rearrangement in the tissue block but not in the histological slide.
Conclusion: Archived cytological slides appear to be well suitable both for EGFR and ALK analysis.

OFP-18-004
Accuracy and efficiency of intraoperative pathologic consultations of thoracic surgery specimens

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Objective: Intraoperative consultations are indicated to influence the type, nature and extent of surgery. The aim of the current study was to compare frozen section (FS) and final histological diagnoses (FHD) of thoracic surgery specimens and to investigate discordant diagnoses to enhance diagnostic accuracy of FS.
Method: The diagnoses obtained by FS and FHD were compared in thoracic surgery specimens between 2005 and 2011 retrospectively. Specimen sites were divided into five groups (thorax/supradiaphragm, diaphragm, subdiaphragm, resection margins and lymph nodes) according to the indications of intraoperative consultations. Sensitivity and specificity of FS were calculated.
Results: A total of 2949 (99.6 %) FS diagnoses and 2580 (87.2 %) FHD were obtained in 1612 patients. Concordance between FS diagnoses and FHD was 98 % for malignant and 97.5 % for benign categories. 15.3 % of intraoperative consultations were deferred. While 16 diagnoses were regarded as "overdiagnosis", 35 were interpreted as "underdiagnosis". Sensitivity and specificity of FS diagnosis and AUC (95 % confidence interval) were calculated to be 0.92, 0.94 and 0.9817 (0.9760–0.9861), respectively according to Binormal ROC Curve. Discordant diagnoses were mostly due to sampling errors and misinterpretation.
Conclusion: FS examination of thoracic surgery specimens is associated with a high degree of accuracy and efficiency.

OFP-18-005
Increased sirtuin expression in lung adenocarcinoma and squamous cell carcinoma

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Objective: Non-small cell lung cancer (NSCLC) represents a heterogeneous group of cancers consisting mainly of squamous cell carcinoma (SCC) and adenocarcinoma (AD). Increased sirtuin (SIRT-1) expression leads to deacetylation of p53 that could be important in the pathogenesis of lung cancer. Differences of the molecular mechanisms in NSCLC subtypes may follow subtly different pathways to tumorigenesis. The aim of our study was compare SIRT-1 expression in lung adenocarcinoma, squamous cell carcinoma and control group.
Method: 25 patients with stage 2 lung cancer were enrolled in the study. 14 patients had adenocarcinoma, but 11 patients had squamous cell carcinoma. Lung tissue for control group were selected from 15 autopsy cases. Immunohistochemical and western blot methods were used to evaluate SIRT-1 expression in lung tissue.
Results: Obtained results showed that patients with lung cancer had increased SIRT-1 expression compared to control group (146±111 vs. 21±16 cells/mm2, $p<0.0001$). In addition, patients with squamous cell carcinoma had increased SIRT-1 positive cells compared to patients with adenocarcinoma (203±143 vs. 95±49 cells/mm2, $p=0.03$).
Conclusion: Lung cancer is characterized by an increased SIRT-1 expression which ir more prominent in squamous cell carcinoma. Supported by ERAF Project 2010/0202/2DP/2.1.1.2.0/10/APIA/VIAA/013.

OFP-18-006
A new experimental model of orthotopic lung transplantation: Padova experience

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Objective: Transplantation is the only treatment for several end-stage lung diseases but limited by chronic allograft dysfunction particularly obliterative bronchiolitis (OB) and its correlate bronchiolitis obliterans syndrome. The development of preclinical models is crucial to better identify immunological/non-immunological mechanisms leading to OB.

Method: Lung allografts from Lewis rats were orthotopically transplanted into Fisher 344 rats [21 cases]. At 30 [group A] and 90 days [group B and C] post-transplant, animals were sacrificed. In animals from group C, cyclosporine was administered at sub-optimal dose. Lung rejection was graded according to the working formulation of ISHLT and the presence of circulating donor-specific (DSA) antibodies determined by flow cytometry.
Results: In group A, acute rejection (AR) or OB occurred in 33 % and 17 % of animals, respectively. AR occurred in 33–44 % of animals in group B and C respectively. OB was detected in 33 % and in 44 % of group B and C respectively. High levels of DSA IgG were observed in cases with AR.
Conclusion: A novel model of pulmonary OB was developed in the rat. To obtain a reproducible onset of OB, short-term and sub therapeutic cyclosporin administration appears indispensable, at least in our species combination.

OFP-18-007
Epithelial dysplasia and lung cancer in end-stage idiopathic pulmonary fibrosis: Padova experience

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Objective: Idiopathic pulmonary fibrosis (IPF) is associated with increased risk of lung cancer. The prevalence of high grade dysplasia/lung cancer was studied only in a small number of IPF patients. The aim of our study was to investigate the prevalence of precancerous/cancerous changes and their relationship with both metaplastic changes and clinical data.
Method: Native lungs from 66 IPF patients were studied. The degree of honeycomb changes and squamous, cuboidal and bronchial cell metaplasia were graded (score: 0–3). The presence or absence of precancerous/cancerous changes were also evaluated.
Results: Three patients showed neoplastic transformation (4 %) and nine high grade dysplasia (14 %) ("cancer" group). The "cancer" group had similar smoking history, sex, age and duration of disease than the "no cancer" group. All lungs showed metaplasia, the score of squamous (p= 0.0001), cuboidal (p=0.018) and bronchial cell (p=0.018) metaplasia was significantly higher in the "cancer" than in the "no cancer", while the honeycomb score was similar in the two groups.
Conclusion: Advanced IPF patients have a high prevalence of high grade dysplasia/lung cancer, complex epithelial metaplasia, particularly squamous type, is more frequent in "cancer" group, independently from all clinical parameters, including smoking history.

OFP-18-008
Primary pulmonary adenocarcinoma with enteric differentiation, morphologically indistinguishable from metastatic colorectal adenocarcinoma: Case report with a history of metastatic colon adenocarcinoma

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Objective: According to a computerized medline search in the English literature, the present case is thought to be the first primary pulmonary adenocarcinoma with enteric differentiation, completely resembling metastatic colorectal adenocarcinoma morphologically, with a history of metastatic colon adenocarcinoma.
Results: A 62 year old man with a history of colon adenocarcinoma which was detected in 2007 underwent radiologic evaluation. A chest computed tomography scan revealed a 7 mm solitary nodule in the left lower lobe which enlarged in 1 year. The patient underwent left lower lobe wedge resection. Macroscopically, an irregular whitish nodule of 1.5 cm in greatest diameter was detected. Microscopically, the nodule was entirely composed of glandular and papillary structures, some of which had a cribriform pattern, lined by tumor cells that were cuboidal to tall columnar with nuclear pseudostratification, eosinophilic cytoplasm, brush-border, luminal necrosis and nuclear debris. Tumor cells were diffusely positive for cytokeratin (CK)7 and negative for thyroid transcription factor-1, surfactant protein-A, CDX-2 and MUC2. Only a very few tumor cells stained for CK20.
Conclusion: Enteric morphology with consistent expression of CK7 and a scattered positivity for CK20 helped in the distinction from metastatic colon adenocarcinoma and favored the diagnosis of primary pulmonary adenocarcinoma with enteric differentiation.

OFP-18-009
Expression of CXCR4 and CXCL12 in pulmonary carcinoids

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Objective: CXCR4 and its chemochine ligand CXCL12 seem to play an important role in the process of tumor metastasis and, possibly, homing of metastatic tumor cells. The chemochine seems to be responsible for creating micro-enviromental predispositions for survival of metastatic cells, in a similar way it is done for developing immuno-competent cells. In contrast, expression of CXCL 12 in primary tumor cells, is thought to be associated with lower metastatic potential. CXCR4 is expressed in a wide range of tumors, and is thought to be crucial for the metastatic process and tissue-specific spread firstly of breast and prostate cancer. The role of CXCR4 signaling has been poorly

evaluated in carcinoids in general and not at all in pulmonary carcinoids.
Method: Immunohistochemically we investigated the expression of CXCR4 and CXCL12 in pulmonary carcinoids.
Results: Together 60 tumors (47 typical and 13 atypical) where investigated. In 6 there was a metastatic process (in 4 typical and 2 atypical). Ligand CXCL12 expression was negative in all of the metastatic tumors and in two without known metastasis in contrast to only two non-metastatic tumors showing negative reaction. CXCR4 positivity was found in both metastatic and non-metastatic carcinoids. The other investigated parameters where present in both metastatic and non-metastatic tumors.
Conclusion: These results point on a antimetastatic role of CXCL12 expression in lung carcinoids.

Monday, 10 September 2012, 17.00–19.00, Club D
OFP-19 Oral Free Paper Session Pulmonary Pathology III

OFP-19-001
Increased decorin and type V collagen in SSc pulmonary fibrosis
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Objective: To evaluate COL V and decorin expression in pulmonary tissue and to characterize biochemical profile of COLV from lung fibroblasts culture from SSc patients.
Method: We evaluated COL V and decorin expression and tridimensional reconstruction (3D) of 6 patients with SSc without pulmonary hypertension that underwent surgical lung biopsy and as control was obtained lung fragments from 6 normal individuals who died from trauma. COL V amount in lung sections was evaluated with immunofluorescence. To biochemical characterization of COL V from lung fibroblasts culture was used quantitative immunoblot.
Results: It was found that the structure of COL V fibers was distorted and strongly thickened in lung tissue from SSc patients compared with thin fibers pattern in the healthy controls. Decorin was distributed around COL V fibrils in the bronchovascular interstitium and vascular walls. Histomorphometric analysis of SSc lung demonstrated increased expression of both COL V and decorin when compared to the control ($p<0.01$). The semiquantitative imunoblot detected an increased high molecular weight COLV fraction in patients when compared to the control.
Conclusion: The over expression and unusual organization of COLV fibers with biochemical changes associated to increased decorin indicates that matrix signalization pathway is involved in COLV fibrillogenesis process in SSc pulmonary fibrosis.

OFP-19-002
Application of combined light microscopy and confocal laser endomicroscopy diagnostics in studying of solitary and multiple lung consolidations
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Objective: Probe-based confocal laser endomicroscopy (pCLE) is a new method used during bronchoscopy by means of special miniprobe Alveoflex and based on the visualization of intraalveolar structures which possess autofluorescence. Aim: to compare the visual signs of a healthy and pathologically changed lung tissue received at pCLE in patients with infiltrative and local lung nodules with the diagnosis, delivered by light microscopy.
Method: An autopsy and surgical material was fixed in 10 % neutral formalin solution and was analyzed by studying with a new method for visualization of structures. Histological specimens were studied at that spaces, where the pCLE was applied. We compared our results by using qualitative method.
Results: Normal lung tissue structures include alveolar septum with the high light emission and light-negative spaces - the alveolar spaces. In case of pneumonia alveolar septum were saved, but the light density of alveolar spaces was higher in compare with the normal tissue. In case of alveolar proteinosis we observed unique globules, which had the highest light emission. We found out several authentic signs, which are representative for each kind of pathological feature. Moreover, we revealed some other characteristics, which help us to distinguish some types of lung cancer.
Conclusion: pCLE can be used as an additional method of noninvasive diagnostics in vivo.

OFP-19-003
Increased copy nember of alk gene is not associated with increased immunoreactivity of alk protein in lung adenocarcinomas
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Objective: Anaplastic lymphoma kinase (ALK) gene rearrangements represent an important predictive marker and promissing therapeutic target in small subset of non-small cell lung carcinomas (NSCLC). Immunohistochemical (IHC) screening of ALK abnormalities in NSCLC was reported to have variable reliability. We analyzed

association between ALK immunoreactivity and increased number of ALK gene copies often seen in NSCLC.
Method: We examined 10 clinically selected EGFR negative lung adenocarcinomas. ALK protein expression was detected by IHC using antibody clone ALK1 (Dako). ALK gene status was assessed by fluorescent in situ hybridization using LSI ALK Dual Color Rearrangement probe (Abbott) and SPEC ALK/EML4 TriCheck probe (ZytoVision).
Results: Increased ALK gene copy number was identified in 7 cases, 3 of them showed cytoplasmic ALK positivity. In 2 of these cases we detected rearrangement of ALK locus, once represented by ALK-EML4 fusion combined with more complex cytogenetic abnormalities. Remaining third ALK + case was negative for ALK rearrangement.
Conclusion: IHC seems to be useful method for initial screening of ALK rearrangements in NSCLC. There is no clear association between ALK protein expression and number of ALK gene copies. Prognostic relevance of ALK copy gains or amplification in lung adenocarcinomas remains to be determined, together with role of ALK-inhibitors in those cases.

OFP-19-004
Expressions of EGFR, ERCC-1, ß Tubulin III, RRM-1 in advanced non-small cell lung carcinoma
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Objective: EGFR, ERCC1, RRM1 and βTubulinIII predicts sensitivity to therapeutic agents and provide prognostic information in Nonsmall cell lung cancer (NSCLC) which is the most frequent worldwide cause of cancer death.
Method: We investigated the expressions of EGFR, ERCC1, βTubulinIII, RRM1 immunohistochemically in 42 advanced NSCLC cases and their correlations with other pathologic features.
Results: The age distribution was 30–82 with an average of 63,02. Male/female ratio was 34/8. ERCC1 protein was detected in nuclei of carcinoma cells in 38 patients (90,5 %) (H score >1). BTubulinIII expression was detected in cytoplasm of cancer cells in 41 patients (97,6 %) (score ≥ 50). ERCC1 and βTubulinIII expression were not associated with pathological factors. RRM1 was negative (score<9) in 29 (69 %) cases and negativity was significantly correlated with male gender (p<0,032). EGFR was negative (score<200) in 40 (95,2 %) cases and negativity was nearly correlated with absent necrosis (p<0,065). No significant correlations were found between EGFR, ERCC1, βTubulinIII, RRM1 and the pathological parameters.
Conclusion: In our study, as a first step, EGFR, ERCC1, βTubulinIII, RRM1 showed no significant correlation with pathologic features. We look forward to obtain further results in the next study consisting of correlations with follow ups.

OFP-19-007
Proliferative markers in idiopathic pulmonary fibrosis: Clinical, radiological and functional significance
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Objective: Natural course of idiopathic pulmonary fibrosis (IPF) could be predicted by proliferative markers of the fibrotic process, such as myofibroblasts and interleukins (IL)-13 and IL14. Our primary aim was to determine whether these proliferative markers influence the course of IPF course measured by a radiological/functional score.
Method: Twenty-eight patients with biopsy-proven IPF disease, who underwent pulmonary evaluation by high-resolution computed tomography (HRCT) fibrosis score and pulmonary function tests were studied. Five normal lung tissues (NLT) were included Biomarkers in lung tissues were detected by immunohistochemistry and quantified by histomorphometry for myofibroblasts alpha-smooth muscle actin (α-SMA), anti-interleukin (IL)-4 and IL-13.
Results: Myofibrobalst amount, IL-4 and IL-13 expression were higher in IPF than in NLT (p<0.01). Myofibroblast expression of α-SMA was positively correlated to IL-14 and IL-13 expression. Lung tissue from patients with high HRCT fibrosis scores expressed significantly greater α-SMA+, IL-4 and IL-13 when compared with patients with low HRCT fibrosis scores (p<0.05). Negative correlations were found between myofibroblasts α-SMA + and VC and DLCO.
Conclusion: Proliferative markers, detected by immunohistochemistry, in lung tissue allowed recognizing a dichotomous distribution of HRCT fibrosis course and influenced pulmonary function tests, suggesting that they may be promising markers of prognosis in these patients. Financial Support: FAPESP, CNPq.

OFP-19-008
Comparison of survival of patients with different histological subtypes of epithelioid pleural mesothelioma
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Objective: Epithelioid mesothelioma is the most common histologic type of the diffuse malignant pleural mesothelioma, also having the best prognosis. Although a great variety of histological patterns within epithelioid type has been described, a clear impact of histological subtyping on clinical outcome is unknown (Kadota et al., 2011.). Here we compared median survival of six histological subtypes of epithelioid mesothelioma.

Method: We examined hematoxylin and eosin-stained slides of 74 patients diagnosed with epithelioid mesothelioma. According to previously described predominant histological features we grouped them into six subtypes: trabecular, solid, microglandular, tubulopapillary, micropapillary and pleomorphic.
Results: The median survival of all 74 patients with epithelioid mesothelioma was 14.5 months. The best median survival was in trabecular and micropapillary subtypes (each 18 months, $n=20$ and $n=5$, respectively), followed by tubulopapillary (17 months, $n=18$), microglandular (16 months, $n=7$) and solid (11 months, $n=19$) subtypes. The worst median survival was in pleomorphic subtype (5 months, $n=5$).
Conclusion: Epithelioid type of diffuse malignant pleural mesothelioma shows a great diversity of histological patterns that likely have an impact on the clinical outcome and patient's survival. Further investigations of genetic variations among different subtypes may provide valuable information for better understanding of pathogenesis of these tumors.

Tuesday, 11 September 2012, 17.00–19.00, Meeting Hall V
OFP-20 Oral Free Paper Session Uropathology

OFP-20-001

Comprehensive characterization of ploidy and proliferation levels in prostate cancer: Progression and prediction of lymph node metastasis

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Objective: Genetic instability resulting in both aneuploidy and polyploidy are discussed to be involved in prostate cancer (PCa) development and progression. Aim of this study was to comprehensively characterize the ploidy status and proliferation levels in PCa with regard to disease progression.
Method: Using FISH, we assessed 112 localized PCa, 75 PCa with 125 corresponding lymph node metastases, and 42 hormone-refractory distant metastases for losses and gains of all 24 chromosomes. The proliferation rate was assessed using pHH3 and Ki67 immunohistochemistry.
Results: We observed significant increases in aneuploidy with advancing tumor stage ($p<0.05$). Chromosomes X, 21, Y, 14, 16, and 8 were most frequently numerically altered. Increased levels of proliferation were significantly associated with the extent of aneuploidy and tumor stage ($p<0.01$). Combining aneusomy of chromosomes 4, 6, 20, and X with PHH3 immunoreactivity resulted in a prediction model for lymph node metastases with a sensitivity of 73.3 % and a specificity of 72.6 %.
Conclusion: We present evidence that genomic instability leading to aneuploidy is an important factor in PCa progression. Furthermore, we demonstrate that increased Ki-67 and PHH3 expression are potential indicators of metastatic disease. Lastly, we suggest a new approach to preoperatively determine lymph node metastasized disease in PCa.

OFP-20-002

ERG protein expression and genomic rearrangement status in primary and metastatic prostate cancer: A comparative study of two monoclonal antibodies

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Objective: Overexpression of the ERG protein is highly prevalent in prostate cancer (PCa) and most commonly results from gene fusions involving the ERG gene. Recently, an N-terminal epitope targeted mouse and a C-terminal epitope targeted rabbit monoclonal anti-ERG antibody have been introduced for the detection of the ERG protein. Here, we are the first to compare the mouse ERG-MAb to the rabbit ERG-MAb for their concordance on the same PCa cohort. Furthermore, we assessed if the ERG protein expression is conserved in lymph node and distant metastases.
Method: We evaluated tissue microarrays of 278 specimens containing 265 localized PCa, 29 lymph node, 30 distant metastases, and 13 normal prostatic tissues. We correlated the ERG protein expression with the ERG rearrangement status using an ERG break-apart fluorescence in-situ hybridization (FISH) assay and IHC of both ERG antibodies.
Results: ERG protein expression and ERG rearrangement status were highly concordant regardless of whether the mouse or rabbit ERG-MAb was used (97.8 % versus 98.6 %, respectively).
Conclusion: This is the first study to comprehensively compare the two ERG-MAbs. By demonstrating a broad applicability of IHC to study ERG protein expression using either antibody, this study adds an important step towards a facilitated routine clinical application.

OFP-20-003

Improved method of detecting the ERG gene rearrangement in prostate cancer using combined dual-color chromogenic and silver in-situ hybridization

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Objective: The recently detected ERG rearrangement revealed as a recurrent and prevalent prostate cancer (PCa) specific event. To detect this alteration, FISH is the method of choice. However, FISH harbors disadvantages for widespread adoption in clinical practice. Subsequently, the

chromogenic in-situ hybridization (CISH) and the enzymatic metallography silver in-situ hybridization (SISH) emerged as promising bright-field alternatives. We aimed to develop a combined CISH and SISH (CS-ISH) gene break-apart assay on the example of the ERG gene.
Method: We assessed and compared 178 PCa and 10 benign specimens for their ERG rearrangement status applying a dual-colour FISH and CS-ISH ERG break-apart assay on consecutive sections.
Results: We observed a highly significant concordance (97,7 %) between FISH-based and CS-ISH-based results (Pearson's correlation coefficient 0.955, $P<0.001$).
Conclusion: We demonstrate that the ERG rearrangement status can reliably be assesed by CS-ISH. Further, we confirm that the CS-ISH technique combines the accuracy and precision of FISH with the ease of bright field microscopy. We developed a tool which allows a broad spectrum of applicants to study the biological role and clinical utilization of ERG rearrangements in PCa. Moreoever, our study is the first proof-of-principle for bright-field CS-ISH gene fusion or break-apart assays.

OFP-20-004
Rearrangement of the ETS genes ETV-1, ETV-4, ETV-5 and ELK-1 is a clonal event during prostate cancer progression
M. Braun*, Z. Shaikhibrahim, W. Vogel, D. Boehm, R. Menon, N. Wernert, G. Kristiansen, S. Perner
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Objective: ETS gene rearrangements are frequently found in prostate cancer (PCa). Recently, we observed that ERG rearrangement in primary PCa transfers into lymph node metastases, suggesting it to be a clonal expansion event during PCa progression. Here, we investigated whether this also applies to the less frequent ETS genes, ETV-1, ETV-4, ETV-5 and ELK-4.
Method: Using break-apart FISH assays, we evaluated the status of above mentioned ETS gene rearrangements on a cohort comprising of primary PCa, corresponding lymph node and distant metastases.
Results: ETV-1, ETV-4, ETV-5 and ELK-4 rearrangements were found in 10 %, 6 %, 1 % and 2 % of the primary PCa, respectively, and in 8 %, 6 %, 6 %, 1 % of the corresponding lymph node metastases, respectively. Rearrangements of ETV-1 and ETV-5 were not found in any of the distant metastases cases, whereas ETV-4 and ELK-4 rearrangements were found in 4 % and 4 % of the distant metastases, respectively.
Conclusion: Our results suggest that rearrangement of the less frequent ETS genes is a clonal event during prostate cancer progression. Our findings provide insights into potential clonal expansion events during PCa progression and may have significant implications in understanding the molecular basis of the metastatic cascade of PCa.

OFP-20-005
Comparative analysis of two prostate biopsy systems: A study of 120 cases
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Objective: It's expectable that the higher the number of prostate biopsies the greater the probability of prostate cancer detection, presumably improving the diagnostic accuracy and treatment decision.
Method: Under this assumption, since May/2010, Santo António's Hospital implemented a prostate mapping system, increasing the number of biopsies performed from 8–12 to 16–18 and processing each core independently. We intend to establish a comparison between the traditional prostate biopsy system (TS) and the prostate mapping system (MS). For this study, all biopsy slides and corresponding surgical specimens from 60 patients subjected to MS and 60 patients subjected to TS were reviewed. Gleason score, percentage of tumor present in prostatic tissue (expressed as small ≤ 5 %, medium 6–19 % and large ≥20 %) and presence of tumor in prostate apex and base were analyzed.
Results: Comparing MS with TS, the correlation coefficient was 53,5 % and 31,9 % for Gleason score and 46,9 % and 37,4 % for the percentage of tumor present in prostatic tissue, respectively. Mapped biopsies were able to detect the tumor in the apex and base in 72 % and 80 % of cases.
Conclusion: These results suggest that prostate MS improves the diagnostic accuracy of prostate cancer and has a good ability to predict the presence of tumor in prostate apex and base.

OFP-20-006
Frequency and prognostic significance of TMPRSS2-ERG gene fusion in lymph node positive prostate cancers
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Objective: TMPRSS2-ERG incidence and prognostic significance in lymph node positive prostate cancer are virtually unknown.
Method: A tissue-microarray was constructed from 119 hormone-naïve nodal positive, surgically treated prostate cancers containing samples from all Gleason patterns (GP) present in every primary tumor (PT) and corresponding lymph node metastases (MET). TMPRSS2-ERG status was determined by fluorescence in-situ hybridization and correlated with various histomorphological tumor features (Gleason score, stage, cancer volume, nodal tumor burden) and biochemical recurrence-free, cancer-specific and overall survival.
Results: TMPRSS2-ERG fusion was present in 43.5 % (homogeneous 25.2 %, heterogeneous 18.3 %) of the PT and in 29.9 % (homogeneous 28.7 %, heterogeneous 1.2 %) of the MET. Percentage of TMPRSS2-ERG in GP3/4/5 of PT and

MET were: 38 %/37 %/24 % and 23 %/30 %/39 %. Concordance in TMPRSS2-ERG status between PT and MET was poor (Kappa 0.39) showing 20.9 % and 8.1 % of cancers with gene fusion solely in the PT and MET, respectively. TMPRSS2-ERG fusion was not correlated with histopathological tumor features and predicted late biochemical recurrence independently (p=0.041) when present in PT.

Conclusion: TMPRSS2-ERG fusion in PT is more frequent and its distribution more heterogeneous compared to MET. The gene fusion in primary tumors independently predicts late biochemical recurrence.

OFP-20-007

WNT and SHH pathways activation in penile carcinoma

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Objective: Penile carcinoma (PC) is rare in developed countries, accounting for less than 1 % of all neoplasms in men, and biological characteristics of this tumor are poorly known. WNT and SHH pathways are important for cell proliferation, differentiation and survival, and therefore, play a role in carcinogenesis of various organs. The goal of this study is to investigate the expression profile of WNT and SHH pathway proteins in PC, characterizing the expression of target proteins from WNT (Wnt-1, Wnt-2, Wnt-2 Gsk3β, β-catenin, D1 Cyclin, MMP7, C-myc, CD44) and SHH (Shh, Smo, Gli, EGFR) pathways.

Method: For that, 18 samples of PC were obtained from the files of Anatomic Pathology department from A.C. Camargo Hospital (Brazil) and submitted to immunohistochemistry.

Results: We observed that Wnt-1 and Wnt-2 were expressed in 15 and 16 cases, respectively, out of the 18 evaluated samples. Strong Shh expression was detected in 16/18 cases, whereas weak and negative expression was seen only in one case each. Smo and Gli-1 proteins were expressed in almost all cases (17/18), and also D1 Cyclin, b-catenin and EGFR were frequently expressed.

Conclusion: These preliminary results suggest that WNT and SHH pathways may be active and participating in the progression of penile cancer.

OFP-20-008

Expression of the multidrug resistance protein 4 correlates with longer PSA relapse free survival and androgen receptor and forkhead box A protein expression in prostate cancer

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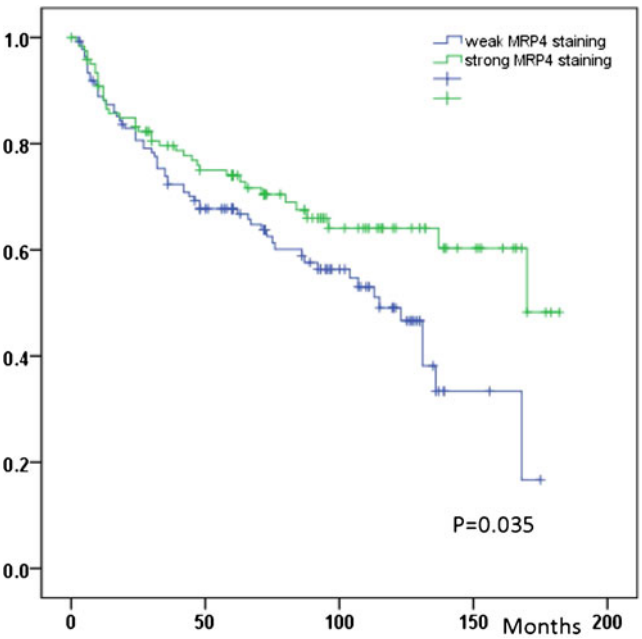
Objective: Multidrug resistance protein 4 (MRP4) a transmembranary transport protein has shown to be expressed in prostate cancer cell lines and cancer cell specimens and turned out to be among the highest upregulated genes in an array-based transcription analysis. Its expression is regulated in an androgen dependent manner, possibly modulated by forkhead box A (FoxA), an androgen receptor (AR) co-activator. Therefore, we investigated its expression in a large cohort of neoplastic and non-neoplastic prostate tissues (n=441) and evaluated its prediction of PSA relapse free survival (RFS).

Method: TMA (n=441) stained for MRP4, FoxA, AR, ER, PSA, Ki-67: radical prostatectomies (RPE) (n=332), castrate resistant prostate cancer (CRPC) (n=26), metastases (n=39) and non-neoplastic (n=187). PSA-RFS of 258 patients; mean 70 months.

Results: MRP4 expression decreases with tumor progression into castrate resistant disease, correlates with PSA, AR and FoxA expression and inversely correlates with Gleason score. Moreover, a strong MRP4 expression is significantly associated with a longer PSA RFS in RPE patients. Normal tissues from the transitional zone show a weak MRP4 expression compared to the peripheral and central zones.

Conclusion: MRP4 expression seems to predict PSA relapse free survival in prostate cancer patients. Since its expression is androgen dependent it decreases with tumor progression into CRPC.



OFP-20-009

Synchronous Angiomyolipoma and renal tumors in patients without Tuberous Sclerosis: Clinico-pathological study of 18 cases

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Objective: Simultaneous existence of AML and renal neoplasia is frequent in Tuberous Sclerosis (TS) patients, but uncommon in non-TS cases.
Method: A total of 18 cases of coexistent renal neoplasia and AML in non-TS patients were identified. Clinico-pathological features were studied.
Results: 18 patients: 10 M/8 F (mean age 62,77 year; range: 35–83). Mean AML size: 0,82 cm (range: 0,2–3,4). The main size of the renal neoplasms was 5,09 cm (range 1,2–15). AML morphology: 6 leiomyomatous, 4 classic-triphasic, 4 lipomatous, and 4 epithelioid. Three cases had multifocal AML. 15 cases had ipsilateral tumors associated with AML: 6 CCRCC (1 sarcomatoid), 4 ChRCC, 1 RO, 1 TFE3 RCC, 1 hybrid (RO-ChRCC) renal-cell tumor, 1 urothelial carcinoma, and 1 case had 2 tumors: MTSC-RCC and concomitant PRCC. 2 cases had contralateral tumours associated with AML: 1 ChRCC and 1 RO. One patient had bilateral tumors associated with AML: an ipsilateral RO and a contralateral CCRCC. The median follow-up was 36,85 mths (range 0,4–199,8): all patients were alive without disease.
Conclusion: The coexistence of renal tumors with AML is a rare event, usually incidental. If AML is found incidentally together with other renal tumors, it is important to exclude TS retrospectively.

OFP-20-010

Primary renal synovial sarcoma: A clinicopathologic, immunohistochemical and molecular genetic study of 16 cases

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Objective: Primary renal synovial sarcoma (R-SS) is a rare malignant neoplasm. Approximately 45 cases have been described, chiefly as case reports or as part of relatively limited small studies. We studied the clinicopathological, immunohistochemical (IHC) and molecular genetic features of 16 well-characterized R-SS.
Method: All available slides for 16 institutional and consultation cases of R-SS were reviewed. An IHC panel (TLE1, BCL2, cytokeratins, S100, CD34, INI1) was performed. RT-PCR for SS18-SSX1/2 or FISH for SS18 rearrangement was performed. Follow-up was obtained.
Results: The patients (9 M, 7 F) ranged from 17 to 78 years (mean 46). All tumors were of monophasic fibrous type. IHC results: all cases were strongly positive for TLE1 and BCL2; focally positive or negative for cytokeratins; negative for S100 and CD34; and showed retained INI1 expression. Molecular genetic results were: SS18-SSX1 (5 cases), SS18-SSX2 (10 cases), SYT rearrangement (1 case). Follow-up (5 cases): 3 dead of disease, 2 alive without disease.
Conclusion: Our data show a striking overrepresentation of the SS18-SSX2 fusion subtype among R-SS, in contrast to other SS, in which the SS18-SSX1 fusion subtype accounts for two-thirds of cases. The reasons for this difference are unclear. The prognosis for R-SS appears similar to that of SS of more common locations.

Poster Sessions

Sunday, 9 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-01 Poster Session Pulmonary Pathology

PS-01-001

Histological and immunohistochemical study of lung carcinomas from the files of the Institute of Pathology of Medical Faculty of the P.J. Safarik University in Kosice (2007–2011)

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Objective: New data related to the diagnosis and therapy of lung cancer have also affected the position of the pathologist in this area. Principal changes in its classification have appeared in relation to adenocarcinoma and partly also in the large cell type of lung cancer.
Method: Presented data represent a five-year retrospective study of a series of 546 cases of lung cancers analyzed in our Institute. Besides routine HE staining the following immunohistochemical reactions were used: antibody against TTF-1, Surfactant A, Chromogranin, Synaptophysin, CK7, AE1/AE3, p63, 34βE12, CD56 and Napsin A.
Results: Using the WHO, 2004 Classification of Lung Cancer, an unusual phenomenon of the return of squamous cell cancer (SCC) prevalence over adenocarcinoma has been documented, which in the earlier years has equated the SCC. The difference in obtaining the tissue samples, and changes in the geographical origin of certain patients of Eastern Slovakia may partly explain these differences. Though the new Travis classification (J Thorac Oncol, 2011) was not used, there prevailed mixed forms also in our series.
Conclusion: It is important to respect new information regarding the Classification of Lung Cancer, especially in the category of adenocarcinoma. The constructive collaboration of pathologists with clinicians is recommended.

PS-01-002

An exceptional coexistence of MALT lymphoma and carcinoid tumor in the lung

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Objective: Extranodal marginal zone lymphoma MALT lymphoma and carcinoid are neoplasms occurring most frequently in the gastrointestinal tract and respiratory system. Although each of them occurs relatively frequently and separately, the simultaneous appearance of these two neoplasms is exceptionally rare.
Method: We report an exceptional synchronous association of MALT lymphoma and typical carcinoid in the lung.
Results: A 52-year-old male with Sjögren's syndrome presented with cough and chest pain with no improvement after antibiotherapy. Bronchial fibroscopy was normal. Computed tomography showed a diffuse interstitial pneumopathy with a persistent left lower lobe nodule suspected of malignancy. A surgical resection of the nodule was achieved. Histopathologically, it measuring 1.2 cm in diameter and was composed of association of malt lymphoma and typical carcinoid tumor which were focally admixed. Immunohistochemical stains were strongly reactive to endocrine marker in carcinomatous component. Tumor cells were diffusely CD20 positive in lymphomatous component. Assessment of extent of lymphoma revealed a gastric location. The patient received chemoptherapy. He's still alive since 8 months.
Conclusion: The best of our knowledge, this is the first report of such a collision lung tumor at the same anatomical site. The aim of this study is to describe the pathogenesis and clincicopathological feartures of such exceptional association.

PS-01-003

Primary mucoepidermoid carcinoma of lung: Clinicopathological analysis of 15 cases

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Objective: Primary mucoepidermoid carcinoma is rare comprise less than 1 % of all lung tumors. It is characterized by the presence of squamoid cells, mucin-secreting cells and intermediate type. On the basis of morphological and cytological features, it is divided into low and high-grade types.
Method: We report a retrospective study of 15 cases diagnosed during a 15-year period. Diagnosis was made by histological examination of specimen obtained from lobectomy in 13 cases and pneumonectomy in 2 cases. No patient had history of salivary mucoepidermoid carcinoma.
Results: There were 13 men and 2 women ranging in age from 10 to 76 years. Computed tomography showed a well circumscribed tumor arising in bronchus in all cases. A bronchial fibroscopy showed a main, lobar or segmental mass. Bronchial biopsy revealed a non-small-cell carcinoma in only one case. Histologically, tumors were classified into 7 low grade mucoepidermoid carcinoma and 8 high grade mucoepidermoid carcinoma. Patients with low grade carcinoma remain alive after surgery alone. Patients with high grade carcinoma received chemotherapy, four of them developed distance metastasis.
Conclusion: Mucoepidermoid carcinoma is a rare primary malignancy of the tracheobronchial tree which is difficult to diagnose by limited biopsy. The prognosis is variable and depends upon the histological grade.

PS-01-004

Primary pulmonary marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue: Clinicopathological analysis of 6 cases

E. Braham*, E. Boudabbous, S. Aouadi, A. Ayadi Kaddour, M. Mlika, O. Ismail, M. Yahia, I. Drira, T. Kilani, F. El-Mezni
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Objective: Primary pulmonary MALT lymphoma is considered to originate from MALT of the bronchus secondary to autoimmune or inflammatory processes. Although, it comprises more than two-thirds of all primary non-Hodgkin's lymphoma of the lungs, it is a rare entity and accounts for less than 1 % of all lymphomas.
Method: We report a retrospective study of 6 cases of Malt pulmonary lymphomas diagnosed during an 8-year period. Diagnosis was made on surgical pulmonary biopsy in 2 cases, bronchial biopsy in 3 other cases and on lobectomy in one case.
Results: There were 4 women and 2 men ranging in age from 48 to 74 years. Two patients had a history of Sjoren's syndrome and one had a history of previous mammary carcinoma. Computed tomography revealed bilateral nodules in 3 patients, lung mass in 2 patients and an area of consolidation in one patient. Fiberoptic bronchoscopy showed bronchial stenosis in only 3 cases. Morphologically, the neoplasms had features typical of MALT lymphoma. One patient was treated with surgery alone and 5 received chemotherapy. Five patients remained alive while one patient presented with recurrence.
Conclusion: Pulmonary MALT lymphomas are characterized by an important dissociation between clinical expression and radiological pattern. Therefore, histological documentation is mandatory to ensure diagnosis.

PS-01-005

Expression of Carbonic Anhydrase IX in malignant mesothelioma

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Objective: Malignant mesothelioma (MM) is an aggressive tumour with a poor prognosis. Carbonic anhydrases and their inhibitors offer an opportunity for developing novel anticancer drugs, as well as diagnostic and prognostic tools. Carbonic anhydrase IX (CAIX) is a membranous metalloenzyme involved in cell adhesion and pH homeostasis. It is a direct target of hypoxia-inducible factor and serves as a marker of hypoxia. This study was designed to assess systematically CAIX expression in MM of pleura and peritoneum, and their benign counterparts.
Method: 47 MMs of pleura (41 epithelioid, 1 biphasic, 2 sarcomatoid) and peritoneum (3 epithelioid), and 14 normal or reactive pleural samples were analyzed. CAIX expression was determined using immunohistochemistry. Membranous immunoreactivity was evaluated semiquantitatively. Specimens were divided into five subgroups according to the staining pattern and intensity.
Results: 95,7 % (45/47) of MMs expressed CAIX. All epithelioid mesotheliomas showed at least a weak focal (8,5 %, 4/47), but predominantly a strong diffuse (70,2 %, 33/47) staining with CAIX antibody, without any perinecrotic pattern. Sarcomatoid mesotheliomas were negative. Normal mesothelial cells were diffusely positive.
Conclusion: These data suggest that mechanisms of CAIX overexpression in MM are different than due to hypoxia and appear promising in prospective use of specific therapeutic CAIX targeting in advanced mesothelioma.

PS-01-006

ALK expression in pulmonary adenocarcinomas

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Objective: EML4-ALK crizotinib therapy needs validation at lower cost and rapid answer in Pathology routine.
Method: Histological/WHO 2004 and CK7, TTF1, CK5.6, CD56/chromogranin and vimentin panel classifications with ALK (clone 5A4, Novocastra Laboratories Ltd, Newcastle, United Kingdom) were applied to paraffin sections of 35 bronchial-pulmonary carcinomas: 20 adenocarcinomas, 6 epidermoid carcinomas, 4 pleomorphic carcinomas (mixed type adenocarcinomas with large/giant/fusiform cells), 4 neuroendocrine carcinomas (NEC) (1 combined large cell NEC with adenocarcinoma and 2 with epidermoid carcinomas; 1 SCLC chromogranin positive combined with adenocarcinoma) and 1 adenosquamous carcinoma.
Results: The applied antibodies specified bronchial pulmonary carcinomas subtypes clearly. In 3 over 60 years old non-smoking females mixed type adenocarcinomas ALK expression was over 50 %: acinar, solid, micropapillary and microacinar patterns; one glandular mucinous pattern (mucinous BA pattern) and one BA pattern, all expressing TTF-1.
Conclusion: In this study, 3/20 adenocarcinomas of older women had ALK protein expression, only one with a mucinous pattern. As protein positivity cases comprise a lower number, FISH described by S. Lantuejoul seems to be the most appropriate method. It is now necessary to decide whether KRAS and EGFR mutations have to be determined together and/or select TTF-1 positive adenocarcinomas (from terminal respiratory unit) raised by this approach.

PS-01-007

Pet activity for bronchial-pulmonary carcinomas and adenocarcinomas subtyping

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Objective: The 5 year survival of bronchial-pulmonary carcinomas remains poor, between 6 % and 14 %/men and 7 % to 18 %/women. Treatment orientation is influenced by clinical staging and morphological classification in biopsies of 70 % of the cases.
Method: This study comprised 41 surgical specimens where we compared immunohistochemistry in-between Adenocarcinomas (18), Epidermoid Carcinomas (12) and the heterogeneous groups of Large Cell Neuroendocrine Carcinoma (3), Small Cell Lung Cancer (1), Large Cell Carcinoma (2), Adenosquamous Carcinoma (2) and Pleomorphic Carcinomas (3) with Max 18 F-Fluordesoxiglucose (FDG), a clinical parameter based in PET to preview diagnosis and prognosis.
Results: We found significant differences ($p=0.028$) between TTF-1 positive and negative Adenocarcinomas where the 18 F-FDG capture was lower in TTF-1 positive cases, indicating lower metabolic activity. TTF-1 negative Adenocarcinomas have similar and higher metabolic activity as Epidermoid Carcinomas. The other histological types have FDG capture similar in between the two defined groups.
Conclusion: Immunohistochemical and 18 F-FDG analysis correlate with clinical differences between Adenocarcinomas and Epidermoid Carcinomas, where TTF-1 negative Adenocarcinomas are biologically similar to Epidermoid Carcinomas, requiring a different medical approach as well as molecular pathology particular interpretation. These results strain the classification of bronchial TTF-1 negative Adenocarcinomas because they are different from the terminal respiratory unit TTF-1 positive Adenocarcinomas.

PS-01-009

Influence of microorganisms on activation of monocytes in bacterial pneumonias

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Objective: According to researchers pneumonias are characterized by increase number of alveolar macrophages population after increased migration of monocytes from bone marrow and blood into the alveolar space.
Method: We examined 60 observations of pneumonia with bacteriological, histological and blood monocytes examination in all cases. Bacteriological study was performed at the Institute of antimicrobial chemotherapy. Histological examination was performed in the Smolensk regional institute of pathology.
Results: In the foci of pneumonias we discovered mainly mixed gram positive and gram negative microorganisms. Ten observations were characterized by an increase in the absolute number of blood monocytes. Fifty observations did not reveal excess levels of blood monocytes. In all cases with an increase in the number of blood monocytes, gram negative bacteria were isolated. In cases with normal number of blood monocytes some of the microorganisms were gram positive.
Conclusion: Gram negative bacteria result in activation of the monocytes and their entry from the bone marrow into the blood more than gram positive bacteria.

PS-01-010

Carcinoid and schwannoma in lung: Two cases

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Objective: Bronchial carcinoids and schwannomas are uncommon, slowly growing, low-grade neoplasms. Carcinoid tumors are thought to arise from neuroendocrine/Kulchitsky's cells of bronchial epithelium. Schwannomas are thought to originate from schwann cells. Clinically they may be asymptomatic or present with non resolving recurrent pneumonia, hemoptysis, respiratory distress.
Conclusion: We present two cases of respiratory distress in two teenage patients.

PS-01-011

Pulmonary hamartomas mimicking metastatic carcinomas

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Pulmonary hamartomas are usually found incidentally and they mimick metastic tumours. We report a case of a 47 year-old man who admitted to Chest Disease service for cough. He had laryngectomy operation formerly and diagnosed as squamous cell carcinoma. Chest-X-ray and computed tomography revealed pulmonary nodules. It was removed but there was not metastatic carcinomas. This case was presented because it can be difficult to make diagnosis when the patient has malignancy.

PS-01-012

Collagen V is modulated by IL-17 in late stage of experimental pulmonary fibrosis: A possible new pathway of fibrosis

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Objective: Experimental models of pulmonary fibrosis (PF) has been proposed and its later phase tend to the resolution in different degrees depending on the drug/strain/inflammatory-pattern. Thus the maintenance of these mechanisms may participate in the PF-progression. Our objective was to determine the immune-fibrotic-pattern in models of pulmonary fibrosis in the late stage (21d).
Method: Distinct animal models were used, including Balb/c, C57BL/6 and IL17RA-KO-C57BL/6 mice by Bleomycin and Paraquat. We analyzed the amounts of total peribronchiolar-interstitial collagen (TPC-TIP) by picrosirius and Col3-Col5 by immunofluorescence through the morphometric evaluation. These data were validated by RT-PCR.
Results: The TPC did not differ between the treated groups. TIC was higher in the C57BL/6 strain, independent of the absence of IL-17RA. The Col5-immunoexpression was higher in control and BLM-treated IL17RA-KO-C57BL/6 than in wild-mice and lower in BLM-Balb/c mice. The Col3immunoexpression was higher in BLM-Balb/c. Likewise, the Col5 gene expression was higher in the IL17RA-KO mice and lower in the BLM-Balb/c.
Conclusion: The perpetuation of fibrosis in PF-susceptible-mice can be modulated by IL-17-dependent Col5-hiperexpression and by Col3-subexpression. This suggests that Col5 is an important component responsible for the development of PF.

PS-01-013

The prognostic role of Filamin A protein expression in patients with non-small-cell lung cancer

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Objective: An actin-binding protein Filamin A (FLNA) serves as a scaffold in various signaling pathways. Recently, it has been reported that FLNA interacts with BRCA1 protein and is required for efficient regulation of early stages of DNA repair processes. As DNA repair proteins are important prognostic markers for non-small-cell lung cancer (NSCLC) patients, we aimed to investigate the role of FLNA protein expression in NSCLC, as well as its correlation with BRCA1 protein expression.
Method: We performed a preliminary study of FNLA and BRCA1 protein expression in 50 NSCLC patients. Formalin-fixed paraffin-embedded tissue sections were stained by immunohistochemistry using antibodies against FLNA C-terminus (EP2405Y, LSBio), BRCA1 N-termunus (MS110) and against phosphorilated forms of BRCA1 at ser1524 and ser1423 (Abcam). Staining intensity was estimated semi-quantitatively and correlated with all available clinico-pathological factors.
Results: FLNA expression was significantly higher in cancer, compared to normal lung tissue. Positive correlation has been revealed between FLNA and BRCA1 phospho-ser1423 expression. Also, 5 year overall survival rate was higher in patients with strong FLNA expression.
Conclusion: According to our preliminary study results the prognostic role of FLNA protein expression deserves to be a subject for further studies in patients with NSCLC.

PS-01-014

Pulmonary nodular lymphoid hyperplasia ("pulmonary pseudolymphoma") – The significance of increased numbers of IgG4 positive plasma cells

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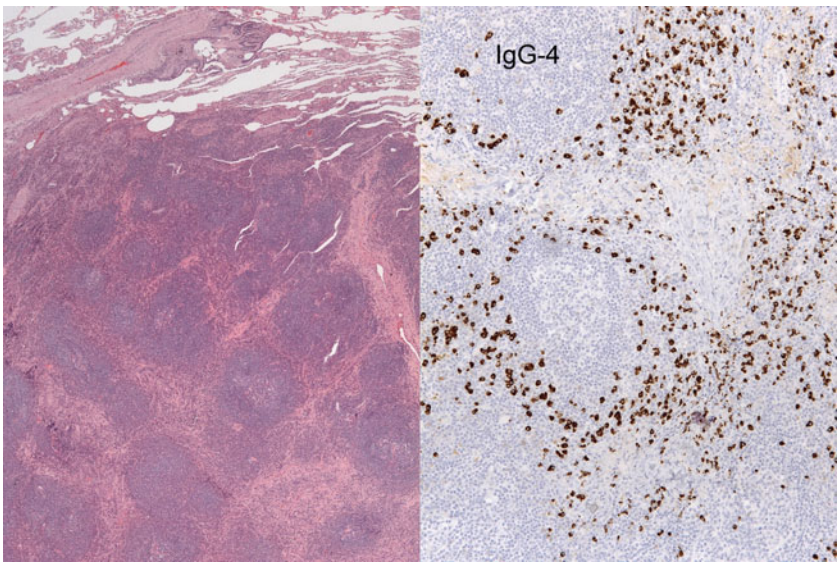
Objective: Pseudolymphomas of the skin, breast, and lacrimal glands show an increase in IgG4 positive plasma cells. We hypothesized that a similar increase in IgG4 positive plasma cells occurs in pulmonary nodular lymphoid hyperplasia (PNLH).
Method: Immunohistochemical stains for IgG4 and IgG were performed in 2 cases of PNLH, 7 cases of BALT lymphoma, 8 cases of intraparenchymal lymph nodes (IPL) and 1 case of follicular bronchiolitis (FB). The mean number of IgG4- and IgG- positive plasma cells and the IgG4/IgG ratio was obtained from a manual count of three separate high power fields (hpfs) of areas of highest cellularity.
Results: The average number of IgG4 positive plasma cells and the IgG4/IgG ratio was increased in PNLH (case 1: 225/hpf, ratio: 0.39, case 2: 280/hpf, ratio: 0.59). In comparison, average IgG4 positive plasma cells per hpf were much lower in BALT lymphoma (range=0–2.3/hpf, ratio=0–0.03), IPL (range IgG4/hpf=0–102, ratio=0–0.23) and FB (1/hpf, ratio=0.03).
Conclusion: The increase in IgG4 positive plasma cells and IgG4/IgG ratio in PNLH aids in diagnosis and supports our current understanding of PNLH as a distinct form of reactive lymphoid proliferation. The relationship between PNLH and IgG4-related sclerosing disease requires further study.



PS-01-015

Calretinin, CK5/6, TTF-1, CEA, Ber-EP4, and CD15: A useful combination of immunohistochemical markers for differentiating pleural mesothelioma from pulmonary adenocarcinoma

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Objective: The distinction between pleural epithelial mesothelioma and peripheral lung adenocarcinoma involving the pleura is still an important diagnostic problem for surgical pathologists. The aim of our study was to identify the most specific and sensitive markers for the positive identification of mesothelioma.
Method: Paraffin-embedded blocks from surgical material of 19 pleural epithelial mesotheliomas and 22 pulmonary adenocarcinomas were retrieved from the files in our department. The primary antibodies used in each case were the following: antibody anticalretinin, EMA; CEA, BerEP4, TTF-1 and CD15.
Results: Of the mesotheliomas, 100 % stained for calretinin, 63.2 % for CK5/6, 78.9 % stained for EMA and AE1/AE3. Of the lung adenocarcinomas, 9.1 % cases showed reactivity for calretinin, 27.3 % for CK5/6, 77.3 % for CD 15, all for TTF-1, 50 % for CEA, 59.1 % for Ber-EP4, 90.1 % for EMA, and all for AE1/AE3.
Conclusion: Calretinin were the highly specific positive mesothelial markers, whereas CK 5/6 showed high sensitivity but low specificity. Among negative markers, we advocate the use of TTF-1, CEA and CD15 which were the most specific in differentiating mesotheliomas from adenocarcinomas.

PS-01-016

Cyclooxygenase-2 expression in NSCLC

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Objective: Overexpression of COX-2 correlates with aggressive disease of NSCLC. Aim of our study was to determine the COX-2 expression levels by two methods.
Method: Analysis was done on 24 consecutive surgical specimens of NSCLC fixed in Paxgene tissue system. Relative quantification of COX-2 mRNA expression was performed by quantitative RT-PCR using intron-spanning primer-probe set. COX-2 protein expression was assessed by immunohistochemistry (IHC). Scoring was performed using an intensity-extent system, both parameters on the scale 0-3 and multiplied to give IHC index.
Results: There were 12 cases of adenocarcinoma, 11 cases of squamous cell carcinoma and one typical carcinoid. COX-2 mRNA expression was detectable in all specimens. The median COX-2 mRNA expression value, normalized against he internal reference gene GADPH, was 0,53 (range 0,08–12,49). We observed cytoplasmic and membranous immunohistochemical reaction patterns. Average IHC index was 3,8. There was positive correlation between mRNA and protein COX-2 expression (R2=0,31). Adenocarcinoma cases had average relative mRNA expression value 2,45 and IHC index 5,08, while squamous cell carcinoma had average relative mRNA expression value 0,67 and IHC index 2,73.
Conclusion: COX-2 is expressed in NSCLC with various IHC reaction patterns. Adenocarcinoma and squamous cell carcinoma have different COX-2 expression levels.

PS-01-017

Clinicopathological correlations of mTOR and pAkt expression in non-small cell lung cancer

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Objective: The Akt/mammalian target of rapamycin (mTOR) pathway is up-regulated in many human cancers, and agents targeting the mTOR pathway are in various stages of clinical development and application.
Method: Expression of pAkt and mTOR was studied by immunohistochemical analysis of 574 surgically resected non-small cell lung cancer (NSCLC) specimens on a tissue microarray (TMA).
Results: The results were correlated with clinicopathological features. Expression of mTOR showed a strong correlation with the expression of pAkt ($p<0.001$) and was significantly associated with female gender, tumor size ≤3 cm, adenocarcinoma (ADC), non-smoker status, and lower pathological stage. Expression of pAkt was correlated with older age (≥ 65), ADC, non-smoker status, and lower T stage. Univariate survival analysis revealed that the mTOR and pAkt positive group had a significantly longer cancer-specific survival than the mTOR and pAkt negative group ($p=0.038$ and $p=0.024$, respectively). Coexpression of pAkt and mTOR correlated with better prognosis than either single or double negative pAkt and mTOR groups ($p=0.016$). However, multivariate analysis proved that mTOR and pAkt expression are not independent prognostic factors for cancer-specific survival.
Conclusion: Expression of pAkt and mTOR expression is more significantly associated with ADC than squamous cell carcinoma (SCC) and expression of these proteins is associated with better prognosis.

PS-01-018

PAK 6 immunohistochemistry marker in non-small cell lung cancer (NSCLC)

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Objective: PAK 6 is a member of P21-activated kinase family. Many human tumor express and activate this family. Because of their role in cell transformation, they become therapeutic targets. They have important roles in cell survival, cell proliferation and cell migration. They affect cell growth and tumor invasion.

Method: 175 cases with NSCLC reported in Gaziantep University Pathology Department between 2000 and 2010, reviewed retrospectively. Immunohistochemically nuclear and cytoplasmic PAK 6 stainings were considered positive and scored according to degree of staining.

Results: Our cases included 110 squamous cell carcinoma, 49 adenocarcinoma, 9 adeno squamous carcinoma and 7 large cell carcinoma. There was no significantly associated between tumor types and PAK6 staining. 38 of 175 patients showed recurrence and of 23 cases showed nuclear staining but there were no statistically significance (p:0,267). 31 cases died from the disease and in 21 of these cases nuclear stainig was very intresting, inspite of statistical results.

Conclusion: In this study PAK 6 staining patern and score were compared with tumor type, size, recurrence, mortality and lymph node involvement in NSCLC. And we found no statistically significance. 150 of 175 case with NSCLC stained with PAK 6. These results suggest that PAK 6 was expressed in lung like prostat, plasenta and breast.

PS-01-019

Pleural Fibroelastosis is a similar spectrum of Histopathology in Chronic Fibrosing Lung Disorders

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Objective: Parenchymal fibroelastosis in chronic fibrosing lung disorders has been much investigated, but little attention has been directed at the visceral pleura (VP) participation in these situations. Our aim was to verify whether elastic deposition accompanies collagen deposition in the repairing process of chronic lung injury. In this work we studied the distribution of these fibrous components of VP in bullous disease type I and II, smoking-related interstitial fibrosis and usual interstitial pneumonia (UIP).

Method: We employed histochemical methods on conventional histological slides. We measured, by image analysis, the content of fibres of the collagenous and elastic systems of the visceral pleura in histological slides sampled from surgical lung biopsies and bullectomy, using the picrosirius-polarization method and Weigert's resorcin-fuchsin stain, respectively.

Results: Four groups were studied: I, 7 patients with spontaneous pneumothorax due to type I bullous disease; II, 12 patients with spontaneous pneumothorax due to type II bullous disease; III, 5 smoking-related interstitial fibrosis; and IV, 5 patients with idiopathic pulmonary fibrosis. The first two groups were used as controls. The content of fibers of the collagenous systems was similar in groups I (40.58± 15.95), II (40.71±15.86) and IV (40.99±13.99) when compared with group III (26.51±1.01).

Conclusion: A similar spectrum of histopathology was found in chronic fibrosing lung disorders.

PS-01-020

Autopsy: Undifferentiated tumor in men with type II Pneumocytes experimental transplantation

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Patient diagnosed with Idiopathic pulmonary fibrosis (2009), in which experimental transplantation was performed of type II pneumocytes, ingress to the hospital for further study groundmass of the right lung. In the postmortem study a 2340 gr. mass was identified, the mass was formed by sarcomatous cells habit, undifferentiated and pleomorphic, with the presence of multiple implants and adhesions in rib cage, diaphragm, pericardial fat. IHC profile was performed: vimentin (+), EMA focally (+), WT1, CK8, TTF1, CKAE1/AE3, S100, CD34, CD31 and CD45 (−) and low proliferation index, the diagnosis undifferentiated malignant tumor. With inconclusive IHC profile, so blocks were sent to Clinic Barcelona Hospital, for study. The estimated prevalence of idiopathic pulmonary fibrosis is 20 cases per 100,000 population in men, with a mortality of 50 % at 5 years of diagnosis. Cancer rate of in transplanted patients is within the range between 4 % and 18 %. Could the appearance of this tumor be related either to transplanted pneumocytes or it is inmunosupression the main risk factor? Current treatments for idiopathic pulmonary fibrosis are not effective, which requires the study and development of new therapeutic options, using fibroblast proliferation inhibitors, as well as prospective studies, in the long term, the evolution of these patients and the development of secondary entities to it.

PS-01-021

Mediastinal hemangioma: A retrospective study about 5 cases

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Objective: Mediastinal hemangiomas are rare tumors accounting for 0,5 % of all mediastinal tumors. These tumors are challenging because of the lack of clinical and radiologic specific signs. Their diagnosis is mainly based on microscopic study.
Method: We report a 10-year-experience of a single institution. We describe 5 cases of mediastinal hemangioma.
Results: Our study contained 2 men and 3 women with a mean age of 60.4 years. Symptoms consisted mainly in chest pain. Neurologic signs were observed in 2 patients. Surgical treatment was performed in all patients dealing with a total resection in 4 patients. The most used surgical approach was a posterolateral thoracotomy. Video-assisted thoracic excision was tried in one patient and was converted into a median sternotomy. Microscopic examination concluded to a mediastinal hemangioma in all cases. All the patients presented no complications after a follow up periods varying from 9 months to 2 years.
Conclusion: Mediastinal hemangiomas are rare tumors whose diagnosis is based on microscopic findings. Their surgical management may be challenging because of their connection to the adjacent structures. Video-assisted thoracic excision is being more frequently used by experienced surgeons. These tumors are benign with a good behavior.

PS-01-022

Pulmonary actinomycosisa retrospective study about 6 cases

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Objective: Actinomycosis is an infectious disease caused by Actinomyce israeli in 85 % of the cases. It is mainly observed in alcoholic patients and affects mainly cervicofacial, abdominal and thoracic regions. Pulomnary actinomycosis accounts for 15 % of the localizations and is caused by the inhalation of septic particles causing granulomatous lesions, the extension to the adjacent organs and a cutaneous fistulae. It represents a real pitfall and mimics malignant lesions, tuberculosis or other infectious diseases.
Method: We report a retrospective study about 6 cases of pulmonary actinomycosis diagnosed over a 17-year-period.
Results: We describe the cases of 6 men aged between 35 and 46 years who presented with respiratory signs. Radiologic investigations showed in all cases parenchymal masses with irregular margins mimicking malignant processes. Positivie diagnosis was based on microscopic examination. The treatment was based on surgical excision associated to a medical treatment without complications after a follow up period ranging from 3 months to 18 months.
Conclusion: Pulmonary actinomycosis shares usually the same clinical and radiologic features as malignant lesions. Positive diagnosis is based on microscopic findings. It inducesusually surroundng organs and may affect, in some cases, the vital prognosis.

PS-01-023

Over expression of hyaluronan syntehase-2 activity has impact in the remodeling process and survival evolution in patients with idiopathic pulmonary fibrosis

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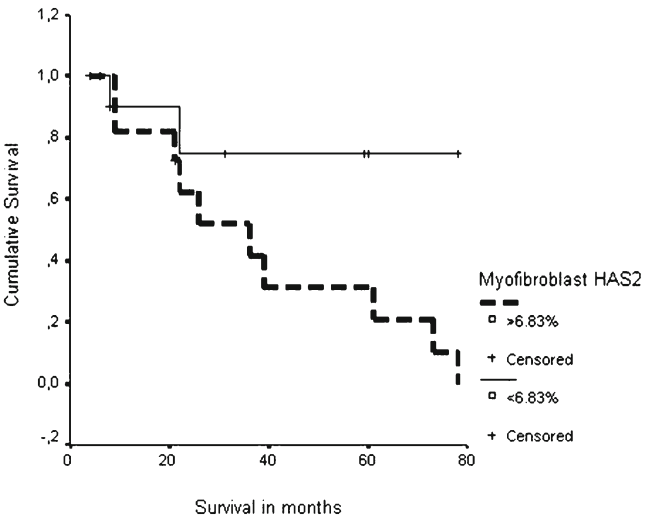
Objective: The idiopathic pulmonary fibrosis (IPF) is a terminal illness characterized by unremitting extracellular matrix (ECM) deposition in the lung. In this regard, the myofibroblasts and the ECM components such as collagen and hyaluronan (HA) have an important role in the fibrosis. We analyzed the expression of HAS1 (HA synthase 1), HAS2, HAS3 and hyaluronic acid receptor (CD44) by epithelial and myofibroblasts cells in patients with IPF and we correlated with a survival.
Method: HAS-1, HAS2, HAS3 and CD44 epithelial and myofibroblast expression were evaluated in 27 surgical lung biopsies from patients with IPF in minimal and severe fibrosis by the point-counting technique. Impact of these markers was tested on pulmonary functional tests and follow-up until death from IPF.
Results: HAS2 and CD44 expression were significantly increased and directly associated with severe fibrosis. Myofibroblast HAS2 activity was indirectly associated to DLO/VA (r= −0.584; p=0.05). Kaplan Maier curves determined a higher risk of death for patient with high HA2 (>6.83 %) expression than in low expression (Log Rank p=0.05, Figure).
Conclusion: The increased HAS-2 activity in epithelial and myofibroblast cells have impact in the remodeling process and the survival evolution, suggesting that strategies aimed at preventing the effect of this ECM component may have a greater impact in patient's outcome. Financial Support: FAPESP, CNPq.



PS-01-024

Viral antigens are more frequently observed in acute interstitial pneumonia than in other types of idiopathic interstitial pneumonias

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Objective: The etiology of idiopathic interstitial pneumonias (IIPs) remains unclear. Many researches assumed that viruses can represent an important factor of aggression to the lung provoking fibrosis. In this regards, we researched the presence of virus infections in patients with IIPs.
Method: Biopsy samples from 13 patients with idiopathic interstitial pneumonia (IPF); 8 patients with nonspecific interstitial pneumonia (NSIP); 13 patients with acute interstitial pneumonia (AIP) and 4 patients with idiopathic cetrilobular fibrosis (ICLF) were used to investigate by microarray and immunohistochemistry the presence of measles virus (MV), hepatitis-C virus (HCV), adenovirus (ADV), respiratory syncytial virus (RSV), Epstein-Barr virus (EBV), herpes I and II viruses (HVI and HVII).
Results: We detected the epithelial alveolar infection by MV and CMV in 30.8 % and 15.4 % in AIP, respectively. Endothelial CMV infection was observed in 25 % of ICLF group. When we compared with the age of these patients, patients with ≤ of 43 years old had more infection by MV and CMV than the group with ≥ 72 years old. The other viruses were not detected in the different groups.
Conclusion: The viral infections observed in AIP and ICLF groups reinforce the possible viral participation in these pulmonary diseases. Financial Support: FAPESP.

PS-01-025

Abnormal up regulation of cyclooxygenase-2 is observed in idiopathic pulmonary fibrosis

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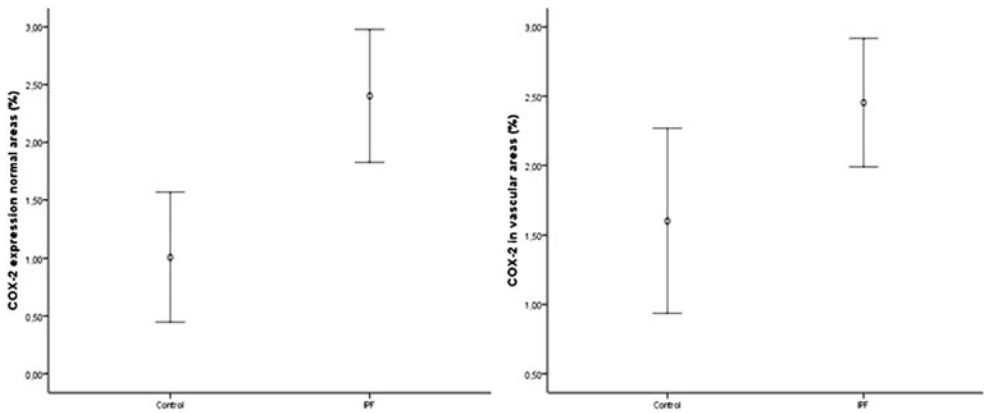
Objective: Several factors modulate fibroblast proliferation and collagen deposition in pulmonary fibrosis diseases, including cyclooxygenase (COX). The main of this study was observed the relationship between COX1 and COX2 in surgical lung biopsies from patients with idiopathic pulmonary fibrosis (IPF).
Method: Twenty four patients (64±8.9 year) were characterized with IPF. Immunohistochemistry and histomorphometry were used to evaluate the amount of COX1 and COX2 expression in lung specimens. The expression of these markers was tested with their pulmonary function tests.
Results: Significantly a higher amount of COX-2 was observed in IPF patients principally in normal and vascular areas (p=0.05) when compared with control group (Figure), contrasting with similar amounts of COX-1 in both groups. An important negative correlation was observed between total lung COX-2 expression and DCO/VA (r=0.694, p=0.01) in IPF patients.
Conclusion: Higher vascular expressions of COX2 probably mediated the inflammatory reaction in patients with IPF and have an important impact with pulmonary function tests, suggesting that a participation in the pathway of IPF. Financial Support: FAPESP.

Error barr shows the correlations between COX-2 expression in normal and vascular areas of IPF compared with control group



PS-01-026

Multiplex Ligation Probe-dependent Amplification (MLPA) as an ancillary method for the diagnosis of malignant pleural effusion

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Objective: A definitive diagnosis provided by the finding of malignant cells in pleural fluid (PF) can be established in around 50 % of patients with pleural malignancy. However, underdiagnosis risk in cytological suspicious cases is high, which makes the cytological diagnosis quite limited. This is an important clinical problem, especially if we consider that some patients, in bad clinical conditions, can not be submitted to a guided thoracoscopic biopsy.
Method: Using multiplex ligation probe-dependent amplification (P315-MRC-Holland) we have studied sequence variations of EGFR gene and amplifications/deletions of chromosomal regions frequently associated to tumors (ATG4B, PAHs, PROS, NSD1, and CDGIF genes).
Results: Forty-three malignant PF samples from patients with different cancers were evaluated, even in those cases with scarce pellet cells. Four benign pleural effusions were used as control. Gene sequence changes were observed in 13 (30.2 %) cases, while others copy number abnormalities were found in 19 (44.2 %).
Conclusion: The findings suggest that MLPA could be considered an alternative tool to detect molecular genetic changes in malignant pleural effusions, since this technique is relatively low expensive and not time consuming. Our next challenge is to find the best combination of probes capable to recognize malignant cells of any origin in fresh samples of PF.

PS-01-027

Multiple primary pulmonary myopericytoma: Case presentation

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Objective: Myopericytoma is described as a perivascular myoid tumor which usually develops as a solitary mass in the subcutaneous tissues of the extremities, in adults.
Method: The chest radiography of a 52-year-old woman showed multiple, bilateral lung nodules. After the surgical excision of one of them, the histopathologic examination revealed a well circumscribed nodule, composed of fusiform or oval cells, with eosinophilic cytoplasm and ovoid nuclei, without atypia, in a concentric pattern, intimately associated with thin-walled vessels, within a myxoid stroma.
Results: The spindle cells were diffusely positive for vimentin, smooth muscle actin (SMA) and occasionally for desmin. CD31 and CD34 were positive only in endothelial cells. Ki 67 was positive in less than 4 % of neoplastic cells.
Conclusion: The histological and immuno-histochemical findings led to the diagnosis of multiple primary pulmonary myopericytoma.

PS-01-028

Five cases of lung pneumocytoma: Clinico-pathological, immunohistochemical and ultrastructural study

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Objective: Lung pneumocytoma (LP), also called sclerosing hemangioma, is an uncommon tumor of uncertain histogenesis.
Method: We analyzed the clinical, morphological, immunohistochemical and ultrastructural features of 5 LP.
Results: All 5 patients were women, with median age of 48 year (range: 29–73). Mean size was 26 mm (range 15–45 mm). All tumors were located within the right lung (upper-lobe: 1; middle-lobe: 2; lower-lobe: 2). All cases showed solid, papillary, sclerotic, and hemorrhagic patterns. The tumors were composed of 2 cells types: pale polygonal and surface cells. EMA, TTF1, and PR were observed in both type cells. The surface cells showed also positivity for CK7, Napsin-A, and surfactant-A, whereas the polygonal cells for vimentin. Surface cells had short microvilli and lamellar bodies in their cytoplasm. Polygonal cells contained abundant microfilaments and rough endoplasmic reticulum. All patients were alive and well without recurrence at the last follow up.
Conclusion: LP is likely to be an epithelial tumor with a differentiation toward type II pneumocytes, which exhibits various architectural patterns. The IHC profile provides useful clues for the diagnosis of this lung neoplasm when typical features are absent. All our cases had an excellent prognosis with no evidence of recurrence following surgery.

PS-01-029

Rare tracheobroncheal lesions diagnosed by small bronchoscopic biopsies

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Objective: Six different, rarely seen tracheobronchial lesions, taken by bronchoscopy as small fragments were discussed with an emphasis on morphological findings and differential diagnosis.
Results: Six patients were men and two patients were women with an age range of 50 to 70 years. Most of the lesions were symptomatic and discovered as small masses by

bronchoscopy. The tracheobronchial lesions varied from polypoid, nodular, well-demarcated, fragile masses to nodular thickenings. Microscopically, a polyp composed of a fibrovascular stroma with scattered mononuclear inflammatory cells was compatible with fibroepithelial polyp. Mature adipocyte proliferation in two cases, S-100 and CD68 positive polygonal or ovoid cells with abundant eosinophilic, granular cytoplasm having small, hyperchromatic nuclei, smooth muscle actin and desmin positive spindle cells in interlacing fascicles within a myxoid and collagenous stroma with mononuclear inflammatory cells, CD34 and CD31 positive thin-walled vascular channels, filled with red blood cells and S-100 positive spindle cells having palisading of wavy nuclei in two cases, located in the submucosa were main findings of lipoma, granular cell tumor, inflammatory myofibroblastic tumor, cavernous hemangioma and schwannoma, respectively.

Conclusion: Tracheobronchial biopsies, even with small fragments of lesions can allow to render rare specific histopathological diagnoses, some of which need to be confirmed by immunohistochemistry.

PS-01-030

Immunohistochemical expression of matrix metalloproteinases 1,2 and 9 in small cell lung carcinoma

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Objective: Small cell lung carcinomas (SCLC) are aggressive neoplasms that give very early distant metastases. Matrix metalloproteinases (MMPs) are a family of endopeptidases which degrade extracellular matrix and modulate cell adhesion, playing a crucial role in cancer cell invasion and metastasis. The aim of the present study is to investigate the immunohistochemical expression of MMP-2, MMP-9 (type IV collagenases) and MMP-1 (interstitial collagenase) in patients with SCLC.

Method: Formalin-fixed, paraffin-embedded lung biopsy specimens from 40 patients with SCLC (M:F=29:11, median age=66.7) were immunostained for MMP-1, MMP-2 and MMP-9 (anti-MMP-1 polyclonal antibody, anti-MMP-2 72 kDa Collagenase IV antibody, anti-MMP-9 92 kDa Collagenase IV antibody, Spring Bioscience).

Results: Immunohistochemical expression of MMPs was detected in the cytoplasm of neoplastic cells. Immunoreactivity was designated positive when >10 % of neoplastic cells were stained. Overall, MMPs were expressed in the majority of SCLC. Specifically, MMP-1 was positive in 90 % (36/40), MMP-2 in 87.5 % (35/40) and MMP-9 in 82.5 % (33/40) of SCLC. Non-neoplastic lung parenchyma did not stain for MMPs.

Conclusion: The majority of SCLC express immunohistochemically MMP-2, MMP-9 and MMP-1. Given the role of MMPs in cancer progression and metastasis, their expression in SCLC may contribute to their aggressive course.

PS-01-031

Diagnosis of pulmonary adenocarcinoma by immunohistochemistry

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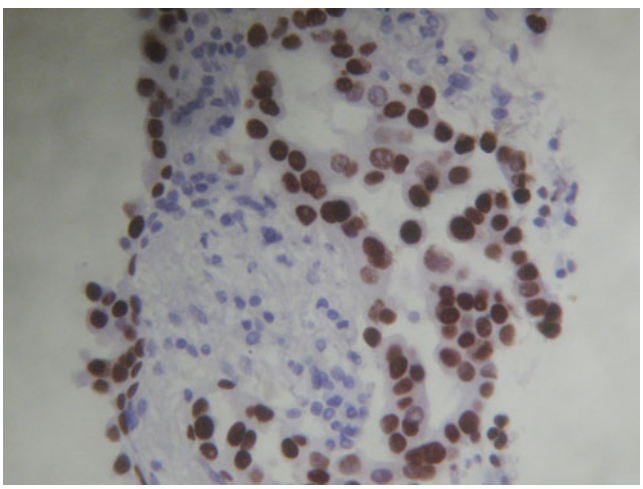
Objective: Number of pulmonary adenocarcinoma (ADC) patients increasease. Treatment of non-small cell pulmonary carcinoma depends of its histological type in era of target molecular therapy particulary of ADC: Diagnosis of ADC is established on small-sized pulmonary biopsies obtained on bronchoscopy and by transthoracic needle pulmonary biopsy. The aim of this study was to evaluate optimal panel of monoclonal antibodies in diagnosis of pulmonary ADC on small-sized biopsy pulmonary samples.

Method: Analysis of 50 small-sized biopsy pulmonary samples. Diagnosis of ADC was established on hematoxillyn-eosin stained (H&E) samples and confirmed immunohistochemicaly by Thyreoid Transcription Factor-1 (TTF-1), Napsin-A, Surfactant B and Cytokeratin7 (CK7). Descriptive statistical method (%) was used.

Results: TTF-1 specificity was 86 %(43/50), Napsin-A-82 %(41/50), SurfactantB – 56 %(28/50) and CK7-90 %(45/50) in ADCs. Two monoclonal antibodies were positive in 24 % (12/50) ADCs, one of them was necessary TTF-1 or Napsin-A. Three monoclonal antibodies were positive in 40 %(20/50) and 4 in 36 %(18/50) ADCs, respectively. There is not statistical significans in number of monoclonal antibodies for diagnosis of ADC.

Conclusion: No one monoclonalantibody is specific for one histological type of carcinoma and its origin. TTF-1, Napsin-A, SurfactantB and CK7 belong in optimal panel for diagnosis of pulmonary adenocarcinoma.



PS-01-032

Expression of CD44, E-Cadherin and Bcl-2 in lung cancer

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Objective: Lung cancer represents major problem in oncology as the incidence and mortality is high (Parkin et al., 2005). Molecular studies could reveal additional targets for intervention or prognostic evaluation. However, the published data are controversial (Renouf et al.,2009; Leung et al.,2010; Maraz et al.,2011; Ko et al.,2011).
Method: Consecutive lung cancer cases (278) were retrieved by retrospective archive search. The diagnostics has been performed systematically in accordance with WHO classification (Travis et al.,2000). The expression of CD44, E-Cadherin and Bcl-2 was analysed by immunohistochemistry and evaluated semiquantitatively.
Results: The intensity of Bcl-2 expression was highest in small cell cancer, reaching the mean value 2.25. No or very low Bcl-2 expression was found in adenocarcinoma, carcinoid and squamous cell cancer. The membranous expression of E-Cadherin showed significantly higher mean intensity in adenocarcinoma (1.93) and carcinoid (1.90) than in small cell cancer (0.14) and squamous cell cancer (0.85). Cytoplasmic E-cadherin expression was observed in small cell cancer. CD44 expression was widespread and frequent in non-small cell lung cancer.
Conclusion: The main histological types of lung cancer show different immunophenotype. Bcl-2 expression is found in small cell cancer. The expression of E-Cadherin is characteristic in adenocarcinoma and carcinoid. CD44 is expressed in non-small cell lung cancer.

PS-01-033

Localized nodular pulmonary and thoracic cage amyloidosis

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Objective: Localised amyloidosis represents a rare differential diagnosis of neoplasms. However, in some cases amyloid deposits are manifestation of tumour itself. To increase awareness about these uncommon but important differential diagnostic issues, we show here three well-characterised cases of thoracic cage or pulmonary localised nodular amyloidosis.
Method: The cases were identified by systematic retrospective archive search, 2000–2011. Congo red stain, polarisation microscopy and immunohistochemical analysis was applied.
Results: There were 2 males and 1 female among the patients diagnosed with thoracic cage or pulmonary amyloidosis. The patients were 67–84 years old and had no history of previous malignancy. Clinically, either lung cancer or sternal osteochondroma was suspected. Radiologically, 1–2 nodules measuring 1.5–9.0 cm were found in lungs (2 cases, one of these being bifocal) or sternum (1). Surgical treatment was applied in all cases. Amyloid deposits were identified by Congo red stain and polarisation microscopy. AL type of amyloid was confirmed. In case of bone lesion, the plasma cells were monoclonal justifying the diagnosis of multiple myeloma.
Conclusion: Localised amyloidosis can involve lung or sternum as tumour-like mass. The lung lesions can be single or multiple. Association with haematologic neoplasm is likely if bone is affected. Clonality analysis of plasma cells surrounding amyloid deposits is mandatory.

PS-01-034

Pleural localization of Castleman Disease: A rare entity

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Objective: Castleman disease (CD) comprises a heterogeneous group of disease with various clinical presentations and prognosis. By definition; CD is a lymphoproliferative disorder of the mediastinal lymph nodes and extranodal tissues with follicular and interfollicular abnormalities. Pleural localization is an unusual presentation of CD.
Method: A 27-year-old man applied to the hospital because of cough. Chest x-ray and CT images showed an irregular, 35×56×67 mm sized intrapleural-extrapulmoner mass in the paramediastinal region. Surgical specimen was consisting of a 7×5×3.5 cm sized, irregular-round shaped, gray colored calcified mass. Microscopically, a lymphoid proliferation with distorted follicles and increased dendritic cells (with CD21) was detected. Lymphocyte depleted germinal centers resembling "onion skin" appearance with penetrated sclerosing hyalinized blood vessels were also seen. Interfollicular region was composed of proliferating blood vessels lined by plump endothelial cells and few lymphoplasmositer infiltration. There was heterogeneous positivity with CD3 and CD20. Expanded mantle zones showed diffuse bcl2 positivity. Ki67 proliferation index was low. The mass was diagnosed as "Castleman Disease, hyaline vascular type". Typical appearance of the follicular and interfollicular abnormalities allowed definitive differentiation from mesothelioma and solitary fibrous tumor of the pleura.
Conclusion: Pleural CD is a rare lesion but should be considered especially on young patients in the differential diagnosis of pleural masses.

PS-01-035

Collagen V-induced nasal tolerance increase FOXp3 in systemic sclerosis model

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Objective: To evaluate FOXp3 expression in bronchus-associated lymphoid tissue (BALT) and correlate with the inflammatory process and collagen content in the lung tissue in an experimental model of scleroderma (SSc) after type V collagen (COL V)-induced nasal tolerance.
Method: Female New Zealand rabbits (N=12) were immunized with 1 mg/ml of COL V in Freund's adjuvant (IM). After 150 days, six immunized animals were nasally tolerated with COL V (25 νg/day), during 60 days (IM-TOL). Animals (N=6) only tolerated served as control (CT). FOXP3 expression in BALT and inflammatory cells in pulmonary interstitium were evaluated by point counting method. Types I, III and V collagen gene expression were evaluated by Real-time PCR.
Results: IM-TOL when compared to IM presented decreased lymphocytes, macrophages and monocytes and types I (p=0,002) and V (p=0,009) collagen mRNA expression in pulmonary tissue. T lymphocytes FOXp3 were expressed in 100 % of IM-TOL and 33,3 % of CT (p= 0,03). Additionally, BALT was higher expressed in IM-TOL in relation to CT.
Conclusion: COL V-induced nasal tolerance in SSc model induces FOXp3 regulatory T cells in BALT which can trigger an immune regulatory mechanism resulting in decreased inflammation and collagen expression. It suggests that COL V tolerance could be a promising therapeutic for human scleroderma treatment.

PS-01-036

IgG4-related lung disease

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Objective: IgG4 –related lung disease is one of the manifestations of IgG4-related systemic disease. Obliterative vasculitis is considered an organ specific feature of IgG4-related disease in the lung. We report a case of a 78-year-old man with multifocal subpleural consolidations in both lungs. Histologic examination revealed IgG4-related lung disease with obliterative lymphoplasmacytic vasculitis.
Method: Histological sections from paraffin blocks were used for hematoxylin-eosin and special stains (elastica-Masson trichrome, PAS, Geimsa, Grocott), for immunohistochemistry (antibodies against kappa and lambda light chains, CD20, CD3, IgG, IgM, IgA, IgG4, LMP1) as well as for EBER in situ hybridisation and PCR.
Results: The lung tissue was irregulary fibrotic with dense lymfoplasmacytic infiltration concentrated in the walls of pulmonary arteries. Some arteries were obliterated by intimal fibrosis. Infiltrating lymphocytes were small and without atypias. The majority of lymphocytes were CD3 positive, nearly all plasmocytes showed IgG positivity. IgG4/IgG ratio was 60 %. EBER in situ hybridisation was negative and monoclonal reaarangement of T cell receptor or immunoglobulin heavy chain genes were not detected.
Conclusion: IgG4-related lung disease is rare. Obliterative vasculitis and high percentage of IgG4 positive plasmocytes are main histological features of this entity.

PS-01-037

Primary lung adenocarcinoma with heterotopic osteocartilaginous formation

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Objective: Primary lung carcinoma with heterotopic osteocartilaginous formation is exceedingly rare. To date only 38 cases have been reported in the literature and the pathogenesis is not fully investigated. We report a case of pulmonary adenocarcinoma with osteocartilaginous formation with immunohistochemical staining of bone morphogenetic proteins (BMPs).
Method: A 59-year-old man was admitted to our hospital for a lung tumor in his left upper lobe. An open lung biopsy followed a lobectomy was done. The resected tissue was fixed with 10 % formalin and embedded in paraffin. Sections, cut from paraffin blocks, were subjected to hematoxylin and eosin (HE) staining and Masson-Goldner staining, in addition to immunohistochemical staining.
Results: The tumor was poorly differentiated adenocarcinoma with heterotopic ossification. Some of the tumor cells were positive for BMP-2, 6, and 7. Some of mesenchymal cells in tumor interstitium were positive for osteoblast (OB)- cadherin or BMP receptor-IA.
Conclusion: We report a case of primary lung adenocarcinoma with heterotopic osteocartilaginous formation and reviewed previously published reports. To our best

knowledge, this was the first case that not only BMP was expressed in tumor cells but also OB-cadherin or BMP receptor in some mesenchymal cells of tumor interstitium.

PS-01-038

Expression of transforming growth factor ß1 and e-cadherin in lung adenocarcinoma

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Objective: There is evidence supporting the concept of tumor progression from pulmonary adenocarcinoma in situ (formerly bronchioloalveolar carcinoma, BAC) to adenocarcinoma with varying degrees of invasion. The aim of this study was to investigate the role of TGFß1in tumor invasiveness in lung adenocarcinoma, and to determine the potential relationships between its expression and immunophenotypes of cell adhesion molecules.
Method: Tumor samples (n=40) from adenocarcinoma in situ (n=13), minimally invasive adenocarcinoma (formerly BAC with ≤5 mm invasion, n=2), and lepidic predominant invasive adenocarcinoma (formerly mixed adenocarcinoma showing non-mucinous BAC features with >5 mm invasion, n=25) were examined for the expression of TGFß1, E-cadherin, N-cadherin, and H-cadherin proteins using immunohistochemistry.
Results: Twenty-five tumors (63 %) were positive for TGFß1. The frequency of immunoreactivity in patients with adenocarcinoma in situ, minimally invasive adenocarcinoma, and lepidic predominant invasive adenocarcinoma was 23 % (3/13), 50 % (1/2), and 84 % (21/25), respectively (p=0.001). Loss of E-cadherin expression was more frequently observed in invasive adenocarcinomas than in adenocarcinomas in situ (p=0.034). TGFß1 expression showed a statistically significant correlation with H-cadherin expression (p=0.040), but not with E-cadherin expression (p=0.752).
Conclusion: These results suggest that TGFß1 and E-cadherin may play an important role in invasive progression of lung adenocarcinoma through regulating epithelial-to-mesenchymal transition.

PS-01-040

LIN28A expression as prognostic indicator in lung adenocarcinomas

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Objective: LIN28A is implicated in stem cell pluripotency by blocking let-7miRNAs and Oct-4 is a transcription factor highly expressed in embryonic stem cells. The present study investigates the prognostic significance of both markers in lung adenocarcinomas.
Method: We evaluated, by immunohistochemistry, LIN28A and Oct-4A expression in formalin-fixed, paraffin-embedded tissues from 92 lung adenocarcinomas. Immunoreactivity was scored as 1+, <1 % positive tumor cells (ptc); 2+, 1–5 % ptc; 3+, 5–10 % ptc; and 4+, >10 % ptc and was compared with clinicopathologic features and overall survival.
Results: Regarding LIN28A expression 23 % of tumors were recorded as 1+, 51 % as 2+, 14 % as 3+ and 12 % as 4+. The stratification for Oct-4 expression was 19 % (1+), 50 % (2+), 23 % (3+) and 8 % (4+). LIN28A and Oct-4 expression was not significantly associated with age, gender and tumor grade or stage. LIN28A 4+ expression predicted a shorter overall survival (P<0.05) on univariate analysis. Oct-4 was not associated with patients' prognosis. Cox multivariate analysis showed that age, TNM and LIN28A 4+ expression were independent prognostic factors of survival.
Conclusion: LIN28A expression appears to be an independent predictor of poor outcome in lung adenocarcinomas. Further studies are warranted in order to investigate its role in stratifying patients at increased risk for poor outcome.

PS-01-041

Comparison of the mutation status of EGFR and KRAS on pulmonary adenocarcinoma and corresponding brain metastasis

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Objective: EGFR and KRAS mutation statuses have been known associated with the sensitivity of tyrosine kinase inhibitor treatment in pulmonary adenocarcinoma. However, the mutation analyses were usually performed on the primary tumors only, due to the availability of the tumor tissue.
Method: To compare the KRAS and EGFR mutation statuses between pulmonary adenocarcinomas and corresponding metastases, we performed direct sequencing, followed by Scorpion ARMS method on wild-type cases for EGFR analysis, and allele-specific real-time PCR for KRAS analysis, on the paired samples of pulmonary adenocarcinoma.
Results: Thirty-one (63.3 %) pulmonary adenocarcinomas and 30 (61.2 %) brain metastases out of the 49 paired specimens have EGFR mutations, and 30 (61.2 %) paired specimens were concordant for the EGFR mutation status between the primary and metastasis. In addition, 17

(51.5 %) pulmonary adenocarcinomas and 17 (51.5 %) brain metastases out of the 33 paired specimens have KRAS mutations, and only 16 (48.5 %) paired specimens were concordant between the primary and the metastasis.
Conclusion: The status of EGFR mutation is relatively consistent between primary and metastasis comparing to that of KRAS mutation in pulmonary adenocarcinomas. However, discordance for the mutation statuses does happen. Accordingly, repeat analysis is recommended if tissue from metastatsis or recurrence is available.

PS-01-042
Morphologic analysis of pulmonary neuroendocrine tumors
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Objective: We tried to measure and analyze characteristics of neuroendocrine tumors in lung by image analysis and help to diagnose them.
Method: It was analysed that sixteen cases of typical carcinoid tumors, five cases of atypical carcinoid tumors, fifteen of small cell carcinomas, fifty one cases of large cell neuroendocrine carcinomas. We analyzed the nuclear area, perimeter, major axis and minor axis using i-solution image analyzer software package.
Results: The mean nuclear area was 488.00 μm2 in the typical carcinoid tumors, 499.30 μm2 in the atypical carcinoid tumors, 481.48 μm2 in the small cell carcinomas, and 684.05 μm2 in the large cell neuroendocrine carcinomas. After the statistical results, every method was effective to distinguish large cell neuroendocrine carcinoma from other tumors and the circumferences of nucleus was the most effective to distinguish among them.
Conclusion: Pulmonary neuroendocrine tumors were the nuclear morphologic differences of each tumors. Therefore, diagnosis that considers morphologic differences of pulmonary neuroendocrine tumors contributes to increase reproducibility and accuracy.

Sunday, 9 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-02 Poster Session Cytopathology

PS-02-001
Cytolytic vaginosis: May cause infertility?
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Objective: Vagina is covered by the flora dominated by Lactobacillus spp. durig the term from puberty to the menopause. An abundant growth of lactobacilli may result in lysis of vaginal epithelial cells, named as Cytolytic Vaginosis. This cytolytic process may cause the symptoms as seen in candidiasis. We observed Pap smears to evaluate if cytolysis has a relationship with infertility.
Method: In the Pathology department of Mardin Maternity Hospital, 2011–2012 period, we examined Pap smear cases suffering from the similar syptoms as candidiasis. Of the 4672 smears, 82 were diagnosed as "Cytolytic Vaginosis". No growth was observed in cultures.
Results: The number of the cases suffering from the infertility was 261 (%5.58) among 4672 cases. In the cytolytic vaginosis group this ratio was %32.9 (n=27). The ratio of the infertil cases of cytolytic vaginosis group over general population was significantly higher (p<0.05).
Conclusion: Our results are in favour of supporting the hypothesis of the relation between cytolytic vaginosis and infertility. Lactobacilli are thought to have inhibitive role in fertility by changing the vaginal ph and adhering to the epithelial cells so inhibiting the sperm penetration.

PS-02-002
Penicillium and aspergillus spp. on pap smears from the surprising origin
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Objective: Fungal organisms are commonly seen on smears. Some unusual species as Aspergillus and Penicillium are so rare and generally seen via contamination. In this study, we investigated the origin of the many extraordinary fungal organisms seen on Pap smears in series in only a few months.
Method: In Pathology department of Mardin Maternity Hospital, we observed both smear and vaginal discharge materials, came from the same hospital but different clinicians, for 3 months.
Results: 149 smears came from clinician A and 335 smears from clinician B. Curious fungal organisms with huge branching hyphas and macrochonidias were seen in 15 smears among 149 smears (2 Aspergillus and 4 Penicillium species were recognized morphologically). No growth was observed in cultures. Interestingly, among all 335 smears came from clinician B, there was no abnormal funguses. The smear samples with unusual fungal components all came from the same gynecologist. This made us strongly consider the probability of contamination.
Conclusion: Penicillium and Aspergillus spp. are extremely rare in vaginal smears. In our study, these funguses are thought to be airborne passed from the thick layer of the mold spreading on the ceiling of the office.

PS-02-003

Hybrid Capture 2 and Cervista: Comparison in the determination of HPV

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Objective: Nearly all cervical cancers are related to human papillomavirus (HPV) infection. Hybrid Capture 2 - HC2 (Qiagen, Hilden, Germany) is the method to determine the presence of high risk HPV (HR HPV) in cytology samples with the best clinical sensitivity.
Method: In our study we compared the results of the HPV test in 742 ThinPrep® cervical samples using first HC2 and secondly Cervista (Hologic, Madison). Samples were divided in two groups for the statistical analysis. The first group were HSIL cases confirmed by biopsy (n=65) and the second group cytology samples reported as negative, ASC-US or LSIL (without biopsy or biopsy, not HSIL) (n=677).
Results: Overall, concordance between the two techniques was 92 % (683/742). There were 23 cases HC2+ Cervista−, and 36 cases HC2 −Cervista+. The average HC2 viral load in discordant cases was 2.83. In our series the HC2 sensitivity for ≥ CIN2 was 100 % (65/65) and the specificity was 85.4 % (578/677). Cervista results were 98.5 % (64/65) and 83.3 % (564/677), respectively. In the HSIL cases the coincidence was 98.5 % (64/65).
Conclusion: Cervista results showed good clinical sensitivity and high concordance with HC2, with a slightly lower specificity. In conclusion, according to our data the determination of HPV with Cervista is comparable with HC2.

PS-02-004

Mammary analogue secretory carcinoma of salivary glands: 2 cases including Cytology, Histology, IHC, EM, RT-PCR and FISH

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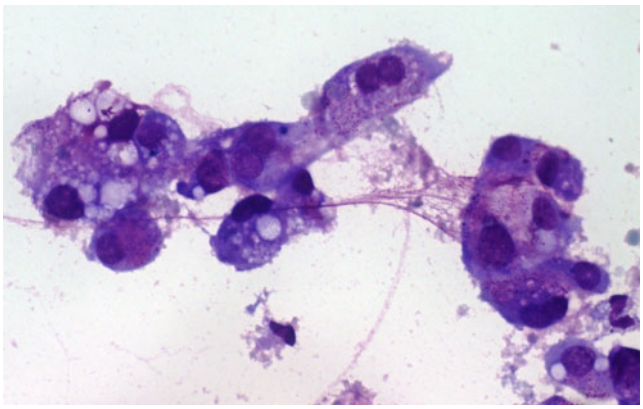
Objective: Mammary analogue secretory carcinoma (MASC) of the salivary glands was described in 2010 by Skálová et al. in a series of 16 cases. We present 2 new molecularly confirmed cases with focus on detailed cyto-morphological features and correlation with special studies.
Method: A 75 year old man and a 68 year old female presented with history of slow growing parotid and submucosal buccal tumors, respectively. Two fine needle aspiration biopsies (FNAB) were performed in each case. The surgical resection specimens were routinely processed and special studies applied on paraffin tissue section. The FNAB smears were retrospectively studied.
Results: All smears showed similar features of abundant proteinaceous background, moderate cellularity including macrophages and irregular and variable sized groups of cells with slightly enlarged round hypercromatic nuclei and abundant bluish vacuolated cytoplasm frequently containing small reddish granulations. The first FNAB reports confirmed salivary origin and the second ones alert for possible neoplastic nature, advising surgical resection. Electron microscopy performed in the parotid case caracterized the granules as mucigen. Subsquent pathologic evaluation and molecular confirmation was carried out.
Conclusion: MASC is a low grade malignant tumor capable of simulating a benign salivary gland process so it is important to know its cytological characteristics.



PS-02-005

Adenosquamous lung carcinoma: The importance of cyto-histologic correlation

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Objective: Adenosquamous lung carcinomas (ASC) are uncommon and aggressive tumors. Identification of a squamous component within a NSCLC is critical as it excludes anti-VEGF therapy. Likewise, recognition of an adenocarcinoma component is also relevant because it prompts the search for EGFR mutations. Since 70 % of lung cancers are diagnosed in small biopsies/cytological specimens, cyto-histological correlation is crucial for correct diagnosis. Thus, we aimed at determining the relevance of combining cytologic and histologic findings in initial diagnostic work-up of ASC.
Method: We searched for cases of ASC diagnosed at our institution from March 2011 to April 2012. Cytologic and histopathologic findings were evaluated and their accuracy for diagnosing ASC was assessed.
Results: Of 184 cases of lung cancer in biopsy, 11 (6 %) corresponded to probable ASC and in 9 cases cytologic examination was also performed. In 7 cases, cytology was

not conclusive, but in 2 cases it demonstrated cytomorphological features of probable ASC. We emphasize one case in which only the squamous component was valued by histology, but cytology provided clues that prompted immunohistochemical analysis which led to the diagnosis of probable ASC.
Conclusion: Cyto-histological correlation augments the diagnostic accuracy in ASC of the lung, emphasizing the complementarity of both procedures.

PS-02-006
The impact of the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC): A retrospective study of 828 aspirates with emphasis on the prior "indeterminate" category
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Objective: We evaluated the impact of implementing TBSRTC in an academic community hospital.
Method: FNAs from Jan/2004 to Dec/2010 were reclassified in TBSRTC: nondiagnostic (ND), benign (B), atypia or follicular lesion of undetermined significance (AUS/FLUS), suspicious for follicular neoplasm (FN), suspicious for malignancy (S) and malignant (M). FLUS and FN were classified according to presence of Hürthle cells as HCLUS and FN-HC.
Results: A total of 828 FNAs (480 patients) were obtained: 46 ND (5.55 %), 682 B (82.4 %), 9 S (1.1 %) and 25 M (3.0 %). The 66 (8.0 %) indeterminate categories were reclassified: 1 ND (1.5 %), 8 B (12.1 %), 5 AUS (7.6 %), 34 FLUS (51.5 %), 5 HCLUS (7.6 %), 3 FN (4.5 %), 9 FN-HC (13.6 %) and 1 S (1.5 %). Thyroidectomies were performed in 125 patients (26 %): benign lesions in 83 (66.4 %), 7 (5.6 %) follicular adenoma and 2 (1.6 %) follicular carcinomas, 1 (0.8 %) medullary carcinoma, 21 (16.8 %) papillary carcinomas and 16 (12.8 %) papillary microcarcinomas (PMC). Risk of malignancy (RM) excluding PMC: B 1.4 %, AUS/FLUS/HCLUS 5 %, FN/FN-HC 11.1 %, SM 50 % and M 77.8 %.
Conclusion: TBSRTC criteria led to more specific diagnosis. FN/FN-HC category has a two-fold RM when compared to AUS/FLUS/HCLUS.

PS-02-007
FNA of thyroid lesions: A brief report
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Objective: The material of this study is consisted of selected FNA biopsies performed in the last 10 mounths period and followed by the Endocrinology Department.
Method: The Bethesda System of reporting thyroid cytopathology was used. Slides were stained with Papanicolaou preparations.
Results: Totally 380 cases were examined, 288 of which were female and 92 were male. Age of the patients varied between 5 and 88. 121 cases were diagnosed as nondiagnostic or nonsatisfactory. 211 cases diagnosed as consistent with a benign follicular nodule. Only 4 cases were diagnosed as a consistent with lymphocytic thyroiditis in corelation with the clinical features. Only 1 case diagnosed as a granulomatous thyroiditis. Diagnosis as "Atypia of undetermined significance or follıcular lesion of undetermined significance "was made only in 2 cases whereas "Follıcular neoplasm or suspicious for a follıcular neoplasm" was diagnosed in 1 case. "Suspicious for malignancy" diagnosed in 15 cases. 2 cases were diagnosed as malignant.
Conclusion: Although diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions are well established in The Bethesda System, difficulty in categorizing the cases and underestimation or overdiagnosis are quite frequent issues. To solve this problem, retrospective studies which include surgical and cytopathologic reports, to examine slides by at least two different pathologists in different times will be helpfull.

PS-02-008
Metastatic pulmonary adenoid cystic carcinoma: Report of a case diagnosed by fine-needle aspiration cytology
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Objective: A rare case of adenoid cystic carcinoma of ceruminal gland with pulmonary metastasis presented with characteristic cytological and histological findings.
Method: The biopsy specimen of the patient, a 45 year-old man with painfull, growing mass in his external auditory canal was interpreted as an adenoid cystic carcinoma. He was treated surgically and received post-operative radiotherapy. After 8 years, a distant metastasis relapse was observed. Computed tomography (CT) of the chest depicted multiple spiculated masses suggestive of metastases throughout both lung fields, the diameter of the largest measuring 2 cm. CT guided percutaneous transthoracic fine needle aspiration biopsy was performed from the largest lesion.
Results: Cytological examination of the aspirates revealed large spherical hyaline globules representing basement membrane material surrounded by neoplastic cells. The cells were cohesive, closely packed, and had uniform round to oval hyperchromatic nuclei with scanty cytoplasm. These features were suggestive of an adenoid cystic carcinoma.
Conclusion: Patients with adenoid cystic carcinoma could be frequently encountered with disease recurrence confined to the lung. Fine-needle aspiration cytology provided a conclusive diagnosis of adenoid cystic carcinoma.

PS-02-009

Diagnostic usefulness of MUC1 and MUC4 for distinguishing between metastatic adenocarcinoma cells and reactive mesothelial cells in effusion cell blocks

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Objective: Differentiating metastatic adenocarcinoma cells (MAC) from reactive mesothelial cells (RMC) in effusion fluids based on cytomorphologic features alone can be very challenging. The aim of our study was to determine the value of MUC1 and MUC4 for distinguishing between MAC and RMC in effusion fluids.
Method: A total of 237 cell block specimens including 196 malignant effusions with MAC and 41 benign effusions with RMC were stained with antibodies against MUC1 and MUC4.
Results: MUC1 immunoreactivity was observed in 194 (99.0 %) of 196 cases of MAC and 20 (48.8 %) of 41 cases of RMC. MUC4 immunoreactivity was observed in 174 (88.8 %) of 196 cases of MAC and 4 (9.8 %) of 41 cases of RMC. In distinguishing MAC from RMC, the presence of MUC1 reactivity was found to be 99.0 % sensitive and 51.2 % specific. The sensitivity of MUC4 for MAC was 88.8 % and the specificity was 90.2 %. The combination of positive staining for MUC1 or MUC4 was 100 % specific for MAC, whereas a combination of negative staining for both MUC1 and MUC4 was 97.6 % specific for RMC.
Conclusion: The combination of MUC1 and MUC4 is a useful diagnostic adjunct with which to distinguish MAC from RMC in cell block preparations.

PS-02-010

Polyvinyl alcohol foam cell blocks from a needle hub residue device

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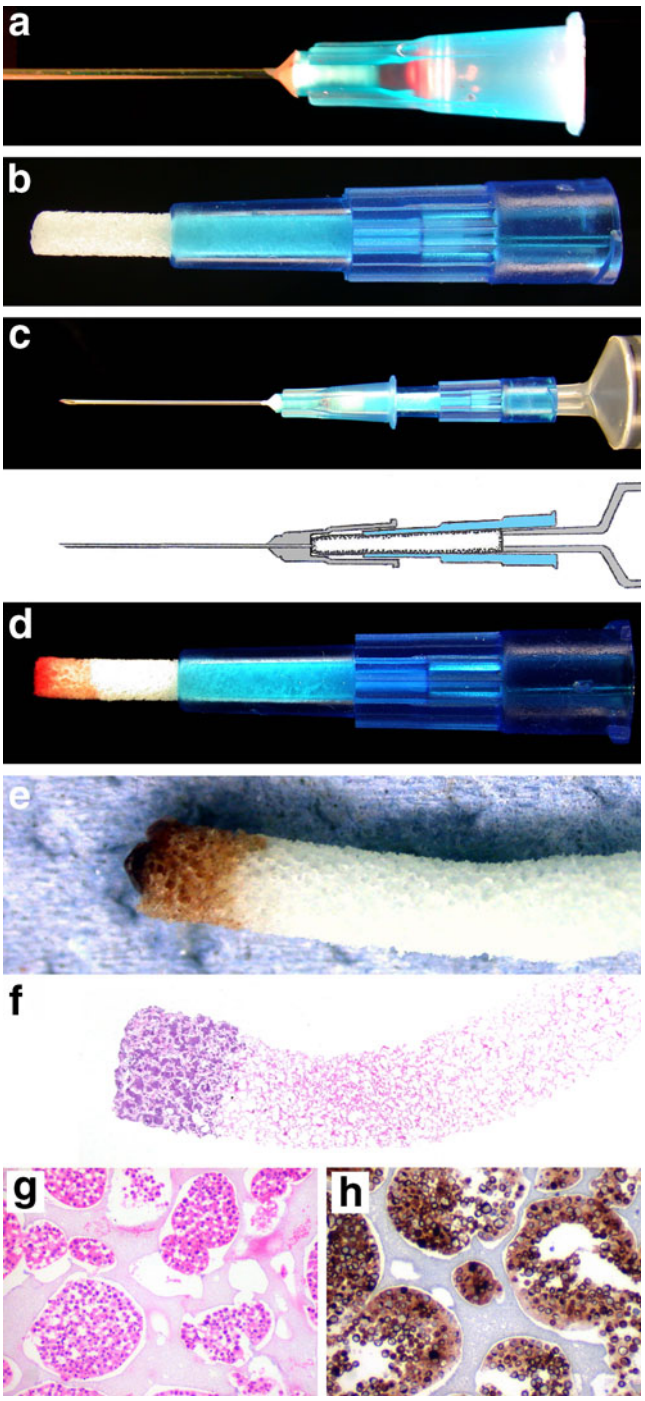
Objective: Often some of a fine needle aspiration (FNA) sample is left behind in the hub of the needle when the specimen is ejected on the slides (Figure 1A).
Method: We have designed a device that collects this material. It consists of a plastic adaptor that has a core of polyvinyl alcohol foam protruding from its lumen at one end (Figure 1B). The other end of the adaptor then fits on to the syringe (Figure 1 C). As the FNA is being performed the sample material flows up the lumen of the needle's shaft and emerges into the hub of the needle where it is absorbed into the tip of the foam core (Figure 1D). Smears are made by ejected the specimen from the needle onto a slide by air pressure from an attached syringe. The air passes through the foam forcing some of the sample in the foam back down the needle but some remains behind. The device is then removed and placed in a formalin specimen pot. Once fixed the core is pulled from the adaptor (Figure 1E), processed and sectioned as for routine histology specimens (Figure 1 F). On microscopic examination cells are seen in the spaces in the foam matrix (Figure 1 G). Immunohistochemistry and other molecular investigations can be performed (Figure 1 H; Cytokeratin 7) as for routine histology specimens.



PS-02-011

Assessment of Dendritic/Langerhans Cells (DCs) in cytological specimens and corresponding histology of Papillary Thyroid Carcinoma (PTC) by immunochemistry

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Objective: The presence of DCs has been studied histologically in PTC, but their presence and potential diagnostic value in thyroid FNAs has not been evaluated.
Method: We assessed the presence of DCs in cytological samples of histologically confirmed PTCs (n=31) and benign thyroid nodules (BTN) (n=29) using CD1a. Corresponding PTCs (n=11) and BTN (n=10) from surgical excisions were stained with both CD1a and Langerin.
Results: CD1a + DCs were identified in 30/31 PTCs on cytology (97 %). They were either isolated in the background or more typically closely associated with tumor cell clusters. The 3 PTC cases with the least DCs corresponded to the follicular variant on histology. In contrast, most BTN (69 %) lacked CD1a + DCs. When DCs were present, they were primarily isolated in the background although 5/29 cases (17 %) contained rare DCs among tumor cells. Tumor-infiltrating DCs and background DCs were both higher in PTCs than in BTN, but only the former was statistically significant (P<0.0001 and P=0.1173 respectively). Similar findings were found on histology where all PTCs contained CD1a + and Langerin + DCs while only 2/10 BTN (20 %) contained rare DCs.
Conclusion: DCs are present in FNAs of PTC, typically among tumor cell clusters, while they were absent or rare in FNAs of BTN. Thus DCs may be useful as an additional diagnostic marker for PTC.

PS-02-012

Significance of p 16 immunostaining in postmenopausal women with atypical squamous cells

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Objective: The evaluation of postmenopausal Pap smears can often be challenging. Degeneration associated with atrophic vaginitis, hyperchromatic crowded groups, parabasal cells with organophilic cytoplasm or variations in nuclear size may be falsely interpreted as squamous atypia or even more severe lesion.
Method: The study included 25 postmenopausal Papanicolaou patients (26 smears) with the initial cytological diagnosis of ASC-US or ASC-H. The smears were decolorized and immunostaining for p16(Ink4a) was applied. In 21 patients (22 smears) tissue biopsy and histological examination was performed and four ASC-US cases had cytological follow up only.
Results: Among cases with histological examination positive p16 reaction was found in 17 patients (18 smears). The histological diagnoses were: CIN1 (3), CIN 1-2 (2), CIN2 (1 case), CIN3 (5 patients/6 smears), AIS (1 case) and invasive squamous carcinoma (2 patients). Two p16 positive patients with three smears and initial negative histology had CIN3 after 2 years. Among p16 negative patients there were two with CIN3 and two with normal histology. Four ASC-US patients without histological examination had normal cytological follow up.
Conclusion: P16 is a useful marker in detecting of clinically significant cervical lesions in postmenopausal women.

PS-02-013

Endoscopic-ultrasound guided fine needle aspiration cytology of intraductal papillary-mucinous neoplasms of the pancreas: Report of two cases and review of the literature

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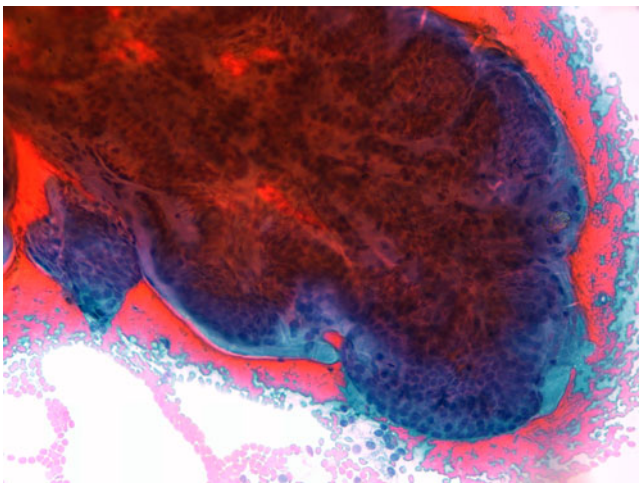
Objective: Intraductal papillary-mucinous neoplasms (IPMN) of the pancreas are mucin-producing tumors recently recognized as a distinct entity among other mucinous pancreatic tumors. Endoscopic-ultrasound guided fine needle aspiration (EUS-FNA) is a sensitive technique which can be very useful in the accurate diagnosis of these neoplasms.
Method: We present a case of a 30-year-old female with recurrent episodes of acute pancreatitis and a 49-year-old male with abdominal pain. TC showed a 26 mm-cystic tumor at the uncinated process of the pancreatic head and cystic dilatation of the main pancreatic duct, respectively. In both cases EUS-FNA was performed.
Results: Smears showed medium-to-large, cohesive groups and complex papillary clusters set in a clean, mucoid background, composed of cuboidal or columnar epithelial cells with abundant clear or mucinous cytoplasms. A honeycomb arrangement was occasionally seen. Although nuclei were predominantly medium-size and uniform, some groups showed some nuclear enlargement and pleomorphism with visible nucleoli. A diagnosis of “mucinous neoplasm with papillary pattern”

was rendered in both cases, followed by partial pancreatectomy. The histologic examination was consistent with IPMN.

Conclusion: The cytologic features of intraductal mucinous papillary neoplasms of the pancreas, evaluated by EUS-FNA, seems to be quite characteristic of these tumors and allow to suggest a correct preoperative diagnosis.



PS-02-014

IGH FISH-CISH DNA probe split signal: An additional tool in clonality assessment of lymphoproliferative processes

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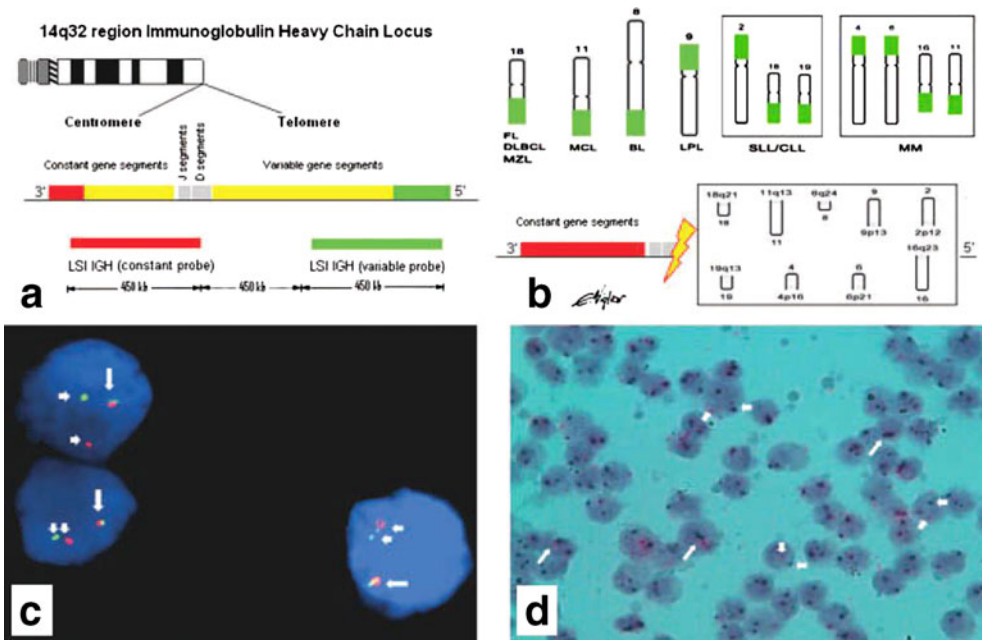
Objective: The human IGH locus at chromosome 14q32 is frequently involved in different translocations of non Hodgkin Lymphoma (NHL), and the detection of any breakage involving the IGH locus should identify a B-cell NHL. The split signal IGH FISH-CISH DNA probe (IFCD) is a mixture of two fluorochrome-labeled DNAs that binds the telomeric and the centromeric segments, on the IGH breakpoint respectively. We tested the capability of the IFCD to detect IGH translocations and diagnose B-cell NHL on cytological samples.

Method: Fifty cytological specimens from lymphoproliferative processes were tested using the IFCD and the results compared to light chain assessment by flow cytometry (FC), IGH status by PCR, and to clinical-histological data.

Results: IFCD analysis detected 29 positive, 15 negative and 6 inadequate cases; there were 29 true positive (66 %), 9 true negative (20 %), 6 false negative (14 %) and 0 false positive cases (0 %). Comparing the sensitivity of the IFCD with FC and PCR, the highest sensitivity was obtained by FC followed by IFCD and PCR.

Conclusion: The IFCD is effective in detecting any translocation involving the IGH locus; it can be employed on different samples from different B-cell NHL whereas it is not useful to classify the specific entities.



Sunday, 9 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-03 Poster Session IT in Pathology

PS-03-001
Recognition of the cross-section of colon glands in histological images based on sequential algorithm as a introduction to morphometry
T. Markiewicz*, R. Koktysz, M. Muszynski, W. Kozlowski, M. Szczepkowski, A. Kobus
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Objective: Morphometric analysis of the glands and inflammatory cells proportions in colon mucosa may be crucial for distinction of subtle changes. The most important step is a recognition and proper segmentation of the separate glands, even branched, atrophic or distorted.
Method: New sequential algorithm has been proposed, based on mathematical morphology transformations, such as extended regional maxima, hit-or-miss, opening and closing operations. For lumen opened glands snake algorithm with closing has been applied to surrounding elements with sequential elimination of the closed contours under decreasing area criterion. Proposed method has been used to evaluate 47 cases of diversion colitis to compare specimens sampled from functional part of colon and defunctioned distal one.
Results: The appropriate results were obtained for specimens with different section planes with efficiency 89 %. In comparison of the B to A was observed decreased participation of epithelium in the glands area measured in deep region (an average 57 % instead 68 %). In addition, the area of the gland was slightly reduced from 51 % to 46 % of the mucosa.
Conclusion: The proposed method can be useful to automatic morphometry analysis of the gland shape in colon mucosa. The recognition of the opened glands improves previously designed algorithms.

PS-03-002
Various approaches of image segmentation explored in immunohistochemical histological samples with nuclei reaction
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Objective: Quantitative analysis of the immunohistochemical histological samples plays an important role in the diagnosis and prognosis of many cancers. The commercial and non-commercial software's to computerized image analysis of microscopic images based in several approaches.
Method: The advance segmentation scheme usually consists of preprocessing, nuclei extraction and classifier blocks. When the preprocessing step includes filtering and conversion to the most discriminative representation and the classifier can be realized by various tools, especially Support Vector Machine as a state-of-art, nuclei extraction is the most crucial part of any algorithms. We compare single thresholding methods such as Otsu, Kurita, minimum error, entropy thresholding, with the sequential thresholding approaches combined with area criteria, local threshold value or extended regional maxima. All of them are accompanied by watershed method and filtration.
Results: For Ki-67 stained meningioma specimens in the fields of view without overlapping nuclei the most advance methods are adequate. When increasing the cell number, only sequential thresholding with area criteria and extended regional maxima give acceptable results. The mean relative error is 2.6±2.2 and 5.4±6.4 % respectively.
Conclusion: The results confirm the efficiency of using sequential methods for segmentation of cell nuclei. For best results, use sequential thresholding with area criteria.

PS-03-003
NHS improvements: Enhanced IT project for histopathology
F. Mayall*
*Musgrove Park Hospital, Dept. of Cellular Pathology, Taunton, United Kingdom

Objective: Many histopathology laboratories are using antiquated software that hobbles their performance.
Method: We developed open source Filemaker Pro based histopathology reporting software with innovations based on Lean principles to enhance work flow. These include: - Colour coded visual workflow control - “One-click” extra-work requests with order tracking - User defined template reporting - Reporting of complex cases using benchmark profomas - Exportable data-sets using Open Database Connectivity - Easy local customisation and enhancement by the user.
Results: The software was used by 15 staff to report more than 7000 histopathology specimens at two histopathology laboratories. Many of these cases were complex cancer resection cases requiring key data capture. The histopathology staff using the software were surveyed on their experience of using the software.
Conclusion: The key steps in Lean IT development: - Start with a small idea - Develop software with multiple Plan, Do, Study, Act (PDSA) cycles - Ask users for more ideas for enhancements - Recruit others into the project by allowing them to use the software and experience its benefits - Standardise new reporting process by achieving agreement between users - Design a project that requires minimal financial investment This open source software is available for download from www.FreeDP.org.

Sunday, 9 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-04 Poster Session Neuropathology

PS-04-001
Sacrococygeal extraspinal mass: A rare presentation of myxopapillary ependymoma
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Objective: Myxopapillary ependymomas (MPE) often occur at the filum terminale but occasionally occur outside the central nervous system (CNS). Common site for these extraneural tumors is sacrococcygeal area.
Method: A cocygeal MPE with radiologic, gross and microscopic features will be presented.
Results: A 39 year old female admitted Neurosurgery Department with painful coccygeal mass. Magnetic resonance imaging revealed a coccygeal, well-demarcated, non-enhancing mass of 4×5 cm in diameter. The mass did not have any connection with the spinal cord. It was completely excised and grossly the cut surface of the encapsulated mass was soft. Microscopically the tumor was comprimised of myxoid stroma with pseudopapillary structures around hyalinized vessels. The tumoral cells showed intracytoplasmic dot-like positivity with EMA. There were no mitosis, and the Ki67 labeling index was low.
Conclusion: Extraspinal MPEs are rare and the most common location is sacrococygeal area. These masses are often preoperatively misdiagnosed as pilonidal sinus. Unlike the CNS MPEs, extraspinal MPEs have a potential to metastasize even if they do not show any anaplastic morphological feature. Long term follow-up is recommended as metastases can occur up to 20 years after initial presentation.

PS-04-002
Cerebellar liponeurocytoma: Report of two cases
L. Andres*, I. Hernandez, B. Mateos, J. I. Lopez, L. Zaldumbide, A. Perez Zabala, N. Cerda, G. Muniz
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Objective: Cerebellar liponeurocytoma (CL) is a rare neoplasm with neuronal, astrocytic and lipomatous differentiation arising in adults. The entity is considered as a grade II neoplasm in the last WHO classification of central nervous system tumours. We show two typical cases of this entity stressing the spectrum of histological changes and its differential diagnosis.
Method: Patient 1 is a 72-year-old woman with a history of headaches and instability. CT scans and MRI showed a 5 cm in diameter relatively ill-defined, poorly enhanced, round tumour mass in the left hemisphere. Patient 2 is a 56-year-old woman with a history of headaches and instability. MRI showed a 6.5 cm in diameter well-defined triangular lesion in the right hemisphere.
Results: Complete surgical resection was achieved in both cases. Both tumours showed highly cellular neoplasms composed by round to polygonal cells with scant cytoplasm and round nuclei with fine chromatin pattern. Mitoses were not seen. Well differentiated lipomatous cells grouped in irregular nests were intermingled with the predominant neuronal component.
Conclusion: Cerebellar liponeurocytomas are located in the cerebellar hemispheres and pursue a non aggressive clinical course, with local recurrences detected mainly after incomplete resections. The typical adipous tissue is the result of a lipidization process and not a true metaplasia.

PS-04-003
Giant cell tumor of the temporal bone: Report of a case
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*Saint Savvas Hospital, Dept. of Pathology, Athens, Greece

Objective: Giant cell tumor of bone is an uncommon neoplasm that accounts for about 5 % of all bone tumors. It usually involves long bones and is very rarely encountered in the skull where it mostly involves the sphenoid and temporal bones. It is a benign neoplasm but can be locally aggressive.
Method: We present a case of a 32 year old woman with history of multiple sclerosis whose routine CT scan revealed a mass with corrosive features and calcification situated at the petrous portion of her left temporal bone. A biopsy was sent to our laboratory.
Results: Histopathologic examination revealed a neoplasm composed of sheets of oval mononuclear cells, with uniformly distributed nuclear chromatin, evenly intermixed with numerous giant cells that contain a variable number of nuclei with features similar to those of mononuclear cells. Cytoplasm of either cell type was eosinophilic and cell borders were indistinct. Mitoses were scarce and regular. Foamy histiocytes, hemosiderin and microscopic nodules of cartilage formation were also noted.
Conclusion: Although giant cell tumor is a benign neoplasm its' localization in this case posses a threat that should be managed surgically and by adjuvant radiotherapy if complete excision is unobtainable.

PS-04-004
Leptin and leptin receptor expression in pituitary adenomas
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Objective: Leptin is a regulatory hormone which is mainly synthesized by adipocytes and regulates body fat mass. Leptin also has regulatory function on anterior pituitary. In

this study, we have investigated the expression levels of leptin (Ob) and its receptor (Ob-R) in various types of pituitary adenomas and normal anterior pituitaries.
Method: 50 pituitary adenoma cases between 2006 and 2011 were selected. Immunohistochemistry for leptin (Ob) was performed for each 10 cases of null cell, GH, ACTH, prolactin and FSH/LH secreting adenomas. Western blot was performed for leptin receptor (Ob-R) in 9 cases consisting of all five subtypes.
Results: Immunohistochemical staining showed greater immunoreactivity for leptin in normal pituitaries compared to adenomas. Except for ACTH-secreting pituitary adenomas, all other four subtypes showed widespread and intense staining for leptin ($P<0.0001$). Null and FSH/LH-secreting subtypes were mainly showed cytoplasmic and nuclear staining. Western blot analysis showed leptin receptor expression in all types of adenomas except null cell.
Conclusion: Leptin immunoreactivity is decreased in pituitary adenomas compared to normal pituitary. Leptin receptor is found in various types of pituitary adenomas except null cell adenoma. This finding shows regulation of leptin and leptin receptor n has role in secretory function of pituitary adenomas.

PS-04-005
Association between expression of KAI1, MMP-2, CD44v6 and malignancy of human primary brain tumors
J. Bar*, B. Paradowski, A. Halon, A. Lis-Nawara, L. Zub, M. Jelen
*Wroclaw Medical University, Dept. of Pathomorphology, Poland

Objective: Primary malignant brain tumors often present local invasive growth. The study aimed to estimate the expression of KAI1 protein, MMP-2, CD44v6 and their correlation in gliomas of different grade of malignancy.
Method: Expression of MMP-2, CD44v6 and KAI1 was evaluated on 154 formalin fixed paraffin-embedded tissue blocks divided into: pilocytic astrocytoma ($n=15$), fibrillary astrocytoma ($n=17$), anaplastic astrocytomas ($n=27$), anaplastic oligodendrogliomas ($n=27$), glioblastoma multiforme ($n=54$) and normal brain tissue ($n=14$) using immunohistrochemistry.
Results: MMP-2 and CD44v6 was observed frequently in gliomas with high grade of malignancy. KAI1 immunoreactivity was mainly observed in specimens with low degree of malignancy. MMP-2 and CD44v6 expression was significantly increased when the degree of malignancy of the gliomas increased ($p<0.05$). Whilst KAI1 expression increased when the degree of gliomas malignancy decreased ($p=0.03$). Positive correlations between MMP-2 and CD44v6 ($p=0.01$) and inverse between KAI1 and MMP-2 expression ($p=0.02$) were found in gliomas.
Conclusion: These results indicate that association between MMP-2 and CD44v6 expression may increase dissemination of tumor cells. Whereas, high expression of KAI1 protein might suppress the function of MMP-2 in gliomas.

PS-04-006
Pediatric glioblastoma: A case report
A. Barin*, S. Ekici, C. Altunkaya, S. Yilmaz, G. S. Yalcin, G. Hatipoglu, M. Caydere, H. Ustun
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Objective: Glioblastoma is the most common malignant tumor of central nervous system in adults which characterized by malignant pleomorphic astrocytic cells with marked nuclear atypia, mitotic activity, necrosis and/or microvascular proliferation. Glioblastoma may manifest at any age but usually affects adults especially older than 50 years. In this case, we present a pediatric glioblastoma case because it has seen rarely under 20 years and it is so important owing to its prognosis.
Method: An 11-year-old boy has had headache for 20 days. According to radiological imagings 23×20 mm in diameter infiltrating mass has seen in temporal lobe contains 15×7 mm in diameter cystic component and contrast enhancement was noted. Clinically grade 3 astrocytoma has thought primarily and he has been operated.
Results: In microscopic examination nuclear atypia, mitotic activity and microvascular proliferation has seen without necrosis.
Conclusion: This case has reported as Glioblastoma (WHO grade IV).

PS-04-007
Gliosarcoma: A study of 3 cases
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Objective: Gliosarcomas are biphasic neoplasms composed of a glioblastoma admixed to a sarcomatous component with different lines of differentiation. Histogenesis of these tumors is still discussed. Our objective is to specify pathological characteristics of this neoplasm its related to or not to glioblastoma.
Method: 3 cases of gliosarcomas diagnosed in our department of pathology. Clinical, radiological, therapeutic and follow-up data were reviewed. Histological features and immunohistochemical results were also established.
Results: 3 female patients with a median age of 46 years (ranging 30–69 years). intracranial hyperpressure and paralysis are main symptoms. The brain imaging showed frontal, fronto- parietal and intra ventricular expansive process, respectively. Microscopically, a biphasic pattern, with anaplastic astrocytic cells alternated with malignant mesenchymal areas,

demonstrating a fibrosarcoma pattern, in two cases and rhabdoïd pattern in one case. Immunohistochemical stain confirmed the diagnosis of gliosarcoma in each case. Patients were treated by surgical excision; One patient was lost on follow-up. One patient died by postoperative complications.
Conclusion: Clinical, radiological and follow-up features of gliosarcomas share great similarities with glioblastomas. Histopathological, histochemical and immunohistochemical studies are helpful in accurate diagnosis. Cytogenetic and molecular data support a monoclonal origin for these tumors.

PS-04-009
Synoviosarcoma of nerve: Case report
S. Costantini*, A. Tosi, G. Fraternali Orcioni, D. De Biase, Y. Ishikawa, V. Eusebi
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Objective: Case of biphasic synovial sarcoma of nerve in a 59 year-old female located between flexor muscles and radial diaphysis and adherent to median nerve and ulnar artery is presented.
Method: Tissue was fixed in formalin, embedded in paraffin and stained with Haematoxylin and Eosin. Periodic Acid-Schiff stain without diastase pre-digestion was obtained. Ventana antibodies were employed: TTF-1, ER, EMA, S100, CK 14, CK 7 and MNF 116. SS18-SSX fusion gene transcript was detected with conventional RT-PCR and qRT-PCR.
Results: Macroscopically nodule had smooth circumscribed borders, grey-yellowish colour and measured 3,7×3×2,5 cm. Histologically it was delimited by a dense sclero-hyaline capsule and constituted of numerous glands lined by one layer of cuboidal-columnar cells showing eosinophilic cytoplasm and round to ovoid nuclei with a single small nucleolus. They contained dense eosinophilic strongly PAS and EMA positive material. Glands were immersed within tightly packed spindle cells. Mitoses were scanty. Necrosis was absent. EMA strongly stained most of the glandular as well as scanty spindle cell elements. Chromosomal reciprocal translocation t (X; 18) with positive signal for SS18-SSX1 transcript was seen.
Conclusion: Synovial sarcoma of nerve is a rare condition that has to be distinguished from histologically similar lesions.

PS-04-010
Rabdoid meningioma: Presentation of a rare case
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Objective: In 1998, Keppes and later Perry suggested the term rhabdoid meningioma which was adopted into the WHO classification (grade III) in 2000.
Method: We present a rare case of a rabdoid meningioma and study the clinicopathological characteristics of the neoplasm.
Results: A 68-year-old woman was submitted in surgical excision of an endocranial tumour (d:3 cm) in our hospital. The histological examination revealed entirely rabdoid morphology. The neoplastic cells expressed the following immunohistochemical phenotype: S100+, Vimentin+, EMA+, GFAP−, PR+, HMB45−, A1/AE3+(focally), CK8/18+(focally), SMA−, Ki-67 (<1)%.
Conclusion: Rabdoid phenotype represents an indicator of malignant transformation regardless of the tumor's histogenesis. Expression of Ki-67 antigen correlates with recurrence even in meningiomas with minimal atypical features, which should prompt closer surveillance after excision. Rabdoid meningiomas behave aggressively and have bad prognosis contrary to the classic meningioma. Prognosis is influenced by it's complete excision and the expansion within the intracranial cavity. It has to be distinguished from glioma, melanoma and metastatic carcinoma. The patient after 1 year is in generally good health, and is followed up by oncologists.

PS-04-012
Atypical Extraventricular Neurocytoma (Case Report)
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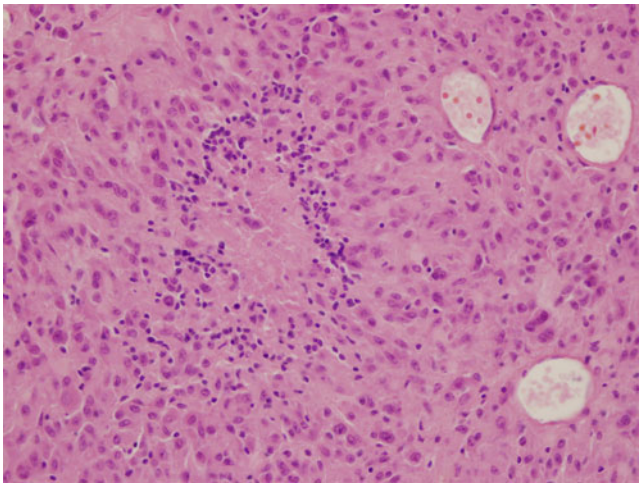
Objective: Central neurocytomas are rare intraventricular tumors with neuronal differentiation, typically located in the ventricles while tumors located outside the ventricles designated as "extraventricular neurocytomas" (EVN). Neurocytomas are classified as atypical if they exhibit a MIB-1 labeling index >2 % or atypical features, like focal necrosis, vascular proliferation, and increased mitotic activity. We here report a case of atypical EVN of the left frontal lobe.
Method: A 60-year-old woman patient admitted to hospital for headache. CT scan showed a large partially calcified cystic mass. MR imaging showed circumscribed, solid mural nodule within the cystic mass. The patient underwent a left frontal craniotomy. Specimens were fixed in 10 % formalin and stained with hematoxylin and eosin. For immunohistochemistry, sections were incubated with monoclonal antibodies to synaptophysin, neurofilament protein, MAP-2, NSE and GFAP. The proliferative index was assessed with MIB-1.
Results: Histopathological examination revealed a neuronal neoplasm composed of uniform cells in solid sheets. Small necrosis areas and mitotic figures were evident. Immunohistochemical examination revealed positive results for synaptophysin, neurofilament protein, MAP-2, and NSE. GFAP staining was negative. MIB-1 index was calculated as 5 %.

Conclusion: In general, central and extraventricular neurocytomas have a good prognosis. Atypical extraventricular neurocytomas are quite rare like this case with malignant histopathological properties.



PS-04-013

Meningioma and Schwannoma associated with Neurofibromatosis Type 2: A case report of rare genetic disorder

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Objective: Neurofibromatosis is a group of genetic disorders referred as phakomatoses. There are two main forms called NF1 and NF2 which have different incidence, molecular characteristics, and clinical exhibitio. Both have higher risk for the development of certain rare malignant tumors that occur in the brain, nerves or spinal cord.
Method: Here, we present a rare case in which multiple meningiomas and vestibular schwannomas diagnosed in the same operation.
Results: A 23 year old woman presented with hearing loss clinically. She underwent surgical treatment for tumoral lesions in two different localization in the same session. One of them resected from pontoserebellar location was diagnosed as a schwannoma and the other one located on dura was diagnosed as a meningioma respectively.
Conclusion: NF2 is far less common than NF1 and strict diagnostic criteria have been described each of them. Since difficulty to detect genetic abnormalities and no single criteria is pathognomonic, clinical characteristics much more valuable for differentiation. Knowledge of associated clinical features will help to correct diagnosis and to predict much more devastating clinical course for NF2.

PS-04-014

Diagnostic confusion: Central neurocytoma

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Objective: Central neurocytoma is a rare intraventricular brain tumor that affects young adults and presents with increased intracranial pressure secondary to obstructive hydrocephalus. They are usually located in the supratentorial periventricular region. Because of some clinical and radiological findings CNS neurocytomas were confused with other intraventricular lesions.
Method: A 37-year-old male was admitted with chronic headache with 6 months duration on July 21, 2011, when there were no neurological deficits or physical abnormalities. Computed tomographic (CT) scans showed 51×40 mm a mixed density mass with amorphous calcification in the right lateral ventricle, which was irregularly enhanced by contrast medium. Light Microscopy showed sheets of monotonously neoplastic cells with uniform round-to-oval nuclei and inconspicuous nucleoli. The cytoplasm was clear or eosinophilic with indistinct border. Capillary networks were well developed and divided the tumor cells into groups. No nuclear pleomorphism or mitosis was seen. We present a case of intraventricular neurocytomas confirmed by immunohistochemical studies.
Conclusion: This rare tumor causing diagnostic confusion, discussed by the literature.

PS-04-015

A case of oligodendroglioma with neuronal differentiation

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Objective: We report a case of oligodendroglioma showing marked neuronal differentiation.
Method: A 46-year-old female visited an emergency room because of an attack of convulsion. Imaging analyses disclosed a calcified, 3.5×3 cm tumor in the right frontal lobe.
Results: The resected tumor was composed of a mixture of oligodendroglioma-like (OLG) and gangliocytoma-like (GC) areas. In the former, fried-egg appearance and more cellular nodules were recognized. In the latter, there were numerous small neuron-like cells with basophilic cytoplasm. OLG areas showed immunoreactivity for Olig2, GFAP and mutant IDH1, while GC areas were positive for synaptophysin and NeuN. Ki-67 labeling index was about 10 % in cellular nodules of OLG areas. At least one allelic loss of 1p/19q was detected in 53.4/61.2 % cells in OLG areas and 47.2/40.6 % in GC areas with FISH analyses. Furthermore, an identical mutation of IDH1 (G395A, R132H) was demonstrated in both OLG and GC areas.

Conclusion: Genetic abnormalities including 1p/19q loss and IDH1 mutation indicate that this case is an oligodendroglioma associated with prominent ganglion cell differentiation. Oligodendrogliomas with neuronal differentiation like our case may suggest a close relationship between oligodendroglial progenitor cells and neuronal cells.

PS-04-016

Gemistocytic astrocytoma with granulomatous inflammation

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Objective: The coexistence of granulomatous inflammation and astrocytoma is extremely rare. Hemostatic agents are used to control intraoperative bleeding in many surgical subspecialties, including neurosurgery. There are occasional reports of granulomatous reaction to biomaterials.
Method: We aimed to present a 35 year old female patient, who was operated because of the tumor at left frontoparietal region. Tumor was histopathologically reported as oligoastocytoma. However, no granulomatous inflammation was detected beside the tumor. After 6 months, patient was reoperated because of tumor recurrence, abscess and inflammatory necrotic tissue beside the tumor. Histopathologically, gemistocytic astrocytoma with granulomatous inflammation and abscess formation was reported. No micro-organism had grown in any kind of cultures. At our neurosurgery department surgicel is used after craniotomy as hemostatic agent. It's raw material is cellulose and absorbed in about 3 months.
Results: In the literature, germinoma accompanied by granulomatous inflammation have been reported. However, astrocytic tumors don't express such an association. The patient doesn't use any drugs forming granuloma reported in the literature.
Conclusion: We encountered that Surgicel causing granulomatous inflammation in very few cases in the literature. The findings might be secondary to surgicel that used in the first operation.

PS-04-017

Allelic loss and microsatellite instability in astrocytic tumors

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Objective: Astrocytic tumors show various molecular and genetic alterations in its development and progression. Glioblastoma multiforme (GM) develops as either de novo or by progression from diffuse astrocytomas (DA) or anaplastic astrocytomas (AA) by genetic alterations.
Method: Loss of heterozygosity (LOH) and microsatellite instability (MSI) was investigated in 40 cases of astrocytic tumors (DAs [n=12], AAs [n=15] and GMs [n=13]) with 14 microsatellite markers and 5 microsatellite markers harboring p53 and PTEN, respectively. The patients' age ranged from 27 to 77 years (mean, 50 years).
Results: LOH was statistically significant in AAs and GMs, compared to that of DAs (p=0.023). LOH for 17p13 and LOH-H group for 10q23 were statistically significant in AAs and GMs (p=0.045 and p=0.001). MSI rate in DAs, AAs and GMs was detected in 16.7 %, 13.3 %, 23.1 %, but it showed no significant correlation with prognosis factors. MSI and MSI-H rates were correlated with younger (〈50 years) group (p= 0.040, p=0.011, respectively).
Conclusion: Alterations on PTEN and p53 may contribute to the development and progression of astrocytic tumors. Especially, LOH-H for 10q23 and 17p13 is considered as clinical application of discriminating the AAs and GMs from DAs. MSI might be involved in the tumorigenesis of relatively young patients.

PS-04-018

Histopathologic findings of three Charcot-Marie-Tooth patients with PMP22 mutation and Dejerine-Sottas Syndrome

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Objective: Charcot-Marie-Tooth disease (CMT) III or Dejerine-Sottas syndrome is a severe hereditary demyelinating motor and sensory neuropathy presenting in infancy or early childhood with delayed motor milestone and extremely slow nerve conduction velocities.
Method: Among 530 unrelated Korean CMT patients, mutational screen for well known CMT genes reveals three patients with PMP22 de novo mutation showing DSS. The histopathological findings of distal sural nerves are analyzed in all patients twice; Cases 1 and 2 with 10 years interval and Case 3 with 17 years.
Results: On semi-thin transverse sections, all the remaining axons (thinly myelinated or demyelinated) are surrounded by classic or basal lamina onion bulbs (OBs). The first biopsy of Case 1 (2 years-old) shows OBs (4,452/mm2), which consists of 2,295 (51.55 %) MFs with OBs and 2,157 (48.45 %) demyelinated axons with OBs. The second biopsy shows OBs (2,275/mm2), consisting of 425 (18.68 %) MFs with OBs, 489 (21.49 %) demyelinated axons with OBs, and 957 (42.07 %) OBs with no discernible axons.

Cases 2 and 3 show similar histopathologic findings with main differences in numbers of OBs.
Conclusion: Although the differences noted in two biopsies are probably due to age of the patients, correlations with clinical symptoms will be helpul for management of the patients.

PS-04-019
Histopathological findings of sural nerves in three patients with seipin gene mutation
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Objective: Two mutations of the seipin gene (N88S and S90L) have been reported and known to cause neurodegenerative disorders. We performed whole exome sequencing in two Charcot-Marie-Tooth families and identified three patients with two causative heterozygous mutations (N88S and S90W) and S90W is a novel mutation.
Method: The histopathological findings of distal sural nerves are analyzed in two patients (Cases 1 and 2) with S90W novel mutation (FC305) and a patient (Case 3) with N88S mutation (FC51).
Results: Transverse semi-thin sections reveal increased numbers of myelinated fibers (MFs) (11,898/mm2; 11,429/mm2; 9,430/mm2) with increased small MFs forming regenerative axon clusters and loss of large MFs. Histogram shows unimodal distribution pattern. Cases 1 and 2 show the similar ranges and average of diameter of MFs (1.46~13.24 μm, 5.13 μm). Case 3 shows more numbers of small MFs (0.82~10.50 μm, 3.73 μm). Ultra-structural examination reveals MFs with myelin abnormalities, pseudo-onion bulb formation including single axon or axon clusters, and thick MFs.
Conclusion: The findings are consistent with axonal neuropathy with features of demyelination. Additional cases will be necessary to know the significance of differences between these cases.

PS-04-020
Immunohistochemical subtyping of primary and secondary glioblastomas
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Objective: Glioblastomas (GBLs) may develop de novo (primary GBL; P-GBL) or through progression from low-grade or anaplastic astrocytomas (secondary GBL; S-GBL). For subtyping of GBLs, we tried immunohistochemical anaysis.
Method: We collected 150 cases of GBLs in SNUBH and SNUH. The mean age at the time of the primary surgery was 58.8 years (range 19–85). Immunohistochemical studies were performed for EGFR, p53 and IDH-1.
Results: According to clinical history, GBLs consisted of 146 primary and four secondary GBLs. However, EGFR(+)/p53(−) immunohistochemical features of P-GBL consisted 41.3 % and EGFR(−)/p53(+) immunohistochemical features of S-GBL consisted 28.6 % among 150 cases. EGFR(+)/p53(+) was noted in 20.6 % and EGFR(−)/p53(−) in 9.3 %. Immunohistochemical expression of IDH-1 was noted in 14 cases (9.7 %) out of 144 cases. Expression of IDH-1 and EGFR(−)/p53(+) showed positive correlations with young age. Characteristic features of S-GBL were noted in 3.5 % of clinically P-GBL.
Conclusion: We analyzed immunohistochemical subtypes of Korean glioblastomas. Combination of EGFR and p53 was unsatisfactory but combination of EGFR, p53 and IDH-1 can be a good tool for immunohistochemical subtyping of glioblastomas.

PS-04-021
Contribution of muscle biopsy to the diagnosis of extraocular mitochondrial myopathies: Survey of case series
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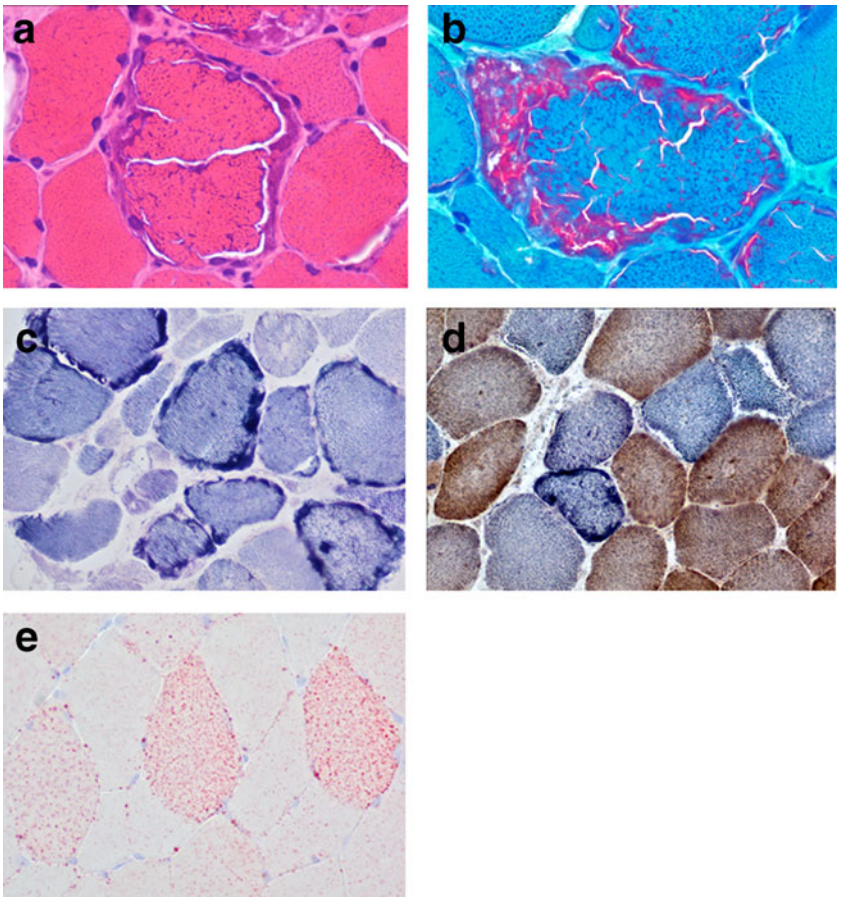
Objective: The diagnosis of mitochondrial myopathy depends on a variety of clinical findings, family history, muscle involvement features, specific laboratory abnormalities, and results of histological, biochemical and genetic analysis. Chronic progressive external opthalmoplegia (CPEO) is the most common phenotypic syndrome of the mitochondrial myopathies, characterized by slowly progressive paralysis of the extraocular muscles.
Method: Retrospective study of the utility of histochemical stains in muscle biopsy of 12 patients over 14 years old with clinical diagnosis of CPEO. Muscle sections were stained with hematoxylin and eosin (HE), Masson trichrome (MGT), oil red (OR), and enzyme histochemistry for succinic dehydrogenase (SDH) and cytochrome oxidase (COX).
Results: The mean number of abnormal muscle fibers with increased cytoplasmic granularity and basophilia on HE and Ragged Red Fibers (RRF) on MGT was 10 %; 14 % showed blue ragged on SDH; 40 % were negative on COX stain. Mild lipid droplets accumulation on OR stain were demonstrated in just a few individual muscle fibers of 7 cases of the series.
Conclusion: Histochemical stains of muscle biopsy may provide helpful clues for specific mitochondrial syndromes, despite the need for genetic analysis for accurate diagnosis. CPEO is characterized by RRF, strong SDH staining and

COX-deficient fibers on muscle biopsy, reflecting respiratory chain complex deficiency.

Fig. 1. Staining procedures showing morphological findings of extraocular mitochondrial myopathy in a patient diagnosed with CPEO: (A) abnormal granular fibers (HE, 40x); (B) characteristic RRF (MGT, 40x); (C) blue ragged fibers (SDH, 20x); (D) cytochrome C oxidase negative fibers creating a mosaic appearance (COX, 20x); (E) increased lipid droplets deposits (OR, 20x)



PS-04-022

An immunohistochemical study of HER2 expression in meningioma and its correlation with tumor grade

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Objective: Meningiomas account for about 15–30 % of all primary intracranial tumors. According to the 2007 WHO classification, meningiomas are divided into three grades (I, II and III). Recurrence is an issue following surgical treatment of meningioma, especially in grades II and III. HER2 (also known as erbB-2) is a 185-kD transmembrane glycoprotein with tyrosine kinase activity. HER2 is expressed in some human malignancies and can be a potential target for therapeutic intervention with selective inhibitors. There are only a few studies on the relationship between meningioma and HER2 expression, and the results are different as well. The aim of this study was to determine this relationship.
Method: Seventy-two paraffin blocks of meningioma were selected randomly and immunohistochemical staining was then performed for each specimen.
Results: Thirty-one of the 72 meningiomas were HER2-positive. HER2 expression was observed in 11 (55 %) of the 20 grade II/III, and 20 (38.5 %) of the 52 grade I meningiomas.
Conclusion: Consequently, HER2 expression was detected in 43 % of meningiomas. No significant difference was seen between grade I and II/III meningiomas, primary and recurrent tumors, and males and females from the point of view of HER2 expression.

PS-04-024

Is accumulation of iron in the human brain dependent on the microenvironment in certain regions?

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Objective: In our previous papers we studied accumulation of iron and proteoglycans in the brain. The aim of this analysis is to build on our previous results alongside other authors to investigate the reason for the presence of excessively accumulated iron observed in Parkinson disease (PD).
Method: Postmortem samples taken from the globus pallidus were prepared for light microscopy for iron and proteoglycans detection. Patients had neither iron metabolism disorders nor had clinical signs of neurodegeneration. The samples were analysed using electron paramagnetic resonance (EPR) to investigate the bounds between iron and proteoglycans.
Results: EPR measurements confirm the presence of complex bounds between Fe(III) and proteoglycans.
Conclusion: Previous data showed a possible dependance between accumulated iron, proteoglycans, ferrireductive alpha-synuclein and Lewy bodies. We propose a mechanism of toxic iron accumulation in the brain in PD. This cyclic process of amplification is presented by onward steps. It is completed by our own observations into one cycle. The initiator of this vicious circle is probably an impirement of the equilibrium in the presence of useful amount of iron. Understanding these relations could bring new insights to the neurodegenerative disease.

PS-04-025

Role of PDGFR overexpression in Schwannoma, and its diagnostic and therapeutic implications

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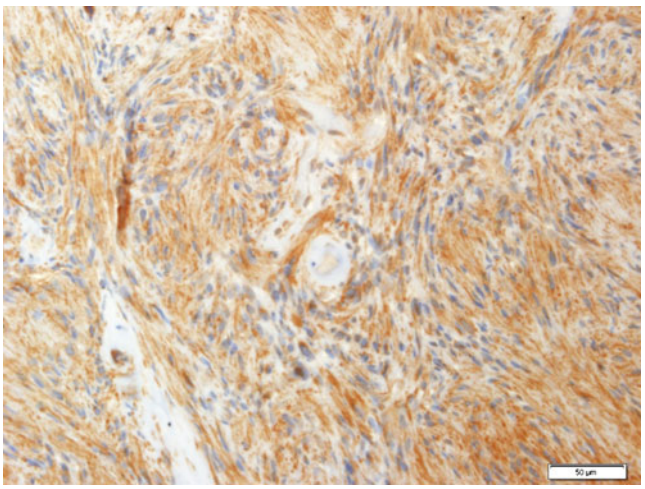
Objective: Platelet-Derived- Growth- Factor- Receptors (PDGFR) are transmembrane tyrosine kinase receptors that function as relay points for signaling pathways. They play a key role in numerous processes that affect cell proliferation, tumor genesis, cancer invasion, metastasis, and modulation of apoptosis. Recently, PDGFR has been demonstrated to be overexpressed in Schwannoma in vivo, and in a small series of acoustic neuromas. However, its phenotypic expression in different variants of Schwannoma remains largely unclear.
Method: Immunohistochemical staining was used to detect PDGFR expression in archived formalin-fixed, paraffin-embedded Schwannoma tissue samples (n=24). Clinical and pathological data including age, sex, location, histological variants and staining patterns were correlated with kinase expression.
Results: PDGFR was expressed in 22 (91.6 %) out of 24 Schwannoma samples. In two of these cases PDGFR overexpression was a key feature in the pathological diagnosis of Schwannoma.
Conclusion: Exploring PDGFR overexpression in Schwannoma, as demonstrated in our study might serve in the pathological diagnosis of challenging cases. Also, there are implications regarding the molecular targets involved in the development of this tumor and possible treatment by Gleevec (Imatinib Mesylate) was suggested.



PS-04-026

Spinal Schwannomatosis: Three cases of Spinal Schwannomatosis

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Objective: Schwannomas are slow growing benign peripheral nerve tumors. Schwannomatosis is defined as an extremely rare tumors characterized by the presence of multiple schwannomas in the absence of typical signs of NF1 and NF2 syndromes, and show a distinct clinical and genetic syndrome.
Method: We reviewed 63 cases of patients with pathologically defined schwannomas and identified those with schwannomatosis. All 3 cases was retrospectively reviewed clinical-pathologic and radiologic findings.
Results: Case 1.) A 41-year-old man with a 3 months history of low back pain. MRI showed well enhanced intradural-extramedullary mass 2.9 cm at L4-L5 level, and 0.9 cm at L2-L3. Case 2.) A 55-year-old woman with low back and buttock pain. MRI presented 0.6 cm well enhancing mass at T12-L1 level, and 0.3 cm at L2-L3. Case 3.) A

68-year-old woman with a 1 month of leg pain. MRI revealed well enhanced mass 3.3 cm at T12-L2 level, and 0.5 cm at L2-L3. Follow-up ranged from 10 months to 7 years without recurrence.
Conclusion: We presented three cases of spinal schwannomatosis without recurrence or any other lesion after surgery. Schwannomatosis is a different disorder distinct from neurofibromatosis. Molecular diagnosis rules out NF2 and follow-up with careful monitoring is necessary.

PS-04-027
Spinal Meningiomas in male
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Objective: Spinal meningiomas are relatively rare in comparison to the intracranial compartment accounting approximately 1.2 % of all meningiomas of the central nervous system. Spinal meningiomas are predominant in women. On the other hand, atypical and particulary anaplastic meningiomas show a male predominence.
Method: We reviewed 54 patients with meningiomas were surgically treated in our hospital between 2005 and 2011. Clinicopathological and radiological features were analyzed.
Results: Among 54 spinal meningiomas patients. 8 patients were male and 46 were female. All spinal meningiomas in male were located in thoracic area, and presented meningothelial subtype. Mean age was 45 (range 26–74). Follow-up range was from 1 month to 9 years. There is no evidence of recurrence. In 46 female spinal meningiomas, there were clear-cell (1 case), rhabdoid (1 case), and metaplastic subtypes (1 case).
Conclusion: Although good prognosis and same treatment in both sex groups, spinal meningiomas showed different clinicopathological findings including age, location, and subtype.

PS-04-028
Brain metastases of pancreatic ductal carcinoma as the first symptom of disease: Case and autopsy report
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Objective: Pancreatic ductal carcinoma (PDC) has one of the worst prognoses. Up to 90 % of pancreatic cancers are diagnosed at the locally advanced or metastatic stage. However, brain metastases from pancreatic carcinoma are extremely rare since less than 20 cases have been reported in the literature since 1978.
Method: We report a case of a brain metastasis from pancreatic adenocarcinoma occurred in a 66 years old women.
Results: 62-year-old woman developed severe neurological symptoms and progressively decreased consciousness. CT revealed cystic tumor in cerebral peduncle and medulla oblongata. Stereotactic biopsy revealed metastasis of carcinoma. The patient died from of the twelfth day after STB because of recurrent hemorrhage. Autopsy revealed well-differentiated papillary adenocarcinoma in the head of pancreas and with multiple metastases in liver and two metastases in medulla oblongata and cerebral peduncle. IHC staining for cytokeratins 7, 18 and 19, mucin 1 and 5 AC types was strongly positive. Ki67 labeling index was 14 %.
Conclusion: We reported an autopsy case of brain metastases from pancreatic cancer, in which the patient initially developed symptoms of a neurologic disorder without exhibiting any symptoms of pancreatic disease.

PS-04-029
The use of Bone Morphogenetic Proteins (BMP2) with nunostrucnure Grey implant in reparation of bone tissue defect
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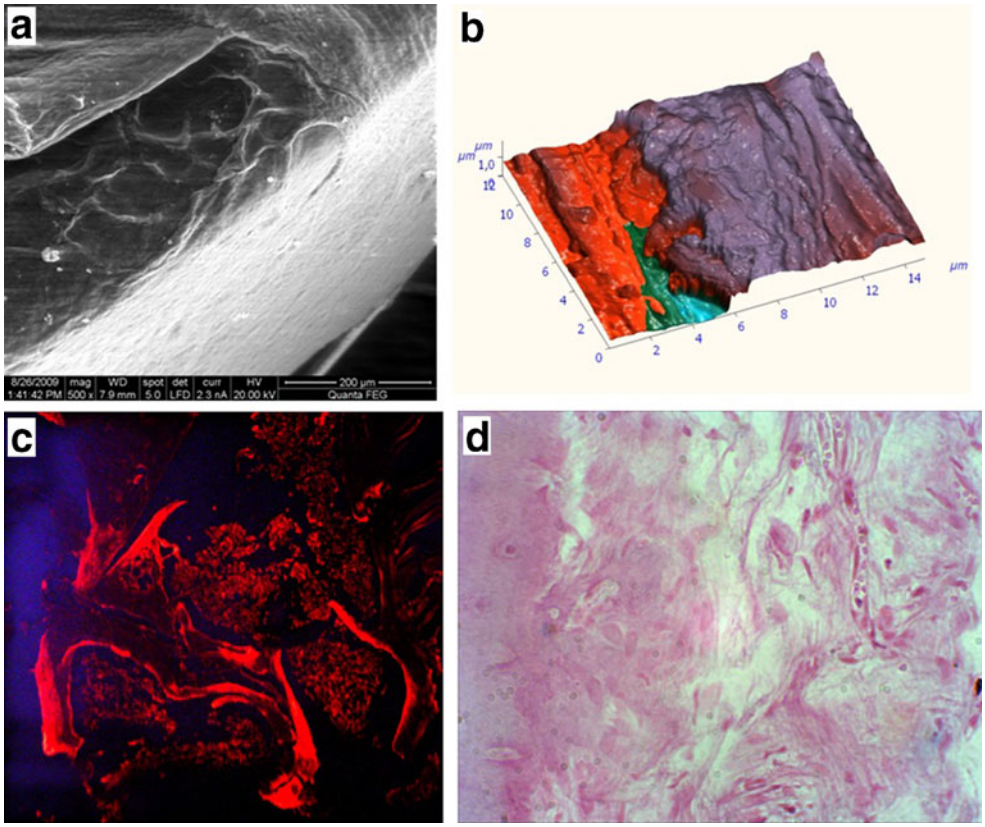
Objective: The matters of materials development of scull bones defect plastic are obviously necessary this time. The experience in use of nanocostructive titans, composites, bone morphogenetic proteins was accumulated.
Method: Implant, made of nanoconstructed titan Grey, covered by 1 layer (gelatin, dextran), 2 layers (1- gelatin, dextran, 2- hydroxyapatite, collagen, dextran) and by 2 layers with use of bone morphogenetic proteins BMP-2. The experiment was conducted on 240 rat-males. In order to study the regeneration processes it were used light, fluorescence, probe and scanning microscopy with the trace element analysis.
Results: The most active changes were registered in the experimental group with use of composite from titan Grey with 2 layers of covering and BMP-2. The covering compound increase the rate of regeneration processes due to creation calcium and phosphorus ion depot and perform support function for again-formed tissue. Increase in the concentration of calcium, phosphorus, sodium, magnesium in trabeculae of bones in comparison with matrix bone at term of 12 weeks testify about active regenerative processes; the mature smooth surface with structured relief of bone trabeculae and diploic veins were detected.

Conclusion: Results can be used in neurosurgery, traumatology-orthopedics, dentistry, plastic and cosmetic surgery.



PS-04-031

Alpha-synuclein (AS) pathology of the Peripheral Autonomic Nervous System (PANS) in Parkinson Disease (PD) and other Lewy Body Diseases (LBD)

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Objective: PD and other LBD have been associated with AS aggregates in the central nervous system (CNS). However, autonomic dysfunctions may appear at any time in the course of the disease. Our objective was to investigate the distribution of AS in the PANS in synucleinopathies.

Method: We examined PANS structures obtained at post mortem from 28 subjects (19 female, age range 69–93, mean 81) at our Brain Bank with a diagnosis of PD (10); Lewy body dementia (5); Alzheimer's disease (9); mixed dementia or other (4). A complete neuropathological study of PANS was performed, including dorsal spinal ganglia, vagus nerve, paraspinal sympathetic ganglia, mesentery, adrenals, digestive and genitourinary systems, heart, and skin. Routine and immune stains for AS and tyrosine-hydroxylase were applied. Cases were semiquantitatively assessed.

Results: 71 % of cases showed AS pathology in the CNS. Of them, AS aggregates were additionally present in the PANS in 80 %. A gradient in involvement was observed, being the paraspinal chain (particularly the stellate ganglion) the most constantly involved structure, followed by digestive system, adrenals, and GU system.

Conclusion: These findings indicate that AS aggregates are extensively found in PANS in synucleinopathies. The highest expression is found in the paraspinal ganglion chain and decreases in other PANS regions. Our results provide valuable information about potential development of new diagnostic and therapeutic strategies.

PS-04-032

Chordoid meningioma: A case report

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Objective: Chordoid meningioma is an uncommon histopathological variant of meningioma.
Method: We report one case of chordoid meningioma occurring in adult patient. Paraffin embedded tissue was stained with hematoxylin–eosin. We used immunohistochemical markers such as CEA, EMA, vimentin and TLE3.
Results: A 81-year-old woman was hospitalized with clinic of an intracranial hemorrhage. Axial computed tomography (CT) of the brain revealed a 3.1*5.2*4.9 cm lesion with perilesional edema in the left temporoparietal region. Foci of intratumoral hemorrhage were also seen. Compression of the left lateral ventricle and midline shift to right side was seen. The patient underwent a left temporoparietal craniotomy for resection of the tumor and died 3 days after surgery. Histologically, sections revealed sheets, trabeculae and lobules of tumour cells scattered in a pale basophilic myxoid matrix. Some of these cells exhibited characteristic cytoplasmic vacuolization. A typical focal meningiomatous pattern was also observed. The tumor cells were diffusely positive for epithelial membrane antigen, vimentin and a strong nuclear immunoreactivity for TLE3. These cells showed negative immunostaining for CEA.
Conclusion: Chordoid meningioma should be distinguished from chordoma, chondrosarcoma, metastatic mucinous carcinoma and other variants of meningioma.

PS-04-033

Morphology of non-specified encephalopathy in cases of polymerase chain reaction proved presence of human herpesvirus-6

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Objective: The morphology of non-specified encephalopathy is a complex medical problem. Human herpesvirus-6 (HHV-6) infection can be discussed as a predisposing factor. The aim of the present study was to investigate the presence of beta HHV-6 in non-specified adult encephalopathy cases.
Method: The blood, meninges and brain tissue were obtained in adult (aged 42–74 years) autopsies including 21 cases with encephalopathy and 23 cases in the control group. Tissues were submitted for routine histology including haematoxylin-eosin stain. The presence of HHV-6 genome (DNA) was analysed by nested polymerase chain reaction (nPCR), HHV-6 variants by restriction endonuclease analysis.
Results: The gross and microscopic structure did not reveal any specific changes. In the encephalopathy group, HHV-6 DNA sequence was found in meningeal tissues (16/21 cases; $p=0.0036$), in brain tissues (15/21 cases; $p=0.0007$), and both in brain and meningeal tissues (10/21 cases; $p=0.0174$). In the control group, the viral DNA was identified in meningeal tissues (7/23 cases), in brain tissues (4/23 cases), both in brain and meningeal tissues (3/23 cases). HHV-6B variant was detected in all cases.
Conclusion: On the basis of the present study it can be concluded that HHV-6 is a pathogenic factor that can predispose to encephalopathy.

PS-04-034

Pathological variants of brain metastases of breast carcinoma and their prognostic and predictive role in different age groups

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Objective: Brain metastases of breast cancer (BMBC) are biologically heterogeneous group of tumors with different molecular changes and behavior. Aim: To evaluate prognostic and predictive role of pathological variants in BMBC in patients of different age groups.
Method: Sixty patients with BMBC after neurosurgery were divided into two age groups: Group I contained patients<50 years of age (43 %, 26/60), and Group II contained patients>50 years (57 %, 34/60). Tumor tissues were stained with H&E and antibodies for Ki-67, ER, PR, Her-2-neu. To clarify the Her-2-neu when its score was 2+ by IHC, FISH method was performed. For statistical analysis STATISTICA 8.0 software was used.
Results: All BMBC were divided into 5 IHC variants: luminal A, luminal B, luminal Her+(prevalent in Group II (35 %), classic Her+, and triple-negative BC (predominant in Group I (31 %). Recurrent BMBC was observed in 50 % (13/26) in Group I and in 21 % in Group II (7/34). Recurrence free-survival in Group I was significantly worse ($p=0.019$).
Conclusion: In younger patients (Group I), more BMBC patients had triple-negative BC, which had more

aggressive behavior. Recurrence-free survival in younger patients was significantly worse than that in older patients, where most frequent variant of BMBC was Luminal Her +.

PS-04-035

Meningeal hemangiopericytoma a pathological dilemma: Immunohistochemical and genetic study

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Objective: Meningeal Hemangiopericytoma (MHPC) is vascular tumor arising from pericytes. Most intracranial hemangiopericytomas apparently arise from the meninges, and often misdiagnosed as meningiomas.
Method: We report 8 cases of MHPS in comparison with 5 cases of meningiomas collected from Departement of histopathology in University Hospital of Sousse (Tunisia) in the period from 2007 to 2011. Immunohistochemistry (IHC) was performed by using EMA, Vimentine, CD99, Bcl-2, CD56, S100, Synaptophisine, P21, CD34, NSE, ACE, FVIII, Desmine, GFAP, P16 antibodies. Additionally we focused on the analysis of a large panel of genetic markers using molecular technique: Multiplex Ligation Probe Amplification (MLPA).
Results: Both MHPC and meningioma showed 100 % Vimentine positivity. The four useful IHC markers (Bcl2, EMA, CD34 and CD99) were 87 %, 37 %, 62 % and 62 % respectively in MHPC. However, the P21 antibody was seen positive in 62 % of HPC and less than 1 % in all meninigiomas.
Conclusion: Meningiomas and MHPC seems to be as spectrum of tumor that IHC can not absolutely differentiate between them because of their unspecific IHC profile. Despite of the help given by genetic investigations to characterize these two tumors, their prognosis still depends on histological grade.

PS-04-036

Intramedullary spinal cord metastases as initial presentation of lung cancer

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Objective: It is extremely rare that the intramedullary spinal cord metastases (ISCM) are the first manifestation of cancer.
Method: In database of neurosurgery biopsies from 2002 to 2011 two cases of ISCM were found without preoperative signs of primary neoplasm. Surgically removed tissue was stained with hematoxylin-eosin and immunohistochemically using following markers: AE1/AE3, CK7, CK20, mammaglobin, TTF-1, GFAP, S-100 and vimentin.
Results: One patient was male aged 51 and another female aged 44. They presented with neck pain and rapidly progressive upper and lower limb weakness. Imaging analysis showed contrast-enhancing mass at the level C4-C6 in male and C2-C4 in female, reported as an ependymoma. Grossly, tumor tissue was of soft consistency and grey white color with yellowish foci of necrosis. Histopathology revealed moderately differentiated adenocarcinoma with distinct border to surrounded glial tissue. In both cases, tumor cells were immunopositive for AE1/AE3, CK7 and TTF-1 indicating primary lung origin. Postoperatively primary cancer was found in upper lobe of the left lung in both cases, without evidence of lymphadenopathy and other distant metastatic lesions in female.
Conclusion: Diagnosis of ISCM in both cases without preoperative signs of neoplasm in other organs was surprising. Immunohistochemical analysis was essential for determination of cancer origin.

PS-04-038

Meaning of alpha internexin (INA) expression related with molecular characteristics in adult glioblastoma and oligodendroglioma

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Objective: Alpha-internexin (INA) is a proneuronal gene-encoding neurofilament interacting protein. INA is related to 1p/19q codeletion, and is a favorable prognostic marker. We studied INA expression in oligodendrogliomas (ODGs) and glioblastomas (GBMs) to verify its association with several molecular phenotypes, 1p/19q codeletion, and epidermal growth-factor-receptor (EGFR) amplification.
Method: A total of 230 low- and high-grade ODG and GBM cases were analyzed for INA expression by immunohistochemical staining, and 1p/19q and EGFR gene status was examined by fluorescence in-situ hybridization.
Results: INA was positive in 80.3 % of ODGs and in 34.3 % of GBMs. 1p/19q codeletion was detected in

77.0 % of ODGs and 5.5 % of GBMs. INA and 1p/19q codeletion were strongly correlated ($p<0.0001$). The specificity of INA expression for 1p/19q codeletion was 70.8 %, sensitivity was 100 % in all 228 tumors. INA expression was correlated with better progression- free survival (PFS) and overall survival (OS) [$p=0.0001$].

Conclusion: In conclusion, INA expression had high specificity and sensitivity to predict 1p/19q codeletion, and it was well correlated with PFS of both ODGs and GBMs. Therefore, INA expression could be a simple, reliable, and favorable prognostic and surrogate marker for 1p/19q codeletion.

PS-04-039

Atypical Teratoid/Rhabdoid Tumor Arising in Pleomorphic Xanthoastrocytoma: A Case Report

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Objective: Atypical teratoid/rhabdoid tumor (AT/RT) is a rare, highly malignant, true rhabdoid tumor in the central nervous system predominantly presenting in young children. AT/RT typically shows rhabdoid cells which can be seen in other tumors also, but it is differentiated from other tumors by the specific genetic alteration involving the INI-1/hSNF5 gene. Only a few cases of AT/RT arising in low-grade glioma have been reported.

Method: A 13-year-old girl presented with headache, dizziness, nausea and vomiting. A 4.7 cm cerebellar mass was found on MRI image. The mass was totally removed.

Results: Histologically, the tumor revealed 2 distinct morphologic appearances: central areas of AT/RT containing rhabdoid cells and sarcomatous component in the background of pleomorphic xanthoastrocytoma (PXA). Immunohistochemically, PXA areas retained nuclear expression of INI-1 and low Ki-67 proliferation index, whereas AT/RT component showed loss of INI-1 nuclear expression and markedly elevated Ki-67 proliferation index. Epithelial membrane antigen (EMA), smooth muscle actin (SMA), and p53 protein were positive only in AT/RT and sarcomatous component. BRAF V600E mutation was identified in PXA by real-time polymerase chain reaction.

Conclusion: We report a rare case of AT/RT arising in PXA which is supposed to progress by inactivation of INI-1 in a pre-existing PXA.

PS-04-040

Prognostic Significance of Tetraspanin CD151 in Newly Diagnosed Glioblastomas

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Objective: Tetraspanin CD151 is a positive effector of cancer invasion and metastasis in many tumor types.

Method: We investigated the protein expression of CD151 in 211 cases of WHO grade I to IV gliomas. Additionally, we performed O6-methylguanin-DNA methyltransferase (MGMT) methylation analysis using real-time methylation-specific PCR in 36 glioblastomas, and the prognostic significance of these biomarkers in glioblastomas was evaluated.

Results: CD151 was overexpressed in a significant proportion (55.6 %) of glioblastomas, while it was not deetected in most of grade I to III glial tumors except for rare overexpression in anaplastic astrocytoma (2/10, 20 %) and oligoastrocytomas (3/23, 13 %). CD151 overexpression was closely associated with MGMT methylation ($P=0.014$), and it was a prognostic factor for predicting worse overall survival (OS; $P=0.002$) and progression-free survival (PFS; $P=0.043$). Combination of CD151 overexpression and MGMT methylation better stratified the patients' OS ($P=0.001$) and PFS ($P=0.009$). In multivariate analysis, CD151 overexpression was an independent prognostic factor for predicting OS over MGMT methylation ($P=0.012$).

Conclusion: CD151 seems to have a critical role for high grade progression in astroglial tumors. CD151 is a good tissue marker for predicting worse prognosis in glioblastomas.

PS-04-041

Role of Hippo Pathway molecules in meningiomas

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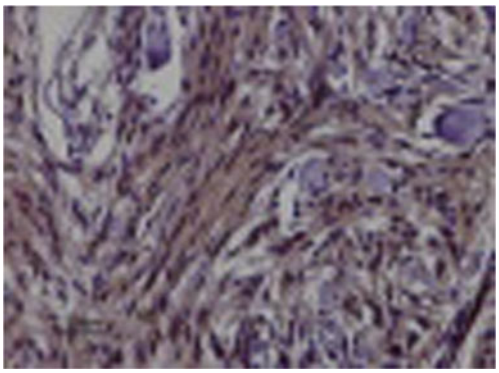
Objective: Meningiomas are frequently diagnosed primary brain tumors. Most of them are benign, but 10 % exhibit malignant features. Hippo signaling pathway is a kinase cascade. Its inhibition leads to translocation of YAP and TAZ transcription co-activators into the nucleus. This result in over expression of their target genes with anti- apoptotic and proliferative function. We hypothesize that inhibition of the hippo

pathway may be correlated to the malignant behavior of meningiomas.
Method: The expression of CD44, YAP, TAZ components of the Hippo pathway was studied by immunohistochemistry in 53 cases of meningiomas (34/53 WHO I, 19/53 WHO II/III).
Results: Nuclear YAP and TAZ immunopositivity and cytoplasmic CD44 immunolocalization significantly correlated with high grade meningiomas compared with low grade tumors.
Conclusion: Our findings suggest that Hippo pathway seems to be critically implicated in high grade memingiomas pathogenesis. Further studies are needed in order to clarify its exact role in meningiomas aggressive biological behaviour.



PS-04-042
Myxomas and neurothekeomas of the meninges. A single entity with two names?: Report of a case and review of the literature
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Objective: Myxomas are benign tumors arising from cells of primitive mesenchymal origin, accounting for about half of the benign cardiac tumors. Primary intracranial myxoma is an exceedingly rare tumor with only eight cases reported in the literature.
Method: We report a case of a 30-year-old man with a 1 year history of oppressive bitemporal headaches. Neurological examination was unremarkable. Magnetic resonance imaging demonstrated a heterogeneously enhancing extra-axial mass arising from the falx cerebri, resembling a meningioma.
Results: A gross total resection of the tumor was achieved. Histological examination revealed a paucicellular tumor with lobulated architecture and abundant myxoid stroma, containing stellate or spindle cells lacking mitotic activity. Alcian blue and mucicarmin histochemical stains were diffusely and strongly positive. Immunohistochemical analysis showed diffuse reactivity for vimentin and scattered cells positive for CD34. Stains for EMA, GFAP, S100 protein, cytokeratin and smooth-muscle actin were negative.
Conclusion: Primary intracranial myxoma should be distinguished from other myxoid intracranial tumors such as myxomatous meningioma, epithelioid hemangioendothelioma or sarcoma through appropriate pathological and inmunohistochemical analysis. A metastasic cardiac myxoma should also be ruled out through cardiac evaluation including an echocardiography. The distinction between this entity and the reported neurothekeoma of the meninges needs to be re-evaluated.

PS-04-043
Holocord pylocitic astrocytoma associated to syringomyelia
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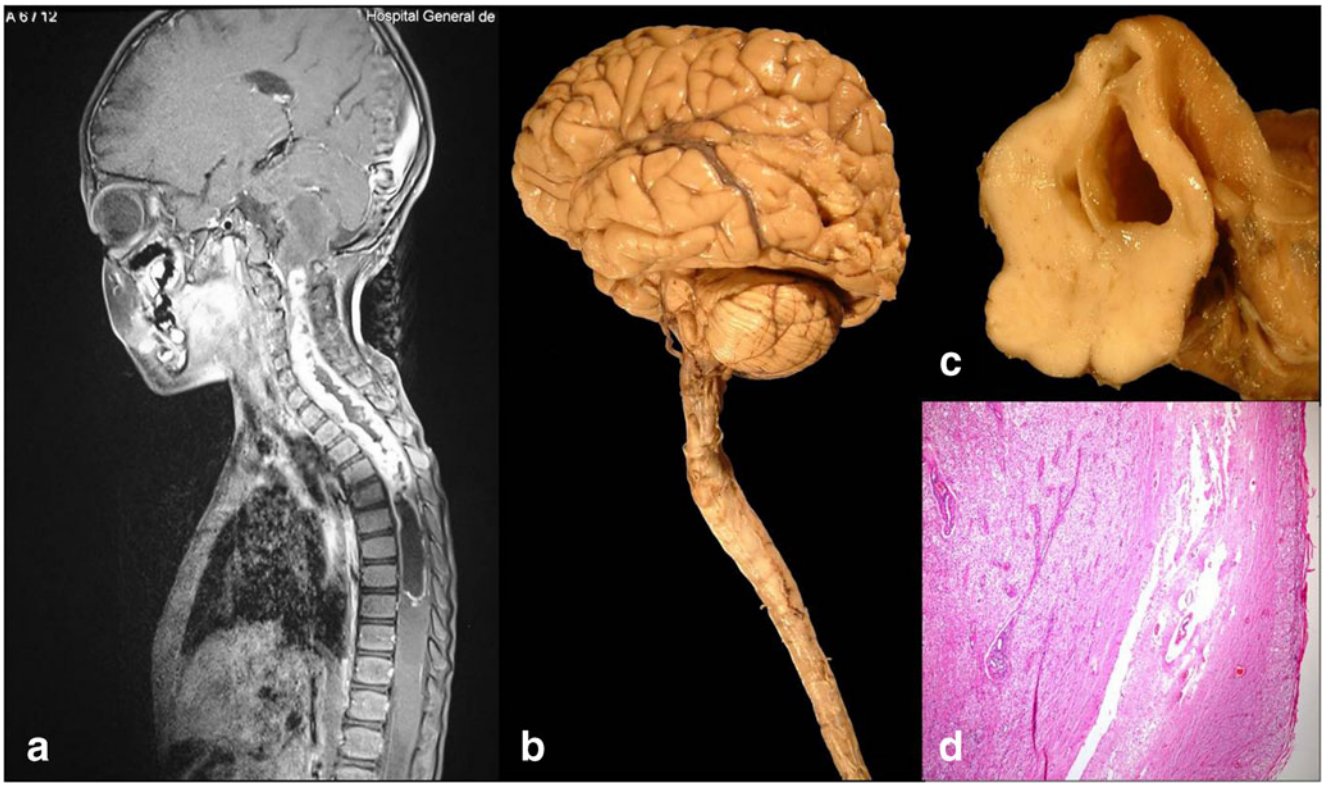
Objective: Spinal intramedullary tumors sometimes extend both superiorly and inferiorly along almost the entire cord, and those diagnosed as pilocytic astrocytoma are rare. The syringomyelia is an ependimary or periependimary cavitation of the spinal cord and is considered a suffering of degenerative and irreversible type, 58 % of the cases is associated with intramedullars tumors.
Method: A three-year-old girl with history of headache, progressive weakness, 3 months before, she was hospitalized for pneumonia, had impairment of neurologic functions and died of cardiac arrest. The autopsy was performed.
Results: The neuropathologic study revealed a intramedullary holocord tumor with secondary syringobulbia, cervical and lumbar syringomyelia. Histopathological examination of all specimen resulted in diagnosis of a pilocytic astrocytoma. Although no signs of atypia were present, an elevated proliferative activity of endothelial vessels was noted.
Conclusion: Gross total resection of holocord and longitudinally extensive intramedullary spinal cord tumors can be

achieved with preservation of long-term neurological function and also solved the syrinx.



Sunday, 9 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-05 Poster Session Endocrine Pathology

PS-05-001
Immunohistochemical expression of Epithelial Cellular Adhesion Molecule (Ep-CAM) in Thyroid Tumors using Ber-EP4

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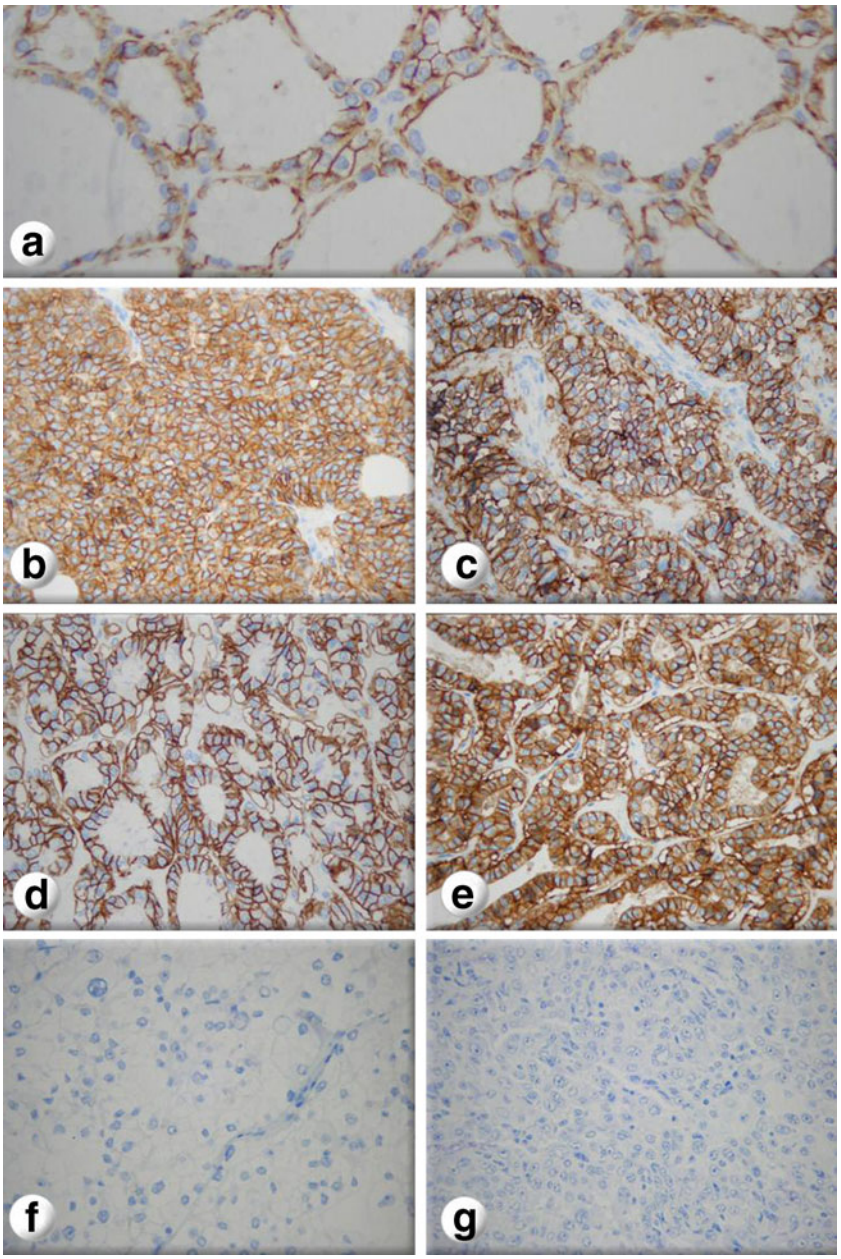
Objective: Epithelial cellular adhesion molecule (Ep-CAM) has been studied in many tissues and neoplasm, including thyroid and thyroid tumors. This is a preliminary study to assess the immunohistochemical expression of Ep-CAM in thyroid tumors using Ber-EP4.

Method: We examined the expression of Ep-CAM using the monoclonal antibody Ber-EP4 in 36 cases of thyroid tumors, including 4 adenomas, 11 papillary carcinomas, 5 follicular carcinomas, 8 medullary carcinomas, 2 poorly differentiated carcinomas, and 6 anaplastic carcinomas. We assessed the positivity as a predominantly membranous staining of the cells, and was scored according to the estimated percentage tumor cells in the total tissue section (negative: 0–10 %; positive: ≥10 %).
Results: Ber-EP4 expression was detected in normal thyroid tissue (perilessional), in all the adenomas, follicular carcinomas, and medullary carcinomas. Papillary carcinomas showed in 36 % lacking areas of expression, coinciding histopathologically one case with poorly differentiated component. All of the poorly differentiated and the anaplastic carcinomas were negative.
Conclusion: The expression of Ep-CAM, using Ber-EP4, was related to normal thyroid tissue and well differentiated neoplasms. Our study suggest that lost of expression is

associated to dedifferentiation. This results match up with the literature. In addition, clinical data and follow up are required to correlate focal areas of lost of expression of Ber-EP4 with dedifferentiated areas of the tumor.



PS-05-002

The pathological effects of estradiol valerate on testis tissue: Size and weight in male rat

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Objective: Studies show that estrogens can influence reproductive system differentiation. The main aim of this study was to determine pathological effects of estradiol valerate on testis histology and morphology in male rats.

Method: Adult male albino Wistar rats were divided to control and estradiol valerate (200 μg/kg/day) receiving groups. Estradiol valerate was applied subcutaneously. After 4 weeks, testes were excised and studied morphologically and histologically. Data were

statistically analyzed and compared between groups using ANOVA.
Results: Our findings revealed that estradiol valerate injection resulted in reducing of testes weight and size ($P<0.05$). Semeniferous tubules were apparently deformed in estradiol valerate receiving animals and cellular density was also reduced. Number of spermatocytes, spermatids and sperms was decreased in estradiol valerate receving rats compared with control animals ($P<0.001$).
Conclusion: Estradiol valerate has considerable pathological effects on testes morphology and histology in male rats.
Key words: Estradiol, Testes.

PS-05-003

Are tumor-dimension, Galectin-3 and CyclinD3 useful to characterize oncocytic adenomas and carcinomas?: Preliminary results

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Objective: Routine histology of follicular oncocytic lesions is not always clear-cut. Therefore, we investigated the usefulness of morphometric and immunohistochemical criteria.
Method: All oncocytic follicular adenomas and carcinomas (OFA, OFC) between 2003 and 2007 have been retrieved from the archive of our institution. After a review of the histology and measuring the dimension (cm) of all tumors (nine Adenomas and eight Carcinomas, four oncocytic Metaplasia) immunohistochemistry with Galectin-3 and Cyclin D3- antibodies was performed.
Results: The mean of diameter of malignant lesion was significantly larger than that of the adenomas (3.77 ± 1.85 vs 1.77 ± 0.64 $P=0.0084$). Galectin-3 stained all but one carcinoma and two adenomas: percent of positive cells carcinoma vs adenoma (34.4 % vs 2.2 % $P=0.0029$). Cyclin D3 stained all carcinomas and six adenomas (40 % vs 13.4 % $P=0.17$). A panel using both markers has a high sensitivity (93.7) % but a low specificity (55.5 %). The positive predictive value was 65.7 % and the negative predictive value was 90.9 %.
Conclusion: These preliminary results suggest that additional criteria (dimension and immunostaining with Galectin-3 and Cyclin D3) can help distinguishing between OFA and OFC if the routine histology is doubtful.

PS-05-004

Heterogeneity in mutation status between primary tumour and metastases in papillary thyroid carcinomas

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Objective: Papillary thyroid carcinoma (PTC) is the most common thyroid malignancy, harbouring BRAF-V600E mutations in about 45 % of cases. The first clinical manifestation of this tumour is often represented by lymphatic metastases.
Method: Twelve cases of PTC and respective lymph node metastases were retrieved from our archive from 2010 to present. Formalin fixed paraffin embedded tissue sections were stained with routine hematoxilin-eosin and representative tissue areas for both tumour and metastases were microdissected and DNA was extracted. After PCR amplification the mutational status of BRAF and RAs was determined by DNA sequencing.
Results: Seven cases of twelve (58 %) showed a BRAF-V600E mutation. Interestingly, only in three these cases (43 %) there was concordance in the mutational status between primary tumour and metastases. Moreover, all metastase of wild type carcinomas were also wyld type.
Conclusion: Even with an overall good prognosis, PTC is characterized by high incidence of lymph node metastases. As BRAF mutational status correlates well with prognosis and tumour progression, a correct molecular assessment is of paramount importance. Our data may indicate that, because the possibility of discrepancy in the mutational status between primary tumour and metastases, molecular analysis should be performed on the primary tumour.

PS-05-005

Carcinoma Showing Thymus-like Elements (CASTLE) of the thyroid: Case report with immunohistochemical and molecular study

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Objective: Carcinoma showing thymus-like elements (CASTLE) is a rare thyroid tumour thought to arise from the ectopic thymus, thymopharingeal duct or branchial pouch remnants in the thyroid gland and neck.
Method: Here we report the pathological, immunohistochemical and molecular findings in a CASTLE presented in a 36-year-old woman.
Results: The left thyroid lobectomy showed a solid, well circumscribed, slightly lobulated, gray tumor, with 34 mm of largest diameter. Microscopically, the neoplastic cells were arranged in broad anastomosing islands surrounded by desmoplastic stroma associated with lymphocytes and plasma cells. Tumour cells were squamoid with mild pleomorphism and occasional Hassal-like corpuscles. Less than 4 mitotic figures per 10 high-power fields were found. Positivity was found for keratins (CK7, CK19, CK34βE12, CKAE1/AE3), CD5, CEA, c-KIT (CD117), p63, p53, p27, cyclin D1 and Bcl-2, whereas no immuno-reactivity for CK20, TTF-1, thyroglobulin, thyroperoxidase, calcitonin,

and Epstein-Barr virus was detected. The proliferative index (Ki-67) about 20 %. No PAX8/PPARgamma rearrangements nor BRAF, N-RAS, H-RAS or K-RAS mutations were detected in the molecular analysis. There was no evidence of recurrence after a follow-up of 48 months.
Conclusion: Molecular alterations typically found in well differentiated follicular-cell derived neoplasms are lacking in CASTLE, and its phenotype suggests differentiation along a thymic/branchial line.

PS-05-006
Neurotensin and Chitosan-based dressings repair ulcers of diabetic mice
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Objective: Diabetes may cause chronic and non-healing diabetic foot ulcers (DFU) decreasing the welfare of patients. Some neuropeptides, Substance P and neurotensin (NT), may act as inflammatory modulators and improve wound healing. Natural biopolymers, chitosan derivatives, are receiving great attention as powerful wound dressing materials for wound healing applications due to their favorable properties. The work aim was to use 5-methyl pyrrolidinone chitosan (MPC) as a platform for the delivery of NT.
Method: Diabetes was induced by intraperitoneal injection of 200 mg/kg streptozotocin. Mice were anesthetized and two 6 mm excision wounds were created dorsally. MPC alone, NT alone, MPC loaded with NT or PBS were placed daily on wounds. Histological analysis of skin, at days 0, 3 and 10, was done through H&E and Masson´s Trichrome stainnings.
Results: In diabetic mice, the healing process was slower, showing an engulfment of acute inflammatory cells that triggered macrophage activity when compared with controls. At day 3, MPC treatment leaded to a faster healing with retraction of the wound site, NT induced a slower non-contracting healing and combined application delayed inflammatory repair with persistent neutrophils.
Conclusion: At day 10, all treatments induced a total healing however, MPC + NT reduced neutrophils infiltration compared with MPC alone.

PS-05-007
Acth producing nasal paraganglioma: Case report
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Objective: Female patient with chronic sinusitis and hypertension presents with lipothymia, dizziness, polyuria and polydipsia. Laboratory studies showed hyperglicemia, leucocytosis, hypokalemia, hypercortisoluria and elevated serum ACTH levels. Head MRI revealed tumor in the right nasal cavity with implantation at the cribiform plate of the ethmoid bone.
Method: Microscopically the tumor had lobular architecture with big, round cells and with eosinophilic granular cytoplasm. These cells were NSE+, synaptophysin+, CD56+, CD57+ and ACTH+. Surrounding the tumor lobules were several spindle cells S-100+ (sustentacular cells).
Results: The lobular growth pattern, the presence of sustentacular cells (S-100 positive), and the ACTH producing granules favours an ACTH producing nasal paraganglioma diagnosis.
Conclusion: Head and neck paragangliomas account for 0,12 % of the tumors in this region, and are mainly located in the carotid bodies. Paragangliomas arising in the nasal cavity are rare, only 23 cases reported so far. They affect the middle or upper turbinates, and also the etmoid, maxillary and sphenoidal sinuses. We report the third case in literature of a ACTH producing paraganglioma in the nasal cavity.

PS-05-008
Sporadic aggressive silent somatotroph pituitary adenoma in the young: Report of two cases
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Objective: Silent pituitary adenomas are infrequent tumors in adults and exceptional in young.
Method: We describe two cases of 20-year-old girls with pituitary adenoma without genetic history, revealed by visual field defects, with panhypopituitarism in one patient. In both cases, MRI showed giant pituitary adenoma, with invasion of the cavernous and sphenoidal sinuses. Hormone assays revealed normal GH, PRL and IGF1 plasma values. Surgery was incomplete in both cases.
Results: Both tumors presented a diffuse pattern. The cells exhibited large nuclei with prominent nucleoli. By immunocytochemistry, focal and low percentages of GH- and PRL-immunoreactive cells were observed respectively in both tumors (GH=1–30 % and PRL=1–5 %). CgA was positive. Cytokeratin and others antibodies against pituitary hormones were negative. Both tumors had high proliferative indexes: Ki-67>3 % (4–10 %) and elevated mitotic number (1–13 mitoses). Detection of p53 was also positive (0.5–5.7 %). The cases were diagnosed as atypical adenomas, according to the WHO classification.
Conclusion: The pathological diagnosis of these aggressive GH-PRL tumors has to be taken into account by the clinician to choose the optimal therapeutic strategies. Despite of the important side effects of the radiotherapy, this aggressive treatment might be proposed earlier, even for the young patients, to avoid the tumoral progression.

PS-05-009

Intrauterine growth retardation with high fat diet in rats markedly disturbs islet morphology characterized by peri-islet inflammation, fibrosis and haemosiderosis

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Objective: Pre- and post-natal factors such as intrauterine growth retardation (IUGR) and high fat (HF) diet contribute to type 2 diabetes (T2D). Our aim was to determine if IUGR and HF diets interact in T2D pathogenesis.
Method: A surgical model of IUGR (bilateral uterine artery ligation) in Sprague–Dawley rats with sham (SH) controls was used pups were fed either HF or chow (CH) diets from weaning. Serial measures of body weight and glucose tolerance were made. At 25 weeks, rat pancreases were harvested for histological assessment.
Results: IUGR vs SH pups weights were 17 % lower. HF diet caused excess weight gain, dyslipidaemia, hyperinsulinaemia and mild glucose intolerance not further aggravated by IUGR. Markedly abnormal islet morphology was evident in 0/6 SH-CH, 5/8 SH-HF, 4/8 IUGR-CH and 9/9 IUGR-HF rats (chi-sq, $p=0.008$). Abnormal islets were characterised by larger size, irregular shape, peri-islet inflammation with CD68 positive cells and marked haemosiderosis. Overall beta-cell mass was not altered by IUGR, with a trend for it to be mildly increased in both HF-fed groups.
Conclusion: HF and IUGR independently and together contribute to islet injury. The marked islet haemosiderosis associated with IUGR and HF diets warrants further investigation as iron is toxic to β-cells.

PS-05-010

Malignant adrenocortical tumour in the setting of adreno-hepatic fusion

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Objective: Adreno-hepatic fusion (AHF) is defined as adhesion of the liver and right adrenal gland with or without a fibrous capsule dividing both organs. We report a surgical case of AHF in which a virilising malignant adrenocortical tumour protruded into the liver mimicking a hepatic mass.
Method: A 36-years-old woman presented with mid-right abdominal pain and marked hirsutism. Computed tomography (CT) revealed an apparently intrahepatic solid tumour suggestive of a giant hepatic adenoma. The right adrenal gland was not visible on CT and the right kidney showed marked downwards displacement. A radical right adrenohepatectomy was performed, with a satisfactory outcome.
Results: Grossly, a giant, partially encapsulated mass was seen to protrude from the right adrenal gland into the liver. Microscopically, the tumour was constituted by atypical clear cells with nuclear polymorphism, necrosis and moderate mitotic activity. Tumour cells expressed vimentin and Melan-A protein.
Conclusion: To our knowledge, this is the first description of a malignant adrenal tumour in the setting of AHF. As illustrated by this case, awareness of AHF as an entity and attention to its distinctive gross and histologic features are essential to avoid confusion between adrenal and hepatic lesions, especially when imaging studies have provided misleading findings.

PS-05-011

ACTH producing pheochromocytoma: A case report

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Objective: Cushing's syndrome (CS) is a rare disease, resulting in the majority of cases from ACTH hypersecretion. 70 % is of pituitary origin, 20 % of adrenal origin, and only 10 % from ectopic ACTH production.
Method: We reported a rare cause of ectopic ACTH dependent CS, caused by a pheochromocytoma.
Results: A 54-year-old male was hospitalized for severe high blood pressure, depression and weight loss. Biological investigation revealed serious hypokaliema, severe ACTH dependent hypercortisolism with elevated urinary free cortisol secretion, loss of diurnal variation, and excess plasma ACTH level. CT-scan revealed a nodular lesion in the right adrenal gland with hyperplasia in the left one. The nodular lesion was assumed to be a pheochromocytoma based on the elevated serum and urinary catecholamine and metabolites and local uptake in right adrenal gland in 131 I-MIBG scan. Right adrenalectomy was performed. Macroscopic examination revealed a 4 cm, well-circumscribed, tan-brown tumor, associated with diffuse adrenocortical hyperplasia. Histological examination confirmed the diagnosis of pheochromocytoma, without signs of aggressiveness. The tumor cells were immunopositive for Chromogranin A, Synaptophysin and ACTH. After surgery, catecholamine secretion returned quickly to normal level. Biological and clinical CS regression was noted.
Conclusion: Despite the rare association of CS with pheochromocytoma, preoperative diagnosis is required to an appropriate therapy.

PS-05-012

A rare case: Extralobar pulmonary sequestration mimicking neuroblastoma

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Objective: Extralobar intraabdominal pulmonary sequestrations are rare congenital malformations which are characterized by disorganized and nonfunctioning pulmonary parenchyma. These lesions have no communication with the bronchial tree and pulmonary arteries. They receive their blood supply from the systemic circulation.
Method: We describe a 5 days old male infant admitted to the hospital with a left subdiaphragmatic, 50×40×35 mm, hiperechogenic and, solid mass that was identified during ultrasonography on the 26th week of gestation.
Results: Abdominal computerized tomography demonstrated a 48×37×33 mm, solid, vascularized, encapsulated, mostly cystic suprarenal mass with no calcification reported to be highly suspicious for neuroblastoma. The mass was completely excised. Gross pathologic examination revealed a well circumscribed spongy lesion that mimicked a lung tissue. On microscopic examination, a disorganized lung tissue that was composed of alveoli, alveolar ductus and bronchioles was seen. Normal adrenal tissue was not observed. Later, we learnt that the lesion's arterial blood supply was from the abdominal aort. Based on these findings, our diagnosis was intraabdominal extralobar pulmonary sequestration.
Conclusion: Intraabdominal extralobar pulmonary sequestrations should be kept in mind in cases of the adrenal masses as the surgical resection is the adequate treatment method for these lesions.

PS-05-013

Axillary lymph node metastasis of papillary thyroid carcinoma showing anaplastic transformation with cutaneous metastasis

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Objective: Papillary thyroid carcinoma (PTC) rarely metastasizes to axillary lymph nodes. Although anaplastic transformation (AT) may occur in the cervical lymph node metastasis from PTC, it is rarely observed in the metastatic axillary lymph nodes. Furthermore, cutaneous metastasis from anaplastic thyroid carcinoma (ATC) is extremely rare.
Method: A 65-year-old male patient who had operated for multinodular goiter 8 years ago presented with neck swelling on the right side. Residual thyroid tissue was detected and the lesion was removed surgically in combination with a right neck dissection. Histopathologic examination was consistent with PTC and metastatic lymph nodes. The patient received radioactive iodine therapy. Afterwards, the patient presented with a right axillary mass 14 years after the first operation and underwent surgical excision.
Results: Histopathologic examination showed PTC with anaplastic transformation. Histopathologically confirmed multiple skin metastases from ATC emerged in thoracic and abdominal regions 3 months after the last operation. Patient died 3 months after the diagnosis of anaplastic carcinoma.
Conclusion: Although most PTCs show an indolent course and have a favorable prognosis, distant metastasis and anaplastic transformation of the metastatic lymph nodes may occur even more than many years after the primary treatment.

PS-05-014

Local „bystander"effect of gene therapy on human tumor cells of medullary thyroid carcinoma in vivo

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Objective: Gene therapy acts on change of prodrug into cytotoxic drug inside tumor cells transfected by foreign enzyme. It uses also "bystander" effect on surrounding tumor cells without enzyme. We used yeast Cytosine deaminase (yCD) in combination with 5- fluorocytosine (5FC) converted into 5- fluorouracil (5FU) and its metabolites. Medullary thyroid carcinoma (MTC) is a malignant tumor often with therapy resistant distant metastases. Patients with sporadic form have metastases at the time of diagnosis, mostly in bones, lungs and liver. The aim of this study was to evaluate the efficiency of yCD/5FC in MTC treatment using xenotransplants derived from model TT cell line in nude mice.
Method: Tumors were immunohistochemically stained with polyclonal antibody anti-EGFP (enhanced green fluorescence protein) and monoclonal antibodies anti-PCNA and anti-Ki67. Positivity was semiquantitatively evaluated.
Results: Diffuse positivity for PCNA was seen in untreated and treated tumors, respectively. Positivity for Ki-67 was diffuse in untreated and only sporadic in treated tumors.
Conclusion: Diffuse PCNA positivity in treated tumors suggests that the tumor cells stopped in S phase. Scattered positivity of Ki-67 after treatment document suppressed proliferation mediated by yCD/5FC gene therapy, which implies therapeutic application in patients with metastatic MTC. (ITMS 26240220052, VEGA 2/008/11, VEGA 2/0146/10).

PS-05-015

E-cadherin/ß-catenin immunoexpression in thyroid carcinomas

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Objective: The aberrant activation of Wnt signaling pathway may be a common denominator for the development of thyroid tumorigenesis. It was announced that the loss of E-cadherin rather than β-catenin mutation represents a crucial

event in determining the degree of differentiation of thyroid carcinomas. The aim of the study was to evaluate the expression of E-cadherin and β-catenin in the thyroid cancer tissue and to correlate these data with some histological and clinical parameters of the tumors.
Method: We investigated 57 patients, having thyroid tumors – papillary, follicular, anaplastic and oncocytic carcinomas immunohistochemically with antibodies against E-cadherin and β-catenin. Survival analyses were done.
Results: E-cadherin expression was focally retained in the tumor cell membranes and in the tumor cell cytoplasm of the papillary, follicular and oncocytic thyroid cancers, weather in anaplastic cancers it was almost lost (p=0.0042, and p=0.019, respectively, Fisher's Exact Test). The expression of β-catenin in tumor cytoplasm and membrane in papilary cancers was higher as compared to that in the other tumors (p=0.111, and p=0.0104, respectively).
Conclusion: Not surprisingly, the presence of aberrant expression of E-cadherin and/or β-catenin in thyroid cancer has been associated with better patients' prognosis and more well differentiated tumor histology.

PS-05-016

Correlation between Estrogen receptor and progesterone receptor with some prognostic factors in papillary thyroid carcinoma

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Objective: The more prevalence of papillary thyroid cancer in women shows the probability of the role of sex hormones in the cancer. The aim of this study was determination of relation between sex hormones receptors and some prognostic factors.
Method: We studied 92 patients with pathology report of papillary thyroid carcinoma after thyroidectomy between 2006 and 2009. The specimens were stained immunohistochemically for ER and PR. The other informations such as sex, age, tumor size and lymph nodes involvement obtained from the patients documents.
Results: The average age of patients was 39.32+16,93. 46.7 % t of samples were ER positive while this was 6.5 % for PR. The percentage of lymph nodes involvement was 23.9 %. The size of tumors was 3.60+2.21 cm. There was a direct relationship between female sex and positivity of ER ($p \leq 0.014$). But there was no significant relationship between ER and PR with age, tumor size and lymph nodes involvement.
Conclusion: It seems to be that ER is more prevalent in females but for showing of its role in prognosis, further studies are recommended.

PS-05-017

Mixed pituitary adenoma/craniopharyngioma: Clinical, morphologic, immunohistochemical and ultrastructural study of a case

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Objective: Mixed pituitary adenoma/craniopharyngiomas are rare tumors, accounting for about 15 reported cases. Most of them are composite neoplasms and tumors showing combined features are extremely rare.
Method: We describe the clinical, morphologic, immunohistochemical and ultrastructural features of a case.
Results: A 75-year-old woman presenting with diplopia due to a sixth left nerve palsy underwent head CT scan and MR which showed a sellar mass suggestive for a pituitary macroadenoma. Endocrine testing demonstrated only a slightly increased prolactin. The patient underwent endoscopic endonasal transphenoidal approach with resection of multiple fragments. The tumor was composed by a pituitary ACTH adenoma admixed with islands of adamantinomatous craniopharyngioma representing 40 % of the lesion. Electron microscopy showed cells of a sparsely granulated ACTH adenoma admixed with craniopharyngioma component and some cells showing both patterns. The patient completely recovered the nerve palsy and the post-operative endocrine tests were normal. A 5 months post-operative head MR confirmed the complete resection of the lesion.
Conclusion: We report a rare mixed sellar tumor showing an ACTH secreting pituitary adenoma admixed with an adamatinomatous craniopharyngioma, with some hybrid cells suggestive of a common histogenesis of the two components of the neoplasm.

PS-05-018

Sitagliptin treatment delays the progression of pancreatic and renal lesions and reduces tissular oxidative stress in a type 2 diabetes animal model

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Objective: Type 2 diabetes mellitus (T2DM) treatment aims to control metabolic effects, preserve pancreatic function and reduce complications, such as nephropathy. This study intends to evaluate the effects of sitagliptin, a dipeptidyl-peptidase-4 inhibitor, in pancreatic and renal lesions in Zucker Diabetic Fatty (ZDF (fa/fa)) rats, an animal model of T2DM.
Method: Male obese diabetic ZDF (fa/fa) rats, 20-weeks-old, were treated with vehicle or sitagliptin (10 mg/kgBW/

day) for 6 weeks, and compared with lean control ZDF rats (n=8 each). Biochemical parameters as well as pancreatic and renal lipid peroxidation and histopathology profile were assessed. Specimens we stained with haematoxylin-eosin and periodic acid of Schiff, and examined by light microscopy. Lesions were evaluated by a semiquantitative rating. Endocrine/exocrine pancreas and renal glomerular, tubulointerstitial and vascular lesions were assessed and scored (0 3/0-2). Results are mean ± SEM; ANOVA and Duncan's post-hoc analysis ($P \leq 0.05$ was considered as significant).
Results: Sitagliptin improved metabolic parameters, reduced lipid peroxidation ($p<0.001$) in both organs and significantly prevented major diabetic pancreatic and renal lesions in obese diabetic ZDF rats.
Conclusion: Sitagliptin seems to comply with the three main objectives of T2DM therapeutic management. Underlying molecular mechanisms deserve further elucidation, but could be related with metabolic improvement and reduction of oxidative stress.

PS-05-019

HBME-1, Cytokeratin-19, Galectin-3, CD56 and p63 expression in thyroid tumors of uncertain malignant potential

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Objective: Thyroid tumors of uncertain malignant potential (TT-UMP) include follicular and well-differentiated tumors of UMP (FT-UMP/WDT-UMP), as it refers to the presence of questionable capsular/vascular invasion or incompletely developed papillary thyroid carcinoma (PTC)-type nuclear changes. However, a diagnosis of TT-UMP is difficult in most cases. We aimed to investigate whether immunohistochemistry (HBME-1, Cytokeratin-19, Galectin-3, CD56 and p63) provides additional information concerning such lesions.
Method: We performed an immunohistochemical analysis on 14 WDTs-UMP and 4 FTs-UMP.
Results: In the WDT-UMP group, HBME-1 was positive in 6/14 (42.9 %) cases. CD56, a marker whose expression is reduced in thyroid carcinoma, showed a "malignant" profile (no expression) in 9/14 (64.3 %) cases. 6/14 (42.9 %) cases were positive for both antibodies. One case showed the co-expression of HBME-1, CD56, Galectin-3 and Cytokeratin-19. Only one FT-UMP case was positive for HBME-1. The follow-up data revealed no distant metastases or persistent disease.
Conclusion: TT-UMP demonstrated very heterogeneous immunohistochemical profiles. WDTs-UMP revealed a certain tendency toward a PTC profile, suggesting a possible pathogenetic link between these two entities. However, immunohistochemistry is to be regarded more as a supporting factor, while morphological criteria should always prime in the diagnostic decision.

PS-05-020

CD68, TGF-ß1, Smad4, Smad7 and TGFßRII and thyroid cancer

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Objective: Many growth factors such as TGFbeta promote macrophage recruitment, survival and differentiation in tumors. In many human tumors a high frequency of infiltrating tumor associated macrophages (TAMs) has been asssociated with tumor development and poor prognosis. It was shown that in poorly differentiated thyroid cancers TAMs support tumor progression. The aim of our study was to investigate the association between TAMs and the proteins of the TGFbeta signaling pathway for the progression of thyroid cancer.
Method: We investigated 57 patients, having thyroid tumors – papillary, follicular, anaplastic and oncocytic carcinomas immunohistochemically with antibodies against CD68, TGFbeta, Smad4, Smad7 and TGFbetaRII. Survival analyses were done.
Results: The higher expression of TGFbeta and TGFbetaRII in papillary and follicular cancers was associated with higher CD68 infiltration in the invasive margin (median 20.7 cells/mm2, $p=0.052$, median 20.7 cells/mm2, $p=0.035$, respectively, Mann–Whitney U test) compared to anaplastic cancers. Similarly, the expression of Smad4 and Smad7 in papillary and follicular cancers was associated with higher CD68 infiltration in tumor stroma (median 19.7 cells/mm2, $p=0.012$, Mann–Whitney U test) in comparison to anaplastic cancers, with mising TGFbeta immunoexpression (median 2.4 cells/mm2).
Conclusion: Our results suggest that TAMs may facilitate tumor progression.

PS-05-021

Immunohistochemical seperation of thyroid papillary carcinoma follicular variant from follicular adenoma and RET/PTC correlation

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Objective: The accurate diagnosis of benign and malign thyroid tumors is very important for the clinical management of patients. The distinction of thyroid papillary carcinoma follicular variant and follicular adenoma can be difficult.

Method: We applied immunohistochemical markers; CK19, HMWCK, Galectin-3, HBME-1 and Fibronectin and PCR analyses for detecting RET/PTC rearrangement. Formalin-fixed parafin embedded tissues from 46 surgically total resected thyroids, included 26 thyroid papillary carcinoma follicular variant (TPCFV), 8 Follicular Adenoma (FA), 6 Minimal invasive follicular carcinoma (MIFC) and Follicular Carcinoma (FC).

Results: There was a positive correlation between TPCFV and HMWCK, CK 19, HBME1, Galectin 3, Fibronectin ($p<0.05$), but there was no correlation with TPCFV and RET/PTC ($p>0.05$). HBME-1 and CK 19 stained strong and diffuse positive in TPCFVs but weak and focal in FAs.

Conclusion: Our study suggests that morphologic features combined with immunohistochemical panel of HMWCK, CK19, HBME-1, Galectin-3 and fibronectin can help to distinguish benign and malign thyroid neoplasms and TPCFV from follicular adenomas. RET/PTC expression has been non-specific but its detection can be a useful tool combined with immunohistochemistry for diagnosing TPCFV.

PS-05-022

Morphological features of the system mother-placenta-fetus during pregnancy on diabetes mellitus

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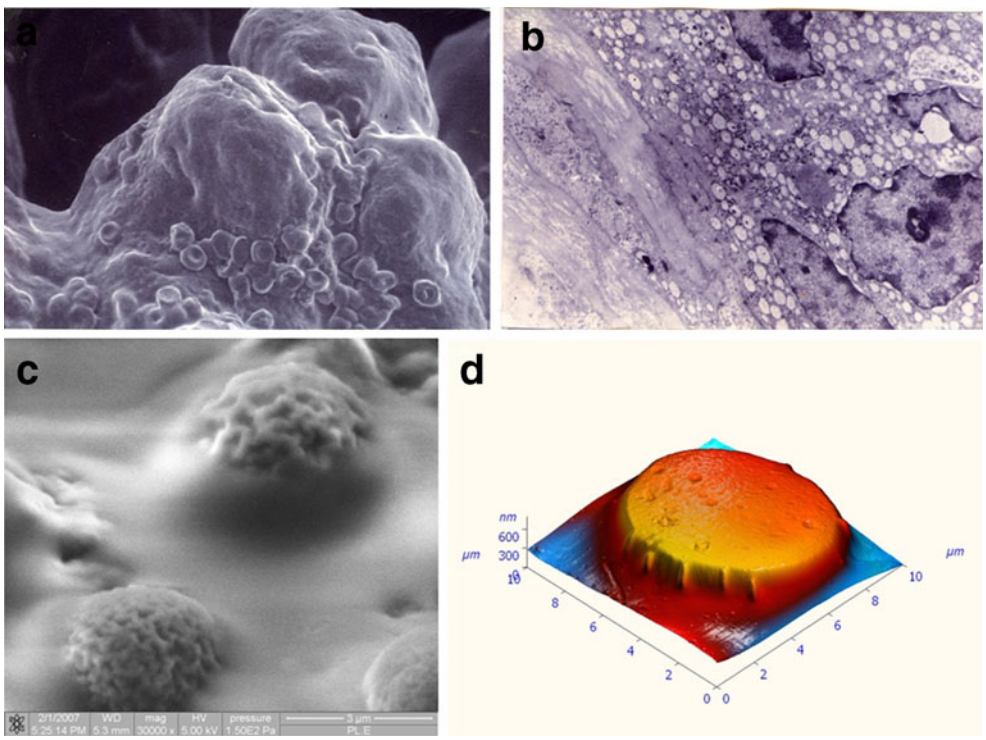
Objective: Combination of diabetes mellitus and pregnancy has a special concern.

Method: It were studied 50 pregnants with diabetes mellitus type 1 and 29 pregnant with gestational diabetes mellitus (GDM). The methods were used: light, transmission, electron, probe and scanning microscopy with microelement analysis.

Results: The pregnancy at diabetes mellitus type 1 and GDM proceeds with complications: treat of pregnancy termination (64,0 % and 50,0 %), hydramnion (27,0 and 62,5 %), preterm birth (36,0 and 12,5 %). It was displayed decreasing of oxygen in mother's erythrocytes. At the diabetes mellitus in uterus of women in birth there are violations of spiral arteries as well as circulatory disorders (stasis, sludge, thrombosis and diapedetic bleedings), that is significantly expressed at gestosis. Tendency to cell form changing is observed in erythrocytes at diabetes mellitus, especially at diabetes mellitus type 1. The frequency of placental insufficiency in pregnant with diabetes mellitus type 1 were 75 %, at GDM- 50 %. The gestosis accession were resulted to birth's increasing of children with prenatal injury of central nervous system at diabetes mellitus type 1 in mother and diabetic fetopathy at GDM.

Conclusion: The clinical and morphological parallels of the system mother-placenta-fetus were presiced ad diabetes mellitus type 1 and GDM.



PS-05-023

Sclerosing mucoepidermoid carcinoma of the thyroid in a 13 year-old female

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Objective: Sclerosing mucoepidermoid carcinomas (SMECs) are low-grade malignant tumours with both squamous and mucinous differentiation representing less than 1 % of thyroid malignancies. SMECs are usually associated to Hashimoto thyroiditis and classically disclose eosinophilia.
Results: A 13 year-old female with Hashimoto thyroiditis presented a 2.5 cm nodule in the left lobe of the thyroid. The total thyroidectomy specimen disclosed a firm, well circumscribed, non-encapsulated tumour. Microscopically, the tumour was composed by anastomosing clusters of squamoid cells in a sclerotic background without eosinophils. Intra-cytoplasmatic PAS/diastase positive material was focally found. The tumour cells expressed AE1.AE3, TTF-1 and p63 whereas no expression was observed for thyroglobulin, calcitonin and CD5. The Ki-67 labeling index was 5 %. In the molecular analysis no mutations were detected in BRAF or (K-, N-, H-) RAS genes nor RET/PTC or PAX8/PPARgamma rearrangements. The remaining thyroid showed Hashimoto-type thyroiditis. A cervical lymph node metastasis was identified. The patient was treated with radioactive iodine and is alive without signs of disease after 10 months of follow-up.
Conclusion: SMECs may not disclose the classical eosinophilia and represent rare low-grade tumours that can give rise to metastases. The most frequent molecular alterations found in thyroid tumours were not detected in this case.

PS-05-024

ALK1 and BMP-9 overexpression as a cause of ossifying papillary thyroid carcinoma

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Objective: Ossification is an often encountered finding in papillary thyroid carcinoma (PTC). We hypothesized that osteogenic signaling may be related to osteogenesis of PTC. Bone morphogenic protein (BMP)-9 is the most osteogenic subtypes among BMPs. And as a cellular receptor, activin receptor-like receptor (ALK)1 has been emphasized in BMP-9 induced osteogenic signaling. We investigated the expression of ALK1 and BMP-9 and their correlation with ossification in PTC.
Method: ALK1 and BMP-9 expression were investigated by immunohistochemistry in tumors and adjacent normal follicles of 78 PTCs with bone formation and 64 PTCs without bone formation. ALK1 and BMP-9 expression were further verified by quantitative real time polymerase chain reaction in each group of 15 cases of PTCs with or without bone formation.
Results: ALK1 and BMP-9 immunoreactivity were increased in PTC with bone formation when compared to those without bone formation ($P<0.001$ and $P=0.001$). Both mean values of ALK1 and BMP-9 mRNA expression were elevated in PTCs with bone formation compared with those without bone formation ($P=0.037$ and $P<0.001$).
Conclusion: ALK1 and BMP-9 overexpression may be underlying the molecular alteration that accounts for osteogenesis in PTC.

PS-05-025

Multiple metastases of renal clear cell carcinoma within adenomatous nodule in multinodular goiter

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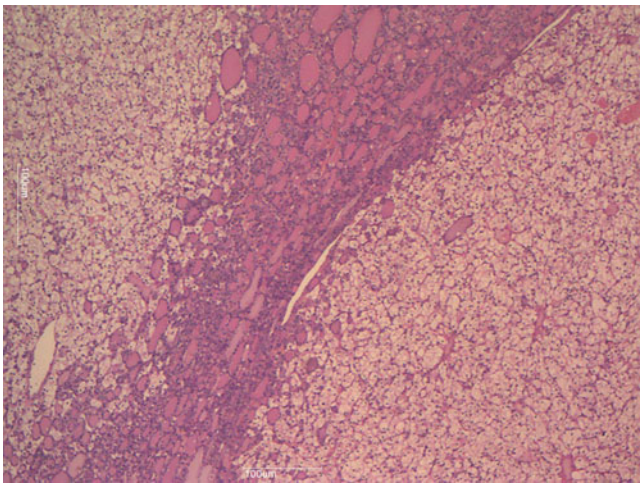
Objective: Thyroid is an extremely rare site of metastases. Renal clear cell carcinoma (RCCC) is one of the most frequent primary malignancies causing thyroid metastases as a single nodule (77 %) or multiple nodules (23 %). We report the case of a 62-years-old female patient affected by multinodular goiter, who was diagnosed with RCCC, treated with nephrectomy.
Method: Due to compressive symptoms, 6 years after nephrectomy, the patient underwent thyroidectomy and the thyroid was sent for histology.
Results: Histology showed multinodular goiter. In the largest hyperplastic adenomatous nodule (left lobe, diameter mm 53), multiple solide yellow-orange areas were detected grossly. These areas were microscopically composed of sheets of large cells with clear cytoplasm and small hyperchromic nuclei, with a focally infiltrative growth pattern. At immunohistochemistry clear cells were negative for TTF1, HBME1, galectin-3 and positive for CD10.
Conclusion: This is a rare case of multiple RCCC metastases within an adenomatous nodule in goiter. Clinical diagnosis of RCCC metastases to thyroid is extremely difficult, even more if metastases grow in multinodular goiter. It

should be always suspected in patients with a clinical history of RCCC.



PS-05-026

A case of follicular carcinoma, oncocytic variant, misdiagnosed as medullary carcinoma by fine-needle aspiration cytology

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Objective: Follicular carcinoma, oncocytic variant, is a rare type of thyroid carcinoma. We examined a case of oncocytic carcinoma misdiagnosed as medullary carcinoma on fine-needle aspiration (FNA) because it was associated with amyloid material.
Method: A 73-year-old female rheumatoid arthritis (RA) patient had a 4.0 cm mass in the right lobe of her thyroid, which showed no enhancement effect on CT scan and was diagnosed as a "cyst". FNA was performed, and she subsequently died of unrelated causes. An autopsy was performed.
Results: Cytology: Large and small round-shaped tumor cells were present with round nuclei with granular chromatin. Double- or triple-nucleated cells and amyloid material were observed. Histology: oncocytic round cells proliferated diffusely in the fibrous capsule. Extra-capsular invasion and vascular infiltration by the tumor cells were recognized. Electron microscopy: the cytoplasm of tumor cells was full of mitochondria. Therefore, we diagnosed this as follicular carcinoma, oncocytic variant. Amyloid deposition was also observed in several other organs.
Conclusion: Amyloid deposition was caused by amyloidosis secondary to RA. Narrowing of the tumor feeder artery due to amyloidosis may have prevented early enhancement on the CT image.

Sunday, 9 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-06 Poster Session Digestive Diseases Pathology I: Upper Gastrointestinal Tract

PS-06-002

Immunoexpression of metaloproteinases 2 and 14 and tissue inhibitor of metaloproteinases-2 in gastric cancer

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Objective: Gastric cancer is the second leading cause of cancer death worldwide. Metaloproteinases 2 and 14 (MMP-2; MMP-14) and Tissue Inhibitor of Metaloproteinases-2 (TIMP-2) are involved in epithelial-mesenchymal transition and tumor progression in cancer. Aim: to evaluate their immunoexpression and correlations with clinicopathological parameters in gastric carcinomas.
Method: Samples from intestinal (n=53) and diffuse (n=30) gastric carcinomas (Lauren classification), underwent tissue microarrais and immunohistochemistry. Immunoxpression of MMP-2, MMP-14 and TIMP-2 was measured according to scores 0=negative; 1=discrete; 2=moderate; 3=strong, (all staining in >50 % of cells), modified from Buskens et al. 2003, Gut, 52:1678-83. CD68 antibody was used to characterize mononuclear cells.
Results: MMP-2 was stained more often in women (67 % & 19 %-men; p<0.005, Fisher's exact test). MMP-2 and MMP-14 were mostly expressed in mononuclear (macrophages) than in epithelial cells, in both sites, principally, lymph nodes (MMP-2: lymph node=81 % & 35 %-stomach; p<0,005). Moreover, TIMP-2 was observed mainly in neoplastic cells of primary intestinal tumours.
Conclusion: In this study, MMP-2 immunoexpression was far more prevalent in women. MMP-2 and MMP-14 predominant expression in mononuclear stromal cells in the lymph node metastases reinforces the central role of these cells in the tumor microenvironment in the progression of gastric carcinoma.

PS-06-003

The relationship between tumor infiltrating immunologic cells and the survival of gastric carcinoma patients

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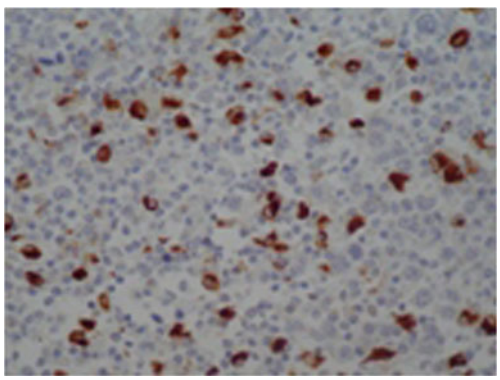
Objective: We investigated the prognostic significance of immune cell counts in the gastric cancer stroma.
Method: This historical cohort study was conducted on50patients with non-metastatic intestinal-type adenocarcinoma who have been undergone curative gastrectomy during2004-2008in Mashhad Medical University. Immunohistochemistry staining forCD56, CD68, CD117 andCD1a was performed to detect NKCmacrophages, mast cells and Langerhans cells, respectively. The immune cells were counted. The prognostic significance of two grouping (low or high immune cell counts) was analyzed using the Kaplan Meier method and Cox proportional hazards regression modeling.
Results: 38(76 %) male and 12(24 %) female patients enrolled the study with a mean (±SD) age of 66.0(±9.2) years old. The median survival time was 15.0(95 % CI: 5.5-24.5) months. Natural killer cells, mast cells and Langerhans cells showed positive effect on survival, whereas the reverse was true for macrophages. Multivariate analysis showed that the independent prognostic factors were location of the tumor (cardia/non-cardia), stage, the presence of extra-cytoplasmic mucin, tumor associated macrophage status (low/high), and tumor associated Langerhans cell status (low/high).
Conclusion: In the studied population, gastric carcinoma proved to have a very poor prognosis. Multivariate analysis showed that the prognostic effect of natural killer and mast cells in tumoral tissue were dependent on the Langerhans cell count.



PS-06-004
Correlation of p53, HER2 and E-cadherin expression with clinicopathological parameters of gastric carcinoma
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Objective: Gastric cancer is the second most common cancer in humans. Numerous genes are possibly involved in carcinogenesis and tumor progression of gastric cancer.
Method: Material of 45 patients diagnosed with gastric carcinoma at the Institute of Oncology, Sremska Kamenica was analyzed using antibodies to P53, HER2 and E-cadherin and correlated with following clinicopathological parameters: gender, age, endoscopic type of cancer, localization, histologic type, grade, vascular and neural invasion, depth of infiltration, distant metastasis.
Results: 78 % of patients were aged over 60 years. p53-positivity was found in 47.17 %, HER2-positivity in 6.52 % and loss of E-cadherin expression in 43 %. p53-positivity showed statistically significant relevance correlated to gender, age, histologic type, localization, vascular invasion and depth of infiltration. HER2 overexpression was statistically relevant compared to endoscopic type of cancer and vascular invasion. E-cadherin was positive in all female and 33.3 % of male subjects. Loss of E-cadherin expression didn't differ among histological types but it showed statistically significant relevance correlated with high grade, deeper infiltration and vascular invasion. Loss of E-cadherin expression was verified in 83.3 % of HER2-positive tumors ($p<0.005$).
Conclusion: P53, HER2 expression and loss of E-cadherin expression may give valuable information for predicting vascular invasion and aggressive tumor behavior.

PS-06-005
Does immune profile of gist differ up to localisation?
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Objective: Though immune profile of gastrointestinal stromal tumor (GIST) has been documented detailly, there has been no attracting data about correlation of the immune profile and localisation.
Method: Archival data of GIST cases has been documented as regards age, localisation, tumor size, mitotic activity rate, CD117 and CD34 immunopositivity. Results have been compared.
Results: Most of the 91 GIST cases were gastric and ileal ones. Mean age and mitotic activity rates were similar, abdominal (extra gastrointestinal tract) tumors were larger than the others. CD117 expression was significantly lower in colonic tumors and CD34 expression was significantly lower in abdominal ones (attached comparison chart).
Conclusion: CD117 and CD34 expressions are significantly lower in colonic and abdominal GISTs consequently. For the diagnosis of colonic and abdominal GISTs these data should be regarded.

	Stomach	Small bowel	Colon	Abdomen	Total
91 cases	30	37	9	15	91
Mean age	60	58	58	52	58
Mean Tm size (cm)	7	7.62	7.27	17.7	9.7
Mitosis	4/50 hpf	14/50 hp	20/50 hpf	14/50 hpf	11/50 hpf
CD117 (+)	26 (86.6%)	30 (81%)	3 (33.3%)	14 (93.3%)	73 (80.2%)
CD34 (+)	28 (93.3%)	25 (67.5%)	7 (77.7%)	5 (33.3%)	65 (71.4%)

PS-06-006

Whipple's Disease: A challenge of clinical, histopathological and electronomicroscopical diagnosis. Experience of a Romanian Tertiary Center - A five-case series

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Objective: Whipple's disease is an infectious disease caused by Tropheryma whipplei, an ubiquitous Gram-positive Actinobacteria. The incidence of the disease is less than 1 per 1 milion. We report five new consecutive cases, four males and one female, diagnosed in our clinic from August 2002 to January 2012.

Method: Diagnosis was reached with the help of gastroduodenal endoscopy and histopathological examination of the duodenal biopsies, by lymph node biopsy and by electron microscopy.

Results: The main symptoms were arthralgia, weight loss and diarrhea. The endoscopic aspect of the small bowel mucosa varied from congestion, granularity of the mucosa to whitish plaques. All patients showed PAS positive, diastase resistant, Ziehl-Neelsen negative macrophages in the lamina propria of the duodenal mucosa and, in one patient, suspected for lymphoma, in an abdominal lymph node. The diagnosis was confirmed by electron microscopy in all cases. Classic Whipple's disease was the diagnosis in all five cases, but one patient showed involvement of the endocardium and two patients showed lymphadenopathies.

Conclusion: Clinical evolution was favorable under long-term antibiotics (Cephtriaxone/Trimethoprim-Sulfamethoxazole) and follow-up biopsies in three patients showed a normal endoscopical mucosa and a reduced but persistent number of PAS positive macrophages in the duodenal mucosa.

PS-06-007

Neuroendocrine Neoplasms of gastrointestinal tract: Forms of presentation and histological characteristics in a series of 11 Tunisian patients

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Objective: Neuroendocrine neoplasms (NENs) of the gastrointestinal tract are rare tumors with an estimated incidence of 1 to 2 per 100,000.

Method: We reviewed the cases of gastrointestinal tract's neuroendocrine neoplasms presented to our department during 1 year (2010–2011) and we assessed the occurrence, form of presentation and histological characteristics of these tumors (we used the new OMS classification of NEN proposed on 2010).

Results: Eleven cases of NEN of gastrointestinal tract were identified. They were 6 men and 5 women with a mean age of 53.09 years. The most common localization was the appendix (7 cases). The 4 other cases were localized in the small intestine, the ileo caecal valve, the fundus and the bulb. The mean tumor's size was 13.8 mm. Mitoses were absent in the majority of cases (72,7 %). All the tumors were well differentiated classified as grade 1 in 9 cases and grade 2 in 2 cases. The tumor was aggressive in 2 cases. The small intestine's NET was multifocal infiltrating the subserosa with lymph node metastasis classified pT3 N1. The ileo caecal valve's NET was also aggressive with lymph node and hepatic metastasis classified pT4N1M1. All patients underwent surgical treatment.

Conclusion: Gastrointestinal NENs are complex tumors whose incidence is rising and whose treatment requires precise classification and risk stratification.

PS-06-008

Multiple duodenal stromal tumors associated with Neurofibromatosis-1

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Objective: Gastrointestinal stromal tumors (GIST), most commonly occur sporadically, but there seens to be some increased tendency for these tumors to develop in patients with neurofibromatosis1(NF1). There is no histological difference between the NF1 assocaciated cases and the sporadic cases. However, tumors associated with NF1 frequently show multiplicity.

Method: A case of multiple duodenal gastrointestinal tumor arising in a 45 year old mal with NF1 is reported. The

abdominal exploration revealed multiple solid nodules in the duodenum, and the pancretecticoduodenectomy was performed.
Results: Macroscopy: the resected segment of the duodenal showed seven suberosal solid masses. The largest mass measured 3,5 cm×2 cm×3 cm, and is coupled with the bors lower pancreas but remains limited by a capsule. The cut surface was smooth and white in appearance. Microscopy: the tumors were composed of interlacing fascicles of the uniform spindle cells with elongated cytoplasm. The tumor cells lacked pleomorphism, and mitotic figures were absent. Immunohistochechemistry: the tumors cells were diffusely positive for CD117, CD34, and negative for desmin, AML and pS100.
Conclusion: GIST are rarely noted in association with neurofibromatosis-1. Duodenal GISt are most frequently diagnosed in the workup of symptoms not specific to these masses. Duodenal resection is rarely indicated except in the case of duodenal GIST and early-stage adenocarcinoma or if the tumor appeared involve the pancreatic parenchyma on preoperative imagings.

PS-06-009
Periampullary adenomyoma: A true trap diagnosis
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*CHU Frantz Fanon, Dept. of Pathology, Blida, Algeria

Objective: Adenomyoma is a term generally applied to nodular lesions showing proliferation of both epithelial and smooth muscle components. It is usually presented as biliary obstruction. Most cases are misdiagnosed as adenoma or carcinoma by preoperative endoscopic or radiologic. Therefore, it is frequently treated with extensive surgery.
Method: We report a case of a 28 year-old man with an adenomyoma located in the ampulla of vater diagnosed by endoscopic piecemeal resection.
Results: On histologic examination, the lesion consisted of hyperplastic glandular lobules, mainly located in the muscle layers of the vaterian system. The lobular formations consist of small glands surrounded by myofifroblastic, fibroblastic proliferation, sparse capillaries and inflammatory cells. IHC: Ki67: rare cells with a positive nuclear staining were presenting in the epithelial and mesenchymal components AML: The myofibroblastic of most spindle cells was confirmed by a strong cytoplasmic expression.
Conclusion: Real incidence of adenomyoma of the vaterian system is difficult to appreciate as different names (adenomyoma, adenomyomatosis, myoepithelial hamartome) are used to designate the same histological lesion. Adenomyoma was diagnosed only in adult patients –mean age: 63 y). The histogenesis is still a subject of controversy. The most widely accepted hypothesis is that the lesion may represent a form of incomplete heterotopic pancreas. Adenomyoma is considered as benign and slow growing, but its potential neoplastic nature cannot be excluded.

PS-06-010
So-called carcinosarcoma of the duodenum: Case report and review of the literature
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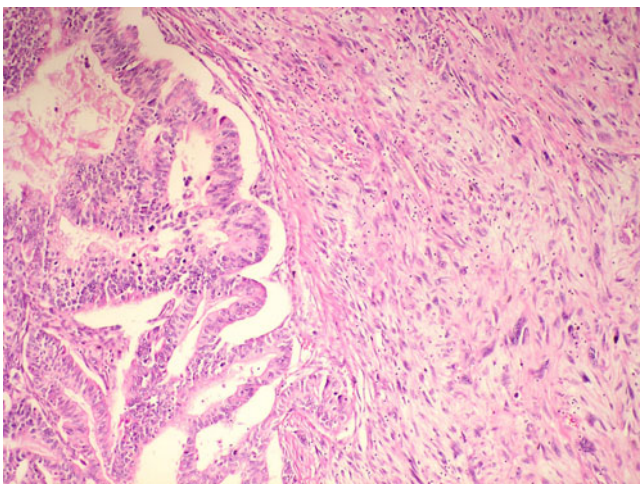
Objective: Carcinosarcomas are rare tumors. Duodenal carcinosarcomas of the duodenum are rare.
Method: H-E and IHC staining.
Results: We present a polypoid so-called carcinosarcoma of the duodenum in the Papilla Vater region in a patient of 59 years old. Tumor of 7 cm resected together the pancreatic tissue from the head of the pancreas. The tumor was diagnosed as Popypoid so-called carcinosarcoma of the duodenum with a wide peduncul infiltrating the Vater papilla. It contains two histologic components, one of well-differentiated adenocarcinoma that covers and infiltrates the tumor and a malignant fusiform component that serves as a stalk to the tumor.
Conclusion: Our case must be the fourth reported in the english literature. They have been reported in various forms, but most of them have been so-called carcinosarcomas. However, the histogenesis of these tumors is subject to further study. Carcinosarcoma of the digestive organs has been reported to exhibit aggressive behavior. Carcinosarcomas in digestive organs have been reportedly associated with a poor prognosis.12,13 However, some cases that have been treated with a curative operation showed long-term survival.



PS-06-011
Analysis of HER2 expression level in gastric carcinomas
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Objective: The expression of HER2 – an oncoprotein belonging to tyrosine kinase family belongs to recently evaluated prognostic and predictive factors in gastric cancer. Overexpression of HER2 is observed in about 8–27 % gastric cancers. According to many authors, overexpression and/or amplification of HER2 correlates with poor prognosis. The aim of our study was to analyze HER2 expression in gastric cancer in material routinely examined in Pathomorphology Department, JUMC.
Method: We have analyzed 50 cases of gastric cancers. The material came from 19 females and 31 males, age: 21-86. Immunohistochemical reactions were performed automatically on BenchMark BMK Classic (Ventana) using PATHWAY HER-2/neu (4B5) antibody. Scoring system for HER2 expression was ranged from 0 to 3+ where: 0 and 1+ were regarded as a negative, 2+ as equivocal and 3+ as positive.
Results: Most cases of gastric cancers were HER2-negative (45/50): including 0 score (38 patients) and 1+ (7 patients). Three cases were equivocal and two cases showed 3+ expression level.
Conclusion: The lower level of HER2 expression in the analyzed material in comparison with literature could be related to a relatively small group of cases but one cannot exclude that there exist some other factors that stand behind this and surely the investigations should be continued.

PS-06-012
MAPKAP kinase 2 overexpression influences prognosis in gastrointestinal stroma tumors, associates with copy number variations on chromosome 1, and expression of p38 MAP kinase and ETV1
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Objective: ETV1 has been proposed to be activated by KIT-mutations in gastrointestinal stromal tumors (GISTs). Aim of the study was to evaluate the role of ETV1 and associated proteins in GIST.
Method: Expressions of ETV1, MAPKAP kinase 2 (MAPKAPK2), phosphorylated p38 MAP kinase (pp38), phosphorylated MSK1, phosphorylated RSK1, COP1 and KIT were determined immunohistochemically in 139 GISTs. Sequence analysis of KIT, PDGFRA and MAPKAPK2 and FISH of ETV1 and chromosome 1 was performed.
Results: Prominent ETV1 expression was seen in 50 % of GISTs, but no correlation with clinical outcome was found. Correlation of ETV1 expression and KIT mutation was seen in 60 % of cases. MAPKAPK2 overexpression (n=62/44.6 %) correlated with pp38 expression (p=0.021) and alterations of chromosome 1 (p=0.024). In one cases with high MAKAPK2 expression, a MAPKAPK2 gene mutation was found. All relapsing GISTs with very low/low risk showed high MAPKAPK2 and KIT expression. MAPKAPK2 overexpression was an independent prognostic factor for disease free survival (p=0.006).
Conclusion: ETV1 is not universally overexpressed in GIST and seems to be induced also by other pathways than KIT-mutation. MAPKAPK2-overexpression is associated with shorter survival in GIST. Patients with low risk GISTs overexpressing MAPKAPK2 might profit from adjuvant tyrosine kinase inhibitor therapy.

PS-06-013
Gastrointestinal stromal tumors: Comparison of two risk stratification systems in a multicenter study of 1963 Turkish cases
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Objective: A nationwide database was performed for gastrointestinal stromal tumors (GISTs) in a large series of primary GISTs surgically treated at centers all around Turkey. The aim of this multicenter study was to analyze and compare the performance of the National Institute of Health (NIH) and Armed Forces Institute of Pathology (AFIP) risk criteria to determine the ideal risk stratification system.
Method: Statistical analysis of a nationwide database is consisted of age, gender, location, risk groups, histopathologic features and the results of CD117, CD34, Desmin, SM Actin, S-100 protein, and Ki67 immunohistochemistry.
Results: In 1965 cases registered in database, male to female ratio was 1.20 and mean age was 57.64 years. Most common location was stomach (47.5 %) followed by small intestine, omentum- peritoneum, large intestine, and esophagus (30.3 %, 12.1 %, 9.1 %, 1.0 % respectively). Comparison of the two risk-stratification systems demonstrated that proposed modified AFIP seems to be better when compared with NIH system. Many histopathologic and immunohistochemical findings showed significant correlation with risk groups of AFIP, even with 'not sufficient data' group (p<0.005).
Conclusion: The results of this multicenter study demonstrates that although follow up results are not provided, AFIP risk criteria seems to be more useful in prognostication for GISTs among the two systems.

PS-06-014
HER2 and Kras in gastric cancer patients
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Objective: HER 2/neu overexpression or amplification is an important biomarker for identifying patients with intestinal-

type gastric cancer who respond to therapy with Trastuzumab. Moreover, intestinal type gastric cancer shares many phenotypic and molecular genetic changes with colorectal cancer. In particular a progression from chronic gastritis to intestinal metaplasia, dysplasia, and finally malignant transformation is probably the sequence of gastric carcinogenesis. Somatic mutation of K-ras gene is common in colorectal cancer, being found in more than one-third of cases, but it seems to have, mostly in intestinal-type gastric cancer, a low incidence (7–20 %). The purpose of this study is to assess HER2 gene amplification and K-ras mutational status in a series of intestinal-type gastric carcinoma patients.
Method: Twenty paraffin embedded gastric cancer specimens were tested for HER2 amplification by chromogenic in situ hybridization (CISH) and K-ras mutational status (codon 12 e 13) by PCR-RFLP.
Results: Six (30 %) cases were HER2 amplified. Only one case (5 %) was found to have K-ras mutation (codon 12), but it was HER2 not amplified.
Conclusion: The frequency of K-ras mutation and HER2 amplification are in agreement with other studies on this topic. In our study, the two seem mutually exclusive events.

PS-06-015
IL-6-174 as a gastric carcinogenesis marker in biopsies
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Objective: Gastric carcinoma is related with cancer genetic susceptibility that can be investigated as single nucleotide polymorphisms (SNPs) and as cytokine genes are known to predispose to malignant disease, several polymorphisms of Interleukin-6 (IL-6) gene have been reported to in some may be associated with tumour progression including inhibition of malignant epithelial cells apoptosis and stimulation of angiogenesis.
Method: The aim of this study was to clarify the association between IL-6 polymorphisms and the risk of gastric cancer and chronic gastritis development or maintenance. PCR-SSP genotyping for IL-6 -174 C>G polymorphism was performed in 100 biopsies of gastric carcinoma and in 100 biopsies of chronic gastritis.
Results: There was association between IL-6 -174 C allele (p=0,0466) and -174CC, low producer, genotype (p= 0,0466) and gastric carcinoma, whereas IL-6 G allele (p= 0,0278) and IL-6GG (p<0,0001), high producer, genotype was associated with gastritis.
Conclusion: We conclude that IL-6 -174, low producer genotypes, may have an important role in gastric carcinogenesis and the polymorphism study of this molecule could be a good marker for gastric carcinoma susceptibility when high grade dysplasia is seen in biopsies.

PS-06-016
Giant Gastric Stromal Tumor in a 25-year-old man
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Objective: Gastrointestinal stromal tumors are the most common mesenchimal tumors of the gastrointestinal tract, representing 1–3 % of all the malignant tumors.
Method: We present the case of a 25-year-old man with a giant gastrointestinal stromal tumor of the stomach. The patient was admitted in the hospital for a palpable abdominal mass and a suboclusive syndrome. CT examination revealed a giant abdominal tumor. For the immunohistochemical (IHC) study we used the following antibodies: Vimentin, CD117, PDGFR, Nestine, D2- 40, PKC, CK MNF116, CK7, Synaptophysine, S100, CD34., En Vision system, visualization with diaminobenzidine.
Results: On gross examination, the tumor of 40/27 diameter, was soft, relatively well circumscribed, brown-tan on cut section, with cyst formation. Microscopically the tumor had an epithelioid growth pattern; the tumor had a low mitotic activity. Immunohistochemical stains showed, in the tumor cells, positive reaction for Vimentin, CD117, PDGFR, Nestine, D2- 40, PKC, and lack of reactivity for panCK, CK7, Synaptophysin, S100, CD34. Based on data offered by gross examination and by usual stains in conjunction with IHC profile we established a diagnosis of gastrointestinal stromal tumor.
Conclusion: Gastrointestinal stromal tumor have always been challenging for pathologists. The particularity of our case is the patient's young age and the large size of the tumor.

PS-06-017
Analysis of microsatellite instability in gastric malt lymphoma
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Objective: In Helicobacter pylori gastritis, constant antigenic stimulation triggers a sustained B-cell proliferation. Errors made during this continuous DNA replication are corrected by the DNA mismatch repair mechanism. Failure of this mechanism has been described in HNPCC and results in a replication error phenotype. Inherent to their instability during replication, microsatellites are the best markers of this replication error phenotype. We aimed to evaluate the role of defects in the DNA mismatch repair mechanism and

microsatellite instability (MSI) in gastric mucosa-associated lymphoid tissue (MALT) lymphoma.
Method: We examined 10 microsatellite loci (BAT25, BAT26, D5S346, D17S250, D2S123, TGFB, BAT40, D18S58, D17S787 and D18S69) for instability in 28 patients with MALT lymphomas. In addition, these tumors were also immunostained for MLH1, MSH2 and MSH6, as well as screened for the presence of t(11;198)(q21;q21) by real time polymerase chain reaction (RT-PCR).
Results: We found MSI in 5/28 (18 %) lymphomas, with one tumor displaying high levels of instability. MSI occurred in both t(11;18)(q21;q21)-positive and –negative tumors.
Conclusion: Our data suggest that a MMR-defect may be involved in the development of gastric MALT lymphomas, and mutations in the MSH6 MMR gene or hypermethylation of the MSH6 promoter might be associated with MSI-driven gastric lymphomas.

PS-06-018
Mitosis-specific marker phospho-histone H3 in the diagnosis of gastrointestinal stromal tumors
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Objective: The assessment of proliferative activity is one of the major parameters in the proper grading of gastrointestinal stromal tumors (GISTs). In the low level of mitotic activity it is difficult to calculate dividing cells correctly. Phospho-histone H3 (PHH3) is a recently introduced immunomarker for mitotic cells.
Method: Immunohistochemical study of 46 cases of GISTs of different malignant potential, statistical analysis.
Results: The count of PHH3-immunoreactive cells demonstrates the strong correlation (Gamma 0,756; $p<0,05$) with malignant potential of GISTs detected by standard parameters. It clearly separates true mitotic cells from apoptotic and piknotic nuclei. In all cases PHH3 count was slightly higher than the mitotic index in H&E stained slides. We have found that PPH3 demonstrated the two types of staining: nucleosomal dot-like type and mitotic homogenous type. The first type, probably, reflects the fraction of cells just before the prophase, which cannot be identified in H&E slides.
Conclusion: Immunostaining of PPH3 is a useful additional marker in detection of proliferative activity in GISTs, helping to identify true dividing cells correctly.

PS-06-019
HER2 assessment in gastric carcinoma using IHC and FISH
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Objective: HER2 in gastric cancer (GC) should be assessed following guidelines - recommended testing algorithm employs IHC as a screening tool and is followed by ISH to clarify equivocal cases. Reported incidences of HER2+ GC vary substantially and discordant results are frequent. In a series of GC HER2 was assessed by IHC and FISH to determine incidence of HER2+ GC, concordance of the methods and reevaluate the recommended algorithm.
Method: HER2 was assessed by both IHC (Pathway 4B5™) and FISH (PathVysion™) in 164 GC samples. Reactions were evaluated according to guidelines. HER2 was considered positive in case of strong protein expression (3+) and/or gene amplification (ratio ≥ 2.0). Frequencies of IHC and FISH scores, incidence of HER2+ GC and concordance (chi-square) of applied methods were analysed.
Results: IHC score distribution: neg(0) 63.3 %, neg(1+) 19.1 %, equiv(2+) 10.8 % and pos(3+) 10.8 %. FISH results distribution: nonampl 85.4 %, ampl 13.4 % and equiv 1.2 %. 36.5 % of IHC equiv 2+ tumors were amplified. There were no discordant cases resulting in excellent concordance ($p< 0.0001$).
Conclusion: Approximately 15 % of GC are HER2+. Application of standardised tests results in excellent concordance and, consequently, the proposed testing algorithm enables detection of all HER2+ GC.

PS-06-021
Glomus tumor of the stomach: A case report
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Objective: Gastric glomus tumors are rare neoplasms originated from modified smooth muscle cells of the glomus bodies. Such lesions present a diagnostic challenge in biopsy material. Herein, we report a case of gastric glomus tumor in a 35-year-old woman.
Method: A 35-year-old woman presented with refractory epigastralgy. A gastrointestinal stromal tumor of the gastric antrum was suspected. The diagnosis was made after ultrasound-guided endoscopic biopsy, followed by an endoscopic submucosal resection.
Results: The biopsy showed tight convolutes of capillary-sized vessels surrounded by collars of small, rounded cells set in a hyalinized, myxoid stroma. Immunohistochemically, these cells were positive for smooth muscle actin and type IV collagen (pericellular pattern), synaptophysin (focal positivity) and negative for CD34, CD117, desmin, S100 and cytokeratins. The diagnosis of gastric glomus tumor was rendered. The resection specimen revealed a submucosal well-circumscribed 2×1,5×1,5 cm nodule with identical histological features. The patient was disease-free 12 months postoperatively.

Conclusion: Visceral glomus tumors are rare neoplasms. When they arise in the gastrointestinal tract, the stomach (antrum) is the most frequent location. The differential diagnosis includes NET, epithelioid GIST and hemangiopericytomas. They usually behave in a benign fashion, although malignant cases have been reported. Surgical excision is the standard treatment.

PS-06-022

Immunohistochemical evaluation of replication Protein-A1 in gastric cancer: Clinicopathological associations

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Objective: Replication protein A1 (RPA1) is required for stabilization of single-stranded DNA at early and later stages of DNA replication being thus critical for eukaryotic DNA replication. In this study, we investigated for the first time the immunohistochemical expression of RPA1 protein in a series of 73 gastric carcinomas in relation with clinicopathological parameters (age, sex, Lauren's histologic classification, histologic grade, lymphovascular invasion, tumor size, depth of invasion (T), lymph node metastasis (N) and stage).
Method: A standard immunohistochemical method and a semi-quantitative evaluation for the detection of RPA1 Labeling Index (LI) were applied.
Results: Nuclear RPA1 immunoreactivity was seen in all carcinomas with a mean value of 26.5 %. Statistical significant correlations emerged between: 1. RPA1 LI and low T-category (p=0.009) 2. RPA1 LI and absence of lymph node metastasis (p=0,014). RPA1 LI was higher in cases without lymphovascular invasion; however this association did not reach statistical significance.
Conclusion: The widespread expression of RPA1 in gastric carcinomas suggests that this protein is implicated in gastric cancer growth. The observed significant associations between RPA1 LI and low T as well as N0 tumors could imply that RPA1 might offer a growth advantage in the early stages of gastric cancer progression.

PS-06-024

Pigmented histiocytic "Pseudotumoral" reaction due to endoscopic tattooing of the duodenum with India Ink

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Objective: India ink has been used for endoscopic tattooing to facilitate localization of a luminal abnormality at the time of surgery or repeat endoscopic examination. Recognition of this phenomenon is important to prevent misinterpretation of this _nding as other cause of black tissue deposits. Some of them can be easily excluded by microscopic examination; the others, however, necessitate special stains or, as illustrated by our observation, an adequate clinical information!
Method: A 76-year-old man was referred for enteroscopy for microcytic anemia. The procedure revealed a 2 cm flat umbilicated lesion of the duodenum. Endoscopic tattooing was performed to guide surgical excision.
Results: Histologic examination of the surgical specimen revealed a tubulovillous adenoma with low-grade dysplasia. The submucosa showed numerous aggregates of large cells containing a heavy black pigmentation. Special histologic stains were inconsistent with melanin or iron. This submucosal cellular infiltration was linked to the preoperative use of India ink when the notion of tattooing was "kindly" provided by the surgeon!
Conclusion: Despite a striking and misleading appearance, the microscopic finding of such phenomenon does not represent a pathologic state. Nevertheless, communication between enterologists, surgeons and pathologists are mandatory to assure prompt recognition and avoid unnecessary investigations.

PS-06-025

Altered gastric surface marker and mucin expression in first degree relatives of gastric cancer patients

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Objective: Gastric cancer phenotypes may be classified according to mucin secretion and surface markers as intestinal, gastric type or unclassified. This is the first study to assess the surface marker and mucin phenotype in first degree relatives of gastric cancer patients.
Method: 48 patients were prospectively recruited at out institution. Sections of gastric mucosa were stained immunohistochemically for CD10, MUC1, MUC2, MUC5AC and MUC6, and scored based on stain extent and intensity.
Results: Expression of CD10 was intermediate in 8 and 5 controls (p=0.02). MUC1 in superficial glands was intermediate in 12, high in 7 (p=0.015). In the deep glands MUC1 expression was intermediate in 8 and 2 controls, and high in 32 and 6 controls (p=0.66). One case show intermediate MUC2. MUC5AC expression was high in superficial mucosa in all cases and controls, and in the deep glands was intermediate in 8 and 2 controls (p=0.67). MUC6 was absent in superficial glands of all cases and controls, but highly expressed in deep glands. H. pylori was found in 8 cases and 2 controls (p=0.67).
Conclusion: Gastric CD10 expression is reduced and MUC1 expression is increased in first degree relatives of gastric cancer patients.

PS-06-026

Primary gastric choriocarcinoma: Two case reports

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Objective: Choriocarcinoma is a malignant neoplasm secreting β-hCG that grows rapidly and metastasizes widely. Primary gastric choriocarcinoma is very rare. We report two cases of primary gastric choriocarcinoma, one of which combined with adenocarcinoma.
Method: Two patients are 73-year-old woman and 77-year-old man. Gastroscopy revealed the protruded tumors with ulceration approximately 8.5 cm and 5 cm in size, respectively. In both cases, urine β-hCG was high. Both patients died 8 months and 1.5 months after the initial diagnosis due to distant metastasis.
Results: Histological examination confirmed the choriocarcinoma composed of intimate admixtures of cytotrophoblasts and syncytiotrophoblasts, associated with hemorrhage and necrosis. In one case, a small area of well to moderately differentiated tubular adenocarcinoma was contiguous to the choriocarcinoma component with relatively well-defined. The choriocarcinoma foci and adjacent adenocarcinomatous area showed positive immunoreactivity for β-hCG, but negative for CEA. However, adenocarcinoma component was positive for CEA, but negative for β-hCG.
Conclusion: In coexistent choriocarcinoma and adenocarcinoma of the stomach, a transitional form of tumor cells is occasionally found, so that a retrodifferentiation theory from adenocarcinoma to choriocarcinoma is supposed.

PS-06-027

Gastrointestinal stromal tumors and rare synchronous neoplasms

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Objective: Gastrointestinal stromal tumors are mezenchimal tumors which originatte from interstitial cells of Cajal or related stem cells from the gastrointestinal wall and have a typical immunoreactivity for CD117(c-kit protein). The most frequent localization is the stomach (about 50-60 %), followed by the duodenum and small intestine (30–40 %), esophagus (about 5 %), rectum (about 5 %), colon (about 2 %). Their association with other gastrointestinal tumors has been reported rarely in literature most frequently with adenocarcinoma or lymphoma and less with neuroendocrine tumors or squamous cell carcinoma.
Method: We present two cases of synchronous tumors.
Results: First case is that of a 73 years old man who underwent surgery for gastric neuroendocrine carcinoma accompanied by a gastric stromal tumor. The second case refers to a 74 years old male with squamous cell carcinoma in the middle third of the esofagus coexisting with gastric stromal tumor with a very low risk.
Conclusion: In literature there are reported less then 30 cases of sinchronous gastrointestinal stromal tumors with neuroendocrine tumors or scuamous cell carcinoma. A multidisciplinary approach is vital for treatment succes.

PS-06-028

The number of metastatic lymph nodes in adenocarcinoma of ampulla of Vater as a prognostic factor

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Objective: Although the increase of the number of lymph node (LN) metastasis indicates worse prognosis in carcinomas from other gastrointestinal tract organs, the prognostic implication of the number of metastatic LNs has not been well characterized in adenocarcinomas of ampulla of Vater (AAs).
Method: The number of metastatic LNs was evaluated with 1058 surgically resected AAs having at least 12 examined lymph nodes from the population based SEER database. A complex pattern of survival versus the metastatic LNs was captured by censored local regression. The effect of metastatic LNs on patient's survival time was investigated by the adaptive partitioning algorithm for identifying the most significant cutoff points of metastatic LNs.
Results: Two significant cutoff points (0 and 2) for the metastatic LNs were identified. These cutoff points segregated the patients into 3 groups with the statistically significant difference in median survival (no metastatic LNs, 478 cases, median survival time, 99 months; 1-2 metastatic LNs, 279 cases, 29 months; >3 metastatic LNs, 301 cases, 19 months, $p<0.01$).
Conclusion: On the basis of the present results, we propose that the nodal classification of AAs should be further classified into N0 (no metastatic LNs), N1 (1–2 metastatic LNs) and N2 (>3 metastatic LNs).

PS-06-029

Correlation of expression of yes-associated protein and phosphorylated yes-associated protein with clinicopathologic parameters in esophageal squamous cell carcinoma

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Objective: Yes-associated protein (YAP) has been investigated in carcinomas as a candidate human oncogene serving as a transcription co-activator in nucleus. The phosphorylated

form of YAP (pYAP) locates to the cytoplasm, preventing cellular proliferation by spatially segregating YAP from the nucleus.

Method: Samples from 142 patients of esophageal squamous cell carcinoma (ESCC) were studied using immunohistochemistry for YAP, pYAP and Ki-67.

Results: In 142 cases of ESCC, higher nuclear expression of YAP was correlated with tumor diameter, pathologic T category (1 versus 2–4), pathologic TNM stage (I versus II–IV) and Ki-67 expression in univariate analyses. Higher nuclear expression of YAP was significantly associated with worse overall and disease-free survival from Kaplan–Meier plots. Multivariate analysis showed higher nuclear expression of YAP to be an independent prognostic marker for overall survival. The cytoplasmic expression of pYAP in ESCC was not correlated with Ki-67 expression and was higher than in the normal esophageal epithelium, whereas nuclear expression of pYAP was not different in the two tissues.

Conclusion: Our results suggest that YAP shifts from the nucleus to the cytoplasm as a consequence of phosphorylation and is inactivated in ESCC. The nuclear expression of YAP is correlated with tumor growth and is an independent predictor for a worse prognosis of ESCC.

PS-06-031

Oesophageal metastasis from ovarian serous adenocarcinoma: A case report

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Objective: Oesophagus is an uncommon site of metastases, mainly originating from lung and breast. Ovarian carcinomas usually metastasize to pelvic structures and peritoneum and only two cases of ovarian metastasis to the oesophagus have been reported in the literature. We report a rare case of metastatic ovarian serous adenocarcinoma to the esophagus.

Method: Our patient, a 67 year-old woman, was diagnosed with carcinoma of the left ovary 8 years ago. She received neoadjuvant chemotherapy and underwent total hysterectomy. After a disease free interval of 5 years she complained of progressive dysphagia. An oesophageal biopsy was taken endoscopically.

Results: Microscopic examination showed infiltration of oesophageal mucosa by a moderately to poorly differentiated papillary adenocarcinoma, immunohistochemically positive for CK8/18, CK7, CA-125 and WT-1. Morphological and immunohistochemical features of the neoplasm were consistent with metastatic ovarian serous adenocarcinoma to the esophagus. The patient received adjuvant chemotherapy and was free of symptoms for 2 years, until recently, when her condition dramatically worsened.

Conclusion: Oesophageal metastases are rare, constituting approximately 2,7 % of malignant oesophageal neoplasms, and must be differentiated from primary tumours. Metastatic neoplasms may reach the oesophagus by haematogenous or lymphatic dissemination. Chemotherapy is the treatment of choice and ultimate prognosis is poor.

PS-06-032

Lesions associated with gastric cancer with implications in gastric carcinogenesis

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Objective: Recently, the pathological aspects implicated in "Correa's cascade" of gastric carcinogenesis were assessed.

Method: Our batch: 61 gastric cancer patients,43 males,18 females, average age=59.34 years. Witness group: antral biopsies from 96 patients with dyspeptic syndrome. We assessed the incidence of premalignant lesions.

Results: Gastric carcinomas: intestinal type(IT)(62.3 %), diffuse type(DT)(27.9 %), and mixed type(MT)(9.8 %). IT develop on the background of atrophic chronic gastritis (ACG)(65.8 %), with intestinal metaplasia(IM). ACG: more frequent in IT vs. DT(65.8 % vs.29.4 %, $p=0.0122$). IM: significantly more frequently in IT(68.4 %) and MT (66.7 %) vs. DT(23.5 %) ($p<0.001$). Type III IM: more frequent in IT(29 %) and MT carcinomas (33.3 %) vs. benign lesions(3.1 %) ($p=0.00006$). Witness group:10 patients presented epithelial dysplasia(10.4 %). Dysplastic lesions: more frequent in carcinomas of MT(66.7 %) and IT (60.5 %) vs. DT(23.5 %) ($p=0.0011$). Incidence of bacterial colonization: greater in IT(73.7 %) and DT(64.7 %) vs. witness group(51 %) ($p=0.00729$).

Conclusion: Our observations sustain the different histogenesis of cancers divided after Lauren classification and the etiopathogenic role of H.pylori in the development of gastric carcinomas. Assessment of type III IM is useful in early diagnosis of gastric cancer.

PS-06-033

The role of endo-biopsy in evaluating inflammatory and pre-neoplastic gastric lesions

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Objective: Our aim was to assess the concordance between the endoscopic and histopathologic diagnosis of gastritis.

Method: We included 96 dyspeptic patients; according to the Sydney system, we designed a protocol for description of endoscopic lesions and taking of the biopsies.

Results: We included 96 patients (58 females;38 males), mean age 60.1 years were. More severe gastritis: gastric body vs. antrum (p=0.041). In patients with endoscopic antral gastritis, histological confirmation had: sensitivity 97.9 %, specificity 50 %, PPV 98.9 %, NPV 33.3 %. In patients with endoscopic aspect of body gastritis, histological confirmation had: sensitivity 41.3 %, specificity 100 %, PPV 100 %, NPV 6.897 %. Infection with H. pylori:51 % of antral and 37.5 % of gastric body biopsies. Most cases of erosive antral gastritis, diffuse erythematous and petechial body gastritis were H. pylori(+). In some cases the endoscopy was normal, but histopathological examination identified H.pylori. Atrophy:48 % of antral and 54.2 % of gastric body biopsies, more frequent in older patients. Intestinal metaplasia:20.8 % antral 25 % gastric body biopsies. Dysplastic lesions:10.4 % of patients, 2(2,1 %) with high-grade dysplasia, in patients with antral diffuse erythematous gastritis.
Conclusion: Histopathological exam is mandatory for the diagnosis of gastritis, identifying pre-neoplastic lesions and confirmation of H.pylori.No concordance between endoscopic and histologic diagnosis of atrophy.

PS-06-034
Coexistence of Mixed Adenocarcinoma with Neuroendocrine tumor G1 (MANEC) and Leiomyomas of the stomach
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Objective: Mixed adenocarcinoma of the stomach with a NET as the neurondocrine component of the tumor is rare, as well as intramural leiomyomas. We present a case of a combined mixed epithelial carcinoma and neuroendocrine tumor with a random finding of mesenchymal tumor.
Method: A 72 year-old male came to our hospital complaining of abdominal pain. Endoscopic biopsy revealed the presence of invasive adenocarcinoma and a total gastrectomy was performed.
Results: The histopathological report concluded the presence of MANEC. The neuroendocrine component comprised a NeuroEndocrine Tumor (NET) G 1, which showed a strong immunoreaction to Chromogranin A, Synaptophysin and CD56 and none to Gastrin, Serotonin and ACTH. Mitotic rate, Ki-67 measured 1 %. The immunohistochemical control of the exocrine component was positive for CK7, CK20. That of the incidental finding of four small leiomyomas was positive for a-SMA and Desmin and negative for CD117, DOG-1 and CD34.
Conclusion: Gastric MANEC with a NET G1 component is a rare tumor. Gastric leiomyomas are also considered a rare finding. The coexistence of the two different neoplasms is even rarer, thus making it an interesting case report.

PS-06-036
Refractory celiac disease: Clinicopathological features of 12 cases
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Objective: Intraepithelial lymphocytes (IEL) in celiac disease (CD) are CD3+ and CD8+ and exhibit a polyclonal profile for T-cell receptor (TCR) rearrangement. In contrast, refractory CD (RCD) may be subdivided into type I (IELs polyclonal and normal phenotype) or type II (IELs monoclonal and/or aberrant phenotype). The aim was to analyze the RCD cases in our institution.
Method: The clinical, pathological, immunophenotypical and molecular findings of 12 RCD cases were reviewed.
Results: Our series comprised 7 men and 5 women with a median age of 57 years (range: 20–76). One patient had RCDI and 11 patients had RCDII. Six patients presented with no prior clinical or biopsy evidence of gluten sensitivity. Three patients developed RCDII after a history of CD of 12, 60 and 144 months and 1 of them developed EATL. Two patients presented IEL and EATL simultaneously. Phenotype was aberrant in 8 out of 11 and TCR was monoclonal in 10 out of 10 tested cases.
Conclusion: In our series, 6 cases presented as RCDII de novo. The IEL phenotype study and the TCR rearrangement were useful for identifying cases with RCD.

PS-06-037
Gastritis cystica polyposa in an unoperated stomach treated by endoscopic polypectomy
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Objective: Gastritis cystica polyposa is a unique lesion found on occasion at the stoma of a gastrojejunal anastomosis. However, GCP is rarely found in an unoperated stomach.
Method: A 51-year-old woman with abdominal discomfort and vomiting. Physical examination, routine hematological examination and biochemical tests were within normal limits, exept mild anemia.
Results: Upper GI endoscopic examination revealed a pedanculated polyp, in the greater curvature. Endoscopic ultrasonography revealed a polypoid heteroechoic mass with cystic area and 20×22 mm diameter in posterior wall of gastric body. Polypectomy was performed without any complications. Histological examination of the protruding lesion revealed some misplaced cystic glands were entrapped in dense disorganized bundles of smooth muscle of muscularis mucosa surrounded by a rim of lamina propria. These findings were consistent with gastritis cystic polyposa.

Conclusion: GCP is a unique type of chronic gastritis represented by a sessile elevated lesion along a suture line, occurring a long time after Billroth- II surgery or simple gastrojejunal anastomosis. When these findings are considered, it may be reasonable to speculate that there are close relationships among DGR, GCP and gastric stump carcinomas.

PS-06-038

Gastrosplenic Fistula from Hodgkin‘s Lymphoma, manifesting as upper gastrointestinal bleeding

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Objective: Primary gastric Hodgkin's lymphoma is reported in only 2 % of patients with primary gastric lymphomas. Most cases are observed in the course of systemic disease.
Method: We report a case of Hodgkin's lymphoma that was complicated by gastrosplenic fistula manifesting as upper gastro-intestinal hemorrhage.
Results: We report the case of a 52 years old man with a 10 years history of untreated Hodgkin’s lymphoma. He was hospitalized for a massive upper gastrointestinal bleeding. The gastroscopy showed a large malignant ulcer of the small curve of the stomach. A gastric fistula on the posterior fundus was objectived. Histological examination of biopsies taken showed the ulcer to be benign and the edges of the orifice of the fistula to be Hodgkin lymphoma by detection of Reed Sternberg cells. A panel of immunohistochemical markers were stained for. A predominant expression of CD30 and CD15 were seen in the cells while being negative of CD3 and EMA. An abdominal CT demonstrated a cavitary splenic lesion with an air-fluid level and extravasation of gastric contrast into the hilum of the spleen, consistent with a gastrosplenic fistula. The diagnosis of gastrosplenic fistula from Hodgkin’s lymphoma was made.
Conclusion: Gastrosplenic fistula is an unusual occurrence and should be recognized as a possible complication of Hodgkin’s lymphoma with splenic or gastric involvement.

PS-06-039

An extremely rare tumor of distal duodenum: Adenosquamous carcinoma

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Objective: Tumors of the duodenum commonly arise around the ampulla of Vater, and most common tumor type is adenocarcinoma. A review of the English literature revealed a few cases of pure squamous cell carcinoma of the duodenum and only one case of adenosquamous carcinoma. Here, we reported a primary adenosquamous carcinoma of duodenum unrelated to papilla vateri.
Method: A fifty-seven years old female was admitted to our hospital with weakness, constipation and back pain after meals. The endoscopic examination revealed a duodenal tumor distal to the ampulla of vater. Computed tomography also detected a mass in the head of the pancreas. After the endoscopic biopsy of duodenum was reported as 'adenocarcinoma with squamous differentiation', Whipple procedure was performed.
Results: Macroscopically, tumoral lesion was seen in duodenum, 2 cm distal to the papilla vateri, infiltrating the adjacent pancreatic tissue. Distal stomach and papilla vateri were tumor-free. Microscopic examination revealed adenosquamous carcinoma, and immunohistochemical-histochemical studies displayed the two different component of the tumor. One peripancreatic lymph node was metastatic.
Conclusion: Adenosquamous carcinoma is an extremely rare tumor of duodenum. Only one case has been published in the literature so far. Although we assume that it may derived from the pluripotent stem cells, its exact pathogenesis is still unclear.

PS-06-040

Significance of mucin expression patterns, EGFR expression and HER2 expression/amplification in gastric carcinoma

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Objective: The gastric carcinomas with MUC1 expression are more likely to be advanced stage. MUC5AC is expressed in diffuse type, MUC2 is expressed in mucinous carcinoma. EGFR overexpression commonly leads to radiation resistance. HER2 gene amplification has been detected in 10–20 % of gastric adenocarcinomas. Expression of these markers are important to predict clinical outcome and targeted therapy modalities.
Method: Fifty-five patients were included to clarify the relationship between histopathologic features and immunohistochemical MUC1, MUC2, MUC5AC, EGFR, HER2 expression profiles, HER2 amplification status in gastric carcinoma.
Results: Of the 46 MUC1(+) cases, 37 were T3/T4, 31 showed perineural invasion. There was a statistically significant correlation between MUC2 expression-mucinous subtype; MUC5AC expression-poorly cohesive subtype ($p<$ 0.01. HER2 expression was 0 in 78,2 %, 1+ in 9,1 %, 2+ in 5,5 % and 3+ in 7,3 % of the samples. Of the 6 HER2 amplified 4 cases were (+++) and 2 cases were (++) by IHC. HER2 overexpression showed a significant association with HER2 amplification ($p<0.001$). EGFR expression levels were 0 in 80 %, 1+ in 10,9 %, 2+ in 1,8 %, 3+ in 7,3 % of the cases. HER2 amplified 4 cases showed negative immunoreactivity with EGFR antibody.

Conclusion: Although we studied a small group, all the results were concordant with the literature data.

PS-06-041

HER2 status in gastric cancer: A comparison of two novel in situ hybridization methods (IQ FISH and dual colour SISH) and two immunohistochemistry methods (A0485 and Herceptest)

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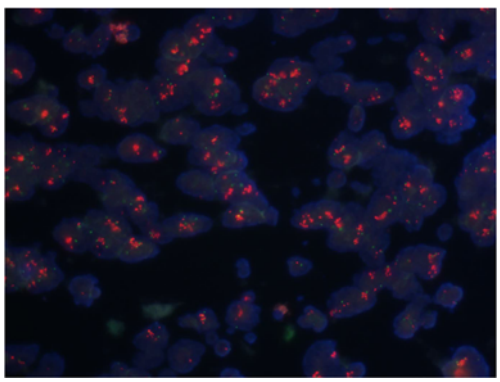
Objective: Contrary to breast HER2 testing, optimal ISH method and antibody for gastric HER2 testing is unclear. The aim of the study was to examine HER2 status in gastric adenocarcinomas comparing rabbit polyclonal antibody A0485 and Herceptest immunohistochemistry (IHC) with dual probe HER2 IQ fluorescence in situ hybridization (FISH) and fully automated dual colour silver in situ hybridization (SISH) methods.
Method: IHC and ISH were carried out on gastrectomy specimens of 88 patients.
Results: HER2 expression was (−) in 65, (+) in 5, (++) in 6, (+++) in 12 cases by A0485 IHC. IHC (+) 3cases and (++) 3 cases were (−) by Herceptest. IHC (−) amplified one case was (++) by herceptest. All A0485 and Herceptest (+++) 12 cases were amplified and HER2 amplification was detected in 15.9 % of the cases by SISH and FISH. IHC (+) two cases showed focal heterogeneous low level amplification by SISH and IHC (++) 2 cases also showed focal amplification by FISH and SISH.
Conclusion: In focal amplified cases it's diffucult to decide if the percentage of the amplified cells meet the '10 %' cut off value. The concordance between HercepTest/A0485 IHC and ISH is perfect in (+++) cases. But (+)/(++) rates are lower and less related with amplification in HercepTest than routine IHC.



PS-06-042

The distribution and intensity of amyloid deposition in gastric biopsies

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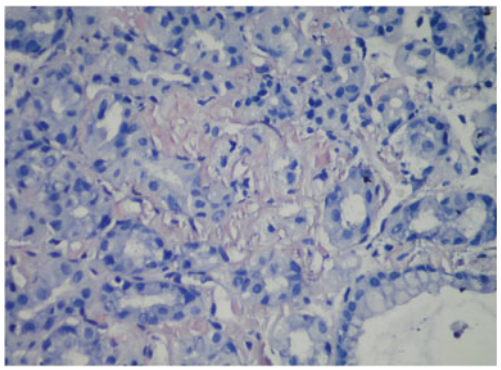
Objective: Amyloidosis is characterized by localized or systemic amyloid deposition. Although rectal biopsies are generally preferred for diagnosis of systemic amyloidosis, upper gastrointestinal tract is not infrequently involved. However, less is known about the presence, distribution and intensity of amyloid deposition (AD) in gastric biopsies.
Method: Hematoxylin-eosine (HE) sections of endoscopic biopsies of 77 patients with systemic amyloidosis were reevaluated and Congo-red staining was used for definitive diagnosis.
Results: AD was found in 69 (89.6 %) cases. The intensity was severe (easily visible at scanning magnification on HE) in 48.1 %, moderate (suspicious on HE and positive with Congo-Red) in 32.5 % and mild (barely visible even with Congo-red) in 9.1 % of them. AD was most frequently encountered in vasculary walls (88.2 %) followed by muscularis mucosa (62.3 %) and lamina propria (46.8 %). Fourteen patients (18 %) had only vascular and one patient (1,29 %) had only muscular deposits, Thirty cases (39 %) showed vascular, muscular and stromal AD. Stromal involvement was only seen in widely distributed cases. ADs tended to involve more than one localization as intensity increased ($p<0.0001$, chi-square).
Conclusion: Upper gastrointestinal involvement is frequently seen in systemic amyloidosis. AD can be either vascular, stromal or muscular and easily be detected by HE.



PS-06-043

Histopathological aspects of gastric neuroendocrine tumors with and without lymph nodes metastases and prognostic significance

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Objective: Gastric NETs are uncommon tumors with increasing incidence in the latest decades. The aim of this study was the histopathological analysis of 8 cases.
Method: We present 8 cases of gastric NETs (surgical resected) diagnosed in Fundeni Clinical Institute between 2005 and 2011, reviewed according to the WHO 2010. The

mean age was 67.37 (range 53–78 years), a female to male ratio of 1:1. One of the tumors was multicentric. The average size is 6.82 (range 0.3–14 cm). Six (75 %) present metastases in lymph nodes. One (12.5 %) is pT1, four (50 %) pT3 and one (12.5 %) pT4. Immunohistochemistry for general neuroendocrine markers (synaptophysin, chromogranin A, Ki 67) was performed in all cases.
Results: According to WHO 2010 classification, one (12.5 %) was neuroendocrine neoplasm G1, four (50 %) were neuroendocrine carcinomas G2, all of these four (100 %) with lymph nodes metastases. Three (37.5 %) were neuroendocrine carcinomas G3, 2 of them (66.6 %) with lymph nodes metastases. The patients with lymph nodes metastases had a worse clinical outcome.
Conclusion: The type and stage of the gastric NETs are among the most important things for best management. With an exact diagnosis and adequate treatment has improved the prognosis.

PS-06-044
Eosinophil granulocytes: New players in gastric carcinogenesis induced by Helicobacter pylori?
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Objective: Popp and Micu are first authors in equal proportions Helicobacter Pylori (HP) induces a continuum of lesions (chronic gastritis, glandular atrophy, intestinal metaplasia and dysplasia – carcinogenetic cascade [CC]) evolving towards intestinal type gastric carcinoma, but also potentially reversible after HP eradication.
Method: Our study included 3069 gastric endoscopic biopsies diagnosed using Sydney criteria by two independent fully trained pathologists. We evaluated several histopathological parameters, correlating the degree of inflammation, atrophy, metaplasia, regenerative hyperplasia and dysplasia with the presence of HP infection.
Results: Some of our results confirmed theory of HP-triggered CC, several data suggesting the idea that there are understudied factors involved in modulating carcinogenesis. Correlations of intestinal metaplasia and activity of gastritis showed that the number of neutrophils is directly proportional with extension of intestinal metaplasia and inverse proportional with gastric atrophy (P=1.01028E-07), suggesting that the presence of neutrophils is the trigger of phenotype alterations leading to metaplasia. Simultaneous presence of numerous eosinophil granulocytes and very few neutrophils was identified associated with mild or absent intestinal metaplasia, supporting the idea that eosinophils favor regenerative changes to the detriment of intestinal metaplasia.
Conclusion: This study identifies histopathologically quantifiable factors interfering in carcinogenesis which can influence management of HP infected patients.

PS-06-045
Gastric carcinoma with osteoclast-like giant cells
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Objective: Throughout the vast variety of gastric neoplasms, gastric carcinoma with osteoclast-like giant cells (OGCs) is one of the rarest. To the best of our knowledge only 9 other cases have been reported in the English literature. We present a case of gastric carcinoma with OGCs in an 81 year-old male patient.
Method: We received a specimen of subtotal gastrectomy and lower esophagectomy. At the gastro-esophageal junction an exophytic tumor, 2.2 cm in greatest diameter, was observed. Multiple sections from the tumor were examined histologically and immunohistochemically.
Results: Sections from the tumor showed gastric carcinoma of intestinal type, stage pT1bpN0. Diffusely among the neoplastic cells giant multinuclear cells, resembling osteoclasts, were observed. Those cells were positive for CD68, lysozyme, vimentin and negative for AE1/AE3, CK8/18, hHCG and LMP1. Moreover in a random section from the gastric fundus a spindle cell lesion was revealed, which was positive for CD117 and CD34 and was diagnosed as GIST.
Conclusion: The presence of OGCs is an extremely rare finding in gastric carcinomas. Due to the low number of reported cases its prognostic value is under discussion. Furthermore this is the first reported case of co-existence with GIST.

PS-06-046
Assessment of human papillomavirus DNA in esophageal squamous cell carcinoma
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Objective: Human papillomavirus (HPV) infection is a known risk factor for the development of squamous cell carcinoma (SCC) of the cervix, the oropharynx and the anogenital region. The aim of our investigation was to assess the prevalence of HPV DNA in patients with esophagus cancer in the Western population.
Method: Formalin-fixed paraffin-embedded blocks from 37 consecutive patients who underwent esophageal endoscopic mucosal resection or esophagectomy for SCC were tested for the presence of HPV DNA by polymerase chain reaction using consensus primers GP5+/GP6+. Viral genotyping was determined by type-specific primers.

Results: Among the total of 37 cases, no HPV DNA was detected in 33 cases (89.2 %). 4 cases were tested HPV positive (10.8 %), of which 1 was HPV 16+, 1 was HPV 18+ and 2 were non-high-risk HPV type. The non-high-risk HPVs were detected in patients with previously treated SCC of the mouth ($n=1$) and the oropharynx ($n=1$). Patients with high-risk HPV-positive tumors had no history of oropharyngeal cancer.
Conclusion: Our study revealed the presence of oncogenic HPV genotypes in a subset of esophageal cancer. The low rates of viral infection detected suggest that HPV unlikely represents a significant etiologic factor in esophageal carcinogenesis. Further studies are needed to confirm these data in larger populations.

PS-06-047

pERK activation in esophageal carcinomas: Clinicopathological associations

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Objective: MAPK (Mitogen-Activated Protein Kinase) pathway is considered a control regulator in various malignant tumors. In our study we examined the possible prognostic significance of MAPK pathway in Greek patients with esophageal cancer.
Method: We searched for mutations in exons 18, 19, 20, 21 of EGFR gene, codons 12 and 13 of K-RAS gene and exon 15 of B-RAF gene by High Resolution Melting Analysis (HRMA) and Pyrosequencing in 44 esophageal carcinomas. Immunohistochemistry was performed in 29 cases in order to evaluate expression levels of pERK (Extracellular - signal Regulated Kinase).
Results: A somatic K-RAS mutation at codon 12 was detected in one laser microdissected squamous cell carcinoma, whereas none of the cases displayed mutations in EGFR and B-RAF genes. Elevated nuclear as well as cytoplasmic pERK expression (100 % and 62 % of cases respectively) was observed independently of EGFR and B-RAF mutational status. Increasing pERK nuclear and cytoplasmic expression as well as the intensity of nuclear staining was found to be significantly correlated with tumor grade in univariate and multivariate statistical analysis.
Conclusion: Our findings demonstrate the presence of activated ERK despite the low frequency of upstream alterations, implicating ERK activation in the acquisition of a more aggressive phenotype in esophageal cancer.

PS-06-048

Gastroblastoma: A rare epitheliomesenchymal biphasic tumour of the stomach

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Objective: Gastroblastoma is a recently described gastric tumour that occurs in children and young adults, displaying epitheliomesenchymal biphasic features.
Method: An 18-year-old female, asymptomatic until 4 months before admission, complained of abdominal pain. Imaging evaluation disclosed a solid and cystic tumour involving the stomach. The surgical specimen displayed a nodular, solid and cystic tumour with 10.5 cm largest dimension. Histologically, the tumour was biphasic with epithelial and predominantly mesenchymal components. The epithelial component was arranged in nests, cords and tubules; the mesenchymal component comprised short bundles of spindle cells, foci of multinucleated cells and variable myxoid/collagenous stroma. Tumour cell atypia was mild and mitotic index low. There was no evidence of lymphovascular/perineural tumour invasion. Lymph nodes were free of metastases. Immunohistochemically, epithelial cells expressed AE1/AE3, CAM5.2, CD56 and, focally, CD10; mesenchymal cells expressed vimentin, CD10 and, focally, CD56. Altogether, these features support the diagnosis of gastroblastoma.
Conclusion: Gastroblastoma is a rare tumour (only 4 cases reported so far by Miettinen et al., 2009 and Shin et al., 2010). In the differential diagnosis, synovial sarcoma, carcinosarcoma and teratoma should be considered. Gastroblastoma behavior remains unsettled, having been suggested to be a low-grade malignant tumour.

PS-06-049

Mixed adenoneuroendocrine carcinomas among gastrointestinal tract carcinomas

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Objective: Mixed adenoneuroendocrine carcinomas (MANECs, WHO,2010) of the gastrointestinal tract are rare neoplasms, presenting at least 30 % of each component. Aim: To increase the awareness of MANECs in gastrointestinal tract carcinomas.
Method: We present a series of four cases of gastrointestinal MANECs admitted in Fundeni Clinical Institute (2007–2010)-two of the stomach, one of the colon and one of the choledocus.
Results: All of the patients were males with the age range between 38 and 62 years. All of them underwent surgical resections. The tumors varying in size from 1 cm (choledocus) to 12 cm (stomach); all of them were infiltrative, invading the adjacent organs (except one case of the stomach). Microscopically, the tumors had two distinct components: adenocarcinoma with varied grade of differentiation (G1-G3) and neuroendocrine carcinoma, grade 2 or 3. One case had mixed lymph node metastases. The immunohistochemistry were

performed in all cases and included panCK, CK7, 19, 20-pozitive in epithelial component, Chromogranine, Synaptophysine, NSE-pozitive in neuroendocrine component and Ki67. One of the patients died in 2 days after surgery, other three were alive at the time of report.
Conclusion: Gastrointestinal MANECs constitute a diagnostic challenge because of frequent identification only of one component of the neoplasm, which leads to an incomplete diagnosis and suboptimal treatment.

PS-06-050
GIST and adenocarcinoma combination in digestive system
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Objective: GIST and adenocarcinoma combination are rare diseases, mechanism of its development is not clear. Histogenesis and morphogenesis of these oncological pathology discuss.
Method: We have 3 cases of GIST and adenocarcinoma of the gaster, colon during 2000–2012 year. Clinico-morphological analysis was performed. Histological, imminohistochemical, histochemical techniques were used.
Results: GIST demonstrated spindle-like and epithelioid types tumours, invading wall of the gaster with secondary changes (hemorrhages, necrosis, infalammation). In 1 case we found metastasis of GIST in gastric lymphatic nodes. Sizes of tumours were more than 5 cm in diameter. Adenocarcinoma was tubular, mucous types of the colon with deep invasive character of growth all wall the colon.
Conclusion: We concider that combination of GIST of the gaster and adenocarcinoma of the colon have common pathogenesis. Cells of the GIST have multifunctional capacities. Combination of the GIST and adenocarcinoma can reflect mutations of the genes participating in its development but this position need to future investigation.

PS-06-051
Her-2/neu assessment for gastric carcinoma: Validation of scoring system
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Objective: Gastric cancer is the second leading cause of cancer mortality in the world. Amplification of HER-2/neu oncogene has become an important biomarker for identifying patients who will respond to HER-2 targeting therapy. The rate of HER2 positivity in gastric cancer is variable, ranging from 6 % to 35 %.
Method: In our study HER-2/neu expression was assessed on 73 samples of primary gastric cancer, using immunohistochemistry. For 19 patients preoperative biopsy samples and resected specimens were available. Additionally, internal ring study was performed to estimate intraobserver variability of IHC scoring among pathologists at our Department.
Results: HER-2/neu overexpression was found in 10 (13.6 %) of the tested samples, and it was more common in intestinal (22.5 %) than the diffuse type (3.7 %). Not one of the 6 analyzed mixed type tumors showed HER-2/neu expression. For the paired samples (preoperative biopsy samples and resected specimens) the concordance rate for HER-2/neu expression was 94.7 %. Concordance rate of 95 % was established among pathologists with Fleis kappa 0.88.
Conclusion: According to high concordance rate in paired samples we consider appropriate to evaluate HER2 expression on biopsy specimens, especially in unresectable cases, and to re-evaluate it on resected specimens if available, due to high heterogeneity of a gastric cancer.

PS-06-052
Apoptosis and cytotoxic T-cells in lymphocytic oesophagitis
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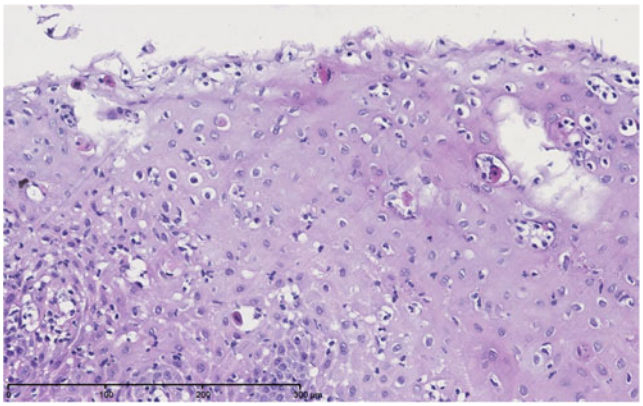
Objective: Lymphocytic oesophagitis is a poorly understood disease of unknown origin, said to be characterized by an epithelial infiltration of lymphocytes. Up to date only few and non-specific histological changes were described.
Method: We collected 37 biopsies of 32 patients with lymphocytic oesophagitis (20 men, 12 women). Grading was done according to Purdy et al. and by the number of intraepithelial lymphocytes (50/HPF as cut off value). The inflammatory cells were characterized by using the t-cell and chemokine STRATIFYER robot (STRATIFYER Molecular Pathology GmbH, Cologne, Germany).
Results: Apoptotic keratinocytes could be detected in 71,4 % of severe cases (15/21) as well as in 25 % of mild cases (4/16) and were found in all epithelial layers. High levels of cytotoxic T-cells were present in 80 % of severe cases with apoptosis (12/15) and in 5 cases without apoptosis, mostly mild cases.
Conclusion: Our data show that apoptosis is usefull in grading of lymphocytic oesophagitis, as it can be found predominantely in severe forms. Due to the presence of cytotoxic T-cells an underlying form of lichenoid inflammation can not be fully excluded in these cases. Further studies should focus on the question, whether

our findings are a hint to an autoimmunologic mechanism or not.



PS-06-053

CDX2 and mucins expression in gastric intestinal metaplasia

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Objective: The homeobox protein CDX2 is a transcription factor involved in early intestinal differentiation and regulates the transcription of several intestinal genes, including intestinal mucin (MUC2). The genetic events responsible for the transdifferentiation that occurs in intestinal metaplasia (IM) are not well understood.
Method: In the 6 year period between 2005 and 2010 a 152 gastric biopsies were examined at the Pathology Department of VNMU. Our panel of primary monoclonal antibodies included: CDX2 (1:100; DAKO, Denmark), anti-MUC5AC (1:100; Novocastra, UK), anti-MUC2 (1:100; Novocastra, UK), anti-MUC6 (1:100; Novocastra, UK).
Results: CDX2 protein was strongly expressed in the nuclei of both goblet cells (GC) and absorptive cells (AC) in the foci of complete IM, but it was significantly decreased in the foci of incomplete. MUC5AC was expressed in the cytoplasm of both GC and AC in incomplete IM, whereas it was expressed in only a few GC but not AC in complete IM. MUC6 was expressed in several deeper glands of incomplete IM but not in complete IM.
Conclusion: CDX2 can be used as an important marker in the pathological diagnosis of early gastric IM. IM with low expression of CDX2 and MUC5AC may serve as predictive markers for gastric cancer.

PS-06-054

Gastrointestinal stromal tumor mimicking pancreatic carcinoma

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Objective: Gastrointestinal stromal tumors (GISTs) are primary mesenchymal tumors that arise in the GI tract. Only 3–5 % of GISTs occur in the duodenum. Here, we report a rare case of duodenal GIST with extramural growth that mimicked a pancreatic tumor.
Method: A 57 years old male patient was admitted to our hospital for duodenal ulcer and gastrointestinal bleeding which was diagnosed in an another clinic by endoscopy. Abdominal MR of the patient showed a 5×5,5 cm necrotic mass in the uncinate process of the pancreas which was excised by whipple operation.
Results: Macroscopically, the resected specimen consisted of solid mass that was connected to the patient's duodenal wall but not to the parenchyma of the pancreas. Microscopic examination of the tumor showed spindle shaped and epithelioid cells with mild nuclear pleiomorphism. Immunohistochemistry revealed that the cells are strongly positive with CD117, with focal expression of CD34 and SMA.
Conclusion: GISTs are low-grade malignant mesenchymal tumors of the GI tract and are believed to originate from the neoplastic transformation of the Cajal cells, which are located between the longitudinal and circular layers of the muscularis propria. They most frequently arise from the second part of the duodenum where they push or infiltrate into the pancreas. In our case report, the patient's tumor exhibited extramural growth and mimicked a pancreatic tumor.

PS-06-055

Reflux oesophagitis: A delusion of endoscopist and/or pathologist?

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Objective: Reflux oesophagitis comprises patients diagnosed as endoscopic oesophagitis (EO) with minimal histologic abnormality and those showing "microscopic oesophagitis" (MO) with normal endoscopy. We, therefore, aimed to evaluate the discriminatory value of histologic criteria for both groups with reflux oesophagitis.
Method: The study group comprised of 416 patients (145 children and 271 adults) who underwent upper gastrointestinal endoscopy where 113 were diagnosed as EO. Histological assesment for basal cell hyperplasia (BH), papillary elongation (PE), dilatation of intercellular spaces (DIS), intraepithelial eosinophils, neutrophils and lymphocytes was performed. Chi-square test was used for statistical analysis.
Results: All morphologic parameters were more commonly observed in patients without EO. The presence of severe PE (p=0.001) and DIS (p=0,01), together with high lymphocyte and neutrophil counts (cut off values of >10 and >2,

respectively) ($p<0.001$) were the most discriminatory features for the diagnosis of MO. EO was significantly more frequently observed in children compared to adults ($p<0.005$). The presence of DIS ($p<0,001$), PE ($p=0,001$), and high neutrophil counts ($p<0.05$) was significantly more common in adults.
Conclusion: The results of our study suggest that endoscopic biopsy is necessary in all patients with or without EO for the diagnosis of reflux oesophagitis.

PS-06-056
Invasion line complexity analysis in resectable gastric cancer cases reveals differences in histoarchitectonic and invasiveness
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Objective: Characterization of gastric cancer invasiveness seems to be one of most important predictor of clinical outcome, dependent on a G and pT grade. Moreover, image differs along tumor invasion line. From the other side, fractal measurement seems to be appropriate for complexity analysis. Thus we attempted to characterize gastric cancer invasion line using complexity measurements, fractal parameters as fractal dimension (D and ΛD), lacunarity and image statistics.
Method: The study based on 19 resectable gastric cancer cases, 13 Laurén intestinal type gastric cancer and 6 diffuse type. Full depth gastric wall slides were stained with pan-cytokeratin. Serial digital images were collected, local pT, G, and image fractal measurements were established for each image.
Results: The presence of necrosis played an significant role in estimating complexity only in Laurèn intetstinal type (lowering ΛD and lacunarity). Histoarchitectonic elements in intestinal cancer type could be characterized by D, inflammation intensity was dependent on the length of the invasion line and ΛD. The pT showed dependence on lacunarity, budding type reflected in D. In gastric cancer diffuse type only inflammation and pT showed dependence on fractal dimensions.
Conclusion: Fractal analysis and image statistics provides a new diagnostic support in gastric cancer studies.

PS-06-057
The factors influencing on histological tumor regression grade (TRG) in gastric cancer
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Objective: The identification of factors influencing on the histological tumor regression grade (TRG) seems to be important in therapy planning. The aim was the assessing of histological features and other parameters influencing on the grade of TRG.
Method: The study encompassed 66 cases with gastric cancer subjected to gastrectomy, after preoperative radio-chemotherapy (years 2003–2010) in our Institute. The dependences between the TRG grade, and sex, age, tumor localization, tumor gross morphology, tumor histology, and invasion data were statistically assessed. (nonparametric methods).
Results: Patients age varied between 36 and 78 years old, (mean 58,6±9,4 years; 25 females and 50 males). Despite radio/chemotherapy histological examination showed in 12 % no response, in subsequent 30,6 % - partial response low grade, whereas in 34,7 % - partial response high grade and in 22,7 % complete therapeutic response. Analysis of cancer types in resected tissues showed in 66 % adenocarcinoma, in subsequent 30 % poorly cohesive carcinoma, 4 % specific type of gastric cancer. Only histological type of tumor, pT and N stages were correlated with TRG grade.
Conclusion: Tumor response to radio/chemiotherapy depends mainly on tumor histotype and clinical staging.

PS-06-058
Clinicopathological and prognostic significance of p53 and TGF-beta 1 in patients with gastric cancer
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Objective: The aim of this study is to investigate p53 value and it relationship with TGF-beta1 expression, clinicopathological parameters and survival in patients with gastric cancer.
Method: In 53 patients who had undergone gastrectomy for gastric cancer, the expression levels of p53 and TGF-beta1 in gastric cancer tissues were examined immunohistochemically (IHC). p53 gene alterations were examined by fluorescence microscope after in situ hybridization performing.
Results: We found p53 expression in all of gastric cancer specimens. Also, 47.2 % of specimens were TGF-beta1 expression positive. The patients with p53 expression had worse prognosis after surgical therapy compared to those without. The median survival of p53-positive patients was 4.8 months whereas the median survival of p53-negative patients was 9.1 months ($p=0.027$; log-rank test). Also, 88.9 % from patients with p53-positive status is in T1-T2 stage vs. 37.8 % in T3-T4 ($\chi 2=7.88$, $p=0.005$). Finally we found that 56.1 % from p53 expressive tumors have TGF-beta1 expression and 16.7 % were non-expressive ($\chi 2=5.79$, $p=0.016$).

Conclusion: In conclusion our results suggest that low expression of p53 and TGF-beta1could be useful as a marker of poor prognosis and had prognostic value for gastric cancer patients.

PS-06-059

Primary gastric mantle cell lymphoma diagnosed from gastrectomy specimen: A case report

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Mantle cell lymphoma (MCL) is relatively a rare subgroup of non-Hodgkin lymphoma. We have experienced an uncommon case of MCL. A 65-year-old man was admitted to emergency service for upper gastrointestinal bleeding as melena. Gastric corpus wall thickness found increased and splenomegaly determined at whole abdominal ultrasonography. Endoscopic examination revealed subsequently, 1 cm diameter polypoid lesion at corpus anterior wall and 2 cm dimensioned elevated and vascularised lesion at corpus posterior wall. Endoscopic biopsy had reported as active gastritis and mucosal reactive hyperplastic changes with ulcerative background. After than total gastrectomy and splenectomy specimens examined diffuse infiltration of monotonous medium-sized, atypical lymphoid cells with hyperchromatic nuclei. These cells were positive for CD20, CD5, CD43, bcl-2 and CD79a, but negative for CD10, CD23 and bcl-6. Atypical lymphoid cells were present even in splenic hilus and lesser curvature lymph nodes. We reported this case as Primary Gastric Mantle Cell Lyphoma according to morphologic and immunohistochemical staining features.

PS-06-060

How about gastric HER2 positivity in our institute?

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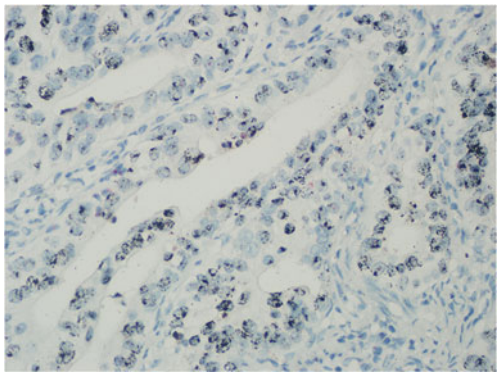
The published data of the multicenter phase III trial (ToGA study) showed that patients with tumors which overexpress HER2 as defined by immunohistochemistry (IHC) 2+ and ISH positive or IHC 3+ are eligible for the targeted therapy. The aim of this study was to find out HER2 overexpression and amplification rates in gastric cancer cases from our archives. Eighty eight formalin fixed and parafin embedded tumor tissue samples from Turkish gastric carcinoma patients were studied with (IHC) and brightfield double in situ hybridization (BDISH). The criteria defined by Hofmann et al. was uesd for IHC evaluation. HER2 expression was found (−) in 65 (73.9 %), (+) in 5(5.7 %), (++) in 6 (6.8 %), (+++) in 12 (13.6 %). BDISH showed that HER2 gene was amplifie (d in 18(20.5 %) of the patients. Of the amplified cases 12(66.6 %) was (+++), 3(16.6 %) (++), 2 (11.2 %) (+), 1(5.6 %) (−). Highly, homogenous amplified cases were neither (+++) nor (++) and correlated with protein overexpression. IHC (−)/(+) cases showed heterogeneous, low level amplification. HER2 amplification was significantly associated with HER2 overexpression, histological subtype, location, depth of invasion, size ($p<0.05$). IHC and BDISH correlation is perfect for (+++) cases. Unlike breast carcinoma, 5 % of IHC (−)/(+) gastric carcinoma cases show heterogeneous amplification.



PS-06-061

Morphometric analysis in gastrointestinal stromal tumors

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Objective: Gastrointestinal stromal tumors (GISTs) have a spectrum from minimal indolent neoplasms to sarcomas. In this study the tumor behavior are compared with morphometric results.

Method: Morphometric cellular parameters such as mean nuclear area (MNA), mean nuclear length (MNL), mean nuclear width (MNW), mean nuclear density (MND), mean cytoplasmic area (MCA) and mean nuclear-cytoplasmic ratio (MNCR) were evaluated in hematoxylin and eosin stained slides of 36 spindle-cell GISTs (11 benign and 25 malignant) by using a computer-assisted image analysis system. Morphometric results were compared with tumor behavior.

Results: MNA, MNL, MNW and MCA are 50.57±5.63, 15.35±1.18, 4.49±0.56 and 135.72±13.85 mcm in benign GISTs, respectively. MND and MNCR are 179±13.6 and 1:2.7 also in benign group. MNA, MNL, MNW and MCA are 51.03±5.55, 14.75±0.70, 4.72±0.43 and 127.22±11.58 mcm in malignant GISTs, respectively. MND and MNCR are 193.9±16.6 and 1:2.5 also in malignant group. No correlation was found between morphometric features and gastrointestinal stromal tumor behavior ($p>0.05$).

Conclusion: This study showed that the tumor cellularity and nuclear-cytoplasmic ratio aren't the parameters to predict

aggressiveness of GISTs. These morphometric parameters may not be used in the prognosis of GISTs behavior.

PS-06-062

Signet ring cell carcinoma of stomach diagnosed with bone marrow metastasis: A case report

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We report a 74-year-old man who had been searched for bicytopenia (anemia and thrombocytopenia). Bone marrow examination revealed extensive bone marrow metastasis of signet ring cell carcinoma. PAS, d-PAS and mucin histochemical markers performed to bone marrow sample which were all positive. Immunohistochemical markers were positive with MUC-1, MUC-5 AC, MUC-2 (focal staining), CK7, CK20, EMA, CEA and negative with vimentin, CD10, chromogranin. According to morphologic and immunohistochemical results we thought primarily gastrointestinal system malignancy, particularly stomach carcinoma. Upper gastrointestinal endoscopy performed subsequently, hemorrhagic ulcerative lesion had seen and taken biopsies. Endoscopic biopsy results showed metastatic signet ring cells origin from stomach. We report this case because bone marrow metastasis can be found commonly in some malignant tumors but diagnosing a nonhematologic malignancy from bone marrow is an unusual event.

PS-06-063

Gastric Her2 Immunocytochemistry: Differences in methodology affecting membrane staining and interpretation. Findings of the UK NEQAS ICC & ISH external assessment service

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Objective: Gastric cancer patients showing IHC 3+ & 2+ and ISH amplified expression benefit significantly from Trastuzumab treatment. With increasing numbers of laboratories carrying out gastric HER2 immunohistochemistry (HER2 IHC) testing, UK NEQAS ICC&ISH has developed a gastric HER2 IHC service to closely monitor staining methodologies and interpretation.
Method: Participating laboratories were sent unstained composite slides consisting of 3+,2+,1+ and negative tumours to stain using their routine method. Participants were requested to return the slide along with a stained in-house control section along with methodological details. Slides were assessed for quality of staining and interpretability by a panel of expert assessors.
Results: Data showed an 'acceptable' pass rate of 54 % (N=89); Borderline pass 17 % and unacceptable staining in 29 %. In-house slides showed an acceptable rate of 33 %, borderline pass 38 % and unacceptable rate 29 %. The Ventana 4B5 system, used by 51 % (n=45), had an overall pass rate of 76 %. The second most popular method was the 'home-brew' (15 %, n=13), with a pass rate of only 15 %.
Conclusion: Using 'home-brew' methods for gastric HER2 testing can result in misinterpretation of membrane staining. An EQA for gastric IHC testing can help ensure reliable results and rectify suboptimal performance.

Sunday, 9 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-07 Poster Session Other Topics

PS-07-001

Evaluation of accuracy of frozen section in diagnosis of ovarian neoplasms by revision of the slides in Urmia, Iran

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Objective: Ovarian neoplasms are a heterogenous group of benign, borderline and malignant tumors of epithelial, stromal and germ cell origin. Since different therapeutic methods are used to treatment of different tumors, intraoperative diagnosis provide guidance for appropriate surgical management. Frozen section is a usual method for this purpose. This study was done to determine the accuracy of frozen section in diagnosis of ovarian neoplasms in Urmia University of Medical Sciences.
Method: In this cross sectional study the slides of all 154 frozen section samples of ovarian neoplasms in teaching hospitals of Urmia University of Medical Sciences during 2003–2009 revised by 2 pathologists separately. Then the results compared with their final permanent section diagnoses.
Results: We had 102 cases of benign, 39 cases of malignant and 13 cases of borderline ovarian tumors. The most common subtypes were teratoma (16 %), benign mucinous cyst (15 %), papillary serous carcinoma (12 %) and benign serous cyst (11 %). Accuracy, sensitivity, specificity, positive and negative predictive values of frozen section were 98 %, 94.8 %, 99 %, 97.3 %, and 98.2 % respectively.
Conclusion: The results showed that in this university, interpretation of frozen section in diagnosis of ovarian neoplasms is done with acceptable accuracy and can be performed for intraoperative diagnosis as a reliable method.

PS-07-002

The pathological effects of salvia officinalis extract on serum level of alkaline phosphatase in male rats

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Objective: Studies show that there is association between salvia officinalis extract administration and liver or heart functions. The main aim of this study was to determine the effects of salvia officinalis extract on serum level of alkaline phosphatase in male rats.
Method: Male wistar rats were randomly divided into control, normal saline receiving and salvia officinalis extract (100, 150 or 200 mg/kg/day) receiving animals of 5 in each group. After a period of 6 weeks, blood samples were collected using cardiac puncture method. Following serum collection, serum alkaline phosphatase levels were measured by spectrophotometry method. Data were statistically analyzed and compared between groups using ANOVA.
Results: The results indicated that Serum alkaline phosphatase levels were significantly increased in salvia officinalis extract (100, 150 or 200 mg/kg/day) receiving animals compared with control rats.
Conclusion: Our findings show that salvia officinalis extract is enhancer of serum alkaline phosphatase according to which, impairing effect of the extract on certain tissues is conceivable.

PS-07-003

The pathological effects of waterpipe smoking on serum levels of CEA, alkaline phosphatase or creatine kinase in male and female rats

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Objective: Various studies show that smoking can influence serum levels of tumor markers such as carcino embryonic antigen (CEA) and kinase or phosphatase enzymes. The main aim of this study was to determine the pathological effects of waterpipe smoking on serum levels of CEA, alkaline phosphatase (ALP) or creatine kinase (CK) in male and female rats.
Method: Male and female Wistar rats were randomly divided into control and waterpipe smoking groups of 5 in each. After a period of 10 weeks, blood samples were collected using cardiac puncture method. Following serum collection, serum CEA, alkaline phosphatase or creatine kinase levels were measured. Intestinal tissue was also examined histologically. Data were statistically analyzed and compared between groups using ANOVA.
Results: The results indicated that serum CEA, ALP or CK levels were significantly increased in male and female waterpipe smoking animals ($P<0.01$, $P<0.01$ or $P<0.001$, respectively). There was not gender effect on serum CEA, ALP or CK levels. There were also histological changes in intestinal tissue including increased tissue plasma cells infiltration and inflammation.
Conclusion: Our findings show that waterpipe smoking is an enhancer factor of serum CEA, alkaline phosphatase or creatine kinase levels, according to which, damaging effects of waterpipe smoking on various tissues, particularly intestine should be considered seriously.

PS-07-004

The effects of acute or chronic immobilization stress on serum level of creatine kinase and alkaline phosphatase in male rats

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Objective: Studies show that immobilization stress has a variety of effects on serum levels of liver enzymes. The main aim of this study was to determine the effects of immobilization stress on serum level of creatine kinase and alkaline phosphatase in male rats.
Method: 50 male Wistar rats weighing 200±30 g were randomly divided into control, acutely or chronically immobilized animals of 5 in each group. Animals were immobilized for 2 h/day or 8 h/day for a period of 3 weeks or 1 week in chronically or acutely immobilized groups, respectively. Blood samples were collected using cardiac puncture method. Following serum collection, creatine kinase or alkaline phosphatase level was measured by spectrophotometery method. Data were statistically analyzed and compared between groups using ANOVA.
Results: The results indicated that serum creatine kinase level was significantly increased in rats enduring acute or chronic immobilization compared with control animals ($P<0.001$), however, there was not significant difference between serum alkaline phosphatase levels in immobilized animals compared with control rats.
Conclusion: Immobilization stress may leave pathological effects in liver or other organs leading to enhanced serum creatine kinase level.

PS-07-005

Immunoexpression of lactoferrin in bone metastases and corresponding primary carcinomas

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Objective: With reference to primary bone tumors, we previously found lactoferrin (Lf) immunoreactivity in chondroblastomas, chondromyxoid fibromas, giant cell tumours and osteoid osteomas, while no immunoexpression for this

protein was detected in chondrosarcomas and osteosarcomas. Herein we aimed to analyze Lf distribution in bone metastases from cancers of different sites.
Method: Lf immunohistochemical expression was investigated in 25 formalin-fixed and paraffin-embedded specimens of human bone metastatic lesions as well as in the primitive corresponding carcinomas. The primitive sites of carcinomas were: breast (8), prostate (4), kidney (4), lung (3), colon-rectum (2), uterus (4). A Lf intensity-distribution (ID) score was calculated for each case by multiplying the values of the area staining positivity and the intensity staining.
Results: Lf immunostaining, with variable ID scores, was encountered in 11/25 (44 %) metastatic bone lesions. Immunoreactivity for Lf was found in primary carcinomas with a percentage of neoplastic cells ranging between 50 tand 75 %, although this positivity decreased in breast carcinomas (37.5 %) and was totally absent in lung cancers.
Conclusion: The immunohistochemical concordant evidence of Lf in bone metastases and corresponding primary carcinomas strongly supports the hypothesis of an autoctone production of this protein by the neoplastic elements themselves in order to get a greater availability of iron for their increased turnover.

PS-07-006

Retroperitoneal mature teratoma simulating liposarcoma

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Objective: Teratomas are germ cell tumors, uncommon in retroperitoneum. Their diagnosis can be difficult on biopsy material where they can be easily confused with ovarian tumors.
Method: A 26 year-old man presented with history of abdominal pain and vomiting. On computed tomography, there was a multiloculated retroperitonal cyst of 18 cm in length.
Results: A biopsy was performed, showing an adipous tissue with thick fibrous septa, there were many large cells with a clear, vacuolated cytoplasm simulating lipoblast. In front of the retroperitoneal location and cells morphology, a liposarcoma was suspected. The tumor was surgically removed. At gross, It measured18×12×8 cm, containing a combination of solid areas and multilocular cystic spaces containg sebaceous material and hair. Microscopic examination revealed a mature cystic teratoma characterized by cystic spaces lined with either a Malpighian or respiratory regular epithelium. There were areas of cartilage, bone, striated muscle and bronchial glands. Calcifications were also noticed.
Conclusion: Teratomas are uncommon in retroperitoneal area; On biopsy material, histopathological diagnosis can be difficult, simulating either benign or malignant lesions.

PS-07-007

Extracellular Microenvironment in Methotrexate (MTX): Treated rheumatoid arthritis patients

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Objective: The pathogenesis of rheumatoid arthritis (RA) is mainly produced by an imbalance between pro-anti-inflammatory factors and other molecules released by different cell types in the synovial extracellular microenvironment. Aims: Assessing Foxp3 positive lymphocytes and some molecular mediators in the joint microenvironment of patients with rheumatoid arthritis (RA) treated with MTX compared with untreated patients.
Method: Synovial fluid (SF) and synovial membrane (SM) from 24 patients with RA were analyzed for the expression of Foxp3, IL1, IL 6, IL17, TGF beta, VEGF, MMP9 by immunohistochemistry (IHC) and IL1, IL6, IL17, by flow cytometry (FC). Twenty patients were treated with MTX and five untreated patients served as control.
Results: It was observed a negative correlation between IL1/IL6 and IL17/Foxp3 concentration in the SF as measured by FC, before the treatment. In the SM, IL6 and MMP9 were strongly expressed in macrophages, fibroblasts, endothelial cells and the extracellular matrix of control cases, but reduced significantly in the treated cases ($p<$ 0, 05). Il 17 and Foxp3 positive cells remained costantly in a reduced number in the MS.
Conclusion: As the proinflammatory cytokines decreased after the therapy, we can conclude that these are more efficiently influenced than some immune cells participating in the autoimmune process.

PS-07-008

Histological evaluation of the spleen after acute bleeding followed by blood replacement with two different physiologic solutions

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Objective: The spleen is important for many hematopoietic and immunological functions, namely hemodynamic compensation during hemorrhagic shock, with a crucial role in the compensation of hypovolaemia, on restoring blood volume in situations of acute haemorrhage. Also, the administration of physiological solutions is of great importance for the correction of circulating volume, avoiding the complications of hypovolaemia. Objectives: To evaluate spleen's histopathological changes in pigs associated with volume

replacement using two different physiologic solutions, after acute bleeding.
Method: 31 Large White pigs under general anaesthesia with propofol and remifentanil. A total of 25 ml/kg of blood was passively removed during 20 min. Intravascular volume was replaced using Ringer Lactate 25 ml/kg (Group 1- thirteen pigs) and HES 130/0.4 20 ml/kg (Group 2- eleven pigs). Spleen samples were processed for routine hystologic evaluation. Congestion, inflammatory infiltrate, ellipsoids enlargement and follicular lymphoid hyperplasia were evaluated in a semi-quantitative score.
Results: Follicular lymphoid hyperplasia was exacerbated in group 1 (84.6 %; grade III), when comparing with group 2 (36.4 %; grade III). The remaining lesions did not show differences between group 1 and group 2.
Conclusion: Volume replacement with HES 130/0.4 may reduce follicular lymphoid hyperplasia when compared with volume replacement with Ringer Lactate.

PS-07-009
Project Uganda and haemopathology: St. Mary's Hospital Lacor, Gulu, Uganda
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Objective: Lacor Hospital is the second hospital of Uganda and serves almost 3 million inhabitants. In 2005, the figures were as follows: for the 34.498 patients admitted, 245.086 patients were treated in the out patient departments. There were available surgery, X-Rays and ultrasound, vaccinations, laboratory tests, but no pathology service was available until 2008.
Method: In 2008 the Italian NGO"Patologi oltre Frontiera" launched a project aiming at establishing a pathology laboratory at Lacor. Spaces were assigned by the hospital and equipments for specimen processing were provided thanks to the Province of Bolzano, Italy. The project aims also at ensuring the local presence of pathologists, on a voluntary base.
Results: 11 pathologists have been working at Lacor since 2008, for time periods of 1–4 months. The most frequent biopsy sites were: Soft tissue, Prostate, Skin, Uterus cervix, Lymph nodes, Liver, Breast. PAP smears were offered to women comming to the hospytal for different reasons (AIDS clinic, delivery, bleeding). At the moment no screening program is present at Lacor. Thanks to the establishment of a pathology service in loco, differential diagnosis was improved since 2008.
Conclusion: The project is still ongoing. Future steps will include the establishment of immunohistochemistry, and the presence of a local pathologist, who will be trained and assisted by volunteer pathologists.

PS-07-010
Splenic localization of the peritoneal mesothelioma: Case report
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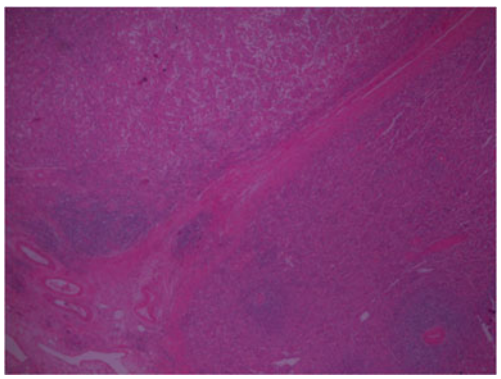
Objective: Peritoneal mesothelioma is a very rare diagnosis. It accounts for 20–30 % of all mesothelioma type cancers. We report a case of a 65-years-old woman was operated because of mass in the spleen and was performed total splenectomy.
Method: Operation specimen included spleen as well as various sizes of nodular peritoneal lesions. Sectioning of the spleen material revealed tumoral lesion ranging in size from 4×3,5×3 cm and it was located in hilus as well as it infiltrated parenchyma. On the other hands, multinodular tumoral tissues were observed and this tissues derived from periton. Tissue sections were prepared by H.E. and immunohistochemical stainings.
Results: Microscopically, tumoral tissue consisted of atypical epithelial cells with abundant eosinophilic cytoplasm and with eosinophilic nucleolus and characterized by acinar or glandlike structures. Sections of tumoral tissue included atypical mitotic figures and necrosis focuses. In immunohistochemical examination, it was shown that calretinin, mesothelioma Ab-1, vimentin, pancytokeratin was positive.So, the tumoral lesion was diagnosed as peritoneal mesothelioma based on these findings.
Conclusion: Peritoneal mesothelioma is a rare form of malignant mesothelioma, making up <30 % of diagnosed mesothelioma cases. The reported case refers to a particular localization of a peritoneal mesothelioma, the spleen, discovered only after a splenectomy.



PS-07-011
Chondromyxoid fibroma, a report from the Turkish bone and soft tissue pathology study group
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Objective: Chondromyxoid fibroma is a rare benign lesion accounting for less than 0.5 % of all primary neoplasms of bone. A study was conducted to assemble a national study group for rare entities and share the experience of different centers.
Method: The data was collected from the pathology archives of 13 referral hospitals in Turkey.
Results: Among the 61 cases enrolled in the study, 57.4 % (n=35) of them were male. Median age was 35±18 years-old (Range: 6–67). The most frequent localizations were tibia (28 %, n=17), femur (n=10, 16.4 %) and pelvic bones (n=9, 14.8 %), followed by feet bones (11.5 %), fibula (8.2 %), humerus (4.9 %), hand bones (4.9 %), cranium (3.3 %), costa (3.3 %), radius (1.6 %), scapula (1.6 %), and vertebrae (1.6 %). Although the cases with appendicular skeleton involvement was younger than the others (median age: 29.5±17.03 vs 53±11.5 respectively) no significant correlation was found between age, gender and localization.
Conclusion: Cases displayed a wide age-range with a slight male predominance. The most frequent localizations were tibia, femur and pelvic bones. Rare localizations such as temporal frontal bones, vertebrae and scapula were also observed. The study, which may serve as a preliminary work for future studies was presented to share our experience on this rare entity.

PS-07-012
Histological changes and granulocytes redistribution in adjuvant arthritis
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Objective: Adjuvant arthritis (AA) is an induced systemic disease primarily with inflammatory joints destruction similar to human rheumatoid arthritis (RA). Spleen and the thymus are organs of immune system involved in RA development. Polymorphonuclear leukocytes (PMN) are cells of first defence line participating at joints affection. First line therapy in RA is Methotrexate (MTX). The aim of the study was to evaluate histological changes of the spleen during AA and effect of MTX on granulocytes redistribution.
Method: Tissues of spleen, thymus and knee joints were histochemicaly stained for detection of chloracetatesterase activity, which showed granulocyte infiltration that was morphometrically evaluated.
Results: We observed significant reduction of spleen white pulp in AA and correction to normal level after MTX administration. The same was seen also in number of PMN. The opposite tendency was observed in knee joints with massive PMN infiltration in AA, which was significantly reduced after MTX administration. No significant changes were observed in the thymus.
Conclusion: Our results indicated the connection between the PMN accumulation in sites of inflammation during AA mirroring their decreased number in the spleen and effect of MTX on spleen histological changes. This observation points to the eventual mechanism of MTX effect on lowering the inflammatory reaction in vivo. (APVV 51-017905, VEGA 2/0093/08).

PS-07-013
Spectrum of histopathological changes in the livers of organ donors: Microscopic evaluation of livers unused to transplantation
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Objective: Liver transplantation is the only chance of rescue for patients with end-stage of many diseases of this organ. The aim was the histopathological assessment of retrieved livers but not used for transplantation.
Method: Forty-four livers were analyzed. The age range of donors was between 23 and 69 years (mean 51). Microscopic preparations were stained with standard HE and van Gieson's methods.
Results: The following categories of organs were distinguished: I – liver with no microscopic changes: 7 cases; II – I° steatosis only: 4; III – II° steatosis only: 1; IV – cholestasis only: 1; V – I° and II° steatosis with cholestasis: 1; VI - G0/G1 inflammation with cholestasis: 2; VII - G0/G1 inflammation with steatosis (<35 % hepatocytes): 6; VIII – III° steatosis only: 2; IX - steatosis (<35 %), G0/G1 inflammation with cholestasis: 5; X – III° and IV0 steatosis: 2; XI – steatosis (>35 % hepatocytes) with inflammation: 1; XII – inflammation with fibrosis: 1; XIII – steatosis, inflammation with fibrosis: 8; XIV – steatosis, inflammation, fibrosis with cholestasis: 3.
Conclusion: The livers which were classified to the I-IV categories are either good or very good organs with no contraindications to transplantation. The livers qualified among the V- IX categories may be in some specific circumstances an additional and valuable pool of organs.

PS-07-014
Metal debris in inguinal lymphadenopathy after mega prosthesis for malignant fibrous histiocytoma
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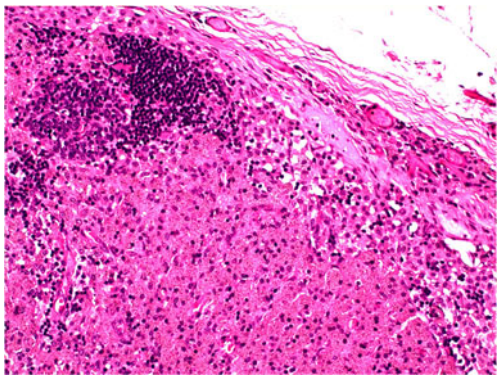
Objective: Surgical treatment options of malignant tumors of the knee includes reconstruction with incorporation megaprosthesis. Inguinal lymphadenopathy due to the lymphatic uptake of metal debris has been described, and may be clinically confused with tumor metastasis.
Method: We report the case of a 39-year-old woman with inguinal lymphadenopathy caused by metallic debris from a knee mega prosthesis for Malignant Fibrous Histiocytoma.
Results: The histopathological changes seen in lymph node were metal debris containing sinusoidal macrophages in a background with numerous epithelioid granulomata in the remaining lymph node.
Conclusion: The identification of regional lympadenopathy in patients with past history of malignancy usually indicates metastatic disease. Post-prosthesis lymph node histiocytosis resembling metastatic disease is described, and that is why we need resect and examine lymph nodes with the use of polarized light microscopy to identify birefringent particles of prosthetic debris for an accurate histologic diagnosis.



PS-07-015
Fine needle aspiration diagnosis of Rosai-Dorfman Disease in patient with multiorgan neoplastic, infectious and autoimmunity pathology
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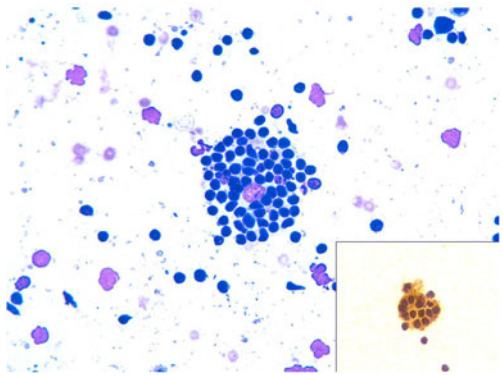
Objective: Sinus Histocytosis with Massive Lymphadenopathy, also known as Rosai-Dorfman disease, is an idiopathic histiocytic proliferation affecting lymph nodes. the cause is still unknown, but it's related to an immune dysregulatory process. Patients publications sometimes includes autoimmune disorders and any neoplasm, being exceptional a case with multiorgan neoplastic, infectious and autoimmunity pathology as the present.
Method: A 77-years-old woman with breast cancer, tuberculosis, rheumatic heart disease, diabetes mellitus, eosinophilic gastroenteritis, intestinal angiodysplasia, chronic hepatopathy non-alcoholic and penicillin allergy among other diseases, consulting for constitutional syndrome with conglomerate inguinal lymph nodes.
Results: Fine needle aspiration cytology revealed histiocytes showing emperipolesis with mature lymphocytes and plasma cells background. Hence, diagnosis of Rosai-Dorfman disease was made.
Conclusion: The case report is a rare presentation of Rosai-Dorfman disease associated with a wide range of illness, some simultaneous. We believe that all the patient illness are related, and it could correspond with a complex disease as a immune system alteration expression.



PS-07-016
Causes of death of psychiatric patients: An autopsy study
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Objective: Numerous researches documented disproportionate somatic morbidity and earlier death among people with psychiatric diseases.
Method: Causes of death of psychiatric patients was analyzed on 5 years autopsy records on Institute of Pathology, Medical Faculty, University of Belgrade. Equal number of randomly selected non-psychiatric cases (n=80) formed control group.
Results: Life longevity of psychiatric patients was approximately 10 years shorter, than in control group (57.8±14.0 vs 68.3±11.8; p<0.001) with significant predominance of males (55:25; p<0.001). Most common causes of death in decreasing order was: bronchopneumonia, pulmonary thromboembolism, COPD, hypertensive heart disease, left heart failure, acute cor pulmonale, diabetes mellitus and food aspiration. Bronchopneumonia (p< 0.01), acute cor pulmonale, diabetes mellitus and food aspiration (p<0.05) was more frequent in group of psychiatric patients. There was statistically significant high relative risk only for bronchopneumonia as cause of death in psychiatric patients (RR=1.79; 95 % CI=1.09–2.89) either they were

hospitalized in psychiatric hospital or not ($p>0.05$). Contrary, pulmonary thromboembolism was more frequent in those hospitalized in psychiatric hospitals ($p<0.05$).
Conclusion: Lung and heart diseases and diabetes mellitus are more frequent in psychiatric patients and cause earlier dying, particularly in males, than in those without psychiatric diseases.

PS-07-017
Intraarticular osteoid osteoma: Case report
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Objective: Osteoid osteoma occupies %11 of all benign bone tumors.It commonly affects the extraarticular portions of the long bones in young patients.It frequently causes persistent pain that worsens at night and is relieved by NSAIDs. The typical radiographic appearance is that of a lucent nidus with surrounding dense cortical thickening.
Method: We present a case of an intraarticular osteoid osteoma in 24 year-old man.He had progressive pain in the right patella, occured 1 year before hospital application and also the pain was not relieved by NSAIDs. The patient applied to the orthopaedic clinic of our hospital in March 2012. The Magnetic Resonance (MRI) imaging results showed the lesion in the anterior epiphysis of the proximal tibia. This lesion located subcortical and the diameter of the lesion was 6 mm.
Results: Microscopically, the nidus was a well-demarcated osteoblastic mass and consisted of interlacking network of osteoid trabeculae with different levels of mineralization, rimmed by abundant short spindled or polygonal osteoblasts and numerous osteclast –like multinucleate giant cells. The diagnosis was osteoid osteoma.
Conclusion: Because intra-articular localization is rare in osteoid osteoma and the pain was not relieved by NSAIDs in our patient, we present the case here.

PS-07-018
Human frozen tissue biobank in Latvia: The first results
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Objective: The incidence of malignant disease in Latvia is closed to the average in Europe and still is inadequately high. The aim of project was to create a modern human tissue biobank containing samples of malignant tumours, precancer conditions as well as autoimmune diseases. The project is funded from the European Social Fund Project „Mutidisciplinary research group for early cancer detection and cancer prevention".
Method: Frozen tissue samples, blood as well as clinical information was collected from each patient. DNA samples were extracted and stored in collaboration with Latvia Genome centre. Standartized pathology reports were used. The hospital pathologist was involved in biobank work: 1) in making diagnostic decisions and 2) in rewiewing specimens.
Results: In total 1870 patients with oncological and premalignant diseases were enrolled in the research during the 2010–2012. Frozen tissue samples were obtained from 211 patients (101 breast, 80 gastric and 30 colorectal cancer cases). Tissue material were examined according to the established morphological protocols. Blood samples were taken from 699 patients (10 melanoma, 206 gastric, 250 breast, 178 prostatic, 55 colorectal cancer and premalignant diseases cases). Tissue biobank material is enrolled in scientific research both in Latvia and abroad (Lithuania, Israel).
Conclusion: We expected that our biobank will join international biobanking network and organizations.

PS-07-019
A case of paravertebral mediastinal chordoma without bone destruction
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Objective: Chordoma is a slow-growing malignant bone tumor that exhibits notochordal differentiation. Nearly 90 % of cases occur in the sacrococcygeal region and in the base of the skull. The remaining cases develop in the mobile spine, predominantly in the cervical and lumbar vertebrae. We report a rare case of paravertebral mediastinal chordoma without bone destruction.
Method: Case report.
Results: A 47-year-old Japanese woman was admitted to hospital after a tumor was incidentally detected on a plain chest X-ray image. The tumor was located in the paravertebral region of the mediastinum and did not show any destruction of the thoracic vertebra radiologically. The tumor was clinically diagnosed as a benign neurogenic tumor and the tumor was easily removed surgically. Microscopically, the tumor mainly consisted of tumor cells with extensively vacuolated cytoplasm, arranged in cord- and nest-like fashion in a myxoid matrix background. Immunohistochemically, the tumor cells showed diffuse positivity for pancytokeratin (AE1/AE3), vimentin. The tumor cell nuclei were positive for brachyury, which is a key transcription factor of notochordal development.

Conclusion: These results confirmed the tumor to be an extraosseous chordoma in the paravertebral mediastinal region, which is rather an extremely rare location for usual chordoma.

PS-07-020

Testicular papillary mesothelioma: A case with borderline features

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Objective: Well-differentiated papillary mesothelioma occurs rarely in the paratesticular region, with only a few published case reports.
Method: We describe a case of a 37-year-old man who initially presented with discomfort in the left testis and underwent resection of a hydrocele in the left testis. A hydrocelectomy was performed, during which a pedunculated mass, 2,5 cm in greatest dimension, was found attached to the testis.
Results: Microscopically, the mass was composed of multiple branching papillary structures with fibrovascular cores covered by a single layer of low cuboidal to cuboidal cells with predominantly bland nuclear and cytologic features and rare microscopical necrosis. Immunohistochemical staining for calretinin and cytokeratines 5/6 was positive and proliferative marker Ki67 was <2 %. Accordingly the diagnosis of a well-differentiated papillary mesothelioma was made. The patient has not received additional therapy and is disease free 15 months after diagnosis.
Conclusion: In conclusion, we report a rare case of a well-differentiated papillary mesothelioma of the tunica vaginalis of the testis. The combination of benign and semimalignant characteristics can make the diagnosis of such a lesion problematic and pathologic distinction from malignant mesothelioma is crucial, although it may be difficult because of the variability of associated histologic features.

PS-07-021

Occurrence of Kimmelstiel-Wilson like lesions in the absence of diabetic nephropathy in dogs, may provide a natural model for further research in the corresponding human form

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Objective: Nodular glomerulosclerosis occurring in non-diabetic patients is an unexplained renal condition that resembles Kimmelstiel-Wilson lesions (K-W), associated almost exclusively with diabetic nephropathy. This study aimed to assess the presence of nodular glomerulosclerosis in dogs with non-diabetic chronic kidney disease (CKD) and evaluate similarities with human condition, and thus, establish the dog as a natural disease model for further studies.
Method: Kidneys from dogs (n=27) with non-diabetic CKD were evaluated for the presence of nodular glomerulosclerosis. Samples were stained with haematoxylin-eosin and periodic acid of Schiff. Lesions were classified as absent or present, the later, classified as non- convincing and convincing K-W like lesions.
Results: Nodular glomerulosclerosis was present in 66.66 % of evaluated cases (n=18), of which, 38.88 % (n=7) were convincing K-W like lesions and the remaining 61.11 % (n=11), although similar, didn't exhibit typical microscopic characteristics and were classified as non-convincing. Fibrosis was positively associated to diagnosis of K-W lesions (OR=6; p<0.05).
Conclusion: As in man, Kimmelstiel-Wilson like lesions may also occur in dogs in the absence of diabetic nephropathy and reveal similar microscopic aspects to the description related in humans and, that some factors, others than hyperglycaemia, may be responsible for the appearance of these lesions. Thus, dogs may provide a model of natural disease for further elucidation.

PS-07-022

Modulated electro-hyperthermia induced programmed cell death in HT29 colorectal carcinoma xenograft

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Objective: Modulated electro-hyperthermia (mEHT) is a non-invasive technique for targeted tumor treatment. The mEHT generated capacitive coupled modulated radiofrequency selectively accumulates in the tumor tissue without major effect in the surrounding normal tissues.
Method: HT29 human colorectal carcinoma cell line xenografted to both femoral region of BalbC/nu/nu mice was treated when reaching ~1.5 cm by using a single shot mEHT treatment (LabEHY, Oncotherm Ltd, Páty, Hungary) for 30 min. Sampling was made after 0, 1, 4, 8, 14, 24, 48, 72, 120, 168, 216 h in 3 mice each group by keeping 5 untreated animals. Histomorphologic, immunhistochemical and TUNEL assay results were tested in digital slides and analyzed semi-quantitatively. The apoptosis protein array results were evaluated using the ImageJ software.

Results: mEHT caused programmed cell death related destruction from the tumor centre. TRAILR2 and FAS proteins were upregulated 8 h post treatment. Cleaved caspase-3 positive cells appeared only at the tumor periphery between 4 and 14 h. AIF nuclear translocalisation at 14–24 h and massive TUNEL positivity at 24–48 h indicated DNA fragmentation. At 72–216 h myeloperoxidase positive leukocyte infiltration ring supported tumor elimination.
Conclusion: In HT29 colorectal cancer xenograft mEHT caused programmed cell death. DNA fragmentation followed rather a caspase independent and AIF dependent subroutine.

PS-07-023
Metaphyseal parosteal lipoma of the distal femur: Case report
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Objective: Lipoma of the bone is a rare benign adipocytic tumor that arises intraosseous and rarely on the cortex or on the surface of the bone (parosteal lipoma). Parosteal lipoma affects the long bones diaphysis of adults over 40 years old.
Method: We present the case of a 23 years old female with clinical diagnosis of femoral exostosis. Conventional radiographs shows the presence of a 5 cm length area of lucency on the femoral metaphyseal surface with a periostal reaction at the base of the lesion.
Results: Gross examination reveals a 5 cm osseous tumor, whitish on the surface and yellow on the section. On microscopic examination there are mature adipocytes with small foci of bone scattered throughout the adipocytes and hyaline cartilage at the perifery of the lesion. The gross and microscopic examinations correlated with conventional radiographs led us to diagnosis of parosteal lipoma.
Conclusion: This case is interesting being a rare bone tumor, the young age of the patient and the location on the surface of the bone.

PS-07-024
Application of Scanning Acoustic Microscope to evaluate lymph node lesions
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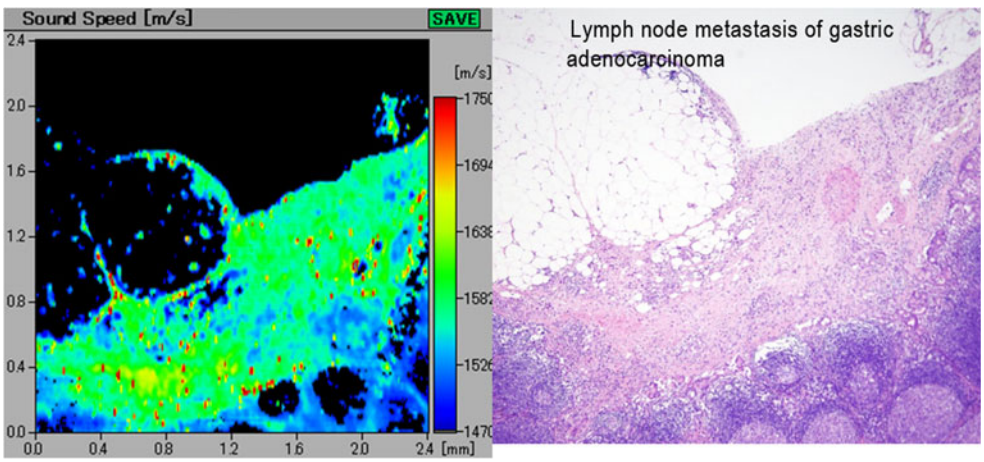
Objective: A scanning acoustic microscope (SAM) is a device that uses ultrasound (frequency, >20 kHz) to image an object or tissue. Because it is known that the harder the tissue, the more the speed of ultrasound, SAM can provide data on the elasticity of cells and tissues.
Method: We compared lymph node lesions between acoustic and light microscopic images to evaluate the usefulness of SAM.
Results: SAM system discriminated lymph node components and demonstrated distinct acoustic images of the lymph nodes such as cancer metastasis, lymphomas, granulomatous diseases, and deposition diseases such as amyloidosis. Areas with desmoplastic reactions associated with cancer invasion or post-inflammatory fibrosis showed the greater speed of sound than normal lymph nodes. These results corresponded well to those obtained using the conventional microscope.
Conclusion: SAM provides the following benefits: (1) images are acquired in only few minutes without requirement for staining, (2) imaging pattern is similar to that of light microscope, and (3) speed of sound from each lesion is digital and statistical analysis is possible among diseases. Although resolution of SAM is little lower than that of light microscope, the SAM can be an ancillary tool for histological diagnosis and clinical research.



PS-07-027

Oxidative stress parameters in patients with Parkinson Disease

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Objective: Parkinson's disease (PD) is considered one of the major neurological disorders of the population, and there is increasing data provides enough evidences confirming the involvement of free radicals and other reactive oxygen species (ROS) in a number of physiological and pathological processes. The aim of the present study was to evaluate, the effect of therapy in patients with Parkinson disease on biomarkers of oxidative stress, such as products of lipid peroxidation by two different methods: Electron Paramagnetic Resonance and visible spectrophotometry.
Method: The study was performed in blood samples of patients with PD -with therapy, patients with PD -without therapy and healthy volunteers as controls. The products of lipid peroxidation were measured as malondialdehid (MDA), spectrophotometrically by thiobarbituric acid (TBA) method. The levels of lipid radicals were determinated ex vivo at room temperature on an X-band EMX-micro spectrometer, Bruker, Germany.
Results: By the present study we reported higher levels of oxidative stress in PD patients without therapy compared to those with therapy. These results were comfirmed by the EPR method.
Conclusion: The increase of oxidative stress, in PD patients' might be an additional reason for many secondary complications.

PS-07-028

Melanoma incidence rate in the Republic of Mordovia according to the cancer-register covering the period from 2006 to 2010

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Objective: Objective – epidemiology of melanoma incidence in the Republic of Mordovia covering the period from 2006 to 2010.
Method: Based on cancer-register data.
Results: Melanoma incidence in the Republic in 2006 amounted to 7,3 0 000, in 2007 – 4,8 0 000, in 2008 – 7,2 0 000, in 2009 – 5,8 0 000, in 2010 - 6,6 0 000. The first time proven case is morphologically confirmed in 2006 – in 87,3 %, in 2007 – in 85,3 %, in 2008 – in 95,0 %, in 2009 – 97,9 %, in 2010 – in 98,1 % of cases. Detectability at early stages increased. In 2006 cases of I – II, III and IV stages amounted to 36,5 %; 27,0 %; 8,0 %, in 2007 – 51,2 %; 21,9 %; 12,2 %, in 2008 – 50,8 %; 32,7 %; 8,2 %, in 2009 – 51,0 %; 14,2 %; 14,2 %, and in 2010 – 56,3 %; 5,4 %; 7,2 %. Peak incidence at 55–60 years of age for males and at 50–55 years of age for females.
Conclusion: There is an increase in skin melanoma incidence rate in the region; increase in morphologically confirmed diagnoses and in disease detectability at early stages.

PS-07-029

Rare association between malignant phyllodes tumor of the breast and cutaneous malignant melanoma: Case report

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Objective: Popp and Petre are first authors in equal proportion Phyllodes tumors are rare (<1 %), biphasic breast tumors composed of a hypercellular mesenchimal proliferation layered by epithelial cells.
Method: We present the case of a 60 years old woman diagnosed with malignant melanoma of the right calf in Nov. 2011 and with malignant phyllodes tumor of right breast in Jan. 2012.
Results: The patient underwent resection of a tumor of the right calf which proved to be a malignant melanoma (superficial spreading type, Clark V, Breslow 4,45 mm); regional lymph node biopsy showed no metastasis (pT4apN0). During postoperative evaluation, a second tumor was discovered in her right breast. Intraoperative histological diagnosis was phyllodes tumor with unknown biological behavior. Microscopic examination on paraffin embedded sections showed a proliferation of mesenchymal elongated cells, with basophilic or clear cytoplasm and elongated, irregular nuclei in a fibrous, hyaline stroma with myxoid areas. Immunohistochemical assays were performed for establishing the biological potential of the tumor (Ki67, p53, CD10, VEGF) and the final diagnosis was malignant phyllodes tumor.
Conclusion: This is the first reported association of these two malignant tumors, in our knowledge, raising the question if is only an incidental association or there is a subsequent connection between them.

PS-07-030

X-linked lymphoprolifetative syndrome: A case of autopsy

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X-linked lymphoproliferative disease (XLP) is caused by mutations in the genes SH2D1A and XIAP. The 3 most commonly recognized phenotypes of SH2D1A related XLP are hemophagocytic lymphohistiocytosis (HLH)

associated with Epstein -Barr virus (EBV) infection (58 %), dysgammaglobulinemia (31 %), and lymphproliferative disorders (30 %). A 10 month old male with clinical history of fever and diagnosis of Infectious Mononucleosis (EBV+), presented with hepato-splenomegaly, high liver enzymes, and clinic hemophagocytic syndrome. Posteriorly he presented dyspnoea, bradycardia, seizures and death. Autopsy examination showed pleural effusion and ascites. Congestive lungs. Liver of 785 g, spleen of 130 g; both with congestive aspect, and multiple adenopathies (we send material to the hospital department of immunology). Histological examination showed on liver and spleen a prominent lymphocytic infiltrate, positive to CD4, CD8, LMP and EBER immunohistochemistry stain with hemophagocytic lymphohistiocytosis, also seen in lymphoadenopathies. There were T lymphocyte cell perivascular in brain and lung. Making an immunology and autopsy outcome of X-linked lymphoproliferative disease. The diagnosis of XLP must be considered in males with fatal or near fatal EBV infecttion, HLH resulting from EBV or other viral disease, hypogammaglobulinemia or common variable immunodeficiency, lymphoma and family history of XLP.

PS-07-031

Aneurysmal bone cysts of hands and feet: A clinical and pathological review of 10 cases out of a series of 78

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Objective: Primary Aneurysmal Bone Cyst (ABC) is a histologically complex and mainly cystic lesion that accounts for 2 % of all primary bone tumors. Information regarding its clinical presentation and management in hands and feet remains sparse.
Method: The medical records ABC in hands or feet in Hospital La Paz Pathology Department from 1966 to 2011 were retrospectively reviewed and compared with existing data. We also propose pathological criteria for differential diagnosis between ABC and giant cell reparative granuloma (GCRG).
Results: Ten ABC in hands or feet were identified, out of 78 (12.8 %), Five tumors were in metacarpals, 4 in metatarsals and 1 in phalanx. Radiographs showed expansile lytic lesions in metadiaphyseal region, sometimes with aggressive appearance. Histologically, ABC showed a mixture of blood-filled spaces with connective tissue septae containing osteoclast giant cells and foci of osteoid. Scattered areas of so called "blue bone" were present in 5 cases (50 %). There were two solid variants. Five patients underwent resection and 5 curettage, three of which relapsed (30 %).
Conclusion: ABC should be considered in the radiologic differential diagnosis of hands and feet tumours because these lesions can even mimic malignancies. Although clinicopathologically some authors consider GCRG is related to the ABC solid variant, we believe they are different entities.

PS-07-032

Carb-3 is the superior anti-CD15 monoclonal antibody in optimized protocol settings

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Objective: Immunohistochemical detection of CD15 is important in diagnosis of Hodgkin lymphoma and may be relevant in classification of renal tumours. In four tests with 71–121 participating laboratories conducted by the NordiQC external quality assessment scheme only 50–76 % of CD15 stains were sufficient, mainly because of too diluted primary antibody concentration, insufficient HIER and less successful antibody clone. The purpose of this study was to evaluate three anti-CD15 antibodies based on vendor and in-house optimized protocols.
Method: Multitissue blocks with various malignant lymphomas, renal tumours and normal tissues (n=218) were stained with three concentrated (conc) antibodies (Carb-3, MMA and BY87) according to predetermined in-house optimized protocols on two staining platforms. Ready-to-use (RTU) solutions of Carb-3 and MMA were also examined. Extension and intensity of stains was scored using the H-score method.
Results: Carb-3conc with an in-house optimized protocol gave the highest H-scores in classical Hodgkin lymphoma, renal tumours and normal kidneys. Carb-3RTU and MMA-conc gave slightly lower scores, while MMARTU and BY87conc gave the lowest scores and a large proportion of false negative reactions. All in-house optimized protocols gave better staining results than vendor protocols.
Conclusion: The importance of antibody selection and protocol optimization in immunohistochemical laboratories is emphasized.

PS-07-034

Markers of early myocardial infarction - To increase autopsy quality

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Objective: Autopsy-based morphologic diagnosis of early phase of myocardial infarction is a challenge. Therefore, specific diagnostic methods are needed to confirm the early myocardial infarction. Recent reports indicate that h-FABP and MYBPC3 protein are highly sensitive and specific markers for the early myocardial infarction. The objective of this study was to evaluate the diagnostic value of h-FABP

and MYBPC3 proteins as markers of early myocardial infarction in autopsy tissue section.
Method: 20 cases of myocardial infarction and 20 cases with suspected myocardial infarction were selected from 236 autopsy examination performed in 2006–2010 at the Department of Pathology. The control group consisted of 20 sections of normal myocardium. The immunohistochemistry was performed on formalin fixed paraffin embedded tissue sections using antibodies against h-FABP and MYBPC3.
Results: h-FABP and MYBPC3 proteins revealed various expression levels in selected groups. The control group revealed strong cytoplasmic expression of both determined proteins. The expression of h-FABP and MYBPC3 in patients with suspected or diagnosed myocardial infarction was reduced.
Conclusion: H-FABP and MYBPC3 proteins may be usefull markers in diagnosis of early myocardial infarction, especially in patients with uncertain cause of death.

PS-07-035
The Pathological Effects of Immobilization Stress on Testes Tissue and Serum Testosterone level in Rats
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Objective: Studies show that there is association between stress and pathophysiological changes in reproductive system. The main aim of this study was to determine the pathological effects of immobilization stress on testes tissue and serum testosterone level in male rats.
Method: Wistar rats were randomly divided into control, acutely or chronically immobilized groups of 10 in each. Animals were immobilized for 2 h/day or 8 h/day for a period of 3 weeks or 1 week in chronically or acutely immobilized groups, respectively. After 6 weeks, blood samples were collected using cardiac puncture method. Following serum collection, testosterone level was measured by radioimmunoassay method. The effect of immobilization stress on testes histology was also examined. Data were statistically analyzed and compared between groups using ANOVA.
Results: Serum level of testosterone was decreased in acutely or chronically immobilized rats compared with control animals ($P<0.001$). In histological study, semeniferous tubules were significantly deformed and cellular concentration was reduced in immobilized rats compared with control animals ($P<0.05$). The number of spermatocytes, spermatids or sperms was also decreased in immobilized rats ($P<0.001$) and this pathologic change was more prominent in acutely than chronically immobilized rats.
Conclusion: Our findings show that immobilization stress can leave pathological effects in male reproductive system leading to reduced cellular concentration in semeniferous tubules and decreased serum level of testosterone.

PS-07-036
Aggressive systemic mastocytosis with Charcot-Leyden crystals-associated crystal storing histiocytosis in bone marrow
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Objective: Crystal storing histiocytosis (CSH) is a rare phenomenon characterized by cytoplasmic accumulation of crystaline material in macrophages. Several different subtypes of CHS have been described depending on etiology or according to the chemical nature of the crystals.
Method: We report a 56 -year-old man with 3 year history of systemic mastocytosis with slight splenomegaly and hepatomegaly. Laboratory investigations showed severe macrocytic anaemia (Hb85g/L; Hct 0.251 L/L; MCV 108.2 fl; MCH 36.6 pg; RDW 17.1), slight leukopenia and eosinophilia.
Results: Microscopic examination of bone marrow revealed sheets of polygonal or spindle-shaped mastocytes with no associated clonal hematological malignancy. Around mast cell infiltrates were interspersed histiocytes with abundant opaque cytoplasm containing eosinophilic crystaline inclusions (Charcot –Leyden crystals).
Conclusion: We report a case of crystal storing histiocytosis of bone marrow in a 56-year-old men with systemic mastocytosis. Around 90 % of CSH is associated with lymphoproliferative or plasma cell disorders, but not all cases are hematologically related. Only small number of non-immunological variants of CSH is reported in the literature.

PS-07-037
Do we overestimate on counting mitosis?
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Objective: The number of mitotic figures in a particular microscopic area is an important criterion, changes the diagnosis or determines the prognosis of many tumors. These criteria are generally accepted for each case in the light of the original studies and determined by counting mitotic figures in certain number of fields. The detected number of mitotic figures is affected by the field of view. Field of view depends on the ocular diameter and magnification value. The ocular lens diameters of the old types of microscopes used in original literature were smaller than

current microscopes with a narrower field of view. The purpose of this report was to emphasize these differences in the mitotic counting.
Method: In this report, the mitotic counting criteria for pathological diagnoses were reviewed from the original literature. Whether there is a difference between original literature criteria and evaluation with current microscopes according to ocular diameter, field of view and assessed total area were investigated.
Results: Review carried out was determined certain differences between the criteria of the original literature and evaluation with current microscopes.
Conclusion: Due to wider field of view in modern microscopes used in the current, number of field counted in original criteria though to need correction.

PS-07-038
Analysis of Nestin expression in pediatric and adult cases of high-grade osteosarcoma
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Objective: Nestin, an intermediate filament protein, has been detected in different tumors. In addition, nestin expression is associated with worse prognosis in some malignancies. Our study analyzed clinical significance of nestin expression in pediatric and adult cases of high-grade osteosarcoma.
Method: Using immunohistochemistry and immunofluorescence, nestin expression was examined in osteosarcoma tissue samples taken from 45 patients [24 males, 21 females; median age 19 years (range 6–85 years)]. In both methods, the frequency of nestin + tumor cells was stratified into three categories and clinicopathological correlations were statistically analyzed.
Results: Variable frequent nestin + tumor cells were identified in all examined osteosarcoma samples. In the entire cohort of 45 patients, high levels of nestin expression detected by immunofluorescence were associated with significantly worse clinical outcomes (OS, p=0,031; EFS, $p<$ 0,001). However, only statistically nonsignificant trends for shorter survival were revealed using generally more sensitive immunohistochemistry. Analogical results were obtained when comparing groups of patients by age or gender.
Conclusion: Despite significantly shorter survival rates observed in patients with high levels of nestin expression assessed by immunofluorescence, nestin does not seem to represent a powerful prognostic marker for patients with high-grade osteosarcomas.

PS-07-039
Benign atypical intravascular CD30+ T-cell proliferation: A reactive condition mimicking intravascular lymphoma
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Objective: Intravascular lymphoma (IVL) is a very aggressive disease that can involve the skin in 40 % of the patients. The majority of IVL are of B-cell lineage, although cases with a T-cell phenotype and, rarely, natural killer (NK)-cell phenotypes have been reported. Indeed, two cases of intravascular large CD30+ T-cell lymphoma were described in the literature, both with a fatal outcome.
Results: Herein, we report two patients with skin lesions showing an atypical intravascular CD30+ T-cell proliferation. The rearrangement of immunoglobulin heavy chain gene and T-cell receptor gamma gene studied by the polymerase chain reaction were polyclonal. Indeed, both patients did not present systemic disease and therefore exhibit a favorable outcome.
Conclusion: To the best of our knowledge, this is the second report of a benign intravascular CD30+ T-cell proliferation that represents an intriguing differential diagnosis for intravascular lymphoma.

Monday, 10 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-08 Poster Session History of Pathology

PS-08-001
Medical research through historical resources: Talking objects at the Pathology Museum of Florence
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Objective: The Pathology Museum of the University of Florence is an example of an institution in which pathological specimens from the nineteenth century become talking objects. Through analysis of the original Catalogue and investigation by means of modern scientific techniques, discovering the story behind the object becomes a feasible challenge.
Method: A case of a parasitic perineal monstruosity from the Museum collection is described on the basis of the original medical records and illustrations.
Results: The surgeon Giorgio Pellizzari (1814–1894) first reported this extraordinary case of sacrococcygeal teratoma containing rudimentary arm bones and a hand. Reader of Descriptive Anatomy, Pellizzari was a well-known Anatomy Dissector and Curator of the Physiological Museum of the Regio Arcispedale di Santa Maria Nuova in Florence.

Conclusion: This report underlines the importance of studying the archive material in order to thoroughly comprehend a single museum object. This handling of matters will help to turn anatomical collections into a unique teaching tool for modern medical practice and a noteworthy documentation of scientific, artistic and historical value.

PS-08-002

The importance of Prof. Dr. Hamdi Suat Aknar in the history of pathology in Turkey

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Objective: A system of pathology based on practice, training and research could be institutionalized in Turkey in earlier 20th. century. Until 19th. century medical education was theoretical. It is known that dissection and autopsy was allowed in 1841 and Turkish became the lecturing language in 1870 during Ottoman Empire era.
Method: It is Prof.Dr. Hamdi Suat Aknar who had founded modern and organizational pathology in Turkey. After training in pathology in Germany (1900–1904), he returned and remained as a dedicated professor until 1933. He was the first who taught pathology in systematic order. Along with his routine work and lecturing, Prof. Aknar conducted numerous researches basically on skin lesions and tumors. He published 40 articles in German and French.
Results: Through the publications and presentations at the congresses, he obtained an important standing and became a well-known pathologist in Europe. He was selected as the member of editorial board of the distinguished journal Acta Cancrologica published in Budapest. He pioneered the first organized activities against cancer in Turkey and contributed to the foundation of the Society Against Cancer.
Conclusion: Pathology, founded in Turkey under the leadership of Prof. Aknar, has further developed with the efforts of eminent scholars.

Monday, 10 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-09 Poster Session Head & Neck Pathology

PS-09-001

Clear cell odontogenic carcinoma: A distinct odontogenic neoplasm with squamous differentiation

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Objective: Clear cell odontogenic carcinoma (CCOC) is a rare odontogenic neoplasm with a propensity for recurrence and distant metastasis. We report a case of CCOC of the anterior maxilla in a 53 year old male.
Method: CT scans revealed a destructive lytic expansile lesion originating from the anterior alveolar process of the maxilla. Histology disclosed a biphasic neoplasm with nests of central clear cells and peripheral polygonal hyperchromatic cells with marked cytoplasmic eosinophilia.
Results: The tumour cells were immunoreactive for MNF116, CK14, CK19, CK5 and EMA. Both cell types were negative for S100 protein, vimentin, SMA, RCC, CD10, CK7 and CK20. The proliferation index, Ki67, was low and its expression, similar to CK14, was confined to the peripheral cells. Electron microscopic examination showed desmosomes and tonofilaments confirming the squamous origin of the lesion.
Conclusion: CCOC is a distinct odontogenic neoplasm of squamous phenotype. Surgical resection with wide tumour free margins remains the mainstay of therapy. Its overall high recurrence rate even after radical surgical excision, necessitate close follow up of the patients.

PS-09-002

Extramedullary plasmocytoma of the sinonasal tract: Report of a case

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Objective: Extramedullary plasmocytoma is an uncommon plasma cell tumor localized preferentially in the upper aerodigestive tract, with no evidence of underlying multiple myeloma. It accounts for less than 1 % of head and neck tumours.
Method: We report a case of a 57-year-old male patient with reccurent left-sided epistaxis and nasal obstruction. CT-scan showed a left maxillary mass eroding the lateral wall of the nasal cavity. The tumor was surgically removed.
Results: Histologic examination showed a diffuse infiltrate of neoplastic cells in the submucosa, arranged in a scant vascularized stroma. The neoplastic cells were large to medium- sized with amphophilic cytoplasm, irregular nuclei and proeminent, eosinophilic nucleoli. Mitotic figures were frequent. Imunohistochemical stains were performed in order to make a differential diagnosis: the tumor cells were positive for CD38 and CD138 and they expressed cytoplasmic immunoglobulin with kappa light chain restriction. Most of the tumor cells were also CD56 and EMA positive.
Conclusion: Even though extramedullary plasmacytoma of the sinonasal tract is rare, it should be included in the differential diagnosis. The cooperation among the otorhinolaryngolists, pathologists and hematologists are required to manage the patients effectively in order to provide optimal treatment.

PS-09-003

Carcinosarcoma of the parotid gland featuring foci of malignant giant cell tumor

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Objective: Malignant mixed tumors of the salivary glands are uncommon. Salivary gland carcinosarcoma is a rare neoplasm in which both the stromal and epithelial components meet the microscopic criteria for malignancy. Seventy-four cases have been reported in English-language literature to date.
Method: Case report.
Results: An 81-year-old male patient with a carcinosarcoma of the parotid gland featuring foci of undifferentiated carcinoma, and sarcomatous components characteristic of chondrosarcoma, high-grade undifferentiated sarcoma and malignant giant cell tumor. Stromal areas of the tumor expressed vimentin and smooth muscle actin. Positive staining for the S-100 protein was noted in areas of chondroid differentiation. Giant cells from areas identified as malignant giant cell tumor were positive for CD68, in contrast to the bizarre/atypical giant cells of the high-grade sarcomatous component, which were CD68-negative.
Conclusion: Foci of malignant giant cell tumors in salivary gland carcinosarcomas has been described in only two previous reports. This case highlights the occurrence of a giant cell tumor component, which may be indistinguishable from its counterparts in the bone and soft tissues and may lead to the diagnosis of salivary gland osteoclast-like giant cell tumor. Extensive sampling may be crucial to correctly identify carcinosarcoma in such cases.

PS-09-004

Osteopontin expression is an independent factor for survival in oral squamous cell carcinoma

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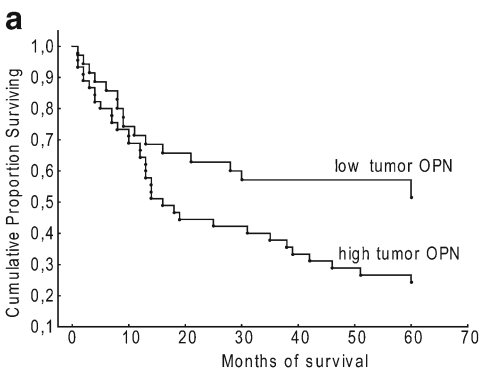
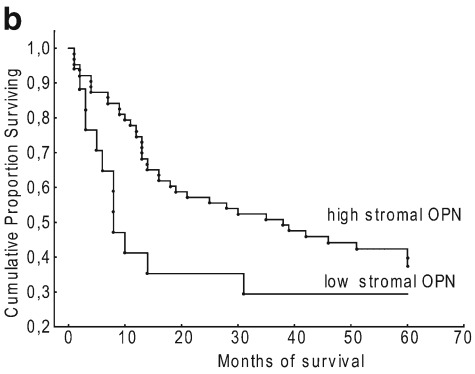
Objective: Ostepontin (OPN) is phosphorilated glycoprotein involved in various physiological and pathological events, including tumor progression. The aim of this study was to analyze the expression of OPN in oral squamous cell carcinoma (OSCC), and to assess its prognostic significance.
Method: The expression of OPN was immunohistochemicaly analyzed in 86 OSCC tissue microarrays and compared with clinicopathological variables such as tumor size, nodal stage, WHO clinical stage, Ki-67 proliferation index, and patients' outcome.
Results: The expression of OPN protein was observed in OSCC tumor cells (tOPN) and various stromal cells (sOPN), including granulocytes, macrophages, lymphocytes, plasma cells, and fibroblasts. OPN expression was higher in OSCC tumor cells compared to adjacent normal mucosa ($p<0.001$), and was associated with advanced nodal stage ($p=0.03$), WHO clinical stage ($p=0.045$), and poor clinical outcome ($p=0.023$). In multivariate analysis tOPN emerged as an independent factor for survival ($p=0.049$). There was no association between sOPN and clinicopathological variables, although a trend for higher sOPN toward the longer patients' survival was found ($p=0.12$).
Conclusion: OPN protein is upregulated in OSCC. While tOPN is involved in OSCC progression and can independently predict the clinical outcome, the role of sOPN is probably different and needs to be further elucidated.





PS-09-005

Immunohistochemical evaluation of non-intestinal sinonasal adenocarcinomas

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Objective: Non-salivary sinonasal adenocarcinomas can be divided into intestinal and non-intestinal, both with low-grade and high-grade subtypes.
Method: We analyzed two patients, one 78-y-o female and one 79-y-o male, presenting nasal obstruction and epistaxis

for the last 18 month. Specimens were obtained by endoscopic biopsies, fixed in formalin and embedded in paraffin. Three micrometers thick sections were used for immunohistochemistry.
Results: The tumors were morphologically characterized by proliferation of glands lined by a single layer of columnar epithelium with minimal cellular and nuclear atypia. Tumor stroma contains lymphocytes, plasma cells and extravasated erythrocytes. CK 18 and 20 were intensely positive in the cytoplasm of tumor cells, but with heterogeneous distribution. The reaction for CK19 and CK7 was weakly, with cytoplasmic and granular pattern, emphasizing the brush border. CK8, 34βE12 and MUC2 were negative. The immunoreaction for S100 protein was heterogeneous, with strong positive areas alternating with negative ones and cytoplasmic pattern. Proliferation index determined by Ki-67 antibody clone MIB1 was less than 5 %.
Conclusion: Sinonasal non-intestinal type adenocarcinomas are very rare tumors, which can pose serious diagnostic problems. Immunohistochemical findings and clinical information stand out in the differentiation of adenocarcinoma's subtypes.

PS-09-006
Histological and ultrastructural features of cutaneous free flaps employed in the oral cavity
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Objective: Cutaneous free flaps (CFF) are routinely used to repair tissue defects resulting from oral surgery. The concept of "mucosalisation" has been proposed although some Authors recently have supported the preservation of the cutaneous phenotype. The aim of this study was to re-evaluate histological and ultrastructural features of skin flaps in order to make a valid contribution to the debate.
Method: Five cases of forearm free flaps were compared, by histological examination and micrometric measurement, with 1 case of forearm skin and with 12 cases of oral mucosa. Ultrastructural examination was performed on 5 cutaneous flaps, 1 case of forearm skin and mucosa.
Results: At histology the CFF showed hyperkeratosis, a variable inflammatory infiltration and the presence of atrophic adnexa. Micrometric measurements revealed that the epidermis and the mucosal epithelium had similar average thickness related to the hyperkeratosis and the hypergranulosis occurring in the transplanted skin. Electronic microscopy highlighted the presence of intraepithelial Langerhans cells (LC) lacking Birbeck granules. Immunohistochemical S-100, CD1a and Langerin positivity also confirmed LC identity.
Conclusion: Histological and ultrastructural analysis confirmed that the cutaneous phenotype was preserved in all cases of CFF.

PS-09-007
Detection of EBV and HPV-high risk viruses in lymphoepithelial carcinoma of head and neck
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Objective: EBV is accepted as the main virus related to lymphoepithelial-like undifferentiated carcinoma (LEC), but recent reports indicate that HPV-16 is involved in the above type of Head and Neck carcinomas (HNC).
Method: Our aim is to compare the association of the above viruses with LEC in HNCs using immunohistochemical (p16 and LMP1) and chromogenic in situ hybridization (CISH). In the BondMax autostainer, the ready to use probes (Leica) for EBER and HPV-high risk were used. 17 cases with histological features of LEC were studied: nasopharyngeal (11), oropharyngeal (1), parotid (3) and oral cavity (2). p16 positive cases were nuclear and/or cytoplasmic in >70 % of cells while LMP-1 cytoplasmic positivity was assessed. EBER and HPV detection was always nuclear.
Results: 72.7 % of cases express EBER with cytoplasmic LMP1 positivity in 21.45 %. Six out of 17 LEC strongly expressed p16 (35.3 %) with an interesting finding 3/3 positive parotid cases. Fifty per cent of p16(+) were expressing HPV. Dual infection with CISH was observed only in one case of parotid gland LEC.
Conclusion: EBV remains the predominant virus in LEC, but several cases show strong expression of p16 with HPV detection in a substantial number, evidence of HPV-High Risk involvement in LEC HNC.

PS-09-008
Prognostic relevance of CD105 and HIF-1 L in laryngeal squamous cell carcinoma
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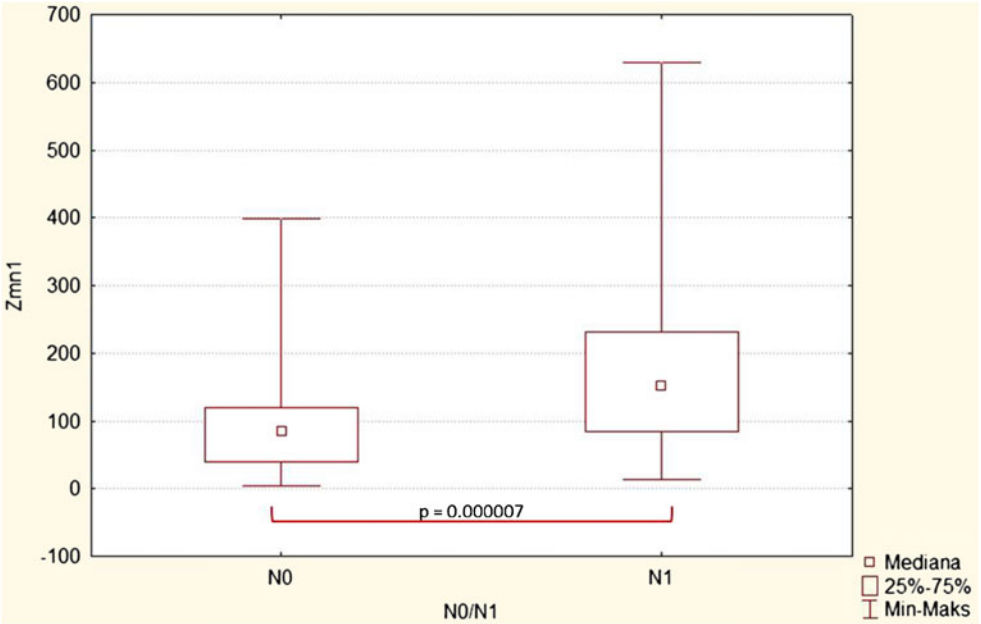
Objective: Neoangiogenesis is the crucial process in tumor progression and promoted by HIF-1α which is associated with endoglin (CD105) overexpressed in de novo formed endothelial cells.
Method: The immunohistochemical analysis for CD105 and HIF-1α expression was performed on 78 samples of 60 laryngeal squamous cell carcinoma (SCC) and 18 of normal mucosa. Automated morphometric methods were

used based on ImageJ software and own developed protocols. Analysis of microvessels density was performed in three hot spots, and included the area of positively stained endothelial cells (0-100), level of CD105 expression (0-255) and MDV/CD105 factor was calculated. We correlated morphometric data with clinico-pathological data (lymph nodes without [N(0)] and with metastases [N(+)]).
Results: The median value of MVD/CD105 in laryngeal SCC was 119.3163 (SD=103.42). It was higher in N(+) group (MVD/CD105 was 151 (SD=108)) than in the N(0) group (MVD/CD105 83.59 (SD=71.42)). Analysis of correlation of CD105 expression in N(0) vs N(+), demonstrated a statistically significant difference (p= 0.000007). Expression of HIF-1α in tumor and tumor stroma was found as nuclear and/or cytoplasmic. Expression of HIF-1α was higher in N(+) vs N(0) cases.
Conclusion: MVD/CD105 and HIF-1α could be an important prognostic factors in laryngeal SCC.



PS-09-010
Sinonasal malignant melanoma: A case report of 2 cases
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Objective: Sinonasal malign melanoma is a rare antity, mostly arising from nasal cavity and accounting for <5 % of all sinonasal tract neoplasms.
Method: We report two patients complaining of nasal obstruction and epistaxis. Endoscopy revealed partially haemorrhagic mass obliterating nasal passage. In one patient diagnosis was done as a plasmacytoma by pathologist in an another hospital. Multiple biopsies were taken. Microscopically, the tumour was consisted of medium sized cells, which had high nuclear to cytoplasmic ratio with pleomorphic nuclei containing eosinophilic nucleoli and intranuclear cytoplasmic inclusions. The cytoplasms contained variable amount of melanin pigment. Mitoses – including atypical forms- were easily detectable. There were mild inflammatory infiltrate against the tumour and rare tumour necrosis. One was showed pseudopapillary growth pattern and lymphovascular invasion.
Results: Immunhistochemically, tumour cells showed immunreactivity for S-100, Vimentin, HMB-45 and Melan-A(MART-1). Tumour cells were negative for CD-20, CD-3, CD-138, CD-56, SMA, Pan-CK and Desmin. Submandibulary lymph node metastasis was observed in one patient. This patient has undergone chemotherapy of temozolomide and 23 cures of regional radiotherapy. For the other patient, there were no metastasis detected by PET-CT.
Conclusion: Sinonasal malign melanoma is a rare malignacy, but this entity could be kept in mind to avoid missdiagnosis with other tumors sharing similar morphology.

PS-09-011

The remodeling of the human vocal fold in muscular-lamina propria interface is age-related

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Objective: Significant changes in the voice occur after 50 years. Vocal quality is dependent on the vocal fold (VF) tissue biomechanics that derive from the extracellular matrix composition and organization. We studied muscular-lamina propria interface of human VF in the aging.
Method: Two authors evaluated density of vessels and the thickness of the deep and muscle layer by HE and IHC (collagenIV) with semiquantitative score. These data were validated by point-counting morphometric method.
Results: With the aging of the vocal folds we identified increased of vessels density in the muscle and deep layers, increasing the matrix density and thickness of the deep layer, and "dissection" of muscle fibers by dense connective tissue.
Conclusion: The progressive structural changes in muscle-lamina propria interface play a crucial role in the remodeling and vocal quality. The increased density of vessels and matrix in aging may contribute to the preservation of vocal function by the physiological repairing.

PS-09-012

"Lymphoepithelioma-like" thymic carcinoma in Parotid Gland

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Objective: We report a 27-year-old woman presented with a slow growing painless mass beneath the right ear. A fine-needle aspiration revealed Whartin tumour. The patient underwent parotidectomy and histopathological examination showed thymic carcinoma with areas of thymoma.
Method: Histopathological examination was done according to conventional protocols. Immunohistochemical stainings were performed using LSAB methods. PanCK, CD3, CD20, CK5/6, CK7, Vimentin, Ki-67, CD5, Bcl-2, CD1a, S100, SMA, TdT antibodies were used.
Results: Histopathologically, a well circumscribed, nodular, hybride neoplasm finely seperated from parotid gland had two components, uniform spindle cells in basaloid form lobulated by fibrous septae and large epitheloid cells with vesicular nuclei and meganucleoli, suggesting thymoma and thymic carcinoma, respectively. Prominent lymphocytic reaction with germinal centers, high mitotic activity, small necrotic foci and microabcesses were also seen. Immunohistochemisty revealed PanCK, vimentin, CD5 and CD1a positivity. The diagnosis of "lymphoepithelioma-like" thymic carcinoma was made.
Conclusion: Thymic carcinoma is a rare tumor most commonly located in the anterior mediastinum. Thymic carcinoma which originates from ectopic rests of thymic tissue caused by defective migration of the embryonic thymus, is extremely rare. In the presented case a thymic carcinoma was found in parotid gland which is an unusual site.

PS-09-013

Evaluation of Wnt Pathway in the development of human oral tissue and Oral Squamous Cell Carcinoma

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Objective: Activation of Wnt pathway can modulate cell proliferation, survival, cell behavior, and cell fate in both embryos and adults. Its deregulation has been linked with carcinogenesis of a variety of human cancers. Oral diseases present a major and prevalent public health problem. This study investigated the role of Wnt pathway in the development of human oral mucosa and oral cancer tissue.
Method: Expression of Wnt-1, Wnt-2, Frizzled-1, β-catenin, Gsk3-β, axin, Mmp7, and c-myc was investigated in 30 human fetuses oral samples, 16 normal oral tissue from adults and 75 OSCC samples using immunohistochemistry.
Results: We observed similar and high expression, in almost all proteins analyzed in oral fetuses and OSCC tissue (Wnt-1, 89 % and 90 %; Wnt-2, 100 % and 84 %; Frizzled-1, 96 % and 93 %; β-catenin, 89 % and 89 %; Gsk3 β, 78 % and 96 %; Axin, 93 % and 100 %, Mmp7, 89 % and 97 %; c-myc, 96 % and 87 %, respectively). Additionaly, in normal oral tissue from human adults these proteins showed lower expression than in fetuses and OSCC samples (Wnt-1, 56 %; Wnt2, 67 %; Frizzled, 85 %, β-catenin, 75 %, Gsk3 β, 94 %, Axin 76 %, Mmp7, 64 % and c-myc, 76 %).
Conclusion: We suggest important roles for Wnt signaling activity in human oral development that could contribute to OSCC progression.

PS-09-014

Thyroid glands involvement in advanced Acquired Immunodeficiency Syndrome (AIDS): An autopsy-based study

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Objective: The course of HIV infection and the AIDS can be complicated by a variety of endocrine abnormalities. The aim of this study was to assess the frequency and the major

histopathological characteristics of thyroid involvement in autopsy of patients with AIDS.
Method: The thyroid were obtained from 60 patients with AIDS that were autopsied in the Death Verification Service of the Capital, Faculty of Medicine, University of São Paulo (SVOC-FMUSP) between 1996 and 1999, from a time before the use of highly active antiretroviral regimens.
Results: The anatomopathological lesions detected in 23 glands (38.3 %) were colloid goiter (52.2 %); colloid goiter + follicular hyperplasia (8.7 %); follicular hyperplasia (4.3 %); thyroiditis lymphocytic cronic (8.7 %); papilary carcinoma (4.3 %); cryptococcosis (4.3 %); tuberculosis (8.7 %); epithelioids granulomas (8.7 %) which were negatives for Ziehl-Neelsen staining. Although thyroid disease had not been clinically diagnosed, its involvement was significant and in 3 cases (13 %) it was related to the immunodeficiency, with Mycobacterium tuberculosis being the most common opportunistic agents.
Conclusion: Thyroid lesions are not uncommon in AIDS patients, occurring over a third of the patients studied. Thus, the analysis of the thyroid from autopsies of patients with AIDS can help identify most frequent lesions and help in early diagnosis and appropriate treatment for these diseases.

PS-09-015
Imaging by confocal endomicroscopy: New insight for in vivo tissue diagnosis of head and neck cancer
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Objective: Fibered confocal endomicroscopy (CEM) is a non invasive technology which allows the achievement of in vivo "optical biopsies". A morphological correlation study was performed between CEM, confocal microscopy (CM) and optical microscopy (OM) images.
Method: Forty-seven non cancerous and cancerous tissue samples of head and neck cancer and precancerous lesions were taken from fresh surgical specimens. After topical application of two fluorochrome agents, samples were imaged with CEM and CM. A morphologic correlation study was subsequently performed on CEM images, CM images and Hematoxylin-Eosin-Safran (HES) slides. The images were randomly interpreted by three pathologists. Statistical correlation between CEM, CM and HES has being finalized.
Results: CEM and CM allowed to differentiate invasive carcinoma from normal tissue with high sensitivity and specificity. They however were less performent to distinguish intra epithelial neoplasia from normal tissue or invasive carcinoma.
Conclusion: This study demonstrated the CEM ability to provide "histological-like images" that can be interpreted by pathologists, even in case of complex images as provided by head and neck cancers. Our study conducted jointly with engineers and a surgeon has identified the conditions of transfer of confocal endomicroscopy into clinical conditions and showed that this technique could help significantly the clinician during endoscopy or surgical procedure.

PS-09-016
Tumors of the salivary glands express receptors for growth hormone - Releasing hormone: Diagnostic and therapeutic implications
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Objective: Recent in vitro and in vivo studies have shown that several malignant tumors express an alternatively spliced variant of the receptor of growth hormone –releasing hormone (SV1), which operates by a ligand-dependent and independent manner.
Method: Nine (9) adenocarcinomas, 11 pleomorphic adenomas and 11 Warthin tumors were studied by immunohistochemistry for SV1 expression and visualized by diaminobenzidine staining.
Results: SV1 expression was cytoplasmic and was detected in 6/8 malignant (75 %) and 11/11 (100 %) Warthin tumors. However, only 1/11 (9 %) pleomorphic adenomas expressed SV1 ($p<0.05$, $x2$-test). Immunoreactivity ranged from mild to intense in all positive specimens, with the exception of Warthin tumors at which only intense immunoreactivity was recorded.
Conclusion: Our study, for the first time reports the presence of anti-SV1 immunoreactivity in tumors of the salivary glands. Furthermore, the high association of SV1 expression with the malignant as opposed to the benign neoplasms implies a role of SV1 in the progression of the disease. A surprising finding of our study was the high positivity for SV1 exhibited by the Warthin tumors that implies biological similarities between these histopathological entities of the salivary glands. These results imply that the use of antagonistic analogs of GHRH merit further investigation.

PS-09-017
Sialadenoma Papilliferum with inverted pattern: A case report in a young patient
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Objective: Sialadenoma papilliferum (SP) is a rare, benign neoplasm of salivary gland origin which manifests as an exophytic papillary excrescence of the mucosa. Indeed, SP is both an exophytic proliferation of papillary stratified squamous epithelium above the mucosal surface and an endophytic salivary ductal proliferation

beneath the mucosa. It arises predominantly in minor salivary glands and usually affects patients in the age range of 32–87 years, with reports in young patients being exceedingly rare.
Method: We report a case of a previously healthy 20 year-old man diagnosed with a nodular mass in the upper lip buccal mucosa. The tumour was excised and submitted for microscopic examination.
Results: Histologic examination revealed a biphasic proliferation of papillary stratified squamous and salivary ductal epithelia, both underneath the mucosal surface.
Conclusion: In this unique case, as the classical SP, the tumour has a biphasic proliferation of squamous and ductal epithelia. However, unlike the classical SP, both epithelia grow under the mucosal surface. As a result, it didn't manifest as an exophytic proliferation, but as a nodule. We excluded squamous papilloma, inverted ductal papilloma, intraductal papilloma and mucoepidermoid carcinoma, the principal entities in the differential diagnosis of SP, and concluded it to be a SP with inverted pattern.

PS-09-018
Interest of histopronostic classification in three grades in the therapeutic management of primary epithelial parotid carcinoma
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Objective: The surgical management of primary parotid cancers (PPC), which is drove by tumor staging and histological grade, remains controversial. A two-grade histological classification is used in therapeutic recommendations. Following new information in salivary gland carcinoma outcomes we assessed the value of a three-grade histological classification.
Method: A 20-year standardized single center treatment including total parotidectomy, neck dissection and radiotherapy has been assessed retrospectively. The histological review of 155 consecutively treated parotid malignancies identified 98 suitable cases for univariate and multivariate survival analyses.
Results: Treatment involved total parotidectomy in 91.6 % of cases, partial or total facial nerve resection respectively in 16.7 % and 13.5 %, neck dissection in 83.3 % and postoperative radiotherapy in 70.8 %. Tumors were high grade in 61.5 % of cases. The 5-year overall survival, disease specific and recurrence free survival rates were 79.4 %, 83.5 % and 70.8 % respectively. Univariate analysis confirmed the classical prognostic factors, whilst multivariate analysis identified clinical stage and grade, especially when analyzing three groups, as the most important prognostic factors.
Conclusion: This study supports total parotidectomy with neck dissection for the treatment of PPC and identifies the possible prognostic significance of intermediate grade tumors.

PS-09-019
Epithelial-myoepithelial carcinoma of salivary gland with pleural metastasis: A case report
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Objective: Epithelial-myoepithelial carcinoma (EMC) is a rare neoplasm occurring predominantly in the parotid gland. The histological hallmark is a biphasic cell arrangement. EMC is a low-grade malignant tumor.
Method: A 45-year-old white woman presented right chest pain for few weeks. The chest computed tomography revealed pleural effusion and thickening in the right lower lobe. There were no parenchymal nodules. Excisional biopsy was performed.
Results: Microscopic examination showed a biphasic tumor with a prominent myxoid stroma and tumor cells with clear cytoplasm involving pleural tissue. Immunohistochemistry showed tumor cells positive for keratin, S100 protein, smooth-muscle actin, p63 protein, vimentin. Histological and immunohistochemical features confirmed the diagnosis of epithelial-myoepithelial carcinoma. The patient underwent a right parotidectomy 3 years earlier for removal of 3.5 cm mass diagnosed as EMC.
Conclusion: Epithelial-myoepithelial carcinoma of salivary gland is a rare low-grade malignant neoplasm with a potential for local recurrence and metastases. Rare metastases for lungs, kidney and brain were reported. We described an additional case of pleural metastasis.

PS-09-020
Fetal parotid gland morphology complicated with growth retardation at late gestation
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Objective: Salivary defense system recognized as an important protective factor of the child oral environment. Research data reveal that bacterial infection, dental caries and periodontal diseases have a higher incidence in cases of salivary glands dysfunction. The aim of present study was to find out the morphological peculiarities of the fetal parotid gland in cases of restrictions of its intrauterine growth (IUGR) at late gestation.

Method: Parotid gland of twenty human fetuses with IUGR from the late spontaneous abortions material were compared with fifteen fetal glands in cases of induced abortions due to psychological reasons (control group). Tissue samples were stained with hematoxylin and eosin. Stereological examination was done to find out volume fractions of parotid gland structural components.
Results: Results have shown the reduction of the area of acini, large collected ducts, striated and intercalated ducts in IUGR group. The volume fractions of vessels were also lower than on controls. The foci of immature secretory lobes in cases of growth restriction occupied wider zones within loose, poorly cellular, fibrous stroma.
Conclusion: Our study demonstrates the delay of the parotid gland structural maturation in pregnancies complicated with IUGR. Impaired growth and secretory gland's dysfunctions may cause pathological changes in oral ecosystem of a child.

PS-09-021
Carcinoma ex pleomorphic adenoma successfully treated with trastuzumab and radiotherapy
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Objective: Carcinoma ex Pleomorphic Adenoma (CXPA) is an aggressive tumour with metastatic disease and rapid clinical course. Some CXPA harbour HER-2 gene amplification and protein overexpression suggesting potential role for Trastuzumab therapy. There are occasional reports of such treatment in salivary duct carcinoma but little is known for CXPA.
Method: A 59 year old man presented in February 2010 with T2N2 M0 CXPA treated by nerve-sparing total parotidectomy and adjuvant radiotherapy. In May 2011 he relapsed in cervical nodes (biopsy proven) along with multiple metastases to the bone, adrenals and retroperitoneum. Tumour cells showed high levels of HER2 gene amplification when tested with in silver situ hybridization (SISH).
Results: The patient received palliative radiotherapy to the spine and commenced trastuzumab, at 3 weekly intervals on 5th August 2011. He experienced resolution of symptoms and repeat CT scans after 3 cycles revealed a good partial response. He continues on maintenance trastuzumab to date.
Conclusion: This case illustrates that Trastuzumab therapy can be successfully used in CXPA. The histological features of salivary duct carcinoma may not be present in the subtype of CXPA and the tumour may still benefit of this targeted treatment. Pathologists should be performing HER2 status in presence of CXPA.

PS-09-022
Chondroid chordoma of cervical spine: A case report
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Objective: Chondroid chordoma was described by Heffelfinger as a biphasic malignant neoplasm possessing elements of both chordoma and cartilaginous tissue.
Method: A 47-year-old man presented with a painful mass in the pharynx area. MRI revealed an ill-defined mass, arising from the body of (C4) vertebra, which extended to the around soft tissue. The diagnosis of chondroid chordoma was suspected in the material biopsy from the pharynx and the patient underwent a radical excision of the mass. The surgical specimen consisted of multiple pieces of whitish tissue measuring 0.8×1.7×2.8 cm in aggregate. The sections were examined with H + E stain and followed by immunohistochemical study.
Results: The lesion was composed of a mixture of areas that resembled typical chordoma and others low grade chondrosarcoma. Immunohistochemical study: chordoma areas, (AE1/AE3+, Ck 8/18+, Ck19+, EMA+, S-100+, Vimentin, CD34−, CD31−, SMA−), low grade chondrosarcoma's areas (Vimentin+, Ki-67:3 %). The above findings confirmed the preoperative diagnosis.
Conclusion: The extent of surgical resection, the histological subtype, and the Ki-67 index can help to predict the clinical outcome for chondroid chordoma's patients. The patient after 3 months is in generally good health, and is followed up by oncologists.

PS-09-024
Basaloid squamous cell carcinoma of the head
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Objective: Basaloid squamous cell carcinoma is an uncommon variant of SCC and seems to have a poorer survival than classical SCC.
Method: Pathologically specimens can have nearly pure basaloid features or a mixture of basaloid and squamous features. Basaloid squamous cell carcinoma is also commonly confused histologically with poorly differentiated SCC.
Results: The presence of particular histologic features may be associated with poorer outcome survival in the basaloid squamous cell carcinoma group was less than half in the poorly differentiated squamous cell carcinoma groups. Distant metastases occured in 73 % of patients with basaloid squamous carcinoma and 10 % of patients in the poorly differentiated squamous cell carcinoma groups.

Conclusion: Considering the high distant metastatic rate of basaloid squamous carcinoma and poorer overall survival rate a more extensive survey is indicated in these patients before surgery is recommended.

PS-09-025

Clinical and pathological characteristics of polymethylmetacrylate and hialuronic acid in the rat tongue: An experimental model to evaluate the effect of dermal fillers

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Objective: Dermal fillers are injectable products commonly used in aesthetic medicine. This type of treatment, which often replaces traditional surgical procedures provides satisfactory cosmetic results. It is known, however, that there is a risk of undesired effects at the site of injection of the product or even at a distance. Literature reports numerous cases of orofacial injuries caused by dermal fillers. The aim of this study is to evaluate two of the most widely used facial dermal fillers for aesthetic purposes in an effort to identify adverse reactions they may produce.
Method: Two of the most commonly used materials for aesthetic purposes by dermatologists and plastic surgeons, polymethylmetacrylate and hialuronic Acid were injected in rat tongues: 10 % polymethylmethacrylate (n=16) and 20 mg/mL hyaluronic acid (n=18), compared to an inert solution for control (n=16). After 7, 60 and 90 days, local clinical and histological alterations were analyzed.
Results: The following factors were verified: intensity of the inflammatory response (H&E), amount of newly formed blood vessels (IHC) and macrophages and collagen fibers density (picrosirius). Results showed that both filling materials triggered local inflammatory response to a greater or lesser degree.
Conclusion: polymethylmethacrylate showed cases of foreign body reaction, while hyaluronic acid demonstrated characteristics suggesting biocompatibility.

PS-09-026

Comparison of effects of clodronate and zoledronic acid on the repair of maxilla surgical wounds: Histomorphometric, receptor activator of nuclear factor-kB ligand, osteopro-tegerin, von Willebrand factor, and caspase-3 evaluation

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Objective: The aim of this study was to compare clodronate and zoledronic acid regarding their influence on the repair of surgical wounds in maxillae (soft tissue wound and tooth extraction) and their relation to osteonecrosis.
Method: Thirty-four Wistar rats were allocated into three groups according to the treat-ment received: (i) 12 animals treated with zoledronic acid, (ii) 12 animals treated with clodronate and (iii) 10 animals that were given saline solution. All animals were subjected to tooth extractions and surgically induced soft tissue injury. Histological analysis of the wound sites was per-formed by means of hematoxylin–eosin (H&E) staining and immunohistochemical staining for receptor activator of nuclear factor-kB ligand (RANKL), osteoprotegerin (OPG), von Willebrand factor, and caspase-3.
Results: The zoledronic acid group showed higher incidence of non-vital bone than did the clodronate group at the tooth extraction site. At the soft tissue wound site, there were no significant differences in non-vital bone between the test groups. RANKL, OPG, von Willebrand factor, and caspase-3 did not show significant differences between the groups for both sites of surgical procedures.
Conclusion: Both of the bisphosphonates zoledronic acid and clodronate are capable of inducing maxillary osteonecrosis. Immunohistochemical analysis suggests that the involvement of soft tissues as the initiator of osteonecrosis development is less probable than has been pointed out.

PS-09-027

Differential diagnosis of lichen planus and lupus erythematosus oral lesions using PAS and immunohistochemistry

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Objective: The aim of this study was to evaluate the expression of CD1a, CD4, CD8, CD20, caspase-3, tryptase and basement membrane thickness in oral lesions of lichen planus (LP) and lupus erythematosus (LE).
Method: Oral lesions of LP (n=21) and LE (n=23) were biopsied. After confirmation of diagnosis, the specimens were submitted to PAS and immunohistochemistry.
Results: CD1a expression was significantly greater in epithelium and connective tissue in LP. Epithelial CD4 and CD20 did not differ between the diseases, but were greater in connective tissue in LP. CD8 expression was greater in both epithelium and connective tissue in LP. Caspase-3 did not differ between the groups, whereas tryptase was greater in LE epithelium. Basement membrane thickness did not differ between LP and LE.
Conclusion: CD1a, CD4, CD8, CD20, caspase-3 and tryptase expression and the basement membrane thickness are

not definitive criteria for differential diagnosis of oral lichen planus and lupus erythematosus.

PS-09-028

Usefulness of p16 immunostaining in Squamous Cell Carcinomas (SCC) of the larynx and hypopharynx

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Objective: HPV status has been surrogated in routine practice by p16 immunostaining. The aim of this study is to define the histological features and overall survival of p16(+) versus p16(−) laryngeal and hypopharyngeal SCC cases.
Method: A total of 80 SCC of the larynx and hypopharynx diagnosed during the 4 years were randomly selected, their histological sections were re-evaluated and follow up was retrieved from the medical files. P16 and p53 immunostaining was performed. Viral status was analyzed by PCR and in situ hybridization. Kaplan-Meier survival curves and log rank test was performed using SPSS software.
Results: 31 % (25/80) were p16 (+)/p53 (−), and 68 %(55/80) were p16(−)/p53(+). The 92 %(23/25) of p16(+) cases were in males with an average age of 54,4 years (range 20–77). The 72 %(18/25) of p16(+) tumors were well-moderately differentiated SCCs. Viral status was obtained in 44 %(11/25) of the cases, 63 %(7/11) being HPV-16. 5-year survival was 84 % for p16(+) tumors and 56 % for p16(−)s (log rank, $p<0.05$).
Conclusion: With reliability, p16 immunostain may surrogate the determination of HPV status in SCC of the larynx and hypopharynx. Overall survival is significantly better in p16(+) cases, most being SCC well-moderately differentiated neoplasms.

PS-09-029

Screening for Human Papillomavirus (HPV) in Squamous Cell Carcinomas (SCC) of the Upper Aerodigestive Tract (UADT): A clinicopathologic study of 136 cases

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Objective: HPV detection in UADT cancer have prognostic implications. This study try to establish the clinicopathological features and overall survival differencies between p16 (+) versus p16(−). Method:
Method: A total of 136 SCC diagnosed during 3 years were randomly selected, their histological sections were re-evaluated and follow up was retrieved. P16 and p53 immunostaining was preformed. Viral status was determined by PCR and in situ hybridation. Kaplan-Meier, log rank and Cox tests was preformed using SPSS software.
Results: 31 %(43/136) were p16(+)/p53(−) and 68 %(93/136) were p16(−)/p53(+). In 92 % (35/38) of p16(+)/p53(−) cases DNA viral was present, being the most frecuent HPV 16, 33 types, mostly located in larynx (41 %, 18/43). Significative correlations was established between HPV(+) and p16(+) cases (Spearmen). Interestingly, 10 of patients develop metachronic second primary tumor. Thirty months overall survival was 81 % for p16(+) tumors versus 53 % for p16(−), log rank $p=0{,}0089$ ns. Differences are related with existence of second primary neoplasms (Cox $p=0{,}0004$).
Conclusion: The immunostaing for p16 is a tool for identification HPV related tumors. In our material HPV(+) cases are located more in larynx than oropharynx. The overall survival differences were due to the presence of second primary tumors.

PS-09-030

Case report: An 80 year old man with odynophagia

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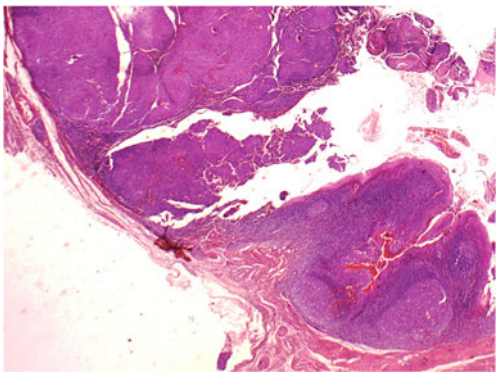
Objective: Odynophagia may be caused by inflammatory/infectious conditions and tumors arising within the oropharynx. We present an unusual case of a follicular dendritic cell sarcoma (FDCS) of the tonsil manifesting with odynophagia.
Method: An 80 year-old man presented with odynophagia refractory to medical therapy; a 0.9 cm left tonsillar mass was noted on inspection. Bilateral tonsillectomy was performed. A panel of antibodies was applied on paraffin tissue section.
Results: Grossly, the left tonsil featured a 1.2 cm well circumscribed grey lesion. Histologic examination showed a proliferation of spindle to ovoid cells arranged in fascicles with swirling qualities admixed with scattered lymphocytes. Frequent mitoses and apoptotic bodies were seen but no "tumoral" necrosis was recognized. Tumor nests were separated by thin stromal septi containing a prominent glioblastoma-like microvascular proliferation with focal formation of glomeruloid tufts. The tumor cells were immunoreactive for CD21, CD23 and vimentin.

Conclusion: FDCS'-s are rare recently described and likely under-recognized malignant tumors capable of simulating poorly differentiated carcinoma, melanoma or lymphoma. In the initial assessment, an extended panel of antibodies inclusive of FDC markers is of valuable diagnostic help.



PS-09-031

Ceruminal gland derived pleomorphic adenoma with intrasialodochal and intracapsular epithelial proliferation of atypical ductal hyperplasia or low-grade ductal carcinoma in situ breast-type

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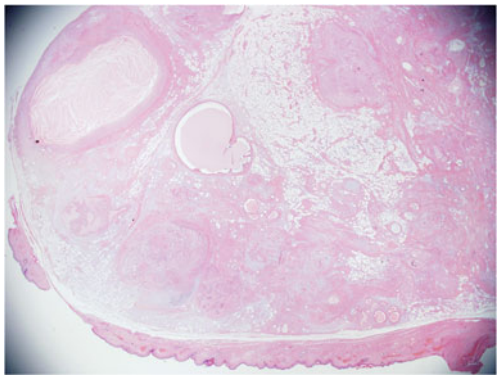
Objective: Primary tumors of the external auditory canal are rare and often difficult to diagnose. We present a case of ceruminal gland derived pleomorphic adenoma with unusual features.
Method: A 55 year-old man presented with a slow growing lesion in the left external auditory canal. The resection specimen was routinely processed.
Results: The specimen consisted of a 1.8 cm sized well circumscribed yellowish nodule covered on one side by skin. The histological examination revealed a partially encapsulated tumor composed of fat and myxochondroid tissue separating biphasic epithelial-myoepithelial elements of diverse patterns and including an intraductal (intrasialodochal) epithelial proliferation of ADH or low-grade DCIS-like character. Ductal tumor cells were immunoreactive AR, ER, Mammaglobin, S-100, CK-HMW, CK5, E-cadherin and Vimentin; Ki-67 (2–4 %). Ductal structures were surrounded by intact myoepithelial layer. ETV6-NTRK3 gene rearrangement was negative. The preferred diagnosis was ceruminal gland derived pleomorphic adenoma with intrasialodochal and intracapsular atypical proliferation of ADH/LGDCIS-breast type. Our differential diagnosis also included ceruminal gland adenoma NOS, polymorphous low grade adenocarcinoma and mammary analogue secretory carcinoma.
Conclusion: Ceruminal gland pleomorphic adenoma is rare and can develop atypias along the carcinoma ex pleomorphic adenoma spectrum.



PS-09-032

Cystic lesions of the jaws

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Objective: A great variety of cystic lesions can affect the jaws, varying from epithelial or non-epithelial, odontogenic or non-odontogenic, developmental, inflammatory or neoplastic in origin. It is important to recognize and correctly diagnose these lesions.
Method: All cases of cystic jaw lesions present in the files of the Anatomic Pathology of the University of Bologna at Bellaria Hospital in the period 1-01-1992\\31-12-2011 were retrieved.
Results: The cases series consisted of 1141 cases. The most frequent types were radicular cysts (537 cases, 47.06 %), keratocystic odontogenic tumours (Keratocyst)(TcO)(199 cases, 17.44 %) and dentigerous cysts (120 cases, 10.52 %). In patients younger than 18 years of age the percentage of radicular cysts was lower (38 %) than in adults, while increased the percentage of dentigerous cysts (35 %). The percentage of TCO was 17 %, being related to the Gorlin-Goltz syndrome.
Conclusion: The present series confirms that the radicular cyst is the most common type of cystic lesion affecting the jaws. The similar neoplastic cystic lesion as TCO is the second most frequent type. Therefore attention should be taken in order to provide the correct diagnosis of cystic lesions of the jaws and to avoid misdiagnosis of neoplastic odontogenic cysts.

PS-09-033

Risk of neoplastic transformation in oral epithelial precursor lesions

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Objective: Oral squamous cell carcinoma (OSCC) is usually preceded by epithelial precursor lesions (EPL). The aim of the present study is to assess the risk of developing OSCC in EPL, as graded according to WHO 2005 criteria. The Ljubljana classification will be followed.

Method: All oral biopsies diagnosed as EPL in the period 1992–2006 were retrieved from the files of the Section of Anatomic Pathology of the University of Bologna at Bellaria Hospital. The details Follow-up was obtained from clinical records.

Results: Follow-up varied from 12 to 216 months. OSCC arose in 2/54 cases of simple hyperplasia (3.7 %), in 2/16 cases of basal-parabasal cell hyperplasia (2.5 %), in 9/32 cases of atypical hyperplasia/carcinoma in situ. Time elapsed from the initial biopsy and OSCC appearance varied from 99.5 months (range 67–132) in simple hyperplasia; 22 months (range 19–25) in basal/parabasal hyperplasia, and 50,4 months (range 12 to 156) in cases of atypical hyperplasia or carcinoma in situ.

Conclusion: The data presented demonstrates that simple hyperplasia has a low risk (<4 %) of neoplastic transformation. The risk increases when EPL appear and is related to the degree of epithelial atypia.

PS-09-034

The prognostic value of resection margins in oral squamous cell carcinoma

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Objective: Resecting oral squamous cell carcinoma (OSCC) with appropriate margins of uninvolved tissue is of critical importance.

Method: 180 surgically resected OSCC with follow-up varying from 6 to 120 months (media 40 months) were histologically reviewed.

Results: Lymph-node metastases were found in 43 % of cases showing depth of invasion >5 mm and in 14.5 % of cases which showed depth of invasion <5 mm. Furthermore they were found in 53.2 % of cases with nerve invasion and in 28.3 % of cases without nerve invasion. Recurrences appeared in 39.4 % of cases with minimum distance from resection margins <5 mm, and in 23.45 % of cases with minimum distance >5 mm. The second OSCC appeared in 37.5 % of cases with high grade epithelial precursor lesions (EPL) on surgical margins and in 16.12 % of cases without EPL on surgical margins.

Conclusion: The present data confirms that accurate evaluation of histological features has a strong prognostic impact on lymph-node metastases, recurrences and appearance of second OSCC.

PS-09-035

Peripheral cemento-ossifying fibroma: A clinicopathologic and immunohistochemical study of 11 cases

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Objective: Peripheral cemento-ossifying fibroma (PCOF) is a growth of the gingival tissues that predominantly affects women and is usually located in the maxilla anterior to the molars. Its pathogenesis remains unknown. We present a study of a series of PCOF and discuss pathogenesis, clinical, histologic and immunohistochemical features as well as differential diagnosis.

Method: This is a five-year (2006–2010) retrospective study of 11 cases of PCOF. Medical files and histologic slides of all eleven patients were reviewed.

Results: There were 3 male and 8 female patients. The mean age was 31.8 years (range 30–87). Patients presented with a polypoid gingival lesion measuring 0.7 to 2.5 cm. The definitive diagnosis was established by histological examination which showed a cellular connective tissue containing focal areas of cementum-like material or trabecular bone. The immunohistochemical study revealed that the proliferating cells showed myofibroblastic characteristics and weak focal positivity with progesterone receptors but did not express estrogen receptors.

Conclusion: Our results indicate that PCOF can be considered as a myofibroblastic proliferation with focal calcifications of odontogenic origin and a putative hormonal influence. Although, PCOF is a benign lesion, we think it deserves recognition because of its relatively high postoperative recurrence rate, up to 20 %.

PS-09-038

Myoepithelioma of tongue

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Objective: Myoepitheliomas are rare benign neoplasms that may be located in various organs as salivary glands, breast, skin, lung. The most of them are usually seen in the parotid gland and the minor salivary glands of the hard palate. They consist mostly of myoepithelial cells with variable cellular morphologies including spindle, epithelioid, plasmacytoid, or clear cells. A variable stromal component can be seen in these tumors.
Method: A 25-year-old female patient who complained with a tongue swelling was admitted to the Otorhinolaryngology Service. Intraoral examination revealed a mass measuring 2.5 cm in diameter on the right side of her tongue. Excional biopsy was performed and the surgical specimen was sent for histopathological analysis.
Results: Histopathologically, the tumor was thinly encapsulated and had got oedematous/myxoid stroma. It was composed of spindled and plasmositoid cells. 1 or lower mitotic figure per 10 high power fields was seen. The positive staining for pancytokeratin, epithelial membran antigen, smooth muscle actin, S-100 protein, and glial fibrillary acidic protein were seen in tumoral cells on immunostaining. Ki-67 labelling index was 2–3 %.
Conclusion: Theoretically, a myoepithelioma in the tongue may be seen. But, to date, and in our knowledge, none of the myoepitheliomas has been reported in the tongue.

PS-09-040

Nasopharyngeal carcinoma and prognostic indicators: EGFR, P53 and LMP1

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Objective: Nasopharyngeal Carcinoma (NPC) is the most common epithelial malignancy of the nasopharynx. Undifferentiated NPC (UCNT), the most frequent histological type, represent a distinct entity.
Method: The study involved 75 patients (pts), 50 H/25 F, an average age of 37 years. All our pts had a nasopharyngeal biopsy with overexpression of EGFR research by immunohistochemistry and 13 pts have benefited from the search for LMP1 and P53, in addition to the EGFR.
Results: Among 75 pts, 15 did not overexpress EGFR (20 %) 60 overexpress EGFR (80 %). Among the 60 positive patients, EGFR is correlated to a chemoresistance, a decrease in response time (p=0.0008), a decrease in disease-free survival (p=0.0008) and a decrease in overall survival (p=0.0001). The results on 13 pts revealed a positive immunostaining for EGFR and LMP1, negative for P53. 100 % of pts are at stage IV with a time of relapse average of 4 months, a Diesease free survival 7.2 months and overall survival of 8 months.
Conclusion: The overexpression of EGFR in UCNT is proved with a 80 % overexpression, it is a prognostic factor certain to be systematically integrated with other conventional factors. In addition to its prognostic value, EGFR positivity can be used to indicate an anti-EGFR targeted therapy in NPC.

PS-09-041

Immunohistochemical Characterization of Salivary Gland Tumors

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Objective: Salivary gland tumors reveal a broad morphology and immunohistochemistry may be helpful.
Method: We examined 12 mucoepidermoid (MEC), 8 adenoid cystic (ADC), 3 asinic cell (ACC) and 4 salivary duct carcinomas (SDC); 2 myoepitheliomas (ME), 5 basal cell (BCA), 31 pleomorphic adenomas (PA) and 18 Warthin tumors (WT) for SMA, Calponin, S100, CD10, GFAP, p63, CEA, GCDFP15, GLUT1, 34BE12, CK14, CK19, CD117 and Galectin3, using tissue microarray.
Results: Tumors expressing myoepithelial markers were ADC (SMA, Calponin), BCA (SMA, Calponin, p63), PA (SMA, Calponin, S100, CD10, GFAP, p63), ME (S100, CD10, GFAP), MEC (p63) and WT (p63); PA being the only tumor expressing all of the markers in the panel. GFAP, S100, CK14, p63, CK5/6 and Galectin3 expressions were higher in benign and CK19 was higher in malignant tumors (p<0.05). Some of our findings helping in differential diagnosis are as follows: In differentiation of PA from ADC: GFAP, CD10, GCDFP15 positivity; higher expression of S100; lower expression of CK14 and CD117 favors PA. In differentiation of PA from BCA: GFAP and CD10 positivity favors PA. In differentiation of MEC from SDC: CD10, CK14, p63 and CK5/6 positivity favors MEC.
Conclusion: We conclude that salivary gland tumors may be well characterized by using distinct markers in each differential diagnosis.

PS-09-042

Salivary immunoglobulins for assessing cariogenicity in children with intrauterine growth retardation

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Objective: It is known that salivary glands pathology results in oral homeostasis disturbances and increases risk of infection diseases like caries.It is known that salivary glands pathology results in oral homeostasis disturbances and increases risk of infection diseases like caries.
Method: Oral examinations were performed in 30 children aged 6 years with IUGR (group I) and 20 controls without IUGR in anamnesis (group II). Non stimulated whole saliva samples were collected. The concentration of sIgA was determined using an immunoassay kit. The salivary flow rate was determined from the volume yielded within 5 min; the pH was measured by pH-electrode. Microbiologically the level of MS in saliva was found.
Results: The results have shown the increased level of sIgA and MS in group I. It was accompanied with the lowered saliva flow rate and buffer capacity. Caries experience was also higher in group I.
Conclusion: This finding tends to support the hypothesis that structural and functional retardation of salivary glands may decrease the oral immune defense and stimulate the early childhood caries development.

PS-09-044
Urbach-wiethe disease (lipoid proteinosis); A case report
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Objective: Lipoid proteinosis is a rare autosomal resessive disorder of variable severity that may involve the skin, mucous membranes of the upper respiratory tract and internal organs that may display different clinical manifestations based on the site of involvement.
Method: A 34 year old male patient was admitted to our hospital with a complaint of hoarseness present since childhood but had worsened in recent years. A dermatological examination revealed light brown papillomatous skin lesions on the dorsum of both hands and elbows present for a long duration. Endoscopic examination of the larynx revealed widespread mucosal thickening and irregularity.
Results: Microscopic examination reveales the deposition of PAS positive eosinophilic hyaline materials negative for Congo red stain in the dermis and submucosal regions. His final diagnosis was lipoid proteinosis with skin and larynx involvement.
Conclusion: The case presented here, which is a typical sample, has been reported to draw attention to the fact that lipoid proteinosis is also included in the differential diagnosis in patients presenting with hoarseness in childhood in otolaryngology.

PS-09-045
Nasal septal lobulary capillary hemangioma
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Objective: Lobulary capillary hemangioma (LCH) is a benign, rapidly growing vascular lesion of the skin and mucous membrans. It may rarely present as a mass of considerable size and thus entirely fill the nasal cavity. It occasionally appears in the nasal region as a pedunculated or broad base mass. Trauma and hormonal influences are the most common presumed etiologic factors. LCH usually involves the gingiva, lips, tongue, and buccal mucosa. The most common symptoms are epistaxis and nasal obstruction.
Method: In this report; a case of 14 years old boy operated surgically of LCD of the nasal septum, which occurred post delivery was described.
Results: On examination, a red pedunculated bloody swelling 3,5*2 cm was noted arising from the posterior part of the nasal septum to nasopharinx. Histopathologically LCH has characteristics consistent with lobular prolifeation of capillaries in a fibromyxoid stroma.
Conclusion: We emphasise that rarely seen LCH must be kept in mind in the differantial diagnosis of a rapidly growing mass, who is cured surgically. Follow up 2 months later showed no recurrance. Although the head and neck is not an uncommon region, the nasal cavity is extremely rare sites for LCH in children.

PS-09-046
Large Cell Neuroendocrine Carcinoma as mucosal lesion (M-LCNEC) of the head and neck regions in Japanese patients: A new clinico-pathologic entity
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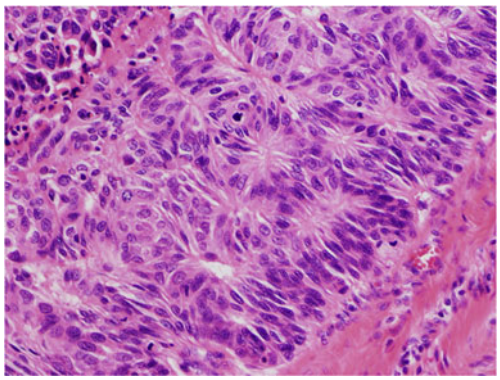
Objective: Large cell neuroendocrine carcinoma (LCNEC) is well known as a subtype of lung cancer. Our objective is to establish mucosal LCNEC (M-LCNEC) as a new entity in the head and neck regions.
Method: We re-estimated 814 surgically resected specimens of the primary mucosal carcinoma in the head and neck regions during 2002–2009. The immunostainings for neuroendocrine (NE) markers such as CD56, chromogranin-A and synaptophysin were performed. In the cases, which were positive for>two NE markers, we re-diagnosed as "M-LCNEC".
Results: Only eight cases (0.98 %) were re-diagnosed as M-LCNEC. All cases were male and their mean age was 64.6 years old. Three cases occurred in the oro-pharynx, four cases in the larynx and one case in hypopharynx. A half

of the cases showed dead of disease. Histologically, M-LCNEC showed the organoid pattern growth of large basaloid cells, in which were seen the central necrosis, rosette formation, peripheral palisading, and high mitotic figures (>15/hpf). Immunohistochemically, M-LCNEC indicated to be positive for two or three NE markers.
Conclusion: M-LCNEC, which occurs as mucosal lesion in the head and neck regions, indicated relatively poor outcome. We propose that M-LCNEC is a new clinico-pathlogical entity.



PS-09-047
Expression of claudins −1, −3, −5, −7 and −11 on the progression of squamous cell carcinoma of the lip
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Objective: Claudins are integral transmembrane proteins of tight junctions, critical for maintenance of cell adhesion and polarity. Altered claudin expression has been detected in carcinomas and correlates with tumour progression. Actinic cheilits is a pathologic condition that affects the lower lip, caused by chronic exposure to solar radiation; it corresponds to the early phase of squamous cell carcinoma. We investigated claudin patterns in phases of actinic cheilitis, as alterations in adhesion molecules are considered important during the progression of this process.
Method: Immunohistochemistry against claudins −1, −3, −5, −7 and −11 was performed in 100 cases of actinic cheilitis/squamous cell carcinoma; results were analysed qualitatively.
Results: Actinic cheilitis (low grade intraepithelial squamous cell carcinoma), and the invasive front of superficially invasive squamous cell carcinoma and in situ squamous cell carcinoma were negative for claudins −1, −3 and −7. Claudin −5 was present on all epithelial layers in most cases evaluated. Claudin −11 was present in all epithelial layers in actinic cheilitis, but negative in cases of superficially invasive and deeply invasive squamous cell carcinoma.
Conclusion: Altered expression of claudins is present in AC from its incipient phase throughout the progression of the disease to invasive squamous cell carcinoma.

PS-09-048
Fibrous dysplasia vs ossifying fibroma of the jaw: Immunological characterization performing osteoprotegerin, RANK and RANKL proteins
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Objective: Fibrous dysplasia of the jaws and ossifying fibroma are maxillofacial fibro-osseous lesions that should be distinguished from each other as they show distinct patterns of disease progression. However, both lesions often show similar histological and radiological features, making distinction between the two a diagnostic challenge.
Method: In this study, we performed immunological analyses of 16 ossifying fibromas and 16 cases of gnathic fibrous dysplasia with typical histological aspects. We examined the difference between fibrous dysplasia and ossifying fibroma in the expression of the OPG/RANK/RANKL markers. This cascade is a final mediator of osteoclastogenesis as well as osteoclastic development demands specific factors produced by preosteoblastic/stromal cells.
Results: Osteocytes, osteoblasts and osteoclasts showed similar expression patterns for all markers tested. Immunoreactivity for RANKL and OPG was positive in 75 % and 81,25 % of the osteoblasts, respectively in the cases of FD, however RANK was expressed in the giant cells (osteoclasts) in all cases they were present (50 %). The OFs expressed RANKL in 56,25 % and OPG in 87,5 % of the osteoblasts and RANK in 56,25 % of the cases in osteoclasts.
Conclusion: These findings suggest a mild suppression of the osteoclastogenesis in both lesions, mostly in OFs, although RANKL was expressed in the majority of the cases.

PS-09-049
Unusual tumours of the mandible? Think of metastases!
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Objective: Metastases to the jaw bones are uncommon and are most likely to arise from primary lung, breast, prostate or kidney tumours. Jaw bone metastases from a primary oesophageal carcinoma are especially rare, with only seven reports published in the literature.
Method: Here, we describe the case of a 69 year-old male patient where 7 years elapsed between the

diagnosis and successful treatment of a poorly differentiated, stage pT2N0 primary oesophageal adenocarcinoma and re-presentation with jaw pain due to a metastatic mandibular deposit.
Results: The morphological appearance of the metastasis and immunohistochemical positivity with CK20, CK7 and CDX2 strongly supported an adenocarcinoma of upper gastrointestinal tract origin.
Conclusion: This case is of particular interest as there is an unusually long time between the detection of the primary oesophageal adenocarcinoma and diagnosis of metastatic disease. The longest period of time we have found for this reported in the literature is 9 months, although it is known that some oral metastases may appear more than 10 years following the primary tumour diagnosis.

PS-09-050
Melanotic oncocytic metaplasia of the nasopharynx - A report of three cases and review of the literature
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Objective: Melanotic oncocytic metaplasia of the nasopharynx is a rare condition which is characterized by the presence of usually a small, brown to black colored pigmented lesion around the Eustachian tube opening. Although it is a benign lesion, it may be clinically misdiagnosed as malignant melanoma. Microscopically, melanotic oncocytic metaplasia is a combination of oncocytic metaplasia of the epithelium of the gland and melanin pigmentation in its cytoplasm.
Method: In our present study, we report three cases of melanotic oncocytic metaplasia of the nasopharynx.
Results: All the three cases occurred in men and were presented as multiple black pigmented lesions around the torus tubarius. Microscopically, mucous glands with diffuse oncocytic metaplasia and numerous black pigments were observed. No cellular atypia was observed. Immunohistochemically, the scattering of S-100 protein-positive, and HMB-45-negative dendritic melanocytes was evident.
Conclusion: This is the first report of cases of oncocytic metaplasia of the nasopharynx in Korea.

PS-09-051
Hemangioma in a lymph node: A case report
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Objective: Hemangioma is a benign vascular tumor that is extremely rare in lymph nodes. Up to date, only 21 cases of lymph node hemangioma, including ours, have been reported in the literature. We report a case of a hemangioma arising in a cervical lymph node.
Results: A 42-year-old man, presented with a palpable right-sided submandibular mass. He had no significant prior medical history, or any other complaints. The ultrasound of the neck revealed a 4.8×2.7 cm hypervascular, hyperechogenic cervical node, at the level of the right common carotid artery bifurcation. It was recommended for surgical resection. On gross examination, it appeared as a well circumscribed, firm and whitish, node, with small punctuate hemorrhagic foci. Whereas, histopathological examination revealed a dense proliferation of small capillary-sized blood vessels with elastic change, that almost entirely had replaced the lymph node parenchyma. Intercapillary stroma was scant. Immunohistochemically, it was immunoreactive for CD34, confirming the diagnosis of a primary capillary hemangioma of the lymph node. There was no indication of malignancy. Fifteen months after surgery, no recurrence was seen.
Conclusion: Despite its rare occurrence lymph node hemangioma should be considered in the differential diagnosis of malignant vascular tumors. Surgical resection is curative in primary nodal hemangioma.

PS-09-052
Adhesion molecules in primary oral mucosal melanoma: Study of integrins, claudins and immunoglobulins in a series of 35 cases
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Objective: Primary oral mucosal melanoma is a rare and aggressive tumor. Recent studies have reported a correlation between increased tumor invasion and metastatic phenotype with an altered expression of adhesion molecules profiles. The present study analyzed the expression of integrins, claudins and immunoglobulins in oral mucosal melanomas and correlated results with clinical features of patients.
Method: Immunohistochemistry against these molecules was performed in thirty-five cases of primary oral mucosal melanomas organized into “tissue microarray” and the results were related to clinical and histological features of patients.
Results: Some subunits of integrins presented downregulation and this was associated with vascular invasion. Increased expression of integrin beta3 and immunoglobulin CD166 (ALCAM) was statistically associated with cases with extensive vascular invasion ($p<0,05$). Lower

expression of the immunoglobulin CD54 (ICAM) was associated with cases with extensive necrosis. Most cases with metastasis were negative for immunoglobulin CD66 (CEACAM). Several subunits of claudins showed down-regulation in the cases analyzed, and, although not statistically significant, it showed to be partially related with histological factors of poor prognosis.
Conclusion: Altered patterns of adhesion molecules, mainly integrins and immunoglobulin seem to participate in the pathogenesis and outcome of oral mucosal melanomas.

PS-09-053

A rare carcinoma of minor salivary gland

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Objective: Clear cell tumor is an uncommon subgroup of salivary neoplasia, and case with predominantly myoepithelial differentiation is extremely rare. It is important to recognize the clinicopathologic features of this unusual tumor, because of its histological similarity to several other primary and metastatic clear cell tumors and its aggressive behavior.
Method: We report a case of minor salivary gland clear cell myoepithelial carcinoma of the retromolar region.
Results: A 49-year-old man, presented with recent fall of left mandibular molars Computed tomography scan identified an osteolytic expansile mass of the horizontal branch of the mandible with definite margins. The patient underwent mass resection. Grossly, the tumor mass, measuring 4 cm on its greater diameter, was indurated, multilobulated, and whitish gray. Microscopically, the tumor was arranged in nests, trabeculae, and cords. Tumoral cells had abundant eosinophilic or clear cytoplasm, focally accompanied by spindle cells and plasmacytoid cells. Immunohistochemically, the tumor cells were positive for S100, cytokeratin (KL1) and Smooth Muscle Actin (SMA) while negative for CD10 and vimentin.
Conclusion: Clear cell myoepithelial carcinoma is an extremely rare tumor. Due to the rarity of this tumor and its histologic similarity to other neoplasms, resulted in difficult diagnosis, treatment, and prognosis estimation.

PS-09-054

Mixed Adenoneuroendocrine Carcinoma (MANEC) of the nasal cavity: Clinico-pathologic and molecular study of a case

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Objective: Mixed adenoneuroendocrine carcinomas (MANEC) of the nasal cavity are extremely rare and their molecular alterations are largely unknown.
Method: We describe the clinico-pathologic features, methylation profile, chromosomal gains and losses, and mutation analysis of KRAS, BRAF and p53 in such neoplasm.
Results: The tumor was composed of an intestinal-type adenocarcinoma (ITAC) and of a poorly differentiated neuroendocrine carcinoma (NEC) positive for CK20, CDX2, p53, serotonin and glicentin, and CK7 negative. Gains and losses were found at 17p13 (TP53), 14q24 (MLH3), 19q13 (KLK3), 5q21 (APC), 7q21 (CDK6), 9q34 (DAPK1), 12q13 (TNFRSF 1A, CDKN1B), 13q12 (BRCA2), 17p13.3 (HIC1), 18q21 (BCL2), and 22q12 (TIMP3). Aberrant methylation of APC and DAPK1 genes was detected only in the NEC component. No mutation of KRAS, BRAF, and p53 was found.
Conclusion: The genetic relationship between ITAC and NEC component supports the hypothesis of a monoclonal origin of the tumor from a pluripotent cell that undergoes a biphenotypic differentiation after carcinogenesis is initiated, as already proposed for MANEC of other sites. In agreement with previous molecular studies, the NEC component showed a more complex genetic profile, suggesting that the neuroendocrine differentiation is from an exocrine to an endocrine pathway.

PS-09-055

A rare case of solitary oral angiokeratoma in an adult

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Objective: Angiokeratoma is a rare cutaneous lesion. Mucosal involvement is occasionally found as part of a more generalized cutaneous disease. Isolated angiokeratoma in the oral mucosa is extremely rare with only a few cases reported thus far.
Method: We report the case of a 61-year-old female presented with a painless lesion on the left bucal mucosa, of 4 months duration. On clinical examination, a solitary purple lesion of approximately 4 mm in diameter was found.
Results: The lesion was excised and the histological examination revealed a tumour involving lamina propria, composed of large dilated vascular spaces, lined by normal appearing endothelium and filled with blood or with fibrin thrombi. The overlying epithelium showed variable degree of acanthosis and hyperkeratosis. Accordingly the diagnosis of angiokeratoma was made. On clinico-laboratory examination no angiokeratomas were found anywhere on the skin as well as no other malformation or metabolic disorder. The patient received no further treatment and 2 years later remains disease free.

Conclusion: In conclusion we report a case of a solitary angiokeratoma of the oral mucosa. Although rare, it should be included in the differential diagnosis when evaluating any lesion in this location and further investigations should be performed to rule out a metabolic or systemic disease.

PS-09-056

Primary nasal meningioma: A case report

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Objective: Primary extracranial meningiomas are rare neoplasms, frequently misdiagnosed, resulting in inappropriate clinical management.
Method: We present a case of 37 years old man, admitted to our hospital with complaint of nasal obstruction and nasal discharge that had arisen 1 year earlier. Rinoscopic examination revealed soft mass in right nasal cavity between the septum and the turbinates. After the computed tomography evaluation the patient underwent a nasal endoscopic surgery.
Results: The nasal lesion was composed of lobules and whorls of neoplastic epithelioid cells with indistinct borders. The nuclei were round and oval, with occasional pseudoinclusions. Psammoma bodies were identified. Immunohistochemical stains showed strong and diffuse positivity for EMA and Vimentin. Isolated tumor cells showed nuclear labelling with ki-67. The patient had a good transoperative and postoperative course. After 6 month of follow-up, the patient is asymptomatic, with normal nasal endoscopic examination and no sign of recurrence.
Conclusion: Primary ectopic meningiomas involving the nasal cavity and paranasal sinuses should be distinguished from the extracranial extension of an intracranial meningioma. This tumors require separation from other types, by both histologic and immunohistochemistry studies, because they behave as slow growing neoplasms with a good prognosis, with longest survival associated with younger age and complete resection.

PS-09-057

MicroRNA miR-203 and protein p63 in verrucous and conventional squamous cell carcinoma of the head and neck

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Objective: Verrucous carcinoma (VC) is a variant of well differentiated squamous cell carcinoma (SCC). In contrast to conventional SCC, VC doesn't metastasize. Foci of SCC in VC (hybrid carcinoma) harbour metastatic potential and must be properly recognised pathohistologically. Molecular basis of morphological and clinical differences between VC and SCC is poorly understood.
Method: We compared the expression of miR-203 and protein p63 between VC and SCC, by using real-time polymerase chain reaction and immunohistochemistry. 30 cases of VC, 10 cases of hybrid carcinoma, 30 cases of well/moderately differentiated and 20 cases of poorly differentiated SCC of the head and neck were included. Control group consisted of 30 samples of normal squamous epithelium of similar localisation.
Results: In comparison to normal epithelium, miR-203 was upregulated in VC, but downregulated in poorly differentiated SCC. p63 was downregulated in VC, but upregulated in SCC. Differential expression of miR-203 in VC and SCC correlated inversely with expression of p63. Immunostaining against p63 labeled foci of SCC in VC.
Conclusion: Differential expression of miR-203 and its target p63 between VC and SCC could be associated with morphological and clinical differences between these tumours. p63 could be used as marker for pathohistological detection of hybrid carcinomas.

PS-09-058

Osteochondrolipoma of the lip: Case report

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Objective: Lipomas are common, benign, slow-growing, soft tissue neoplasms of mature adipocytes. They are uncommon in the oral region. The incidence of oral lipomas is thought to be 1 % to 4 % of all benign oral lesions and lips are the last affected region of oral cavity. Lipomas with osseous, cartilaginous metaplasia are rare histological variants and these lesions have been called chondrolipoma, osteolipoma, lipoma with chondroid and osseous metaplasia, lipoma with cartilaginous, osseous change and ossifying lipoma. In this article we report a case with a osteochondrolipoma of lower lip.
Method: Case: 60-years old male patient admitted to hospital because of swelling of his lip. Physical examination detected a tumoral mass in lower lip. The tumor was excised totally.
Results: Macroscopically there was a well circumscribed nodular tumor below the oral mucosa, it was yellow-white in color and 1,5 cm in greatest diameter. Microscopically the tumor was composed of mature adipocytes and chondrocytes. There were mature osseous tissue in focal areas. The lesion had a pushing pattern of growth and therefore had a pseudocapsule. With these features our diagnosis was osteochondrolipoma of the lip.
Conclusion: We present this case due to its unusual localisation and to remind this rare entity.

PS-09-059

A middle ear adenoma

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Objective: 56 year-old female patient with pain, tinnitus and hearing loss complaints is diagnosed to have a hearing loss of 73–23 dB in her left ear and left tympanic membrane was intact but abnormally thicker.
Method: Temporal CT (64 sliced) showed soft tissue densities in left external ear and mastoid antrum and tympanic cavity enclosed with ossicules. Tympanic membrane couldn't be discriminated from the soft tissue densities.
Results: Histopathologically in macroscopy, the cystic lesion was determined as a small part of tissue in white –grey color, in sizes of 0,6×0,5×0,3 cm. In microscopic evaluation, the epithelial tumor cells were formed mostly tubular, partially in solid form and broadly making pseudopapillary pattern in stromal tissue. In the luminal structures formed by tumor cells, there has been mucin as dark basophilic stained with PAS/Alcian blue (PH: 2, 5). The tumor cells are strong and have common positivity with CK7, and have negativities with CK20 (B-SA method). In the focal area that the tumor cells got the solid pattern, synaptophysin and chromogranin to evaluate the neuroendocrine differentiation wasn't determined.
Conclusion: The lesion in the medial part of the tympanic membrane of the patient was reported as colesteatom and the lesion in the middle ear was reported as middle ear adenoma.

PS-09-060

Histopathologic evaluation for Helicobacter Pylori as a possible etiopathogenic factor in chronic tonsillitis

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Objective: Helicobacter Pylori is the major gastric pathogen which has an important role in the etiopathogenesis of chronic gastritis. We investigated the presence of Helicobacter Pylori as an extragastric reservoir in the tonsillectomy specimens to display if it is an etiologic factor in the development of chronic tonsillitis.
Method: In the current study, 100 cases with chronic tonsilitis were examined in bilateral tonsillectomy specimens. The colonization of the microorganism have been evaluated with Hemotoxylin-eosin and Giemsa stains under the the light microscope.
Results: Helicobacter Pylori has been detected in 33 cases (33 %) on one side of the bilateral tonsillectomy specimens while it has been seen in 15 cases (15 %) on both sides which demonstrated positivity in 48 cases (48 %) in total. No colonization has been observed in the remaining 52 cases (52 %).
Conclusion: Due to the considerable positivity in our study, the histopathologic evaluation of tonsillary Helicobacter Pylori colonization may be instrumental in the etiologic association with chronic tonsillitis.

PS-09-061

Inverted papilloma with squamous cell carcinoma

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Objective: Inverted papillomas are benign sinonasal lesions that have tendency to recur and associated with squamous cell carcinoma in approximately 5 % of patients. We present a 80 year old male patient with clinic, radiologic and pathologic findings to remind coexistance of inverted papilloma and squamous cell carcinoma in the same case.
Method: 80 year old male patient referred to our hospital Otolaryngology outpatient clinic with difficulty in breathing and persistant mass in his nose. A vegetative polypoid mass in his right nasal cavity that extended to nasopharynx has been determined in anterior rhinoscopy and computer tomography scan. The mass has been excised by endoscopic surgery and sent to pathology laboratory for examination.
Results: Grossly the polypoid mass was in 40 cc volume, grey white and easily dispersible. Histologically, there has been polipoid structures that have edematous and inflammatory stroma surrounded with squamous epithelium. We have determined carcinoma insitu and invazive focuses in the epithelium.
Conclusion: The etiology of inverted papillomas is unclear. Malignant transformation has been observed in less than 7 % of cases. Total excision is the preffered therapotic approach but recurrence rates are not uncommon.

PS-09-062

Anaplastic Large T cell lymphoma, ALK negative presented with tonsillar hypertrophy and systemic lymphadenopathy with granulomatous infiltrate

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Objective: Tonsils are uncommonly affected by granulomatous inflammation, been systemic disease and infections more frequent causes than neoplasms. Regarding tonsillar lymphomas the vast majority are of B-cell origin and with intermediate to high-grade histology.

Method: We present a case of a 64 year old caucasian male, with obstructive sleep apnea syndrome, odynophagia and cervical lymphadenopathy. The physical examination showed severe right tonsillar hypertrophy and the scanners revealed generalized lymphadenopathy.
Results: The histological features of the tonsil and cervical lymph node specimens were similar, both presented a pleomorphic lymphoid infiltrate surrounded by abundant epithelioid histiocytes forming non-necrotizing granulomas. Granulomatous infection diseases were dismissed. The neoplastics cells were positive for T cell markers, MUM-1 and CD30, and negative for ALK1. The proliferative index Ki67 was 60 % of the tumor cells. The molecular study showed T-cell clonal population The morphologic and immunophenotypic features, together with the molecular results were consistent with anaplastic T cell lymphoma ALK-negative.
Conclusion: The morphology and immunophenotype features, with the molecular study report support the diagnostic of anaplastic T cell lymphoma ALK- negative, with Lennert pattern. This case illustrate how a granulomatous infiltrate can mask a lymphoproliferative disorder, mostly of T-cell type, although a careful study of the biopsy allow a correct diagnosis.

PS-09-063
Salivary duct carcinoma, oncocytic variant: Case report
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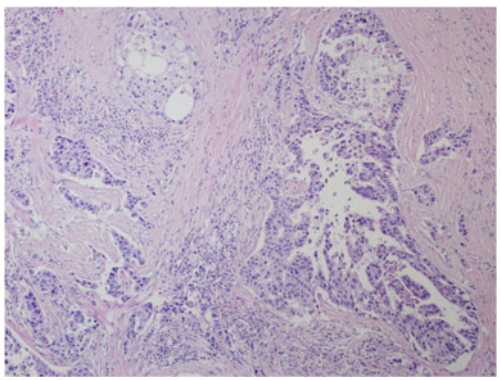
Objective: Salivary duct carcinoma (SDC) is a rare, aggressive malignancy with poor prognosis. Its histomorphology is distinctly reminiscent of the ductal carcinoma of the breast.
Method: A 48-year-old man was admitted with a mass of the right preauricular area. The mass had been enlarging steadily for the past 7 months. Computed tomography (CT) of the neck revealed 4×3×3 cm contrast enhancing solid mass with irregular borders at the right parotid region. Thorax CT, abdominal and thyroid ultrasonography were unremarkable. As the aspiration cytology was malignant right parotidectomy and right cervical lymphadenectomy was performed.
Results: Histopathological examination showed a mixture of ducts, nests and cords of cells often embedded in a desmoplastic stroma with comedonecrosis of some ductal structures. The tumor cells were polygonal with vesicular nuclei, prominent nucleoli and eosinophilic, oncocytic cytoplasm. The tumor margins were lobulated and irregular with perineural invasion. Mucin stains were negative. We noted high proliferative index and cerbB2 overexpression. The tumor was classified as a salivary duct carcinoma, oncocytic variant of parotid gland. The resection margins were negative and the lymph nodes were reactive.
Conclusion: As high proliferative index and cerbB2 overexpression are predictive factors, close clinical follow up is recommended for the risk of local recurrences and metastasis.



PS-09-064
Immunohistochemical expression of Bcl-2 and Ki-67 in oral lichen planus and leukoplakia with different degrees of dysplasia
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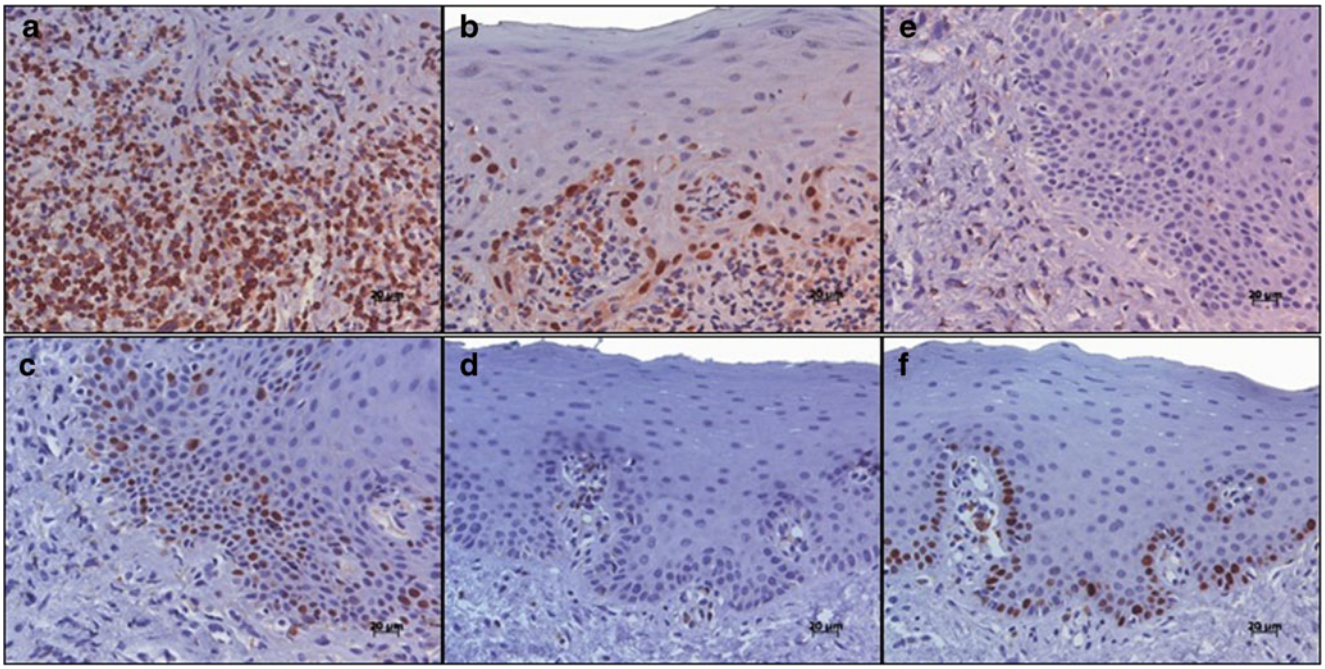
Objective: The oral lichen planus (OLP) is a chronic inflammatory disease of unknown cause, and its malignant potential is a very controversial issue. Therefore, the aim was to evaluate the immunohistochemical expression of apoptosis-related proteins and cell proliferation in OLP and epithelial dysplasia in order to investigate changes related to carcinogenesis and emphasize the importance of long-term follow-up of patients with OLP.
Method: For this purpose, we selected 14 samples of OLP, 14 samples of leukoplakia with epithelial dysplasia, and 09 samples of normal oral mucosa as controls. The evaluation of the expression of Bcl-2 and Ki-67 was conducted in accordance with the immunoperoxidase technique.
Results: There was also a high expression of Blc-2 protein in inflammatory cells in OLP lesions and leukoplakia with epithelial dysplasia. The expression of Ki-67 marker was higher in all analyzed tissue levels in the lesions of OLP and leukoplakia with epithelial dysplasia when compared with the control group.

Conclusion: The highest expression of proteins Bcl-2 and Ki-67 in cases of OLP and leukoplakia with epithelial dysplasia may reveal the possible presence of molecular alterations morphologically imperceptible.



PS-09-065

Evaluation of benign and malignant tumors of the oral cavity using DNA flowcytometric analysis

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Objective: Biologic behaviour of benign and malignant tumors of the oral cavity is influenced by many factors. Proliferative activity of the tumor is one of these factors, serving to estimate prognosis and design of treatment. Flowcytometric analysis allows quantitative estimation of DNA content and measurement of cells in the S phase fraction (SPF) representing the proliferative potential of the tumor.

Method: DNA content and S-phase fraction (SPF) of oral tumors from Egyptian patients were measured by flowcytometry and related to clinicopathologic parameters.

Results: Thirty percent of malignant cases were diploid and 70 % were aneuploid. Sixty-six point seven percent of diploid cases showed low SPF and 33.3 % showed high SPF. Only 16.7 % of aneuploid cases showed low SPF, and 83.3 % showed high SPF. All benign cases were diploid with a low SPF with a statistically significant difference from malignant cases ($p<0.001$). There was a directly proportionate relationship between flow cytometric parameters and histopathologic grade. SPF correlated significantly to the presence of lymph node metastasis ($p=0.03$).

Conclusion: DNA ploidy and SPF are important prognostic factors in tumors of the oral cavity and maxillofacial region. Management decision for individual patients could make use of these parameters.

PS-09-070

DNA copy number alterations in pleomorphic adenomas and carcinoma ex-pleomorphic adenomas

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Objective: Pleomorphic adenoma (PA) is the most common benign salivary gland neoplasm of the major and minor salivary glands. Pleomorphic adenoma was shown sometimes to undergo malignant transformation in its natural course. Carcinoma ex pleomorphic adenoma (CPA) is a rare salivary gland malignancy that may develop from either a long-standing primary or a recurrent PA. The genetic mechanisms involved in the progression of adenoma to a carcinoma is still unclear. To identify the predictors of disease, more knowledge about their genetic profiles is necessary. This study aimed to characterize alteration in the DNA copy number of PA and CPA.

Method: We used next-generation sequencing technologies to produce genomic copy number data on three formalin-fixed paraffin-embedded CPA, three PA and one PA with carcinoma insitu areas.
Results: Aberrant chromosomal areas were detected in all tumors. The most common frequent gains in bening tumors were detected at 20p, whereas loss at 5q, 6q, and 16q. Our analysis detected DNA copy number changes in carcinomatous components of CPA, mostly gains compared to PA. The chromosomal regions including 3p, 8q and 18p, 6q abnormalities were consistently identi_ed.
Conclusion: All of the three carcinomatous components and all of the four adenomatous components showed various DNA copy number changes.

PS-09-072
Clinic-histologic aspects of twenty-five cases of minor salivary gland sialolithiasis
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Objective: Sialolithiasis in minor glands is rare. Presently we analyze clinical and microscopic findings as well as clinical data and also clinical diagnosis since many cases are misdiagnosed at first. Data were obtained from the Department of Oral Pathology file (2000–2011).
Method: Cases were selected among those with a final diagnosis of sialolithiasis, or others that might lead to a histological suspicion such as sialadenitis and duct ectasia. Gender, age, site, clinical diagnosis, gland and ductal alterations and aspects of sialoliths were analyzed.
Results: Twenty-five cases were retrieved. Age average was 62.5 years (26–76), mostly on 7th or 8th decades (55.0 %). Male/female ratio was 1.3:1, mostly involved upper lip (46 %) and buccal mucosa (38 %). Main clinical diagnosis were mucocele and fibroma. Clinical misdiagnosis was 88.0 %. Sialoliths were commonly superficial (66.7 %) and composed by concentric layers (70.8 %) with varied grades of mineralization. Chronic periductal and/or intraparenchymatous inflammation were frequent (64 % for each). Ducts commonly presented squamous metaplasia (58.3 %) and also ectasia, squamous and mucous metaplasia, mucous plugs and/or cellular debris.
Conclusion: In conclusion, clinical suspicion of sialolithiasis should be encouraged for upper lip and buccal mucosal lesions. Based on histomorphological diversity of sialolith and gland alterations it is possible to suppose a multifactorial cause.

PS-09-073
Expression of p27 in oral leukoplakias in smokers and nonsmokers
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Objective: Leukoplakia is an oral premalignant white lesion. Although its etiology may vary, smoking has been implicated as a possible risk factor. The p27 protein has been shown to inhibit kinases, and it is known that its expression is decreased during carcinogenesis. The reduced expression of p27 has been correlated with poor prognosis in carcinoma. In this study a role for the smoking habit in the expression of this protein was investigated.
Method: Forty cases clinically diagnosed as oral leukoplakias and that presented a mild to intense degree of epithelial dysplasia and could not be diagnosed as any other disease were selected. Twenty cases were from current smokers (more than 20 cigarettes/day for at least 1 year) and never-smokers. Thirty-six cases of leukoplakia without dysplasia were used as controls. Histological sections of each lesion were subjected to the estreptoavidin biotin immunohistochemical method for detection of p27.
Results: A semi quantitative analysis was performed and the results showed that the expression of p27 was independent of the smoking status of the patient (p=0, 5237), using Kruskal-Wallis and Mann–Whitney tests.
Conclusion: Although not statistically significant, due to the small number of cases, the results indicate that the counting of p27 in leukoplakia correlates inversely with degree of epithelial dysplasia.

PS-09-074
Low-level laser therapy may influence on the Akt/mTOR signaling pathway in oral cancer cells
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Objective: Distinct cells respond differently to low-level laser therapy (LLLT), while the exact molecular mechanisms involved in cell proliferation or growth inhibition, after light stimulation remain poorly understood. Although LLLT has shown promising results in accelerating wound healing and preventing or treating oral mucositis, there is no evidence-based consensus of what this energy could cause in cancer cells. This should be highly pondered when an oral cancer patient is treated with LLLT due to oral mucositis, for example.
Method: Two tongue squamous cell carcinoma cell lines (SCC9 and SCC25) were utilized to find the effect of low-level laser irradiation on the Akt/mTOR signaling pathway. Laser irradiation (660 and 780 nm) consisted on 40 mW of power and energy densities of 2, 3 and 6 J/cm2. After a single irradiation the most significant energy densities found with MTS assay were employed to analyze Akt/mTOR signaling pathway related proteins through immunofluorescence and western blotting.
Results: Beyond modifying the growing rates of cancer cells, low-level laser irradiation was able to induce different variations in the studied pathway, however a direct correlation among the proteins was not found.

Conclusion: LLLT may act on Akt/mTOR/Cyclin D1 signaling pathway, which has a widely recognized role in head and neck cancer progression.

PS-09-076

Mucins as predictors of recurrent pleomorphic adenoma of salivary glands: An immunohistochemistry analysis of over 60 cases

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Objective: Pleomorphic adenoma (PA) is the most common tumor of salivary glands and, despite its benign behavior, the recurrence after primary surgery is significant. In attempt to find a marker capable to predict the recurrence of this lesion, this study aims to analyze the expression of mucins MUC 1, 2, 4, 5 AC and 6 in 62 cases of PA, considering that mucins have been related to tumour growth of some organs.
Method: This study was performed in 62 cases in PA, which 5 of them presented recurrence after the initial surgery. All the primary tumors were histologically processed and submitted to the immunohistochemistry reaction. The antibodies for MUC 1, 2, 4, 5 AC and 6 were used and then analyzed with conventional optical microscope.
Results: MUC1 was the only mucin significantly expressed in most of all cases (88 %), being present within ductal lumen and cytoplasm. The other mucins showed a focal positivity in few cases, where MUC 2, 5 AC and 6 were cytoplasmic, while MUC4 was expressed in ductal lumen and blood vessels.
Conclusion: The most relevant expression of MUC1 could suggest a contribution of this mucin to predict the development of PA recurrences or even predict cellular dysfunctions capable to promote adenomas.

PS-09-077

CA EX pleomorphic adenoma: A clinicopathologic study of six cases

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Objective: Ca ex pleomorphic adenoma (Ca ex PA) is a rare salivary neoplasm with aggressive behavior arising from a primary or recurrent pleomorphic adenoma.
Method: Six cases of Ca ex PA are presented. Three females and three men (median age of presentation 66 years) were diagnosed in our department during six last years in a total of 214 salivary neoplasms (2,8 %), comprising 10.8 % of salivary malignancies and 8.6 % of PA.
Results: Three cases were arising de novo and the rest from a PA recurring seven, twenty -seven, and thirty years after initial diagnosis. Three cases were localized to parotid and the rest to submandibular gland. Microscopically all tumors were composed of a mixture of PA and carcinoma of various type. All tumors, except one, had areas of necrosis. Four cases were encapsulated. All patients were underwent an ablative surgical procedure. Two women, both with extensively infiltrating tumors, died with recurrences and distal metastasis, within one and four years respectively, after carcinoma diagnosis, despite the application of combined radiotherapy and chemotherapy.
Conclusion: Ca ex PA, a rare salivary malignancy, occurs either as a primary involvement or as a PA late recurrence. The disease has a fatal course relating with tumor invasiveness.

PS-09-078

HPV existence, TP53 and E-Cadherin expressions and correlations between clinicopathologic variables in squamous cell carcinoma of larynx

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Objective: In our study we purposed that to detect interactions between HPV existence and squamous cell carcinoma of larynx (SCCL), and the correlations among the clinicopathologic variables; levels of p53 and E-cadherin expressions, and surveillance.
Method: The 149 SCCL and 50 control cases are included the study. Immunohistochemically p53 and E-cadherin antibodies were performed and polyclonal HPV was analyzed with polimerase chain reaction (PCR). In positive cases, HPV types 16, 18, 31, 33 were investigated.
Results: Polyclonal HPV was detected in 149 of 9. Six cases were positive for HPV16 and one case was positive for HPV18. Remain two were negative for HPV 31 and 33. So type of these cases could not be identifiedSignificant correlations were detected between gender, survey and LN metastases and p53 and E-cadherin expressions. Also significant results were obtained between p53 positivity and grade and between E-cadherin positivity and TNM stage.
Conclusion: Contribution of HPV existence shows geographic diversities in tumorigenesis. The preoperative detection of LN metastases is crucial for patient management. LN metastases increase in tumors with high p53 positivity and low E-cadherin expressions. These features can be informative for clinicians.

PS-09-080

Gingival metastasis from prostatic adenocarcinoma: A case report and review of literature

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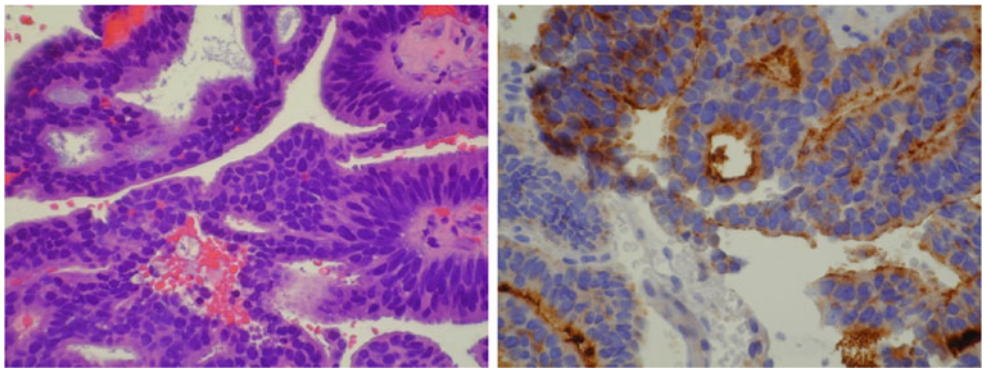
Metastatic disease of the oral cavity is extremely rare. Only 1 % of oral tumors are considered to be due to metastasis. Jaw bones are affected more often than soft tissues. The

clinical presentation of metastatic lesion in the oral cavity can be deceiving and extremely challenging for the clinicians and the pathologists and can lead to misdiagnosis of either a benign process or primary tumor. Therefore, in any case of unusual clinical presentation, especially in patients with known malignancy elsewhere a diagnostic biopsy should be mandatory. We present a rare case of a 92-year-old male patient with previously diagnosed and treated prostate cancer who presented with a gingival mandibular mass and lower lip paresthesia. Only two cases of oral soft tissue metastasis from prostate have been reported in the literature.



PS-09-081

Correlation between fine needle aspiration cytology and histopathology results of salivary gland masses

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Objective: In this study, we evaluated the diagnostic value of fine needle aspiration cytology (FNAC) in salivary gland masses retrospectively.We compared FNAC and postoperative histopathologic results of patients.

Method: Ninety-two patients (47 females, 45 males; mean age 46,6; range 15 to 78 years) having salivary gland masses who underwent FNAC and surgical treatment between January 2007 and November 2011 were included in the study. FNAC and histopathologic results were compared retrospectively. The sensitivity, specificity, positive and negative predictive values and accuracy rate of FNAC in salivary gland masses were evaluated under the light of the results.

Results: The most common benign and malignant FNAC results were pleomorphic adenoma (38 patients, %41) and mucoepidermoid carcinoma (3 patients, %3). FNAC results of six patients were nondiagnostic and this patients were excluded. According to the FNAC and histopathologic results, sensitivity has found %64, specificity %100, positive predictive value %100, negative predictive value %93 and accuracy rate of FNAC %92.

Conclusion: FNAC is a reliable method that has high specificity to distinguish between benign and malignant salivary gland lesions. Our sensitivity has found lower than expected because the samples didn't represent lesion exactly.

Monday, 10 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor

PS-10 Poster Session Molecular Pathology

PS-10-001

Regulation of multidrug resistance in NSCLC by miRNAs

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Objective: Drug resistance remains a major problem in the treatment of NSCLC cancer patients for both, conventional chemotherapeutic and novel biological agents. Intrinsic or acquired resistance is caused by a variety of mechanisms, including increased drug elimination, decreased drug uptake, drug inactivation and alterations of drug targets. Recent data showed that drug resistance mechanisms might also be regulated by microRNAs (miRNAs).

Method: We tested 65 lung cancer samples. The total RNA was isolated from individual specimens and then RT-PCR and pre-amplification were performed. We detected levels of miR-21, miR-23a, miR-23b, miR-126, miR-205, miR-335*, miR-3163, miR-491-3p, miR-548p, miR-548x, miR-576-5p, miR-590p, miR-655, miR-656 and miR-944 using TaqMan® MicroRNA Assays by LightCycler® 480 Real-Time PCR System. We assigned obtained results using statistical methods.

Results: Our results suggest that miR-590-5p and miR-655 are involved in apoptosis. The higher levels of miR-590-5p correlate with Bcl-2 positivity and pro-apoptotic protein BAX seems to be regulated by miR-655. The level of LRP protein responsible for drug resistance in lung cancer patients seems to be regulated by miR-255.

Conclusion: Within our cohort of NSCLC patients we did not find any correlations between the expression profiles of the abovementioned miRNAs and survival.

PS-10-004

The role of secondary mutations in the mechanisms of the drug development in the gastrointestinal stromal tumors

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*University Hospital Motol, Dept. of Pathology and Molecular Medicin, Prague, Czech Republic

Objective: Gastrointestinal stromal tumors (GISTs) are characterized by a gain of function mutations of the KIT or PDGFRA genes. Activated KIT and PDGFRA proteins are important therapeutic targets of the therapy with imatinib mesylate (IM). Although most patients with advanced GIST benefit from IM treatment, a portion of patients develop resistance to the agent. The most common mechanism of the acquired resistance of GIST is the acquisition of secondary mutations.

Method: Mutation analysis was performed on genomic DNA extracted from formalin-fixed, paraffin-embedded or fresh frozen tumor tissues. Exons 9, 11, 13 and 17 of the KIT gene and exons 12, 14 and 18 of the PDGFRA gene were evaluated for mutation by PCR amplification and direct sequencing of the amplification products.

Results: We analyzed 95 tumor samples acquired from 82 patients treated with IM. In 11 specimens from 7 patients we detected secondary mutations. Secondary mutations were clustered in exon 13 or exon 17 of the KIT gene.

Conclusion: The acquired resistance is an important phenomenon of the targeted biological therapy failure. Molecular analysis of GISTs and detection of secondary mutations might become a clue to the design and management of second generation kinase inhibitors or alternative therapeutic strategies. Support: PCDRO (MH CZ) 00064203.

PS-10-005

Modified methacarn fixation as an excellent preservation of histology, protein immunoreactivity and RNA integrity in paraffin embedded tissue specimens

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Objective: Fixation techniques preserving morphological fidelity, immunoreactivity and integrity of nucleic acids may have a high impact on both basic and applied research and diagnostic pathology.

Method: We investigated the effect of formalin, absolute ethanol and methanol; ethanol supplemented with acetic acid and modified methacarn fixative on the tissue morphology and immunoreactivity of different types of tissues and the preservation of RNA fragments of different lengths.

Results: The modified methacarn fixation provided a histomorphological quality comparable to the formalin-fixed tissue specimens. The immunoreactivity was superior in the buffered than in the untreated formalin and the preservation of protein antigenicity in normal and pathologically changed tissues tested with several antibodies was excellent with the use of alcohols with acetic acid. The acidic ethanol and the modified methacarn fixative showed the best preservation of the integrity of RNA in satisfactory quantity and quality of fragments up to 577 bp, which was reliable for relative evaluation of gene expression.

Conclusion: The presented data provide evidence that the modified methacarn fixative is an excellent alternative to formalin when tissue specimens are evaluated for tissue morphology, immunoreactivity and RNA expression profile. Supported by ITMS: 26240220052.

PS-10-006

Differential connexin expression in giant cell tumour of bone (GCTB)

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Objective: Intercellular communication through connexin (Cx) channels is known to regulate cell homeostasis and play crucial roles in promoting signals and nutrients between osteoblasts and osteocytes. Giant cell tumour of bone (GCTB) is an aggressive osteolytic lesion, in which neoplastic stromal cells drive osteoclastogenesis. Here we tested if Cx expression correlates with GCTB progression.

Method: Tissue microarrays of 94 primary and 82 recurrent GCTB cases were immunostained for connexin isotypes and the results were scored in digital slides including image quantitation.

Results: Cx37 and Cx40 were detected only in endothelial cells and Cx23, Cx26, Cx43 and Cx46 were found primarily in mononuclear cell fraction. Double labelling revealed connexins both stromal and monocytic lineage cells. Cx23 was also seen consistently and Cx46 occasionally in giant cells. None of the Cx isotypes showed statistical preference between primary and recurrent cases, though Cx43 displayed a tendency for upregulation in recurrent cases. Concerning clinico-radiological stage, only Cx26 showed significantly elevated ($p<0.05$) expression in aggressive compared to active GCTB cases.

Conclusion: Though a wide range of connexins can be detected in GCTB, some of them have not been published in osteoblasts, stromal cells or monocytes, their expression is not statistically lined with GCTB progression/recurrence.

PS-10-007

Heterogeneity of KRAS mutational status in colorectal adenocarcinomas with a mucinous component

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Objective: KRAS mutations in colorectal cancer (CRC) are predictive of nonresponse to anti-epidermal growth factor receptor therapy. More than 90 % of CRCs are adenocarcinomas and some of these show mucinous areas. Only when more than 50 % of the lesion is composed of pools of extracellular mucin containing malignant epithelium the CRC is considered as a histopathological variant and it is classified as mucinous adenocarcinoma.
Method: We analyzed the mutational status of KRAS on a series of 20 formalin-fixed, paraffin-embedded, advanced CRC specimens taken from an equal number of patients. Each sample was classified as adenocarcinoma with mucinous areas (<50 %) and DNA extraction was performed by laser-microdissection with respect to the different histological types present in the same section. A reverse-hybridization-based assay was utilized in the identification of the most frequent KRAS mutations.
Results: We found a KRAS single mutations in 10/20 (50 %) patients. In particular, in 9 patients the same mutation was detected in adenocarcinomatous as well as in mucinous areas. On the contrary, in one case we found a mutation (Gly12Asp) in the adenocarcinomatous area but not in mucinous component of the same tumour.
Conclusion: Intratumoral heterogeneity of KRAS status is not frequent in adenocarcinomas with a mucinous component.

PS-10-008

cFLIP supports the maintenance of resistance to apoptosis in thymic carcinoma cell line 1889c

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Objective: cFLIP prevents the apoptosis by caspase 8 inhibition, its overexpression correlates with the progression of different tumors. Thymomas and thymic carcinomas are thymic epithelial tumors, in which the regulation of apoptosis is still unknown. We investigated the role of cFLIP in regulating the viability of thymus carcinoma cell line 1889c using an RNA Interference. The cell line HaCat was used as a control.
Method: 1889c and HaCat cell lines were transfected with an established "short Hairpin" pIRES/PURO cFLIP-shRNA expression vector. CFLIP suppression and its Effect on pro and antiapoptotic molecules were analyzed using q-PCR and western blot. Apoptosis was quantified using the flow cytometry.
Results: The 1889c-shcFlip, but not the shcFlip-HaCat, showed sensitivity to TRAIL (tumor necrosis factor-related apoptosis-inducing ligand), accompanied by an overexpression of both the pro-apoptotic protein Noxa ($p<10–4$) and the anti-apoptotic proteins BIRC2, BIRC3 and XIAP compared to the non-transfected cells ($p<10–4$).
Conclusion: cFLIP shRNA seems to induce apoptosis in the thymus carcinoma cell line. Simultaneously antiapoptotic proteins (AIPs) BIRC2, BIRC3 and XIAP were up regulated in order to protect the cell from apoptosis. Could these AIPs provide the way to escape the cell death? AIPs Selective inhibitions could represent a promising therapeutic approach for malignant thymic carcinomas.

PS-10-010

Quantitative measurement of cyclin D1 mRNA expression level helped with diagnosis in small lymphocytic lymphoma type B-CLL with aberrant protein cyclin D1 expression detected by immunohistochemistry

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Objective: Cyclin D1 is a molecular marker of mantle cell lymphoma (MCL) and it may be examined by immunohistochemistry at the protein level or by PCR at the mRNA level. Despite the cyclin D1 specifity for the MCL diagnosis we discovered rare cases of small B-cell lymphocytic lymphoma of B-cell leukemia type (B-CLL/SLL) with aberrant cyclin D1 protein expression detected by immunohistochemistry.
Method: Using quantitative PCR we analyzed cyclin D1 mRNA expression level in 10 B-CLL/SLL cases with immunohistochemically positive cyclin D1 protein. Simultaneously we measured the mRNA cyclin D1 level in 289 MCLs, 67 other B-cell non-Hodgkin's lymphomas (B-NHL) and 5 reactive lymphadenopathies.
Results: The cyclin D1 mRNA level was overexpressed above the cut-off limit that we established in the MCL specimens specifically. The 10 B-CLL/SLL cases with cyclin D1 protein immunohistochemical positivity showed

the cyclin D1 mRNA level below the cut-off limit within the range of nonMCL B-NHLs and reactive lymphadenopaties.
Conclusion: A precise cyclin D1 mRNA level measurement was useful in distinguishing between the cyclin D1 overexpression that is a MCL hallmark and the aberrant expression in B-CLL/SLL, and thus helped to decrease the risk of MCL misdiagnosis in cyclin D1 immunohistochemically positive B-CLL/SLLs. Support:CZ.2.16/3.1.00/24022, 00064203.

PS-10-011

Monphasic synovial sarcoma of the pleura: A potential diagnostic challenge

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Objective: Synovial sarcoma is a very unusual malignancy that often affects the extremities in proximity of large joints. The diagnosis of this tumour in pleura may be a challenge due to the broad spectrum of differential diagnosis.
Method: Pleural biopsy of a 35 years old female patient was performed in chest-surgery department because a relapsing pleural effusion, there is no history of trauma or asbestos exposition. Formalin fixed paraffin embedded blocks were stained with routine Haematoxylin and Eosin and two representative blocks were selected for immunohistochemistry and real-time PCR (RT-PCR).
Results: The tumour is composed of monotonous spindle cells with a high mitotic activity (18 M/10 HPF). There are neither necrosis nor epitheliod areas. The tumour stained with bcl-2 and vimentin, with only focally reaction for Epithelial Membran Antigen (EMA) and for CD99. There was no reaction for WT-1, Calretinin, Pan-Cytokeratin CD 34, desmin, smooth muscle actin and S-100. RT-PCR showed a distinct 98 bp product of the translocation t (X;18).
Conclusion: Synovial sarcoma of the pleura is very rare, with to our best knowledge only 35 cases reported in the literature. A multidisciplinary approach, based on clinical, pathological and molecular information is crucial for a correct diagnosis and therapy.

PS-10-012

Nuclear and cytoplasmic expression of nucleolin depends on accurate validity

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Objective: Nucleolin is a multifunctional DNA-, RNA- and protein-binding protein, involved in fundamental aspects of transcription, cell proliferation and growth. It is located in the nuclei/nucleolus, cytoplasm and on the cell surface. The present study aimed at optimizing the histological identification of nucleolin.
Method: Mamary invasive ductal carcinoma 3 μm paraffin sections were pretreatead with pronase at room temperature (5–10 min) to epitope exposure. Biotinilated peptide against nucleolin was applied (1/1.5 mM dilutions), incubated at room temperature for 30 min/overnight at 4 °C; after phosphate-buffered saline, peptide binding was identified by peroxidase-conjugated streptavidin and 3,3-diaminobenzidine tetrahydrochloride applied according to manufacturer's instructions before haematoxylin counterstaining.
Results: Pretreatment for 5 min at 1.5 mM of biotinilated peptide showed only nuclear expression, as 1 mM/10 min pretreatment with overnight peptide incubation; positive cytoplasmic expression was obtained also after 30 min incubation/room temperature. At 1.5 mM concentration for 10 min epitope retrieval, cytoplasmic and nuclear positivity raised over 75 % expression, independently of peptide exposure (overnight/room temperature).
Conclusion: For optimizing peptides/antibodies, we have to be aware that nuclear/cytoplasmic expressions depend on digestion and peptide concentration. Histological morphology is also important and discordant results may be erroneously obtained.

PS-10-013

KRAS testing in clinical laboratory: Optimizing targeted therapy

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Objective: Activating mutations in the KRAS gene are found in more than 30 % of colorectal tumors, where they are associated with a poor response to anti-epidermal growth factor receptor therapies. Mutation testing techniques have therefore become an urgent concern. Several methods for KRAS mutation detection have been described in the literature. Most of these are laboratory developed tests and only a few commercial assays are currently available.
Method: We studied the performance characteristics of a KRAS mutation detection assay on the ABI-3130XL genetic analyzer using a new commercial mutation detection kit. Samples were analyzed in parallel by different reference laboratories using alternative methodologies. Various sample types were used including formalin-fixed paraffin-embedded tissue, fine-needle aspirates, and cyst fluid specimens.
Results: A high level of agreement (100 % correlation for formalin-fixed paraffin-embedded tissue and fine-

needle aspirate samples and 93 % correlation for cyst fluid specimens) was obtained despite the use of different methodologies.
Conclusion: Shift termination assay is a simple, robust, and sensitive method for the identification of KRAS mutations in wide variety of specimen types.

PS-10-014
DNMT over-expression based on microRNA modulation in HIV-related aggressive B-cell lymphomas
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Objective: Immune activation of B-cells contributes to the increased frequency of B-cell malignancies observed in HIV-infected individuals. The Tat protein may participate in B-cell abnormalities as it may be released by infected cells. Tat increases the expression of specific cellular genes, as IL6, which may upregulate the expression of DNA methyltransferase 1 (DNMT1), which epigenetically regulates gene expression. Dyregulation of DNMTs results in abnormal patterns of DNA methylation, which is frequent in cancer. HIV is reported to upregulate DNMT1 expression. We have analyzed the expression of DNMTs and their regulatory microRNAs in HIV-positive tumors and in Tat-transfected cell lines.
Method: HIV-positive and HIV-negative DLBCL and BL were tested for their expression of DNMTs by qRT-PCR and IHC. The expression of specific microRNAs was then investigated. The in vivo results were further confirmed in Tat-transfected human cell lines.
Results: DNMTs were found upregulated both in HIV-positive primary tumors and in Tat-transfected cell lines. In accordance, the expression of specific microRNAs was found downregulated. Up-regulation of DNMTs resulted in the aberrant methylation of genes, as INK4/p16, and microRNAs.
Conclusion: Dysregulation of DNA methyltransferases may result in the aberrant methylation of important tumor suppressor and cell cycle regulatory genes, eventually initiating neoplastic growth.

PS-10-015
EBV-Bart-6-3p induces cell proliferation and escape of immunosurveillance in BL cell lines and primary tumours
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Objective: Burkitt Lymphoma is an aggressive B-cell lymphoma presenting in three clinical forms: endemic, sporadic and immunodeficiency-associated. More than 90 % of eBL carry latent EBV, whereas only 20 % of sBL are associated with EBV. Recent data suggests a microRNA dysregulation in sBL and eBL cases. Furthermore, EBV itself encodes viral miRNAs, which may partecipate in BL pathogenesis. We profiled human and viral miRNA expression in eBL and sBL cases.
Method: Fresh tissues of eighteen BLs (six EBV-pos and twelve EBV-neg) were used for this study. For miRNA profiling Agilent® microRNA expression microarray technology was used.
Results: Comparison between EBV-pos and EBV-neg BL revealed that a few cellular miRNAs are differentially expressed. The profiling identified viral miRNAs expressed in EBV-pos BL cases. Target genes of differentially expressed miRNAs were searched, which were then classified in functional categories, according to the Gene Ontology. In particular, the role of EBV-BART6-3p was evaluated. Among others, Bart6-dependent dysregulation of PTEN and IL6 receptor was observed.
Conclusion: PTEN downregulation results in enhanced cell proliferation whereas gp130 downregulation determines escape of immunosurveillance. Viral miRNAs are of particular interest, as they may affect the expression of cellular genes which may represent targets for tailored therapies.

PS-10-016
Expression of MicroRNAs in pediatrics astrocytomas paraffin embedded
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Objective: MicroRNAs (miRs) are small RNAs that modulate protein expression via post-transcriptional regulation of mRNA. They are related to malignancy in several tumors. Deregulation of miRs expression has been described in high grade astrocytomas of adult patients, however there is scarce information in pediatric patients. In this work we quantified the expression profiles of miRs in pediatrics astrocytomas.
Method: Total RNA was extracted from 59 astrocytomas and 8 normal brain (NB) tissues, formalin fixed paraffin embedded. The expression levels of miR-124, miR-128-1 and miR-221 were quantified by using miRNA-specific TaqMan miRNA assays.
Results: The miR-128-1 was more abundant in NB against to miR-124 and -221 ($p<0.05$). MiR-124 and

miR-128-1 were significantly down-regulated in all grades compared to NB ($p<0.05$) but in grade IV was more decreased: 8000- and 1200-fold, respectively. In patients with recurrent tumor, the expression of miR-221 was lower ($p<0.002$). Live patients expressed high levels of miR-128 ($p<0.02$) and miR-221 ($p<0.0026$) against deceased.

Conclusion: MicroRNAs are differentially expressed between astrocytomas and NB. The low expression of miR-128 and -221 could be a potential marker in recurrent pediatric astrocytomas, and both are associated to less survival. Embedded tissue is useful to describe and evaluate expression of molecular markers of malignancy.

PS-10-017

Gene protein detection platform: An automated technique of combined immunohistochemistry and Brightfield double in situ hybridization in the Context of HER2 protein, gene and chromosome 17-centromere evaluations for breast cancer

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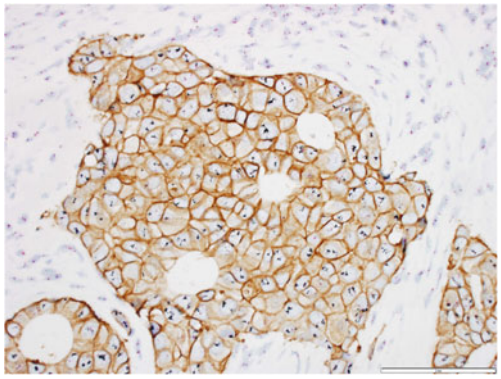
Objective: Human epidermal growth factor receptor 2 (HER2) immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) are semiquantitative assays for selecting breast and gastric cancer patients for HER2 antibody therapy. However, current procedures are labor intensive, require skilled technologists and pathologists trained in FISH, and FISH slides cannot be stored and reviewed. Our aim was to test a recent automated technique of combined IHC and brightfield double in situ hybridization (BDISH) – Gene Protein Detection Platform – in the context of HER2 protein, gene and chromosome 17-centromere status evaluations.

Method: The combined IHC-BDISH technique performance was evaluated in 50 consecutive invasive breast cancer cases with HER2 IHC 2/3+ scoring results. Interpretation of HER2 IHC, BDISH, FISH and Gene-protein stains were conducted by 2 pathologists using conventional brightfield and fluorescence microscopes with 60x objectives.

Results: This recent combined IHC-BDISH technique has equivalent results compared to standard separate IHC, BDISH and FISH protocols.

Conclusion: The combined IHC/BDISH technique is robust and has the advantages of being less tissue and time consuming. Most pathologists prefer the brightfield solution and stains can be stored. Furthermore, the advantage of assessing gene and protein status simultaneously on all cases may improve the performance of the integrated testing algorithm.



PS-10-018

Formalin Fixed Paraffin Embedded (FFPE) Reference Standards B-Raf, EGFR, K-Ras and PI3Ka Validated using Droplet Digital™ PCR

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Objective: Isolation of genomic DNA from formalin fixed paraffin embedded (FFPE) tissues is a critical step for molecular diagnostic assays. Horizon Diagnostics has generated FFPE cell line reference standards containing defined mutant allelic frequencies, enabling the quality control of both assay sensitivity and DNA extraction.

Method: A panel of X-Man™ (gene-X, Mutant And Normal) cell lines were developed using our patented gene editing technology (GENESIS™) including; B-Raf V600E, V600K; EGFR ΔE746-A750, T790M, L858R, L861Q; K-Ras G12A, G12C, G12D, G12R, G12S, G12V, G13D; PI3Kα E542K, E545K, H1047R. FFPE blocks containing specific allelic frequencies including: 50 %, 33 %, 25 %, 20 % or 5 % were generated and sections cut. DNA was extracted using five different extraction methods and analysed using Droplet Digital™ PCR.

Results: Mutant alleles could be detected using Droplet Digital™ PCR at each defined allelic frequency and the reproducibility of each test was very high. The allelic frequency was consistent throughout each block. The total DNA yield from each section was consistent using the same extraction method but varied between methods.

Conclusion: This study has demonstrated Horizon Diagnostic's FFPE Reference Standards have a highly accurate defined mutation specific allelic frequency together with a consistent DNA quantity.

PS-10-019

Transcript variants and isoforms of the phosphatase subunit PPP2CA and its regulatory binding partners in haematological malignancies

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Objective: The importance of feedback mechanisms involved in suppression of growth factor-induced signals is gaining importance both to understand molecular mechanisms of disease and also as potential therapeutic targets. Our previous studies show that erythroid differentiation can be blocked by constitutive expression of the pp2a inhibiting subunit, alpha4. The aim of this study was to identify variants and transcript isoforms of PPP2CA and the inhibiting subunits alpha4 and SET, using (1) cell lines derived from haematopoietic disease, and (2) Chronic Myeloid Leukemia (CML) and Acute Myeloid Leukemia (AML) patient material.
Method: High Resolution Melting (HRM) analysis was used to scan the cDNAs for variants and isoforms. Principle component analysis clustered the amplicons into genotypic groups. These genotypes were further analysed by direct sequencing.
Results: HRM identified mutants in SET and alpha4. Of interest the cell line, U937 has multiple mutations in the coding region of SET. PPP2CA isoforms were identified in patient material. One of the isoforms lacking exon5, is predominantly expressed in 15 % of CML (n=19) and AML (n=344) patients.
Conclusion: The presence of SET variants result in deregulated pp2a activity. The PPP2CA isoform (del.exon5) results in loss of phosphatase function, predicting sensitivity to the pp2a activator, FTY720.

PS-10-020

PAXgene® Tissue fixation technology for simultaneous preservation of morphology and biomolecules

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Objective: PAXgene Tissue (PAXgene) is a new, formalin-free fixation technology. PAXgene fixed, paraffin embedded (PFPE) tissue is suitable for conventional histochemical and immunohistochemical staining as well as for extraction of high quality nucleic acids and proteins including phosphoproteins.
Method: Cases of human cancer were divided and fixed in formalin, PAXgene, or snap frozen in liquid nitrogen (LN2). FFPE and PFPE tissue were stained with H&E and IHC stains. Nucleic acids were isolated and analyzed in RT-qPCR, by agarose gel electrophoresis, long-range, and multiplex PCR. Proteins and phosphoproteins were evaluated by western blot analysis.
Results: Morphology of PFPE samples and IHC staining intensities were similar to that for FFPE tissue. High correlation of RNA and miRNA expression between PFPE and LN2 samples, but poor correlation between FFPE and LN2 was observed. DNA from LN2 and PFPE was of high molecular weight and performed well in PCR, but DNA from FFPE failed in most PCR assays. Signal intensities for phosphoproteins in western blots were comparable between LN2 and PFPE, but weaker for FFPE tissue.
Conclusion: PAXgene Tissue simultaneously preserves morphology and biomolecules for morphological and multimodal biomarker testing within one sample. For research use only. Not for use in diagnostic procedures.

PS-10-022

STAT3 plays a pivotal role in cell adhesion in mouse hepatocytes by regulating E-cadherin expression

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Objective: Epithelial cells grow by proliferation and adhesion, which will form an organ/tissue. STAT3 is involved in cell proliferation and various cellular events. In the present study, we studied the role of STAT3 in cell adhesion in hepatocytes.
Method: STAT3 knockout cells (S3KO cells) and liver-specific STAT3KO (L-S3KO) mice were generated. Cellular adhesion was analyzed by light/electron microscopy. Expression of adhesion molecules was examined by immunohistochemistry and western blot analysis. Protein expression and cellular adhesion were also examined in the pre-/post-hepatectomy liver tissue in control and L-S3KO mice.
Results: mRNA and protein of E-cadherin were not expressed in S3KO cells. IL-6 up-regulated E-cadherin in control cells but not in S3KO cells, and induction of constitutively active mutant of STAT3 restored E-cadherin level in S3KO cells. Interestingly, membrane-bound beta-catenin expression was not affected, but released to cytosol in S3KO cells. S3-KO cells showed almost normal proliferation but did not form cell cluster due to lack of E-cadherin. Electron-micrograph confirmed lack of intercellular adhesion structures (desmosome) in S3KO cells. Also in L-S3KO mice, hepatocytes lack desmosome structure and cell adhesion.

Conclusion: STAT3 may play a pivotal role in cell adhesion by up-regulating E-cadherin expression.

PS-10-023

CXCR4 mRNA overexpression in high grade prostate tumors: Lack of association with TMPRSS2-ERG rearrangement

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Objective: Many prostate carcinomas (PrCa) harbor the fusion TMPRSS2-ERG, that results in ERG protein expression. Different studies have suggested an association between CXCR4 and ERG protein overexpression resulting from TMPRSS2-ERG rearrangement. The aim of this study is to investigate the relationship between CXCR4 expression, TMPRSS2-ERG fusion and Gleason grade in PrCa
Method: TMPRSS2-ERG rearrangement was investigated by FISH (n=44), ERG protein expression by IHC (n=84), and CXCR4 mRNA expression by quantitative RT-PCR (n=44) in primary PrCa (Parc de Salut MAR Biobank, Barcelona, Spain).
Results: TMPRSS2-ERG rearrangement and ERG protein overexpression were present in almost 50 % of cases, without statistical differences among Gleason groups. There was a very high concordance between FISH and IHC (Kappa= 0.954). 70 % of Gleason ³ 8 tumors overexpressed CXCR4 mRNA (p=0.009), without association between ERG protein and CXCR4 mRNA expression.
Conclusion: CXCR4 mRNA overexpression is associated with high Gleason grade, regardless of TMPRSS2-ERG status. TMPRSS2-ERG is not associated with grade. ERG IHC is very useful for TMPRSS2-ERG rearrangement detection.

PS-10-024

Oncogenic KRAS copy gain in colon carcinoma is associated with higher tumor grade

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Objective: Oncogene gain of function mutations in cancer are traditionally considered as heterozygous mutations, i.e., the malignant cell is expected to contain one copy of mutated gene and one copy of the wild type gene. However, recent studies have demonstrated a phenomenon of mutant allele imbalance, characterized by gaining additional copies of mutant allele. The purpose of this study was to determine the extent of this phenomenon and its clinical relevance in colon carcinoma.
Method: Based on the results of previous molecular morphometric study that quantitated the amount of wild type and mutated alleles among the tumor cells we now calculated the mutated allele gain in 42 samples of colon carcinoma harboring KRAS mutation and evaluated its association with tumors' grade and stage.
Results: Of the 42 samples 14 (33 %) showed mutant KRAS gains. The tumors with gains were associated with lower differentiation (4/21 in the well differentiated as compared to 10/21 in the moderately to poorly differentiated group, p=0.05). No association was found between copy number gains and tumor T stage or metastasis.
Conclusion: Our data indicates that oncogenic KRAS copy gain is associated with colon carcinoma grade. Further studies are needed to determine the role of this parameter in clinical practice.

PS-10-026

Molecular diagnosis of ALK positive anaplastic large cell lymphoma

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Objective: ALK positive anaplastic large cell lymphoma (ALCL) is characterized by anaplastic lymphoma kinase (ALK) expression, most commonly associated with the t (2;5)(p23;q35), fusing the ALK and nucleophosmin (NPM) genes. However, in a significant proportion of cases the ALK gene has a number of other than NPM translocation partners. The aim of the study was to detect the NPM/ALK fusion gene and the other possible fusion genes.
Method: NPM/ALK was detected by RT-PCR, NPM/ALK negative lymphomas were analyzed by ALK specific Rapid Amplification of 5´cDNA Ends (5´ RACE). We prepared Q-RT-PCR assay for quantification of 3´ ALK mRNA. Molecular findings were correlated with I-FISH.
Results: We analysed 42 ALK positive ALCL. Chromosomal breakpoints affecting the ALK locus were detected by I-FISH in all patients. The NPM/ALK was detected in 32/42 patients. 5´ RACE identified ATIC/ALK in 3, CLTC/ALK in 2 patients. Other fusion genes (TPM4/ALK, TPM3/ALK, ALO17/ALK) were found in one patient. In all specimens, overexpression of 3´ALK mRNA suitable for the minimal residual disease (MRD) detection was found.
Conclusion: Molecular diagnostics allows for detecting of various ALK gene translocation partners. Q-RT-PCR based analysis of 3´ALK mRNA is a promising and rapid approach for diagnosis and MRD monitoring in patients with ALK positive ALCL.

PS-10-027

Clonality analysis of giant cell tumor of bone and aneurysmal bone cyst

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Objective: A 17 year-old girl, presented with an osteolytic epiphyseal lesion of the distal ulna. Based on histopathological examinations, the lesion was classified as giant cell tumor of bone (GCT). Four years later, the girl developed a second lesion at the same site. The histopathological examination revealed aneurysmal bone cyst (ABC) with solid spindle celled and giant celled areas which raised a question of a recurrent GCT or a primary ABC. The aim of this study was to analyze the clonality of these two processes. Determination of maternal and paternal X chromosome activation status is useful in the diagnostic analysis of nonrandom X inactivation patterns.
Method: The human androgen receptor (HUMARA) gene polymorphism assay was used to identify the clonality of these two processes.
Results: The patient was identified as heterozygous for the HUMARA allele. The GCT and ABC samples exhibited a monoclonal pattern, but one of them was with maternal and the other with paternal X chromosome origin.
Conclusion: The findings of this case report demonstrate the clonal behavior of both lesions with different clonal patterns. The above investigation proved to be helpful in distinguishing between recurrent GCT and de novo ABC in the field of previous surgical intervention.

PS-10-028

Study comparison of different methods cytogenetic vs. QRT-PCR in the diagnosis of gastric cancer for HER2/NEU

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Objective: In approximately 20 % of gastric adenocarcinoma was found expression of Her2 receptor which correlate with worse prognosis.
Method: For immunohistochemistry (IHC) was used certified kits (HercepTestTM, Dako) and (PATHWAY® HER2/neu (4B5) Ventana, Roche). For in situ hybridizacion (ISH) was used fluorescence in situ hybridizatiom (FISH) (PathVysion HER-2 DNA Probe Kit Abbott molecular, USA), and FISH ZytoLight® SPEC HER2/CEN 17 Dual Color Probe Gastric Cancer and robotic method SISH (HER2 Dual Colour ISH, Ventana, Roche). In all specimens gen Her2/neu was quantifed agains reference gen by qRT-PCR method (LyghtCycler® 480 II, Roche).
Results: The results of cytogenetic analysis have been showed in 40 % that didn´t corespond with the results of qRT-PCR quantification. On the contrary the results of IHC was correlated with the results of qRT-PCR in 100 %. Methods SISH vs FISH has in 25 % different of results. In regard to the quality of ISH signals the SISH is more preferable for determination Her2/neu.
Conclusion: A pilot study conducted on a group of 20 patients showed that among the methods used in the process of determining HER2/neu amplification are significant differences, even in evaluation and interpretation of test results. Regardless of the histological type of tumors (diffuse and intestinal type) as problematic for the evaluation of samples proved to be endoscopic route.

PS-10-029

The use of molecular methods in diagnosis of malignant melanoma of biopsy

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Objective: Distinction between benign and malignant melanocytic lesions commonly represents a big challenge for the pathologist. In this case it appears as a useful auxiliary method of fluorescence in situ hybridization (FISH). The aim of this study was by using fluorescently labeled probes detection of numerical changes occurring in malignant melanoma and thus supply or confirm the diagnosis.
Method: The retrospective study included 14 samples tissue with an established histological diagnosis (6x malignant melanoma, benign melanocytic lesions 8x). For detection was used probe Vysis LSI RREB1/LSI Myb/LSI CCND1/CEP6 (Abbott Molecular, USA), Olympus AX70 fluorescent microscope (immersion lens 1000x). In the area of the tumor were calculated signals of individual probes and evaluated according to the manufacturer's instructions.
Results: Evaluable results were obtained in 10/14 Cases (71 %) of the melanomas were 4 and 6 benign melanocytic lesions. In all four cases of malignant melanoma have been burdened with genetic changes, mainly in the CCND1 (in 55 %) gene amplification and PREB1 (in 40 %) and MYB (in 5 %). In contrast, for all 8 benign melanocytic been demonstrated normal findings.
Conclusion: DNA abnormalities detected by FISH occurr in the vast majority of malignant melanomas but are not seen in benign nevi. This fact make the FISH test an important extra step in the differential diagnosis melanocytic lesions with ambiguous or borderline histological findings.

PS-10-030

Gene expression analysis of MEN1 and EGFR in operated for primary lung cancer patients

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Objective: EGFR is a receptor on the cell membrane with tyrosine-kinase activity and which is a regulator of proliferation, apoptosis, angiogenesis, tumor invasion. He is found to be overexpressed in some lung cancer histological subtypes. MEN1 is a tumor suppressor gene, with a role in cellular growth and differentiation, DNA reparation, and apoptosis.

Method: Surgically resected specimen from 99 patients (men $n=66$; women $n=33$, age 57 ± 11) with lung cancer were studied: carcinoid tumors (CT)-23, small cell lung carcinomas (SCLC)-13, large cell neuroendocrine carcinomas (LCNEC)-6, adenocarcinomas (AC)-29, and squamous cell carcinomas (SCC)-28. The histological subtype, pTNM stage, and gene expression of MEN1 and EGFR in tumor and normal lung tissue were evaluated.

Results: Overexpression of EGFR was observed in 34 %(SCC–61 %, AC–31 %, SCLC–23 %, LCNEC–17 %, CT-13 %). Decreased expression was observed in 22 %(LCNEC–66 %, SCLC–54 %, CT–22 %, AC–14 %, SCC–7 %) ($p<0.001$). Overexpresssion of MEN1 was observed in 57 % of all tumors (SCLC-69 %, CT-65 %, SCC-57 %, LCNEC-50 %, AC-48 %) ($p>0.05$). Significant correlation between overexpression of MEN1 and early stage SCC was observed ($p=0.03$).

Conclusion: EGFR is a target for therapy with monoclonal antibodies, so the tumors that overexpress EGFR can be considered for treatment with these drugs. MEN1 can eventually be a marker for good prognosis and a potential target for therapy.

PS-10-031

PROX1 overexpression alters gene expression profile in oral squamous cell carcinoma cell lines

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Objective: Homeobox genes encode transcription factors controlling cellular proliferation and differentiation. Altered expression of PROX1 homeobox gene is related to many cancers, including breast, esophagus, lymphatic and oral.

Method: After overexpression of PROX1 gene in SCC9 cell line, total RNA was extracted from three overexpressing-PROX1 clones (OC) and one control-transfection cell clone (CC). Microarray analyses were performed using the Whole Human Genome 44 K according to the manufacturer's instructions. Genes with a fold change of greater or lower than 2.0 in OC versus CC, were considered as increased or decreased, respectivelly. Gene Ontology (GO) was used to assign biological process related to significantly differentially expressed genes.

Results: Down-regulated genes MMP2, TIMP3 and NOTCH1 were further validated by qRT-PCR. Comparative gene analysis of OC and CC revealed 925 up-regulated and 789 down-regulates genes. Pathways induced upon PROX1 overexpression in GO terms included vascular development control, cellular adhesion, regulation of proliferation, among others. MMP2, TIMP3 and NOTCH1 expression by qRT-PCR showed reduced expression leves in OC. These genes are commonly overexpressed in oral squamous cell carcinoma and have been related with metastatic tumors and worse prognosis.

Conclusion: Overexpression of PROX1 alters the expression of genes involved in oral squamous cell carcinoma development. MMP2 and TIMP3 reduced expression following PROX1 overexpression suggest this gene function as a tumor suppressor.

PS-10-032

Analysis of alterations in epithelial DNA methylation as potential epigenetic biomarkers of neoplastic progression in Barrett's Esophagus

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Objective: Barrett´s Esophagus is the unique known precursor for esophageal adenocarcinoma (EAC), in a gradual progression to dysplasia. Our objective is to determine the correlation between the hypermethylation in CpG islands of the promoter region of p16 tumoral suppressor gen in epithelial DNA and the histopathological pattern, as possible biomarker for risk of progression.

Method: 1. A study was performed about the evolution of precursor lesions, in a group of 55 patients diagnosed following the Vienna classification. 2. p16 hypermethylation is analyzed in paraffin embedding samples, through laser microdissection, DNA extraction, PCR amplification, pyrosequencing and quantification.

Results: 1.14 of 20 cases with 2 to 5 biopsies remained as ND, ID or LGD, and 6 cases progressed to HGD and/or EAC. 2. Within the control group the methylation grade is 6.53 % and in the diagnostic groups is 12.04 % (ND), 7 % (ID), 17.05 % (LGD), 8.50 % (HGD) and 23.33 % (EAC).

Conclusion: 1. 70 % remained stable, but those reaching HGD all progressed to ACE (only in 50 % of the latter, HGD is recognized with H&E). 2. Methylation´s grade is higher in all diagnostic groups comparing to the control group, progressively increased as the dysplasia grade found with H&E, so it may be a good biomarker for neoplastic progression.

PS-10-033

Comparison of HPV OncoTec and NucliSENS Easy Q Test in preneoplastic lesions of the cervix

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Objective: In High Risk HPVs the expression of oncoprotein E6 is responsible for the degradation of p53, while E7 inactivates pRb and causes the progression to S phase of cell cycle, both sustaining the conversion to and the maintenance of malignancy. The aim of this study is to compare the performance in the detection of the E6 and E7 mRNA expression of HR-HPV using the NucliSENS Easy q test (bioMerieux) or HPV OncoTect (IncellDx) a test based on Flow cytometry-FISH method.
Method: We enrolled 50 patients positive for HR-HPV DNA and/or pap smears. All subjects underwent a colposcopy histological evaluation and were tested both for the NucliSENS Easy q test and HPV OncoTect.
Results: 31 out of 50 subjects resulted positive for RNA expression. The patients were divided into two cohorts based on the histological diagnosis: low grade lesions (CIN1) and high grade lesion (CIN2+). Patients with CIN1 were 26 with NucliSENS Easy q test and 13 with HPV Onco Tect, those with CIN2+ were 5 with either tests.
Conclusion: These preliminary results suggest that HPV OncoTect have a better specificity than NucliSENS Easy q test, while more samples need to assess the difference in sensitivity.

PS-10-034

Detection of PIK3CA/AKT mutations in human meningiomas

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Objective: The PI3K/AKT pathway is a major signaling pathway frequently activated in human cancer due to PIK3CA and AKT1 gene mutations thus representing a potential therapeutic target and prognostic biomarker. In this study, we examined the mutational status of PIK3CA and AKT1 in meningiomas.

Method: 91 meningiomas were screened for activating mutations in "hot spot" exons 9, 20 of PIK3CA using Real Time PCR and High Resolution Melting Analysis. PIK3CA wild-type samples were analyzed for mutations in exon 4 of AKT1. The mutations were verified by sequencing and/or pyrosequencing
Results: Mutations were detected in 2 out of 91 samples (2 %) in exon 9 of PIK3CA and were identified as p.E547K and p.S541F. Regarding exon 20, 7 out of 91 samples (7,5 %) showed the following mutations: p.R1023Q, p.T1025T, p.H1020V, p.M1043I, p.H1047R (2 cases), p.H1046T. Finally, in exon 4 of AKT1, 8 mutant cases were detected (9 %) all identified as p.E17K. In 19 % of the patients the activation of the PI3K/AKT pathway is due to mutations in the two examined genes.
Conclusion: Aberrant activation of the PI3K/AKT pathway due to PIK3CA and AKT1 mutations is commonly observed in human meningiomas and these genes could be considered as potential targets in new therapies for cancer.

PS-10-035

Study of PI3K/AKT/mTor pathway in urothelial bladder carcinoma

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Objective: Deregulation of the PI3 kinase-AKT/mTOR pathway is a frequent event in tumorigenesis. We examined the possible significance of the components of this pathway in bladder urothelial carcinoma (UC).
Method: 108 cases with bladder UC were screened for mutations in exons 9, 20 of PIK3CA gene and exon 4 of AKT1 by PCR-SSCP, HRMA, sequencing and/or Pyrosequencing. The expression of p-mTOR, p-4E-BP1, p-p70S6K, p-AKT, FGFR3 and p-ERK was evaluated by immunohistochemistry.
Results: 4,6 % of the cases were mutant in PIK3CA gene and 3 % in AKT1. Cases with wild type AKT1 displayed higher FGFR3 receptor expression (p=0.0521). p-4E-BP1 expression was more frequent in low grade (p=0.018) and in pTa-T1 tumors (p=0.053). Furthermore, superficial tumors presented higher levels of p-p70S6K expression (p=0.035) and lower levels of p-AKT expression (p=0.048). In multivariate survival analysis, p-4E-BP1 immunoexpression emerged as an independent prognostic factor of adverse survival (HR=9.207, p=0.0039), along with tumor grade and T-category.
Conclusion: Activation of PI3K/AKT/mTOR pathway in bladder UC is not exclusively related to the presence of AKT1 and PIK3CA mutations. Expression of p-4E-BP1 could serve as an independent prognosticator.

PS-10-036

Comparison of DNA extraction methods of formalin fixed, paraffin-embedded archival tissues

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Objective: Formalin fixed, paraffin-embedded (FFPE) archival tissues are valuable resources for many molecular studies. The goal of this study is identify the optimal method for DNA extraction from FFPE tissues.
Method: 32 human gingival tissues which has obtained from patients with gingival hyperplasia were used. Serial sections of 10 μm thickness obtained using a standard microtome. Half of the sections were deparaffinized on glass, the other half collected directly to a 1,5 ml tube. In order to identify the optimal method for DNA extraction, we compared phenol-chloroform protocol and DNA Extraction Mini Kit. The duration of proteinase K digestion were also compared. Spectrophotometric evaluation of the yield and purity of DNA was conducted. To deteminate the amplifiablity of extracted DNA, three different bp fragment of the beta-globin gene were amplified using PCR.
Results: The phenol-chloroform method had the lowest yield and purity. Deparaffinized specimens on glass, digested for 72 h and isolated using mini kit had the highest yield. Amplification of the 120 bp fragment of beta-globin gene was successful in all samples.
Conclusion: According to our results deparaffinization on glass, increasing the time of proteinase K digestion and using commercial kits for isolation seems the best method to obtain amplifiable DNA from archival specimens.

PS-10-037

MicroRNA signatures associate with Fallopian tubal implantation in humans

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Objective: MicroRNAs are small non-coding RNA molecules that regulate a large number of cellular pathways and deregulation or altered expression of miRNAs is associated with many disease states. The function of the Fallopian tubes appears to involve orchestrated spatiotemporal alterations in transcriptome profiles, the regulation of tubal gene expression and function by miRNAs may thus be of primary importance in tubal ectopic pregnancy.
Method: Both implantation sites and non-implantation sites of Fallopian tubes from women with EP and decidual biopsies from women undergoing therapeutic surgical termination of pregnancy were collected and analyzed by miRNA array. The unique miRNA profiling results were validated by TaqMan qRT-PCR, and bioinformatics' analysis was employed to further predict the miRNA targets.
Results: A total of 47 miRNAs were differentially expressed in implantation sites compared with those in non-implantation sites of Fallopian tubes after comparison of decidual miRNAs, among which 19 were up-regulated while 28 are down-regulated. The miR-424 was significantly increased, whereas let-7i, miR-149, and miR-182 were significantly decreased. Differentially expressed miRNAs were predicted to be related with several signaling pathways in normal intrauterine implantation.
Conclusion: Our findings establish an miRNA signature associated with tubal implantation and provide the experimental basis for further understanding the molecular and cellular mechanisms of initiation and development of tubal EP in humans.

PS-10-039

Does Hsp90AA1-2 and Hsp90AB1 expression in lung tissue can be a marker of increase of warming in Mexico from 1970 to 2009?

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Objective: In Mexico the maximum increase of the temperature from 1971 to 2009 is 7.5 °C with a mean of 1.6 °C. Lung is an organ that can sense any perturbation of the air, due to its constant interaction (long live) of the air. Our hypothesis was that lung could be an organ sensor of climatic change observed today.
Method: This preliminary study analyzed the expression of 3 isoforms of the genes of Hsp90. The cases were chosen from archive of autopsies from 1970 to 1979, with different diagnosis, and were matched in sex and age with a same number of cases chosen from 2000 to 2009. The expression was studied by RT-PCR from lung tissue embedded in paraffin, 20 samples of each decade.
Results: The expression levels of Hsp90 were normalized to β-actine. We found expression in six cases of 2000–2009: five for Hsp90AA1-2, and 1 for Hsp90AB1, one case expressed both. Their matched cases in 1970–1979 never expressed any isoform. The cause of dead in all cases doesn't fit with any pattern.
Conclusion: With these results we propose than the lung could be a sensor of global warming, and the expression of these genes could be molecular markers of this climatic change.

PS-10-040

Apoptosis associated genes and their role in predicting responses to neoadjuvant breast cancer therapy

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Objective: Neoadjuvant chemotherapy is used in the treatment of breast carcinoma because it substantially reduces the size of the primary tumor and lymph node metastases. This present study is aimed at the investigation of biomarkers that can predict a pathologic response to the therapy.
Method: The transcriptional profile of 84 key apoptosis genes was evaluated in both pre-therapeutically obtained tumor tissue by core needle biopsy and in specimens removed by final surgery, using a pathway-specific Real-Time PCR assay.
Results: On the basis of a hierarchical cluster analysis of 13 significantly changed genes, we divided patients into good and bad prognosis groups, which correlate well with progression-free survival. In the good prognosis group, we found a statistically significant downregulation of the expression of MCL1 and IGF1R genes after neoadjuvant treatment. We also found a statistically significant overexpression of BCL2L10, BCL2AF1, CASP8, CASP10, CASP14, CIDEB, FADD, HRK, TNFRSF25, TNFSF8 and CD70 genes. In contrast, we found upregulation of IGF1R after the treatment in the group with poor prognosis.
Conclusion: As we have shown, gene expression profiling after neoadjuvant chemotherapy is a valuable research tool for investigating molecular markers, which may better reflect tumor biology and treatment response than standard prognostic and predictive factors.

PS-10-041
Genetic changes in non-small cell lung carcinoma
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Objective: Non-Small Cell Lung Carcinoma (NSCLC) is one of the most serious cancers. Identification of genetic changes (mutations, amplifications or rearrangements) within EGFR, KRAS and ALK oncogenes, associated with NSCLC, allows choosing the patients, benefit from biological therapy with tyrosin kinase inhibitors.
Method: DNA is isolated from formalin fixed paraffin embedded specimens or cytology specimens. Mutation detection is performed by real-time PCR, fragment analysis, primer-extension analysis and mutant-enriched PCR. Wt-EGFR patients (e.g. with no mutation detected) are tested for ALK gene rearrangement and EGFR gene polysomy or amplification using the fluorescence in situ hybridization (FISH) method.
Results: Since 10/2010 till 2/2012, 238 DNA samples were analyzed. Out of these, 17 patients (7,14 %) were found to be positive for activating mutations within EGFR gene. Since 07/2011 till 2/2012, 80 patients were analyzed for ALK gene rearrangement, EGFR gene polysomy or amplification. ALK gene rearrangement has been proven in 5 (6,25 %) cases, ALK gene amplification in 2 (2,5 %) cases and EGFR gene polysomy or amplification in 35 (43,75 %) cases.
Conclusion: Determination of genetics changes in tumor can provide powerful tool for setting up strategy and therapeutic protocols in NSCLC patients.

Monday, 10 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-11 Poster Session Digestive Diseases Pathology II: Lower Gastrointestinal Tract

PS-11-003
Primary peritoneal mesothelioma complicating intussusception
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Objective: A 61 year old gentleman, ex-smoker with a history of asbestos exposure presented to the emergency department with a 1 day attack of severe abdominal pain and bilious vomiting. History of abdominal pain, lethargy, and weight loss over the last 12 months and 4 years of recurrent pleural effusion. Pleural aspirates and a video-assisted thoracic biopsy were negative.
Method: X-ray confirmed small bowel obstruction and an emergency laparotomy performed. The terminal ileum was intussuscepted into the caecum causing proximal obstruction. A right hemi-colectomy was performed.
Results: On gross examination there was intussusception of the terminal ileum secondary to a polypoid mass at the ileo-caecal valve. Histology showed an oncocytic tumour with neuroendocrine features arising from the serosa of the small bowel. The tumour cells were positive for CK7, calretinin, and vimentin but negative for CK20, chromograninA, CD56 and TTF-1. The features were in keeping with a malignant peritoneal mesothelioma infiltrating the small bowel wall.
Conclusion: Peritoneal malignant mesothelioma is an uncommon tumour which rarely causes mechanical small bowel obstruction. To our knowledge this is the first case of localised primary peritoneal mesothelioma presenting with intussusceptions.

PS-11-004
Giant mesenteric cystic lymphangioma in adult; rare tumor, unusual location and uncommon age of occurrence: A Tunisian case report
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Objective: Cystic lymphangioma is a rare benign neoplasm arising from the lymphatic system. It occurs as a result of congenital malformations of the lymphatics, leading to the obstruction of local lymph flow and the development of lymphangiectasia. Lymphangioma is common in pediatric patients, but it is extremely rare in adults, with only about 100 cases reported in literature. Most lymphangiomas are found in the head and neck; intraabdominal and specially mesenteric locations are very unusual. The aim of this work was to study its clinical, histological and therapeutic features and their diagnostic difficulties.
Method: We report the case of a 46 years-old woman, who presented a painful syndrome of the right iliac fossae (RIF). The physical examination found a mass of the RIF. Abdominal ultrasonography and magnetic resonance image showed a mesenteric cystic formation. At laparotomy, a large cystic tumor of the caecal mesentery, measuring 23 cm, was found. Histopathology showed a fibrous and thin walled cyst, lined by flat low lying epithelium with surrounding tissue of scattered lymphoid cells.
Results: The diagnosis of cystic lymphangioma was retained.
Conclusion: Mesenteric lymphangiomas are very rare, but they can cause acute abdomen that requires an emergent surgery. Therefore, they should be included in the differential diagnosis of cystic intra-abdominal lesions raises several possibilities, including both malignant and benign soft tissue tumours.

PS-11-005
Multiple splenic metastasis from colon cancer
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Objective: The spleen metastases from colon cancer are rare conditions and usually associated with extensive disease. There are only eight reports in English-language literature of isolated splenic metastases from colorectal carcinoma, which generally metastasize to regional lymph nodes, liver and abdominal peritoneum.
Method: We report a case of multiple splenic metastases in a 60-year-old woman.
Results: In November 2009, the patient had undergone right hemicolectomy, lymphadenectomy and chemotherapy for stage III tubular adenocarcinoma of the ascendant colon with positive pericolic lymph nodes. In December 2011, she was admitted in our hospital for diffuse abdominal pain and intestinal transit disorders. Computed tomography of the abdomen revealed multiple metastases of different sizes in liver and spleen. During the surgery, which was performed with the goal of curing metastatic disease, there were found two nodular hepatic secondary tumors, and numerous spleen metastases, with diameters from 0.2 cm to 1.5 cm. The histopathological evaluation of splenectomy specimen revealed a metastatic tumor deposit, histologically similar to the primary tubular adenocarcinomas of colon.
Conclusion: This is the ninth documented case of splenic metastasis from colon cancer. Previously reported cases of this type were isolated tumor, this one being the first reported with multiple splenic metastases.

PS-11-006
The role of fatty acid synthase in Inflammatory Bowel Disease (IBS)
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Objective: It was demostrated that FAS expression increases not only in mucosa involved by active colitis but also in normal mucosa of ulcerative colitis (UC) patients. Our aims were to evaluate the role of FAS expression in differential diagnosis of IBD, to search for any possible change during the progression of the disease in patients with clinical and endoscopic follow-up.
Method: Among 82 colonoscopic biopsy samples of 50 UC cases,13 samples were classified as remission,15 as resolution, and 54 as active period;35 samples of 30 Crohn Disease (CD) cases were classified as active period. Fifteen cases with normal endoscopic and morphologic findings comprised the control group.
Results: Between UC and CD active periods and control group, a significant difference was found (p=0,0001). There was a statistical correlation between FAS expression of basal crypt of normal mucosa in UC active period and the disease duration (p=0,036).
Conclusion: The increasing in FAS expression in patients with IBD can not be explained only by the inflammation. FAS expression can not aid us in the differential diagnosis of UC and CD, but it seems that it is related to the extent of inflammation in UC. The relation between the disease duration and an increase in FAS expression active UC, might have a significant role in carcinogenesis in UC.

PS-11-007
Micropneumatosis – An (un) usual finding in gastrointestinal specimen?
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Objective: A rather rare disease, micropneumatosis describes the findings of cyst-like cavities devoid of lining epithelium in the gastrointestinal wall. Micropneumatosis is often secondary to intestinal bacterial infection or mechanical factors. This

study evaluates the incidence of micropneumatosis in our institute.
Method: We analyzed all cases of micropneumatosis obtained in our institute between 2001 and 2011. Available data were retrieved from patients' records.
Results: Out of 300.000 specimens obtained between 2001 and 2011, 71 cases (0.02 %) presented with micropneumatosis (37 female, 34 male; mean age 61 years, age range 18 to 85 years). Most common site was the colon (32 cases), followed by stomach (30), small intestine (8) and greater omentum (1).
Conclusion: Micropneumatosis represents a rare but harmless diagnosis in gastrointestinal specimen. Due to the histological picture, which may be confused with dilated lymphatic vessels, submucosal lipomas, and, to the untrained eye, even with signet ring cell carcinoma, incidence may even be higher. In unclear cases, where there seems to be a endothelial layer, immunohistochemistry may be necessary to confirm diagnosis of micropneumatosis. This study shows that micropneumatosis should be considered in differential diagnosis in every age and sex.

PS-11-008
Predicting lymph node metastasis in pT1 colorectal cancer – A meta-analysis providing rationale for therapy decisions
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Objective: We conducted a meta-analysis of published reports on the predictive value of risk factors for lymph node metastases (LNM) in pT1 colorectal cancer in order to provide a rationale for choosing follow-up or radical surgery after local excision.
Method: Local excision is an attractive treatment option for colorectal cancer, but is only safe in the absence of LNM. Several pathological factors have been associated with LNM, however it remains unclear how to integrate these in clinical decision making.
Results: A Pubmed search revealed 17 studies totaling 3741 patients. Strong predictors of LNM were lymphatic invasion (RR 5.2 [95 % CI 4.0–6.8]), budding (RR 5.1 [95 % CI 3.6–7.3]), and high grade histology (RR 4.8 [95 % CI 3.3–6.9]). Deep submucosal invasion was also strongly associated with LNM, however in a risk stratification model this factor was of limited added value.
Conclusion: The absence of lymphatic invasion, budding and high grade histology may justify withholding radical surgery. The independent role of submucosal invasion depth is probably limited. Models for risk stratification based on these factors need to be validated.

PS-11-009
S 100 reactive protein in the intestinal wall with Crohn's Disease and in colitis ulcerosa
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Objective: Dendritic S100+ cells in intestines have been described in more studies. Their connection to S100+ fibres of nervous system is lesser of an object of interest.
Method: We have processed the samples of intestinal mucosa of people with Crohn's disease and colitis ulcerosa by the means of form-paraffine technique and anti S100 antibodies.
Results: In lamina propria and in submucosa at Crohn's disease were S100+ the fibres of various width and orientation. Outside of them the diffusely scattered round S100+ mononuclear cells could be seen. Contrary to colitis ulcerosa the granulation tissue at Crohn's disease contains in the area around abscesses a thick accumulation of S100+ cells and this is similar also in the formed lymphoid tissue.
Conclusion: The positive fibres can be seen in submucosa at the edge as well as in LPM between the bases of the glands. In between the plexus/ring and longitudinal muscle there are massive bands of connective tissue which contains bundles S100+ of ganglion cells and nerve fibres. The fibres are present in ring as well as in longitudinal muscle. In this area S100+ fibres can also be seen in vessel walls. Numerous bundles of granulatory tissue do not contain positively reacting substance. In the basal part lamina propria there are visible S100+ cells as well as long, smooth, positively reacting fibres.

PS-11-010
NCF1-deficient mice with impaired oxidative bursthave a more agressive progression of Dextran Sulfate Sodium (DSS) -induced colitis
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Objective: Intestinal Inflammatory Disease (IID) as a primary immunodeficiency depends on mutations in the NADPH oxidase complex, responsible for the production ofreactive oxygen species (ROS). One of the most common clinical patterns in IID is chronic colitis. Ncf1-mutation in mice leads to deficiency in ROS, rendering them susceptible to autoimmunity. Here we studies how ROS-deficiency in Ncf1-mutant mice influenced the immune response to DSS colitis, its recovery and answer to a second induction.
Method: Colitis was induced in wild type (WT) and Ncf1-mutant (Ncf1) B10.Q mice by administration of 3.5 % DSS in the drinking water for 1 week. After 1 week recovery, DSS

was administered for another week. Mice were sacrificed at days 0, 7, 14 and 21, the colon was removed and folded into a Swiss roll. Sections of the colon were stained with HE, and monoclonal antibodies against B cells (B220), CD3+ T cells; and macrophages (Mac1/CD11b) were applied.

Results: Colitis was more severe in Ncf1 than WT mice, with epithelial dysplasia, hyperplasia of Peyer's patches and poor epithelium recovery (hyaline scars). At all time-points the amount and location of colonic B cells, T cells and CD11b + cells was distinct between groups. These results suggest that ROS are crucial for leukocyte recruitment and tissue-repair in DSS-induced colitis.

PS-11-011

Histopathological pattern of polypoid lesions of colon in Albanian population

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Objective: Our aim was to study histopathologic pattern of the polypoid lesions in Albania.

Method: We studied 216 lesions, 184 polypectomies and 32 colorectal surgery in 139 patients in Tirana.

Results: There were observed 216 polypoid lesions of large intestine in 122 males and 91 females.105(48.6 %) were adenomatous polyps, 31(14.35 %) were hyperplastic, 24 (11 %) were inflammatory polyps with ulcerative colitis, 10 (4.6 %) were inflammatory 6(2.77 %) were juvenile polyps, 2(0.92) non Hodgkin's lymphoma and 1 (0.46) was fibrolipoma. Tubular adenomatous polyps were the commonest polyps. They were more common 56 (25.9 %) in male population as compared to female 19(8.79 %). High grade dysplasia was present in 50 (23.14 %) and malignant change in 26 (12 %). The size of the polyps range from 0.5 to 4 cm.

Conclusion: Adenomatous polyps were the most frequently found polyps in our study; the approximately 24 % were advanced lesions.

PS-11-014

The role of cancer stem cells in biology and prognosis of colon cancers

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Objective: This study was designed as a retrospective clinicopathological observation based on immunohistochemical and statistical findings to show the relationship between the disease progression and the intensity of the stem cell population within the tumor for colorectal cancers.

Method: For this purpose, we investigated 97 colorectal carcinoma cases, retrospectively. Paraffin embedded blocks was obtained from pathology archive and demographical patients' data from the patient's files of Gastroenterological Surgery Department. Immunohistochemically, we used CD133 and Musashi-1 antibody to determine the stem cells within the tumor. We noted the age of the patients, histopathological diagnose, tumor location, grade, TNM status, clinical stage, disease-free-survival and the outcome. Then we statistically compared all prognostic data with the immunohistochemical findings

Results: All of the cases were immunoreactive for both antibodies, furthermore we found a significant statistical correlation ($p=0.043$) between CD133 expression value and patient outcome. When the value of CD133 expression was high, clinical outcome was poor. In addition, there was a relation between high Musashi-1 expression and poor outcome.

Conclusion: Based on these findings we reported that overexpression of both CD133 and Musashi-1 antibodies may be a poor prognostic factor in colorectal cancers.

PS-11-015

Immunohistochemical evaluation of VEGF expression in colorectal carcinomas

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Objective: Vascular endothelial growth factor (VEGF) is an important angiogenic glycoprotein secreted by the tumor cells and host cells which proved to be a powerful prognostic factor in various human cancers. The aim of our study was the evaluation of VEGF expression in colorectal carcinomas using immunohistochemistry, in order to identify the relationship between the presence of the protein in the tumor cells and a series of morphological parameters.

Method: We analyzed 30 consecutive surgically removed colorectal carcinomas. Immunohistochemistry was done on formalin-fixed and paraffin embeded tissue sections, using the anti-human VEGF-A monoclonal antibody (clone VG1, Dako). The extent and intensity of staining were graded and used to calculate the immunoreactive score for each case. Statistical analysis was performed with SPSS (Statistical Package for the Social Sciences), using non-parametric tests. The level of statistical significance chosen was $p<0.05$.

Results: VEGF was expressed in all tumors, with a heterogeneous distribution. The only parameters that correlated with high VEGF positivity were the extent of the tumor necrosis and the presence of lymph node metastases ($p=0,001$).

Conclusion: High levels of the VEGF expression may be an indicator of poor prognosis in colorectal carcinomas.

PS-11-016

Collision tumour of the appendix: Mucinous cystadenoma and carcinoid - Report of a case

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Objective: Appendiceal carcinoids are usually located at the tip of the appendix and occur as incidental findings. Epithelial neoplasms of the appendix are uncommon and consist of mucinous adenomas, carcinomas and neoplasms with features of both carcinoid and adenocarcinomas.
Method: A case of dual mucinous cystadenoma and carcinoid of the appendix is reported.
Results: The patient, a 57-year old- asymptomatic female presented with a cystic right iliac fossa mass. The excised specimen was appendix cystically dilated measuring up to 8,5 cm in diameter. The luminal content consisted of viscid mucin. The base of the appendix was thickened (up to 1,5 cm) and firm. Microscopically the cystic part of the specimen had features of mucinous cystadenoma with adenomatous epithelium extending as well over the thickened appendiceal wall. At that area the wall was involved by a well differentiated neuroendocrine neoplasm WHO gr I (carcinoid). The neoplastic cells infiltrated the entire thickness of the appendiceal wall, the mesoappendix and reached the serosal surface. The two neoplasms where separate and there was no transitional zone between them.
Conclusion: Dual carcinoid/epithelial neoplasia is a rare occurrence in the appendix. The prognosis appears to be no worse than for either of the two components alone.

PS-11-017

Gastrointestinal Stromal Tumor (GIST) of the anal canal: A case report

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Objective: Gastrointestinal stromal tumors (GIST) are mesenchymal tumors derived from interstitial cells of Cajal. They are found more frequently in the stomach, small intestine while colon and rectum represent unusual sites. GIST's of the anal canal are extremely rare.
Method: 43-years-old woman who presented bleeding, pain and constipation for several months. The rectal examination revealed a well defined mass located within 10 cm of the anal verge. The magnetic resonance imaging confirmed a well-circumscribed mural mass without adenopathy. The local excision of the tumor was performed for pathological study.
Results: Gross examination showed a 4.5×3.0 cm fibrous mass. Histological examination revealed a spindle cell tumor with moderate atypia and mitotic count of 6 mitosis/50HPF. Neoplastic cells showed marked positivity for c-Kit and CD34 and negativity for muscular markers. A diagnosis of GIST with intermediate risk of aggressive behavior was made.
Conclusion: GISTs of the anal canal are extremely rare with only few cases reported in the literature. We described an additional case of GIST of the anal canal with histological and immunohistochemical study.

PS-11-018

Intestinal graft versus host disease with giant cells

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Objective: Graft-versus-host disease (GVHD) is a common complication of allogeneic bone marrow transplantation in which immune cells in the transplanted marrow attack the immunocompromised host. It can occur in either an acute or in a chronic form and may affect various organs. Intestinal GVHD is particularly important because of its frequency, severity and its effects on the general condition of the patient.
Method: Here we report a 68-year-old man who developed GVHD, 8 months after receiving allogeneic non-myeloablative peripheral blood stem cell transplantation for refractory chronic lymphocytic leukemia. Colonic biopsies revealed an edematous and congested lamina propria, dilated crypts lined by flattened epithelium, increased apoptotic figures and vanishing crypts. Notably there were some giant cells in between crypts. However subsequent sections and special stains didn't show any granuloma formation or presence of an infectious agent.
Results: To our knowledge presence of giant cells in GVHD hasn't received proper attention before. Although we don't know the actual importance or clinical consequences of the entity yet, we report this case to increase awareness of this feature within the context of GVHD. We have seen more cases with giant cell GVHD afterwards; comparison with other cases of GVHD without giant cells may help clarifying their significance.

PS-11-021

Differential mutation patterns of KRAS and BRAF in adenomatous and serrated neoplastic sequences

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Objective: Colorectal carcinomas develop through adenomatous or serrated neoplastic sequence. Different molecular mechanisms underly these morphologic sequences which may be translated into different therapies. We aimed to assess adenomatous and serrated neoplastic sequences in terms of KRAS and BRAF mutations.
Method: The study group comprised of adenomatous polyps (APs, n=20, 13.6 %), conventional adenocarcinomas (ConCA, n=30, 20.4 %), serrated polyps (SPs, n=67, 45.6 %) and mucinous adenocarcinoma (MucCA, n=30, 20.4 %). KRAS mutation was assessed for exon 2 and exon 3 using pyrosequencing while BRAF V600E mutation was analysed using allele specific PCR. Chi square test was used for statistics.
Results: KRAS mutations were observed in 41.5 % of carcinomas and 25.3 % of polyps. KRAS mutation rate was significantly higher (p<0.05) in ConCA (85 %) than in MucCA (50 %), and in APs (55 %) than in SPs (16.4 %). BRAF mutation was found in one MucCA (1.7 %) while all SPs were mutated. TSAs had the highest KRAS mutation rate (36.8 %) in comparison to SSA/Ps (17.6 %) (p<0.001) whereas SSA/Ps and HPs had significantly higher rates of BRAF mutation (64.7 %, 61.1 %, respectively) than TSAs (26.3 %) (p<0.001).
Conclusion: KRAS seems to take part in adenomatous sequence while BRAF, seem to play a significant role in serrated neoplastic progression of the colorectum.

PS-11-022
Characterizing quiescent ulcerative colitis: Pathologic review of 45 cases
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Objective: Quiescent ulcerative colitis (Q-UC) is morphologically characterized by typical architectural and cellular mucosal changes that define the process as chronic. It is not clear which of these changes are more ubiquitous in Q-UC. Our aim was to evaluate which classical histological findings of Q-UC are more prevalent in rectal samples.
Method: Rectal biopsies were collected from patients with clinical and endoscopical Q-UC. The biopsies were evaluated for mixed inflammation in the lamina propria, crypt architectural abnormalities, basal plasmacytosis, fibrosis, and Paneth cell metaplasia as well as for features of active disease (cryptitis, lamina propria neutrophils and erosion).
Results: Forty-five patients (64 % female; median age 56 years) were included. Thirteen (28,9 %) biopsies showed focal activity and four cases (8,9 %) had criteria for active disease. Epithelial distortion, chronic inflammatory infiltrate and basal plasmacytosis emerged as features present in 95, 81 and 73 % of biopsies. Overall, 4 biopsies were histologically normal (no chronic features, no active disease).
Conclusion: Rectal mucosa from patients with clinical and endoscopical Q-UC can show microscopic active disease, which illustrates that endoscopy alone may be insufficient to identify quiescent disease. In Q-UC, the most frequent changes (present in over 75 % of the biopsies) were epithelial distortion and chronic inflammatory infiltrate.

PS-11-023
Vacuum-based preservation of colorectal cancer specimens: A comparison with formalin fixation
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Objective: In Pathology, an alternative to immediate fixation in neutral buffered formalin (NBF) is vacuum sealing and cooling (VSC) ("Tissue safe" system). There have been few evaluations of VCS.
Method: We assessed MSI, KRAS, BRAF in colorectal cancers, conserved with VCS before fixation (51 cases with surgery in a hospital distant from our centre), or immediately fixed in NBF (56 cases with surgery during the same period in our hospital). DNA was extracted from paraffin embedded tissue. MSI was assessed by MLH1 and MSH2 immunohistochemistry and PCR; KRAS and BRAF were screened by multiwell-plate based real-time PCR (LightCycler® 480, Roche), confirmed by Sanger sequencing.
Results: There was no difference regarding morphological analysis. Immunohistochemistry was interpretable in all cases, with 4 negative cases in the VCS group (4 MLH1), 11 negative cases in the NBF group (10 MLH1, 1 MSH2), and a 100 % correlation between immunohistochemistry and PCR. DNA extraction was possible in all cases. KRAS and BRAF mutations were detected in 21 and 1 cases in the VCS group and 16 and 7 cases in the NBF group, respectively.
Conclusion: We show that analysis of MSI, KRAS and BRAF is feasible in surgical specimens after VCS. This procedure can be an alternative to formalin fixation.

PS-11-024
Clinical significance of CD204-positive M2 macrophage in colorectal cancer
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Objective: Tumor-associated macrophages are divided into two phenotypes, termed M1/M2 macrophages. M1 macrophages promote tumoricidal responses whereas M2

macrophages assist tumor progression and metastasis. In this study, we have analyzed a clinical significance of M2 macrophages in excised sections from patients with colorectal cancer.
Method: Patients who had surgical resection for colorectal cancer between 2005 and 2006 were identified from a prospective database. Tissue sections with adenocarcinoma in pT3 category were employed in this study. The sections were stained with anti-CD204, a marker of M2 macrophages. The relation between the staining pattern and tumor budding or patient prognosis was examined.
Results: Fifty-two patients (30 male, 22 female) with a median age of 67 years (range 23–86) were studied. The tumors were classified into four subtypes according to the staining patterns of CD204-positive cells, i.e. sparse type (n=9), invading-tip type (n=6), peri-nest type (n=18), and dense diffuse type (n=19). Only a dense diffuse type was related to the high degree of tumor budding. The prognosis with a dense diffuse type demonstrated a poor prognosis as compared to the other types.
Conclusion: Even the case with comparable tumor depth, CD204-positive macrophages with dense diffuse distribution was related to the poor prognosis.

PS-11-025

Analysis of the pathological response in patients with locally advanced rectal cancer after pre-operatory treatment

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Objective: The treatment of locally advanced rectal cancer has shown a significant development over the last decade. The total mesorectal excision and the use of pre-operative radio (chemo)-therapy are leading the patients to a gradual improvement of local control of the disease. The aim of this study is to evaluate the pathological tumour response to pre-operative treatment through correlation between the clinical stage (cTNM) and the pathological stage (ypTNM).
Method: Since 2009, 35 patients with locally advanced rectal cancer, assessed by high resolution magnetic resonance imaging (HR-MRI) and TNM staging system, have been evaluated by the Colorrectal Multidisciplinary Team. Pre-operative radio (chemo)-therapy was mandatory before undertaking standard surgery. Surgical specimens were evaluated according to the Vikingo Project's protocol implemented by The Spanish Association of Surgeons.
Results: 34 patients completed the pre-operatory treatment. After evaluation of clinical and surgical study specimens, we observed variable degree of downstaging in 27 (79,5 %) patients, 5 of whom showed complete response. The 7 (20,5 %) remainig patients were assessed as stable disease. No local progression of tumours was observed.
Conclusion: In this study, approximately 80 % of patients, who were staged by HR-MRI and underwent preoperative radio (chemo)-therapy for locally advanced rectal cancer, showed some degree of downstaging. We remark the fact that nearly 15 % of patients reached complete response.

PS-11-026

The density of macrophages in colorectal cancer is inversely correlated to TGF-BETA1 expression and patients' survival

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Objective: The role of macrophages in colorectal cancer tumorogenesis is complex because they can both prevent and promote tumor development. We investigated CD68 infiltration in tumor tissue and its correlations with proteins ot TGF-beta1 signaling pathway.
Method: A nonselected panel of 206 primary tumors of colorectal origin was investigated immunohistochemically with antibodies against CD68, TGF-beta1, Smad4, Smad7, TGFRII and levels of TGF-beta1 were measured by ELISA.
Results: Lower CD68 infiltration in tumor nests was associated with expression of TGF-beta1 (chi2=9.236, p=0.002) and Smad4 (chi2=2.871, p=0.090) in tumor cells and with TGFRII expression (chi2=5.699, p=0.017) in tumor cells membranes. There was not correlation between CD68 cell numbers in tumor tissue and TGF-beta1 serum levels. We have found higher frequency of liver metastases in patients with lower infiltration with CD68 in invasive margin (chi2=11.364, p=0.001). The survival time was shorter for patients with low CD68 infiltration in tumor nests and invasive margin, compared with the survival time for patients, with higher CD68 infiltration in both tumor compartments (p<0.001).
Conclusion: The increased levels of TGF-beta1 in the tumor have an immunosuppressive effect on CD68 infiltration.

PS-11-027

Inflammatory myofibroblastic tumor of the colon: The 25th reported case

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Objective: Inflammatory myofibroblastic tumor (IMT) is a very rare tumor of the colon in which the diagnosis is

especially based on immunohistochemistry. In the colon, we report the 25th case of IMT.
Method: Case presentation
Results: We report the case of a 56-year old male who presented with symptoms suggesting colon cancer. A 20 mm protruded tumor was endoscopically described in the ascending colon. Right hemicolectomy was performed. Macroscopically the tumor was well defined, covered by normal mucosa with a central depressed area, suggesting a GIST (Gastrointestinal Stromal Tumor). Microscopically spindle cells with fascicular arrangement admixed with mononuclear leukocytes were observed. The tumor cells expressed Vimentin, SMA, Desmin and ALK and were CD34 and CD117 negative. Intense angiogenesis and CD117 expression in the endothelial cells were also observed.
Conclusion: In the IMT of the colon, clinical endoscopic and gross feature can imitate a carcinoma or a GIST. The IHC pattern of IMT can offer informations about its histogenesis. Based on the immunophenotype, we hypothesize that this tumor seems to occur from the the pluripotent stromal cells, CD34 positive which can be either differentiated in the interstitial cells of Cajal (telocytes), which are also CD34 positive or, during differentiation, can loss CD34 positivity.

PS-11-028
Development of a computerized morphometry application for assessment of tumor fraction in colon carcinoma tissue samples
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Objective: Determining the fraction of tumor cells in colon carcinoma samples analyzed for KRAS mutation is important for choosing the proper testing modality. However, when asked to determine tumor cell fraction in tissue samples, different pathologists give considerably different estimations, possibly leading to erroneous interpretation of KRAS mutation analysis results and poor treatment choices.
Method: We developed a free, easy to use computer program that estimates tumor cell fraction on colon carcinoma slides that are immune-stained with anti-cytokeratin antibody. Sixty samples were evaluated by the program and results were compared to actual measurement of tumor fraction.
Results: The tumor cell fraction estimated by the computer program showed highly significant correlation with the actual measurements (R=0.64, p<0.001). Additionally, we found that a short calibration step prior to beginning the computer estimation increased the accuracy of the results. In four cases (7 %) there was some discrepancy between the computer estimation and the actual measurements, however, this was attributed to lower quality immunohistochemical staining.
Conclusion: In conclusion, we believe that this program can be used for standardizing the evaluation of tumor cell fraction in colon carcinoma, and that its use might aid in making better diagnosis and treatment choices for these patients.

PS-11-029
Magnetic resonance imaging assisted tumour block selection in colorectal cancer
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Objective: Inadequate sampling may result in understaging in colorectal cancer. Fat clearance techniques and whole mount sections are time consuming and costly. We hypothesise that high resolution Magnetic Resonance Imaging (MRI) of the colorectal cancer specimen may aid histological sampling and result in upstaging.
Method: Patients undergoing resection are prospectively recruited, and randomised to "conventional histology" or "MRI assisted histology". In addition to routinely selected tumour blocks, 4 additional blocks and any additional lymph nodes are selected with the aid of specimen MRI or visual inspection and palpation according to group. T stage, depth of extramural invasion, distance to resection margin, lymph node (LN) number and involved LN are compared between the two groups.
Results: To date, 116 of 218 patients have been recruited. We present the methods and preliminary results. There is a trend towards greater T stage and LN yield. No difference in N stage, extra-mural vascular invasion or involved non-peritonealised resection margin has yet been observed.
Conclusion: Early results suggest that specimen MRI may upstage colorectal cancer specimens by aiding tumour block selection. We will complete recruitment of 218 colorectal cancer patients over the next 12 months to determine whether observed differences are significant.

PS-11-030
Diverticular disease of transverse colon is rare and perforation may occur in Crohns Disease
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Objective: Diverticular disease commonly affects the sigmoid colon in the West and the right colon in Asia. Perforation is uncommon affecting 4/100 000 per year. Perforated diverticular disease of the transverse colon is therefore very rare. We present a case of Crohns disease complicating

transverse diverticular disease that lead to perforation and unfortunate death.
Method: Radiological and histopathological features are presented with a review of the literature
Results: To the best of our knowledge, this is the first reported case of Crohns disease complicating diverticular disease of the transverse colon. We suggest that distal stricturing leading to increased intraluminal pressure or increased weakening of the colonic wall due to coincident Crohns fissure and diverticulum are possible pathogenic mechanisms.
Conclusion: Crohns disease complicating transverse diverticular disease is uncommon, but may be one pathogenesis leading to the rare event of transverse colon diverticular perforation.

PS-11-031
Analysis of acute cellular rejection in a series of 16 adult intestinal transplants of the Hospital 12 de Octubre (series 2004–2011), Madrid, Spain
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Objective: Intestinal transplantation is a therapy for irreversible intestinal failure. Acute rejection (AR) is the main cause of morbi-mortality.
Method: Review of 12 intestinal and 4 multivisceral transplants in 15 adult recipients with follow-up of 745 days (31-2019) to investigate the incidence, significance and outcome of AR.
Results: There were 12 episodes in 9 patients. They start between day 7 and 499 (178±159 days). Duration ranged from 3 to 87 days (27±22). The three moderate and the three mild AR reversed with treatment. Of the 6 severe AR, 3 caused the failure of the graft. Five episodes de AR began as moderate or severe directly. Severity in the course of each episode was fluctuating. Sixteen indeterminate rejections were seen in 9 grafts (did not reach definitive criteria). They lasted 1–31 days (mean: 5±8 days).
Conclusion: 1-Acute rejection is the most common cause of morbidity in the intestinal transplant (56 % of the grafts). 2-It can develop at any time and relapse. 3-The duration and severity of the episodes are fluctuating. 4-In our series, 75 % reversed, but severe rejection often lead to graft loss (50 %).

PS-11-032
Histopathological study of 7 intestinal grafts lost in a series of 16 adult transplants. Hospital 12 Octubre. Madrid. Spain
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Objective: Intestinal transplantation is a therapy for irreversible intestinal failure. In 2004- 2011, 16 transplants were performed (12 isolated, 4 multivisceral) in 15 adults with a follow-up of 745 days (31-2019). Our goal is to determine the causes of intestinal graft loss (IGL).
Method: We studied 4 explants and 2 autopsy. The autopsy was not authorized in one death.
Results: Seven grafts were lost in 6 patients (3 multivisceral). Two types of failure were seen. A) local: 3 severe acute rejections (AR) (days 77, 158, 511) and 1 lymphoproliferative syndrome (LPS) in day 148; B) systemic: 3 sepsis (days 31,88,161). AR showed 3 types of morphology: ulcerative, pseudomembranous and with disappearance of the villi preserving the crypts. LPS was a high-grade B lymphoma and affected the graft and the lymph mesenteric nodes with venous thrombosis that cause ischemic necrosis. The 3 sepsis were due to acinetobacter, to adenovirus in the graft and pulmonary aspergillosis and to pseudomona aeruginosa with necrohemorrhagic pancreatitis.
Conclusion: 1- The incidence of IGL was 44 %. 2- The cause of IGL was local (AR and LPS) in 57 % and sepsis in 43 %. 3- Severe AR was the most frequent cause of failure. 4- Histological examination properly determine and document the causes of IGL.

PS-11-033
Cap polyposis: Report of two cases
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Objective: Cap polyposis is a rare colorectal disease characterized by mucoid, bloody diarrhea associated with multiple inflammatory polyps covered by a cap of fibrinopurulent mucous. The disorder was first described in 1985 and up to date a small number of cases has been reported in the literature.
Method: We report two cases with multiple polyps of rectum and sigma, which were histologically diagnosed as cap polyposis.
Results: The cases were two males on age of 18 years and 64 years. In both cases there was a history of mucoid and bloody diarrhea. On the basis of colonoscopy findings, in the young patient there was a broad differential diagnosis including M. Crohn, inflammatory pseudopolyps and Cronkhite–Canada syndrome. In the second case the clinical diagnosis was polyps of sigma. Endoscopic biopsies and polypectomy were done. In both cases, the histology showed typical histological features of cap polyposis - polypoid lesions containing elongated, tortuous and often distended crypts covered by a cap of inflammatory granulation tissue.

Conclusion: The recognition of this rare disease is of practical significance because its clinical symptoms have some similarity with inflammatory bowel disease or irritable bowel syndrome.

PS-11-034

Histopathological findings in 496 consecutive appendectomies: A retrospective analysis

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Objective: Appendectomy is one of the most common surgical procedures. Histology usually confirms the clinical suspicion of acute inflammation, but sometimes other clinically relevant diagnoses are made. The aim of our study was to audit the appendectomies at our institution and summarise atypical pathological findings with emphasis on benign and malignant tumours.
Method: We reviewed the histopathology results of 496 consecutive appendectomies received in a 5-year period.
Results: Excluding three cases of metastatic process, appendiceal tumour was found in 21 cases (4.2 %), which is a higher rate than reported in the literature. There were four endocrine tumours, all G1, three cases of classical adenomas, 10 cases of low-grade appendiceal mucinous neoplasm (one associated with pseudomyxoma peritonei) and three cases of carcinoma (one mucinous adenocarcinomas, one intestinal type, one undifferentiated carcinoma). We also diagnosed one case of multicystic mesothelioma. Endometriosis was diagnosed in seven cases. In 18 cases appendicitis was associated with diverticula, in 6 cases changes were suggestive for Crohn's disease and in one case for cystic fibrosis. Negative appendectomy rate was 10.3 % that falls within the range reported in the literature.
Conclusion: Histopathological examination of appendectomy specimens may reveal many different conditions not previously suspected; therefore, it should be performed in all cases.

PS-11-035

CDX2 and MUC protein expression in small intestinal adenocarcinomas and their prognostic significances

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Objective: Clinicopathological and prognostic significances of CDX2 and mucin core (MUC) proteins expression have not been comprehensively evaluated in the small intestinal adenocarcinoma (SIAC).
Method: Immunohistochemical expressions of CDX2, MUC1, MUC2, MUC5AC, and MUC6 in tissue microarrays of 189 surgically resected SIAC cases were examined and compared with clinicopathologic variables, including patients' survival.
Results: CDX2, MUC1, MUC2, MUC5AC, and MUC6 expression was observed in 39.7 % (75 cases), 35.4 % (67 cases), 27.5 % (52 cases), 28.6 % (54 cases), and 16.9 % (32 cases), respectively. While SIAC patients with CDX2 expression showed less nodal metastasis ($p=0.01$), those with MUC1 expression tended to have SIACs with nodular or infiltrative growth ($p=0.003$), poor differentiation ($p=0.005$), and more lymphatic invasion ($p=0.04$). MUC5AC expression was associated with SIACs with well differentiation ($p=0.02$) and frequent pancreatic invasion ($p=0.04$). Patients with CDX2+/MUC1- had more polypoid ($p=0.02$) and well differentiated ($p=0.006$) tumors and a significantly better survival (median, 80.8 months, $p<0.0001$) than those with other immunophenotypes (CDX2−/MUC1+, CDX2+/MUC1+, and CDX2−/MUC1−). Patients with CDX2 expression (median, 71.2 months) had a significantly better survival than those without CDX2 expression (23.0 months) by univariate and multivariate analyses ($p<0.0001$).
Conclusion: CDX2 expression is an independent good predictor of survival in surgically resected SIAC patients.

PS-11-036

Small neuroendocrine tumor of appendix with metastasis in the ileocecal lymphnode: A case report

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Objective: Neuroendocrine tumors (NET) of appendix are believed to behave less aggressively than NETs at other sites. Separate staging criteria have therefore been proposed, and tumor size >2 cm appears to be the dominant criterion for aggressive behavior in appendiceal NETs. However, it is controversial whether radical surgery is indicated in tumors measuring >2 cm. We report a case of a 13-year-old girl with acute appendicitis in whom appendectomy and right-sided hemicolectomy were performed.
Method: Surgical specimens were sampled and processed according to standard histological and immunohistochemical (IHK) procedures.
Results: In the base of appendix, there was a tumor measuring 1.5 cm in diameter, focally invading mesoappendix, with free resection margins. Microscopically, tumor exhibited characteristic features of NET G1, with positive IHK for chromogranine and synaptophysin, and Ki67 index <2 %. IHK for podoplanin revealed focal lymphovascular invasion. In the right-sided hemicolectomy specimen, there was no residual tumor, metastasis was found in one ilecoecal lymphnode.
Conclusion: Our case shows that appendiceal NET smaller than 2 cm can metastasize to regional lymphnodes. IHK against podoplanin might be helpful in searching for lymphovascular invasion, helping to separate it from the

retraction clefts, thus providing additional information concerning risk factors for a more aggressive behavior.

PS-11-037

Lipomatosis of ileocaecal valve causing small bowel obstruction mimicking Crohn´s Disease

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Objective: Lipomatosis of ileocaecal valve is a rare cause of small bowel obstruction.
Method: We describe a 41-year-old male treated for Crohn´s disease and clinical and imaging presentation of chronic small bowel stenosis and obstruction.
Results: A right hemicolectomy was performed, and hypertrophy of Bauhin´s valve causing intestinal obstruction was found. Microscopical examination of the specimen revealed morphological changes consistent with lipomatosis of the ileocaecal valve. The ileum and colon were macroscopicaly unremarkable and histomorphological features of Crohn´s disease were absent.
Conclusion: Many patients with lipomatosis of the ileocaecal valve are asymptomatic, or the lipomatosis gives causes insignificant symptoms only or rarely obstruction may occur. Then, as in the presented case, the surgical resection with ileo-colic anastomosis is the only effective treatment.

PS-11-038

Overexpression of CXCR4 in tumor buds is a strong predictor of lymphatic invasion and lymph node metastasis in colorectal cancer

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Objective: CXC chemokines enhance tumor cell survival and proliferation. Especially CXCR4 promotes tumor development by stimulating angiogenesis and favoring metastasis. In contrast, CXCR3 is angiostatic and may exert an anti-tumor effect. Since tumor budding is linked to vascular/lymphatic invasion and lymph node (LN) and/or distant metastasis in colorectal cancer (CRC), here we explored the expression of CXCR3+4 in relation to tumor budding.
Method: A multiple-punch tissue microarray of 220 CRCs with full clinicopathological information including therapy underwent immunohistochemistry for CXCR3 and CXCR4. Expression was evaluated in tumor-center, -front and -buds and correlated to clinical data.
Results: CXCR3-expression was homogeneous throughout tumor-center, -front and -buds (average 40 %) and was unrelated to clinicopathological features or survival. CXCR4-expression was high in tumor-center and -front but reduced ($p<0.001$) in buds (76 %, 77 %, and 20 %, respectively). Maintenace of CXCR4-expression within buds was predictive of LN-positivity ($p<0.0001$) and lymphatic invasion ($p<0.0001$) but not of venous invasion or distant metastasis. CXCR4-positivity in buds was associated to poor outcome ($p=0.0048$) in LN-negative CRCs ($p=0.0191$).
Conclusion: Maintenance of CXCR4-expression in buds has a profound effect on tumor aggressiveness and prognosis in LN-negative CRC-patients. This would help in establishing a tumor budding "profile" especially linked to LN-metastasis in CRC.

PS-11-041

COX-2 expression in serrated polyps of the colon does not discriminate specific histological subtypes

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Objective: COX-2 expression was investigated in colorectal cancer and colorectal precancerous lesions. Its expression in adenomas is associated with increasing size and neoplastic potential. Little is known about COX-2 expression in subtypes of serrated colonic polyps, which constitute substantial number of colon cancer precursors. The aim of the study was to assess COX-2 expression in serrated polyps of the colon and to investigate its potential discriminative role.
Method: 175 consecutive serrated polyps were analyzed. They included: 26 traditional serrated adenomas (TSA), 36 sessile serrated polyps (SSP) and 113 hyperplastic polyps (HP). COX-2 expression was assessed semi-quantitatively (0–3). Kruskall-Wallis test was used for the comparison of COX-2 expression between serrated categories ($\alpha=0.05$).
Results: We found COX-2 positivity in 19 of 26 TSA (73.0 %), 27 of 36 SSP (75.0 %), 78 of 113 HP (69.0 %), respectively. No differences in COX-2 expression were found between serrated subgroups.
Conclusion: The results may suggest no discriminative role of COX-2 within serrated neoplasia pathway.

PS-11-042

Heterogeneous expression of Ki67 staining in tumor buds implies different prognostic outcomes in colorectal cancer

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Objective: In colorectal cancer (CRC), tumor buds represent a more aggressive tumor cell type at the invasive front

with apparently low proliferation. The aim of this study was to determine the proliferation potential of tumor buds by comparing Ki67 staining across different tumor areas and adjacent normal tissue.
Method: Whole tissue sections from 197 patients with CRC underwent immunohistochemistry for Ki67. 10 high-power-fields were evaluated for each of the following regions: normal mucosa, tumor center, tumor front and tumor buds. Ki67-positivity was correlated to patient outcome.
Results: Average Ki67-positivity was 5.2 % in normal mucosa and significantly higher in the tumor center (38.2 %; $p<0.0001$) and invasion front (34.9 %; $p<0.0001$). Strikingly, only 0.3 % of all tumor buds showed Ki67-positivity ($p<0.0001$). Although Ki67-positivity in the tumor center or front was unassociated with clinicopathological features or patient survival, the greater the number of Ki67-positive tumor buds, the worse the prognosis. This effect was also found after adjusting from TNM stage (HR (95 % CI): 2.25 (1.1–4.5); $p=0.0193$)).
Conclusion: A marked absence of Ki67 staining is found in most tumor buds, suggesting a substantially decreased proliferation rate. However, the association of Ki67-positivity with worse prognosis in 15 % of cases points towards a heterogeneous population of tumor buds.

PS-11-043
Kayexalate and intestinal necrosis: An underrecognised entity
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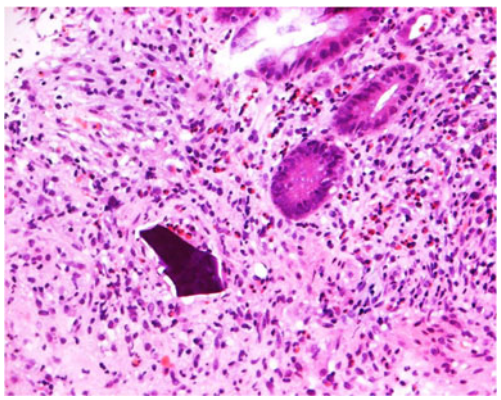
Objective: There are only few cases of intestinal necrosis secondary to administration of kayexalate described in the literature, most of them from postoperative patients, having the largest study only 11 patients in 9 years. We report our experience in the last 4 years with a brief review of the pathophysiology and histologic aspects of the lesions induced by the kayexalate.
Method: Between 2008 and March 2012 seven patients were diagnosed with ischemic necrosis related to kayexalate administration, five in colon biopsy and two in resection specimens. They're comorbidities and clinical evolution was extracted from the medical records.
Results: The patients' age ranged between 47 and 78 years. In one case we had the clinical information of chronic renal insufficiency. In three of them, there was no previous history of renal impairment. One patient developed symptoms after one single administration of kayexalate. The clinical presentation ranged from abdominal pain, gastrointestinal bleeding and three of them had a fatal outcome.
Conclusion: The administration of kayexalate can have associated risks with different clinical impact in any patient. We must be aware of the related complications, as the histological identification of the kayexalate crystals indicates the etiology of the ischemic lesions to the clinicians and alerts them to the dangers of this therapeutic.



PS-11-044
Absence of K-Ras mutations in colorectal cancer is associated with EGFR overexpression
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Objective: EGFR plays an important role in colorectal cancer (CRC) progression and represents a natural target for molecular anticancer drugs. In this study we evaluated 800 consecutive CRC aimed to analyze K-Ras mutational status in relationship to: different clinical-pathological parameters, EGFR immunohistochemical (IHC) expression, response to cetuximab treatment.
Method: K-Ras mutations and EGFR expression were determined by direct cycle sequencing and IHC respectively in 565 surgical specimens and 235 biopsies. IHC findings were evaluated using four different score systems.
Results: The distribution of K-Ras mutations did not significantly vary between surgical or bioptic specimens or with respect to different anatomic tumor localization. In contrast, K-Ras is more frequently mutated in EGFR negative/low score tumors than in positive ones ($p<0.0001$). Focusing on the 419 surgical treated CRC patients, we found a higher percentage of K-Ras mutations in T4 CRC ($p=0.01$) and in younger patients ($p=0.002$). Finally, we observed that 6 % of primary CRC, concomitantly evaluated with their paired metastases, changed K-Ras mutational status during progression.
Conclusion: Our data showed that tumor size, patient age and EGFR IHC expression significantly influenced K-Ras

mutations. Interestingly, we observed that cetuximab treated patients, had a better clinical outcome when EGFR presented a high IHC score.

PS-11-045

Multiple Immunohistochemical investigation of signaling pathways in colorectal cancer

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Objective: Despite the recent advances in therapeutic armamnet colorectal cancer (CRC) remains one of the leading cancer deaths worlwide. CRC has a heterogenous molecular background with known prognostic and predictive markers, but the whole picture is rather complex with many unexplored connections.
Method: We performed multiple immunohistochemical stainings on tissue microarrays (TMA) made of 95 CRC cases to study the correlations between EGFR-RAS, cell cycling, apoptosis, cell adhesion and tumor invasion pathways. We evaluated digitized slides using matrix scores considering both the frequency and positivity of cells and statistical analysis followed.
Results: We found strong linear correlation between positivity and (p-1068, p-1173) phosphorylation of the EGFR receptor and p53 positivity detected with different clones. Furthermore, phospho-NF-KB p65 positivity was strongly linked to Survivin-expression.
Conclusion: Activation of EGFR-related pathways including NF-kB is a key factor in CRC-growth. The strong link between cancer promoting EGFR signaling and the mutational lack of the p53 driven apoptosis suggests a deadly cooperation, which can be further aggravated by forced tumor survival through survivin. Correlation of these markers potentially predict poor disease outcome but can be specifically targeted by the upcoming new molecules of tailored therapy.

PS-11-047

KRAS status in colorectal carcinoma: Assessment in primary and metastatic tumors

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Objective: KRAS mutational status is important in colorectal carcinoma (CRC). It is unclear, however, which is the most informative tissue source for study in CRC cases showing more than one tumor mass. To explore this issue we determined KRAS status in a series of primary (PT) and metastatic CRCs.
Method: A total of 68 tumors belonging to 25 patients (17 males and 8 females) with ages ranging between 46 and 80 years (average, 64 years) were studied. KRAS mutation hotspots in codon 12 and 13 were analyzed by polymerase chain reaction and sequentiation. wt-KRAS cases were confirmed with the KRAS StripAssay TM.
Results: KRAS mutations were found in 11 (44 %) of the 25 PTs, 8 (73 %) in codon 12, and 3 (27 %) in codon 13. PTs and their metastases showed similar genotypes in 21 (84 %) cases. The 4 (16 %) cases with dissimilar results showed the following combinations: wt-KRAS/KRAS c.35 G>A:p. Gly12Asp (n=1); wt-KRAS/KRAS c.35 G>T:p. Gly12Val (n=1); wt-KRAS/KRAS c.50 G>T:p. Ser17Ile (n=1) and KRAS c.35 G>A:p. Gly12Asp/wt-KRAS (n=1).
Conclusion: Most primary CRCs and their metastases are genotypically very similar. Even so, if metastatic tumor tissue is available we recommend its study over that of the PT, since de novo mutations may supervene in CRC metastases.

PS-11-048

Usefulness of EPCAM expression in the algorithmic approach to Lynch Syndrome in colorectal carcinoma

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Objective: Lynch syndrome (LS), the most frequent form of hereditary colorectal cancer (CRC), is caused by germline mutations in the mismatch repair system genes. A recently identified mechanism involving the EPCAM gene is responsible for 6.3 % of MSH2-negative LS cases. We herein explore EPCAM protein expression in LS-associated, MSH2-negative CRCs to evaluate its potential value in the algorithmic approach to LS population screening.
Method: We studied a total of 19 MSH2-negative CRCs from 14 different patients in whom we were able to perform a complete germline analysis. Expression of both MSH2 (1:200 dilution, clone G219-1129, Pharmingen) and EPCAM (1:100 dilution, clone Ber-EP4, Dako) was evaluated by immunohistochemistry (IHC).
Results: Nine patients showed a deleterious germline mutation that involved the MSH2 gene in three instances and the EPCAM gene exon 9 in six instances. All patients harbouring the EPCAM mutation belonged to the same family. Of the19 CRCs, EPCAM expression loss was seen in only five, all of them were from patients with a germline EPCAM deletion.
Conclusion: Due to the high specificity of EPCAM protein loss for identifying LS patients with an EPCAM deletion, we recommend adding EPCAM IHC to the LS diagnostic algorithm in MSH2-negative CRC cases.

PS-11-049

BRAF mutation in colorectal carcinomas with signet ring cell component

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Objective: Colorectal carcinoma with signet ring cell component (CRC-SRC) is a rare and distinct subtype with little molecular information. We investigated the frequency of BRAF mutation in 28 CRC-SRCs and its relation with clinicopathologic parameters.
Method: We categorized tumors into groups 0–9 %, 10–24 %, 25–49 % and >50 % according to signet ring cell component. Genomic DNA was isolated from parafin blocks and analyzed for BRAF V600E mutation by polymerase chain reaction - restriction fragment length polymorphism (PCR-RFLP).
Results: Eleven of cases showed BRAF mutation (39.3 %). The results were also confirmed with sequence. No statistically significant differences were found in clinicopatologic parameters between BRAF wild-type and mutant CRC-SRC. On the other hand, when we adjusted age, gender, percentage of signet ring compenent and stage, we found a statistically significant increased risk in BRAF mutant group compared to BRAF wild-type in Cox regression analysis (HR=7.68, 95 % CI=1.06–55.78, p=0,044)
Conclusion: BRAF mutation is frequent in CRC-SRCs. This finding may support its diverse molecular pathogenesis and could have important therapeutic implications for those patients. To clarify the relation of BRAF mutation with clinicopathologic parameters and prognosis in CRC-SRC, studies with multi-instutional larger series are needed.

PS-11-050

Coexisting lipomas and adenocarcinoma of the colon: Case report

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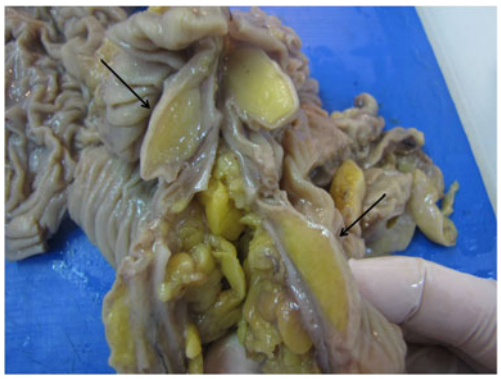
Objective: Lipomas of the large bowel are rare, they are invariably submucosal and therefore may intussuscept. Infrequently lipomas may also present in the form of multiple polypoid masses in the colon. We present a 69-years old female with 3 submucosal lipomas and a coexisting adenocarcinoma of transverse colon.
Method: 69-years old female patient was admitted to hospital because of rectal bleeding for 3 months. Colonoscopic examination revealed mucosaly intact polypoid tumoral masses and an ulcerated tumoral mass in transverse colon. Biopsy of the ulcerated mass was diagnosed as adenocarcinoma. Extended right hemicolectomy was performed.
Results: Grossly, ulcerated tumor was 1,5×1×0,4 cm and there were 3 polypoid tumors in cecal area of the right colon which were 2.5–2.0–1.5 cm in their greatest dimensions. Polypoid tumors were yellow, lipomatous on cut surfaces. Microscopically ulcerated tumor was composed of adenocarcinoma morphology and the other polypoid tumors were composed of submucosal mature adipocytes with a thin capsule around them. The diagnosis was colonic adenocarcinoma (pT1N0M0) and submucosal lipomas of colon. The patient had no additional therapy and she is healthy with no evidence of recurrence.
Conclusion: This case is presented to remind that there may be multiple lipomas of colon with coexisting malignant epithelial tumors.



PS-11-051

Myxoid liposarcoma of the ileum: A case report

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Objective: Primary liposarcoma of the small intestine is exceedingly rare. To our knowledge, only 7 cases have been reported so far. We report a case of the primary myxoid liposarcoma of the ileum.
Method: The patient was 77-year-old woman. CT and MRI revealed a 6-cm-intrapelvic mass, which was proved to be a tumor of the distal part of the ileum, and, therefore, partial ileectomy was performed.
Results: The tumor was 6.7×6.3×3.7 cm in size, relatively well circumscribed and located within the intestinal wall without invasion to the neighboring tissues. Microscopically, the tumor had mixture of cellular and myxoid areas, showing proliferation of short spindle and stellate shaped cells in a delicate capillary vasculature. Univacuolated tumor cells and a small number of lipoblast-like cells were also seen. Immunohistochemically, these proliferating cells were positive for S-100 protein. According to these pathological findings, we diagnosed the tumor as myxoid liposarcoma. FISH methods showed the tumor had chromosomal translocation t(12;16)(q13;p11).
Conclusion: The differential diagnosis of this includes other spindle cell tumors such as GIST and myogenic tumors. But we could arrive at the proper pathological diansosis following the above morphological features and the specific chromosomal

translocation. We will also discuss the clinico-pathological features of the cases including ours.

PS-11-052

Prognostic significance of selected immunohistochemical markers in colorectal cancer

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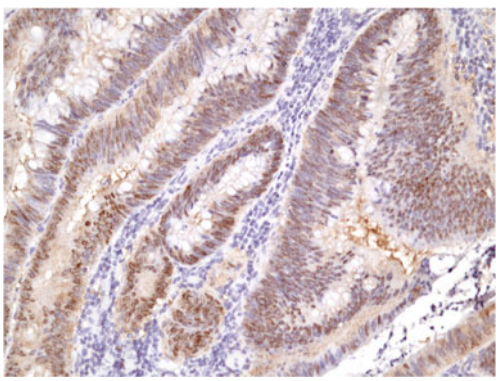
Objective: The aim of our study was to identify a combination of markers whose expression is predictive of invasion and metastasis of colorectal carcinoma.
Method: The expression of E-cadherin, β-catenin, tenascin C, KAI-1, epidermal growth factor receptor (EGFR) and vascular endothelial growth factor (VEGF) was studied immunohistochemically and correlated clinicopathologically in 72 primary colorectal carcinoma cases (26 with metastatic lymph nodes). 17 patients (24 %) developed haematogenous metastases at median 6,5 months postoperatively (3–11).
Results: Expression of following markers significantly correlated with depth of tumour invasion: cytoplasmic accumulation of E-cadherin (p=0,035), nuclear staining for β-catenin (p=0,03), increased tenascin C expression (p=0,001), and loss of EGFR and VEGF expression (p=0,015 and 0,02, respectively). Decreased tenascin C and KAI-1 expression associated with the presence of lymph node metastases (p= 0,027 and 0,046, respectively). Weak cytoplasmic E-cadherin expression correlated with distant metastases (p=0,045).
Conclusion: Our results suggest that abnormal expression of proteins involved in cell adhesion and migration (E-cadherin, β-catenin, tenascin C, EGFR) and angiogenesis (VEGF) may be related to the invasion of colorectal carcinoma. Detecting the expression of E-cadherin, tenascin C and KAI-1 probably possesses clinical significance in evaluating lymph node and distant metastasis and predicting the prognosis of colorectal cancer.



PS-11-053

p53 and PTEN immunoexpression in colon adenomas

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Objective: The PI3K signaling pathway is antagonized by phosphatase and tensin homologue (PTEN) activity. In human cells, the activation of PI3K signaling by mutations in PTEN can lead to activation of p53.
Method: We studied immunoexpression of PTEN and p53 in 59 colon adenomas and polyps (A/P): hyperplastic polyps (HP), serrated adenomas (SA), tubular adenomas (TA), tubulo-villous adenomas (TVA), and 7 in situ carcinomas (CC), using the Ultravision Labeled Polymer System method. We established frequency (p53, PTEN) and intensity of the reaction (PTEN).
Results: PTEN expression was decreased in 42 % of A/P and in 57 % of CC. PTEN expression is more frequently lower in HP, A/P with dysplasia, A/P located in the left colon and in case of young patients. A/P are mainly p53+/PTEN+, while CC are p53+/PTEN−. The majority of TA and SA are p53+/PTEN+, and HP are p53+/PTEN−.
Conclusion: p53 overexpression is associated with altered PTEN expression in colorectal carcinogenesis. Acknowledgments: This study is partially supported by the Sectoral Operational Programme Human Resources Development, financed from the European Social Fund and by the Romanian Government under the contract number POSDRU/89/1.5/S/60782.

PS-11-054

Immunohistochemical expression of mismatch repair proteins in colorectal carcinomas of the Epirus region

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Objective: In colorectal adenocarcinomas (CRCs) microsatellite instability (MSI) can be documented by immunohistochemical detection of mismatch repair proteins (MMR). The aim of the present study is to identify the percentage of MSI-positive CRCs, in the Epirus region of Greece and compare it to the international data.
Method: A total of 50 cases of sporadic CRCs, 25 adenomas and 10 hyperplastic polyps, formalin-fixed paraffin-embedded, were examined immunohistochemically using standard methods (En Vision system), with the antibodies MLH1 (Clone ES05), MSH6 (Clone PU29) and PMS2 (Clone M0R4G) (Novocastra-Menarini). Immunostained sections were evaluated semi-quantitatively, taking in account the percentage of neoplastic positive cells and estimating nuclear staining intensity, compared to the internal positive controls (normal epithelium, lymphocytes).
Results: All hyperplastic polyps and adenomas expressed the examined MMR. Two out of 50 CRCs were negative for MSH6 and PMS2, while one of them was also negative for MLH1. Interestingly, one of these two CRCs had an

adjacent adenoma, which also showed negative staining for MSH6 and PMS2.

Conclusion: Immunohistochemical staining for MMR is possible in archival material. Loss of MMR varies, depending on the protein examined. In CRCs from the Epirus region the estimated loss of at least two MMR is 4 %.

PS-11-055

Gelatinases expression in 53 Tunisian sporadic colorectal cancer cases

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Objective: Matrix metalloproteinases (MMPs) are a family of zinc-dependent neutral endopeptidases collectively capable of degrading essentially all extracellular matrix (ECM) components. Genetic alterations in MMP-2 and MMP-9 have been implicated to play an important role in colorectal carcinogenesis (CRC). The aim of this study was to investigate the hypothetic correlations between the MMP-2 and 9 mRNA expression and the clinicopathologic variables of the CRC.

Method: The expression of MMP-2 and -9 mRNA was assayed by RT-PCR for 53 Tunisian sporadic colorectal adenocarcinomas.

Results: MMP-2 was highly expressed in the 53 cases. MMP-9 was not detected in 18 cases and moderately or highly expressed in 35 cases. Absence of MMP-9 mRNA expression was significantly related to an advanced tumoral invasion stage (pT3) ($p=0.003$).

Conclusion: Our study suggests that the overexpression of MMP-2 could be the result of an imbalance in the system of transcriptional regulation of MMP-2, which would involve the loss of expression or activity of its inhibitor: TIMP-2. A variable expression of transcripts of MMP-9 could be explained by the hypothesis of hypermethylation of the promoter or degradation of its transcript after protein translation.

PS-11-056

Relationship between matrix metalloproteinases 2 and 9 promoter polymorphisms and colorectal cancer risk

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Objective: The carcinogenic schema of colorectal cancer (CRC) follows a multistep process governed by mutational events that affect multiple micro-environmental factors, including matrix metalloproteinases (MMPs). This present work aims to contribute to a better understanding of MMP-2 and -9 promoter polymorphisms involvements in the genesis and progression of sporadic CRC in Tunisian population.

Method: The MMP-2 and MMP-9 promoter genotypes were determined by PCR-RFLP in 53 Tunisian patients with sporadic colorectal cancer and 69 healthy control subjects.

Results: No significant associations were found regarding MMP-2 (-1306 C/T) polymorphism and CRC susceptibility. There was a connection between the MMP-2-1306 promoter polymorphism and gender ($p=0.012$). The MMP-9 (−1562 C/T) was significantly associated with CRC (OR= 2.39 [1.023 to 5.58]). No implication of MMP-9-1562 promoter polymorphism in the clinicopathological parameters of CRC was evident.

Conclusion: Our findings suggest that the MMP-2 promoter polymorphism was not a predictive factor for the CRC occurrence while the MMP-9-1562 CT genotype was a risk factor for CRC susceptibility.

PS-11-057

Hodgkin's lymphoma in distal rectum in a patient with Crohn´ Disease treated by biologic therapy – A case report

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Objective: Rare cases of Hodgkin`s lymphoma have been reported in the setting of inflammatory bowel disease.

Method: We report a case of Hodgkin`s lymphoma in a 37 years old male patient with corticosteroid-dependent Crohn´ Disease (CD) who had been medicated with azathioprine for many years. In the last 4 years he began periodical therapy with infliximab, till the time when he complained of worsening of symptoms and the appearance of asthenia, tenesmus and weight loss. Infliximab was withdrawn and replaced by adalimumab. A colonoscopy with several biopsies revealed the presence of a Hodgkin Lymphoma.

Results: The histological examination revealed granulation tissues where we identified atypical cells (Reed-Sternberg cells) with the following immunohistological staining: CD30+, CD15+, LMP1+LCA-, CD20-, CD3-, ALK-. These results in conjunction with the morphological aspects and the clinical history of CD favored the diagnosis of Hodgkin Lymphoma in a patient with preceding CD. The patient was subjected to radical colectomy. Postoperative pathological examination showed CD with involvement of the distal rectum by Hodgkin's lymphoma.

Conclusion: The present report may serve as a reminder to clinicians of the possibility of occult lymphoma in patients with colonic CD treated with biological therapy.

PS-11-058

Immunohistochemical testing of microsatellite instability in Stage II Colon Cancer: Outcome analysis of 352 cases

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Objective: DNA mismatch repair (MMR) status in sporadic colonic cancers (CCs) had provided valuable prognostic and predictive information in the appropriate clinical setting; however there are no definitive guidelines for microsatellite instability (MSI) testing. We evaluated the expression of MMR proteins and correlated them with outcome in a cohort of patients with sporadic colon cancer.
Method: We reviewed 352 cases of sporadic stage II colonic cancer from Abril 27th 1995 to December 12th 2009. Clinical data including tumor grade, prognostic factors, therapy and outcome were searched for. Tissue microarrays using a manual Beecher system were constructed and stained with antibodies for MLH1, MSH2, PMS2 and MSH6.
Results: 8 % (28) of 352 CCs had loss of expression of one or more MMR proteins, including defect in 1 protein 3.7 % (13), 2 proteins 3,7 % (13) and tree proteins 0,6 %(2). The mean overall survival was 144 months with no significant differences in patients between microsatellite stable and unstable tumors.
Conclusion: We detected a fairly low prevalence of the loss of immunohistochemical expression of MMR proteins. This result might have influence our mean overall survival between microsatellite stable and unstable tumors.

PS-11-059

The pathological effects of orchidectomy on intestine tissue and serum level of carcino embryogenic antigen

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Objective: Carcino Embryogenic Antigen (CEA) is a well-known tumor marker influenced by carcinogenic changes in intestine tissue. The purpose of this study was to determine the effects of orchidectomy on serum level of CEA and histological changes of intestine in male rats.
Method: Male Wistar rats were randomly divided to control, sham, uni-orchidetomised and biorchidectomised groups of 5 in each. 10 weeks after operation, blood samples were collected using cardiac puncture method. Serum CEA level was measured using ELISA method. The effect of orchidectomy on intestine tissue was also histologically studied. The results were statistically analyzed using ANOVA.
Results: Serum level of CEA was significantly increased in orchidectomised rats compared with control animals ($P<0.001$). The increase in serum CEA level was more in biorchidectomised than uniorchidectomised rats ($P<0.001$). There was also an enhancement in tissue lymphocytes, plasma cells and inflammation in intestine of orchidectomised animals.
Conclusion: The results showed that orchidectomy results in pathological changes in intestine tissue leading to increased serum CEA level.

PS-11-060

The plasma cells density in pararectal lymph nodes of patients with rectal cancer after neoadjuvant therapy

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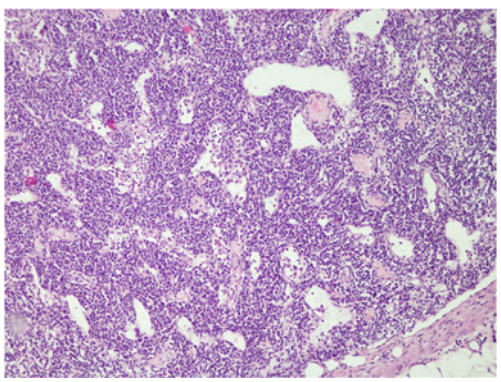
Objective: Neoadjuvant chemoradiotherapy (NT) is standard procedure for locally advanced rectal cancer. In this study, we compared the morphology of lymph nodes and the amount of plasma cells in the interfollicular region of lymph nodes in rectal tumour surgical excision material, between two groups who had received and not received NT prior to surgery.
Method: Fifty cases with NT and forty cases without NT were included. The number and diameter of lymph nodes were recorded. The morphology of the lymph nodes were evaluated, and the percentages of interfollicular plasma cells were demonstrated immunohistochemically (CD138). Tumor regression grade was assessed using Mandard scoring system.
Results: Average number and diameter of lymph nodes were greater in patients without NT ($p<0,05$). Atrophy of germinal centers was noted as 54 % in NT group, versus 5 %. The amount of plasma cells in the interfollicular region was found to be higher than fifty-one percent in 54 % of NT group versus 5 % ($p<0,05$), as well. Complete response rate (Mandard's: 1) was 18 %. No significant association was found between the amount of plasma cells and tumor regression.
Conclusion: NT leads to a decrease in the volume of the lymph nodes and atrophy of germinal centers, conversely, causes stimulation of the proliferation of interfollicular plasma cells.



PS-11-061

Adenomyoma of the ileum: Pathohistological features with reference to pathogenesis

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Objective: Adenomyoma is a rare benign non-neoplastic tumor-like lesion. It originates from abnormal embryonic buds but its pathogenesis has not been fully elucidated.
Method: A 63-year old man with severe pain, intussusception and ileus underwent a resection of a part of the intestine containing a tumor mass acting as a lead point. Tissue was analysed using H&E, histochemical and immunohistochemical stains.
Results: Lesion located in the mucosa, submucosa and muscularis propria consisted of glandular structures varying in size and morphology, the larger ones containing papillary projections and the smaller ones being similar to Brunner's and peribiliary glands, both of them surrounded by smooth muscle bundles. The lesion was not accompanied by ectopic pancreas, and it indicated a diagnosis of adenomyoma of the ileum. Glandular elements were CK7+ and CK20− and CDX-2−, opposite to intestinal mucosa.
Conclusion: Adenomyoma is a mass lesion rarely found distal to the duodenum, which bares close clinical and morfological resemblance to a tumor and some non-neoplastic conditions. Cytokeratin expression favors the heterotopic pancreas theory of pathogenesis, but abnormal interaction between the endoderm- and mesoderm-derived tissues can not be excluded.

PS-11-062

Smoothelin in biopsies of colorectal carcinomas as marker of muscularis propria invasion

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Objective: Staging of colorectal carcinomas is of eminent importance for prognostication and treatment; preoperative distinction between high grade dysplasia, invasion of submucosa (with permigration of the muscularis mucosae MM) and infiltration of muscularis propria (MP) is difficult in biopsies, due to similarities of smooth muscle cells in MM and MP. Smoothelin is a robust marker of the MP in normal colon, not expressed in MM.We analysed it value for distinguishing MP and MM near carcinomas.
Method: 50 colorectal carcinomas, diagnosed in biopsy particles and staged in the surgical specimens were analysed by IHC for expression of smoothelin (MoAb R4A, DCS Hamburg).
Results: Desmin and SMA were consistently expressed in the smooth muscle cells of MM and MP near and distant to carcinoma cells. Smoothelin showed little expression in MM. In MP however, the invasion by carcinoma cells caused a total or subtotal loss of Smoothelin in the cytoplasm of the smooth muscle cells.
Conclusion: Expression of Smoothelin correlates to mechanical tension in the cells. The reliable difference in the IHC-expression of Smoothelinin MM and MP in normal colon is not seen in near infiltrating carcinomas. Relying on Smoothelin in biopsies for the determination of the depth of invasion is dangerous.

PS-11-063

Anal tuberculosis: Report of a case

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Objective: Tuberculosis can affect any part of the gastrointestinal tract. Anal localization, in particular, has a very low incidence (0,7 %).
Method: A 66 year-old male presented, complaining of perianal pain, constipation, weight loss of 5 kilos the last 4 months and night sweating. Physical examination was normal, except for an ulcerated lesion in the anal region. The patient was submitted to computerized tomography (CT) and incisional biopsy of the lesion.
Results: The CT of the chest revealed multiple, scattered, calcified nodules in the upper zones of both lungs and histological examination showed confluent, non-necrotizing, epithelioid granulomas with the presence of Langhans' multinucleated giant cells. Acid-fast bacilli were detected both within the anal lesion and in the sputum. Mantoux test was positive. The patient had a history of pulmonary tuberculosis 40 years ago. A diagnosis of anal tuberculosis was made and the patient was put on a four drug anti-tuberculous regimen. In 6 months the symptoms improved and the perianal lesion healed.
Conclusion: A tuberculous origin must be considered when the cause of anal and perianal lesions is unclear. Therefore histological and bacteriological confirmation is essential in order to avoid undue delay in diagnosis and treatment.

PS-11-064

The relation of BRAF V600E Mutation and microsatellite instability in colorectal carcinomas

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Objective: Colorectal carcinogenesis is associated with various morphological and molecular pathways. Microsatellite instability (MSI) pathway has familial and sporadic forms.

Among CRC's %15 of the sporadic cases are associated with MSI and these have hypermethylation of the MLH1 promoter associated with BRAF V600E gene mutation. Familial forms do not show BRAF V600E mutation.
Method: We investigated the microsatellite instability (MSI) by immunohistochemical study of MLH1, PMS2, MSH2 and MSH6 together with the BRAF mutation presence and their correlation with standard histopathological parameters in 54 sporadic CRC cases.
Results: The age distribution was 25–88 with an average of 67,9. Immunohistochemical expression loss of MLH1, PMS2, MSH2 and MSH6 was seen in 18,5 %, 22,2 %, 7,4 % and 11,1 % of the total 54 cases respectively. MSI was seen in 27,8 % of the cases. The BRAF V600E gene mutation was seen in 18 cases and among these 8 cases (44,4 %) showed MSI, while MSI frequency was 19,4 in non-mutated group. And this was statistically significant ($p<0.05$). MSI was found significantly correlated with grade and lymph node number ($p<0.05$).
Conclusion: Our study confirmed that sporadic cases of CRC with MSI are associated with the BRAF V600E gene mutation. MSI is correlated with histologic grade and dissected lymph node number.

PS-11-065
Colon biopsy diagnostics may reliably be performed using virtual microscopy
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Objective: Virtual microscopy using whole slide images (WSIs) is a feasible alternative to optical microscopy, offering major advantages for pathology practice. The present study aims to prove reliability of this promising technique for colon biopsy diagnostics.
Method: Colon biopsies ($n=295$) were assessed (into 7 main diagnostic groups) using both glass slides and WSIs by 4 pathologists and 2 residents. Two of the pathologists having ample experience using WSIs, scored the biopsies in a primary diagnostic setting. For each case the criterion standard diagnosis was defined based on glass slide diagnoses. Accuracy was defined as the percentage of concordance with the criterion standard. Kappa statistics were calculated as a measure of observer agreement.
Results: The overall concordance rates were 89.5 % for WSIs and 91.4 % for conventional microscopy. The intraobserver (WSIs versus glass slides) agreement was good to excellent, with kappa values ranging from 0.73 to 0.87 (mean 0.78) and was higher than the interobserver agreement for glass slides (mean 0.71). Concordance with the criterion standard varied less between WSIs and glass slides in the diagnoses of pathologists with virtual experience.
Conclusion: This study showed good diagnostic accuracy and reproducibility for WSIs, indicating this technology may be used for colon biopsy diagnostics.

PS-11-066
Intestinal occlusion due to colonic lipoma: A case report
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Objective: Lipomas of the digestive tract are rare benign tumor and most often found incidentally during a colonoscopy, computed tomography scan, surgery or autopsy. Lipomas of the colon were first reported by Bauer in 1757 and are most often located in the ascending colon. The incidence of this lesion is estimated between 0.2 and 4.4 % and represents 1.8 % of the colonic benign lesions. We report a case of patient with symptoms of ileus due to colonic lipoma.
Method: A 78-year-old man patient was urgently admitted with symptoms of ileus. Right hemicolectomy was performed, and clinical impression was that it was a malignant tumor.
Results: Examination of the cecum we found polypoid whitish yellow tumor, size 4×2,5 cm. On histology the tumor was composed of mature adipose tissue without cellular atypia. The tumor was located into submucosa. Larger parts of the surface mucosa was eroded. The postoperative course was uneventful and intestinal passage was quickly established.
Conclusion: Although colonic lipomas seldom cause severe symptoms in patients and are easily removed by endoscope while they are small, severe symptoms like abdominal fullness, intestinal obstruction, intestinal bleeding and intussusceptions may appear as a lipoma grows larger. In some cases lipoma may clinically mimic colonic carcinoma.

PS-11-067

Prognostic impact of lymph node ratio outperforms positive lymph nodes and lymph nodes harvested: A time-dependent analysis in mismatch repair-proficient and -deficient colorectal cancers

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Objective: We compare the prognostic strength of the lymph node ratio (LNR), positive lymph nodes (+LNs) and collected lymph nodes (LNcoll) using a time-dependent analysis in colorectal cancer patients stratified by mismatch repair (MMR) status.
Method: 580 stage III-IV patients were included. Multivariable Cox regression analysis and time-dependent receiver operating characteristic (tROC) curve analysis were performed. The Area under the Curve (AUC) over time was compared for the three features. Results were validated on a second cohort of 105 stage III-IV patients.
Results: The AUC for the LNR was 0.71 and outperformed + LNs and LNcoll by 10–15 % in both MMR-proficient and –deficient cancers. LNR and + LNs were both significant ($p<0.0001$) in multivariable analysis but the effect was considerably stronger for the LNR [LNR: HR=5.18 (95 % CI: 3.5–7.6); +LNs=1.06 (95 % CI: 1.04–1.08)]. Similar results were obtained for patients with >12 LNcoll. An optimal cut-off score for LNR=0.231 was validated on the second cohort ($p<0.001$).
Conclusion: The LNR outperforms the + LNs and LNcoll even in patients with >12 LNcoll. Its clinical value is not confounded by MMR status. A cut-of score of 0.231 may best stratify patients into prognostic subgroups and could be a basis for the future prospective analysis of the LNR.

PS-11-068

Prognostic value of tumor-stroma ratio in rectal adenocarcinomas

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Objective: Recently, tumor-stroma ratio (TSR) has been identified as a strong predictor for survival in colorectal cancer. Despite an identical biology clinical implications are quite different for colon and rectal cancer regarding to anatomical differences.
Method: TSR was estimated on H&E stained histological sections of 154 patients who underwent resection for rectal adenocarcinoma between 1996 and 2006. None of these patients had received neoadjuvant chemo- or radiotherapy. The TSR was determined, by two independent investigators, in different layers of the rectal wall at the point of highest tumor infiltration and at the border of the tumor. TSRs were categorized into three categories: TSR-low, TSR-moderate and TSR-high.
Results: Patients with stage I and II disease (T1-4 N0) and TSR-high showed significantly better 5 year survival rates for overall survival compared to TSR-low and TSR-moderate ($p=0.010$) and a trend to a better disease specific survival ($p=0.067$) and disease free survival (0.057). In a multivariate Cox regression analysis the TSR remained an independent prognostic factor for overall survival, when adjusted for age, pT-status and grading.
Conclusion: TSR as a prognostic tumor characteristic can be used to identify patients with a good and a poor outcome in lymph node metastasis negative cases.

PS-11-069

A mixed neuroendocrine tumor loceted in appendix vermiformis: "Goblet cell carsinoid"

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Objective: Goblet cell carcinoid (GCC) of appendix vermiformis is a rare neoplasm that share histological features of both adenocarcinoma and carcinoid tumor. While its malignant potential remains unclear, GCC's particularly show transmural dissemination and are more aggressive than conventional carcinoids. Patients usually present with acute appendicitis. They usually lack the formation of a well-defined tumor mass; thus, it is somewhat difficult to accurately assess their size.
Method: Case Presentation: Fifty years old male patient applied to the emergency service with abdominal pain and laparatomy was performed with suspicion of acute appendicitis. Grossly, conjestion and exudation on the distal edge of appendectomy material were seen. A 1×1 cm lesion which was spreading into peripheral adipose tissue was seen on the cut surface. Microscopically, tumor was composed of goblet cell groups resembling “signet ring cells”. Tumor was infiltrated into muscularis propria and mesoappendix. Immunohistochemically, chromogranin, synaptophysin, cytokeratin 20, mCEA and p53 were stained positive. Ki67 (MIB 1) proliferation index was 18 %.
Conclusion: Adenocarcinoid of the appendix is a rare tumor, which is very difficult to diagnose preoperatively and even macroscopically, making histological examination essential. Immunohistochemical staining is required for definitive and differential diagnosis. Here, we present this rare case with literature reviewed.

PS-11-070

Normal colon tissue and colon carcinoma show no difference in heparanase promoter methylation

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Objective: Heparanase, the sole heparan sulfate degrading enzyme, has a role in cellular invasion. Accordingly, a large number of studies have demonstrated an association between heparanse expression and tumor stage and patients' prognosis. In colon carcinoma, heparanase shows increased expression in tumor compared to normal tissue and its expression correlates with the presence of metastasis. One of the regulatory mechanisms of heparanase expression is methylation on its promoter. In the present study we evaluated the role of heparanse promoter methylation in colon carcinoma.
Method: Analysis of heparanse promoter methylation was done on 32 samples of colon carcinoma as well as 30 sample of normal colonic mucosa. DNA was extracted from FFPE tissue and subjected to bisulfite conversion. The relative fraction of methylated and unmethylated DNA was evaluated with real-time PCR.
Results: The fraction of methylated DNA was 1 %±0.6 in the colon carcinoma group, and 2.4 %±0.6 in the normal colon group (P=0.11). Only one case in the normal group and one case in the tumor group showed more than 10 % methylation in the heparanase promoter.
Conclusion: We did not find any difference in heparanase promoter methylation between colon carcinoma and normal colonic mucosa, suggesting that heparanase overexpression in colon carcinoma is mediated by other mechanisms.

Monday, 10 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-12 Poster Session Haematopathology

PS-12-001
Neural cell adhesion molecule (CD56) expression in diffuse large B cell lymphomas
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Objective: Among B-cell non-Hodgkin's lymphomas, neural cell adhesion molecule/CD56 expression is exceptional. The aim of this study is to report unusual CD56 (neural cell adhesion molecule, NCAM) expression on diffuse large B cell lymphoma (DLBCL).
Method: The panel of antibodies included CD3, CD20, CD10, bcl-2, bcl-6, MUM-1 and CD56.
Results: A total of 50 cases of DLBCL were identified and one case was also detected positive for CD56. The subject was female, 48 years old. The patient had presented generalized lymphadenopathy. She had not documented involvement of extranodal sites. The case is alive with disease 1 year after diagnosis and chemotherapy treatment.
Conclusion: CD56 expression is an uncommon finding in B cell lymphomas. To date the literature reports a variable expression of CD56 in B cell lymphoma, ranging from 0.5 to 5.5 % of all B cell lymphomas. The presence of CD56 reported by the literature on certain DLBCL with extranodal presentation might be related to mechanisms involved in growth and expansion. Our case had not documented involvement of extranodal sites. The reason why CD56 expression is present in B cell lymphoma is not yet clear. Further studies are necessary to clarify the biological role of Cd56 in B cell lymphoma.

PS-12-002
Indolent onset of a T cell lymphoblastic lymphoma: Case report
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Objective: A case of mediastinal T-cell lymphoblastic lymphoma with indolent clinical course in a 52-year-old man was studied by immunohistology and molecular biology.
Method: Formalin-fixed sample. Histology with Ematoxilin&Eosin and Giemsa; immunohistochemistry by APAAP method. T-cell receptor gamma rearrangement by BIOMED2 protocols.
Results: After one fainting episode the patient was found to have pericarditis caused by a XX-cm-diameter mediastinal mass. The 2 first biopsies were unsuccessful and the third diagnostic one was done 6 months later. In this time-period the patient was well without symptoms and the mass stable. After two mediastinal biopsies with unspecific features (Castleman disease?), the diagnostic one showed fibrosis, abundant small reactive lymphocytes (CD20+/CD3+) and areas with diffuse small-medium size lymphocytes positive for CD3, TdT, CD34, CD7, LMO2 and high Ki67. T-cell receptor gamma genes were monoclonally rearranged.
Conclusion: Indolent T-LBL is exceedingly rare: for this reason in our case LMO2 was a key marker for the diagnosis which was delayed for the presence of fibrosis and reactive B cells.

PS-12-003
Granulocytic sarcoma of the spinal cord: Case report
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Objective: Granulocytic sarcoma (GS), also termed myeloid sarcoma or chloroma, is a rare malignant solid tumor

resulting from the extramedullary proliferation of myeloblasts or immature myeloid cells. GS most frequently occurs in patients with acute myeloid leukemia, myeloproliferative neoplasms or myelodysplasia. GS rarely presents in the absence of systemic myeloid disease. GS most commonly occurs in the soft tissues of the head and neck, bone, skin and less often in the central nervous system and spinal cord.

Results: A 40 year old woman presented with 1 month history of weakness of both legs. MRI of the thoracal spine showed 4 cm diameter epidural mass compressing the dural sac in the spinal canal at the T9-10 levels. Decompressive laminectomy and tumor removal were performed resulting in neurological improvement. Histologically neoplastic cells have round nuclei with finely dispersed chromatin and scant cytoplasm proliferating in a diffuse pattern. Immunohistochemically, tumor cells were positive for MPO, CD117, CD45, CD99. Diagnosis was GS without bone marrow involvement.

Conclusion: We report the case of GS due to unusual localization and nonleukemic presentation.

PS-12-004

Hairy cell leukemia: Retrospective study of 6 cases

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Objective: Hairy cell leukemia (HCL) is a rare indolent B cell non Hodgkin's lymphoma with a characteristic presentation of pancytopenia, splenomegaly, and immunophenotype circulating hairy cells.

Method: Retrospective study about 6 cases of HCL diagnosed between 1993 and 2007 at the Hematology Department, Farhat Hached Hospital.

Results: There were 5 males and 1 female with a median age of 40 years (22–79 years). Physical examination shows splenomegaly in all cases and hepatomegaly in 2 cases, hematological parameters shows lymphocytosis with peripheral hairy cells in all cases. Flow cytometric immunophenotyping was done in 2 cases, and confirmed the diagnosis of HCL with CD11c, CD25+, CD103+, CD123 +, and CD5-, CD10-, and CD23-. Bone marrow biopsy was done in all cases, showing massive infiltration with villous cytoplasmic projection cells that were CD20 positive. The treatment consists of blood transfusion in all cases, associated with splenectomy in 3 cases, only 1 patient was treated with (2 CDA: cladribine) with a complete remission after a follow up of 24 months.

Conclusion: HCL has consistent cytologic histologic and immunologic features that make classification reliable and reproducible; it remains problematic because of the variety of the disorders and the differential diagnosis of splenic lymphoma of the marginal zone.

PS-12-005

Primary cerebral lymphoma: A retrospective study of 5 immunocompetents

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Objective: Primary CNS lymphomas (PCNSL) are uncommon tumors in immunocompetent patients, they represent up to 1 % of non Hodgkin lymphomas (NHL) and 3–5 % of all brain tumors. The majority of PCNSL are diffuse large B cell lymphomas, 2–5 % are T cell lymphomas, in rare instances low grade B cell lymphomas. We determine clinical characteristics, histological findings and treatment outcome of PCNSL.

Method: Five cases of PCNSL occurring between 1993 and 2007 were retrospectively reviewed.

Results: They were 4 males, 1 female, median age 50 years, range (23–74). Most common symptom was neurological deficits (4cases). MRI of the brain revealed an expansive tumor affecting the parietal bone in 3 cases, the temporal bone in 1 cases and the frontal bone in 1 case. Immunohistological finding showed large B- cell NHL in 2 cases, anaplastic lymphoma in 2 cases, and large- cell immunoblastic lymphoma in 1 case. Treatment consists on exclusive tumoral resection in 3 cases, surgery and chemotherapy (1 case), complicated by death in all these cases. Surgery followed by high dose chemotherapy and radiotherapy (1 case) with complete remission after a follow-up of 7 years.

Conclusion: Chemotherapy followed by involved field irradiation appears to be an adapted therapy.

PS-12-006

Primary cutaneous lymphoma: A retrospective study

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Objective: Primary cutaneous non-Hodgkin's lymphoma (PCNHL) is defined as lymphoma limited to skin without extra-cutaneous involvement at presentation. We describe here epidemiological and histo-pathological aspects of PCNHL.

Method: Retrospective review of clinical data of PCNHL patients diagnosed in Hematology Department, Frahet Hached Hospital, Sousse (1993–2012).
Results: Fourty three patients with PCNHL, median age: 48 years (11–84), sex-ratio was 2.3. The site of cutaneous involvement was upper lumb in 4 cases, lower lumb in 7 cases and disseminated in 23 cases. PCNHL was small T cell lymphoma in 13 cases, large B cell lymphoma in 16 cases, anaplastic, CD4+ CD56+ hematodermic neoplasm, and follicular type in 1 case respectively. According to TNM classification 21 cases were T3bNxMx, 12 cases were T1N0M0. After first line therapy, 26 patients in CR, PR was obtained in 1 case and failure in 6 cases, 10 patients relapsed within 1 to 72 months (median 6 months), all of them were disseminated cases.
Conclusion: Our study indicate that the extend of cutaneous involvement at the time of diagnosis is a significant prognostic factor in PCNHL.

PS-12-007
Follicular lymphoma: Multicentric retrospective study
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Objective: Follicular lymphomas (FLs) account for one third of non Hodgkin lymphomas (NHLs) in adults. The disease is characterized by a response to initial treatment, followed by relapses, sometimes associated with histologic transformation into high grade NHL. Analyze epidemiological characteristics of patients with FL.
Method: Retrospective study of 22 of adult FLs diagnosed in Hematology Department (2000–2011).
Results: Median age was 59 years (29–77), sex-ratio: 1.7 The most frequent clinical symptom at diagnosis was lymphadenopathy in 13 cases. Involvement of the spleen in 3 cases. B symptoms were present in 10 cases. Performance status was more than 1 in 4 cases. According to the international prognostic index (FLIPI), 7 patients have low index, 5 have intermediate index, and 10 have high index. Grade 2 FL was seen in the majority of cases. Treatment modalities varied over time and according to the disponibility of drugs especially to anti CD20 monoclonal antibody. CR was obtained in 13 cases, PR in 6 cases; 3patients relapsed within 8–48 months. Histologic transformation was seen in 3 cases, we have noted 10 deaths related to the disease in 7 cases.
Conclusion: Treatment results in FL might not only be improved by more effective induction regimens but also by maintenance treatment.

PS-12-008
Primary mediastinal large B-cell lymphoma: A single center study of clinicopathologic characteristics
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Objective: Primary mediastinal large B – cell lymphoma (PMLBCL) is a subset of LBCL with unique clinicopathologic features. Objective: Study clinical, biological, histogenesis and phenotype of patients with PMLBCL.
Method: Retrospective clinicopathologic analysis of 10 patients with PMLBCL from a single center from 2001 to 2009.
Results: Six were women and 4 were men, aged from, aged from 17 to 73; 3 were at stage I-II, 3 at stage III, and 4 at stage IV, all patients had bulk disease with superior vena cava syndrome,8 had contiguous infiltration, 7 had lactate dehydrogenase elevation, Bsymptoms were present in all cases Microscopic examination shows infiltration of medium-large cells surrounded by collagen fibrosis, neoplastic cells express B-cell markers, CD30+ in 1 case, CD3 negative in all cases Five patients received chemotherapy plus Rituximab and radiotherapy in 2 cases with complete remission in 4 cases, 5 patients received chemotherapy only with relapse in 3 cases.
Conclusion: The relative rarity of this type of lymphoma necessitates clinical trials in order to define the better treatment.

PS-12-009
A potantial diagnostic pitfall: Frequent CD99 and FLI-1 coexpressions in diffuse large B cell lymphoma
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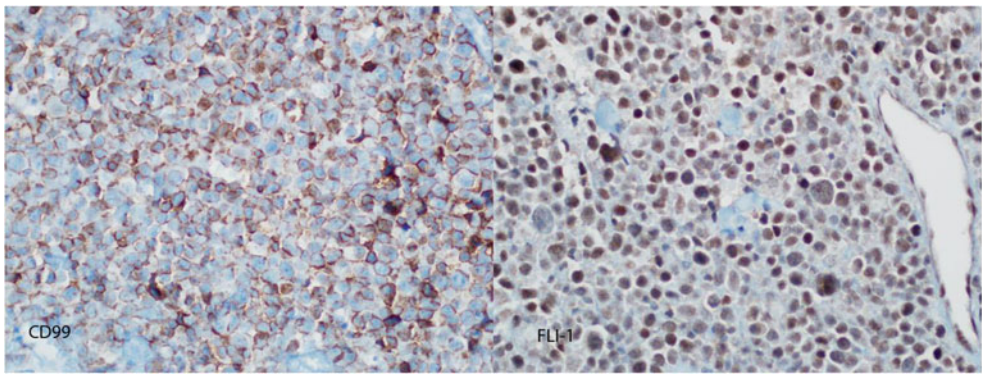
Objective: CD99 and FLI-1 are widely used for their diagnostic utility in Ewing sarcoma/peripheral neuroectodermal tumor (ES/PNET). CD99 expression has been documented in a variety of tumors, including lymphoid malignancies of T cell origin. Also FLI-1 expression is common in different tumor types. However, few studies have investigated the CD99 and FLI-1 immunoreactivity in diffuse large B-cell lymphoma (DLBCL). We aimed to determine the frequencies of CD99 and FLI-1 immunohistochemical expressions in DLBCL which may lead to a misdiagnosis.
Method: CD99 and FLI-1 expressions are retrospectively investigated by immunoperoxidase staining in prechemoterapy primary tumors of 42 DLBCL cases.

Results: Out of 42 cases, CD99 and FLI-1 expressions were observed in 14 (33.3 %) and 7 (16.7 %) tumors, respectively. Concomittant expressions of CD99 and FLI-1 proteins were found in 5/42 (11.9 %) cases.

Conclusion: The present study revealed that CD99 and FLI-1 are frequently expressed in DLBCL, thus DLBCL should be considered in the differential diagnosis of CD99+ and FLI-1+ neoplasms.



PS-12-010

Primary cutaneous marginal zone lymphoma with biclonality

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Objective: Primary cutaneous marginal zone lymphoma (PCMZL) represents a B-cell lymphoma which presents with papules, plaques or nodes. The presence of a monotypical light chain B cell population supports the diagnosis of PCMZL. We describe a case of PCMZL which showed different light chain restriction in two heterochronous lesions.
Method: A 50 year-old male patient presented in 2004 with a cutaneous nodule in the anterior surface of the tibia, which was totally excised. The patient did not show other lesions since 2011, when a new cutaneous nodule located in the right ankle, was appeared. Immunohistochemical analysis was performed in both biopsies.
Results: Histological and immunohistochemical findings of both biopsies were consistent with marginal zone lymphoma of the skin with lambda light chain restriction in the biopsy of the first lesion and kappa light chain restriction in the biopsy of the second lesion. Blood laboratory studies, chest and abdominal computerized tomography scans revealed no evidence of systemic involvement by lymphoma.
Conclusion: The finding of both kappa and lamda light chain restricted B cell populations in PCMZL is unusual. The monoclonal light chain switching in PCMZL is rare and its pathogenesis is discussed.

PS-12-011

Microvascular density assessed using CD34 immunostaining does not have prognostic significance in mantle cell lymphoma: Retrospective clinicopathological analysis of 177 patients of the Czech Lymphoma Study Group

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Objective: Microvessel density (MVD) has prognostic significance in some malignancies. Little information exists about angiogenesis in mantle cell lymphoma (MCL), although antiangiogenic drugs are used experimentally. Prognostic factors of MCL are needed as outcome and therapy are heterogeneous and often unsatisfactory. The aim is to assess MVD in MCL and to evaluate its prognostic significance.
Method: 177 MCL specimens (FFPE) were examined by immunohistochemistry with anti-CD34 antibody. MVD was quantified using systematic uniform random sampling and unbiased counting frames. Clinical data were analyzed in Kaplan-Meier survival curves and log-rank test.
Results: Median survival (MS) of all patients was 46 months, median progression-free survival (MPFS) 22 months. Mean MVD was 172,7 microvessels/mm2, median 158,2/mm2. Dividing cases into quartiles: <117,4/mm2, <158,2/mm2, <206,6/mm2 and ≥206,6/mm2 (43, 44, 45, 45 cases), MS and MPFS did not differ statistically significantly between these groups (P=0,307; similar for therapy groups). Visible differences are only between the fourth quartile and the rest:

MS of the first three quartiles (132 cases): 56 months, of the fourth quartile (45 cases): 30 months (P=0,084); MPFS: 22 versus 18 months (P=0,069).
Conclusion: MVD assessed using CD34 immunostaining does not have prognostic significance in a large series of MCL with a long follow-up.

PS-12-012

Clinico-pathological study of 5 cases of Plasmablastic Lymphoma in HIV positive and negative patients

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Objective: Plasmablastic lymphoma (PBL) is a rare aggressive subtype of diffuse large-B-cell lymphoma which occurs primarily in the oral cavity of HIV-positive patients. It is extremely rare in immunocompetent patients.
Method: A total of 5 cases of PB were retrospectively analyzed. All cases had tissue available for immunohistochemistry and in situ hybridization.
Results: The age range of the 5 patients was 35–81 years (median 68) and all were men. Three patients were HIV negative. HIV + patients: tumors involved the oral cavity (n=1), and small intestine (n=1). HIV- patients: tumors were located in bone marrow (n=1) and lymph nodes (n=2). All tumors were composed of monomorphic plasmablastic cells. Tumors were negative for CD45 and CD20, while they showed diffuse positivity for CD138, CD38, MUM1 and EMA. By ISH, monoclonal light chain restriction was detected. EBV (EBER) was positive in all cases. The median overall survival was 21,4 months regardless of the intensity of chemotherapy. Only one patient is alive 1 month after diagnosis.
Conclusion: PBL may appear in non immunocompromised patients and other locations than oral cavity. Any patient diagnosed with PBL should be tested for HIV. Patients who had HIV-negative PBL have lower rates of oral involvement.

PS-12-013

Spinal granulocytic sarcoma preceding clinical manifestation of acute myeloid leukemia

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Objective: Granulocytic sarcoma is a rare malignant neoplasm of primitive myeloid cell origin, most commonly found in association with acute myeloid leukemia. Granulocytic sarcomas generally occur in the soft tissues, bone, and skin.
Method: We report a case of a 55-year old man with spinal granulocytic sarcoma manifesting as rapidly progressive paraplegia preceding clinical manifestation of acute myeloid leukemia.
Results: Magnetic resonance imaging revealed a tumor in lumbal spine (L1-L3). Baseline laboratory data were normal. He underwent emergent laminectomy and the tumor was totaly resected. Histological examination of lesion demonstrated diffuse proliferation of large atypical cells with round nuclei with delicate chromatin and one or more prominent nucleoli. Immunohistochemical studies revealed positive staining for LCA, CD33, CD43, CD163, Lysozyme and CD15 while myeloperoxidase, lymphoid, neuroendocrine markers, S-100 and CD99 were negative. The final histological diagnosis was granulocitic (monoblastic) sarcoma. No chromosomal aberrations were detected by FISH. A month later, acute myelomonocytic leukemia was diagnosed upon a peripheral blood and bone marrow examination showing an increased number of abnormal monoblasts. Chemotherapy, with multiple regimens for leukemia in combination, did not affect the tumor and the patient died.
Conclusion: Granulocytic sarcoma should be considered in the differential diagnosis of spinal tumors.

PS-12-014

Survivin expression in patients with newly diagnosed nodal diffuse large B-cell lymphoma treated with immunochemotherapy

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Objective: Survivin, a member of the inhibitor of apoptosis family might play an important role in the pathogenesis of diffuse large B cell lymphoma (DLBCL). We investigate clinical and prognostic significance of survivin expression in nodal DLBCL.
Method: Biopsy specimens obtained from 56 patients with newly diagnosed nodal DLBCL treated with immunochemotherapy (R-CHOP) were immunostained for survivin.
Results: Survivin immunoexpression (>45 % positive tumor cells) has been found in 22 (39.28 %) patients. Significant difference in immunoexpression was noticed between GCB and non-GCB subtype of DLBCL (p=0.031). There was no significant association with IPI, „bulky“disease, Ki-67 immunoexpression or other clinico-pathological parameters. Univariate analysis showed that survivin expression was unfavorable factor for therapy response and shorter survival in patients with DLBCL (p=0.048 and p=0.034, respectively). Patients with survivin overexpression experienced relapse more often that the patients without expression of this apoptotic protein (27.3 % vs. 11.8 %), but this difference did not reach statistical significance (p=0.131).

Conclusion: The results of this study showed that disregulation of survivin expression had the important role in determination of course of disease in pateints with nodal DLBCL treated with R-CHOP. Therefore, survivin represent potential therapeutic target in DLBCL.

PS-12-015

Langerhans cell histiocytosis of the jaws: A report of ten cases with an analysis of the mechanism of eosinophilic infiltration

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Objective: Langerhans cell histiocytosis (LCH) frequently presents eosinophilic infiltration. Here we report ten cases of LCH that involved the jaws and our investigation of the mechanism underlying eosinophilic infiltration in LCH.
Method: We evaluated the CCL-11/eotaxin-1 expression of LCH cells via immunohistochemical staining. Toluidine blue staining was used to inspect the densities of mast cells, with ten periapical granuloma specimens serving as a control group.
Results: Every patient was classified as having single-system LCH, even though acute lymphoblastic leukemia occurred in one patient during LCH treatment. The ratio of mandible to maxilla LCH was 5:1. The jaw lesions were the earliest manifestation in seven patients with multifocal LCH. Toluidine blue staining revealed that the number of mast cells in LCH lesions was not significantly higher than in periapical granulomas. However, upon immunohistochemical examination, most of the patients showed diffuse positivity for eotaxin-1 in LCH cells, while few eosinophils/T cells were immunoreactive.
Conclusion: We surmise that the eotaxin-1 expression of LCH cells may be relevant to eosinophilic infiltration in LCH. Further studies of the eotaxin-1 functions including its influence on the immature state of LCH cells may be needed to understand the pathogenesis of LCH as well as the role of tissue eosinophilia in LCH.

PS-12-016

Sclerosing Angiomatoid Nodular Transformation (SANT) of the spleen: The unusual entity

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Objective: Sclerosing angiomatoid nodular transformation (SANT) is an unusual and rare nonneoplastic vascular lesion of the spleen well characterized by Martel et al. in 2004.
Method: We report a case of SANT in 53 years-old man presented with abdominal discomfort and pain in a left lumbal region. Abdominal computed tomography scan revealed a massive haematoma extended from spleen to the enlarged left kidney and left retroperitoneal space. The patient also had a spontaneous rupture of right kidney 2 years ago.
Results: Macroscopically, the cut surface of spleen showed multiple well circumscribed red brown nodules. Microscopically, SANT consists of multiple well-circumscribed angiomatoid nodules showing plump endothelial cells and extravasated erythrocytes. Nodular formations are surrounded by a variable lymphoplasmacytic infiltrate, spindle cells and collagenous stroma. Immunohistochemical staining displayed endothelial phenotype that resembled splenic capillaries (CD34+/CD31+/CD8−). Expression of CD68 was also present.
Conclusion: The differential diagnosis of SANT includes splenic hamartoma, inflammatory myofibroblastic tumor, littoral cell angioma and hemangioendothelioma. It has been postulated that SANT represents a peculiar hamartomatous transformation of splenic red pulp in response to an exaggerated nonneoplastic stromal proliferation. SANT has a benign clinical course and splenectomy has been supposed as curative.

PS-12-017

Collision tumor of menningioma and non Hodgin malignant lymphoma of cerebellum

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Primary central nervous system lymphoma (PCNSL) constitutes a rare group of extranodal non-Hodgkin's lymphomas (NHLs), primarily of B cell origin, whose incidence has markedly increased in the last three decades. Immunodeficiency is the main risk factor, but the large majority of patients are immunocompetent. This report presents the case of a 71-year-old woman with a collision tumor of primary malignant lymphoma and meningioma in the cerebellum. Collision tumor of primary malignant lymphoma and meningioma have not been described in the literature. The morphological aspect is interesting with regard to the problem of collision tumors.

PS-12-018

Prognostic significance of immunohistochemical expression of the angiogenic molecules VEGF-A, VEGFR-1 and VEGFR-2 in patients with Classical Hodgkin Lymphoma

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Objective: Classical Hodgkin Lymphoma (cHL) is characterized by the presence of a small percentage of

malignant Hodgkin and Reed-Sternberg (HRS) cells amongst a reactive background. The role of angiogenesis in cHL is still unclear. The aim of the study was to evaluate the expression of VEGF-A, VEGFR-1 and VEGFR-2 and their correlation with clinicopathological parameters and prognosis.

Method: The immunohistochemical expression of VEGF-A (VG1, Dako), VEGFR-1 (RB-9049, Neomarkers) and VEGFR-2 (sc-6251, Santa Cruz) was studied in a large cohort of 199 patients with cHL and the results were correlated with clinical characteristics and patient outcome.

Results: The neoplastic HRS cells expressed VEGF-A, VEGFR-1 and VEGFR-2 in 90.3 %, 97.2 % and 94.1 % of the cases respectively and their expression levels were intercorrelated. Expression of VEGFR-1 and VEGFR-2 was significantly and positively correlated with early disease stage, absence of B-symptoms, WBC <15.000, Alb ≥4, IPS ≤2. VEGFR-2 was additionally positively correlated with male gender and ESR <50. All three molecules were statistically correlated with ramifications of blood vessels but not with microvessel density.

Conclusion: Based on our results, we could speculate that, in contrast to solid tumours, the process of angiogenesis is probably an early event in neoplastic progression in the context of Hodgkin's Lymphoma.

PS-12-019

P53 upregulation is associated with proliferation and is not capable of inducing apoptosis in Hodgkin's lymphoma

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Objective: P53 is a tumor suppressor protein described as the "guardian of the genome". In a normal cell, p53 is inactivated by its negative regulator, Mdm2. Once activated, p53 induces cell cycle arrest and apoptosis by activating various cell cycle related genes, like WAF1/CIP1 encoding for p21. Although mutations that deactivate p53 are the most common genetic alteration found in cancer, they are rare in the context of Hodgkin's lymphoma (HL).

Method: P53 immunohistochemical expression was investigated in a subset of 81 cases of primary HL. The study of the p53-downstream protein p21 was used as an indirect way of analyzing its functional status. P53 expression was correlated with proliferation, apoptosis, clinicopathological data and prognosis of the patients.

Results: P53 showed a median value of 32.4 %, suggesting an upregulation of the p53 gene in HL, and a significant correlation with p21 (p=0.043) and the proliferation marker MIB1 expression (p=0.038).

Conclusion: Although p53 overexpression is a frequent finding in HL and there is indication of its functionality, this upregulation does not lead to apoptosis. It can be speculated that this is possibly due to Mdm2-p53 interactions.

PS-12-020

Simultaneous gastric adenocarcinoma and B cell lymphoma of the stomach

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Objective: The simultaneous association of gastric carcinoma with gastric lymphoma is a rare event.

Method: We describe a 52 years old man, who had been diagnosed as marginal zone lymphoma in a cervical lymph node biopsy 3 years previously.No endoscopic examination was evaluated then. There was no pathological appearance in the gastrointestinal system by CT scanning and patient was considered nodal marginal zone lymphoma. Patient had taken 8 cycles of chemotherapy which consisted of rituximab, cyclophosphamide, vincristine, and prednisolone.2,5 years after completion of chemotherapy, a gastric wall thickening compatible with gastric lymphoma or linitis plastica was detected on CT and gastroscopic examination was indicated. Endoscopic examination revealed an erosive, fragile, hemorrhagic, malignant-looking lesion with a diameter of 4.5 cm in the cardia. Besides, rugae of fundus and corpus were severely rough and hyperemic suggesting a diffuse malignant infiltration. Multiple biopsies were taken from cardia, fundus and corpus of the stomach.

Results: Cardiac samples showed pancytokeratin positive signet ring cells which contain neutral and acidic mucine in microscopic examination. Samples of corpus and fundus did not show similar carcinoma cells, instead, there was diffuse infiltration of atipical lymphocytic infiltration consistent with marginal cell lymphoma both morphologically and immunophenotypically.

Conclusion: Co-occurrence of carcinoma and marginal zone lymphome is a rare event and dramatically exacerbates prognosis of a patient with such an indolent lymphoma.

PS-12-021

Assessment of demographic data, staging and experesion of CD20, CD30, CD15, Bcl-2 in Reed-Sternberg cells of Hodgkin lymphoma cases in their first admission in Urmia Imam Komini Hospital

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Objective: Immunohistochemistry plays an important role in diagnosis of Hodgkin lymphoma. Beyond diagnostic importance of Immunohistochemistry, so far many studies

have investigated the correlation between cellular markers and the prognosis of patients with Hodgkin lymphoma. Amongst other markers, CD20 is one of the most studied marker with a lot of controversy around it.
Method: Retrospectively 66 eligible patients entered the study. Clinical and laboratory Data and Immunohistochemistry findings analyzed for possible correlation between disease stage and other parameters.
Results: In our study 63.6 %, 90.9 % of cases respectively expressed cellular markers CD15 and CD30 while only 18.2 % of cases expressed CD20. Furthermore statistical analysis revealed that CD15 was inversely correlated with disease staging. (P=0.027). In contrast we didn't find any relation between CD20 or CD30 positivity with disease staging. (P=0.482, P=0.376). However in our study expression of CD20 was not related to stage or other parameters of poor prognosis which proposes that in our patients this marker possibly was not related to disease prognosis.
Conclusion: Therefore we suggest that cellular marker CD20 is not beneficial beyond IPS factors and its usage should be confined to diagnostic purposes.

PS-12-022

Primary naturall killer cell lymphoblastic leukemia/ lymphoma of central nervous system

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Objective: A 25-year old woman with a 2-year history of a multifocal lesion occupying the cerebellum who periodically received cortisol and etoposide as it was considered tumor-forming multiple sclerosis.
Method: Two years after initial clinical diagnosis a stereotactic biopsy was performed. Immunohistochemistry and in situ hybridization were performed on the tissue sample.
Results: The perivascular (Virchow-Robin) space of microvessels was occupied by middle sized lymphocytes with blastic chromatin and scant cytoplasm. The neoplastic cells were negative for: 1. B-cell markers: CD19, CD22, CD20, CD79a, Pax-5, 2. Myelogenous differentiation antigens: MPO, CD13, CD33, 3. Plasmacytoid dendritic differentiation antigens: CD123, TCL1, 4. Blastic cells markers: CD34, CD117 5. T-cell markers: CD3, CD5 with restricted expression of CD2 and CD7 in a few cells, 6. Cytotoxic enzymes TIA-1, Granzyme-B and perforin. All cells expressed intensely CD56 and TdT and some of them CD16. In situ hybridization for EBV virus (EBERS) was negative. PCR analysis: T-cell receptor and immunoglobulin genes were in germ line. Bone marrow was negative.
Conclusion: The diagnosis of Natural Killer Lymphoblastic Leukemia/Lymphoma, leukemia of ambiguous lineage was established according to the WHO/2008 classification of lymphomas. To our knowledge this is the first case of primary CNS NK lymphoblastic lymphoma in the literature.

PS-12-023

Combined immunological, morphological and cytochemical research of cells with the usage of microarrays

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Objective: Tumor cells immunophenotyping with the usage of flow cytofluorimetry, immunoenzymometric and immunofluorescence methods is quite expensive. The new method of cell surface antigens detection with the usage of immunological microarrays was proposed.
Method: The microarray represents a solid substrate, on which the specified antibodies are immobilized in the particular places ("stains"). During the analysis the microarray is incubated with the cell suspension. The cells which possess determined cell surface antigens, specifically communicate within stains. Different cell surface antigens on various cells can be indentified through one microarray. Microarrays are manufactured on transparent and chemically-proof substrates and it allows to carry out the coloring of communicated cells for research with the help of light microscopy. The whole procedure can be performed on cells from the blood, bone marrow during 1–2 h.
Results: With the help of microarrays we conducted researches dedicated to the study of various types of normal blood cells, cells of acute and chronic leukemia, non-Hodgkin's lymphoma. The big spectrum of cell surface antigens and the histological types of cells which possess each type of defined antigens were simultaneously determined.
Conclusion: The techniques of the combined research of cells proposed by us make microarrays convenient method for solving diagnostic and research problems.

PS-12-024

Epidemiology, morphology of nodal/exstranodal lymphomas in the Ural region of Russia

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Objective: Lymphomas constitute 33,65 cases on 100 000 inhabitants annually, its frequency grows.
Method: This work presents epidemiological, morphological analysis of nodal/exstranodal lymphomas. Analysis of data from Izhevsk cancer center during 2009–2011 was carried out.
Results: Lymphoma appeared in 2.94 % among first diagnosed malignant tumors. The panel of monoclonal antibodies was used for tumor immunophenotype identification. Nodal lymphomas presented 183 cases: 55 - Hodgkin lymphoma (HL), 128 – non-Hodgkin lymphoma (NHL). Exstranodal

lymphomas presented 111 cases, various variants of NHL were more frequent. Small lymphocyte lymphoma - 37, diffuse large B-cell lymphoma (DLBCL) - 36, follicle center lymphoma - 18, mantle cell lymphoma – 8 were frequent among nodal lymphomas. T-cellular NHL presented 16 cases (6 - peripheral T-cell lymphoma, 7 - angioimmunoblastic T-cell lymphoma). Among other organs of lymphatic system lymphomas appeared in tonsils (19), thymus (15) and spleen (9). Exstranodal NHL were registered in stomach (25), rarely in other organs - testis (7), central nervous system (3), nose (3), breast (3). As rule DLBCL was more frequent (36).
Conclusion: Results coincide with data on lymphoma's frequency and morphological characteristic in other regions.

PS-12-025
In situ mantle cell lymphoma in nasopharynx
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Objective: The nasopharynx normally contains abundant lymphoid tissue and it can be the site of both lymphoid hyperplasia and lymphomas. We present the first case of the recently described in situ mantle cell lymphoma (MCL) in nasopharynx.
Method: A 70 year-old woman presented with nasal obstruction in 2008. A mass located in nasopharynx was found. Biopsy was sent for histological examination. A new biopsy was taken 3 years later. Histological, immunohistochemical and FISH studies were performed.
Results: Histological examination of both biopsies revealed lymphoid hyperplasia, characterized by CD5 and cyclinD1 positive cells of mantle zones, findings consistent with in situ MCL. The diagnosis of in situ MCL confirmed by FISH analysis for t(11;14). The patient examined thoroughly and has remained free of an overt lymphoma to the present day.
Conclusion: Pathologists and otorhinolaryngologists should be aware that in situ MCL may be observed in nasopharynx. It may be appropriate to perform cyclinD1 immunostain, even in cases with clinical and histological findings compatible with lymphoid hyperpasia. The patients should be examined thoroughly, since in situ MCL may accompanied by an overt lymphoma in other sites or it may be a precursor of an overt MCL.

PS-12-027
Multisystem Langerhans' cell histiocytosis coexisting with metastasizing adenocarcinoma of the lung
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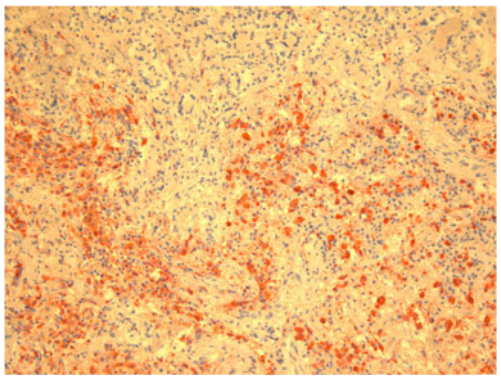
Objective: Langerhans' cell histiocytosis (LCH) is an uncommon disease of unknown etiology characterized by uncontrolled proliferation and infiltration of various organs by Langerhans' cells. To our knowledge, this is the first case reporting an association of multisystem LCH with metastasizing adenocarcinoma of the lung.
Method: We present the case of a 54-year-old man, heavy smoker, with dispnea, cough, hemoptyses, headache and ataxia, who died shortly after admission to our hospital. On the autopsy, we found tumor in the posterior segment of the right upper pulmonary lobe as well as a right-sided occipito-parietal lesion which penetrated into the right ventricle resulting in internal and external hematocephalus. Histologically and immunohistohemically, the diagnosis of primary lung adenocarcinoma with brain metastasis was made (tumor cells showed positivity for CK 7 and TTF-1 which confirmed the diagnosis). Light microscopic examination of the other organs showed LCH involving the pituitary gland, hypothalamus, spleen, mediastinal lymph nodes, and lungs. Immunohistochemical studies revealed CD68, S-100 and CD1a immunoreactivity within the Langerhans' cells.
Conclusion: Multisystem form of LCH with extensive organ involvement was an incidental finding, while the metastatic lung adenocarcinoma to the brain, that led to hematocephalus, was the cause of death.



PS-12-028
Langerhans cell histiocytosis associated with extramedullary hematopoiesis in a 65-year-old male patient
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Objective: Langerhans cell histiocytosis is a rare disease histologically characterized by the proliferation of Langerhans cells.
Method: A 65-year-old male came to our attention presenting with erythematous-squamous lesions all over the body, axillary and inguinal adenopathies and hepatosplenomegaly. We have taken a cutaneous and an axillary lymph node biopsy.
Results: Microscopic examination of the cutaneous fragment revealed the presence of a dermal infiltrate of large cells with an eosinophilic cytoplasm and vesicular, nucleolated nuclei

with an irregular nuclear margin, raising suspicion of a cutaneous lymphoma. Immunohistochemical stains for CD45, CD20, CD79a, CD3, CD5, CD15, CD30, and Bcl-2 were negative, and the previous diagnosis was not confirmed. The microscopic examination of the axillary lymph nodes showed foci of extramedullary hematopoiesis, raising suspicion of a lymphoproliferative process, but the immunohistochemical stains and the paraclinical data didn't confirm it. Based on the intense positive reaction for CD68, S100 and Ki-67 showed by the tumoral cells from the prelevated tissues, correlated with the clinical and paraclinical findings, a diagnosis of Langerhans cell histiocytosis was established.

Conclusion: The particularity of our case consists in the presence of extramedullary hematopoiesis in the lymph nodes of a patient diagnosed with Langerhans cell histiocytosis.

PS-12-030

Unusual primary cutaneous presentation of B-cell chronic lymphocytic leukaemia

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Objective: B-cell small lymphocytic lymphoma/chronic lymphocytic leukaemia (B-CLL) is a low-grade lymphoproliferative disorder and cutaneous lesions are rarely the presenting findings.

Method: We report the case of a 62-year-old woman who presented in winter with erythematous plaque on her nose, of 3 months duration. Laboratory data showed elevated white blood cell count (40.000/mm3) with small mature lymphocytes predominance (60 %).

Results: Histopathologic examination of the skin lesion reveals infiltration of the reticular dermis and subcutis, consisting mostly of small lymphoid cells, without epidermotropism. Immunohistochemical examination revealed positivity for CD20, CD79a and CD5 in the neoplastic cells. According to the laboratory and histopathologic findings the diagnosis was consistent with B-CLL with a primary cutaneous presentation. A staging bone marrow aspiration and biopsy showed 80 % infiltration by a clonal B-cell proliferation with typical CLL immunophenotyping. CT-imaging was normal, so stage I according to Binnet classification was confirmed. The patient received 6 cycles of chemotherapy and remained in remission for 1 year, when the skin lesion recurred in winter, at the same location.

Conclusion: In conclusion we report an extremely rare case of subclinical B-CLL with cutaneous presentation. It is important to maintain a high index of suspicion for a lymphoproliferative process in skin lesions with atypical lymphocytic infiltration.

PS-12-031

Myeloid sarcoma mimicking nasal polyp

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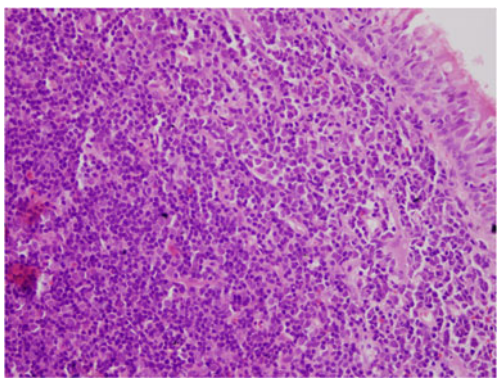
Objective: A myeloid sarcoma is a tumour mass consisting of myeloid blasts with or without maturation occuring at an anatomical site other than the bone marrow. Every site of the body can be involved, skin, lymph node, gastrointestinal tract, bone, soft tissue and testis. %10 cases presents at multiple anatomical sites.

Method: The current case is 75 year old woman presenting with nasal polyp and underwent polypectomy. The polyp was 2,5 cm in diameter and had a bloody appearance. By microscopic examination there was a diffuse infiltration of neoplastic cells under the cilliated epithelium. The mitotic index was high in neoplastic lymhoid cells. Immunohistochemical study was helpful for the differential diagnosis.

Results: The immunohistochemical panel was LCA(+), Myeloperoksidase (+), CD117(+), CD34 (−), CD20 (−), CD3 (−), CD2 (−), S100 protein (−), CD56 (−), CD99 (−), CD79a (−), CD138 (−), CD30 (−), ALK (−), Desmin (−), Pancytokeratin (−), Pax5 (−), Synaptophysin (−), Myogenin (−), CD5(−). The bone marrow aspiration showed a ratio of %20 myeloblasts.

Conclusion: We report a rare case of myeloid sarcoma presenting with nasal cavity involvement. The differential diagnosis include lymphoblastic lymphoma, Burkitt lymphoma, diffuse large B-cell lymphoma, small round cell tumors.



PS-12-032

Ear, nose and throat lymphomas in Central Tunisia: Epidemiological and anatomoclinical study of 34 cases

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Objective: The aim of this study was to describe the epidemiology and anatomo-clinical features of the ear, nose and throat (ENT) lymphomas in the Centre of Tunisia.
Method: All ENT lymphoma cases diagnosed in the Pathology Department, Farhet Hached Hospital, Sousse during a 15-year period were analyzed.
Results: A total of 34 cases of ENT lymphoma were reported (21 males, 13 females) with a sex-ratio of 1.4. The age at diagnosis varied from 9 to 85 years with a median age of 56.5 years. The majority of ENT lymphoma cases (81 %) were of B cell type including large B-cell lymphoma (58 %) and small-cell B lymphoma (23 %). Nasopharynx and tonsils were the most involved areas with 44 % and 42 % of cases, respectively. According to the Ann Arbor staging system, these lymphomas are diagnosed in the stage II (42 %) followed by stage I (30 %).
Conclusion: The most frequent lymphoma developed in ENT region was B cell lymphoma, especially located in nasopharynx and Tonsils.

PS-12-033

Paediatric lymphomas in Central Tunisia: Epidemiological and anatomoclinical study of 44 cases

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Objective: Lymphomas are the most second tumour in children worldwide. In Tunisia, lymphomas are ranked second after leukaemias (25.7 %). The aim of this research was to describe the epidemiology and anatomo-clinical features of childhood lymphomas in the Centre of Tunisia.
Method: All paediatric lymphomas diagnosed in the Pathology Department, Farhet Hached Hospital, Sousse during 15-year period were analyzed.
Results: A total of 44 cases were reported (26 males, 18 females) with a sex-ratio of 1.4. The median age was 10 years (range: 3–15 years). Lymph node lymphomas were the most frequent accounting for 63.6 %, followed by ENT, mediastinum, and haematopoietic system (6.8 % each one); cutaneous and digestive location were less frequent (4.5 % each one). Among the 44 patients, 23 (52.3 %) had had Hodgkin's lymphoma and 21 (47.7 %) had had non-Hodgkin's lymphoma (NHL). Diffuse large B-cell lymphoma was the most diagnosed (57 %) followed by Burkitt lymphoma (23.8 %) and T-cell lymphoma (9.5 %). According to the Ann Arbor staging system, 29.6 % of patients were diagnosed in an advanced stage.
Conclusion: Lymphomas are the second paediatric tumour in the Centre of Tunisia. Large B-cell lymphomas are the most frequent. Third of cases are diagnosed in advanced stage.

PS-12-035

EBV positive diffuse large B-cell lymphoma in angioimmunoblastic T-cell lymphoma (a composite B and T -cell lymphoma)

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Objective: Angioimmunoblastic T-cell lymphoma (AILT) is a rare neoplasm with an Epstein-Barr virus (EBV)–infected B-cell population and occasional Reed-Sternberg-like cells (RS).
Method: We present a case of composite AILT and diffuse large B-cell lymphoma (DLBCL) A 45-year-old woman with multiples lymph nodes. Biopsy of inguinal node was performed. Three months later the patient had enlarged cervical node which was removed.
Results: Firstly, the inguinal lymph node was diffusely infiltrated by small-medium size lymphocytes with scanty cytoplasm. The nuclei were irregular. Several large cells were observed in a background of prominent arborizing high endothelial venules. The small cells were CD3 positive. The large cells were CD79a, CD30 positive. Theses cells showed nuclear positivity for EBER by ISH. Secondly, the cervical lymph node showed large areas of necrosis admixed with pleomorphic and medium size T lymphocytes. There were a population of neoplastic EBV + pleomorphic B lymphocytes; some of them with RS-like morphology. We performed B and T-cell clonality studies. We detected TCR-gamma T-cell and IgH B-cell gene clonal rearrangement.
Conclusion: Occasionally IgH gene rearrangement has been detected but only a few cases have demonstrated, morphologically, composite AILT and EBV-associated diffuse large B-cell lymphoma (DLBCL).

PS-12-036

Typhlitis as initial manifestation of granulocytic sarcoma of the appendix: A case report

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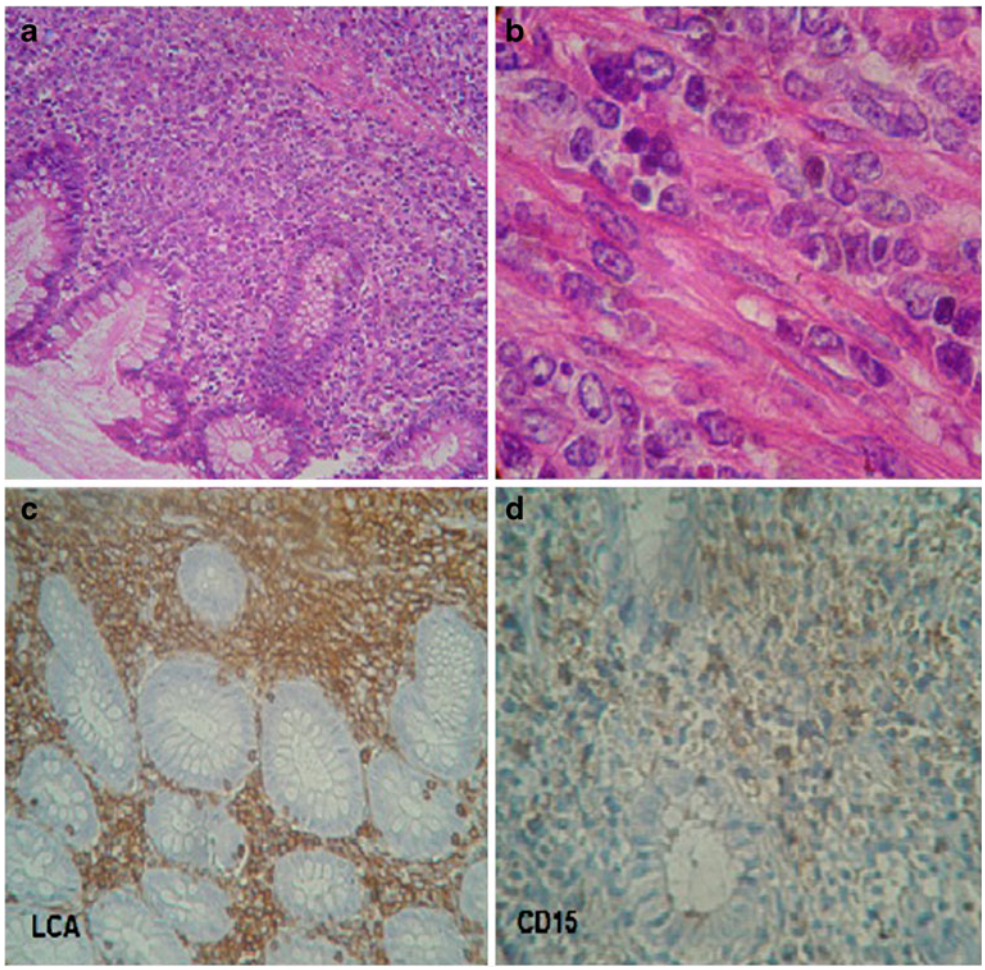
Objective: Myeloid sarcoma is a localized mass of myeloblasts or immature myeloid cells involving any extramedullary site. Reports in the literature documenting leukemic infiltration of appendix are uncommon and extremely rare when symptoms mimicking typhlitis.

Method: A 30-year-old man with a history of relapsed acute myelogenous leukemia (FAB classification, M2) admitted for receiving induction chemotherapy. After 10 days of chemotherapy, he presented with fever, nausea, vomiting, abdominal pain and severe neutropenia (0.026×109/L as absolute neutrophil count). This manifestation was attributed to typhlitis and he received antibiotic therapy, but he came back 50 days later with acute abdomen prompting exploratory laparotomy which revealed inflamed appendix.

Results: Histologic examination showed diffuse appendiceal wall infiltration of mononuclear cells with medium-to-large vesicular nuclei, conspicuous nucleoli and pale eosinophilic cytoplasm. Immunostains showed the diagnosis of granulocytic sarcoma with myeloperoxidase, leukocyte common antigen, CD15, CD117 and CD68 positivity and epithelial membrane antigen, keratin, CD3, CD5, CD10, CD79a and CD20 negativity.

Conclusion: Our case declares that physicians and surgeons should be aware of granulocytic sarcoma in the differential diagnosis of mild tenderness on palpation of the abdomen as a complication of acute myelogenous leukemia.



PS-12-037

Angioimmunoblastic T-cell lymphoma: A report of 3 cases

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Objective: Angioimmunoblastic T-cell lymphoma (AITL), one of the most frequent entities among peripheral T-cell lymphoma, is characterized by lymphadenopathy, B-symptoms, and an aggressive behaviour.
Method: We reported 3 cases of AITL during a period of 4 years (2004–2007).
Results: The age of patients varied between 20 and 73 year-old. They hadn't any pathologic history. Two patients presented with a multiple cervical lymphadenopathy, and weight loss. The other patient had fever and sweat. Physical examination found multiple lymph nodes with hepatosplenomegaly in 2 patients. Abdominal ultrasound and CT-scan showed diffuse lymphadenopathy with features raising the possibility of lymphoma. The diagnosis of AITL was confirmed by a microscopic and an immunhistochemical study of lymph node or liver biopsy. 2 patients received a cure of chemotherapy
Conclusion: Angioimmunoblastic T-cell lymphoma (AITL) is an aggressive non-Hodgkin T-cell lymphoma. AITL is frequently associated to immunological and hematologic diseases such as autoimmune hemolytic anemia, vasculitis, rheumatoid arthritis, and autoimmune thyroid disease. Its natural history has been the subject of controversy, considered for many years to be a non-malignant disorder or a dysimmune disease, until the clonal nature of AITL was proven by molecular studies. Although patients are usually treated with corticosteroids, chemotherapy, and/or plasmapheresis, outcomes were dismal.

PS-12-038

The indolent Nodal B-cell Lymphomas (NBCL) in the Center of Tunisia: A series of 50 cases

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Objective: Low grade lymphomas (indolent) are commonly located on extranodal sites. nodal location are relatively of low incidence. Our aim is to describe the epidemiological status of NBCL and to assess their pathological features in the center of Tunisia.
Method: We report 50 cases of indolent NBCL diagnosed in the department of pathology, during a period of 10 years (2000–2009). Clinical, pathological and immunohistochemical (large panel of antibodies), treatment and outcome data are collected.
Results: The mean age was 63 year old (33 and 89 years). The sex ratio was 1.27. NBCL was 6.5 % of all N H lymphomas and 42.73 % of indolent NBCL of any sites. Nodal enlargement and hepatomegaly were the main symptoms. Small Lymphocytic lymphomas were the most frequent variant (56 %), followed by follicular lymphomas (26 %). Mantle cell lymphoma and marginal zone B cell lymphoma were rare (12 % and 6 %, respectively). They were exclusively of B cell type. 76 % of cases were in stage III-IV. 90 % of patients received chemotherapy. 2 % of recurrence and 48 % of death were found.
Conclusion: NBCL in the center of Tunisia are relatively uncommon. Small lymphocytic lymphoma is the most frequent in our population. They are still of relatively worse prognosis.

PS-12-039

Bone marrow metastasis of signet ring cell carcinoma with an unknown primary site

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Objective: Bone marrow metastases can be found in some malignant tumors, but diagnosing a nonhematologic malignancy from marrow is an unusual event. Herein we present a case of metastatic signet ring cell carcinoma with an unknown primary site.
Method: A 39 year-old woman admitted to the Hospital with weakness and bone pain. Positron emission tomography/computed tomography (PET/CT) revealed disseminated bone lesions showing increased metabolic activity. Bone marrow biopsy and aspiration were performed.
Results: Bone marrow biopsy revealed extensive necrosis and nearly total replacement of normal bone marrow elements by atypical tumoral cells. Tumoral cells were arranged individually or in small clusters, having hyperchromatic, eccentric located nuclei and abundant cytoplasm with signet ring cell morphology. Even after thourough investigation of all the systems, a primary site of malignancy could not be detected. She received nine cycles of chemotherapy. Craial MRI revealed multiple metastatic lesions. 9 months after the initial diagnosis, she died of disseminated metastatic lesions.
Conclusion: Even after thorough investigations, a primary site of malignancy could not be detected. In the literature, all the presented cases had very short survival varying from days to a few months. Our patient lived for 9 months with multidiciplinary approach.

PS-12-043

Most t(14;18) negative follicular lymphomas are nodal marginal zone lymphomas

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Objective: Approximately 20 % of follicular lymphomas (FLs) are bcl2 negative and 10–15 % of FLs lack a translocation t(14;18). Previously we have found that negative bcl2 staining in cases that do have a t(14;18) is caused by mutations in the epitope for the bcl-2 antibody, but this is never the case in bcl-2 negative, t (14;18) negative cases. Now that translocation detection is more commonly performed we noticed that many of the cases that were referred to us as translocation negative FL are actually often nodal marginal zone lymphomas (NMZLs) with extensive follicular colonization.
Method: t(14;18) negative cases that on H&E sections look like FL were analyzed by morphology and immunohistochemistry, including antibodies against CD10, bcl-2, Ki-67, and CD23.
Results: Careful observation of the bcl-2 staining pattern revealed that follicles that appeared positive at low power contained negative cells at high magnification. The amount of negative cells varied from follicle to follicle and was associated with the extent of Ki-67 positivity.
Conclusion: Based on morphology and immunohistochemistry we reclassified many cases of bcl-2 positive, t(14;18) negative FL into NMZL. Although there is presently no positive marker for NMZL, we believe that such cases are responsible for most t(14;18) negative FL.

Monday, 10 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-13 Poster Session Electron Microscopy

PS-13-002

Ultrastructure of cutaneous lichen planus lesions evidenced in various types of disease correlated with tissue levels of gelatinase-B

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Objective: Recent studies do not provide a definite answer on the origin and pathogenesis of lichen planus (LP). Histologic findings are the same, regardless of the area involved. Electron microscopy is useful to confirm the diagnosis in atypical cases and monitoring LP development. This study aimed an ultrastructural characterization of keratinocyte degeneration in pemphigoides, hypertrophic, and follicular LP types correlating this with levels of gelatinolytic activity caused by metalloproteinase-9 (MMP-9).
Method: Skin biopsies were processed conventionally and examined in a JEOL 1011 transmission electron microscope. MMP-9 expression was detected immunohistochemically.
Results: LP pemphigoides demonstrated intact basal keratinocyte cell membrane, and the lamina densa lining blister cavity correlating with moderate basal MMP-9 expression of weak intensity. Hypertrophic type demonstrated good preservation of keratinocytes and their junctions along with strong basal and suprabasal MMP-9 expression of moderate intensity. Both types demonstrated diffuse and strong MMP-9 immunostaining in dermal lymphohistiocytic infiltrate. A hypertrophic type revealed an increase of expression within dermal sweat glands comparing with LP pemphigoides. A diffuse and strong epidermal and follicular MMP-9 staining was noticed in follicular variant of LP.
Conclusion: Ultrastructurally keratinocyte involvement displays deviations in various types of LP, and these changes correlate with levels of gelatinolytic activity caused by MMP-9.

PS-13-004

Ultrastructural findings of myopathy induced by long-term therapy of clevudine

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Objective: Clevudine is a recently introduced anti-viral agent that shows efficacy against hepatitis B virus related chronic liver diseases. However, it has been reported that certain patients who have received long-term administration of clevudine exhibit myopathy involving mitochondrial abnormalities. To make a differential diagnosis congenital mitochondrial myopathy and drug induced mitochondrial myopathy, we investigate ultrastructural findings of drug induced myopathy.
Method: We studied histopathological features of myopathy focused on the various ultrastructural mitochondrial abnormalities found in 18 patients with long-term clevudine therapy.
Results: In every case, ragged red fibers and multinucleated fibers with eosinophilic granules were observed. Additionally, type 2 fiber atrophy was found in 6 cases. Mainly concentrated in subsarcolemmal or inter-fibrillar areas, the abnormal mitochondria were enlarged and swollen, showing a variety of morphological types. Most of the abnormal mitochondria indicated structural abnormalities in cristae, including the apparent decrease in the number, concentric lamellar pattern, and structure that is branched or lattice-like.
Conclusion: From the overall analysis, clevudine-induced myopathy is characterized by ragged fibers showing proliferation of abnormal mitochondria with various forms of inclusion bodies and abnormal cristae. Another particular feature of interest is the presence of multinucleated fibers, which, in most cases, are filled with abnormal mitochondria.

PS-13-006

Ultrastructural features of human mature oocytes subjected to cryopreservation

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Objective: Oocyte cryopreservation protocols have not been fully optimized yet. Our aims were to evaluate and compare the ultrastructure of human mature oocytes frozen-thawed (F/T) after slow freezing and vitrification.
Method: The oocytes, fixed at sampling (fresh controls) and after freeze/thawing, were processed for light and transmission electron microscopy (LM and TEM) observations.
Results: By LM, both fresh and F/T oocytes were rounded cells surrounded by an intact zona pellucida (ZP) and containing uniformly distributed organelles. By TEM, numerous vacuoles were found in F/T oocytes after slow freezing. On the contrary, vacuoles were only occasionally detected in F/T oocytes after vitrification, and in fresh controls as well. Amount and density of cortical granules (CGs) appeared abnormally reduced in F/T oocytes, irrespective of the protocol applied.
Conclusion: In conclusion, a) cryopreservation currently ensures a good overall preservation of the oocyte; b) however, vacuolization appears as a recurrent form of cell damage during slow freezing, whereas the quasi absence of vacuoles seems the most relevant marker of quality in vitrified oocytes; c) premature CG exocytosis - and the consequent hardening of the ZP - seems a non-specific, ubiquitous phenomenon occurring during freeze/thawing, suggesting the appropriateness of the use of ICSI as the preferred insemination method after cryopreservation.

Tuesday, 11 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-14 Poster Session Digestive Diseases Pathology III: Liver, Biliary and Pancreas

PS-14-001

Pancreatic mucinous cystadenocarcinoma: Study of 5 cases

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Objective: Mucinous cystic epithelial neoplasms of the pancreas are uncommon with 2–5 % of all exocrine pancreatic tumours. They occur exclusively in aged women. Here, we report the pathological, clinical and prognosis particularities of pancreatic mucinous cystadenocarcinoma (PMC).
Method: Retrospective study was performed on 5 cases of PMC diagnosed in the Pathology Department, Farhat Hached Hospital, Sousse.
Results: There were 3 women and 2 men with a median age of 60 (range 45–80 years). Symptoms were dominated by abdominal pain, jaundice, vomiting, and alteration of the general condition. Radiologic investigation showed multiloculated cystic mass of the pancreas, associated to splenic thrombosis and bone metastasis in one case. In gross, we received multilocular cysts of 3 to 16 cm in wall, their wall was fibrous, and thick, the internal surface showed many papillary projections and mural nodules. There was no communication with the duct system. On histologic examination, cysts had a fibrous wall lined by mucinous atypical cells showing frank anaplasia, wall's cyst was invaded by anaplastic glands; the stroma was of ovarian type in all cases.
Conclusion: PMC are uncommon neoplasia, their diagnosis is based on the histopathologic exam, their diagnosis is better than duct carcinoma and depends on the extent of tumour invasion.

PS-14-002

Heterotopic pancreas of the gallbladder associated with acute cholecystitis

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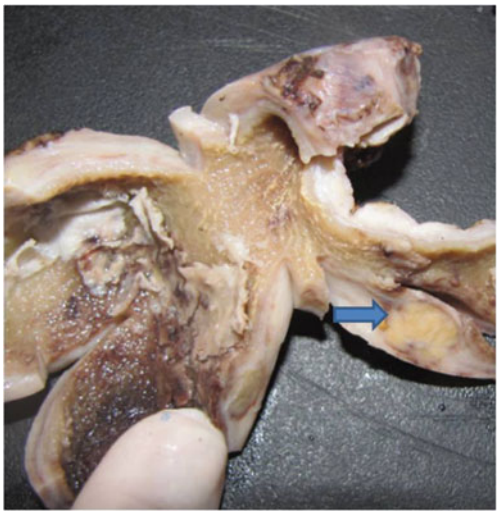
Objective: Pancreatic heterotopia is a rare entity, which is commonly found in the stomach, duodenum, jejunum and Meckel's diverticulum. Heterotopic pancreas is extremely rare in the gallbladder. Despite being a congenital condition, it takes years to become symptomatic. It can be associated with cholecystitis or cholecystolithiasis.
Method: A 21-year-old female patient was admitted to emergency service with abdominal pain. On physical examination, right upper abdomen was tender without defense or rebound. Abdominal ultrasonography revealed small sized gallstones and pericholecystic fluid. Magnetic resonance cholangiography showed dilated intrahepatic and extrahepatic bile ducts. Laparoscopic cholecystectomy was performed.
Results: Cholecystectomy specimen was 75×35×30 mm. On gross examination we noted a few milimetric yellow colored stones and 12 mm yellow solid intramural nodule. The mucosa was covered with fibrinopurulent exudate. Microscopic examination revealed acute cholecystitis and aberrant pancreatic tissue consisting of acini and ductules. The phlegmonous inflammation of the gallbladder infiltrated the aberrant pancreatic tissue. The patient recovered completely after cholecystectomy.
Conclusion: We found this case worth reporting because, pancreatic heterotopia of the gallbladder is a rare, clinically

silent entity unless complicated with gallstones and acute cholecystitis.



PS-14-003

Expressions of c-erb-B2, EGFR, p27, PTEN, mTOR, PI3K in hepatocellular carcinomas and adjacent liver tissues

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Objective: We investigated the expressions of c erb B2, EGFR, PTEN, mTOR, PI3K, p27 in Hepatocellular carcinomas (HCC) cases and their correlations with other pathologic features.
Method: Fifty HCC cases were stained immunohistochemically with these markers. Correlations between the markers and pathologic characteristics were analyzed.
Results: The cases had an average age of 56,72. Male/female ratio was 44/6. HBV is more common in advanced stages and right lobe location ($p<0.05$). Tumor size is significantly larger in patients older than 50 years ($p<0,04$). No membranous c erb B2 staining was seen while cytoplasmic positivity was present in 92 % and significant correlation was found with multiplicity ($p<0.041$) and p27 positivity ($p<0,011$). EGFR membranous positivity was present in 90 % and significantly correlated with stage ($p<0.05$). p27 was negative in 92 % and PTEN is reduced or absent in 56 %. All markers were similarly expressed in adjacent noncancerous tissue. No significant correlations were found between PTEN, mTOR, PI3K and the pathological parameters.
Conclusion: In our study, as a first step, none of the markers among c-erb-B2, EGFR, p27, PTEN, mTOR, PI3K was found significant in correlation with pathologic features. We look forward to obtain further results in the next study consisting of correlations with follow ups.

PS-14-004

The value of echo guided liver biopsy in the positive diagnosis of a rare primary liver tumor – pathological approach

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Objective: Hepatic angiomyolipomas are rare mesenchymal hepatic tumour. The most important problem about their diagnosis on biopsy specimens is to exclude a hepatocellular carcinoma.
Method: We present two cases of hepatic angiomyolipoma diagnosed in Fundeni Clinical Institute, Bucharest. Both females patients, 39 and 43 years old, were imagistically diagnosed with a 13 cm hepatic left lobe tumor in the first patient, respectively a 10.5 cm hepatic right lobe tumor in the second one. Both tumors were echo guided biopsied. The biopsy specimens measured about 8 mm, respectively 20 mm. The tumors were surgical removed. The biopsy and resection specimens were analyzed in light microscopy, including immunohistochemistry.
Results: Initial diagnosis on HE stain was cell variant hepatocellular carcinoma, in the 8 mm biopsy, respectively suspicious for angiomyolipoma in the second case. Further immunohistochemical studies showed positivity for Vimentin, HMB45, MELAN A, S100 and actin, and negativity for OCH1E5, CK7, CK8/18, CEA, CD34, Ki67 and Factor VIII in both biopsy specimens, consistent with hepatic angiomyolipoma diagnosis, confirmed on surgical specimens too.
Conclusion: Diagnosing a hepatic angiomyolipoma is not easy to do especially on a biopsy. The size of biopsy specimens plays a very important role in a correct diagnosis.

PS-14-005

Adult pancreatic hemangioma: Case report and literature review

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Objective: Pancreatic vascular neoplasms are rare lesions accounting for 0.1 % of all pancreatic tumors. Adult pancreatic hemangiomas are extremely uncommon. Only 12 cases of adult pancreatic hemangiomas have been reported in literature since 1939.
Method: We report a new case with literature review.
Results: A 62-year-old woman presented with a 2-day history of nausea, fever and diffuse abdominal pain. CT scan revealed a well circumscribed small lesion of the pancreatic body. On arterial phase imaging, the mass was of low density relative to the pancreas without marked contrast enhancement. Based on these findings, the patient underwent surgical resection of this mass and a distal

spleno-pancreatectomy was performed. Microscopic examination showed a well circumscribed but non encapsulated soft tissue proliferation consisted of blood vessels lined by a single layer of uniform flattened cells, with dilated lumen filled with red blood cells and inflammatory cells. Immunohistochemical staining confirmed the vascular nature of the lesion. The diagnosis of pancreatic hemangioma was made.
Conclusion: Adult pancreatic hemangioma is an extremely rare tumor. The review of all published cases showed that this tumor often do not demonstrate the contrast-enhanced CT features typical of an hemangioma, so a poor arterial phase enhancement cannot rule out pancreatic hemangioma and the histological examination is very important in these cases.

PS-14-006

Hepatocholangiocarcinoma - Clinicopathological features: Case report

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Objective: Hepatocholangiocarcinoma (HCC-CC) is an uncommon form of primary liver cancer with features of hepatocellular and biliary epithelial differentiation. It accounts for 0.4–14.2 % of all primary liver carcinomas. Many of the demographic and clinical features of this tumor remain unclear. It was previously suggested that coexisting chronic liver diseases were rarely seen in patients with HCC-CC.
Method: We report a case of HCC-CC diagnosed in patient with cirrhosis.
Results: A 48 year-old man presented with ascites, jaundice, vomiting and symptoms of portal hypertension. On abdominal CT scan the right hepatic segment was heterogeneous, hypervascular in the late arterial phase and low-attenuated on portal venous phase. Based on a these clinicoradiological informations, diagnosis of infiltrating hepatocellular carcinoma was made and hepatic biopsy was performed. Histopathologic examination showed, in addition to features of liver cirrhosis, the presence of malignant proliferation composed of tubular structures as well as microtrabecular and compact foci. On Immunohistochemical stainings the tumor cells expressed cytokeratins 7 and 20. Cells lining the tubular structures reacted with cytokeratin 19 allowing the diagnosis of hepatocholangiocarcinoma.
Conclusion: Hepatocholangiocarcinoma is a rare primary liver cancer. Preoperative noninvasive diagnosis with conventional radiography is often difficult especially when occurring in patients with liver cirrhosis or other hepatic chronic disease. The diagnosis is frequently made only after histological and immunohistochemical examination.

PS-14-007

Morphological changes in different zones of the gallbladder in cholelithiasis

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Objective: Gallstone disease remains a serious problem of modern surgery. An important aspect of the problem is the question of the urgency of surgical intervention, depending on the condition of the gallbladder.
Method: It was carried out the analysis of 1130 case histories and excised gallbladder with different forms of cholelithiasis. 81.3 % were women in the age of 41–50 years. Acute catarrh cholecystitis was found out in 20 % cases, acute phlegmonous - in 21 % cases, acute gangrenous - in 11 % cases, chronic – in 28 % and chronic relapsing – in 21 % cases.
Results: All forms of cholecystitis characterized by a maximum thickness of the body wall, minimal at the bottom of the gallbladder. In all forms adipose tissue inflammation in the connective tissue layer was increased and it was found out the atrophy of the mucosa. In the inflammatory infiltrate in acute forms of inflammation were found neutrophilic and basophilic leukocytes: with simple acute cholecystitis - in the bottom, and with acute phlegmonous and gangrenous cholecystitis - in the area of the body of the gallbladder. In the cases with chronic cholecystitis were dominated mononuclear cells in all areas, and in the cases with chronic relapsing - neutrophilic and basophilic leukocytes in the bottom and the body, and mononuclear cells - in the neck of the gallbladder.

PS-14-008

Histological features of chronic hepatitis C in hemodialysis patients

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Objective: Chronic hepatitis C (CHC) in hemodialysis patients has not been thoroughly investigated, despite its high frequency. The present comparative study aims to highlight the histological features of CHC and its association with putative pathogenetic parameters in this specific group of patients.
Method: Sixty-one biopsies of hemodialysis patients and 326 biopsies from the general population with CHC were comparatively evaluated for the severity and specific histological features of CHC. Results were examined in relation to age, time of dialysis, viral load and genotype.
Results: Patients on hemodialysis were older than patients of general population (p=0.031), showing a similar genotype distribution (p=0.328) and lower viral loads (p=0.001). CHC on hemodialysis was significantly milder according to stage

(p=0.033), activity and its parameters (p<0.001). Significantly reduced was also the frequency of lymphoid aggregates (p< 0.001), bile duct damage (p<0.001) and steatosis. (p=0.033). Severity of hepatits was not associated with time on hemodialysis. In multivariate analysis the differences were independent of age, which was associated with more severe disease. Steatosis was associated with hemodialysis duration and age.
Conclusion: CHC in hemodialysis patients is significantly milder than in general population. Limited necroinflammatory activity and absence of immune mediated lesions are indications of defective immune response although involvement of low viral load cannot be overlooked.

PS-14-009

Inflammatory (myofibroblastic) pseudotumor of the liver: Case report

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Objective: Inflammatory pseudotumor of the liver (IPT) is a rare, benign tumor-like lesion of which etiology is not fully known. It is confused with primary and metastatic malignant tumors as it seems as an occupying mass on radiologic examinations.
Method: Thirtyeight-year-old male patient who had fatigue and dyspepsia was detected to have elevated liver enzymes and hepatomegaly. On computed tomography, two masses of which middle is mildly hypometabolic, measuring 34× 31 mm in right liver lobe and 45×39 mm in left liver lobe were detected. Biochemical tests were normal except elevated AST and ALT levels. Ultrasound-guided needle biopsy was done for two masses.
Results: On microscopic examination, a lesion composed of abundant fusiform fibroblastic cells and vascular structures among inflammatory cells composed of lymphocytes, plasmocytes, histiocytes and eosinophillic leucocytes and including sharp margins between regenerated liver tissue was observed. On immunohistochemical examination, SMA was stained focal positive in fibroblastic cells. Staining with desmin, S-100, PanCK, CD34, Ki-67 and CD117 was not seen.
Conclusion: IPT does not have a specific radiologic finding and definite diagnosis is made with pathologic examination. This case is presented as it is rarely seen, radiologically resembles to malignant tumors and for review of pathological differential diagnosis.

PS-14-010

Enhancer of Zeste Homologue 2 (EZH2) expression in malignant and benign hepatic tumors

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Objective: The immunohistochemical demonstration of Enhancer of zeste homologue 2 (EZH2) proved to be a useful marker in several tumor types, including hepatocellular carcinomas.In order to recognize the diagnostic value of this protein in hepatic tumors we have investigated the presence of EZH2 in the most common liver neoplasms.
Method: The presence of EZH2 has been studied by standard immunohistochemistry in several formalin-fixed paraffin-embedded tumor samples (hepatocellular adenoma, hepatocellular carcinoma, cholangiocarcinoma, hepatoblastoma, metastatic liver tumors and primitive childhood tumors).
Results: Forty of 44 hepatocellular carcinomas, 22 of 23 cholangiocarcinomas, 29 of 31 hepatoblastomas and 14 of 17 metastatic liver tumors stained positively, but all the investigated hepatocellular adenomas (n=24) and proliferating biliary structures were negative. The other primitive childhood tumors that were examined all expressed EZH2.
Conclusion: Based on these results EZH2 is a sensitive marker of malignancy in hepatic tumors regardless of their histogenesis. In routine surgical pathology EZH2 could be helpful to diagnose hepatocellular carcinomas and it might be the first marker to distinguish transformed and reactive cholangiocytes.

PS-14-011

Nuclear ploidy as a marker of intraductal papillary-mucinous pancreatic neoplasms malignancy

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Objective: Intraductal papillary-mucynous pancreatic neoplasm (IPMN) represents 0,5 to 9.8 % of all tumors of exocrine pancreas. Our aim was to study nuclear ploidy of malignant and benign IPMNs cells.
Method: We studied 20 pancreatic surgical specimens from 5 females and 15 males. We performed histological, morphometrical and ploidy analysis of all specimens.
Results: IPMN cells nuclear perimeter and size was higher than in normal pancreatic duct cells. This parameters were higher in malignant noninvasive IPMN than in benign tumor. Nuclear size and perimeter of invasive malignant IPMN were in intermediate position between benign and malignant noninvasive tumor. Mean nuclear ploidy (MNP) of normal ductal pancreatic cells was 2.4c. MNP of benign IPMNs was 2.5c, borderline tumors – 3.0c. MNP of noninvasive malignant IPMNs was 5.1c, of invasive IPMNs – 4.5c. We also revealed that aneuploidy coefficient (AC) of benign IPMNs was 0 (there weren't aneuploid nuclei in its cells). AC of borderline IPMNs was 0.11. Maximal level of

AC was in malignant noninvasive IPMNs whereas AC of invasive IPMNs was lesser.
Conclusion: Nuclear morphometric parameters and mean nuclear ploidy level as well as aneuploidy coefficient could be used as additional criteria for determining malignant potential of IPMNs.

PS-14-012

An intraductal papillary mucinous neoplasm of the pancreas with concomitant neuroendocrine tumor: A case report

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Objective: Intraductal papillary mucinous neoplasms (IPMNs) are a recently classified pancreatic neoplasm with an increasing incidence. IPMN of the pancreas is a lesion consisting of mucin-producing cells with neoplasic potential, characterized by papillary intraductal growth and varying degrees of cytologic atypia. Neuroendocrine tumors of pancreas (PNET) are rare pancreatic neoplasms comprising 1–2 % of all pancreatic tumors. PNETs express neuroendocrine markers, however the true cell or cells of origin are not fully understood. PNETs are classified as functional or nonfunctional based on the presence or absence of a specific clinical syndrome associated with hormone oversecretion. Intraductal papillary mucinous neoplasm of the pancreas with concomitant Neuroendocrine tumor are a highly rare occurrence.
Method: A literature review of IPMNs and PNET was made, as well as a review of the clinical data of a patient with IPMN and concomitant PNET.
Results: A 60-years-old Caucasian female, underwent a laparoscopic distal pancreatectomy with splenectomy for IPMN. Macroscopic examination revealed discrete dilatation of pancreatic ducts and nodule in the pancreas tail. Hystologic examination revealed neoplasic lesion of intraductal papillary-mucinous in the body and tail of pancreas with moderate dysplasia (IPMN borderline) and Neuroendocrine Tumor grade 1 (WHO 2010).
Conclusion: This case reports a highly rare occurrence.

PS-14-014

Glypican 3 and agrin expression in hepatocellular carcinoma and cholangiocellular carcinoma: A immunochemistry study

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Objective: Glypican 3 (GPC3), which plays a role cellular growth, differentiation and migration is one of members of glypican family. Although GPC3 expression in the liver, glypican upregulation of the vast majority of tumors are available. Agrin is found the surface on the cells and the extracellular matrix, the micro-vessels
Method: In this study, formalin-fixed, paraffin-embedded surgical specimens from 20 patients with hepotocellular carcinoma and 20 patients with cholangiocellular carcinoma diagnosed between 2000 and 2011 years in Ataturk University, Faculty of Medicine, Department of Pathology were studied with immunohistochemistry Agrin and GPC3.
Results: We detected agrin in around bile ducts and blood vessels within the portal areas in the normal liver. İn the malignant hepatocellular carcinoma (HCC) is seen in a dramatic increase in the quantity of agrin. GPC3 immunpositivity showed in %85 of HCC and %15 of cholengiocellular carcinoma. Agrin immunpositivity showed in %95 HCC and %50 of cholangiocellular carcinoma.
Conclusion: GPC3 and Agrin, that is useful in early diagnosis of HCC cases; cholangiocellular carcinoma, or not enough was understood to be very limited.

PS-14-015

Value of glypican 3, Hep Par and alpha fetoprotein in diagnosis of hepatocellular carcinoma

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Objective: Glypican 3 showed high expression of the embryonic liver and intestine, is silenced in normal adult tissues. It is an oncofetal protein. İn general, oncofetal proteins, while having a critical role in tumor progression or immunotherapy is a potent tumor marker used as a target. Alpha fetoprotein, clone C3 localized, normally produced by gestational age, fetal liver and yolc salc, glycoprotein structure emerging marker for patients with HCC. Hep Par 1 antibody was developed in 1993 using fixed liver as immunogen.
Method: İn this study formalin-fixed, paraffin-embedded surgical specimens from 20 patients with hepatocellular carcinoma diagnosed between 2000 and 2011 years in Ataturk University, Faculty of Medicine Department of pathology were studied with immunohistochemistry GPC3, Heppar 1, and AFP. GPC3, Heppar 1 and AFP expression was divided into 2 categories negative (negative or weak under %5 tumor cells cytoplasmic staining) and positive (and %5 over of tumour cells) moderate or strong cytoplasmic with membranous accentuation.
Results: Immunpositivity at GPC3, Hep Par 1 and AFP were 85 %, 95 %, 75 % respectively.
Conclusion: İn this study, GPC3, AFP and Hep Par 1 may aid in the accurate diagnosis of HCC.

PS-14-016

Expressions of fibroblast growth factor receptors as an independent prognostic factor in hepatocellular carcinoma

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Objective: Fibroblastic growth factor receptor (FGFR) family is known to be related to the development and progression of various types of cancers. The aim of this study is to determine the clinical implication of FGFR expressions in patients with hepatocellular carcinoma (HCC).
Method: Immunohistochemical analysis was done in 842 cases of HCC using tissue microarray. Diffuse cytoplasmic staining for FGFR1, 2, 3 and 4 in more than 10 % of tumor cells were designated as positive. The results were analyzed in terms of various clinicopathologic parameters.
Results: On univariate analysis, the overall survival rates of patients with FGFR2 expression (152 cases, 18.1 %) were significantly lower than those with no expression (HR 1.838, 95 % CI 1.452–2.328, $P<0.001$). However, the overall survival rates of patients with FGFR4 expression (446 cases, 59.6 %) were significantly higher than those with no expression (HR 0.636, 95 % CI 0.521–0.776, $P<0.001$). There was no statistical significance between patients' overall survival rates and expressions of FGFR1 (46 cases, 5.5 %) or FGFR3 (33cases, 4.0 %). On multivariate analysis, only FGFR2 expression is independently associated with reduced OS (FGFR2: HR 1.790, 95 % CI 1.404–2.282, $P<0.001$).
Conclusion: The FGFR2 expression can be used as an independent prognostic factor in patients with surgically resected HCC.

PS-14-018
Hurp overexpression in pancreatic adenocarcinomas correlated with worse prognosis
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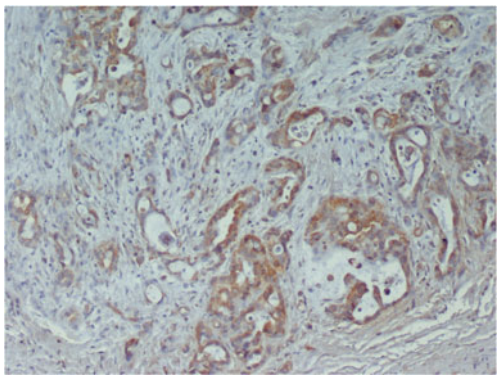
Objective: HURP (hepatoma upregulated protein) is a putative oncogene, overexpressed in many human cancers, including hepatocellular carcinoma. It has also been shown recently that high HURP protein levels correlate with resistance to chemotherapeutic agents. In the present study we investigate the expression of HURP and its correlation with pancreatic adenocarcinoma, prognosis and patient survival. Pancreatic adenocarcinoma is one of the most aggressive types of cancer and represents the fourth most common cause of death, either in the male or in the female population of the United States of America.
Method: HURP immunoreactivity was assessed by immunohistochemistry in a series of 28 primary pancreatic adenocarcinomas. In parallel, HURP expression was examined in 10 normal pancreatic tissues. Statistical analysis related HURP expression levels with clinicopathological characteristics and survival.
Results: Results showed a positive correlation between HURP overexpression and grade as well as lymphovascular invasion. All non malignant biopsies were negative. Furthermore, positive expression of HURP appeared to be an important independent prognostic factor too, related with poor survival rates.
Conclusion: Our results showed that HURP overexpression is associated with poor prognosis in pancreatic adenocarcinoma and indicated a diagnostic potential of this protein. Its role in the carcinogenetic process awaits further elucidation.



PS-14-019
Hepatocellular carcinoma in patient with hepatic porphyria: A case report
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Objective: Hepatocellular carcinoma (HCC) is frequently associated with liver cirrhosis or chronic hepatitis of various etiology, less often with other chronic hepatopathies, including hepatic porphyria. We present a case report of HCC diagnosed in patient with clinically unrecognized porphyria cutanea tarda (PCT).
Method: A 70-year old male was admitted to hospital complaining of a pressure below low costal margin, anamnesis of a trauma 1 year ago and clinical suspicion of a posttraumatic intrahepatic haematoma. By a surgery, a partialy necrotic and hemorrhagic tumor mass 10 cm in diameter was removed.
Results: The mass corresponded histologicaly to moderately differentiated clear cell HCC, resembling renal clear-cell carcinoma. The surrounding parenchyme showed steatohepatitis with fibrosis and distinct intracellular porphyrin crystals.
Conclusion: Development of HCC is a well documented complication of PCT, a disorder of porphyrin biosynthesis. PCT can be inherited (autosomal dominant trait), the acquired form (sporadic PCT) is more common. Known etiological factors of PCT include toxins, alcohol abuse, estrogens or chronic viral hepatitis, or association with other

hepatic diseases like iron overload (including hereditary haemochromatosis) or chronic hepatitis C, increasing the risk of malignancy. However, in the presented case none of these associations was recognized and its etiology remains obscure.

PS-14-020

Undifferentiated carcinoma with osteoclast-like giant cells – Rare variant of pancreatic cancer– Case report

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Objective: Undifferentiated carcinoma with osteoclast-like giant cells is a rare pancreatic tumor that could be associated with an adenocarcinoma or a mucinous cystic neoplasm of the pancreas.
Method: We present the case of a 63 years old man with clinical diagnosis of hemorrhagic retroperitoneal tumor penetrating the tail of the pancreas, spleen, inferior cava vena and posterior gastric wall.
Results: Gross examination reveals multiple whitish tumor fragments with necrosis and hemorrhage. Microscopically: round to spindle atypical cells and large non-neoplastic multinucleated giant cells infiltrating the pancreas. First impression is that it looks like a giant cell MFH infiltrating the pancreas. On closer examination we see can small areas of adenocarcinoma that have been better highlighted by citokeratin antibody. Immunohistochemically: the mononuclear tumor cells are positive for vimentin and part of them for p53 and CD68, the multinucleated giant cells are positive for CD68 and adenocarcinoma tumor cells for citokeratin.
Conclusion: The diagnosis is made by the microscopic features associated with pancreatic adenocarcinoma that sustains the pancreatic origin and exclude the giant cell MFH that, usually, arises in deep intramuscular soft tissue of the extremities.

PS-14-021

Unusual malignant tumor of the gallbladder

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Objective: Signet ring cell carcinoma is an extremely rare type of gallbladder carcinoma composed overwhelmingly (90 %) of signet ring cells. Only a few cases of this histologic type have been published and detailed knowledge of this disease is not available.
Method: We report a case of signet-ring cell carcinoma of the gallbladder in a 70-year-old woman who was admitted with epigastric pain. Under the preoperative diagnosis of cholangiocarcinoma, which was based on findings of CT scan and ultrasonography. Cholecystectomy was performed.
Results: Microscopic examination revealed a signet ring cells tumor that arose from the sub epithelial layer of mucosa and involved all the layers of gallbladder. Nuclear atypia and mitoses were present. Periodic acid schiff (PAS) stain highlighted the intracellular mucin in the tumor cells. Lympho-vascular emboli were detected in the subserosal layer. The cystic duct surgical margins were invaded.
Conclusion: Gallbladder adenocarcinomas are seen frequently, but signet-ring cell carcinoma is a rare entity. Owing to the location of the gallbladder, dissemination of the tumour to the adjacent tissues is usually presented at the time of the diagnosis. It is necessary to exclude a gastric or colonic signet ring cell carcinoma secondarily involving the gallbladder.

PS-14-022

Extragastrointestinal stromal tumor of the pancreas: A case report

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Objective: Gastrointestinal stromal tumors (GISTs) are mesenchyme neoplasms of the gastrointestinal tract which express CD117. GISTs can occur in the entire length of gastrointestinal tract, but very seldom can also arise in omentum, mesentery and retroperitoneal space, kidney, urinary bladder etc. There they are located adjacent to stomach or intestine, but not originated from the latter. These tumors are designated as "extra-gastrointestinal stromal tumors" (EGISTs). There are only 14 description of the Primary EGISTs reported in the literature.
Method: We report a case of a pancreatic EGIST in a 38-year-old female patient.
Results: CT scan showed a mass in the head of pancreas. Grossly encapsulated tumor, 9 cm in diameter, was found in the head of the pancreas (Figure 1). Histologically, tumor demonstrated spindle-cell pattern consisted of distinct fascicles and bands. The number of mitoses was 1-2/50 high power fields in “hot-spot” areas. IHC revealed strong positivity for CD117, CD 34 in neoplastic cells and negative for SMA, desmin, S-100. Ki67 labeling index was 3 %.
Conclusion: We presented a rare case of pancreatic GIST. The tumor has very good prognosis.

PS-14-023

Hepatoblastoma in adult age

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Objective: Hepatoblastoma is a rare malignant tumor of the liver and usually occurs in the first three years of life.

Hepatoblastoma is classified as epithelial (56 %) or mixed epithelial/mesenchymal (44 %). Epithelial hepatoblastoma is further divided to pure fetal (31 %), embryonal (19 %), macrotrabecular (3 %) and small cell undifferentiated (3 %).
Aim: To increase the awareness regarding possibility of hepatoblastoma in adult age.
Method: We review four cases of hepatoblastoma epithelial type diagnosed in Pathology Department of Fundeni Clinical Institute between 2009 and 2012. Immunohistochemistry was done in all cases: CEA, Vimentin, CK 8/18, CK 19, CK 20, Ki 67, TTF1, CD 10, CD 34, CD 56, MUC 5A, alpha-fetoprotein.
Results: Two of the patients were males and two females with age ranging between 17 and 27 years. The tumors varying in size from 8 to 12 cm. On microscopic examination the tumor was composed mainly of epithelial elements. The pathological diagnosis was epithelial hepatoblastoma epithelial type.
Conclusion: Hepatoblastoma is a rare tumor in adult age and epithelial type is the rarest from all type of hepatoblastoma in adult age. The pathological diagnostic is quite difficult even using immunohistochemistry because none of the markers are not specific for hepatoblastoma.

PS-14-024
Submassive hepatic necrosis with regenerative nodules: A series of cases
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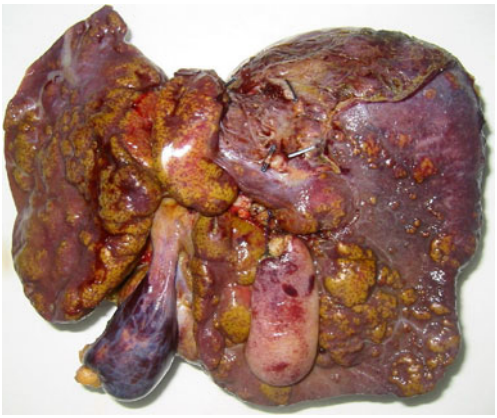
Objective: Confluent hepatic necrosis is the morphological correlate of fulminant liver failure. A group of these livers develop a combination of areas of necrosis and regenerative macronodules (RMN).
Method: Sequential biochemical and clinical data and tissues from two groups of patients were compared. Group 1: 10 cases of submassive necrosis associated with RMN; Group 2: 19 cases with total confluent necrosis without nodular regeneration.
Results: Group 1: mean age was 33,6 years (ranged 10 months-63 years); group 2 mean age was 42,6 years (ranged 18 months-63 years) ($p>0,05$). A longer course (42,8±34,6 days vs 12,6±6,0, $p<0.05$) and higher maximum serum bilirubin levels (23,5 mg/dl ±13,08 vs 14,9 mg/dl± 10,9, $p<0.05$) were observed in group 1. Serum AST, ALT and gamma-GT were lower in group 1 ($p>0.05$). Morphologically livers from group 1 showed well defined regenerative green-yellow nodules with large regenerative hepatocytes in acinar pattern without surrounding fibrosis. The remaining parenchyma showed confluent necrosis, haemorrhage, mixed inflammatory infiltrate and ductular proliferation.
Conclusion: A special anatomoclinical form of subacute liver failure was characterized by regenerative macronodules in a background of extensive confluent liver necrosis. Illness duration was longer and had higher maximum bilirubin levels than those without RMN.



PS-14-025
Immunohistochemical study of MUC gene family in pancreatic cancer
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Objective: Investigation of the MUC gene in pancreatic ductal adenocarcinomas (PDA).
Method: In the present study, we examined the expression of MUC1, 2 and 5 AC types by immunohistochemical analyses in PDA from 74 patients. Overall survival curves were drawn by the Kaplan-Meier method. For all analyses, $p<0.05$ was considered to be statistically significant.
Results: In our cases most of the PDA was presented as MUC1+/MUC5AC + phenotype - 42 % cases (31/74). The group with intestinal phenotype mucin, which characterized by positive expression of MUC2 and CDX2, was only 7 % (5/74). The group which characterized by positive expression only MUC5AC (gastric phenotype), was 15 % (11/74). The survival rate of patient better in group with MUC2 expression. Cumulative survival at 12 months after surgery was 1.0 and the median postoperative follow-up period was 17 months. The most aggressive behavior was PDA with expression only MUC1 ("true pancreatobilliary type"). Cumulative survival at 12 months after surgery was 0.25 and the median postoperative follow-up period was 7 months.
Conclusion: The mucin profile as a prognostic factor is important not only for intraductal pancreatic mucinous neoplasm, but and for ductal pancreatic adenocarcinoma.

PS-14-026
Hepatocellular carcinoma microvessels density depends on tumor differentiation: Radiologic-pathologic correlations
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Objective: Prognosis and recurrence level in hepatocellular carcinoma (HCC) depends on microvessels density.
Method: We performed CT and pathological correlations in 22 cases of HC (5 cases of highly (h-HCC), 11 cases of moderate (m-HCC) and 4 cases of low differentiated HCC (l-HCC)).
Results: Vessels number in w-HCC in compare to m-HCC was higher by 26.1 % ($p<0.05$). Total vessel area was higher in m-HCC and l-HCC than in w-HCC by 11.7 % and 20.4 % accordingly. We observed positive correlation between CT density of h-HCC and number and total vessel area. Correlation between h-HCC CT density and mean vessel area was negative. We also revealed modest negative correlation between m-HCC density and the number vessels in all phases of CT. Negative correlation between total and mean vessel area and m-HCC density was revealed in native and arterial CT phases in compare with venous and delayed phases where positive correlation was revealed. In all phases of CT we revealed strong negative correlation between l-HCC density and the number of vessels whereas correlation between l-HCC density and mean vessel area was strongly negative.
Conclusion: We revealed decreasing in angiogenic activity in HCCs neoplastic progression and growth. CT signs correlate with HCC histological differentiation.

PS-14-027
Primary sporadic liver schwannoma: An extremely rare diagnosis
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Objective: Primary liver schwannoma (PLS) is extremely rare.
Results: Case Report: A 69-year-old female with previous history of cholecystectomy, appendectomy, arterial hypertension and diabetes mellitus was admitted due to an intrahepatic nodular lesion identified in routine ultrasound examination. She was submitted to partial hepatectomy with postoperative uneventful evolution. Macroscopically, the specimen disclosed a 2.1 cm nodular, well circumscribed, yellowish tumour. Histologically, the tumour displayed an expansive growth pattern, comprising short bundles of spindle cells with mild atypia, without mitotic figures or necrosis. Immunohistochemically, the tumor cells expressed diffusely vimentin, S-100 and GFAP, in the absence of AE1/AE3, CAM5.2, CD117, and HMB45; Ki-67 index was 2 %. Staging procedures did not disclose evidence of any other tumor. There was no personal or family evidence of neurofibromatosis. These features are consistent with sporadic PLS.
Conclusion: Schwannoma is a rare benign tumour in the gastrointestinal tract with few cases reported in the liver. The clinical presentation is usually an upper abdominal pain but they can be asymptomatic. Secondary cystic degeneration and hemorrhage are common in large tumours. Differential diagnosis by imaging evaluation includes several benign and malignant, namely metastatic, tumours. Therefore, the pathological examination is crucial for the diagnosis of primary liver schwannoma.

PS-14-028
Metastases of hepatocellular carcinoma to the costa and soft tissue: A very rare entity
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Objective: Hepatocellular carcinoma (HCC) is the most common primary tumor of the liver with a potential of metastasis primarily to the lung, abdominal lymph nodes and bone. However, metastases to the costa, soft tissue are rare.
Method: An 82-year-old man was admitted to hospital with weakness, anorexia. Chest x-ray and CT-scan demonstrated a 5×5 cm sized, intrathoracic mass on the lateral-side of the left 2.costa and also infiltrating the axillary soft tissues.A secondary mass with the identical radiological features was also detected within the C7-vertebra. Whole-body CT-scan was planned.A 2×2 cm sized nodular, hipodense mass was detected in the upper segment of the liver. Interestingly, none of these masses demonstrated a significant pathological FDG-uptake in the PET.A trucut biopsy was taken from the axillar. Microscopically, large tumoral nests were observed in connective tissues. Polygonal shaped tumoral cells were found to have granular cytoplasm, pleomorphic nuclei. Immunohistochemistry results: Positive cytoplasmic reaction with Heppar, TTF-1; canalicular staining with Polyclonal-CEA, CD10; weak cytoplasmic staining with pankeratin, B72.3; Negative reaction with Vimentin, AFP, CK7, CK20.
Results: These histomorphological, immunohistochemical findings strongly supported to the diagnosis of HCC metastasis.
Conclusion: HCC that is, in general, morphologically similar to mesenchymal and epithelial tumors, should be considered among the differential diagnosis of unknown primary tumors.

PS-14-029
Morphological justfication of using pulsed electric discharge in surgical treatment of echinococcosis
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Objective: Echinococcosis is characterized by lesions of internal organs, severe complications, often lead to disability and death.
Method: New method of processing of the residual cavity with impulsive electric discharge after echinococcectomy was experimentally developed and introduced into clinical practice. The effectiveness of the method is confirmed by morphological examination of operational bioptic of the liver tissue.
Results: 20 patients underwent surgical treatment with the new method (Patent of the Republic of Kazakhstan ¹ 63558). Parasitic cysts with an inner germinal layer and protoskoleks, outdoor layer - chitinous shell with a productive reaction with lymphocytes infiltration, single eosinophils, separate groups of hydatid bubbles with their invasion in the liver tissue were detected in the histological examination of material taken intraoperatively prior processing of residual cavity with electropulse discharge. Fibrinoid necrosis, destruction of germinal elements, single lymphoid infiltration, hyperemia of blood vessels, absence o inflammatory reaction were marked in the histological material after processing by impulsive electric discharge.
Conclusion: The results showed that echinococcectomy with processing of the residual cavity with impulsive electric discharge is an alternative for pericystectomy and liver resection.

Tuesday, 11 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-15 Poster Session Paediatric and Perinatal Pathology

PS-15-001
Congenital peribronchial myofibroblastic tumor: Case report and review of the literature
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Objective: Congenital peribronchial myofibroblastic tumor is a rare, solid mesenchymal tumor of the fetus and neonate, usually associated with nonimmune hydrops fetalis. We report the case with clinical, radiological and pathologic findings and review the other cases in the English language literature.
Method: We present a case of CPMT, whom a right lung mass was detected in intrauterine life. 12 days after delivery by cesarean section, right lobectomy was performed.
Results: The tumor was limited to lung, and composed of spindle cells, proliferating around bronchial unit. Central necrosis and 4-5/10 hpf was present. Patient is well 15 months after surgery.
Conclusion: Congenital peribronchial myofibroblastic tumor is a rare solid pediatric tumor of lung which was named differently in the past, such as congenital fibrosarcoma, congenital leiomyosarcoma, congenital mesenchymal malformation of the lung, neonatal pulmonary hamartoma. albeit it resembles sarcoma with high cellularity, mitosis and necrosis features microscopically, no additional therapy to tumor resection is needed. So it is important to keep in mind this scary looking, but innocent tumor both in prenatal and postnatal evaluation.

PS-15-002
Morphologic alteration of metastatic neuroblastoma in bone marrow after chemotherapy
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Objective: The aims of our study are to evaluate the histologic features of metastatic neuroblastoma in bone marrow (BM) in comparison with those of primary neuroblastoma, and to compare the histologic characteristics of metastatic neuroblastoma in BM before vs. after chemotherapy.
Method: Total 92 biopsies from 19 children diagnosed as stage 4 neuroblastoma with BM metastasis were examined histologically; 19 primary neoplasm biopsies, 19 BM biopsies before chemotherapy, 19 primary neoplasm excision biopsies after chemotherapy, and 35 BM biopsies after chemotherapy.
Results: 1) Primary neoplasms were classified as neuroblastoma poorly differentiated (n=10), neuroblastoma differentiating (n=5), ganglioneuroblastoma intermixed (n=1) and neuroblastoma type unclassifiable (n=3). 2) Metastatic foci in BM before chemotherapy were composed of undifferentiated and/or differentiating neuroblasts but not ganglion cells, in neuropil but not schwannian stroma. 3) Metastatic foci of BM after chemotherapy showed differentiation such as ganglion cells and schwannian stroma, which was more prominent after more cycles of chemotherapy. 4) Metastatic neuroblastomas in BM after chemotherapy were as mature as or less mature than those in primary neuroblastomas after chemotherapy.
Conclusion: Metastatic neuroblastomas in BM initially consist of more immature components than primary neuroblastomas, whereas they become differentiated as primary neuroblastomas after multi-cycle chemotherapy.

PS-15-003
Morphometric evaluation and clinical correlations in malignant small round cell tumors
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Objective: Nuclear size increases in malignant tumors and reflects DNA content, ploidy and proliferation index. Present study investigated; could nuclear morphometery

differentiate histomorphologically similar paediatric malignant small round cell tumors in H & E stained sections for using in a poor resource country?
Method: Morphometric analysis was done in 26 confirmed but difficult to differentiate round cell tumors histomorphologically and were analyzed by cell images from 6 different areas in each section, using Leica Q win 500 images software.
Results: Nuclear measurements were obtained for retinoblastoma (9), Hodgkin lymphoma (6), Wilms tumor (3), medulloblastoma (2), Ewing's sarcoma (2), alveolar rhabdomyosarcoma (1), malignant hemangiopericytoma (1), non-Hodgkin lymphoma (1) and neuroblastoma (1). Amongst the retinoblastomas, maximum mean nuclear area percent (24.93) was seen in cases with nerve involvement and metastasis, followed by cases with only nerve involvement (21.60) and smallest area (16.57) was in non-nerve involving, non metastatic cases. Wilms tumor cases with metastasis had higher nuclear area (21.25) than non metastatic (19.47). Non-Hodgkin lymphoma nuclear area (20.03) was more than Hodgkin's (18.60). Amongst all tumors, minimum value (14.93) was seen in malignant hemangiopericytoma.
Conclusion: Morphometric evaluation in paediatric malignant round cell tumors have generated useful data, and needs further multicentric confirmation for implementation.

PS-15-004
Immunohistochemical expression of survivin in Wilms tumor
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*School of Medicine, Inst. of Pathology, Belgrade, Serbia

Objective: Survivin, a bifunctional protein that regulates cell division and suppresses apoptosis, may play an important role in tumorigenesis. The aim of this study was to determine survivin expression patterns in Wilms tumor (WT) and to analyze it in relation to stage, prognostic category and histological type.
Method: Immunohistochemical expression of survivin was analysed in 59 cases of primary WT and in 10 normal kidney specimens uninvolved by the tumor.
Results: Fifty one out of 59 cases of WT (86.44 %) showed decreased cytoplasmic survivin expression compared to the expression in normal kidney tissue. Decreased cytoplasmic expression (in all components of WT) of survivin was found significantly more often in low stage compared to high stage WTs (86.7 % vs. 27.3 %; p=0.002). Tumors of intermediate risk group showed more often decreased cytoplasmic expression of survivin in comparison to high risk group, but the difference was not significant. Decreased survivin expression was found more frequent in WTs with diffuse anaplasia and in epithelial WTs compared to other histological types, but without statistically significant difference.
Conclusion: Decreased survivin cytoplasmic expression may be associated with the favorable prognosis WT.

PS-15-006
Uncommon solid hepatic tumor in a fetus
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*Menzah, Tunisia

Objective: Hepatic tumors accounted 5 % of congenital neoplasms. Mesenchymal hamartoma of the liver is a rare benign tumor of children. We report a case of hepatic mesenchymal hamartoma in a premature male neonate.
Method: A premature neonate born at 33 gestational weeks from 34 year-old mother, G3P3 with non-consanguineous marriage; prenatal ultrasonography showed a fetal macrosomia, a highly vascularized abdominal mass occupying two-third of the abdomen and displacing the bowel loops associated with poly-hydramnios. The newborn examination showed abdominal firm lump. Ultrasound found and anterior highly vascularized mass displacing the left lobe of liver. The infant died few hours later. A complete autopsy was performed.
Results: External examination showed a male neonate anatomically of 34–35 week having an increased periombilical diameter and a macrosomia, ascitis, pulmonary hypoplasia, cardiomegaly, pleuropericardial effusion, liver tumor developed in left lobe and dilation of renal vessels. Histologically the tumor showed a mixture of normal liver tissues with blood or lymphatic vessels, bile ducts within an abundant edematous and myxoid stroma.
Conclusion: In neonate and fetus, prenatal diagnosis is possible by ultrasonography. Large tumors can affect the viability of the newborn. Adequate excision is curative in most of cases.

PS-15-007
NCAM polysialylation as potential initiator of differentiation and proliferation of renal progenitors in human fetal tissue
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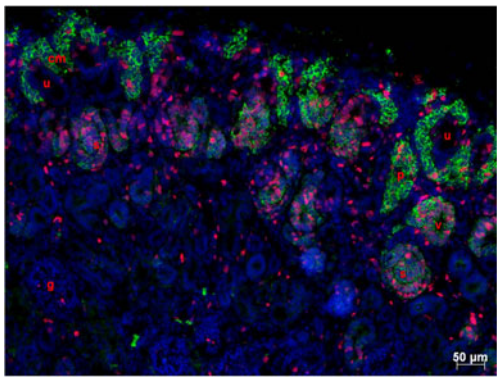
Objective: Objective: Neural cell adhesion molecule (NCAM) is widely expressed on mesenchymal and early tubular epithelial cells during kidney development although with still undefined function. NCAM can be polysialylated and as PSA-NCAM has been shown to be involved in proliferation and migration of neuronal cells during brain

development. The aim of this study was to evaluate the presence of PSA-NCAM in nephron precursors in relation to the expression of renal progenitor and proliferation markers.
Method: Human fetal and neonatal kidneys were analyzed using double-immunofluorescence (dIF) staining and Western Blot (WB) analysis. Specific antibodies against NCAM, PSA-NCAM, EpCAM, CD24 and Ki-67 were applied.
Results: On WB only fetal tissue samples have bands with NCAM at 140 to 250 kDa which suggest that NCAM molecule is polysialylated; dIF analysis of fetal tissue show PSA-NCAM + Ki-67+ cells in all structures known as nephron precursors. While in neonatal tissue PSA-NCAM and Ki-67 were positive only on rare single cells in intersticium.
Conclusion: PSA-NCAM expression appears to characterize a very early stage of induced nephron progenitors differentiating from NCAM + EpCAM- mesenchymal cells. According to PSA-NCAM localization and coexpression with Ki-67 during development and its practically absence in neonatal tissue, suggest that PSA-NCAM present potential initiator of proliferation and differentiation of renal progenitor.



PS-15-008
Autopsy findings in fetuses with cystic hygroma colli: A perinatal survey in a Greek University Hospital
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Objective: Cystic hygroma (CH) typically develops in utero, late in the first trimester to early in the second trimester of gestation. Many of the fetuses with CH present additional malformations commonly associated with chromosomal anomalies.
Method: A review of 548 fetal autopsies performed over a 10 year period revealed 19 cases of CH (3,4 %). The results of cytogenetic analysis and the prenatal ultrasound findings were retrieved and compared to the autopsy findings.
Results: Fetal death was due to therapeutic abortion in 9/19 cases, intrauterine death in 8/19 cases, and spontaneous abortion in 2/19 cases. Cytogenetic analysis was available in 12 cases. The results showed an abnormal karyotype in 7 cases (5 cases of Turner syndrome and 2 cases of trisomy 21). The mean size of CH was 5,4 cm. Other findings suggestive of the cause of fetal death were diagnosed in 10/19 cases (52,6 %). The most common autopsy findings were hydrops and central nervous system anomalies. The autopsy findings were in agreement with the prenatal ultrasound findings in 14/19 cases, while in 5 cases (26,3 %) additional findings were detected during autopsy.
Conclusion: Our study is confirms the strong correlation between CH and chromosomal anomalies of the fetus.

PS-15-009
Immunohistochemical expression of E-cadherin in primary and metastatic nephroblastoma cases
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Objective: In nephroblastoma cases association between decreased E-cadherin expression and higher stage of tumor (Safford SD, 2005) and lower expression in metastatic tumors (Alami J, 2003) was described. Some authors considered that E cadherin is not likely to play tumor suppressor role in nephroblastoma (Shulz S, 2000). Purpose of this study was to compare the expression of E-cadherin in metastatic and primary tumor cases in Latvia.
Method: 26 cases of primary tumors, 8 metastases and 1 case of relapse were analyzed immunohistochemically using visualization system EnVision. The number of E-cadherin positive structures per field was assessed (magnification× 100). Comparison between primary tumors and metastatic/relapse tumors groups was made using Mann–Whitney test.
Results: In primary tumor group the number of positive structures in the field ranged from 0 to 86, average 27.19, SD 24.13. In the metastatic tumor group, the number of positive structures varied from 0 to 40, average 9.89, SD 14.87. Comparison of expression observed in both primary and metastatic tumors groups showed the decreased E-cadherin expression in metastatic tumor group ($Z = -2.33$, $p = 0.046$).
Conclusion: Expression of E-cadherin is lower in metastatic tumor group that may suggest about negative correlation between it and higher tumor grade.

PS-15-010
Testicular fibrous hamartoma: A case report
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Objective: Fibrous Hamartoma (FH) of childhood is uncommon benign tumor. They are generally seen in the head

and neck region, gastrointestinal system and lung. As in the case we report, they may also occur in other unusual sites such as groin and testis. The clinical presentation is almost always a mass or swelling, however our case was admitted to our hospital because of a left testicular atrophy. We report a FH in the testis, which has a rarely location and clinical presentation.
Method: A 7-year-old male presented to department of pediatric surgery because of left testicular atrophy. Left orchiectomy was performed.
Results: In macroscopic examination, testis dimension was 1.5×1.3×0.4 cm. Its cut surface was smooth and dirty-white. In microscopic examination, the tumor showed disorganized matur tissue that composed of fibrocollagen stroma, vessels, muscular and adipose tissue. By this findings, it was diagnosed as testicular fibrous hamartoma (TFH).
Conclusion: In conclusion, TFH should be always kept in mind with testicular atrophy not only testicular mass or swelling. And knowledge of this particular type lesion is important to distinguish the FH of childhood from other situations in testis such as testicular torsion, incarcerated hernia, malign neoplasm, etc. in order to allow a correct diagnosis and avoid inadequate treatment.

PS-15-011
Placental pathologic features in diabetes and hypertension
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Objective: The aim of this study was to evaluate the most frequent placental findings in diabetes and hypertension and their main differences.
Method: Retrospective study of 229 selected placentas from 19 to 41 weeks gestation, in a universe of 3231 placentas examined over the last 10 years (6 % associated with hypertension, 1,5 % with diabetes and 0,4 % with both diabetes and hypertension (DwH).
Results: In diabetes the most frequently found abnormalities were immature villi (35 %) and infarction (27 %). In DwH the most frequent lesions were the immature villi (29 %) and inflammatory lesions (either acute or chronic) (29 %). In the hypertension group the most frequently found lesions were infarction (54 %) and accelerated maturation of the villi (23 %). In 35 % of placentas in diabetes, 21 % in DwH and only 15 % in hypertension, no lesions were found. The incidence of fetal death was 8 % in diabetes, 0 % in DwH and 5,5 % in hypertension. When evaluating placental weight, small placentas were more frequent in the hypertension group (37 %), and large placentas were more frequent in diabetes (27 %).
Conclusion: Our findings may contribute to evaluate the consequences of diabetes and hypertension in fetal outcome. As inflammatory conditions are usually not directly attributed to diabetes or hypertension, placental examination may help in diagnosis of associated pathology like infection.

PS-15-013
Placental villi morphometry in preeclampsia
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Objective: Terminal villi structure abnormalities could play an important role in preeclampsia (PE) and its complications development. Our aim was to perform comparative morphometric study of the placentas from mild and severe PE pregnancies.
Method: Complex morphological and morphometric study of 9 term placentas from mild PE (mPE) cases (1st group), 6 term placentas from severe PE (sPE) cases (2nd group) and 10 term placentas from uncomplicated pregnancies (control group) was performed.
Results: We revealed significant decreasing in terminal villi size in both preeclamptic groups in compare to control. This decreasing was much prominent in sPE group. We also observed significant terminal villi perimeter decreasing in both PE groups without any difference between mPE and sPE groups. Morphometry of CD31 stained specimens revealed significant decreasing in mean capillary number in both PE groups. Single capillary area and perimeter were significantly lower in mPE and sPE groups and these changes were much prominent in sPE group. Total villous capillary area and perimeter were significantly lower in both PE groups with minimal values in sPE group. Degree of villous capillarisation was significantly lower in both PE groups.
Conclusion: Revealed features reflect villous structure changes in preplacental hypoxia, caused by mild and severe preeclampsia.

PS-15-014
Sudden intrauterine death: The usefulness of autopsy
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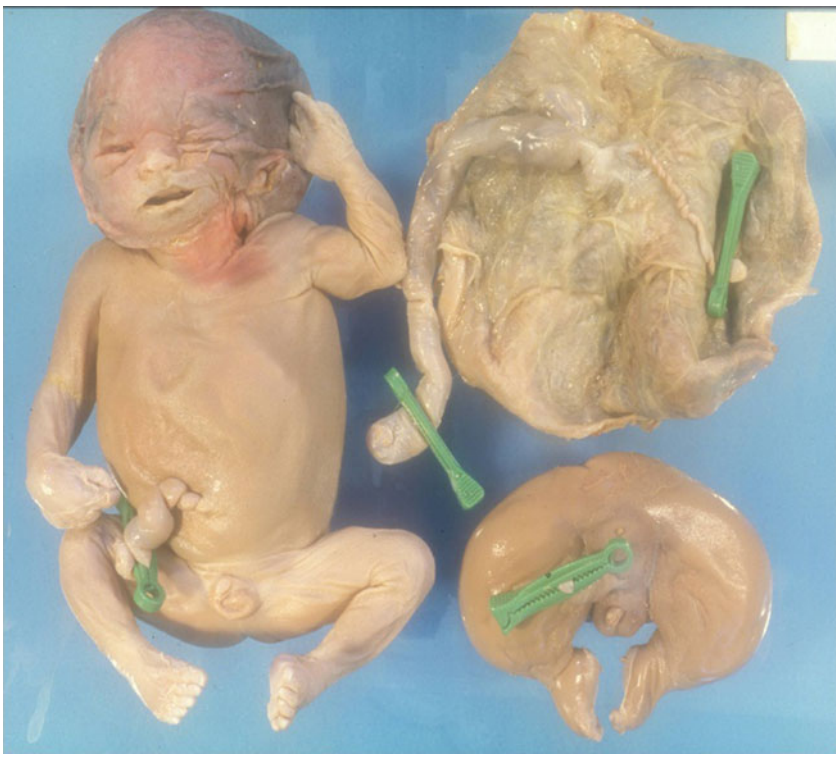
*University of Palermo, Section of Pathology, Italy

Objective: We investigated in 1006 autopsies of stillbirths the usefulness of autopsy even in the absence of risk factors and/or apparent anatomical/clinical causes which could explain the death.
Method: From January 1990 to December 2010 (Institute of Pathology, Paolo Giaccone- Palermo) 2643 autopsies on dead uterine foetuses were performed. 1637 cases were abortions (<25 weeks), 1006 were stillbirths (≥25 weeks). In all cases the autopsy included

a macroscopic and microscopic examination both of the foetus and the placenta. The final diagnosis of death was based on both the morphological and clinical data. Of the 1006 stillbirths, 715 cases were "risk factor pregnancies", 291 non.

Results: The stillbirth mortality was classified as follows: - Sudden Intrauterine Unexplained Death (SIUD,"-sine materia" and absence of risk factor autopsies),4 cases; - Explained Intrauterine Death ("cum materia" with or without risk factor autopsies),987 cases; - Borderline Intrauterine Death ("sine materia" and presence of risk factor autopsies),15 cases.

Conclusion: In the absence of autopsy in 715/1006 cases it was possible to establish the cause of death based on the presence of risk factors. In the absence of risk factors the autopsy showed a certain anatomical cause in 287/1006, only in 4/1006 it was "sine materia".



PS-15-015

The role of "traditional" and "tomography" autopsy in foetal Congenital Heart Disease (CHD)

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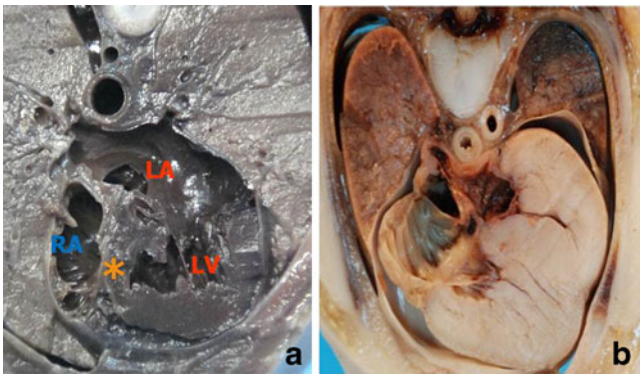
Objective: The role of systematic autopsy in foetal CHD is to identify the morphology of cardiac and possible associated extracardiac malformations (ECM) and the correlation between morphology, suspected clinical etiology and genetics. We evaluated the role of autopsy in 643 foetal CHDs with/without prenatal diagnosis.

Method: From January 1990 to December 2010 (Institute of Pathology, Paolo Giaccone – Palermo), 2371 foetal autopsies were performed. The autopsy protocol used was "tomography" for abortions, the "traditional" technique was adopted for stillbirths.

Results: In 643 cases CHDs were identified. In 196 cases CHD diagnosis was made only through autopsy, in 447 after a certain (244) or suspect (203) clinical/genetic diagnosis. The etiology of CHD associated to ECM (621) was: chromosomic type (271), syndromic/sequence type (233), association type (117). The etiology of CHD without ECM (22) was never syndromic.

Conclusion: "Traditional" and "tomography" autopsy plays a key role in the diagnosis and counselling of CHD, either when it represents the only diagnostic tool (30,48 %) or when it is preceded by a clinical/genetic study. In the latter cases, its value depends on the detection of ECM, useful to "consolidate" a suspect clinical diagnosis (31,57 %) and to

"complete" a malformative picture etiologically known thanks to a clinical/genetic analysis (37,9 %).



PS-15-016

Amplification of cyclin A gene in Wilms tumor

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Objective: Deregulation of cell cycle control is a hallmark of cancer. We have examined protein expression and gene amplification of cyclin A in Wilms tumor (WT) and to analyze it in relation to tumor stage, prognostic group and histological type.
Method: Real-Time Quantitative PCR was used to detect gene amplification of cyclin A in tumor tissue from 36 patients with WT, while immunohistochemistry was applied to detect protein expression of the same cyclin.
Results: Cyclin A gene amplification was found in 4 out of the 36 (11.8 %) cases of WT. Cyclin A protein overexpression was detected in all four cases, but was also found in 84.7 % of cases without detectable gene amplification. So, there was no significant correlation between cyclin A gene amplification and protein overexpression. All cases with amplification of cyclin A were of favorable histological type, intermediate risk group and three out of four cases were low stage WTs. On the other hand, overexpression of cyclin A was found significantly more often in high stage WTs compared to low stage WTs (p=0.04).
Conclusion: Cyclin A gene amplification might be associated with the favorable prognosis of WT (low stage, intermediate risk group and non-anaplastic tumors).

PS-15-017

Alveolar capillary dysplasia with misalignment of pulmonary veins: Pathological and molecular diagnosis

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Objective: Alveolar capillary dysplasia (ACD) with misalignment of pulmonary veins (MPV) is a rare cause of persistent pulmonary hypertension in newborns (PPHN). The gold standard to diagnose is lung biopsy or necropsy. Up to 40 % of cases have mutations or deletions in the gene FOXF1 (cr16q24.1) who plays a crucial role in the development of the lung vasculature.
Method: We report a case of a term newborn female affected of ACD/MPV who was diagnosed by a lung biopsy. She died at 38 days of life. Autopsy and molecular diagnosis were also performed
Results: In the biopsy and autopsy specimens a decline in the number of capillaries in the alveolar septa and detachment of the epithelial lining was observed. Secondary proximal plexiform arteriopathy, muscularization of arterioles and venous-venular dilatation and proliferation were evident. A pathogenic mutation in the gene FOXF1 (frame shift mutation in the first exon) confirmed our diagnosis.
Conclusion: ACD is defined by a decrease in capillaries with alveolar septal thickening and hypertrophy of the middle muscular layer of arterioles. MPV suggests an imbalance of angiogenesis. The FOXF1 mutation helps to prenatal diagnoses of high risk families and to give the diagnosis to patients who fail to perform biopsy or autopsy.

PS-15-018

Notch pathway activation in childhood rhabdomyosarcoma

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Objective: Prognosis of Rhabdomyosarcoma (RMS) has improved significantly over the last 20 years. Overall survival (OS) is>80 % in the majority of patients; even though, children with metastatic tumors have a dismal prognosis with an OS <30 %.
Method: We analyzed in 18 cases, the possible correlation of Notch activation with histology, presence of metastasis and outcome. Immunohistochemistry (IHC) was performed for the Notch downstream effectors Hes1 and Hey1.
Results: Hes 1 was strong or moderate in 95 % of the cases. Hey1 was positive in 50 %. 3 out of 4 alveolar RMS (aRMS) were positive for Hes1 and 1 was positive for Hey1. Both stains were negative in the fusion-negative aRMS. In embryonal RMS (eRMS), eight out the 9 were Hey1 positive and 14 of the 17 were Hes1 positive. The 2 patients whit metastases had staining for Hes1 and Hey1. 3 patients who died showed Hes1(+). 14 of the 15 patients in remission showed positivity for Hes1 and 7 for Hey1.
Conclusion: Hes1 expression was found in the majority of RMS while Hey1 was more eRMS specific. Is no correlation between pathway activation, metastasis or outcome. The blockage of the pathway with specific inhibitors could offer a new therapeutic option for this patients.

PS-15-019

A renal epithelioid angiomyolipoma in a young woman with tuberous sclerosis complex, cortical tubers by neuroimaging, facial angiofribromas and lung lymphangioleiomyomatosis

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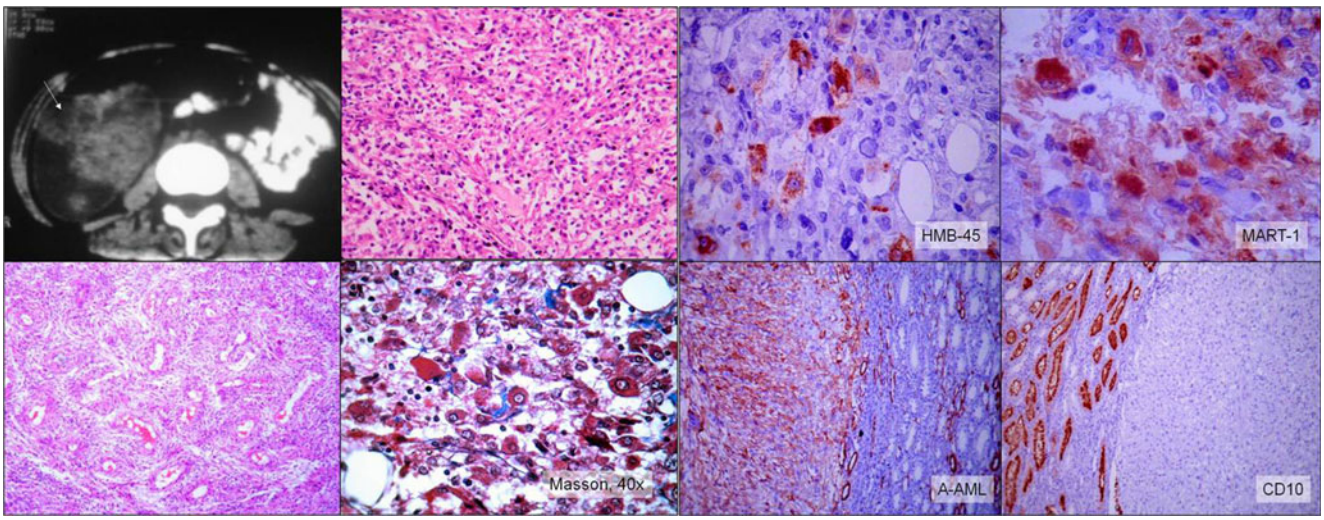
Objective: Tuberous sclerosis (TS) is a genetic disorder affecting cellular differentiation and proliferation, which results in hamartoma formation in many organs like skin, brain, lung, kidney and heart.
Method: A seventeen-year-old female with history of facial angiofibromas a 10 years before, right renal tumor diagnosed a year before as theratoid-rhabdoid tumor, with chemoradiation as adjuvant treatment, cortical tubers by neuroimaging a few months before, and diagnosis of lung lymphangioleiomyomatosis recently. After last diagnostics, we reviewed again the renal tumor, new orientation of tissue, with new histological sections were performed. (Fig)
Results: At histological examination, the kidney showed an infiltrating tumor, very cellular, consisting mainly of polygonal cells with eosinophilic cytoplasm, other multinucleated similar to the ganglion cells, also small hamartomatous areas with smooth muscle, fat and blood vessels proliferation. The tumor cells expressed HMB45, MART-1, SMA, VIM and CD10, CKAE1/3 were negative. (Fig)
Conclusion: The majority of renal angiomyolipomas is sporadic and 50 to 80 % occurs as part of TS, and their partnership is more close with epithelioid variant, recently, a rare entity with aggressive behavior, difficult histological characterization and poor prognosis.



PS-15-020

Pulmonary mast cells in sudden infant death syndrome (SIDS)

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Objective: Several theories of the underlying mechanisms of SIDS have been proposed, one of them is focusing on shock including anaphylaxis. Increased concentrations of mast cell tryptase in post mortem blood have been observed without increased mast cell numbers in lung tissue. The aim was to evaluate the age-related distribution of pulmonary mast cells in infants dying of sudden infant death syndrome and controls.
Method: 6 infants (up to 1 year of age) who died of SIDS and 23 controls who died of other non-pulmonary causes were examined. Peribronchial mast cells exhibiting tryptase immunoreactivity were evaluated and quantified in high power fields in lung sections.
Results: The number of mast cells in peribronchial regions amounted to 18,9 (± 6,6)/mm2 in children aged 1 month up to 13 months. Mast cells in SIDS cases were 21,2 (± 4,5)/mm2. The difference was not significant (P=0,113, Student's t test).
Conclusion: It is unlikely that increased pulmonary mast cells are indicators of SIDS. The role of mast cells in SIDS remains controversial.

PS-15-021

Trophoblast apoptosis in placentas from pregnancies complicated by preeclampsia

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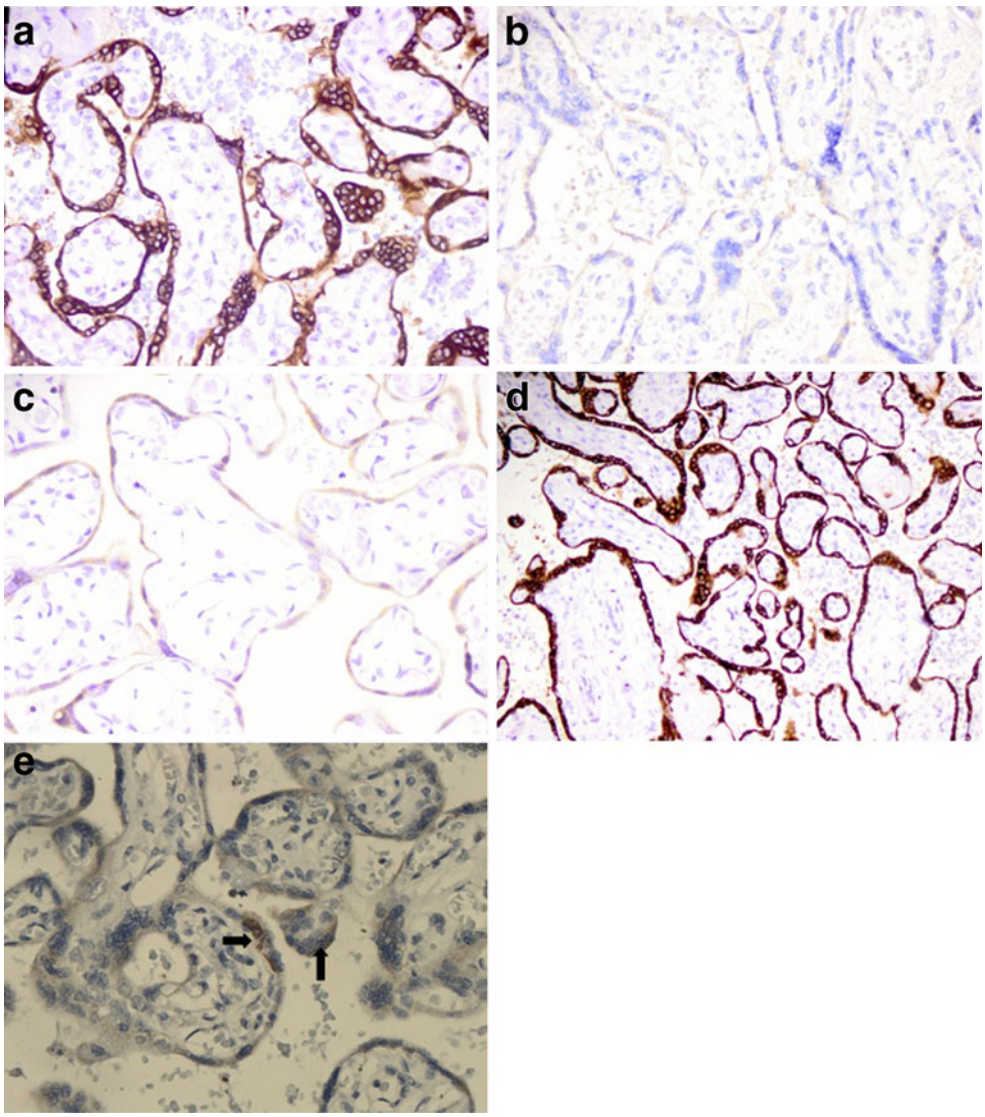
Objective: To assess trophoblast apoptosis separately in cytotrophoblast, syncytiotrophoblast, total villous trophoblast and syncytial knots, as well as to investigate the expression of apoptotic factors Fas ligand (FasL), Bcl-2 and proliferation marker Ki-67 in trophoblast of placentas from preeclamptic patients.
Method: The study included placental samples from 25 preeclamptic and 25 normal pregnancies. For the detection of apoptosis and proliferation antibody M30 and antibody against Ki-67 antigen were used. Expression of Fas ligand and Bcl-2 was assessed using semi quantitative HSCORE method. Syncytial knots were expressed as the number of syncytial knots per individual villus and as the total number of syncytial knots in each placental sample.
Results: apoptosis in all stages of trophoblast differentiation, number of syncytial knots per individual villus and the total number of syncytial knots were significantly higher in preeclamptic placentas than in control group placentas. Fas ligand expression was significantly less, and Bcl-2 expression significantly greater in the villus trophoblast among the study subjects compared with controls. There was no difference in the trophoblast proliferation between groups.
Conclusion: our findings might suggests that increased apoptosis and syncytial knots formation combined with reduced Fas ligand expression could be involved in pathophysiological mechanisms of preeclampsia.



PS-15-022

Contribution of fetal autopsy for diagnosis of Meckel-Gruber Syndrome

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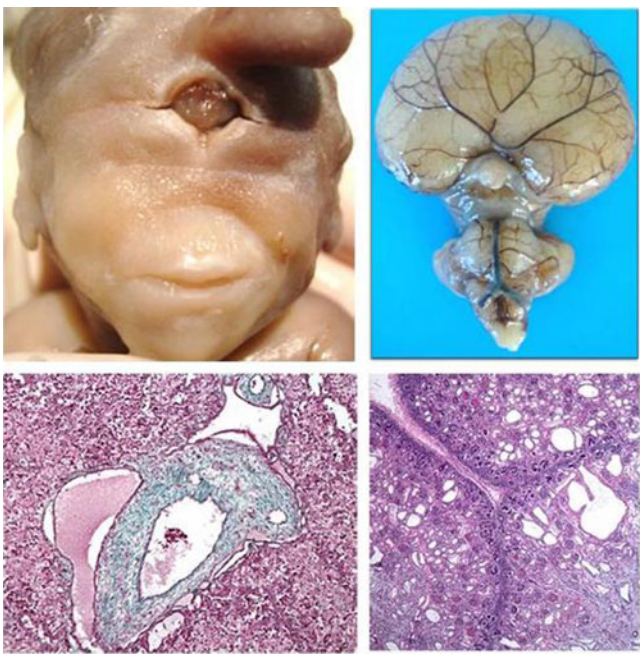
Objective: Meckel-Gruber Syndrome (MGS) is a lethal rare autosomal recessive malformation. The six implicated genes encode proteins involved in primary cilia function. Groups of families in Finland, India and North of Africa have been identified.
Method: A fetus,46 XY, karyotype, therapeutically aborted at 21 weeks with alobar holoprosencephaly in ultrasound. Fetal autopsy was performed. Genetic counseling was proposed to the family revealing Moroccan origin and consanguinity, the parents were first cousins.
Results: A male fetus showing cyclopia, proboscis and a single opening with two rudimentary eyes was the external morphology. Histological examination confirmed holoprosencephaly and also showed bilateral corticomedullary renal multicystic and periportal hepatic fibrosis with bile duct dilatation. The main diagnosis was MGS although other ciliophaties and non-ciliopathies conditions were considered, such as Bardet-Bield, Joubert, Smith-Lemli-Opitz syndrome and trisomy 13. However, the pathological characterization, parent's consanguinity and their North African origin makes MGS the likely diagnosis.A genetic study on paraffin-embedded material was requested, the poor quality of DNA stopped definitive genetic diagnosis.
Conclusion: The pathologist may encounter atypical cases that require morphologic diagnosis to determine the type of underlying mutation and provide genetic counseling to parents.A meticulous autopsy is necessary to establish the diagnosis of MGS. Fresh material would have to be frozen in order to make current diagnostic techniques of molecular pathology.



PS-15-023

Mesenteric cysts in the pediatric age group

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Objective: Mesenteric cysts are extremely rare lesions arising with an incidence of 1/20,000 admissions in children. Clinically, mesenteric cysts are generally comprehended as a unique diagnostic entity, although they exhibit histological diversity. The objective of this study was to determine the incidence and the histology of the mesenteric cysts in the pediatric age.
Method: All cases of mesenteric cysts operated at the University Children's Hospital Belgrade over the 10-year period of 2002 to 2011 were reviewed using pathology reports from the files of the Institute of Pathology. Histological slides were re-examined and immunohistochemistry was applied, when necessary.
Results: A total of 27 cases of mesenteric cysts were identified. Cysts of lymphatic origin (cystic lymphangiomas) were recorded in 12 patients (44 %), cysts of enteric origin - in 14 patients (52 %): 13 duplication cysts and one isolated enteric cyst of the mesenterium. Only one example of the cyst of mesothelial origin, i.e. benign cystic mesothelioma was diagnosed (4 %). The most frequent site was mesenterium and mesocolon (86 %), followed by omentum (7 %) and the retroperitoneum (7 %).
Conclusion: Cysts of enteric origin are easily recognized. It is important to differentiate between cystic lymphangioma and cystic mesothelioma due to their different natural history.

Tuesday, 11 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-16 Poster Session Soft Tissue Pathology

PS-16-001

Myxoid liposarcoma of the breast

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Objective: Myxoid liposarcoma belongs to the group of soft tissue sarcomas with lipomatous differentiation. Breast is a rarely affected (only 0.3 % of breast sarcomas), and often misdiagnosed.
Method: A 67-years old woman presented with a painful timorous lump of the left breast. Mammography showed oval, lobulated lesion between medial quadrants, while ultrasonography revealed hipoechogenic, inhomogeneous nodule. Patient underwent core biopsy which was histologicaly inconclusive and followed by quadrantectomy with excision of both medial quadrants.

Results: A lump (6 cm) was visible on the skin surface. Serial sectioning revealed solid gray–white tumor with cystic and prominent necrotic areas. The tumor was located in the deep mammary tissue an it infiltrated the overlying dermis without involving the epidermis. It consisted of atypical stelate and spindle cells with infrequent mitoses and low Ki-67 proliferative index. On the periphery mature adipocytes and lipoblasts were present. Stroma was abundant, myxoid with plexiform capillary pattern. The myxoid substance stained slightly Alcian-blue positive and tumor cells showed cytoplasmic immunopositivity for S100. Phyllodes tumor was excluded because of absence of epithelial component.
Conclusion: Myxoid liposarcoma has a distinct morphology, rarely confused with other soft tissue tumors, although on cytological smears or biopsy samples it may be unrecognized.

PS-16-002
INI-1 and TLE-1 expression in five synovial sarcomas diagnosed by fluorscent in situ hybridization
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Objective: Synovial sarcoma poses a difficult diagnostic challenge since it can be confused with other benign or malignant entities.
Method: Four biphasic and one monophasic synovial sarcomas were studied. We used the break apart/split signal kit (VYSIS) to detect the t(X;18) translocation and we performed immunohistochemistry for TLE-1, INI-1, D2-40, CD56, CD99, bcl-2, EMA, CK7, CD34, S-100, Desmin and Claudin-1.
Results: Immunohistochemically we observed: TLE-1+(5/5), INI-1 (4/5) with reduced nuclear and (1/5) with no expression, D2-40+(1/5), CD56+(5/5), CD99+(5/5), bcl-2+(5/5), EMA focal expression (5/5), CK7−(5/5), CD34−(5/5), S-100−(5/5), Desmin−(5/5), Claudin-1+(5/5). FISH revealed the split signal between the centromeric and telomeric end of the SYT gene.
Conclusion: t(X;18) translocation remains the diagnostic hallmark of synovial sarcoma. INI-1 which is typically negative in atypical teratoid/rhabdoid tumor, epithelioid sarcoma and myoepithelial carcinoma seems to be reduced or even negative in synovial sarcomas. The focal expression of D2-40 must be considered when the differential diagnosis includes mesothelioma. Finally TLE-1 is a very sensitive marker for synovial sarcoma.

PS-16-004
"Mixed aneurysmal bone cyst" and "simple bone cyst", represent a different group of cystic lesion
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Objective: There are some mixed cysts (MC) with overlapping histological features of aneurysmal bone cyst (ABC) and simple bone cysts (SBC).
Method: We reviewed 69 pure ABC, 40 SBC and 23 "Mixed Cysts (MC)", and compared them by nonparametric tests.
Results: MCs, mainly showed two paterns as "Type 1: SBC with secondary ABC foci (n=18)"and "Type 2: Cysts with fully developed SBC and ABC areas (n=5)". The median age for ABC, SBC, and MC were 16±18.2 (range: 3–53), 21±13.7 (range: 3–54) and 9±11.47 years old (range: 3–50) respectively. MCs were more frequent in males than ABC and SBC (p=0.017) and the most frequently involved bones were humerus-femur-pelvic bones in descending order (p= 0,021). "Type 1 MC" showed more frequent cementum-like amorph material (p<0.001), ectatic venules (p=0.040), calcifications (p=0.044), less cholesterol deposition, necrosis and no different fracture and osteoid matrix when compared with Type 2 MCs and SBCs.
Conclusion: Cysts with overlapping features of ABC and SBC are not uncommon. Though they usually represent "SBCs with secondary ABC component", they have dissimilarites with ordinary SBCs which needs to be further clarified with larger series.

PS-16-005
Pitfalls in evaluating neoadjuvant chemotherapy response in bone resection specimens
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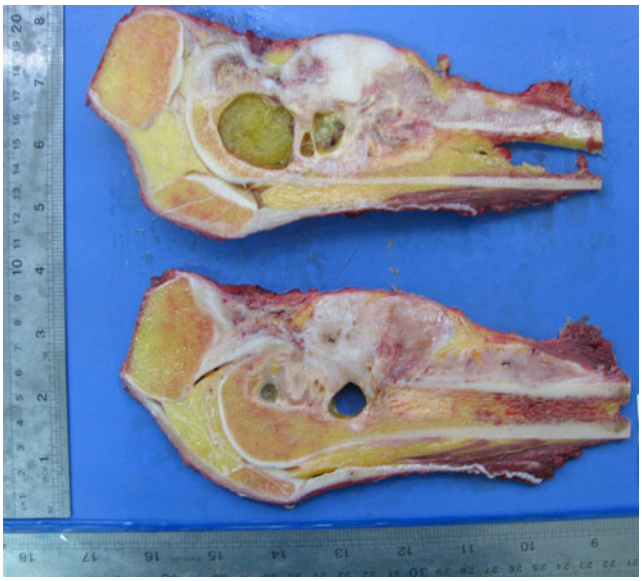
Objective: Percent of tumor necrosis after neoadjuvant chemotherapy, determined by detailed specimen mapping, has a high prognostic value. However both the mapping and grading systems has some practical problems.
Method: 128 cases were reviewed for potential pitfalls in handling and reporting processes and correlated with radiological findings by nonparametric-tests.
Results: Most of the tumors were osteosarcoma (74.2 %) and Ewing Sarcoma (16.4 %), located in femur (53 %), tibia (22,7 %) and humerus (10.2 %). Cortex, soft tissue and joint invasion was observed in 94 %, 77.6 % and 30.3 % of the cases, respectively. A median of 27.5 tumor blocks (9–74± 14,64) were submitted for histology. Tumors were totally necrotic in 30 cases (24 %) (Huvos Grade-HG-IV), HG III in 20.3 %, HG II in 28.1 % and HG I in 24.2 % of the cases. Overall good (HG III-IV) and poor responders (HG I-II) correlated well with radiological findings (p<0.001). Discrepant cases showed extensive oedema and congestion enhancing contrast medium, patchy necrosis unabling accurate histologic evalation, or failure to prove tibiofibuler joint involvement because of sagittal sectioning (p<0.05).

Conclusion: Evaluating chemotherapy responce is a laborious work. Radiologic orientation prior to grossing and applying morphometric technics may enhance more accurate evaluation.



PS-16-006

Atypical Ewing sarcoma/Primitive neuroectodermal tumor with unusual melanocytic differentiation – A case report

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Objective: Atypical Ewing sarcoma/primitive neuroectodermal tumor with the melanocytic differentiation is a very rare, malignant tumor which occurs in infants and adolescents. It is localized mainly in soft tissues. Its biological behavior is aggressive, but its response to the chemotherapy is prognostically good.
Method: A 4-month old male is presented with the 17×11 cm tumor of the soft tissue, localized in the right front over the cranial margin of the orbit. The tumor was surgically exstirpated and then sent to the histological investigation with the additional immunohistochemistry and the FISH.
Results: Microscopically, the tumor is hypercelullar and consisted of oval to polygonal cells with the vesicular nuclei, the prominent nuclei and the amphophilic cytoplasm. In other parts of the tumor, there are smaller neoplastic cells with hyperchromatic nuclei. Some neoplastic cells contain the melanin pigment in the cytoplasm, which was positive in Fontana-Masson method. The immunohistochemical stains for vimentin, AE1/3, CK7, CD99, HMB-45, FLI-1 were positive. The FISH investigation demonstrated the translocations (t 11;22, q24;q12) in 95 % of neoplastic cells and (t 21;22, q12;12) of 5 % ones.
Conclusion: In literature, the Ewing sarcoma/PNET showing the myogennic differentiation is usual, but the melanocytic differentiation is rare and can be confirmed not only immunohistochemically, but also by FISH investigation.

PS-16-007

Expresion of poly(ADP-ribose) polymerase-1 protein in neoplasms and its importance in their biological behavior

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Objective: Poly(ADP-ribose) polymerase-1 (PARP-1) is a nuclear enzyme involved in the repair of DNA single-strand breaks. PARP-1 inhibitors may be efficient in therapy of malignancies. This report evaluates the expression of PARP-1 in primary testicular germ cell tumors and correlates expression patterns with histological subtypes and patient/tumor characteristics.
Method: Group of 124 patients with testicular germ cell tumors were investigated for PARP-1 expression by immunohistochemistry, scored by the multiplicative quickscore (QS) method and compared to PARP-1 expression in normal testis.
Results: We observed higher expression of PARP1 in testicular tumors compared to normal testis (mean QS=10.04 vs. 3.60, $p<$ 0.0000001). The PARP-1 overexpression (QS>9) was most often detected in intratubular germ cell neoplasia ITGCN (100 % of specimen with PARP-1 overexpression), compared to 1.9 % of normal testicular tissue specimen. There was no association between PARP-1 expression and clinical variables.
Conclusion: PARP-1 expression is higher in tumor tissue than in normal testis. PARP-1 could represent a novel treatment target in TGCTs and the assessment of PARP-1 expression in tumor samples may lead to the consideration of TGCTs patients for PARP inhibitor therapy. Supported by 2007/30-NOU-01, VEGA 1/0724/11 and ITMS: 26240220052 cofinanced by European Regional Development Fund.

PS-16-008

Gardner fibroma - implications of a diagnosis

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Objective: Gardner fibroma (GAF), a rare lesion, typically occurs in infants, children and young adults, with predilection for the trunk (particularly paraspinal region) and no gender predominance. GAF is an ill-defined plaque-like

mass, with rubbery consistence, usually asymptomatic, ranging from 0.3 to 12 cm. Although benign, 70–90 % of the cases may be associated with APC mutations, familial adenomatous polyposis (FAP) and/or Gardner Syndrome (GS). We report 2 cases of GAF, which allowed the identification of 2 families with GS.
Results: CASE 1: 7-month-old boy, with 2 nodules in the left paraspinal region, the largest with 2.5 cm. CASE 2: 5-month-old boy, presenting a 1.5 cm ill-defined deep right scapular mass. Both lesions were infiltrative, paucicelular densely collagenized proliferations of bland spindle cells. A GAF diagnosis was made and clinical/genetic investigation advised. APC gene sequentiation revealed, in both cases, a frameshift germline mutation in exon 15. Additionally, case 1 presented a del(5)(q11q35). Heredogram showed typical manifestations of GS: CASE 1: Mandibular osteomas, epidermoid cysts, "soft-tissue tumours", colo-rectal carcinoma. CASE 2: Hepatoblastoma, colo-rectal carcinoma.
Conclusion: Given the high association with GS and the fact that it can be its first manifestation, GAF is considered a sentinel lesion for this syndrome. Therefore, an accurate diagnosis is of the utmost importance.

PS-16-009

Prognostic significance of bcl-2, c-myc and survivin in synovial sarcoma

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Objective: In this study, we evaluated 81 synovial sarcoma cases, who had been referred to our tertiary tumor center during the last 20 years. We applied bcl-2, c-myc and survivin as immunohistochemical markers and evaluated the relation with conventional prognostic findings and prognosis for those 64 patients who have follow-up.
Method: In this study; ten-year tumor free survival rate was 38 % reflecting the agressive behaviour of synovial sarcoma. Tumor grade was the most valuable prognostic input. Progression free survival (PFS) was 159 months for gradeII cases (40 cases) and 36 months for gradeIII cases (24 cases) (p=0,000).
Results: Immunohistochemically, there was weak relation between bcl-2 staining intensity with prognosis. Overall survival was 211 months for weak or negative cases (9cases), 132 months for focally intense cases (21cases) and 101 months for diffuse and intense cases (34 cases) (p= 0,042). There was also weak relation with c-myc staining pattern with prognosis. Overall survival was 193 months for c-myc negative cases (25cases), 114 months for cytoplasmic positive cases (23cases) and 68 months for nuclear positive cases (16 cases) (p=0,043). There was no relation between survivin and prognosis.
Conclusion: In conclusion; tumor grade is the most valuable prognostic parameter in synovial sarcomas. Immunohistochemically c-myc and bcl-2 staining have weak relation with synovial sarcoma prognosis.

PS-16-011

Immunohistichemical profile of primary and recurrent desmoids

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Objective: Desmoids is a locally recurrent and invasive but not metastatic tumor. Our aim was to study immunohistochemical profile of primary and recurrent desmoids.
Method: Complex morphological study of 16 abdominal desmoids. All the tumors were divided into 3 groups: primary, first recurrent and second and more recurrent cases. We used antibodies against β-cathenin, COX-2, APC, survivin and Ki-67 for immunohistochemical study.
Results: Nuclear and cytoplasmic β-cathenin expression levels were significantly higher in recurrent than in primary desmoids. APC cytoplasmic expression level was also significantly higher in recurrent tumors. We revealed only cytoplasmic COX-2 expression in desmoids, and its level was significantly higher in recurrent tumors with the activity increasing accordingly to the number of recurrences. Survivin expressed both in nuclei and cytoplasm of the tumor cells and its expression levels were significantly lower in recurrent desmoids.
Conclusion: Revealed immunohistochemical properties of primary and recurrent desmoids reflect tumor transformation and progression and could be used as additional prognostic markers in this disease.

PS-16-012

Chemokine expression in a xenograft model of human sarcomas

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Objective: Many bone and soft tissue sarcomas (BSTS) are aggressive tumors with fatal prognosis. The importance of angiogenesis for the growth and progression of solid BSTS is now well recognized. A variety of chemokines have been described that either promote (angiogenic) or inhibit (angiostatic) angiogenesis. The aim of this study is to characterize the expression profile of some chemokines in a series of xenotransplanted human BSTS.
Method: One Ewing sarcoma (ES), 1 grade 3 chondrosarcoma (Chs), 1 osteosarcoma (Os), 1 synovial sarcoma (SS), 1 fibrosarcoma and 1 gastrointestinal stromal tumor (GIST)

were xenotransplanted into the backs of nude mice (athymic Balb-c nude mice). When the tumor size reached the 3 cm, animals were sacrificed and tumors analyzed for the expression of CXCL1/2/3, CXCL9 and CXCL10, using two-color staining fluorescence on each slide under a confocal microscope (Olympus FV1000).
Results: We observed that angiostatic chemokines (CXCL9 and CXCL10) presented higher expression than angiogenic (CXCL1/2/3) chemokines in ES, grade 3 Chs, Os and GIST whereas fibrosarcoma and SS were more positive for angiogenic chemokines.
Conclusion: The expression profile of angiostatic and angiogenic chemokines depends on the type of BSTS and could be related to their different biological behaviour. Other elements such as angiogenic or pro-inflammatory markers should also be considered.

PS-16-013
Predictive diagnostics of rhabdomyosarcomas
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Objective: The wide range of differential diagnostic possibilities of rhabdomyosarcomas (RMS) shows the need for more specific and sensitive markers. Low survival rates of high risk RMS patients require new prospective therapeutic targets.
Method: Archival material FFPE samples of 15 RMS (12 embryonal -eRMS, 3 alveolar -aRMS) and non-RMS soft tissue tumors were evaluated by immunohistochemistry for myogenin, MyoD1, EGFR, VEGF, COX-2, p-Akt and p-mTOR expression. The presence of PAX3/7-FKHR forming translocations, myogenin, MyoD1, gamma subunit of fetal acetylcholine receptor (AChR) and K-RAS mutational state were determined by RT-PCR.
Results: 10/12 eRMS and 3/3 aRMS showed expression of myogenin, MyoD1 and gamma AChR. Non-RMS tumors were negative. Translocations were only found in aRMS. EGFR expression was characteristic for eRMS, without the presence of activating K-RAS mutation. Strong expression of VEGF was detected in all samples. p-AKT and p-mTOR showed overlapping expressions in 86,7 % RMS. In most of the samples weak COX-2 positivity was demonstrated.
Conclusion: Myogenin, MyoD1 and the fetal AChR are specific and sensitive diagnostic markers of RMS. RMS subtypes are identifiable by PAX3/7-FKHR detection and probably EGFR expression. The results indicate VEGF, EGFR, COX-2 and Akt-mTOR pathway directed therapy to be considered in RMS. Supported by ITMS 26240220052.

PS-16-014
Immunohistochemical analysis of potential targets in desmoid tumor therapy
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Objective: Desmoid tumors (DTs) are clonal fibroblastic/myofibroblastic proliferations. Although histologically benign, desmoids are locally invasive and often have an unpredictable clinical course. DTs are infrequent lesions, but they have a high incidence in patients with familial adenomatous polyposis (FAP). The treatment of DTs needs to be individualized.
Method: To explore the molecular bases of potential pharmacologic targets in DTs we evaluated the immunohistochemical expression of steroid hormone receptors (ERa, ERb, PR) and COX-2 protein in sporadic (n=6) and FAP-associated desmoid tumors (n=9) together with GI adenomas of FAP patients (n=5).
Results: Nuclear ERb expression was found in 14/15 DTs. All adenoma samples showed nuclear ERb positivity, which was weaker than in the surrounding normal epithelial cell. ERa and PR expression were lacking in all samples. COX-2 was found in 14/15 DTs. Adenomatous polyps showed intense COX-2 expression compared to surrounding normal mucosa.
Conclusion: High incidence of ERb positivity in DTs supports the usage of hormonal therapy in these lesions. Open question is the effect of anti-estrogen therapy in DT patients with adenomatous polyps, as in adenomas estrogen seems to have preventive potential. COX-2 expression suggests the benefit of anti-inflammatory treatment in DTs adenomatous polyps. Supported by ITMS: 26240220052.

PS-16-015
Retroperitoneal sarcomas: Clinicopathological features in a series of 68 cases
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Objective: Retroperitoneum is the less common site of origin accounting for approximately 10 % of soft tissue sarcomas.
Method: Between January 1990 and December 2010, our hospital's records of 68 patients with retroperitoneal sarcomas were retrospectively studied.

Results: The patient median age was 57 years and there was no sex predominance. Median tumor size was 18.5 cm (ranging from 6 to 55 cm) with 60 % of them being larger than 10 cm. The most common histological type was liposarcoma (36/68–52,9 %), followed by leiomyosarcoma (16/68–23,5 %) and undifferentiated soft tissue sarcoma (7/68–10,2 %). The remaining 9 tumors (13,2 %) included 2 chondrosarcomas, 2 well-differentiated fibrosarcomas, 1 PEComa, 1 hemangiopericytoma, 1 Ewing sarcoma and 1 malignant peripheral nerve sheath tumor. 44 of the sarcomas were high grade (65 %) and 24 (35 %) low grade. 1-year recurrence rate was 34,3 %. The 3- and 5-year overall survival rates were 56,2 % and 53,1 % respectively. Seven patients received adjuvant chemotherapy.
Conclusion: The most commonly encountered histologic subtypes are liposarcoma and leiomyosarcoma, which are consistent with the results of the present study. Complete tumor resection at first operation is the only treatment factor that consistently predicts improved survival.

PS-16-016
Abdominal desmoid tumor
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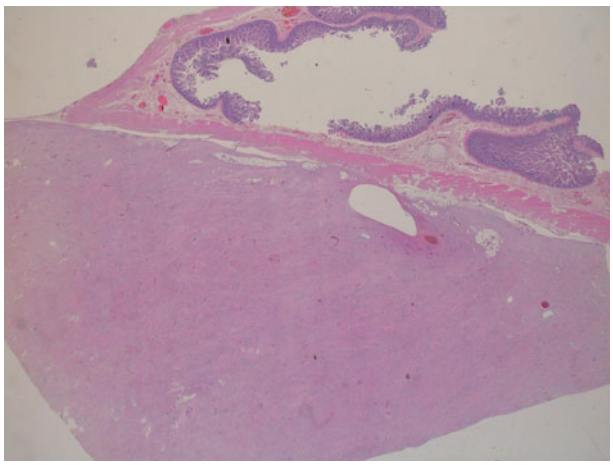
Objective: Abdominal desmoid tumours are rare benign neoplasms. They are commonly found in the mesentery, while they are rarely found in the intestinal wall. Most cases are sporadic, although there is a link with colonic polyposis, trauma, and oestrogen. They predominate in 25–35 year-old women. This present case is notable due to its location in the jejunal wall, possible relation with previous surgery, and the age and sex of the patient.
Method: We present a 51-year-old male patient previously operated for umbilical hernia years before. He came to the consultation on noticing an abdominal mass. Since the initial suspicion was of jejunal wall GIST tumour, surgery was performed.
Results: The histopathological and immunohistochemical findings, support the diagnosis of desmoid tumour.
Conclusion: Desmoid tumours consist of fibroblastic monoclonal proliferation developed from aponeurotic muscle structures. Some authors consider them non-neoplastic processes given their limited aggressiveness while others classify them within distinct low-grade sarcomas. Their origin is not well established, although there are known factors involved such as mutations in the APC gene or beta-catenin and trisomy 20 and 8. The originating cell, the myofibroblast, is involved in post-traumatic cellular regeneration. This explains why we find these tumours associated with previous surgery.



PS-16-017
Treatment of advanced dermatofibrosarcoma protuberans with imatinib mesylate with or without surgical resection
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Objective: Dermatofibrosarcoma protuberans (DFSP) is a rare soft tissue sarcoma of the skin characterized by the presence of specific COL1A1-PDGFB fusion protein, which appears as a consequence of the t(17;22) (q22;q13) translocation.
Method: The aim of the study was to perform an analysis of patients with advanced DFSP treated with imatinib, with or without surgery. We examined 15 patients (6 male, 9 female; median age 56 years) with locally advanced/initially inoperable and/or metastatic DFSP treated with imatinib 400–800 mg daily between 12/2004 and 06/2009. All diagnoses were ascertained cytogenetically (fluorescent in situ hybridization). Median follow-up time was 16 months (range: 4–81).
Results: Metastases were present in 8 cases (two lungs, two soft tissue, two lymph nodes). Fibrosarcomatous transformation was confirmed in 7 patients. After treatment with imatinib overall responses were: 10 partial responses, 2 stable diseases (13 %) and 3 progressive diseases (20 %). Seven patients (47 %) after resection had residual disease confirmed by pathologic examination and remained free of disease.
Conclusion: We proved that anti-tumour effect of imatinib in DFSP with presence t(17;22) had in most cases good responses. Imatinib therapy may in some cases leads to tumour resection because of lesser size.

PS-16-018

Clinicopathologic features of osteosarcoma in Turkish population: A 10 year report of 745 cases

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Objective: At an estimated incidence of 2 cases per million per year, osteosarcoma is the most common malignant primary bone tumor.
Method: We conducted a retrospective study to identify the osteosarcoma cases diagnosed at major tertiary care hospitals in Turkey.
Results: Our study group was made up of 745 cases: 440 men, 305 women, aged 3–82 years (mean 23.7 year). All patients had been diagnosed with skeletal osteosarcoma between 2001 and 2011 at one of the 10 tertiary care referral center. Tumor was most frequently located in femur (50.4 %) followed by tibia. Apart from the long bones, pelvic and gnatic bones were the next in location, 4.4 % and 1.6 % respectively. There were 16 (2.1 %) secondary osteosarcomas, related to previous irradiation and various underlying diseases. For the histological types conventional osteblastic intramedullary tumors were most prevalent, making 71.8.% of the cases. Chondroblastic and telengiectatic osteosarcoma are the next common histologic types. Surface tumors were detected in 51 (6.8 %) cases. Rare histological types like small cell, epitheloid, chondroblastoma like and fibrous dysplasia like were also reported.
Conclusion: This study is conducted as a preliminary work to form the basis of a pathologic database for the osteosarcoma cases diagnosed in our country.

PS-16-019

Kaposi's sarcomas in Central Tunisia: Epidemiological and anatomoclinical study of 71 cases

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Objective: Kaposi's sarcoma is a rare disease likely associated with human herpes virus 8 infection, and occurs predominantly in Jewish, Mediterranean and middle eastern men. Since there is a paucity of reports on the pattern of its occurrence in Tunisia, we here analysed the epidemiological pattern and anatomoclinical features.
Method: We retrospectively studied 71 consecutive cases of Kaposi's sarcoma diagnosed in the Pathology Department, Farhet Hached Hospital, Sousse during a 15-year period.
Results: Kaposi's sarcoma represented 21 % of soft tissue sarcomas. There were 23 (32.4 %) females and 48 (67.6 %) males (male-to-female ratio: 2.1:1). Median age at diagnosis was 69 (range: 10–98 years). The age distribution showed that elderly (≥60 years) were the most affected patients with a frequency of 66.2 %, followed by patients aged 31–59 years (25.3 %), and patients under 30 years (8.4 %). The most common location was the lower limbs, particularly the distal lower extremity (73.3 %), followed by contiguous location (7 %), and soft tissue, NOS (7 %).
Conclusion: Kaposi's sarcomas were more frequently diagnosed in elderly. The distal lower extremities were more involved.

PS-16-020

Rhabdomyosarcomas in Central Tunisia: Epidemiological and anatomoclinical study of 47 cases

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Objective: Rhabdomyosarcoma is the most common soft tissue sarcoma in the first two decades of life. In this study, we analysed the epidemiological pattern and antomoclinical features of rhabdomyosarcoma in Central Tunisia.
Method: We retrospectively studied all cases of rhabdomyosarcoma diagnosed in the Pathology Department, Farhet Hached Hospital, Sousse during a 15-year period.
Results: There were 15 (31.9 %) females and 32 (68.1 %) males (male-to-female ratio: 2.1:1). Median age at diagnosis was 9 (range: 0–85 years). Rhabdomyosarcoma was more frequently diagnosed in childhood (63 %) than in adults (37 %). In children, the tumour size was higher than 5 cm in 73 % of cases, the embryonal subtype was the most frequent (60 %) and the two most common sites of disease were the head and neck (50 %) and genito-urinary tract (23.3 %). In adults, the tumour size was higher than 5 cm in 90 % of cases, the pleomorphic subtype was the most diagnosed (41 %), and limbs were the most involved sites (41 %).
Conclusion: Rhabdomyosarcomas is more frequently diagnosed in children than in adult. Head and neck locations were the most involved and embryologic type was the most diagnosed. In adults, rhabdomyosarcomas were more frequently localized in limbs and diagnosed as pleomorphic type.

PS-16-021

Microarray-based DNA methylation study in Ewing sarcoma of bone

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Objective: Alterations in the DNA methylation pattern are a hallmark of malignancy and also of Ewing sarcomas. However, most epigenetic studies in Ewing sarcoma have focused on the analysis of few candidate genes and comprehensive studies are required.
Method: Here, we report for the first time a microarray-based DNA methylation study of 1505 CpG sites of cancer-related 807 genes in 69 Ewing sarcomas. We used Illumina's GoldenGate Methylation Cancer Panel I microarray.
Results: Using appropriate controls (n=14), we identified a total of 104 CpG sites hypermethylated in Ewing sarcoma. Most of hypermethylated genes are related with cell adhesion, cell regulation, development, and signal transduction. We compared the methylation mean of each tumor according to the survival data. The methylation mean was significantly higher in the alive patient group (0.25±0.03) compared to the dead patient group (0.22±0.05) (p=0.0322). However, the methylation mean was not significantly correlated with age, sex, or tumor location. We selected the most popular hypermethylated genes, GDF10, OSM, APC, and HOXA11, but, their methylation levels were not significantly correlated with the survival data.
Conclusion: We have characterized the DNA methylation profile of Ewing sarcomas and detected 104 CpG sites that were significantly hypermethylated in Ewing sarcomas. These might therefore play an important role in the development of Ewing sarcomas.

PS-16-022

Pleomorphic and dedifferentiated leiomyosarcoma associated with Lynch syndrome: A case report

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Objective: The Lynch syndrome or hereditary non-polyposis colorectal cancer (HNPCC) is a hereditary syndrome that predisposes to different types of colonic and extracolonic cancer, mainly in endometrium, stomach, ovary, and hepatobiliary and urinary tract. Occasional sarcomas have been reported in HNPCC patients.
Method: We describe a pleomorphic and dedifferentiated leiomyosarcoma of the gluteus in a patient with Lynch syndrome. We study her clinical, pathology, immunochemistry and molecular alterations.
Results: We present a 71 year old woman with previous colorectal, endometrium and breast cancers in a Lynch syndrome with mutations in exons 1 and 2 of MLH2, which appeared with a right gluteus mass. Grossly, it was encapsulated, whitish-yellowish with necrotic areas and measured 7,2 cm. Microscopically, the tumor was composed by a diffuse and polymorph spindle cells with fascicular pattern, focally myxoid and zones of necrosis and large hyalinization. The cells had large nuclei, sometimes giant multinucleated, with a brisk atypical mitosis activity. There was IHQ variability: positivity to desmine, MSA, calponin and negative to caldesmon and SM. There was loss of MSH2 and MSH6 repair proteins.
Conclusion: We must suspect a Lynch Syndrome relational sarcomas if we found one in a patient with HNPCC in order to test to mismatch repair proteins.

PS-16-023

Immunohistochemical review of 42 synovial sarcomas, including expression of TLE1: A "new" marker, with molecular confirmation in 21 cases

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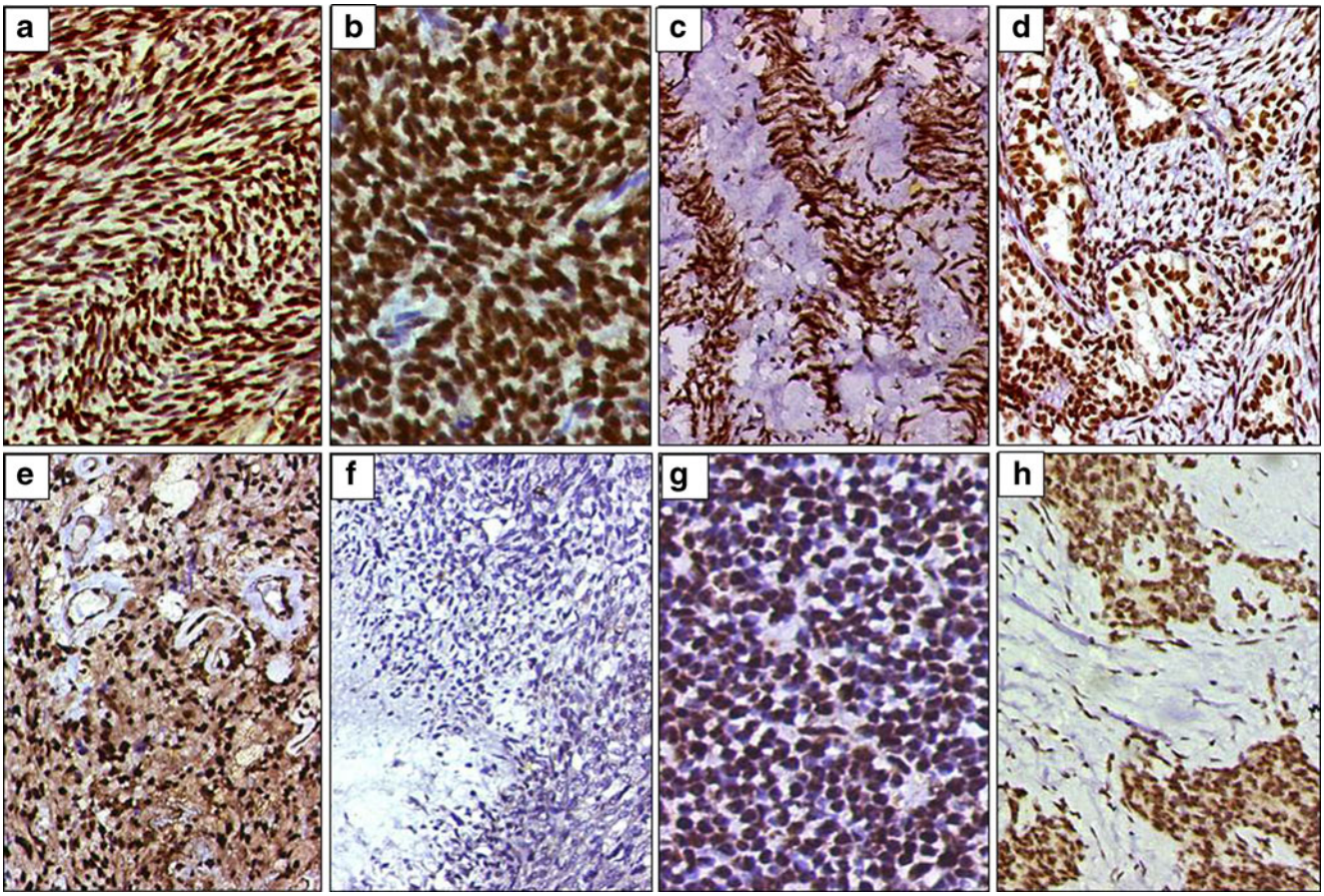
Objective: Synovial sarcoma displays a wide clinicopathological spectrum and a specific translocation t(X; 18)(SYT-SSX)(p11.2; q11.2). Cost constraints limit molecular confirmation in every case. Lately, TLE1 has been recognized as a useful IHC marker. Herein, we present IHC review of 42 synovial sarcomas, including TLE1 expression.
Method: Forty-two synovial sarcomas included monophasic spindle-cell type (26) (61.9 %), biphasic 13 (30.9 %), calcifying (2) (4.7 %) and poorly-differentiated type (1) (2.3 %). 21 tumors were confirmed with molecular analysis. TLE1 immunostaining was graded from 0, 1+, 2+, 3+, with 2+ or 3+ grades interpreted as positive staining.
Results: On IHC, various synovial sarcomas were positive for EMA (26/34)(76.4 %), CK7 (6/10) (60 %), CK/MNF116 (6/21)(28.6 %), BCL2 (36/37)(97.3 %), MIC2 (23/31)(74.1 %) and TLE1 (40/42)(95.2 %), while negative for CD34 (0/21). Among 70 other tumors, TLE1 was positive in schwannomas (5/5) (100 %), neurofibromas (2/2)(100 %), MPNSTs (2/12)(17 %) and PNETs (4/10)(40 %). Sensitivity and specificity of TLE1 for synovial sarcoma was 95.2 % and 72 %.

Conclusion: Although molecular confirmation remains its diagnostic gold standard, TLE1, EMA, BCL-2, MIC2, CKs and CD34 constitute an optimal for synovial sarcoma. Awareness of TLE1 expression in other tumors and its correct interpretation are necessary.



PS-16-024

HER3 (ErbB3) overexpression in Peripheral Nerve Sheath Tumors (PNST)

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Objective: Malignant peripheral nerve sheath tumors (MPNST) comprise 5–10 % of sarcomas. Prognosis is poor and the search for new treatments is ongoing. HER3 is a crucial receptor for neuregulin signalling in Schwann cells but to date, has not been studied in sarcomas. Our aim was to determine the prevalence of HER3 receptor expression in soft tissue tumors, including MPNST.

Method: HER3 expression was evaluated by immunohistochemistry in a total of 50 benign and 71 malignant mesenchymal tumors, including 16 neurofibromas, 16 schwanomas, 14 MPNST and 75 other lesion (uterine and non-uterine leiomiomas and leiomiosarcomas, synovial sarcomas, undifferentiated pleomorphic sarcomas (UPS)).

Results: HER3 overexpression was found in 31 % of cases. Significantly, HER3 positivity was present in

50 % of PNST (75 % of schwanomas, 50 % of MPNST and 25 % of neurofibromas). In contrast, HER3 positivity was observed in 20 % of other mesenchymal tumors (28 % uterine and 9 % non-uterine leiomiomas, 18 % uterine and 25 % non-uterine leiomiosarcomas, 29 % UPS).
Conclusion: HER3 overexpression is frequently found in PNST, including 50 % of MPNST. Due to the crucial role of HER3 receptor in cell signalling as a main activator of the PI3K pathway, these results support the rationale of developing new therapeutic approaches in MPNST.

PS-16-025
Giant cell tumor of tendon sheath with t(1;2)(p13;q37) translocation: A case report
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Objective: Tendosynovial giant cell tumor (TGCT) is a common neoplasm of synovium and tendon sheath. However, clonal chromosome aberrations characteristic for TGCT have been reported in no more than 30 cases. The aim of the study is a presentation of solitary TGCT with morphological, ultrastructural and cytogenetic analysis of tumour.
Method: A 44 year-old male was operated on because of a nodule, localized in soft tissue of medial ankle region and attached to the tendon of flexor muscle of toes. Small fragments of fresh tumour tissue were taken for ultrastructural, flow cytometric and cytogenetic studies. Paraffin-embedded material was examined histologically and immunohistochemically.
Results: Histologically, the tumor was built of ovoid and epithelioid mononuclear cells which present a moderate amount of cytoplasm and round nuclei with a single prominent nucleolus. Together with mononuclear cells, there was a moderate number of osteoclast-like multinucleated giant cells, foam cells and siderophages. Both the mononuclear and multinucleated cells stained with CD68, whereas only giant cells were positive for CD45. At the ultrastructural level, mononuclear cells displayed features of both histiocyte-like and fibroblast-like cells. Cytogenetic studies detected a clonal translocation: 46, XY, t(1;2)(p13;q37)[5]/46, XY[6].
Conclusion: The clonal genetic aberrations support the concept of neoplastic nature of the TGCT.

PS-16-026
Nonneural granular cell tumour of the breast: A case report
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Objective: Nonneural granular cell tumour (NNGCT) is a rare neoplasm described in 1991 by Leboit et al. Till now, no more than 35 cases have been presented in the literature, nearly all were limited to the skin. We report the first NNGCT of the breast and present its morphological and immunohistochemical characteristics.
Method: A 39 year-old female underwent lumpectomy because of tumour of the breast. After routine histological examination, the immunohistochemical studies were performed using commercially available antibodies against cytokeratins (AE1/AE3), CD68, CD1A, S100, CD34, smooth muscle actin, desmin, miogenin, inhibin, and Ki67 antigen (MiB1).
Results: Microscopically, the tumour was composed of ovoid and polygonal cells with abundant granular, eosinophilic cytoplasm. The cells presented mild or moderate polymorphism and trace mitotic activity. They were arranged in diffuse sheets with no evidence of nesting or fasciculation. The histological texture of the tumour resembled that of classical granular cell tumour of Abrikosoff. However, the tumour cells were strongly immunoreactive for CD68 and inhibin, whereas the reactions against S100 protein as well as other antigens studied gave negative results. The value of Ki67 index did not exceed 2–3 %.
Conclusion: The differential diagnosis of granular cell myoblastoma (Abrikossoff tumour) should include the nonneural granular cell tumour.

PS-16-027
Low grade fibromyxoid sarcoma: A study of 10 cases
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Objective: Low grade fibromyxoid sarcoma (LGFMS) is a specific type of fibrosarcoma with deceptively banal appearance and malignant behavior.
Method: A 5 year retrospective study revealed 10 LGFMS cases. Morphological and immunohistochemical analysis was performed. Follow-up information was obtained for 5 cases.
Results: All tumors occurred in adults (mean 40 year). They developed in neck (1), extremities (6) and trunk (3). Beside classical morphology of LGFMS following features were observed: necrosis (3), rosettes (3), areas of increased cellularity (5), foci of epithelioid cells (5), marked nuclear pleomorphism (1), prominent myxoid change (3), invasive border (6), bone formation (1), focal retiform pattern (1) and sclerosing epithelioid fibrosarcoma-like areas (1). Immunoprofile was the follow: vimentin (100 %), EMA (30 %), CD34 (10 % focally), S100 (0), SMA(0), desmin (0), AE1/AE3 (0). Two patients were without evidence of disease, one developed lung metastasis after 1 year. Two patients developed secondary tumours in 6 and 12 years after initial diagnosis. There were differences in the location and histologic features compared with primary ones. Secondary

tumors were less cellular, without necrosis or epithelioid cells. Behavior of secondary tumors did not fit to the classical concept of tumor progression that implies increase of malignancy.
Conclusion: LGFMS is a distinctive but unusual type of soft tissue sarcoma demonstrating a wide histologic spectrum and behavioral range.

PS-16-031
Immunohistochemical and mutational study of synovial sarcomas
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Objective: Synovial sarcomas are mesenchymal tumors of unknown histogenesis. Their molecular signature is a specific t(X; 18)(p11.2;q11.2) translocation. No effective targeted therapies are currently available. The aim of this study was to evaluate the expression and mutational status of potential molecular therapeutic targets.
Method: 38 molecularly confirmed cases of synovial sarcomas were included in this study. Immunohistochemical stainings of the EGF-R family (EGF-R, HER2/neu, HER3), and signaling molecules implicated in the mTOR pathway (AKT, mTOR, PTEN), as well as E-Cadherin and snail was performed. In addition, cases were screend for mutations in the EGFR, PIK3C, B-RAF, K-RAS, and N-RAS genes.
Results: EGF-receptor family members as well as E-Cadherin and snail are important for defining the tumor phenotype by determining epithelial-mesenchymal transition of synovial sarcomas. Activation oft the mTOR pathway is seen in a significant number of cases. Mutations of the genes studied are an overall rare event in synovial sarcomas and other types of sarcomas studied.
Conclusion: EGF-R expression is found in many synovial sarcomas, however, mutations of EGFR or downstream molecules appear to be rare. Activation of mTOR pathway is frequently seen in synovial sarcomas. The benefit of targeted therapy against these genes in synovial sarcomas remains to be determined.

PS-16-032
Collagen V induces differentiation of rabbit adipose tissue-derived stem cells in chondrocyte-like phenotype
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Objective: Stimulated mesenchymal stem cells (MSCs) have capacity of differentiation in many cell types. It is being used in degenerative diseases treatment protocols. We evaluated the collagen V (COL V) and collagen XI (COL XI) influence in the differentiation of rabbits adipose tissue-derived MSCs in a chondrocyte-like cell phenotype.
Method: MSCs isolated of New Zealand rabbits adipose-tissue were maintained in culture by 4 weeks. COLV, COLXI and COLV/XI (10 μg/ml) were added to culture during 72 h. The cells aggregates were stained with Toluidine blue, Alcian blue and Picrosirius. Chondrocyte-like phenotype was confirmed by immunofluorescence to CD34, vimentin and collagens I, II and III.
Results: MSCs stimulated with COLV expressed proteoglicans and collagen, when compared with COLXI and COLV/XI and control. In the presence of COLV, MSCs was capable to increase collagen II expression confirming its chondrocyte-like cell phenotype. In contrast, MSCs cultured with COLXI and COLV/XI express collagen I and III.
Conclusion: The data suggest that COLV may facilitate the differentiation of rabbit adipose tissue-derived stem cells into a chondrocyte-like phenotype. Further studies are urged in order to evaluate the influence of COLV in the ability of chondrocytes to remodel osteoarthritic joint surface at ultra structural and molecular levels.

Tuesday, 11 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-17 Poster Session Breast Pathology

PS-17-001
Targeting XRCC1 (X-ray Repair Cross-complementing Gene 1) deficiency in human cancer for personalized cancer therapy
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Objective: XRCC1 is essential for DNA base excision repair, single strand break repair and nucleotide excision repair.
Method: We evaluated XRCC1 immunohistochemically in early stage breast (n=2046), ovarian (n=157), gastric (n=140), colorectal (n=250) and pancreaticobiliary cancers (n=240). Pre-clinically, we evaluated a panel of XRCC1 deficient and proficient Chinese hamster ovary and human cancer cell lines. Double strand break repair (DSB) inhibitors targeting ATM (KU55933), DNA-PKcs (NU7441) and ATR (NU6027) were evaluated for synthetic lethality and cisplatin alone or in combination with DSB inhibitors for chemopotentiation.
Results: In breast cancer, XRCC1 loss (16 %) was associated with a 2-fold increase in risk of death and metastasis (p< 0.0001). In ovarian cancer, XRCC1 positive tumours (44 %) were more resistant to platinum chemotherapy (p=0.0001). XRCC1 positivity conferred a 2 fold increase of risk of death

(p=0.002) and independently associated with poor survival (p= 0.002). Pre-clinically, KU55933, NU7441 and NU6027 were synthetically lethal in XRCC1 deficient compared to proficient cells as evidenced by DSB accumulation, G2/M cell cycle arrest and apoptosis. XRCC1 deficient cells were hypersensitive to cisplatin which was enhanced by DSB repair inhibitors compared to in proficient cells.
Conclusion: Conclusions: XRCC1 deficiency in human tumours may be suitable for synthetic lethality application and exploited for cisplatin chemotherapy potentiation.

PS-17-004
Analysis of BCL2 oncoprotein expressing breast cancer by molecular subtype
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Objective: Breast cancer is the most common malignancy in Western women. Despite the progress in morphological investigation, active research is devoted to potentially important targets for prognosis and intervention. BCL2 oncoprotein represents such factor.
Method: Consecutive breast cancer cases were examined by routine protocol approach. The BCL2 oncoprotein expression was detected immunohistochemically. Expression was considered positive if it was in more than 25 % of tumour cells. The molecular subtype (Luminal A(LA), Luminal B(LB), HER2 positive(HER2) or triple negative(TN)) was determined as well.
Results: Among 159 invasive breast cancer cases, positive expression of BCL2 was detected in 66.7 %. The BCL2 positive group included: LA 86.8 % [95 % confidence interval 79.0–92.0], LB 4.7 % [2.0–10.6], HER2 0.9 % [0.2–5.2] and TN 7.6 % [3.9–14.2]. The BCL2 negative group consisted of LA 34 % [22.7–47.4], LB 3.7 % [1.0–12.8], HER2 26.4 % [16.4–39.6] and TN 35.8 % [24.3–49.3].
Conclusion: 1. BCL2 positive breast cancer possesses mostly Luminal A molecular subtype. Among BCL2 negative tumours, there is significantly higher fraction of HER2-positive and triple negative subtypes. 2.In breast cancer, BCL2 expression is associated with favourable prognostic indicators and should be analysed in complex with other parameters.

PS-17-005
Extramammary tumour metastasis in the breast
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Objective: Breast cancer is the most common malignant tumour of Latvian women (www.csb.lv). Correct diagnosis, including identification of tumour histogenesis, is the prerequisite for appropriate treatment.
Method: Consecutive breast tumour cases were selected by systematic retrospective archive search and were examined by breast cancer panel. If expression of oestrogen and progesterone receptors and HER2 protein was negative, mammaglobin, cytokeratin AE1/AE3, vimentin, CD45, CDX2, cytokeratin 20, TTF-1 and melanosome protein HMB-45 were detected.
Results: Five patients (0.89 %, 95 % CI=0.38–2.10 %) with secondary breast tumours were identified among 559 cases. Breast was affected by metastatic small cell lung cancer (1), malignant neuroendocrine tumour of small intestine (1) as well as by epithelioid melanoma metastasis in breast tissues (2) or intramammary lymph node (1). Analysing medical records, multiple synchronous and/or metachronous metastasis, involving brain, kidneys and ovaries, were found in all patients with haematogenous tumour metastases in the breast. In contrast, the lymphogenic tumour spread was isolated.
Conclusion: 1. Lymphogenic or haematogenous metastasis rarely (0.89 % of malignant breast tumours by morphology) can develop in breast tissues. It should be taking into account when planning the differential diagnostic approach, especially immunohistochemistry. 2. Haematogenous metastases in breast are associated with a wide synchronous or metachronous extramammary tumour spread.

PS-17-006
The prognostic significance of tumor-associated stroma in invasive breast carcinoma
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Objective: Fibroblasts in the stromal component of a tumor may influence tumor progression in various organs. The prognostic significance of tumor-infiltrating lymphocytes is also frequently reported. However, the prognostic significance of the stromal component in breast cancers, particularly those of high grade, has not been established.
Method: In this study, we analyzed surgically resected specimens from 545 patients with breast carcinoma, including 193 high grade tumors, for tumor-stroma ratio, dominant stroma type (collagen (C), fibroblast (F) or lymphocyte (L) dominant type), and central fibrosis on hematoxylin-eosin stained histological sections. We correlated these features with clinical prognosis.
Results: Among the 533 specimens examined, 127 (23.3 %) were of C type, 292 (53.6 %) of F type, and 114 (20.9 %) of L type. Central fibrosis was found in 99 tumors (18 %). The dominant stroma type was a significant prognostic factor on univariate and multivariate analyses, together with T classification, nodal status and Bloom-Richardson grade. Tumor-stroma ratio and central fibrosis did not predict survival on multivariate analysis. Even in high-grade tumors, relapse-

free intervals differed significantly according to dominant stroma type.
Conclusion: Conventional hematoxylin-eosin stained tumor slides may contain more prognostic information than previously thought; in particular, the dominant stroma type in invasive breast cancer may potentially be used to predict outcome.

PS-17-007
Pathology in breast implants substitution
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Objective: Health alert concerning breast implants brand PIP led to a review of patients harboring these prosthesis and in many cases replacement by new ones. Anaplastic lymphoma described in these patients has been an additional problem to be faced by plastic-surgeons and pathologists.
Method: Ninety two cases of women with breast implants were studied. Most of them had PIP implants (although no information of prosthesis type was available in all cases). Eighty of them presented with ruptures of different size. After implant replacement, histopathologic analysis of fibrous capsules and liquid from seromas in periprosthetic cavities was carry out. Following FDA recommendations, immunohistochemical studies to rule out lymphoma was performed in 85 cases.
Results: Fibrous capsules showed synovial metaplasia in all cases. Morphology was practically identical that in real articular synovial cells, and occasionally intracavitary nodules were seen detached from the surface in a process similar to synovial chondromatosis. No cases of lymphoma were seen and no expression of CD30 or ALK markers occurred. A case of pericapsular ductal invasive carcinoma was discovered.
Conclusion: Synovial metaplasia seems to be very common in capsules around breast implants. Development of conventional breast carcinoma is probably much more frequent than lymphomas independently of the possible implant influence.

PS-17-009
Post-radiation angiosarcoma of the breast: Report of a case
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Objective: Post-irradiation angiosarcoma generally occurs after breast conservation and radiation therapy. It affects the dermis of the breast within the radiation field. The incidence of post-radiational angiosarcoma is about 0.14 %.
Method: An 82-year-old woman who had undergone conservative surgery and radiotherapy for breast cancer 10 years ago presented with multiple red-purplish papules on the skin of her right breast. Excisional biopsy followed by simple mastectomy was performed.
Results: Excisional biopsy revealed a neoplasm composed of highly pleomorphic cells with prominent nucleoli forming solid areas and neoplastic slit-like vascular channels. Many mitotic figures and some individual apoptotic cells were also present. The tumor cells were positive for endotelial cell markers (factor VIII, CD31, CD34) and negative for CK7. The gross inspection of the mastectomy specimen showed multiple reddish-purple papule-like lesions on the skin, spreaded in an area of 12×10 cm. Sectioning showed numerous homogenous slightly hemorrhagic white nodules measuring from 2 to 12 mm located in the dermis. Histopatology and immunohistochemistry findings were consistent to those of the excisional biopsy. Infiltration of the subdermis was noted.
Conclusion: Diagnosis was high grade post-irradiation angiosarcoma. Simple mastectomy is the treatment of choice. Adjuvant chemotherapy should be considered in high grade neoplasms like this one.

PS-17-010
Prognostic factors in invasive lobular carcinoma of the breast
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Objective: Determination of molecular features in breast carcinomas, such as hormone receptor expression, can guide clinicians to the optimal choice of therapy. In this study, the relationship between the histologic grade, pathologic stage and the prognosis of invasive lobular carcinoma of the breast, and the tissue expression levels of ER, PR, HER-2/neu, p53, bcl-2, Ki-67 and E-cadherin was investigated.
Method: 31 cases of invasive lobular carcinoma of the breast, from 2003 to 2011, were included in this study. A single best representative paraffin block was selected for each case and H&E staining and immunohistochemistry procedures were performed. Ki-kare test was used for statistical method.
Results: 24 of 31 cases had classical lobular carcinoma, 7 cases had tubulolobular, pleomorphic, signet ring cell, or apocrine features. The median age of patients was 54 years. ER and PR were positive in 28 cases. All cases were negative for E-cadherin. Ki-67 was greater than %15 in 2 cases with pleomorphic lobular carcinoma. p53 positivity increased with grade. In 14 cases p53 was negative and bcl-2 was positive. Bcl-2 and p53 were positive in 29 and 17 cases respectively.

Conclusion: In contrast to the literature, there was no correlation between bcl-2 status and other molecular markers, including p53.

PS-17-012

Rapid immunohistochemistry in intraoperative sentinel axillary lymph node evaluation

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Objective: Sentinel lymph node (SN) examination is the current procedure to establish the status of axillary lymph nodes in breast cancer. To avoid a two step delayed surgical procedure, a reliable and quick method of SN evaluation is advocated. Rapid immunohistochemical technique (UICH) for keratin has been only recently proposed. Aim of this study is to apply keratin UICH in frozen sections (FSs) of SNs.
Method: A consecutive series of 231(Series A) SN cases was studied at FS level followed by two sections stained with keratin UIHC. All procedure requires 23 min. For comparison 131 consecutive cases (series B) of SN were studied with FS only. All residual tissue from both series was paraffin embedded (PS).
Results: Series A: SNs showed tumour involvement in 41 cases (17.7 %). In only 8 cases (3.75 %), PS sections evidenced additional neoplastic cells (micometastases) not seen with keratin UIHC, that led to a delayed axillary dissection. Series B: PS sections revealed metastatic deposits (micrometastases) not seen in FS in 6.1 % of cases.
Conclusion: FS coupled with keratin UHIC of all the entire lymph node accurately evidences carcinoma cells in SNs.

PS-17-013

High concordance of 6 HER2 in situ hybridization methods with Abbott FISH

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Objective: We conducted a comprehensive concordance study of 6 ISH methods with Abbott FISH in a large series of breast carcinomas.
Method: Tissue Micro Arrays (TMA) were constructed by taking 3 tissue-cores from praffin blocks of 402 primary breast carcinomas. Up to 384 cases were analyzable in 7 ISH assays. Scoring was performed by two independent observers without knowledge of the other ISH data according the ASCO-guidelines for HER2-testing. Cases were considered positive when the ratio was ≥2.0. Discordant cases were reviewed and scores were reassigned on consensus of opinion. Concordance and Cohen's kappa score were calculated in relation to FISH, Abbott.
Results: In 372 cases analyzable with Abbott HER2 FISH, 12.1 % were HER2-positive. Concordances (kappa-scores) of the 6 other assays were: DAKO FISH 98.1 % (0.90), DAKO duoCISH 97.2 % (10.4 %), Zytovision FISH 99.1 % (0.96), Zytovision duoCISH 99.1 % (0.96), single probe SISH Ventana 98.9 % (0.95), dual probe SISH Ventana 99.4 % (0.97).
Conclusion: Conclusion: Concordance of 6 HER2 ISH assays with Abbott FISH were shown to be 97.2 % or higher. In this study, DAKO assays had a lower kappa score with Abbott FISH than Ventana or Zytovision assays.

PS-17-014

Which is the best method to measure multiple breast cancer?

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The size of the breast tumor is relevant in a patient s management also affecting the prognosis. For unifocal lesions, tumor staging depends on the maximum diameter of the tumor, whereas in multiple lesions, this issue is not standardized. The aim of this paper is to study which is the best method in the assessment of the tumor size in multiple invazive carcinomas (multifocal and multicentric) in correlation with the lymph node metastases developement. Two different assessments of the tumor size (diameter of the largest focus=LD, and combined, aggregate diameter of all the foci=AD) were used in 418 primary invasive breast lesions (91 multiple, 327 unifocal) and compared with the nodal status (CHI- test). The use of combined tumor focus upstaged 23 (25.27 %) patients with multiple tumors (16 upstaged from pT1 to pT2 and 7 from pT2 to pT3). There was no difference in nodal positivity based on pT status between LD and AD. We observed a statistically significant difference in the mean diameter of the largest focus between the unifocal and multifocal group (31,47 vs 39,67 mm) (p=0,0013). Aggregate diameter in multiple breast cancer is not correlated with an increase of axillary metasases and should not be used for staging.

PS-17-015

Central nervous system metastases in women with invasive breast carcinoma, not otherwise specified, are associated with estrogen receptor status

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Objective: Central nervous system metastases (CNSM) from breast cancer (BC) are relatively common and can

present as the first site of disease progression. Lymph node status and tumor size are regarded as important prognostic indicators for disease-free and overall survival in BC. The aim of this study was to investigate prognostic/predictive pathological data in BC that could define a high-risk group to develop CNSM.
Method: The authors evaluated 97 female patients with invasive breast carcinoma, not otherwise specified, previously submitted to setorectomy/mastectomy, in order to determine lymph node status, tumor size, histologic grade, estrogen receptor status (ER) and immunoexpression of HER2/neu. Of these cases, 10 patients developed CNSM.
Results: The patients who developed CNSM were younger (median age 54.7±8.152 years/p=0.251) and more likely to have T2N2 disease than patients with no CNSM. The presence of encephalic disease was associated with ER (p=0.031). Lymph node status (p=0.84), tumor size (p=0.339), histologic grade (p=0.933), and HER2/neu expression (p=0.31) were not significant risk factors.
Conclusion: Although the literature data discriminate that HER2/neu overexpression in BC is related with CNSM, the authors suggests that these lesions can be related to ER too. Efforts to determine other risk factor for development of CNSM may be warranted.

PS-17-018

Androgen receptors and sex hormone serum levels in breast carcinoma: Study of the ORDET cohort

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Objective: Androgens and androgen receptors (AR) are involved in breast cancer (BC) pathogenesis. High testosterone serum levels increase the risk of developing mainly ER + BC, especially after menopause, although androgen role in tumor progression is not clearly elucidated.
Method: Correlations between serum sex hormones and clinico-pathological features of 131 BC arisen among 10,786 women previously recruited for ORDET study were investigated. Prediagnostic estradiol, testosterone (free/total) and SHBG serum levels were available. Immunohistochemistry for AR was evaluated along with ER, PR, HER-2 and MIB-1.
Results: AR + was found in 90.8 % of BC. Higher estradiol (p=0.0001), free testosterone (p=0.02) and SHBG (p=0.02) were seen in premenopausal patients. In dead patients higher free testosterone was observed (p=0.0003). No correlation was found for hormone levels vs stage, histotype and grade. Higher SHBG was seen in PR-rich tumours (p=0.02). HER-2+/ER- cases showed a trend for a higher total testosterone (p=0.18) and SHBG (p=0.2). Testosterone, estradiol and SHBG were similar in AR + and AR- tumors. Among triple negative, AR + tumours showed higher free testosterone (p=0.04). BC with few AR + cells showed higher total testosterone (p=0.0004) and a worse outcome (p=0.29).
Conclusion: Our results confirm the role of AR in BC and suggest the androgen involvement in tumour progression.

PS-17-019

Mitotic count in metastatic breast carcinoma to lymph nodes: Preoperative study

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Objective: Axillary lymph node metastasis (ALNM) is one of the most important prognostic factors in breast cancer. The reasons why tumours are capable to result in axillary metastasis remain unclear. The evaluation risk of ALNM would improve the treatment planning. We study the metastatic breast carcinoma to the lymph node to obtain information about the metastatic risk.
Method: We study 65 patients with metastatic breast carcinoma to the lymph node diagnosed preoperatively by needle biopsy. We study the mitotic average (×10 HPF), metastasis size, positive lymph nodes, total lymph node studied, lymph node ratio (nº of positive node/total nodes nº), primary tumour size and grade.
Results: All the cases with high mitotic count were associated with macrometastasis. We didn't find any relation between the mitotic rate or the metastatic size with the number of lymph node affected, and the lymph node ratio. Breast carcinomas G1, T1, <6 mitosis/HPF lymph nodes showed 25–50 % of positive lymph nodes.
Conclusion: We tried to obtain information from the metastatic breast carcinoma to the lymph node to predict the axillary status. In our cases we couldn't predict the lymph node involvement based in the tumour size, grade, metastatic size, and metastatic mitotic rate. The preoperative study of a breast tumour and their lymph node metastasis don't allow predicting the lymph node status in our series.

PS-17-020

RASSF1A hypermethylation is associated to the presence of tumoral cells detected by One-step Nucleic Acid Amplification (OSNA)

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Objective: One-step nucleic acid amplification (OSNA) is used in routine clinical use for sentinel lymph node biopsy (SLNB). It consists of the molecular quantitation of a

tumoral marker (cytokeratin-CK 19 mRNA). Gene hypermethylation is one of the most common mechanisms of inactivation of suppressor genes. RASSF1A gene, is a region frequently hypermethylated in breast cancer.
Method: 51 patients with breast cancer were included in the study, and a total of 87 lymph nodes were analysed.
Results: 41 %, 33.3 % and 21.6 % of the tumours were of low, intermediate and high-grade, respectively. In 40.8 % of the cases there are not tumoral cells, in contrast to 12.2 %, 4.1 %, 14.3 %, 28.6 % that showed low number of cells/ITC (<250 copies/sample), Micro- (<5000 copies/sample) and Macro-Mtx, respectively. There is a very clear association between RASSF1A hypermethylation and the presence of tumoral cells (p= 0.004), being more frequent in Macro-mtx compared to the rest of groups (P=0.007). RASSF1A hypermethylation is also correlated to unfavorable histologic grade in the tumour (P=0.025) and lymph node involvement at the diagnosis (0.001).
Conclusion: The analysis of RASSF1A hypermethylation could provide additional information to OSNA to detect tumoral cells in lymph nodes. The spare tissue material derived from OSNA could be good material to consider new molecular studies.

PS-17-021
Breast Cancer profile in young Romanian women
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Objective: A variety of previous studies have shown a higher prevalence of prognostic parameters associated with poor survival in young women with breast cancer. The aim of this study is to reveal the morphologic aspects and hormonal status in patients with breast cancer under 35 from the Pathology Department of Targu Mures.
Method: 949 patients with breast cancer have been diagnosed in 5 years (2006–2011), 17 being under 35 years old (1,79 %).
Results: Of these, 15 patients (88,23 %) had palpable tumor at presentation, 12 (70,58 %) with palpable axillary adenopathy. In 10 cases (58,82 %) the tumor diameter was over 2 cm at the time of diagnosis. In 15 cases (88,23 %) the histological type was infiltrative ductal carcinoma, with 13 cases having high grade. Most of the tumors expressed ER and PR and were Her-2 negative (none was triple negative). However, in 11 cases (64,70 %) the ki-67 index was more than 50 %.
Conclusion: Young women with breast cancer have been shown to have a poorer prognosis because of the high grade and hormonal status. Our study shows some similar aspects, but the hormonal status is totally different from the dates in the literature, revealing a possible better response to hormonal treatment and a better survival.

PS-17-022
Immunohistochemical predictive markers for trastuzumab resistence
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Objective: HER2 positivity defines a clinically challenging subgroup of patients with breast cancer with variable prognosis and response to therapy. The main aim of this study is to identify immunohistochemical markers to predict trastuzumab resistence.
Method: Tumours from 57 patients with Invasive Ductal Carcinoma, who were previously treated with trastuzumab, were included in a tissue microarray and stained for ER, Ki67, p53, cyclin D1, p16 and for HER2 and SISH (silver in situ hybridization).
Results: After 5 years of follow up, 80 % of patients with p53 negative tumours were disease free (p 0.029) and 90 % were alive (p 0,014) and the patients cyclin D1 positive, 90 % were alive (p 0.031) and 84 % were disease free (p 0.005). Among HER2 3+, 10 % did not amplify (polysomy 17). Moreover, 12 % of treated patients were HER2 0−2+ and did not amplify by SISH.
Conclusion: The best immunohistochemical markers to predict a good response to trastuzumab treatment were P53 negative and/or cyclin D1 positive. All HER2 positive 3+ tumours should be confirmed by hybridization, since polysomy 17 is found in 10 %, and these tumours should not be treated with trastuzumab. Variations in the immunostaining techniques could induce trastuzumab treatment to patients with HER2 non amplified tumours.

PS-17-023
CD99 expression in breast carcinoma
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Objective: CD99 is a membraneous protein that is expressed widely among various soft tissue tumors. There is growing evidence that its expression in some carcinomas correlates with epithelial to mesenchymal transition (EMT) and is a poor prognostic factor. Its importance in the breast carcinoma remains unsettled.
Method: The analysis was performed on breast cancer samples from 122 patients. Tumors were graded histologically according to the Nottingham system. CD99 expression was scored by grading system used for HER-2. Only cases showing grade (3+) were regarded as positive. Additionally,

expression of estrogen (ER) and progesterone receptor (PR), HER-2, E-cadherin, Vimentin, Twist, Ki-67, c-myc, cyclin D1 and Topoisomerase 2alfa was performed. Expression of the CD99 was correlated with all these markers and with clinical outcome.
Results: Expression of CD99 was observed in 11 patients and correlated significantly with negative PR status (p=0,01), higher histological grade (p=0,05), positive Twist (p=0,04) and Topoisomerase2alfa expression (p=0,04). There was also a trend toward higher frequency of cyclin D1 positivity (p= 0.09). No impact on prognosis for CD99 expression was found.
Conclusion: Expression of CD99 correlates with high histological grade, negative progesterone receptor status and expression of certain EMT and proliferation markers, but it does not influence prognosis in breast carcinoma.

PS-17-024
Primary plasmacytoma of the breast: A case report
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Objective: extramedullary plasmacytomas of the breast are extremely rare, especially those that are not associated with multiple myeloma and they can mimic mammary carcinoma.
Method: case report:69-year-old woman presented a palpable mass in the left breast previously diagnosed as a lobular carcinoma by core biopsy performed in other service. In our institution a conservative surgery with lymph node dissection was proposed.
Results: Frozen section was required and the gross examination showed a 4.0×4.0×3.0 cm firm-elastic nodule with surgical margins free of tumor and the microscopic examination showed tumor cells with abundant cytoplasm with hyaline appearance. The paraffin sections showed a proliferation of plasma cells with moderate atypia. The immunohistochemical study confirmed the diagnosis of plasmacytoma. There was no axillary lymph node involvement. There were no bone lesions in the additional investigation.
Conclusion: primary plasmacytomas of the breast are extremely rare and have to be included in the differential diagnosis with breast carcinomas especially in material of core biopsy.

PS-17-025
Sentinel lymph node in breast cancer: Form morphology to molecular examination
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Objective: Sentinel lymph node (SLN) examination is a standard in breast cancer treatment. It can be performed on formalin-fixed paraffin-embedded material (FFPE) or on frozen sections (FS). FFPE or FS suffer two drawbacks: 1) partial examination; 2) operator's dependence. To avoid these limitations, a molecular technique (OSNA) targeted to quantify a tumoral fingerprint (CK19), has been introduced. Our aim is to compare the performance of FFPE, FS and OSNA.
Method: We evaluated the clinical-pathological features of three series of SLN-patients from a single Institution. The series consists of 540 FFPE (2000–2005), 390 FS (2009) and 198 OSNA (from October-2011 to march-2012) patients.
Results: Positive SLN were disclosed in 162/540 (30 %) FFPE, 87/390 (22 %) FS and 55/198 (28 %) OSNA and represented by metastases-micrometastases [FFPE: 61–38 %, FS: 74–26 %, OSNA: 71–29 %]. After axillary dissection, additional metastasis were observed in 53/162 (33 %) FFPE, 27/87 (31 %) FS and 16/53 (30 %) OSNA patients, with further involvement more frequent with metastasis (FFPE 43 %, FS 36 %, OSNA 36 %) rather than micrometastasis (FFPE 16 %, FS 17 %, OSNA 14 %).
Conclusion: OSNA provides results overlapping to those of FFPE and FS, thus representing a valid and objective alternative for intraoperative SLN examination in breast cancer.

PS-17-026
HER2 assessment in invasive breast cancer using IHC and FISH: Results from 7479 consecutive cases
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Objective: HER2 in invasive breast cancer (IBC) should be assessed according to recommended algorithms employing IHC as screening tool and ISH only in equivocal cases. Therefore there is little data on possible missdiagnosis in discordant cases.
Method: HER2 was assessed by both IHC and FISH in 7479 consecutive IBC. Distribution of IHC and FISH scores, incidence of HER2+ IBC, concordance and level of amplification in discordant cases were analysed.
Results: IHC distribution: neg(0) 49.6 %, neg(1+) 27.0 %, equivocal(2+) 11.3 %, pos(3+) 12.1 %. FISH distribution: nonamplified 84.6 %, amplified 13.6 %, equivocal 1.8 % of which in 42.1 % ratio was ≥2.0. 15.0 % IBC were HER2+ and 0.7 % were double-equivocal. 14.4 % of equivocal(2+) were amplified. Discordance was infrequent (1.2 %) (p< 0.0001): among neg(0) and neg(1+) 0,3 % and 1,6 % were amplified, while among pos(3+) 4.7 % were nonamplified. 64 IHC negative tumors, representing 5.7 % of all HER2+, were amplified, however in 89.1 % ratio was ≤4.0.

Conclusion: 15 % IBC are HER2+. Application of two standardised methods results in excellent concordance and enables detection of all HER2+ IBC, while recommended algorithms lead to missdiagnosis in 6 % of HER2+ IBC, but in these amplification is low-level.

PS-17-027

Case report: Unusual breast cystic lesion in a 46-year-old female

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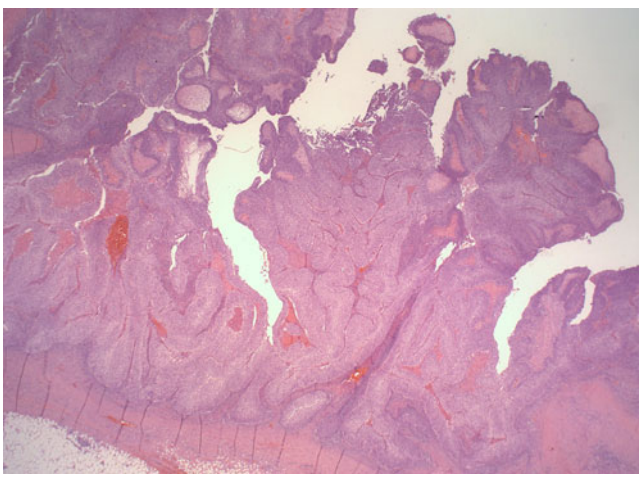
Objective: Papillary carcinoma of the female breast may exhibit a broad phenotype. We present an unusual case of a pseudoencapsulated invasive papillary carcinoma featuring transitional cell features.
Method: A specimen of internal right female breast biquadrantectomy was routinely processed and a panel of antibodies applied on paraffin tissue section.
Results: Grossly, the specimen showed a 12.5 cm cystic lesion with fibrino-hematic material and multiple pinkish-grey papillary structures, the largest measuring 4 cm. The histological examination revealed a malignant epithelial papillary proliferation reminiscent of transitional cell carcinoma, with high nuclear grade, frequent mitotic figures, multiple areas of invasion and rare necrotic foci. Tumor cells were immunoreactive for p63, 34βE12 and Ki-67 (90 %) and negative for other stains including HER2/neu, estrogen and progesterone receptors. Our differential diagnosis included a metastasis from a primary urothelial carcinoma, an intraductal papillary lesion, a metaplastic carcinoma and a papillary adnexal neoplasm, all reasonably excluded after careful clinico-pathologic evaluation.
Conclusion: Metastatic involvement of the breast is uncommon but it should be considered if tumor phenotype is inconsistent within usual or "special type" breast carcinoma. Yet, some rare primary misleading lesions are difficult to recognize.



PS-17-028

Volume measurement of female Sprague–Dawley mammary tumors induced by N-methyl-N-nitrosourea: Comparing ultrasonography and caliper

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Objective: N-methyl-N-nitrosourea (MNU) is a chemical carcinogen frequently used to induce mammary tumors in female rats, which experimental evaluation requires the monitoring of tumor's volume. For this purpose several methods are described, namely: caliper and ultrasonography measurement. The aim of this work was to compare data obtained by caliper and ultrasonography.
Method: Twelve female Sprague–Dawley rats with 187.7± 14.3 g body weight were intraperitoneally injected with MNU (50 mg/Kg) at 50 days of age. Thirty-six weeks after MNU administration forty-one tumors volume was determined by caliper (Vito®) and ultrasonography (LOGIQP6®, General Electric Healthcare) measurement. The tumor volume (V) was calculated according to the following formula $V=\pi$. ⟦S_1^2⟧ ^ .S_2⁄12, being S_(1) and S_2 the tumor diameters (S_(1)<S_(2)).
Results: The means tumor caliper and ultrasonography measures were 4.116±5.801 cm3 and 2.578±4.302 cm3, respectively. The ICC for scoring reproducibility was 0.75 (95 % Confidence Interval, 0.57 to 0.86) and Paired-Sample *T*-Test was significant ($p<0.01$).
Conclusion: Usually mammary tumors in rat are measured by caliper. However, our results showed that there are volume differences between both methods studied. Ultrasonographic method is more accurate and more precise than caliper. Therefore, we recommend the use of ultrasonography to rat tumor evaluation.

PS-17-029

Involvement of PI3K/Akt pathway alterations in breast cancer treated with trastuzumab

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Objective: There is a significant percentage of patients with breast cancer and HER2 receptor overexpression that do not respond to trastuzumab-directed therapy. The aim of this paper is to study the alterations of one of the HER2 signalling pathways related to trastuzumab response in breast cancer.
Method: The study comprised 127 cases of breast carcinoma in different stages of evolution with HER2

overexpression (HercepTest 3+) or gene amplification (FISH). All patients were treated with trastuzumab. The assessment of PTEN and pAkt expression was based on staining intensity and percentage of stained cells. We also determined the molecular alterations in PIK3CA.
Results: Our series showed a statistically significant association between a positive expression of PTEN and the absence of PIK3CA mutations with better overall survival from treatment onset with trastuzumab (p=0.022 and p= 0.003, respectively). The association with the expression of pAkt was statistically significant if survival is evaluated from the pathological diagnosis of the tumor (p=0.043), pAkt positive tumors had worse survival.
Conclusion: PTEN expression and PIK3CA mutations could be considered prognostic biomarkers in trastuzumab-treated breast cancer. The relationship with pAkt expression depends on other factors, not just the mechanism of action of trastuzumab.

PS-17-030
Mammaglobin expression in primary breast cancer and corresponding metastases
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Objective: Expression of mammaglobin A (MG-A) in breast cancer has been reported to be of prognostic value and to be associated to hormone receptor-positivity. MG-A is also useful in the diagnosis of metastatic breast cancer. The present study evaluates the differential MG-A expression in two subsets of primary breast cancer (metastasizing vs. non-metastasizing) and in their correspondent metastases.
Method: Immunohistochemical analysis of MG-A (clone 304-1A5) was performed in 55 non-metastasizing primary breast tumors and 19 paired primary and metastatic breast cancers. A percentage of 1 % of stained tumor cells was considered positive. The expression of MG-A in the different groups, together with other clinicopathologic factors (grade, size, hormone receptors, HER2, etc.) was analyzed by t-test.
Results: Expression of MG-A was significantly higher in estrogen receptor-positive (ER+) tumors (p<0.003). A trend was noted for ER + metastasizing primary breast cancers to show a higher expression of MG-A, compared to those non-metastasizing (p=0.064). No significant differences were noted in the expression of MG-A between metastasizing primary tumors and their correspondent metastases, with a good correlation (p=0.033).
Conclusion: These results suggest that MG-A might be of prognostic value in determining a subset of ER + breast cancers prone to progression. Larger series are needed to confirm these observations.

PS-17-031
Concordance of St. Gallen intrinsic subtypes in core biopsies and related surgical specimens of breast cancer
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Objective: To evaluate the relevance of intrinsic breast cancer subtyping (IBCS) on core biopsies (CB).
Method: IBCST was performed on CB and related surgical specimen (SSP) of 398 breast cancers according to the clinicopathological criteria of the St. Gallen Consensus 2011. To discriminate Luminal A and Luminal B Her2 negative tumors we used the Mitotic Activity Index with a cut-off of ≥10 for high proliferation (WHO 2003, Baak 2008). Agreement rates of CB and SSP and positive predictive values (PPV) of CB based IBCS were calculated.
Results: IBCS of SSP came out with 52 % Luminal A, 22 % Luminal B Her2neg, 6 % Luminal B Her2+, 2 % Her2+, 11 % Triple-negative, and 8 % Special Type. The CB/SSP-agreement rate of IBCS was complete with exception of Luminal B with only 33 %. Accordingly, the PPV of CB based Luminal A was 78 % whereas IBCS for all other types was 100 %. Both exceptions are due to underestimation of proliferation in CB.
Conclusion: Agreement of IBCS in CB and SSP and the PPVs of CB based IBCS are generally high. This means that IBCS on CB specimen can be used for preoperative decision making in the vast majority of cases.

PS-17-032
HER2 testing in Russia: The results of the 10 years of experience. ASCO/CAP recommended score system
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Objective: We analyzed using of score system criteria for HER2 testing in breast cancer.
Method: In 2001–2011 176028 new invasive breast cancer cases were investigated in Russia. IHC testing was made using HER2 antibody (A0485, Dako and Confirm HER2 Ventana) in 79 regional laboratories, samples were retested in 8 reference centers with HerceptTest (Dako). Equivocal results IHC (2+) were retested using ISH: FISH (Dako), BDISH (Ventana). Scoring criteria was 10 % of tumor cells (till 2009) and 30 % of tumor cells according to the ASCO/CAP recommendations (2010).

Results: 39384 samples were tested in 2009. Score 0 was found in 45.43 % cases, 1+ in 28.86 %, 2+ in 12.97 %, 3+ in 14.73 %. The amplification was revealed in 32.12 % of 2+ cases, 15.82 % tumors were 3+/FISH+. 43485 cases were tested in 2011: score 0 −38.42 %, 1+ 30.61 %, 2+ 15.65 %, 3+ 15.32 %. The amplification was seen in 28.17 % 2+ cases and 18.68 % tumors became 3+/FISH+. There was no significant distinction using 10 % and 30 % cells score system for 3+ tumors, whereas for groups 1+ and 2+ it was.
Conclusion: ASCO/CAP scoring criteria developed in 2007 have no effect on HER2-positive tumors detection but increases number of cases with equivocal result, what require retesting with ISH.

PS-17-033
Microvessel density in triple-negative breast cancer: Characteristics and prognostic implications
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Objective: We assessed topography and characteristics of blood vessels in triple-negative breast cancer (TNC) and examined their association(s) with clinicopathological features, basal-like phenotype and influence on patient prognosis.
Method: Blood vessels were assessed in tissue sections from 133 TNCs stained for CD34. Slides were scanned using ScanScope® XT and analysed with Aperio ImageScopeTM, Microvascular Density v1 algorithm. Microvessel density (MVD) was assessed in three areas: intratumoural (IT), peripheral tumoural (PP) and peritumoural (PT), and correlated with clinicopathological features and prognosis.
Results: The majority of blood vessels were located largely at the peripheral tumoural and peritumoural areas. Tumours with higher total MVD and PT-MVD were significantly associated with the presence of recurrence (p=0.05; 0.01), distant metastasis (p=0.01; 0.005), hematogenous metastasis (p=0.006; 0.01); and shorter overall survival (OS; p=0.006; 0.01) and disease free interval (DFI; p=0.04; 0.09). High PT-MVD correlated with a higher stage at diagnosis (III and IV; p=0.02), lymph node (LN) metastasis (p=0.04), basal-like phenotype (p=0.01), high histologic grade (p=0.05), presence of distant metastasis (p=0.02), and shorter OS (p=0.01).
Conclusion: Blood vessels are mainly located at the peritumoural and peripheral areas in triple negative breast cancers and seem to have a major role in tumour progression by representing means for disease dissemination.

PS-17-034
Expression of CD44 and CD24 in primary ductal invasive carcinoma of breast and metastatic lymph nodes
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Objective: Cancer stem cells are believed to have certain role in progression, metastatic potential and outcome of ductal invasive carcinoma of breast.
Method: The archived materials of 2008–2012 years from the Department of Pathological Anatomy, N. Kipshidze Central University Clinic were used for the research. 196 cases of ductal invasive carcinoma were chosen for the study. The CD44, CD24 immunohistochemistry (Biocare Medical) was used for staining. Evaluation was performed using SPSS software.
Results: The results showed: 68.5 % of grade II cases and 90.5 % of grade III cases were lymph node positive. CD24 positivity in grade II tumors was seen in 29.6 % of primary site and 45.9 % of metastasis; in grade III tumors-50 % of primary site and 55.2 % of metastasis. CD44 positive cases in grade II-48.1 % for primary tumor and 27 % in metastasis, for grade III- 73.8 % for primary tumor and 39.4 % for metastasis.
Conclusion: The results show that CD44 positivity is significantly less frequently seen in metastasis than in primary tumor; CD24 positivity is more frequently seen in metastasis for grade II cases. This indicates, that cells with stem cell phenotype decrease in metastasis reflecting heterogeneity between primary and metastatic sites, which should be taken into consideration for assessing progression and treatment.

PS-17-035
Solid neuroendocrine breast carcinoma: Three case reports
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Objective: It seems that neuroendocrine breast carcinoma (NEBC) is underrecognized in routine practice. 2003 World Health Organization classification of tumors of the breast defined NEBC as a subtype of invasive mammary carcinoma in which >50 % of the tumor cells express neuroendocrine markers. Three cases compatible with solid NEBC are discussed with an emphasis on identifying features useful in recognition of this tumor type.
Results: The patients were 35, 55 and 57 years old women. All patients presented with a palpable mass, two in the right and one in the left breast. Microscopically, infiltrating, solid cohesive nesting pattern with delicate sinusoidal vasculature

or peliosis and papillary pattern were observed. The tumor cells were round or polygonal with abundant granular, eosinophilic cytoplasm. The nuclei had hyperchromatic/vesicular or "salt and pepper" chromatin. Two cases had ductal carcinoma in situ component. All cases were positive for synaptophysin and chromogranin A in >50 % of tumor cells. While a positive status for estrogen receptor was detected in all cases, progesterone receptor was observed in two cases. None of the tumors displayed HER2 overexpression.
Conclusion: Morphological clues suggestive of NEBC must be recognized for immunohistochemical confirmation for appropriate classification of this clinically distinct subtype of invasive breast carcinoma.

PS-17-036
Comparison of automated and manual FISH for evaluation of HER2 gene status on breast carcinoma core biopsies
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Objective: Automation of HER2 FISH may improve HER2 gene testing. The aim of our study was to evaluate an automated HER2 FISH assay for assessing the HER2 genomic status.
Method: Core biopsies of 100 invasive breast carcinomas were analysed in parallel using the manual PathVysion™ HER-2 DNA Probe Kit and the automated Leica HER2 FISH System for the BOND™ instrument. To assess inter-method agreement, concordance analysis was performed for various numerical and categorical parameters.
Results: Carcinomas with all HER2 immunohistochemical scores were included (0+: 20; 1+: 20; 2+: 30; 3+: 30). Using either HER2/CEP 17 ratio >2.2 or ≥2.0 as criterion for HER2 amplification, high levels of concordance were observed between automated and manual FISH (concordance rate 96 %, K coefficient 0.92). High levels of inter-method agreement were also found for HER2 copy number, CEP17 copy number, HER2/CEP17 ratio, the percentage of carcinoma cells with HER2/CEP17 ratio >2.2, and the presence of HER2 genetic heterogeneity, HER2 clusters and CEP17 polyploidy.
Conclusion: HER2 testing using automated FISH is feasible on breast carcinoma core biopsies. Automated HER2 FISH using the Leica HER2 FISH System for BOND is an alternative to manual HER2 FISH in evaluating the HER2 status of primary invasive breast carcinomas.

PS-17-037
Myofibroblastoma of the breast: Presentation of three cases
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Objective: Myofibroblastoma is a rare, usually solitary, benign spindle cell tumour composed of myofibroblasts. It affects both genders equally.
Method: Three cases diagnosed in our laboratory are presented.
Results: Two patients were postmenopausal females (53 and 75 years old) and one was male (55 years old). The tumour was 1,6 cm in greatest diameter in the first case, 7 cm in the second and 2 cm in the third. Microscopically, all neoplasms were circumscribed and consisted of uniform, bland spindle cells separated by broad bands of hyalinized collagen. The neoplasmatic cells had abundant eosinophilic cytoplasm, oval nuclei and were arranged in fascicles. Cellular atypia was found only in one case and mitoses were scarce. Immunohistochemically, all neoplasms were strongly positive for vimentin, CD34 and Bcl-2, while the expression of desmin and SMA varied. S-100 protein was negative. The neoplasms of the female patients were strongly positive for ER and negative for PgR. The stains for estrogen and androgen receptors were not carried out in the case of the male patient.
Conclusion: Differential diagnosis can be complex. Fibromatosis of the breast, nodular fasciitis, myoepithelioma, myofibrosarcoma, solitary fibrous tumor, inflammatory myofibroblastic tumour should be excluded based on the histological and immunohistochemical findings.

PS-17-038
Morphological analysis of stromal population of mast cells in breast cancer
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Objective: Mast cells in breast cancer are not studied enough.
Method: Using light- and transmission electron microscopy fragments of mammary gland tumors, received intraoperative, from 58 patients 26–82 years with infiltrative ductal breast cancer were studied.
Results: Most of the mast cells were localized in the areas of infiltrative growth, at a background of lymphohistiocyte infiltration and in peripheral part of the tumor. Intratumourous mast cells were totally degranulated. The mast cells with intact structure at a background of cells and tissue destruction were also in mammary gland. In destructive mast cells the nucleus with electron-dense circle and chain of granules were observed. On transmission electron microscopy their deformations and the decrease of density were revealed. The mast cells were of elongated of rounded shape with large nucleus and invaginations of karyolemma. The nucleus occupies almost completely the cell's area. It has a ring of large but pale granules. Small protuberances were observed

on the surface of the cell membrane. Their number decreased in direct proportion to the size of must cells and their remoteness from microvessels. Such protuberances are necessary for mast cells in moving. Destructively changed cells with the signs of swelling, vacuolization and clasmatosis were frequent in breast cancer.

PS-17-039

Study of the effect of concurrent mutations of HER-2 and TP53 on angiogenesis of invasive ductal carcinoma and other tissue prognostic factors

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Objective: Determination of eligibility of breast cancer patients for treatment with anti-angiogenic drugs has been always considered as a challenge for oncologists. Each mutation in the genes of proliferation phase enhances the angiogenesis of tumor. We aimed to determine the effect of concurrent mutations of HER-2 and TP53 on angiogenesis.
Method: 32 Women affected by invasive ductal carcinoma (IDC) sporadic breast cancer were included. Immunohistochemical study was performed with HER-2, TP53, Ki-67 and AnnexinV markers. Angiogenesis index was semi-quantitatively calculated by MVD-CD34 technique. Statistical associations between parameters were evaluated.
Results: Prevalence of HER-2 positive and TP53 positive cases were 21.4 % and 20.0 %, respectively. 6.5 % of patients showed concurrent mutation of these genes. Concurrent mutation led to significant increases in both angiogenesis and proliferation and a significant decrease in apoptosis. There was no statistically significant association between concurrent mutation and tumor grade.
Conclusion: This study demonstrates that most of the tissue prognostic factors are poor in concurrent mutation of both genes. Also, our study illustrates that the concurrent mutation correlates with a higher angiogenesis and thus an increased risk of recurrence. We can conclude that in priority setting for administration of anti-angiogenic agents, patients with concurrent mutations are more eligible.

PS-17-040

Adenoid cystic carcinoma in male breast: A case report

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Objective: Adenoid cystic carcinoma of the breast is a rare variant of breast cancer that accounts for 0.1 % of all breast carcinomas and occurs commonly in women between the ages of 25 to 80. In the literature, only a few examples have been reported in men. It is well-differentiated tumour with favorable prognosis and generally presents as a painful breast mass.
Method: Here, we are presenting a 60 years old male patient with a 13×8 mm diameter solid mass on left breast retroareolar region. On fine needle aspiration biopsy, there were 'atipical proliferating ductal epitelial groups'. Then, hookwire localization and excision have been performed. Microscopically, there were tubulary and cribriform islands composed of basaloid type cells with eosinophilic cytoplasm and myxoid material in the cribriform spaces at the center of the islands. We used immunohistochemical markers such as P 63, S 100, CK 7, CD 117, CK 14 and Smooth Muscle Actin for differential diagnosis.
Results: The diagnosis was 'Adenoid Cystic Carcinoma'. The margins of the tumor were positive, so radical mastectomy was performed for treatment.
Conclusion: Because adenoid cystic carcinoma of the breast in male is a very rare example, we present our case here.

PS-17-041

Comparison between the Bond Oracle HER2 immunohistochemical system, the polyclonal HER2 Dako antibody and Chromogenic In Situ Hybridization in breast carcinoma

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Objective: The sensitivity and specificity of immunohistochemical (IHC) methods for HER2 testing are very important given the therapeutic implications. This study compares the concordance between Oracle and the HER2 Dako polyclonal antibody (HER2), in breast carcinomas (BCs) that were equivocal (2+ or not evaluable/NE), by HER2 staining, considering as gold standard the chromogenic in situ hybridization (CISH).
Method: BCs (n=34), problematic by HER2 staining (1−2/2+ or NE), and studied by CISH in our institution, and 24 additional consecutive BCs were stained with HER2 and Oracle, and scored separately by three pathologists. Consensus scoring for each IHC method and CISH results were recorded. Descriptive statistics and measurement of the Cohen's Kappa coefficient were performed.
Results: The overall agreement between the 2 tests in a 3×3 analysis shows a concordance in 62 % of cases (κ=0.405). Among the cases studied by CISH, equivocal were 26 and 11 cases, for HER2 and Oracle, respectively. Seventeen HER2 equivocal cases were negative with Oracle and CISH. In problematic cases, using CISH as gold standard, the sensitivity, specificity, positive and negative predictive values for HER2 and Oracle were 100, 20.7, 17.9, 100 and 100, 72.4, 38.5, 100, respectively.

Conclusion: In problematic cases, Oracle testing shows higher specificity and positive predictive value.

PS-17-042

Stromal P53 and Ki67 expressions of the mammary phyllodes tumors: Are they the clues in determination of tumor grade?

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Objective: Conventionally growth pattern, stromal overgrowth, stromal cellularity, stromal mitotic activity are the main parameters in grading of phyllodes tumors. Recent studies revealed that P53 and Ki67 expressions are both correlated with grade of phyllodes tumors of the breast.
Method: We searched for p53 and Ki67 expression rates of benign and malignant phyllodes tumors in our archival data and correlated them with conventional parameters such as stromal cellularity and mitotic activity rates. 17 benign, 9 malignant phyllodes tumors were reevaluated as regards stromal cellularity (low/moderate and high), mitotic activity (low and high), p53 expression (low, moderate, high), Ki67 expression (low and high) rates. Statistical correlation amongst the whole parameters were searched with Chi-Square test.
Results: Stromal cellularity, mitotic rate, p53 and Ki67 expression rates were all closely correlated (p=0.000–0.001) for benign and malignant histologic subgroups. Ki67 expression was significantly correlated with histologic subgroups, stromal cellularity and mitotic rate (p=0.000–0.001). Similarly P53 expression was correlated with histologic subgroups, stromal cellularity and mitotic rate (p=0.000–0.002).
Conclusion: Both Ki67 and p53 expression rates are statistically significantly correlated with grade of mammary phyllodes tumors, so they can be used in determination of tumor grade, especially for differential diagnosis of benign and malignant ones.

PS-17-043

Quantitative measure proliferative markers by image analysis of invasive ductal carcinoma

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Objective: We analyzed a total number of tumor cells) in invasive ductal breast carcinoma, proliferative activity (% Ki67-positive cells) and mitotic index (% phh3 – positive cells) to establish absolute quantity tumor cells per sq.mm of histological slide and relations this measure with proliferation and mitosis.
Method: The study included 46 patients diagnosed with breast carcinoma from Baku Oncology Hospital during the 2001–05. After whole slide scanning by Mirax scanner (3DHistech, Budapest) of HE, Ki67 and phh3 stained slides we juxtaposed all three slides in one screen to the found area with maximal ki67 level in tumor and the corresponding area in other slides. Morphometric analysis was performed using the Pannoramic Viewer software (3DHistech, Budapest). For each case we analyzed a total number of tumor cells in1 mm2, number of Ki67 and phh3 positive cells.
Results: Mean tumor cells in 1 mm2 of histology slide was 4180+\\−251 cells, median – 3976 cells, 1185+\\−166 (31 %) were positive for Ki67 and 124+\\−23 (3 %) were in mitosis. There was moderate correlation between cell density and Ki67 r=0,44 (p=0,0032) and phh3 r=0,42 (p=0,0018).
Conclusion: By analysis of breast cancer, was established a total tumor cell per mm2 and main proliferative characteristics for invasive ductal carcinoma.

PS-17-044

Malignant adenomyoepithelioma of the breast

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Objective: Adenomyoepithelioma of the breast is a very rare benign tumor with biphasic proliferations of epithelial and myoepithelial elements. It is morphologically and immunohistochemically identical to epithelial-myoepithelial cell carcinoma of the salivary gland. The histologic criteria of malignant AME is not well-established because of the rarity of AME. We report a case of malignant adenomyoepithelioma in a 65-year-old woman.
Method: On ultrasonography, a well-marginated and lobulated solid mass was found at LIQ of the right breast.. An ultrasono-guided core biopsy was performed. The diagnosis of core biopsy was myoepithelial lesion. She subsequently underwent a wide local excision of the lesion.
Results: Microscopically the tumor mass was composed of biphasic patterns which showed formation of tubules lined by an inner layer of ductal epithelial cells surrounded by proliferation of myoepithelial cells that also formed solid nests. But this tumor had foci of infiltrating margins and proliferation of spindle cell components. Also noted are numerous mitotic figures and increased mylepithelial Ki-67 positivity (10–15 % of tumor cells).
Conclusion: Breast lesions which have predominently myoepithelial cells can be divided into myoepithelial hyperplasia, adenomyoepithelioma and malignant adenomyoepithelioma. Tavassoli divied AME into tubular, papillary, and solid subtypes. The criteria of malignant AME is not well-established but some criterias can apply to make a diagnosis of malignant AME.

PS-17-045

Association among residual cancer burden, molecular subtype, and chemosensitivity-related protein expression in breast carcinoma treated with neoadjuvant chemotherapy

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Objective: Neoadjuvant chemotherapy (NACT) is available for patients with breast carcinoma. However, resistance to chemotherapy is still a main cause of mortality.
Method: Differentially expressed genes were identified from previously published studies that examined chemoresistant and chemoresponsive cell lines or patients with breast carcinoma. The expression of 14 selected gene products was assessed in tissue microarray slides comprising 75 post-NACT resection specimens from breast carcinoma patients using immunohistochemistry, and analyzed according to the molecular subtype and Residual Cancer Burden (RCB) grade.
Results: Most cases were positive for ABCB1 (97.7 %) and MYC (96.0 %), but negative for TOP2A (100 %). RCB-II cases expressed much higher levels of MUC1 (p=0.011) and CLU (p=0.021) than RCB-III cases. Positive expression for CALR (p=0.002) and LGALS3 (p=0.018) was observed more often in triple negative types than in luminal types, and cytoplasmic CDKN1B expression was observed more often in luminal types (p=0.014).
Conclusion: Positive expression of ABCB1 and MYC and negative expression of TOP2A in the residual carcinoma after NACT implies general resistance to NACT. Expression of CALR, LGLAS3 and cytoplasmic CDKN1B may be associated with resistance depending on the subtype. Expression of MUC1 and CLU can be used to predict the RCB grade or response to NACT.

PS-17-046

Primary and metastatic melanoma of the breast-review of 4 cases

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Objective: Primary breast melanoma is a very rare tumour accounting for <5 % of all malignant melanomas. The malignant melanoma can be with different manifestation in the breast (primary breast tissue or primary breast skin melanoma as well as metastatic melanoma).
Method: In this study 4 cases of breast melanoma were identified from our records of the past 3 years (0.41 % of all breast cancer cases). A histological and an immunohistochemical (IHC) study was performed using antibodies against CKAE1/3, HMB-45 and Melan-A on both the biopsy and operation material.
Results: Obtained results showed that in 3 cases pigmented, epitheloid and spindle cell melanoma, but in one case epitheloid cell amelanotic melanoma was found. By IHC the melanoma cells expressed HMB45 in three cases, melan-A and S100 in all cases. No expression of CKAE1/3 was observed.
Conclusion: Careful histological and immunohistochemical examination of malignant tumour is essential for adequate diagnosis, follow-up and treatment of breast melanoma.

Age,year	The manifestation of melanoma in the breast	Location	Treatment	Follow-up status
48	Melanoma metastasis to the breast 5 years after primary surgery	Left and right breast, multiple	INF2α	Died after 14 months with distant metastasis
49	Melanoma metastasis to the breast from unknown primary site	Right breast, 1.8 cm diameter	Mastectomy+ ALND	Alive for 2 years with distant metastasis
59	Melanoma metastasis to the breast from unknown primary site	Left breast	Biopsy, INF2α	Disease free for 11 months
71	Primary melanoma of the breast skin	Left breast with ulcerated tumour, 12.0 cm diameter	Mastectomy+ ALND	Disease free for 15 months

PS-17-047

Stem cell expansion in ductal carcinoma in situ of breast

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Objective: The aim is to study the ability of a cell marker panel - ALDH1, CD44 and Ki67 – to identify breast stem cells in no malignant and ductal carcinoma in situ.
Method: Double-color triple-immunohistochemistry - to ALDH1, CD44 and Ki 67 - was done in 169 paraffin

embedded tissue specimens from 111 patients arrayed in tissue microarray blocks. Statistical was done using Chi-square probability test: differences were considered significant when $p<0.05$.

Results: Significantly higher immunoreactivity was seen in DCIS than in benign lesions of breast ($p<0.01$) with used markers. In a total of 169 specimens, CD44+/ALDH1+/Ki67- cells were identied in 110 cases. The distribution was as follows: DCIS (79/57); fibroadenoma (45/29), Atypical hyperplasia (23/13); other benign lesions (22/11) Individually, expression of ALDH1 was: DCIS - 72/79; FAD - 45/45; ADH - 23/23; OBL - 21/22. For CD44: DCIS - 77/79; FAD - 44/45; ADH - 22/23; OBL - 21/22. For Ki67: DCIS - 67/79; FAD - 43/45; ADH - 22/23; OBL - 21/22. The expression values of ALDH1 and Ki-67 were significantly higher in DCIS than in benign lesions ($p=0.028$ and $p<0.01$).

Conclusion: Stem cell expansion is higher in DCIS than in non malignant, supporting their participation in the carcinogenesis of the breast.

PS-17-048

Expression of Calcium Sensing Receptor (CaSR) in patients with disseminated breast cancer

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Objective: Data from in vitro and clinical studies suggest that CaSR expression can be associated with the development of bone metastases. Most probably CaSR stimulates production and secretion of PTHRP via EGFR pathway. The aim of our study was to assess expression of CaSR in the primary breast cancer and correlate it with the risk of bone metastases.

Method: We have analysed 170 patients with the breast cancer. Bone metastases were diagnosed in 102 cases, 68 patients died without skeletal involvement (control group). CaSR expression was assessed in primary tumors using tissue microarray (TMA) and immunohistochemical technique (polyclonal antibody Pierce Bio. PA1-37213). To evaluate cytoplasmatic CaSR expression we have used 0–1 point scale in which 1 was defined as uniformly strong or medium staining in more than 50 % of tumor cells.

Results: Strong or medium staining in more than 50 % was identified in most studied cases, however it was more predominant in patients diagnosed with bone metastases than in the control group (93,14 % vs 83,82 %), $p=0,053$.

Conclusion: Expression of CaSR is common in primary tumors of patients with disseminated breast cancer irrespectively of the metastatic site. However, the patients with bone involvement have higher rate of expression, that is borderline significant statistically. As a result, a group of patients with very high risk of bone dissemination might be separated.

PS-17-049

Bcl2 expression is associated with centromere 17 alterations in luminal B breast cancer

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Objective: Bcl2 is an important established prognostic parameter in human breast cancer (BC) and chromosome 17 centromere (CEP17) copy number is proposed to be the same too. We evaluated Bcl2 expression in different BC's molecular subtypes in relation to increased CEP17 level (CEP17>3 per nucleus).

Method: Immunohistochemistry for Bcl2 assessment and fluorescence in situ hybridization for detection of CEP17 alterations were used. Statistical analysis was performed with Fisher's exact test.

Results: A total of 226 cases of female invasive BC's were analyzed (2010–2011). The tumour subtypes were as follows: luminal A (ER/PR+, Her2/neu-, Ki67<14 %) – 118; luminal B (ER/PR+, Her2/neu-, Ki67>14 % or ER/PR+, Her2/neu+) – 62; Her2/neu+(ER/PR-, Her2/neu+) – 24; triple-negative - 20. In our study group, Bcl2- cases were preferentially ER- in agreement with previous reports. However, 20,5 % tumours of luminal B subtype were Bcl2- too and all of them had increased CEP17 copy number ($p=$ 0,0011, $r\varphi=0,57$). We therefore hypothesized that not only ER had influenced Bcl2 in luminal B BC but CEP17 alterations also.

Conclusion: Centromere 17 alterations are associated to bcl2 downregulation in luminal B BC's. The mechanisms responsible for that remain to be established but the underlying cause could be promoter methylation or transcriptional repression.

PS-17-050

Outcome of excision of radial scar diagnosed on core biopsy: A single centre analysis

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Objective: Radial scar (RS) is a sclerosing lesion of the breast which may be associated with a spectrum of epithelial proliferative lesions and carcinoma. It is frequently subject to biopsy when presenting as a mammographic abnormality. The need to excise RS diagnosed on core biopsy (CB) remains controversial. The aim of our study is to determine the frequency of upgrade in diagnosis after excision of RS.

Method: A retrospective study of RS diagnosed on CB in our department between 01/01/2000 and 31/12/2011 was performed.

Results: 117 cases were retrieved, all women, with a median age of 53 years. Of these, 101 pairs of CB/resection specimens were obtained. CB diagnosis was RS without atypia in 79 cases, RS with atypia in 19 cases and RS with in situ carcinoma in 3 cases. After excision, 21/79 (26,6 %) cases diagnosed as RS without atypia were upgraded: 17 to atypia, 3 to in situ carcinoma and 1 to invasive carcinoma. Of those cases diagnosed on CB as RS with atypia, 9/19 (47,4 %) were upgraded: 8 to in situ carcinoma and 1 to invasive carcinoma.
Conclusion: Our results support the excision of all lesions diagnosed on biopsy as RS. *FM and MC are joint first authors.

PS-17-051
Outcome of excision of papillary lesions diagnosed on core biopsy: A single centre analysis
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Objective: Papillary lesions of the breast (PLB) comprehend a spectrum of entities with different morphologies and malignancy risk, which present a diagnosis challenge on core biopsy (CB). Although diagnostic accuracy has improved with immunohistochemistry, the need to excise benign PLB remains controversial. The aim of our study is to determine CB diagnosis accuracy in PLB, and subsequent need to excise all lesions.
Method: A retrospective study of PLB diagnosed by CB in our department between 01/01/2000 and 31/12/2011 was performed.
Results: 96 cases were identified, with a median age of 59 years. CB diagnosis was benign in 66 cases, some kind of atypia found in 10, and malignant lesions ('in situ' and encysted/invasive types of carcinoma) in 20. Surgical excision was performed on 70 cases, including all cases with carcinoma. Following excision, 6/42 and 4/42 benign CB results were respectively upgraded to atypical and malignant; 3/8 with atypia were upgraded to malignant. Overall, 14 % (7/50) of benign and atypical PLB CB diagnosis therefore missed malignancy.
Conclusion: Our results show that, despite good correlation between CB and excision diagnosis, some cases of carcinoma are missed on CB, so the excision of all PLB remains advisable. *FM and MC are joint first authors.

PS-17-052
Myoepithelial carcinoma of the breast: A case report
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Objective: Myoepithelial carcinoma of the breast is an extremely rare tumor, composed purely of myoepithelial cells, predominantly spindle, with identifiable mitotic activity.
Method: We report a case of a 50 year-old female patient with a palpable, well demarcated lump in her left breast, measuring 3,5 cm in its maximal diameter. Surgical excision and axillary lymph node dissection were performed.
Results: Histologically, the tumor displayed an infiltrating growth pattern and consisted of spindle cells, that appear to emanate from myoepithelial cells of ductules entrapped in the center of the lesion. Mitotic activity did not exceed 5 mitotic figures/10 HPF. Immunohistochemically, the tumor cells revealed positivity for p63, cytokeratin 5/6, cytokeratin 34βE12, smooth muscle actin, CD10 and S100 protein, whereas they were negative for desmin, cytokeratin 7, CD34, HMB45, estrogen, progesterone receptors and Her-2 oncoprotein. Approximatelly 25 % of tumor cells showed nuclear positivity for MIB-1/Ki-67. All axillary lymph nodes were free of metastases.
Conclusion: Myoepithelial carcinoma of the breast is a potentially highly aggressive neoplasm and its differential diagnosis is fairly broad, including metaplastic spindle cell carcinoma and a variety of myofibroblastic lesions.

PS-17-055
Differential expression of biomarkers in stromal and epithelial cells from invasive primary ductal breast carcinomas and paired lymph node metastasis
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Objective: We investigated the differential expression of several biological markers between primary invasive breast carcinomas and their paired lymph node metastasis analyzing separately epithelial and stromal components.
Method: Representative samples of 42 IDC and paired compromised lymph nodes were arrayed in a TMA and 15 selected markers: hormonal receptors, HER-1, HER-2, proliferation (p53, c-myc, pAKT, pmTOR, TGFβ1), motility (CD9 and CXCR) and basal markers (CK5, CK14, c-kit) were evaluated by IC.
Results: In the primary tumor, p53, MIB-1, TGFβ1, CD9 and CXCR4 were more expressed in epithelial cells ($p<0.05$), while pAKT, pmTOR, c-myc and c-kit showed a similar frequency in both components. Hormone receptors, HER-1/HER-2 and cytokeratins were not expressed in stromal cells. The proliferative biomarkers were concordant in the epithelial component. CD9 frequency was similar but cytoplasmic CXCR4 as opposite to nuclear was predominantly expressed in lymph nodes ($p=0.008$). Stromal cells from lymph node showed a reduced frequency of CD9 ($p=$

0.029) and c-myc (p=0.003) when compared to the stromal component of primary tumors.
Conclusion: Epithelial CXCR4 expression may facilitate lymph node metastasis whereas the low frequency of c-myc and CD9 in the lymph node stromal component indicated decreased proliferation enhanced motility of stromal cells in this site.

PS-17-056
Expression of hypoxia-inducible factor-1a and associations with vascular endothelial growth factor expression, high microvessel density and features of aggressive tumors in African breast cancer
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Objective: Breast cancer in Africans is reported to have poor clinical outcome. Whereas hypoxia-inducible factor-1α (HIF-1α) expression has been linked to treatment failure and poor prognosis in breast cancer, there is a lack of reports about HIF-1α expression in Africans. The aim of this study was to evaluate HIF-1α expression in relation to vascular endothelial growth factor (VEGF) expression, angiogenesis, and other tumor characteristics in an African population.
Method: In total, we analyzed 192 breast cancers by immunohistochemical staining. We determined microvessel density (MVD), proliferating microvessel density (pMVD), and vascular proliferation index (VPI) in the most vascularized areas as well as expression of HIF-1α and other biomarkers using tissue microarrays.
Results: Expression of HIF-1α (in 128/182 tumors; 70 %) was associated with VEGF expression (p<0.0005), MVD (p=0.037), high tumor grade (p=0.001), high Ki-67 proliferative rate (p<0.0005), and p53 expression (p=0.032).
Conclusion: There is a high expression of HIF-1α in this series of breast cancer which is strongly associated with VEGF expression and increased MVD. More studies are required to assess the therapeutic implications of HIF-1α expression in this population.

PS-17-057
Breast metastasis: An unusual manifestation of a primary occult appendiceal goblet cell carcinoid
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Objective: Breast metastases from nonmammary malignant neoplasms are uncommon, accounting for approximately 2 % of breast tumors. Primary appendiceal goblet cell carcinoid (GCC) metastasizing to the breast have only sporadically been reported in the literature.
Method: A 47-year-old woman presented with a lump in her left breast.
Results: Clinical examination revealed a firm suspect mass in the breast. The Mammography revealed an irregular mass of 38×25 mm in the upper inner quadrant of the left breast. The patient underwent lumpectomy. The gross specimen had a tan grey firm nodule of 25×15×15 mm. Histological examination revealed a proliferation made of signet ring cell and glandular structures, with islands of goblet cells. Immunohistochemistry revealed strong positive staining with CK7 and CK20, and a sparse positive staining with synaptophysin and chromogranin.ER, PR and HER2 were negative. The patient underwent appendicectomy with a final diagnosis of breast localization of a primary occult appendiceal GCC.
Conclusion: The differential diagnosis between primary carcinoid tumor of the breast and signet ring cell carcinoma metastatic to the breast is often controversial in surgical pathology. Diagnoses need to be made correlating clinical and histological examination in difficult cases in which there is not a diagnosis of carcinoid tumor elsewhere. Their histological appearance may mimic ductal adenocarcinoma of the breast. The distinction is important due to differences in management and prognosis.

PS-17-058
Determination of HER2 gene amplification by chromogenic in situ hybridization (CISH) in breast carcinoma
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Objective: Detection of Her2neu amplification is an integral part of breast carcinoma diagnostics to decide therapy.
Method: We study 55 cases of breast carcinoma embended paraffin tissues, both CISH and FISH were performed on each case using (SPoT-Light HER2) for CISH and both Her-2 and chromosome 17 probes for FISH (Vysis). Sixty tumor cells were evaluated in each case. The scoring system and interpretation of CISH – INVITROGEN.
Results: Concordance between CISH and FISH was found in 94,8 % cases, considering FISH as gold standard, sensitivity of CISH was 97.5 % and specificity 94 %. CISH is more practical alternative due to lower cost, no requirement of fluorescence microscope, use of existing bright-field microscopy and techniques it s similar to IHC, archivable and quantitative results, it s easy to observe both the tissue morphology and the gene amplification evaluation Of the 55 cases analyzed, 53 showed similar results for both methods. Two cases were discordant. In these cases, low-level amplification was suggested by CISH but nonamplification by FISH.
Conclusion: our results, suggest that CISH is a useful technique to determine Her-2/neu oncogene status, in breast

carcinoma for paraffin embendded tissues, is a highly accurate, reproducible and practical technique, with a high sensitivity.

PS-17-060

Usual ductal hyperplasia with central necrosis, microcalcifications and multiple foci of pseudoinvasion arising in a radial scar: A potential diagnostic pitfall

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Objective: The diagnosis of radial scar (RS) is often difficult, especially when associated with proliferative changes, pseudoinvasion and necrosis.
Method: A 41-year-old woman was referred to the Surgery Department for a palpable mass in her left breast, regarded as a possible fibroadenoma on ultrasonography.
Results: Lumpectomy was performed and the macroscopy revealed a tan-white 11 mm diameter lesion, with irregular margins and firm consistency. On light microscopy, a sclerosing lesion, with a stellate arrangement of ducts surrounding a central fibro-collagenous zone was identified. Haphazardly arranged, distorted ducts associated with massive intraductal proliferation, highly suspicious of infiltrative were also present in the center of the lesion. The proliferating ducts showed slit-like, irregular, secondary lumens, several containing central necrosis and a heterogenous cell population. The presence of central necrosis and pseudoinvasion were, however, worrisome. Immunohistochemistry for p63 demonstrated the presence of myoepithelial cells surrounding all the areas with pseudoinfiltrating features, while CK 5/6 displayed a heterogenous, mosaic-like positivity, characteristic for usual ductal hyperplasia (UDH).
Conclusion: Because pseudoinvasion in benign RS can easily be misinterpreted as invasive carcinoma, immunohistochemistry is mandatory to establish the presence of myoepithelial cells. Although rare, central necrosis may occur in UDH and should not be used as a single diagnostic criterion of malignancy.

PS-17-061

Phenotypical and morphological heterogenity of breast cancer: Our experience

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Objective: Breast cancer is the most frequent malignant tumor in women with a rising incidence. About 4 500 new cases are diagnosed in Czeck republic every year, up to 43 % die on it´s account.
Method: In CGB laboratory are investigated 500 of malignant breast tumors every year. We evaluate the morphology, grade of differentiation and phenotype properties- hormone receptors expression, overexpression and amplification of HER-2/neu gene. 2 % of carcinomas posses significantly morphologically and phenotypically heterogenic tumor population in one and the same tumor leasion.
Results: The most often sign of phenotype heterogenity found is hormone receptors expression or overexpression of HER-2/neu gene. Often we see two morphologically different tumor populations coexisting. The most interesting cases from our practice are on the poster.
Conclusion: As for now, studies about the origin of heterogenity inside the same leasions, did not find a single theory to resolve it. A possible answer gives the theory of tumor stem cells and the model of clonal evolution. Our observations demonstrate and may explain the practical reason of different phenotype properties found in core cut biopsy where one population may be held, against the heterogenic properties of the tumor shown when resected as a whole.

PS-17-062

High grade infiltrating carcinoma with squamous features - A case report

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Objective: Apocrine carcinoma is a rare and histologically distinct type of invasive breast carcinoma.
Method: The patient, a 73 years-old woman was admitted to the hospital for a tumor mass in the upper internal quadrant of the left breast. Tissue fragments from the quadrantectomy specimen were routinely processed by paraffin embedding. For the immunohistochemical (IHC) study we used the following antibodies: CK7, androgen receptors (AR), estrogen receptors (ER), progesterone receptors (PR), high molecular weight cytokeratin (HMWCK), p63, gross cystic disease fluid protein-15 (GCDFP-15), En Vision system, visualization with diaminobenzidine.
Results: The gross examination revealed a nodular, well delineated mass of 2,5/2,7/3 cm, firm, gray-beige with areas of necrosis on cut section. Microscopically, the tumor had a predominantly solid, partially cystic and less tubular growth pattern. The tumor cells had abundant eosinophilic granular cytoplasm and pleomorphic high-grade nuclei. A small tumor contingent presented squamoid features. IHC stains showed the following profile: CK7+, AR+, GCDFP-15+, ER-, PR-, p63/HMWCK + (focal/zonal). A diagnosis of high-grade infiltrating apocrine carcinoma with squamous differentiation was established.
Conclusion: There are only a few cases of apocrine carcinoma on record and our case is even more special because of his peculiar aspect, the squamous differentiation.

PS-17-063

The effects of treadmill exercise in the number and weight of mammary tumors chemically induced in female Sprague–Dawley rats: Preliminary results

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Objective: We hypothesized that moderate exercise in Treadmill may affect the mammary tumor development. N-methyl-N-nitrosourea (MNU) is a commonly used carcinogen to induce mammary carcinomas. The aim of this study was to evaluate the influence of Treadmill exercise in the development (number and weight) of female rat mammary tumors.

Method: In this experimental protocol were used 21 female Sprague–Dawley rats. MNU was intraperitoneally administered at 50 days of age in a dose of 50 mg/Kg. Animals were randomly divided in two groups: sedentary (n=11) and exercised (n=10). The exercise program was started after carcinogen administration. Animals were exercised in a Treadmill Control LE8710® after an initial period of familiarization. Thirty-six weeks after MNU administration animals were sacrificed and tumors were counted and weighted.

Results: Sedentary and exercised group presented 25 and 20 tumors, respectively. Pearson Chi-Square value was not significant (p>0.05). The mean tumors weight of sedentary group (5.34±10.58 g) was lower than exercised group (8.64 ±13.01 g). The difference between groups was not significant (p>0.05).

Conclusion: We observed that exercised group showed minor number of tumors, however the lesions presented higher volume. Future morphological and biochemical analysis of tumors will allow a better understanding of the relation between mammary cancer and physical exercise.

PS-17-064

Multifocal malignant lymphoma of the breast

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Objective: Primary non-Hodgkin's lymphomas is an uncommon disease representing approximately 0.15 % of all reported malignant mammary neoplasms. Clinically they are mainly observed as solitary lesions but may also be seen as multiple foci. Herein, we present a very rare case with the diagnosis of multifocal malignant lymphoma of the breast with a detailed clinicopathologic evaluation.

Method: A 56-year-old-female patient with a right palpable breast lump admitted to the hospital. Mammography and ultrasonography findings showed 2 different foci of hypoechoic solid mass forming lesion in the right breast. Excisional biopsy has been performed.

Results: In the histopathological evaluation, both lesions demonstrated diffuse infiltration of mammarian tissue with foci of necrosis; mitotically active tumor cells with large nucleus and prominent nucleoli. The immunohistochemical analysis revealed diffuse and strong LCA, CD20, CD43, focal CD68 positivity while pancytokeratin, EMA, CD34, SMA were negative. The case was diagnosed as Diffuse Large B-cell Lymphoma.

Conclusion: Breast is an uncommon site for primary malignant lymphomas. We report a very rare case with a diagnosis of multifocal primary non-Hodgkin's lymphoma of the breast.

PS-17-065

Cytological, histopathological and clinical correlation at differential diagnosis of granulomatous mastitis-malignancy

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Objective: Idiopathic Granulomatous Mastitis (IGM) is a rare disease that is difficult to diagnose by only radiological methods and clinical findings.

Method: First case; a 30 years old woman with a well circumscribed mass of 5 cm diameter at right breast applied to our hospital general surgery outpatient clinic. In the examination of fine needle aspiration biopsy (FNAB), palisaded epitheloid histiocytes and scattered atypical cells have been seen on a bloody and inflammatory background. We suggested excisional biopsy. Second case; a 39 years old woman applied to our hospital general surgery outpatient clinic with a sore mass in her left breast. The mass has been excised for malignancy suspect. Foci of abscesses, active chronical inflammation, areas of hemorrhage and numerous granulomas containing epitheloid histiocytes are observed microscopically.

Results: In microscobic evaluation of the excisional biopsy of the first case prediagnosed as granulomatous mastitis invasive ductal carcinoma has been our diagnosis. In the second case there have been numerous granulomas containing epitheloid histiocytes, microscopically. Our diagnosis was Granulomatous mastitis in this patient prediagnosed as malignancy.

Conclusion: Especially FNAB findings are easy to confuse with malignancy. We wanted to emphasize to clinician and pathologist to be more alert on distinction of granulomatous mastitis and malignancy.

PS-17-066

Immunohistochemical characteristics of triple negative breast cancer

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Objective: Triple-negative-breast-cancer (TNBC) that accounts for 10–20 % of all breast carcinomas is defined by the lack of estrogen receptor, progesterone receptor, HER2 expression with agressive clinical behavior. TNBC is categorized into basal like subtype which is characterized by the expression of basal cell markers and normal breast subtypes.
Method: We studied on 41 immunohistochemically TNBC patients to determine EGFR, Cytokeratine5/6 (CK5/6), p53, Ki67, GCDFP15 expression patterns by immunohistochemistry, HER2/Chromosome 17 gene status by FISH.
Results: Most of the tumors (90,2 %) were invasive ductal carcinomas. p53, Ki67, GCDFP15 mean positivity rates were 55,6 %; 51,7 %; 3,2 % respectively. GCDFP15 positivity was noted in 8 cases of which 6 were CK5/6(−). The cut-off value for CK5/6 positivity was 5 %. EGFR immunoreactivity was grouped into 0, 1+ as negative; 2+, 3+ as positive categories. CK5/6 was positive in 56,1 %, EGFR was positive in 51,2 % of the patients. The relation between CK5/6 and EGFR expression was statistically significant ($p < 0.01$). HER2 FISH was negative in all cases.
Conclusion: As a result GCDFP15 alone is not a useful marker to detect the metastasis of basaloid type breast cancers. CK5/6 and EGFR coexpression can be used to diagnose basaloid tumors with 5 % cut-off value.

PS-17-067

The clinical significance and incidence of lobular neoplasia: Multicenter study

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Objective: Lobular neoplasia (LNs) of the breast include atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS). Because LNs do not present typical clinical or radiologic findings, the diagnosis is incidental. Many reports suggest that LN is not only a risk factor of invasive lobular carcinoma but also is as a precursor. It is important to know about the incidence of LNs and associated disease in Korea.
Method: A total 1551 cases of breast biopsy or excision from five major hospitals in Daegu were reviewed independently by 5 pathologists of the Daegu Breast Pathology Study Group. The incidence of ALH and LCIS, associated disease, the presence of microcalcification and necrosis were reviewed. All suspected cases of LNs were confirmed on E-cadherin immunohistochemical staining.
Results: Only 46 cases out of 1551 cases (2.9 %) revealed LNs. Associated disease were 17cases of invasive ductal carcinoma, 10cases of in situ ductal carcinoma, 6 cases of invasive lobular carcinoma, 5 cases o f other benign disease, and 3 cases of florid ductal hyperplasia or columnar cell change.
Conclusion: The incidence of LNs was similar to western women. Incidental LNs were frequently associated with invasive ductal carcinoma and further excision is suggested if it was present on the needle biopsy specimen.

PS-17-068

Silver-enhanced in Situ Hybridization (SISH) detection assay for HER2 gene status determination in breast carcinoma: A four year experience in our laboratory

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Objective: Assessment of HER2 status in breast cancer is important in the clinical management of patients and can be identified by a number of methods. In this study we present the results of the SISH technique used in our laboratory in the last 4 years.
Method: We analyzed 398 cases of invasive breast carcinoma, including 41 core biopsies, which were previously characterized immunohistochemically (CB11) as equivocal on a protein level (HER2 2+). All cases were evaluated by bright-field SISH using the automated Ventana Benchmark XT machine. Evaluation was independently performed by two pathologists (FP, GB) based upon the algorithms of the manufacturers and ASCO/CAP guidelines.
Results: Out of 398 cases the HER2 gene was amplified in 82 cases (20.6 %), while in 302 cases (75.9 %) there was no gene amplification. Fourteen of the cases (3.5 %) were characterized as equivocal. The concordance between the two pathologists was high (97.6 %).
Conclusion: The SISH method is new, fully automated and very rapid. Furthermore the bright-field SISH signal does not decay and can be visualized by any standard bright-field microscope even after long periods of time, making it particularly suitable for routine application in surgical pathology.

PS-17-069

Breast fibromatosis: A clinicopathological study of 5 cases

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Objective: Breast fibromatosis (BF) represents 0.2 % of breast tumours that simulate carcinoma. The aim of this study is to characterize the cases of BF diagnosed in our institution.
Method: BF cases diagnosed from 1999 to 2009 were evaluated with clinicopathological and immunohistochemical parameters. We also studied mutations in exon 3 of the gene for β-catenin in 4 cases. Ultrastructural study (US) was performed in 1 case.
Results: There were 5 women between 33 and 69 years old. Radiologically they showed deeply located hypoechoic irregular lesions. Size ranged between 1 and 23 cm. Histologically they were characterized by an ill-defined spindle cell proliferation without epithelial elements or atypia. Immunohistochemical study was negative for AE1/AE3, CK5/6, P63, CD34 and BCL2. Actin was diffusely positive in 4/5, and S100 and Desmin focally positive in 4/5. β-catenin showed cytoplasmic(5/5) and nuclear(1/5) expression. The US showed double smooth muscle and myofibroblastic differentiation. Three patients showed mutations in exon 3 of the β-catenin gene (2 with substitution at codon 41 (T41A) and 1 deletion of 33 base pairs (A43_E65del)).
Conclusion: Focal desmin expression and US suggest smooth muscle differentiation in some BF. All cases showed cytoplasmatic positivity for β-catenin but nuclear expression was seen in only 20 % of cases. 75 % of the valuable cases showed genetic alterations of β-catenin.

PS-17-070

Do BRAF and KRAS mutations exist in triple negative breast carcinomas?

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Objective: Breast cancer is a heterogenous disease consisting of distinct entities characterized by different gene expression patterns. Gene expression profiling of breast cancer revealed 4 major subtypes, including hormone receptor (HR) positive luminal A and B, HER-2 positive and basal-like breast cancer. Most of the basal-like carcinomas are triple negative (HR and HER-2 negative). As most triple negative breast cancers express EGFR, mutations in the signal transducing cascade of RAS/RAF/MAP kinase might play a role in tumor progression. The aim of this study was to determine the incidence of KRAS and BRAF V600 mutations in triple negative breast carcinomas.
Method: Total genomic DNA was obtained from 37 formalin-fixed, paraffin embedded, triple negative breast tumors. KRAS was analyzed by pyrosequencing of codon 12, 13, 61. BRAF (exon 15, V600) mutations were analyzed with AutoGenomics INFINITI BRAF assay on the Autogenomics INFINITI analyzer.
Results: We found KRAS mutation in only one case (2.7 %), apocrine carcinoma which was Gly12Asp (GGT> GAT) mutation. The BRAF V600 mutations were not detected in all analyzed tumors.
Conclusion: We concluded that KRAS mutation was rare in triple negative breast carcinomas and high frequency of EGFR overexpression in this subtype might be related to other pathways in EGFR signaling.

PS-17-071

The pre-lymphatic system and the lymphatic network of the breast in menstruating and in menopausal women: A comparative study

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Objective: The pre-lymphatic system was initially described in the 1960s by Casley-Smith and Florey. It consists of CD34 positive fibroblasts lined stromal spaces communicating with the lymphatic capillaries. The aim of the following investigation was to compare the lympho-vascular density and pre-lymphatic network density of breast tissues in the context of the menstrual status of the patients.
Method: Formalin-fixed, paraffin embedded tissue specimens from 105 patients with primary breast cancer were studied. Tumor-free tissue materials were selected. Tissue processing and immunohistochemical staining with D2-40 and CD34 antibody was performed in accordance to standard laboratory protocols. Quantitative evaluation of the lymphatic and pre-lymphatic system was performed. The Kruskal – Wallies test was used to compare differences between the median values of the studied variables. Statistical significance of the differences was considered if $p<0.05$.
Results: The pre-lymphatic network was found to be significantly more dense in menstruating, compared to menopausal women K-W=61.04; $p<0.0001$ $n=105$. Lymphatic vascular density was higher in menstruating compared to menopausal women K-W=7.60882; $p=0.006$; $n=105$.
Conclusion: Involution changes in the pre-lymphatic and lymphatic system of the breast were found to appear in postmenopausal women. This may be the explanation for the slow local progression of breast cancer observed often in elder patients.

PS-17-072

Comperative study of Herceptest and fluorescence in situ hybridization results in breast carcinoma: Indeterminate (2+) group must not be a wide range uncertainty category

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Objective: HercepTest is an exclusively used immunohistochemistry method for testing Her2/neu overexpression in breast carcinomas. The purpose of this study is to select the proper patients candidate to in situ hybridization, with an indeterminate Her2 score.
Method: A retrospective analysis of 163 cases with invasive breast carcinoma were evaluated for Her2 status using immunohistochemistry and fluorescence in situ hybridization. İmmunohistochemistry of cases that had been previously evaluated by nine different pathologists in our department, were reviewed by two experienced pathologists. Interpretation of the immunohistochemistry results was made without knowing the first results.
Results: Compared to the first evaluation; cases with score 0, 1+ and 3+correlated with the review of immunhistochemistry and none of score 0 and 1+ tumors were positive with in situ hybridization. Gene amplification was detected in 43 cases; 23 of them with 2+score. Three of 3+ tumors and 106 of 2+ cases were negative with in situ hybridization. Discordance was detected in 21 cases in 2+ score; 17 of them were reclassified as negative and 4 were technically unsatisfactory.
Conclusion: Using a different cut-off value for indeterminate Her2 results and training of pathologists to minimaze the interpretational differences, will maximize the accuracy, while not submitting to unnecessary molecular tests.

PS-17-073

Clinicopathological significance of excision repair cross-complementation 1 (ERCC1) enzyme status in breast cancer patients

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Objective: The excision repair cross-complementation 1 (ERCC1) enzyme plays an essential role in the nucleotide excision repair pathway and is associated with resistance to platinum-based chemotherapy in different types of cancer. The aim of the present study was to evaluate the clinicopathological significance of ERCC1 expression in breast cancer patients.
Method: We used immunohistochemical to analyze ERCC1 expression in a tissue microarray from 135 breast carcinomas. ERCC1 expression analysis was available for 109 cases and was correlated with clinicopathologic factors and outcome data.
Results: ERCC1-positive was observed in 58 (53.2 %) cases and was correlated with smaller tumor size (P= 0.007) and with positivity for estrogen receptor (P=0.040). ERCC1 expression did not correlate with overall and disease-free survival rates. The majority (72.7 %) of special histological types of invasive breast carcinomas was positive for ERCC1 compared to invasive ductal carcinomas (ERCC1-positive in 51.1 % of the cases). Similarly, triple negative breast cancers (TNBC) were more frequently negative for ERCC1 (61.5 % of the cases) compared to the non-TNBC (41.5 %).
Conclusion: ERCC1 expression correlated significantly with favorable prognostic factors, such as smaller tumor size and ER-positivity, suggesting a possible role for ERCC1 as a predictive and/or prognostic marker in breast cancer.

PS-17-074

A study of CD10 positive basal/myoepithelial cells in a consecutive series of in situ lobular neoplasia of the breast

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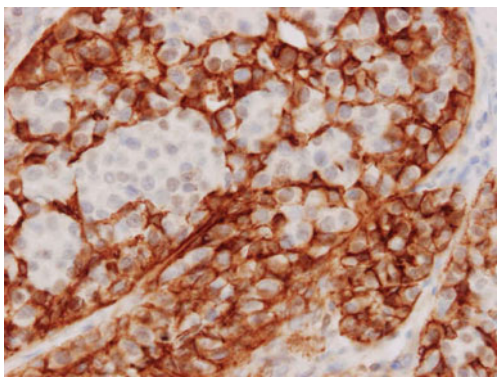
Objective: We have previously reported a few sporadic cases of in situ lobular neoplasia (ILN) associated with marked proliferation of CD10 positive basal/myoepithelial cells.
Method: Twenty consecutive cases of pure ILN and 9 DCIS were studied. New sections were cut and stained for E-Cadherin and CD10.
Results: One out of the 20 cases showed foci of invasive lobular carcinoma in the new cut sections. All 20 ILN cases showed increased proliferation of CD10 positive basal cells, varying from a focal mild increase to a marked proliferation surrounding or mingling with the lobular cells. CD10 positive cell proliferation was least observed in a case of ILN with central necrosis and in foci of ILN seen adjacent to the invasive carcinoma. The invasive tumour cells were CD10 negative. All cases of DCIS had a thin layer of CD10 positive myoepithelial cells, that was incomplete or absent in some foci.
Conclusion: Our findings confirm the presence of a unique relationship between excess proliferation of CD10 positive basal cells and ILN; an association which is not seen in DCIS or invasive carcinoma. This is particularly interesting as recent evidence indicates that CD10 is involved in the regulation of mammary stem and 'sphere forming' cells.



PS-17-075

Breast cancer in young Czech women: An institutional review

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Objective: Breast cancer in young women poses unique diagnostic and management challenges however, very few large studies investigating clinico-pathologic and immunophenotypic characteristics within this group exist and varied, arbitrary age-limits are used to define 'young'.
Method: An institutional archive search was performed for breast cancer diagnosed in women <50 in 2006–2007. Age at diagnosis, tumor histological type and grade, estrogen and progesterone receptor (ER and PR), HER2/neu, Ki-67 and p53 status as well as clinical course during the follow-up period were recorded. Patients were sub-classified into age-groups of 5-year intervals for statistical analysis.
Results: Ninety of 516 carcinomas were diagnosed in women <50. They frequently displayed aggressive morphology, high proliferative activity, increased expression of p53 and high incidence of lymph node metastasis. We found a statistically significant decrease in HER2/neu over-expression with increasing age using 40 as the cut-off (<40: 42 %, ≥40: 11 %; $p=0.0032$, chi-square test). No significant age-related differences in ER or PR expression were observed within the group of women <50.
Conclusion: We show that 40 should be used as the cut-off for defining young women; in whom breast cancer is most likely to over-express HER2/neu. The mechanisms behind this finding and its significance are yet to be elucidated.

PS-17-076

Expression of cytokeratin-19 in breast carcinoma and its implication in the study of lymph node by OSNA method: An analysis of 345 cases

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Objective: OSNA is a molecular assay for lymph node in breast carcinoma (BC) based on m-RNA detection of CK19. The aim of this study is to evaluate the rate of negative o heterogeneous immunohistochemical expression of CK19 in BC.
Method: CK19 was assessed in 345 consecutive samples. Cases were categorized as positive, negative and heterogeneous. Other parameters recorded where histological type and grade (Nottingham) and molecular subtype (St. Gallen2011).
Results: 319 cases (92.4 %) were CK19+. Ten (2.8 %) were CK19- and 16(4,6 %) were heterogeneous. There were 2 intraductal carcinomas, 1 heterogeneous and 1Ck19-. Among 24 invasive carcinomas, there were 9CK19-: 6 ductal, 2 papillary and 1 metaplastic. Three cases corresponded to G1, 4 G2, 1 G3 and 1T1mi not available. Five cases were Luminal A(LA), 1 Luminal B/HER2-(LB-), 1 HER2+ and 2 triple negative (TN). Among 15 heterogeneous cases, 13 were ductal, 1 metaplastic, and 1 atypical medullary carcinoma. Eleven were G3, and 4 G2. Four were LB- and 11 cases were TN.
Conclusion: All lobular carcinomas expressed CK19 CK19 was negative in 2.8 % and heterogeneous in 4.6 % of BC. They represent a heterogeneous group but half of these cases are either G3 or TN. 74 % of heterogeneous cases were TN and 26 % LB- with no LA cases in this subgroup.

PS-17-077

Case report of an extremely rare tumor of the breast: Mucoepidermoid carcinoma

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Objective: Staniceanu and Socoliuc are first authors in equal proportions Mucoepidermoid breast carcinoma, classified in category of purely epithelial metaplastic carcinomas, is rarely encountered with only a few female cases described in literature. It is composed by mucous, intermediate and epidermoid cells, similar to its salivary gland counterpart.
Method: We present the case of a 67 years old man with a 2,2/1,6 cm breast tumor located under the nipple, poorly circumscribed, with increased consistency and central cystic area containing serous fluid. Tissue samples were preserved using 10 % formalin. All sides were stained using hematoxylin-eosin. Immunohistochemistry was performed using labeled streptavidin-biotin method.
Results: Microscopic examination reveals islands and sheets of polygonal cell with clear/pale cytoplasm, "signet cells" figures, areas of squamous metaplasia and centrally located hyperchromatic nuclei, some with visible nucleoli and rare mitoses. Tumoral parenchyma contains ducts and cysts of varying sizes, with pale eosinophilic luminal accumulation PAS, D-Pas and Alcian Blue positive (mucin). Immunohistochemical tests were performed. Differential diagnosis was made among several benign and malignant lesions, the final diagnostic being mucoepidermoid carcinoma, low grade.
Conclusion: Mucoepidermoid carcinoma of the breast is an extremely rare entity; however its specific morphologic and prognostic features (similar to its salivary gland counterpart) allow proper diagnostic.

PS-17-078

Malignant transformation of adenomyoepithelioma of the breast by monophasic population with triple negative and bilinear immunophenotype: Report of 2 cases

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Objective: Malignant adenomyoepitheliomas are rare tumours of the breast and 34 cases have been so far reported in the English literature of which only 16 cases with spindle morphology.
Method: Two cases of adenomyoepithelioma of the breast with malignant transformation by monophasic spindle population of cells are presented in a 56 and 41 year old patient respectivelly.
Results: The underlying benign adenomyoepithelioma with typical biphasic architectural pattern was identified and represented at least 30 % of the tumor volume in each case. In both cases, malignant portion of tumor was composed of relatively uniform monophasic population of highly atypical cells. The malignant component in case 1 was positive for pan-cytokeratin, myoepithelial markers, and basal-type cytokeratins and also focally positive for luminal-type of cytokeratins; but negative for hormone receptors (estrogen and progesterone) and HER-2/neu protein overexpression. The malignant component in case 2 was positive for spectrum of myoepithelial markers but negative for luminal cytokeratins and hormone receptors and HER-2/neu protein overexpression.
Conclusion: The bilinear immunophenotype in the case 1 suggests that the malignant tumor may have developed from precursor multipotent stem cells that can differentiate into both luminal epithelial and myoepithelial cells, while malignant component in case 2 appears to be the of pure myoepithelial phenotype.

PS-17-079

Primary neuroendocrine carcinoma of the breast: Can it be suspected on histomorphologic grounds?

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Objective: Primary neuroendocrine carcinomas (NEC) of the breast are defined by the WHO classification as a group of neoplasms that express neuroendocrine markers in more than 50 % of the cells. These tumors can exhibit different morphologic appearances including solid, nested or alveolar pattern, papillary or mucinous differentiation or conventional ductal structures. The aim of this study is to identify histomorphological features useful in the recognition of this tumors.
Method: 160 invasive breast carcinomas were reviewed, none of them previously typified as NEC. 154 were ductal carcinomas (26 grade I, 61 grade II and 66 grade III) and 6 lobullilar carcinomas. In all cases immunohistochemical staining for the neuroendocrine marker synaptophysin was performed.
Results: Eight of the 160 cases showed intense immunoreactivity for synaptophysin. All of them were predominantly composed of solid, confluent nests and cords of cells with medium-to high grade nuclear atypia. Two cases showed intense desmoplastic or sclerotic stromal response. A colloid component was identified in another two cases.
Conclusion: Due to its morphologic variability, mammary NEC is frequently underrecognized. A predominantly solid pattern of confluent nests and trabeculae associated with a prominent sclerotic stromal response or colloid differentiation should prompt to perform additional immunohistochemical staining in order to exclude neuroendocrine differentiation.

PS-17-080

Expression of Aurora kinase A and Gamma-tubulin in breast carcinomas of patients undergoing neoadjuvant chemotherapy

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Objective: Association between centrosome abnormalities and response to chemotherapy has not been fully elucidated in breast carcinomas (BC). Here we analysed the association between Aurora kinase A (AURKA) and Gamma-tubulin (GT) and response to neoadjuvant chemotherapy (PST) in patients treated with BC.
Method: The immunohistochemical expression of AURKA and GT was analysed in 44 core biopsies of BCs taken before administration of PST. AURKA expression was analysed using a modified Allred-like scoring system (intensity and percentage of staining combined). Cells containing one or two centrosomes as determined by GT were considered negative, whereas cells containing more than two centrosomes were regarded as positive. Centrosome amplification was graded in each specimen as follows: negative (0–2 % of cells); weak (2–10 %); moderate (11–20 %); and strong (21 %<). Pathological response rates were assessed using Chevallier's classification.
Results: Centrosome amplification was significantly higher in patients achieving complete response when compared with the cases where partial remission or no response was

defined (p=0.03), whereas we found no significant correlation between the expression of AURKA protein and response rate to neoadjuvant chemotherapy (p=0.24).
Conclusion: BCs showing centrosomal amplification as determined by GT present higher response rates to neoadjuvant chemotherapy, but need further validation.

PS-17-081

Breast granulocytic sarcoma with aleukemic presentation: A case report

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Objective: Granulocytic Sarcoma (GS), a rare solid tumor of immature myeloid cells in exrtamedullary sites, usually occurs during the natural course of acute myelogenic leukemia (AML). Rarely is presented without overt hematological disease. The breast is an uncommon site of localization.
Method: We report a case of breast GS with aleukemic presentation, condition that is extremely rare and requires a high index of suspicion for diagnosis. A 46 year old woman, presented with a solitary, non-tender, palpable left breast mass. A lumpectomy was done.
Results: Histopathology revealed breast parenchyma diffuse infiltration, in a targetoid pattern, by immature small cells intermingled with eosinophils. Lobular carcinoma and lymphoma were considered in differential diagnosis. The myeloid origin of the neoplasm was established by immunohistochemical analysis that revealed LCA, MPO, CD34, HLADR, CD68 (Kp1) positivity. There was no evidence of leukemia in the peripheral blood and bone marrow. The patient was treated as AML with systemic chemotherapy and 5 months after the diagnosis she is without evidence of disease.
Conclusion: Breast GS is a challenging situation both for pathologists and hematologists. Available evidence strongly favors the application of systemic chemotherapy despite the appeared localized nature of the disease.

PS-17-082

Molecular subtypes of breast cancer according to expression of surrogate immunohistochemical markers: Study of 152 cases

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Objective: To classify breast cancer into molecular subtypes based on immunohistochemical profile: luminal A (ER + and/or PR+; HER-2-), luminal B (ER + and/or PR+; HER-2+), HER-2-positive (ER-; PR-; HER2+), basal (ER-; PR-; HER2-; at least one of three basal markers positive), 5-negative (ER-; PR-; HER2-; CK5/6-; CK17-; EGFR-).
Method: Paraffin blocks of tumor tissue of 152 breast cancer cases collected at our Cancer Centre for 3 years. The immunohistochemical study was performed by standard techniques using following antibodies (Dako): ER, PR, HER-2, EGFR, CK5/6, CK17, Ki67.
Results: All cases were classified into the 5 subtypes: luminal A (n=91; 59.8 %); luminal B (n=13; 8.6 %); HER-2-positive (n=19; 12.5 %); basal (n=19; 12.5 %); 5-negative (n=10; 6.6 %).
Conclusion: Luminal breast cancer phenotype predominates in our collection, predictive/prognostic value of molecular genetic subtypes is planned to be investigated. We recognized statistically significant differences (P<0,001) in five-year survival rates between tumors of luminal (A, B) and basal subtypes.

PS-17-083

Proliferating trichilemmal cyst with atypical cytological features

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Objective: Proliferating trichilemmal cysts are relatively common occurring within the scalp of elderly women. Proliferating trichilemmal cysts of the breast, however, are rare. These cysts are benign with very few demonstrating malignant transformation.
Method: We report a case of proliferating trichilemmal cyst of the breast with atypical cytology which prompted excisional biopsy. Cytological assessment was useful in this case as it indicated excisional biopsy rather than a more extensive excision.
Results: Smears produced from the FNA showed sheets of atypical epithelial cells with foamy histiocytes, multinucleate cells and fibrotic material with evidence suggestive of fat necrosis. A cell block was acellular. A specific diagnosis was not made. An excision specimen was advised and a proliferating trichilemmal cyst was demonstrated.
Conclusion: The cytological features in this case are in keeping with previous cases reported in scalp lesions. These benign cysts can uncommonly undergo malignant transformation. While rare, proliferating trichilemmal cysts of the breast do occur and complete surgical excision is required. Cytological features are thus important to recognise. No previous cytological diagnoses of this rare breast lesion have been reported.

PS-17-084

Morphological and molecular biological features of breast cancer in patients till 35 years of age

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Objective: A large clinical value has determination of molecular subtype of breast cancer (BC). To clarify morphological and molecular biological similarities and differences between BC depending on age, we compared features between tumors of younger and older women.
Method: 573 patients with BC are included in research: from 18 till 86 years, among them 254 patients were till 35 years. ER, PR, Her-2/neu, p53, p63, Ki67, CK5/14, p21, Bag1, Mcl1, pS2, VEGFR, Her-1 were analyzed in all cases by immunohistochemistry.
Results: The younger patients with BC had higher expression of p53, p63, p21, Bag1, Mcl1, Ki-67, VEGFR, HER-1 ($p<0,001$) than older patients. There was a basal-like molecular subtype of BC 3-fold more frequent compared with older patients (21,6 % versus 7,2 %; $p<0,0001$). Three-years overall survival in patients till 35 years was by 11,5 % and a five-year overall survival was by 15,5 % lower than in patients over 35 years ($p<0,001$).
Conclusion: Aggressive clinical course of breast cancer in patients till 35 years is related to the molecular biological features of tumor.

PS-17-086
Breast HER2 Insitu Hybridization (HER2 ISH): Acceptable and unacceptable staining criteria impacting on interpretation
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Objective: Breast HER2 ISH relies on correct enumeration of HER2/CEP 17 signal. However, as with immunohistochemistry, there are technical pitfalls which may render ISH difficult/unreliable to interpret. The UK NEQAS has established a 'technical' ISH module to provide feedback to laboratories using both chromogen and fluorescence based tehcniques.
Method: Unstained slides consisting of 4 breast cancer cell lines were distributed. Laboratories were asked to demonstrate HER2 gene amplification using their routine assay, and then return the slides for assessment. Chromogen based methods were assessed around a multi-header microscope with 4 assessors scoring each slides, whilst the fluorescent ISH method was assessed by a single individual. Assessors scored the 'readability' of each slide, without counting the probes, and provided feedback where the hybridisation technique could hinder interpretation.
Results: CISH based methods showed acceptable staining in 50 % ($N=32$) of cases. Staining problems ranged from loss/poor HER2/CEP17 signal, non-specific staining and morphological damage. The FISH pilot assessment showed an acceptable rate of 32 % ($n=21$), with the low pass rate being attributed to poor preservation/quenching of fluorescence signal.
Conclusion: Greater emphasis needs to be placed on the 'readability' of an ISH slide, prior to carrying out the process of enumeration.

Tuesday, 11 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-18 Poster Session Cardiovascular Pathology

PS-18-001
A rare tumor in the right atrium
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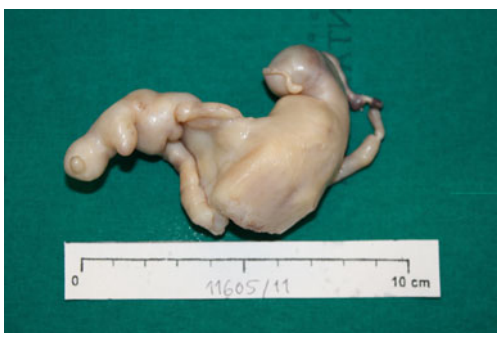
Objective: Intravenous leiomyomatosis is a very rare growth pattern variant of leiomyoma in which nodular masses of tumor grow within venous channels. Occasionally the tumor can extend to vena cava and the right heart.
Method: We present a case of a 45-year-old woman, who was admitted in the emergency room with rapidly evolving exertional dyspnea. Cardiac ultrasonography revealed a "big mass in the right chambers". She was submitted to a right atriotomy with resection of part of the tumor, which was sent for intraoperative consultation.
Results: Grossly, the tumor was polypoid, firm, with a smooth surface. The frozen section showed a lesion composed of tortuous vessels and in some areas a fibrillar eosinophil extracellular matrix and others with spindle cells. No significant atypic or pleomorphic cells, mitosis or necrosis were observed. The diagnosis was deferred for definitive paraffin sections. In the definitive H&E and with immunohistochemical stains, the case was diagnosed as an intravenous leiomyomatosis, and the diagnosis was confirmed in the hysterectomy specimen.
Conclusion: Intravenous leiomyomatosis with cardiac involvement is an extremely rare condition. Clinical information is essential for the correct diagnosis in frozen section.



PS-18-003

Characterization of a specific mechanism for late loss of cardiac allograft: The antibody mediated rejection (AMR) as a major factor of cardiac allograft vasculopathy (CAV)

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Objective: The rational of this study was to investigate explanted failing grafts in the light of new concepts in rejection mechanisms, namely AMR.
Method: This retrospective multicentric study collected 31 explanted cardiac grafts failing ≥1 year posttransplantation. The vasculature of the grafts was assessed from epicardial coronary arteries to myocardial microcirculation. Immunohistochemistry was performed for C4d complement fraction deposition and CD68-positive macrophages in the explanted grafts and previous endomyocardial biopsies. Donor specific antibodies (DSA) were retrospectively assessed using Luminex SA technique.
Results: A pure classical coronary atherosclerosis pattern was observed in 6/31 (19 %). A pure pattern of CAV was present in 12/31 (39 %) and a mixed pattern associating CAV and atherosclerosis features in 9/31 (29 %). Interestingly the CAV pure and mixed patterns were associated with vascular inflammation within the arteries and/or the microcirculation with C4d deposits and macrophages (15/21) in the explanted grafts versus nil (0/6) in pure atherosclerosis pattern ($p<0.002$). Furthermore they were associated with previous AMR episodes on endomyocardial biopsies (11/21) and by positive DSA (10/14) versus nil in pure atherosclerosis pattern ($p<0.05$ and $p=0.05$, respectively).
Conclusion: In failing cardiac grafts CAV lesions are associated with makers of AMR. CAV should be the consequence in coronary arteries of an ongoing AMR process.

PS-18-004

Age related histopathological changes in cardiac conducting system in Turkish population: Evaluation of 202 autopsy cases

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Objective: Histopathological features of cardiac conducting system (CCS) in Turkish population have not been investigated previously.
Method: We examined CCS of 202 autopsy heart specimen dissected between the years 2004 and 2005 in Bursa Forensic Medicine Institution. Of the 202 cases from all age groups, 154 were male and 48 were female.
Results: In our cases increase in fibrous and adipose tissue concordant with age, indicating an age related nature, were detected. Fibrous and fatty tissue infiltration appeared at the age of 35. Fatty infiltration started at the age between 20 and 34 at sinoatrial node. In 4 cases calcification and in 19 cases inflammation was observed. Amyloid accumulation was not present. In 7 cases myocardial infarction not involving CCS was seen. In 1 case fibroelastoma was detected.
Conclusion: In Turkish population age related fibrosis and fatty infiltration in CCS appeared at the age of 35 and increased with age. Fatty infiltration in sinoatrial node started at a younger age than that of reported in the literature. In cases whom the cause of death could not be determined we could not detect lethal pathologic features. However we think that examination of the CCS will improve the quality of autopsy diagnosis.

PS-18-005

Periadventitial adipose tissue in human coronary atherosclerosis: A neurotrophin study

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Objective: Recent evidence demonstrates that epicardial adipose tissue, including coronary periadventitial adipose tissue (tunica adiposa), are paracrine sources of bioactive mediators (adipokines, NO, H2S) which may be involved in coronary atherogenesis. Because of the increasing interest for extra-neuronal effects (inflammation, wound healing, lipid and glucose metabolism) of the neurotrophins nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF), including in human coronary atherosclerosis in autopsy samples, the aim of the present study is to evaluate the expression of NGF and BDNF and their receptors (TrkA and TrkB, respectively) in cardiosurgery biopsy samples of pericoronary adipose tissue.
Method: Immunohistochemistry of NGF, BDNF and their Trk receptors.
Results: NGF, BDNF, Trk A and TrkB expression was lower in periadventitial adipose tissue of atherosclerotic coronary arteries as compared to non-affected coronaries.
Conclusion: We provide the first evidence for a possible role of neurotrophins in the molecular remodeling of tunica adiposa in human coronary atherosclerosis. This study is dedicated to 103rd Anniversary of Rita Levi-Montalcini, the Nobel laureate for the discovery of NGF.

PS-18-006

Apoptosis in dilated cardiomyopathy and myocarditis

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Objective: In normal myocardium, apoptotic myocytes are usually absent, or if affected, with most of 28 positive cells per million.
Method: The apoptosis was measured by the TUNEL method in 60 patients with dilated cardiomyopathy (DCM) and myocarditis (MC), and expresed by apoptotic index (AI) in 30 patients within both groups, and to correlated with ejection fraction (EF) and with different morphological stages of these entities. Statistical analisys was performed, and p values ≤ 0.05 were considered statistically significant.
Results: AI in MC cases was 4,23+12,16, and in DCM cases the value was significantly higher 5,41+9,33 ($p=0.005$). In the group MC patients, we didn't found statistically significant correlation between AI and different values of EF ($p=0.701$). The analysis of the value of AI between patients with different morphological stages of MC didn't show statistically significant correlation ($p=0.535$), as well as in DCM ($p=0.312$).
Conclusion: Apoptosis play a significant role in DCM and MC but its significance in the progression to heart failure has still to be established.

PS-18-007

"Contusio Cordis": A concealed cause of unexpected death

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Objective: Cardiac lesions following blunt chest trauma are multiple and of various degrees of severity. "Cardiac Contusion" is a difficult diagnosis, especially antemortem and if signs of thoracic trauma are not evident on external habitus and on the underlying internal plans of cardiac area. Is the contusion a cause of death per se?
Method: The authors present two cases of road accident male victims, aged 43 and 50 year-old, submited to complete postmortem examination with ancillary diagnostic methods.
Results: No traumatic lesions or underlying pathology was found at the autopsy. Epicardial and myocardial hæmorrhagic foci were histologicaly documented. Toxicology was negative.
Conclusion: Cardiac Contusions are caused by one of the following mechanisms: 1) heart compression between bone structures, 2) sudden acceleration-deceleration movements and 3) sudden thoracic/abdominal pressure increase. They may be asymptomatic or lead to rhythm disturbances responsible for unexpected death (10 %). They seem to be underdiagnosed, thus suspecting the entity "Contusio Cordis" is crucial, not only antemortem for correct surveillance and treatment, but also postmortem to adequately establish causality nexus in cases of post-thoracic trauma deaths.

PS-18-008

The influence of bone marrow-derived multipotent stromal cells on myocardial scar healing in experimental myocardial infarction

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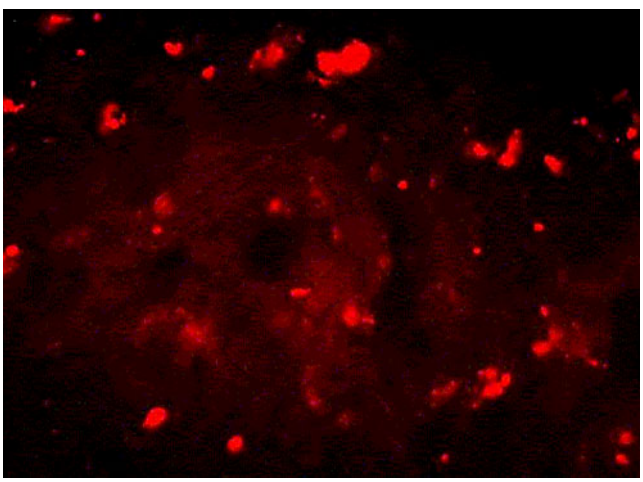
Objective: Previous studies have shown the benefits of intracoronary infusion of bone marrow-derived multipotent stromal cells (BM-MSCs) in heart disease. Our aim was to study engraftment, differentiation of BM-MSCs and its role in myocardial reparation.
Method: Acute myocardial ischemia was produced by transient occlusion (total of 20 min) of the proximal left anterior descending coronary artery and followed by reperfusion. BM-MSCs were isolated, expanded by standard and labeled with PKH26 (Sigma). Cells were CD90 and CD105 positive. 30 days after occlusion during cross-clamping of aorta the cells were administered into the cavity of the left ventricle at the concentration 5×106 in saline solution. In 1 day, 2, 4 and 6 weeks after transplantation the labeled cells were detected in the cryosections and heart morphometry was performed.
Results: BM-MSCs were detected only in the scar tissue and had a fibroblast-like phenotype. They neither differentiated into cardiomyocytes nor into the cells of blood vessels. In 4 weeks after transplantation the scar thickness was higher in the group with cell transplantation ($p<0.001$).
Conclusion: Engrafted BM-MSCs promote myocardial fibrosis only in the scar, but not in the perifocal myocardium, provided strengthening of the scar, remodelling of outflow tract, and improvements the myocardial function.



PS-18-009

Endomyocardial biopsy value in differential diagnosis of hypertrophic cardiomyopathy

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Objective: Endomyocardial biopsy (EMB) may be used to diagnose different types of cardiomyopathies, to monitor transplant rejection, evaluation of myocarditis, heart failure of unknown origin, arrhythmias, drug toxicity and heart neoplasmas. The aim of this case is to show how non-invasive cardiac investigations are sometimes not sufficiently conclusive for distinguishing between hypertrophic obstructive cardiomyopathy (HOCM) and the other cardiac diseases.
Method: Thirty-one representative left ventricle biopsies were obtained following suspected HOCM. Samples underwent routine standard and special staining procedures. Five histologic parameters were used for assesment (disarray and hypertrophy of myofibers, myocardial short runs, perinuclear halo and bizarre nuclei and fibrosis) and graded from 0 to 3, presenting in summary Histological HOCM Index (HHI- ranging from 0 to 15).
Results: The histological findings in EMB of thirty-one patients, in 8 (25,8 %) patients HOCM diagnosis was confirmed, in 6 (19,35 %) patients HHI was under or equal to 50 % (8) so HOCM diagnosis couldn't be confirmed, amyloidosis in one (3,22 %) patient, myocarditis in 4 (12,9 %) patients, dilatative CMP in 6 (19,35 %) patients and unspecific cardiac changes in 6 (19,35 %) patients.
Conclusion: A definitive diagnosis can be obtained by means of a multidisciplinary approach including EMB findings.

PS-18-010

Morphometric study of structural changes in the heart of people who abused alcohol for more than 5 years

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Objective: The information about structural changes in the heart of people abused alcohol (PAA) is very contradictory.
Method: We studied 22 hearts of PAA (>100 g per day), 10 hearts of patients with ischemic heart disease (IHD) and 10 hearts of healthy persons. At the morphometric study of heart we measured the mean cardiomyocyte diameter (MCD), the relative areas of fatty infiltration (FI), fibrosis, cardiomyocytes. Immunohistochemistry was performed using antibodies against CD3-antigens to count the number of antigen-positive cells per 1 mm².
Results: The average heart weight, the MCD of the PAA were not significantly different compared to the ones of the control group. The average relative area of FI of RV for the group of PAA was 21±15 % and was significantly different compared to the one of both the control group and the group with IHD. The relative area of RV fibrosis in the group of PAA was 9.9±6.5 % and was not significantly different compared to the ones of the other two groups. The mean number of CD3+ lymphocytes/mm² of 23 % of PAA was more than 14.
Conclusion: The PAA did not have myocardial hypertrophy. 23 % of them had chronic myocarditis. Marked FI in PAA was significantly higher than the other two groups.

PS-18-011

Expression of angiotensin-converting enzyme 2 in ischemic myocardium

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Objective: The aim of the study was to evaluate the expression of angiotensin-converting enzyme 2 (ACE-2) in left ventricular myocardium in the presence of chronic myocardial ischemia.
Method: Heart specimens with persistent ischemia (n=43, pre-infarction ischemic heart disease (IHD) group) and post-infarction scar (n=32, post-infarction IHD group) from dissected males and heart explants (n=15, end-stage ischemic heart failure group) were studied. Heart specimens (n=29) selected at autopsy from individuals who died from accidents were used as controls. The slides of myocardium were incubated with polyclonal antibody against the ACE-2 (1:1000, ab15348, Abcam).
Results: ACE-2 expression in cardiomyocytes of the pre-infaction IHD and post-infarction IHD groups did not differ from the controls and was increased only in the end-stage ischemic heart failure group (p<0.05). ACE-2 expression in vascular endothelial cells, smoth muscle cells and macropages of the pre-infarction IHD group did not differ from the controls; but the number of ACE-2 expressing cells in the post-infarction IHD and in the end-stage ischemic heart failure groups was greater, as compared with the pre-infarcion IHD group and the controls (p<0.05).
Conclusion: Expression of ACE-2 is increasing in progression of ischemia-induced myocardial dysfunction.

PS-18-012

Thrombotic occlusion of the peripheral pulmonary arteries: Anatomical "trigger" of the massive pulmonary thromboembolism (PTE)

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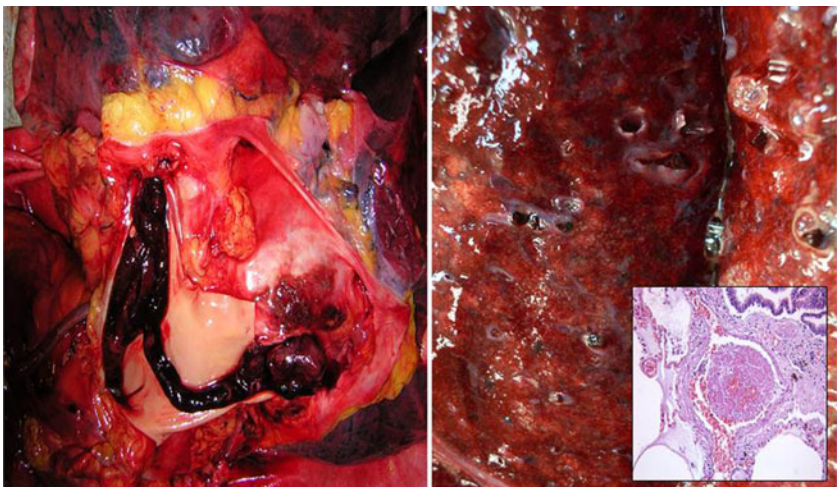
Objective: From January 2000 to December 2009 (Institute of Pathology and Legal Medicine, Paolo Giaccone – Palermo) 57 autopsies were performed on 37 males and 20 females who died of a massive PTE.
Method: Systematic autopsy.
Results: Saddle pulmonary thrombosis in 33 cases, in 24 isolated in both the main pulmonary arteries. In all cases the transverse heart diameter was 1,5–2 cm superior to the longitudinal one, the interventricular septum became rectilinear with a right ventricular dilation. The coronary artery anatomy was: critical stenosis through fibroatheromatous plaque of the dominant right coronary artery (RCA, 2), non dominant left coronary artery (LCA, 3); non critical stenosis of RCA (14), LCA (8); absence of stenosis (30). Histological ventricular examination showed hypoxic-ischaemic and/or reperfusion and overload lesions. In all cases, the lungs showed plurifocal occlusive thrombosis of intramural pulmonary arterial (IPA) vessels associated with adjacent infarctual necrosis (49); acute partially haemorrhagic basal oedema (35) and desquamative macrophagic alveolitis (28).
Conclusion: In all cases of massive PTE the thrombosis of IPA vessels associated with an adjacent infarction (86 %) is constant. This suggests that death is nearly always preceded or triggered by one or more episodes (clinically silent or with non specific symptoms) of thromboembolism of IPA vessels.



PS-18-013
Cardiac findings in routine fetal autopsies: More than it meets the eye?
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Objective: Congenital heart disease (CHD) is the most common malformation in newborns. Our aim was to evaluate the spectrum of CHD in consecutively performed fetal autopsies and to correlate prenatal and postmortem diagnoses.
Method: A retrospective study of 726 fetal autopsies was performed in a tertiary referral hospital. CHD was classified in seven categories: left ventricular outflow tract obstruction-LVOTO, right ventricular outflow tract obstruction-RVOTO, septal defects, connection anomalies, conotruncal anomalies, complex anomalies and others. Cardiac defects were also classified as isolated or associated with others anomalies.
Results: CHD was identified in 99 (13.6 %) fetuses. Most common categories were septal defects and complex anomalies. Associated anomalies were found in 67 fetuses (67.7 %). In this group, septal defects were the most common CHD, frequency being significantly higher than in the group of isolated cardiac anomalies (p=0.012). Comparison of prenatal and postmortem diagnoses (50 cases) showed complete or partial agreement in 36 and 10 cases (72 % and 20 %, respectively) and complete disagreement in 4 cases (8 %). In the latter group, prenatal diagnosis had not been done by a pediatric cardiologist.
Conclusion: The high prevalence of CHD in lost pregnancies highlights the importance of systematic fetal autopsy performed by a specialized pediatric pathologist.

PS-18-014
Morphogenetic biomineralization aspects in the human heart valve affected by atherosclerosis
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Objective: The appearance of pathological calcification, which leads to significant changes of vascular wall, which underlie the development of atherosclerotic complications, has a great importance in the morphology of atherosclerosis development. Purpose of the work is the study of pathological biomineralization in heart valves affected by atherosclerosis.
Method: The study was conducted on sectional material of mitral and aortic valves obtained during autopsy. The tissue of heart valves was studied by methods of histology, electron microscopy, X-ray diffraction, infrared spectroscopy.
Results: Macroscopically mitral and aortic valves are thickened, opaque, dull whitish, sometimes with deformity and ulceration. Histology observed the formation of atherosclerotic plaques, fibrous changes, and inflammatory infiltration. According to X-ray phase analysis biominerals in heart valves are represented by apatite crystalline phase. Sizes of crystals have distinct age dependence. The results of infrared spectroscopy revealed absorption bands of carbonate apatite replacement; in all instances they correspond to the type of substitution B (CO3 2– replaces PO4 3–).
Conclusion: The study of pathological mineral formations on human heart valves by the range of morphological and physicochemical methods show that they are aggregates of interacting organic and mineral components, their ratio changes with "maturation": the organic component decreases and the mineral component, represented by carbonate containing hydroxyapatite doped with chlorine grows while improving, so the process is dynamic.

PS-18-015

Relationship between myocardial injury, oxidative stress mechanism and sepsis/septic shock in infants submitted to surgery for congenital heart defects

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Objective: A progressive ventricular dysfunction caused by ischemic myocardial injuries remains one of the leading causes of death during the postoperative course in congenital heart disease (CHD). The aim of this study was to investigate the role of oxidative stress in these myocardial injuries.
Method: Myocardial injuries and oxidative stress mechanisms were assessed by histopathology and immunohistochemistry and quantified by morphometrical analyses.
Results: Myocardial injury was observed in pediatric patients submitted to surgery for CHD with cardiopulmonary bypass, followed by lethal exit. Oxidative stress mechanisms were directly related to these particular types of myocardial injuries. Importantly, 4- hydroxynonenal (4-HNE), a marker of lipid peroxidation, is strongly expressed, especially in irreversible myocardial lesions. Although morphologically similar, myocardial injuries observed in patients who evolved with sepsis in the peri-operatory period exhibited a completely different set of oxidative stress mechanisms. Increased concentrations of nitrotyrosine protein adducts were observed in these patients, suggesting that peroxynitrite-mediated protein nitration may be the predominant oxidative stress mechanism found in these situations.
Conclusion: The underlying mechanisms of these lesions seem to be related to the development of ischemia or ischemia/reperfusion followed by oxidative stress mechanisms that vary depending on whether sepsis was present. While the exact mechanism is not fully understood, it has been suggested that endogenous catecholamine release could have a role in this process.

PS-18-018

Increase of ABCG2/BCRP + side population stem cells in the myocardium after ventricular unloading

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Objective: A significant decrease of the mean cardiomyocyte DNA content and increased numbers of diploid cardiomyocytes after ventricular unloading was demonstrated, suggesting a numerical increase of cardiomyocytes. The heart harbours several stem cells populations including c-kit (CD 117) + cells and side population cells (SPC), that might proliferate after unloading and generate diploid cardiomyocytes. It was tested, whether there is an increase of ABCG2+ SPC and CD117+ cells after unloading.
Method: In paired myocardial samples (before and after LVAD), the number of cells with immunoexpression of ABCG-2, c-kit/CD 117 and MEF-2 was assessed by immunohistochemistry and morphometrically determined.
Results: A significant increase of SPC and cells with coexpression of c-kit and MEF-2 after unloading was observed (p=0.001). A significant positive correlation between both SPC and cells with coexpression of c-kit and MEF-2 expression was observed (p=0.007 and 0.01). No correlation was found between the number of SPC and the mean cardiomyocyte DNA content.
Conclusion: SPC are significantly increased in the myocardium after ventricular unloading, suggesting a role of stem cell proliferation during “reverse cardiac remodelling”. These cells might proliferate and commit to different cell lineages such as cardiomyocytes or endothelium, and thus ameliorate cardiac function.

PS-18-019

Role of elastin gene polymorphism in ascending aorta aneurysm development in patients with essential hypertension

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Objective: There is supposition about genetic propensity in the ascending aorta aneurysm (AAA) development. Aim: to investigate role of elastin gene polymorphism (rs2071307) in AAA development in essential hypertension (EH).
Method: DNA samples from persons with AAA and EH (1 group), with EH only (2 group) and healthy subjects (3 group) were examined. Polymorphism rs2071307 was studied with real-time PCR. Histological examination of AAA walls was performed in 1 group.
Results: Distribution on genotypes A/A, A/G, G/G was the following: 1 group - 42.1 %, 42.1 %, 15.8 %; 2 group - 68 %, 24 %, 8 %; 3 group - 18.5 %, 45.6 %, 35.9 %. Fragmentation of elastic membranes and media collagen component strengthening were revealed in persons with A/A, A/G, G/G genotypes in 54.2 %, 70.8 %, 11.1 % respectively. Persons with G/G genotype have more frequently (66.6 %) than others (A/A – 16.6 %, AG – 12.5 %) signs of inflammation, which promote AAA development parallel to EH.
Conclusion: We obtained evidence that elastin gene polymorphism (rs2071307) plays important role in EH and AAA development. In persons with allele A in rs2071307 risk of EH and AAA development is higher than in G/G genotype. Mostly allele A in rs2071307 is accompanied with elastic membranes fragmentation and their substitution by collagen that decreases arterial wall elasticity.

Tuesday, 11 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-19 Poster Session Ophthalmic Pathology

PS-19-001

Conjunctival reticulohistiocytoma

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Objective: Reticulohisticytoma is an uncommon lesion of non Langerhans histiocytes with a solitary form and a multicentric variant associated with other pathologies including malignancies. It is related to juvenile xanthogranuloma, but presents a peculiar giant cell type with occasional prominent nucleoli.
Method: A 83 years old man presented with a solitary conjuctival lesion clinically suspicious of CIN or squamous cell carcinoma. Previously patient reported surgery for a pituitary adenoma. Conjunctival lesion was completely removed and histological and immunohistochemical study was performed.
Results: The lesion appeared composed mainly by giant cells with wide granular cytoplasm and one or several nuclei, intermingled with lymphocytes. Macrophage cell markers were positive (CD68 and CD163). S-100, CD1a, CD21 and CD23 were negative.
Conclusion: Reticulohistiocytoma is a benign disease but clear distinction from systemic reticulohistiocytosis is important. Other similar non Langerhans histiocytosis share the risk of developing a systemic disease with much worse prognosis.

PS-19-002

Tumors metastatic to the orbit: Presentation of two cases

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Objective: Our aim is to inform on the frequency, clinical aspects, and histopathological features of the tumor metastatic to the orbit. In adults, the most common tumor metastatic to the orbit are carcinomas, breast carcinoma the most frequent. Less common are the metastases from gastrointestinal tract, kidneys, and prostate. Cutaneous malignant melanoma is the most common nonepithelial tumor metastatic to the orbit.
Method: Orbital metastatic tumors may occur at any age, but most often between 40 and 70 years of age. Most reported statistics reveal a slight predominance of women, accounted for by the fact that breast carcinoma is causing metastases most frequently. A frequent finding in the cases of metastatic carcinoma is enophthalmos that is associated with scirrhous carcinomas. We present two cases of orbital metastatic tumors in which the primary tumors were a basal cell carcinoma and a cutaneous malignant melanoma.
Results: As to the metastasis from a basal cell carcinoma, the primary tumor was located in the external angle of the eyeball and metastasized the external 1/3 of the orbit. In the case of malignant melanoma, the primary tumor was located in the upper lid and invaded the orbital floor and fat. In both patients eyeball enucleation was performed.
Conclusion: We chose to present these cases given the differential diagnostic challenge and rarity of their location.

PS-19-003

Uveal melanoma

A. Dumitriu*, S. Dumitriu
*UMF Iasi, Dept. of Neurology, Romania

Objective: Uveal melanoma which arises from melanocytes residing in the stroma is the most common primary intraocular cancer in adults.

Method: We report a case of uveal melanoma presenting as complicated cataract in a 65 years-old male.
Results: The right eye was blind for 6 months. The patient underwent extended enucleation and histopathology was consistent with uveal melanoma.
Conclusion: We present this case in order to provide the medical community a basic reference that would help to make further progress in this rare disease, which remains difficult to treat.

PS-19-004
Is uveal malignant melanoma different in Brazilian patients?
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*São Paulo, Brazil

Objective: Background: Information on uveal melanoma is derived chiefly from European and USA studies, with little data from the rest of the world, including Brazil.
Method: This was a retrospective chart review of 285 enucleated cases of uveal malignant melanoma from the AC Camargo Hospital in São Paulo, Brazil, from January 1988 until December 2005. Epidemiologic characteristics were studied in relation to histological findings.
Results: There were more women than men (52 % versus 48 %). Metastases developed in 39 % (total group mean follow up of 7.14 year). Mixed tumors were most common overall (43.5 %): for non metastasizing tumors there were 41.1 % mixed, 36.1 % fusiform and 17.2 % epithelioid types. For metastatic tumors there were 46.7 % mixed, 21.5 % epithelioid and 21.5 % fusiform types. The difference between cell type and metastatic development was significant in all but epithelioid compared with mixed tumors. Epithelioid type had a relative risk of mortality of 3.51 and mixed had 2.18 compared to fusiform cell type.
Conclusion: Our patients were younger, with larger tumors and different histological proportions from those of the Collaborative Ocular Melanoma Study. Five year survival times were similar to those for Europe.

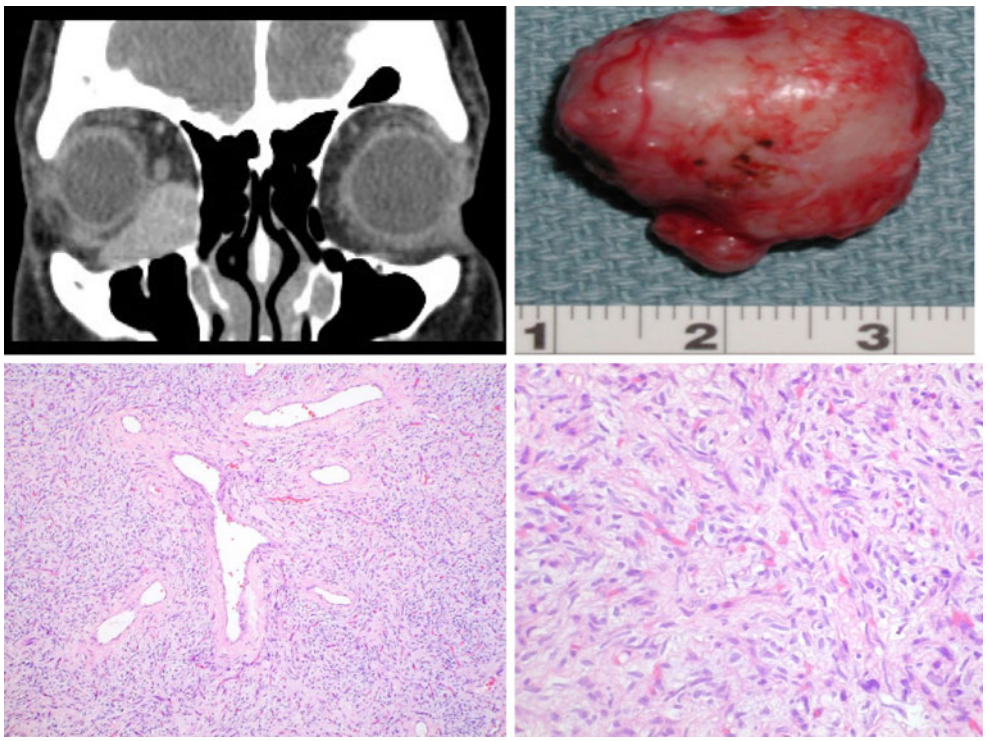
PS-19-005
Uveal melanoma between preserving vision and prolonging survival. Pathological contributions to a better clinical management
M. Mera*, L. Blaga
*UMF Cluj-Napoca, Anatomic Pathology, Romania

Objective: Uveal melanoma has a high metastatic potential which is invariably fatal. There is an ongoing debate on the impact of ocular treatment on metastatic disease and survival. Improved prognostication is needed to identify cases that could avoid unnecessary loss of vision while avoiding unethical care. Our study is aimed at contributing to the developing of reliable tools to assess the metastatic risk.
Method: An accurate prediction should include both clinical features and histologic parameters as biopsy techniques continuously advance. 120 cases of uveal melanoma, either reviewed or prospectively managed in our Pathology Department, were included in a Log-logistic multivariate survival model that we have considered would best accomodate our data. The performance of the model was assessed by bootstrap re-sampling.
Results: Extravascular matrix patterns, optic nerve invasion, tumorinfiltrating lymphocytes, tumor cytomorphology, nucleolar size and the mitotic count together with initial visual acuity have been found to be the most important predictors, ahead of the traditional TNM stage. The results are provisional but encouraging.
Conclusion: There is still need for multidisciplinary approach and multicenter collaboration in an effort to elucidate the uncertainty related to the best management of one of the most traumatising types of cancer.

PS-19-006
Orbital hemangiopericytoma: A case report
E. Omoscharka*, K. Lankachandra
*University of Missouri, Dept. of Pathology, Kansas City, USA

Objective: Hemangiopericytomas are rare vascular tumors arising from Zimmerman's pericytes, which ubiquitously surround blood capillaries and post-capillary venules. They rarely occur in the orbit, accounting for only 1 % of all orbital neoplasms. In most cases the primary presentation is progressive proptosis.
Method: A 26-year-old female was first seen for the evaluation of a right orbital mass which has been causing proptosis. Associated symptoms included peripheral vision loss in the right eye, persistent headache with occasional balance problems. A palpable, 3.2× 2.5 cm well circumscribed mass with a smooth surface, resting on the inferior orbital wall was completely removed through right anterior orbitotomy. H&E stained histologic sections were studied. In addition, tissue sections were subjected to immunohistochemical stains for CD34, CD99, BCL2, SMA, desmin, EMA and S-100.
Results: The mass was composed of spindle cells with very low mitotic activity. Staghorn vascular channels were evident, and in several areas the tumor cells invaded the pseudocapsule. The tumor cells were positive for CD34, CD99 and bcl-2 supporting the histopathologic diagnosis of benign hemangiopericytoma.

Conclusion: Orbital hemangiopericytoma is a slow growing tumor with a potentially malignant behavior, and a high local recurrence rate if incompletely excised. Complete, intact removal prevents tumor recurrence and provides a good outcome.



PS-19-007

Expression of SOD family in rat lacrimal gland after intermittent light exposure

C. L. Zamfir*, F. E. Zugun, E. Cojocaru, R. O. Temneanu, R. Folescu, M. Spataru
*University of Medicine Iasi, Dept. of Histology, Romania

Objective: Any disturbance of chronobiological rhytms represents a potential stressor, acting like a strong oxidant trigger. SOD family (CuZn-SOD, Mn-SOD and EC-SOD), is one of the most significant enzymatic complexes involved in antioxidant defense. Monitoring local SOD distribution in lacrimal gland after intermittent light exposure can be able to provide insights into the distinct links of antioxidant adaptative mechanisms.So long as lacrimal gland morphology and functions are dependent to a normal light exposure, mobilisation of its own antioxidant resources, especially SOD, is an usefull starting point in antioxidant ophtalmic therapy.
Method: Immunohistochemistry was performed in microscopic analysis of glandular fragments prelevated from 30 male Wistar rats, randomized in control/intermittent light exposed groups for 45 days. There have been used specific antibodies for each enzymatic member of SOD family. Blood samples were prelevated to control SOD levels. The study respected all imposed ethical criteria.
Results: Lacrimal glandular tissue exhibits a strong CuZn-SOD immunoreactivity, a moderate one for Mn-SOD and only a small EC-SOD reactivity, while the level of sanguin SOD is high, as a marker of oxidative aggression.
Conclusion: Oxidative stress may be engagged in a deep alteration of lacrimal gland. Mobilisation of SOD, depending on their specific glandular location and tissular receptivity, should be regarded as a promising alternative for antioxidant therapy.

Tuesday, 11 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-20 Poster Session Thymic and Mediastinal Pathology

PS-20-001

Mediastinal liposarcomas: Clincicopathological study of 4 cases

E. Braham*, M. Yahia, M. Zarrouk, O. Ismail, M. Mlika, A. Ayadi Kaddour, E. Boudabous, T. Kilani, F. El Mezni
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Objective: Liposarcoma is the most commonly diagnosed soft tissue sarcoma in adults and occurs predominantly in the lower limbs and retroperitoneum. Primary mediastinal liposarcomas are rare accounting for less than 1 % of all mediastinal tumors.
Method: We report a retrospective study of 4 cases of mediastinal liposarcoma during an 8-year period. Diagnosis was made on mediastinal biopsy in 2 cases and on resected specimen in the 2 other cases.
Results: There were 3 men and a women ranging in age from 28 to 81 years, explored for respiratory symptoms. Radiological findings showed an anterior inhomogeneous mediastinal mass in all cases with extension to left hemithorax in one case. A surgical resection was achieved in only 2 cases but was incomplete. Histopathologically, tumors were classified into 2 well differentiated lipoma-like liposarcoma, one myxoid liposarcoma and one mixed liposarcoma (sclerosing liposarcoma with myxoid liposarcoma). All patients received adjuvant radio or chemotherapy. One of them presented lung metastasis during the follow up and another died from respiratory failure. The two other are still alive.
Conclusion: Mediastinal liposarcomas include a heterogeneous group of bulky tumours, the progression of which depends on the histological type. Histopathologic examination is always necessary as much for diagnosis as prognosis.

PS-20-002

Mediastinal epithelioid hemangioendothelioma with a high-grade clinical course

A. Konstantinova*, K. Shelekhova, V. F. Klimashevsky
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Objective: Epithelioid hemangioendothelioma (EH) is a rare neoplasm usually presenting in soft tissues. About twenty cases of EH have been reported in the mediastinum. Most of these mediastinal EH exhibited an indolent course.
Results: A 21-year-old woman presented with focally encapsulated mass, 5.5×4 cm in size, in the anterior mediastinum. The tumour of bone density was adhered to the lung tissue and occluded left subclavian vein. Microscopically, the tumor consisted of foci of so-called blister cells typical for EH, anastomosing cords of small epithelioid cells embedded in myxohyaline matrix with haphazardly distributed metaplastic bone and hemorrhagic cellular stroma. Spindling of the tumor cells was prominent. The tumor cells demonstrated moderate atypia, but mitotic figures were not found. Immunohistochemically, cells of primary tumor were positive for Fli1, vimentin, CD31 and CD34. Focal staining with EMA was observed. Multiple metastases were subsequently found in the liver and lungs. Metastatic deposits had the same morphology as a primary tumor.
Conclusion: We present the case of rare mediastinum epithelioid hemangioendothelioma with peculiar histological features such as prominent spindling of neoplastic cells and abundant metaplastic bone formation in aggregate with aggressive clinical behavior that exhibited a profound metastatic poteintial.

PS-20-004

Immunohistological characterization of thymic dendritic cells

A. Papoudou-Bai*, M. Bai, M. Doukas, K. Stefanaki, V. Galani, A. Goussia, A. Batistatou, P. Kanavaros
*Ioannina, Greece

Objective: Dendritic cells play key roles in the thymic histophysiology and histopathology. Therefore, we analyzed the immunotopographical distribution of cells expressing markers of dendritic cells and macrophages in thymus.
Method: In paraffin sections of postnatal thymuses were performed immunostainings for S-100, CD1a, CD207 (langerin), CD11c, CD123, CD68 and CD163. The Streptavidin-Biotin Peroxidase labeled (LSAB) and the double LSAB/Alkaline Phosphatase/anti- Alkaline Phosphatase (APAAP) immunohistochemical procedures were used.
Results: S100, CD1a, CD207, CD11c and CD123 positive cells, many of them with morphology of dendritic cells, were detected in the cortex and mainly in the medulla. These markers, except CD123, were also detected in cells of juvenile and immature Hassall Bodies (HB). CD68 and CD163 positive cells were detected in the cortex and the medulla but not in HB.
Conclusion: The immunohistological detection of S100, CD1a, CD207 and CD11c positive dendritic cells in juvenile and immature HB may reflect an important role of HB in the cooperation of epithelial and dendritic cells in the process of T-cell differentiation.

PS-20-005

Primary thymic carcinoma: Report of three cases

P. Xirou*, M. Koumpanaki, G. Balis, S. Barbanis, N. Barbetakis, N. Vladika, B. Christoforidou, F. Patakiouta
*Theagenion Cancer Hospital, Thessaloniki, Greece

Objective: Thymic carcinomas comprise rare malignant epithelial neoplasms, which exhibit a disproportionately large variety of growth patterns. We present three cases of primary thymic carcinomas, including two squamous cell carcinomas and one papillary adenocarcinoma.
Method: All three patients were males, aged 51, 61 and 77 years, and presented with mediastinal masses measuring 17 cm, 6.5 cm, 3.7 cm in maximal diameter respectively.
Results: Microscopically the first two tumors were poorly differentiated squamous cell carcinomas, immunohistochemically positive for CD5 and CD117, whereas the third

tumor was a papillary adenocarcinoma, positive for CD5 and negative for CD117 and TTF-1. Immunohistochemical features of the tumors were supportive of thymic derivation.
Conclusion: Primary thymic carcinomas are rare malignant tumors with clear-cut atypia, largely lack of organotypic features and a very diverse differentiation. Squamous cell carcinoma is the most frequent subtype. They are often a diagnosis of exclusion, since metastases to thymus and anterior mediastinum, mainly from the lung, are far more common. Immunoreactivity to CD5, CD70 and CD117 may support the thymic origin of neoplastic squamous cells. Treatment options include surgical excision, radiation and/or chemotherapy depending on tumor stage and patient's condition. The prognosis is generally poor with squamous cell carcinomas having a slightly more favorable outcome.

Wednesday, 12 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-21 Poster Session Nephropathology

PS-21-002
Histopathological assessment of renal lesions after volume replacement with HES 130/0.4 or Ringer solution, following acute bleeding
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Objective: Surgical blood loss can lead to ineffective tissue perfusion of vital organs. Physiologic solution chosen for blood volume replacement may be determinant for preserving renal integrity. Our aim is to study kidney histopathological changes in a hemorrhagic model, followed by intravascular volume replacement with Ringer's lactate or Hydroxyethylstarch (HES) 130/0.4 solutions.
Method: Thirty one pigs under general anaesthesia with propofol and remifentanil underwent haemorrhage at a volume of 30 ml kg-1, over 20 min. After a waiting period of 20 min, intravascular volume was replaced using HES 130/0.4 (G1) and Ringer's lactate (G2). One hour after, pigs were euthanized with IV potassium chloride and sixty two renal samples were taken for histopathological examination, using PAS staining. Renal damage was assessed for glomerular, tubulointerstitial and vascular lesions.
Results: Mean arterial pressure reached 40 mmHg after bleeding, and recovered for values above 60 mmHg in both groups after volume replacement. Histopathological lesions observed in G2 were more frequent than those in G1.
Conclusion: HES 130/0.4 may reduce the incidence of histopathological lesions secondary to renal hypoperfusion after severe bleeding when compared with Ringer Lactate. Results suggest that the reestablishment of intravascular volume with HES 130/0.4 may preserve renal integrity secondary to blood loss.

PS-21-003
Expression of AEG-1, P53 and its clinicopathological significances in the malignant lesions of renal cell carcinomas
H. Erdem*, M. Oktay, U. Yildirim, A. K. Uzunlar, M. A. Kayikci
*Duzce University, Dept. of Pathology, Turkey

Objective: Astrocyte elevated gene-1 (AEG-1 also known as Metadherin) is associated with various aspects of tumor malignancy. The aim of this study was to investigate P53 relationship between AEG-1 and prognostic parameters.
Method: This study was made 50 paraffin blocks (tumoral samples), which were histopathologically diagnosed at department of pathology from 2005 to 2011. Subtypes of the cases were 24 (48 %) clear cell renal cell carcinomas (RCC) and 26 (52 %), non-clear RCC respectively. By immunohistochemical analysis, we investigated AEG-1, P53 expression in carcinomas of kidney and we determined its relationship with clinicopathological parameters.
Results: There were significant relationship between increased AEG staining score and tumor capsule (P=0.01), lymphovascular invasion (p=0.015) and significant relationship between the increased diameter with the increase of p53 (p=0.028). There were significant correlation between increased diameter of tumor and degree of increase the Fuhrman (p=0.02).
Conclusion: High AEG-1, P53 expression correlates with prognostic parameters in the RCC. In addition, AEG-1, P53 expression in RCC may be associated with tumor progression.

PS-21-004
Relationship of CD95, COX-2 and P53 in renal cell carcinomas with survival and other prognostic parameters: A tissue microarray study
H. Erdem*, U. Yildirim, A. K. Uzunlar, M. A. Kayikci
*Duzce University, Dept. of Pathology, Turkey

Objective: Renal cell carcinomas (RCC) is the seventh most common human malignancy. RCC is now recognized to be a complex neoplasm consisting of several different tumor subtypes, each with distinct genetic and clinical features. The aim of this study was to investigate the expressions of cyclooxygenase-2 (COX-2), P53 and CD95 in RCC that has different clinicopathologic characteristics.
Method: This study was conducted on a total of 49 paraffin embedded kidney samples (tumoral samples), which were histopathologically diagnosed at department of pathology

from 2005 to 2011. IHC stains for COX-2, P53 and CD95 were performed on tissue microarray using standard procedures.
Results: There were significant correlations between COX-2 and subtype (p=0,044), COX-2 and diameter (p=0,026). Significant relationships were found between p53 and age (p=0,050), P53 and diameter (p=0.050). Besides, there were significant correlations between CD95 and furhman grade (p=0,050).
Conclusion: CD95, COX-2, P53 expression correlates with prognostic parameters in the RCC patients. In addition, COX-2, P53, CD95 expression in RCC may be associated with tumor progression.

PS-21-005
Soft-tissue tumors and Ebstein Barr Virus (EBV) in kidney grafted patients
J. C. Goldberg*, M. d. Carmen Rial, J. Petroni, L. Leon, M. Amante, G. Hillchenbach, D. Casadei
*Buenos Aires, Argentina

Objective: EBV related malignancies (skin cancers, lymphomas, Kaposi sarcomas) complicates organ transplantation EBV-associated smooth-muscle tumors are rare.
Method: Among 1500 kidney grafted patients, three developed EBV-SMT. Case 1. Female 51 y, with EBV-SMT (Generalized) Case 2. Female 46 y, breast phylodes sarcoma, reviewed diagnosis: EBV-SMT. Case 3. Male 23 year, severe abdominal pain, 2 gut tumor-like nodules were excised suspection of TBC. EBV-SMT was microscopic diagnosis.
Results: Progressive weight-loss all 3patients, chronic cough in patient 1, chest X ray multiple pulmonary lesions, on CT-scan paravertebral lesions. Transthoracic biopsy: spindle cells proliferation with mixed cellularity eosinophilic cells intermingled fascicles resembling smooth muscle, mononuclear inflamatory cells and capillarie evoqued myofibroblastic tumor. No mitosis, mild nuclear atypia. Negative immunohistochemestry: CD21, CD34, CD99, EMA, cytokeratin, S100, CD117. Alpha-smooth muscle actin diffusely positive, EVB-LMP negative. In situ hybridization : EBV + nuclei. EBV-SMT was established.
Conclusion: SMT in immunocompromised are EBV associated. Primary target of EBV are B lymphocytes, may infect smooth-muscle through receptor for EBV CD21 Mechanisms of EBV related-tumor genesis is integration of EBV-DNA within ALK locus in tumor cells. ALKgene rearrangement and expression; associated with inflammatory myofibroblastic tumors, anaplastic large-cell lymphomas etc. Clonally of multifocal EBV-SMT using southern blot showed, multiple tumors constitute independent primary lesions.

PS-21-006
Glomerulosclerosis is a major contributor for chronic renal allograft dysfunction in IgA nephropathy developing after transplantation
H.-J. Jeong*, B.-J. Lim, D.-J. Joo, M.-S. Kim, Y.-S. Kim, S.-I. Kim, M.-J. Koh
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Objective: To explore the significance of glomerulosclerosis and glomerular injury in posttransplant immunoglobulin A nephpropathy (IgAN), we reviewed 131 renal allograft biopsies diagnosed with IgAN after transplantation.
Method: The degree of glomerulosclerosis was scored into 0–3, mesangial proliferation was scored into 0 (absent) and 1 (present), and the degree of crescents was scored into 0–2. Glomerular injury score (GIS) was obtained by adding the above 3 scores and grouped into 3 categories (group 1, score 0–1; group 2, 2–4; group 3, 5–7).
Results: Serum creatinine level was significantly increased (1.3±0.4, 1.8±0.9, 2.2±0.8 mg/dL, p=0.007), estimated glomerular filtration rate (eGFR) was significantly decreased (68.5±17.6, 52.1±22.5, 40.9±20.4 mL/min, p=0.001) and proteinuria was significantly increased as GIS increased (1.3±2.7, 1.9±1.6, 4.6±7.1 g/24 h, p=0.030). Interstitial fibrosis of more than 25 % of cortical area increased as GIS increased (2.3, 26.0, and 57.1 %, p<0.001). When a multivarate analysis was done, GIS group 3 was the most important predictive factor of eGFR (p=0.009) and proteinuria (p=0.014).
Conclusion: In conclusion, glomerular injury is a dominant feature of posttransplant IgAN and a simple surrogate marker for chronic graft dysfunction.

PS-21-007
Causes of early graft impairment after deceased donor kidney transplantation
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Objective: The aim of the study is to evaluate the histopathological finding and the C4d staining patterns of the patients who were biopsied due to graft dysfunction (GD) after initial well-function within 1 month of deceased donor kidney transplantation (DDKT).
Method: Histological analysis and C4d immunostaining were performed 34 on needle core biopsies.
Results: Thirty-four patients (mean age: 37±8 years, male: 59 %) were included. Histological analysis revealed acute rejection (AR) (n:7), acute tubular injury (ATI) (n:8), allograft infection (n:1), borderline changes (n:8), normal morphology (n:3), and donor-related changes (n:7). C4d

staining was detected in 44 % (15 of 34) biopsies; staining patterns were diffuse (n:5), focal (n:5) and minimal (n:5). Diffuse (n:3) and focal (n:1) C4d positivity accompanied 4 of 7 cases of AR. In remaining 27 patients having non-AR histological picture, diffuse or focal C4d positivity were detected in 2 and 4 cases, respectively. Peritubular capillaritis was detected in 41.1 % (14/34) of biopsies, of which four had C4d diffuse, one had C4d focal positive.
Conclusion: Beyond cold ischemia time-induced ATI, immunological causes including antibody mediated process may play an important role in early impairment of graft function after DDKT.

PS-21-008
Immunohistochemical analysis of the renal interstitial fibroblasts
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Objective: Renal fibrogenesis is a process common to all progressive kidney diseases. The main executive cell of this process is the fibroblast, by secreting and remodeling the extracellular matrix. The number of fibroblasts is minor in healthy kidney interstitium, but it increases during the process of fibrosis. Their morphology and immunophenotype vary due to different intrinsic and extrinsic factors, thus making their identification and visualization, as well as determination of their origin, very difficult.
Method: We performed morphological and immunohistochemical analyses on kidney biopsies with primary glomerulopathy and interstitial fibrosis, using the following antibodies: Vimentin, α-SMA, S100A4, Cadherin 9 and CD34.
Results: Interstitial fibrosis with focal, rather than diffuse distribution, was present in all analyzed cases. The total interstitial fibroblast population was positive for Vimentin, majority of the cells were positive for S100A4, and a smaller proportion of cells were positive for α-SMA, Cadherin 9 and CD34. Furthermore, different cells in the fibroblastic population showed positivity for different markers.
Conclusion: The above stated observations contribute to the theory that different subpopulations of fibroblasts, with different origin, take part in the renal fibrogenesis.

PS-21-009
Soluble epoxide hydrolase inhibition reduce blood pressure and organ damage independently of Nitric Oxide (NO) in mice with Goldblatt two kidney, one clip model (2K1C)
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Objective: Investigate the role of NO in the blood pressure (BP)-lowering effects of soluble epoxide hydrolase (sEH) inhibition in 2K1C model.
Method: The endothelial NO synthase gene knockout mice and their wild-type controls were used. Renal concentrations of epoxyeicosatrienoic acids (EETs) and dihydroxyeicosatrienoic acids (DHETs) were measured in nonclipped kidney. Renal NO synthase activity was determined by measuring the rate of formation of L-[14 C]citruline.
Results: Treatment with the sEH inhibitor caused the same BP decrease that was associated with increase in daily sodium excretion in both types of mice. The ratio of EETs/DHETEs in the nonclipped kidney was increased and did not alter renal NOS activity. sEH inhibition reduced significantly glomerular and tubulointestitial injury.
Conclusion: BP-lowering effects of chronic sEH inhibition in 2K1C mice are associated with normalization of the reduced availability of biologically active EETs in the nonclipped kidney and their direct natriuretic actions.

PS-21-010
Total inflammation in 6-month surveillance renal transplant biopsies is associated with decreased renal function and de novo class 2 donor specific antibody
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Objective: The goal was to correlate inflammation and acute rejection (AR) with renal function and antibody status in 6-month renal transplant surveillance biopsies.
Method: Relative risks of inflammation and AR in 380 6-month biopsies was calculated by Multivariable Poisson regression.
Results: AR was seen in 7.3 % (n=28), borderline change in 19.7 % (n=75), and C4d positivity in 2.1 % (n=8) of all biopsies. Total cortical inflammation (ti), present in 32.6 % (n=124) cases, was associated with 7 ml/min/1.73 m2 lower eGFR at 6 months (95 % CI= −10.8, −3.2). De novo HLA Class 1 was identified in 17.4 % (n=44) and Class 2 DSA in 26.1 % (n=66), with most having MFI values <1000. Increased risk of AR was seen with higher levels of de novo Class 1 (RR 1.49, 95 % CI=1.08, 2.0) or Class 2 DSA (RR 1.34, 95 % CI=1.04, 1.72). Class 2 (but not class 1) DSA was associated with a higher risk of ti (RR 1.40 for ti-score ≥1, 95 % CI=1.13, 1.72) at 6 months.
Conclusion: Both ti and AR in 6-month surveillance kidney transplant biopsies are strongly associated with de novo HLA Class 2 DSA. Total inflammation at 6 months correlates with decreased kidney function.

PS-21-012

Acute renal failure in a HIV patient with Fanconi syndrome, nephrogenic diabetes and hypokalemia: Report of a case and correlation between clinical symptoms and histology, showing tenofovir toxicity

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Objective: Tenofovir disoproxil fumarate has been used in the treatment of HIV patients producing occasional renal dysfunction and Fanconi Syndrome.
Method: A 38-year-old patient was referred with severe acute renal failure and important metabolic acidosis and glycosuria with normoglycemia in urine analysis, altogether with urinary alkaline pH and proteinuria with a protein/creatinine ratio of 4. He was HIV and B positive diagnosed 17 years earlier. His medication regimen consisted of lopinavir, ritonavir, tenofovir and lamivudine. The patient had a history of nausea, vomiting and some diarrhea with low fluid intake for a week. Besides slight dehydration, the physical examination was unremarkable. Renal ultrasound showed normal kidneys. With adequate fluid restoration, the renal function improved but other metabolic alterations like nephrogenic diabetes remained.
Results: Renal biopsy revealed toxic acute tubular necrosis predominantly involving proximal tubules with prominent eosinophilic inclusions within proximal tubular cell cytoplasm, which represented giant, abnormal mitochondria, consistent with tenofovir toxicity. Some histochemichal studies (COX and SDH) were performed.
Conclusion: Although prospective clinical trials have demonstrated a low incidence of renal toxicity with tenofovir, there are several such reports in the literature. Current recommendations suggest close monitoring of renal function after initiation of therapy with tenofovir, specially at the beginning and when used in combination with certain antiretroviral agents.

PS-21-013

Nutcracker syndrome (NS): A case report

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Objective: Nutcracker syndrome (NS) is caused by compression of the left renal vein between the aorta and superior mesenteric artery. The main presenting symptom of this rare entity is haematuria, with various degrees of proteinuria. The diagnosis of NS syndrome is primarily by imaging and can sometimes be challenging.
Method: A 21-year-old male was referred to nephrology with a 3 months history of intermittent gross haematuria. All blood test including blood cell count, biochemistry, immunoglobulin electrophoresis, antinuclear antibody were normal. Urinary analysis revealed numerous red blood cells and a protein/creatinine ratio of 0.3. A previous cystoscopic examination was normal. Renal ultrasound revealed a diffuse increased echogenicity.
Results: Renal biopsy showed a normal histology with no immunofluorescence deposits. CT scan revealed dilatation of the distal left renal vein with narrowing between the superior mesenteric artery and the aorta.
Conclusion: NS is a rare entity causing haematuria. There are few reported cases with histology, although it usually shows no abnormalities. The proposed mechanism for the haematuria is an abnormal communication between the submucosal venous plexus and the calyceal system presumably induced by renal venous hypertension.

PS-21-014

Banff Initiative for Quality Assurance in Transplantation (BIFQUIT): Reproducibility for BKV immunohistochemistry in renal allografts

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Objective: Detection of BK virus associated large T-antigen is crucial for the diagnosis of polyomavirus nephropathy.
Method: In an international multi-centre trial we assessed the inter-observer and inter-laboratory variability for BK immunohistochemistry. A tissue microarray was constructed comprising 23 specimens representative of the whole analytical spectrum from negative over mild to strong SV40 positive cases. 81 participants at 60 centers stained the TMA slides using local protocols. Participants evaluated their slides following a provisional Banff grading schema. Details regarding local staining protocols and evaluation scores were collected online. Stained slides were returned for centralized panel re-evaluation. Weighted kappa statistics were used to determine the variability.
Results: The BK inter-observer reproducibility was substantial (mean kappa 0.64), but inter-laboratory reproducibility was below chance (kappa −0.22). Separating components of BK evaluation schema into stain intensity and stain percentage showed no significant improvements in reproducibility. However, collapsing the proposed BK scoring schema into a simple positive/negative call improved BK inter-laboratory variability to 0.77.
Conclusion: These results indicate a significant variability between laboratories for detecting the SV40 large-T antigen by immunohistochemistry in paraffin sections. Any

proposed grading schema for BK nephropathy, which is dependent on percentage and intensity of nuclear staining, will essentially not be reproducible between laboratories.

PS-21-015

Diagnostic significance of myelin figures in renal biopsies

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Objective: Myelin figures (MF) in podocytes is the major finding in Fabrys`s disease. MF are also found in metabolic disorders and following application of cationic amphiphilic drugs. We posed the question: Can M. Fabry and metabolic and/or drug induced MF be differentiated by LM and EM?
Method: Case reports of 7966 renal biopsies containing the terms myelin, phospholipid or Fabry were selected, then we noted sex, biopsy indications, drug therapy and pathological diagnosis. EM pictures were screened for frequency and distribution of myelin figures and curvilinear bodies (CLB).
Results: MF were rare (n=42), mainly found in podocytes (31/42), less frequently in endothelial/mesangial cells (each 8/32) or proximal tubules (6/42). CLB were seen only once in podocytes. In most cases, usually, only few cells had single MF. CLB and foam cells were absent. The etiology was usually unknown. In one case, CLB were found with MF, alongside moderate numbers of MF in moderate numbers of podocytes. Foam cells were not seen. The patient had received chloroquine.
Conclusion: In all cases with podocytic foam cells (12/31) and/or numerous MF in many podocytes and other renal cells, without detectable CLB, M. Fabry was present. Foam cells together with many MF are suspicious of M. Fabry, MF and CLB are indicative of chloroquine therapy.

PS-21-016

Simultaneous transplant glomerulopathy and recurrent glomerulonephritis in kidney allograft

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Objective: We present three cases of simultaneous Transplant Glomerulopathy (TG) and recurrent glomerulonephritis in kidney allografts.
Results: CASE 1:56 year old man with Chronic Renal Failure (CRF) secondary to IgA Nephropathy who recived a kidney transplant. Five years later the patient present asthenia, deterioration of renal function, proteinuria and hypertension. Allograft biopsy showed on light and electron microscopy characteristic features of TG, but also recurrent IgA Nephropathy with mesangial staining of IgA and mesangial electrodense deposits in the glomeruli. CASE 2:43 years old man. CRF secondary to Membranous Glomerulonephritis Kidney transplant on July 2000 with decrease renal funtion and proteinuria 9 years later. Allogratf biopsy showed again characteristic features of TG and granular IgG and C3 inmunostaining in glomerular basement membranes. Ultraestructural studies confirm the TG and the subepithelial deposits. CASE 3:52 year old woman CRF secundary to membranoprolipherative glomerulonephritis type 2(DDD). Third kidney transplant on August 2006. Renal function deterioration on March 2010. Allogratf biopsy showed characteristic features of TG on light and electron microscopy but also features of DDD with C3 deposition on inmunofluorescence and ribbon-like highly electrodense intramenbranosous deposits.
Conclusion: We must consider the possibility of simultaneous transplant glomerulopathy and other recurrent or de novo glomerulonephritis in the graft biopsy. Prognosis when both entities develop in the allograft is disastrous.

PS-21-017

Cryopyrin-associated periodic syndrome with secondary amyloidosis

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Objective: Cryopyrin-Associated Periodic Syndrome (CAPS) is a rare hereditary inflammatory disorder with three differents phenotypes: familial cold autoinflamatory syndrome, Muckle-Wells syndrome and neonatal-onset multisysten inflamtory disease CAPS results from a mutation of the NLRP3 gene (1q44) coding for cryopyrin, which forms intracellular protein complexes (inflammasomes).
Results: Case report: 41 year old women with chronic renal disease stage 3 (creatinin 2,2 mg/dl and proteinuria 180 mg/24 h) who developed urticarial episodies since 6 months old related to cold exposure. After 11 years old patient describe associated to these episodios bilateral arthritis (knes, ankles and elbows), conjunctival inflammation, shivers, and asthenia, more frequently in winter and precipitated by cold exposure, air conditioning, stress and menstruatión. Aditionaly the patient developed in last years bilateral hypoacusis A kidney biopsy showed a amorphous, acellular and acidophilic material Congo red positive deposits at interstition, arteries and arterioles and less frequent at glomeruli. This material displays apple green birefringence by polarizad light microscopy. Diagnosis: SECONDARY RENAL AMYLOIDOSIS

Conclusion: The clinico-Pathologial findings of this case are compatible with Muckle-Wells syndrome. Secondary amyloidosis is a severe complication which occurs in 25 % of Muckle-Wells cases. Amyloidosis is cause by increase of C-protein and A amyloid during the episodies before described and deposition of the A amyloid in differents tissues.

PS-21-018

Glomerulocystic disease associated with thrombotic microangiopathy in two kidney allografts

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Objective: Glomerulocystic kidney disease (GCKD) is a rare condition usually congenital and reported in infants and young children. Only few cases of adquired GCKD had been reported often following Hemolytic Uremic Syndrome (HUS).
Method: Histological study of two kidney graft explants.
Results: We present two cases of kidney transplant who developed HUS in allografts. Both cases showed at the histological examination typical vascular and glomerular changes of Thrombotic Microangyopathy (TMA). A cystic transformation with increase of urinary space and retraction of glomerular tuft was frequently observed. Chronic transplant vasculopathy was found in the two cases. Humoral active rejection was also demonstrate in one case with moderate peritubular capillaritis and glomerulitis and diffuse C4d deposition at peritubular capillaries.
Conclusion: In a few cases GCKD appear to develop after another kidney disease includes single case reports of GCKD associated with mesangial glomerulonephritis, Wegener's granulomatosis, progressive systemic sclerosis, after HUS (include some case in adult patient). Our two cases represent a initial stage of adquired GCKD. The ethiopathogenetic relationship is not clear but some authors propous that cystic dilatation of the Bowman's capsule associated to TMA/HUS may be secondary to ischemic mechanism.

PS-21-019

Case report: Cytomegalovirus gastritis in renal transplanted man

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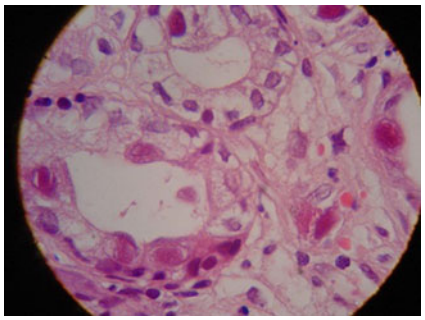
Objective: CMV is an important pathogen in immunocompromised hosts, including patients with AIDS, neonates and transplant recipients. This infection develops in 70–90 % of transplant patients. Upper GI symptoms in solid organ recipient are common (20 %) and clinical signs are more serious in 10 % of cases.
Method: We report a 30 year old man with end stage renal disease underwent kidney transplantation from a CMV negative donor on June 2011. After 1.5 months he admitted with fever, generalized body pain, oral aphtous ulcers and epigastric pain accompanied by malaise. Endoscopic examination revealed multiple antral erosions with surrounding erythema. Clinicopathological investigations revealed CMV viremia with a Ig-M antibody titer and CMV gastritis confirmed by histopathological examination.
Results: The patient was started on intravenous (IV) ganciclovir 5 mg/kg per day every 12 h initially for 3 weeks, afterwards the fever decreased; cell blood counts throwback to normal ranges and general condition of the patients improved.
Conclusion: CMV infection develops in 70–90 % of the transplant patients. The colon and stomach are the most common sites of gastrointestinal infection. Though the rate of GI affliction by CMV is high, localization to the gastric antrum is not common.



PS-21-020

Immunohistochemistry study of C-Kit expression in renal cell carcinoma

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Objective: Renal Cell Carcinomas include about 2–3 % of adults neoplasms and 90–95 % of all renal tumors. In many cases, it is possible to distinguish. RCC subtypes on the basis of hematoxylin-eosin staining alone. However, overlapping morphologic features pose some difficulties in making a proper diagnosis. To render an accurate diagnosis, additional methods like immunohistochemichal staining against C-Kit have been recommended.
Method: We reviewed 65 cases of RCC diagnosed during 9 years. Formalin fixed, paraffin embedded specimens was available in 65 cases. The expression of C-kit was evaluated using immunohitochemistry.
Results: Six cases of 39 clear cell type (15.4 %), 8 of 13 papillary type (61.5 %), and 11 of 11 chromophobe type (100 %) were positive for C-kit that considering Chi-Square test there is significant relevation between RCC's subtypes

and C-Kit expression (P: 0.001). From 8 cases with renal vein invasion, 3 showed positive expression of C-Kit (37.5 %) and in 55 cases with no venous invasion, C-kit expression was detected in 22 (38.6), so no significant relation was found between renal vein invasion and C-kit expression.
Conclusion: The expression of C-Kit in RCC may have diagnostic significance.

PS-21-022
Tubulointerstitial Nephritis (TIN) in IgG4-Related Systemic Disease (IgG4-RSD) with lung and lymph node involvement
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Objective: IgG4-RSD shows abundant IgG4-positive plasma cells, diffuse fibrosis, and increased serum IgG4 levels. Although IgG4-RSD typically results in autoimmune pancreatitis (AIP), any organ may be involved. Thus, IgG4-RSD TIN often goes unrecognized in the absence of AIP. This is an IgG4-RSD TIN case with mediastinal lymph node and pulmonary involvement.
Method: A 73-year-old male presented with rapidly progressive renal failure, hypergammaglobulinemia, hypocomplementemia, and enlarged mediastinal lymph nodes and bilateral pulmonary nodules on CT. Renal and mediastinal lymph node biopsies were performed and IgG4 IHC was done on both after standard techniques.
Results: The renal cortex and medulla showed diffuse interstitial fibrosis with tubular atrophy and abundant plasma cells (25 IgG4-positive cells/HPF), numerous lymphocytes and some eosinophils. IF showed IgG, C3, kappa, and lambda granular deposits in tubular basal membranes and Bowmann capsules. Lymph node follicular and paracortical hyperplasia with abundance of mostly IgG4-positive plasma cells was seen. An IgG4-RSD diagnosis was rendered and high serum IgG4 levels were demonstrated. Steroid therapy resulted in lymph node and lung nodule reduction.
Conclusion: TIN with abundant plasma cells and diffuse interstitial fibrosis, especially if accompanied by hypergammaglobulinemia, hypocomplementemia, or extrarenal involvement, should suggest IgG4-RSD and prompt serum IgG4 level determination and renal IgG4 IHC.

PS-21-023
An unusual case of osmotic nephrosis
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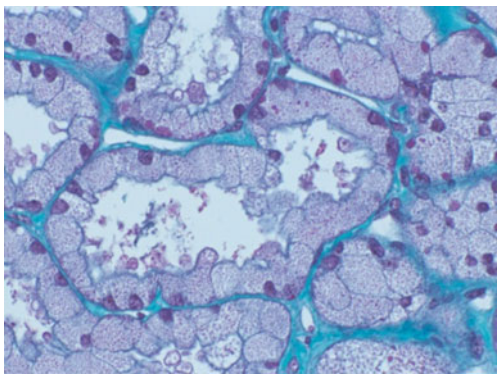
Objective: A 39-year-old woman was admitted for chronic renal failure. Clinical examination was normal. Biological explorations showed creatinin clearance around 55 ml/min, tubular proteinuria with Bence Jones κ protein. Serum immunoelectrophoresis identified abnormal monoclonal immunoglobulin G and κ-light chains (LC). Bone marrow histology was normal.
Method: Kidney biopsy revealed diffuse intracytoplasmic vacuoles in the proximal tubules resembling osmotic nephrosis. Distal tubules, glomeruli, vessels and interstitial compartment were normal. Immunofluorescence (including anti-κ and -λ staining) was negative. Electronic microscopy (EM) revealed intracytoplasmic immunoglobulinic crystals containing κ LC inside the vacuoles, leading to the diagnosis of Light Chain Proximal Tubulopathy (LCPT).
Results: LCPT is a rare complication of dysglobulinemia. It may be associated with crystals within the cytoplasm of proximal, less frequently distal, tubular cells, consisting more frequently in κ LC. Rarely, diffuse tubular vacuolization is present, often indistinguishable from osmotic nephrosis. In our case, there was no proximal tubular dysfunction and immunofluorescence was negative. The first evocated diagnosis by light microscopy was "osmotic nephrosis". However, we failed to identify any causal factor. Finally, the diagnosis was performed by immunoEM.
Conclusion: In conclusion, before a picture of osmotic nephrosis without obvious cause, EM and immunoEM may be helpful for the diagnosis of LCPT, often revealing a dysglobulinemia.



PS-21-024
Opportunistic infections in renal transplantation – A case series
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Objective: Oporto's Hospital Centre is one of the portuguese hospitals with more renal transplantation activity (performed since 1982). Although increasingly rare, opportunistic infections (OI) in transplanted patients remain a

major diagnostic challenge and are associated with high mortality rate.
Method: In order to evaluate the incidence of OI in renal transplant patients and to identify the location of infection, the respective techniques of diagnosis used and the survival time after infection, we conducted a retrospective study using the Nephrology Department's database on renal transplants. We consulted the registries from 2004 to 2012.
Results: We investigated 2041 cases and found 82 cases of OI caused by Herpes virus (n=7), Cytomegalovirus (n=27), Polyomavirus (n=16), Aspergillosis (n=4), Alternaria (n=2), Mucormycosis (n=1), Candidiasis (n=12), Tuberculosis (n=9), Cryptococcus (n=2) and Pneumocystis (n=2). The lung and urogenital system were the most affected systems. Kidneys were affected in 3 cases respectively by mucormycosis, tuberculosis and cryptococcus. Of all the cases of OI, 39 were diagnosed by the Department of Anatomic Pathology (21 by biopsy; 16 by cytology; 2 by biopsy and cytology).
Conclusion: In many cases the diagnosis could only be performed through histologic/cytologic examination. Prompt diagnosis and treatment are necessary to avoid life threatening complications and may greatly improve prognosis.

PS-21-025

Papillary renal cell carcinoma with osseous metaplasia and bone marrow elements: A case report

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Objective: Renal cell carcinomas might display foci of calcification and even ossification. This rare event has been reported mostly in the clear cell variant. Herein, we present the case of a 69 year-old man, previously diagnosed with colon cancer, incidentally found to have a calcified mass in the kidney, which was interpreted as non-characteristic for renal cell origin.
Results: Radical nephrectomy was performed. A 5.5×5.0×4.0 cm tumor was found, with a heterogeneous brown cut surface, containing areas of necrotic tissue and extensive calcifications. Histopathologic examination disclosed papillary structures covered by small cells with scant cytoplasm, dispersed among mature bone tissue enclosing marrow elements. Epithelial tumor cells were imunorreactive for cytokeratins, CD10 and PAX2, and negative with HMB-45. Hale`s colloidal iron was negative. Trisomy of 3p, 7p and 17p was detected by FISH. A diagnosis of PRCC type 1, Fuhrman grade 2, with extensive osseous metaplasia was rendered.
Conclusion: Ossification of renal cell tumors is rare, occurring mostly in clear cell type and the underlying mechanism is unclear. These tumors show atypical radiological features and might be confused with non-renal cell tumors. To the best of our knowledge, this is the first report of PRCC with osseous metaplasia and bone marrow elements.

PS-21-026

The effect of doxycycline on glomerulosclerosis in 5/6 renal ablation

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Objective: The effect of matrix metalloproteinase (MMP) inhibitors in segmental sclerosis is unknown. The aim of this study is to investigate the effect of a MMP inhibitor, doxycycline, on glomerulosclerosis (GS) in renal ablation nephropathy.
Method: Fourteen of the 32 female Wistar albinos were 5/6 nephrectomised. Doxycyline was given to half of each group (40 mg/kg/day total 28 days). After sacrification, the GS, MMP-2, MMP-9, TIMP-2 expressions were analyzed histopathologically. Pro and active MMP-2 and -9 were analyzed by gelatin zymography. TIMP-1 and TIMP-2 were measured with ELISA assay.
Results: Doxycycline administration to the 5/6 nephrectomy group improved GS, but did not inhibit glomerular MMP-9 or cortical pro- and active-MMP-2 and pro-MMP9 but increased TIMP-1 and TIMP-2 expression in all groups in cortical tissue. MMP-9 expression and GS were increased in all groups receiving doxycycline.
Conclusion: We have demonstrated improved GS in renal ablation model by doxycycline administration but also doxycycline has an unexpected adverse effect. The effect of doxycycline on the expression of MMP-2 and -9 cannot explain the improvement in GS, but increased cortical TIPM-1 and -2 may be an important contributing factor for inhibition of MMPs.

PS-21-027

Digitally reinforced hematoxylin-eosine polarization in diagnosis of renal amyloidosis

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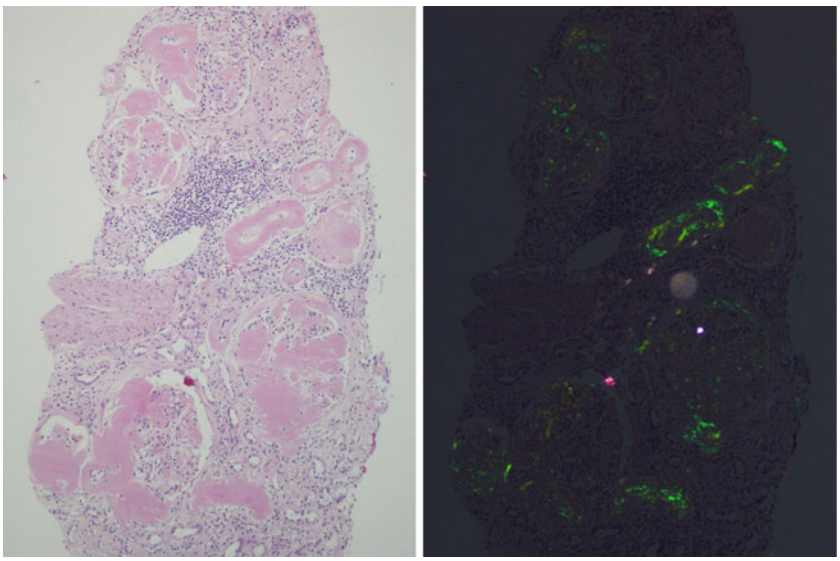
Objective: Systemic amyloidosis is a rare disorder, characterized by extracellular accumulation of Congo-red (CR) positive fibrillar amyloid protein deposits. The kidney is the most commonly affected organ by systemic amyloidosis. CR staining which increases the positive birefringence of the weakly birefringent unstained amyloid. In this study we investigated potential power of digitally reinforced birefringence of routine Hematoxylin-eosine (HE) slides on the renal biopsies.

Method: We reviewed 130 HE stained slides for polarization. Sixty five amyloidosis cases were diagnosed by renal biopsy from 2008 to 2012 at our laboratory. All biopsies were evaluated by light and immunofluorescence microscopy. Slides were reevaluated blindly using a microscope (Olympus BX51) attached polarization filter and connected to a digital camera (Olympus DP21, SAL). Depositions which show green birefringence on HE with digitalized microscopy were considered as positive and results were confirmed using CR.

Results: Of the 65 CR confirmed amyloid positive biopsies, 61 showed green birefringence with HE. Of the 65 CR confirmed amyloid negative biopsies, two were considered as false positive. The sensitivity, specificity, positive and negative predictive values were estimated as 94 %, 97 %, 97 % and 94 %, respectively.

Conclusion: We concluded digitally polarized HE sections can be used as a fast and first step diagnostic method for renal amyloidosis.



PS-21-028

Sirolimus ameliorates cyclosporin-induced nephrotoxicity in a rat model – focus on renal lesions, oxidative stress, inflammation, proliferation and angiogenesis

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Objective: Sirolimus (SRL) have been pointed as a feasible option for minimize the use of Cyclosporin A (CsA), especially because of putatively less nephrotoxicity. This study aimed to characterize the histological lesions and the molecular pathways implicated in CsA-induced nephropathy and prevention when converted to SRL.

Method: The following 4 groups ($n=6$) were tested during 9 weeks: Vehicle, CsA, SRL and Conversion (CsA 3 weeks + SRL 6 weeks). BP and HR were monitored. Blood was collected and kidney gene expression of markers of inflammation, proliferation, angiogenesis and oxidative stress were assessed. Histology: H&E, PAS and Gordon & Sweets staining. Statistics: ANOVA and Post´hoc tests ($p<0.05$).

Results: After 9 week of CsA treatment, there was important kidney lesions, including glomerular, tubulointerstitial and vascular: mesangial expansion, atrophy, bowman capsule enlargement, hyaline cylinders formation, tubular calcification and vascular congestion, as well as arteriolar vacuolization and arteriolosclerosis. Conversion to SRL, HT and tachycardia were reduced, accompanied by amelioration of kidney dysfunction and lesions (glomerulosclerosis and tubulointerstitial fibrosis), together with reduction of oxidative stress, proliferation and angiogenesis.

Conclusion: In conclusion, SRL ameliorates CsA-induced nephrotoxicity in a rat model, which might be due to protection against oxidative stress, proliferation and angiogenesis, but these mechanisms deserve better exploitation.

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PS-21-029

Non-lupus "full-house" nephropathy in Serbian population in last six years

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Diffuse glomerular and sometimes focal mesangial staining of immune complex depositas (IgA, IgG, IgM, C3, and C1q), also known as "full-house" pattern commonly indicates lupus nephritis. However, some non-lupus nephropathy also can be present with a "full-house" immunofluorescence pattern, mimicking lupus nephritis. The aim of this study was to define the clinicopathological spectrum of originally non-lupus "full-house" nephropathy. Biopsies from January 2005 till December 2011 were analyzed in order to identify all renal biopsies cases showing "full-house" pattern. The study included 192 "full-house" renal biopsy diagnosiss. From all analyzed cases 117 (60 %) had lupus nephritis expressing "full-house" pattern and 75 (40 %) cases had non-lupus "full-house" nephropathy. In the absence of clinical and/or serological evidence of systemic lupus erythematosus (SLE), at the time of renal biopsy, in 36 cases diagnose was membranous glomerulonephritis (GN), than 11 mesangioproliferative GN, 9 membranoproliferative GN, 7 IgA nephropathy, 6 rapidly-progressive GN and 6 membranous/membranoproliferative GN cases. Non-lupus "full-house" nephropathy is present in broad spectrum of different types of GN, predominantly in cases of membranous GN. The possibility of "full-house" nephropathy preceding the emergence of overt SLE remained to be clarified.

PS-21-031

A prostacyclin analogue inhibits the mitochondria-dependent endothelial apoptosis in the kidney of glomerulonephritis rats

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Objective: Although the renoprotective effects of prostacyclin have been demonstrated in many studies, the protection mechanisms of prostacyclin in chronic kidney disease, especially at the terminal stage, are still remained unclear. In the present study, we performed pathological and pathphysiological analyses of prostacyclin renoprotective effects using a stable prostacyclin analogue, beraprost sodium, in the disease kidney of anti-GBM glomerulonephritis (GN) rats.
Method: Beraprost was administrated from 2 weeks after induction of GN. The condition of renal microvascular network and localization of apoptotic cells were examined using renal vascular corrosion casts, immunostainings and TUNEL-staining. The intracellular apoptotic signaling pathway was analyzed by Western blot and qPCR.
Results: In the kidney of beraprost-treated rat, significantly high density of renal microvascular network was maintained, and apoptosis of vascular endothelial cells was suppressed even at the terminal stage of anti-GBM GN. Pathophysiological analyses revealed that transcriptional and post-translational modifications of Bcl2 and XIAP, which were anti-apoptotic proteins in mitochondria dependent apoptotic pathway, were occurred in the kidney of beraprost-treated rat.
Conclusion: These results suggested that prostacyclin protects renal vascular network by inhibiting mitochondria dependent endothelial apoptosis, and it play an important role for preservation of renal function in the chronic kidney disease.

Wednesday, 12 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-22 Poster Session Uropathology

PS-22-001

Villous adenoma of the urinary bladder

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Objective: Although villous adenomas commonly occur in the gastrointestinal tract villous adenomas of the urinary tract, including the bladder, are infrequently encountered.
Method: We report a case of urinary bladder villous adenoma in a 72-year-old man. The patient was undergone cystoprostatectomy because of diagnosis infiltrative urothelial carcinoma in the transurethral resection of bladder.
Results: Histopathological examination of cystoprostatectomy specimen there was no urothelial carcinoma. A 2,5 cm polypoid mass was seen at the dome of the urinary bladder. Histopathology confirmed that this tumor was a villous adenoma with a polypoid growth of the glandular epithelium consisting of small tubular glands, dilated cystic glands or papillary fronds lined by a columnar epithelium. The glandular epithelial cells displayed mild nuclear atypia and nuclear pseudostratification with some mucus cells admixed. The patient was diagnosed with a rare case of villous adenoma of the bladder. Over the past 5 months of follow up, the patient is alive and no metastasis.
Conclusion: Patients with isolated villous adenomas in the urinary bladder have an excellent prognosis and surgical resection is curative. However, it is uncertain whether an untreated lesion might eventually develop into an adenocarcinoma. Therefore, close follow up is recommended because of the possibility that this condition might be premalignant.

PS-22-002

Caprin 1 overexpression in urothelial carcinomas of bladder

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Objective: Caprin1 encoded by Cytoplasmic Activation/ Protein-1 gene located in 11p13 chromosome region. It

has been reported that Caprin 1 is associated with cell proliferation in various types of cell lineages.
Method: We researched whether Caprin 1 might be overexpressed or not in urothelial carcinoma of bladder and its overexpression could be correlated with clinicopathologic parameter (age, sex, invasion). Fifty urothelial carcinoma of bladder (29 infiltrative; 21 non-infiltrative) were stained by immunohistochemically in tissue microarrays.
Results: The expression of Caprin 1 was observed in 24infiltrative urotelial carcinoma cases (%82) and 18 non-invasive urothelial carcinoma cases (%85). Age range was 32–85. Eight patients were female, 42patients were male.
Conclusion: In the literature Caprin 1 overexpression was reported in different types of tumors including esophageal, stomach, prostate, lung, liver. Caprin 1 overexpression might be correlated with the cellular proliferation potential. To determine of importance of Caprin -1 overexpression new studies are necessary.

PS-22-003
Pseudohyperplastic squamous cell carcinoma of the penis: A lichen sclerosus related tumor
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Objective: Pseudohyperplastic squamous cell carcinoma of the penis (PSCC) is a low grade tumor with specific clinical and pathological features. This very uncommon tumor occurs in association with lichen sclerosus, the main location is foreskin, and the high degree of differentiation may difficult its discrimination with pseudoepitheliomatous hyperplasia.
Method: A 66-year-old male presented a penis lesion involving glans and foreskin, clinically suspicious of malignancy. Size was 1,6×1,4 cm and a conservative resection was done. Pathological study was performed, and HPV detection with a commercially available kit: PCR amplification and reverse hybridization with probes to 35 HPV types.
Results: The lesion showed a non-verrucous well differentiated squamous cell tumor. Upper layers lacked any atypia but infiltrative growth was evident in basal layers, with atypical cells and mitosis. Lichen slerosus changes were evident bordering the tumor. HPV was negative for all types studied. No further treatment was employed and after a 18 months follow-up no recurrence has been observed.
Conclusion: PSCC should be taken in mind when handling penis tumors. A correct differentiation from benign lesions and a knowledge of its low grade to avoid overtreatment will benefit patients. Lichen sclerosus and not HPV seems to play a precancerous role.

PS-22-004
Evaluation of sunitinib malate and meloxicam as single agents or in combination in bladder cancer cell lines
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Objective: Currently accepted for the treatment of advanced renal cancer, sunitinib malate is a small molecule inhibitor of the VEGFR family, with ability to regulate tumor growth, progression, angiogenesis and metastasis. Several reports have suggested that encouraging effects can be achieved by combining COX-2 inhibitors with anticancer agents. The goal of this work was to evaluate the effects of sunitinib malate and meloxicam isolated and combined on three human bladder cancer cell lines.
Method: T24, 5637 and HT1376 cells were treated with several concentrations of sunitinib malate and meloxicam, as single agents or in combined schedule. Their influence on cell proliferation was determined by MTT method after 72 h of treatment. Control samples were processed in the same way as treated samples but in drug-free medium. Absorbance values of each well were read at 492 nm using an ELISA plate reader.
Results: A reduction in cell proliferation rate was observed when all cell lines were treated either with sunitinib malate or meloxicam isolated. Simultaneous exposure to both agents enhances the inhibition of cell proliferation. Statistical significances were obtained when treatment groups were compared with control group.
Conclusion: These results suggest a potential clinical application of sunitinib malate in combination with meloxicam on bladder cancer.

PS-22-005
Bcl-2 expression in prostate carcinomas
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Objective: The disturbance of apoptosis represents an important event in the genesis of tumors with different localization. The study of anti-apoptotic protein Bcl-2 expression from the perspectives of the prognostic and predictive value in prostate cancer has led to inconsistent results, even contradictory.
Method: Expression of Bcl-2 was analyzed in 3 groups of prostatic carcinoma: localized, locally advanced and with distant metastases. For histological grading of carcinomas we used Gleason score. Classification of the tumors into prognostic subgroups was made according to NCCN Guidelines. For the immunohistochemical study we used anti-Bcl-2 antibody (clone 174), EnVision system, visualization with

diaminobenzidine. The results of immunohistochemical reaction were assessed by evaluating the extent and intensity of immunostaining. Statistical analysis was performed using STATA 9.2.
Results: 17 of the 59 analyzed cases of prostate carcinomas showed Bcl-2 over-expression: 5,9 % localized carcinomas, 23,5 % locally advanced carcinomas and 70,6 % carcinomas with distant metastases ($p<0.001$). Although most of the Bcl-2 positive tumors were poorly and moderately differentiated, the correlation between Bcl-2 over-expression and tumor grade did not show statistical significance ($p=0,085$).
Conclusion: Bcl-2 overexpression in advanced prostate carcinomas suggests involvement of this marker in the progression of tumors in this location.

PS-22-006
Urothelial carcinoma of the bladder: A clinicopathologic study of 92 cases
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Objective: Urothélial carcinoma (UC) accounts for nearly 90 % of urinary bladder tumors.A variety of histological variant of UC have been recently recognosed. Some variants have prognostic and therapeutic implications. The aim to this study is to assess the pathological features from our series and to compare our results that of the literature.
Method: We retrospectively studied 92 patients who were diagnosed histopthologically with urothelial carcinoma using the WHO classification system.
Results: The mean age of patients at diagnosis was 60(range, 30–70 years). 86,67 % were male (80 H/12 F). All tumors were classified as urothelial carcinomas: 2,1 % urothelial neoplasm with squamous differentiation,2,1 % with glandular differentiation,2,1 % urothelial tumors nested and 1 % sarcomatoid. In this study most tumors were grade 2 (67 cases) and stage pT1.
Conclusion: Adult urothelium has the capacity to undergo several pathways of phenotypic cellular and structural differentiation as a result of the embryological origin of the bladder from the multipotent tissues of the cloacal endoderm and the mesodermal wolffian ducts. The clinical course of bladder cancer varies depending on the histological type of neoplasm, grade and stage of the tumor. Hight-grade muscle-invasive urothelial cancers and tumors schowing variant microscopic morphology have in general hight mortality and poor prognosis.

PS-22-007
Comparison of insignificant cancer detection rates in prostatectomies performed following 6 and 12-core biopsy schemes
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Objective: Widespread use of extended biopsy protocols have increased the prostate cancer detection rates. Besides this improvement, whether detection of clinically insignificant cancer detection rates are increased by extended biopsy protocols is not well documented. In the study, we aimed to compare the rates of insignificant cancers found in prostatectomy specimens performed following 6 and 12-core biopsy protocols.
Method: Retrospectively, we investigated the low volume/low grade (LV/LG) prostate cancers in 160 prostatectomy specimens. Tumors volumes were calculated digitally as multiplying total tumor areas by 3 mm for average block thickness, and corrected for tissue shrinkage by multiplying a factor of 1.25.
Results: Of the 160 prostatectomies, 54 were performed following sextant technique, and 106 were performed after 12-core protocol. Review of the H&E stained sections revealed 21 insignificant cancers. Number of LV/LG tumors found in 6 and 12-core groups were 3(5.6 %) and 18 (16.9 %), respectively.
Conclusion: When compared to sextant technique, detection of LV/LG tumors were significantly raised in prostatectomies performed following 12-core protocol, and this increase points out the need for new approaches in patient management to avoid overtreatment after extended biopsy protocols.

PS-22-008
Impact of total core length for cancer detection in a lateral zone targetted 12-core prostate biopsy scheme
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Objective: A widely accepted adequacy criteria for histopathologic evaluation of prostate core biopsy protocols has not been defined yet. Selection of patients for repeat biopsies after a negative initial biopsy result is also a matter of debate. We aimed to evaluate the impact of total core length for detecting prostate cancer in a 12-core transrectal ultrasound guided biopsy scheme.
Method: Retrospectively, we investigated the core lengths of 768 patients underwent initial prostate biopsy by a lateral zone targetted 12-core protocol between 2006 and 2011.
Results: Cancer was identified in 292 (38.0 %) patients. Mean total core length for positive and negative patients were 15.3 cm and 14.6 cm, respectively. Cancer detection rates in groups for total core length <12 cm, 12–15 cm, and >15 cm were 30.9 % (55/178), 40.6 % (96/236), and 39.8 % (141/354), respectively. When a threshold of 10 cm was selected for total core length, overall cancer detection rates for <10 cm and ≥10 cm groups were 23.9 % (17/71) and 39.5 % (275/697), respectively.

Conclusion: Total core length is significantly associated with cancer detection rates and may be used as a reliable adjunctive tool in deciding repeat biopsies for patients with negative biopsy result.

PS-22-009

Primitive neuroectodermal tumor of the kidney in an adult: A case report

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Objective: Primitive neuroectodermal tumors (PNETs) are highly malignant tumors of neuroectodermal origin. We report a case of renal PNET in a 52-year-old male with a 6-month history of intermittent hematuria.. He underwent a right radical nephrectomy. Macroscopically, the inferior pole was replaced by a multinodular, grey, glistening tumour measuring 8.7/7/6 cm, with foci of necrosis and hemorrhage.
Method: Serial histological sections have been assessed using hematoxylin-eosin and Van Gieson stain and the indirect immunohistochemical analysis for antibodies: MNF 116, VIM, CD56, NSE, MIC2/CD99.
Results: Histological examination revealed a uniform population of undifferentiated, small-to medium-sized tumor cells, arranged in alveolar-insular patterns, with round to oval nuclei, small nucleoli, numerous signs of mitosis and scattered apoptosis, geographic zones of necrosis. Dispersed cells showed cytoplasmic vimentin positivity favouring the diagnosis of PNET. Few tumoral cells appeared positive for MNF116. Expression of CD56 was positive in a large number of tumoral cells and an area of the tumour exhibit a milder reaction of positive NSE. MIC2 was positive with moderate staining in almost all tumoral cells.
Conclusion: Diagnosis is based on histology and immunohistochemistry but pathological evaluation can be challenging because of the differential diagnosis with other small round cell tumors.

PS-22-010

Nonamyloid fibrillary glomerulonephritis: Presentation of two cases

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Objective: Fibrillary glomerulonephritis (FGN) is a rare disease, characterized by fibrillar deposits in the mesangium and the glomerular capillary loops. These deposits do not have an amyloid – like cross-β structure and are readily distinguishable from amyloid by the larger thickness of fibrils and lack of Congo red staining.
Method: We report two cases of a 52- and 64-year-old women, who presented with severe nephrotic syndrome, rapidly progressive chronic kidney disease and lymphoproliferative disorders. Glomerular crescents were present in about 30 % of both renal biopsy specimens (18 of 54 and 9 of 27 glomeruli, respectively). Immunohistochemical analysis, immunofluorescence and an electron microscopy (EM) studies were performed.
Results: Renal biopsy showed a deposition of an amyloid-like extraneous substance in the mesangium, as well as within the glomerular basement membranes. Congo red staining was negative. The EM examination revealed FGN.
Conclusion: FGN must be included in the differential diagnosis of rapidly progressive chronic renal disease. EM confirm the diagnosis of FGN, which suggests a poor outcome.

PS-22-011

Urachal adenocarcinoma: A report of 3 cases

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Objective: Urachal carcinomas represent less than 1 % of bladder-related cancers. Most are adenocarcinomas, but urothelial, squamous and small cell carcinomas may occur. There are pathological criteria for assessing an urachal origin. A specific staging system is lacking for these tumors.
Method: A mass of the bladder dome was found in two 56 and 58 year-old men. A 76 year-old woman presented an urachal cyst. CT-scan revealed no other tumors and partial cystecomy was performed. Pathological examination showed partially cystic adenocarcinomas, one enteric type G2, and two mucinous type G1. Two tumors extended into the bladder mucosa and one was limited to the urachal cyst. Surgical margins were negative. Immunostainings were positive for CK7, CK20, CDX2, cytoplasmic beta-catenin, and negative for p63.
Results: With a follow-up of 1, 6 months and 6 years, all patients are free of disease.
Conclusion: No TNM classification exists for urachal carcinomas. Specific staging systems have been proposed by Sheldon, and more recently by the Mayo Clinic. Two cases are Sheldon IIIA/Mayo Clinic II, and one Sheldon II/Mayo Clinic I. Since stage, grade and surgical margins are the main prognostic factors, a clear and relevant staging system is needed for these rare carcinomas.

PS-22-014

Renal cell carcinoma with papillary and chromophobe features: An example of hybrid tumor

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Objective: Renal cell carcinoma (RCC) with two different histologies must be included in the unclassified group (WHO classification). Whether these cases should be included in this histological subgroup or be considered hybrid RCC is a matter of debate. We report one of such cases in which papillary and chromophobe phenotypes meet.
Method: A 5 cm in diameter asymptomatic left renal mass was discovered incidentally in the radiological follow-up of a breast carcinoma diagnosed 12 years before in a 62 year-old woman. Follow-up showed right adrenal gland metastasis. Patient died 12 months later.
Results: Grossly, tumor well circumscribed, tan-yellow, with haemorrhagic and necrotic areas. The neoplasm showed two different histologies clearly defined: One showed solid nests of polyhedral cells, with eosinofilic cytoplasm, central and hyperchromatic nuclei, occasional mitosis recapitulating chromophobe RCC. The other component presented a well defined tubulopapillary growth pattern typical of papillary RCC. Focally sarcomatoid transformation, with tumor necrosis and chronic inflammation. By immunohistochemistry, chromophobe and papillary areas retained their specific phenotypes.
Conclusion: Hybrid renal carcinomas do exist, but they are most probably hidden in the unclassified group of renal tumors. However, the exact histological context for which a renal neoplasm deserves the name "hybrid" remains to be defined.

PS-22-015
Thyroid-like follicular renal cell carcinoma of the kidney
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Objective: Renal cell carcinoma with thyroid-like follicular pattern is a rare histological subtype of renal carcinomas that has been very recently described.
Method: A 3.3 cm in diameter asymptomatic left renal tumor was discovered during the study of a macroscopic hematuria in a 32 years old man. The lesion was organ-confined.
Results: Grossly, the tumor was a well circumscribed, solid, brown and homogenous intraparenchymatous nodule. Proliferating cells were arranged in a microfollicular pattern with colloid-like material resembling thyroid adenoma. Cells displayed low grade nuclear features and had eosinophilic cytoplasm. Some areas showed a solid pattern of growth resembling an oncocytoid neoplasm. By inmunohistochemistry, the tumor was negative for thyroglobulin and TTF1, and positive for EMA, CK7, AE1/AE3, and e-cadherin.
Conclusion: Renal cell carcinoma with microfollicular thyroid-like features has been very recently identified in the literature. There is no agreement on the exact nature of this neoplasm so far, and the 2004 WHO classification of renal tumors still does not consider this phenotype as a distinct histological subtype. Anyway, the tumor must be distinguished from metastatic thryroid carcinoma, another quite unusual condition.

PS-22-016
Evidence for clonal fibroblast proliferation and autoimmune process in idiopathic retroperitoneal fibrosis
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Objective: We sought to determine if idiopathic retroperitoneal fibrosis is clonal process and if it is an autoimmune, or IgG4-driven, process.
Method: Thirty cases of idiopathic retroperitoneal fibrosis, in whom known causes of retroperitoneal fibrosis were excluded and those for which paraffin blocks were available, were included in this study. We performed clonality analysis in 16 female patients. Genomic DNA samples were prepared from formalin-fixed, paraffin-embedded tissue sections using laser capture microdissection.
Results: Eight of 15 information cases (53 %) showed nonrandom X-chromosome inactivation, or a clonal process. Of the 26 patients for which IgG4 analysis was performed, 14 (54 %) were positive for IgG4-positive plasma cells and all were negative for ALK. Of the 12 patients, for which both clonality analysis and IgG4 analysis were performed, 4 were clonal and IgG4 negative (33 %), 2 were clonal and IgG4 positive (17 %), 2 were nonclonal and IgG4 positive (17 %), and 4 were nonclonal and IgG4 negative (33 %).
Conclusion: Our data indicate that a significant proportion (53 %) of idiopathic retroperitoneal fibrosis cases in females is associated with a clonal expansion of fibroblasts. In addition, a subset of idiopathic retroperitoneal fibrosis cases could be classified in the IgG4-related sclerosing disease spectrum.

PS-22-017
Histopathology and clinical features of urethral caruncle
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Objective: Urethral caruncle is a benign polypoid mass of the urethral meatus in primarily postmenopausal women. Although a conclusive association with malignancy, urologic disorder, or systemic disease has not been established, often the lesion carries a challenging clinical differential diagnosis that includes malignancy.

Method: We examined clinical and histopathologic characteristics in 41 patients. Medical records were assessed for presentation, clinical diagnosis, associated urothelial carcinoma, radiation treatment, tobacco use, immunologic/urologic disorder, and treatment strategy/outcome.
Results: The mean age was 68 (range 28–87 years). Presenting symptoms were: pain (37 %), hematuria (27 %), and dysuria (20 %), in contrast to asymptomatic (32 %). Clinical diagnosis favored malignancy in 10 % of cases. Concurrent or subsequent urothelial carcinoma was present for five patients (12 %), though none developed urethral carcinoma. Histologic features included mixed hyperplastic urothelial and squamous lining, overlying a variably fibrotic, edematous, inflamed, and vascular stroma. Invaginations of urothelium extending into the stroma were common (68 %), showing rounded nests with cystic or glandular luminal spaces, similar to urethritis cystica/glandularis, without intestinal metaplasia. Two lesions included an organizing thrombus, one with intravascular papillary endothelial hyperplasia. Twenty patients were treated with topical medications without resolution. Three lesions recurred (7 %) after excision.
Conclusion: Urethral caruncle is an uncommon lesion that may clinically mimic benign and malignant conditions, making tissue diagnosis critically important.

PS-22-018

Human Papillomavirus (HPV) is not involved in urothelial tumorigenesis

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Objective: The purposes of this study were to investigate the possible role of human papillomavirus in the development of squamous cell carcinoma of the urinary bladder and to determine if p16 expression could serve as a surrogate marker for human papillomavirus in this malignancy.
Method: Forty-two cases of squamous cell carcinoma of the urinary bladder and 27 cases of urothelial carcinoma with squamous differentiation were investigated. HPV infection was analyzed by both in situ hybridization at the DNA level and immunohistochemistry at the protein level. p16 protein expression was analyzed by immunohistochemistry.
Results: Human papillomavirus DNA and protein were not detected in 42 cases of squamous cell carcinoma (0 %, 0/42) or 27 cases of urothelial carcinoma with squamous differentiation (0 %, 0/15). p16 expression was detected in ten cases (31 %, 13/42) of squamous cell carcinoma and nine cases (33 %, 9/27) of urothelial carcinoma with squamous differentiation. There was no correlation between p16 expression and the presence of human papillomavirus infection in squamous cell carcinoma of the bladder or urothelial carcinoma with squamous differentiation.
Conclusion: Human papillomavirus does not play a role in the development of squamous cell carcinoma of the urinary bladder and urothelial carcinoma with squamous differentiation. p16 expression should not be used as a surrogate marker for evidence of human papillomavirus infection in urinary bladder cancer.

PS-22-019

PAX8 is expressed in the majority of renal epithelial neoplasms: A study of 223 cases using a tissue microarray-based immunohistochemical approach

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Objective: PAX8 is a cell lineage-specific transcription factor and plays a crucial role in organogenesis of the kidney, thyroid, and Müllerian duct. Previous study showed that PAX8 is a specific and sensitive marker for both renal and ovarian carcinomas. The purpose of this study is to investigate PAX8 expression using a new monoclonal PAX8 antibody in a larger number of renal epithelial neoplasms including clear cell renal cell carcinoma, papillary renal cell carcinoma, chromophobe renal cell carcinoma, and renal oncocytoma.
Method: PAX8 immunohistochemical staining was performed on tissue microarrays containing 84 cases of clear cell renal cell carcinoma, 66 cases of chromophobe renal cell carcinoma, 57 cases of papillary renal cell carcinoma, and 16 cases of renal oncocytoma.
Results: PAX8 expression was detected in 93 % (78/84) of cases of clear cell renal cell carcinoma, 80 % (53/66) of cases of chromophobe renal cell carcinoma, 95 % (54/57) of cases of papillary renal cell carcinoma, and 94 % (15/16) of cases of renal oncocytoma.
Conclusion: PAX8 is expressed in the majority of renal epithelial neoplasms including renal cell carcinomas and oncocytomas and this monoclonal PAX8 antibody is more sensitive than polyclonal antibody to detect chromophobe renal cell carcinoma. These results showed that PAX8 is a valuable marker for nephric neoplasms.

PS-22-020

Prostatitis as the presenting sign in Wegener granulomatosis: A case report

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Objective: Wegener's granulomatosis (WG) is a systemic disease that is usually limited to the respiratory tract and kidneys. Prostate involvement is demonstrated histologically in 2–7 % of the patients.
Method: A 41 years old male was hospitalized with symptoms of acute urinary retention due to acute prostatitis, was treated with antibiotics and demonstrated clinical improvement. He underwent transurethral prostatic biopsy and the diagnosis of acute necrotic prostatitis was rendered. A month later, he was admitted to our hospital with features of sepsis. Abdomen CT revealed prostate abscesses and thoracic cavity CT showed bilateral pleural effusion with single peripheral nodule on the left lobe. Bronchoscopy revealed nodules on the main right bronchus. Bronchial biopsy demonstrated candida inflammation. Red cell casts in urinalysis and C-ANCA seropositivity was demonstrated. Prostatic biopsy slides were reevaluated and showed histological features of acute necrotic prostatitis associated with vasculitis and scattered multinucleated giant cells.
Results: Based on the combination of clinical, histological, biochemical and immunological features the diagnosis of WG was established. He received immunosuppressive therapy and showered significant clinical improvement.
Conclusion: Prostate involvement can rarely be the presenting clinical manifestation of WG. Early diagnosis is important expediting aggressive immunosuppressive therapy which may limit a more severe systemic disease progression.

PS-22-021

Transitional cell carcinoma arising within the renal pelvis of a patient with autosomal dominant polycystic kidney disease: A case report

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Objective: Cancer risk for Autosomal Dominant Polycystic Kidney Disease (ADPKD) is still unknown, but reports of Papillary and Clear Cell types of Renal Cell Carcinoma (RCC) are frequent. Transitional Cell Carcinoma (TCC) in patients with ADPKD are less frequent, with only four cases reported.
Method: A review of clinical data from an ADPKD patient with TCC admitted in our hospital and a review of current literature regarding ADPKD and TCC were made.
Results: The patient is a 77 year-old woman with chronic renal failure due to ADPKD, on hemodialysis for 2 years. She was admitted with left lumbar pain, hematuria and fever. Radiological exams revealed various complex cysts with dense material that did not enhance with contrast, compatible with hematic cysts in the context of ADPKD. The whole clinical findings suggested cystic infection complicated with sepsis, so nefrectomy was performed. Macroscopic examination of the ressected kidney revealed a white granulous nodular formation with 4.5 cm diameter in the renal pelvis. Histological examination confirmed a high-grade papillary TCC with parenchymal infiltration (pT3) and extense scamous differentiation.
Conclusion: The present case illustrates that TCC can occur in ADPKD, despite its rarity. It can be difficult to successfully diagnose TCC on ADPKD based on clinical-radiological findings.

PS-22-022

Clear cell renal cell carcinoma with syncytial-type multinucleated giant cells: Report of 4 cases of a rare variant of renal cell carcinoma

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Objective: Renal Cell Carcinoma (RCC) with Syncytial-type cells (SGC) is a rare variant of renal carcinoma, with few cases reported. Our aim is to define the morphologic and immunohistochemical findings of 4 new cases.
Method: Four cases of RCC with SGC have been identified in our files from 1990 to 2011. Histological slides were reviewed in all cases and inmunohistochemistry (CK7, AE1/AE3, CD10, RCC-Ma, EMA, CD117, AMACR, CAIX) performed in 3 cases.
Results: Main clinicopathological data appear in the Table. All tumors were classic clear cell RCC with SGCs distributed along the tumor. SGCs showed emperipolesis and eosinophilic hyaline globules. SGCs immunostaining was similar to conventional clear cells (CD10, EMA, AE1/AE3, RCC-Ma, CAIX positive). Two cases showed extrarrenal extension.

Conclusion: SGCs is a rare finding in clear cell RCC. The immunostaining of syncytial cells is similar to that observed in the adjacent clear cell RCC. This histologic variant seems to be more aggressive than conventional clear cell RCC; additional series are needed to delineate with certainty its clinical behaviour.

Case	1	2	3	4
Sex	M	M	F	F
Age	65	73	61	71
Size	5.5	6	4	5
Laterality	L	L	R	R
Stage	pT1b	pT3a	pT4	
Fuhrman-Grade	III	IV	III	
Direct-Extension	No	Perirrenal fatty-tissue	Adrenal gland	

PS-22-023

Primary renal carcinoid tumor: Report of 2 cases

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Objective: Carcinoid tumor is a very uncommon neoplasm in the kidney. We report the histopathologic and immunohistochemical (IHQ) study of two new cases.
Method: Case 1: 48 year-old female with a 4 cm asymptomatic ¨cystic¨ mass discovered in a routine exam. The patient underwent tumorectomy. Case 2: 77 year-old female with a 3 cm renal mass who underwent left nephrectomy. Two months later a needle biopsy confirmed carcinoid tumor metastasis in the liver. Both patients currently free of disease.
Results: Both tumors showed similar histologic features. Neoplastic cells were grouped in nests, ribbons, and pseudoglands with rosette-like appearance and showed eosinophilic granular cytoplasm and chromatic nuclei. Low mitotic index. IHC: diffuse/intense cytoplasmic staining for CD56, CD57, AE1/AE3, chromogranin and synaptophysin.
Conclusion: Primary renal carcinoid tumor is rare in the clinical practice. The histological findings correspond to a well differentiated neoplasm and are similar to carcinoid tumors in other locations, which makes the diagnosis feasible even without previous personal experience. IHC confirms the diagnosis. It usually behaves as a low grade neoplasm, but recurrences and metastases do occur. Only single cases and short series have been published so far. There is no accumulated experience to establish long term prognosis.

PS-22-024

Prostatic adenocarcinoma occurring simultaneously with large cell neuroendocrine carcinoma of the urinary bladder: An extraordinary collision tumor

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Objective: Radical cystoprostatectomy is a standard surgical procedure for male patients with muscle-invasive urinary bladder (UB) carcinoma. Vast majority of these tumors are urothelial carcinomas, while large cell neuroendocrine carcinoma (LCNEC) is a very uncommon tumor with less than 20 reported cases. Invasive prostate carcinoma is incidentally detected in up to 20 % of cystoprostatectomy specimens. It is usually well differentiated and shows low propensity for dissemination and local recurrence.
Method: Clinical and pathological description of an extremely rare collision tumor composed of LCNEC of

the urinary bladder and a high grade acinar prostate carcinoma.
Results: A 79-year-old male patient was admitted to the urology department due to severe gross haematuria. Cystoscopy revealed large tumor of the posterior-inferior wall of the UB with involvement of the left uretheral orifice. In the radical cystoprostatectomy specimen LCNEC of the UB, involving bilaterally prostate and spermatic vesicle (pT4a), was diagnosed. Additionally both lobes of the prostate were involved by the acinar prostatic carcinoma (pT2c, Gleason score 5+4=9).
Conclusion: High-grade prostate carcinoma may rarely co-exist with UB tumors of uncommon histology.

PS-22-025
Expression of androgen receptors in prostate carcinomas
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Objective: Despite of numerous researches in the field, data regarding immunohistochemical (IHC) expression of androgen receptor (AR) in prostate carcinomas, in terms of prognosis and therapy, are quite controversial.
Method: The IHC expression of AR was analyzed on 3 groups, each of 20 primary diagnosed prostate carcinomas: localized, locally advanced and distant metastasized. The anti-AR antibody (clone AR441) was used. For each tumor was determined the percentage of AR-positive nuclei, assigning a staining score (0 to 4). A value of 64 % was considered to be discriminatory between tumors with high and low AR expression.
Results: All the analyzed carcinomas showed AR. 54.2 % of tumors had high AR expression and 45.8 % showed low AR expression. 7/19 localized tumors (one tumor vanished during processing), 15/20 locally advanced and 10/20 distant metastasized tumors showed high AR expression (p=0.051). 5/18 well-differentiated, 16 of 23 moderately differentiated and 11/18 poorly differentiated tumors showed high expression of AR (p=0.022).
Conclusion: Although not reaching statistical significance, the AR expression tended to correlate with the stage of disease and with the degree of differentiation in terms of an increased expression of AR in advanced, moderately and poorly differentiated tumors.

PS-22-026
Prostate tumors with atypia in the stromal compartment
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Objective: Prostate lesions with atypical stromal component are rare and poorly characterized in terms of evolution and prognosis.
Method: We retrospectively analyzed 3 cases of unusual prostate tumors diagnosed on prostate needle biopsy. The biopsies were performed due to an elevated serum PSA and/or phenomena of bladder outlet obstruction. For the immunohistochemical (IHC) diagnosis there were used the following antibodies: CK AE1/AE3, PSA, PSMA, vimentin, SMA, ER, Desmin, PgR, CD34.
Results: Two of the three patients, one 68 and the other 66 years-old, with serum PSA level of 34 ng/ml and 14.58 ng/ml respectively, were diagnosed with sarcomatoid carcinoma, the former presenting with liver metastases at diagnosis. In evolution, the death of the first patient occurred 3 months after the diagnosis and the second patient refused surgery. The third patient, 75 years-old, with a nodular prostatic mass of 3.3 cm, was clinically suspected to have an unusual malignant prostatic tumor considering that, despite his 7 ng/ml of serum PSA, he presented multiple bone metastases. The histopathological diagnosis was Stromal Tumor of Uncertain Malignant Potential.
Conclusion: The prostate lesions with atypical mesenchymal component are rarities in urologic pathology. An accurate diagnosis relies on meticulous pathological examination techniques and supplemented, for rare cases, with other clinical and laboratory data.

PS-22-027
Immunohistochemistery study in a case of nephrogenic bladder adenoma
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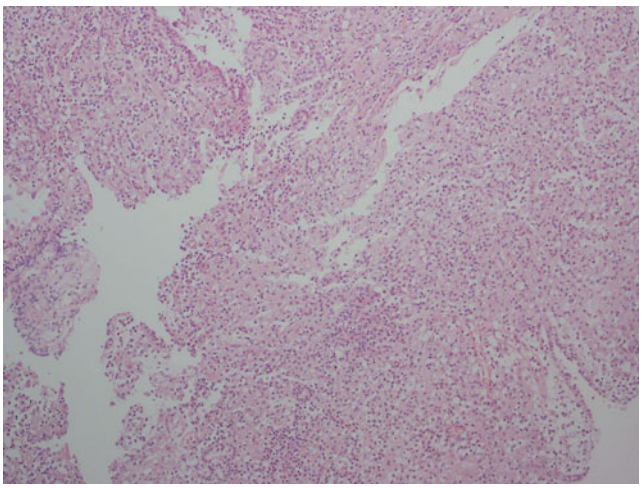
Objective: Nephrogenic adenoma is a rare benign lesion of bladder that may be confused with malignant lesions. There is strong relation with urinary tract irritation and intravesicl instrumentations. Nephrogenic adenoma was initially thought to originate from urothelial metaplasia however no solid proof is available.

Method: We present this 55 years old lady with urinary problem. Cystocopic examination show a sessile mass and biopsy show circumscribed proliferation of tubules, cysts, and papillae lined by cells with low cuboidal to columnar epithelial cell. Nephrogenic adenoma can be a significant diagnostic pitfall as certain histological features, such as the presence of enlarged nuclei with prominent nucleoli

Results: Immunohistochemistery study showed strong reactivity to CK7, P504S, CD10, and EMA but negative for CK20, PSA, and P63.

Conclusion: We recommend that any lesion in cystoscopic examination should be followed and immunohistochmistery examination some times is mandatory to differentiate them from malignant tumors.



PS-22-028

Regulators of apoptosis and the cell cycle are overexpressed in bladder cancer metastases and may predict survival

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Objective: Expression of biomarkers and their prognostic relevance may differ between primary tumours (PT) and its metastases (MET). There is little information about this phenomenon concerning apoptosis and cell-cycle associated biomarkers in urothelial bladder cancer (UCB).

Method: Nodal positive patients (n=152) with UCB underwent cystectomy and lymphadenectomy. Immunohistochemical expression of bcl-2, bcl-6, MDM-2, p53 and CyclinD1 was quantified in tissue microarrays constructed from PT and corresponding nodal MET.

Results: Frequency of MDM-2 positivity increased from PT (17 %) to MET (37 %, p<0.001). This trend was not significant for bcl-2 (PT: 7 %; MET: 10 %, p=0.4) and bcl-6 (PT: 8 %; MET: 12 %, p=0.08). Median percentage of p53 and CyclinD1 immunostained cells increased significantly (p<0.05) from PT (15 %/30 %) to MET (40 %/50 %). MDM-2 and CyclinD1 expression were positively correlated in PT (p<0.004) and MET (p<0.002). p53 and MDM-2 positivity were inversely correlated in PT (p<0.03). Only high CyclinD1 expression in the metastases predicted early death significantly and independently (p=0.017).

Conclusion: Biomarkers of apoptosis and cell-cycle associated are up-regulated in the metastases indicating differences in survival and proliferation of cancer cell compared to primary tumours. Both tumor components may harbor different prognostic information and are not necessarily surrogates for each other.

PS-22-029

Evaluation of histopathologic and histomorphometric changes of testicular tissue and gonadotropins levels following consumption of Methylphenidate in male mice

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Objective: One of the most common psychiatric disorders in children is ADHD (Attention Deficit Hyperactivity Disorder), which is treated extensively by Methylphenidate. This study investigates the assessment of the effects of methylfenidate on Histopathologic and Histomorphometric changes of testes and serum level of gonadotropin in adulthood which produces gametes and has Importance for future generations.

Method: In this study 36 adult male mice (Balb/C) were used. After determining the body weight, the animals were divided randomly into two experimental groups of and one control group. The Experimental groups received Ritalin via gavage as follow: The group 1 received 2 mg/kg/day and the group 2 received 10 mg/kg/day for a period of 40 days. After evaluation of body weight, general anesthesia was used for taking blood samples from the heart in order to measure gonadothropins levels in serum. Then for the purpose of body weighing and measuring of diameter of germinal epithelium the testes were removed and the possibility of any pathologic changes was considered.

Results: The results showed that Methylphenidate with different doses could decrease germinal epithelium and also body weight significantly. Besides some significant changes in serum gonadotropins, without any pathological changes were observed.

Conclusion: Our findings demonstrated that Methylphenidate administration in adulthood due to Influence of

gonadotropin hormones on testis function may affect on spermatogenesis.

PS-22-030

A rare bladder cancer: Report of two cases

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Objective: Small cell urothelial carcinoma (SCUC) comprises less than 1 % of bladder malignancies. It is characterized by an aggressive clinical course, early metastatic spread and high mortality rate. The histogenesis remains controversial and there are no well-defined protocols for therapy.
Method: We report two cases of SCUC. Both of them refer to 50 year-old males, smokers. They presented with gross hematuria. Transurethral resection bladder tumor (TURBT) specimens showed SCUC, followed by cystoprostatectomy and pelvic lymphadenectomy, confirming the initial diagnosis. Immunohistochemistry was used on paraffin embedded tissue.
Results: Microscopically, the tumor cells show a diffuse architectural pattern with occasional nesting, are small, uniform, with scant cytoplasm, nuclear crowding, nuclear molding, inconspicuous nucleoli and finely stippled chromatin. Numerous mitoses, Azzopardi phenomenon and foci of necrosis are present, as well as areas of urothelial carcinoma. Tumor cells are strongly (+) with Ker AE1/AE3, Cam 5.2 (dot-like perinuclear pattern), CD56 (the most consistent neuroendocrine marker), p53, ki-67(60 %), focally (+) with Synaptophysin and (−) with Chromogranin, Ker34βE12, Ker7, Ker 20, TTF-1, LCA.
Conclusion: Pathologic and immunohistochemical data identify SCUC. Differential diagnosis includes metastasis of a small cell carcinoma from another site, poorly differentiated urothelial carcinoma, malignant lymphoma, lymphoepithelioma like carcinoma, plasmacytoid carcinoma, and primitive neuroectodermal tumor.

PS-22-031

Rare variant: Primary renal malignant fibrous histiocytoma

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Objective: Malignant Fibrous Histiocytoma is the most common subtype of soft-tissue sarcoma in adults Typical sites are the extremities followed by the retroperitoneum. Primary MFH of the kidney is extremely rare.
Method: A 77-year-old man presented with left-flank pain and fever of 1 month duration. Clinical examination revealed left renal mass, which on contrast enhanced computed tomography and magnetic resonance imaging was characterized as 8×8×7 cm sized well-demarcated left renal middle- superior polar mass with central necrosis and cystic changes. The contralateral kidney was normal. He underwent left radical nephrectomy by thoracoabdominal approach. Gross examination of the specimen revealed yellowish white 9×9×7 cm sized mass, with multifocal necrozis and cystic changes. Histopathology of these resection specimens; scattered spindle cells and foam cells, fine vascular network and necrosis. Immunohistochemistry revealed CD68-positive xanthoma cells. The tumor also stained positive for vimentin, CD34, but negative for cytokeratin, EMA, desmin, SMA and myoD1. A diagnosis of MFH was made.
Conclusion: MFH is a primitive mesenchymal tumor with some histiosytic and fibroblastic differentiation Primary renal MFH is an extremely rare lesion. Because this malign mesenchymal tumor is indistinguishable clinically and radiologically from renal cell carcinoma diagnosis and histopathology of this rare lesion are discussed.

PS-22-032

Hyaline ring granulomas in the urinary bladder: A case report

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Objective: Hyaline ring granulomas, or pulse granulomas, are rare inflammatory responses to vegetable matter, characterised by aggregates of hyaline rings and other inflammatory components around vegetable matter. The vast majority occur in the oral cavity and only a few specific extra-oral cases have been reported. We present a case of pulse granulomas in the wall of the urinary bladder, occurring in a 50 year-old gentleman with a concurrent history of diverticulitis and colo-vesical fistula. Pulse granulomas were recently described in the bladder in association with interstitial cystitis, in mesocolonic fat and mesocolonic lymph nodes in association with inflammatory bowel disease and in enterocutaneous and recto-salpingeal fistulas in association with diverticulitis. To our knowledge this is the first case reporting the direct association of the occurrence of bladder pulse granulomas in relation to diverticulitis.
Method: The tissue sections were fixed with 10 % buffered formalin and stained with H&E.
Results: Histopathological examination revealed several hyaline ring granulomas within the outer muscle layer and serosa of the urinary bladder, together with hyaline ring

granulomata within the outer wall of the sigmoid colon associated with diverticula.

Conclusion: It is important to differentiate pulse granulomas from parasites, hyaline ring vasculopathy, granulomatous inflammatory disorders and even malignancy.

PS-22-033

Micropapillary urothelial carcinoma of the bladder: A clinicopathologic comparison with urothelial carcinoma with and without divergent differentiation

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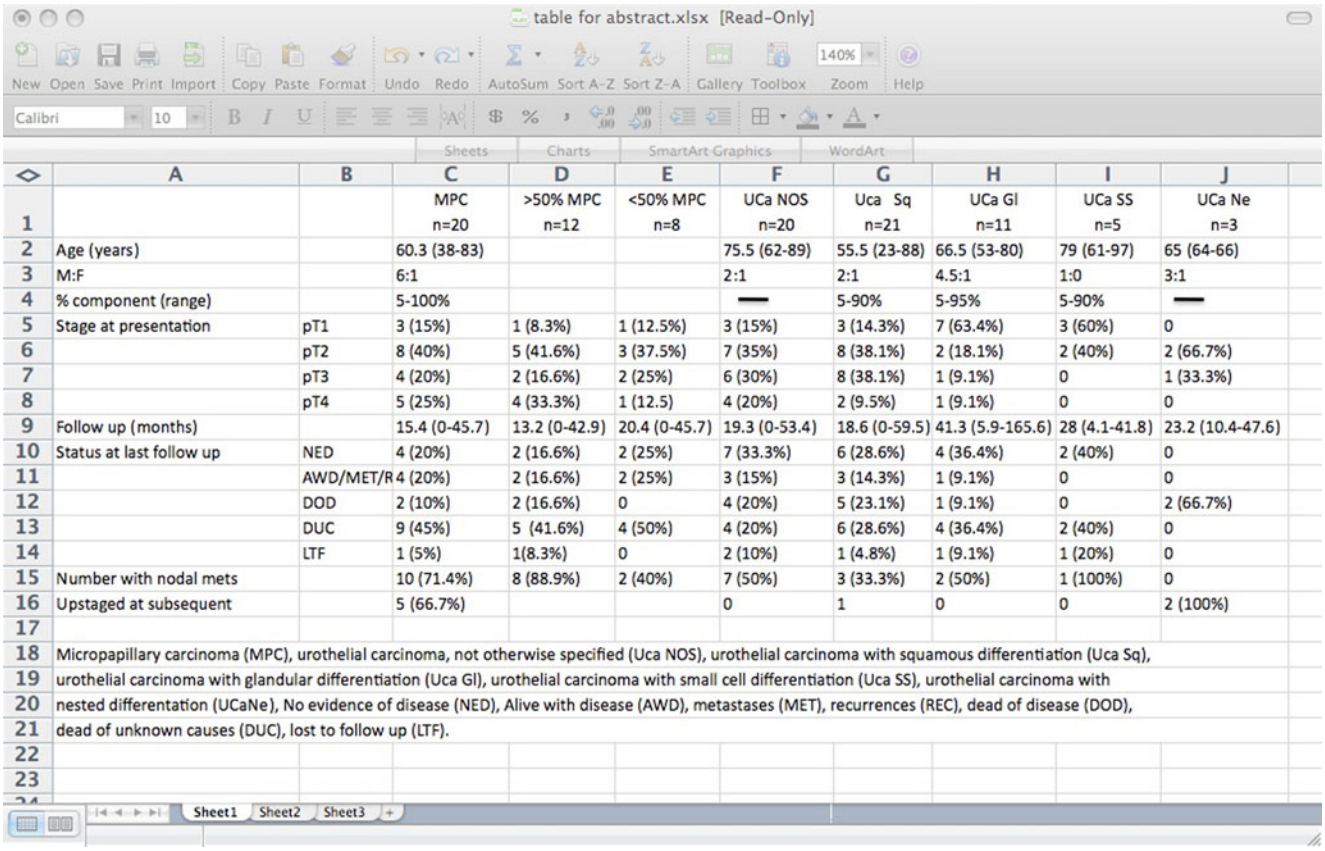
Objective: Micropapillary carcinoma (MPC) is associated with poor prognosis, and may lead to immediate cystectomy irrespective of stage. We study MPC, with "classical" histologic features, to "stage-matched urothelial carcinoma (UCa), not otherwise specified (NOS)", and other UCa with divergent differentiation to compare outcome.

Method: 89 cases from 80 patients with MPC, UCa with squamous (SQ) or glandular (GL) differentiation, small cell carcinoma (SmCa), and nested variant (NeCa) variant of UCa were identified. Histologic and clinical data including stage and outcome were collected.

Results: All groups show male predominance and similar age range. MPC showed the highest rate of nodal metastases (Table 1). Patients with MPC tumor volume of >50 % showed the highest rate of nodal metastases of all other subgroups. The majority of patients with MPC died, a large percentage from unknown causes. Compared to MPC, SQ showed similar presentation at higher stages and similar survival, but a lower propensity for nodal metastases. In our cohort, GL presented at lower stages, showed slightly better survival, and a lower rate of nodal metastases, when compared to MPC. Our cohort included fewer cases of SmCa and NeCa. However, both patients with NeCa died of disease.

Conclusion: MPC, particularly when it represents >50 % of tumor volume, shows higher rate of nodal metastases than remaining subgroups, and is associated with a larger percentage of patient deaths.



	A	B	C	D	E	F	G	H	I	J
1			MPC n=20	>50% MPC n=12	<50% MPC n=8	UCa NOS n=20	Uca Sq n=21	UCa Gl n=11	UCa SS n=5	UCa Ne n=3
2	Age (years)		60.3 (38-83)			75.5 (62-89)	55.5 (23-88)	66.5 (53-80)	79 (61-97)	65 (64-66)
3	M:F		6:1			2:1	2:1	4.5:1	1:0	3:1
4	% component (range)		5-100%			—	5-90%	5-95%	5-90%	—
5	Stage at presentation	pT1	3 (15%)	1 (8.3%)	1 (12.5%)	3 (15%)	3 (14.3%)	7 (63.4%)	3 (60%)	0
6		pT2	8 (40%)	5 (41.6%)	3 (37.5%)	7 (35%)	8 (38.1%)	2 (18.1%)	2 (40%)	2 (66.7%)
7		pT3	4 (20%)	2 (16.6%)	2 (25%)	6 (30%)	8 (38.1%)	1 (9.1%)	0	1 (33.3%)
8		pT4	5 (25%)	4 (33.3%)	1 (12.5)	4 (20%)	2 (9.5%)	1 (9.1%)	0	0
9	Follow up (months)		15.4 (0-45.7)	13.2 (0-42.9)	20.4 (0-45.7)	19.3 (0-53.4)	18.6 (0-59.5)	41.3 (5.9-165.6)	28 (4.1-41.8)	23.2 (10.4-47.6)
10	Status at last follow up	NED	4 (20%)	2 (16.6%)	2 (25%)	7 (33.3%)	6 (28.6%)	4 (36.4%)	2 (40%)	0
11		AWD/MET/R	4 (20%)	2 (16.6%)	2 (25%)	3 (15%)	3 (14.3%)	1 (9.1%)	0	0
12		DOD	2 (10%)	2 (16.6%)	0	4 (20%)	5 (23.1%)	1 (9.1%)	0	2 (66.7%)
13		DUC	9 (45%)	5 (41.6%)	4 (50%)	4 (20%)	6 (28.6%)	4 (36.4%)	2 (40%)	0
14		LTF	1 (5%)	1(8.3%)	0	2 (10%)	1 (4.8%)	1 (9.1%)	1 (20%)	0
15	Number with nodal mets		10 (71.4%)	8 (88.9%)	2 (40%)	7 (50%)	3 (33.3%)	2 (50%)	1 (100%)	0
16	Upstaged at subsequent		5 (66.7%)			0	1	0	0	2 (100%)
17										
18	Micropapillary carcinoma (MPC), urothelial carcinoma, not otherwise specified (Uca NOS), urothelial carcinoma with squamous differentiation (Uca Sq),									
19	urothelial carcinoma with glandular differentiation (Uca Gl), urothelial carcinoma with small cell differentiation (Uca SS), urothelial carcinoma with									
20	nested differentation (UCaNe), No evidence of disease (NED), Alive with disease (AWD), metastases (MET), recurrences (REC), dead of disease (DOD),									
21	dead of unknown causes (DUC), lost to follow up (LTF).									
22										
23										

PS-22-034

Expression of estrogen and progesterone receptors and Wilms tumor 1 in kidneys with chronic obstructive pathology

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Objective: Müllerian-like stroma with ER/PR expression is typical of renal mixed epithelial and stromal tumor and has been described in kidneys with obstructive pathology. WT1 overexpression is not reported in this setting.
Method: Immunohistochemical study for ER, PR and WT1 in autosomal dominant polycystic kidney disease (ADPKD) (n=5), acquired cystic kidney disease (ACKD) (n=5), xanthogranulomatous pyelonephritis (XP) (n=5), and renal lithiasis (RL) (n=5). Controls: fetal (<24 w, n=4; >24 w, n=4) and adult autopsy kidneys (n=5).
Results: Stromal ER was found in 100 % of ADPKD, ACKD, XP and RL; PR expression in 100 % of ADPKD, ACKD and RL and 80 % of XP, and nuclear WT1 in 20 % of XP and RL. ER were negative in 100 % of controls. We found PR expression in 100 % of fetal controls of second trimester. WT1 was negative in the stroma of adult controls (100 %). 80 % of fetal controls showed WT1 expression in the peripheral cortex.
Conclusion: ER and PR expression is frequent in kidneys with chronic obstructive and inflammatory pathology. WT1 is expressed occasionally. More studies are needed to determine whether these findings are a consequence of renal obstruction or they are involved in its pathogenesis, as well as their potential therapeutic implications.

PS-22-036

Telomerase expression in urothelial carcinomas of the urinary bladder: Does it make sense for carcinogenesis or prognosis?

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Objective: Human telomerase reverse transcriptase (hTERT) has been reported as poor prognostic marker in several cancers. In the present study, we examined hTERT expression in urothelial carcinoma (UC) to investigate whether it has a role on the carcinogenesis or prognosis.
Method: Immunohistochemistry was performed to detect hTERT protein expression in tisse microarray blocks consisting of cores of papillary UC (n=63) and infiltrating UC (n=13) cases. Nucleolar staining was considered and staining scores (intensity × distribution) were determined. Tumors were grouped as low or high in terms of histological grade, and as early (Ta, T1), or late stage (T2- T4) in terms of pathological stage.
Results: hTERT expression was significantly higher in the papillary UC group (p=0.028). Tumors in late stage were more likely to show low staining scores of hTERT (p=0.013). No correlation was found with tumor grade and recurrence rate. No effect on survival.was detected.
Conclusion: These findings indicated an association of hTERT protein with early stage UCs as its expression significantly decreased with muscularis propria invasion.

PS-22-037

Incidental multifocal renal cell carcinoma in graft nephrectomy with cellular rejection findings: Concurrence of papillary renal cell carcinoma and renal carcinoma associated with Xp11.2 translocation

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Objective: Malignancy represents the second main cause of death in renal transplant patients and increase markedly by 20 years after transplantation.
Method: A 41 year old male who has been on hemodialysis for 8 months for chronic renal failure, underwent living kidney transplantation from his brother. He received immunosupressive therapy of siclosporin and prednisolon. Twelve years later, due to the impairment of renal functions hemodialysis was started again and ultrasonography revealed chronic renal parenchymal disease. Graft nephrectomy was performed with the pre-diagnosis of chronic rejection.
Results: Macroscopic examination revealed two well-circumscribed tumor nodules with 12 mm and 6 mm in largest diameter. Microscopically, both tumor nodules showed tubulopapillary organization. Larger tumor consisted of clear cells with TFE3 positivity, whereas the small one showed eosinophilic cells with diffuse cytokeratin7 and AMACR positivity, without any TFE3 expression. Concurrence of papillary renal cell carcinoma and renal cell carcinoma associated with Xp11.2 translocation was reported. Non-tumoral renal paranchyme revealed interstitial inflammation, tubulitis and transmural arteritis with fibrinoid necrosis compatible with type III cellular rejection.
Conclusion: As far as we know this is the first case in the English literature demonstrating concurrence of papillary renal cell carcinoma and renal cell carcinoma associated with Xp11.2 translocation in a graft nephrectomy.

PS-22-038

The effect of postoperative intravesical BCG and Mitomycin C therapy on recurrence in superficial bladder cancer

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Objective: To evaluate the efficacy of two mostly used intravesical agent, BCG and mitomycin c, in case of tumor recurrence.
Method: Between 2002 and 2008, we performed TUR-BT to 127 patients whom pathology results were superficial bladder cancer. 41 patients were treated with intravesical BCG once for week 6 weeks then monthly up to one year beginning from 14. day postoperatively. 26 patients were treated with intravesical mitomycin c, beginning from first 6 h postoperatively and once a week for 8 weeks. 60 patients didn't get any further treatment, and excluded from study.
Results: For BCG group, expected disease free interval was 58.1 months, and 34.6 months for mitomycin c group. When two groups compared for expected disease free interval, statistically significant difference observed (p=0.017). For BCG and mitomycin c group, recurrence was seen in 13 and 9 patients, respectively. For patients treated with BCG, 1 and 3 years disease free survival rate was %92.7 and %75.7, respectively. In mitomycin c group 1 and 3 years disease free survival rate was %76.9 and %62.9.
Conclusion: Intravesical adjuvant BCG maintenance therapy is more effective for tumor reccurence than intravesical mitomycin c therapy.

PS-22-039

Papillary cystadenomas of the epididymis: Case presentation

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Objective: Papillary cystadenomas of the epididymis are rare, first described by Sherrick in 1956. They are considered hamartomatous lesions rather than neoplastic and may be seen as intrascrotal swellings in a wide age range. We report here the case of a 32-year-old male who presented with a swelling of the right testis over the past year. His past medical history was otherwise unremarkable.
Method: Ultrasonography revealed the presence of an epididymal cyst. Grossly the cyst had a 2 cm diameter with a cyst wall of 0.2 cm thick attached to a part of epididymis measuring 2×1 cm filled with clear fluid.
Results: Histologically the cyst showed pseudopapillary structures lined by monotonous clear cells. There was mild nuclear pleomorphism, no mitotic activity and no necrosis. Immunostaining for AE1/AE3, EMA, were positive, as well as focally for CK5/6 whereas calretinin and CEA was negative. Similar pattern of staining was seen in the epididymal parenchyma.
Conclusion: Papillary cystadenomas are benign neoplasms and there have been no reports of recurrence or metastasis in the recent literature. Bilateral disease is often associated with von Hippel-Lindau syndrome. Our patient received no further treatment and remains asymptomatic and well 10 months after the intervention.

PS-22-040

Effect of neoadjuvant sorafenib treatment on histology of clear cell renal cell carcinoma and occurrence of circulating tumor fragments

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Objective: Clear cell renal cell carcinoma (ccRCC) generally presents with a micronodular phenotype (MP) due to high expression levels of vascular endothelial growth factor (VEGF-A). Earlier we have shown that MP is associated with shedding of multicellular tumor fragments (MTF) into the circulation and pulmonary metastasis. We hypothesized that VEGF inhibition will destroy MP resulting in less MTF.
Method: 8 ccRCC patients were treated for 4 weeks by daily administration of Sorafenib (400 mg bid). Three days after therapy, nephrectomy was performed and kidneys were perfused via the arteria renalis. Venous perfundate was filtered and processed to AgarCytoblocks for MTF. Treatment effects were studied using immunohistochemistry.
Results: All tumors were ccRCC as demonstrated by high VEGF-A expression. None of the tumors showed MP after Sorafenib treatment. Tumors showed large areas of necrosis and fibrinoid necrosis of the blood vessels, concomitant with profound perivascular inflammation. 6/8 ccRCC patients (75 %) had MFT vs 33 % in a control group (p= 0.03 Fisher's exact test). Individual tumor cells in the MTFs showed increased mitotic activity.
Conclusion: Sorafenib destroys MP in ccRCC, attacks tumor vasculature, causes extensive necrosis and inflammation. Post-treatment MTF are increased in venous perfundate. Care should therefore be taken with neo-adjuvant sorafenib treatment of ccRCC.

PS-22-041

Differential expression of Claudin-1, Claudin-3 and Claudin-4 in bladder lesions

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Objective: Claudins are major transmembrane proteins of tight junctions. As the disruption of their function have important impact on tumorogenesis, invasion and metastasis. Claudins became a focus of interest for targeting therapies. Although their expression profiles have been studied in many organs, researches on Claudin expression in bladder are in limited number. The aim of this study is to present the differential expression of Claudins in invasive urothelial cell carcinoma (IUCC), noninvasive papillary urothelial carcinoma (NPUC), carcinoma in-situ (CIS), papillary urothelial neoplasm of low malignant potentiall (PUNLMP) and control group (CG).
Results: 83 cases (31 IUCC -further divided into:15 muscle invasive UCC, 16 UCC with lamina propria invasion-, 17 NPUC, 13 PUNLMP, 7 CIS and 15 CG) were evaluated with Claudin-1, 3, 4. Interestingly, high Claudin-1 and -3 score in CG (100 %, 80 %), decreased significantly in all non-invasive lesions (mean 18 %, 22 %). Claudin-4 expression appeared to decrease in IUCC vs. Others (%52 vs mean %82).
Conclusion: Higher expression of Claudin-4 in low-grade and non-invasive lesions may be used as a diagnostic tool. In terms of Claudin-1 and -3, their decreased expression in non-invasive lesions when compared to CG and their trend to show more increased expression in IUCC needs to be studied further in larger studies.

PS-22-042

Can we rely on alternative sampling method of radical prostatectomy specimens?

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Objective: Prostatic adenocarcinoma is the most common cancer and second leading cause of cancer death in men. The incidence of prostate cancer has been increasing because of efficiency of modern cancer scanning programs and residual awareness of the patients. For that reason, there is a considerable increase in the number of prostatectomy specimens in the university and research hospitals.It is costly and time-consuming procedure and causes in turn increased workload. The aim of this study is to compare the results of total and alternative sampling methods and to delineate the differences if there are any.
Method: Totally embedded 50 radical prostatectomy specimens were randomly selected and evaluated for key pathologic parameters. These cases then were reevaluated with limited sampling. The limited sampling method was built to include similarly embedded apical margins, bladder neck margins and seminal vesicles. In addition to that new slices were selected by skipping every other slice as differently from totally sampling protocol.
Results: The %37 reduction was achieved in number of blocks. The concordance rates between two sampling methods were %40, %50.4, %70.3, and %60 respectively for Gleason scores, perineural invasion, extraprostatic extension and pathologic stages.
Conclusion: Although the limited sampling protocol provides statistically significant results, because of critical role of pathological assessment in treatment of prostatic adenocarcinoma, they can be found unsatisfactory for many pathologists.

PS-22-043

Expression of nestin in Leydig cell tumors and hyperplasia

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Objective: Initially described in embryonic neuroepithelium, nestin is an intermediate filament involved in cell differentiation and transiently related to vimentin, keratin and glial fibrillary acidic protein (GFAP). In tumoral and vascular proliferation, nestin is recognized in stem/progenitor cells. The octamer-binding transcription factor 4 (OCT-4) is a biomarker of this lineage. Since there are few data concerning the presence of nestin in Leydig cells and testicular tumors, our aim was to investigate a series of Leydig cell hyperplasia and tumors.
Method: 31 cases (13 hyperplasia, 14 adenomas, 2 malignant Leydig cell tumors and 2 lymph node metastases) and controls were immunostained with anti-nestin, vimentin, keratin, GFAP and OCT-4 antibodies.
Results: Twenty-six (84 %) cases (tumors and hyperplasia) were nestin positive with mostly weak, finely granular cytoplasmic staining. Four (13 %) were negative, 1 (3 %) not interpretable. Vimentin was expressed in twenty-seven (87 %) cases. Seventeen (55 %) were focally keratin positive. Only three (10 %) showed OCT-4 positivity. All were GAFP negative.
Conclusion: In Leydig cell hyperplasia, adenomas and malignant tumors nestin and vimentin are expressed frequently, sometimes with keratin. This would be a sign of epithelial-mesenchymal transition. Further investigations are needed to understand the relationship with the malignant potential of these tumors.

PS-22-044

Morphological changes of testis in atherosclerosis

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Objective: Up to now in the field of morphology of reproductive system of men the problems of testis involution and morphogenesis at atherosclerosis haven't been thoroughly investigated.

Method: We have investigated histologically testis of 63 died patients aged 36–89 with general atherosclerosis and testis of 38 men aged 36–89 with minimal manifestations of atherosclerosis died in an accident.
Results: The absolute volume rete testis of patients being ill with atherosclerosis decreases by 65–80 %. Absolute volume of convoluted seminiferous tubules and interstitial tissue decrease by 24–27 %. In testis there are zones of focal sclerosis of seminiferous tubules, whose area goes as far as 12.7 % of shear section area. It was revealed that on the periphery of sclerosis zones there is a reduction of transaction area of seminiferous tubules by 20–33 % with Sertolli cells quantity reduction by 17–24 %. It has been stated the downward changes in index of spermatogenesis in convoluted seminiferous tubules by 63–65.6 %, accounted for the quantity reduction of all kinds of cells.
Conclusion: Morphological changes of testis at general atherosclerosis characterize atherosclerotic testiculopatie, caused by chronic ischemia of testis.

PS-22-046

A Leydig-cell tumor in a cryptorchid testis: Report of a case

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Objective: Leydig cell tumor is a rare form of testicular neoplasm, representing only 1–3 % of all testicular tumors. According to accepted medical knowledge, this type of tumor isn't linked to cryptorchidism, unlike germ cell tumors of the testicles. Herein, a case of Leydig cell tumor in a cryptorchid testis is described.
Method: A 59-year-old, unmarried man was admitted for surgical repair of inguinal hernia. His past medical history included untreated bilateral cryptorchidism first noted in childhood, as well as poliomyelitis that presented at age two. The past surgical history and review of systems were noncontributory. A CT scan of the abdomen and pelvis revealed two 3×3 cm testicles at the level of the inguinal canal. He underwent bilateral inguinal orchiectomy combined with surgical repair of his inguinal hernia.
Results: The right testis contained a solid, well-circumscribed, round, tan-colored tumor 1.5 cm in diameter. The histological appearance was that of a Leydig cell tumor exhibiting no mitotic figure. There was no clinical or radiological evidence of metastatic spread.
Conclusion: Although cryptorchidism is considered to be a risk factor for developing germ cell tumors, there have been a few reported cases of Leydig cell tumors with a history of cryptorchidism. Our case adds to the evidence that there may be a link between the two conditions.

PS-22-047

The role of CD44, E-cadherin, and ß-catenin in lesions of the prostate gland

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Objective: CD44, E-cadherin, β-catenin are "cell adhesion molecules" and appear to influence development, inflammation, cancer invasion and metastasis. We studied the expression of these CAMs in prostatic adenocarcinoma (PCa), high grade prostatic intraepithelial neoplasia (HGPIN) and nodular adenomatous hyperplasia (NH).
Method: 135 specimens of radical prostatectomies were assessed. These CAMs were determined by immunohistochemistry. All sections included PCa, HGPIN, and NH. The expression of these markers was evaluated with three scores. The correlation of immunopositivity with Gleason score and TNM stage was investigated.
Results: CD44 was strongly expressed in 41.5 %, 46.7 % and 37.8 % of NH, HGPIN and PCa, respectively. E-cadherin immunostaining was higly detected in 71.1 %, 78.5 % and 63.0 % of NH, HGPIN and PCa areas while β-catenin immunostaining was exclusively membranous in 80.7 % of NH and nuclear/cytoplasmic in 70.4 % and 48.9 % of HGPIN and PCa areas. All markers were unrelated to Gleason score (p=0.352). CD44 and E-cadherin immunopositivities were inversely associated with TNM stage (p=0.021 and p=0.042 respectively); such an association was not observed in β-catenin (p=0.556).
Conclusion: CD44 and E-cadherin decreased expression is probably associated with invasive potential of prostate cancer. β-catenin staining pattern in neoplastic lesions differs from that in non-neoplastic prostate lesions.

PS-22-048

Expression of E-cadherin in non-neoplastic mucosa, superficial and central portion of the tumor and the tumor invasive front and vimentin in tumor cells in the phenomenon of epithelial-mesenchyme transition in penile carcinoma

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Objective: To analyse the e-cadherin (ECAD) and vimentin expressions in the epithelial-mesenchymal transition (EMT), and their correlation with clinical prognostic factors of patients with penile carcinoma.
Method: 91 cases without neoplasia and 151 cases presenting penile carcinoma were applied to immunohistochemical analysis of ECAD at the non-neoplastic mucosa (NNM), Tumor Superficial and Central Portion (TSCP), Tumor

Invasion Front (TIF) and vimentin expression at the cytoplasmatic portion of tumor cells.
Results: The loss of ECAD expression was significantly higher at the TIF when comparing with TSCP and NNM. The loss of ECAD was correlated with histological grade, infiltrative pattern, lymph node metastasis, perineural and vascular invasion. The vimentin expression showed association with histological grade, infiltrative pattern, T stage, lymph node metastasis, perineural and vascular invasion.
Conclusion: The loss of ECAD and the gain of vimentin expressions occur more frequently at the tumor invasion front and are associated with classic factors of poor prognosis and low survival rates.

PS-22-050
Prognostic value of immunohistochemical markers in bladder cancer
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Objective: The tumor stage and grade of bladder tumors are the major elements to define the prognosis. However, it is sometimes difficult to identify an infiltration of chorion or detrusor muscle. Moreover, the evaluation of tumor grade is subjective and not reproducible.
Method: Our objective is to study the prognostic value of the expression of proliferating cell nuclear antigen (PCNA), Ki67 antigen, the tumor suppressor gene p53, the proto-oncogene c-erb B2, the receptor for Epidermal Growth Factor (EGF-R), the apoptosis suppressor gene bcl2, carcinoembryonic antigen (CEA) and Epithelial Membrane Antigen (EMA).
Results: The study showed that the PCNA expression was significantly associated with the early recurrence ($p=0.010$) and the tumor stage ($p=0.003$). The Mib1 expression was correlated to the early recurrence ($p=0.010$), and tumor progression in stage and/or grade ($p=0.007$). The c-erbB2 expression showed significant association with the tumor grade ($p=0.007$). The prognostic value of other markers has not been proven.
Conclusion: These findings may be useful providing better classification of bladder tumors thus the better management of patients. The c-erbB2 expression contributes to refine the tumor grading. PCNA and Mib1 can predict the early tumor recurrence; they could be relevant for the determination of endoscopic controls rhythms of patients.

PS-22-051
Primary urinary bladder neuroendocrine carcinoma: A report of five cases
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Objective: Primary urinary bladder neuroendocrine carcinoma (PUBNEC) is a rare tumor characterised by an aggressive behaviour and poor prognosis.
Method: We report five cases of PUBNEC diagnosed in the departement pathology of Farhat Hached Hospital between 1990 and 2011.
Results: Our population is composed by four mens and a woman. All patient are heavy smokers. The most common presenting symptom is hematuria and dysuria in all cases. One patient presented a complete urinary retention. A cystoscopic examination with transurethral resection was performed in all cases. The pathological examination with use of immunohistochemical markers of neuroendocrine differentiation were consistent with a large cell neuroendocrine carcinoma in four cases and a small cell neuroendocrine carcinoma in a case. A cystoprostatectomy was made in two cases followed by chemotherapy.
Conclusion: The clinical presentation of PUBNEC is similar to other bladder cancers and is characterized by advanced stage at diagnosis and rapidly progressive disease. The diagnosis of poses several problems: a vesical metastasis has to be excluded and such lesions have to be differentiated from transitional cell carcinoma, lymphoma, paraganglioma and peripheral nerve neuroblastoma. There is no gold standard for the management of patients affected due to low disease frequency

PS-22-052
IgG4-associated Inflammatory Pseudo-tumor (IPT) of the ureter: A case report
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Objective: IgG4-associated inflammatory pseudo-tumor (IPT) is a novel clinico-pathologic entity characterized by intensive infiltration of IgG4-positive plasma cells, associated with systemic IgG4-related sclerosing disease. Many reports described IgG4-related IPT in various locations such as pancreas, salivary glands, liver, breast, lung and recently also ureter.
Method: It is described a case of ureteral IPT with pathologic and immunohistochemical features of IgG4-related IPT, fibrohistiocytic type.
Results: The study case is a 82-year-old female with severe stenosis of the left ureter and hydronephrosis, who underwent to nephroureterectomy and endoscopic resection of multiple lesions in the bladder. The histological examination showed transmural fibrosing inflammatory lesion of the affected ureteral wall, with abundant plasma cells intermixed with many histiocytes, lymphocytes, fibroblasts and scattered eosinophils. The majority of infiltrating plasma cells were positive for IgG4. Bladder lesions showed similar histological

features. The diagnosis was IgG4-related IPT, fibrohistiocytic type.
Conclusion: IgG4-related IPT of ureter is extremely rare, with only few cases reported in literature. Recognition of this entity is clinically relevant because this type of IPT can be treated with steroid therapy and may be associated with sclerosing autoimmune disease in other organs.

PS-22-053
A rare case of malignant fibrous histiocytoma of the urinary bladder
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Objective: Malignant fibrous histiocytoma (MFH) is an extremely rare malignant mesenchymal neoplasm of the urinary bladder with only a few well-documented cases reported in the English literature.
Method: We report the case of an 88-year-old man who was brought to our hospital due to sudden massive haematuria. Catheterization failed to obtain haemostasis so, a suprapubic incision and direct exploration of the bladder was performed. A large solid tumor was found with a shaggy haemorrhagic surface and biopsies were taken.
Results: Histological examination revealed an infiltrating malignant neoplasm composed of variably pleomorphic ovoid neoplastic cells with eosinophilic cytoplasm, bizarre tumor giant cells and prominent stromal osteoclastic giant cell reaction. Immunohistochemical examination was negative for cytokeratin, desmin, smooth muscle actin, PSAP, NSE, S100protein and HMB45 whereas it was positive for CD68 in a large number of tumor cells. Accordingly, the diagnosis of undifferentiated pleomorphic sarcoma with histological features compatible with giant cell MFH of the urinary bladder was made. The patient died 4 days after the diagnosis.
Conclusion: In conclusion, MFH of the bladder should be kept in mind when facing with an undifferentiated malignant tumor. Despite the poor prognosis, early diagnosis and aggressive salvage therapy might offer the chance of long-term survival in selected cases.

PS-22-054
Partial nephrectomy experience at a single tertiary-care oncology centre: A clinicopathologic study of 60 cases
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Objective: Partial nephrectomy (PN) is replacing radical surgery as a gold standard in the treatment of small renal masses. Intra-operative frozen consultation for margin status is aimed at achieving a disease free state in order to reduce chances of recurrence.
Method: A retrospective clinicopathologic analysis of consecutive PNs performed at our institute from 2004 to 2011 was undertaken.
Results: Sixty cases of PN were analysed. Male to female ratio was 1.8:1. Median age was 51 years. Six cases were benign: oncocytomas (3), angiomyolipoma (3); while 54 cases were malignant: renal cell carcinoma (RCC) - conventional (43), papillary (8), chromophobe (1), mucinous tubular spindle cell carcinoma (1) and one case of primitive neuroectodermal tumour. In 4 patients, the renal tumour was a second malignancy. Median tumour size was 3.5 cm with 42 cases of stage pT1. Intra-operative margin was positive in 16 cases. Mean margin for all cases was 2.3 mm. Median follow-up was of 24 months. None of the tumours recurred or metastasized during follow-up.
Conclusion: Conventional RCC is the commonest histology in PN cases. Frozen section analysis has a definite role in achieving margin free status. PN is not associated with increased risk of local recurrence in small renal tumours.

PS-22-057
Clear cell tubulopapillary renal cell carcinoma: A clinicopathologic study of two cases
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Objective: Cleal cell tubulopapillary renal cell carcinoma has been recently identified as a low grade renal cell tumor with distinct histological features.
Method: Patient 1: 65 year old female with a history of fibromyalgia and persistent loin pain. A right renal mass, 2.8 cm in diameter, was discovered in the rheumatologist's follow up. Right nephrectomy was performed and the patient is free of disease 7 months later. Patient 2; 55 year-old female with a history of diabetes mellitus type 2, hypertension and renal failure grade 3 with a 2.5 cm in diameter renal tumor in the routine studies. She underwent tumorectomy.
Results: Grossly, both were cystic tumors with gelatinous fluid and white-yellowish solid areas. Tumors showed a tubular and papillary architecture. Proliferating cells displayed clear cell cytoplasm and hyperchromatic nuclei placed in the luminal side. IHC showed positive staining with e-cadherin, EMA and CK7. Conversely, CD10, CD117 and AMACR were negative.
Conclusion: Clear cell tubulopapillary renal cell carcinoma should be considered a distinct subtype of renal cell carcinoma according to its unique morphologic and inmunohistochemical features. The few cases reported so far behave in an indolent course.

PS-22-058

Tubulocystic renal cell carcinoma: Clinicopathologic study of two cases

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Objective: Tubulocystic carcinoma of the kidney (TCRCC) is a rare variant of renal tumor showing unique gross and microscopic features. Several recent studies favour its inclusion within the papillary renal cell carcinoma (PRCC) group.
Method: Patient 1 was a 55 year-old man with a left asymptomatic renal mass incidentally discovered by sonography. Patient 2 was a 72 year-old man with aortic estenosis and coronary disease. A right renal mass was discovered in the work up for aortic valve replacement and coronary bypass.
Results: Both tumors were well circumscribed masses with "sponge-like" appearance. On light microscopy, the tumors were composed of ectatic tubules and cysts of variable size, lined by a single layer of tumor cells with eoshinophilic cytoplasm, apocrine appearance, rounded nucleus sometimes overlapping, and prominent nucleoli. IHC showed positive staining with CK7, e-cadherin, CD10, and AMACR.
Conclusion: TCRCC has been recently recognized as a distinct subtype of PRCC by some authors. In fact, some few cases reported have histological transition between tubulocystic and papillary phenotypes on routine histological sections. Additionally, TCRCC shows trisomies of chromosomes 7 and 17. The exact location of this tumor within the 2004 WHO classification is a matter of debate.

PS-22-062

HER2 protein expression in urothelial carcinoma of the bladder

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Objective: Our purpose is to evaluate HER2 protein expression in urothelial carcinoma of the bladder. HER2/neu is a tyrosine kinase receptor (family of human epidermal receptors), showing overexpression in a large variety of tumor cells.
Method: 30 bladder biopsy and cystectomy specimens were included in this study. The age of the patients ranged from 25 to 86 (mean 71). Among them 25 (83.33 %) were male and 5 (16.67 %) female. All cases were reevaluated histopathologically according to WHO 2004 grading system. HER2 protein expression was detected by immunohistochemistry (CB11) using the same criteria as for breast cancer.
Results: All 30 bladder neoplasms were low- or high-grade urothelial carcinomas. HER2 protein overexpression was observed in 10 (33.33 %) cases (2+: 5 cases and 3+: 5 cases), while 20 (66.67 %) cases were negative (0: 3 cases and +1: 17 cases). Among HER2 positive cases 9 (90 %) were high-grade carcinomas, while 1 (10 %) was low-grade carcinoma. Among negative cases 14 (70 %) were low-grade carcinomas, while 6 (30 %) were high-grade carcinomas.
Conclusion: These findings indicate that HER2 protein overexpression is predominately correlated with high tumor grade in urothelial carcinoma of the bladder and patients with these characteristics could be potential candidates for targeted therapy.

PS-22-063

Mucinous adenocarcinoma of the renal pelvis: A case report and review of the literature

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Objective: Primary mucinous adenocarcinoma of the renal pelvis is extremely rare and about 50 cases have been reported to date. We present a case of mucinous adenocarcinoma followed by renal cysts.
Method: The patient is a 52-year-old male. A renal cyst in the right upper region was found incidentally. He had no symptom at that time. After 4 years, he came to the hospital because of hematuria and back pain. The examination revealed that the renal cyst was enlarged accompanied with solid lesion. The high serum level of CEA indicated malignancy and tumorectomy was performed.
Results: Macroscopically, a renal cyst (15×10 mm) in the right upper portion was adjacent to a solid mass (22×17 mm). The tumor showed papillary growth (20×15 mm) in renal pelvis. Microscopically, the tumor was consisted of adenocarcinoma with tubular or papillary structure, spreading from cyst wall to pelvis. The tumor cells contained mucin and some showed signet-ring cell-like feature.
Conclusion: Clinically, high serum level of CEA is a marker of mucinous adenocarcinoma originated from renal pelvis. In our case, the tumor has already from pelvis to cyst wall. We thought it originated form renal pelvis, however, the renal cyst is also a candidate for its origin.

PS-22-064

Survivin expression in renal epithelial tumors: Its usage in the differential diagnosis of eosinophilic renal epithelial tumors

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Objective: The differential diagnosis of renal tumors can be problematic due to overlapping morphologic features. The purpose of this study was to assess the potential contribution of survivin expression in the differential diagnosis and determination of therapy modalities of these tumors.
Method: This study consisted of 15 chromophobe (ChRCC), 15 clear cell (CCRCC) and 9 papillary (PRCC) renal cell carcinomas, and 13 oncocytomas. Sections were stained against survivin antibody.
Results: PRCCs and CCRCCs showed diffuse and strong survivin expression. Survivin expression was strikingly prominent in type1 PRCCs and cystic CCRCCs. In CCRCCs, survivin expression was more pronounced in low grade areas than high grade and sarcomatoid areas. In ChRCC, survivin expression was more limited and weaker than that of oncocytomas and other malignant renal tumors. In non-neoplastic renal tissue, survivin expression was more pronounced in podocytes and atrophic tubules than other nephron parts.
Conclusion: Our findings suggest that survivin may contribute to the differential diagnosis of renal tumors because of the partially unique staining patterns. It was purposed that knockdown of survivin reduced growth, induce apoptosis and enhance in vitro radiosensitivity of RCC cells. Taken together, to be known different survivin expression patterns in renal tumors may help to determine new therapeutic strategies for RCCs.

PS-22-065

Adenomatous hyperplasia of the rete testis: Not a true hyperplasia, just proliferation!

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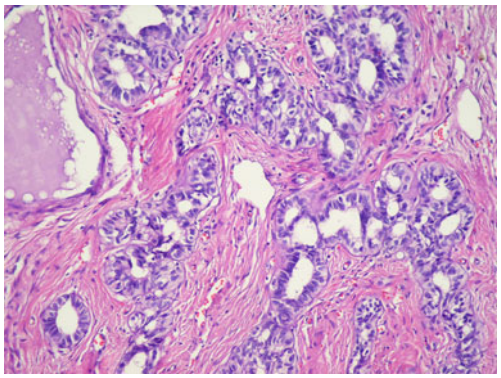
Objective: There are several tumor-like lesions and miscellaneous neoplasms of rete testis. We present a case with adenomatous hyperplasia of rete testis (AHRT).
Method: The patient was 24 years old with undescended testis and referred to our hospital. There was no clinical or endocrin abnormalities. Cryptoorchidism was unilateral and the other testis was normal. Right orciectomy was performed and sent to pathology labarotory for examination.
Results: There was no tumoral lesion in gross examination but in microscobic examination there was gland like tubular structures. Some of these were back to back position with little intervening stroma and mild to moderate atypia. EMA and pancytokeratin immunohistochemistry findings with morphology confirmed the diagnosis of AHRT in this case.
Conclusion: AHRT is a rare proliferatif lesion and can be confused with malignancy. It is incidentally realised in microscobic investigation. It may present as a very small lesion detected in microscobic examination or solid-cystic mass lesion which is macroscobically evident. Clinic history, localization, histologic features and immunohistochemistry are criterias for differentiating these lesions.We present this case for both surgeons and pathologists with its importance to be confused with malignancy.



PS-22-066

AMACR and iNOS expressions in prostate adenocarcinomas

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Objective: Prostate cancer is the second leading cause of death in men. The localized disease often responds to conventional therapies like androgen ablation via castration and/or administration of chemical inhibitors but advanced disease resistant to any curative therapies is still challenge for investigators. There are increasing efforts to enhance the possibility of finding positive and sensitive immune markers for diagnosing and treating prostate cancer.
Method: We applied immunohistochemical markers; AMACR and iNOS. Formalin-fixed parafin embedded tissues of 64 prostate needle biopsy specimens diagnosed as prostate adenocarcinoma between 2005 and 2010 years were enrolled in the study.
Results: AMACR expression has been found in 58 (90.6 %) and iNOS expression in 54 (84.4 %) of 64 prostate adenocarcinomas.No significant relationship of AMACR and iNOS has been obtained ($p>0.05$). There was no significant

correlation of histopathologic grade of the tumors with AMACR and iNOS expression ($p>0.05$).
Conclusion: The expression of AMACR and iNOS might be important diagnostic immune markers for prostate adenocarcinomas especially in needle biopsies when the quantity and quality of tissue are limited.

PS-22-067

A tissue microarray study of Napsin-A expression in renal tumors

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Objective: Napsin-A is an aspartic protease present lung, renal, and thyroid cells. There are few studies evaluating Napsin-A in renal neoplasms. Therefore, we studied IHC expression of Napsin-A in a wide spectrum of renal tumors.
Method: IHC for Napsin-A (rabbit polyclonal antibody) was performed in a series of 334 cases of primary and metastatic renal tumors on TMA. Cytoplasmic immunoreactivity was scored: intensity (0–3+) and extent (% of tumor cells: 0–3). The 2 scores were added: positive case: combined IHC score>2; negative if combined score of 2 or less.
Results: Napsin-A expression was observed in 79 cases (23,7 %). Diagnosis # Napsin-A positive (%) Conventional-RCC: 30/117 (20,4) Papillary-RCC (PRCC): 27/42 (64,3) Papillary adenoma (PA): 10/10 (100) Clear-cell-papillary-RCC (CCP-RCC): 2/2 (100) Mucinous tubular spindle-RCC (MTS-RCC): 3/4 (75) Chromophobe-RCC: 2/74 (2,7) Oncocytoma: 0/34 (0) Bellini-RCC: 0/4 (0) Translocation-RCC: 1/2 (50) Unclassified-RCC: 4/7 (57,1) Urothelial carcinoma: 0/8 (0)
Conclusion: Napsin-A has distinct expression in renal tumors originated from proximal or distal nephron. Napsin-A is frequently expressed in PA, PRCC, CCP-RCC, and MTS-RCC. Napsin-A could be useful in an IHC panel for the identification of PRCC.

PS-22-068

Utility of alpha-methylacyl-CoA racemase and P63 cocktail in the diagnosis of prostatic carcinoma

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Objective: The diagnosis of prostatic carcinoma can be challenging on needle core biopsies. The aim of this study was to assess the utility of alpha-methylacyl-CoA racemase (AMACR/P63) antibody cocktail for prostate cancer diagnosis. A prospective analysis of 50 consecutive radical prostatectomy specimens and 50 prostate needle biopsy semples was performed to select histological sections showing foci of minimal prostatic carcinoma, high grade prostatic intraepithelial neoplasia (HGPIN) and benign mimickers of prostatic carcinoma (atrophy, adenosis).
Method: Serial histological sections were stained with hematoxylin and eosin, Van Gieson and immunomarkers: AMACR and P63 using a prediluted antibody cocktail.
Results: The cocktail was very useful in highlighting prostatic carcinoma associated with HGPIN (flat or cribriform) and distorted foci of minimal carcinoma. AMACR was positive with moderate and strong staining in almost all cases for which the immunohistochemical result converted the atypical diagnosis to a final cancer diagnosis. The cases whose diagnosis was changed from "atypical" to cancer were all highly suspicious for cancer based on HE histology and negative basal cell markers.
Conclusion: This cocktail would be of diagnosis utility when limited tissue is available for histopathological evaluation of small diagnostically difficult foci (prostate needle biopsy and surgical specimens).

PS-22-069

Overexpression of Cytokeratin 20, Ki-67 and Topoisomerase-II-a can significantly stratify the recurrence risk in patients with bladder cancer after transurethral resection

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Objective: The current predictive models based on main clinical tumor features are not accurate for the biggest bladder cancer patient group, who underwent the transurethral resection (TUR).
Method: Overall 103 patients with primary urocarcinoma after TUR were included in this retrospective study. The follow up plan in all cases included cystoscopy and biopsy every 3 months in the first 2 years. The recurrence criteria were cystoscopical and pathological confirmation of the tumor growth. In all cases using TMA technique (TMA Master, 3DHistech) there was done the IHC expression study of p53, p63, CK20, E-cadherine, B-catenin, CD44v6, Ki-67 (10 % cut-off), Topo-II-a (10 % cut-off) and Her2, as well c-erb-B2 amplification study (CISH).
Results: There were no association found between the Her2 expression and c-erb-B2 amplification in urocarcinoma patients. In multivariate regression analysis only CK20, Ki-67 and Topo-II-a showed the significant prognostic power in recurrence prediction. These markers were used to develop the powerful predictive index for bladder cancer patients after TUR.
Conclusion: Although the Her2 overexpression is relatively common event in bladder cancer, c-erb-B2 gene amplification isn't main mechanism of its realization. The CK20, Ki-67 and Topo-II-a are promising prognostic markers for

recurrence and should be validated in further prospective study.

PS-22-070

Solitary fibrous tumor of the urinary bladder associated with a high-grade urothelial invasive carcinoma. A case report

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Objective: Solitary fibrous tumor (SFT) is an unusual spindle cell neoplasm, which can exceptionally occur in the urinary bladder.
Method: We present a case of urinary bladder SFT in a 60 year-old man who complained of pelvic pain. Cystoscopy revealed a large protruding, fleshy mass at the anterior wall of the bladder. A biopsy was first misclassified as inflammatory myofibroblastic tumor (IMT). Subsequent complete transurethral resection was performed.
Results: Macroscopically, a 9×7×5 cm greyish lobulated firm polypoid tumor was seen. Microscopically, it consisted of uniform spindle cells with elongated tapered ends nuclei forming a patternless growth in a collagenous background. Mitotic figures were rare. Immunohistochemically, the neoplastic cells were positive for CD34 and bcl-2, and negative for α-SMA, desmin, CK AE1/AE3 and Alk-1. The bladder urothelium showed foci of high-grade transitional carcinoma with lamina propria invasion.
Conclusion: Initially, SFTs were thought to be of mesothelial origin. Then, these tumors have also been observed in extrapleural and extraserosal sites, which suggests a mesenchymal cell origin. The differential diagnosis should always include other spindle cells lesions such as sarcomatoid carcinoma, leiomyosarcoma and IMT. To date, this is the first reported case of association of urinary bladder SFT and high-grade urothelial invasive carcinoma.

PS-22-072

Renal oncocytomas with unusual features: Clinicopathological study of 9 cases

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Objective: Oncocytoma (RO) is a benign renal neoplasm, with a wide morphologic spectrum and excellent prognosis. Recently, it has been described worrisome morphological features.
Method: RO treated in our centres were reviewed, and we focused on identifying the worrisome and the atypical features.
Results: We identified 9 RO with at least one of the worrisome feature. Patients: 5 M/4 F (mean age 72,89 year; range: 63–88). Mean tumor size: 4,24 cm (range: 1,6–11,5 cm); right kidney: 5, and left: 4 cases. Invasion into the perinephric or renal sinus fat was the most frequent worrisome feature: 7 tumors (77,8 %) and focal chromophobe carcinoma-like areas in 3 cases (33,3 %). Lymphovascular invasion, entrapped renal tubules-glomeruli, necrosis and mitosis were found in 2 (22,2 %) respectively. All but two ROs had at least 2 worrisome features. Follow-up was available for all cases (median 11 months; range 3–108): all patients were alive without recurrence or metastasis.
Conclusion: RO is a tumor which often can show worrisome and atypical morphology. It is necessary to know and recognize the worrisome features to prevent diagnostic errors, if otherwise typical oncocytoma morphology is present. Despite these atypical morphological data, the prognosis is excellent.

PS-22-073

Ki67 and p53 expression in urothelial carcinomas and clinicopathologic correlation

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Objective: The most important predictive parameter for the biological behaviour of urothelial carcinoma is histological grade, except for depth of invasion. The aim of this study was to investigate the expression of p53 oncoprotein and Ki67 antigen in a series of transitional cell bladder carcinoma with papillary morphology (pTa – papillary carcinoma and pT1) with histological grade and recurrence.
Method: This study included 59 cases diagnosed with urothelial carcinoma with papillary morphology (pTa, pT1). Immunohistochemical expression of Ki67 and p53 were examined in each case, and were graded accordingly to the percentage of cells stained, in low, moderate and high-expression groups.
Results: As described previously in other publications the expression of p53 and Ki67 has a relationship with histological grade. We also noted that of the 13 recurrences, 11 were associated with moderate to high expression of either p53 or Ki67, or both.
Conclusion: We concluded that p53 and Ki67 expression combined with histological grade and pathological stage may be helpful in assessing more accurately the biological behaviour of urothelial carcinoma. And the overexpression of p53 and Ki67 are related with an unfavourable prognosis.

PS-22-074

Prostatic glandular and stromal hyperplasia with stromal cell atypia: A follow-up study of 1 case

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Objective: Prostatic stromal hyperplasia with atypia is a rare lesion with fewer than 200 cases reported worldwide. It can be mistaken for sarcoma because of the presence of atypical, bizarre cells. Its malignant potential is uncertain. The follow up study of every case is important.
Method: A 71-year-old man with previously diagnosed atypical prostatic adenostromal hyperplasia with atypia of stromal cells was hospitalized with urinary obstruction after transurethral resection of prostate made 6 years ago. Repeat TURP was performed and tissue specimens were investigated and compared with the initial biopsy.
Results: The second biopsy showed the benign hyperplastic prostatic glands with atypical, bizarre, frequently multinucleated giant stromal cells between them. They displayed intense immunoreactivity for actin, vimentin and androgen receptors. The microscopical picture was identical to that seen in the first specimens. The nuclear abnormalities looked like in an atypical symplastic leiomyoma of myometrium. No evidence of sarcomatous or carcinomatous transformation, mitotic index evaluation was noted.
Conclusion: This case maintains the viewpoint that the prostatic adenostromal hyperplasia with stromal cell atypia is a benign lesion. But it can recur and requires the repeat TURP or radical surgery.

PS-22-075

Cancer risk in patients with precancerous lesions of the prostate

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Objective: Prostatic intraepitelial neoplasia (PIN) and atypical small acinar proliferation (ASAP) has a high predictive value as markers for prostate cancer (PCa).
Method: PCa-risk in patients with precancerous lesions has been assessed on biopsy material in 172 patients having morphological suspicious to PCa. Suspicious foci were estimated with use of cocktail AMACR + HWC + p63.
Results: According to our results revealing of precancerous lesions in biopsy specimens has been associated with PCa identification in re-biopsies (F=0,04). Within the first-5-years the overall incidence of PCa in re-biopsies made 27 % in the group of precancerous lesions and 36 % – in the ASAP group. Life-time-without-PCa median made up 5-years with no reliable difference between PIN and ASAP groups (WW=2,35; p=0,06). Thus, the cumulative share of patients without PCa in the ASAP group formed 86 %-82 %-82 %-73 %-60 % at the end of the first-second-third-fourth-fifth year of supervision respectively.
Conclusion: Within the first 5 years PCa risk makes 27 % in the general group of precancerous lesions of the prostate and 36 % in ASAP group with no difference between ASAP and PIN groups. Cumulative share of patients without PCa in re-biopsy specimens decreased from 86 % to 60 % during these 5 years.

PS-22-076

Benign prostatic hyperplasia and prostate carcinogenesis after the Chernobyl accident in Ukraine

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Objective: The prevalence as well as immunohistochemical (IHC) study of latent, incidentally found prostate cancer (LPC) as well as precancer lesions, in patients, who underwent surgery for BPH were studied.
Method: BPH samples were obtained by prostatectomy from 120 Ukrainian patients consisting of 30 patients from areas without radio-contamination (control group 1) and of 90 patients living in 137Cs contaminated areas of Ukraine (group 2). Ki-67, p53, p27Kip-1, p63 and Bcl-2 proteins were IHC investigated in BPH from all patients.
Results: The incidences of LPC (Gleason score 4), chronic prostatitis, PIA and PIN were 16.67, 53.34, 20, and 26.67 % in group 1; 12.23, 64.45, 43.45 and 36.67 % in group 2, respectively. Greatly elevated levels of p53, Ki-67, Bcl-2 associated with decreased levels of p27Kip-1and p63 in areas of PIA and less LPC and PIN in group 2 to compare with group 1 patients were obtained with statistically significant differences.
Conclusion: Our study suggests that chronic long-term low-dose radiation exposure might result in the increase of chronic inflammation and it is now found to be associated with increased incidences of PIA and PIN in BPH accompanied by p53, p27KIP-1 and Bcl-2 alteration which in turn could lead to prostate carcinogenesis.

PS-22-077

Eosinophilic globules in rete testis mimicking yolk sac tumor in a testicle with seminoma

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Objective: The recognition of a non-seminomatous component in an otherwise typical testicular seminoma changes the choice of adjuvant chemotherapy.

Method: A 37-year old male underwent orchiectomy for a testicular mass. Serum tumor markers levels (β-hCG/AFP/LDH) were normal.
Results: Macroscopical examination revealed a 2.1 cm white–yellow tumor. The tumor was composed of the characteristic for seminoma homogenous, clear cells arranged in nests and islands separated by septa and infiltrated by lymphocytes. Immunohistochemically the tumor cells were positive for PLAP, OCT3/4, CD117 and D2-40 and negative for CD30 and CK8.18. There was also a regular pattern of tubular structures infiltrated by the seminoma cells while retaining a low columnar type epithelium. The presence of sphaerical eosinophilic globules (PAS+/dPAS+/AFP−) within the tubular lumina was strongly reminiscent of the hyaline globules of yolk sac tumor. The tubular structures were positive for CK8.18 and negative for AFP, glypican-3 and OCT3/4.
Conclusion: The presence of tubular structures with sphaerical eosinophilic globules creates a suspicion for a yolk sac tumor component. The absence of AFP and glypican-3 expression, the regular pattern of the tubular structures and their continuity with rete testis excluded this suspicion. Hyaline eosinophilic globules in rete testis should not be confused with the globules produced by yolk sac tumors.

PS-22-078

Beta- catenin expression and CTNNB1 mutations in a series of Wilms tumours

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Objective: CTNNB1 mutations have been found in 15–30 % of Wilms tumour (WT) cases. Nuclear beta-catenin protein has been detected by immunohistochemistry in a higher proportion of WTs, thus suggesting alternative genetic pathways leading to beta-catenin activation in these neoplasms.
Method: Sixteen renal WTs and 7 secondary WT localizations were retrospectively investigated. The series included 17 paediatric patients, 10 females and 7 males, with a mean age of 4.5 years and a 34 year-old female patient. Immunohistochemical analysis of beta-catenin was performed and findings were reported for each neoplastic component (i.e. epithelium, stroma and blastema). Tumour DNA was extracted for direct sequencing analysis.
Results: The majority of WTs showed moderate to strong membranous staining for beta-catenin in the epithelial (76.5 %) and the blastemal (60 %) components. Nuclear beta-catenin expression was observed in combination with cytoplasmic staining in the mesenchyma and/or the blastema of two primary renal tumours. In these cases the deletion of codon 45 p.S45del and the missense substitution p.T41A were detected.
Conclusion: Preliminary results of this ongoing study highlight beta-catenin cytoplasmic and membranous expression in the tumour cells of primary and metastatic WTs, with few cases demonstrating nuclear expression. In our series, beta-catenin nuclear expression was invariably associated to CTNNB1 mutation.

PS-22-079

A preliminary study on O6-methylguanine-DNA methyltransferase and Type 2 transglutaminase expression profile of renal cell carcinomas

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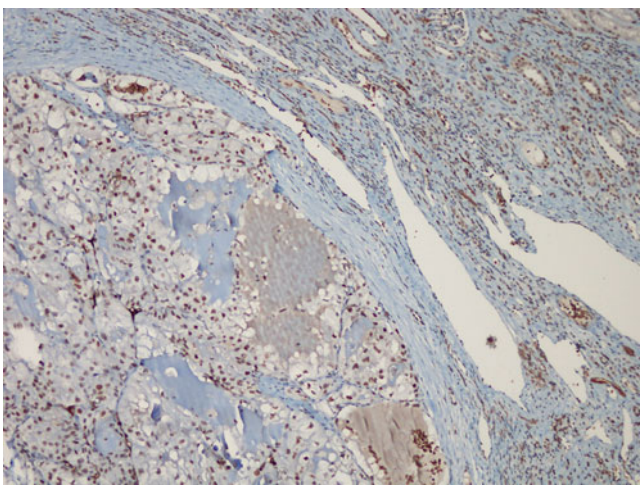
Objective: O6-methylguanine-DNA methyltransferase (MGMT) repairs O6-methylguanine in DNA, therefore provides a tumor supressor effect. Type 2 transglutaminase (TGase–2) is a multifunctional enzyme involved in many biological processes. Few data are available in the literature on their expression in kidney cancers. In this preliminary study, we evaluated immunohistochemical expression of MGMT and TGase–2 in renal carcinoma cases.
Method: Forty cases of renal carcinoma including ten clear cell, ten chromophobe cell, ten papillary and ten urothelial carcinoma were randomly selected. Thirty-one patients were male and average age was 61,5. Staining intensity and percentage of staining tumor cells were scored. Total score was categorized as weak, moderate and strong.
Results: Strong MGMT positivity was demonstrated in 15 cases (38 %). Eight cases (20 %) showed strong TGase-2 expression. Fifty percent of clear cell carcinomas strongly expressed MGMT and TGase–2. No correlation was found between MGMT and/or TGase–2 expression, tumor size and grade. Eighty percent of urothelial carcinomas strongly expressed MGMT.
Conclusion: The prognostic value of MGMT and TGase–2 as well as their potential role in treatment response have been investigated recently. MGMT and TGase–2 may be prognostic factors in renal carcinomas. Further investigation is required to verify our findings.



PS-22-080

Three dimensional topographic analysis of 904 cases of radical prostatectomy

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Objective: Prostate cancer is typically mutifocal, and there has been no report about the exact number of prostatic carcinomas in each case. We have performed topographic analysis using three dimensional mapping technique.
Method: We established data base including 904 cases of radical prostatectomy consisting of 2717 individual adenocarcinomas, and performed comprehensive pathologic analysis.
Results: 728 cases (80.53 %) out of 904 revealed multifocal carcinomas. The mean number of multifocal carcinoma was 3.05 and the maximal number was 11. 88.27 % of carcinomas were noted in both lobes. Among 904 cases, peripheral zone was involved in 95.80 %, transitional zone in 63.83 %, central zone in 22.35 %, and anterior fibromuscular stroma in 44.03 %. Representative Gleason score consisted of 6 (17.70 %), 7 (68.92 %), 8 (2.54 %) and 9 (10.84 %). Regarding individual carcinomas, Gleason score consisted of 6 (51.99 %), 7 (41.16 %), 8 (1.73 %) and 9 (3.94 %). The mean volume of individual carcinoma was 1.68 ml (range: 0.01–93.55). 904 cases consisted of pT2a (8.76 %), pT2b (0.11 %), pT2c (53.10 %), pT3a (26.50 %), pT3b (9.76 %) and pT4 (1.77 %). High grade PIN was present in 90.04 %, and perineural invasion in 76.11 %.
Conclusion: We report comprehensive pathologic features of Korean prostate cancers, including the number and size of individual carcinomas.

PS-22-081

ERG immunohistochemistry and clinicopathologic characteristics in Korean prostate adenocarcinoma patients

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Objective: TMPRSS2-ERG gene fusion is the most common genetic alternation in prostate cancer. It is associated with the expression of oncogene ERG protein. Recently, the immunohistochemical staining method that using anti-ERG antibody was verified strong correlation with ERG protein which is the product of genetic alteration. Aim of this study is to declare that the relationship between ERG expression and clinicopathological factor.
Method: otal 307 cases of radical prostatectomy specimen were assessed. All cases were constructed tissue microarray and immunohistochemical staining was performed.
Results: ERG-positive rate was 24.1 % (74/307) and significantly higher expression of ERG expression was observed in the subgroup that has lower Gleason score. ($p<0.05$) Analysis with the histologic pattern of prostate adenocarcinoma, tumors with discrete glandular unit (Gleason pattern 3) is shown higher frequency of ERG expression ($p=0.007$).
Conclusion: ERG-positive case was smaller than that of western population (about 50 %) and other factors including age, tumor volume, initial PSA level, pathological stage and margin status were not significantly related with ERG expression. In conclusion, positive rate of ERG immunohistochemical staining is meaningful higher in the tumors with well-formed gland that is represented by lower Gleason score.

PS-22-082

Solitary fibrous tumour of the kidney mimicking renal cystic neoplasm

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Objective: Solitary fibrous tumour (SFT) can develop at any anatomic site, but in the kidney is described rarely. In general, SFT forms an unencapsulated solid mass. We report a case of a 57-year old woman with benign SFT of the left kidney. The tumour showed extensive pseudocystic change and mimicked renal cystic neoplasm.
Method: A nephrectomy specimen showed cystic tumour beneath renal capsule and in peripelvic adipose tisssue. Histological sections were used for hematoxylin-eosin and for immunohistochemistry (antibodies against vimentin, smooth muscle actin, desmin, S-100 protein, CD117, CD99, bcl-2, CD34, CK18, AE1-AE3, EMA).
Results: Microscopically the tumour showed uniform spindle cell proliferation with expansive tumour margins, without necrosis or hemorrhagies. Mitotic activity was 1 per 10 high power fields. Cystic spaces without epithelial lining contained eosinophilic proteinaceous fluid. Imunohistochemically tumour showed difuse positivity for CD34, CD99, bcl-2, vimentin and stained negatively for S-100 protein, cytokeratins, EMA, smooth muscle actin, desmin and CD117.
Conclusion: SFT of the kidney is infrequent. Some renal SFT can undergo pseudocystic transformation and mimic renal cystic neoplasm both clinically and macroscopically.

PS-22-083

Epitheloid renal angiomyolipoma with atypia

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Objective: Renal angiomyolipomas are mesenchymal tumors that comprised of adipose tissue, smooth muscle like cells and

abnormal thick walled blood vessels admixed in various proportions. Epithelial renal angiomyolipomas are rare variants and may exhibit atypia. In the literature epithelioid renal angiomyolipomas with atypia are reported to have malignant potential.
Method: Left radical nephrectomy was performed due to renal mass with flank pain and hematuria.
Results: In gross examination; 6.5×3.5×3 cm gray white mass with occasionally necrotic areas at the middle portion of left kidney renal sinus and perinephritic fatty tissue, macroscopically. Microscopic eveluation reveals; tumoral lesion comprised of adipose tissue, smooth muscle and blood vessels, showing areas of epitheloid morphology and moderate to severe degree of nuclear atypia. In addition to histomorphology positivity HMB-45 immunohistocemistry elaborated to the diagnosis of "epitheloid renal angiomyolipoma with atypia".
Conclusion: This case has been presented due to its infrequent occurrence and malignancy potential.

PS-22-084
Correlation of minute focus of prostate adenocarcinoma on random multifocal needle biopsy with radical prostatectomy specimen
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Objective: This work attempts to determine the importance of small foci of prostatic cancer in random multifocal needle biopsy specimens.
Method: 64 patients with a microscopic focus confined to a single core specimen (which defined as tumor less than 1 mm with a Gleason score of 6 or less) were identified from a retrospective review of 1206 needle biopsies of the prostate. Twelve of these 64 subsequently under went radical retropubic prostatectomy at our centre. Clinically significant tumors were defined as those with volume greater than 0.5 cc.
Results: Average tumor volume was 0,9±0,6 cc (range 0,068–2,9 cc). In 41,66 % (5) of the cases was less 0,5 cc (range 0,068–0,458 cc, mean volume – 0,22±0,15 cc). There was 1 (8,4 %) of patient with extraprostatic extension.
Conclusion: Our data have shown high frequency of revealing insignificant tumours (mean 42±28 %; P=0,95). However, about 60 % of patients had clinically significant tumors warranting definitive therapy. The smallest focus of cancer on needle biopsy is not a guarantee of a clinically insignificant tumor.

PS-22-085
E-cadherin in mice: Expression in normal urothelium, pre-neoplastic and neoplastic urothelial lesions
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Objective: E-cadherin is an adhesion molecule that promotes the integrity and stability of the urothelium. A decrease in its expression is associated with more aggressive tumour phenotypes, with the ability to invade and metastasize. Our aim was to describe the expression of E-cadherin in normal urothelium and in urothelium with pre-neoplastic and neoplastic lesions of ICR male mice.
Method: Urothelial lesions were chemically induced by N-butyl-N-(4-hydroxybutyl) nitrosamine in ICR mice, and evaluated by immunohistochemistry in order to determine the staining pattern of E-cadherin.
Results: In normal urothelium, 87.5 % of E-cadherin expression was at the cellular membrane level. In simple hyperplasia, the same pattern was observed in 66.67 % of lesions. Nodular hyperplasia exhibited a mixed pattern (50 % membrane and 50 % cytoplasmic pattern). In 86.67 % of dysplasia, a cytoplasmic pattern was seen. On invasive carcinoma the majority of invasive urothelial cells exhibited a pattern of membrane and cytoplasmic staining. On squamous metaplasia it was observed a membrane pattern on basal and intermediate layers, and a loss of immunoreactivity in the most superficial ones.
Conclusion: E-cadherin is a valuable tool for investigating the cellular adhesion status of the urothelium in mice. Neoplastic lesions exhibited an abnormal, heterogeneous staining pattern.

PS-22-088
New potential prognostic and predictive factors in conventional clear cell renal carcinoma
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Objective: Biological behavior of conventional clear cell renal carcinoma (CCRC) is associated with tumour stage and grade. Cancer progression with metastasis is part of a process epithelial-mesenchymal transition (EMT) and is joined with invasiveness due to adhesion and cytoskeleton change. The central role of the EMT mechanism is attributed to Snail factor. The intermediate filament expression is changed through the progression of many types of neoplasms. These changes are organ or tissue specific and depend also on the degree of malignant transformation (genome instability acceleration). The expression changes of cytokeratin 18 (CK18) are signs of aggressive biological behaviour in some tumour types - e.g. colorectal and breast carcinoma (downregulation of expression) or CCRC (upregulation of expression). The expression of Snail and CK18 molecules and mRNA CK18 levels correlate to stage and grade of CCRC (according Messai et al. 2010). Objective: Study was based on the expression of

immunohistochemical markers (CK18, CK7, vimentin, Snail, CD10) in 15 cases with evaluation of the primary tumour and its metastasis.
Results: The difference and similarity of intensity and percentage of positive neoplastic population between the primary and the secondary carcinoma will be presented.
Conclusion: Snail and CK18 seem to be potential tumour progression factors and may be included in so called personalised medicine.

PS-22-089
Sarcomatoid carcinoma of the prostate: A case report
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Objective: Sarcomatoid carcinoma (SC) of the prostate is a rare variant of prostatic cancer representing less than 1 % of prostate tumors. Tumors are most commonly composed of an admixture of both malignant glandular and spindle cell elements. The sarcomatoid component can vary from 5 % to 99 %.
Method: We report the case of a 63-years-old patient with an invasive tumor of the prostate for which he had a radical prostatectomy. Histopathological examination showed that the tumor was responding to an undifferentiated proliferation made of beaches and clusters of pleomorphic cells usually spindle-shaped, with eosinophilic cytoplasm, and elongated or oval nuclei, which are very irregular, sometimes monstrous, multinucleated, basophils with numerous mitotic figures. In some places, there were areas of glandular differentiation and foci of comedocarcinoma. Immunohistochemical study showed immunoreactivity of spindle and pleomorphic cells with cytokeratin and vimentin.
Results: The diagnosis of sarcomatoid carcinoma of the prostate-grade Gleason 5+5 was confirmed.
Conclusion: SC of the prostate is an exceedingly rare tumor. Retrospective analyses render prostate SC as one of the most aggressive prostate malignancies. The prognosis is dismal regardless of other histologic or clinical findings.

PS-22-091
Primary leiomyosarcoma of the kidney: Three cases
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Objective: Renal sarcomas constitute only %1–2 of malignant renal tumors in adulthood. Leiomyosarcoma is the most common histologic type of renal sarcoma (%50–60).
Method: We present three renal leiomyosarcomas. The tumors diameters were variable between 5 and 9,5 cm. The age range of the patients was 36–81 years. All of them were female.
Results: In the macroscopic examination, the tumors were seen originating from renal capsule, a well-circumscribed, gray-white, swirl cut surface. Renal pelvic and ureteral dilatation was seen in the first case because of the mass effect. Microscopically the alternating spindle tumor cells were detected which were positive with actin, desmin, caldesmon and negative with S100, Pan- CK, CD34 and CD 117.
Conclusion: Sarcoma of the kidney are extremely rare and of varied cell types. These neoplasms exhibit an aggressive biological behavior and an unfavorable prognosis and are, thus, more lethal than sarcomas of any other genitourinary sites. In the literature renal leiomyosarcomas have been reported frequently in female patients as seen as our cases. The renal leiomyosarcomas and other sarcomas should be kept in mind among the reasons of hydroureteronephrosis.

Wednesday, 12 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-23 Poster Session Gynaecological Pathology

PS-23-001
Histopathological features and prognostic factors in uterine leiomyosarcoma (U-LMS): Results from two Portuguese tertiary centers
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Objective: Although rare, U-LMS is the most frequent malignant gynaecological mesenchymal tumor, usually disclosing unfavorable prognosis. U-LMS diagnosis may be controversial. In this study we evaluated clinical-pathological features/prognostic factors of U-LMS.
Method: All consecutive U-LMS diagnosed (1987–2012) at CHSJ and IPO-Porto and with available material were re-evaluated. The clinical files were reviewed, including demographic, clinical, imaging, surgical, staging, and follow-up parameters. The pathology features, including immunohistochemistry evaluation, were re-evaluated and the tumors staged according to most recent consensus criteria.
Results: The mean age at diagnosis of the 38 cases was 57 years (39–83); 68 % were multiparous and 60 % postmenopausal women. The majority (82 %) had symptoms at diagnosis, mostly abnormal bleeding. Histological classification displayed: 63 % spindle, 13 % epithelioid, 3 % myxoid, 10.5 % pleomorphic, and 10.5 % mixed U-LMS. Treatment included surgery (97 %), radiotherapy (67 %), and chemotherapy (63 %). Overall median survival was 49 months (CI 95 % 8.3–89.6), and 48 % 5-year survival rate. In univariate analysis only epithelioid subtype and

extra-uterine extension (FIGO stage II- IV) were significant parameters of poor prognosis. No multivariate analyses were performed due series limitation.
Conclusion: Detailed pathology evaluation, including histological subtype, and FIGO stage are essential in the adequate management decision/prognosis evaluation of U-LMS.

PS-23-002
Two cases of endometrial cancer with unusual presentation
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Objective: Over 90 % of women with endometrial cancer show signs of uterine bleeding, so most cases are diagnosed at an initial stage. This study covers two patients who presented the first signs of this disease in an exceptional manner.
Method: Case-1 A 71-year-old woman was afflicted with a six-month toxic syndrome. An omentum tumor was identified in the x-ray. Eleven days after the excision, she demonstrated oliguria, dysuria, and scant uterine bleeding. The pelvic ultrasound revealed a uterine mass. Case-2 A 56-year-old woman demonstrated disabling right inguinal pain. After an x-ray examination of her pelvis, a metastasis was suspected. A biopsy confirmed it. The immunochemistry pointed to a gynecologic, pancreatic or intestinal tumor. The computer tomography scan revealed a uterine mass.
Results: The first case only suggested an estromal gastrointestinal tumor or a mesothelioma, misdiagnosing and missing the endometrial carcinoma. The second case was uncommon as bone metastasis is found with solid tumors but seldom occurs with endometrial cancer and even less so as a first sign.
Conclusion: We must consider endometrial cancer at signs of uterine bleeding, however, further investigation is required in order to consider the 10 % who do not show the common signs.

PS-23-003
Extrapelvic endometriosis presenting as a retroperitoneal tumor
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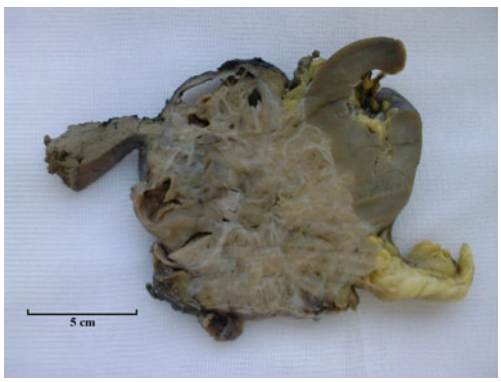
Objective: Endometriosis is a benign disease characterized by the presence of functional endometrial tissue in ectopic locations. Retroperitoneal, liver or kidney involvement are extremely rare.
Method: We present a case of a 52-year-old woman, which was referred to surgical consultation because of a retroperitoneal mass that was found on a routine abdominal ultrasonography (US). A subsequent CT scan showed a 12 cm tumor involving the liver, right kidney and adrenal gland. The gynecological US revealed ovaries with normal size and two probable uterine leiomyomas. She was submitted to a tumorectomy with segmental hepatectomy and nephrectomy.
Results: Grossly, the tumor was 12×8×6 cm, invaded the kidney, the liver and a segment of diaphragm. It was white, fasciculate and with hemorrhagic focus. Histologically the tumor was composed of a biphasic proliferation of endometrial glands and endometrial stroma, both without atypia. The case was diagnosed as deep infiltrating extrapelvic endometriosis. With a 5 years follow-up, the patient is doing well and without evidence of disease.
Conclusion: Despite being an extremely rare presentation, endometriosis can involve retroperitoneal organs and simulate a malignant neoplasm, even without a previous history of pelvic involvement.



PS-23-004
Primary melanoma of the female genital tract: A report of 10 cases and review of the literature
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Objective: Malignant melanoma of the female genital tract is a multifocal disease resulting from a disorder of melanocytes

within the mucosa. We report a retrospective clinicopathological analysis of 10 malignant melanomas of the female genital tract.

Method: A total of 10 patients with malignant melanomas arising in the female genital tract have been treated in our institutions in a 20 year period. Clinical data and follow-up were retrieved from the medical histories and histological slides were reviewed.

Results: The series included 6 vulvar and 4 vaginal melanomas. Average age of patients was 69. Four patients had more than one focus of melanoma. Nodular melanomas were detected in two patients. Melanoma in situ was found in an otherwise normal mucosa in two patients and vaginal melanosis in another two of them. All patients were treated by radical local excisions with or without lymph node dissection. Two patients with local recurrences within the genital tract required new surgical excisions. On follow up, 5 patients died of disease, 3 of them with metastatic disease.

Conclusion: Primary malignant melanomas are exceedingly rare in the female genital tract (2–3 %). It is suggested that melanoma of the genital tract is the result of a multifocal disorder of the melanocytes within the mucosa. The increased local recurrence rate reflects an inherent abnormality of melanocytes.

PS-23-006

Distant metastasis (DM) in uterine leiomyosarcoma (U-LMS): Study of a series and review of the literature

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Objective: U-LMS is the most frequent malignant gynaecological mesenchymal tumor, disclosing DM; several case reports describe DM, but so far the metastatic patterns remains to be clarified. We aim to evaluate sites and timing to U-LMS metastasis in our series and reported cases.

Method: Consecutive CHSJ&IPO-Porto U-LMS (1987–2012) of patients with DM. Review of the literature (1995–2012) using PUBMED and query: uterine and leiomyosarcoma and (metastases OR metastasis).

Results: Our series: 35 (39.8 %) with metastasis; literature: 65 with metastasis. Global mean age at diagnosis: 52 years (28–74); Initial treatment: hysterectomy (96 %), radiotherapy (28 %), and chemotherapy (40 %). Metastatic site: lung (59 %), intracranial (22 %), skin/soft tissues (13 %), bone (10 %), liver (6 %), others including thyroid, pancreas, vulva/vagina, salivary gland, oral cavity, heart, mediastinum, adrenal, and breast; 38 % with metastatic related symptoms. Overall median time to first metastasis: 21 months (CI 95 % 15.5–26.5). Pancreas, heart and mediastinum were the earlier metastatic sites. Metastatic treatment: metastasectomy (55 %), radiotherapy (24 %), and chemotherapy (37 %). Overall median survival: 13 months (CI 95 % 8.5–17.4), and 8 % 5-year survival.

Conclusion: U-LMS disclose wide range DM sites and time to first metastasis, which highlights the need of long-term follow-up, high level of suspicion, and histological confirmation.

PS-23-008

Microglandular adenocarcinoma of the endometrium: Immunohistochemical characteristics and prevalence of human papillomavirus infection

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Objective: Microglandular adenocarcinoma (MGA) of the endometrium, a rare subtype of endometrial mucinous adenocarcinoma, has histologic similarities to the microglandular hyperplasia (MGH) of the cervix. It should not be misdiagnosed as cervical MGH especially in a small endometrial biopsy specimen.

Method: Eight cases of MGA of the endometrium and 5 cases of control MGH of the cervix were immunostained for Ki-67, CD34, p16, p53, p63, vimentin, estrogen receptor (ER), progesterone receptor (PR) and PTEN. HPV DNA analysis was performed using paraffin-embedded MGA tissue by polymerase chain reaction amplification.

Results: P16 was positive in 7 of 8 MGAs and negative in all MGHs. PTEN loss was observed in 4 MGAs, but not in MGHs. ER and PR were positive and p53 was negative in all MGAs and MGHs. Ki-67, p63, and vimentin did not show remarkable differences. There were no signals for HPV DNA in MGAs.

Conclusion: Immunohistochemical staining for p16 and PTEN can be useful in distinguishing endometrial MGA from cervical MGH. Similar to other subtypes of endometrial carcinoma, MGA of the endometrium is related to p16 positivity and PTEN loss and is not associated with HPV infection.

PS-23-009

Cotyledonoid dissecting leiomyoma

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Cotyledonoid dissecting leiomyoma is a benign smooth muscle tumor which can mimic a malignant lesion due to its alarming aspect. There are some variant forms of leiomyomas with an unusual infiltrative growth pattern. Due to its worrying appearance of the gross specimen, it is often mistaken for malignant lesion and it is important to be aware of this entity not to over treat this benign smooth-muscle neoplasm. We report a case of a 55 years old woman who underwent hysterectomy because of the suspect of a tumor growing from the right lateral uterine wall. On gross study the tumor measured 10 mm in diameter and was nodular, brown in color and irregular on cut section. Histological examination showed a nodular tumor composed of smooth muscle cells with a storiform pattern which dissects the uterine wall. The tumor was highly vascularized, included a myxoid component and showed some areas with invasion of vascular components. Cellular atypia, mitosis and necrosis were absent. The patient has had a good clinical course, without relapses until the date, what supports the fact that these tumors have a benign clinical behavior, even though they may have a malignant appearance.

PS-23-010

Uterine leiomyoma with lymphoid infiltration

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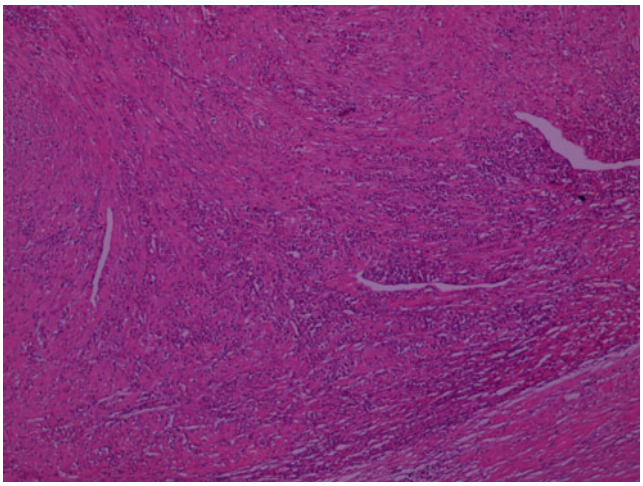
Objective: Although leimyomas of the uterus are common, lymphoid infiltration of leimyomas is a rare occurrence. We presented a case of a 45-year-old woman whose leiomyoma was diffusely infiltrated by lymphocytes. Lymphoid infiltration was analyzed with immunohistochemical methods and infiltration was found to be polyclonal type.

Method: A 45-year-old woman with abnormal uterine bleeding was prediagnosed uterine leiomyoma and she was applied total abdominal hysterectomy and bilateral salphingo-oopherectomy. The analysis of the sample sent to pathology lab showed two leiomyomas. Hematoxylin eosin –stained slides were prepared after sampling. ımmunohistochemical stains were applied.

Results: Microscopic examination of leiomyoma in greater diameter revealed a lesion with well-circumscribed borders composed of interlacing fascicles of bland monomorphic spindle cells diffusely infiltrated by lymphoid cells. The infiltrate not extended into the surrounding myometrium. Immunohistochemical analysis showed positive staining with CD 20, CD3, CD68. It was seen that inflammatory infiltration was polyclonal and involved T cells, B cells and histiocytes. Leiomyoma with lymphoid infiltration was diagnosed. The postoperative course was uneventful within a 6 month follow up period.

Conclusion: Leiomyoma with lymphoid infiltration first described in 1989 by Ferry et all. From that date on, the literature involves few cases. Because it is rare and differential diagnose with malignant lymphoma is crucial, we presented the case and reviewed the literature.



PS-23-011

Differentiated vulvar intraepithelial neoplasia: Relationship with malignant and benign vulvar lesions and immunohistochemical features

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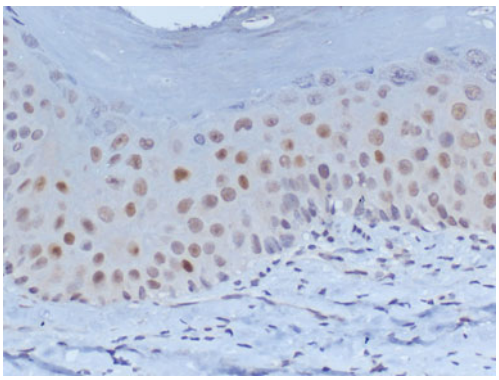
Objective: Vulvar intraepithelial neoplasia is divided into two groups: usual type and differentiated type. The differentiated vulvar intraepithelial neoplasia, which is frequently seen with invasive squamous cell carcinoma, can be confused with some benign lesions. The aim of this study is to analyse p16, p53, and Ki-67 expression characteristics of different histological types of vulvar intraepithelial neoplasia, invasive squamous cell carcinoma, and benign lesions of the vulva.

Method: In this study, immunohistochemical analysis of 18 vulvectomy cases with p16, p53, and Ki-67 was performed.

Results: Of 18 patients who underwent vulvectomy, nine had invasive squamous cell carcinoma and nine had vulvar intraepithelial neoplasia. Four additional vulvar intraepithelial neoplasia lesions were found accompanying the invasive squamous cell carcinomas. Nine benign lesions were found accompanying the invasive squamous cell carcinomas and

vulvar intraepithelial neoplasia. Mean Ki-67 proliferation index was 32.3 % in the usual type of vulvar intraepithelial neoplasia cases and 26.4 % in the differentiated vulvar intraepithelial neoplasia cases. No p53 expression was present in benign lesions.
Conclusion: Ki-67 PI does not recognize the usual type or differentiated type of vulvar intraepithelial neoplasia. p53 positivity can be of value in distinguishing differentiated type vulvar intraepithelial neoplasia from benign lesions.



PS-23-012
An audit of surgical pathology reports of endometrial carcinoma: Experience from a referral centre in India
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Objective: The aim was to see, compliance to minimum data information in carcinoma endometrium reports, in a team of 13 pathologists; and also to analyze these parameters e.g. tumor size, type, grade, depth of myometrial invasion, lymph node yield, pTNM stage etc.
Method: During the period of 2008–2010, from the files of Pathology department of our hospital, reports of operated 114 carcinoma endometrium cases were retrieved and analyzed for various, above mentioned, parameters.
Results: The median age was 58.04 years and median tumor size was 4 cm. Endometrioid adenocarcinoma was the commonest type (82.5 %); followed by MMMT (6.1 %) and Serous carcinoma (3.5 %). Grade 2 was the commonest tumor grade (42.1 %). Less than half of myometrial invasion was seen in 50 % of the cases, =/> half myometrial invasion was seen in 46.5 % of cases. (Information- not available in 4 cases). Parametrial involvement was seen in 5.3 % cases. The pTNM stage was not mentioned in 71.9 % reports. The median lymph node yield was 15.
Conclusion: The compliance to adhere to minimum data information in carcinoma endometrium reports is generally good. Lymph node yield is reasonable. Parametrial involvement and mentioning of pTNM staging is to be done more meticulously. Use of proformas/checklists is recommended.

PS-23-013
Extraovarian granulosa cell tumor: A case report
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Objective: Extraovarian granulosa cell tumor is a very rare neoplasm. We report a case of a tumor located in mesocolon.
Method: A 58-years-old woman presented with abdominal pain and fever. Abdomen CT showed a mesocolic mass adherent to the left kidney and the spleen. She underwent resection of a 22 cm long segment of the left colon with a circumscribed mesocolic tumor measuring 7×10 cm. The tumor was infiltrating the subserosa of the large intestine. Intraoperatively normal ovaries have been identified.
Results: Histologically the tumor is composed by monomorphous cells in solid nests developing cavities which contain serous or hemmorhagic fluid. The tumor cells have scanty cytoplasm and often grooved nuclei. Mitoses are very rare. The tumor cells were immunoreactive for vimentin, inhibin and progesterone receptors. The postoperative course was uncomplicated and the patient is free of disease 18 months later.
Conclusion: Light microscopic and immunohistochemical features of the tumor are similar to those of ovarian granulosa cell tumors (GCT). Since the tumor was resected in toto and the mitotic activity of the cells is very low, we expect a favorable prognosis. Extraovarian GCT are very rare and only 7 cases have been published during the last 50 years. Probably these tumors arise from residual tissue of the genital ridge (so-called secondary mullerian system).

PS-23-014
Detection of amplification of TERC and TERT genes in cytology samples from cervical neoplasias by fluorescent in situ hybridization
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Objective: Increased telomerase activity represents an early event in cervical carcinogenesis allowing cell immortality by recovering chromosomal telomeres. Thus, detection of TERC and TERT gene amplification might represent a diagnostic and valuable prognostic biomarker of cervical neoplasias.
Method: Cervical smears from 13 patients classified according to Bethesda as NILM (n=3), ASC-US (n=2), L-

SIL (n=2), H-SIL (n=4) and SCC (n=2) were analysed for TERC (3q26) and TERT (5p15) gene amplification by fluorescent in situ hybridization (FISH) in 100 cells per slide using a four-color FISH probe (FHACT™).
Results: The numbers of TERC and TERT copies, average ratio of gene copies and average number of cells with ≥4 TERC gene copies were highest in SCC, followed by H-SIL, L-SIL, ASC-US and NILM cases. Correlation between TERC/TERT amplification intensity and oncocytological findings was statistically significant (p<0.0001).
Conclusion: FISH analysis of TERC and TERT genes could be effective tool for the diagnosis of cervical neoplastic lesions. Using together with cytology and HPV DNA testing it can achieve higher sensitivity and specificity to discriminate H-SIL and invasive carcinomas from L-SIL lesions. Supported by projects CEPVII (IMTS:26220120036) and Molecular Diagnosis of Cervical Cancer (IMTS:26220220113) co-financed by EU sources and grant UK303/2011.

PS-23-016

Ovarian stromal hyperplasia and endometrioid endometrial carcinoma in an obese and premenopausal woman

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Objective: Ovarian stromal hyperplasia (OSH) is characterised by non-neoplastic overgrowth of the ovarian cortical. Mild hyperplasia of the cortical and medullary stroma is found in the ovaries of about one-third of perimenopausal and postmenopausal women. It is nearly always diffusely bilateral. We report a case of OSH associated with endometrial carcinoma (EC).
Method: A 40-years-old caucasian woman, obese, smoker, with fatty liver, Gilbert´s syndrome and cholelithiasis. She had endometrial curettage biopsy for dysfunctional uterine bleeding for 5 month, which was diagnosed of complex atypical endometrial hiperplasia. A total abdominal hysterectomy whith bilateral salpingo-oophorectomy were performed.
Results: The diagnosis was Well differentiated endometrioid EC and bilateral OSH with focal stromal hypertecosis.
Conclusion: OSH of moderate to severe degree may be found in women with disorders associated with androgenic and estrogenic manifestations including EC, obesity, hypertension, and glucose intolerance, but these findings are less frequent and less obtrusive than in stromal hyperthecosis. Obese woman are at risk for developing endometrioid EC as a result of the increased capacity in adipose tissue to convert androstenedione to oestrone, and testosterone to oestradiol. A relationship in the origin of hormone-dependent endometrial pathology may exist between OSH, blood androgen levels and EC.

PS-23-017

Detection of micrometastases in para-aortic lymph nodes in patients with carcinoma of the uterine cervix after negative frozen section analysis

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Objective: Previous studies considered the presence of micrometastases (MM) in pelvic lymph nodes as clinically relevant prognostic indicator.
Method: Frozen section analysis was performed in all cases. After FS-examination nodes were examined by one H&E-stained slide. All nodes without metastatic disease after frozen section and permanent section examination were subject of the present study. 43 patients and 418 PAN were enrolled and immunohistochemical staining using two cytokeratin-cocktail antibodies (AE 1/AE 3 and KL-) was performed.
Results: In one case, one single node showed micrometastasis, representing an incidence of 2.3 % of the studied cases and 0.23 % of the examined lymph nodes. In three cases benign endosalpingiosis was seen. The patient with MM is alive without evidence of disease 96 months after surgery. ITC were not observed.
Conclusion: The frequency of MM in PAN is very low. There are only limited data regarding their prognostic impact within the literature. After careful examination of all removed PAN using H&E-staining (and step sectioning), immunohistochmeical ultrastaging cannot be recommend for routine use.

PS-23-018

Serous tubal in situ carcinoma (STIC) in tubal and primary peritoneal carcinomas

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Objective: Serous tubal in situ carcinoma (STIC) has been defined as one important precursor of pelvic serous cancer. Morphologically, STIC is defined by are cytologic atypia, high proliferative index and strong staining for p53.
Method: The present study evaluates the presence of STIC and p53-signature in consecutive cases of 12 prophylactic salpingo-oophorectomy in women with BRCA-1-mutaion (BSO), 11 macroscopically inconspicuous tubes of patients with primary tubal cancer (TC) and 9 cases of primary peritoneal cancer (PPC) using immunohistochemistry against Ki-67 and p53 (clone DO-7).
Results: The frequency of p53-signature and STIC was 8 % and 0 % in cases of prophylactic surgery, 9 % and 18 % in TC and 0 % and 33 % in PPC.

Conclusion: STIC and p53-signature as precursor lesions of pelvic serous cancer is seen in macroscopically inconspicuous Fallopian tubes in unilateral TC in patients with elective BSO and patients affected by PPC. We propose that the sectioning and extensively examining the fimbria protocol be applied to all cases with PPC, TC and in women with prophylactic BSO.

PS-23-021

Primary intestinal-type adenocarcinoma of the vulva

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Objective: Primary adenocarcinoma of the vulva is rare, and enteric differentiation is excepcional. Only a few cases of neoplasms of pure intestinal-type in the low genital tract have been reported. They are considered to arise from cloacal remants or from intestinal heterotopia.
Method: We present the case of a 54 year-old woman, with a histerectomy performed 10 years before. On clinical examination a polipoid lesion in the vulvar vestibule was noticed. Biopsy revealed a tubular adenoma of intestinal type with a focus of adenocarcinoma. The first histologic interpretation was a metastatic intestinal tumor. Clinical examination, recto-colonoscopy and magnetic resonance imaging of the abdomen excluded this possibility.
Results: The immunohistochemical study showed reactivity with citokeratin 20 but didn't with citokeratin 7. All this led to conclude that it was a primary intestinal-type adenocarcinoma of the vulva arisen from an adenoma.
Conclusion: On our knowledge there are less than 100 reported cases of intestinal adenoma in the genital tract. They have been described also in the vagina and cervix but only a few developed an adenocarcinoma. It is important to be aware of this tumor type and to distinguish it from metastatic colorectal adenocarcinoma in order to plan appropriate treatment.

PS-23-023

Ligneous cervicovaginitis and endometritis: Case report

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Objective: Ligneous (wood-like) disease is a rare chronic pseudomembraneous inflammation of the mucous membranes which may also affect genital tract. The underlying pathogenesis is still unclear and an effective method of treatment has not yet emerged.
Method: Here we present a 32 years old female patient presented to our clinic with 7 years of unexplained infertility. Her diagnostic infertility work-up revealed no abnormality. However, at gynecologic examination there was a thick and hard granulation tissue at the cervix extending to the posterior vaginal wall. Transvaginal ultrasound was unremarkable except for increased endometrial thickness.
Results: Cervicovaginal and endometrial biopsy with diagnostic hysteroscopy was performed which demonstrated ligneous inflammation of both cervix and vagina. Endometrial biopsy was reported as chronic non-specific endometritis with dense fibrin deposition.
Conclusion:. The disease may also affect other organs including oral cavity and eyes. This unusual condition is difficult to treat and lack of awareness makes the diagnosis also problematic.

PS-23-024

Benign (LM) and borderline uterine smooth muscle tumors (STUMP) harboring necrosis

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Objective: Differential diagnosis LM vs STUMP may be controversial, especially regarding necrosis evaluation; few studies address the relation between different treatments and their morphological effects. We aim to characterize a series LMs and putative STUMPs harboring necrosis.
Method: Consecutive putative STUMPs (1995–2012) and a series of LMs with necrosis diagnosed at CHSJ & IPOP-Porto. Clinical files, particularly previous hormonal treatment (HT), gross specimen and histology features.
Results: 18 putative STUMPs and 35 LMs with necrosis. LMs mean age at diagnosis: 43 years; mean size: 9.0 cm (2.3–18); 45 % with other LMs; treatment: myomectomy (49 %) and hysterectomy (51 %); 23 % peri-partum, 8.5 % post-uterine artery embolization; 17 (49 %) previous HT: progestin (17 %), oral contraceptive-OC (20 %), hormonal-IUD (8.6 %), and medical assisted reproduction (8.6 %). STUMPs mean age at diagnosis: 45 years; mean size: 10 cm (2.0–20); 44 % with other LMs; low mitotic index-MI (mean 3.16; median 1/10HPF); slight cell atypia; variable ischemic/tumor-type necrosis. Treatment: myomectomy (22 %), hysterectomy (83 %) and radiotherapy (11 %); 12 (67 %) previous HT: progestin (22 %), OC (39 %), hormonal-IUD (11 %); no recurrence in remaining cases (n=6): median follow-up: 97.5 months.
Conclusion: LMs with necrosis and STUMP may display overlapping features. Diagnosis of STUMP should consider previous HT, detailed morphology (necrosis type/atypia/MI), to prevent overdiagnosis of STUMP.

PS-23-025

Malignant deciduoid mesothelioma mimicking a gynecological tumor

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Objective: Malignant deciduoid mesothelioma (MDM) is a variant of epithelioid mesothelioma that might be associated with asbestos exposure and poor prognosis. Described by Nascimento et al. in 1994, frequently mistaken with florid mesothelial hyperplasia or peritoneal deciduosis, 44 cases are reported in the literature.
Method: A 76 year-old woman, without asbestos exposure, discovered vaginal lateral wall tumour, CT: mass in right adnexa/parametrium. RMN: tumour with imprecise boundaries in Douglas cavity. Tumour markers negative. Exploratory laparoscopy with intraoperative biopsy diagnosed a MDM. Consequently; total mass excision was performed including uterus, both annexed, vaginal dome, sigma and rectum.
Results: An 8 cm tumour was revealed in Douglas cavity, histologically, deciduoid morphology was predominant with abundant atypical mitoses and massive neutrophyls infiltration. Immunohistochemical positivity: calretinin, cytokeratin5-6, CAM5.2, cytokeratinAE1AE3, E-cadherin, vimentin, HMBE1, CA125 and negativity: CD99, CD1a, melan-a, MyoD1, Wt-1, CD10, HMB45, actin, thrombomodulin, desmin, alpha-fetoprotein, Moc31, CERB-2, estrogen and progesterone. Normal DNA-repair proteins expression.
Conclusion: MDM is highly aggressive neoplasm, differential diagnosis includes: squamous carcinoma, GIST, deciduosis pseudotumoral, anaplasic large cell lymphoma, trophoblastic tumour, oxyphilic variant of ovarian clear cell carcinoma. This case represent a rare variant of mesothelioma, in which, was possible a complete resection with a probably better pronostic unlike most of these cases.

PS-23-026

Quality assessment of the registration of vulvar and vaginal premalignant lesions at the Cancer Registry of Norway

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Objective: A crucial factor concerning the utility of Cancer Registries is the data quality with respect to comparability, completeness, validity and timeliness. However, the data quality of the registration of premalignant lesions has rarely been addressed. This necessitated evaluation of the quality of registration of VIN and VaIN at the Cancer Registry of Norway (CRN).
Method: We re-collected all notifications with high grade VIN and VaIN diagnoses during 2002–2007 from pathology laboratories, and compared these to the data in the CRN database.
Results: Over the period 2002–2007 we estimated the completeness of the 1556 VIN and 297 VaIN notifications to be 95.0 % and 92.9 %, respectively. The original and reabstracted topography codes showed major discrepancies for 12 of 642 (1.9 %) VIN and 7 of 128 (5.5 %) VaIN notifications. The morphology codes were identical for 724 out of 814 notifications. For the period 2002–2007 the median time elapsed between date of diagnosis and registration was 436 and 441 days for VIN and VaIN cases respectively.
Conclusion: Based on the present analysis of the comparability, completeness, validity and timeliness of premalignant lesions of the vulva and vagina, we conclude that the CRN is able to monitor these premalignant lesions satisfactorily.

PS-23-028

Immunohistochemical properties of the gonad in adult patient with testicular feminization syndrome (TFS). A case report

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Objective: We evaluated morphological features of male gonad in an adult patient with TFS with an accent on its immunohistochemical properties.
Method: Our 47 years old patient had a primary amenorrhea. External genitals were female, without pubic and axillary hair. US confirmed cystic formation of the left gonad and lack of uterus. Tumor markers were normal but testosterone was high. Cystic formation of the left gonad was surgically removed, initially specified as a left ovary, as well as the other gonad. Pathohistological examination and karyotyping was done.
Results: Immunohistochemical analyzes of the gonad sample reveal that Sertoli cells showed positivity for Inhibin α, Vimentin, CD99, CKAE1/AE3 and Calretinin and Leydig cells showed positivity for Inhibin α, Vimentin, CD99, CKAE1/AE3 and Calretinin, and weak positivity for S-100, Synaptophysin i NSE. Immunoreactivity for CD99 in hyperplastic areas of Leydig cells showed the most intensive

positivity. PLAP and Chromogranin were negative. Ki-67 nuclear positivity was found in less than 1 % of Sertoli cells and in about 1 % of Leydig cells in hyperplastic areas. Karyotype was 46xy.
Conclusion: Although, surgical pathologists encounter TFS rare in a clinical practice, they should be aware of this condition, especially in lack of relevant clinical data, when it could be interpreted as a tumor.

PS-23-029
Mucinous tumors of the ovary: Diagnostic challenges at frozen section and clinical implications
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Objective: Frozen section (FS) diagnosis of ovarian mucinous tumors can be difficult due to the size of these tumors, heterogeneity and potential risk of metastasis from gastrointestinal (GI) neoplasms.
Method: We reported 79 ovarian mucinous tumors submitted for (FS) evaluation between January 2007 and Avril 2012 was conducted.
Results: FS and final pathology results were collected. The average tumor size was 22,1 cm (1–55 cm). The FS and final pathology diagnosis were concordant in 84,8 % (67/79) of the cases. Of the 12(15,1 %) discordant cases, one (1,2 %) was downgraded and 8 cases (13,9 %) were upgraded. Of the 30 tumors interpreted as borderline mucinous tumors (BMT) on FS, 8(26,6 %) were malignant at final diagnosis (4 ovarian, 4 GI), 21 (70 %) remain as BMT and 1 (3,3 %) was benign. Of the 18 benign tumors on FS, 3 cases (17, 6 %) were upgraded to BMT at final diagnosis. Tumors with a malignant diagnosis on FS (30 cases) were 100 % concordant with final diagnosis.
Conclusion: Our study showed a 15,1 % rate of discordance between FS and final diagnosis. Given that GI origin is a possible finding, intraoperative assessment of the appendix should be performed in all mucinous ovarian tumors.

PS-23-030
Uterine müllerian adenosarcoma: A clinicopathologic study of 31 cases
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Objective: Müllerian adenosarcoma (MA) is a distinctive type of uterine tumor, traditionally regarded as a low-grade variant of mixed müllerian tumors.
Method: Thirty one cases of adenosarcoma were examined during a period of 19 years (May 1993–February 2012).
Results: Thirty tumors were of the uterine corpus and one of the cervix. The mean patient age was 54,2 years (range: 16 to 73 year). The main clinical manifestations were vaginal bleeding and pelvic pain. Physical examination showed cervical/vaginal mass or pelvic mass. Treatment was known in 25 cases: Patients underwent hysterectomy with bilateral salpingo-oophorectomy in 17 cases and lymphadenectomy in 6 cases. Tumor size ranged from 2,5 to 12 cm (mean: 7.1 cm). Microscopically, sarcomatous overgrowth was found in 4 cases (13 %), heterologous elements in 5 (16 %). Eleven cases (35 %) had myometrial invasion involving the internal half of the myometrial thickness in 9 cases, and more than 50 % in 3 cases (9 %). The cervical tumor presented as an endocervical polyp without invasion of the cervical wall.
Conclusion: Uterine MA are low-grade neoplasms capable of local recurrence and much less commonly distant metastasis. Surgical excision is the main treatment strategy with a good prognosis in the early stage disease. The 2 most important adverse prognostic factors are deep myometrial invasion and sarcomatous overgrowth.

PS-23-032
Spectrum of epithelium changes in adenomyosis
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Objective: Adenomyosis (AM) is a very common gynecological disorder. Despite high incidence of the disease epithelial changes precise developmental events leading to the condition remain controversial. The aim of the study was to investigate and compare epithelium morphologicaly and markers expression of proliferation, apoptosis, invasion and neoangigogenesis in AM foci.
Method: This study was done on biopsy samples of uterus taken from 70 women with adenomyosis. Immunohistochemical staining of tissues was performed with antibodies to ApoCas, Ki-67, MMP-2, TIMP-1, claudins 3, 5 (CL3,5), E-cadherin, COX-2, EGFR, VEGF.
Results: Four variants of epithelium changes were found in AM foci such as proliferative type, hyperplastic type with and without atypia, and atrophic type.

Hyperplastic tipe with and without atypia in AM foci was characterized by increase ApoCas, Ki-67, EGFR, COX-2, VEGF, MMP-2, decrease E-cadherin, TIMP-1. CL-3,5 were revealed in cytoplasm of cells. The level of expression of these markers in the epithelium of AM foci with hyperplasia with atypia was very close to endometrial carcinoma of the uteri body ($p<0.05$).
Conclusion: Atypical epithelium in AM foci may be the source of carcinoma of the uterine body.

PS-23-033
Clinicopathologic and molecular profile in endometrial carcinoma: An immunohistochemical analysis of 95 cases
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Objective: Endometrial carcinoma (EC) displays variable outcomes.
Method: Immunohistochemistry for p53, Ki67, EGFR, HER-2 (%positive), PTEN, estrogen and progesterone receptors (ER/PR), pERK, pJNK (H-score) in TMA from 95 EC: 26 endometrioid (ADE) grade(G) 1, 28 ADEG2, 16 ADEG3, 18 serous(ADS), 4 clear cell (ADCC), 2 carcinosarcomas and 1 undifferentiated carcinoma. Survival and disease status data.
Results: ADE: ER/PR mean H-score from 70/190 to 11/110, from G1 to G3, 34 for PTEN, 13 and 67 for pERK and pJNK, two ADEG3 >75 % p53 and one 20 % Ki67. ADS: 55 % >75 % p53 and 42 % >10 % Ki67, 14/61 for ER/PR, 79 for PTEN, 18 and 116 for pERK and pJNK. ADCC: none ER/PR; 90, 144 and 73 for pERK, pJNK and PTEN, and 50 % >75 % p53 and none >5 % Ki67. HER-2 expression >50 % in one ADS and one ADEG3; EGFR >50 % in one ADEG1 and 25–50 % in one ADEG1, 3 ADEG2 and 1 ADS. 20 patients died of disease (DOD): 9 ADS and 6 ADEG3; 66 were alive without disease: 49 ADEG1 and ADEG2. ADE poor outcome correlated with low ER/PR (16/71G2 and 20/106G3) and PTEN (1G2, 3G3); pERK showed low expression in ADS DOD.
Conclusion: Histologic types of EC show molecular profiles with probable prognostic and pathogenic significance.

PS-23-034
MicroRNA expression in uterine smooth muscle tumors
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Objective: miRNA expression profiling may provide new insights for diagnostic and therapeutic purposes in uterine smooth muscle tumors.
Method: Expression profiling of 654 miRNAs was studied in 10 leiomyosarcomas (uLMS),4 leiomyomas (uLM), myometrium (3), and 6 non-uLMS, using NanoString nCounter™ Assay System. ANOVA was used to identify statistically significant differential miRNAs expression (fold-change>2 and $P<.05$).
Results: 51, 35 and 13 miRNAs were deregulated in uLMS compared to uLM, myometrium, and non-uLMS, respectively. 16 were deregulated in uLM compared to myometrium. 7 identical miRNAs (21/29a/126/139-5p/140-3p/193a-5p/1247) were deregulated in all tumor groups while uLMS and non-uLMS shared 19 deregulated miRNAs (15b/106b/130b/155/494/708/1246/1308 upregulated; 30c/92b/125a-5p/125b/197/199/216a/328/455-5p/873/let-7c down-regulated) compared to uLM and myometrium, several known to be involved in cell-cycle and/or apoptosis pathways (p53, RB, E2F, cyclin-D1/E) and/or metastasis.
Conclusion: Albeit some overlap, miRNA expression profile of uLMS is different from uLM but relatively similar to non-uLMS. uLMS and non-uLMS share deregulation of several miRNAs that may be linked to specific cell-cycle/apoptosis pathways, not dysregulated in uLM. These miRNAs may deserve further study for potential diagnostic, prognostic and/or therapeutic utility.

PS-23-035
Clinicopathological spectrum of 18 adenosarcomas reviewed at a tertiary cancer referral centre
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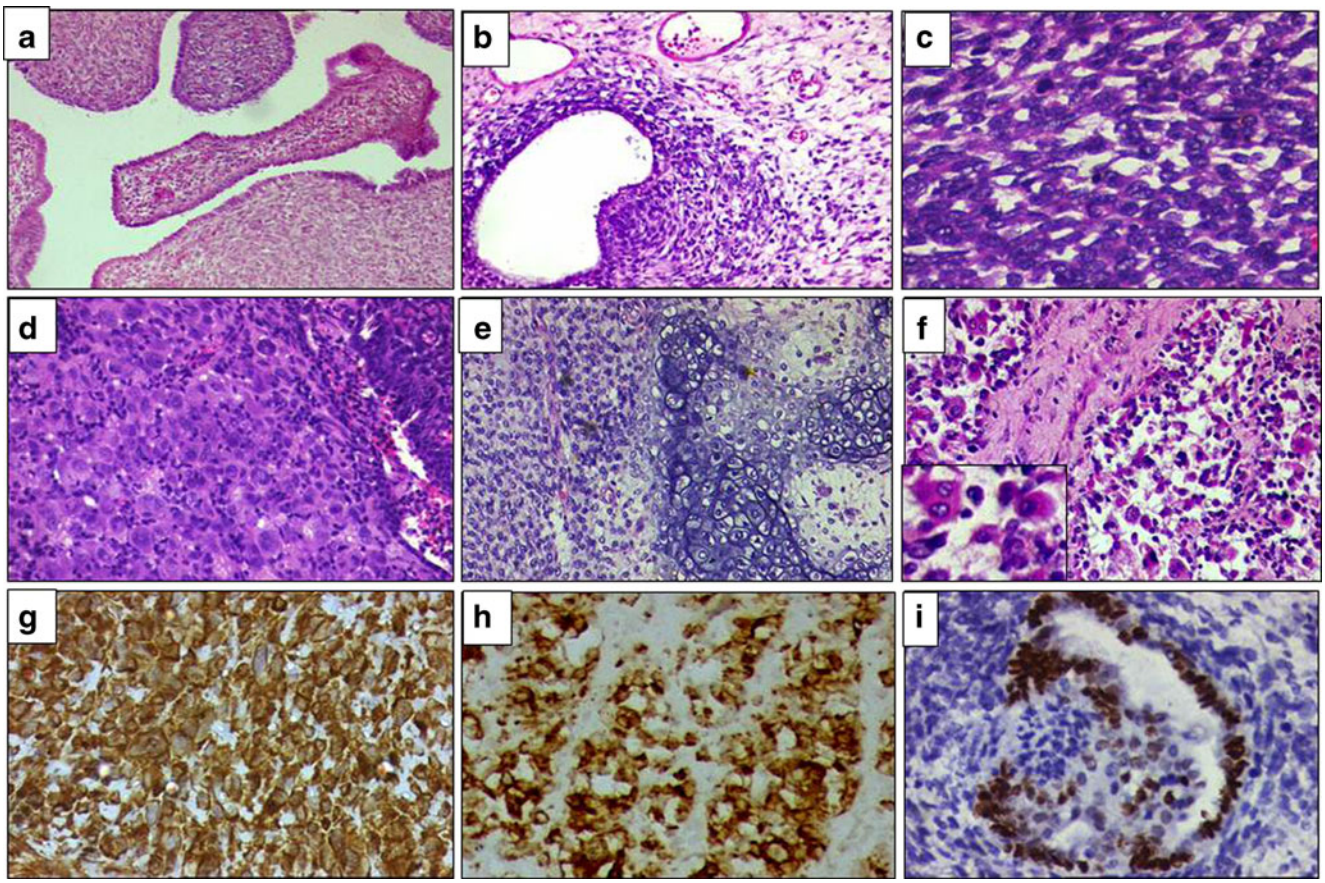
Objective: Adenosarcomas of female genital tract are uncommon.
Method: Over a 7-year period, 18 adenosarcomas were critically reviewed.
Results: Eighteen adenosarcomas occurred within age-range 21–65 years (mean, 42.9), involving uterus (8), cervix (2), uterus + cervix (5) and ovary (2), with size 3–15 cm (mean, 7.4). Histopathologically, tumors were low-grade (10) (55.5 %) and high-grade (8) (44.4 %), latter with sarcomatous overgrowth (SO) (6/8). De-differentiation (9, 50 %) included rhabdomyoblastic (5), cartilaginous (2), adipocytic (1) & sex-cord-type (1). Four cases had leiomyomas; 2 developed on endometriosis; 1 in treated cervix carcinoma and 1 displayed decidualization. Immunohistochemically,

tumors focally expressed CD10 (4/5), SMA (3/8), vimentin (4/4, diffuse) and desmin (9/10), latter mostly in rhabdomyoblasts. MIB1 (5 cases) varied 5–20 %. All 15 cases underwent surgery, mostly TAHBSO (9) (50 %) and 4 high-grade cases received adjuvant treatment. Five tumors recurred (4 high-grade tumors with SO) and 1 metastasized. Among 10 cases, 5 were alive-with-disease (mean, 29.4 months) and 5 free-of-disease (mean, 15 months).

Conclusion: Adenosarcomas are uncommon, with a wide clinicopathological spectrum. Whereas the commoner low-grade adenosarcomas are less-aggressive, high-grade tumors with SO recur more. Surgery is treatment-mainstay. Adjuvant treatment is considered in high-grade subtypes.

A. Polypoid glands with sarcatomatous stroma (phylloides-like pattern). B. Periglandular condensation. C. Sarcomatous overgrowth. D. Decidualization. E. Cartilagenous dedifferentiation. F. Rhabdomyoblastic dedifferentiation (**Inset**). G. Vimentin positivity. H. Desmin in rhabdomyoblasts. I. ER positive glands.



PS-23-036

Morphological changes of complex endometrial hyperplasia with intraepithelial neoplasia during conservative treatment: A report of 3 cases

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Objective: Endometrial endometrioid carcinoma is the most common malignant tumor of the uterine corpus usually developing in postmenopausal women. More seldom it occurs in young reproductive age and sometimes develops from an endometrial intraepithelial neoplasia (EIN). The EIN diagnosis and treatment in such patients have some difficulties.

Method: We have studied curettage tissue specimens from three women with ages 27, 33 and 35, with abnormal uterine bleeding and obesity. The severe complex endometrial hyperplasia with low grade intraepithelial neoplasia was revealed in all cases. These biopsies were repeated some

times during 3 years and investigated using routine light microscopy and immunohistochemistry (IHC) to control the treatment response.
Results: In the course of progestin treatment the complex endometrial hyperplasia with intraepithelial neoplasia became histologically less complicated and than normal. IHC profiles and Ki-67 expression had the same dynamics. In the youngest patient the unusual gland cell atypia with focal calcification was observed one time and hysterectomy was considered.
Conclusion: The study confirms that the repeated curettages with conservative treatment and histological studying can be successfully used in some cases of complex endometrial hyperplasia with intraepithelial neoplasia.

PS-23-037
Value of Ki67, P16 and CK17 markers in differentiating cervical intraepithelial neoplasia and benign lesions
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Objective: The cervical cancer is one of the most common cancers among women worldwide. Diagnosis of CIN affected by high rates of discordance among pathologists. Therefore, we need to other adjunct methods for accurate diagnosis of CIN versus benign lesions in equivocal cases. The aim of this study was evaluation of Ki-67 (MIB-1), CK17 and P16 INK 4a (P16) markers by immunohistochemical method in differentiating CIN from benign cervical lesions.
Method: Seventy-seven cervical biopsies that originally diagnosed as non-CIN (n=31) and CIN (n=46), were reviewed by three pathologists and re-classified as non-CIN (n=54) and CIN (n=23), based on agreement between at least two of three, to obtain a consensus diagnosis. Consensus diagnosis was defined as the "Gold Standard". Then immunostaining for Ki67, P16 and CK17 was performed on all cases and their results were compared with original and consensus diagnosis.
Results: The overall agreement between original and consensus diagnosis was 67.5 % (Kappa=0.39, P-value< 0.001). The sensitivity and specificity of Ki67 immunostaining were 95.6 % and 85.1 % and for P16 were 91.3 and 98.1 %, respectively. The sensitivity and specificity of CK17 negative staining for CIN detection were 39.1 % and 40.7 % respectively.
Conclusion: We recommended using Ki67 and P16 markers as complementary tests for differentiation between dysplastic and non-dysplastic lesions.

PS-23-038
WT1 expression in ovarian borderline and malignant surface epithelial tumors
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Objective: Wilms tumor gene product, a tumor suppressor gene, now is considered to have oncogenic functions. There seems to be differences in WT1 expression among surface epithelial ovarian tumor subtypes.
Method: Immunohistochemistry for WT1 was done on 35 serous & 3 mucinous cystadenocarcinomas, 9 borderline serous & 10 borderline mucinous tumors, 7 endometrioid ovarian carcinomas, 3 clear cell carcinomas, 1 malignant Brenner tumor, 2 metastatic adenocarcinomas and 6 endometrial adenocarcinomas. A tumor was considered negative if<1 % of tumor cells were stained. Positive reactions were graded :1+,1–24 %; 2+,25–49 %; 3+,50–74 %; 4+,75–100 %.
Results: Of serous cystadenocarcinomaes, 30(85.7 %) were positive,4 showed reactivity of<50 % of the tumor cells and one were negative. All borderline serous tumors were positive. All mucinous tumors, endometrioid carcinomas, clear cell carcinomas, metastatic adenocarcinomas and primary endometrial carcinomas were negative. The single malignant Brenner tumor were positive for WT1.
Conclusion: WT1 is a good marker to distinguish primary ovarian serous carcinomas from other surface epithelial tumors (especially endometrioid subtype) and metastatic carcinomas (especially endometrial serous carcinoma), other than malignant mesothelioma. Degree of expression is not an indicator to separate high grade borderline serous tumors from low grade ones.

PS-23-039
Female adnexal tumor of probable Wolffian origin (FATWO): A case report
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Objective: FATWO is a rare neoplasm originating from the mesonephric duct remnants that occurs predominantly in the broad ligament but also in the ovary. It is considered a low-malignant potential tumor. However local recurrences and metastases have been reported.
Method: A 45 year-old female, on routine gynecological physical examination, followed by pelvic ultrasonography and computer tomography was diagnosed with a mass at the right ovary. A salpingo-oopherectomy was performed. On gross examination a well-circumscribed, solid and focally

cystic tumor measuring 10,5×7×5,5 cm arose in the ovarian hilus.
Results: Microscopically the tumor consisted of medium-sized, ovoid to polygonal cells arranged in a solid, tubular and sieve-like pattern. Some cystic spaces were lined by low-cuboidal cells and contained amorphous, eosinophilic material. Cellular atypia and mitoses were rare. The tumor cells were positive for Vimentin, Inhibin-a (focally), CD10, cytokeratins 8/18, 19 and 7 (focally) and negative for cytokeratin 20, epithelial membrane antigen, carcinoembryonic antigen and a-fetoprotein.
Conclusion: Histopathological and imunohistochemical findings consistent with an ovarian FATWO. Differential diagnosis includes endometrioid carcinoma, clear-cell carcinoma, Sertoli-Leydig cell tumors (retiform variant) and rete ovarii adenoma. Surgical excision is the optimal treatment. Radiation therapy, chemotherapy or even targeting molecular therapy is questionable.

PS-23-040
Müllerian adenosarcoma family: Report of two sisters uterine tumors
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Müllerian adenosarcoma is a rare mixed tumor of low malignant potential. Usually presented as a large endometrial polyp in postmenopausal women. They are associated with tamoxifen or radiation therapy. Microscopy shows a mixture of benign glandular epithelium and low-grade endometrial sarcoma is typically concentrated around the glands. The differential diagnosis is made with the adenofibroma, but now is doubted the existence of this tumor and is considered more of a distinct adenosarcoma. The treatment is total hysterectomy. Sisters of 24 and 16 years with a history of dysmenorrhea. Hysteroscopy was performed to the eldest one, in which multiple polyps are observed and partially resected. The pathological diagnosis was Mixed Mullerian tumor, adenofibroma/adenosarcoma. Total abdominal hysterectomy was performed. Histological examination showed a mixed tumor with glandular component and a low-grade sarcomatous, scarce mitosis, mild atypia and no necrosis. The diagnosis was: mullerian adenosarcoma. A year later, a hysteroscopy and endometrial biopsy was performed to the youngest sister, that showed endometrial polyps with stromal predominance, and no significant atypia. With the diagnosis of mullerian adenosarcoma, and taking into account family history, total hysterectomy was performed. Adenosarcoma is a rare tumor whose family presentation is not described in the literature.

PS-23-041
Gliomatosis peritonei is associated with frequent relapse but not affects overall survival in patients with ovarian immature teratoma
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Objective: Gliomatosis peritonei (GP) associated with ovarian teratoma has known to have no adverse prognostic effect. We investigated the clinicopathological features of ovarian teratoma associated with GP, and compared immature teratomas (ITs) with GP to ITs without GP.
Method: We investigated 16 patients with ovarian teratoma with GP and 27 patients with IT without GP, who were diagnosed at Samsung Medical Center (seoul) from January 1995 to August 2010.
Results: Six patients with IT with GP (37.5 % of 16 patients) had recurrence. When IT with GP (n=15) was compared to IT without GP (n=27), patient of IT with GP showed larger tumor size (median, 19 cm vs. median 13 cm) (P<0.001), more frequent relapse (40 %, 6/15 vs. 3.7 %, 1/27) (P=0.005), and frequently elevated pre-operative CA125 level (100 %, 12/12 vs. 50 %, 10/20) (P=0.004). Survival curves showed significantly shorter relapse-free survival in patients of IT with GP (P=0.002). Two-year relapse-free survival rates were 59.3 % and 96.3 % in IT with GP and IT without GP, respectively. However, all patients except one case of IT with GP alive.
Conclusion: Ovarian IT with GP was characterized by larger tumor size and frequent elevation of preoperative CA125 level, and GP was associated with frequent relapse in patients with ovarian IT.

PS-23-042
Corelation between histopathologic diagnosis with p16 and Ki67 immunostaining, cytologic features in cervical neoplasia
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Objective: Frequency of cervical carcinoma decreases nowadays since cytologic screening methods have been using extensively. The incidance of cervical intraepithelial neoplasia increases. Cytologic diagnosis og these lesions are substantially important. So we aim to identify the role of p16 and Ki67 immunostainings for predictive factors of cervical neoplasia.
Method: The study was conducted January 2007 to January 2012. Ninety-three cases (mean age 43,9; range 22–71 years) diagnosed as squamous intraepithelial lesions were included,

which were examined histopathologically, and in terms of cytologic features, p16 and Ki67 immunoexpression.
Results: Cervical smear samples from 93 patients were diagnosed as 6 AGUS, 9 ASCUS, 12 ASC-H, 19 HGSIL, 47 LGSIL cases. 28 of 93 patients (%30,1) were HGSIL and 65 cases (%69,9) were LGSIL in cervical biopsy. 14 of 28(%50) HGSIL cases were diagnosed as HGSIL and 38 of 65(%58,5) LGSIL patients were diagnosed as LGSIL in cervical cytology. All HGSIL cases were positive with p16 and Ki67. 54 of 65(%83,1) LGSIL cases were positive with p16 and 61 of 65(%93,9) LGSIL cases were positive with Ki67. p16 and Ki67 overexpression are independent variables for diagnosing HGSIL and LGSIL (p<0,005).
Conclusion: These immunostaining results have been proven useful for accurately assessing of cervical lesions that hardly diagnosed.

PS-23-043
Cavernous lymphangioma of the uterine cervix
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Objective: Lymphangiomas are rare benign proliferations of the lymphatic system. Three types are generally acknowledged: circumscriptum (or capillary), cavernous, and cystic. We present a case of cavernous lymphangioma of the cervix in a 54-years-old female.
Method: Case Report: A 54-years-old woman presented to the department of obstetrics and gynecology at our hospital. For uterin myoma, she underwent total abdominal histerectomy and bilateral salpingo-oophorectomy. Operation material was sent to pathology department. Macroscopic evaluation revealed, cut surface of cervix was blackish and had many cavities. Microscopic examination showed cavernous lymphangioma; composed of cavernous lymphatic spaces which contain lymphatic fluid. Immunhistochemically, factor VIII, CD 34, SMA were positive in lymphatic endotelium.
Conclusion: Cavernous lymphangioma is a rare lesion in the uterin cervix. To our knowledge this is one of the few cases documented in English literature. As our case, vascular lesions of cervix or another site of female genital tract can be detected coincidentally at histerectomy materials.

Wednesday, 12 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-24 Poster Session Dermatopathology

PS-24-002
Spitz nevus, Atypical Spitz Tumor or Spitzoid Melanoma: Which morphological criteria ensure the diagnosis?
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Objective: Spitzoid lesions continue to be a devastating problem in dermatopathology. Diagnoses as Spitz nevus (SN), atypical Spitz tumor (AST) and Spitzoid melanoma (SM) is an adjunctive classification based on several morphological criteria and survival results.
Method: Thirty-one Spitzoid lesions were reviewed by a scoring system based on seven selected criteria reported previously appreciating characteristics of Spitzoid lesions. As a prevailing criteria, presence of deep mitoses had a score of 2; ulceration, asymmetry, epidermal consumption, solid growth pattern, loss of maturation, pigment heterogeneity were scored as 1 for each. Final diagnosis was SM for scores 4-8, AST for 1-3, SN for 0.
Results: The most frequently seen criteria, loss of maturation was present in 12 SM (n=12), 7 AST (n=16) and epidermal consumption in 8 SM, 3 AST. Deep mitoses were present in only 7 SM. Ulceration was present in 4 SM and 1 AST. Asymmetry, solid growth pattern and pigment heterogeneity were nearly equally seen in SM and AST. First diagnoses of 16 SN switched to AST, 8 to SM, and of 2 AST to SM.
Conclusion: Presence of deep mitoses is the single criteria present only in SM. Loss of maturation, epidermal consumption and ulceration can be used to differentiate AST from SM.

PS-24-003
CD10 and P53 expression in basal cell carcinoma and benign adnexial neoplasm of hair follicle apparatus
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Objective: Basal cell carcinoma (BCC) of the skin is the most common form of human cancer. Sometimes the histological appearances of benign adnexial neoplasm of hair follicle apparatus tumors (trichoepithelioma, trichoblastoma) are diffucult to distinguish from BCC. The aim of this study is to investigate the usefulness of CD10 and p53 in distinguishing BCC and benign adnexial neoplasm of hair follicle apparatus tumor.
Method: This study included 237 BCC and 27 benign adnexial neoplasm of hair follicle apparatus tumor. We used immunohistochemical stains for p53 and CD10 in all cases.
Results: In BCC cases the expression of CD10 was noted in tumor cells in 222 cases. In 20 benign adnexial neoplasm of hair follicle apparatus tumor cells were negative stain with CD10. Only 7 benign adnexial neoplasm of hair follicle apparatus tumor were positive CD10. The rates of p53 immunostaining of BCC and benign adnexial neoplasm of hair follicle apparatus tumor were 91 % and 25,9 %. Chi-square test revealed a significant correlation that P53 and CD10 expression in BCC and benign adnexial neoplasm of hair follicle apparatus tumor were significantly different (p<0,0001).

Conclusion: We conclude that CD10 and P53 expression may be a useful adjunct marker in distinguishing BCC and benign adnexial neoplasm of hair follicle apparatus tumor.

PS-24-004

Pigmented purpuric dermatosis: Study of a series of six patients

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Objective: Pigmented purpuric dermatosis (PPD) comprises a group of vascular disorders of unknown etiology. Histologically, it is characterized by lymphocytic capillaritis in the papillary dermis.
Method: A retrospective and monocentric study concerning the cases of PPD diagnosed in the department of anatomopathology La Rabta over 6 years (from 2006 to 2011). These cases were studied clinically and histopathologically. Hepatitis C and B profile was carried out to evaluate a possible relation.
Results: 6 cases of PPD have been diagnosed; 2 men and 4 women, aged from 20 to 80 years. Only one patient tested positive for hepatitis C with an elevated viral load. she had a profuse eruption involving the trunk and the limbs of 4 years duration, contrary to the other patients in whom only the lower limbs were affected. she has been treated by alpha interferon and ribavirin with a disappearance of the eruption within 3 months. In the five other patients, the lesions resolved spontaneously within a period of 2 to 9 months.
Conclusion: Hepatitis C may play a role in the pathogenesis of PPD especially when the lesions are profuse and long-standing. In our patient, the disappearance of lesions 3 months after the onset of interferon alpha therapy with a significative decrease of viral load is an argument supporting our hypothesis.

PS-24-005

Fibrolipomatous hamartoma of nerve

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Objective: Fibrolipomatous hamartoma of nerve is a benign lesion, very rare in medical practice, occurring in children or young adults. Case report: A 44 year old woman, G. N., presented with a slowly growing plantar mass in the right foot that had been present for 7 years. Neither the patient nor members of her family had a history of neurofibromatosis or other soft tissue tumors. She had no pain at rest, but she had shooting pain while running or walking. Physical examination revealed a mobile, tender mass located in the plantar soft tissue.
Method: After surgical excision, the lesion was well circumscribed, 20/10/8 mm, white colour with yellow areas. Tissues specimens were fixed in 10 % buffered formalin, routinely processed and embedded in paraffin, sectioned at 3 μm, then stained routinely by Hematoxylin – Eosin, than examined by light microscopy.
Results: The lession is characterized by proliferation of mature fatty and fibrous tissue within the epineurium of the nerve accompanied by prominent concentric perineurial fibrosis. The histopathological diagnosis was fibrolipomatous hamartoma of nerve.
Conclusion: The tumour usually affects nerves of the upper extremities, most commonly the median nerve. Involvement of other nerves is rare. The lesion is benign and the recommended treatment is surgical excision.

PS-24-006

Chymase + and tryptase + mast cells and endoglin expression in melanocytic skin lesions

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Objective: Mast cells are known to participate in cancer formation. The aim of the study was to evaluate number of tryptase and chymase positive mast cells and their relationship with neoangiogenesis in pigmented nevi and melanoma.
Method: Material consisted of 24 pigmented nevi (PN), 19 dysplastic nevi (DN) and 18 melanomas (MM). Chymase and tryptase positive cells and CD105 postive vessels were counted inside the lesion and at the interface with the stroma.
Results: The mean intralesional tryptase + cell count was 15.75 for PN, 21.78 for DN, and 8.07 for MM. The chymase + intralesional count was 14.89 for PN, 21.88 for DN, and 11.34 for MM. The tryptase + cell perilesional count was 16.89 for PN, 15.93 for DN, and 15.71 for MM. The chymase + perilesional count was 16.52 for PN, 16.16 for DN, and 14.77 for MM. The mean perilesional CD105 + vessel density was 2. 71 for PN, 4.49 for DN and 33,93 for MM. The vessel density was correlated with intralesional tryptase + mast cells. Perilesional CD105+ vessels were correlated with mitotic activity of melanomas.
Conclusion: The mast cells may participate in angiogenic switch of melanocytic skin lesions.

PS-24-007

HER-3 expression may influence progression of cutaneous malignant melanoma

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Objective: There are several prognostic factors in melanoma. It was suggested that HER-3 expression may influence the tumor behavior. The aim of the study was to investigate the relationship of HER-3 expression with various prognostic factors.
Method: HER-3 expression was evaluated in 52 melanomas, 26 without metastases and 19 with lymph node and 7 with distant metastases. Membranous, cytoplasmic and nuclear HER-3 expression was separately analysed. The staining intensity and percentage of positive tumor cells were evaluated.
Results: The cytoplasmic staininig was seen in all cases, with average intensity of 2 and percentage of positive cells ranging from 5 % to 90 % (mean 48.8 %). The percentage of cytoplasmic HER-3 positive cells was inversely correlated with Clark and Breslow stage ($R=-0.29$ and $R=-0.43$). Cytoplasmic HER-3 reaction was significantly stronger in cases with lymph node metastases (2.3 vs. 1.8 $p<0.03$). In 22 cases a dot-like cytoplasmic reaction was seen. Membranous positivity was seen in 28 cases (54 %).
Conclusion: HER-3 may play a role in melanoma progression. It may be involved in lymphatic dissemination. Further studies of prognostic significance of HER-expression in melanoma are needed.

PS-24-008
Hypopigmented mycosis fungoides with unusual vitiligo-like presentation in child
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Objective: Mycosis fungoides (MF) is the cutaneous T cell lymphoma. Classical, clinical and histopathological findings of MF are detected in most of the patients. However, some of the patients have defined atypical MF. hypopigmented MF (HMF) is one of the atypical forms. HMF could be misdiagnosed with clinical and histopathological examination. HMF is considered mistakenly vitiligo. Therefore, it should be considered differential diagnosis. MF is usually seen in the middle aged and elderly. The occurrence of mycosis fungoides in children is very rare.
Method: An 7-year-old girl child attended dermatology clinic with complaints of pruritus and hipopigmented patches. Lesions was performed punch biopsy and reported HMF.
Conclusion: Herein, this case presented because it was considered vitiligo as clinically and diagnosed HMFas histopathologically.

PS-24-009
Reducing block sampling in wide local excisions for melanoma
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Objective: It is established practice that wide local excision (WLE) is undertaken for the further management of cutaneous melanoma, however, definitive guidelines for macroscopic sampling have not been established. Our aim was to determine whether our sampling of WLE specimens was adequate, inadequate or excessive and to establish guidelines for these specimens.
Method: 128 cases which underwent initial biopsy and subsequent WLE in 2010 were identified. We recorded the specimen size, macroscopic appearance, number of blocks sampled and margins of the original biopsy.
Results: There was wide variation in the number of blocks sampled (range 1–27). Residual melanoma was identified in 7 of the cases (9.4 %) which had clear margins on the original biopsy. Of these, 4 had evidence of a pigmented lesion on macroscopic examination. The remaining 3 cases had margins of 1 mm or less on the original excision. No subsequent surgery was performed on these cases.
Conclusion: Our study has shown that in WLE specimens with no evidence of a macroscopic lesion and in which margins of the original biopsy were clear by greater than 1 mm, little is to be gained from extensive sampling. Reduced sampling would result in saving laboratory resources with a predicted 49 % block reduction in our laboratory alone.

PS-24-010
Functioning oxyphil adenoma of parathyroid gland: A case report
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Objective: The most frequent cause of primary hyperparathyroidism are adenomas of the parathyroid gland, the majority of which are composed of chief cells. Oxyphil adenomas are uncommon and account for 3 % of functioning parathyroid adenomas. Up until 1978 year they have been considered non-functional.
Method: Laboratory findings revealed calcium levels of 2.86 prior to operation. The serum parathyroid hormone level was 151.40 pg/ml. A CT scan of the neck showed normal size thyroid lobes with heterodense structure with an oval hypodense lesion in the lower right pole of the thyroid.
Results: At surgery a mahagony-brown mass measuring 10 mm in diameter was removed and reported as oxyphil adenoma on frozen section. Histopathological examination revealed encapsulated adenoma composed of oxyphil cells with abundant, granular pink cytoplasm and a rim of normal parathyroid tissue. Mitotic figures were absent. Postoperatively, a decrease of the serum

calcium down to 2.31 mmol/l was declared. The follow-up period was unremarkable.
Conclusion: There appear to be a growing evidence that a big part of oxyphil adenomas of parathyroid gland can produce parathyroid hormone and contribute to the cases of primary hyperthyroidism.

PS-24-011
Effectiveness of UVB phototherapy on mycosis fungoides using histologic guitart criteria in Iranian patients
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Objective: Mycosis fungoides (MF) is the most common primary cutaneous lymphoma. Mycosis fungoides often develops slowly over many years, presenting with a generalized erythroderma, skin patches or plaques. The diagnosis of MF requires the integration of clinical and histopathologic findings. Narrowband UVB (NBUVB) is widely used to treat MF. To evaluate the effectiveness of therapy the histopathologic findings before and after NBUVB reviewed using GUITART criteria.
Method: We enrolled 20 patients (12 women, 8 men; age range, 10–80 years; mean age, 45.5 years) with clinically and histologically proven MF. The patients received NBUVB phototherapy three times a week. A biopsy was performed 3 months after onset of the treatment and GUITART criteria used to scoring MF before and after therapy.
Results: Phototherapy was reduced the primary intraepidermal atypical lymphocytes (P value=0.008), dermal atypical lymphocytes (*P* value=0.008), epidermotropism (*P* value=0.001), density of infiltration (*P* Value=0.002) and lymphocytic infiltrate without inflammatory features (*P* Value=0.046) in all patient. But the relationship between the reticular fibroplasia of papillary dermis and phototherapy was not proved (*P* value=0.18). Overall score of patients was significantly lower after phototherapy (*P* value=0.000).
Conclusion: Our data suggest that NBUVB therapy is reduces histiologic score of MF and is effective for the treatment of Iranian patients.

PS-24-012
Nodular colloid degeneration of the skin: Report of three cases
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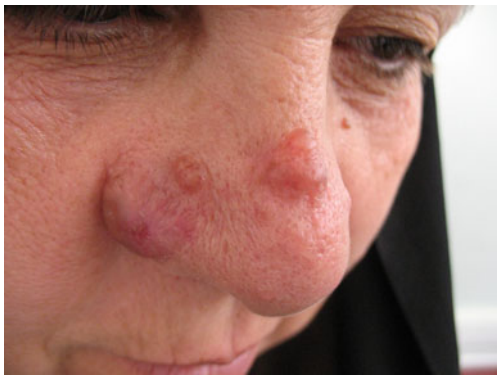
Objective: Nodular colloid degeneration (NCD) is a rare dermatological disorder and also a rare type of colloid milium. The degeneration may be related to sun exposure.
Method: Three cases of NCD were enrolled from the archive of dermatopathology department of Razi hospital during 2009–2011.
Results: In this report, three cases, all presented with multiple plaques and nodules in the nose and the face, are depicted. Histologically, these nodular masses were homogeneous, with eosinophilic clefted materials expanding the papillary dermis and extending into the deep dermis. Histochemical review showed the reactivity of the colloid materials via the PAS, crystal violet and methyl violet staining. All the three cases were finally diagnosed as nodular colloid degeneration.
Conclusion: NCD is a rare disease but it should be considered in any cases with a history of long exposure to the light. We suggest the long term exposure to the sun as an etiologic factor thus, sun protection would be the most preventive and available treatment.



PS-24-013
Glypican-3 protein expression in melanoma: A immunocytochemistry study
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Objective: Glypican-3 (GPC3) is a cell surface heparan sulfate proteoglycan. Serum GPC3 was shown to be expressed in 40 % of melanomas (Ms) but GPC3 expression in Melanoma tissues had not been investigated.In this study, immunohistochemical analysis of GPC3 protein expression was investigated in histologic sections from Melanoma tissues.
Method: 60 melanoma patients, twenty patients with insitu melanoma, twenty patients stage 0 and stage I melanoma, twenty patients stage II and stage III melanoma. All cases were stained with anti-GPC3 antibody. GPC3 expression was divided into 2 categories: negative (negative or weak cytoplasmic staining) and positive (moderate or strong cytoplasmic with membranous accentuation).
Results: GPC3 immunopositivity. showed in 40,3 % of melanomas. GPC3 expression at stage 0, I, II, III were 44.4 %, 40.0 %, 41.6 %, 35 % respectively.

Conclusion: GPC3 is apparently a novel tumor marker useful for the diagnosis of melanoma, especially in early stages of the disorder.

PS-24-014

Cutaneous leishmania in Eastern Anatolia: 6 case reports

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Objective: Leishmaniasis refers to the spectrum of diseases caused by Leishmania species, which are Protozoa of order Kinetoplastida. Clinically leishmaniasis is divided into visceral (kala-azar), cutaneous, mucosal, and mucocutaneous syndromes. The final diagnosis of the disease, lesions of the parasites, as well as shown smear'lerde factor confirmed by histopathological and clinical evaluation.
Method: In our study, 6 patients with the diagnosis of Leishmania cutaneous between 2006 and 2012 in Department of Pathology, Ataturk University Faculty of Medicine were presented.
Results: Four (66.6 %) cases were females and 2(33.3 %) were males. Age ranging of cases was found from 0 to 60 years and median age 31.85±12.15 years. The lesions were found on the face in patients. Facial skin biopsy specimens were taken in all cases. Giemsa-stained touch preparation of the skin biopsy revealed amastigotes inside macrophages, consistent with leishmaniasis. Lesions of 2 patients who have long been different from the rest of them were those who migrated to the Cukurova region.
Conclusion: Leishmaniasis is public health problem in Southeastern Anatolia region of Turkey, especially in Sanliurfa and Çukurova region.

PS-24-015

Autoimmune blistering skin diseases in East Anatolia

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Objective: Autoimmune blistering skin diseases can be divided into pemphigus diseases and subepidermal bullous diseases. In pemphigus, the autoantibodies are directed against intercellular contact structures; in the pemphigoid diseases, the autoantibodies are directed against adhesion molecules of the basal membrane zone.
Method: A retrospective study of 102 cases of autoimmune blistering skin diseases obtained over a period of 7 years from 1st October 2005 to 31st December 2011 in the Department of Pathology, Medical Faculty of Ataturk University was designed.
Results: In the present study, the mean age was 52 years and male: female ratio was 0,7. The most commonly affected sites were the buccal mucosa and the palate. %18 of cases, the oral cavity was the primary site of involvement. In histopathological examination we showed intraepithelial vesicle formation, subcorneal separation with acantholysis, and the presence of Tzanck cells in biopsy specimens.
Conclusion: The incidence of autoimmune blistering skin diseases in our department increased in the past 7 years. Pemphigus vulgaris is the most common of these diseases. %70 of autoimmune blistering skin diseases was pemphigus diseases.

PS-24-016

Prevalence of vasculitis in Sweet syndrome

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Objective: Acute febrile neutrophilic dermatosis (Sweet syndrome) is the most common neutrophilic dermatosis. A dense dermal neutrophilic infiltrate is the usual histological findings. The absence of histological image of vasculitis has been considered a characteristic of the disease and a distinctive feature of the other neutrophilic dermatoses. However, recent reports suggest that vasculitis should not exclude the diagnosis.
Method: This retrospective study examines 32 cases collected over a period of 14 years (1996–2009). We studied its clinical and histological characteristics. Skin biopsy specimens were reviewed to determine the prevalence of vasculitis.
Results: Sweet syndrome is significantly more common in women than in men (sex-ratio=1/15). The patient's mean age was 51 years. Disease developed most often in autumn. Atypical presentation was noted in 18 patients. Skin biopsy revealed a sweet syndrome pattern in all cases. The prevalence of vasculitis (vessel wall damage with fibrinoid necrosis) was 28 % (9 of the 32 patients).
Conclusion: Our series of patients is particular by the frequency of atypical clinical presentation and the presence of vasculitis in histologic examination, a feature that shouldn't exclude the diagnosis. It was suggested that vasculitis in Sweet syndrome represents an epiphenomenon rather than a primary immune-mediated process.

PS-24-017

Dermal lymphangitic carcinomatosis as a primary manifestation of lung carcinoma: Report of an unusual case

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Objective: Although dermal lymphangitic metastases are reported to range between 1 and 4,5 % of all visceral carcinomas, their presence as a primary manifestation of the tumor is rather unusual.

Method: We report the case of a 77 year old man presenting with an erythematous plaque of the right hemithorax.
Results: Macroscopically the lesion had irregular borders and was mildly infiltrative with a violet hue. Microscopic examination revealed tumor cells within lymphatic spaces, without infiltration of the adjacent stroma. The histologic and immunophenotypic characteristics of these cells were compatible with a carcinoma of lung origin. CT scan revealed a lung mass as well as multiple liver and chest wall metastases.
Conclusion: Malignancies originating from the breasts, lungs and large bowl are the most common to involve the lymphatic net of the skin. Melanoma on the other hand is more frequently presenting with lymphangitic invasion, whereas inflammatory carcinomas may also affect lymphatic vessels and may be confused with erysipelas. The revelation of the primary origin is not always easy and differential diagnosis should also include gynecological malignancies, kidney and urinary bladder carcinomas. In our patient the diagnosis was established on the grounds of histology and immunohistochemistry, and was supported by the clinical and radiological findings.

PS-24-018
Inverted follicular keratosis
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Objective: Inverted follicular keratosis (IFK) is almost always a solitary lesion occuring mainly in adult life. Men are affected twice as often as women. Pathologically, They can be confused with a variety of lesions, both benign and malignant. Squamous carcinoma is the most serious differential diagnosis.
Method: We decribe a retrospective study about 7 cases of IFK diagnosed over a 18-year-period (1994–2012).
Results: We collected 7 lesions, all treated by surgical excision. Haemalum eosin sections were studied in all cases. All lesions were single. Five, of them, were situated on the face and two on the scalp. All the patients were adults with a mean age of 34 years, average between 19 and 66 years. They presented mostly as asymptomatic papules and all were small lesions. The different sections of the lesion showed skin well delineated endophytic epithelial proliferations with inverted papillomatous and acanthotic components containing several circumscribed squamous eddies. They was no atypia, mitotic activity necrosis or stromal invasion.
Conclusion: IFK pose very real diagnostic problems unless one is aware of this entity. In fact, they may mimic malignant lesions especially squamous cell carcinoma, both clinically and pathologically.

PS-24-019
Primary cutaneous follicular lymphoma with prominent spindle cell areas. So called spindle cell follicular lymphoma. Case report
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Objective: Spindle cell type variant of cutaneous follicular lymphoma is a rare histologic variant of primary cutaneous follicular lymphomas. It is caracterised by the presence of spindle and bizarr cells. We present a case of a 25 years old man who had a nodule on his scalp and two smaller nodules on his frontal region. We examined an excisional biopsy specimen of the forehead.
Method: HE, Stains all and Immunohistochemical stains were used.
Results: Histology revealed dense lymphoid infiltrate showing nodular pattern in the dermis and in the subcutis. The lymphoid infiltrate predominantly composed of large centrocytes. There were areas where the neoplastic cells show spindle cell morphology with bizarre nuclei and in these areas the stroma were myxoid, mucinous. With immunohistocemical stains the neoplastic cells were positive for CD20, Bcl-6, and negative for CD5, CD10, vimentin, CD34, S100, actin, desmin, AE1/AE3. CD21 showed residual network of follicular dendritic cells in the background.
Conclusion: Spindle cell lymphoma is a very rare variant of cutaneous follicle centre cell lymphoma and the presence of the spindled bizarre cells can cause differential diagnostic problems. The main differential diagnostic entities are primary or metastatic spindle cell sarcoma and spindle cell melanoma. Careful morphological and immunohistochemical analysis are required to the correct diagnosis.

PS-24-020
The histopathologic and immunohistochemical features of mycosis fungoides
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Objective: The histopathologic diagnosis of early mycosis fungoides (MF) is often difficult. The lesions can mimic a variety of inflamatory dermatitis. We aimed to establish and draw attention to the most frequent histopathologic and immunohistochemical features of MF.
Method: We reviewed 115 skin biopsies of clinicopathologically diagnosed MF cases at Medical University of Ankara. We looked for a) epidermotropism, atypical lymphocytes, morphologic features in the epidermis, dermoepidermal junction and dermis b) immunohistochemical

staining ratios of CD3, CD4, CD8, CD20, CD30 and expression loss of CD5, CD7.
Results: Atypical lymphocytes) (96 %), dermal fibrosis (90 %), epidermotropism (86 % single cells, 44 % linear arrangement, 15 % Pautrier's microabscesses, 83 % 'haloed' lymphocytes), epidermal acantosis (72 %), basal vacuolar degeneration (focally 43 %, marked 15 %) and a perivascular lymphocytic infiltrate were the most common and important features. Dermal edema (46 %) extravasated erythrocytes (34 %), spongiosis (27 %), eosinophils (17 %) and necrotic keratinocytes (14 %) were the less seen and non-specific ones. Immunohistochemical results correlated with a ratio of 78 % CD4, 22 % CD8 positive MF. Expression loss of CD7 was seen in 73 %, CD5 in 31 % of cases.
Conclusion: Diagnosis of early MF requires the correlation of morphologic, immunohistochemical and clinical features. Also due to the disease's heterogenity, biopsies from different locations and rebiopsies will enhance the diagnosis.

PS-24-021
Connexins of cutaneous melanocytic tumours
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Objective: Connexins (Cx) form transmembrane channels that can transport ions and small regulatory molecules between adjacent cells. They also function as hemichannels and through protein interactions and are involved in the control of cell replication and maintenance of multicellular homeostasis.
Method: We have tested the expression of connexins in melanocytic tumours using immunohistochemistry in tissue microarrays of 21 common and 73 dysplastic nevi, and 61 primary and 23 metastatic malignant melanomas.
Results: Cx23 was not found in melanocytic tumours despite expressed in the basal epidermis. Cx30.3 reaction showed punctate cell membrane staining in 71 % of naevi in their superficial regions including atypical nests, and displayed cytoplasmic staining in 28 % of melanomas. Low levels of Cx32 were revealed in the cytoplasm of >80 % of naevi and melanomas but only 23 % and 8 % showed membranous positivity, respectively. Cx36 perinuclear/cytoplasmic immunostaining was observed in 57 % of naevi and 24 % of melanomas and as cell membrane reaction in 24 % and 12 %, respectively. Punctate Cx43 reaction was detected in vertical tumour nests in 69 % of naevi, while only 11 % of melanomas proved positive and showed cytoplasmic Cx43 delocalization.
Conclusion: Therefore, most tested connexins were significantly down-regulated in malignant vs. benign melanocytic tumours that possibly contribute to their malignant phenotype.

PS-24-022
Quantitative follow up study of CD 1a, CD 8 and CD 68 positive cells in multiple basal cell carcinoma cases after combined treatment
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Objective: In last years appear more cases with multiple basal cell carcinomas (BCC). Skin immune system reaction is especially important in nonsurgically treated cases. Aim of study is to evaluate the dynamics of CD 1a, CD 68, CD8 marked cells in BCC and in skin adjacent to tumour (5 and 10 mm) before and after the treatment with cryotherapy and imiquimodum.
Method: From 68 BCC cases with multiple tumours investigated immunohistochemically, in dynamics we have characterized 8 patients. Antibodies for CD1a, CD8, CD68+ cells in derma and epidermis were used. They were evaluated in 3 fields of vision (400×) before and after treatment. 5 % imiquimod cream and double freezing was used. Control group: three normal skin samples. Statistical analyses of results were done.
Results: After treatment were erythema, then crust and exfoliation. Microscopically expressed fibrosis instead BCC was found. Amount of immune cells before and after treatment were: CD8 25±3,1/34±4,8 (also in epidermis), Langerhans cells 7±2,3/14±3,4, CD 68 19±3,8/10±2,9.
Conclusion: All immune cells of skin react to the combined treatment of BCC in radius of 5 mm. There is significant statistical difference between the numbers of Langerhans cells in normal epidermis and in BCC cases treated with cryomethod and imiquimodum.

PS-24-023
Regulatory T-cells in invasive and in situ squamous cell carcinoma of the skin and actinic keratosis
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Objective: Regulatory T-cells (Tregs) participate in tumor tolerance and facilitate tumor growth and Foxp3 transcription factor is necessary and sufficient for their development and function. We investigated the presence of T-regs in invasive (IN) and in situ (IS) squamous cell carcinoma (SCC) of the skin and actinic keratosis (AK).
Method: Tregs were identified using immunohistochemistry for Foxp3 and recorded using image analysis in 55 cases of INSCC (and their adjacent IS, AK or benign tissue (BN), when present), in 18 cases of IS and 46 cases of AK (and

their adjacent BN tissue). Statistical analysis was performed using the paired *T*-test. *p*-values <0.05 were considered statistically significant.

Results: In INSCC cases, Tregs in the tumor were more numerous than the adjacent BN (n=46) (mean 155 vs. 79, p <0,001). Additionally, adjacent IS had more Tregs than adjacent AK (n=6) (160 vs. 86, p=0,045). Significant differences between INSCC, and IS or AK were not observed. In IS and AK cases, Tregs were more numerous than the adjacent BN (206 vs. 42, p<0,001 and 148 vs. 47, p< 0,001), respectively.

Conclusion: Treg infiltration of the skin increases early from the precancerous AK, indicating early involvement of Tregs in the development of SCC.

PS-24-024

Cutaneous mastocytosis: Report of 6 cases

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Objective: Mastocytosis is a rare disorder and its true incidence is unknown. Skin is most commonly involved, followed by the bones and the gastrointestinal tract.

Method: Five men presented with many brown lesions in the trunk and one woman with multiple redish brown nonpruritic macules in the extremities. We used immunohistochemistry for c-kit and tryptase for the definite diagnosis. The expression of CD25 and CD2 were also evaluated.

Results: Histology showed five cases of urticaria pigmentosa with severe diffuse infiltration of the papillary dermis by mast cells and one case of telangiectasia macularis eruptiva perstans (TMEP) with scattered mast cells around dilated capillaries and venules of the papillary dermis. The mast cells were positive to c-kit and tryptase and only in one case there was a coexpression of CD25 and CD2 >50 % of the mast cells. In that case involvement of bone marrow was observed and the diagnosis of indolent systemic mastocytosis was established according to WHO 2008 criteria.

Conclusion: Urticaria pigmentosa is the most common form seen in adults while TMEP is an uncommon form that occurs exclusively in adults. The skin involvement in indolent systemic mastocytosis is a part of the spectrum of the disease.

PS-24-025

Subvisual nuclear characteristics are different between keratoacanthoma and keratoacanthoma-like squamous cell carcinoma

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Objective: The differential diagnosis between keratoacanthorna and keratoacantoma-like squamous cell carcinoma may be extremely diffcult. Our objective was to study whether computerized image analysis could be helpful.

Method: In 34 patients biopsies of keratoacantoma-like lesions were taken at admission. One month later surgical excision was performed in growing lesions, whereas regressing lesions were left untreated. A final diagnosis was established combining clinical and histological evaluation, Digitalized images from KI-67 immunostained and hematoxylin counterstained sections of first biopsies were obtained. Tumor nuclei were marked interactively. An inhouse computer program analyzed the geometric relations between the nuclei. Nuclear gray values and their histogram entropy were calculated.

Results: 27 keratoacnthomas and 7 keratoacantomalike squamous cell carcinomas entered this investigation. Basic variables of the geometric analysis did not differ between the two entities regardless whether all nuclei or only the Ki67 positive ones had been examined. Chromatin gray values were significantly lower and their histogram entropy higher in the keratoacantoma-like squamous cell carcinomas.

Conclusion: Basic geometric variables do not seem to be different beteen both lesions, but a shift in the gray value histogram to lower values with increased entropy in carcinomas indicated important differences of the chromatin structure, Supported by FAPESP and CNPq.

PS-24-026

Non-infectious erythematous papular and squamous lesions of the skin in our institute, with clinicopathologic correlation

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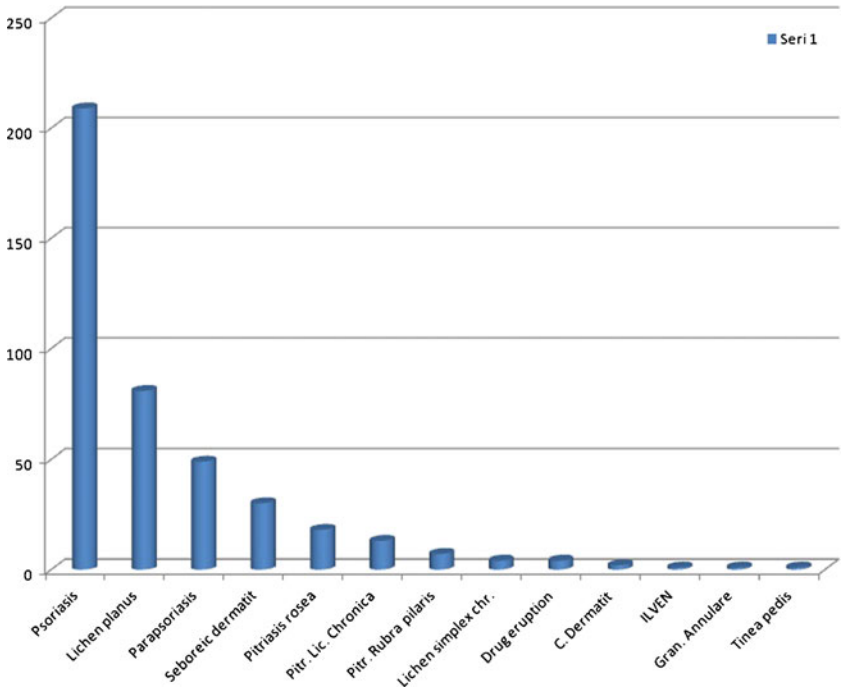
Objective: Non-infectious erythematous, papular and squamous lesions of the skin are basic lesions that pathologists differentiate in routine laboratory examinations. Our aim has been to analyse these lesions by pathologic and clinical findings in our institute with determining clinicopathologic correlation.

Method: In our study 420 cases prediagnosed as erythematous, papular and squamous lesion by dermatologists and evaluated in pathology laboratory between 2004 and 2010 have been reviewed.

Results: The lesions comprised %14.3 of the total load of surgical pathology and 9.1 % of total number of skin biopsies. The highest percentage was in the 41–50 year age group (39.1 %) with a female predominance of 51.2 %. The limbs were most frequently involved (36.9 %). Psoriatic

lesions were the commonest (50.7 %), classic generalized plaque variant psoriasis (89 %) being the most frequent. Correlation with the histopathologic diagnosis was positive in 75.3 % cases and negative in 24.7 % cases.

Conclusion: The contribution of histopathology to the final diagnosis was significant. It confirmed the diagnosis in 75.3 % cases and gave the diagnosis in 7.3 % cases.



PS-24-027

Vulvar lichen sclerosus: A misnomer for an entity with decreased fibrillar components and increased amorphous components in extracellular matrix remodeling

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Objective: The hyalinization of subepidermal skin is one of the histopathological characteristics of the vulvar lichen sclerosus (VLS). It was found that patients with VLS present autoantibodies against the extracellular matrix protein 1 (ECM-1) and the deficiency of this protein is responsible for the development of a different disease, the Lipoid Proteinosis. This disease shows a similar histology with VLS and has better characterized morphology.
Method: We analyzed 20 VLS patients biopsies and the control group was composed by 20 vulva samples from authopsy. The biopsies and control samples were analysed by immunofluorescence for collagen I, III and V and th total collagen fibers by Picrosirius staining. The elastic fibers were stained with Verhoeff and the proteoglycans and glycosaminoglycans with Periodic Acid-Schiff and Alcian Blue. Collagen quantification was performed through image analysis.
Results: It was observed a significant reduction in all studied collagens as well as in the elastic fibers. On the other hand, the proteoglycans were increased in the VLS biopsies.
Conclusion: This study did not found an increase in collagen sclerosis that would justify the term used for the LS. It was observed a predominance of the edema area probably caused by the increase of glycoproteins as in lipoid proteinosis.

PS-24-028

Combined high-grade basosquamous carcinoma and malignant melanoma of the scalp (malignant basomelanocytic tumor) metastasizing to the breast. A case report

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Objective: Background. Basal cell carcinoma (BCC) is a very low grade, usually not metastasizing skin malignancy, which needs to be radically excised.
Method: Methods. An 80 year-old woman was treated for a 3×2,2 cm multinodular mass in the scalp. One month later

an ultrasonography of the left breast showed a 5,5 cm mass which was excised with clean margins. Axillary lymph nodes were free of metastasis.
Results: Results. The dermal tumor presented well demarcated basaloid epithelial nests with squamous differentiation focally connected with the epidermis. They showed peripheral palisading and high nuclear grade with pleomorphism, brisk mitotic activity and multiple prominent nucleoli. Atypical cells, arranged as strips, nests or isolated elements, were observed at the tumor edge, separated by a grey-zone from the overlying malpighian epithelium. Immunostains were positive for cytokeratins, melanocytic (S-100/HMB-45/MART-1) and neuroendocrine (CD56/NSE/Cromogranin) markers. The 4,8 cm breast tumor corresponded to a high grade metastatic BCC with reactivity for epithelial markers, S-100 and CD56.
Conclusion: Conclusions. The literature reported 32 cases of combined tumors composed of BCC and malignant melanoma (MM) with 5 patients showing local recurrences. The term << malignant basomelanocytic tumor >> describes these biphasic tumors. The knowledge of this entity expands the differential diagnosis of skin tumors with melanocytic component.

PS-24-029
Superficial granulomatous pyoderma: Three cases of this rare variant
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Objective: Pyoderma gangrenosum (PG) was described at first by Brocq and named by Brunsting et al. in 1930. Superficial granulomatous pyoderma (SGP) was described as a variant of PG in 1988. We present three cases of this rare variant.
Method: There were two women and one man with age ranging from 40 to 78 years. All of them had a long history of a slowly enlarging, eritematous and ulcerative plaque in different areas including leg and breast skin. A biopsy was performed in all cases.
Results: The superficial dermis showed neutrophilic inflammation with an admixture of granulomatous inflammation and sinus formation. There wasn't vasculitis and fat tissue was not affected.
Conclusion: SGP is a rare variant of PG. Diagnosis of this entity generally is made on the basis of skin biopsy results with all features mentioned previously and a typical clinical appearance. Most of times, these lesions are diagnosed as granulomatous dermatitis, thinking in infectious pathology. This is the most important differential diagnosis, because SGP is responsive to corticosteroids. The pathogenesis of PG is unknown, though is now believed to altered neutrophil chemotaxis and some authors suggest that SGP may be a delayed-type hypersensitivity to an unknown antigen. Pathergy is the inciting factor in several patients.

PS-24-030
High concordance in BRAF status between native-BRAF malignant melanoma and matched lymph node metastases
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Objective: The discovery of selective v-raf murine sarcoma viral oncogene homolog B1 (BRAF) V600 mutation as an oncogenic mutation in cutaneous malignant melanoma (MM) has changed the treatment paradigm for melanoma. Selective BRAF inhibitors have demonstrated response rates far higher than standard chemotherapeutic options. BRAF mutation analysis is usually performed on primary tumour tissue; however, no conclusive data are available on the concordance of test results between primary tumours and corresponding metastases. We assessed the concordance of BRAF mutation status in a study of 16 primary BRAF-native tumours and their corresponding lymph node metastases.
Method: 16 patients with histologically confirmed non-mutated BRAF MM who underwent surgical resection of the primary tumour and positive selective lymph node biopsy or lymphadenectomy were included. Mutation status was determined by means of a realtime PCR assay (Cobas 4800 BRAF V600 Mutation Test, Roche Molecular Systems).
Results: There was a 100 % concordance of the BRAF results in primary tumor and corresponding metastases in 16 analyzed pairs.
Conclusion: Our findings show total concordance in BRAF status between primary BRAF native tumors and their paired metastases, and suggest that acquisition of BRAF V600 mutation in metastases from primary native tumors is a rare event.

PS-24-031
Dermatoscopic and histologic score correlation in atypical Spitz/Reed nevi
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Objective: Different dermatoscopic scores of pigmented skin lesions have provided a valuable tool in daily routine practice to differentiate malignant from benign lesions.

However, these semiquatitative methods have a high rate of false positives in Spitz/Reed nevi. We have compared semiquantitative histopathologic and dermatoscopic findings in a series of Spitz/Reed nevi.
Method: We collected 19 cases (15 female and 4 men) of atypical Spitz and/or Reed nevi. All cases were microscopically confirmed. A histologic index (HI) was constructed scoring the following findings: symmetry, sharp demarcation, architectural dysplasia, melanocytic atipia and nest size, and compared with validated dermatoscopic scores (ABCD score, 7-point checklist and Menzies score). Distributions of these scores for the different dermatoscopic patterns were also analyzed.
Results: Median age at presentation was 15 years (range 1 to 36). The HI varied from 0 to 5 points. We found a strong positive correlation between the HI and Menzies score (r=0,539, p=0,01). In addition, HI values differed significantly when the multicomponent dermatoscopic pattern group was compared with the other patterns (U=22, 5 Z=−2,25, p=0.01).
Conclusion: Menzies is the only dermatoscopic score which strongly correlates with histologic findings in Spitz/Reed nevi and may be useful in the diagnosis of atypical lesions.

PS-24-033
Correlation of nonmolecular and molecular subtyping of inherited epidermolysis bullosa
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Objective: Inherited epidermolysis bullosa (EB) is a heterogeneous group of hereditary mechanobullous diseases with skin blister formation of variable severity and numerous extracutaneous manifestations. EB comprises three main groups and many subtypes and their recognition is important for prognosis and genetic counselling.
Method: We examined skin biopsy samples of 42 patients with EB using transmission electron microscopy, immunofluorescence antingen mapping (AM) and their peripheral blood samples by mutational analysis.
Results: In the total number of 42 cases, concordant results of molecular and nonmolecular methods were found in 35 cases (83 %). In 7 patients (17 %) mutational analysis did not confirm the results of ultrastructural and AM analysis.
Conclusion: Strong correlation in the results obtained by different methods was observed. Using combination of nonmolecular and molecular diagnostics methods high diagnostic accuracy can be achieved.

PS-24-034
Granulomatous Slack Skin (GSS): A case report with evidence of T cell clonality
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Objective: GSS is a very rare variant of MF. We describe an additional case of this rare disorder in a 42 yo female that has been approved by TCRB&G Tcell Clonality Assay.
Method: A 42 yo female with a single bulky skin lesion in the inguinal fold which had first appeared 6 y before and enlarged up to 20 cm, referred to plastic surgery for esthetics. H&E section of the deep skin biopsy of lesion showed a granulomatous infiltrate in the dermis. Nuclear atypia and epidermotropism is not significant. But there is numerous multinucleated histiocytic giant cells. Elastophagocytosis are present. TCRB&GT cell Clonality Assay showed a clonal rearrangement in TCR gamma gene. She was referred to dermatology for treatment and now she is getting UVA1 phototherapy.
Results: The diagnosis of GSS is difficult in early stages of the disease. Clonal rearrangement of TCR genes can be a useful diagnostic tool in early stages of the disease.
Conclusion: 20–50 % of patients with GSS carry a risk for the development of a second malignancy. GSS may be associated with lymphoproliferative disorders. Therefore, follow up of the patient is important. This case report supports that GSS is an indolent variant of MF due to clinical, histological and T-cell gene rearrangement results.

PS-24-035
Unusual occurrence of multicentric reticulohistiocytosis with systemic involvement in childhood
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Objective: Multicentric reticulohistiocytosis (MR) with systemic involvement is an extremely rare disease afflicting mainly adults.
Method: We report a case of SR arising in a 3 year 7 month old boy with concomitant celiac disease.
Results: Since 6–7 months, he developed several brown to dark-red skin nodules (up to 0.8 cm) located mainly on face and arms; current episode include hemorrhagic syndrome, severe pancytopenia and massive hepato-splenomegaly. Bone marrow aspirate ruled out acute leukemia and tezaurismoses; bone marrow biopsy and skin biopsy showed important infiltration with numerous large cells with abundant fine granular/ground glass eosinophilic cytoplasms in a

reactive inflammatory stroma (lymphocytes, few plasma cells and few eosinophils); bone marrow cells were mononucleated, cutaneous cells were both mono&multinucleated; tumor cells immunophenotype was consistent with histiocytes (CD68+, S-100 protein + (faint), CD1a-, langerin-) both in bone marrow and skin biopsies; no hemophagocytosis was seen. MR with systemic involvement of skin, bone marrow, liver and spleen was diagnosed. Cyclophosphamide therapy was instituted with initial diminishing of splenomegaly; latter on, despite adding cyclosporine and etoposide, no further impact on pancytopenia and hepatosplenomegaly was recorded.

Conclusion: Complete hematologic examination is mandatory for patients diagnosed with cutaneous reticulohistiocitosis, irrespective of their age, in order to identify MR and institute proper treatment.

PS-24-036

Primary cutaneous follicle centre lymphoma: A case report and review of literature

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Objective: Primary cutaneous follicle centre lymphoma (PCFCL) is an indolent, primary cutaneous B-lymphoma with an excellent prognosis but a high incidence of reccurence. Apart from standard surgery and local radiotherapy, targeted strategies with anti-CD20 (rituximab) has introduced new treatment modalities.

Method: Woman, aged 82, with solitary skin lesion on her face. After surgical excision, histo- and immunohistochemistry with the ABC system on paraffin embedded tissue was performed.

Results: Microscopically, a non-epidermotropic perivascular and periadnexal neoplastic infiltrate with a follicular growth pattern was observed. The lesion consisted of predominantly medium-sized centrocytes and several centroblasts enmeshed in a network of CD23(+) dendritic cells. Immunohistochemically, the neoplastic lymphoid cells were CD20, CD79a, BCL2 and BCL6 positive. CD30, MUM1 and Ig were all negative. The patient received one cycle of rituximab and 6 months later is free of disease.

Conclusion: Primary cutaneous B-cell lymphomas (CBCL) account for 25 % of cutaneous lymphomas. PCFCL is one of the three major categories of CBCL, recently classified by WHO, (the other two: PCMZL and PCDLBCL, leg-type). BCL-2, except for systemic follicular lymphoma, it can also occur in PCFCL, as in our case. PCFCL, usually locally treated with surgery and radiotherapy, could possibly offer a candidate for anti-CD20 targeted therapy, especially in multifocal lesions.

PS-24-037

Concurrent CD8 and CD30 positivity: Pityriasis lichenoides et varioliformis acuta (PLEVA) or lymphomatoid papulosis?

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Objective: Thirteen and ten years old male patients admitted with 4 months interval, having diffuse hemorrhagic papules on extremities and trunk. The first has not responded to methorexate previously. The second had varicella infection 3 months before and, his rushes spreaded out recently.

Method: Multiple punch biopsies of the first patient revealed epidermal necrosis, basal vacuolisation and subepidermal diffuse infiltrate composed of CD3 and mostly CD8 positive T cells showing a striking angiocentric distribution. There were CD30 positive large cells with vesicular nuclei both in epidermis and dermis. Some of the vessels exhibited lymphocytic vasculitis with fibrinoid necrosis. Punch biopsy of the second patient revealed subcorneal pustule, dyskeratosis and basal vacuolisation, papillary dermal edema, erythrocyte extravasation and severe lymphocyte-rich cellular reaction infiltrating the interface. Lymphocytes were CD3 and mostly CD8 positive. In between, there were large cells with vesicular nuclei exhibiting CD30 positivity.

Results: Diagnoses were PLEVA based on the vascular and interface changes in accordance with clinical findings. Both patients responded to oral antibiotics.

Conclusion: PLEVA is among the reactive conditions that can simulate CD30 positive lymphoproliferative diseases. Although CD8 positive lymphomatoid papulosis is defined in pediatric patients, no response was seen to oral antibiotics.

PS-24-038

Are HMB-45 and MIB1 results reliable for safe diagnosis of nevi?

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Objective: Melanocytic lesions having subtle features suspicious for malignancy create considerable difficulty in decision-making.process. Lack of deep HMB-45 positivity and low dermal MIB-1 index can be reliable tools in association with morphology.

Method: Twenty-seven acquired melanocytic lesions in which HMB-45 and MIB-1 have been performed are reviewed to determine the importance of these markers in routine diagnostic practice. Asymmetry, focal loss of maturation, presence of mitoses, epidermal consumption and lymphocytic inflammation were the morphological features that have created difficulty especially when seen alone in a bland appearing nevus.

Results: All cases with epidermal consumption and/or mitoses and nearly half of cases with inflammation, asymmetry and focal loss of maturation was associated with.focal deep dermal HMB-45 positivity. Thirteen cases had an MIB-1 index of ≤1 %. Two of 3 cases with MIB-1 index of >1 % had also HMB-45 positivity and/or inflammation. The case with a MIB-1 index of 8 % was an acral nevus bearing 4 of the evaluated morphological features.
Conclusion: Focal deep dermal HMB-45 positivity goes parallel with epidermal consumption and dermal mitoses, mostly used prevailing criteria of malignancy in melanocytic lesions but it's expression is not adequate for diagnosis of melanoma. Low MIB1 index can be a reliable marker of benignity.

Wednesday, 12 September 2012, 09.30 - 10.30, Congress Hall Foyer 3rd Floor
PS-25 Poster Session Infectious Diseases Pathology

PS-25-001
Ionic imbalance, renal pathology and lack of effect of adjuvant treatment with methylene blue in the hamster model of leptospirosis
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Objective: Leptospirosis in humans usually courses with hypokalemia and hypomagnesemia, and the putative mechanism may be related to nitric oxide production. Methylene blue is a known inhibitor of inducible nitric oxide synthase, and have beneficial effects on clinical and experimental sepsis.
Method: Serum creatinine and ionic changes were evaluated at various time points (4, 8, 16 and 28 days) in hamsters. We also determined the effect of methylene-blue treatment when used as adjuvant therapy combined with a late start of standard antibiotic (ampicillin) treatment.
Results: Rather than K and Mg depletion, hyperkalemia and hypermagnesemia were observed during acute infection. These findings are probably associated with an accelerated progression to renal failure, since this model is not feasible to mirror the supportive therapy (including fluid expansion) that retards progression to the oliguric/hyperkalemic state. Infected hamsters at day 8 presented diffuse tubular cell swelling with mild or no nephritis. At days 16 and 28 they showed variable degrees of acute tubular changes, regeneration of tubular epithelia and nephritis. Survival and renal pathology did not differ among different treatment groups.
Conclusion: Adjuvant methylene blue had no effect on the survival, renal pathology or Mg and K serum levels during acute-phase leptospirosis in hamsters.

PS-25-002
Occupation of the striated muscle fibre by Trichinella spiralis is associated with increased intracellular sialylation
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Objective: The knowledge about glycoproteome in skeletal muscle is limited and most of the information come from studies on aberrant glycosylation in inherited muscle diseases. This work describes the intracellular changes in sialylation of skeletal muscle fiber during the process of its transformation into a nurse cell after occupation by the nematode Trichinella spiralis.
Results: The study was performed at defined time points post infection. Lectin histochemistry with TML, MAL and SNA detected increased production of sialylated glycoproteins within the affected fibers, and it was evaluated by acidic ninhydrin reaction in muscle homogenates. Increase of total sialyltransferase activity was estimated by measurement of incorporated CMP-N-[14 C]-acetylneuraminic acid, and immunohistochemistry showed higher expression of α-2,3-sialyltransferases II and IV within the affected fibers. SNA lectin affino-blots showed at least four protein bands with approximate molecular weight between 126 and 159 kDa, which were more reactive to SNA compared to their counterparts from the control samples.
Conclusion: It is evident that skeletal muscle injury induced by Trichinella activates biosynthesis of glycoproteins bearing sialic acids, which are not present in the normal muscle fiber. However, the protein identity, function and the biological significance of these sialoglycoproteins remain to be elucidated. BG051PO001-3.3.04/46, 28.08.2009; ITMS: 26240120023.

PS-25-003
Cerebral amebic abscess in immunocompetent patients: Two case report
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Objective: Protozoal and helminthic infestations of the central nervous system (CNS) are rare and their incidence is less than 1 %. They are more common among children, the elderly and immunocompromised individuals and tend to follow a fatal course.
Method: We report 2 cases of cerebral amebic abscess occurring in 2 immunocompetent men.
Results: They were 2 men aged of 43 and 18 years old. Headache; altered mental status and fever were common presenting symptoms. In the 2 cases the diagnosis of cerebral abscess was suspected on cerebral CT scan. Histopathologic analysis revealed extensive areas of necrosis and hemorrhage with granulomatous lymphoplasmacytic inflammatory infiltrate.

Different structures (isolated or forming small clusters) with the morphological characteristics of amoeba trophozoites were identified in the areas of necrosis with and without an inflammatory reaction. The diagnosis of cerebral amebic abscess was then made. The 2 patients received antibiotic treatment.
Conclusion: Cerebral amebic abscess is rare but has poor prognosis. It should be considered as a diagnosis for any patient with subacute and/or chronic meningoencephalitis without evident bacterial etiology. More effective antibiotic drugs can be chosen for post-surgical treatment; furthermore, better survival may be achieved by diagnosing the disease in early stages.

PS-25-004
Morphometric characteries of women placenta which can be different forms of syphilis
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Objective: Many literary information give us about getting down coefficient of fertitity -placenta at women which suffer from pregnancy with syphilis.
Method: Verified data analysis about morphometric placentae and it's comparison with newly- born child at 50 women which suffer from different forms of syphilis.
Results: Research placenta with syphilis show us the area of placenta surface is decreased, it was formed primary syphilis −297,+−42,1 sm, secondary −316,8±28.8sm and with latent form of syphilis 319,7±28.8(at control 331.4±234,8sm2 $p>$ O.l), at that time as a mass, placentary cell was been bigger and it formed (at primary- 589.1±32.7gr and at secondary- 568,2±25,5gr and at latent form of syphilis 582.8±20.7gr, then in control (555,0±35,7) but all this different were been statistically unreliable ($p>0,05$). Comporision mass of placenta and mass newly born- child show us corfficient of fertitity-placenta is make up (5,86±0,21) and actually it is not different at control fact group.
Conclusion: The change coefficient of fertitity -placenta was typifying for until penicillin era, that time. When actual condition, treatment syphilis with antibiotic to bring on development phathomorphism placentae with out different coefficient of fertitity -placenta.

PS-25-005
Influenza B virus-associated pneumonia: Report of one fatal case associated with sickle-cell trait
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Objective: Influenza virus pneumonia complicated with acute respiratory distress syndrome is rare and has a high mortality rate. Patients with sickle cell trait are asymptomatic, however, complications with increased risk of thromboembolism can occur.
Method: Case report: A 30-year-old woman with no preexisting medical conditions presented nonproductive cough and fever for 4 days. For the next 3 days, developed acute respiratory failure. She was treated for septic shock and acute respiratory distress syndrome without success with death. Expectoration and blood cultures were negative and the real-time polymerase (RT-PCR) of the thracheal swab was positive for influenza B virus.
Results: The autopsy showed a diffuse necrotizing alveolitis and intra-alveolar hemorrhage with pulmonary infarction. There was no histological evidence of bacterial pneumonia. An evident blood cell sickling was observed associated with sickle cell trait. RT-PCR was also positive for influenza B virus in pulmonary tissue and the immunohistochemistry was negative for influenza A virus.
Conclusion: Severe hypoxemia caused by the acute respiratory distress syndrome was a possible cause of the blood cell sickling and thrombotic events.

PS-25-006
Report of three lupus vulgaris cases
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Objective: Lupus vulgaris (also known as "Tuberculosis luposa") are painful cutaneous tuberculosis skin lesions with nodular appearance, most often on the face around ears nose, eyelids and lips, cheeks. ıt is still a major health problem in developing countries. Cutaneous tuberculosis is a rare form of extrapulmonary tuberculosis. Lupus Vulgaris (LV) is the most common form of cutaneous tuberculosis. LV should make differential diagnosis other granulomatous disease. All three cases of old female patient.
Conclusion: Herein, three cases were presented which they treatment with correlation clinical and histopathological examination.

PS-25-007
Actinomycosis: A retrospective study of 56 cases
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Objective: Actinomycosis is a rare, chronic, and slowly progressive granulomatous disease caused by filamentous Gram positive anaerobic bacteria from the Actinomycetaceae family. It is often misdiagnosed because it can mimic

other conditions such as malignancy and tuberculosis. It occurs normally in the mouth and tonsils, however, it can sometimes occur in the chest, abdomen, pelvis or other areas of the body.

Method: We describe a retrospective study about 56 cases of actinomycosis diagnosed over a 21-year-period (1990–2011).

Results: The 56 cases were divided in 20 cervicofacial actinomycosis, 18 genito-urinary tract actinomycosis, 8 cutaneous actinomycosis, 7 abdominal actinomycosis and 3 cases occur in central nervous system. All patients were symptomatic. The most frequent symptom consisted in fever. The diagnosis was based on histologic study in all cases. Tissue histologic studies show suppurative and granulomatous inflammatory changes, connective proliferation, in which bacteria form typical granular colonies composed of radiating gram positive filaments.

Conclusion: Diagnosis of actinomycosis is usually made retrospectively by means of histologic examination of surgically obtained specimens, but rarely preoperatively. It is generally treated with long term antibiotics.

PS-25-008

Expression of angiogenesis factors in placentas with intrauterine transmission of HIV

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Objective: Placenta plays an important role in the prevention of the mother-to-child transmission of HIV during pregnancy. The purpose of this investigation was to study expression CD31, bFGF and TGFβ in human placentas in cases of intrauterine HIV infection.

Method: Group A - 11 placentas from women and children with HIV infection. In control – Group B, were 16 placentas from women without HIV infection. On paraffin slices expression of CD31, bFGF, TGFβ and p24 was evaluated. We counted the area of positive cells related to the square of the slice.

Results: In all placentas with HIV infection p24 has been found in placental macrophages and villi's vessels. In group A expression of CD31 in endothelial cells was 4,22±0,85 % of the slice's square (in control - 3,69± 0,53 %) ($p>0,05$). Expression of bFGF in villi's stroma was 5,49±1,48 % (in control - 4,01±0,6 %) ($p>0,05$). Expression of TGFβ in villi's vessels was 11,2±3,6 % (in control - 2,71±0,63 %) ($p<0,05$).

Conclusion: Thus, placentas in cases with intrauterine transmission of HIV are characterized by increased expression of TGFβ the significance of this fact is still to be evaluated.

PS-25-009

1709 unilocular cystic echinococcosis in Erzurum during last 30 years

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Objective: Unilocular cystic echinococcosis which Echinococcus granulosis causes is seen frequently in the animal husbandry practised underdeveloped countries.

Method: The 1709 unilocular cystic echinococcosis cases which were seen in the eastern part of Turkey, in 30 years between 01.01.1981 and 01.01.2010, except Faculty of Medicine of Atatürk University are presented.

Results: Organ distribution: Female: Liver 557 (SD:15.614), lung 259 (SD 15.928), spleen 42 (SD 13.108), abdomen 25 (SD 11.55), kidney 21 (SD 11.92); Male: Liver 331(SD 15.406), lung 233 (SD 18.027), spleen 25 (SD 10.12), brain 23 (SD 11.55), soft tissue 15 (SD 14.197).

Conclusion: The frequently seen organs in both gender are liver and lung. The rarely seen organs were spleen 67, brain 40, abdomen 39, kidney 36, vertebrae 29, soft tissue 27, pleura 26, bone 25, breast22. The others were very rare: eye 4, gallbladder 4, thyroid 4, neck 4, ovary 1, testis 1.

PS-25-010

Relation of the length of appendix and parasitosis: Preliminary report

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Objective: Is there an effect of the length of appendix vermiformis on the settlement of the bowel parasites? We have decided to research.

Method: It was studied retrospectively for not to be under the influence. Randomly chosen from the archives, 65 parasitic appendix (41 women + 24 men) and 65 appendix vermiformis (41 women and 24 men) lengths were compared. The last 65 appendix materials of the appendixes which include parasites (56 E.vermicularis, 8 A.lumbricoides,1 T.saginata) and operated any causes were examined. Placeholder conditions such as fibrous obliteration and tumour were excluded. The premeasured length of the appendix in the series (65+65=130) were listed with the gender.

Results: Appendix length in the control series: The length of appendix in men:7.15 The length of appendix in women:6.85 The length of appendix in both gender:6.95 cm. The length of parasitic appendix: The length of appendix in men:7.30 The length of appendix in women:6.76 The length of appendix in both gender:6.94.

Conclusion: The mean length of appendix in both series was about 6.95 cm. There were no important difference of the length of either parasitic appendixes or all cause appendectomy materials. In this study, it is concluded that there isn't an effect of the length of appendix on the settlement of bowel parasites.

PS-25-011

About a rare and challenging disease: Multiple thoracic hydatidosis

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Objective: Cystic hydatid disease (CHD) is an infection produced by larvae of the parasite platyhelminth Echinococcus granulosus. Living in a rural area is an important risk factor for this disease. It is still an endemic disease in some regions of the world, particularly in many Mediterranean countries. The organs most commonly affected are the liver and the lungs.
Method: We present a new case of multiple thoracic hydatidosis.
Results: We present the case of a 37-year-old Caucasian man who presented chest pain and dyspnea. Chest-x-ray showed a well limited cardiac opacity of the upper lobe and of the right lung. Chest-CT-scan showed a mediastinal cyst evoking a hydatid cyst in the left ventricle associated to a right pleural effusion. The patient underwent surgery that consisted in the drainage of multiple pericardial cysts, cystectomy of a left ventricle cyst and right pleural cystectomy. Microscopic examination showed a pleura-pulmonary and cardio-pericardial hydatidosis. The patient was treated with albendazole and did not present complications or recurrences after 1 year of follow up.
Conclusion: Multiple thoracic hydatidosis is rare. Cardiac location is the most challenging because it is difficult to manage and is life threatening. Treatment modalities are mainly based on surgery. Preventive measures are necessary to avoid disease recurrence.

PS-25-012

Role of peripheral lymph node biopsy in patients with HIV infection

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Objective: Lymphadenopathy is frequently present in HIV positive patients, especially in those with severe immune deficiency and consequently elevated risc of opportunistic infections and neoplasms. Considering the large spectrum of possible differential diagnosis a thorough lymph node analyses should be performed.
Method: We examinated 30 peripheral lymph nodes from 27 patients from latero-cervical, axilar, inguinal and supraclavicular regions; 10 nodes (33,3 %) had diameter less then 1 cm.
Results: Histopathological findings indicated mycobacterial infection in 15 patients (55,5 %), reactive hyperplasia in 7 patients (25,9 %), lymphoma in 3 patients, metastasis from Kaposi sarcoma in 2 and supurative inflamation in 1. Clinically suspected lymphoma was microscopically infirmed in all 4 cases. 4 cases of tuberculosis, 1 of lymphoma and 1 of Kaposi sarcoma metastasis were identified, all of them without prior clinical suspicion We identified tuberculosis, lymphoma and metastasis in 33,3 % of nodes smaller then 1 cm.
Conclusion: In 74 % of cases lymph node biopsy identified tuberculosis or malignancy, and established a reliable diagnosis in various clinical suspicions. We consequently emphasize the importance of lymph node examination in the evaluation of lymphadenopathy in HIV positive patients, even is not prominent. Stăniceanu and Nichita are first authors in equal contribution.

PS-25-013

The importance of autopsy in HIV infected patients

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Objective: Nowadays possibilities of medical investigations offer miriads of accumulating data regarding HIV infected patients status. Correlation and/or validation of these informations with pathological findings is mandatory to establish in order to ensure appropiate management of HIV infection.
Method: We performed a comparative study between clinical/paraclinical and autopsy findings in some of the most frequent afected organs in HIV infection; we studied in 31 HIV positive patients autopsied between 2000 and 2011; all patients had no or incipient (up to 1 year) antiretroviral treatment.
Results: 26 patients presented lung pathology, clinico-pathological correlations revealing 13 discrepancies, 13 total concordances and 5 partial concordances. Most of these inconsistencies referred to opportunistic infections, clinically suspected and pathological refuted in 9 cases and clinically unsuspected and pathological identified in 7 cases. Clinically suspected neurological alterations were microscopically infirmed in 33,3 % of cases, while 3 cases presented unsuspected lesions. Opportunistic infections were

detected in 38,8 % of liver examinations and in 38,0 % of lymph nodes, all of them clinically unsuspected.
Conclusion: Autopsy evaluation allows proper selection of relevant biological/clinical/paraclinical data in order to establish a better understanding of this complex disease. Stăniceanu and Nichita are first authors in equal contribution.

PS-25-014

Morphological features of erythropoietin and mesenchymal stem cells application in experimental sepsis in rats

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Objective: On the basis of recently detected receptors for erythropoietin on the surface of MSCs we hypothesized that introduction of EPO together with MSCs may enhance their effect and improve the results of sepsis treatment.
Method: 50 Wistar male rats were randomized into 5 groups with 10 animals in each: Group1 - the healthy controls, 2–5 Groups were intraperitoneally introduced bacterial LPS 20 mg/kg. Group3–4 got×105 allogeneic MSCs, Group4 - 8.5 μg of recombinant EPO-beta, Group 5 - MSCs and EPO in the same doses. The morphological study of liver, spleen, thymus, lung and kidney was performed. Histological specimens were evaluated by qualitative, semi-quantitative and quantitative methods.
Results: In lung tissue the thickness of alveolar septums progressivly reduced from Group 3 to 5.In kidney and liver tissue the dystrophy of hepatocytes and nefrocytes and a blood vessel's dilatation in studied groups also reduced.In lien tissue we observed hyperplasia of white pulp in groups 4 and 5. Structural features of thymus were connected with patterns of T-lymphocyte proliferation and differentiation.
Conclusion: Combined treatment with EPO and MSCs can reduce acute lung injury and kidney damage, cause hyperplasia of lymphoid tissue and enhance the immune response more than separate treatment in an experimental model of sepsis in rats.

PS-25-015

Mycobacterial spindle cell pseudotumor of the liver

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Objective: Spindle cell pseudotumors are rare manifestations of mycobacterial infections. We describe a case in the liver in an immunocompromised patient with tuberculosis.
Method: A 28-year-old man, with active substance dependency, HIV-1 infection known for 7 years and acquired immunodeficiency syndrome for 3 years, was receiving tuberculostatic medication for disseminated tuberculosis and investigated for persistent fever. A liver ultrasonography confirmed a moderate hepatomegaly and showed multiple dispersed nodules in both lobes, with 1 to 3 cm of greater diameter.
Results: A needle biopsy from one of the nodules showed a proliferation of spindle cells without atypia, grouped in intersecting bundles, with immunoreactivity to vimentin, CD68 and lysozyme and negative for CD34, pS100, SMA and desmin; a Ziehl-Neelsen stain revealed several acid fast bacilli in the spindle cells. They were PAS negative.
Conclusion: Pseudotumoral lesions in hepatic tuberculosis usually correspond to granulomatous inflammation. A spindle cell proliferation, like that seen in other organs are more frequently associated with non tuberculous mycobacteria, is very rare. We found only another case in the literature of liver spindle cell pseudotumor associated with tuberculosis. This lesion must be differentiated from mesenchymal neoplasms.

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Sixteen months follow-up in a treated case of Whipple Disease (WD)

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Objective: WD is a rare, multi-systemic infection caused by a ubiquitous environmental bacteria -Tropheryma whipplei - that affects the duodenum and small intestine but also the brain, endocardium, skin, lungs and joints.
Method: We are presenting a 49 years old man with a 2 years history of diarrhea, malabsorption and weight lost (about 30 kg). Endoscopical examination revealed an unspecific, yet unusual pattern of lesions: small, yellow, multiple, slightly elevated patches involving duodenum and jejunum. Histological examination revealed numerous foamy macrophages in lamina propria with PAS (+), Ziehl-Neelsen (−) material in cytoplasm.
Results: Treatment with trimethoprim/sulfamethoxazole was initiated with a spectacular response: after 2 days of therapy the patient had normal stool and in 6 months he already gained back 20 kg. After 1 year of treatment the biopsy confirmed a partial remission with fewer macrophages persisting in lamina propria of duodenum. After 16 months of treatment (March 2012), very few macrophages with PAS (+) material are still identified on duodenal biopsy.
Conclusion: WD is a potentially fatal disease with unspecific clinical and endoscopical signs that can be diagnosed on duodenal biopsies. Histological follow-up is a useful tool of managing the treatment and histopathological confirmation of the absence of foamy macrophages is mandatory in discontinuing therapy.