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ORIGINAL ARTICLE

Salivary type tumors seen in consultation

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Abstract The aim of this study is to characterize personal consultation practice in salivary pathology and to identify most common diagnostic challenges. Seven hundred sixty consultation requests were prospectively indexed over 12 months, and 205 cases of salivary type tumors were identified. The following data were recorded: anatomic site, patients' age and gender, geographic origin of cases, diagnoses by submitting pathologist and consultant, and turn-around time. Final diagnosis was offered by submitting pathologist in 77 of 205 cases (37.5%). The definitive diagnosis was provided to contributors in 188 of 205 cases (91.7%); diagnostic limitations and potential adequacy issues were addressed in 17 remaining cases. The average turn-around time was 4.4 days. The three most common diagnostic problems were acinic cell carcinoma, epithelial myoepithelial carcinoma, and adenoid cystic carcinoma. Pathologists' adherence to recommendations by Association of Directors of Anatomic and Surgical Pathology regarding consultation practice is described.

Keywords Personal consultations · Salivary gland pathology

Introduction

Pathology consultation cases usually originate from two main sources: referral cases, also known as institutional consults (IC), in which the patient had been referred to a tertiary center for therapy or second opinion; and *consultation-only cases or personal consults* (PC), in which a second opinion was being sought but the patient was not being referred for therapy. These practices are summarized by the Association of Directors of Anatomic and Surgical Pathology (ADASP) in a 1993 report [1].

IC have been the subject of numerous studies [2–6] and included head and neck subsites [7, 8]. The focus of such studies is fairly concrete: accuracy with respect to an expert "gold standard" and impact of expert reclassification on patient management and outcome. Studies of PC are far more challenging, uncommon [9–11], always retrospective, and to date have not been performed in head and neck pathology. For PC, a final diagnosis is not rendered by the contributor, and thus is not exactly "reversed" by an expert. Therefore, assessment of concordance and accuracy is less meaningful here. Thus, a more pragmatic approach to analysis of PC would be to identify problematic areas and document the approach to resolution.

In order to describe the commonly encountered challenges in a head and neck consultative practice, we prospectively collected data on PC received by the Head and Neck Division at University of Pittsburgh Medical Center (UPMC) over a 1-year period. This real-time evaluation of PC revealed that salivary type tumors represent a major diagnostic dilemma. In this study, we focus on the commonly encountered problems in salivary gland pathology.

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Materials and methods

About 40,000 surgical specimens are accessioned annually at UPMC-Presbyterian University Hospital (PUH), and 5,000 are from the head and neck organs. Three pathologists have extensive expertise in Head and Neck Pathology. Two Head and Neck Pathology fellows were in training during the academic year of this study (2007–2008). PC cases referred to UPMC Head and Neck Division were prospectively identified—760 cases over a 12-month period (Aug 2007 to July 2008; excluding endocrine cases). Of 760 cases, 205 cases were salivary type tumors, which are characterized in this study. This study is approved by Institutional Review Board (no. 0601084).

Indexed data The following data were recorded prospectively: age, gender, geographic location, and type of pathology practice where cases originated from academic, community, or commercial laboratory, number of slides and blocks submitted for review, and anatomic site. We categorized initial diagnoses as "none", "preliminary", or "final". In cases where final diagnosis was made, we further looked for the presence of a comment "case sent for additional extradepartmental review, addendum to follow". When no such a comment was present, we recorded who requested the consultation (e.g., clinician, patient) and how much time passed between the original sign out date and the date case was received at UPMC. Turn-around time (TAT) was measured in days, including weekends and holidays. When tissue block was required and was not submitted initially, TAT was calculated from the day block was received. If consultation was delayed for more than 7 days (n=36 cases), a written explanation of the delay was included in the report (e.g., conference time, extensive immunohistochemical [IHC] work-up). Most consultation cases were submitted by the pathologist within 6-week period after tissue was collected. All information was extracted from documentation submitted with pathology material. Since we were not involved in gross evaluation of consultation cases, we generally did not comment on adequacy of excision.

If necessary, *additional information* sometimes unavailable to the referring pathologist, such as radiologic appearance or clinical symptoms, was provided to us by clinician at our request. IHC studies were performed as previously described [12]. Most commonly used abbreviations of salivary type tumors are as follows: acinic cell carcinoma (ACC), adenoid cystic carcinoma (AdCC), epithelial myoepithelial carcinoma (EMCa), mucoepidermoid carcinoma (MEC), pleomorphic adenoma (PA), hyalinizing clear cell carcinoma of salivary origin (HCCC), low-grade cribriform cystadenocarcinoma (LGCCAC), polymorphous low-grade adenocarcinoma (PLGA).

Cost: A $250 fee was charged per consultation case.

Results

General characteristics of consult cases

The demographic and geographic features, submitted material, and TAT along with other general features of consultation cases are summarized in Table 1. The diagnoses rendered by consultants and anatomic distribution of cases are summarized in Table 2. Hematoxylin and eosin (H&E) slides alone were sufficient for diagnosis in only 27% of cases (55 of 205). Tissue blocks were initially submitted along with H&E slides in 43% of cases (89 of 205). Blocks were requested in 30% of cases following the review of initial H&E slides (61 of 205) and were received on average within 4.5 days.

Final or preliminary diagnoses were rendered in 153 of 205 cases (75%). Fifty-two cases were received without pathologists' interpretation: 25% of cases from community practices (36 of 142), 47% of cases from commercial laboratories (eight of 17), and 17% from academic institutions (eight of 46). Most of the cases with a final diagnosis (50 of 73, 68%) had a "disclaimer" in the final diagnosis or diagnostic comment field—"consultation pending".

Adherence to recommendations by Association of Directors of Anatomical and Surgical Pathology [1] All cases were accepted for consultation. The rendered diagnosis was always communicated to the submitting pathologist as a written report transmitted via fax. If the case was sent to more consultants after our opinion was rendered, we were not made aware of this fact. Gross description with cassette summary accompanied all cases. Fifty-one of 205 cases did not include the cover letter explaining the reason for consultation, specific questions to be answered, or working diagnosis. All slides were shipped in an adequate manner—No glass slide was received broken [13]. All materials that cannot be duplicated (tissue blocks and cytology slides) were returned. All recuts and special studies performed at UPMC PUH were retained.

Most common diagnostic challenges: epithelial myoepithelial carcinoma

General features of 21 EMCa are summarized in Table 3. Nineteen EMCas were located in the parotid gland (90.4%), one in submandibular gland (4.3%), and one in sublingual gland (4.3%). Tissue blocks/blank slides were provided in ten cases and requested by consultants after initial H&E evaluation in nine additional cases. Two cases were signed out based on H&E and IHC performed by submitting pathologists. Preliminary and final diagnoses rendered by submitting pathologists in cases diagnosed by consultants

Table 1 Demographic and other characteristics of patients and material

Demographic features	Men (number)/average age (years), %	86/56 (42%)
	Women (number)/average age (years), %	119/59 (58%)
Practice type (number, %)	Academic	46 (22%)
	Commercial	17 (8%)
	Community	142 (70%)
Slides per case, average		10
Cases received with accompanying blocks		89 (43%)
Cases with blocks requested following review of original H&E slides		61 (30%)
Turn-around time		4.4 days
Contributors' diagnoses	Final, with comment "consultation pending" [a]	50 (25%)
	Final, without the comment "consultation pending"	23 (11%)
	Preliminary	80 (39%)
	None	52 (25%)
Geography[b]	31 states; 125 different departments; top 5 contributors—PA (49[c]), CA (15), OH (14), FL (11); ≥5 cases were received from 17 states	

[a] Consultation was requested by clinicians in nine cases and patients in two cases

[b] One international case was received

[c] Of 49 PA cases, 11 were sent by University of Pittsburgh Medical Center-affiliated hospitals.

as EMCa are summarized in Table 4 (Electronic supplementary material).

Histologically, the majority of EMCa (17 of 21, 81.0%) showed a biphasic tubular proliferation of pale eosinophilic cuboidal inner/luminal cell layer surrounded by an often clear cell outer myoepithelial layer (Fig. 1a). However, in this series, clear cells dominated in only 11 of 21 cases (52.3%). Immunohistochemically, luminal cell layer was strongly positive for low molecular weight cytokeratin cocktail CAM5.2 (Fig. 1b), while the outer myoepithelial cell layer was positive for p63 (Fig. 1c), actin, and/or calponin (Fig. 1d). Of note, nine of 21 (42.8%) cases showed at least partial encapsulation (Fig. 1a). Of the named variants of EMCa, oncocytic and apocrine variants were noted in six of 21 (28.6%) cases (Fig. 1e). Here, the bi-layered appearance was maintained. However, the epithelial layer and often, the myoepithelial cell layers, showed abundant granular eosinophilic cytoplasm. In the apocrine EMCa, the epithelial component also showed periapical snouts, large nuclei with vesicular chromatin, and prominent nucleoli. This cell layer was positive for androgen receptor (Fig. 1f).

Adenoid cystic carcinoma

AdCC comprised 20 of 205 (9.8%) of salivary consultation cases. General features of AdCC are summarized in Table 3. Site distribution was as follows: parotid gland—five (25%), palate—two (10%), tongue—two (10%), buccal mucosa—one (5%), maxillary sinus—three (15%), submandibular gland—two (10%), ear—two (10%), nasal cavity—one (5%), nasopharynx—one (5%), neck, and not otherwise specified—one (5%). Preliminary and final diagnoses rendered by submitting pathologists in cases diagnosed as AdCC by consultants are summarized in Table 5 (Electronic supplementary material).

All AdCC were infiltrative basaloid tumors with basement membrane type material deposition (Fig. 2a). These tumors were also biphasic, consisting of an outer myoepithelial and inner ductal layers. However, unlike EMCa, both cell layers were comprised of cells with scant cytoplasm and small angulated, but relatively monomorphic hyperchromatic cells (Fig. 2b and d). Ten of 20 (50%) cases had a tubular or cribriform predominant morphology, while seven of 20 (35%) had solid predominant (Fig. 2c) morphology. The myoepithelial contribution to the tumor diminished as the solid component increased. Additionally, three of 20 (15%) cases had evidence of high-grade transformation (HGT) [14].

Acinic cell carcinoma

Twenty ACC were diagnosed over the period of this study. General features of ACC are summarized in Table 3. Seventeen carcinomas arose in the parotid gland, two in the upper lip (biopsies), and one in submandibular gland. Tissue blocks were provided in seven cases and requested by consultants after initial H&E evaluation in three additional cases. Preliminary and final diagnoses rendered by submitting pathologists in cases diagnosed as ACC by consultants are summarized in Table 6 (Electronic supplementary material).

ACC in this series were characterized by a variety of growth patterns: papillary cystic (n=5; Fig. 3d), solid (n=2; Fig. 3a),

Table 2 Diagnoses and anatomic distribution of salivary lesions

Diagnosis	Anatomic site, number of cases							
	(Para)nasal	Ear	Naso pharynx	Neck	Major salivary glands	Oral cavity	Thorax	Total
Acinic cell carcinoma					18	2		20
Adenoid cystic carcinoma	4	2	1	1	7	5		20
Adenoma, NOS					4			4
Atypical PA					5			5
Basal cell adenocarcinoma			1		3			4
Basal cell adenoma				1	4			5
Carcinoma ex PA					12			12
Carcinosarcoma ex PA					1			1
Canalicular adenoma					2	1		3
Cautery artifact					1			1
Cystadenoma					1			1
EMCA					21			21
HCCC						1		1
LGCCAC					3			3
Lymphadenoma					1			1
MEC					9	8		18[a]
Mucocele						3		3
No definitive diagnosis	1		1	1	1	11	2	17
Oncocytic hyperplasia					1			1
Myoepithelial carcinoma	1				8			9
Myoepithelioma					8			8
Normal histology					1			1
Oncocytoma					4			4
PA			1		12	4		19[b]
PLGA	1				1	5		7
Salivary duct carcinoma					10			10
Sialadenoma papilliferum						2		2
Warthin tumor				1	3			4
Total	7	2	4	4	140	42	2	205[a,b]

Of 140 cases located in major salivary glands, 117 cases involved parotid gland, 21 submandibular gland, one submandibular and parotid glands, one sublingual gland

NOS not otherwise specified, *PA* pleomorphic adenoma, *EMCA* epithelial myoepithelial carcinoma, *HCCC* hyalinizing clear cell carcinoma of salivary origin, *LGCCAC* low-grade cribriform cystadenocarcinoma, *PLGA* polymorphous low-grade adenocarcinoma

[a] One MEC was located at base of skull

[b] One additional PA was located in lacrimal gland and one in the larynx

and mixed microcystic and follicular (n=13; Fig. 1e; Table 7, Electronic supplementary material). The key histologic feature of ACC is the presence of zymogene granules, sometimes more obvious on Periodic Acid Schiff stain with diastase (PASD; Fig. 3b). In all but two cases, granules were smaller, fewer, and less basophilic than in classic cases (a combination of features more commonly seen in ACC arising in minor salivary glands). No case showed dedifferentiation or significant areas of clear cells. Prominent tumor-associated lymphoid response was present and mentioned in the diagnostic line in ten of 20 cases. In four cases, the prominence of vacuolated mucous-like cells (Fig. 3c) prompted the differential diagnosis of a mucoepidermoid carcinoma and "sebaceous" differentiation. In all of these cases, mucin appeared to be intraluminal rather than intracytoplasmic. Four cases were further complicated when the predominant cells were "intercalated duct-type cells" (Fig. 3f).

Consultation cases with no definitive diagnosis

In 8% of cases (17 of 205), no definitive confident diagnosis was rendered by consultants. General features of

Table 3 General features of epithelial myoepithelial carcinomas, adenoid cystic carcinomas, acinic cell carcinomas (three most common diagnostic challenges sent for consultation) and cases with no conclusive diagnosis

Feature, total cases	EMCa, 21	AdCC, 20	ACC, 20	No conclusive diagnosis
Average age, years	61.4	59.8	46[a]	57
Men to women ratio	9:12	11:9	8:12	9:8
Type of practice	C-15; Com–2; U-4	C-13; Com-2; U-5	C-12; Com -5; U -3	C-15; Com-1; U-1
TAT, days	4.8	4	2.6	6

Type of practice: C—community, Com—commercial laboratory, U—university

EMCa epithelial myoepithelial carcinoma, *AdCC* adenoid cystic carcinoma, *ACC* acinic cell carcinoma, *TAT* turn-around time (days)

[a] Four patients were younger than 21 [youngest—12 years of age]

these cases are summarized in Table 3. In 13 cases, it was impossible to distinguish between a benign and malignant process. In four cases, while the malignant nature of the process was apparent, the exact type of the cancer remained unclear. This subset of cases required a more extensive review by more than one consultant within our department, leading to a TAT of 6 days (versus 4.1 days TAT in cases where definitive diagnosis was provided). Preliminary and final diagnoses rendered by submitting pathologists in these cases are summarized in Table 8 (Electronic supplementary material). The anatomic distribution of this subset of cases is summarized Table 9 (Electronic supplementary material). Follow-up excisions were sent for two cases with inconclusive diagnosis: One case was confidently diagnosed as a PA. In another case, although the malignant nature of the neoplasm was firmly established (due to the presence of an invasive growth pattern), further classification was still impossible.

Discussion

The popularity of PC can be potentially attributed to many factors, but among the most prominent is the progressive evolution of sub-specialization in medicine. The refinement of clinical oncology and surgery practice places increasing demands on pathologists to provide a level of expertise and sophistication that satisfies this new and changing "standard of care". Unfortunately, the scope of material encountered by most practicing pathologists is still very broad and general. To address the challenge of providing improved expertise in each area, some academic centers adopt subspecialty sign out practice, but for most practices, this is not feasible. Thus, PC to designated experts in subspecialty area has become a viable option.

The current study is the first prospective analysis of a PC practice. While our data collection included all head and neck lesions (excluding endocrine), for this study, we have chosen to report on our experience with salivary type pathology, as this was the most prominent area of our consultative service (205 of 760 cases). The broad geographic distribution of contributors and demographic features of patients allow us to conclude that the problematic diagnostic patterns documented by this study are representative of challenges experienced by a larger pathology community. Regarding the breadth of material received during this 12-month period, almost all salivary type entities (as described in Head and Neck WHO Classification of Tumors) were represented (with the exception of sebaceous tumors, oncocytic carcinoma, and sialoblastoma). Furthermore, the demographic features of more common salivary neoplasms are similar to those described in the largest studies on the topic. For instance, the female predominance, age and anatomic distribution, and prevalence of ACC in this series mirrors those summarized in Armed Force Institute of Pathology atlas of tumors of the salivary glands [15].

For the first time, adherence to the ADASP recommendations for personal consultations is described. Twenty-five percent of consultation requests were NOT accompanied by final or preliminary diagnoses. This is one area for future improvement. Some criteria of consultation practice were never studied before. For instance, the TAT presented here was 4.4 days. For comparison, in this study, the average time required to receive the block once it was requested was 4.5 days. The only other benchmarks for comparison in the literature are the TAT provided by two retrospective European studies conducted by referring institutions (rather than consultants as in the present analysis): 22 days [16] and 32.8 days [17]. The TAT does depend on the diagnostic difficulty of the consult case. For instance, the recognition of classic H&E features of ACC resulted in faster TAT: these cases were signed out on average in 2.6 days. For comparison, the general TAT for all salivary type consultation cases was 4.4 days, and for cases were definitive diagnosis was not rendered, TAT was 6 days (waiting for additional clinical information, imaging studies, deeper H&E levels, IHC).

In 92% of cases (188 of 205 cases), expert pathologist provided the final diagnosis. It is difficult to appreciate the clinical and financial impact of this service.

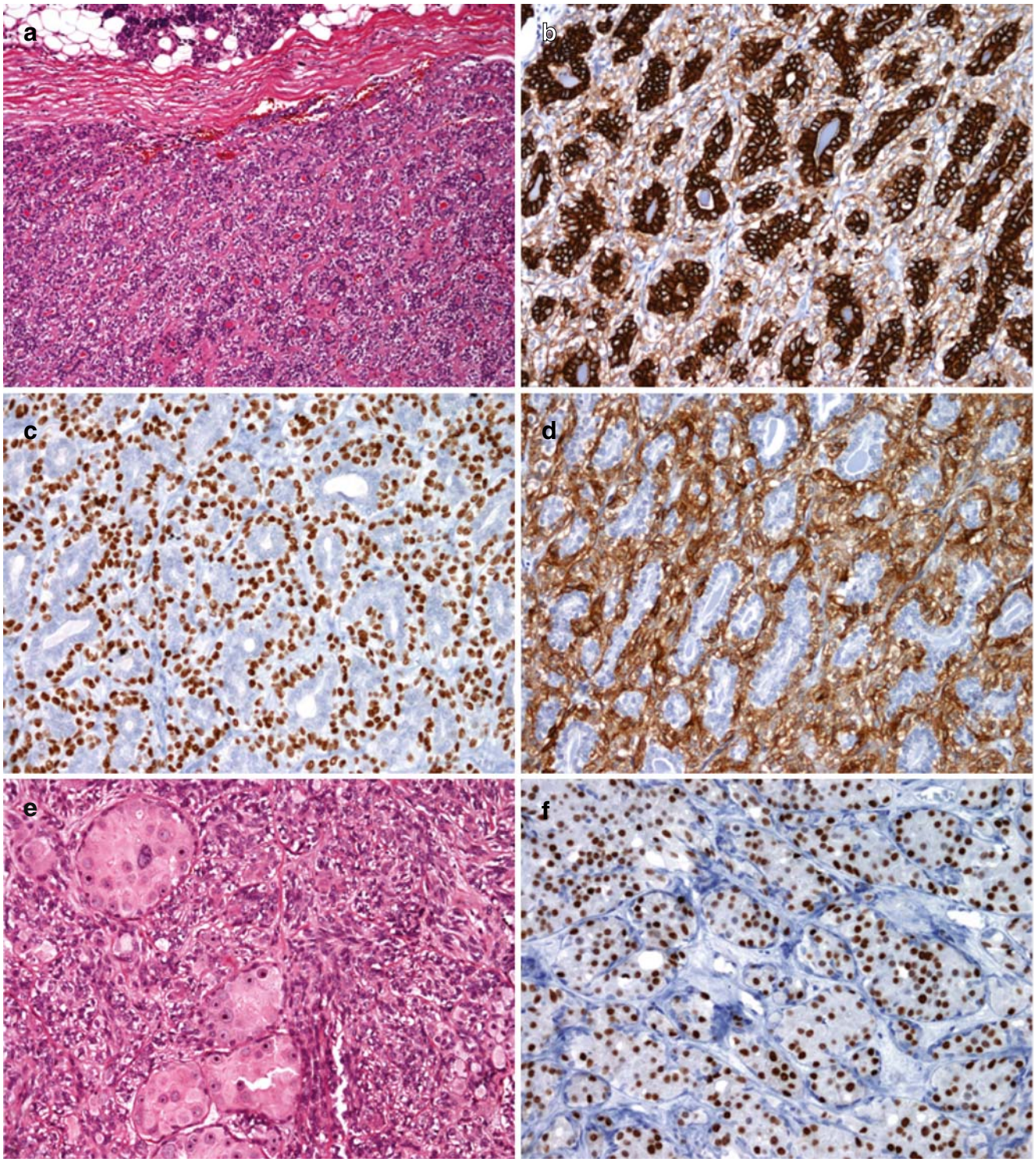

Fig. 1 Epithelial myoepithelial carcinoma diagnostic features. **a** Partially encapsulated EMCa showing a biphasic ductular proliferation of eosinophilic inner cells and clear outer myoepithelial cells, H&E, ×100. **b** CAM5.2 highlights luminal cells, IHC, ×200. **c** The outer myoepithelial cell layer is positive for p63, IHC, ×200. **d** Myoepithelial cells are highlighted by calponin, IHC, ×200. **e** Apocrine variant of EMCa with epithelial layer showing abundant granular eosinophilic cytoplasm, prominent nucleoli, H&E, ×400. **f** Luminal cells with apocrine features are positive for androgen receptor, IHC, ×200

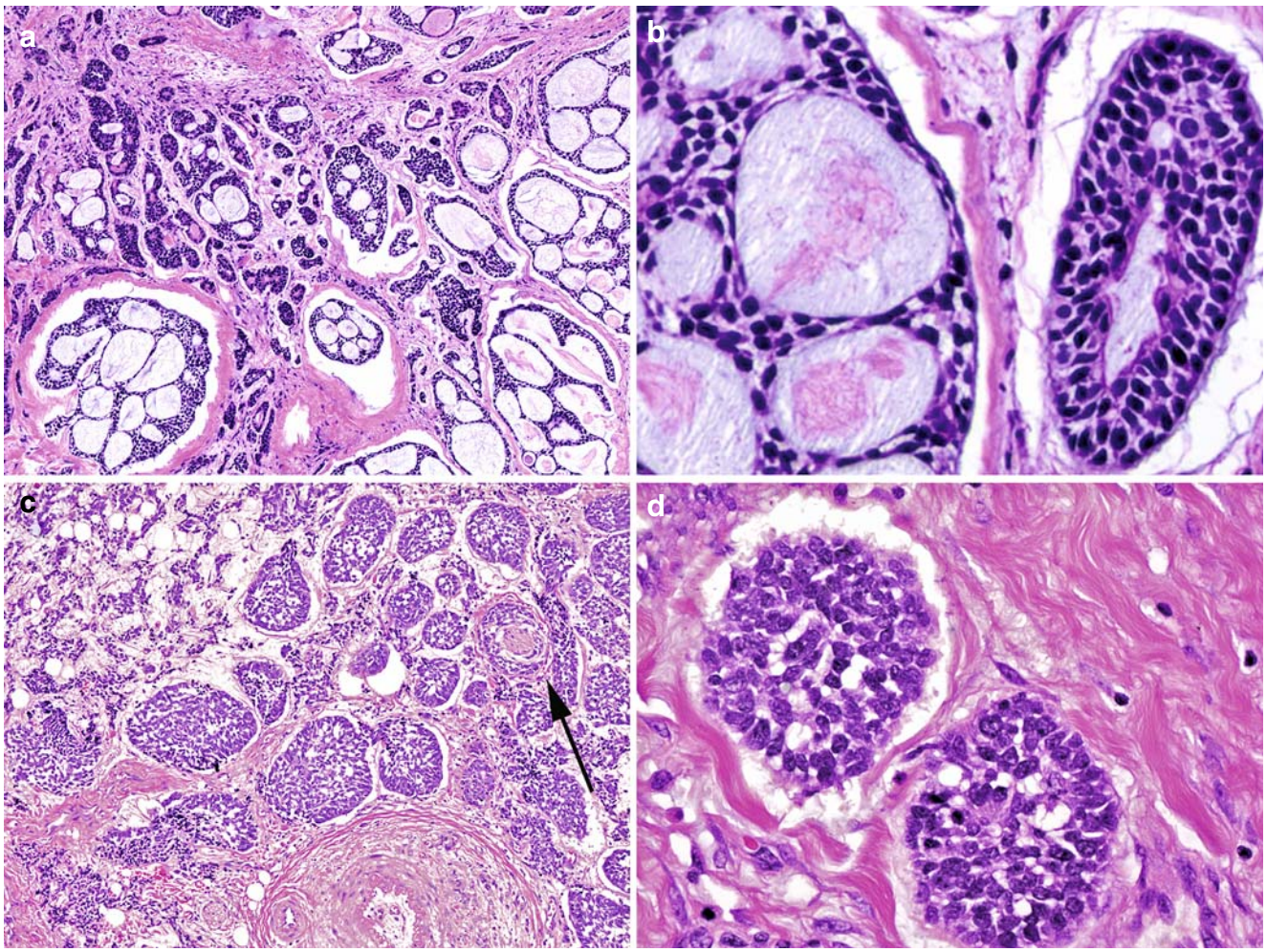

Fig. 2 Adenoid cystic carcinoma diagnostic features. **a** AdCC showing a basaloid cribriform patterned proliferation of tumor cells in myxohyaline matrix, H&E, ×100. **b** The distinguishing nuclear characteristics of AdCC are hyperchromasia, angulation, and monomorphism shown here. Also present is the characteristic clefting of tumor nests from stroma, H&E, ×400. **c** Solid AdCC showing perineural invasion, H&E, ×100. **d** The nuclear features are similar to the cribriform AdCC in Fig. 2b, H&E, ×400

Epithelial myoepithelial carcinoma

These tumors have proved historically to be difficult to recognize and categorize [15]. One of the major challenges in the accurate diagnosis is the rarity of this tumor. Additionally, the biphasic arrangement of tumor cells can show numerous patterns and variants [12]. Occasionally, one component may predominate, obscuring the biphasic nature of the tumor. As shown above, IHC stains can "unmask" the biphasic nature.

Another issue encountered here was the deceptively bland appearance of this low-grade malignancy. These tumors usually infiltrate in a multinodular fashion rather than angulated infiltrative nests. In our consult experience, at least partial encapsulation is relatively common, raising the possibility of a benign biphasic tumor, most notably of a cellular PA. As we noted in our previous series [12], this distinction may be extremely challenging particularly if the EMCa had arisen from PA, as noted in two cases in this study. Distinguishing features from PA include documentation of invasion, even if nodular or minimal, and absence of chondromyxoid stroma in EMCa.

Another perhaps less apparent reason for diagnostic difficulty is the restrictive nature of the AFIP definition requiring that the outer cell myoepithelial cell layer shows clear cytoplasm [15]. We characterized oncocytic and apocrine variants of EMCa that defy the classic definition and yet to date behave in a fashion similar to "classic" EMCa [12]. In this study, oncocytic and apocrine variants comprised over one fourth of our EMCa. This high prevalence of "non-classic" EMCa is likely reflective of "consult bias" towards unusual cases.

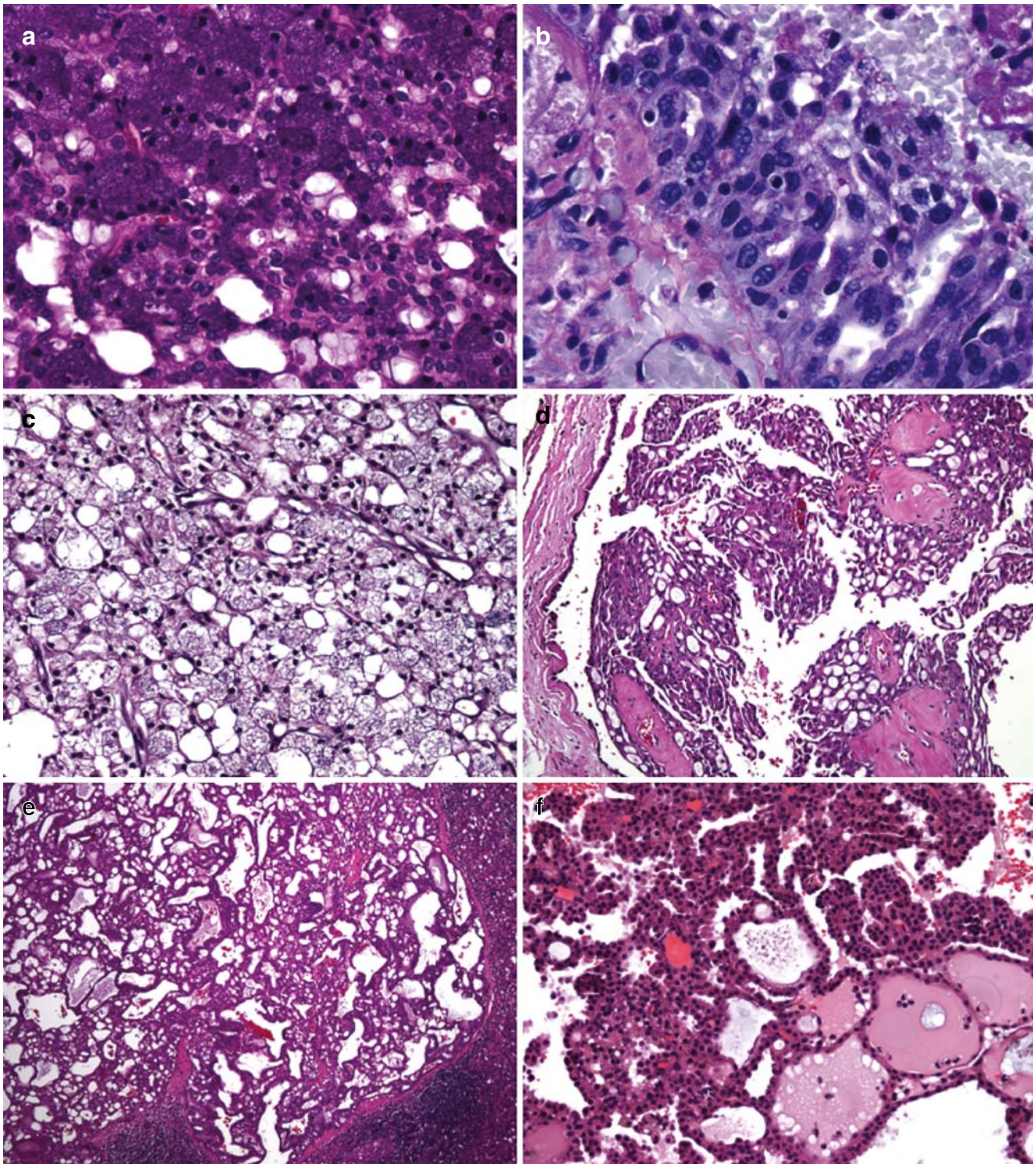

Fig. 3 Acinic cell carcinoma diagnostic features. **a** Classic well-differentiated acinic cell carcinoma with acinic cells with basophilic granular cytoplasm arranged in a solid pattern, H&E, ×200. **b** Rare cytoplasmic zymogene granules highlighted by periodic acid shift stain with diastase treatment (PASD resistant; PASD, ×400). **c** A representative area of acinic cell carcinoma with numerous modified serous/acinic cells showing vacuolated cytoplasm, H&E, ×200. **d** Papillary-cystic pattern of acinic cell carcinoma, H&E, 100×. **e** Mixed follicular and microcystic pattern of acinic cell carcinoma and tumor-associated lymphoid stroma, H&E, 100×. **f** Cuboidal intercalated duct-type cells arranged in mixed follicular and microcystic patterns; minimal to none acinic serous differentiation, H&E, ×200

Once the biphasic nature of a tumor is recognized and is confirmed to be malignant by its permeative growth, perineural, and/or angiolymphatic invasion, the differential diagnosis narrows to AdCC, basal cell adenocarcinoma, and oncocytic carcinoma (with respect to the oncocytic EMCa variant). Both EMCa and AdCC are biphasic tumors with the same phenotype—inner ductal and outer myoepithelial layers. However, AdCC tends to be more infiltrative and comprised of cells with more hyperchromatic and angulated nuclei with scanter cytoplasm. We have also noted clefting of tumor nests from the surrounding stroma/basement membrane type material to be more common in AdCC. In EMCa, the retraction artifact is more commonly seen between the luminal and outer layers (personal observations). Basal cell adenocarcinomas to some extent are biphasic tumors that may show central ducts and some outer myoepithelial cells. A key distinguishing morphologic features from EMCa is the presence of peripheral palisading of the outermost layer in basal cell adenocarcinomas. Only some of the outer basal cells in basal cell adenocarcinoma are myoepithelial (expressing p63 *and* actin/calponin); the rest express p63 only. Oncocytic carcinomas may show p63 positive cells; however, in contrast to a bona fide oncocytic EMCa, these cells are small, indistinct, and randomly distributed [18]. Apocrine EMCa, a newly described variant [19], is also oncocytoid in appearance but the ductal component has vacuolated cytoplasm, periapical snouts, and nuclear pleomorphism typical of apocrine change and reminiscent of salivary duct carcinoma. Additionally, these areas express androgen receptor similar to salivary duct carcinoma [20, 21].

Adenoid cystic carcinoma

AdCC, though more easily recognized, is still a significant part of our consult practice. Contributors are aware that not all basaloid or cribriform patterned salivary gland malignancies are automatically AdCC. To some extent, the predominant growth pattern dictates the differential diagnosis. For tubular/cribriform patterns, the biphasic tumor differential mentioned above comes into play, in addition to low-grade salivary gland malignancies such as PLGA, and rarely benign entities such as a cellular PA or basal cell adenoma. In contrast, solid AdCC and AdCC with HGT evoke high-grade diagnostic considerations, including carcinoma ex PA, salivary duct carcinoma, and non-salivary lesions such as neuroendocrine carcinoma, basaloid squamous cell carcinoma, or even a lymphoma. Our consult data appear to support this concept (see Table 5, Electronic supplementary material).

For the tubular and cribriform patterned AdCC, key diagnostic features are the recognition of the biphasic growth pattern and angulated dark nuclei. A historical differential diagnostic consideration is PLGA. It is interesting to note that this was not a significant issue in our consult practice. In our opinion, this consideration has diminished greatly with the characterization of salient morphologic features of PLGA [22]. PLGA is not a biphasic tumor; it is polymorphous in pattern, but fairly uniform in cell type with characteristic ovoid nuclei with open, "papillary thyroid carcinoma"-like chromatin [22]. PLGA is strongly positive for S100 [22].

For solid conventional AdCC, an epithelial phenotype predominates; however, immunostains will show a residual outer abluminal myoepithelial cell. AdCC with HGT, on the other hand, has the appearance of a high-grade adenocarcinoma or undifferentiated carcinoma, and there is no longer an abluminal myoepithelial layer. If the transformed component is present alone, it would be indistinguishable from an adenocarcinoma, not otherwise specified, or a high-grade carcinoma ex PA. Thus, one important diagnostic criterion is the recognition of a residual conventional AdCC component [14].

Acinic cell carcinoma

We have identified three sources of problems in diagnosis of ACC: abundance of mucous and vacuolated cells, tumor-associated lymphoid response, and predominance of non-specific intercalated ductal-type cells.

The importance of tumor-associated lymphoid response as a potential diagnostic pitfall was previously highlighted by Auclair [23]. Unlike acinic cell carcinoma, benign salivary tissue inclusions within lymph nodes are present in parotid gland only and demonstrate *both* ducts and acini [24]. A careful search for zymogene granules on PASD stain, combination of solid, follicular, microcystic, and papillary-cystic pattern along with the predominantly negative p63 immunostain (i.e., absence of epidermoid cells) will lead to the correct diagnosis of ACC.

In addition to highlighting common diagnostic challenges presented by recognizable nosologic entities, we outline here a *subset of biopsies with inconclusive diagnosis* following expert review. When the cytologic features are bland, the mitotic rate is low, and the classic morphologic features for a malignant category (e.g., ACC) are absent, the delineation of benign versus malignant process relies on evaluation of the periphery of the lesion to assess for invasiveness. In the absence of the tumor/normal tissue interface, it is essentially impossible to evaluate for defining features of malignancy: invasive growth, perineural, or angiolymphatic invasion. This does not imply that useful data cannot be gleaned from such biopsies. Here, morphologic characterization and immunohistochemical studies can at least narrow the differential diagnostic considerations, which were offered in all cases. The most common diagnostic line employed in this group of lesions was "biphasic salivary neoplasm". The differential diagnosis of

biphasic salivary tumors included AdCC, EMCa, and cellular PA. Of note, even when malignant nature of the biphasic carcinoma is obvious, reliably distinguishing between an AdCC and EMCa might still be a difficult task (one case in this series). Clear cell neoplasms were another perennial problem encountered on this biopsy. The differential diagnosis here is broad and occasionally includes non-salivary/metastatic lesions. Again here, characterizing the immunophenotype of the clear cells (i.e., epithelial versus myoepithelial) may exclude several categories. In some cases, the prohibitively small size of the biopsy results in the diagnostic line "insufficient for diagnosis". Thus, in summary, our general practice is not to make the "line diagnosis" of carcinoma unless at least one of the following criteria is met:

1. High-grade cytologic features, including severe atypia, abundant/atypical mitoses, and/or necrosis.
2. Perineural or angiolymphatic invasion.
3. Infiltration as seen at tumor/adjacent normal tissue (stroma) interface.
4. Morphologic features absolutely classic for a malignant category (i.e., adenoid cystic carcinoma, acinic cell carcinoma).

Further prospective studies with follow-up are required to validate these or other "adequacy" criteria for biopsies of salivary type lesions.

In summary, this prospectively accrued study of personal consultations originating from head and neck sites offers insights into the challenges commonly encountered in salivary gland pathology. Demographic characteristics and TAT benchmarks are established, and adherence by both contributor and consultant to most of ADASP recommendations is described. The commonly encountered named entities in this PC practice include AdCC, EMCa, and ACC. We also herein formalize a problem that is commonly encountered in salivary gland pathology, namely the biopsy of a cytologically bland neoplasm without tumor stromal interface, and offer recommendations on reporting for these biopsies.

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