The Daily Dose: Study Tips for Exam and Board Preparation

David E. Klingman, DMD
Diplomate, American Board of Oral and Maxillofacial Pathology
Diplomate, American Board of General Dentistry

The Daily Dose: salivary gland pathology FEEDBACK

Regarding the four cases:

- basal cell adenoma
- polymorphous carcinoma
- secretory carcinoma
- myoepithelial carcinoma

I offer the following opening comments:

- Salivary pathology is quite challenging and the responses are similar to the responses I gave when I began reviewing these cases, so don't be alarmed by the candid input and suggestion some additional reading; communicating with the experts (many of them identified in the readings) and a lot of reading (of literature produced by those said experts) is what has been the most helpful for me
- As commented, immunohistochemistry is perhaps not commonly employed and in my training program we were not highly encouraged to utilize IHC or molecular testing; however, the more I have read about it, the more I believe IHC and molecular testing have utility

Suggestions to assist with appropriate diagnosis:

1. I consider the list of all the salivary tumors to be less useful than characterizing the tumors first as either benign or malignant, and if malignant as either low grade or high grade tumors
2. I consider fragmented or incomplete specimens or specimens missing 'orientation' to either the surface epithelium, deep structures or adjacent organs and tissue planes to be more or less uncharacterized as either benign or malignant (especially for basaloid lesions or lesions resembling either mixed tumor or polymorphous carcinoma)
3. I then try to characterize the lesions as either solely or predominantly myoepithelial in origin (most commonly these will be either benign mixed tumors or myoepitheliomas), as basal or parabasal in origin (these should be the basaloid entities) or as Raja Seethala et.al. characterize, biphasic tumors
4. I'll look for mucin production; this may lead me to favor entities like mucoepidermoid carcinoma, mucin-producing adenocarcinomas (including the papillary and cribriform types of carcinomas), and also consider some of the sinonasal carcinomas (intestinal and non-intestinal type adenocarcinomas) and metastatic tumors (breast, colon, prostate, etc.) or even some of the sinonasal hamartomas (like respiratory epithelial adenomatoid hamartoma and seromucinous hamartoma)
5. I'll look at stroma for features that might suggest mixed tumor (hyalinization or chondromyxoid features) or polymorphous carcinoma (the slate blue or 'blue goo' background)
6. I always look for circular 'swirling' of tumor around nerves (I like to think if this as 'being flushed down the toilet') which may be a characteristic of polymorphous carcinoma, or easily identifiable perineural or intraneural invasion (most often reported in adenoid cystic carcinoma or high grade adenocarcinomas)

Philosophically I've been grouping certain salivary tumors:

Mucoepidermoid carcinoma, acinic cell adenocarcinoma, zymogen poor acinic cell adenocarcinoma which often turns out to be 'mammary analog' secretory carcinoma, polymorphous 'low grade' adenocarcinoma, and all of the cribriform and ductal/intraductal carcinomas: I find these to all have overlapping histologic features and I have been performing IHC panels and stains on these which include myoepithelial markers and S100, mammaglobin, either PAS-D or mucicarmine and in some cases DOG1... because I just want to be sure which tumor I am looking at [this was my motivation to put together the table and summary in the case of 'low grade salivary duct carcinoma in situ' that I presented at AAOMP in 2016]

I group all the basaloid tumors together; these would include both benign and malignant basaloid tumors (basal cell adenoma versus basal cell adenocarcinoma), high grade transformation of other tumors, basaloid variants of adenoid cystic carcinoma... the recurring theme is that unless a complete excision leads me to believe that the tumor is nothing more than a basal cell adenoma, I don't rely on just cytologic features alone given that even basal cell adenocarcinoma can appear identical to its benign counterpart, and since these tumors include adenoid cystic carcinoma, I favor performing a least a few IHC stains to determine if these are myoepithelial only (which might exclude adenoid cystic carcinoma) or might include something with a biphasic character (like epithelial-myoepithelial carcinoma)

With any 'blue' or basaloid tumor, I also consider whether the lesion might not be a salivary tumor, especially if I can find no features of other salivary gland lesions; in these cases I also consider neuroendocrine tumors, in the sinonasal complex I would also consider sinonasal neuroendocrine and undifferentiated carcinomas and tumors with adenoid cystic carcinoma like features

With any salivary tumor with clear cell features, I will consider (at a minimum) variants of mucoepidermoid carcinoma, oncocytic lesions, epithelial-myoepithelial carcinoma and (hyalinizing) clear cell adenocarcinoma

When I report, as for other difficult tumors, I consider a more generic diagnostic line (unless the tumor is clearly one that can be identified by specific characteristic features); examples might include:

LOW GRADE ADENOCARCINOMA
LOW GRADE MUCIN-PRODUCING ADENOCARCINOMA BASALOID SALIVARY TUMOR BASALOID SALIVARY TUMOR, FRAGMENTED SPECIMEN HIGH GRADE ADENOCARCINOMA HIGH GRADE MUCIN-PRODUCING ADENOCARCINOMA PAPILLARY or CRIBRIFORM ADENOCARCINOMA
and so forth

The intent, as for the other cases we've been reviewing, is to communicate the impression and then for the difficult tumors employ additional diagnostic tools to better characterize the tumor; these would include myoepithelial markers, basal/parabasal or ductal epithelial markers, DOG1 if acinic cell adenocarcinoma is to be verified, mammaglobin (useful for mammary analog secretory carcinoma but also reported in some polymorphous adenocarcinomas)

Finally, consider molecular testing in those tumors that may fall into the category of translocation associated carcinomas and which include mucoepidermoid carcinoma, secretory carcinoma, and the clear cell carcinomas; familiarity with these translocations is strongly recommended and the references discussed should provide background.

Regarding responses provided, these included:

BENIGN SALIVARY GLAND TUMOR CONSISTENT WITH BASAL CELL ADENOMA; EXCISIONAL BIOPSY TO RULE OUT ADENOCARCINOMA

MY COMMENTS:

When I signed out the actual case, I made a very similar diagnosis and included a comment that complete excision for evaluation of surgical margins was advised, though I favored the diagnostic terminology of BASALOID SALIVARY NEOPLASM, MOST CONSISTENT WITH BASAL CELL ADENOMA, INCOMPLETELY EXCISED

My philosophy is that these tumors, along with tumors that suggest either mixed tumor or polymorphous carcinoma, should include a comment if the specimen is fragmented or incompletely excised, since this should be a recognized limitation in diagnosis

MALIGNANT SALIVARY GLAND TUMOR FAVOR PLEOMORPHIC ADENOMA, LOW GRADE

This diagnosis is inconsistent since it indicates a malignant neoplasm but identifies a benign tumor and confuses the reader; a more appropriate diagnosis might be MALIGNANT SALIVARY GLAND TUMOR, FAVOR POLYMORPHOUS CARCINOMA or MALIGNANT SALIVARY GLAND TUMOR, LOW GRADE

MALIGNANT SALIVARY GLAND TUMOR CONSISTENT WITH MAMMARY ANALOG SECRETORY CARCINOMA

This is appropriate if the lesion is morphologically consistent with one of the so-called 'zymogen poor acinic cell carcinomas' or an acinic cell carcinoma that as in this case appeared somewhat more 'pink' than the more basophilic acinic cell adenocarcinoma; the consensus in a case like this would be (I believe) to confirm this diagnosis (secretory carcinoma, using the revised nomenclature) with either an IHC panel that might include S100 and mammaglobin; in addition STAT5a has been reported as a sensitive and specific marker in these tumors *or* with molecular analysis for the ETV6-NTRK3 gene fusion

EPITHELIAL AND SPINDLE CELL TUMOR WITH CLEAR CELLS MALIGNANCY FAVOR MYOEPITHELIAL CARCINOMA RULE OUT EPITHELIAL-MYOEPITHELIAL CARCINOMA

This is a reasonable approach but minimizing some of the histologic and cytologic descriptors may clarify the diagnosis; thus consider EPITHELIAL AND SPINDLE CELL NEOPLASM WITH CLEAR CELLS AND GLANDULAR FORMATIONS, FAVOR MYOEPITHELIAL ORIGIN

This was a particularly challenging case, since it took some searching to find the glandular features and areas that seemed to be producing some mucin; this facilitated calling it an adenocarcinoma. However, defining this as either a myoepithelial neoplasm or one of the biphasic tumors (like epithelial-myoepithelial carcinoma) was in my mind and with my skill level not possible without the IHC and even that was challenging to interpret since the IHC did appear to favor both an epithelial and myoepithelial component -- I admit that I sent this case for expert opinion and there was expert commentary that both myoepithelial and epithelial-myoepithelial carcinoma were both strong considerations; this was ultimately one of those cases that might be more academic since the diagnosis is of a somewhat more aggressive tumor which necessitated thorough oncologic evaluation.

Final comments:

1. Consistency in diagnostic terminology is important; describing a tumor as malignant should include a list of malignant lesions and demonstrates the challenges associated with the mixed tumor-polymorphous carcinoma 'spectrum' particularly in fragmented, incompletely excised masses or in specimens that lack orienting surface epithelium or adjacent tissue planes
2. Basaloid lesions which are incompletely excised or lack orienting surface epithelium or adjacent tissue planes may best be treated similarly to the mixed tumor-polymorphous carcinoma 'spectrum'
3. Though the importance of definitive characterization of a tumor as a specific entity cannot be overemphasized, particularly as IHC and molecular analysis continues to identify distinct tumors including the translocation associated carcinomas, first identifying the lesion as either benign or malignant and as either low grade or high grade may be more effective than the potential confusion of attempting to commit a growing list of tumor names (some which change in the new classification) that may confuse both the pathologist and the reader (clinician or potential examiner)