Practical Diagnostic Categories for Salivary Gland Cytopathology

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Disclosures

I have nothing to disclose

Objectives

1. Understand your role as cytopathologist in the workup of salivary gland lesions.

1. Understand and be able to apply a practical diagnostic schema with broad diagnostic categories for FNA specimens from the salivary gland.

Salivary gland FNA

Perceived as one of the most challenging areas of cytopathology

- Wide range of reactive and neoplastic lesions
- >40 subtypes of neoplasms with overlapping cytologic features
- Perceived requirement for precise cytologic classification
The cytopathologist’s role*

- Primary value is to establish need for surgery, not to establish a specific diagnosis
- Helpful to avoid surgery in select patients:
  - reactive lymph node
  - Lymphoma
  - Warthin’s tumor
  - non-neoplastic disorder
- Can guide imaging, extent of surgery discussion, timing of surgery, consultations

* Perspective by David Eisele MD, Chair OHNS, Johns Hopkins

Practical Goals

- Distinguish non-neoplastic from neoplastic lesions
- Provide a definitive diagnosis in approximately 60% of cases where we can be accurate (i.e. PA)
- Classify remainder of cases (~30%) into broad categories
  - “Salivary gland neoplasm” is a legitimate diagnosis

Practical diagnostic algorithm
**Non-neoplastic lesions**

Heterogenous mixture of cell types +/- metaplastic changes in normal tissues.

- Chronic sialadenitis
- Accessory parotid gland
- Sialosis
- Reactive lymph node

**Case 1**

57 year old woman with a discrete 2 cm parotid mass, occasionally painful

- Clinical diagnosis: Pleomorphic adenoma

**Case 1**

Acini absent or scant and atrophic

**Case 1**

Condensed, dark cuboidal ductal epithelium w/metaplastic changes in a background of lymphocytes.
Cytologic diagnosis:

Chronic sialadenitis, no evidence of neoplasm.

Chronic sialadenitis

1. In the setting of Sjogren’s syndrome and/or clinically worrisome mass where lymphoid tissue predominates, submit flow cytometry to rule out lymphoma.

2. Abundant plasma cells in an otherwise hypocellular/sclerotic aspirate suggests chronic sclerosing lesion, a.k.a. Kuttner tumor (IgG4+ by IHC or serology).

Where can you go wrong?

Management: Conservative measures, sialoendoscopy, anti-inflammatory medications

Do not overlook stone fragments!
**Acinic cell carcinoma**

**Practical diagnostic algorithm**

- Neoplastic
- Non-neoplastic
- Primary
- Metastasis

**Metastatic neoplasms**

- Squamous cell carcinoma
- Melanoma
- Renal cell carcinoma
- Breast and prostatic adenocarcinoma

**Case 2**

66 year old woman with a remote history of breast cancer and a left parotid mass for several months

- MRI showed an enhancing parotid mass, no lymphadenopathy
Case 2

Cytologic diagnosis:

Squamous cell carcinoma, primary versus metastatic

Squamous cell carcinoma

- More likely metastasis than primary to salivary gland
- Final determination of site of origin requires clinical history, evaluation of both upper aerodigestive tract and skin
- Histologic features (in situ ductal component) can sometimes support origin in the salivary gland
**Primary vs. met SCC?**

**Management:** Surgical resection + lymph node dissection + radiation

**Note:** Radiation fields are modified to include the primary site and draining lymphatics when cutaneous or mucosal primary is suspected.

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**Primary vs. met SCC?**

- Hyperchromatic, non-keratinizing “basaloid” squamous cell carcinoma in the tail of parotid (cervical level 2 lymph node) is likely a metastasis from the oropharynx (base of tongue/tonsil).

- p16 stain and/or HPV 16 in situ is indicated for this histology.

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**Practical diagnostic algorithm**

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Primary
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- Low grade
- High grade
- Basaloid
- Non-surgical (i.e. lymphoma)

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**Low grade primary neoplasms**

- Pleomorphic adenoma
- Epithelial/myoepithelial neoplasms
- Low grade adenocarcinoma
- Acinic cell carcinoma
- Most mucoepidermoid carcinomas
Case 3

37 year old woman with a 2 cm firm, painless, right parotid mass, present for 6 months

Case 3

Epithelial component includes bland cuboidal cells with oval nuclei and small nucleoli

Case 3

Variable ratio of epithelial and myoepithelial cells along with fibrillar extracellular matrix

Cytologic diagnosis:
Low grade salivary gland neoplasm, favor pleomorphic adenoma
**Pleomorphic adenoma**

Heterogenous cytomorphology – ductules, mucinous and squamoid epithelium

Myoepithelial component frequently imbedded in stromal matrix

**Occasional atypical or multinucleated cell is acceptable.**

**Pleomorphic adenoma**

Diffuse atypia with nuclear enlargement, pleomorphism, and prominent nucleoli is inconsistent with diagnosis of pleomorphic adenoma.

“Salivary gland neoplasm” is a legitimate diagnosis

**Management:** Complete surgical resection guided by pre-operative imaging studies

**Carcinoma ex PA**
Where can you go wrong?

FNA is highly reliable for diagnosis of pleomorphic adenoma.

Review of 182 UCSF surgical specimens with preceding FNA biopsy, FNA diagnosis has a PPV of 96%.

Misses:
- 1 Carcinoma ex pleomorphic adenoma
- 1 Myoepithelial carcinoma
- 2 Schwannomas (1 spindled and 1 epithelioid)

Practical diagnostic algorithm

Low grade vs. High grade

<table>
<thead>
<tr>
<th>Low grade neoplasm</th>
<th>High grade neoplasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small ovoid or angulated nuclei</td>
<td>Large pleomorphic, hyperchromatic nuclei</td>
</tr>
<tr>
<td>Fine chromatin, small nucleoli</td>
<td>Coarse chromatin, prominent nucleoli</td>
</tr>
<tr>
<td>Rare mitoses</td>
<td>Mitoses, necrosis, tumor diathesis</td>
</tr>
</tbody>
</table>

High grade primary neoplasms

- Salivary duct carcinoma
- High grade adenocarcinoma, NOS
- Rare high grade mucoepidermoid carcinoma
Case 4

68 year old man with 6 week history of left parotid fullness and multiple enlarged left cervical lymph nodes

- FNA of an enlarged lymph node in the left upper neck
Case 4. **Androgen receptor**

Cytologic diagnosis:

*High grade salivary gland neoplasm, consistent with salivary duct carcinoma*

**Salivary Duct Carcinoma**

- Similar to high grade apocrine-type ductal carcinoma of breast
- Large oval, nuclei with prominent nucleoli
- +/- luminal or cytoplasmic mucin, comedo necrosis
- Positive for androgen receptor

**Salivary Duct Carcinoma**

Management: Surgical resection + lymph node dissection + radiation

Adjuvant chemotherapy currently controversial, subject of RTOG study
**What about mucoepidermoid carcinoma?**

High grade MEC is very rare and the majority of HG MEC diagnosed histologically are misclassified (i.e. Metastatic breast cancer).

- Recent USCAP abstract*, reviewed 72 cases of MEC for prognostic features and grading. 16 cases of “high grade MEC” were misclassified:
  - 2 salivary duct carcinoma
  - 11 squamous cell carcinoma
  - 3 high grade adenocarcinoma, NOS


**Basaloid neoplasms**

- Adenoid cystic carcinoma
- Basal cell adenoma/Basal cell adenocarcinoma
- Basal cell carcinoma (cutaneous origin)
- Metastatic basaloid squamous cell carcinoma

**Practical diagnostic algorithm**

- Basaloid
- Non-surgical (i.e. lymphoma)
- High grade
- Low grade

**Case 5**

54 year old woman with a firm, slow growing submandibular mass

*Present for at least 2 years, now more “noticeable”*
Case 5

Small, ovoid, basaloid cells with scant clear cytoplasm, uniform nuclei lacking atypia, rare mitoses, no necrosis

Cytologic diagnosis:
Basaloid neoplasm, favor adenoid cystic carcinoma

Characteristic acellular, homogeneous matrix composed of metachromatic spheres or cylinders

Adenoid cystic carcinoma

Squamous differentiation is not a feature of adenoid cystic and suggests a basal cell adenoma/adenocarcinoma, or basal cell carcinoma (skin).

Management: Complete surgical resection guided by pre-operative imaging studies
Practical diagnostic algorithm

Primary

Low grade  High grade  Basaloid  Non-surgical (i.e. lymphoma)

Take-home points

1. Distinction between neoplastic and non-neoplastic lesions in the salivary gland is our primary task.

2. Distinction between primary and metastatic neoplasms has clinical value, i.e. SCC.

3. Discrimination between high grade and low grade neoplasms is helpful, but "Salivary gland neoplasm" is a legitimate diagnosis.

Non-surgical neoplasms

- Lymphoma
  - Low grade (MALT type)
  - High grade (DLBCL)

- Benign lesions in the appropriate clinical context
  - Warthin’s tumor
  - Oncocytic lesions