Diagnostic Problems in Salivary Gland Pathology – An Update

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Lesions Mimicking Adenoid Cystic Carcinoma

Adenoid Cystic Ca. – Cribriform Pattern

Adenoid Cystic Ca. – Tubular Pattern
Adenoid Cystic Ca. – Solid Pattern

Reticular Pattern
Adenoid Cystic Ca. v. Mixed Tumor

Sclerotic Pattern
Adenoid Cystic Ca. v. Mixed Tumor

Lesions Mimicking Adenoid Cystic Carcinoma

- Basal cell adenoma
### Basal Cell Adenoma v. Adenoid Cystic Carcinoma

<table>
<thead>
<tr>
<th>Feature</th>
<th>Basal Cell Adenoma (BCA)</th>
<th>Adenoid Cystic Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basaloid cells</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Hyaline cylinders</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cribriform pattern</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Palisading</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Stromal mucin</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Margin</td>
<td>Capsule</td>
<td>Infiltrating</td>
</tr>
<tr>
<td>Perineural invas.</td>
<td>Absent</td>
<td>Common</td>
</tr>
<tr>
<td>Favored location</td>
<td>Parotid, lip</td>
<td>Any salivary gland</td>
</tr>
</tbody>
</table>

### Lesions Mimicking Adenoid Cystic Carcinoma

- Basal cell adenoma
- Basal cell adenocarcinoma
Lesions Mimicking Adenoid Cystic Carcinoma

- Basal cell adenoma
- Basal cell adenocarcinoma
- Mixed tumor
Mixed Tumor v. Adenoid Cystic Carcinoma

<table>
<thead>
<tr>
<th></th>
<th>Mixed Tumor</th>
<th>Adenoid Cystic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyaline cylinders</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cribriform pattern</td>
<td>Rare</td>
<td>Yes</td>
</tr>
<tr>
<td>S-E junction</td>
<td>Blurred</td>
<td>sharp</td>
</tr>
<tr>
<td>Cell type</td>
<td>Polygonal</td>
<td>Basaloid</td>
</tr>
<tr>
<td>Typical MT pattern</td>
<td>Common</td>
<td>Absent</td>
</tr>
<tr>
<td>Margin</td>
<td>Focal invasion</td>
<td>Diffuse invasion</td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>Absent</td>
<td>Common</td>
</tr>
<tr>
<td>MisDx. as MT</td>
<td>***</td>
<td>Uncommon</td>
</tr>
<tr>
<td>MisDx. as ACC</td>
<td>Common</td>
<td>***</td>
</tr>
</tbody>
</table>
Lesions Mimicking Adenoid Cystic Carcinoma

- Basal cell adenoma
- Basal cell adenocarcinoma
- Mixed tumor
- Polymorphous low-grade adenocarcinoma

Polymorphous Low-Grade Adenocarcinoma

Adenoid Cystic Carcinoma
Polymorphous Low-Grade Adenocarcinoma v. Adenoid Cystic Carcinoma

<table>
<thead>
<tr>
<th>Feature</th>
<th>PLGA</th>
<th>Adenoid Cystic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Margin</td>
<td>Infiltrating</td>
<td>Infiltrating</td>
</tr>
<tr>
<td>Perineural invasion</td>
<td>Prominent</td>
<td>Prominent</td>
</tr>
<tr>
<td>Cribriform pattern</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Solid areas</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Tubules</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Myxoid stroma</td>
<td>Minor</td>
<td>Major</td>
</tr>
<tr>
<td>Cell type</td>
<td>Polygonal</td>
<td>Basaloid</td>
</tr>
<tr>
<td>Location</td>
<td>Oral cavity</td>
<td>Any seromucinous</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Very good</td>
<td>Guarded</td>
</tr>
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</table>

Immunohistochemical Features

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Expression</th>
</tr>
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<tbody>
<tr>
<td>S100</td>
<td>Weak, variable</td>
</tr>
<tr>
<td>CD-117</td>
<td>Strong/all</td>
</tr>
<tr>
<td>EMA</td>
<td>Luminal cells</td>
</tr>
<tr>
<td>CEA</td>
<td>Luminal cells</td>
</tr>
<tr>
<td>MSA</td>
<td>Focal, non-luminal</td>
</tr>
</tbody>
</table>

Polymorphous Low-grade Adenocarcinoma

Adenoid Cystic Ca

S100

PLGA

CD117
Polymorphous Low-Grade Adenocarcinoma
Clinical Features

- **Frequency:** most common oral cavity adenocarcinoma.
- **Location:** *de novo* in oral cavity or as component of malignant mixed tumor
- **Age/Sex:** 26 to 77 yrs, most in 6th to 7th decade, female predominance
- **Clinical Course:** indolent, recurrences uncommon, may be after many yrs. Non-papillary = no mets, may undergo de-differentiation.

Lesions Mimicking Adenoid Cystic Carcinoma

- Basal cell adenoma
- Basal cell adenocarcinoma
- Mixed tumor
- Polymorphous low-grade adenocarcinoma
- **Solid carcinoma**
### Solid Carcinoma v. Adenoid Cystic Ca

<table>
<thead>
<tr>
<th></th>
<th>Solid Carcinoma</th>
<th>Adenoid Cystic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid cell nests</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Comedonecrosis</td>
<td>Prominent</td>
<td>Rare/absent</td>
</tr>
<tr>
<td>Pleomorphism</td>
<td>Prominent</td>
<td>Minimal</td>
</tr>
<tr>
<td>Cell type</td>
<td>Variable</td>
<td>Basaloid</td>
</tr>
<tr>
<td>Mitotic figures</td>
<td>Numerous</td>
<td>Sparse</td>
</tr>
<tr>
<td>L.N. mets</td>
<td>Common</td>
<td>?never</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Rapid, poor</td>
<td>Protracted/guarded</td>
</tr>
</tbody>
</table>

### Lesions Mimicking Adenoid Cystic Carcinoma

- Basal cell adenoma
- Basal cell adenocarcinoma
- Mixed tumor
- Polymorphous low-grade adenocarcinoma
- Solid carcinoma
  - **Basaloid squamous cell carcinoma**
**Basaloid Squamous Cell Carcinoma**

**Light Microscopic Features**

- Sharply defined cell nests close to surface mucosa
- Basaloid cells
- Hyperchromatic to vesicular nuclei, no nucleoli
- Cystic spaces with mucin
- Assoc. with squamous cell ca., often CIS
- Comedonecrosis
- Stromal hyalinosis

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**Basaloid Squamous Cell Carcinoma. v. Adenoid Cystic Carcinoma**

<table>
<thead>
<tr>
<th></th>
<th>BSCC</th>
<th>Adenoid Cystic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyaline cylinders</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td>Cribriform pattern</td>
<td>Focal</td>
<td>Common</td>
</tr>
<tr>
<td>Cell type</td>
<td>Basaloid/pleomorphic</td>
<td>Basaloid/uniform</td>
</tr>
<tr>
<td>Comedonecrosis</td>
<td>Prominent</td>
<td>Rare</td>
</tr>
<tr>
<td>Mitotic figures</td>
<td>Numerous</td>
<td>Sparse</td>
</tr>
<tr>
<td>Squamous diff.</td>
<td>Always</td>
<td>Rare</td>
</tr>
<tr>
<td>Origin</td>
<td>Mucosa</td>
<td>Salivary</td>
</tr>
<tr>
<td>L.N. mets</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Course/prognosis</td>
<td>Rapid/poor**</td>
<td>Protracted/guarded</td>
</tr>
</tbody>
</table>
Clear Cell Salivary Lesions

- Hyalinizing clear cell carcinoma
Hyalinizing Clear Cell Carcinoma
Pathologic Features

- **Size:** 0.5 to 3.5 cm.
- **Microscopic:** trabecula, cords, nests, sheets of cells.
  - Infiltrating margins, hyalinizing stroma
  - Round, clear cells with PAS+ cytoplasm
  - Focal eosinophilic cells
  - Rare mitotic figures, ?correlation with l.n. mets
  - Perineural invasion common

Hyalinizing Clear Cell Carcinoma
Immunohistochemical Features

- Cytokeratins +
- EMA +
- Myoepithelial markers –
- S100 protein –

PAS
Hyalinizing Clear Cell Carcinoma
Clinical Features

- **Sites:** base of tongue >> palate > larynx > salivary
- **Sex:** female to male = 2 : 1
- **Age:** 4\textsuperscript{th} to 8\textsuperscript{th} decades
- **Regional nodes:** ~15%
- **Prognosis:** ?no deaths from disease
Clear Cell Salivary Lesions

- Hyalinizing clear cell carcinoma
- Epithelial-myoepithelial carcinoma
Epithelial-Myoepithelial Carcinoma

**Light Microscopic Features**

- Often lobulated growth pattern
- Distinct, bilayered ducts/glands
- Inner epithelial layer with cuboidal, eosinophilic cells, round nuclei
- Outer myoepithelial layer with polygonal, clear cells, often vesicular nuclei
- Clear cell component may overgrow lesion
- May be associated with adenoid cystic carcinoma

**Clinical Features**

- **Frequency:** ~1% of all salivary tumors, ~11% of minor salivary gland tumors
- **Location:** both major and minor salivary glands, parotid favored, also intraoral
- **Age/Sex:** broad age, peak in 7th decade, occasional pediatric cases, 60% female
- **Prognosis:** low-grade malignancy, 30-40% local recurrence, 18% l.n. mets, 8% distant mets.

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**ENT Clear Cell Tumors**

**Differential Diagnosis**

<table>
<thead>
<tr>
<th></th>
<th>Hyalinizing Clear Cell Ca.</th>
<th>Epithelial-Myoepithelial Ca.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biophasic</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Densely sclerotic</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>S100 Protein</td>
<td>No</td>
<td>Yes (myoepith.)</td>
</tr>
<tr>
<td>SMA</td>
<td>No</td>
<td>Yes (myoepith).</td>
</tr>
<tr>
<td>Glycogen</td>
<td>Yes</td>
<td>?</td>
</tr>
<tr>
<td>Prognosis</td>
<td>good</td>
<td>guarded</td>
</tr>
</tbody>
</table>

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**Clear Cell Salivary Lesions**

- Hyalinizing clear cell carcinoma
- Epithelial-myoepithelial carcinoma
- Mucoepidermoid carcinoma
Clear Cell Salivary Lesions

- Hyalinizing clear cell carcinoma
- Epithelial-myoepithelial carcinoma
- Mucoepidermoid carcinoma
- Sebaceous neoplasia

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Clear Cell Salivary Lesions

- Hyalinizing clear cell carcinoma
- Epithelial-myoepithelial carcinoma
- Mucoepidermoid carcinoma
- Sebaceous neoplasia
- Acinic cell carcinoma
Clear Cell Salivary Lesions

- Hyalinizing clear cell carcinoma
- Epithelial-myoepithelial carcinoma
- Mucoepidermoid carcinoma
- Sebaceous neoplasia
- Acinic cell carcinoma
- Clear cell oncocytoma
Clear Cell Oncocytoma

- A diagnosis to be approached with caution!
- Current case was CD10-, RCC-, CEA-, SMA-, S100-, CK20+
- Surrounding oncocytosis is highly supportive
- Radiologic exclusion of renal cell may still be warranted

Clear Cell Salivary Lesions

- Hyalinizing clear cell carcinoma
- Epithelial-myoepithelial carcinoma
- Mucoepidermoid carcinoma
- Sebaceous neoplasia
- Acinic cell carcinoma
- Clear cell oncocytoma
- Metastatic carcinoma
Lesions Mimicking Mucoepidermoid Carcinoma

- Necrotizing sialometaplasia
Necrotizing Sialometaplasia

Necrotizing Sialometaplasia

Necrotizing Sialometaplasia

Mucoepidermoid Carcinoma
Necrotizing Sialometaplasia v. Mucoepidermoid Carcinoma

<table>
<thead>
<tr>
<th></th>
<th>Necrotizing Sialometaplasia</th>
<th>Mucoepidermoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenosquamous</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pleomorphism</td>
<td>Focal, mild</td>
<td>Mild/moderate</td>
</tr>
<tr>
<td>Lobular pattern</td>
<td>Yes</td>
<td>Variable</td>
</tr>
<tr>
<td>Lobular infarction</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Inflammation</td>
<td>Frequent</td>
<td>Occasional</td>
</tr>
</tbody>
</table>

Lesions Mimicking Mucoepidermoid Carcinoma

- Necrotizing sialometaplasia
- Adenosquamous carcinoma

Adenosquamous v. Mucoepidermoid Carcinoma

<table>
<thead>
<tr>
<th></th>
<th>Adenosquamous</th>
<th>Mucoepidermoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenosq. Pattern</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pleomorphism</td>
<td>Marked</td>
<td>Mild/moderate</td>
</tr>
<tr>
<td>Mitotic figures</td>
<td>Numerous</td>
<td>Variable</td>
</tr>
<tr>
<td>Necrosis</td>
<td>Frequent</td>
<td>Uncommon</td>
</tr>
<tr>
<td>“Non-salivary”</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Course/prognosis</td>
<td>Rapid/poor</td>
<td>Protracted/variable</td>
</tr>
</tbody>
</table>
Lesions Mimicking Mucoepidermoid Carcinoma

- Necrotizing sialometaplasia
- Adenosquamous carcinoma
- Salivary duct carcinoma
Salivary Duct Carcinoma

- **Location:** 86% parotid, 12% submandibular
- **Age/Sex:** 27-86 yrs, 71% male, 29% female
- **Prognosis:** poor, 53% 6-year mortality; high rate of local, regional & distant spread

Lesions Mimicking Benign Lymphoepithelial Lesion

- Lymphoma
- Malignant lymphoepithelial lesion
- Metastatic undifferentiated carcinoma

Benign Lymphoepithelial Lesion
Benign Lymphoepithelial Lesion

Lesions Mimicking Benign Lymphoepithelial Lesion

- Lymphoma

Nodular B-Cell Lymphoma

B-cell Lymphoma with "Epi-myoeplithelial Island"
Benign Lymphoepithelial Lesion

Caveats

- Epi-myoepithelial islands are NOT diagnostic
- BLL is a diagnosis of exclusion. It may be associated with lymphoma or undifferentiated carcinoma.
- Patients with BLL have an increased risk of lymphoma. An increased risk of carcinoma is doubtful
- BLL may be monoclonal*
Lesions Mimicking Benign Lymphoepithelial Lesion

- Lymphoma
- Malignant lymphoepithelial lesion

Malignant Lymphoepithelial Lesion
Undifferentiated Carcinoma of Salivary Gland

- **Incidence:** highly regional, uncommon in the west
- **Ethnic:** strong predilection for Eskimos and Chinese
- **Location:** 90% parotid, 10% submandibular
- **Age & Sex:** range: 10-58 yrs.; mean age: 40 yrs; no male/female predilection
- **Prognosis:** 30% mortality, >50% lived >4 yrs.
Malignant Lymphoepithelial Lesion
Age Distribution

Decade of Life

No. Pts.

EBV