Basic Salivary Gland Pathology

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Agenda

• Common benign lesions
  • Warthins tumor
  • Pleomorphic adenoma
  • Basal cell adenoma
  • Myoepithelioma
• Common Malignancies
  • Mucoepidermoid carcinoma variants
  • Adenoid cystic carcinoma
  • Carcinoma ex pleomorphic adenoma
  • Salivary duct carcinoma

Salivary Glands Background

• Major salivary glands
  • Parotid
  • Submandibular gland
  • Sublingual gland
• Minor salivary glands
  • Throughout respiratory tract
Warthin Tumor

- Incidence
  - Related to smoking
  - Can be bilateral
  - Parotid, minor salivary glands, rests
- Clinical
  - Mass lesion, benign
Warthin Tumor

- Gross
  - Cystic lesion
  - Fluid resembles motor oil
- Histology
  - Oncocytic epithelium
  - Papillary growth
  - Lymphoid stroma
  - Germinal centers
Pleomorphic Adenoma

Incidence
• Most common benign tumor

Clinical
• Mass lesion
• Surgical treatment with margins

Gross
• Bosselated
• Chondroid

Histology: Mixed
• Stromal: chondroid, hyalinized, myxoid
• Epithelial cells: ducts and tubules
• Myoepithelial cells
Pleomorphic Adenoma

- **IHC**
  - Myoepithelial markers positive (GFAP)
  - Ki-67: low proliferative rate (<5%)

- **Prognosis**
  - Local recurrence: 5-10%
  - Malignant degeneration: 5%-25%
    - “Carcinoma ex pleomorphic adenoma”

Recurrent Pleomorphic adenoma
Pleomorphic Adenoma

- Differential diagnosis
  - Basal cell adenoma
  - Unique morphology
  - Myoepithelioma
    - No chondroid, no tubules

Basal Cell Adenoma

- Histology: Solid, trabecular, tubular
  - Two cell types
    - Small, dark nuclei with palisading
    - Larger, lighter nuclei, islands and cords
  - Distinct basement membrane
  - No chondromyxoid stroma
- Immunohistochemistry
  - Epithelial and myoepithelial cells
    - Positive for respective markers
  - GFAP negative
Basal Cell Adenoma

- Histology
  - Membranous type (Dermal Analogue tumor)
  - Similar to dermal cylindroma ("turban tumor")
  - Epithelial islands
  - Peripheral small basophilic palisading cells
  - Central large cells, squamoid whorls
  - Extracellular hyaline material
Myoepithelioma

- Incidence
  - Probably under-recognized
- Clinical
  - Mass lesion

Myoepithelioma

- Histology: Pure myoepithelial cells
  - No ducts/tubules
  - No chondroid matrix
  - Hyalinized and myxoid matrix
- Myoepithelial cells
  - Spindle, epithelioid, clear, mixed
Myoepithelioma

- IHC
  - Positive for myoepithelial markers
  - Variable cytokeratin staining
  - Negative for CEA
Myoepithelial Cells

- Morphologically diverse
- Variable immunohistochemical stains

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<tr>
<th>Myoepithelial Markers</th>
<th>Usually positive</th>
<th>Usually negative</th>
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<tr>
<td>AE1-3</td>
<td>SMA</td>
<td>EMA</td>
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<tr>
<td>Vimentin</td>
<td>SMMH</td>
<td>CEA</td>
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<tr>
<td>S100</td>
<td>CK14</td>
<td>CK7</td>
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<tr>
<td>Calponin</td>
<td>Cam.5.2</td>
<td>B72.3</td>
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<tr>
<td>P63</td>
<td>CK5/6</td>
<td>Desmin</td>
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<tr>
<td>CK903</td>
<td>Maspin</td>
<td>HHF-35</td>
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<tr>
<td>CD10</td>
<td>GFAP</td>
<td></td>
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</table>
Myoepithelioma

• Differential diagnosis
  • Myoepithelial carcinoma
    • Invasive
    • Pleomorphism, mitoses, atypia
    • Clear cell hyalinizing carcinoma
    • CEA positive

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Mucoepidermoid Carcinoma

• Incidence
  • Most common malignant salivary gland tumor (children and adults)
  • Major and minor salivary glands
  • Peak incidence 5th to 6th decades

• Clinical
  • Mass lesion
  • Surgical treatment with margins
Histology

- Mucus cells and cysts
- Epidermoid cells
- Intermediate cells
Tumor Grading

- Tumor specific grading
  - Defined features

- General grading
  - Resemblance to normal
  - Nuclear features

- Grade by definition

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<tr>
<th>Tumor specific</th>
<th>General grading</th>
<th>Grading by Definition</th>
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<tr>
<td>Mucoepidermoid</td>
<td>Oncocytic carcinoma</td>
<td>Salivary Duct carcinoma</td>
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<td>Adenoid cystic carcinoma</td>
<td>Adenocarcinoma, NOS</td>
<td>Polymorphous low-grade</td>
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No Grading
- Acinic cell carcinoma
Mucoepidermoid Translocation

- t(11;19)(q21;p13)
- MECT1-MAML2
  - MECT1: also known as CRT1, TORC1, WAMTP1
  - cAMP response element binding protein (CREB) regulated transcriptional coactivator
  - MAML2: Notch coactivator
- Translocation activates Notch target genes independent of Notch ligands

MECT-MAML2 Translocation

Adenoid Cystic Carcinoma

- Incidence
  - Relatively common
  - Any salivary gland location
- Clinical
  - Mass lesion
  - Nerve palsies
  - Surgical treatment with margins
Adenoid Cystic Carcinoma

- Histology
  - Tubular, cribriform, solid patterns
  - Solid has worse behavior
  - Perineural invasion
  - Nuclei small, dark, and angulated
Adenoid cystic carcinoma, solid

Adenoid cystic carcinoma

Adenoid cystic carcinoma
Adenoid Cystic Carcinoma

- IHC
  - CKIT and bcl-2 positive
  - Epithelial cells: cytokeratins
  - Myoepithelial cells: p63, SMA, CK5/6

High Grade Transformation

- Clinical
  - Tumor progression with aggressive disease
  - May have clinical history of adenoid cystic carcinoma

- Histology
  - Low grade areas and high grade areas
  - Epithelial predominance
  - Necrosis
  - Vascular invasion
Adenoid cystic carcinoma with high grade transformation

Seethala RR. AJSP 3(11):1683, 2007

High Grade Transformation

- Alive & Well: 10%
- Recurrence: 45%
- Death from disease: 45%
High Grade Transformation

- Immunohistochemistry
  - Loss of myoepithelial component
  - SMA, p63, calponin negative
  - All cells stain with cytokeratin
  - Strong p53 staining
  - High proliferative rate (Ki-67)
Adenoid Cystic Translocation

- **t(6;9) (q22-23; p23-24)**
- **MYB-NFIB**
  - **MYB**
    - Transcription factor with an important role in cell proliferation, apoptosis, and differentiation
    - Highly expressed in immature proliferating cells, and down-regulated as cells become more differentiated
  - **NFIB**: nuclear factor 1B
- Deregulation mechanism is not completely understood

Translocation in ACC


Carcinoma ex Pleomorphic Adenoma
Carcinoma ex Pleomorphic Adenoma

- Incidence: Relatively rare
- Etiology: Arises from PA
- Clinical
  - Long standing mass with recent rapid enlargement
  - History of PA
    - Resected incompletely
    - Recurrent

Carcinoma ex Pleomorphic Adenoma

- Histology
  - Residual pleomorphic adenoma
  - Carcinoma component
    - Specific salivary carcinoma (any type)
    - Adenocarcinoma, NOS
- IHC
  - Specific to type of carcinoma
Incidence: Rare
Clinical
- Aggressive clinical course
- Metastases at presentation
- Surgical treatment
- Chemotherapy & radiation
Salivary Duct Adenocarcinoma

- Histology
  - Resembles breast carcinoma
  - Cribriform, micropapillary, solid
  - Comedo-type necrosis
  - Micro and macro calcifications
  - Stromal and perineural invasion
Salivary Duct Carcinoma

- IHC
  - Androgen receptor positive
  - HER2/neu positive
  - PSA occasionally positive
  - ER/PR usually negative
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