Histopathology of Major Salivary Gland Neoplasms

Sam J. Cunningham, MD, PhD
Faculty Advisor: Shawn D. Newlands, MD, PhD
Faculty Advisor: David C. Teller, MD
The University of Texas Medical Branch,
Department of Otolaryngology
Grand Rounds Presentation
November 16, 2005
Introduction

- Neoplasms of the major salivary glands constitute minor portion of head and neck neoplasms
- Less than 2% are malignant
- Most neoplasms in parotid 75%, 0.8% in sublingual glands
- Remainder equally distributed between submandibular gland and minor salivary glands
Introduction

- Incidence rises at age 15 and peaks at 65-75.
- Incidence of malignant neoplasms increases after 4th and 5th decades and peaks 65-75 years.
- Benign neoplasms present slightly earlier
- Malignant neoplasms occur most often in men.
Introduction

- Cancers of the salivary glands account for only 6% of H&N cancers
- Only 0.3% of all cancers
- Proportion of malignant and benign varies with the gland of origin.
Introduction

Bar chart showing the percentage of benign and malignant tumors in different salivary gland regions:

- Parotid: 75% benign, 25% malignant
- Submandibular: 57% benign, 43% malignant
- Minor salivary: 18% malignant

Legend:
- Benign
- Malignant
Salivary Gland Microanatomy

- Saliva transported from central structure (acini) in complex ductal system to the oral cavity
- System is a bilayer with internal luminal layer and external reserve layer.
- Internal layer forms acini and ductal epithelium
- External layer forms myoepithelium and reserve cells
Salivary Gland Microanatomy

ACINUS  INTERCALATED DUCT  STRIATED DUCT  EXCRETORY DUCT

RER  myoepithelial cell  golgi  secretory granules  basal invaginations and mitochondria  basal cells
<table>
<thead>
<tr>
<th>Site</th>
<th>Positive Stains</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acini</td>
<td>Carcinoembryonic antigen</td>
</tr>
<tr>
<td></td>
<td>Epithelial membrane antigen (serous acini only)</td>
</tr>
<tr>
<td>Intercalated duct</td>
<td>Carcinoembryonic antigen</td>
</tr>
<tr>
<td></td>
<td>Epithelial membrane antigen</td>
</tr>
<tr>
<td></td>
<td>Cytokeratins</td>
</tr>
<tr>
<td></td>
<td>S-100 (minor glands only)</td>
</tr>
<tr>
<td>Striated duct</td>
<td>Epithelial membrane antigen</td>
</tr>
<tr>
<td></td>
<td>Cytokeratins</td>
</tr>
<tr>
<td></td>
<td>S-100 (minor glands only)</td>
</tr>
<tr>
<td>Myoepithelial cells</td>
<td>Cytokeratins (serous glands only)</td>
</tr>
<tr>
<td></td>
<td>S-100</td>
</tr>
<tr>
<td></td>
<td>Muscle-specific actin</td>
</tr>
</tbody>
</table>

Bicellular Theory

- **Intercalated Ducts**
  - Pleomorphic adenoma
  - Warthin’s tumor
  - Oncocytoma
  - Acinic cell
  - Adenoid cystic

- **Excretory Ducts**
  - Squamous cell
  - Mucoepidermoid
Multicellular Theory

- Striated duct—oncocytic tumors
- Acinar cells—acinic cell carcinoma
- Excretory Duct—squamous cell and mucoepidermoid carcinoma
- Intercalated duct and myoepithelial cells—pleomorphic tumors
Classification of Salivary Gland Neoplasms

- **WHO**
  - Adenomas
  - Carcinomas
  - Nonepithelial Tumors
  - Malignant lymphomas
  - Secondary tumors
  - Unclassified tumors
  - Tumor-like lesions
Classification of Salivary Gland Neoplasms

- Armed Forces Institute of Pathology
  - Benign Epithelial Neoplasms
  - Malignant Epithelial Neoplasms
  - Mesenchymal Neoplasms
  - Malignant Lymphomas
  - Metastatic Tumors
  - Nonneoplastic Tumor-like Conditions
Benign Neoplasms

- Pleomorphic Adenoma
- Warthin’s Tumor
- Basal Cell Adenoma
- Oncocytoma
- Canalicular Adenoma
- Myoepithelioma
Pleomorphic Adenoma

- Histology
  - Mixture of epithelial, myoepithelial and stromal components
  - Epithelial cells: nests, sheets, ducts, trabeculae
  - Stroma: myxoid, chondroid, fibroid, osteoid
  - No true capsule
  - Tumor pseudopods
Pleomorphic Adenoma

- Necrosis and mitosis rare
- IHC profile consistent with dual architecture
- Glandular areas stain with CEA and S-100, actin, epithelial membrane antigen
- Mesenchymal areas stain with S-100 and actin only
Warthin’s Tumor

- **Histology**
  - Papillary projections into cystic spaces surrounded by lymphoid stroma
  - Epithelium: double cell layer
    - Luminal cells
    - Basal cells
  - Stroma: mature lymphoid follicles with germinal centers
Basal Cell Adenoma

- Solid nests of cells with scant cytoplasm and hyperchromatic nuclei
- Tendency for peripheral pallisading.
Basal Cell Adenoma

- **Solid**
  - Most common
  - Solid nests of tumor cells
  - Uniform, hyperchromatic, round nuclei, indistinct cytoplasm
  - Peripheral nuclear palisading
  - Scant stroma
Basal Cell Adenoma

- **Trabecular**
  - Cells in elongated trabecular pattern
  - Vascular stroma
Basal Cell Adenoma

- Tubular
  - Multiple duct-like structures
  - Columnar cell lining
  - Vascular stroma
Basal Cell Adenoma

- Membranous
  - Thick eosinophilic hyaline membranes surrounding nests of tumor cells
  - “jigsaw-puzzle” appearance
Basal Cell Adenoma
Oncocytoma

- **Histology**
  - Cords of uniform cells and thin fibrous stroma
  - Large polyhedral cells
  - Distinct cell membrane
  - Granular, eosinophilic cytoplasm
  - Central, round, vesicular nucleus
Oncocytoma

- Positive staining for phosphotungstic acid: hematoxylin, cytokeratin, epithelial membrane antigen
- Negative for S-100, glial fibrillary, smooth muscle actin
Canalicular Adenoma

- **Histology**
  - Well-circumscribed
  - Multiple foci
  - Tubular structures line by columnar or cuboidal cells
  - Vascular stroma
Myoepithelioma

- **Histology**
  - **Spindle cell**
    - More common
    - Parotid
    - Uniform, central nuclei
    - Eosinophilic granular or fibrillar cytoplasm
  - **Plasmacytoid cell**
    - Polygonal
    - Eccentric oval nuclei
Myoepithelioma
Malignant Neoplasms

- Mucoepidermoid Carcinoma
- Adenoid Cystic Carcinoma
- Polymorphous Low-Grade Adenocarcinoma
- Acinic Cell Carcinoma
- Adenocarcinoma
- Malignant Mixed Tumor
- Epithelial-Myoepithelial Carcinoma
- Salivary Duct Carcinoma
- Squamous Cell Carcinoma
- Undifferentiated Carcinoma
Mucoepidermoid Carcinoma

- Histology—Low-grade
  - Mucus cell > epidermoid cells
  - Prominent cysts
  - Mature cellular elements
Mucoepidermoid Carcinoma

- Histology—Intermediate-grade
  - Mucus = epidermoid
  - Fewer and smaller cysts
  - Increasing pleomorphism and mitotic figures
Mucoepidermoid Carcinoma

- **Histology—High-grade**
  - Epidermoid > mucus
  - Solid tumor cell proliferation
  - Mistaken for SCCA
    - Mucin staining
Low Grade Mucoepidermoid Carcinoma
High Grade Mucoepidermoid Carcinoma
Adenoid Cystic Carcinoma

- Histology—cribriform pattern
  - Most common
  - “swiss cheese” appearance
Adenoid Cystic Carcinoma

- **Histology—tubular pattern**
  - Layered cells forming duct-like structures
  - Basophilic mucinous substance

- **Histology—solid pattern**
  - Solid nests of cells without cystic or tubular spaces
Adenoid Cystic Carcinoma
Polymorphous Low-Grade Adenocarcinoma

- **Histology**
  - Isomorphic cells, indistinct borders, uniform nuclei
  - Peripheral “Indian-file” pattern
Polymorphous Low-Grade Adenocarcinoma

- Markedly positive staining for S-100, epithelial membrane antigen, and cytokeratins. Less predictable with CEA and muscle-specific actin.
Acinic Cell Carcinoma

- **Histology**
  - Solid and microcystic patterns
    - Most common
    - Solid sheets
    - Numerous small cysts
  - Polyhedral cells
  - Small, dark, eccentric nuclei
  - Basophilic granular cytoplasm
Acinic Cell Carcinoma

- Positive staining with cytokeratins and CEA, mixed results with others
- Vacuolated cells with eccentrically located nuclei and granular, basophilic cytoplasm, scant stroma
Adenocarcinoma

- Histology
  - Heterogeneity
  - Presence of glandular structures and absence of epidermoid component
  - Requires exclusion of other specific salivary gland carcinomas
Adenocarcinoma
Malignant Mixed Tumors

- Carcinoma ex-pleomorphic adenoma
  - Carcinoma developing in the epithelial component of preexisting pleomorphic adenoma

- Carcinosarcoma
  - True malignant mixed tumor—carcinomatous and sarcomatous components

- Metastatic mixed tumor
  - Metastatic deposits of otherwise typical pleomorphic adenoma
Carcinoma Ex-Pleomorphic Adenoma

- **Histology**
  - Malignant cellular change adjacent to typical pleomorphic adenoma
  - Carcinomatous component
    - Adenocarcinoma
    - Undifferentiated
Carcinosarcoma

- **Histology**
  - Biphasic appearance
  - Sarcomatous component
    - Dominant
    - Chondrosarcoma
  - Carinomatous component
    - Moderately to poorly differentiated ductal carcinoma
    - Undifferentiated
Malignant Mixed Tumor
Epithelial-Myoepithelial Carcinoma

- Dual epithelial component
- Irregular, eccentric nuclei w vacuolated cytoplasm
- IHC reveals dual cell origin
  - epithelial: cytokeratins
  - Myoep:S-100, actin
Epithelial-Myoepithelial Carcinoma

- Tumor cell nests
- Two cell types
- Thickened basement membrane
Salivary Duct Carcinoma

- Large polygonal cells with well defined borders
- Pleomorphic nuclei with prominent nucleoli and granular, eosinophilic cytoplasm
- IHC patterns similar to breast CA except neg for estrogen
- CEA, epithelial membrane +
- S-100, cytokeratins -
Squamous Cell Carcinoma

- **Histology**
  - Infiltrating
  - Nests of tumor cells
  - Well differentiated
    - Keratinization
  - Moderately-well differentiated
  - Poorly differentiated
    - No keratinization
Squamous Cell Carcinoma
Undifferentiated Carcinoma

- High grade, high mitotic activity, scant cytoplasm, hyperchromatic nuclei
- IHC: cytokeratins, epithelial membrane antigen
- +/- neuroendocrine
References


Rosen, Salivary Gland Neoplasms. Dr. Quinns online textbook of Otolaryngology. 2002.

The highlighted area represents:

a. the acini  
b. the intercalated duct  
c. the striated duct  
d. the excretory duct
The highlighted area represents:

a. the acini
b. the intercalated duct
c. the striated duct
d. the excretory duct
Question 3

The highlighted area represents:

a. the acini
b. the intercalated duct
c. the striated duct
d. the excretory duct
Question 4

The highlighted area represents:

a. the acini
b. the intercalated duct
c. the striated duct
d. the excretory duct
Question 5

The parotid gland neoplasms are:

a.) Mostly Benign
b.) Mostly Malignant
c.) About equal distribution, benign=malignant
Question 6

The submandibular gland neoplasms are:

a.) Mostly Benign
b.) Mostly Malignant
c.) About equal distribution, benign=malignant
Question 7

The sublingual gland neoplasms are:
a.) Mostly Benign
b.) Mostly Malignant
c.) About equal distribution, benign=malignant
Question 8

Identify the neoplasm:
Question 9

Identify the neoplasm:
Question 10

Identify the neoplasm: