Salivary gland neoplasms

PathoBasic
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Exocrine saliva producing glands

1. Major salivary glands:
   - Parotis
   - Submandibular gland
   - Sublingual gland

2. Minor salivary glands:
   Numerous (500-1000) nonuniformly distributed small aggregations in the mucosa of the oral cavity

Seromucous glands of the nasal cavity, pharynx, larynx and bronchi are morphologically similar and show the same tumors but are sensu stricto not salivary glands
Incidence and Epidemiology

- Rare neoplasms 0.4-6.5/100,000, 2-6% of all head and neck neoplasms
- Peak: 6th to 7th decade
- Risk factors: radiation, genetic predisposition, tobacco use, industrial chemicals, viral infections
- 64-80% parotis, 7-11% submandibular gland, <1% sublingual gland, 9-23% minor gland
Distribution in patients <17 years of age
<table>
<thead>
<tr>
<th>Localisation</th>
<th>%</th>
<th>malignant</th>
<th>benign</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parotis</td>
<td>80%</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>Gl. submandibularis</td>
<td>10%</td>
<td>45%</td>
<td>55%</td>
</tr>
<tr>
<td>Gl. sublingualis</td>
<td>1%</td>
<td>90%</td>
<td>10%</td>
</tr>
<tr>
<td>Minor salivary glands</td>
<td>9%</td>
<td>45%</td>
<td>55%</td>
</tr>
</tbody>
</table>
Site specific differences

Malignant:
• 50% of palatal tumors
• 80%, 93% and 93% of tongue, retromolar and mouth floor

Entities:
• Canalicular adenomas and polymorphous low-grade adenocarcinoma: minor gland sites
• Warthin tumor: parotid gland
Site specific differences

• Pleomorphic adenoma:
  – capsule in major salivary glands
  – no capsule in minor salivary glands
→ CAVE: juxtaposition to acini and ducts or muscles is not a sign of malignancy in minor salivary glands
  – in minor glands often predominantly plasmacytoid, also in myoepitheliomas (CAVE no plasmacytoma)
Difficult diagnosis in FNP

• In 8% a benign lesion was diagnosed as malignant

• In 32% a malignant lesion was called benign

From the College of American Pathologists
Most tumors are thought to arise from the intercalated duct reserve cell or ist precursor that differentiates into acinar, myoepithelial, striated, and intercalated ductal cells. The excretory duct reserve cell differentiates into excretory ductal cells and gives rise to tumors such as mucoepidermoid carcinoma and salivary duct carcinoma.
Benign salivary gland neoplasms

• Most frequent diagnosis in minor salivary glands:
  – Pleomorphic adenoma
  – Myoepithelioma
  – Canaliculular Adenoma
  – Cystadenoma

  60-80% of all cases

Thought to arise from intercalated duct reserve cells within the secretory unit
Pleomorphic Adenoma
Figure 4-3

PLEOMORPHIC ADENOMA OF PAROTID GLAND

The preauricular mass had enlarged to this size over a period of 5 years. (Fig. 4-1 from Fascicle 17, Third Series.)

Figure 4-4

RECURRENT PLEOMORPHIC ADENOMA

The characteristic multinodular growth of recurrent pleomorphic adenoma is obvious in this parotid mass. (Fig. 4-2 from Fascicle 17, Third Series.)
Microscopy

- Cytomorphologic and architectural diversity
  - **epithelial**: spindle, clear, squamous, basaloid, cuboidal, plasmacytoid, oncocytoid, mucous, sebaceous
  - **mesenchymal like**: myxomatous or myxochondromatous mesenchymal like (bone may be present)

- Bland cytology, few mitosis, necrosis only after surgical manipulation

- Translocation: 8q12 (PLAG1 = pleomorphic adenoma gene 1) und 3p21(CTNNB1=humaner beta Catenin-Gen Locus) or 12q13-15 (HMGA2= high mobility group gene A2) ➔ PLAG1 overactivation (in >50% of cases)
Clinical aspects

• Pseudo capsule: Tumor penetration or perforation with «satellite nodules»
• Higher recurrence rate > 5cm
• Recurrences very often multinodular
Differential diagnosis

- None, if classical case
- Small biopsy from the lip: canalicular adenoma and polymorphous low-grade adenocarcinoma (clinical aspect!)
- Chondroid syringoma: closer to skin than salivary gland
Pleomorphic adenoma.
A, Pleomorphic adenoma with cystically dilated ducts.
B, Squamous metaplasia and keratin formation.
C, Mucous cells and crystalline bodies.
Pleomorphic adenoma.
A, Sheets of plasmacytoid myoepithelial cells with focal duct formation.
B, Cells with eccentric pleomorphic nuclei and abundant eosinophilic cytoplasm.
Pleomorphic adenoma.
A, Tumor with extensive hyalinization.
B, Ducts exhibit benign cytology surrounded by densely hyalinized stroma (inset).
Carcinoma ex pleomorphic adenoma of the upper lip.
A, Pleomorphic adenoma with extensive hyalinization and adenocarcinoma (right).
B, Remnant pleomorphic adenoma.
C, Adenocarcinoma with comedonecrosis.
D, Adenocarcinoma with pleomorphic nuclei.
Myoepithelioma

• Benign epithelial neoplasm
• Spindle, plasmacytoid, epithelioid, clear cells that exhibit myoepithelial but no ductal differentiation
• May have abundant acellular, mucoid or hyalinized stroma but no chondroid or myxochondroid foci
• Represents one end of the spectrum of pleomorphic adenoma
  → almost identical biological behaviour
Myoepithelioma.
A, Myoepithelioma showing sheets of myoepithelial cells without duct formation.
B, Plasmacytoid myoepithelial cells with abundant eosinophilic cytoplasm.
Spindle cell myoepithelioma of palate.
A, Spindle cell proliferation with formation of cartilage and fat.
B, Focal area of osseous metaplasia.
C, Spindled myoepithelial cells in myxoid stroma.
**Figure 4-154**

**MYOEPITHELIOMA: SO-CALLED RETICULAR VARIANT**

Ramifying cords of polygonal and basaloid cells are surrounded by ample mucoid stroma. More solid growth of this tumor was evident elsewhere. (Fig. 4-40 from Fascicle 17, Third Series.)

**Figure 4-155**

**MYOEPITHELIOMA: PLASMACYTOID VARIANT**

Top: A well-delineated proliferation of small islands, clusters, and individual cells lies in a richly mucoid stroma. Bottom: Higher magnification shows that a homogeneous population of plasmacytoid cells comprises the cellular component of this tumor. (Fig. 4-41 from Fascicle 17, Third Series.)
Basal cell adenoma
Histologische Typen

- Solide
- Trabecular
- Tubular
- Membranous
**Figure 4-46**

**BASAL CELL ADENOMA**

Some of the nuclei of the epithelial cells adjacent to the stroma along the periphery of the tumor cell nests appear palisaded (arrows).

**Figure 4-47**

**BASAL CELL ADENOMA**

A small lumen and a large lumen (arrows) are lined by eosinophilic cuboidal ductal cells.

**Figure 4-48**

**BASAL CELL ADENOMAS: SOLID TYPE**

In the solid type of basal cell adenoma, the basaloïd tumor cells form variably sized and shaped nodules that appear closely apposed and molded together (left) or more separated and insular (right). Wide anastomosing bands are also evident (left).
Figure 4-52

BASAL CELL ADENOMA: TRABECULAR TYPE

The trabeculae of tumor cells are closely apposed, and there is little stroma.

Figure 4-53

BASAL CELL ADENOMA: TRABECULAR TYPE

The small lumens within some of the trabecular cords of basaloid cells, as in this tumor, have prompted the term tubulotrabecular.
Figure 4-54

BASAL CELL ADENOMA: TUBULAR TYPE

The tubular pattern is characterized by numerous small lumens lined by ductal or basaloid cells. Basaloid cells are usually arranged peripheral to the lumens.
Figure 4-55

BASAL CELL ADENOMA: MEMBRANOUS TYPE
Prominent eosinophilic hyaline material surrounds and separates islands and trabeculae of basaloid cells.

Figure 4-56

BASAL CELL ADENOMA: MEMBRANOUS TYPE
In addition to the marked hyaline material that separates tumor nests, there are prominent hyaline droplets within the tumor nests.

Higher recurrence rate

Cylindroma like

PAS + Basal membrane remnants
Differential diagnosis

• Eccrine dermal tumors: site

• Basal cell adenocarcinoma:
  - Mitosis (>3/10 HPF suggests malignancy but less does not rule out)
  - Infiltrative growth (CAVE multinodular basal cell adenoma), nerve sheet infiltration helps (but only 25%)!

• Adenoid cystic carcinoma (solid variant):
  - Perineural invasion, infiltrative growth, necrosis, mitosis
Canalicular adenoma
Canalicular adenoma.
A, Encapsulated tumor with focal capsular infiltration.
B, Delicate ribbons of cells in myxochondroid stroma.
C, Double layer of basaloid cells with ductal structures and collagen-poor stroma with ectatic vessels.
**Figure 4-126**

**CANALICULAR ADENOMA**

The epithelial tubules are composed of two rows of columnar cells that alternately abut and separate. The stroma is nearly invisible, with few cells, but several small capillaries have an eosinophilic cuff and stand out.

**Figure 4-127**

**CANALICULAR ADENOMA**

Foci of basaloid cells (arrows) among the typical columnar cells appear to be tubular epithelium cut en face. Another focus (arrowhead) suggests a proliferation of basaloid cells.
Differential diagnosis

• Basal cell adenoma:
  no columnar cells, no canaliculi, parotis most frequent localization

• Adenoid cystic carcinoma:
  No rows of columnar cells, no blood vessels in the stroma, dense collagen in the tumor, infiltrative growth (CAVE multifocal canalicular adenoma)
Cystadenoma.
A, Proliferation of cysts of varying sizes with focal adenomatous plaques.
B, Cysts lined by a double layer of columnar cells.
Oncocytic sialocytosis.
A, Salivary gland with dilated ducts within multiple gland lobules.
B, Dilated ducts lined by a double layer of oncocyes and underlying plasma cells; early changes in adjacent glands (arrow).

DD cystadenoma
Sialadenoma papilliferum.
A, Papillary proliferation of surface epithelium and adenomatous proliferation of ducts at base.
B, Inflammation results in spongiosis of epithelium.
C, Adenomatous proliferation with papillary hyperplasia.
Intraductal papilloma.

A, Single, dilated excretory salivary duct with luminal papillary proliferation.

B, Well-organized papillary structures with fibrovascular cores and microcysts.

C, Surface luminal cells are cuboidal/columnar, and mucous cells are present.
Inverted ductal papilloma.
A, Bulbous endophytic growth arising from a duct.
B, Cuboidal-to-columnar cells seen on luminal surface with scattered mucous cells.
C, Cells have bland nuclear morphology, and there is microcyst formation.