MALIGNANT TUMORS OF THE SALIVARY GLANDS

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What you will Learn

- Malignant Salivary gland Tumours:
  1. Mucoepidermoid carcinoma
  2. Adenoid cystic carcinoma
  3. Polymorphous low grade adenocarcinoma
  4. Carcinoma ex pleomorphic adenoma
  5. Adenocarcinoma NOS
Tumor like Lesions:

A. Sjogren’s syndrome
B. Mickulicz Disease
C. Necrotizing sialometaplasia
Tumors of salivary glands constitute a heterogeneous group of lesions of great morphologic variation.

These tumors are relatively uncommon.
HISTOGENESIS OF SALIVARY GLAND NEOPLASMS

Semipluripotential bicellular reserve cell hypothesis

Specific reserve or basal cells of the excretory and intercalated ducts or both are responsible for replacement of all types of cells in normal gland and hence are the sole source for neoplastic transformation.
Multicellular histogenetic concept

- Any of the various cells found in the normal salivary gland could serve as a precursor for neoplasia; thus, this is a multicellular histogenetic concept.
1. BENIGN EPITHELIAL TUMOURS

- Pleomorphic adenoma (mixed tumour)
- Myoepithelioma
- Basal cell adenoma
- Warthin tumour
- Oncocytoma
- Canalicular adenoma
- Sebaceous adenoma
- Sebaceous adenoma
- Sebaceous Lymphadenoma
- Ductal papillomas
  - Inverted ductal papilloma
  - Intraductal papilloma
  - Sialadenoma papilliferum
- Cystadenoma
  - Papillary cystadenoma
  - Mucinous cystadenoma
2. MALIGNANT EPITHELIAL TUMOURS

- Acinic cell carcinoma
- Mucoepidermoid carcinoma
- Adenoid cystic carcinoma
- Polymorphous low grade adenocarcinoma
- Epithelial-myoepithelial carcinoma
- Basal cell adenocarcinoma
- Sebaceous carcinoma
- Sebaceous lymphadenocarcinoma
- Cystadenocarcinoma
- Low-grade cribriform cystadenocarcinoma
- Mucinous adenocarcinoma
- Oncocytic carcinoma
Salivary duct carcinoma
Adenocarcinoma, NOS
Myoepithelial carcinoma

MALIGNANT MIXED TUMOURS
A. Carcinoma ex pleomorphic adenoma
B. Carcinosarcoma
C. Metastasizing pleomorphic adenoma
Squamous cell carcinoma
- Small cell carcinoma
- Lymphoepithelial carcinoma
Malignant pleomorphic adenoma

Clinical features

- Most common in middle age & older adults
- Rapid growth with associated pain or ulceration
- Often fixation
- Slight female predilection
- Tumor of high grade malignancy grows rapidly & produces pain
Facial n. paralysis frequent in parotid tumors
Three categories:

- Carcinoma ex pleomorphic adenoma
- Carcinosarcoma
- Metastasizing Mixed tumor
Histologic features

Carcinoma ex pleomorphic adenoma

- Malignant component appears to overgrow benign
- Bulk of tumor appear benign
- Areas of malignant degeneration of the epithelial component, characterized by cellular pleomorphism & abnormal mitotic activity
Malignant component has an aggressive growth pattern with capsular invasion & infiltration into surrounding tissues.

Carcinosarcoma

Biphasic tumor demonstrating both carcinomatous and sarcomatous areas.
Metastasizing mixed tumor

- Has microscopic features of a benign pleomorphic adenoma, within both the primary and metastatic sites. Malignant histopathologic changes are not observed.
MUCOEPIDERMOID CARCINOMA

- One of the most common salivary gland malignancies; most common malignant salivary gland tumor in children.

**Clinical features**

- Most common in parotid salivary gland
- Minor glands – 2\textsuperscript{nd} most common site especially the palate
- Asymptomatic swelling
- Pain or facial n. palsy may develop
- 2nd to 7th decade
- Slight female predilection
- Some tumors associated with history of radiation therapy
- Trismus, drainage from the ear, dysphagia, numbness of the adjacent areas & ulcerations
- Not encapsulated, tends to infiltrate the surrounding tissue, & tends to metastasize to regional lymph nodes
HISTOLOGIC FEATURES

- Mucus secreting cells, epidermoid type cells and intermediate cells.
- Mucous cells of various shapes seen.
- Epidermoid cells have squamoid features.
- Intermediate cells – progenitor of epidermoid and mucous cells.

- Clear cells may be seen.

- Epidermoid and mucous cells may be arranged in a glandular pattern.
Three histopathologic grades based on the following:

1. Amount of cyst formation
2. Degree of cytologic atypia
3. Relative numbers of mucous, epidermoid and intermediate cells.
GRADED AS

Low grade –

- Well formed glandular structures & prominent mucin filled cystic spaces, minimal cellular atypia & high proportion of mucous cells
Intermediate grade –

- Solid areas of epidermoid cells or squamous cells with intermediate basaloid cells.
- Cyst formation is seen but is less prominent
High grade –

- Consist of cells present as solid nests & cords of intermediate basaloid cells & epidermoid cells
- Prominent nuclear pleomorphism & mitotic activity noted
- Cystic component very less
- Glandular component rare
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<td>Intracystic component &lt;20%</td>
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<td>Neural invasion present</td>
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<td>Necrosis present</td>
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<td>Four or more per 10 HPF</td>
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<td>Anaplasia</td>
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<td>Intermediate</td>
<td>5 - 6</td>
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<td>High</td>
<td>7 - 14</td>
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Variants of tumor

Sclerosing type –
- Characterized by an intense central sclerosis with inflammatory infiltrate of plasma cells, eosinophils & lymphocytes.

Intraosseous –
- May originate within the jaws.
- Central mucoepidermoid carcinoma.
Treatment -

Conservative excision with preservation of the facial nerve
Adenoid cystic carcinoma

(Cylindroma)

**Clinical features**

- 50% in minor salivary glands
- Palate – most common site for minor gland tumor
- Parotid (2-3%) & submandibular (12-17%)
- Middle aged adults – most common
- Equal distribution between men & women
- Appears as a slowly growing mass
- Pain is common finding
- Facial nerve paralysis may develop with parotid tumors
- Palatal tumors are smooth & ulcerated
- Tumors arising in palate or maxillary sinus may show radiographic evidence of bone destruction
Histologic features

- Mixture of myoepithelial & ductal cells

3 patterns

**Cribriform**

- Most classic
- Islands of basaloid epithelial cells that contain cylindric cyst like spaces resembling swiss cheese
- These spaces often contain a mildly basophilic mucoid material, a hyalinized eosinophilic product or combined mucoid-hyalinized appearance
- Small strands of tumor cells are seen within hyalinised stroma
Tubular pattern

- Tumor cells occur as multiple small ducts within a hyalinised stroma
- Tubular lamina lined by one or several layers of cells, & some times both a layer of ductal cells & myoepithelial cells can be seen
Solid variant

- Consists of large islands or sheets of tumor cells that show little tendency towards cyst formations
- Cellular pleomorphism & mitotic activity may be observed
Dedifferentiation of Adenoid cystic Carcinoma

- Solid sheets and cords of anaplastic tumor cells with focal gland formation
Perineural invasion –

- Highly characteristic feature of adenoid cystic carcinoma is its tendency to show perineural invasion
Polymorphous low grade adenocarcinoma

- Malignant epithelial tumor that is essentially limited in occurrence to minor salivary gland sites and is characterized by bland, uniform nuclear features, diverse but characteristic architecture; infiltrative growth; and perineural infiltration.

- Recently described in 1983.
In minor gland sites PLGA is twice as frequent as ACC.

Average age is 59 years; female predilection.

Firm, nontender swelling involving mucosa of hard & soft palates.

Discomfort, bleeding, telangiectasia or ulceration of the overlying mucosa.
Histologic features

- Infiltrative growth with diverse morphology & uniform cytologic features.
- Well circumscribed but unencapsulated & infiltrate into adjacent structures.
- Polymorphic nature refers to variety of growth patterns including solid, ductal, cystic and tubular.
- Pseudocribriform pattern in some tumors resembling ACC.
- Cuboidal to columnar isomorphic cells that have uniform ovoid to spindle-shaped nuclei.
- Scant to moderate amounts of eosinophilic cytoplasm seen.
Perineural invasion is common that makes this tumor mistaken as ACC.

Indian file arrangement shows streaming cords of cells.

**Treatment**

Conservative wide surgical excision.
FIGURE 8-40 Polymorphous low-grade adenocarcinoma showing streaming pattern.
FIGURE 8-42 Polymorphous low-grade adenocarcinoma with a pseudocribiform pattern.
FIGURE 8-45 Polymorphous low-grade adenocarcinoma in perineural spaces.
ACINIC CELL CARCINOMA

ACINIC CELL ADENOCARCINOMA

- Cells show serous acinar proliferation

CLINICAL FEATURES

- 85% occur in the parotid gland
- This neoplasm makes up 1-3% of all parotid gland tumors
- One study showed -8.6% of all parotid tumors.
- Less common in submandibular glands
9% develop in oral minor salivary glands with the buccal mucosa, palate, lips being the most common sites.

- Seen in 2nd - 7th decade
- Mean age - middle 40
- Slow growing mass
- Asymptomatic
- Facial nerve paralysis - an infrequent sign.
Histologic features

- Variable microscopic appearance
- Well circumscribed & sometimes encapsulated
- Some tumors show an infiltrative growth pattern
- Most characteristic cell is serous acinar cell
- These cells are uniform in appearance, and mitotic activity is uncommon.
- Other cells may resemble intercalated duct cells.
- Some tumors have cells with a clear, vacuolated cytoplasm.
Several growth patterns seen-

- Solid variety consists of numerous well-differentiated acinar cells.
- Microcystic- multiple small cystic spaces are created that may contain some mucinous or eosinophilic material.
- Papillary – cystic- larger cystic areas formed that are lined by epithelium having papillary projections into the cystic spaces.
- Follicular- appearance similar to thyroid tissue.
- Lymphoid elements sometimes seen.

**Treatment / prognosis**

- Surgical excision
- Poor prognosis if features like pain or fixation, gross invasion seen
Adenocarcinoma (NOS) not otherwise specified

- Rare but aggressive tumors.

**Clinical features**

- Present in patients over 40 years of age.
- Mostly seen in parotid gland.
- Palate most common in minor salivary gland sites.
Histopathology

- Demonstrate a wide range of growth patterns, and somewhat difficult to classify.
- All adenocarcinomas have in common the formation of glandular structures.
- Grades I, II or III depending upon the degree of cellular differentiation.
TUMOR LIKE LESIONS
- **Mickulicz disease** reserved for cases associated with benign lymphoepithelial lesions.

- **Mickulicz Syndrome** – cases of parotid and lacrimal enlargement secondary to other disease like tuberculosis, sarcoidosis and lymphoma.

- These terms should no longer be used.
Benign lymphoepithelial lesion

- Mikulicz disease is a chronic condition characterized by the abnormal enlargement of the salivary and lacrimal glands.
- Uncommon
- Inflammatory & neoplastic
- Autoimmune disease
- Often occurs in combination with Sjogren syndrome.
CLINICAL FEATURES

- Xerostomia, difficulty in swallowing and result in tooth decay.
- Enlarged lacrimal glands, leading to decreased tears.
- Painless swellings of the salivary glands.
- Recurring fevers accompanied by dry eyes.
- Unilateral / bilateral enlargement (85%)
- Associated with salivary gland pathology such as sialoliths and benign or malignant epithelial tumors.
- 85% cases occur in the parotid gland. Onset – fever, infection
Diffuse enlargement of salivary gland
Size – few cm in diameter
Asymptomatic or associated with mild pain
Women affected more
Middle or later life- mean age 50yrs
Histologic features

- Lymphocytic infiltration destroying or replacing the acini,
- Germinal centers may or may not be seen.
- Acini replaced by epithelial cells
- Lymphoid element diffuse
- Cellular proliferation & loss of polarity
- Solid nests/ clumps of poorly defined epithelial cells
- Epimyoepithelial islands throughout the lymphoid proliferation.
- Eosinophilic material in epithelial islands- seen in advanced lesions.
Treatment

- Surgical excision
- Radiation
- Mild cases – no treatment
- Persistent cases – surgical excision
- Prognosis – good
- Associated malignancy- a malignant lymphoepithelial lesion or lymphoepithelial carcinoma.
Sjogren’s syndrome

- Chronic, systemic autoimmune disorder that involves the salivary and lacrimal glands.

- **Triad of**
  - Keratoconjunctivitis sicca
  - Xerostomia
  - Rheumatoid arthritis

Two forms- **Primary / Secondary**
- **PRIMARY**- sicca syndrome alone: no other autoimmune disorder present

- **SECONDARY**- patient shows sicca syndrome in addition to another associated autoimmune disease.
Etiology

- Genetic
- Hormonal
- Infection
- Immunological
- EBV

- HLA Ag-HLA-DRw52 associated with both forms of the disease.
- HLA-B8 and HLA-DR3 seen in primary form of the disease.
Clinical features

- > 40 years or in middle aged adults.
- 10 : 1 female male ratio
- Dryness of mouth & eyes
- Painful burning sensation of oral mucosa
- Difficulty in swallowing, altered taste or difficulty in wearing dentures.
- Fissured tongue & atrophy of the papillae.
- Denture sore mouth & angular cheilitis
- Dental decay, especially cervical caries
- Secretory glands involved
- Parotid enlargement
- Lymphadenopathy
Histologic features

- Lymphocytic infiltration of the salivary gland
- Destruction of the acinar units.
- Proliferation of ductal & myoepithelium
- Atrophy of gland
- Antisalivary duct antibody
Lab Findings

- **Primary**
  - Hyperglobulinemia
  - Cryoglobulins
  - Multiple organ / tissue specific antibodies
  - Increased ESR
  - Antisalivary duct antibody more in secondary
X - RAY

- Sialography
- Formation of cavitary defects
- Cherry blossom
- **Branchless fruit- laden tree**
- Reduced salivary flow – sequential salivary scintigraphy
- Sialochemistry – IgA, K, Na levels are elevated
Treatment

- No satisfactory treatment
- Symptomatically
- Ocular lubricants- methylcellulose
- Saliva substitutes
- Dental caries
- Oral hygiene
- Surgery in cases of enlargement
- Complications are:
  Pseudolymphoma & malignant lymphoma
Necrotizing sailometaplasia

- Uncommon
- Destructive inflammatory condition
- Ischemia
- Mimics malignancy

ETIOLOGY

- Traumatic injuries
- Radiation therapy
- Dental infections
- Ill fitting dentures
- Upper respiratory infection
- Adjacent tumors
- Previous surgery
- Tobacco use.
Clinical features

- Palatal glands
- 75% posterior palate, hard palate
- 2/3rd unilateral
- Other minor glands & occasionally parotid and submandibular gland.
- Mean age - 46 years
- Males affected twice
- Nonulcerated swelling
Lesions often painless.

Some lesions present as a submucosal swelling, without ulceration of the overlying mucosa.

Necrotic tissue slough out.

Crateriform ulcer of the palate that simulates a malignant processes.

Destruction of the underlying palatal bone.
Histopathologic features

- Acinar necrosis
- Acinar cells lack nuclei, appear pale & basophilic
- Squamous metaplasia of ducts
- Lobular architecture preserved
- Liberation of mucin
- Inflammatory response
Scattered neutrophils & foamy histiocytes
Pseudoepitheliomatous hyperplasia of the overlying mucosa can also be present.

DIFFERENTIAL DIAGNOSIS
- Squamous cell carcinoma
- Mucoepidermoid carcinoma

Treatment
- NS resolves spontaneously.
- No treatment is necessary.
Frequently asked questions

- Short Notes on:
  1. Mucoepidermoid carcinoma
  2. Adenoid cystic carcinoma
  3. Polymorphous low grade adenocarcinoma
  4. Sjogren’s syndrome.
Objective type questions:

a) Name the histopathologic patterns seen in adenoid cystic carcinoma.

b) Which is the classic histopathologic pattern seen in adenoid cystic carcinoma?

c) Name the tumor-like lesion of salivary gland which mimics malignancy clinically as well as microscopically. Which is the most common site of this lesion?
REFERENCES

For any queries, mail to:
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THANK YOU