Salivary Tumours

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Anatomy

- Parotid
  - Paired glands posterior cheek.
  - Superficial and deep lobe divided by the facial nerve.
  - Approximately 10 to 20 intra-parotid lymph nodes principally in the superficial parotid lobe.
- Submandibular
  - Paired glands in a submandibular position.
  - Lymph nodes lie outside the gland.
  - Closely approximates the hypoglossal and lingual nerves.
  - Paired ducts enter the anterior floor of mouth.
  - Higher calcium content in the secretions.
- Sublingual
  - Paired glands in a submucosal position in the lateral floor of mouth.
- Minor salivary glands
  - Throughout the nasal, paranasal, oropharynx, larynx. Highest density on hard palate

Histology

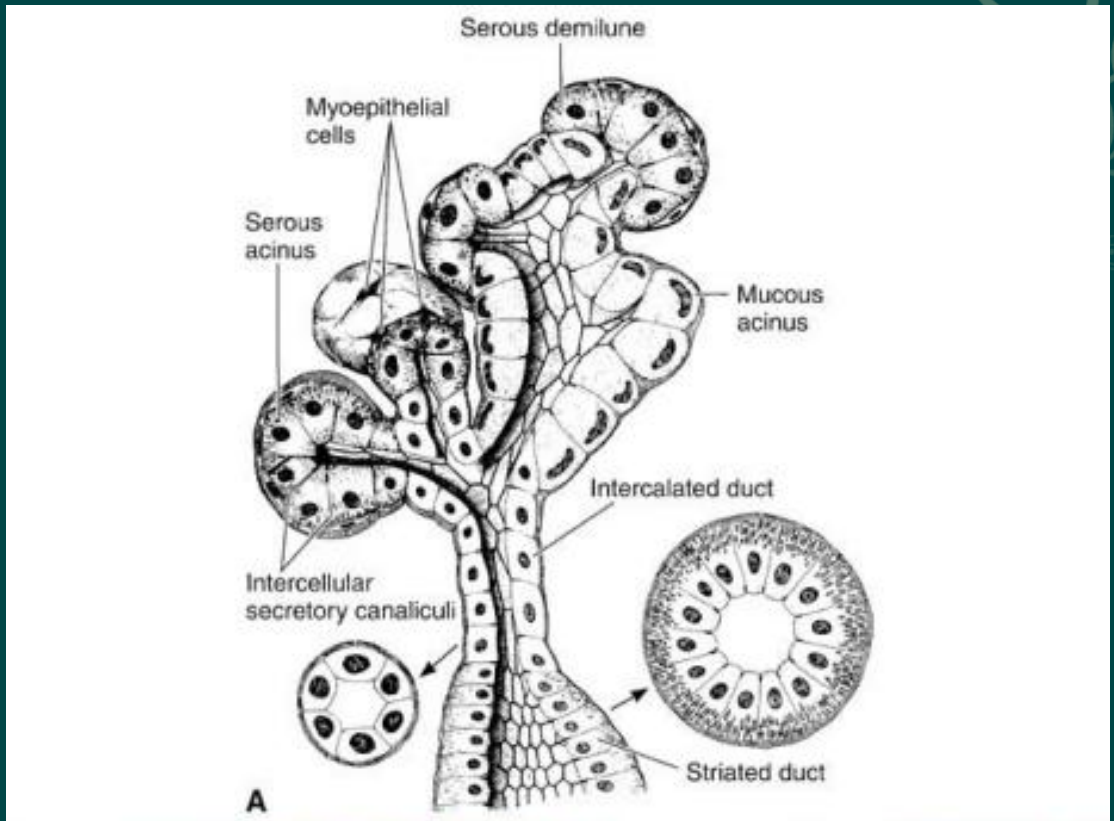
Distal acinus
- Saliva-forming cells around central lumen
- Myoepithelial cells
- Basement membrane

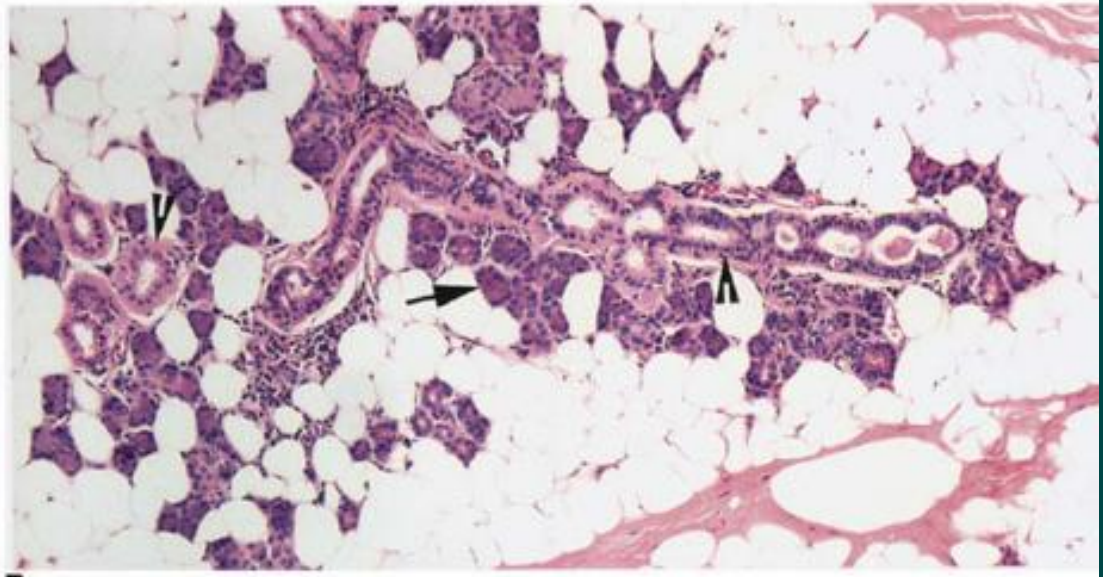
Intercalated duct

Striated duct

Excretory ducts

Arise from undifferentiated reserve cells





Tumourigenesis

- Histogenesis
  - Multicellular Theory
    - Each type of tumour derives from separate cell types within the salivary gland.
  - Bicellular Reserve Cell Theory
    - The basal cells of the excretory or intercalated ducts have potential to differentiate into a variety of epithelial cells.

Aetiology

- Environmental
  - Radiation
    - Increased rate in Atomic bomb survivors
    - Increased risk with head and neck irradiation
    - Highest risk for mucoepidermoid carcinoma and Warthin's tumours
  - Viral
    - Epstein-Barr virus associated with lymphoepithelial carcinoma in the Asian population
  - Toxins
    - Tobacco smoking associated with an increased risk of Warthins's tumour
    - Silica dust exposure increases risk or salivary malignancy

Incidence

- Primary Salivary Gland tumours are 3-4% of head and neck malignancies.
- Parotid: 75% of salivary tumours
  - 80% of parotid lesions are benign
  - 80% of benign lesions of the parotid are pleomorphic adenoma
- Submandibular: 10% of salivary tumours
  - 1/3 malignant
- Minor Salivary glands: 15% of salivary tumours
  - ½ malignant
- Sublingual: Rare (0.3% of salivary tumours)
  - 90% malignant
- NOTE: metastatic SCC to parotid is the most common malignancy in the parotid, but this talk is primary salivary tumours.

Presentation

- Lump or swelling is the usual presentation
- Episodic swelling/acute swelling and pain suggest inflammatory.
- Bilateral parotid swelling suggests inflammatory i.e. Sjogren's
- Long and/or slow growth history, painless, and mobile suggest benign.
- Faster growth rate, mass with fixation, nerve palsy, and pain strongly suggest malignancy.

Investigations

- CT scan or MRI (MRI is at defining tumour extent and architecture)
  - Tumour location, margins, unilateral/bilateral, local destruction, cavitation.
- FNA (Ultrasound guided)
  - Low morbidity
  - Highest error rate for head and neck malignancies
  - Tendency to under-diagnose rather than over-diagnose
  - 68% sensitivity and a 32% false negative rate in malignancy lesions
  - 86 to 99% sensitivity and specificity 95 to 100% for benign lesions
  - Good at diagnosing Lymphoma

Benign Tumour Classification

- Pleomorphic Adenoma
- Warthin's tumour
- Basal Cell Adenoma
- Oncocytoma
- Myoepithelioma

Pleomorphic adenoma

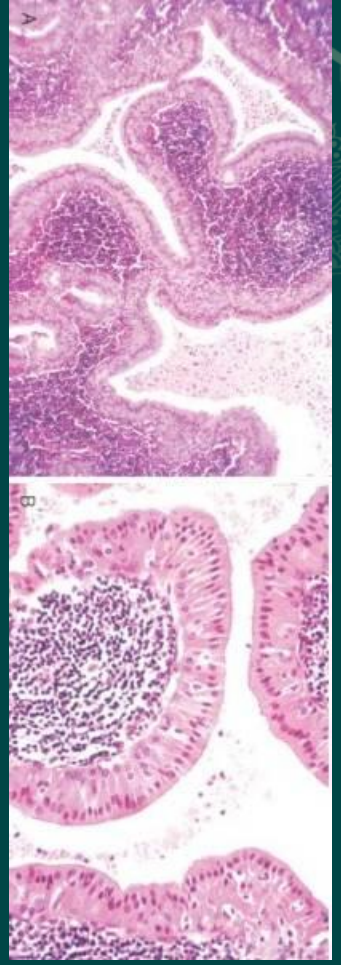
- 75% of all parotid tumours; 45% of all salivary tumours; Second most common paediatric tumour after haemangiomas
- F > M; 3rd to 6th decades
- Etiology unknown
- Clinically a firm, slowing growing, painless mass. Usually solitary. May reach very large sizes.

- Arise from distal portion of salivary gland (reserve cells of the intercalated ducts)
- 90% arise in the superficial lobe of the parotid
- Occasionally extend from the superficial lobe into the deep lobe . (If extending into the parapharyngeal space can form a dumbbell tumour)
- 10% arise in the deep lobe of the parotid or parapharyngeal

Pleomorphic adenoma

- Histopathology– mixture of epithelial/ myoepithelial/ stromal elements
  - Must contain all 3
  - Epithelial cells as well as myoepithelial cells found within a chondroid matrix material.
- 25% have satellite nodules or pseudopodia – need margin
- Well-demarcated tumor with a thin capsule
- Treatment is surgical excision.
- Prognosis excellent
  - 4% recurrence when excised with a margin of normal parotid.
  - 1.5% malignant transformation at 5 years, 10% at 15 years.

Warthin's Tumours



- Papillary cystadenoma lymphomatosum
- Alfred Warthin described in 1929
- 10% of benign parotid tumours (second most common)
- Associated risk with smokers. Associated with ionizing irradiation
- M>F
- 5^{th} to 7^{th} decades
- 10% bilaterality; at least 10% multicentricity

- Exclusively in the parotid gland. Usually in the tail.
- Arises from ectopic ductal epithelium
- Distinctive histology – papillary structures, double layer of oncocytes, cystic changes, mature lymphocytic infiltration
- Usually a slow growing painless mass.
- Treatment is surgical excision.

Other Tumours

- Basal cell adenoma
  - Similar appearance to solid variety of adenoid cystic carcinoma
  - Most occur in parotid or lip
  - Basement membrane intact cf. pleomorphic adenoma.
  - Treatment is surgical excision.
- Oncocytomas
  - Less than 1% of tumours, mostly occur in the superficial parotid.
  - Usually slow growing painless mass.
  - May be diffuse
  - Radioresistant
  - Treatment is surgical excision.
- Myoepitheliomas
  - Well encapsulated, slow growing and painless. Difficult to diagnose on FNA. Treatment is surgical excision. Clinically similar to Pleomorphic adenomas.
- Oncocytic Papillary Cystadenoma
  - Usually in the larynx. Uncommon in the Parotid.
  - ? a true tumour.

Management of Benign tumours

- Benign lesions – appropriate resection with margin
  - Superficial parotidectomy, submandibular gland resection, palatal resection and appropriate reconstruction. etc
- Recurrent Pleomorphic Adenoma
  - Resection +/- radiotherapy
  - Radiotherapy
  - Risk to facial nerve for a benign lesion

Congenital Tumours

- Haemangiomas
  - Most common salivary gland tumour in children
    - 90% of parotid tumors in children <1yo
  - Rapid, proliferative growth -> deformity, airway obstruction
  - Usually present at birth – unilateral, painless mass
- Vascular malformations
  - Venous
  - Arteriovenous
  - Lymphatic

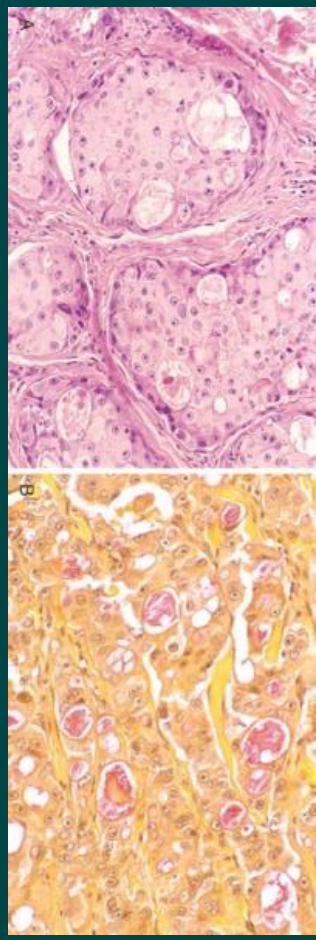
Malignant Tumour Classification

- Mucoepidermoid
- Adenoid Cystic Carcinoma
- Malignant Mixed Tumour
  - Benign Metastasizing Pleomorphic Adenoma
  - Carcinosacroma
  - Carcinoma ex-Pleoporphic Adenoma
- Acinic Cell Carcinoma
- Polymorphous Low Grade Adenocarcinoma
- Adenocarcinoma NOS (when does not fit MED, ACC, acinic or other definable adenocarcinoma)
- Salivary Duct Carcinoma
- Epithelial - Myoepithelial Carcinoma
- Primary Squamous Cell Carcinoma
- Primary Small Cell Carcinoma
- Lymphomas
- Metastatic/ secondary tumours
- Further divided into low/ intermediate/ high-grade histology based on clinical behaviour and tumour differentiation

Mucoepidermoid carcinoma

- Most common salivary gland malignancy
- Most common paediatric parotid gland malignancy
- 80-90% occur in parotid gland
- Also occurs in minor salivary glands of hard palate, RMT and buccal mucosa.
- F:M 4:1
- 5th decade

- Histologically comprised of solid and cystic components. There are three cell types - mucinous, squamoid and intermediate.

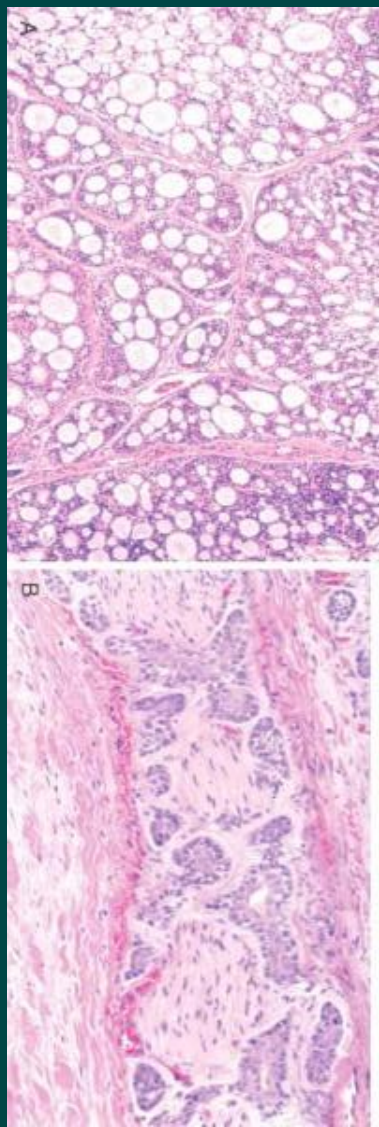


Mucoepidermoid carcinoma

- Grading of the tumour correlates strongly with clinical behavior.
  - Low grade prominent cystic component, with well differentiation, little atypia and low mitotic activity – rarely metastasize
  - Higher grade lesions have more solid and intermediate cells with more atypia, mitoses, necrosis and infiltration
- Clinical staging is also important for prognosis and is as important as histological grading.
- Survival rates
  - 5-year 56.7%
  - 10-year 27.8%
  - 15-year 7.1%

Adenoid cystic carcinoma

- 14% of parotid gland, 35% of minor salivary gland and 40-60% of sublingual gland malignancies
- M=F, peak incidence 50 to 60 yo.
- Presentation – mostly a lump, but 20% paraesthesias, 30% in parotid with partial/compete facial nerve palsy.
- Histological patterns
  - Cribriform (Swiss cheese), tubular and solid.
- Histological grade of tumour determined by extent of solid component
  - I: tubular +/- cribriform; no solid
  - II: cribriform with <30% solid
  - III: cribriform with >30% solid
- Perineural invasion by tumor cells in 75% of cases.
- Discontinuous areas of spread along a nerve



Adenoid cystic carcinoma

- Indolent and protracted clinical course with late recurrences and metastases over many years.
- Distant haematogenous metastases (particularly pulmonary(90% of mets)/ bone/ liver/ brain occurring late, usually 10 or more years later – long term follow up required.
- Medial survival after metastases is greater than 3 years.
- Lymphatic spread rare – not recommended for neck dissection or nodal radiotherapy
- Only the extent of surgery correlated with outcome, suggesting a need for radical surgery and combined with radiotherapy for perineural infiltration.

Acinic cell carcinoma

- 8% of malignant parotid neoplasms.
- F>M 2:1
- Wide age range from childhood to old age. Peak age 30 -60 yo
- Second most common paediatric salivary malignancy
- Presents as a slow grow mass. Rarely facial nerve palsy.
- FNA very difficult to diagnose
- Encased in fibrous capsule
- Low grade malignancy – surgery alone. But 10 -15% will metastasize. (thought a benign adenoma until 1953)
- Average 14 yrs to metastases, generally haematogenous to lung and bone.
- Survival rate
  - 5yr 83%
  - 10yr 76%
  - 15yr 65%
  - 25yr 50%

Malignant mixed tumour

- Three entities
  - Benign metastasizing pleomorphic adenoma – very rare
  - Carcinosarcoma – carcinoma and sarcoma (usually chondrosarcoma) elements – aggressive, rare
  - Carcinoma ex-pleomorphic adenoma - 95% of malignant mixed, uncommon

- Carcinoma ex-pleomorphic adenoma
  - Arise in pleomorphic adenomas
  - Malignant component is purely epithelial
  - Risk of malignant transformation is 1.5% in 5 years and 10% at 15 years.
  - Adverse features include invasion >1.5 mm from capsule and usual high grade features.
  - These tumours do poorly.
  - Surgery + XRT
  - 5yr survival rate 40%, 10 yr 24% and 15 yr 19%

Rarer Salivary Gland malignancies

- Polymorphous Low Grade Adenocarcinoma
  - Arises in the minor salivary glands, most commonly on the palate.
  - Low grade tumour, slow growth
  - F:M 2:1
  - 40-60 yo generally
  - Histology quite variable. Low mitotic rate, no necrosis
  - Conservative resection and lymph node dissection is involved only

- Adenocarcinoma NOS
  - Has ductal differentiation but unable to classify further.

Rarer Salivary Gland malignancies

- Epithelial-myoepithelial carcinoma
  - 1% of salivary gland neoplasms
  - 40% local recurrence, 20% cervical metastases, 40% die of disease
- Salivary duct carcinoma
  - Less than 10% of salivary malignancies
  - High-grade and aggressive – 35% local recurrence, 62% distant metastases, 77% die of disease, Mean survival of 3 years
- Primary SCC
  - Rare (<1% of salivary malignancies)
  - Must excluded high grade mucoepidermoid carcinoma
  - >50% have nodal disease at time of diagnosis.
- Small Cell Carcinoma
  - Less than 2% of salivary malignancies
  - Neuroendocrine tumour, dd merkel and lung small cell tumour

Lymphoma

- 2% salivary gland tumours
- Primary Non-Hodgkin's Lymphoma
  - De Novo or as secondary to lymphoepithelial sialadenitis.
- Full-body evaluation
- Association with Sjogren's syndrome
- FNA high sensitivity and specificity

TNM

- TX Primary tumor cannot be assessed
- T0 No evidence of primary tumor
- T1 Tumor 2 cm or less
- T2 Tumor 2-cm
- T3 Tumor more than 4 cm or extraparenchymal extension
- T4a Tumor invades skin, mandible, ear canal, or facial nerve - resectable
- T4b Tumor invades skull base, pterygoid plates, or encases carotid artery – non-resectable

- NX Regional lymph nodes cannot be assessed
- N0 No regional lymph node metastasis
- N1 Metastasis in a single ipsilateral lymph node 3 cm or less
- N2a Metastasis in single ipsilateral lymph node 3–6 cm
- N2b Metastasis in multiple ipsilateral lymph nodes <6 cm
- N2c Metastasis in bilateral or contralateral lymph nodes <6 cm
- N3 Metastasis in lymph node >6 cm

- MX Distant metastasis cannot be assessed
- M0 No distant metastasis
- M1 Distant metastasis

TNM Staging

- Stage I T1 N0 M0
- Stage II T2 N0 M0
- Stage III
  - T3 N0 M0
  - T1 N1 M0
  - T2 N1 M0
  - T3 N1 M0
- Stage IVA
  - T4a N0 M0
  - T4a N1 M0
  - T1 N2 M0
  - T2 N2 M0
  - T3 N2 M0
  - T4a N2 M0
- Stage IVB
  - T4b Any N M0
  - Any T N3 M0
- Stage IVC
  - Any T Any N M1

Prognostic Vairables

- Clinical Variables
  - T stage (size)
  - Submandibular or sublingual location – worse prognosis
  - Advanced age
  - More rapidly growing tumour
  - Nerve involvement clinically
  - Pain
- Histological Variables
  - Favourable tumours – acinic cell, low grade Mucoepidermoid, PLGA, basal cell adenoCa
  - Unfavourable tumours – high grade Mucoepidermoid, SCC, adenoCa NOS, salivary duct Ca
  - Local tissue invasion
  - Perineural infiltration
  - Incomplete surgical margins

Management of Malignant Tumours

- History and examination
- Investigations and tissue biopsy (FNA, truecut, incisional)
- Review in head and neck clinic.
  - Discussion of management ENT, Plastic, Radiation oncology, Medical Oncology, Speech Therapy, Social worker, Radiologist, Pathologist.
  - Decision based on overall patient situation – tumour, medical, social, their wishes
- Surgical resection
  - Adenoid Cystic – wide resection, frozen section nerves and margins, post op XRT
  - Low grade tumours – complete resection, frozen section for diagnosis if needed, usually no neck dissection.
  - High grade tumours – wide resection, frozen section for diagnosis if needed and for margins, +/- lymph node dissections depending on assessment, +/- XRT

Summary

- Salivary neoplasms are mostly benign.
- Most are in the parotid and a superficial parotidectomy the most common treatment.
- Malignant lesion need management through a head and neck clinic and require wide resection and possible radiotherapy.