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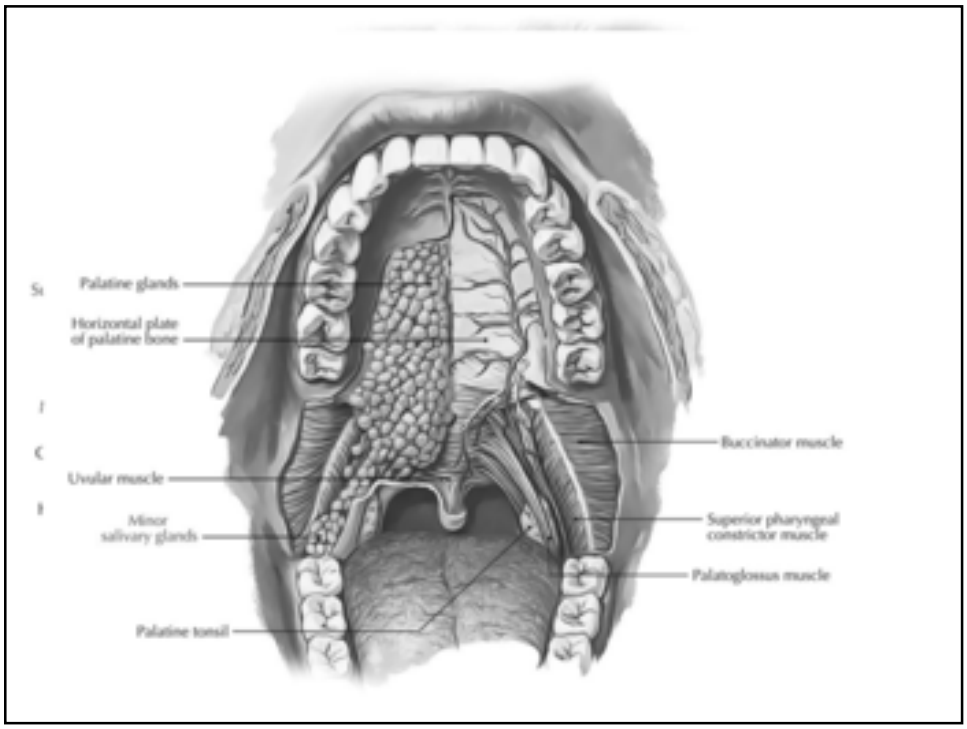
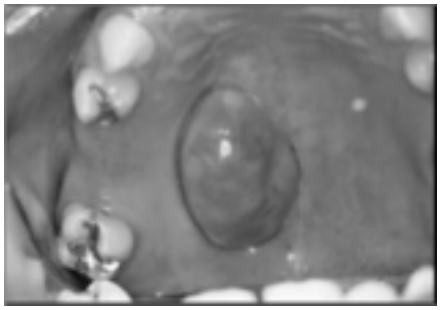
Salivary glands lesions

Dr. Amirah Alnour


Palatine glands
Horizontal plate of palatine bone
Uvular muscle
Minor salivary glands
Palatine tonsil
Buccinator muscle
Superior pharyngeal constrictor muscle
Palatoglossus muscle

Classification

Reactive Lesions
Infectious Sialadenitis
Benign Neoplasms
Malignant Neoplasms
Rare Tumors



Classification

Reactive Lesions

1. Mucus Extravasation Phenomenon
2. Mucus Retention Cyst (Obstructive Sialadenitis)
3. Maxillary Sinus Mucocoele (Retention Cyst and Pseudocyst)
4. Necrotizing Sialometaplasia

Infectious Sialadenitis

1. Sarcoidosis
2. Sjögren's Syndrome
3. Xerostomia
4. Taste Disturbances
5. Halitosis

Classification

Benign Neoplasms

1. Mixed Tumor (Pleomorphic Adenoma)
2. Basal Cell Adenoma
3. Canalicular Adenoma
4. Myoepithelioma
5. Oncocytic Tumors
6. Sebaceous Adenoma
7. Ductal Papilloma

Malignant Neoplasms

1. Mucoepidermoid Carcinoma
2. Polymorphous Low-Grade Adenocarcinoma
3. Adenoid Cystic Carcinoma
4. Clear Cell Carcinoma
5. Acinic Cell Carcinoma
6. Adenocarcinoma Not Otherwise Specified

Classification

Rare Tumors

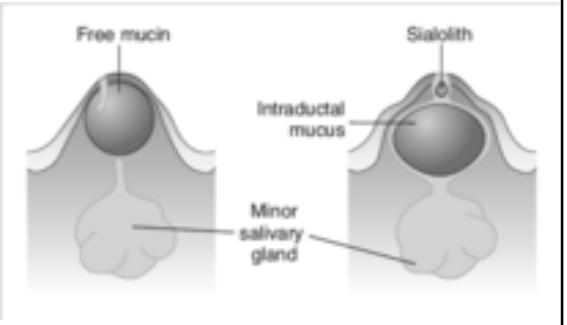
1. Carcinoma Ex-Mixed Tumor/Malignant Mixed Tumor/
2. Metastasizing Mixed Tumor
3. Epimyoepithelial Carcinoma
4. Salivary Duct Carcinoma
5. Basal Cell Adenocarcinoma
6. Mammary Analog Secretory Carcinoma (MASC)
7. Squamous Cell Carcinoma

Reactive Lesions

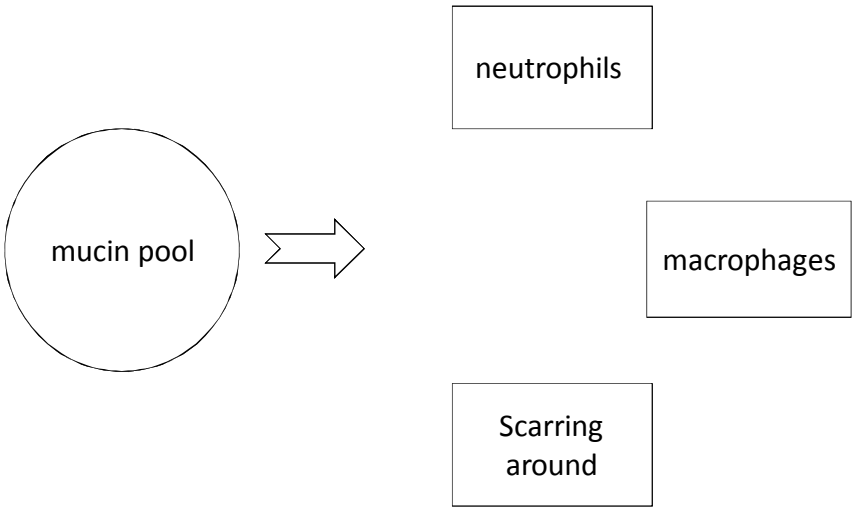
1

Mucus Extravasation Phenomenon

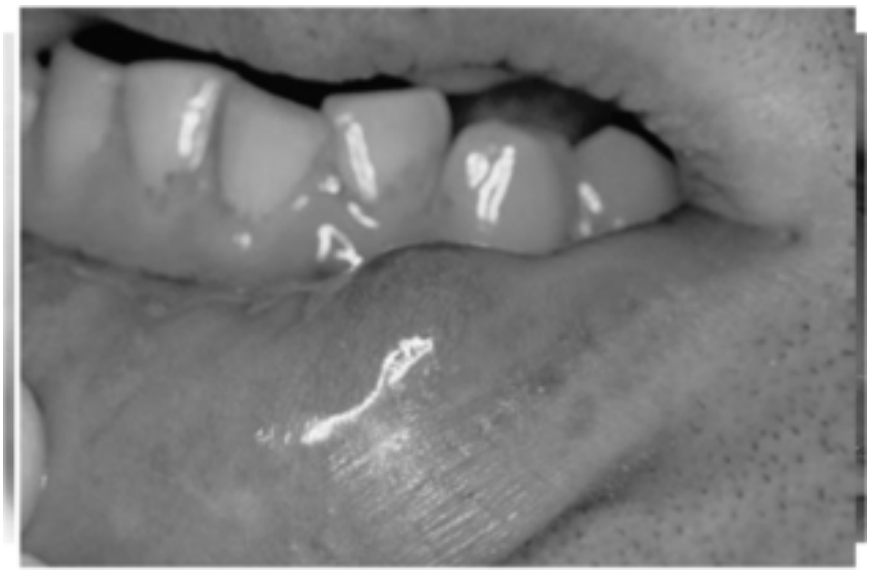
Traumatic severance of excretory duct → *escape of mucus*, into the surrounding connective tissue



Reactive Lesions



Reactive Lesions

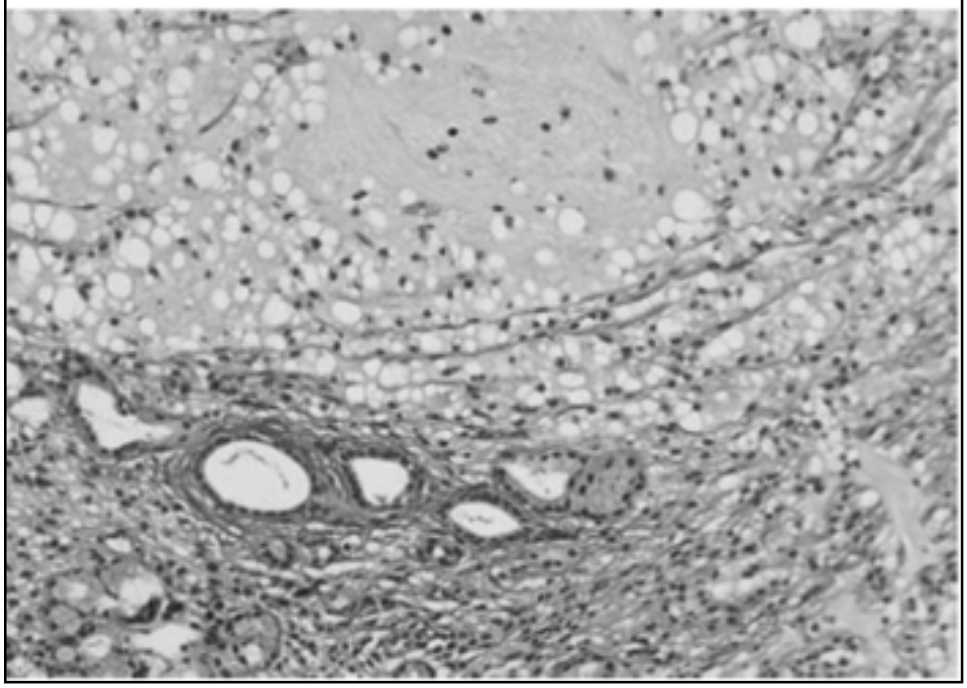


Reactive Lesions

Histopathology

1. Extravasation of *mucin* into the connective tissues
2. incites an inflammation: neutrophils, macrophages, and *granulation tissue*
3. duct *dilation*,
4. chronic inflammation,
5. acinar *degeneration*,
6. interstitial *fibrosis*

Reactive Lesions



Treatment and Prognosis

- *Surgical excision*: to prevent recurrence.

- Superficial mucoceles: *No treatment* is required for : short-lived.

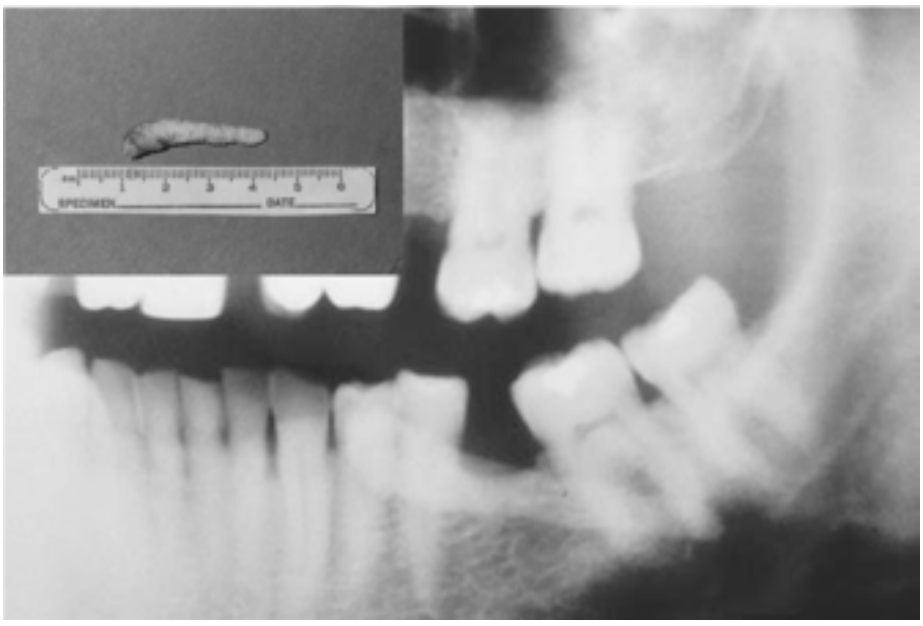
2

Mucus Retention Cyst (Obstructive Sialadenitis)

- *Obstruction* of salivary flow caused most commonly by a *sialolith*.

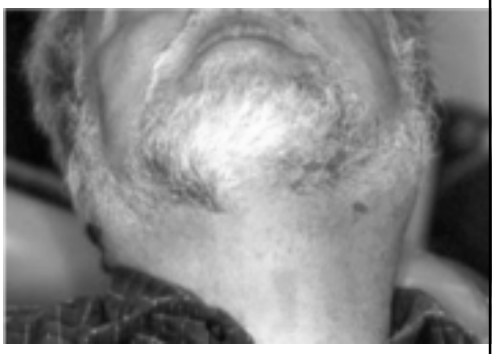
- A *sialolith* (calculus or stone).

Reactive Lesions

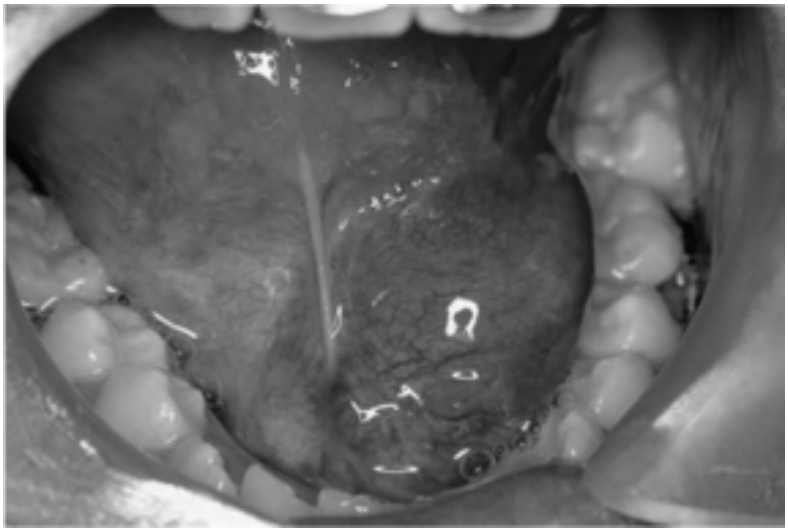


Reactive Lesions

About 20% are seen in the *parotid glands*, and a very small percentage is seen in sublingual and minor glands (especially upper lip).

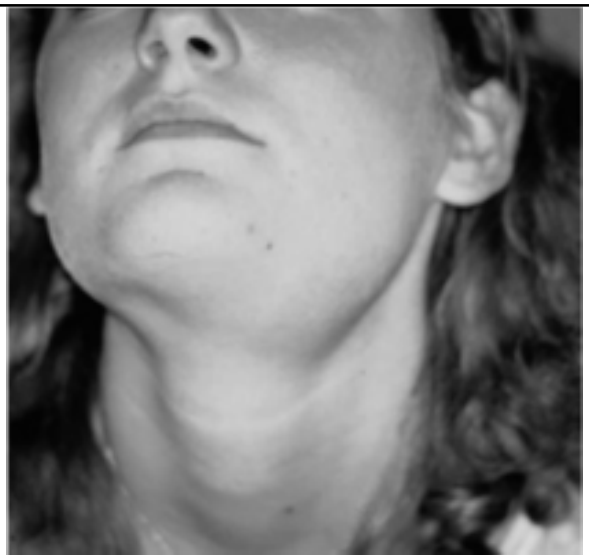


Reactive Lesions



Ranula on the floor of the mouth

Reactive Lesions

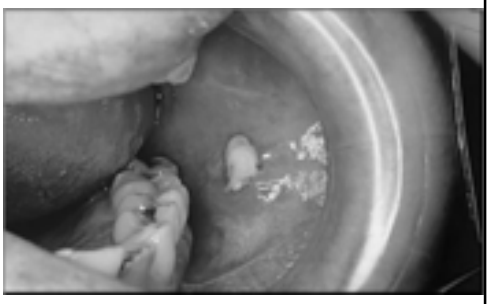


Plunging ranula: . Mucin in the floor-of-mouth lesions may dissect through the *mylohyoid muscle* that separates the sublingual from the submandibular space

Reactive Lesions

Clinical features:

- *Recurrent swelling* and pain worsening at mealtime.
- *Infection*: +/-
- A purulent *discharge* at the duct orifice when massaged,



Reactive Lesions

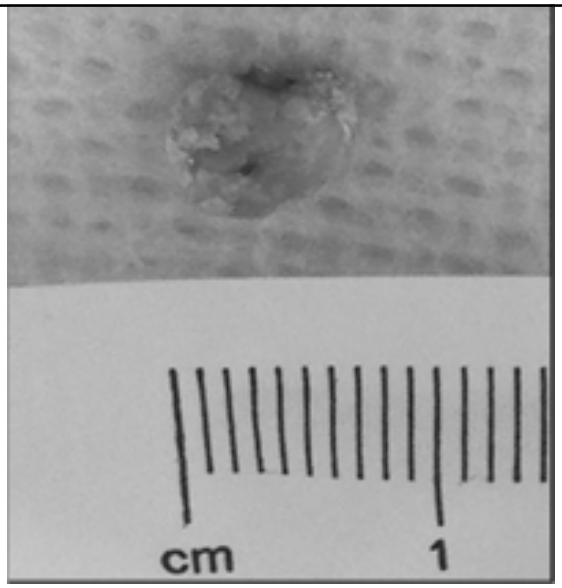
Radiographically

90% of submandibular sialoliths are radiopaque,

90% of parotid stones are radiolucent.

confirmed by:

1. routine radiographs,
2. sialography, or
3. cross-sectional CT imaging.



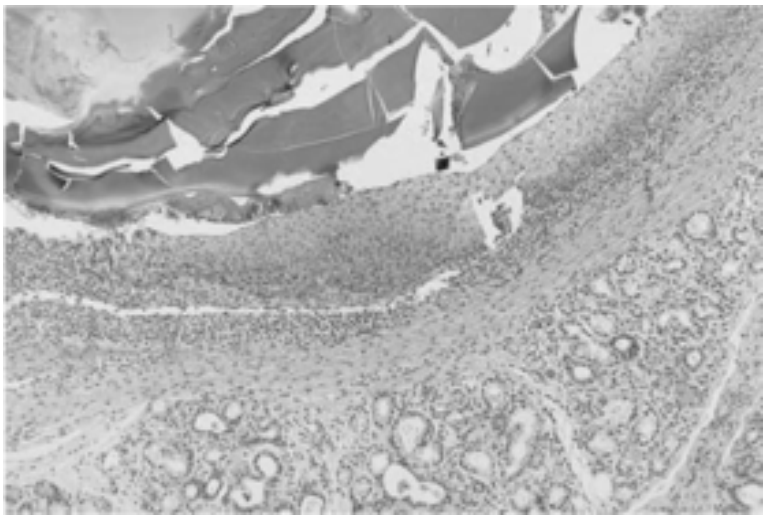
A salivary stone after sialendoscopic removal.

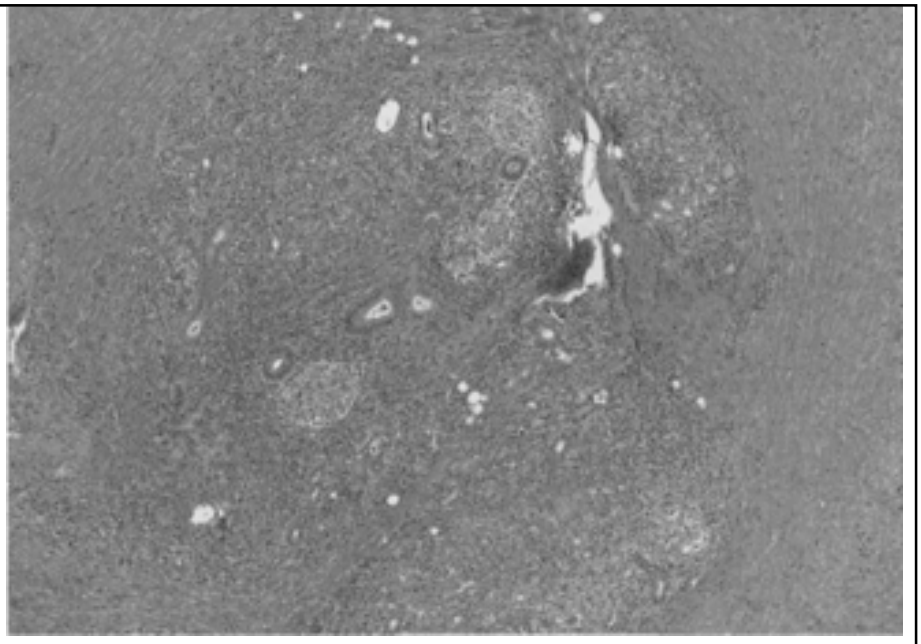
Histopathology

"pseudocyst"

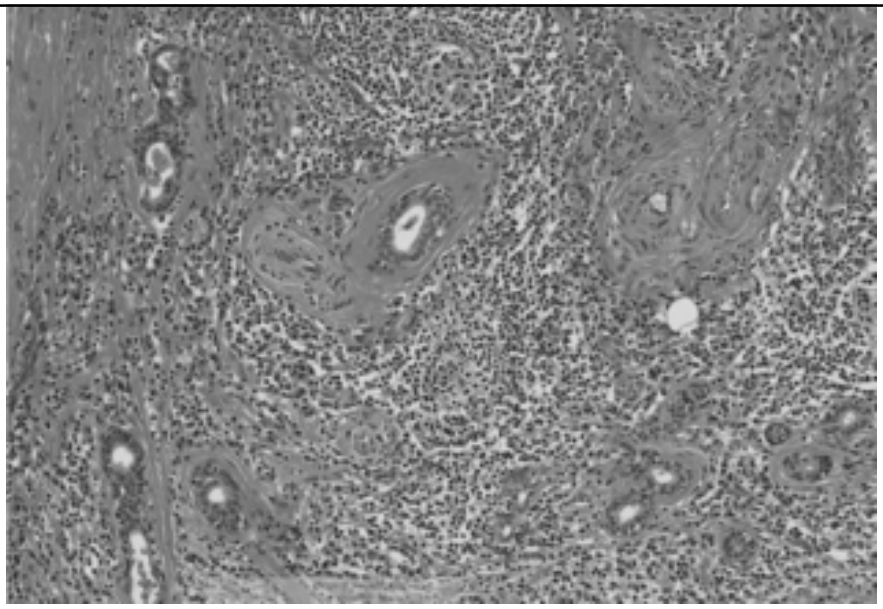
1. *Epithelium*: normal ductal that may range from pseudostratified to stratified squamous or occasionally oncocytic.
2. The *lumen* contains mucin.
3. The *connective tissue*: around the lesion is minimally inflamed

Reactive Lesions

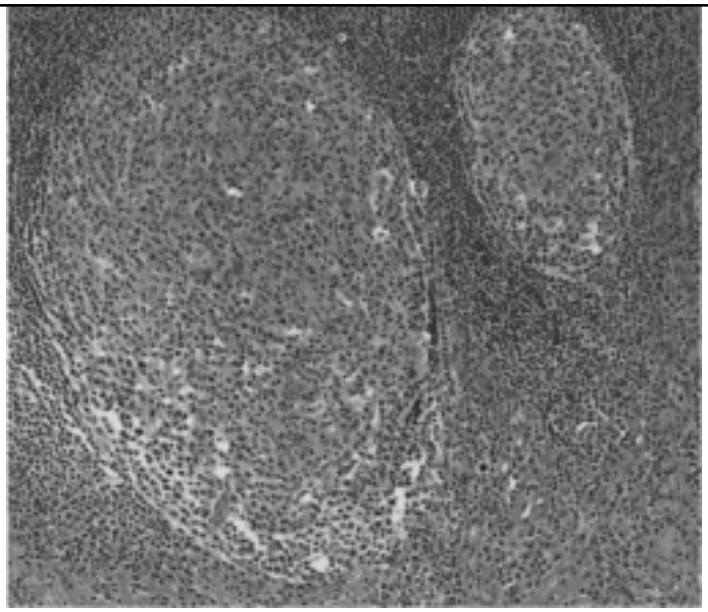




Preservation of lobular architecture



Acinar destruction



Intense chronic inflammation

Prognosis

excessive scar formation could result in obstruction or recurrence. *Recurrence* is noted in up to *20% of cases* following routine treatment.

3

Maxillary Sinus Mucocoele (Retention Cyst and Pseudocyst)

common, incidental findings on panorama

Retention cyst: arise from blockage of an antral seromucous gland,

↓

ductal epithelium-lined cystic structure filled with mucin.

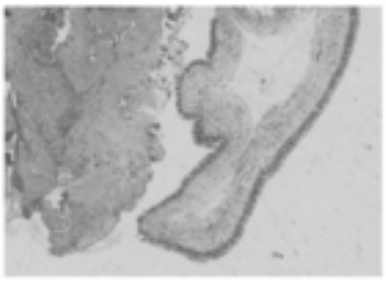
Pseudocysts: inflammatory origin → fluid accumulation within the sinus membrane

may be related to infection or allergy.

Histopathology

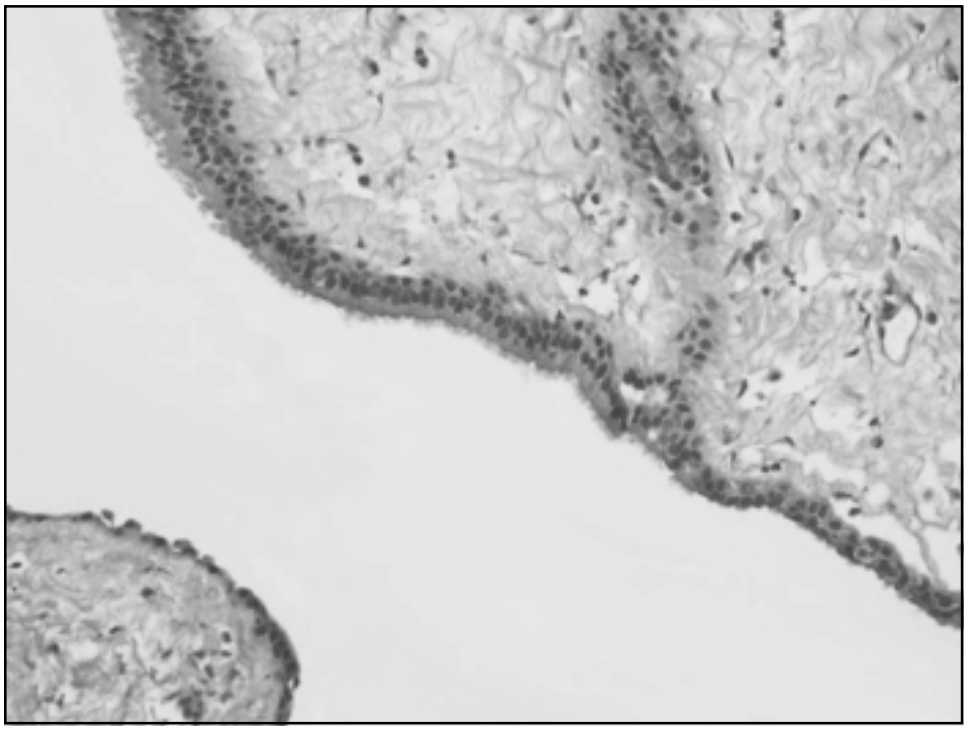
Retention cyst:

- lined by pseudostratified columnar epithelium with occasional mucous cells.



Pseudocyst:

- no epithelial lining
- pools of mucoid material surrounded by inflammatory connective tissue.



Treatment

1. generally left untreated
2. usually rupture spontaneously
3. periodic observation is required.

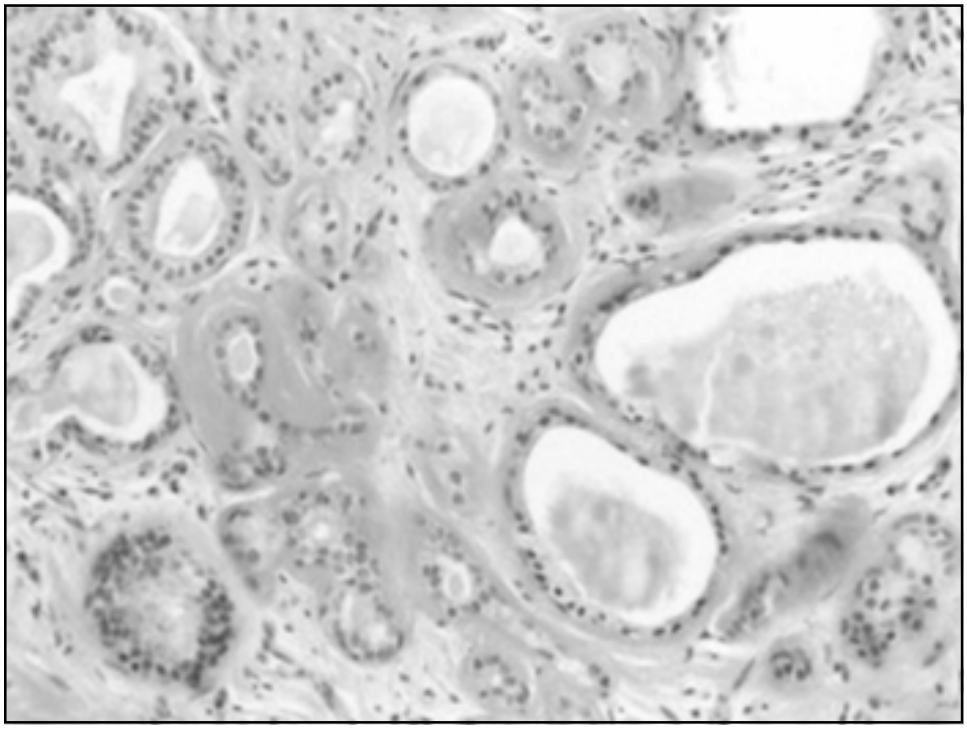
4

Sclerosing polycyctic adenosis

- Benign SG lesion similar to fibrocyctic change and sclerosing adenosis in breast
- It is maybe a pseudoneoplastic sclerosing and inflammatory process
- Local recurrences: 11%
- Rarely: malignant transformation

- In adenosis: atypical changes (low-grade to carcinoma in situ); that raise the possibility that SPA might represent a neoplastic lesion
- Clonality of Human androgen receptor (HUMARA): found in some cases: supporting the neoplastic theory

- Affects female twice as male
- Slow-growing mass in parotid
- Painless (15%: mild pain & parasthaesia)
- On gross: Gland is replaced by multiple discrete firm, rubbery nodules



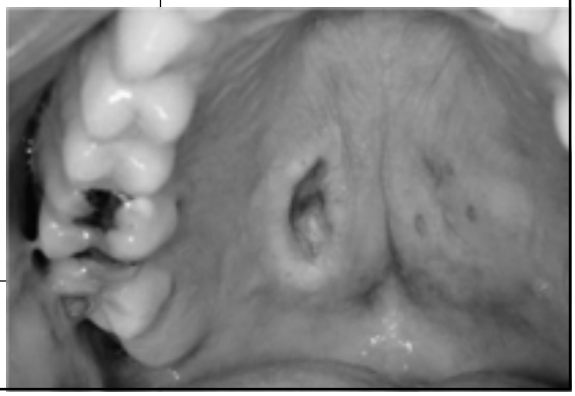
Reactive Lesions

6

Necrotizing Sialometaplasia

- typically affecting the palate.
- mimics malignancy.
- ischemia by:

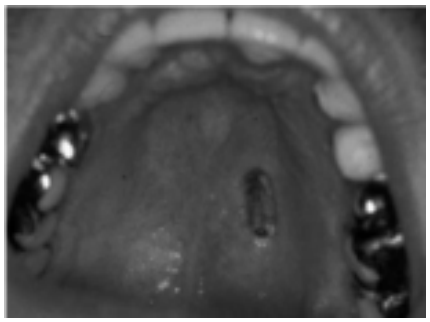
1. local trauma,
2. surgical manipulation,
3. local anesthesia

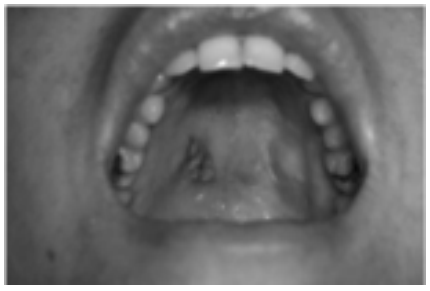


Reactive Lesions

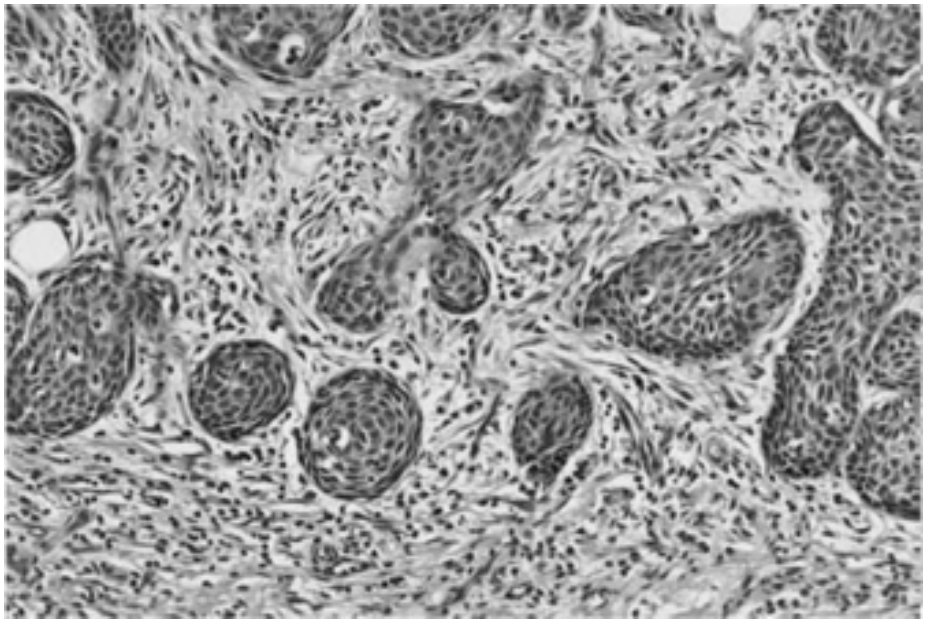
Clinical Features:

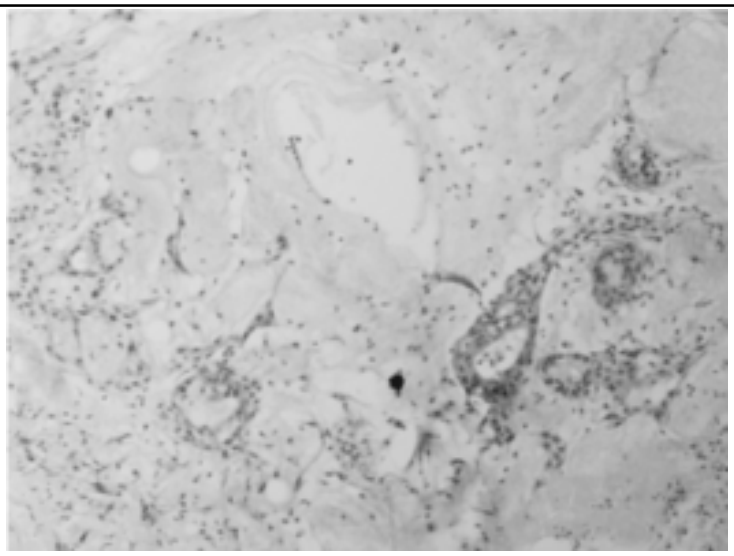
1. tender *swelling*, with a dusky erythema
2. mucosa breaks down (*ulcer*)
3. unilateral or bilateral,
4. Diameter: *1 to 3 cm*
5. Pain
6. Healing: *6 to 10 weeks*.





Reactive Lesions





Section showing necrosis of salivary glands with only partially preserved lobularity, chronic inflammation, and several small dutcs with squamous metaplasia.

Treatment and Prognosis

no treatment is necessary,

no neoplastic potential.

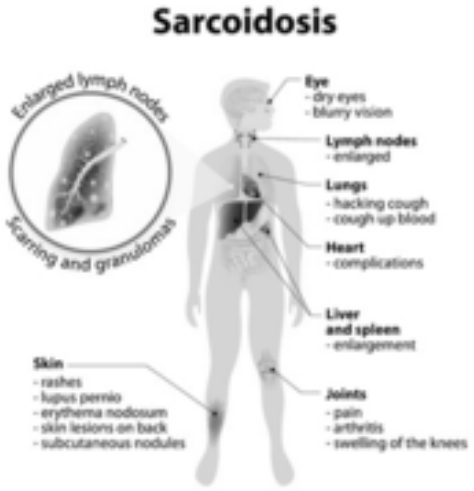
Infectious Sialadenitis

1. Sarcoidosis
2. Metabolic Conditions
3. Sjögren's Syndrome
4. Salivary Lymphoepithelial Lesion
5. Scleroderma
6. Xerostomia
7. Taste Disturbances
8. Halitosis

1

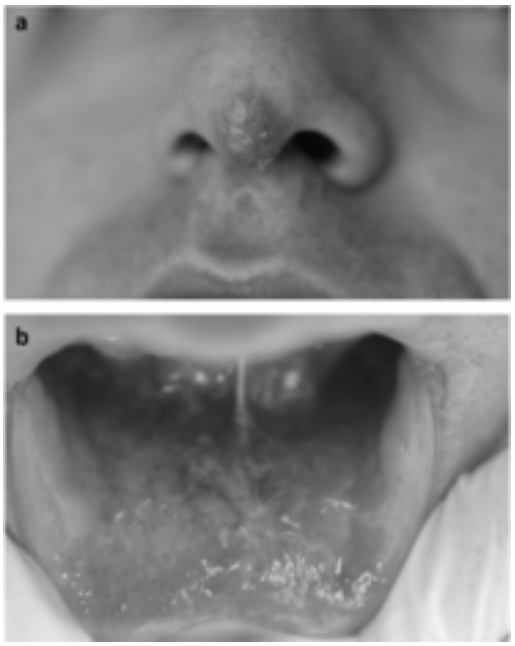
Sarcoidosis

- *multisystem* granulomatous disease of undetermined origin.
- hypersensitivity response to *atypical mycobacteria*
- Causative viruses: (*EBV*) (*HHV8*) viruses.



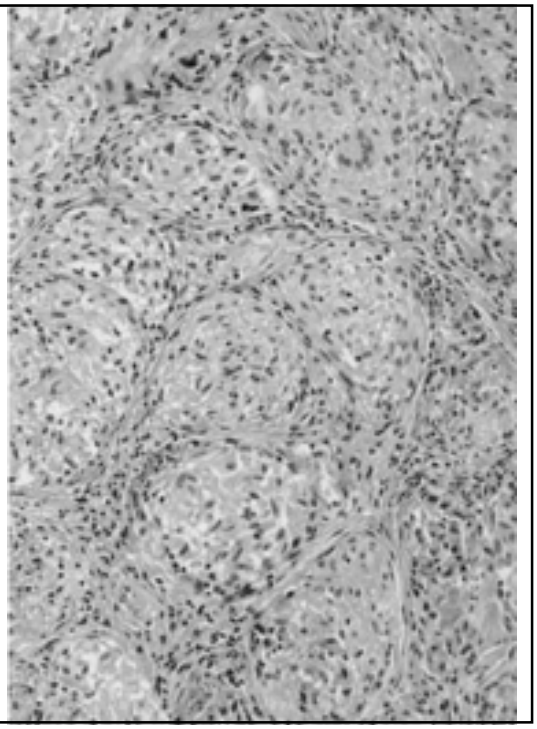
Oral sarcoidosis :

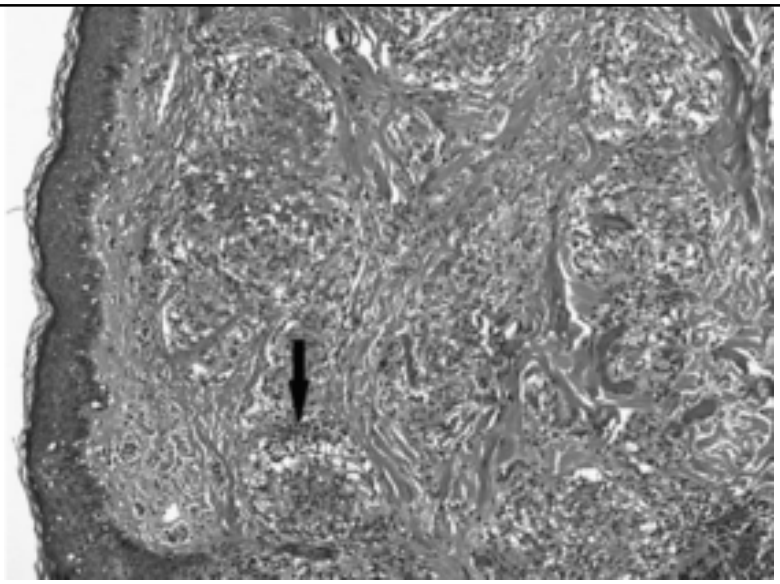
- *nodular swellings* of the buccal mucosa and vestibule (same to Crohn's)
- *Lips*: diffuse or nodular swelling.
- *Parotid* swelling (unilaterally or bilaterally)
- *Melkersson-Rosenthal* syndrome.



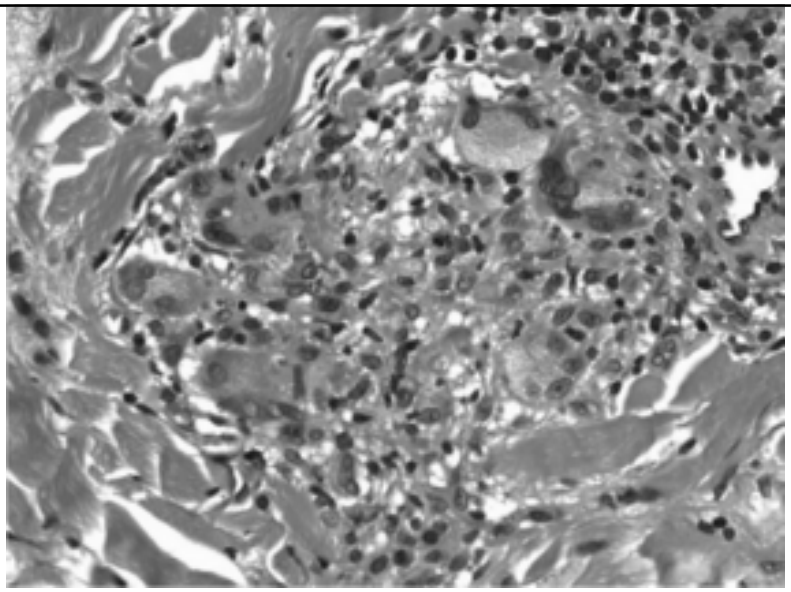
Histopathology

- *noncaseating* granulomas ,
- *Asteroid* bodies
- *Schaumann* bodies





Non-caseating-granulomata. (a) Low power photomicrograph of skin biopsy showing numerous non-caseating granulomata in the dermis and extending into the subcutaneous tissues. The granulomata are surrounded by increased fibrous tissue



High power view of one of the granulomata showing a collection of epithelioid histiocytes with Langhans giant cells. Surrounding the granuloma is fibrosis and a 'collarette' consisting predominantly of lymphocytes

Treatment

1. Spontaneous resolution (65%-70%)
2. Corticosteroids
3. Other agents: Chloroquine,
4. Immunosuppressive drugs
5. thalidomide and infliximab (a TNF-alpha monoclonal antibody)
6. Immunomodulators: levamisole in management of arthritic symptoms

Prognosis

- Good, but patients must be monitored periodically with chest radiographs and serum angiotensin 1–converting enzyme
- Clinical relapses are unusual in cases in which spontaneous resolution has occurred.

Prognosis

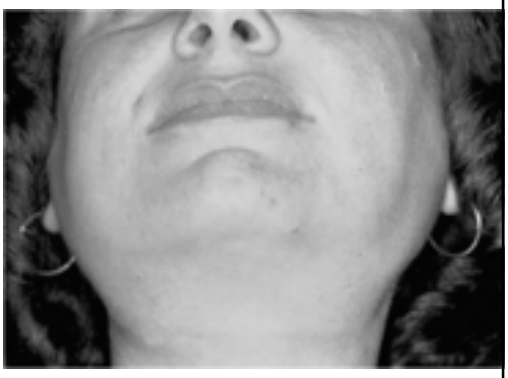
- *Good*, but patients must be monitored periodically

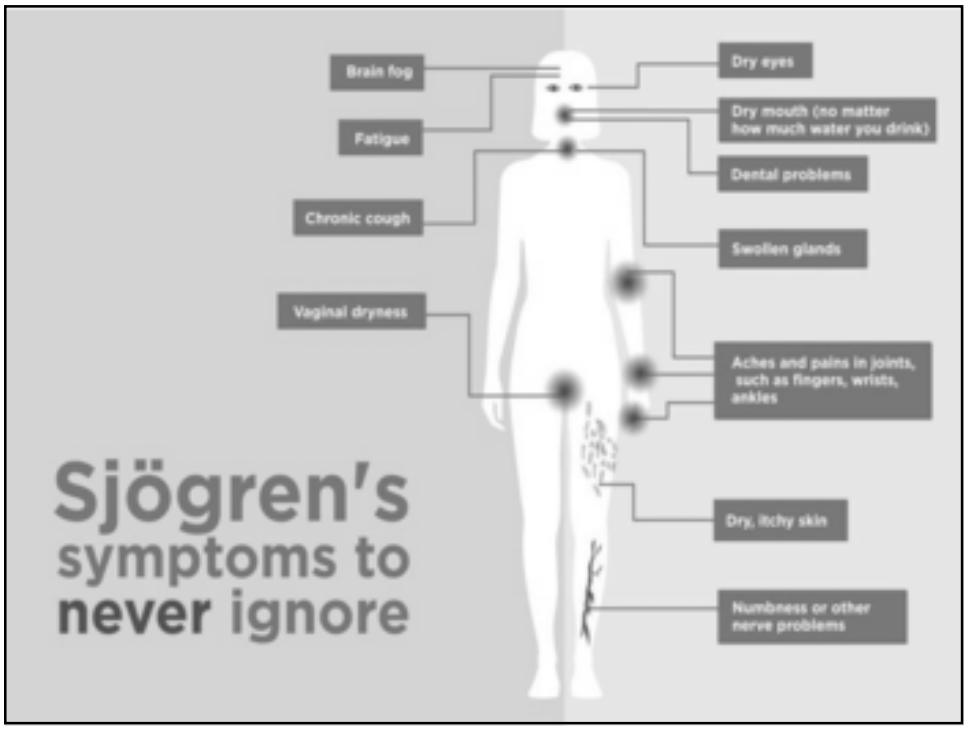
- Clinical *relapses are unusual*

2

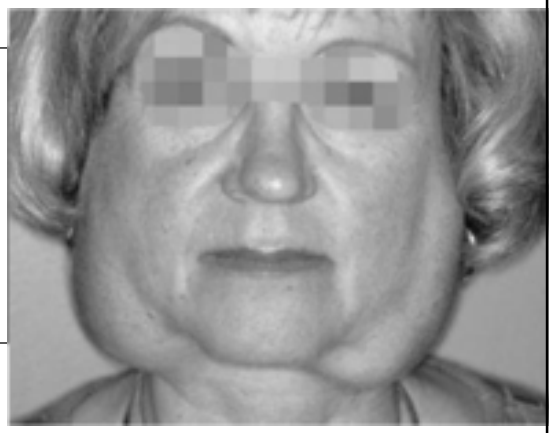
Sjögren's Syndrome

- Systemic *autoimmune* disease
- Lymphocyte-mediated *destruction* of salivary *parenchyma*
- Chronicity: risk of *lymphoma (10%)*





- *Parotid gland enlargement* (50% of patients), often bilateral
- arthralgia, myalgia, and *fatigue*



Diagnosis requires 2 of the following 3 features:

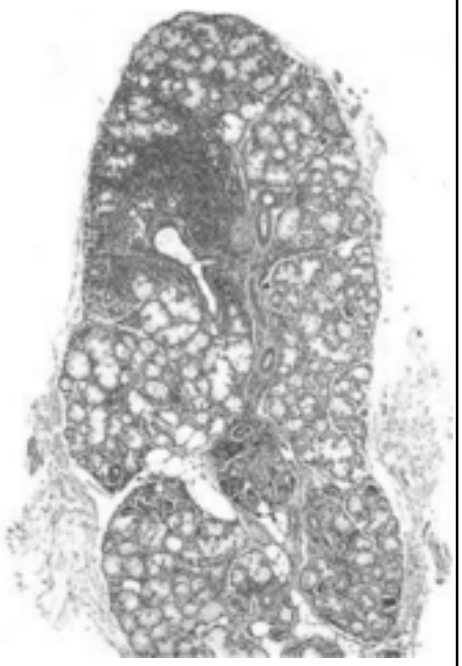
1) anti-SSA and/or anti-SSB / rheumatoid factor /antinuclear antibody titer >1:320

2) ocular staining score by lissamine green >3

3) focal lymphocytic sialadenitis with a focus score >1 focus/4 mm2 in labial salivary gland biopsy

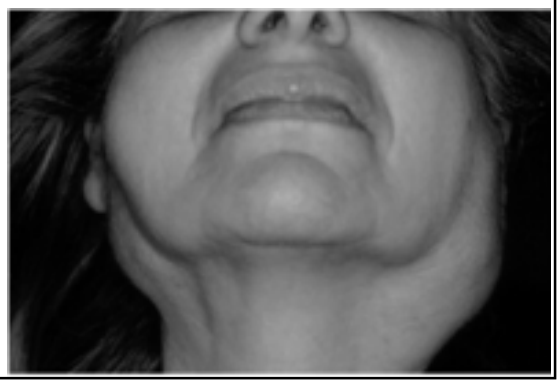
Histopathology

- benign *lymphocyte* infiltrates the parenchyma.
- focal *periductal*
- Then *acinar degeneration*
- *Epimyoepithelial* islands are present in major (40% of cases), rare in minor glands.



Treatment

1. Symptomatic treatment
2. Artificial *saliva* and *tears*
3. Scrupulous oral hygiene necessary to prevent xerostomia associated caries



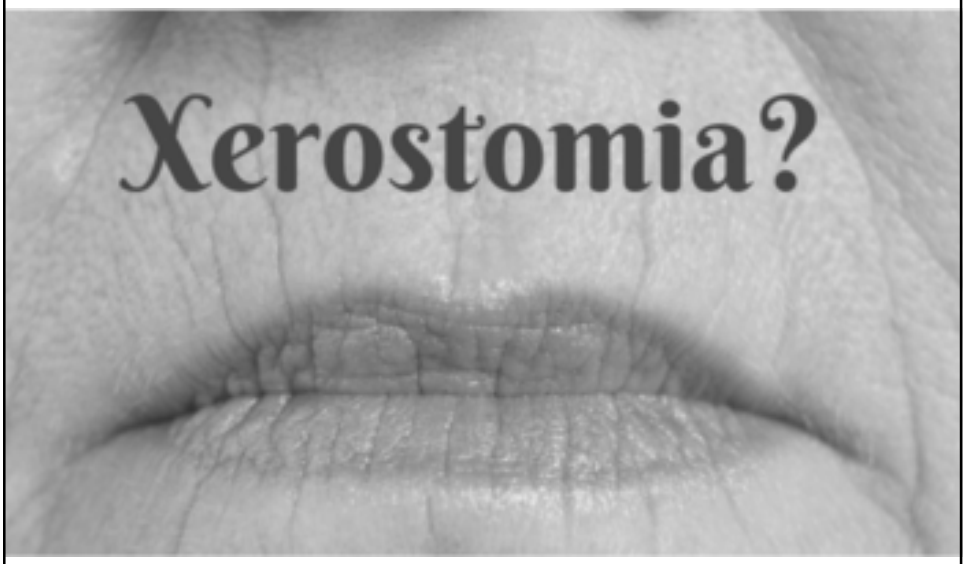
3

Xerostomia

Medications
- Analgesics
- Opioids
- Anticholinergic drugs
- Antihistamines
- Antidepressants
- Selective serotonin reuptake inhibitors (SSRIs)
- Tricyclic and heterocyclic antidepressants
- Atypical antidepressants
- Antihypertensive agents
- Diuretics
- Muscle relaxants
- Sedatives/anxiolytics

Autoimmune or Systemic Diseases
- Sjögren's syndrome
- Primary biliary cirrhosis
- Wegener's granulomatosis
- Sarcoidosis
- Scleroderma

Other Conditions
- Local radiation therapy
- Type 1 or 2 diabetes
- Radioactive iodine treatment
- Human immunodeficiency virus (HIV)/acquired immunodeficiency
- syndrome (AIDS)
- Anxiety/depression



Management :

Palliation

1. Elimination of alcohol and caffeine consumption
2. Elimination of alcohol-containing mouth rinses
3. Gustatory salivary stimulation
4. Sugarless candies, gum
5. Moist sugar-free or complex carbohydrate foods
6. Oral lubricants
7. Carboxymethylcellulose- or hydroxymethylcellulose-based products
8. Other polymer-based rinses

Prescription Strategies

1. Cholinergic agonists
2. Pilocarpine
3. Cevimeline
4. Acupuncture

4

Taste Disturbances

Diseases Associated with Taste Disturbances

1. Bell's palsy
2. Cancer/oral—head and neck irradiation
3. Candidiasis (thrush)—oral
4. Diabetes mellitus with associated peripheral neuropathy
5. Gingivitis, periodontitis
6. Hypothyroidism
7. Multiple sclerosis
8. Parkinsonism
9. Pernicious anemia (vitamin B12 related)
10. Renal failure/hemodialysis
11. Sjögren's syndrome
12. Upper respiratory disturbances and infection/influenza
13. Zinc deficiency

Drug Classes and Agents Associated with Taste Disturbances

1. Angiotensin-converting enzyme (ACE) inhibitors
2. Calcium antagonists
3. Diuretics
4. Antiarrhythmics
5. Antithyroid agents
6. Antidiabetics
7. Antihistamines
8. Antiasthmatics
9. Antidepressants
10. Antipsychotics
11. Antineoplastics
12. Chelating agents
13. Neuromuscular/antiseizure drugs
14. Nitroglycerin
15. Opioids

5

Halitosis

Anatomic Origins of Halitosis

Oral cavity

- Poor oral hygiene/prosthesis hygiene
- Posterior dorsal surface of tongue

Periodontal pathogens

- Porphyromonas gingivalis
- Prevotella intermedia
- Fusobacterium nucleatum
- Bacteroides forsythensis
- Treponema denticola

Oral ulcerative and erosive diseases

Oral infection (primary and secondary)

- Candidiasis
- Pericoronitis
- Postextraction alveolitis

5

Halitosis

Anatomic Origins of Halitosis

Dietary considerations

- Volatile sulfur-containing foods (onions, garlic, others)
- Hydrogen sulfide
- Dimethyl disulfide
- Methyl mercaptan

Xerostomia

Nasal cavity

- Nasal infection
- Sinusitis
- Nasal polyps and nasal foreign bodies

Other airflow obstruction

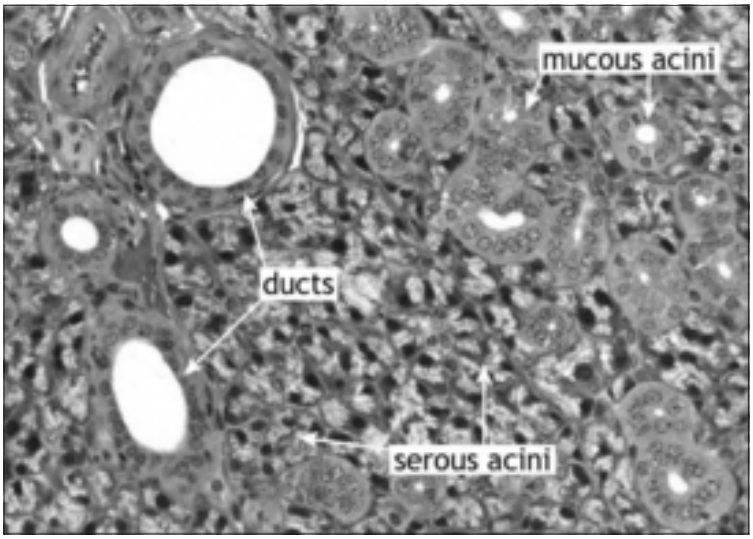
- Tonsils
- Infection
- Tonsilliths
- Neoplasia

Other sites

- Bronchial and pulmonary infection
- Renal failure

Salivary glands tumors

Normal Histology

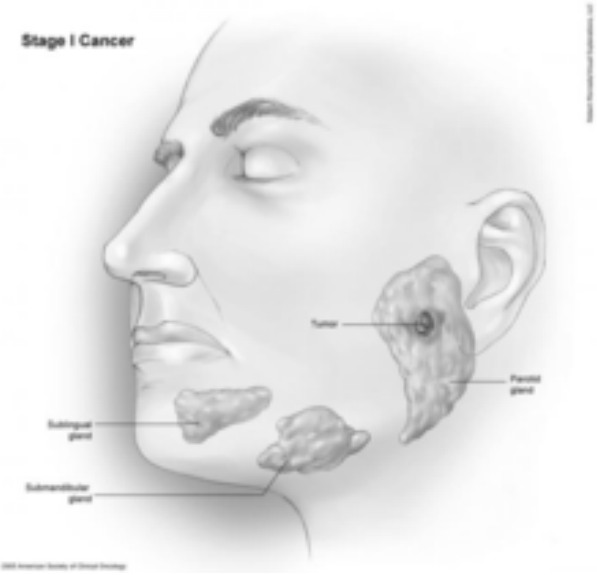


Staging system for major salivary gland cancer

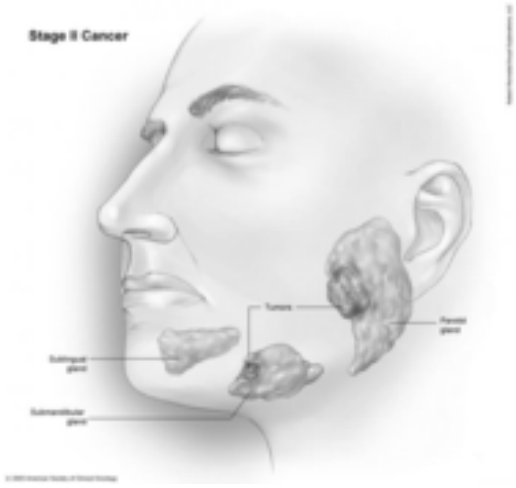
- **Tx** Primary tumor cannot be assessed
- **T0** No evidence of primary tumor
- **T1** Tumor < 2cm in greatest dimension
- **T2** Tumor 2-4 cm in greatest dimension
- **T3** Tumor 4-6 cm in greatest dimension
- **T4** Tumor > 6 cm in greatest dimension

- All categories are subdivided: (a) no local extension; (b) local extension.
- Local extension is clinical or macroscopic invasion of skin, soft tissue, bone, or nerve.
- Microscopic evidence alone is not a local extension for classification purposes.

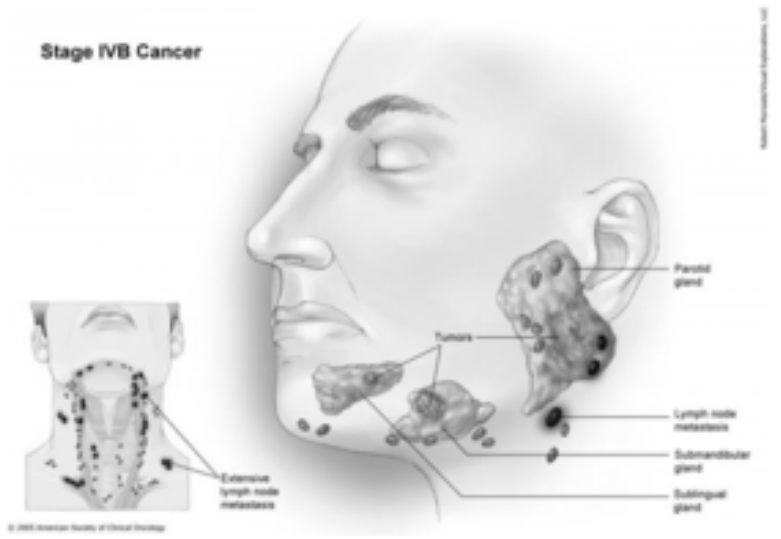
The American Joint Commission on Cancer .



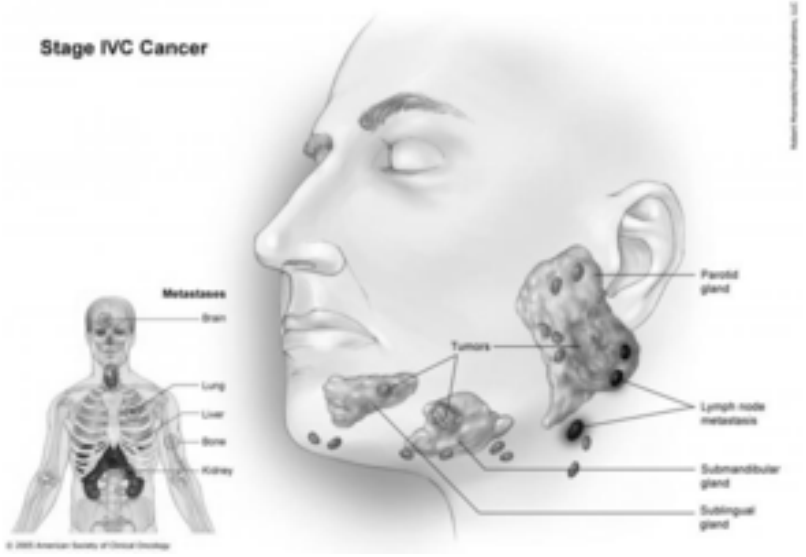
Stage I: Noninvasive tumors (T1, T2) with no spread to lymph nodes (N0) and no distant metastasis (M0).



Stage II: An invasive tumor (T3) with no spread to lymph nodes (N0) or distant metastasis (M0).

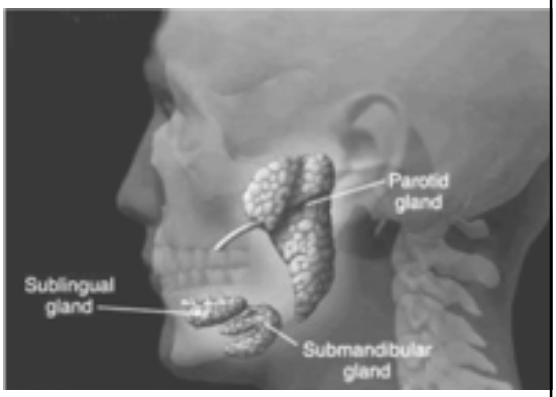


Stage IVB: Any cancer (any T), with more extensive spread to lymph nodes (N2, N3), but no metastasis (M0).



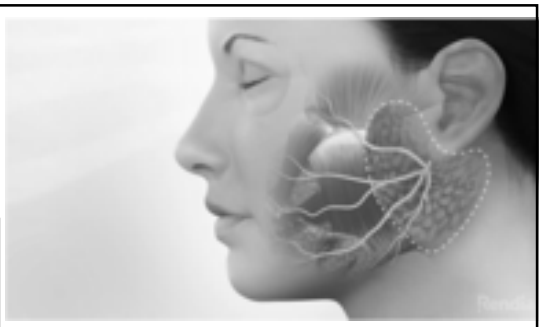
Stage IVC: Any cancer with distant metastasis (any T, any N, and M1).

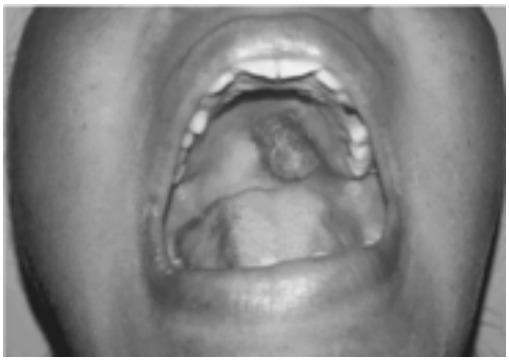
1. Vast *majority* are *benign* tumors
2. Affects *major* more than the minor glands
3. *Slow* growing masses
4. Pain???



Criteria of malignancy:

1. *Facial nerve* involvement
2. Metastasis to *lymph node*
3. Rapid *growth*
4. *Ulceration* of the covering skin/mucosa





Benign Salivary Gland Tumors

1. Mixed tumor (pleomorphic adenoma)
2. Monomorphic adenomas
- Basal cell adenomas—solid, tubular, trabecular, membranous
- Canalicular adenoma
- Myoepithelioma
- Oncocytoma
- Warthin's tumor and papillary cystadenoma
3. Sebaceous adenoma
4. Ductal papilloma
5. Inverted ductal papilloma
6. Sialadenoma papilliferum
7. Intraductal papilloma

Pleomorphic Adenoma\ Mixed tumor

Clinical Features

- Adults; M/F affected equally
- Asymptomatic submucosal mass
- Sites: palate, upper lip, buccal mucosa, other sites

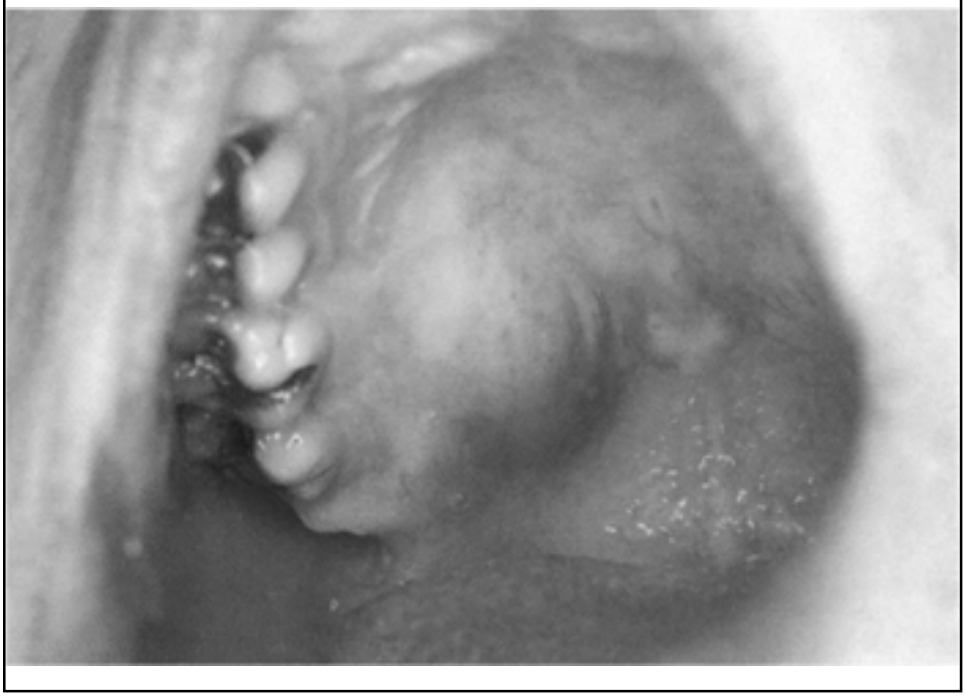
Histopathology

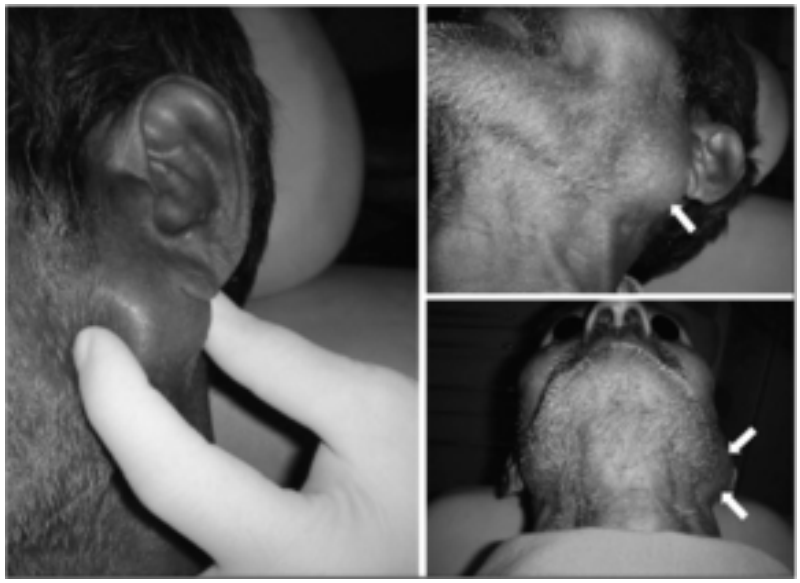
- Encapsulated; variable glandular patterns; epithelial and myoepithelial
- differentiation; no mitoses

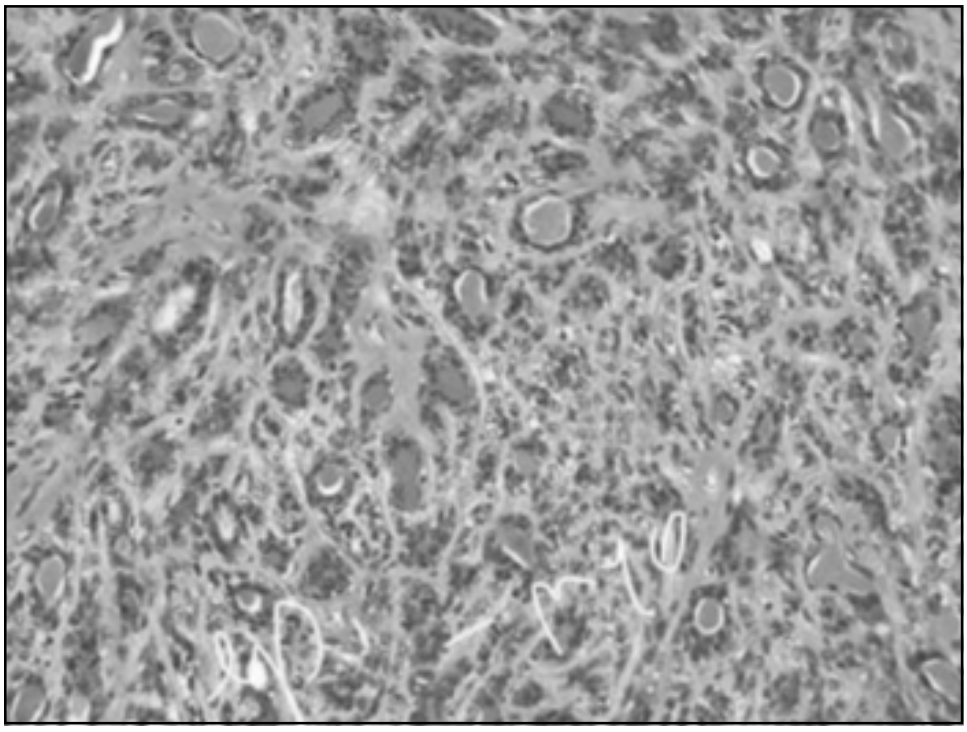
Treatment

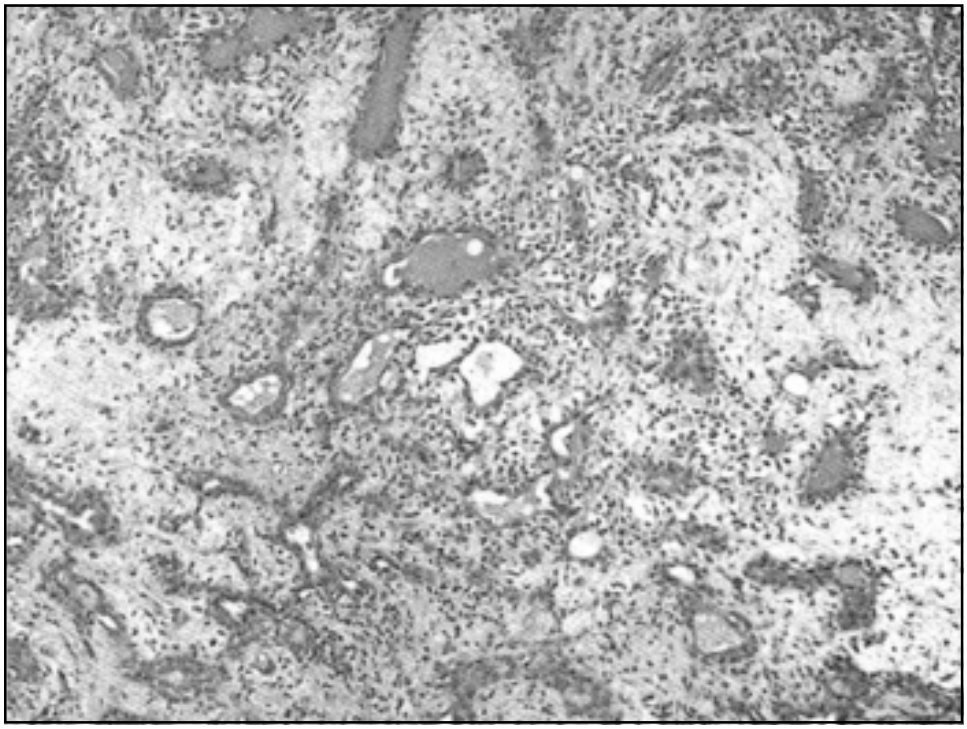
- Excision; occasional recurrence in major glands

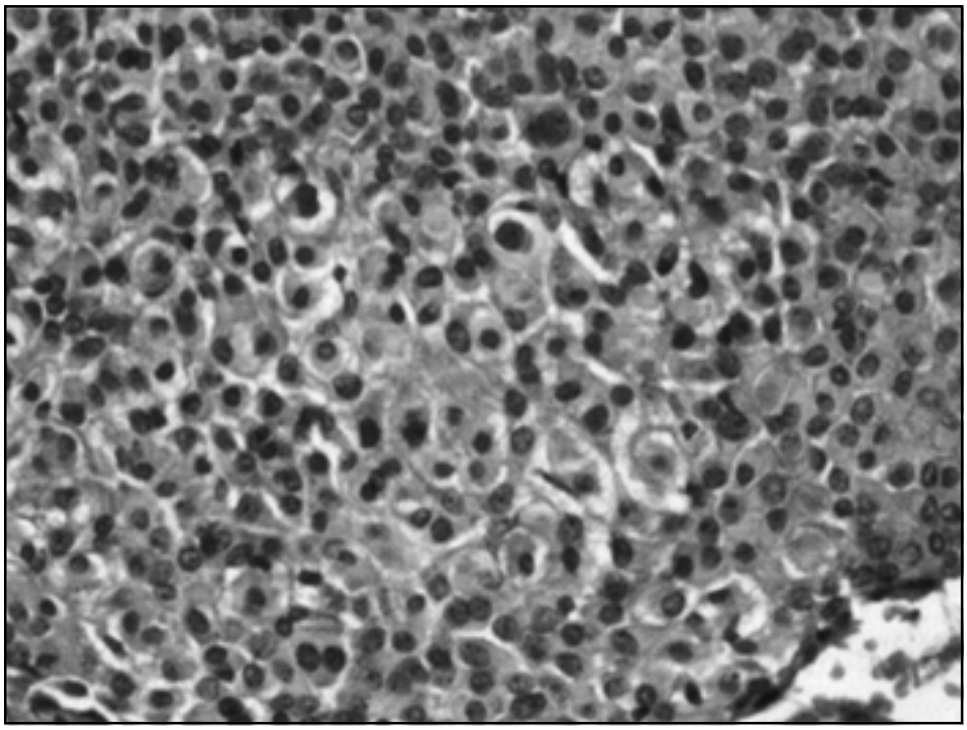
Architecture rather than cellular pleomorphism



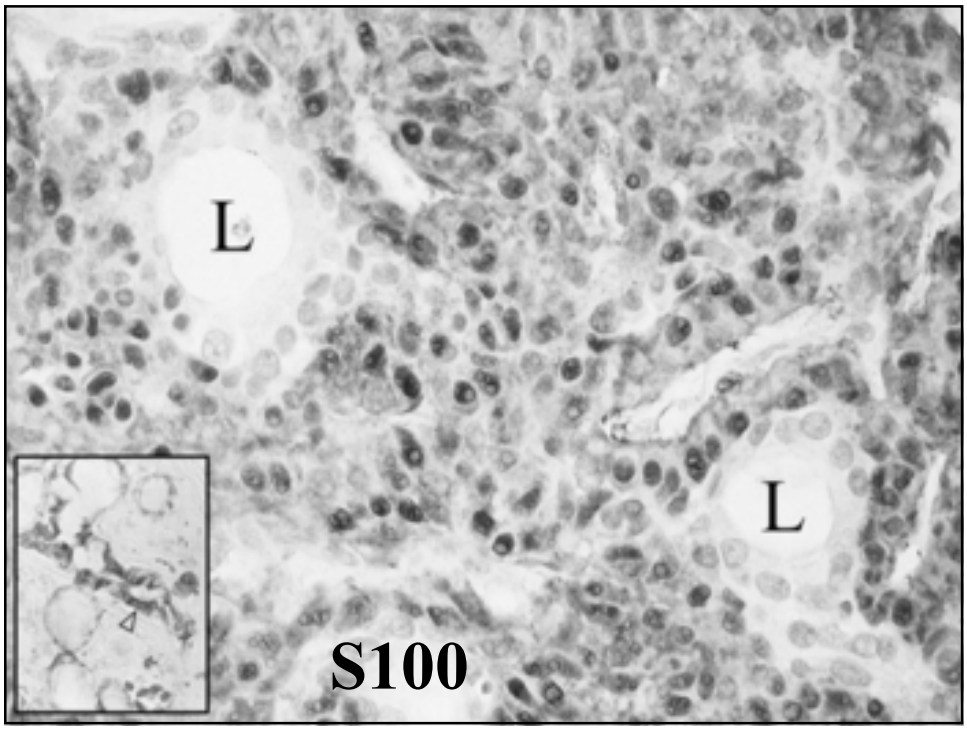


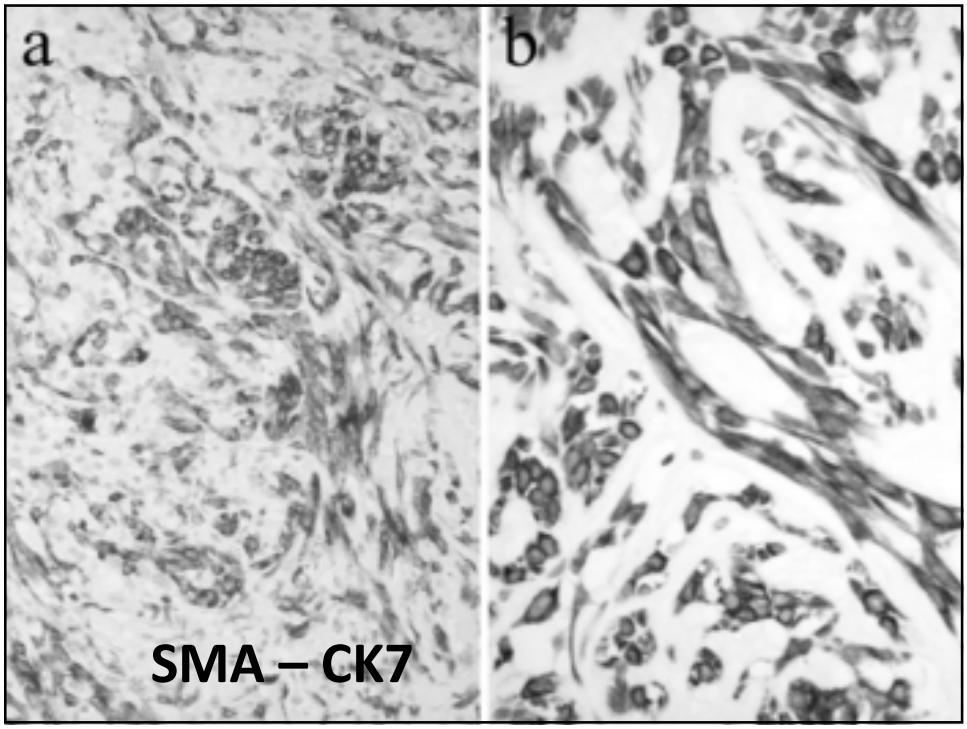


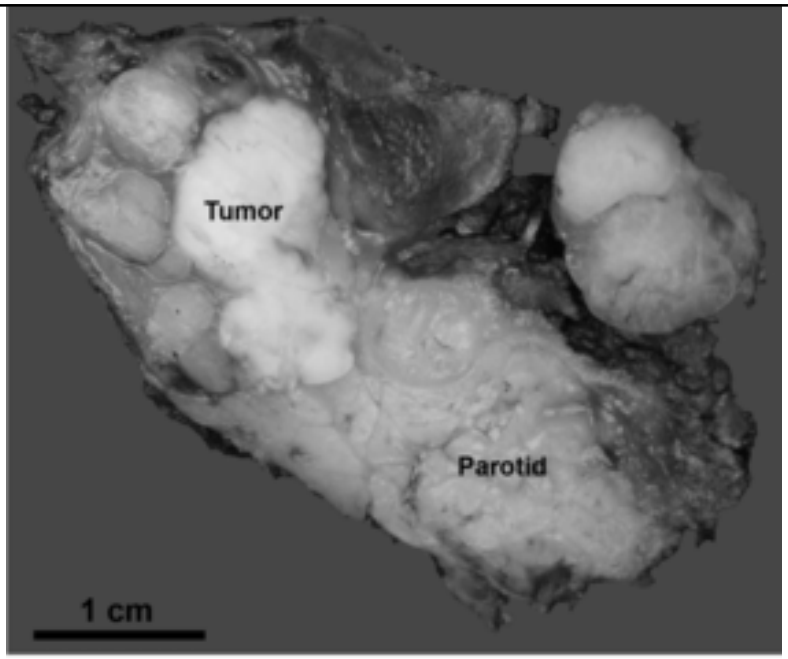




- Rarely: mitosis / necrosis
- IHCs: CEA, S100, actin and epithelial membrane antigene, S100 and actin





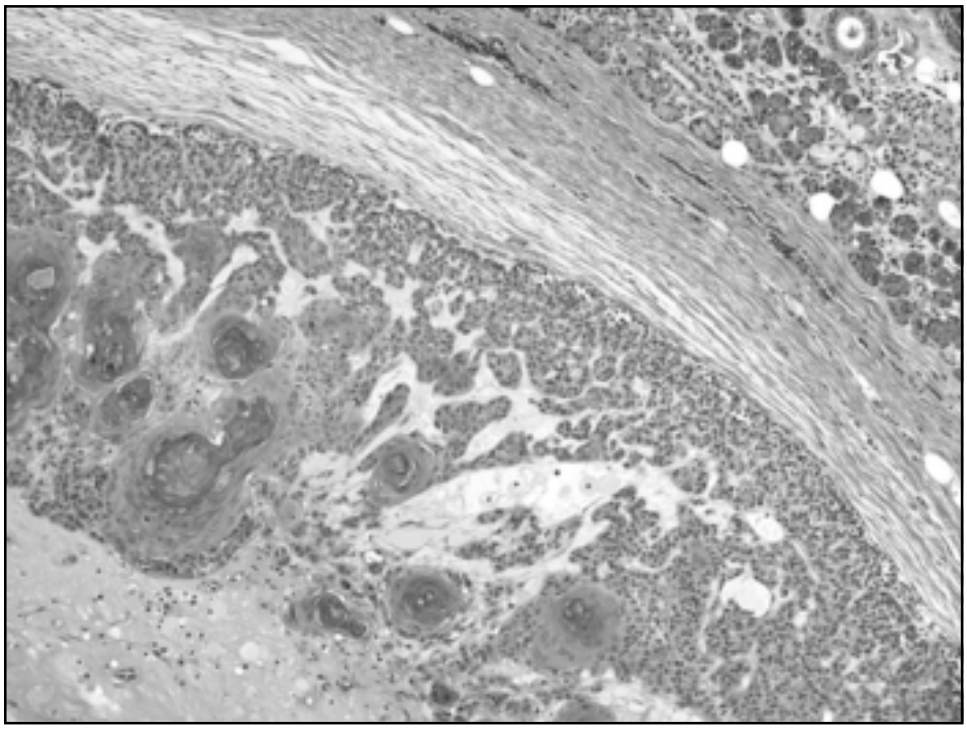


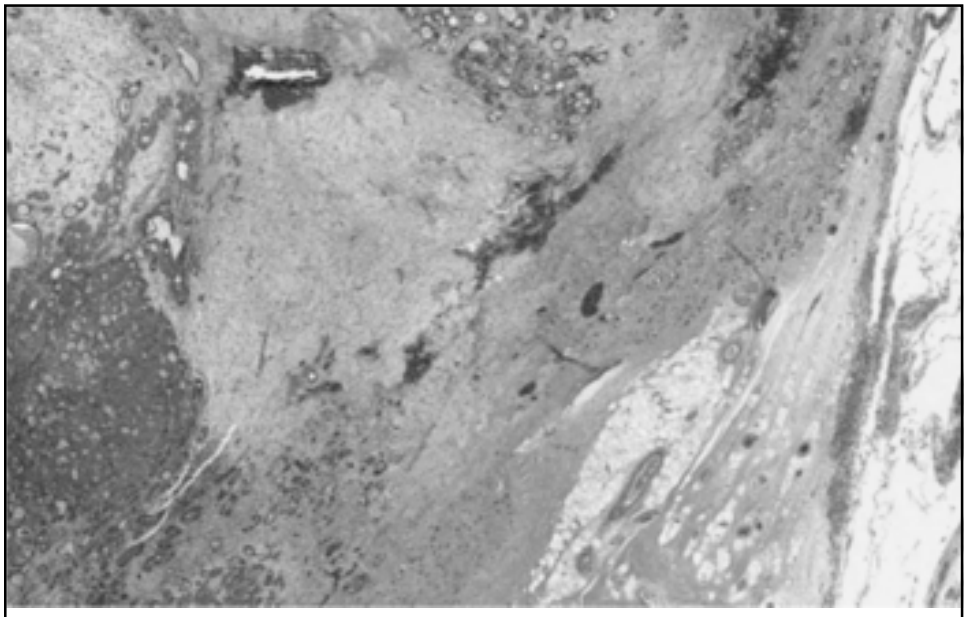
Recurrent pleomorphic adenoma: multiple myxoid to fibrotic tumor nodules of various size involving the parotid gland

1. Carcinoma X pleomorphic adenoma

The main histologic feature to make diagnosis:

1. Benign pleomorphic adenoma with carcinoma
2. The PA is often largely *hyalinized* /and or/ *calcified*

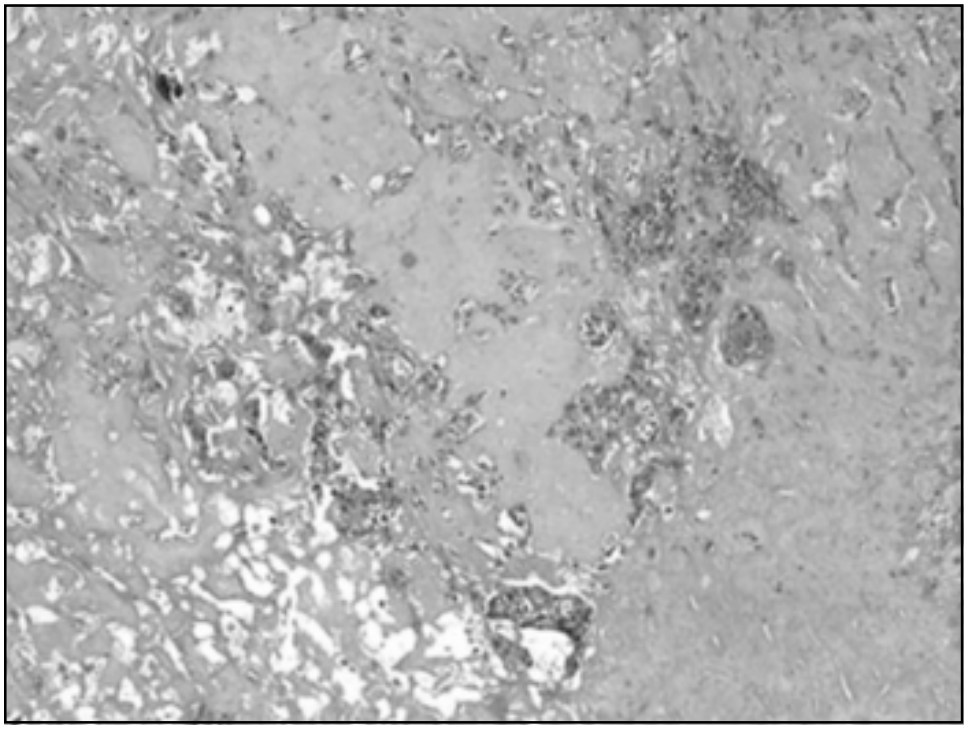




Ca ex PA with invasion outside the capsule. The carcinoma forms tiny glands and nests infiltrating through the capsule into the adjacent adipose tissue

Features to assess breaching the capsule:

1. Intracapsular
2. Minimally invasive
3. Widely invasive



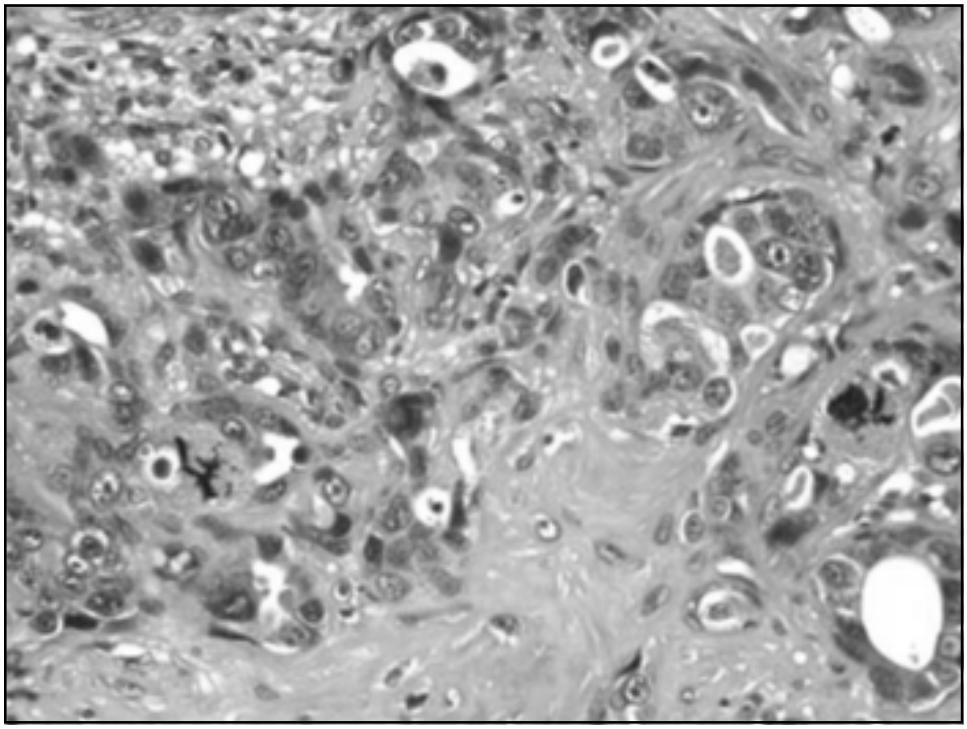
Distinction between invasive and non-invasive tumor:

1. Preservation of outer layer of myoepithelial cells
2. Destructive invasion in the body of PA
3. Extension into surrounding tissues

Distinction between minimal and wide invasion:
More than 2.5 mm from the capsule of residual PA

All high grade tumors show over-expression and amplification of HER2/neu

detect early carcinoma in PA

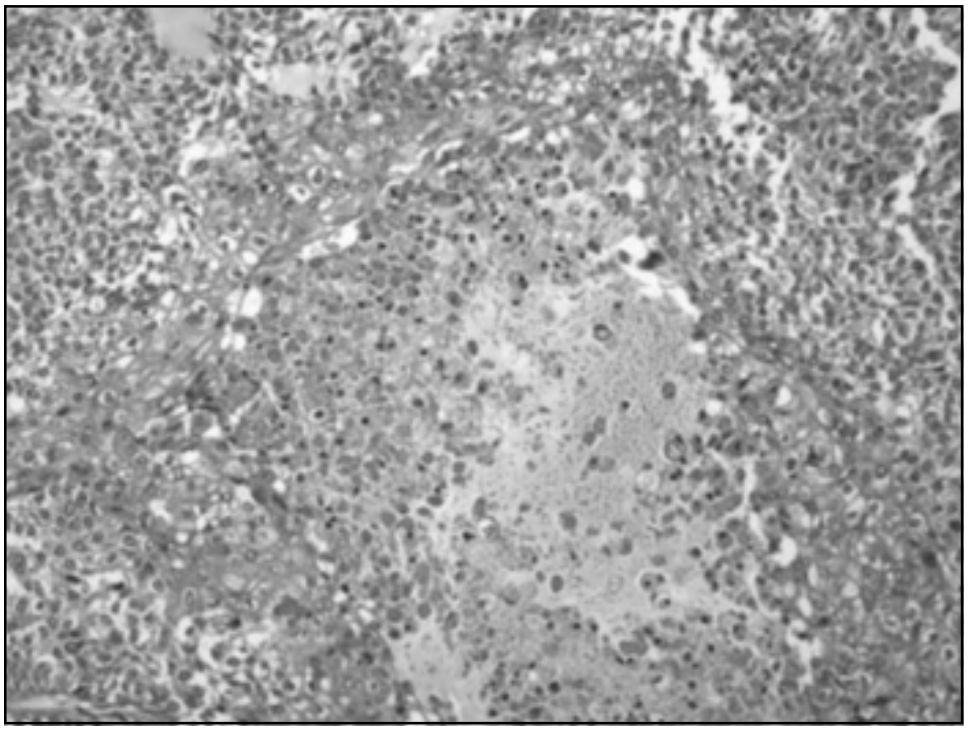


2. Carcinosarcoma in PA

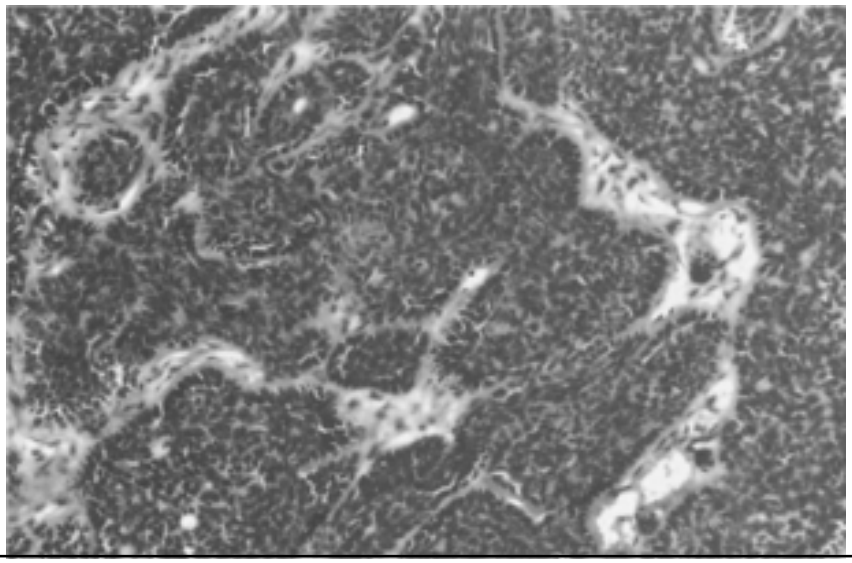
- Exceedingly rare biphasic salivary gland malignancy
- Composed of distinct carcinoma and heterologous sarcomatous components (usually chondrosarcoma)
- Capable of metastasis
- 60% dying by disease
- Mutation of salivary duct carcinoma can be found: in subtype with osteoclast type giant cell was found the same allele on chromosome 17P13

3. Metastasizing pleomorphic adenoma

- “ histologically benign PA that inexplicably manifests local or distance metastasis”.
- Metastasis can be found to: bone, lung and lymph nodes.
- Recommended therapy: wide excision for both primary and metastases

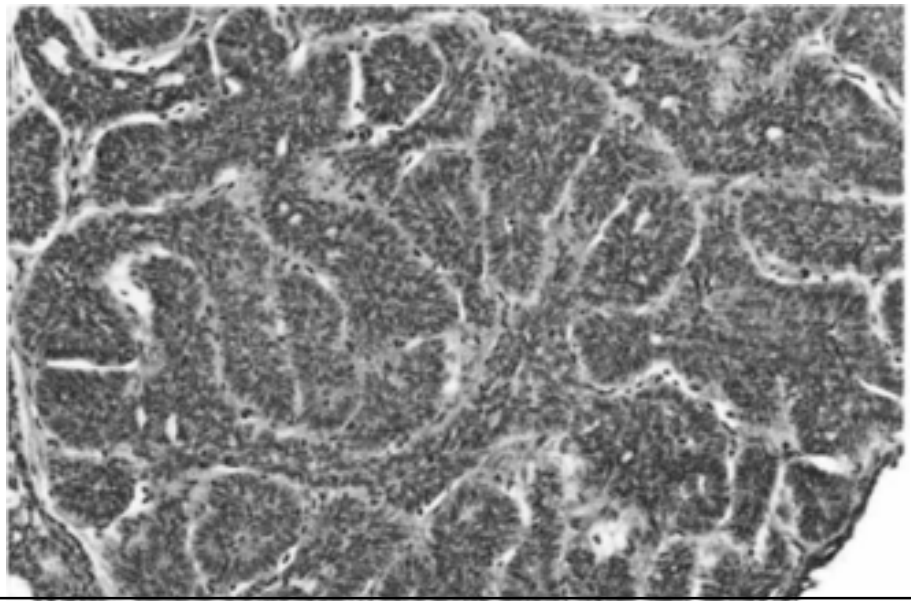


Basal Cell Adenoma



- 1-2% of SG tumors
- 70% in *parotid gland*
- In minor: *upper lip*
- Slow growing mass
- Tend to affect *male* (60 y.o)

Solid type

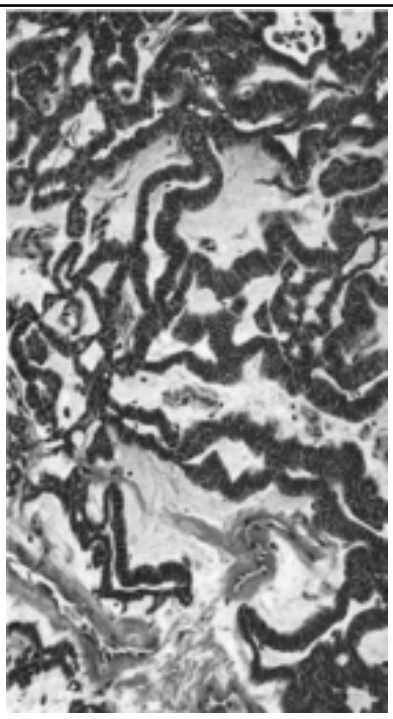


Canalicular Adenoma

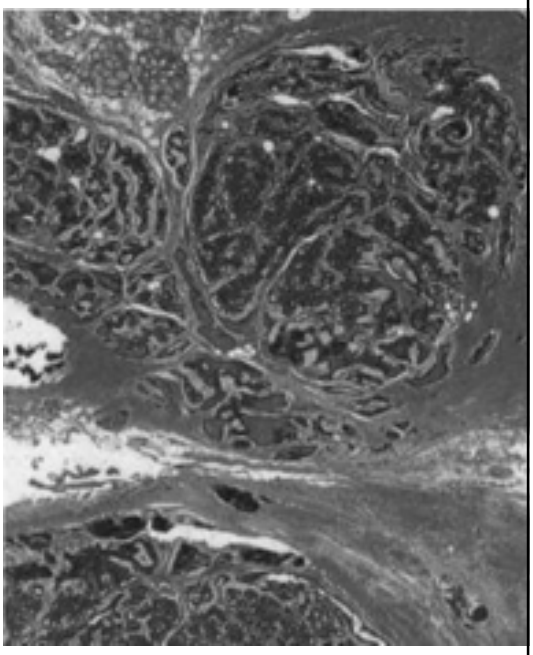
- Upper lip
- F>M
- Movable mass
- Asymptomatic

Histopathology:

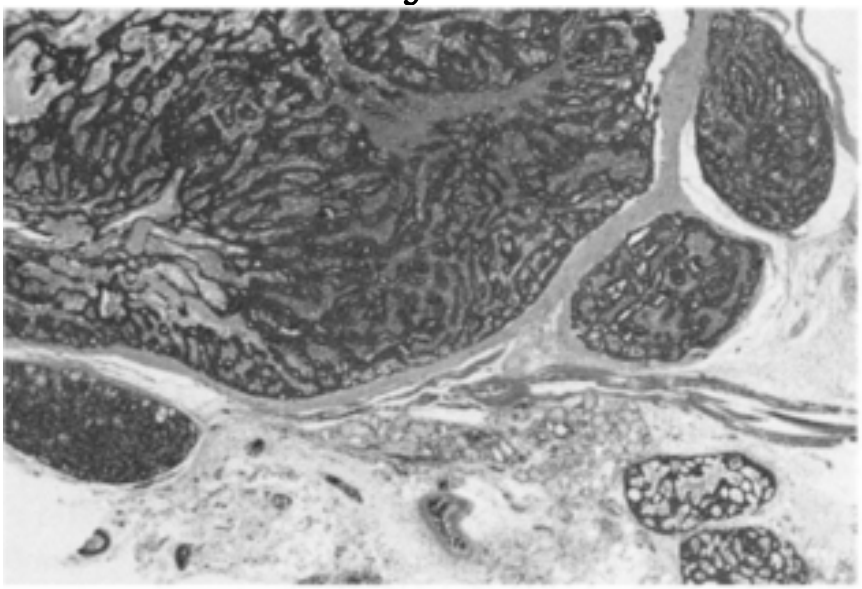
bilayered strands of *basaloid cells* that branch and anastomose within a delicate stroma that is highly vascular .

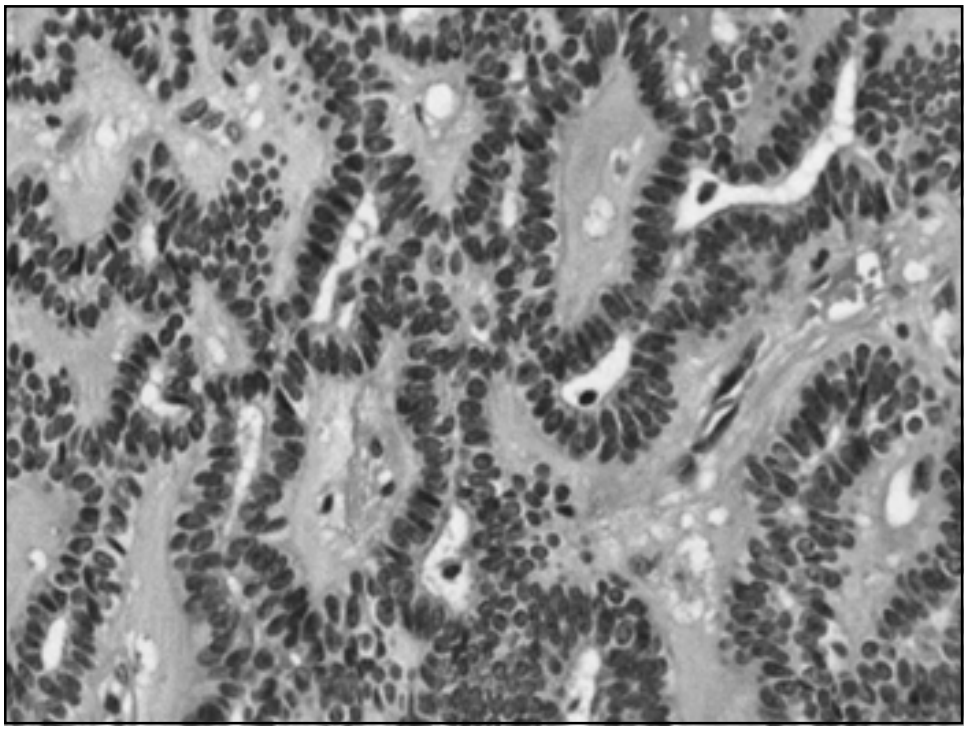


occasionally may not be totally encapsulated, and more than *20%* of cases are *multifocal.*



Multi-foci mass

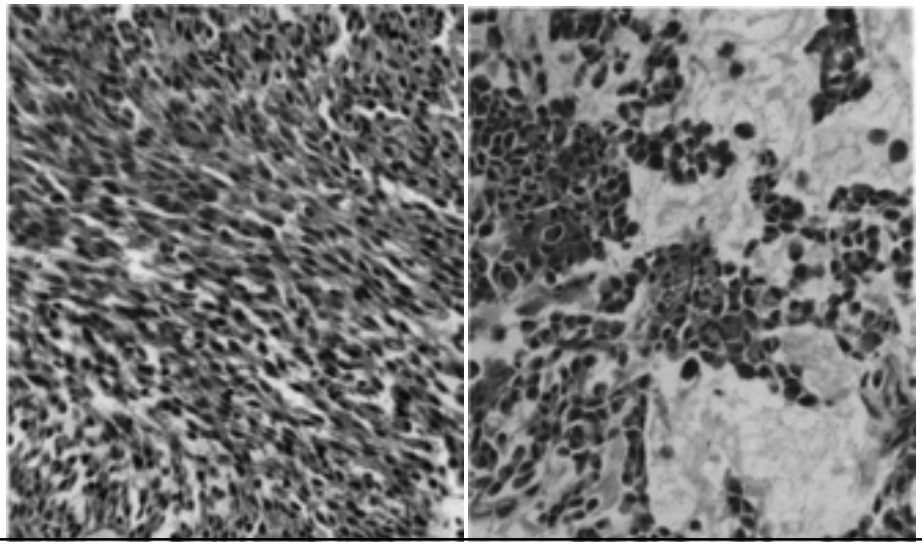


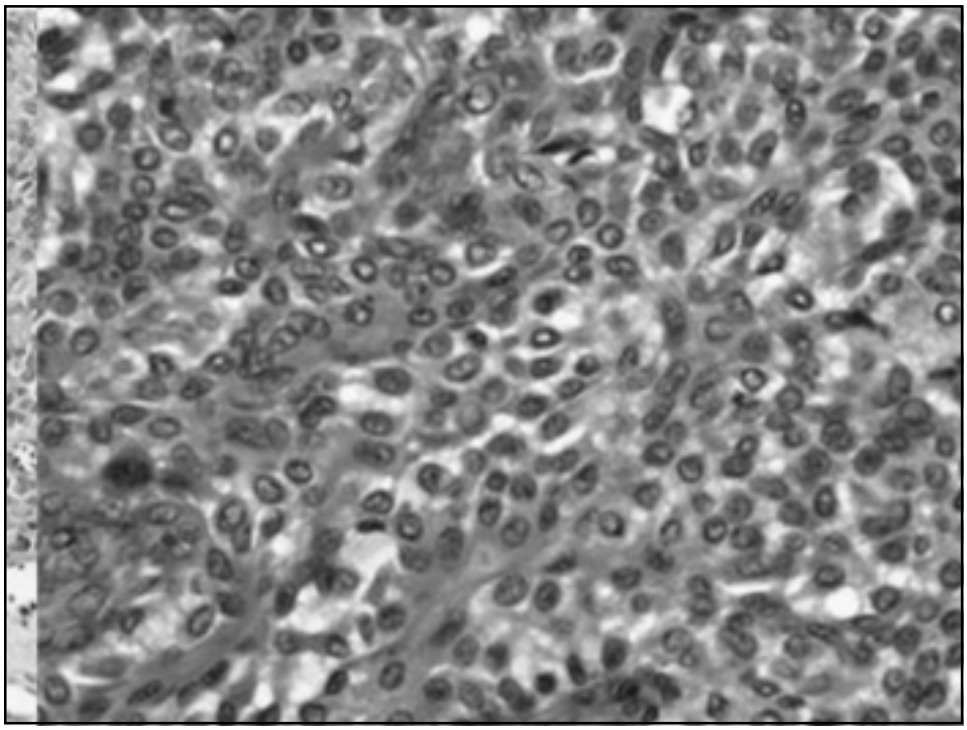


Myoepithelioma

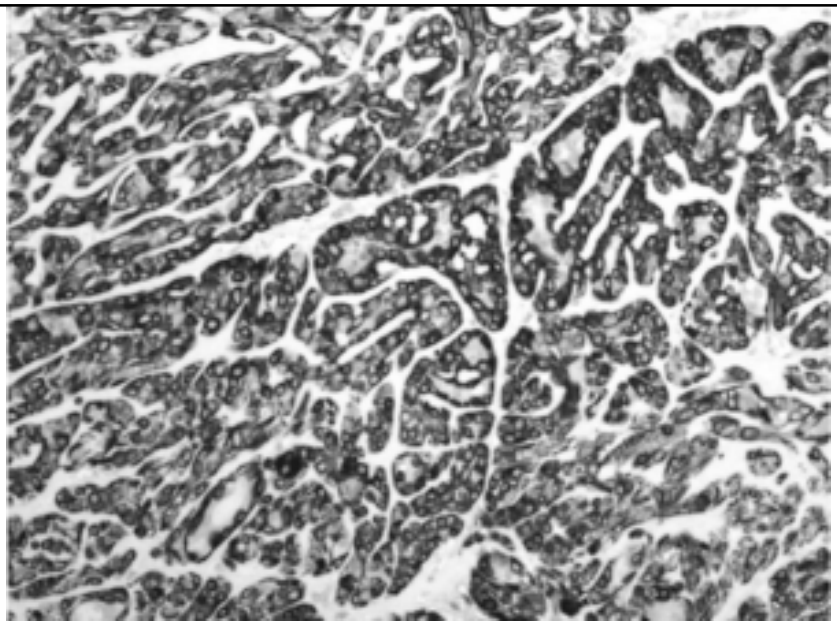
- *epithelial* origin,
- Mostly in *parotid* gland, followed by minor salivary glands.
- *circumscribed* painless masses.
- both genders equally.

70% of cases contain *spindle cells*, and *20%* are composed of *plasmacytoid cells*





IHCs:
p63, actins, cytokeratin, and S-100 protein.



GFAP positivity

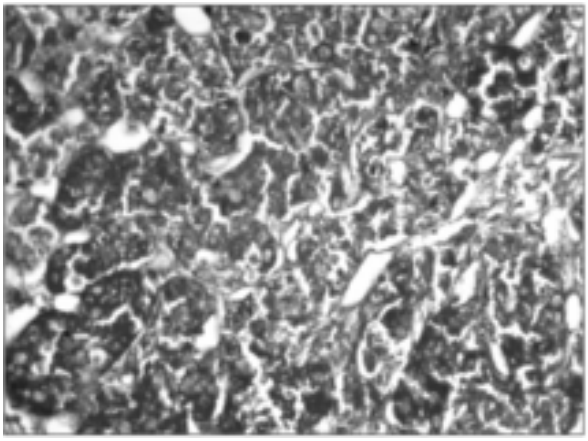
Treatment and Prognosis

- In parotid gland: *superficial parotidectomy* is indicated.

- The overall *prognosis* is *excellent*, and recurrences are not expected.

- sheets of *polyhedral cells*, or *microcystic* spaces and *clear* cell changes.

- The phosphotungstic acid hematoxylin (**PTAH**), highlighting the intracytoplasmic mitochondria: to confirm the diagnosis

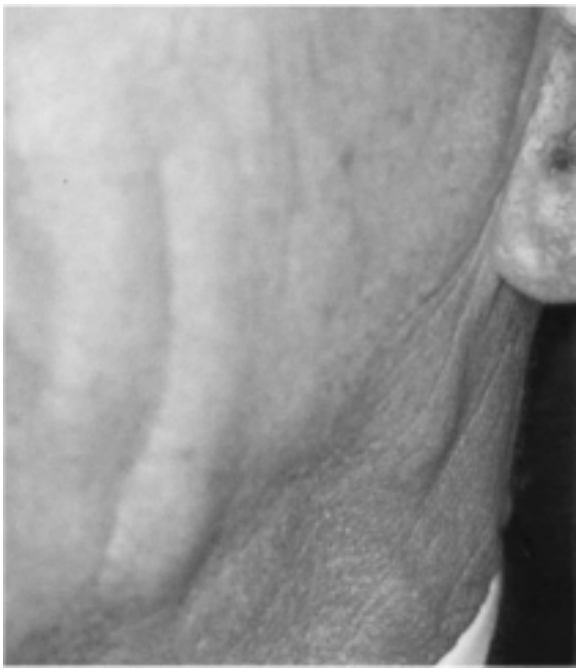


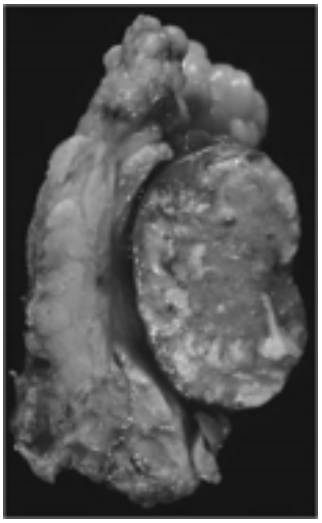
- Treatment: is *conservative*, with superficial parotidectomy
- In minor salivary glands, removal of the tumor with a *margin of normal tissue* is deemed adequate.
- *Recurrence* is *rarely* noted.
- The *malignant* oncocytoma is rare.

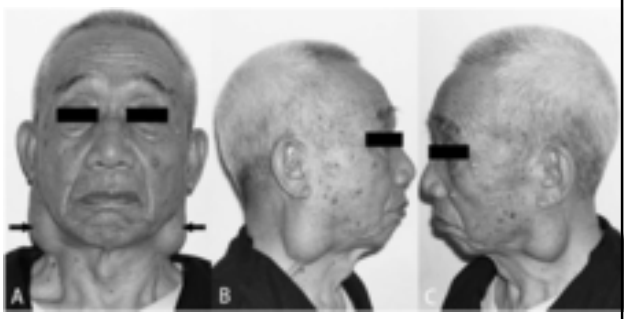
Papillary Cystadenoma Lymphomatosum (Warthin's Tumor)

- 7% of epithelial neoplasms of salivary glands,
- within lymph nodes ??
- chronic inflammation ??

- Mainly in *parotid* gland
- predominantly in *men*,
- a strong positive association with *cigarette smoking*
- Mostly *bilaterally*, and most common associated with other salivary tumors.



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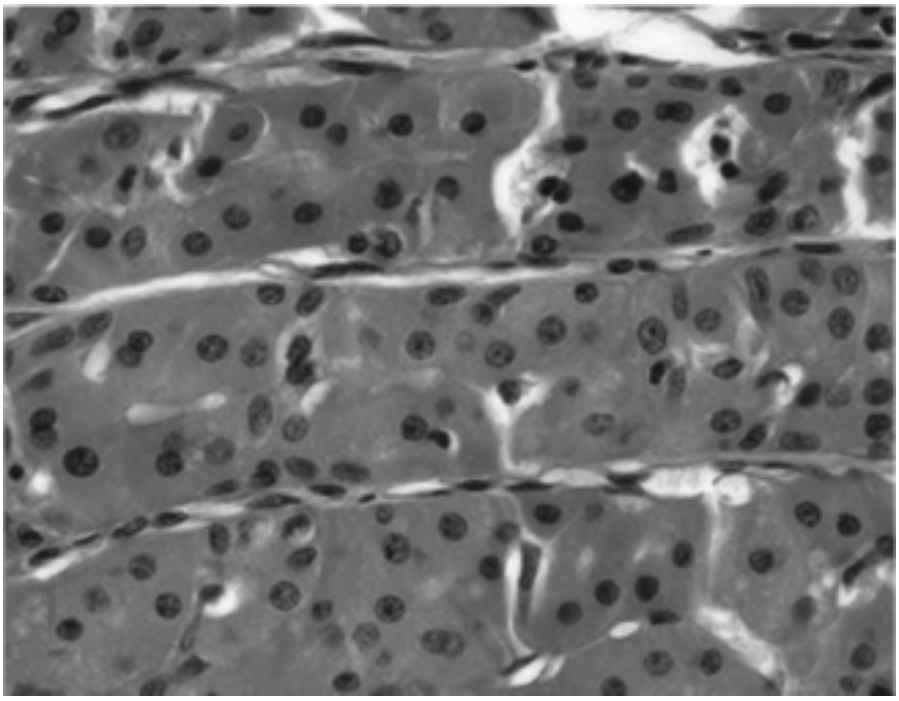
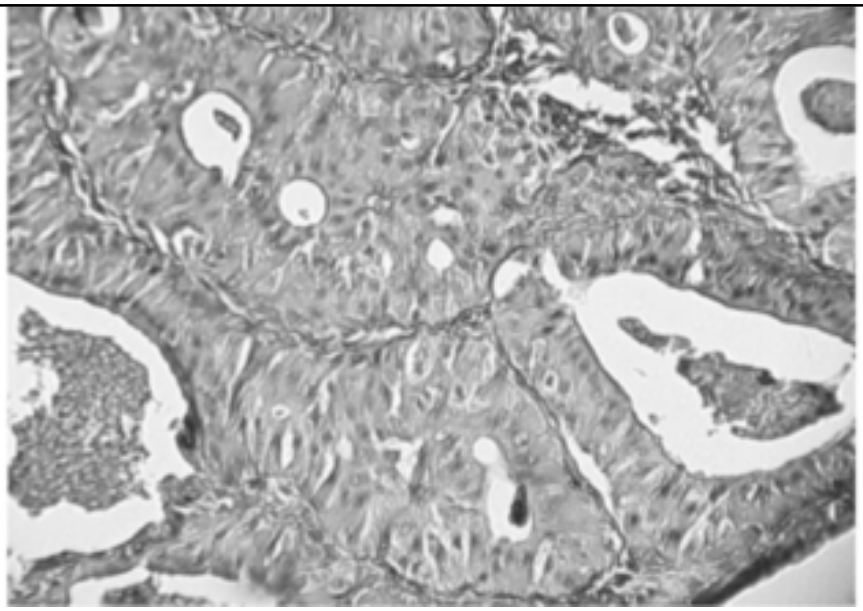




prominent epithelial component with tall oncocytic luminal cells palisading of a basal cell layer

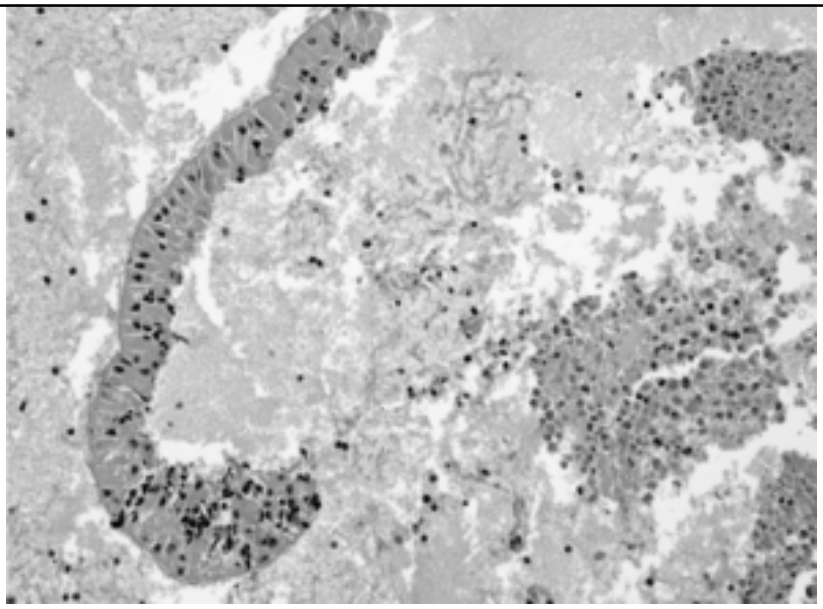
Prognosis:

- *Recurrences* represent second primary lesions.
- *Malignant* transformation, especially as a complication of radiotherapy to the region, is rare.

Metaplastic Warthin's Tumor

One of few diagnostic pitfalls in rare subtype variously termed (6-7% of cases):

1. Infarcted
2. Infected
3. Metaplastic



Infarcted type

Histologic D.D

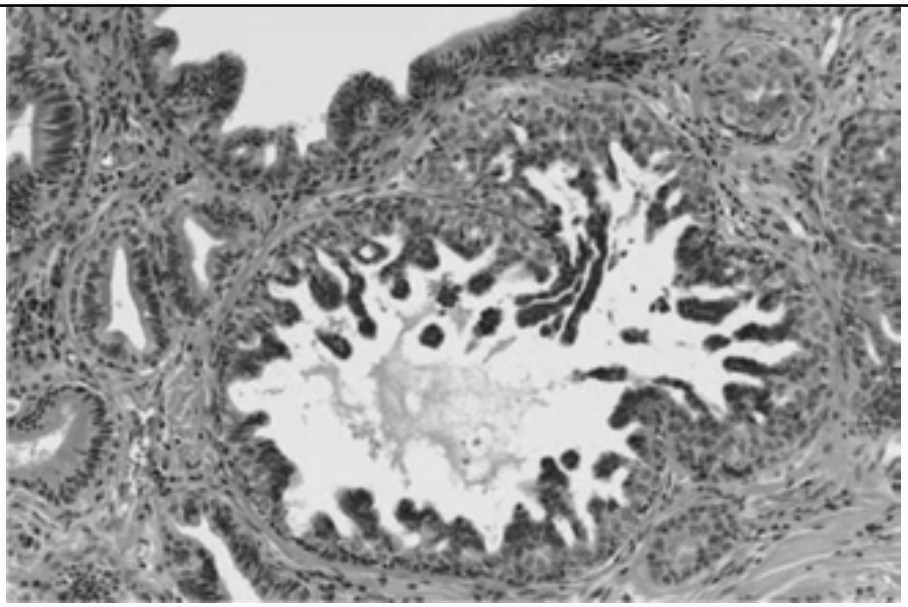
1. **MEC**: FISH testing for MAML2 to rule out MEC
2. **SCC**: either de novo (from squamous metaplasia) or rarely as malignant component of carcinoma X Warthin tumor (in SCC: cellular atypia)

Ductal Papilloma

arise within the interlobular and excretory duct portions of the salivary gland unit.

3 types

1. sialadenoma papilliferum,
2. inverted ductal papilloma,
3. ntraductal papilloma.

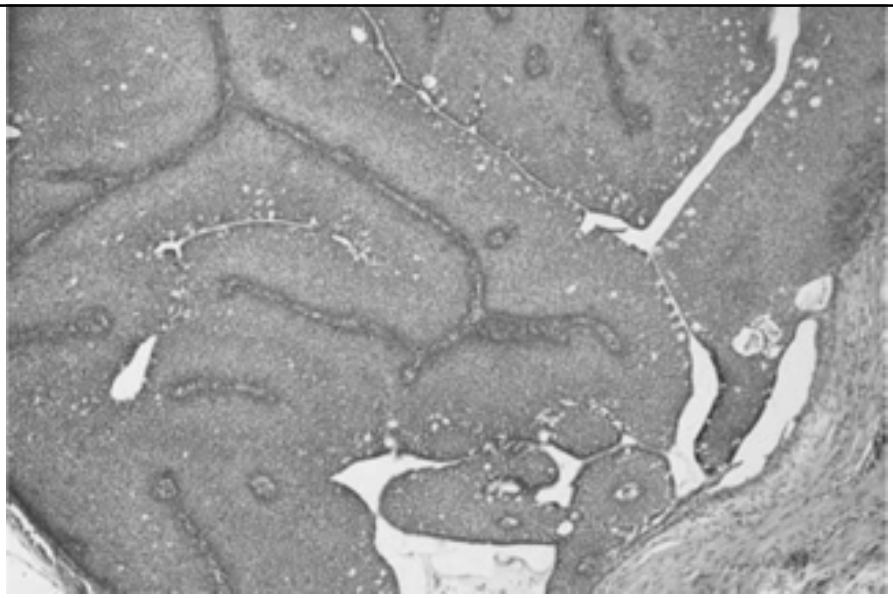


Sialadenoma papilliferum

Inverted ductal papilloma

- marked proliferation of ductal epithelium is seen subjacent to intact mucosa.

- ***Crypts*** and ***cyst-like spaces*** lined by columnar cells with polarized nuclei are interspersed with goblet cells and transitional forms of cuboidal to squamous cells as an intraluminal proliferative process with an endophytic growth pattern.

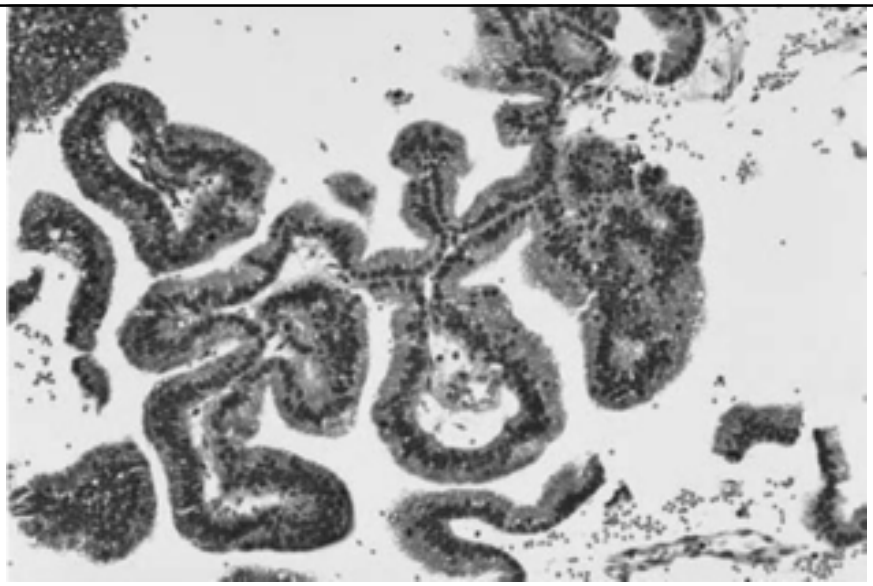


Inverted ductal papilloma

intraductal papilloma

- rare lesion arises from a greater depth within the ductal system, often presenting as a salivary obstruction caused by intraluminal exophytic growth.

- a single or double layer of cuboidal to columnar epithelium covers several papillary fronds that project into a duct, with no evidence of proliferation into the wall of the cyst.



Intraductal papilloma composed of fronds of ductal cells. The duct from which this lesion is derived is not included in the photomicrograph.

- Treatment for this lesion, as well as for inverted ductal papilloma, is *simple excision*.
- There is *little risk of recurrence*

Malignant salivary glands tumors

1. Mucoepidermoid carcinoma
2. Polymorphous low-grade adenocarcinoma
3. Adenoid cystic carcinoma
4. Clear cell carcinoma
5. Acinic cell carcinoma
6. Adenocarcinoma NOS

Rare, predominantly parotid tumors

1. Carcinoma ex-mixed tumor/malignant mixed tumor
2. Epimyoepithelial carcinoma
3. Salivary duct carcinoma
4. Basal cell adenocarcinoma
5. Oncocytic adenocarcinoma
6. Sebaceous adenocarcinoma
7. Mammary analog secretory carcinoma
8. Squamous cell carcinoma

NOS, Not otherwise specified.

Malignant Salivary Gland Tumors: Biological Classification

Low-Grade Malignancies

1. Mucoepidermoid carcinoma (low grade)
2. Polymorphous low-grade adenocarcinoma
3. Acinic cell carcinoma (low to intermediate grade)
4. Clear cell carcinoma
5. Basal cell adenocarcinoma

Intermediate-Grade Malignancies

1. Mucoepidermoid carcinoma (intermediate grade)
2. Epimyoepithelial carcinoma
3. Sebaceous adenocarcinoma
4. Mammary analog secretory carcinoma

High-Grade Malignancies

1. Mucoepidermoid carcinoma (high grade)
2. Adenoid cystic carcinoma
3. Carcinoma ex-mixed tumor
4. Salivary duct carcinoma
5. Squamous cell carcinoma
6. Oncocytic adenocarcinoma

Malignant Minor Salivary Gland Tumors

Clinical Features

- Adults; men and women affected equally
- Mass or ulcerated mass
- Asymptomatic in early stages
- Sites—palate . buccal mucosa . retromolar pad . upper lip .
- tongue
- Low-grade mucoepidermoid carcinoma . polymorphous
- low-grade adenocarcinoma . adenoid cystic carcinoma

Histopathology

- Highly variable but characteristic patterns; infiltrative margins;
- rare mitoses; little pleomorphism

Treatment and Prognosis

- Wide excision; radiation added for problematic cases
- Ranges from low- to high-grade behavior (adenoid cystic carcinoma
- has worst long-term prognosis)

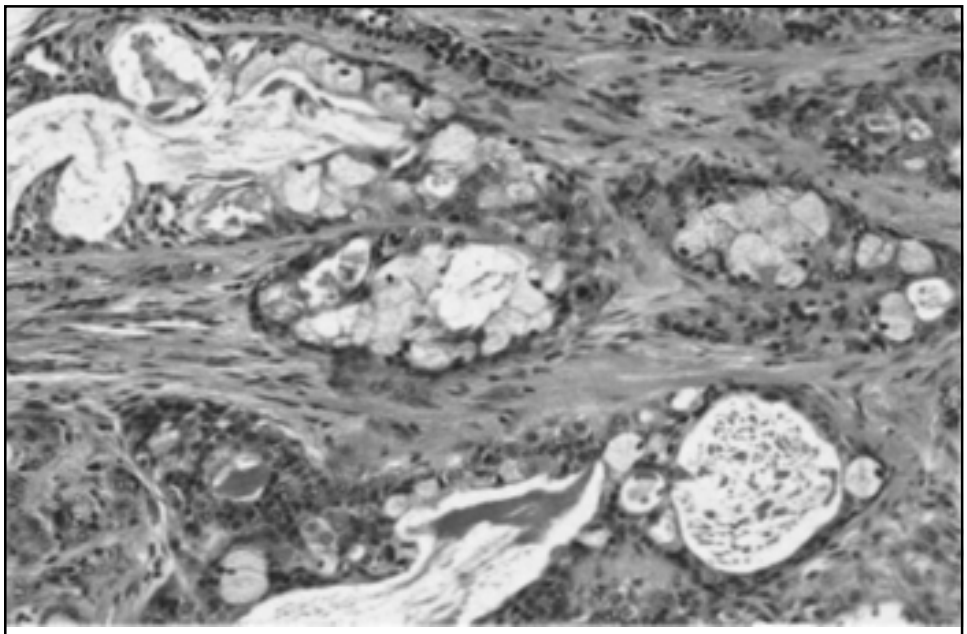
	Benign	Malignant
Growth rate	Slow	Varied, usually rapid
Ulceration	No	Yes
Fixation	No	Yes
Facial nerve palsy	No	Yes
Encapsulated	Yes	No
Natural history	Slow growth	Slow to rapid growth
Metastasis	No	Yes
Treatment	Local excision	Surgery with or without radiation

Mucoepidermoid Carcinoma

- Most common malignancy of SG
- Most common salivary malignancy in children
- In minor: Palate mostly; rare primary intrabony (jaws)
- More ducts and mucous cells in low-grade lesions
- Most oral lesions of low grade

- it is a distinctive salivary gland malignancy composed of:

1. *Mucinous* cells
2. *Intermediate* cells (clear)
3. *Squamoid* cell



Low grade MEC

	Low Grade (Good Prognosis)	High Grade (Fair Prognosis)
Cell type	Numerous mucous cells and intermediate cells; few epidermoid cells	Mainly epidermoid cells and few mucous cells; looks like squamous cell carcinoma
Microcystic spaces	Large and numerous cysts; >20% of area	Few cysts; <20% of area; mainly solid tumor
Cytologic atypia	None to little	Abundant
Necrosis	Absent	Present
Perineural invasion	Absent	Present

- Affects major more than minor SG
- MEC in palate: most commonly in younger age group

Important notes:

- Epidermoid cells have an obvious intercellular bridges which give it the squamous appearance: So it is squamous-like or epidermoid
- Keratinization is rare: (when found: doubt the MEC)

when there is **keratinization** it is part of:

1. squamous metaplasia in PA
2. Myoepithelial carcinoam
3. Metastatic SCC

Polymorphous (Low-Grade) Adenocarcinoma

- first reported in 1983 by two different groups using the terms *lobular carcinoma* and *terminal duct carcinoma*.
- The putative source: reserve cells in the most *proximal portion* of the salivary duct.
- Myoepithelial-differentiated cells: in low to moderate numbers

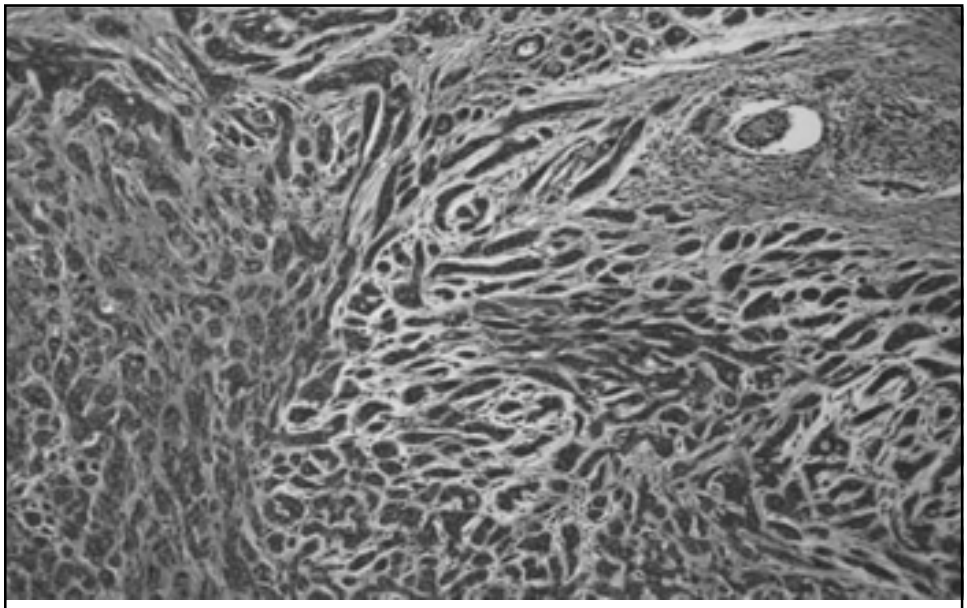
- Malignancy of minor SG; second in frequency to mucoepidermoid carcinoma
- asymptomatic submucosal mass
- most cases show small nerve invasion but no effect on prognosis
- Low-grade malignancy; good prognosis
- Treatment by wide excision; recurrence rate ,10%

Occasional metastasis

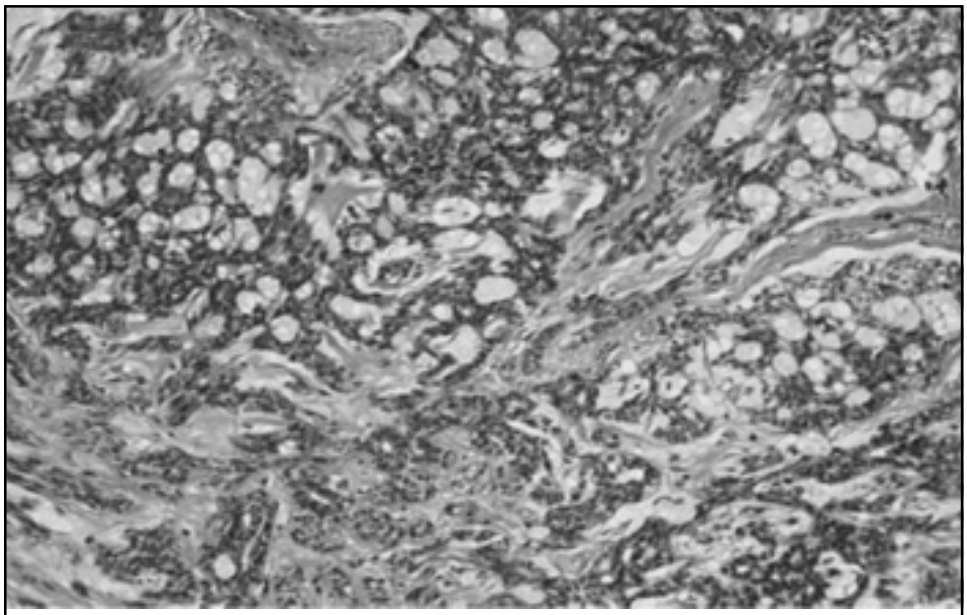
1. Regional nodes ,10%
2. Rare to lungs

Histopathology

- Absence of encapsulation with infiltrating streams of cells and a general lobular morphology characterize this tumor.
- Infiltration into the surrounding salivary gland and connective tissue is evident at low-power examination.
- In most areas, the tumor is composed of a homogeneous population of cells with prominent, bland, uniform, and often-vesicular nuclei surrounded by minimal cytoplasm



Polymorphous low-grade adenocarcinoma showing streaming pattern.



Polymorphous low-grade adenocarcinoma with a pseudocribriform pattern

- S100: + and strong and more diffuse than adenoid cystic carcinoma
- P63, CK7, EMA, vimentin, BCL2: +
- P40: -

Treatment & Prognosis

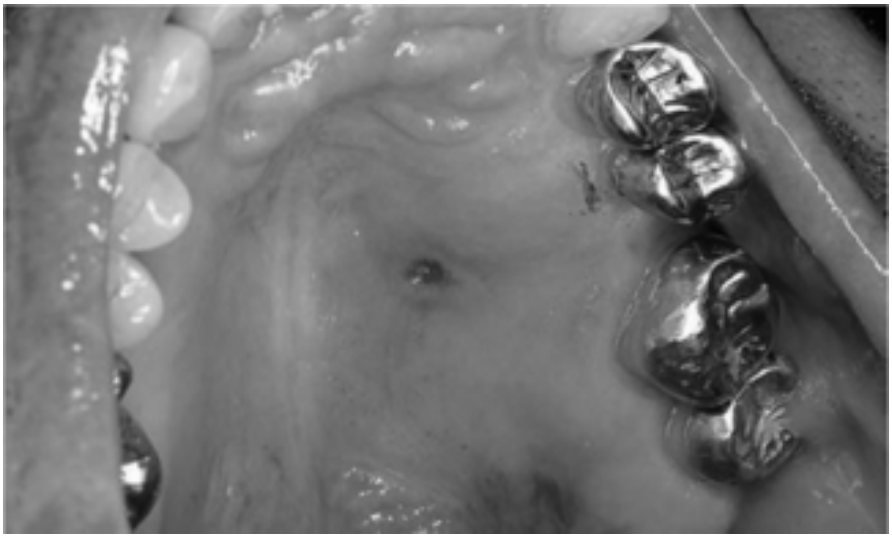
surgical excision, with wide surgical

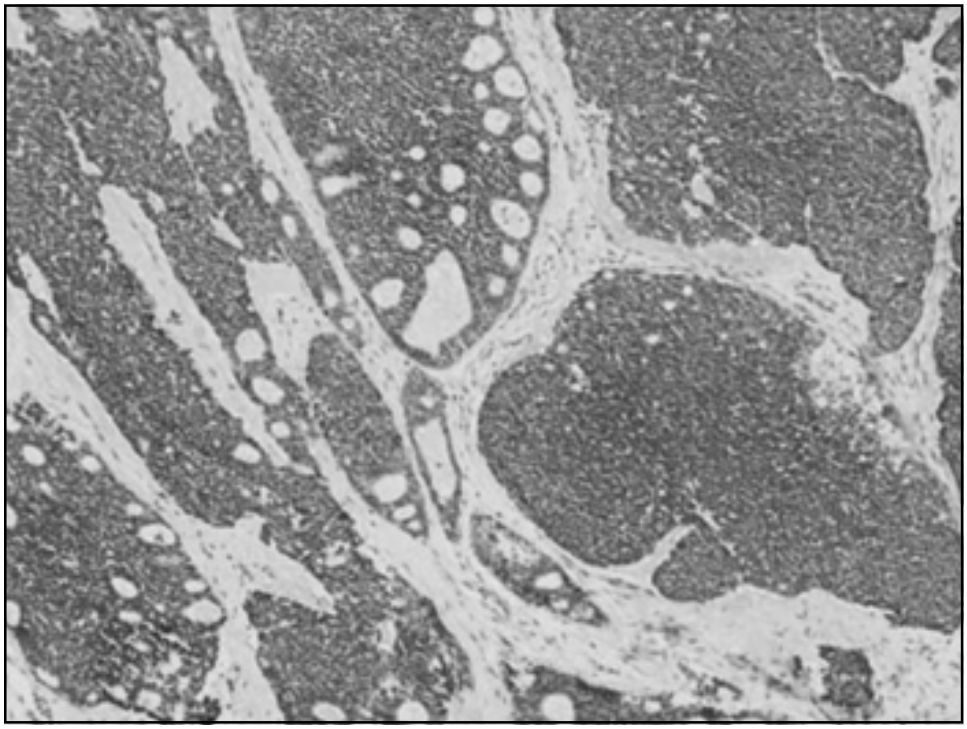
excision, the recurrence rate is approximately 10%, and the overall survival rate is excellent.

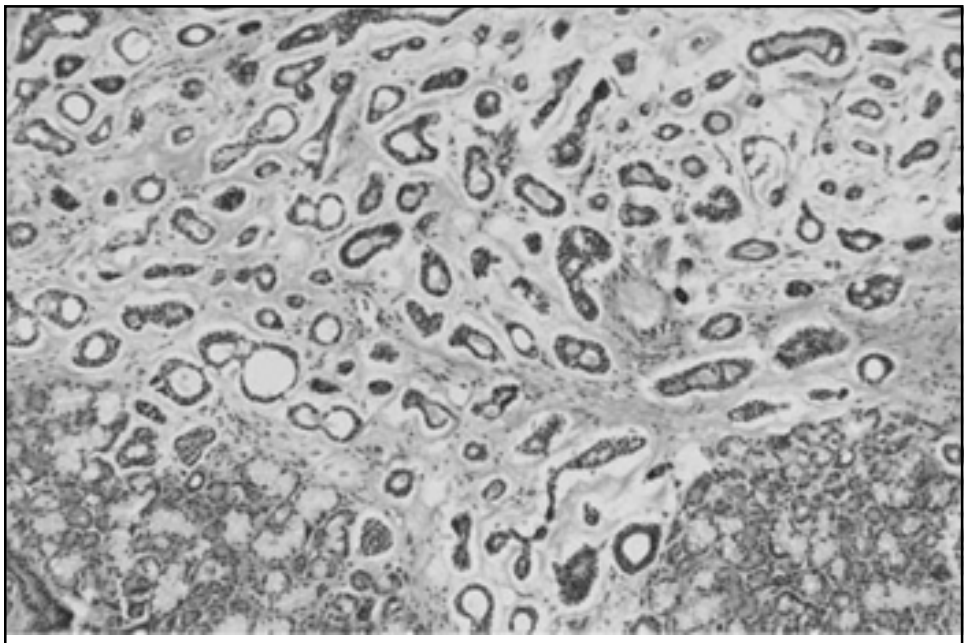
Adenoid Cystic Carcinoma

- a high-grade malignancy that has a fair 5-year survival rate but a dismal 15-year survival rate.
- It is composed of duct-type epithelial cells and myoepithelial cells in variable patterns.
- showing little cellular atypia and only rare mitotic figures

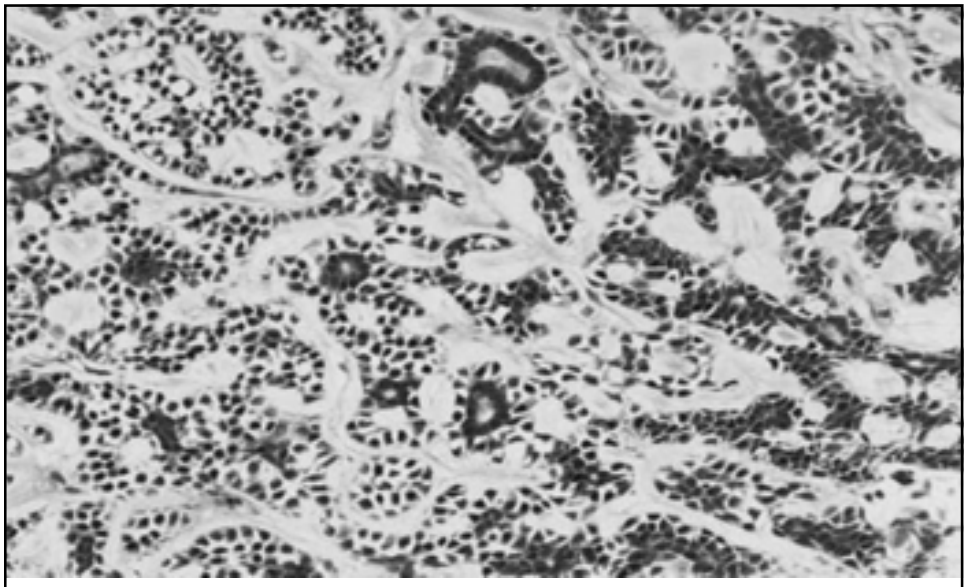
- Adults; palatal mass/ ulceration
- Cribriform microscopic pattern
- Spread through perineural spaces
- Local recurrence and metastasis; lung > nodes
- 5-year survival 70%; 15-year survival 10%



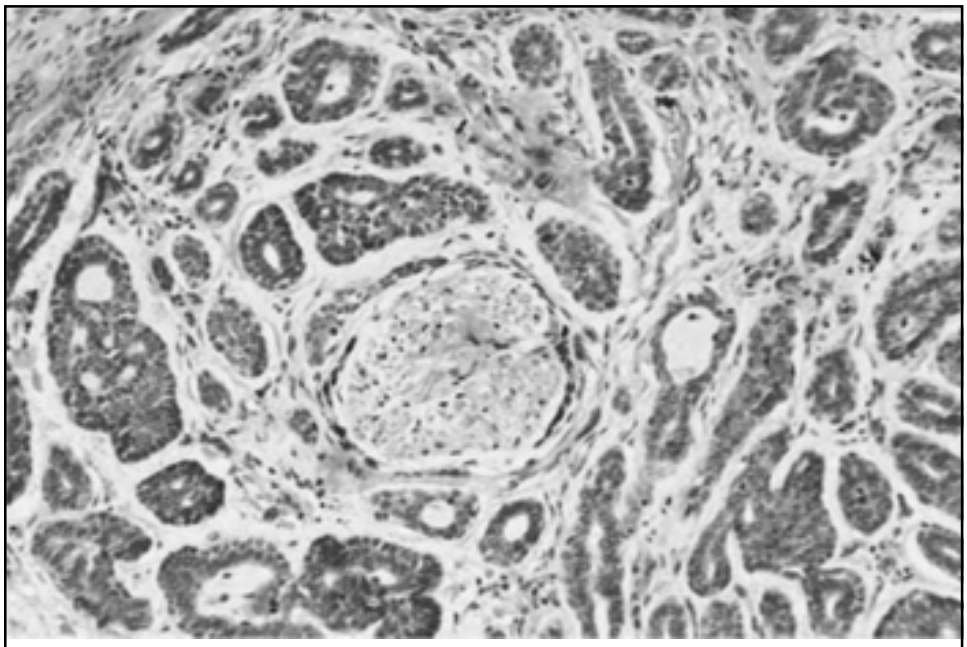




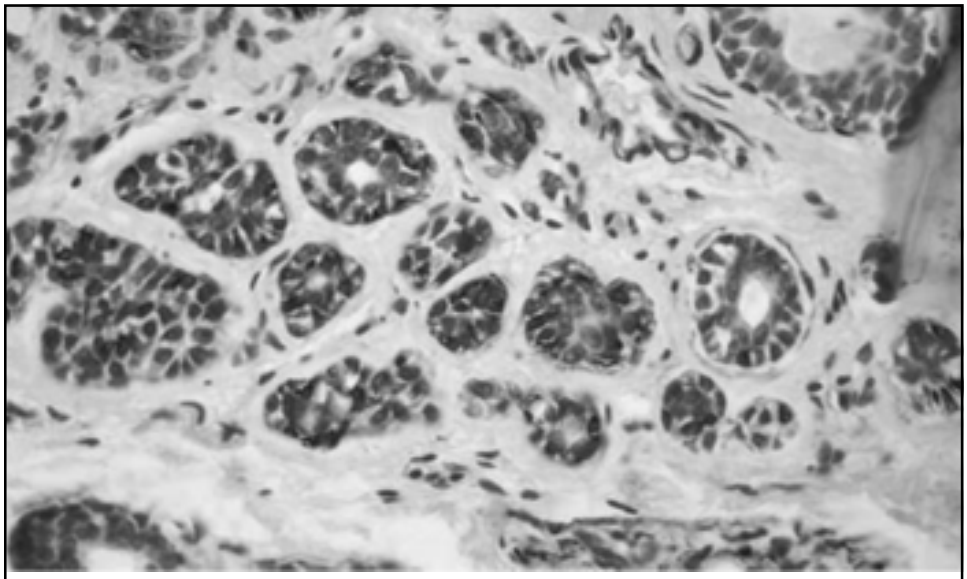
Adenoid cystic carcinoma, microinvasive pattern



Adenoid cystic carcinoma with prominent clear cell layer surrounding inner ductal cells.



Adenoid cystic carcinoma showing perineural invasion.



Adenoid cystic carcinoma stained for muscle-specific actin. Positive staining (red) is seen in the outer layer of cells.

Traetment

- surgery is regarded as the treatment of choice
- parotid glands: superficial parotidectomy or superficial and deep lobectomy is recommended,
- In the parotid region, the debate is whether the facial nerve should be spared; most investigators recommend resection if the tumor surrounds or invades this nerve.
- Intraorally, wide excision, often with removal of underlying bone, is the treatment of choice. Radical surgical excision may be justified to obtain surgical margins that are free of tumor.

	PLGA	AdCC
P40	-	+

Acinic Cell Carcinoma

- occurs predominantly in parotid.
- Source of acinic cell carcinoma is the intercalated duct reserve cell, although there is reason to believe that the acinic cell itself retains the potential for neoplastic transformation

- all age groups
- M=F
- 14% of all parotid gland tumors and 9% of the total of salivary gland carcinomas of all sites.
- 80% of cases develop within the superficial lobe and the inferior pole of the parotid gland

- Slow growing lesion smaller than 3 cm in diameter.
- pain is a common
- Rarely, may assume a dedifferentiated phenotype with corresponding levels of clinical aggressiveness, rapid growth, lymphovascular invasion, and regional lymph node metastasis.

Important note

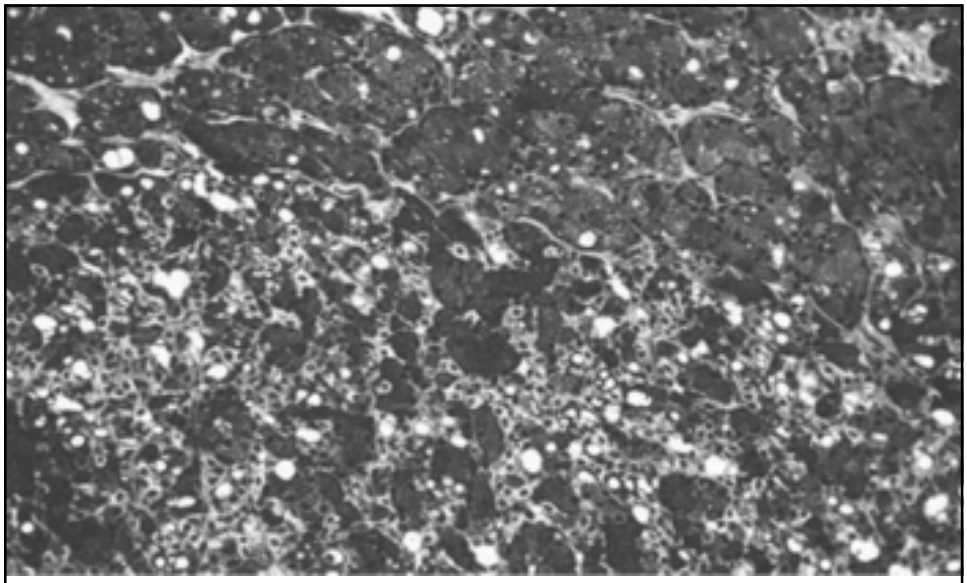
previously classified acinic cell carcinoma often of minor SG harboring the ETV6 translocation should now be classified as secretory carcinoma (MASC: mammary analog secretory carcinoma)

Histopathology

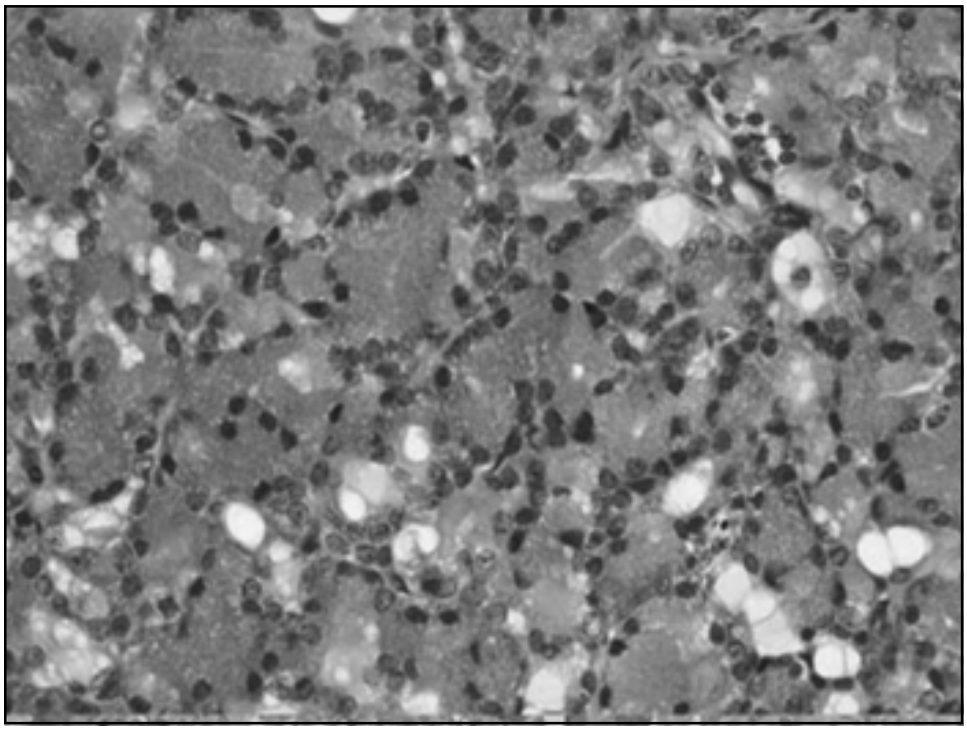
- intraglandular mass , **well circumscribed**.
- solid microscopic pattern, although one third of lesions have a microcystic pattern
- Papillary and follicular patterns may be seen within the solid component, or may represent the majority of the lesion.
- Hemosiderin is often found, and there is little stromal tissue.

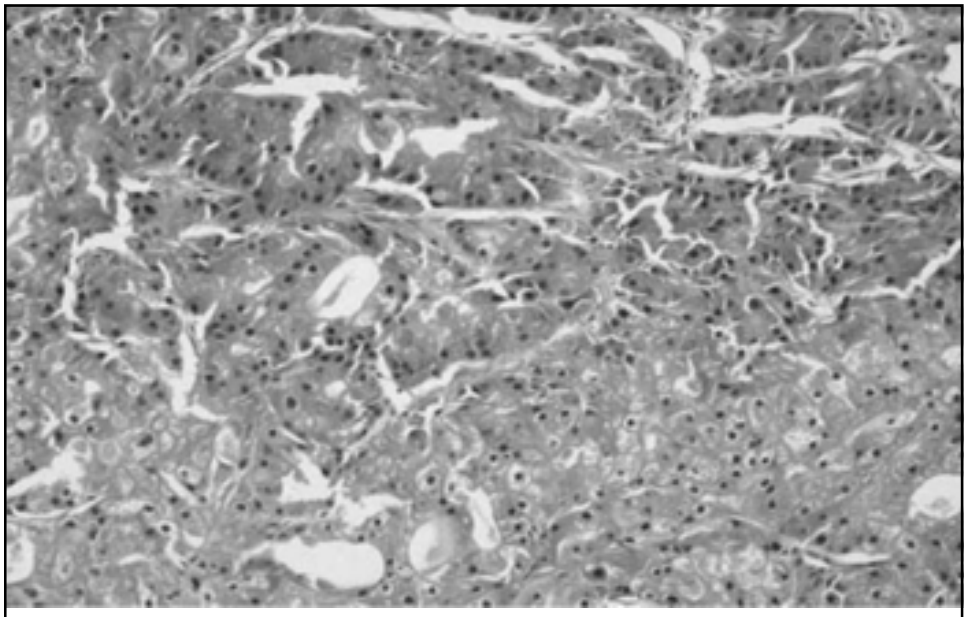
Patterns of cellular growth:

1. Solid/lobular
2. Microcystic
3. Papillary/cystic
4. Follicular pattern



Acinic cell carcinoma with cells containing darkly staining zymogen granules.





Acinic cell carcinoma with clear cell area

- Ki67 > 5% : it is more aggressive
- 6% of cases: clear cells

- High grade transformation is seen in older patients: undifferentiated cells with any type and areas of necrosis
- Thin fibrous pseudo-capsule

Clinical stage is important: poor prognosis with:

1. Large size
2. Involvement of deep lobe of parotid
3. Incomplete resection
4. Multiple recurrence
5. Lymph nodes metastases

Histological features associated with more aggressive tumors:

1. Frequent mitosis
2. Necrosis
3. Neural invasion
4. Pleomorphism
5. Infiltration
6. Stromal hyalinisation

Clear Cell Carcinoma

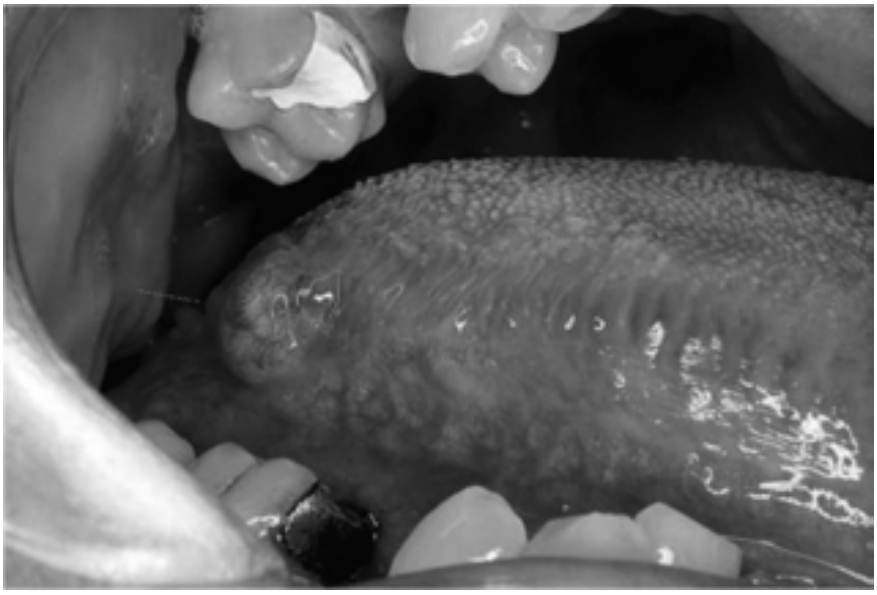
Clear Cell Tumors:

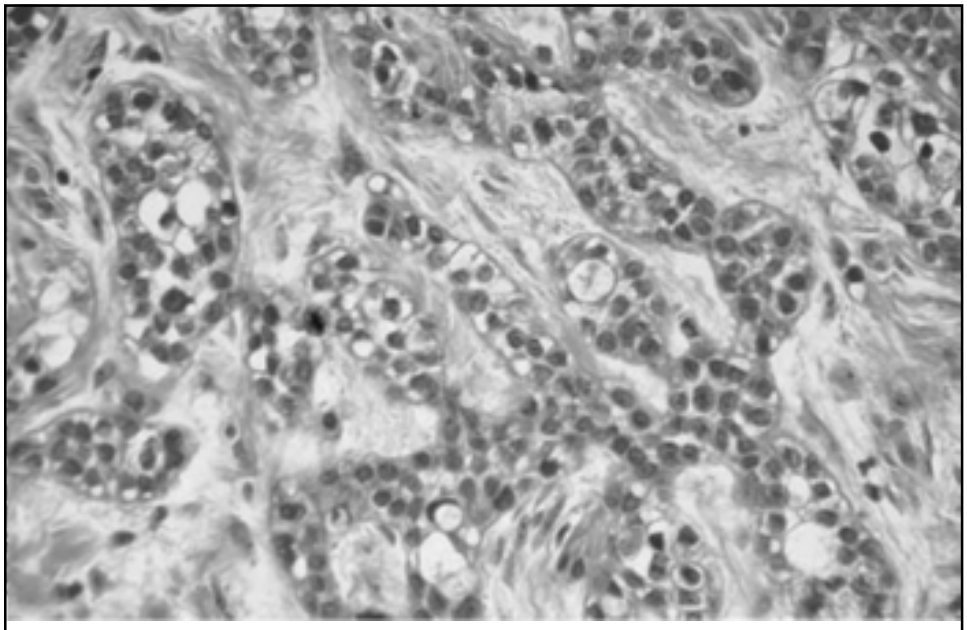
1. Clear cell carcinoma
2. Epimyoepithelial carcinoma

Clear Cell Change/Artifact in other Tumors

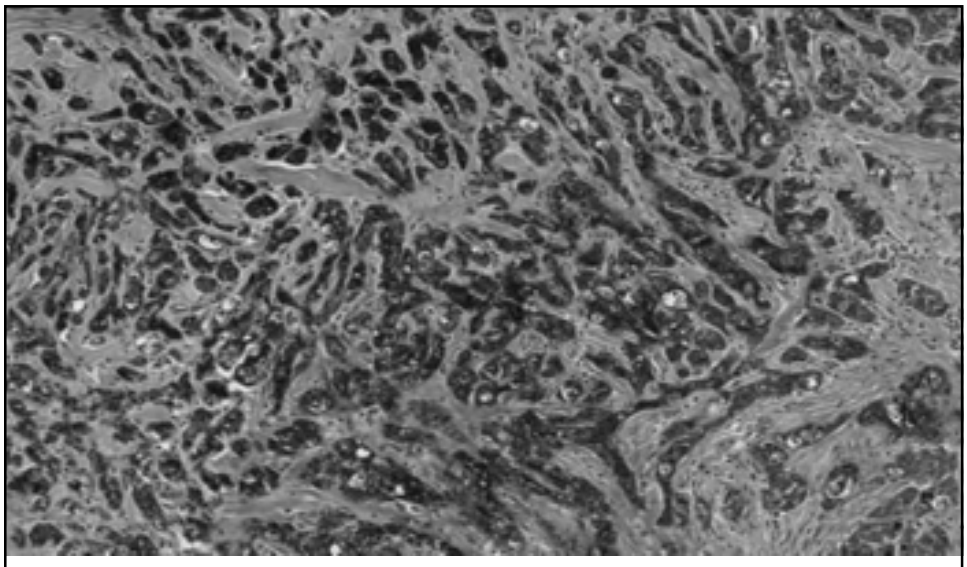
1. Adenoid cystic carcinoma
2. Oncocytoma
3. Acinic cell carcinoma
4. Mucoepidermoid carcinoma

low-grade tumor that occurs predominantly in the minor salivary glands (80% of cases). Most present as submucosal masses in the palate,

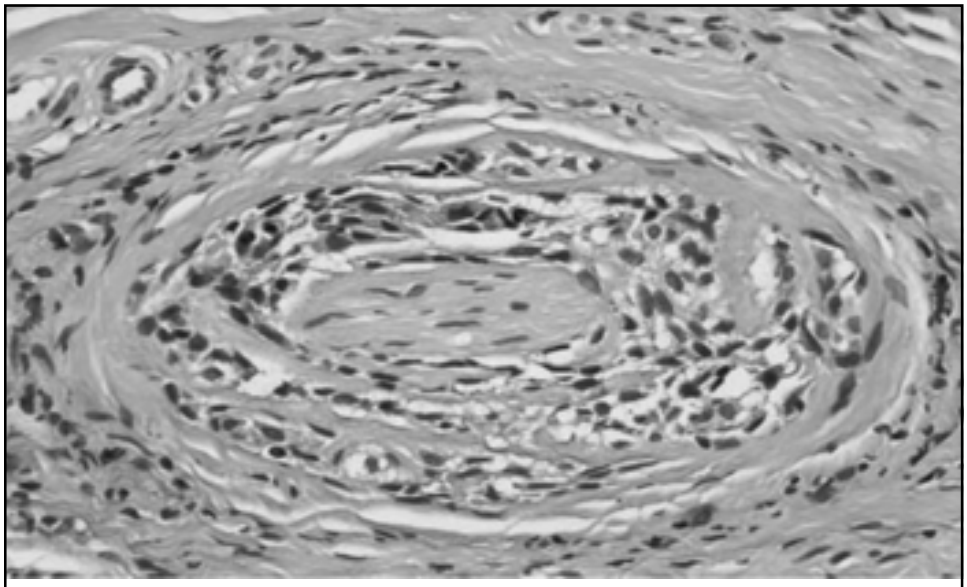




Clear cell carcinoma, trabecular arrangement of clear cells



Positive (red) periodic acid–Schiff (PAS) staining (glycogen) of tumor cells.



Clear cell carcinoma showing perineural invasion.

Classification of clear cell tumors of the salivary glands

Benign:

PA, sebaceous adenoma, oncocytoma and oncocytic hyperplasia (MNOH: multi-focal nodular oncocytic hyperplasia)

Malignant:

- Carcinomas not usually characterized by clear cells BUT with rare clear cell variants: MEC and acinic cell carcinoma

- Carcinomas usually characterized by clear cells:

1. dimorphic: epithelial-myoepithelial carcinoma

2. monomorphic: hyalinized clear cell carcinoma and clear cell malignant myoepithelioma (myoepithelial carcinoma)

3. Sebaceous carcinoma

Malignant, metastatic:

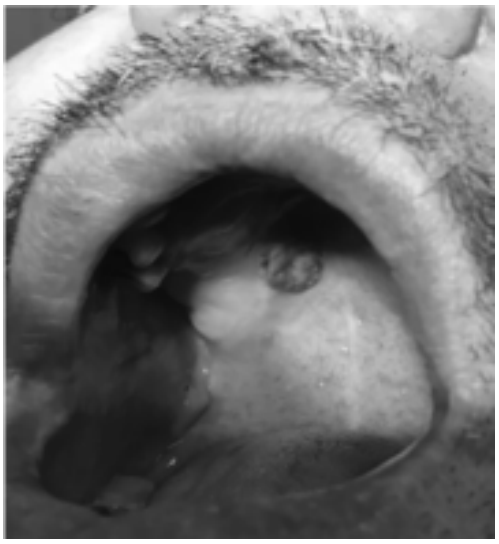
Carcinomas: espically kidney, thyroid also melanoma

Mammary analogue secretory carcinoma (MASC)

It was first recognized in 2010 by Skalova et al, previously it was thought to be " ancient acinic cell carcinoma"

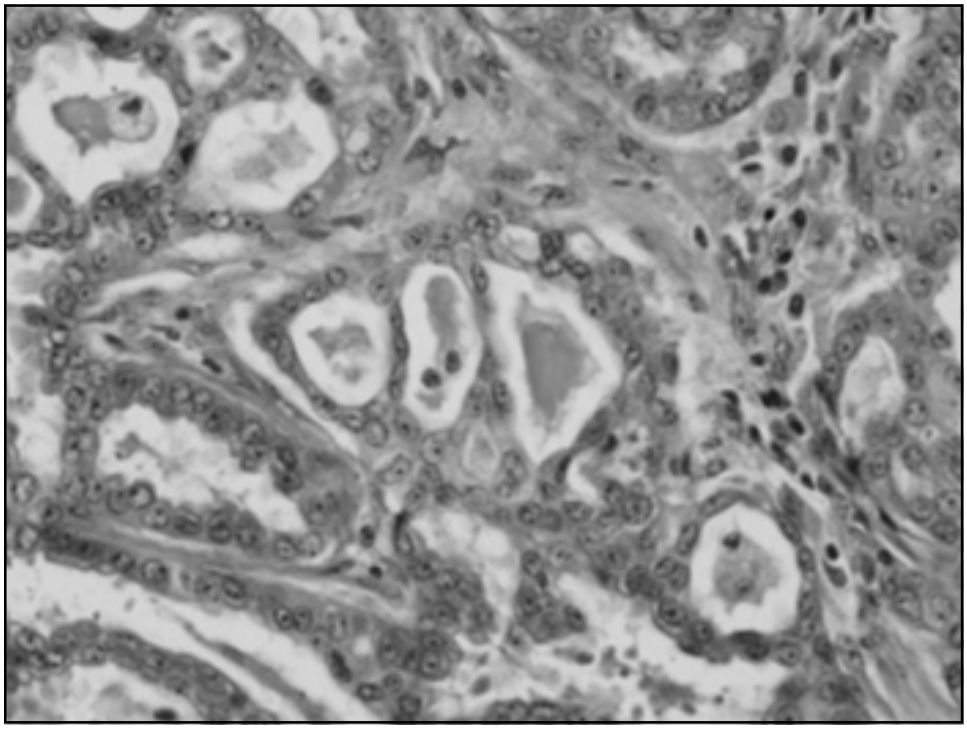
In WHO 2017 classification: " a generally low grade salivary gland carcinoma characterized by morphological resemblance to mammary carcinoma and ETV6-NTRK3 gene fusion.

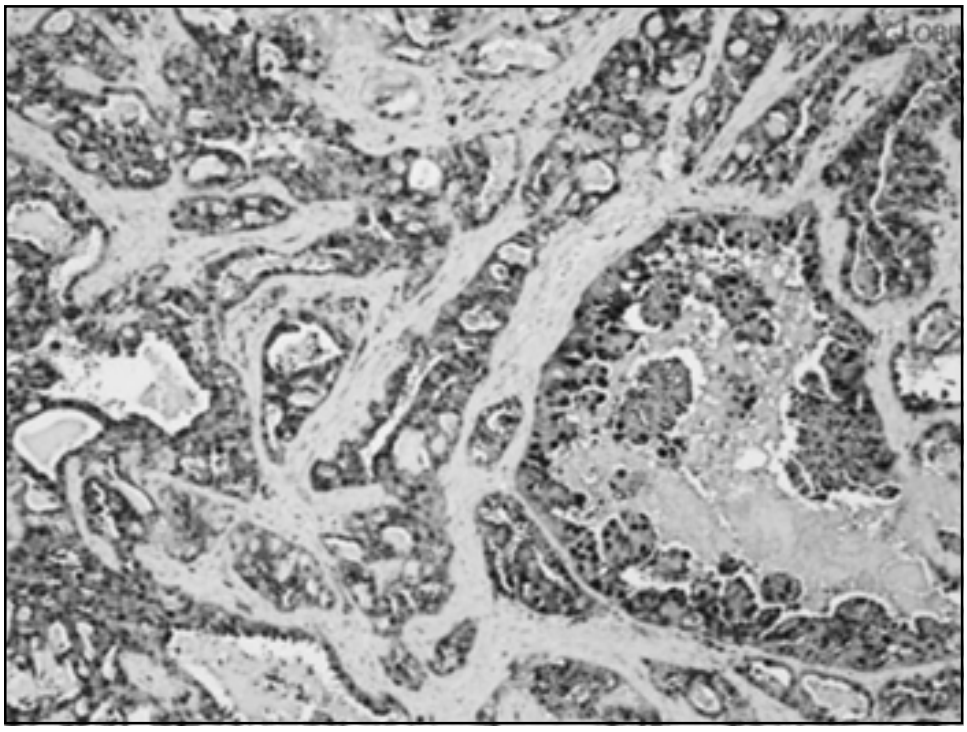
- F =M
- Mostly parotid (also in submandibular)
- Also reported in sinonasal track and thyroid



Histopathology

- Circumscribed but not encapsulated
- Lobulated growth pattern composed of tubular and solid structures with microcystic and glandular spaces
- Low grade vesicular nuclei with centrally located nucleoli and pale vaculated cytoplasm
- Cellular atypia is mild and mitotic figures is rare
- Less frequent: macrocysts, hobnail cells, intracytoplasmic mucin (focal) and thyroid colloid-like areas
- No necrosis and no serous acinar differentiation





MASC harbours a balanced chromosomal translocation t(12;15)(p13;q25) while leads to a fusion gene between ETV6 on chromosome 12 with NTRK3 on chromosome 15

DDx

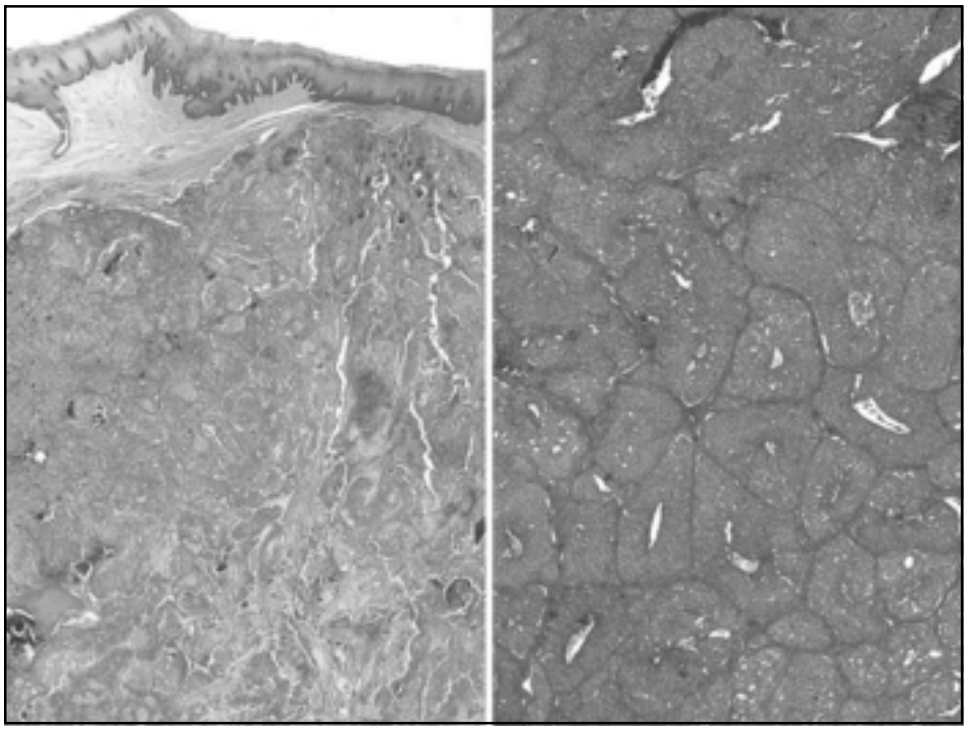
1. Acinic cell carcinoma: some previously diagnosed ACC re-diagnosis as MASC based on ETV6 translocation. ACC outside the parotid is rare BUT diagnosis should be reseved for tumors with obvious zymogen granules

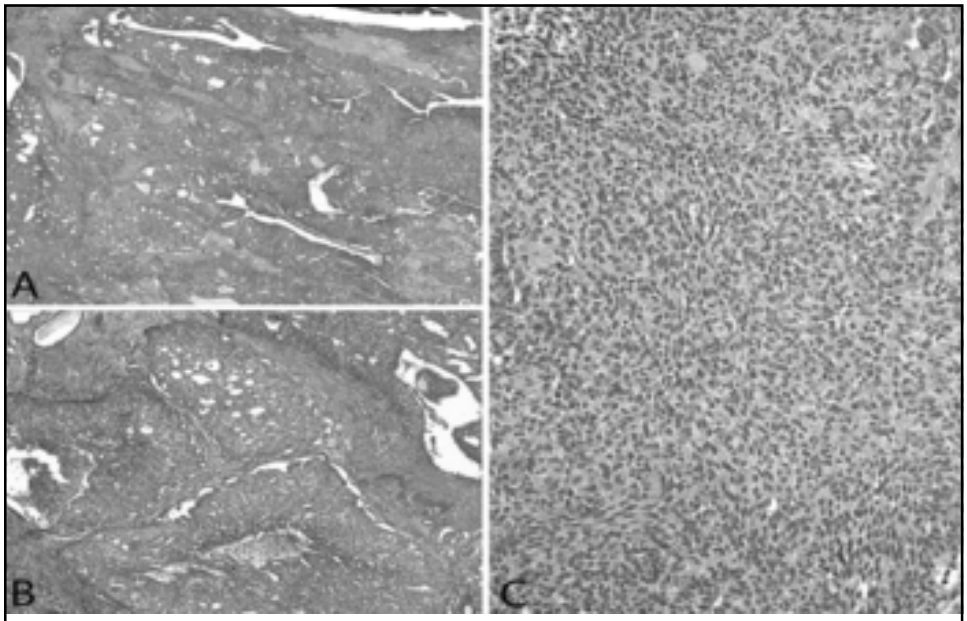
IHCs is useful: MASC: mammoglobin + and DOG-1- While in AcCC usually shows the reverse profile.

MASC in SG appears to be more aggressive than its breast countrepart

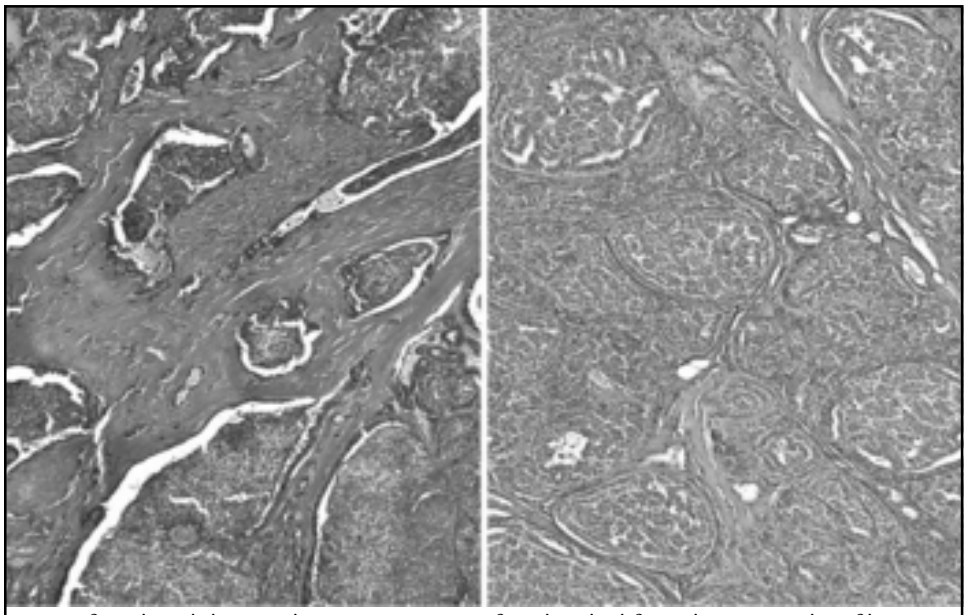
CATS: cribriform adenocarcinoma of tongue and SG-WHO 2017

- In 1999 Michal et al, published a series of distinctive adenocarcinoma in the posterior tongue characterized by lateral neck lymph nodes but no distance spread. Then more cases were collected arising in minor SG other than in tongue. Now it is clear entity distinct from PLGA. In WHO 2017 it was included as variant of PLGA.





The tumors are composed predominantly of cribriform (a) to microcribriform (b) and solid structures (c) in variable proportions



Left in the solid areas, the tumor nests are often detached from the surrounding fibrous stroma by (presumably artifactual) clefts. Right artifactual detachment often results in glomeruloid appearance of tumor lobules

IHCs:

- Spectrum of low weight cytokeratins: CK7, as well as S-100 and vimentin
- Myoepithelial cells markers are + in up to 60% of cells
- Ki67: 2-10% (low)
- NO TTF1 or thyroglobulin

- In 2011: no mutation of BRAF, KRAS or PDGFRa genes
- 80% of CATS display rearrangements by FISH mainly of PRDK1-3 genes; in contrast, only 1/8 PLGA showed a similar abnormality (PRDK-2

IHCs: ACC

- CK7, CK5/6, CK14 or CK20: +
- EMA, CEA, S100: +
- α-amylase: -
- DOG-1, SOX-10 : not completely +
- AR, P63: -

IHCs: MASC

- Vimentin, mammoglobin: -
- Areas of high grade transformation: increased expression of Cyclin-D1 and membranous β-catenin
- DOG-1: -
- Calponin, SMA, CK5/6: -


THE END


Thank
you
so
much!