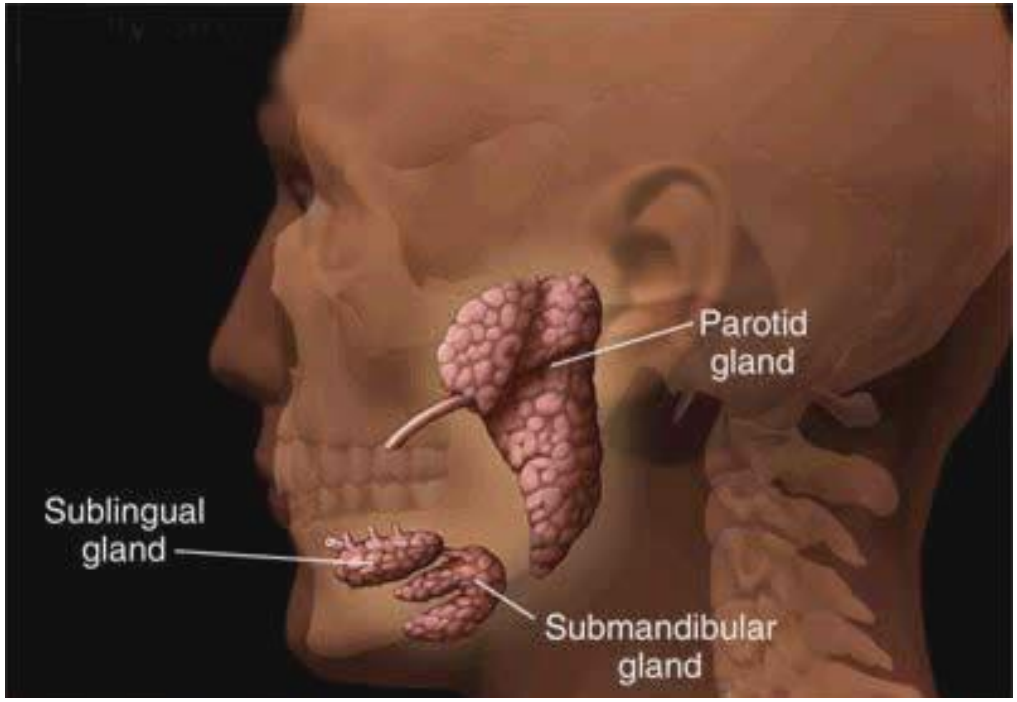
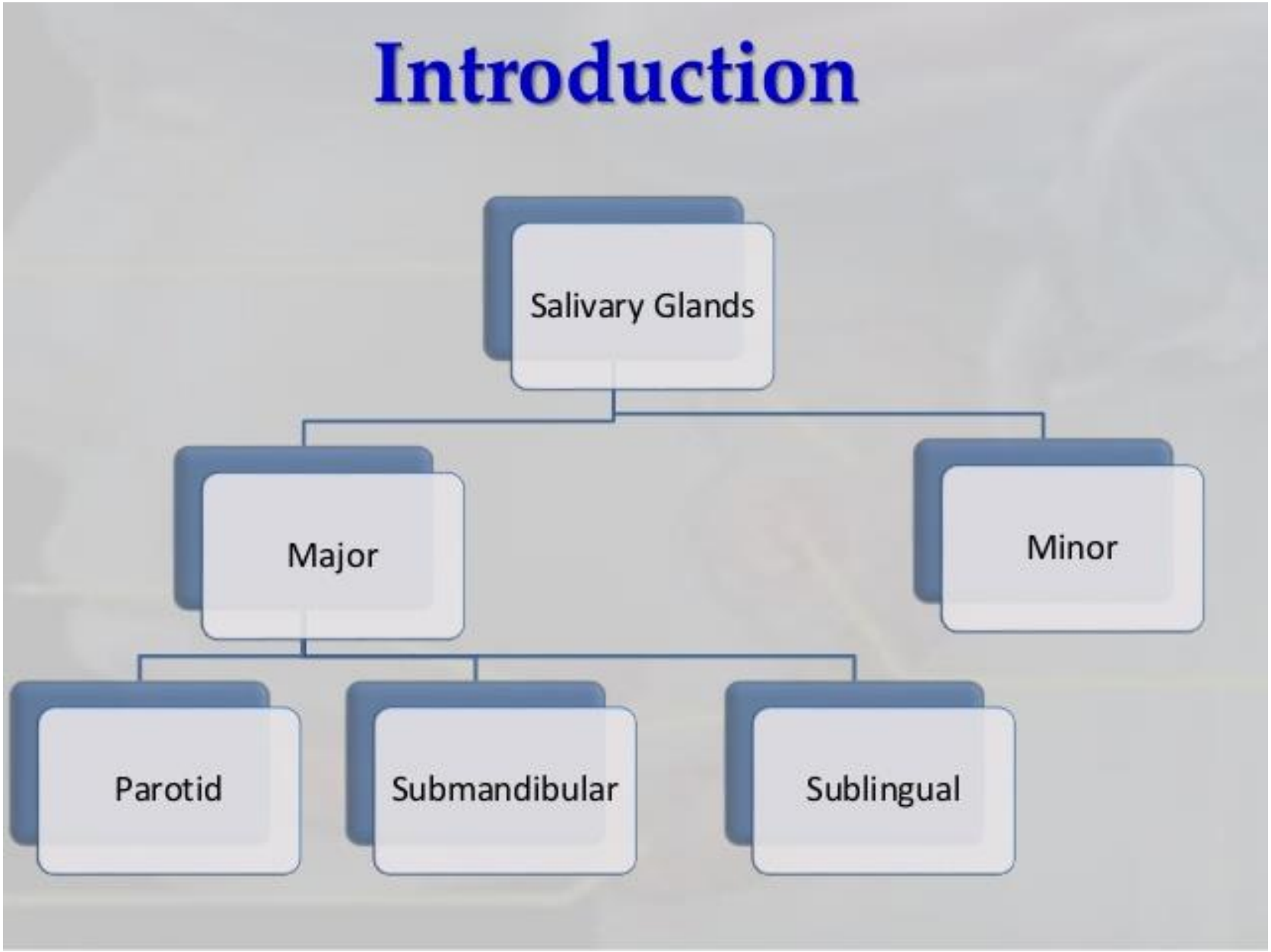
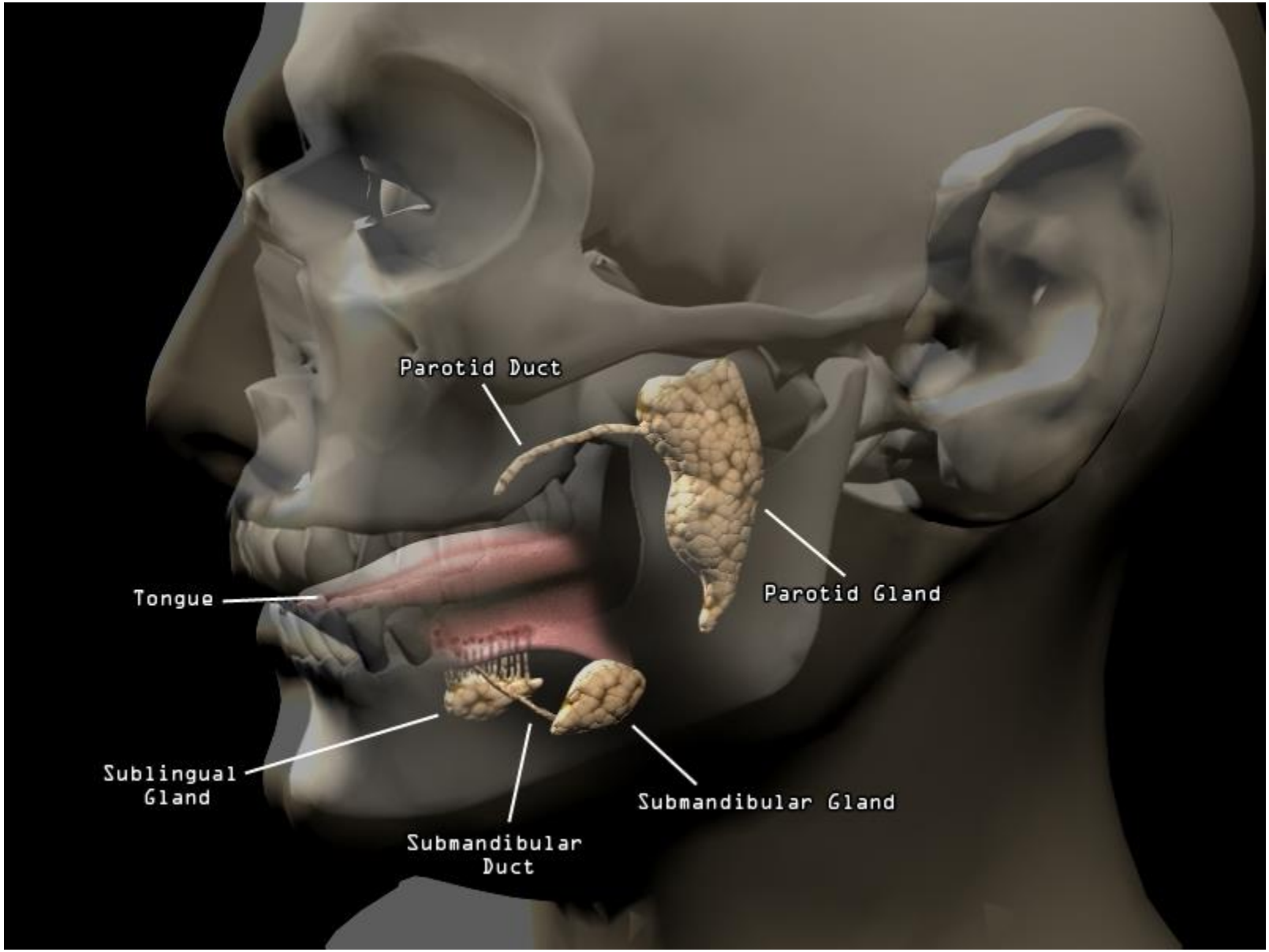
Salivary gland tumors



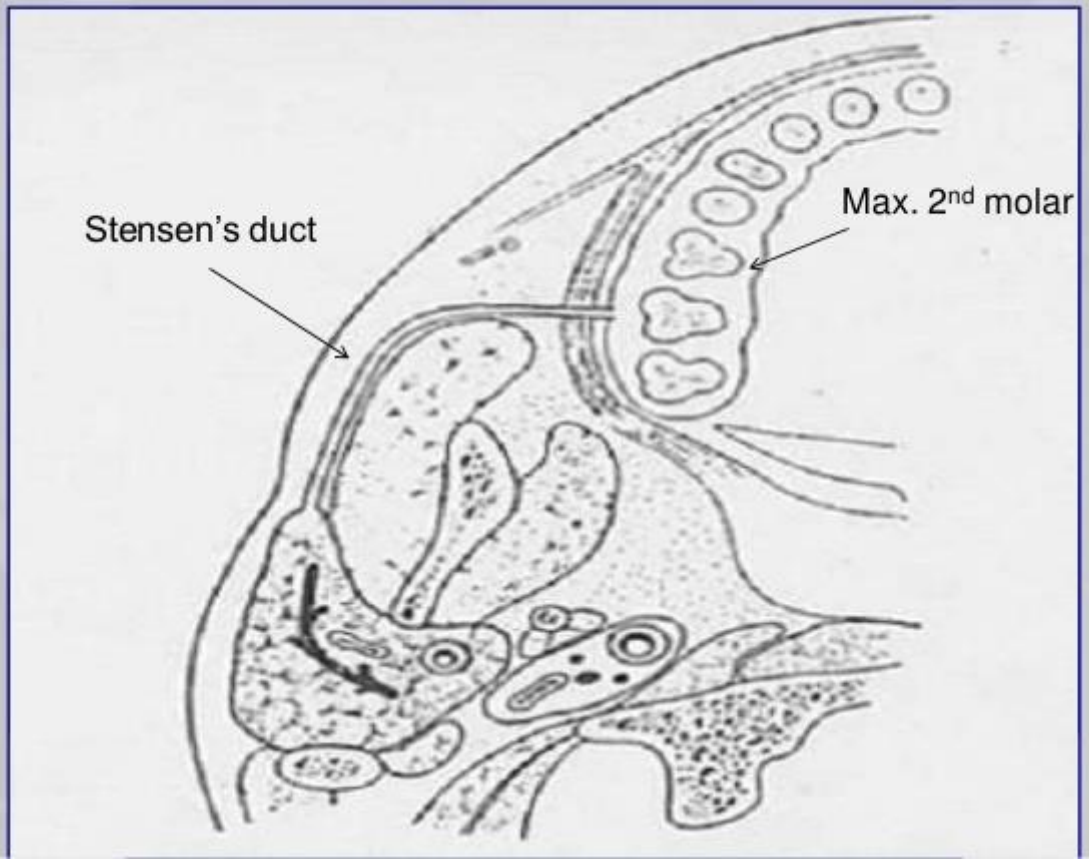
Introduction



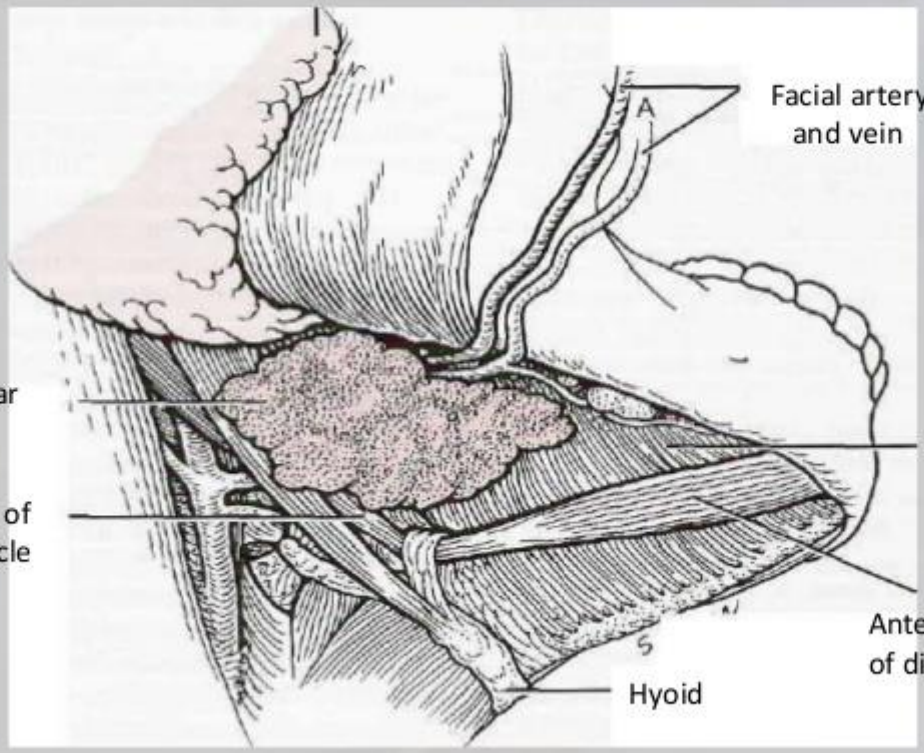
ANATOMY OF SALIVARY GLANDS



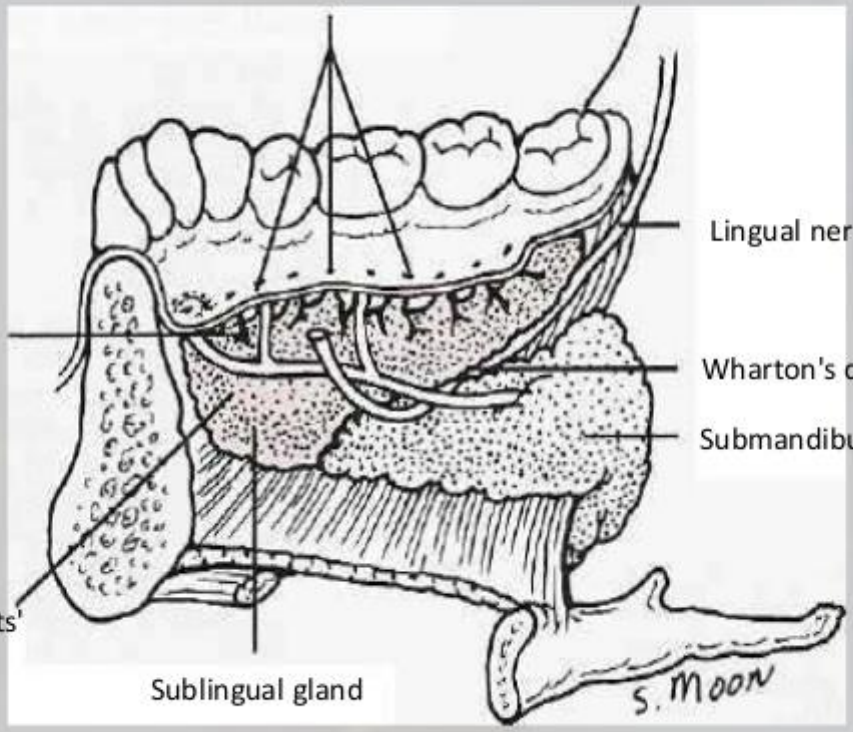
PAROTID GLAND



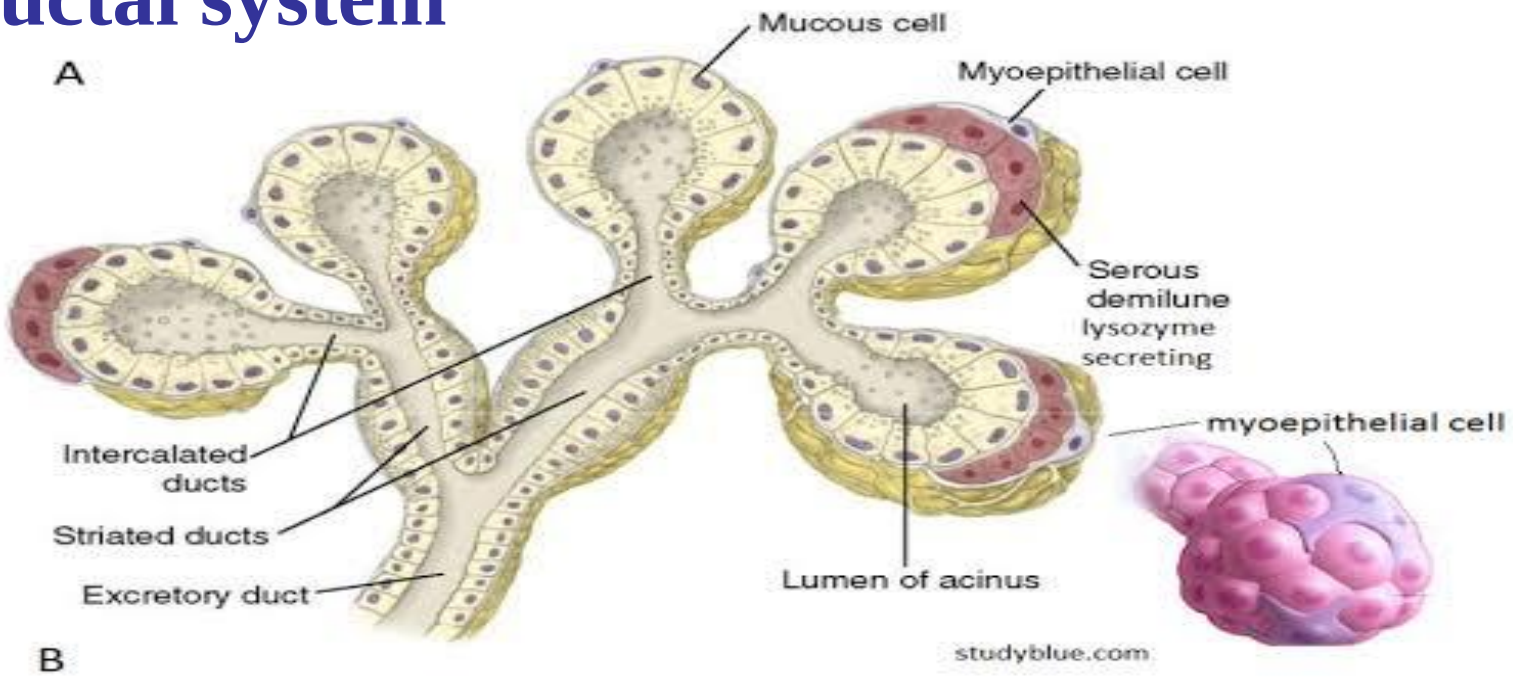
SUBMANDIBULAR GLAND

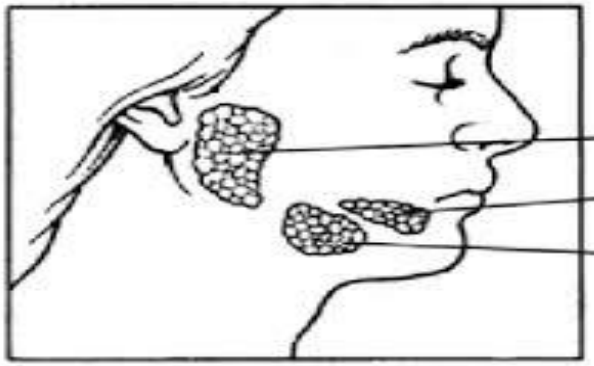


SUBLINGUAL GLAND



Histology of Salivary gland – Cells and ductal system





Salivary glands

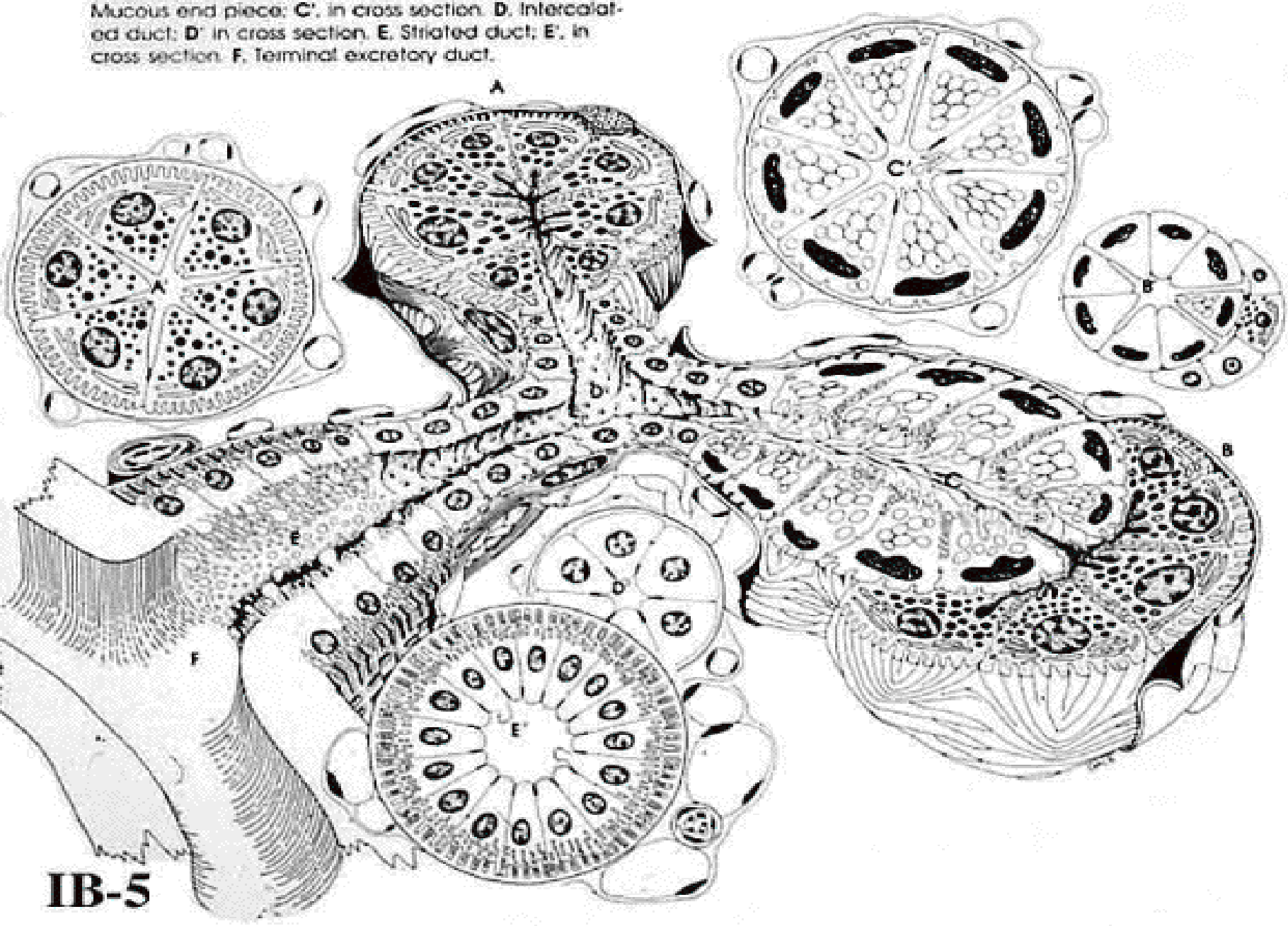
Parotid gland

Sublingual gland

Submandibular gland

//www.cancer.org/cancer/salivaryglandcancer

FIG. 17-27 Schematic diagram of a typical salivary gland. A, Seromucous end piece; A', in cross section. B, Seromucous demilune; B' in cross section. C, Mucous end piece; C', in cross section. D, Intercalated duct; D' in cross section. E, Striated duct; E', in cross section. F, Terminal excretory duct.



IB-5

Introduction

- *Salivary gland tumors comprise 1% of all head and neck tumors.*
- *Known for their remarkable morphological and histological diversity.*
- *Commonly occur in the 6th Decade of life.*
- *Rare in children(except mucoepidermoid carcinoma)*
- *65% of salivary gland neoplasms are benign*
- *35% are malignant.*
- *Pleomorphic adenoma comprise around 65% of all Parotid gland tumors.*
- *85% of benign tumors occur in Parotid.*
- *60% in submandibular and*
- *10% in sublingual glsnds.*
- *75% of parotid gland tumors are benign*
- *75% of sublingual gland tumors are malignant*

Introduction

- The commonest benign salivary gland tumor is Pleomorphic adenoma.

- The most common malignant tumors are
  - Mucoepidermoid carcinoma
  - Adenocarcinoma
  - Acinic cell carcinaoma
  - Adenoid cystic carcinoma.

Histological classification (WHO 1991)

- Adenomas
- Carcinomas
- Nonepithelial tumors
- Malignant lymphomas
- Secondary tumors
- Unclassified tumors
- Tumor-like lesions

1. Adenomas

- Pleomorphic adenoma
- Warthins tumor
- Oncocytoma
- Basal cell adenoma
- Canalicular adenoma
- Myoepithelial adenoma
- Sebaceous adenoma

- Ductal papilloma
  - ✓ *Inverted ductal papilloma*
  - ✓ *Intra ductal papilloma*
  - ✓ *Sialadenoma papilliferum*

- Cystadenoma
  - ✓ *Papillary Cystadenoma*
  - ✓ *Mucous Cystadenoma*

2. Carcinomas

- Acinic cell carcinoma
- Mucoepidermoid carcinoma
- Adenoid cystic carcinoma
- Polymorphous low grade adenocarcinoma
- Epithelial myoepithelial carcinoma
- Basal cell adenocarcinoma
- Sebaceous carcinoma
- Papillary cystadenocarcinoma
- Mucinous adenocarcinoma
- Oncocytic carcinoma
- Salivary duct carcinoma
- Adenocarcinoma
- Myoepithelial carcinoma
- Malignant mixed tumor
- Squamous cell carcinoma
- Small cell carcinoma
- Undifferentiated carcinoma

7. **Tumor like lesions**

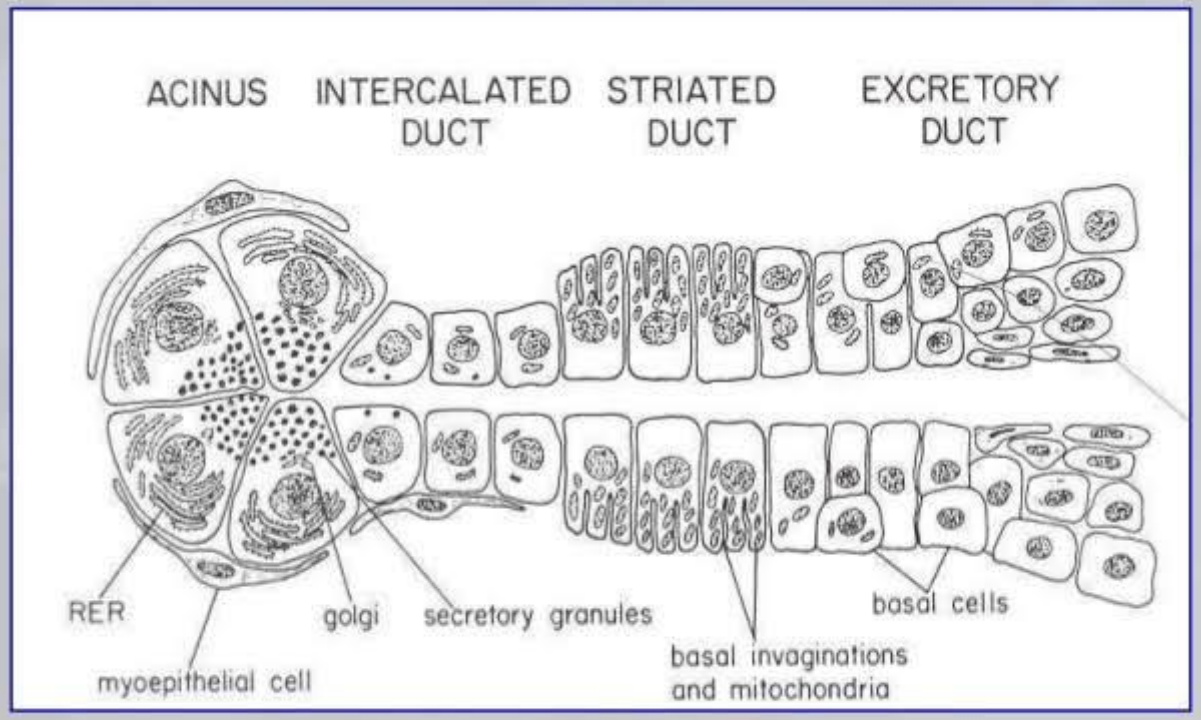
- Sialadenosis
- Oncocytosis
- Necrotising sialometaplasia
- Benign lymphoepithelial lesions
- Salivary gland cysts
- Chronic sclerosing sialadenitis of submandiblar gland
- Cystic lymphoid hyperplasia in AIDS

 Histogenesis: Cell of origin for a neoplasm rather than the developmental process underlying the tumour.

 Morphogenesis: The process of differentiation inherent in the neoplasms and the resulting histopathology characteristic for that particular tumour.

Histogenesis theories proposed by various authors	Proposed hypothesis
Basal reserve cell theory	Basal cells of both excretory and intercalated ducts responsible for differentiation of functional units
Pluripotent unicellular reserve cell theory	Basal cells of excretory duct are responsible for the development of all remaining salivary gland units
Semipleuripotent bicellular reserve cell theory: Advanced by Eversole 1971 and further refined and developed by Batasakis *et al*.	The outer (basal) layer of cells gave rise to inner (luminal) layer. The eventual derivation of intercalated ducts from these excretory ducts was proposed
Multicellular theory	Differentiated cells at all the levels of the gland, including acinar and basal are capable of cell division

ORIGIN



Mounting evidence against current histogenetic concepts for salivary gland tumorigenesis. Eur J Morphol 1998; 36:257-261.

CLINICAL FEATURES

BENIGN	MALIGNANT
Facial nerve not involved commonly	Facial nerve is commonly involved
Pseudoencapsulated	Nonencapsulated
Uiceration not common	Ulceration common
Local invasion	Spread to lymph nodes and metastasis to lung,liver,brain and bones is common

BENIGN TUMORS

Pleomorphic adenoma
(Mixed tumor)

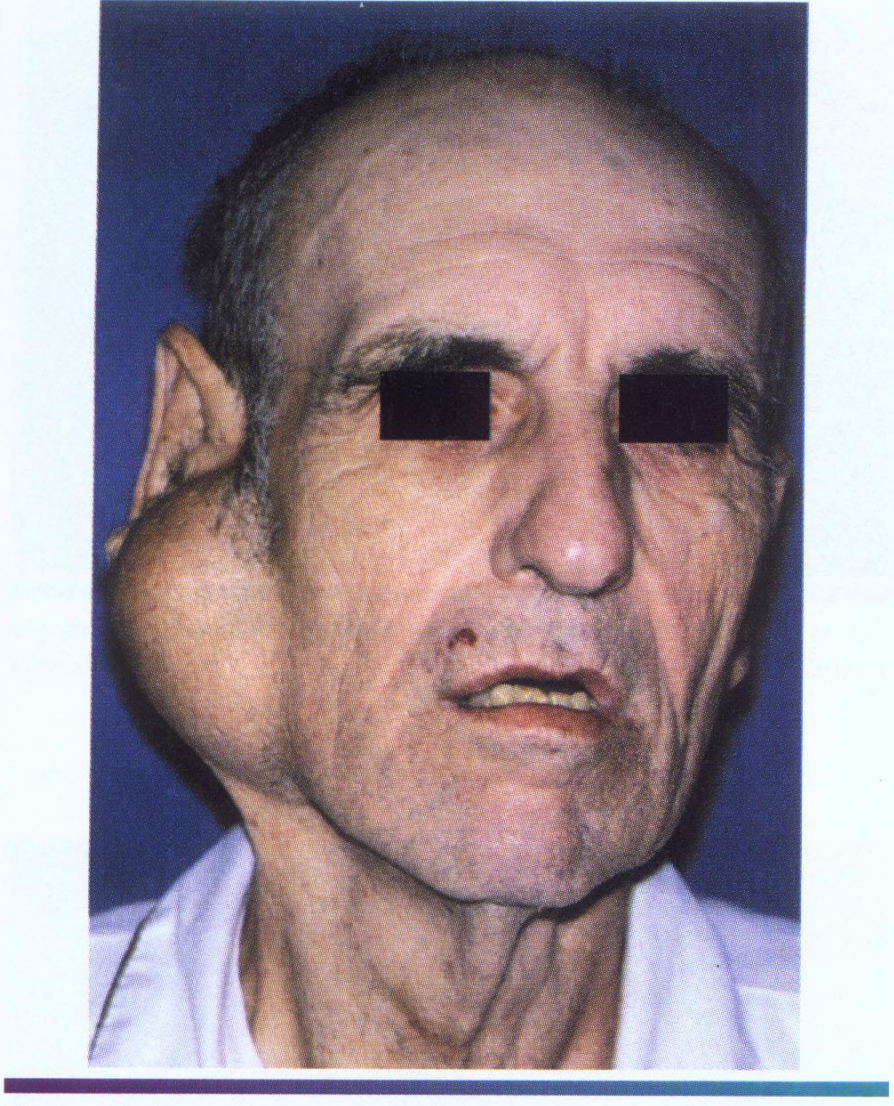
- Most common salivary neoplasm
- Has the unique ability to differentiate to epithelial and mesenchymal cells.
- It is not a ‘mixed tumor’ in the true sense of being derived from more than one primary tissue. It arises as a result of differentiation or metaplasia of the tumor cells or products of the tumor cells per se.

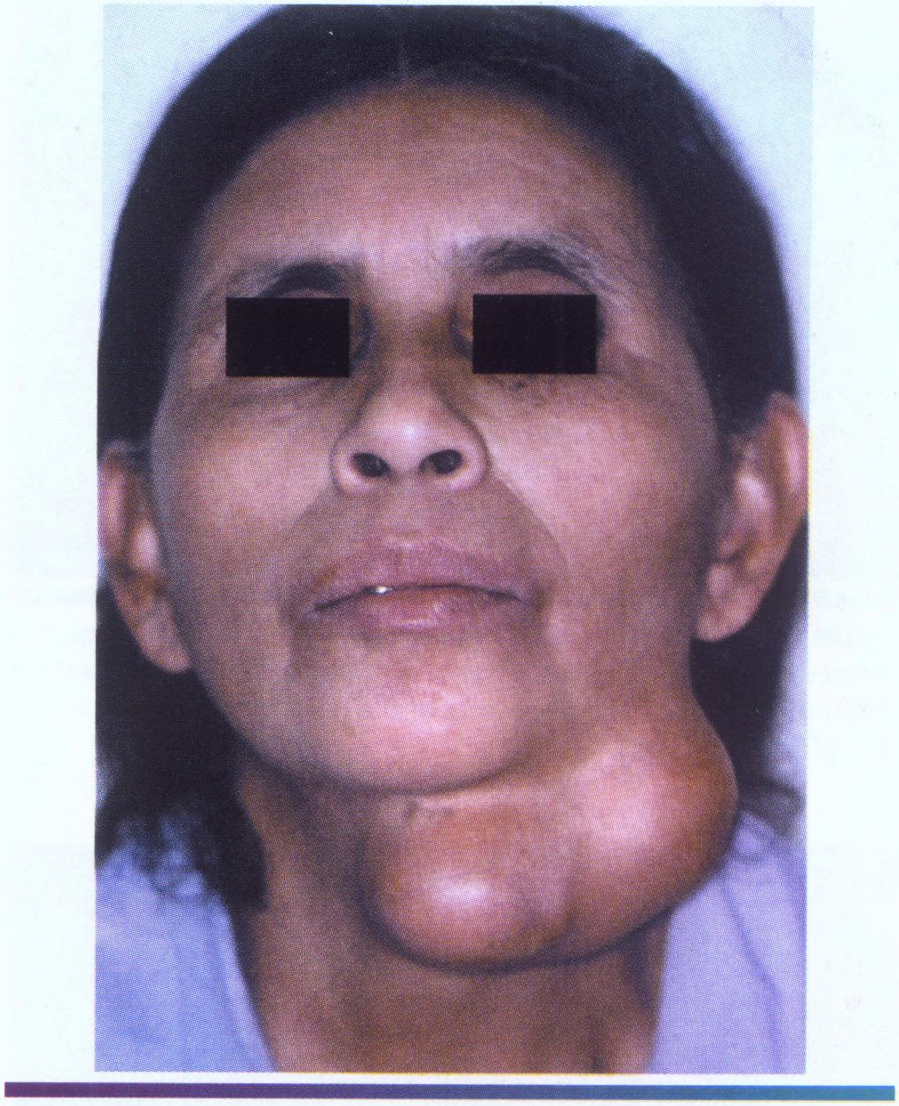
Histogenesis

- Derived from a mixture of ductal and myoepithelial elements.
- Microscopic diversity exists between one tumor to another.
- Hubner and his associates have postulated that Myoepithelial cells are responsible for the morphological diversity of the tumor, including the production of fibrous , mucinous, chondroid and osseous areas.
- Regezi and Baskis postulated that the intercalated duct reserve cell can differentiate into ductal and myoepithelial cells and the latter in turn can undergo mesenchymal metaplasia.
- Dardick and his associates have questioned the role of both types of cells. They say that a neoplastically altered epithelial cell with multidirectional differentiation potential may be responsible.

Clinical features

- Parotid gland is the most common site.
- Among the minor salivary glands, palate is the most common site.
- Painless but may show local discomfort.
- Slow growing firm mass
- May occur at any age but common between 30 to 50 years.
- Female predilection (6:4).
- In parotid appears in the superficial lobe and presents as a swelling in front of the ear.
- Facial paralysis is rare.

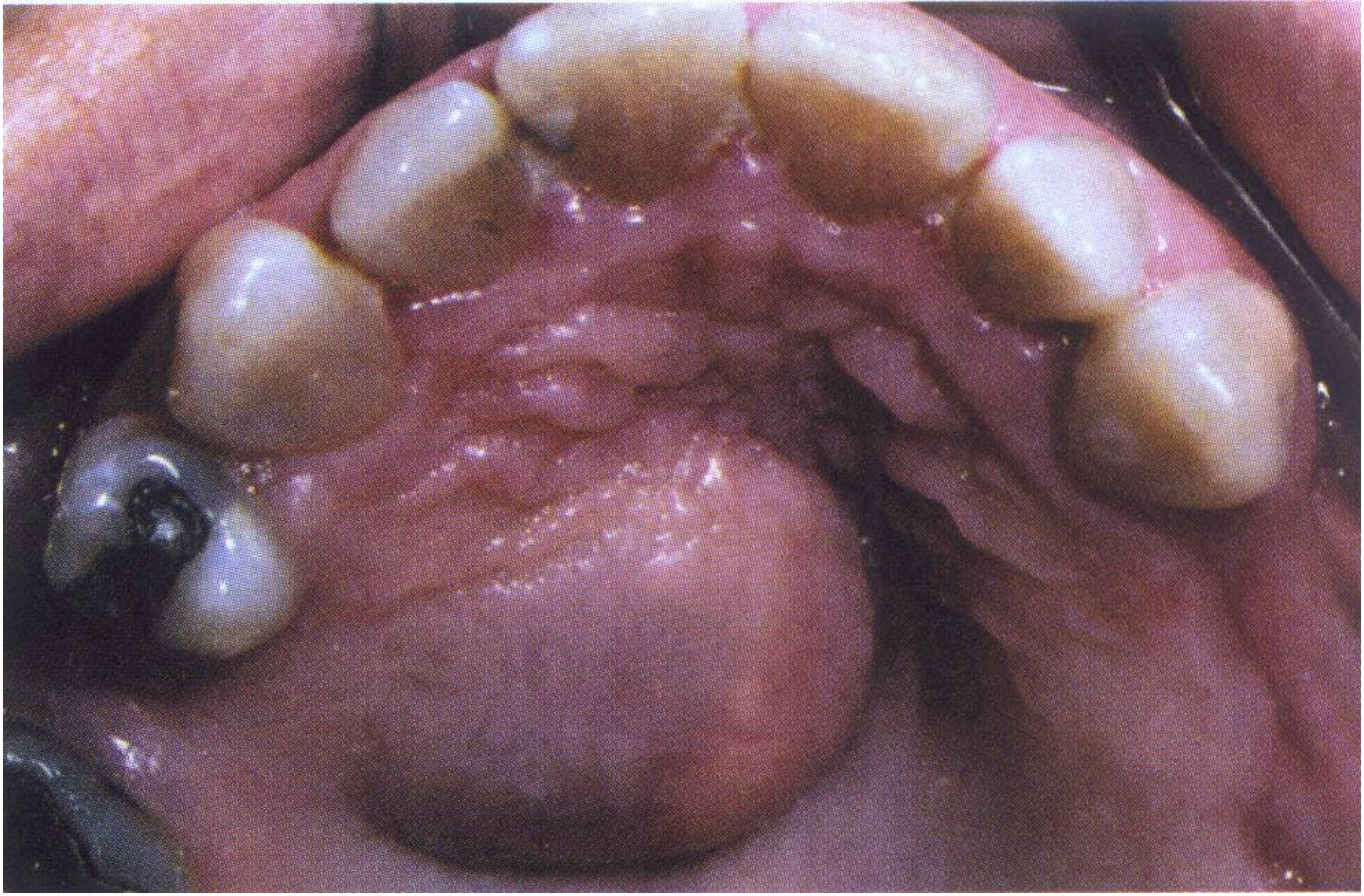




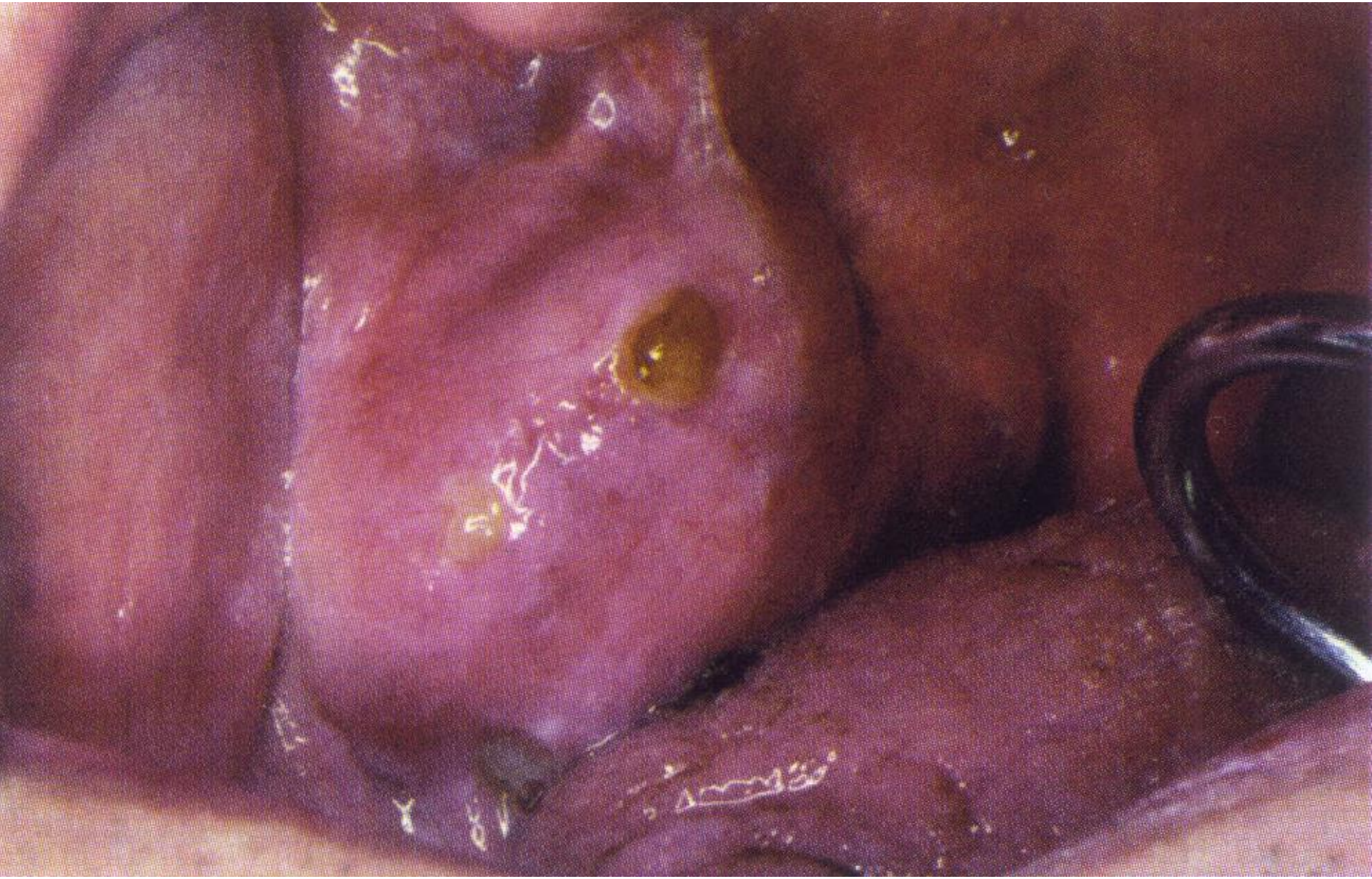
<u>Pleomorphic adenoma –</u>

(L) in parotid gland ,

(R) in submandibular gland



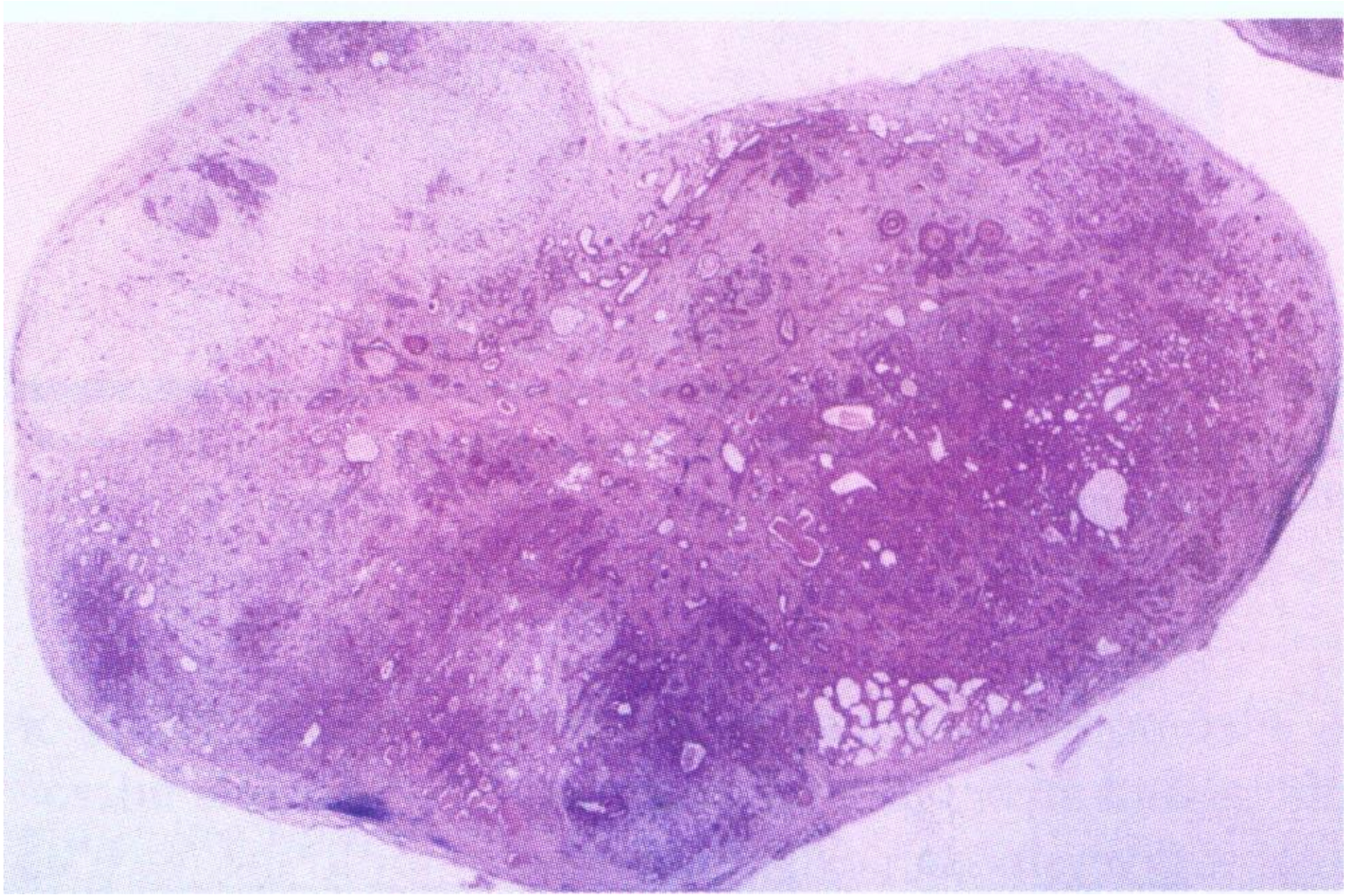
<u>Pleomorphic adenoma</u> – firm mass of the hard palate lateral to the midline



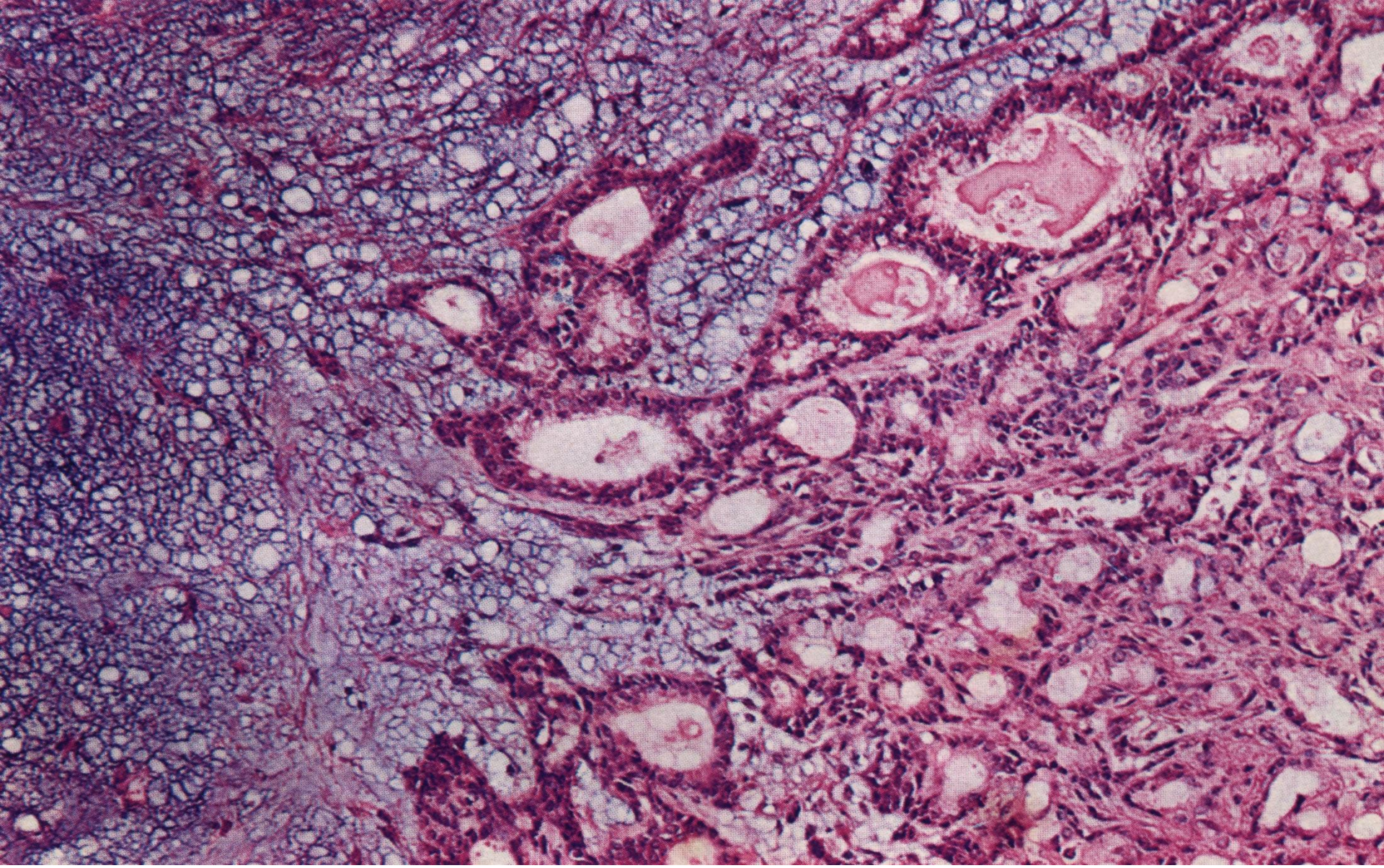
<u>Pleomorphic adenoma –</u> tumor of the pterygomandibular area

Histopathology

- Well circumscribed,
- Encapsulated tumor
- Consists of mixture of glandular epithelium and mesenchyme like tissue.
- The epithelium form ducts and cystic structures or may occur as islands or nests or anastomosing cords or sheets of cells.
- Myoepithelial cells are responsible for the morphological diversity of the tumor. Extensive accumulation of mucoid material around these cells may give a myxoid appearance. Vacuolar degeneration of these cells may result in a cartilaginous appearance. Foci of degeneration, hyalinization and even fat can be noted in some cases.
- When pleomorphic pattern of the tumor is absent and the pattern is highly cellular – **cellular adenoma.**
- When myoepithelial proliferation predominates – **myoepithelioma.**

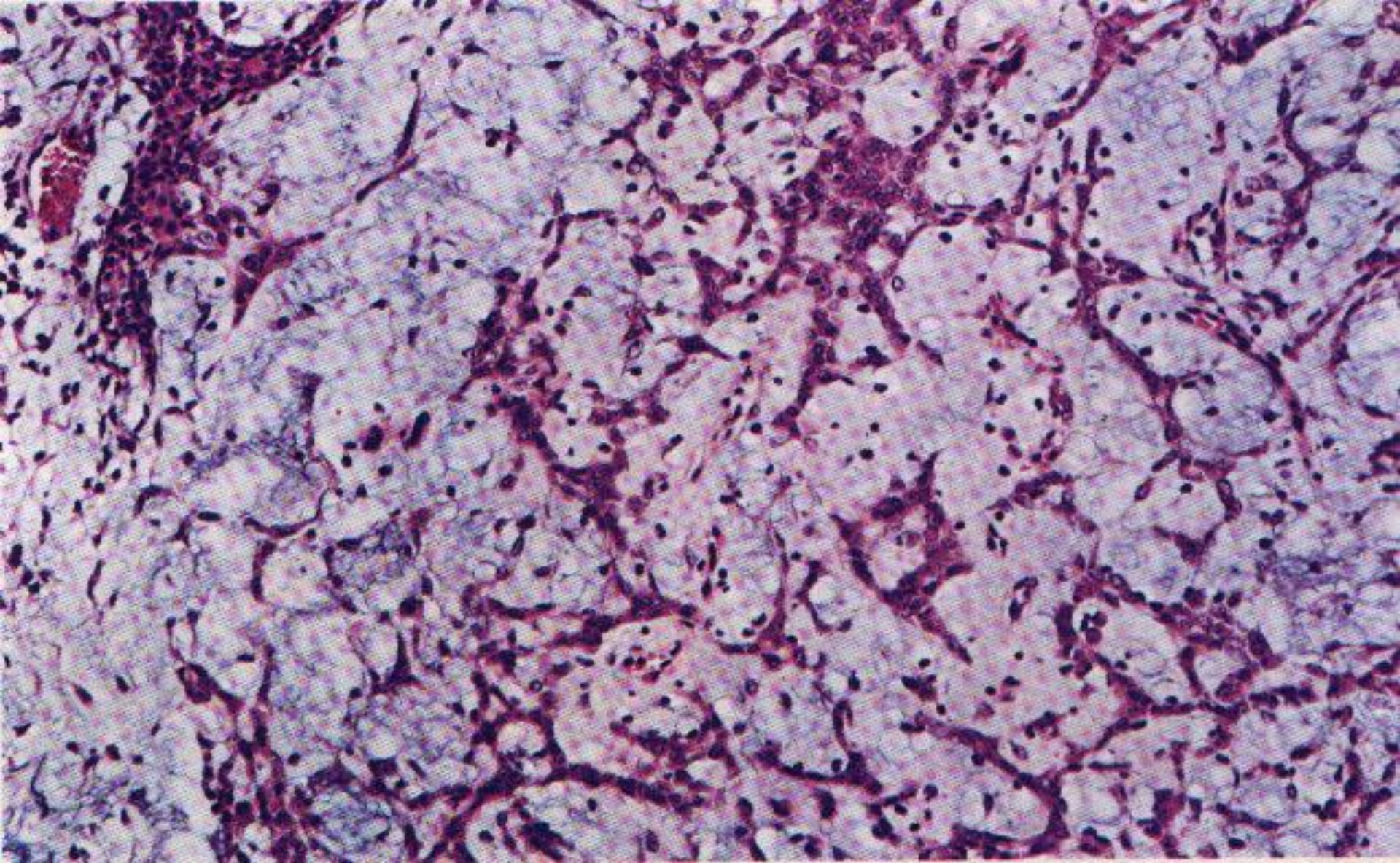


<u>Pleomorphic adenoma –</u> low power view showing a well circumscribed, encapsulated tumor mass, having a variable histologic pattern.



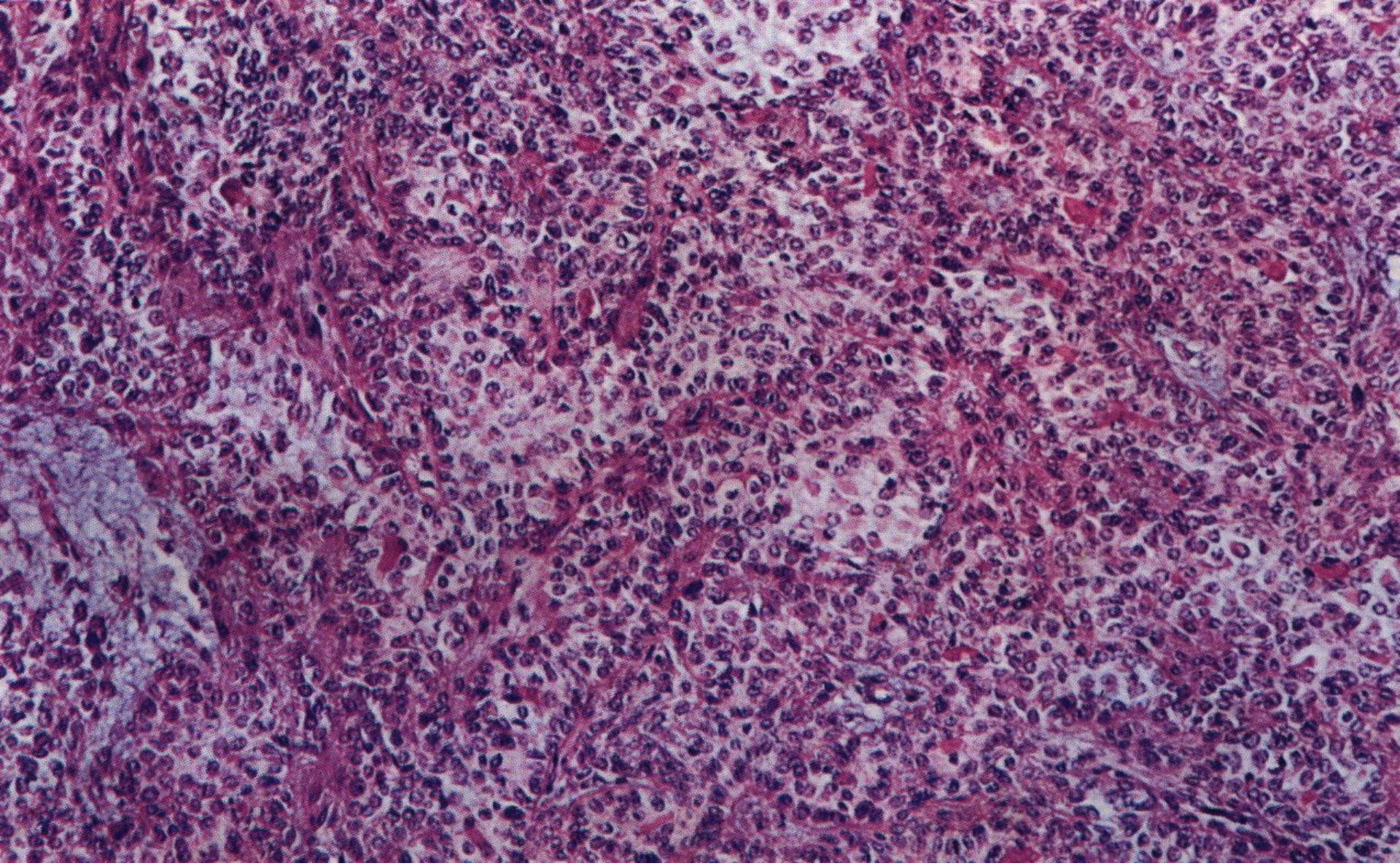
Pleomorphic adenoma

Epithelial ducts merging into myxoid areas



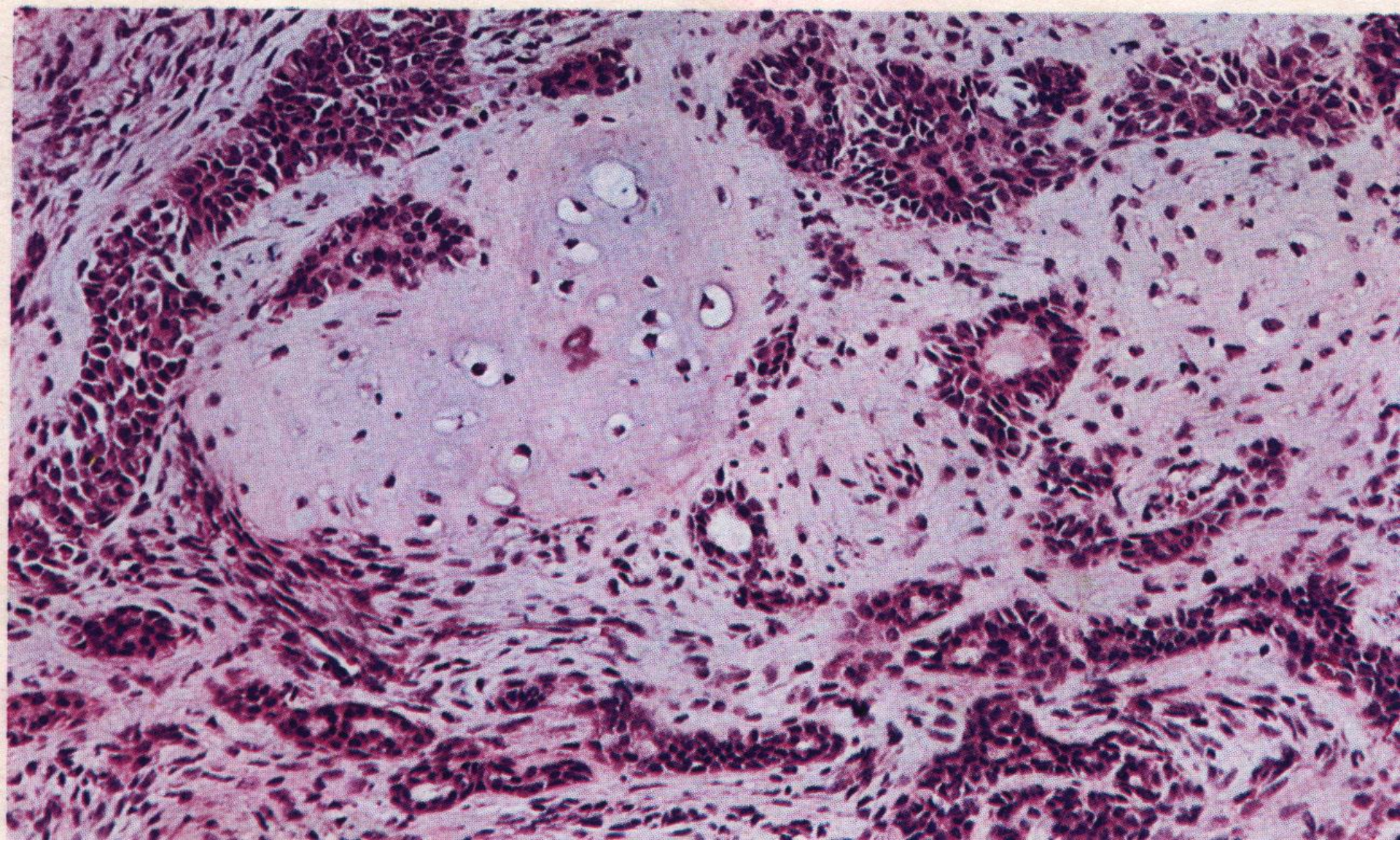
Pleomorphic adenoma

Epithelial cells appear to merge into the myxoid background



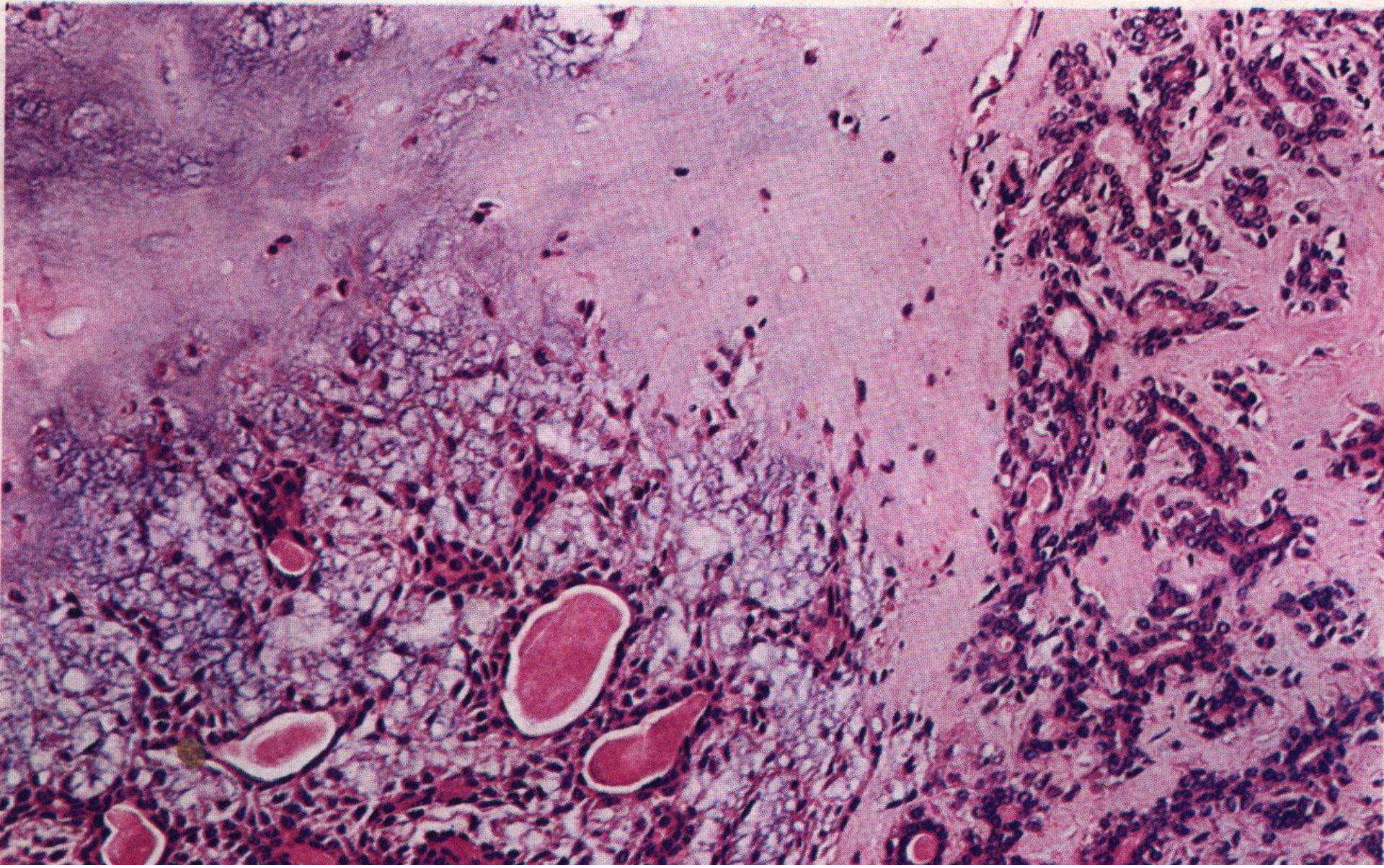
Pleomorphic adenoma

Solid areas of epithelial and myoepithelial cells with minimal stroma



Pleomorphic adenoma

Chondroid focus developing in close proximity to myoepithelial cells



Pleomorphic adenoma

Epithelial ducts in hyaline, myxoid and chondroid background

Treatment and prognosis :

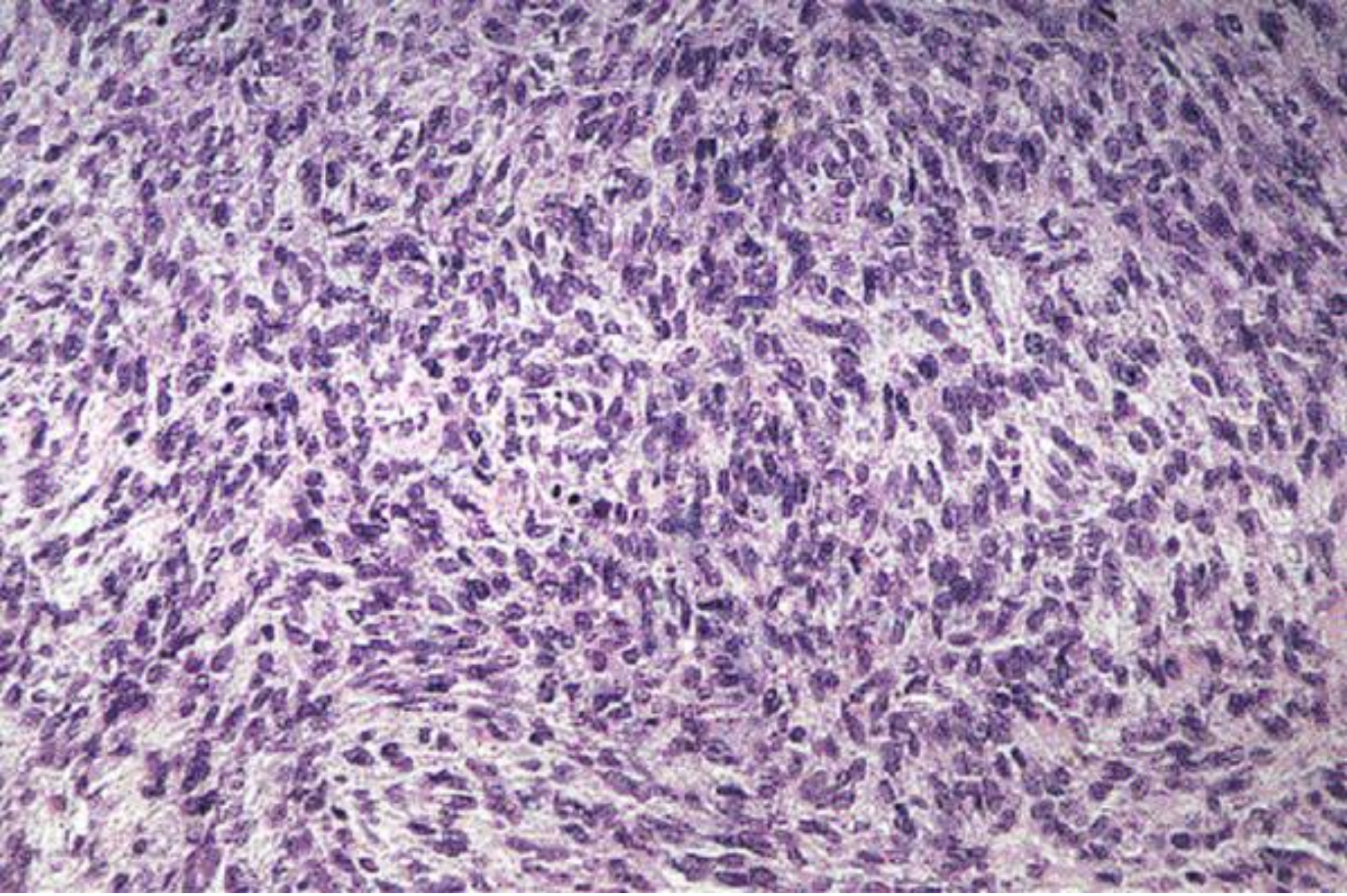
- Surgical excision.
- Intraoral lesions can be treated conservatively by extracapsular excision.
- They are radio-resistant. So radiotherapy is contraindicated.

Myoepithelioma

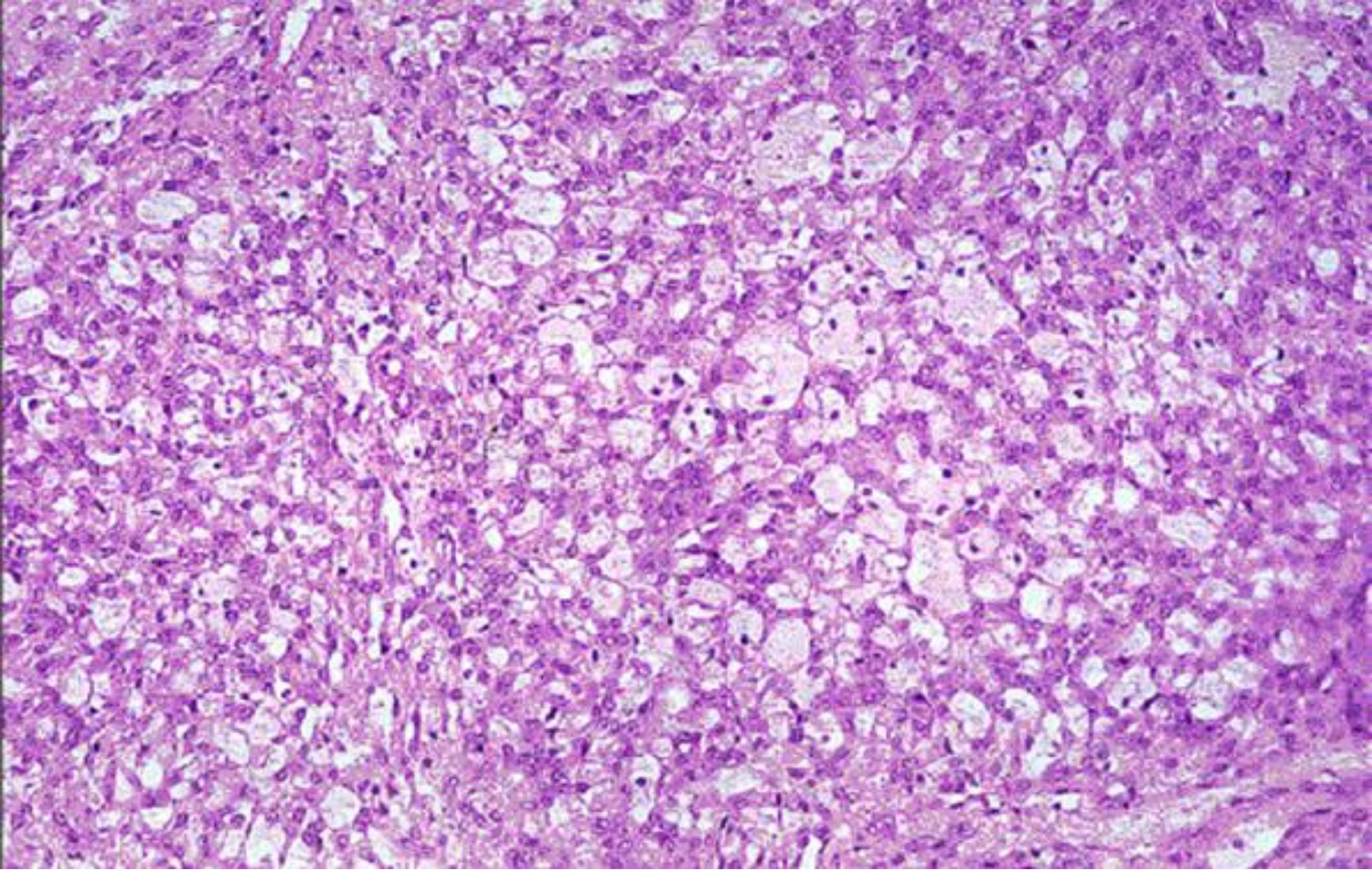
- Same clinical features as the pleomorphic adenoma.

Histologic features :

- Composed almost exclusively of neoplastic myoepithelial cells.
- The neoplastic cells are spindle shaped or plasmacytoid
- Epithelial or clear cells may also be present.
- Either a single cell type predominates or there may be a combination of cell types.
- Tumor consisting predominantly of spindle cells, tends to be more cellular than one consisting of plasmacytoid cells.



Myoepithelioma : composed of spindle shaped myoepithelial cells



Myoepithelioma : composed of plasmacytoid cells separated by a loose myxoid stroma

Treatment :

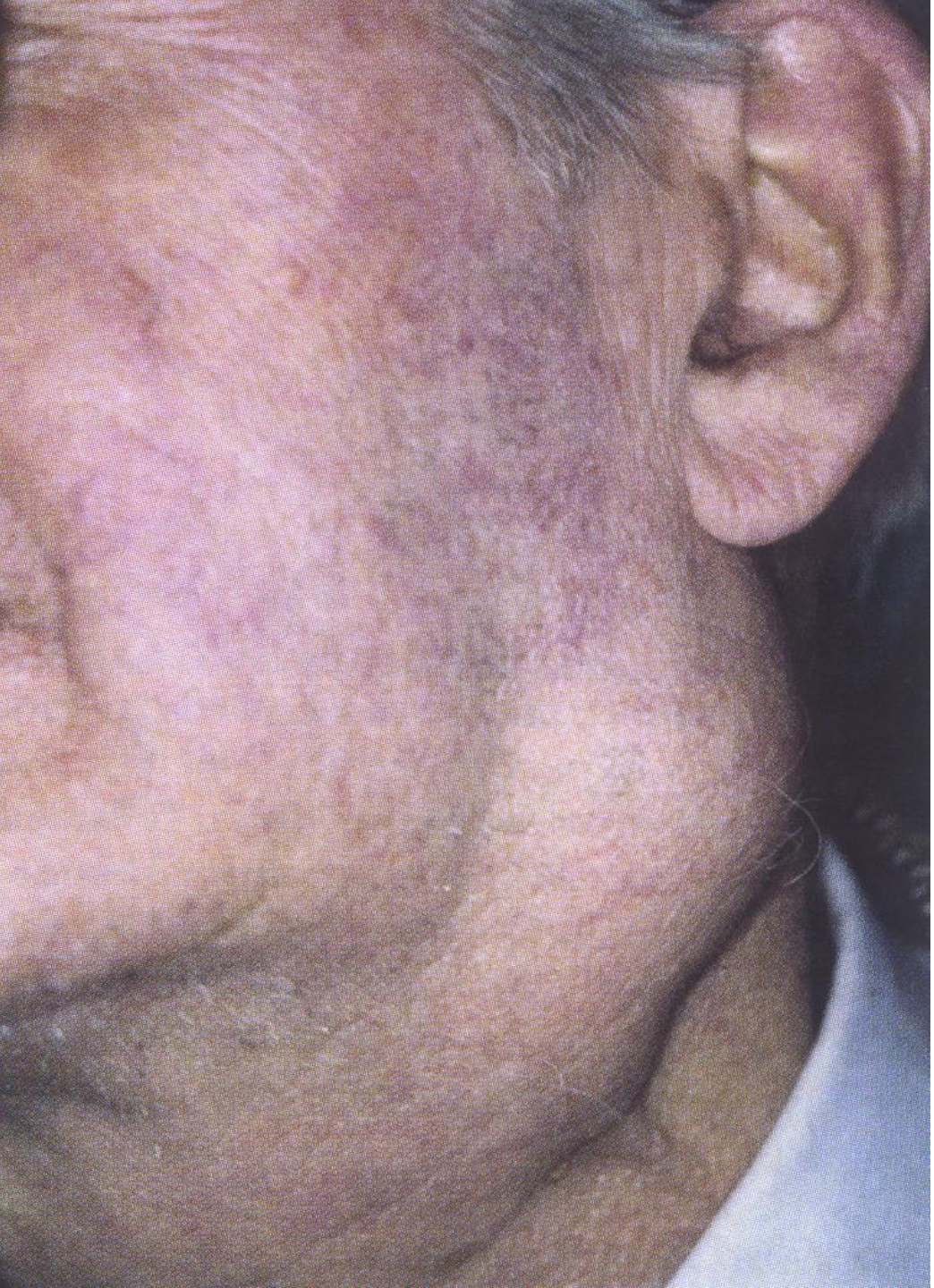
Surgical excision

Warthins tumor (Adenolymphoma, Papillary cystadenoma lymphomatosum)

- Benign neoplasm that occurs almost exclusively in parotid glands.
- Second most common salivary gland tumor.
- Arises from heterotopic salivary gland tissues entrapped in parotid lymph nodes.
- Strong association with smoking.
- EBV has also been implicated in its pathogenesis.

Clinical features :

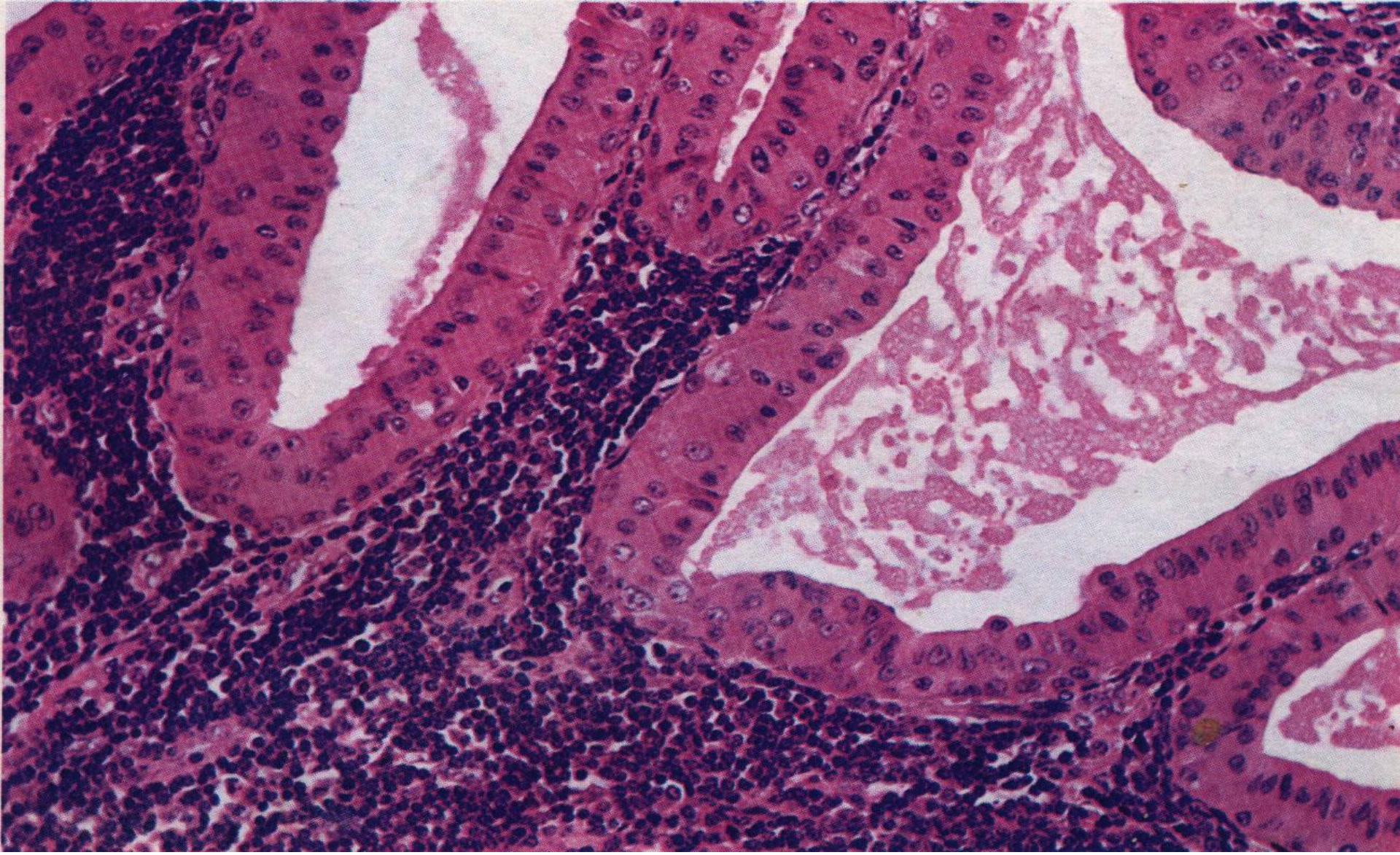
- Slow growing
- Painless
- Nodular mass of parotid gland.
- Most commonly occurs in the tail of parotid, near angle of mandible
- Uniquely occurs bilaterally
- Male female ratio = 10:1
- Most commonly occurs in the sixth and seven decades.



<u>Warthins tumor</u> – mass in the tail of the parotid

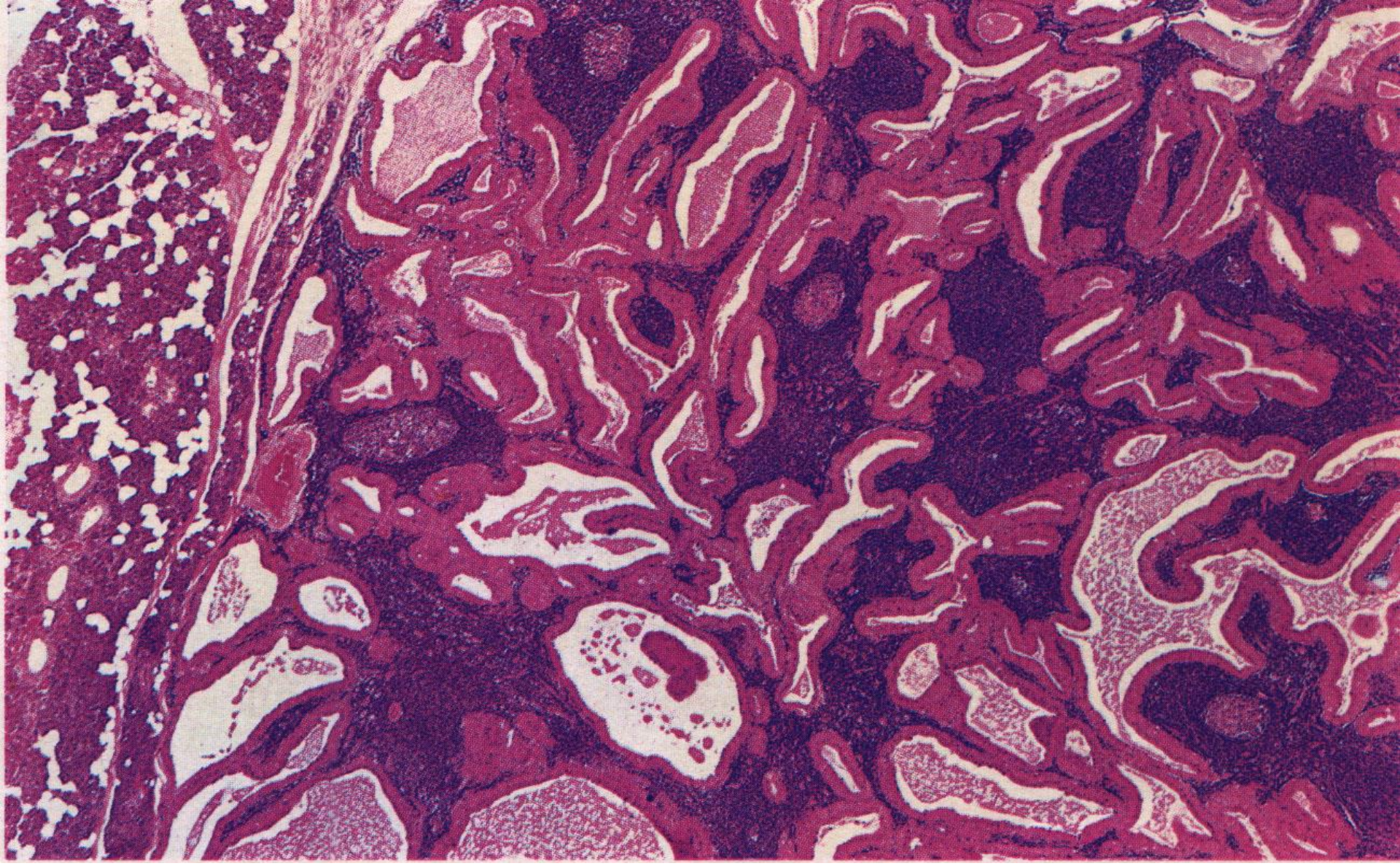
Histopathology :

- Made up of two histologic components – epithelial and lymphoid tissue.
- It is actually an adenoma exhibiting cyst formation, with papillary projections into the cystic spaces and a lymphoid matrix showing germinal centers.
- Cysts are lined by papillary proliferations of bilayered oncocytic epithelium. (Oncocytes – epithelial cells with abundant, granular eosinophilic cytoplasm due to presence of numerous mitochondria)
- Inner layer cells are tall columnar with centrally placed hyperchromatic nuclei and a finely granular and eosinophilic cytoplasm.
- Outer layer cells are usually oncocytic triangular.
- Multiple papillary folds of epithelial lining into cystic spaces.
- The eosinophilic coagulum present in the cystic space will appear like a chocolate colored fluid.



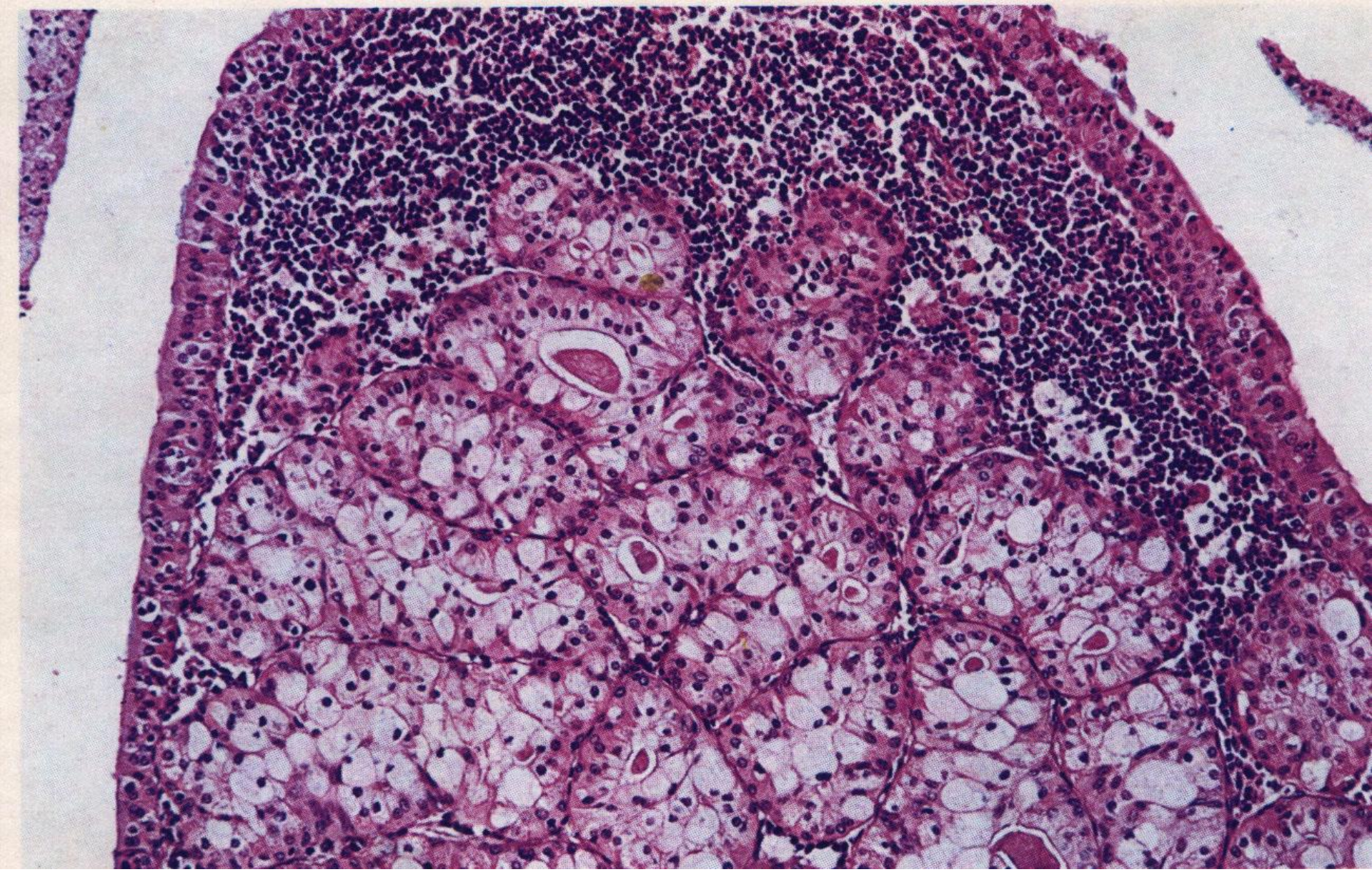
Warthins tumor

Tall columnar double layered epithelium lining spaces; lymphoid stroma.



Warthins tumor

Glandular epithelium, partly in papillary cystic arrangement, with intervening lymphoid tissue.



Warthins tumor

showing sebaceous differentiation

Treatment and prognosis :

- Surgical excision.
- Some cases of mucoepidermoid carcinoma developing in this tumor have been reported.

Oncocytoma
(oxyphilic adenoma)

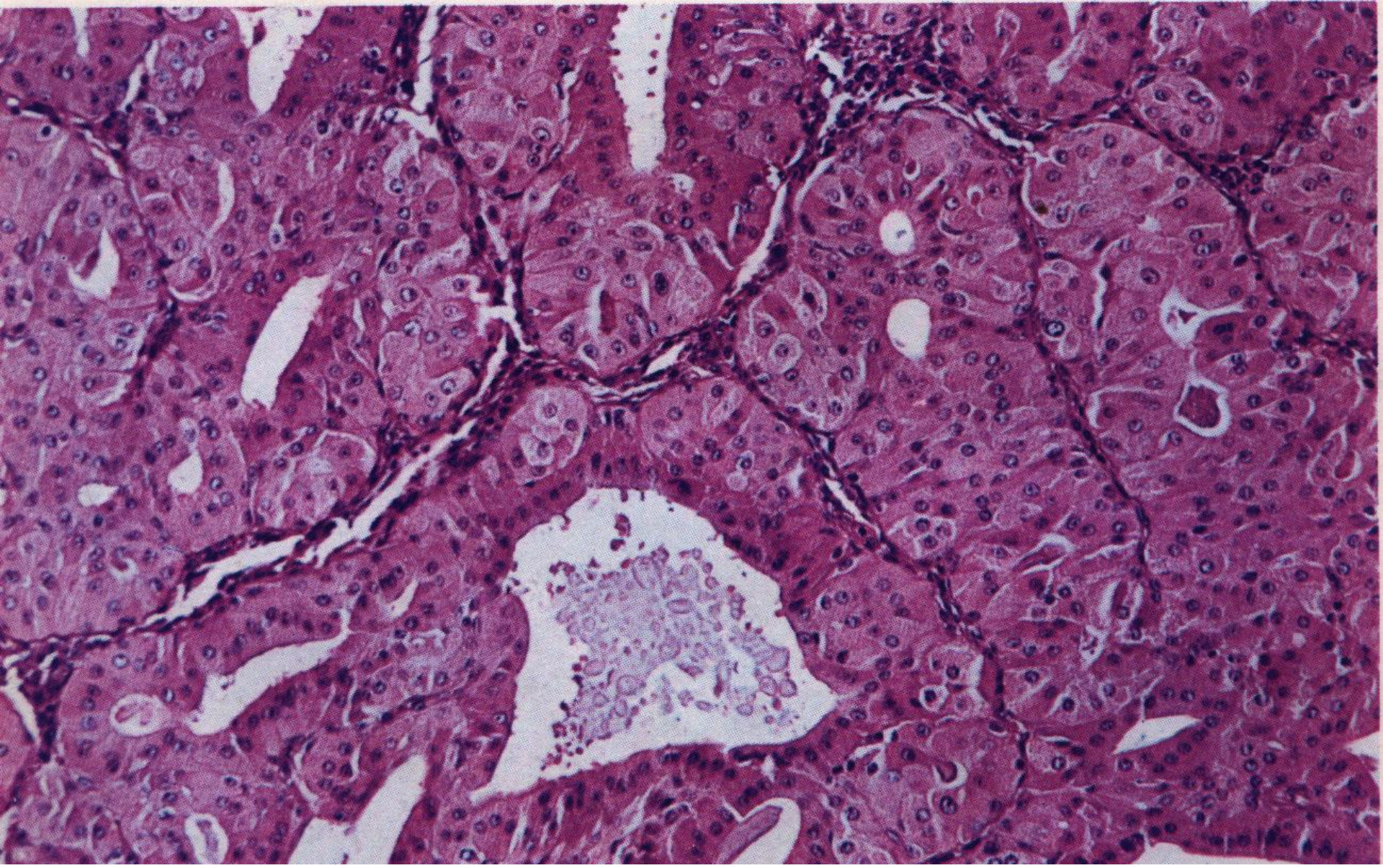
- Composed of oncocytes with granular eosinophilic cytoplasm and a large no. of atypical mitochondria.

Clinical features :

- Usually occurs in the parotid.
- More common in women.
- Almost exclusively in elderly.
- A discrete encapsulated mass, sometimes nodular.
- Painless.

Histologic features :

- Large cells which have an eosinophilic cytoplasm and a distinct cell membrane and are arranged in narrow rows or cords.
- Oncocytes are arranged in sheets or nests or cords which form alveolar or organoid patterns.
- Some degree of cellular atypia, nuclear hyperchromatism and pleomorphism is acceptable.
- Exhibit few mitotic figures, are closely packed and have little stroma.
- Lymphoid tissue is frequently present.
- Cells are engorged with enlarged and morphologically altered mitochondria.



Oncocytoma : cells are of oncocytic type. Tumor may be entirely solid as illustrated

Treatment :

- Surgical excision
- Does not recur.
- Malignant transformation is uncommon.

Basal cell adenoma

- A neoplasm of a uniform population of basaloid epithelial cells arranged in solid, trabecular, tubular or membranous patterns.

Clinical features :

- Occur primarily in major salivary glands, particularly parotid.
- Painless, slow growing mass.
- Greatest dimension is usually < 3 cm.
- Chiefly in adults.
- 2:1 female predilection.

Histologic features :

- Two morphologic forms of basal cells are present – one small with scanty cytoplasm and round deeply basophilic nucleus; another large with eosinophilic cytoplasm and an ovoid pale staining nucleus.
- Can be divided into four subtypes –

✓ Solid

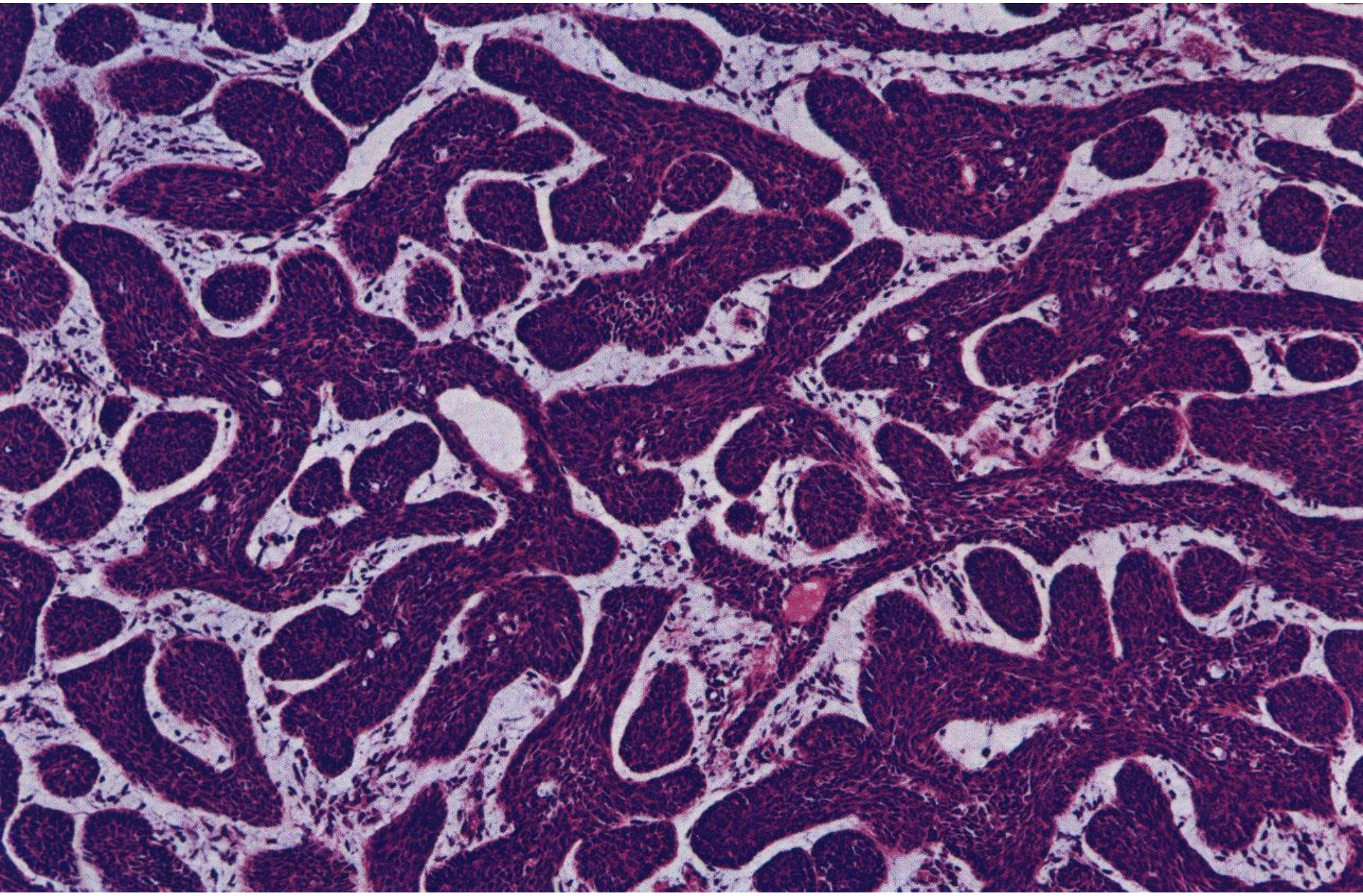
✓ Tubular

✓ Trabecular

✓ Membranous

1. Solid type : most common type.

o Basaloid cells form islands and cords in a lobular pattern and are sharply demarcated from the c.t stroma by basement membrane.



Basal cell adenoma : solid type

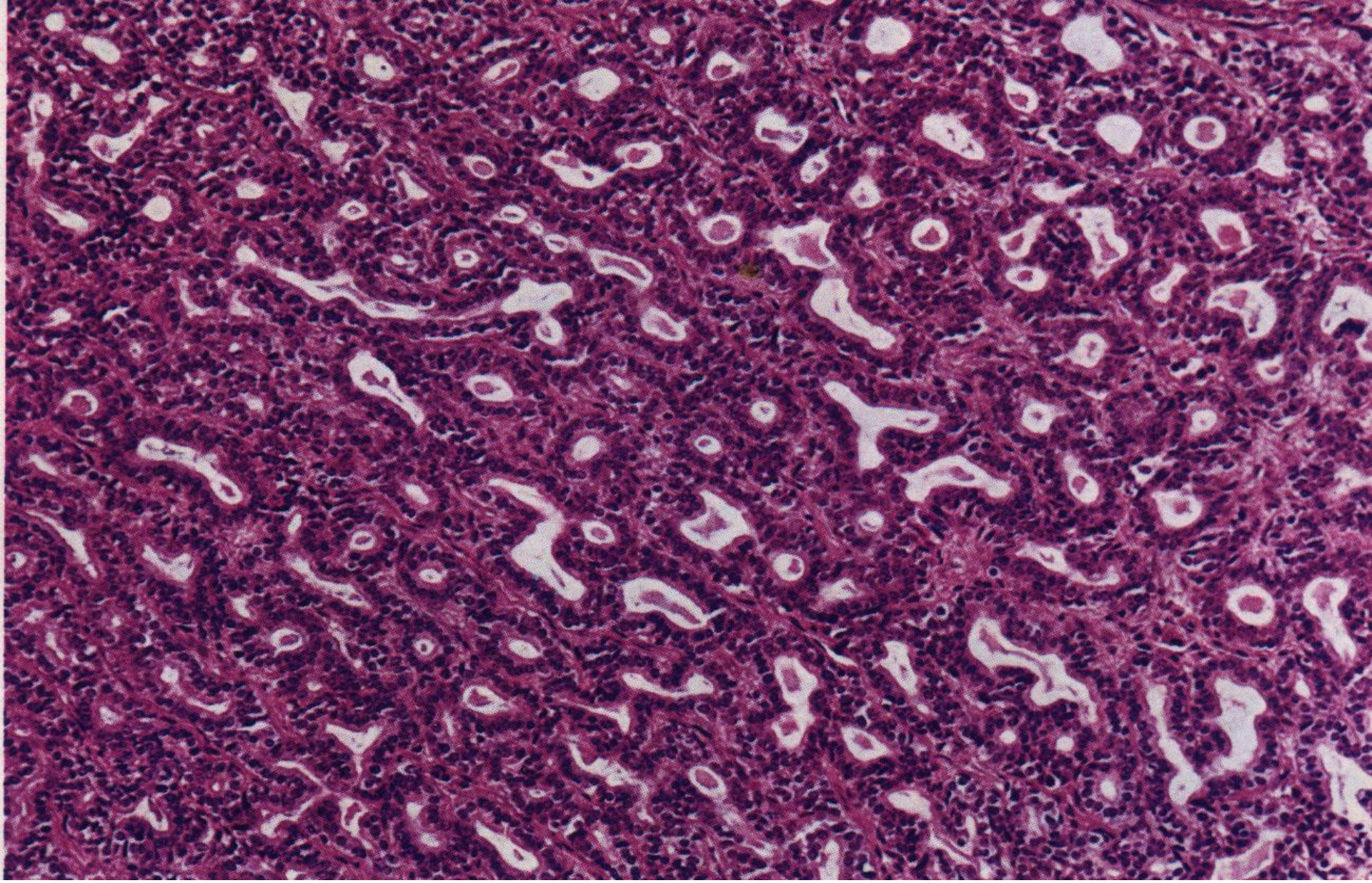
2. Tubular type : least common

- Multiple small round duct like structures, lined by two distinct layer of cells, with inner cuboidal cells surrounded by outer basaloid cells.

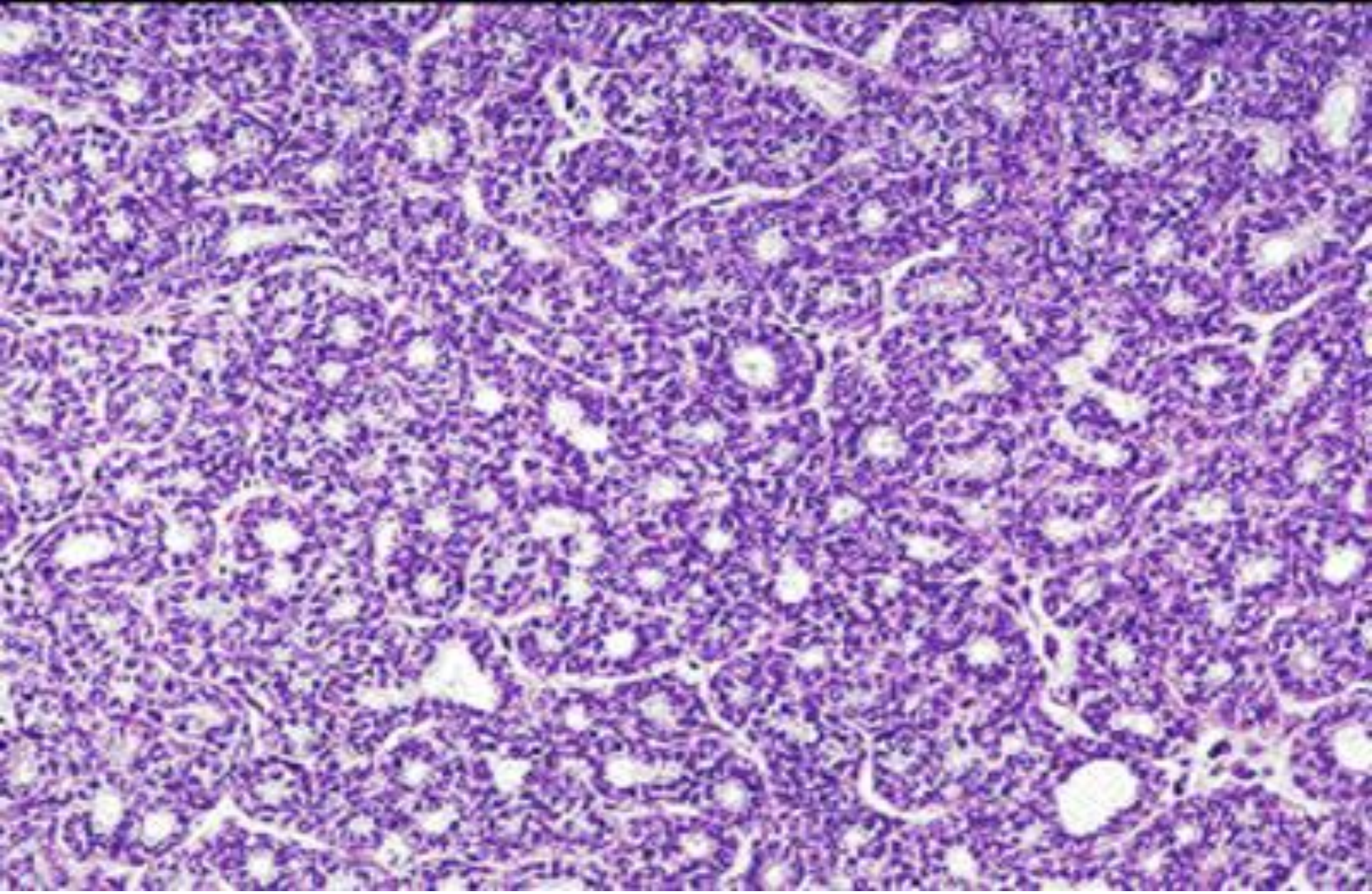
3. Trabecular type : same features as the solid type but the epithelial islands are narrower and cord like, interconnected with one another producing a reticular pattern.

4. Membranous type : presence of abundant thick eosinophilic hyaline layer that surrounds and separates the epithelial islands.

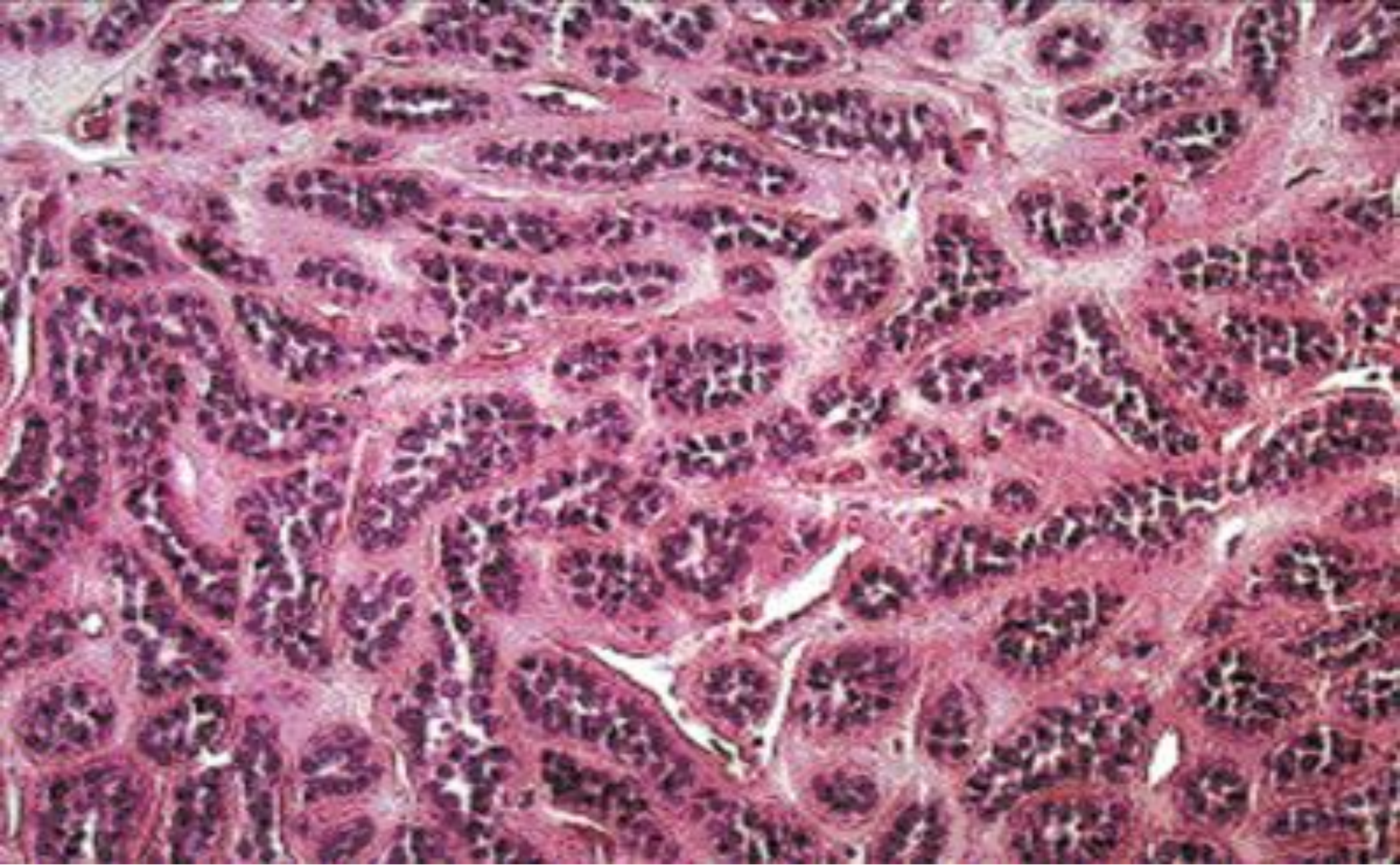
- Epithelial islands are arranged in large lobules and appear to mold to the shape of other lobules to resemble a jigsaw puzzle pattern.



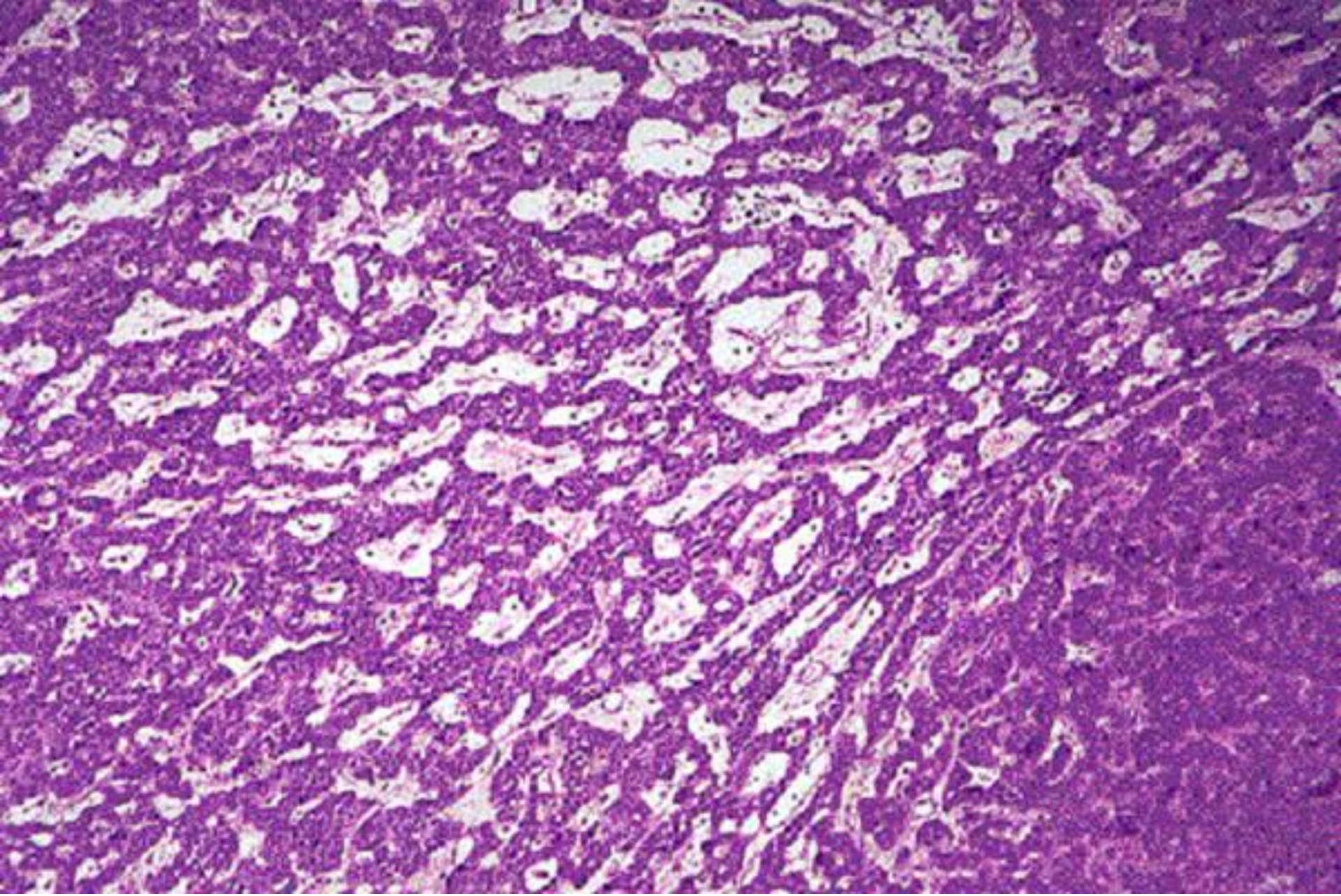
Basal cell adenoma : tubular type



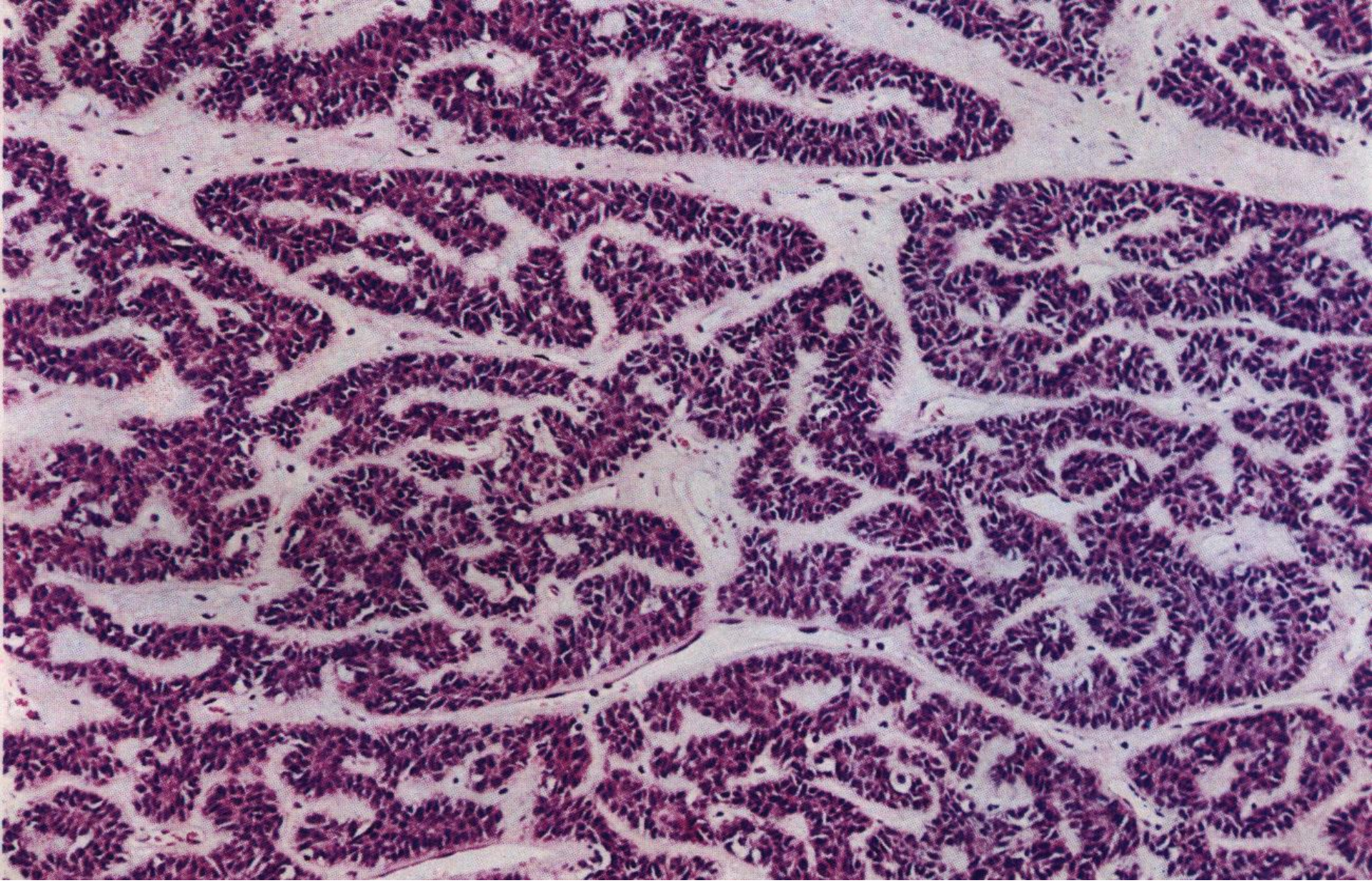
Basal cell adenoma : tubular type



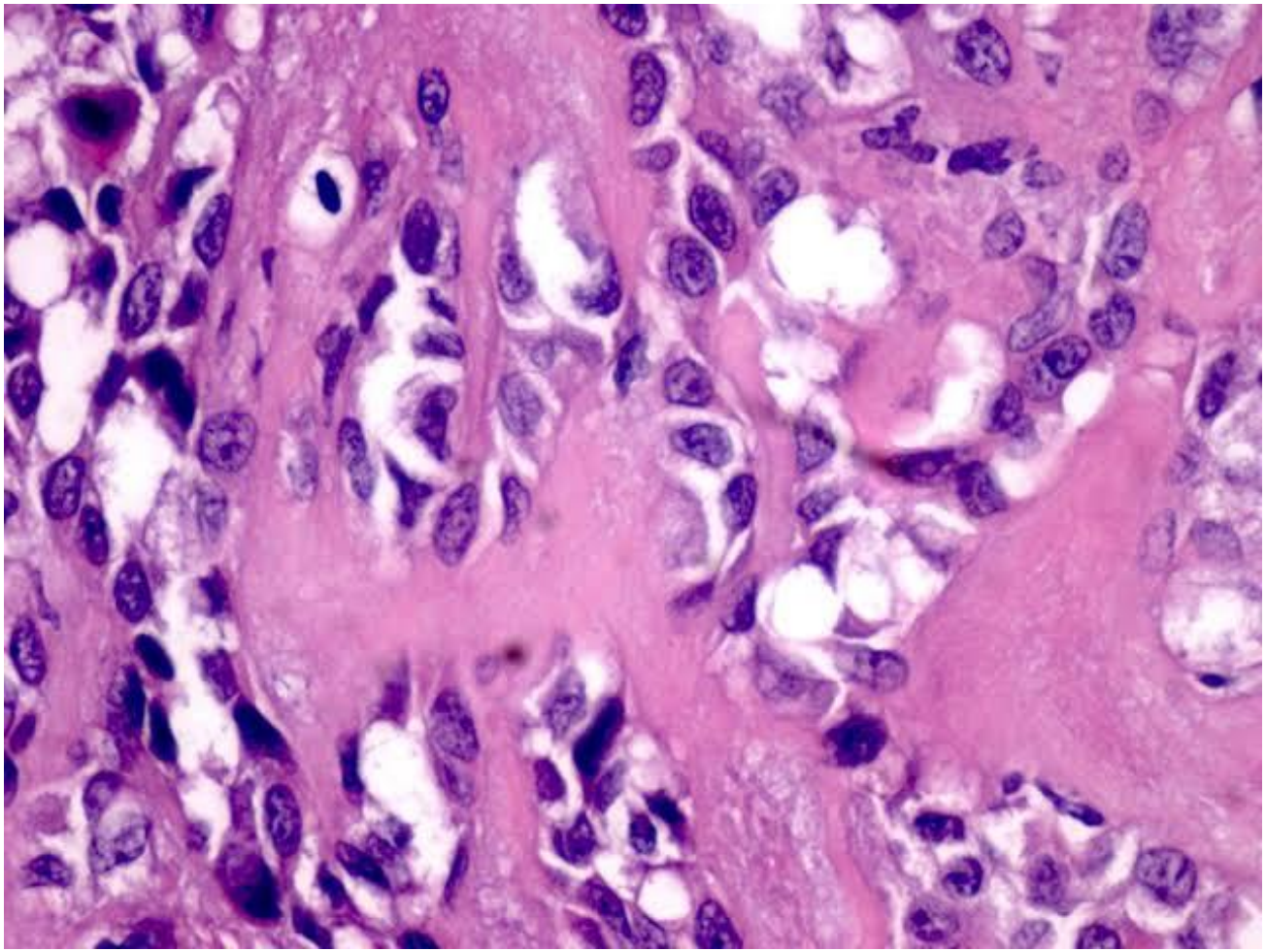
Basal cell adenoma : tubular type



Basal cell adenoma : trabecular type



Basal cell adenoma : trabecular type (high power)



Membranous type

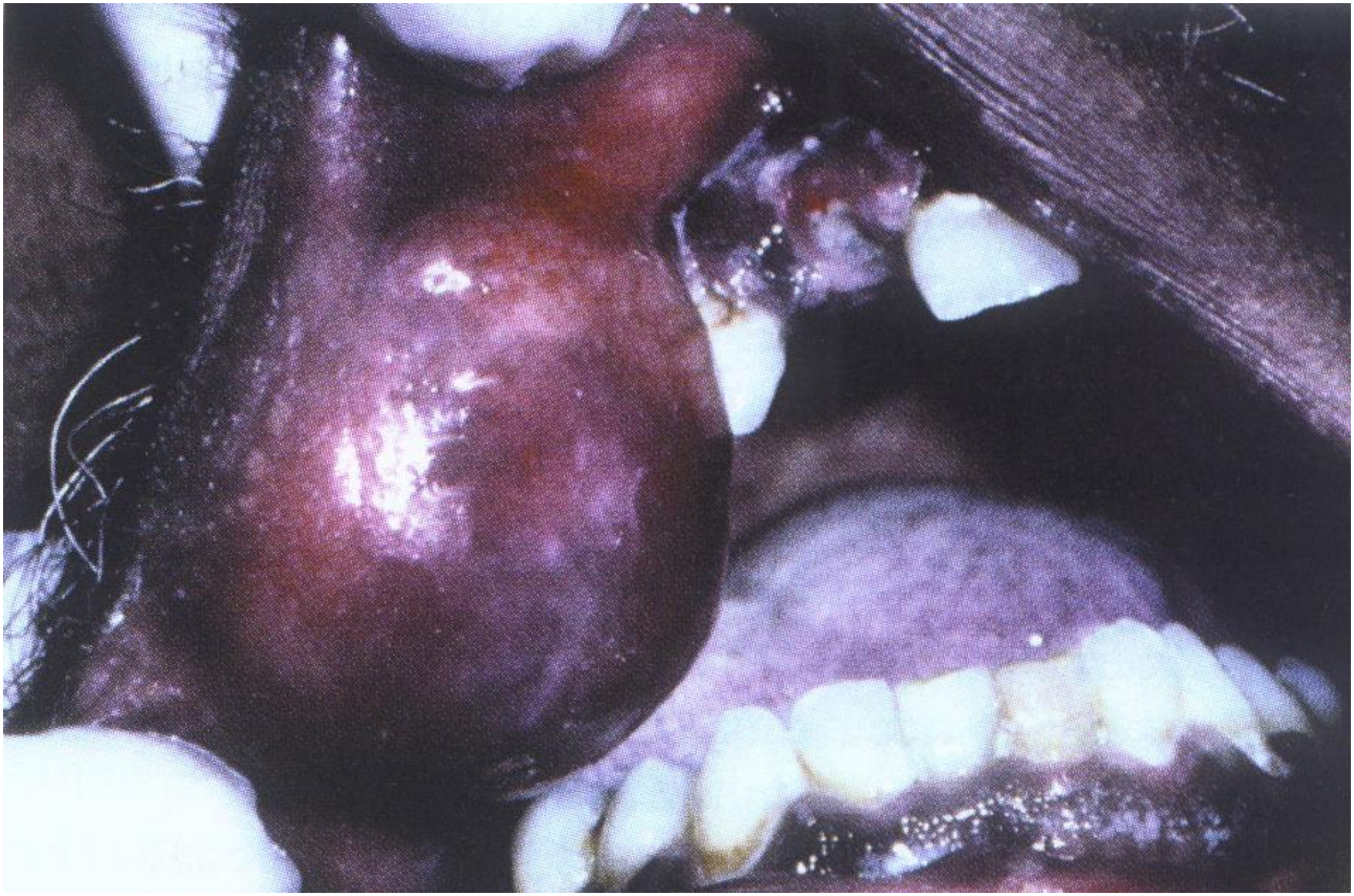
Treatment :

Surgical excision

Canalicular adenoma

Clinical features :

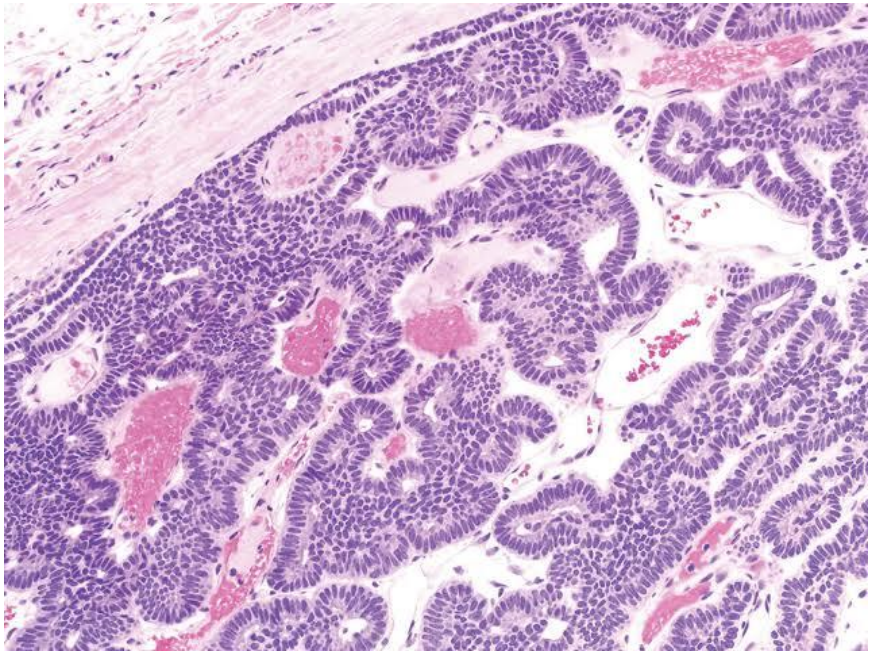
- Mainly in intraoral accessory salivary glands, most commonly the upper lip.
- Age 34-65 years.
- Female : male = 1.8 : 1
- Slow growing, well circumscribed, firm nodule which can be moved.



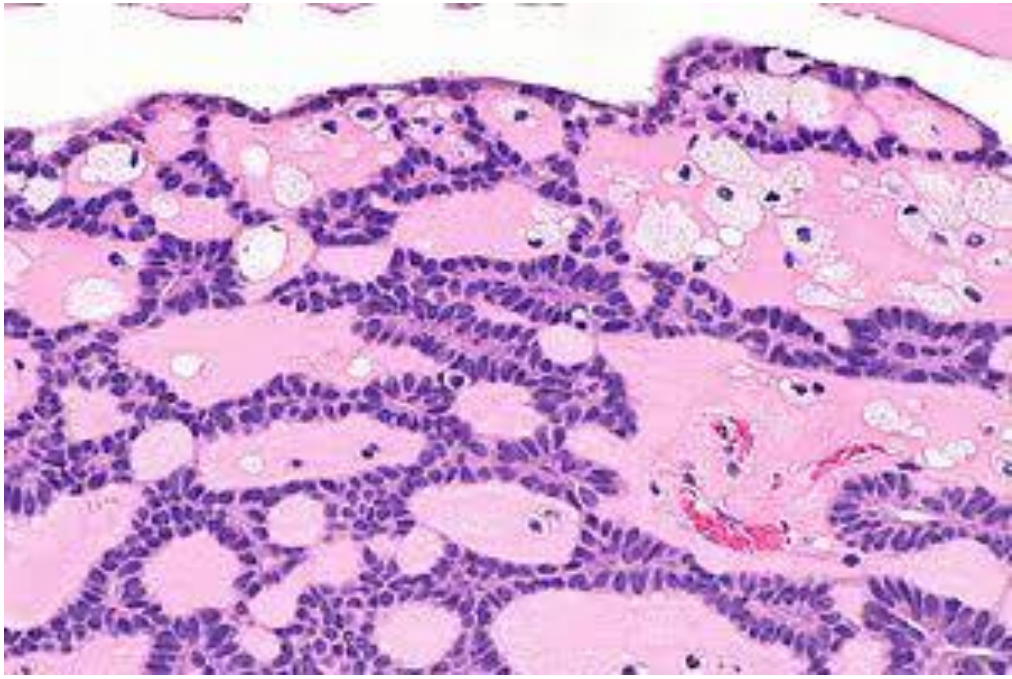
<u>Canalicular adenoma</u> – mass in the upper lip

Histologic features :

- Long columns or cords of cuboidal or columnar cells in a single layer, which are parallel forming long canals.
- Sometimes rows of cells are closely approximated and appear as a double row of cells showing a ‘party wall’.
- Sometimes cystic spaces are enclosed within these cords, usually filled with an eosinophilic coagulum.
- Supporting stroma is loose and fibrillar.
- May be mistaken for an adenoid cystic carcinoma.



Interconnecting cords of cells



Treatment :

Enucleation or simple Surgical excision

Sebaceous adenoma

Clinical features :

- Mean age 58 years.
- More common in men.
- Chiefly found in parotid.

Histologic features :

- Composed of sebaceous cell nests with minimal atypia and pleomorphism & no tendency to invade local structures
- Many tumors are microcystic or may be composed predominantly of ectatic salivary ducts with focal sebaceous differentiation.
- Sebaceous glands may vary markedly in size and in tortuosity and are usually embedded in a fibrous stroma. occasionally marked oncocytic metaplasia and histiocytes &/or foreign body giant cells may be seen focally.

Treatment : conservative excision.

Ductal papilloma

It is a group of three rare benign papillary salivary gland tumors –

A. Inverted ductal papilloma

B. Intra ductal papilloma

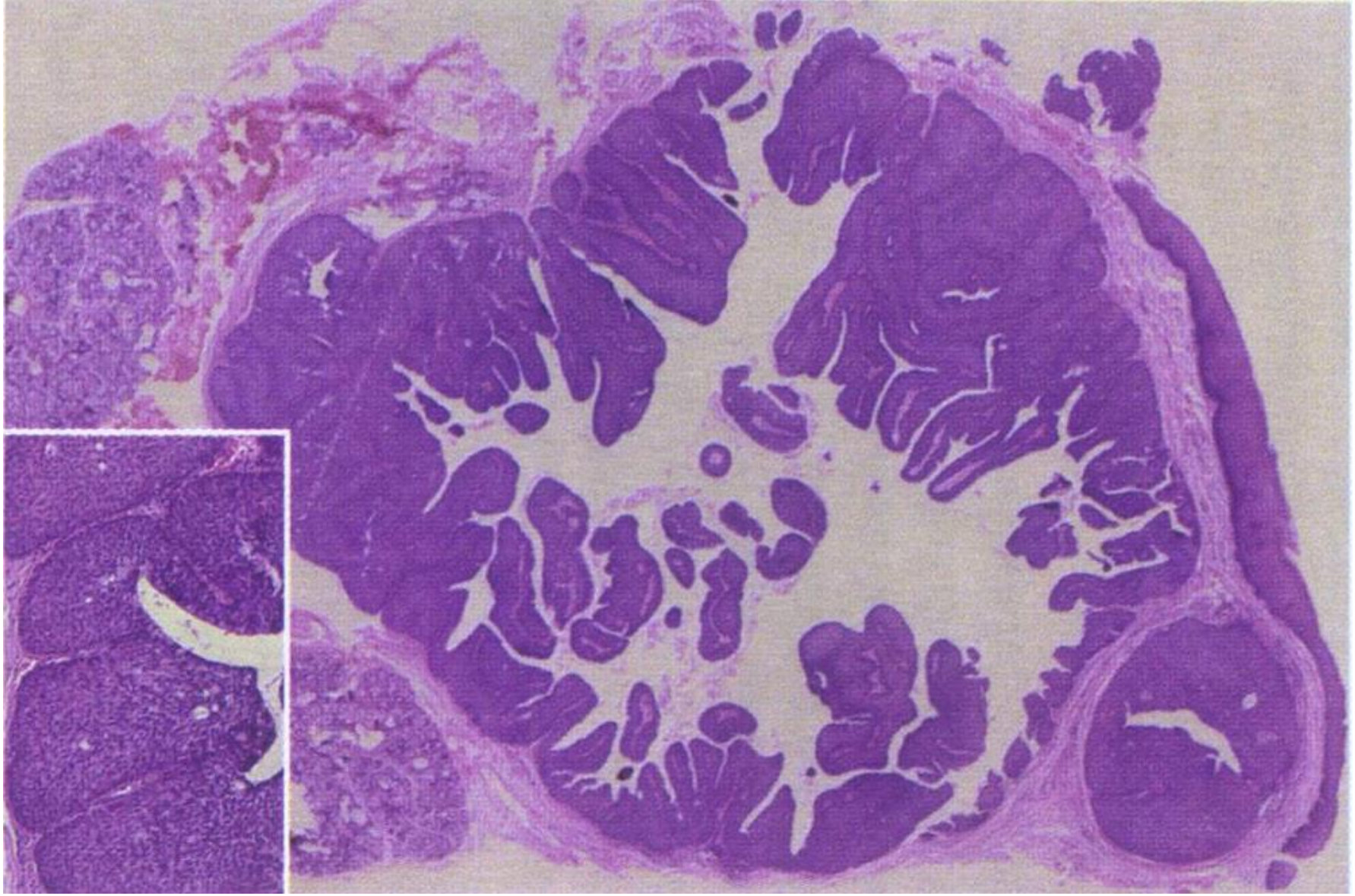
C. Sialadenoma papilliferum

A. Inverted ductal papilloma

- Only in minor salivary glands of adults.
- Lower lip is the most frequently involved site .
- Appear to arise from the excretory ducts near the mucosal surface.
- Seen as submucosal nodules which may have a pit or indentation.

Histological features :

- Basaloid and squamous cells arranged in thick, bulbous papillary proliferations that project into the lumen.
- Lumen is often narrow and in some cases communicates with the exterior.



<u>Inverted ductal papilloma</u> – papillary intraductal proliferation located beneath the mucosal surface.
Inset shows both mucous and squamous cells.

B. Intra ductal papilloma :

- An ill defined lesion usually confused with papillary cystadenoma.
- Usually occurs in adults.
- Common in minor salivary glands, most commonly lower lip.
- Presents as a submucosal swelling.
- Arises from the excretory ducts at a deeper level than the inverted ductal papilloma.

Histological features :

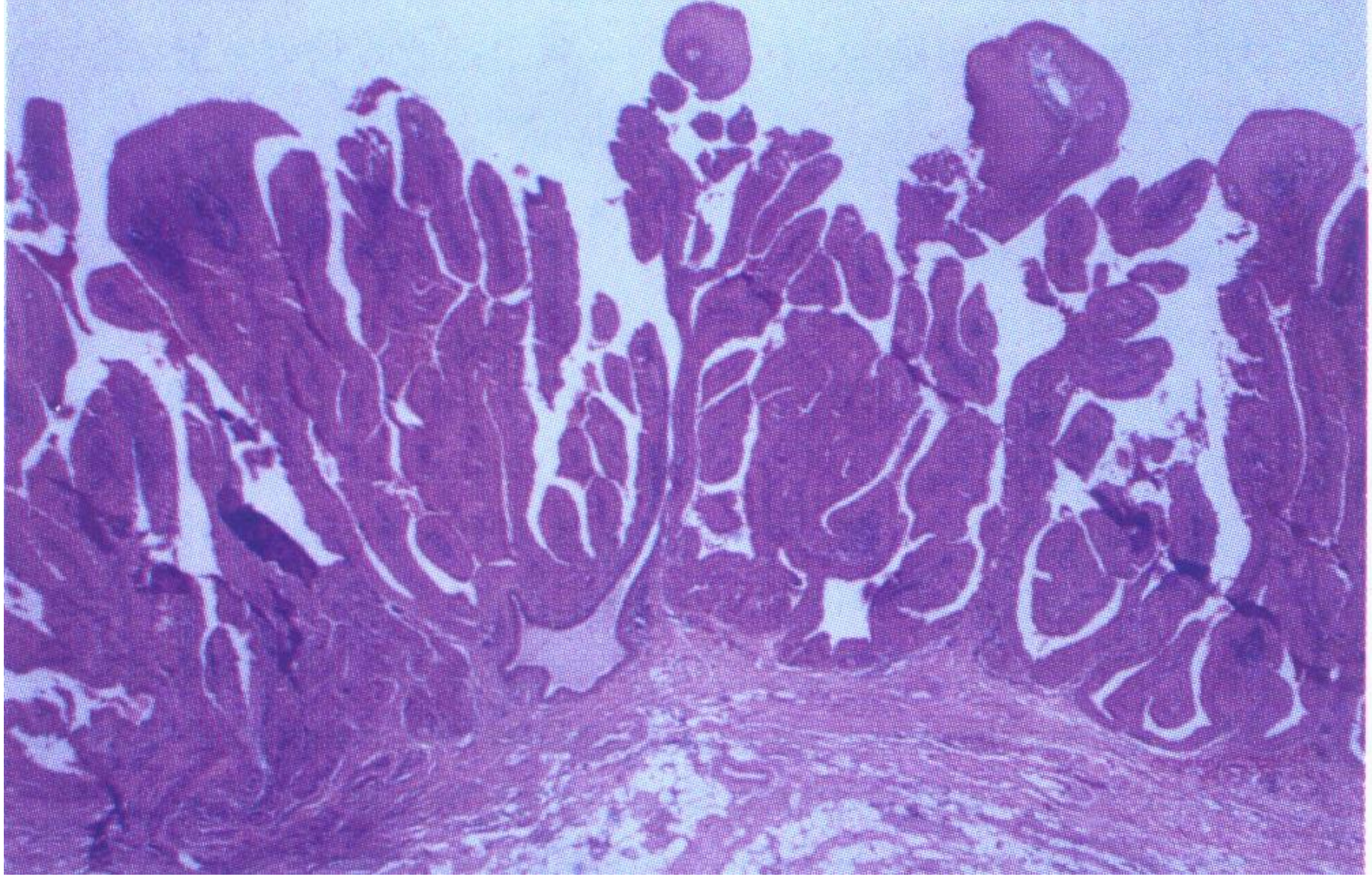
- Exhibits a unicystic dilated structure.
- Cyst wall is lined by a single or double layer of columnar cells which extend into the cyst lumen as papillary projections having thin fibrovascular cores.

C. Sialadenoma papilliferum :

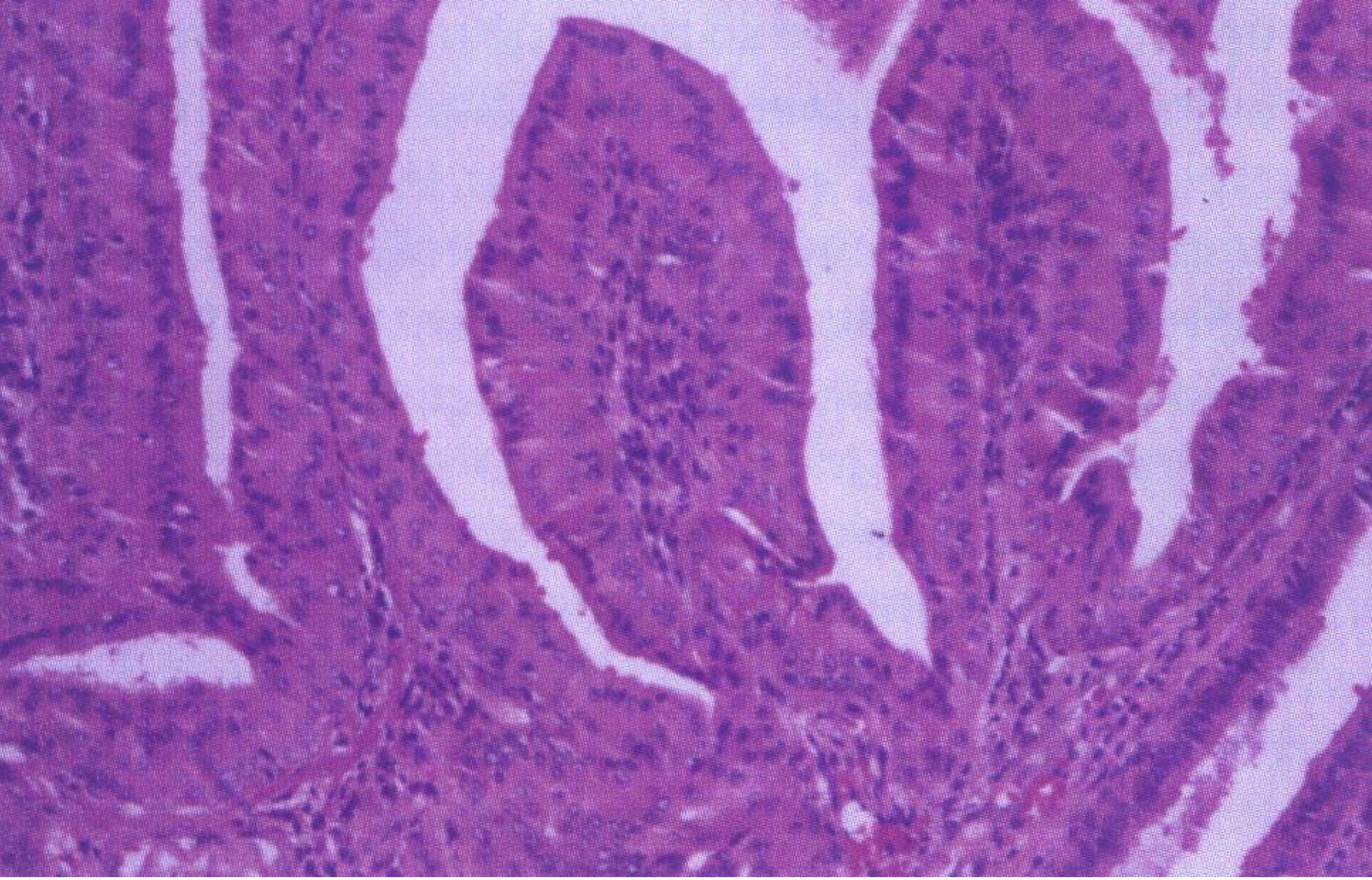
- Most commonly in minor glands.
- Adults.
- Male predilection
- Exophytic papillary surface lesion.

Histological features :

- Biphasic growth pattern of exophytic papillary and endophytic components.
- Papillary projections of epithelium are supported by fibrovascular cores, and are covered by parakeratotic stratified squamous epithelium.
- Fibrovascular cores have a mixed inflammatory infiltrate.
- Ductal epithelium continues downwards into the deeper c.t.
- Multiple ductal lumina are seen which are lined by a double row of cells consisting of a luminal layer of tall columnar cells, resting on a cuboidal basal layer.



<u>Sialadenoma papilliferum –</u> low power view showing a papillary surface tumor with associated ductal structures in the superficial lamina propria.



<u>Sialadenoma papilliferum</u> – high power view showing cystic areas lined by papillary oncocytic epithelium.

Treatment :

Surgical excision

Cystadenoma

- In this benign tumor, the epithelium demonstrates adenomatous proliferation that is characterized by formation of multiple cystic structures.
- **Papillary cystadenoma** is a cystadenoma in which the cystic space is filled with papillary projections. According to WHO, “it is a tumor that closely resembles Warthin’s tumor but without the lymphoid elements, constituting multiple papillary projections and a greater variety of epithelial lining cells.”
- If mucous cells predominate in the cell population of the lining epithelial cells, the tumor is termed as **mucinous cystadenoma.**

Clinical features :

- In both major and minor salivary glands.
- Female :male = 2:1.
- Older age, commonly the eighth decade.
- Clinically presents as a slow growing , painless slightly compressible swelling.

Histologic features :

- Epithelial proliferation results in various sized cystic structures, whose lining varies from flattened to tall columnar cells, and cuboidal, mucous and oncocytic cells may also be seen.
- Limited papillary growth with central connective tissue core is seen.
- Eosinophilic or slightly hematoxyphilic secretions are seen in the stroma.
- Dense fibrous c.t. stroma with scattered inflammatory cells is present.

Treatment :

Conservative surgery.

Malignant tumors

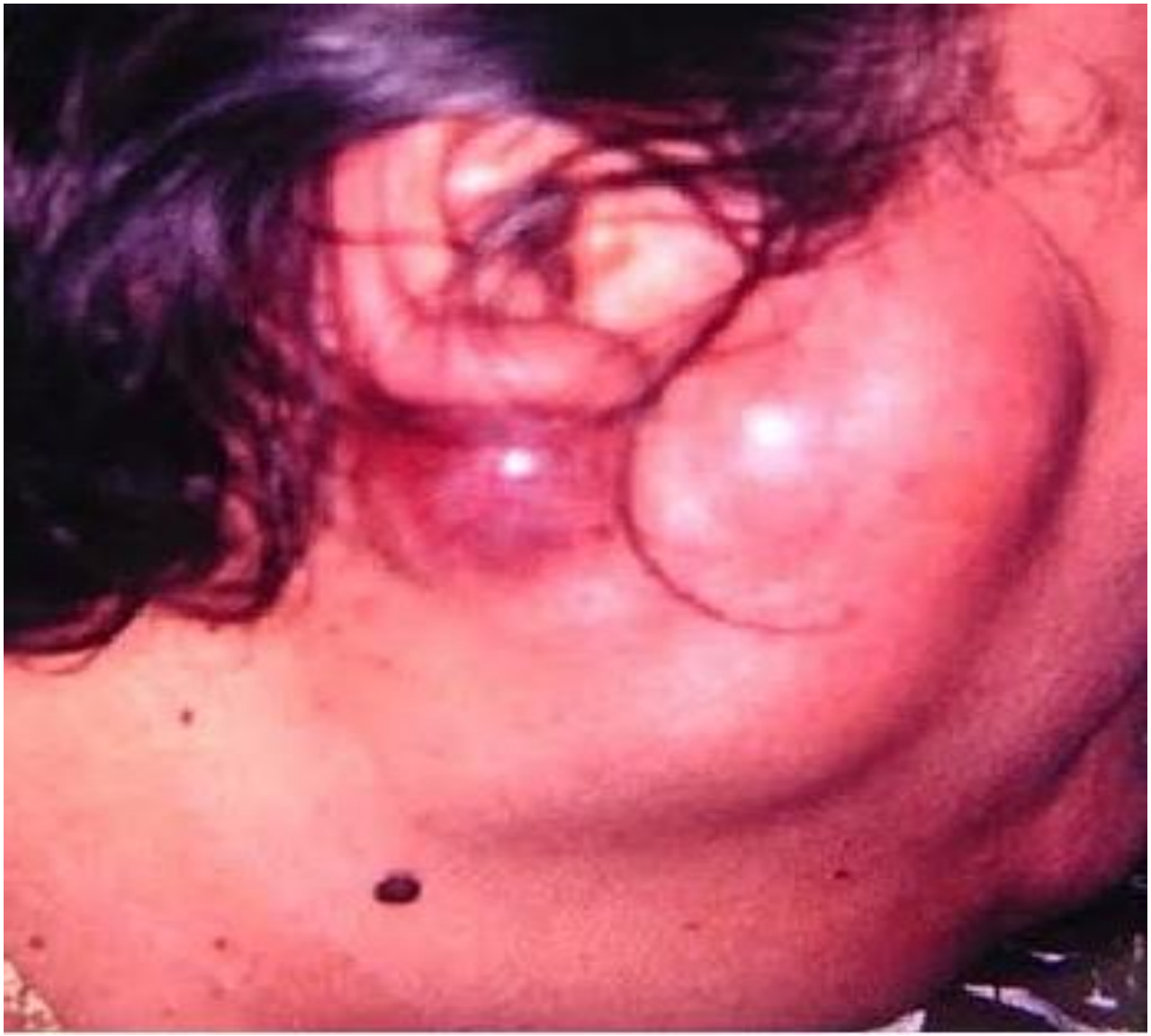
of salivary glands

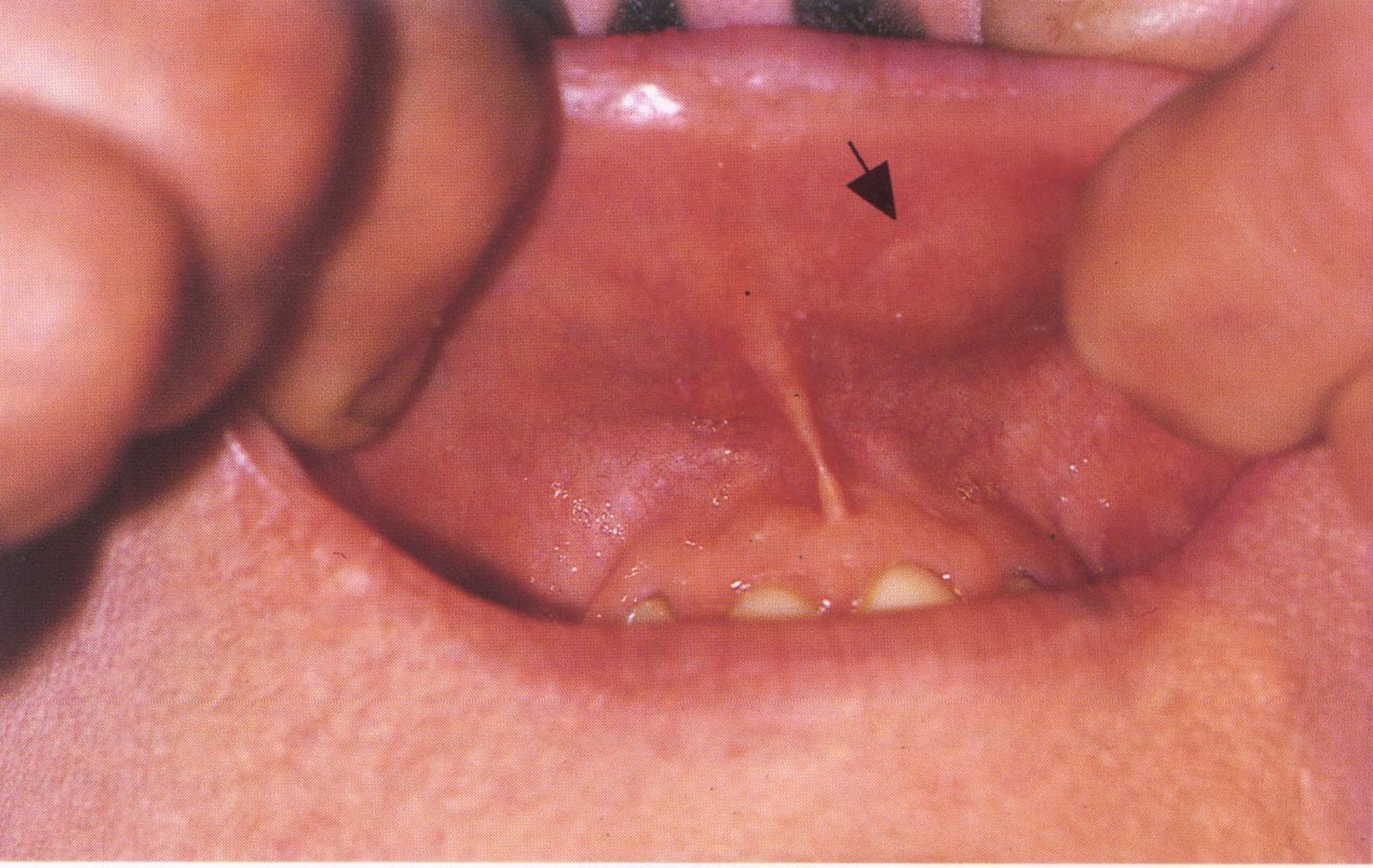
Acinic cell carcinoma

- A malignant epithelial neoplasm in which the neoplastic cells express acinar differentiation.
- All tumors of this type have at least a low grade malignant potential.
- Here the cytologic differentiation is towards the serous acinar cells whose characteristic feature is cytoplasmic PAS positive zymogen-type secretory granules.
- It is the third most common malignant salivary gland neoplasm, after mucoepidermoid carcinoma and adenocarcinoma.

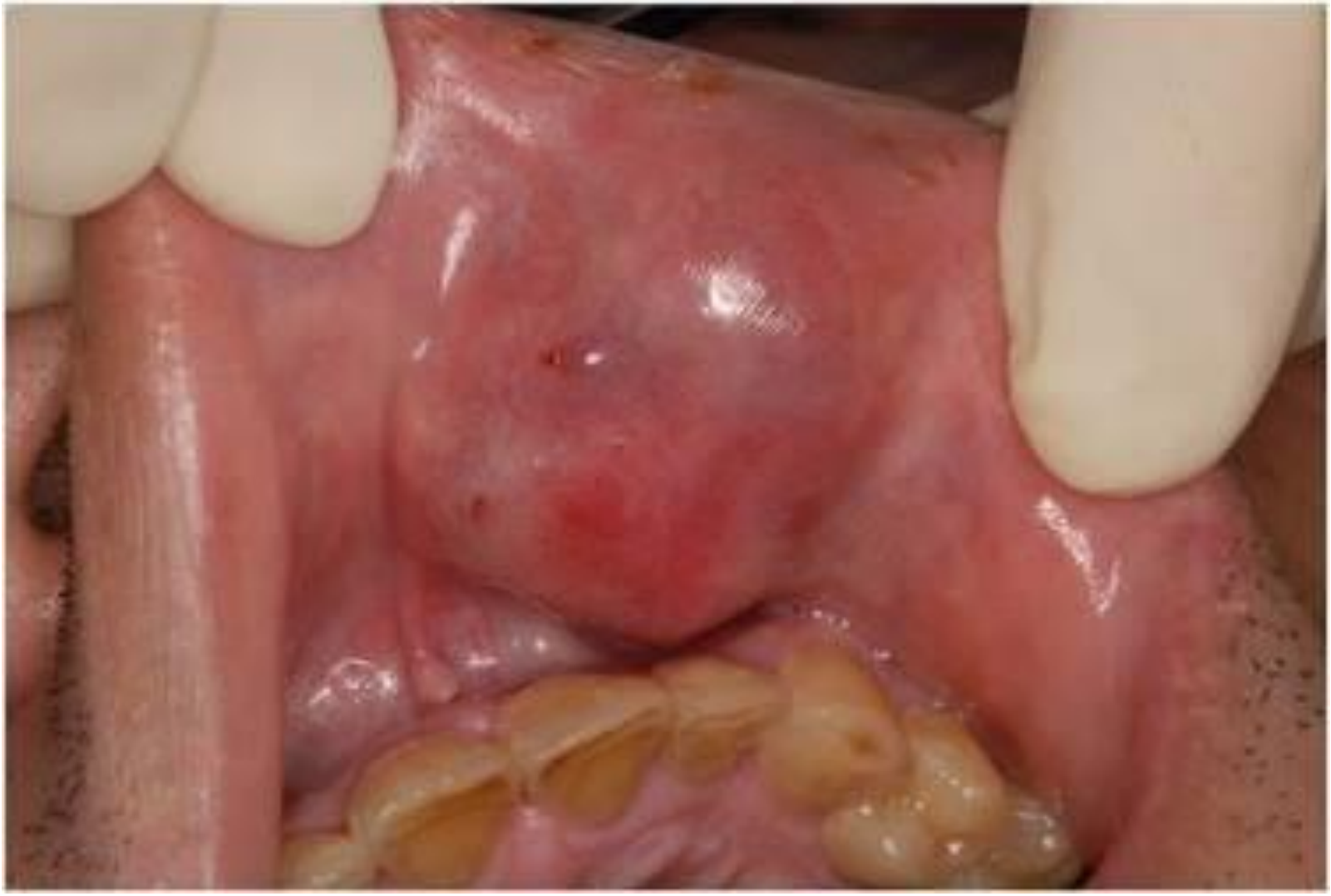
Clinical features :

- Resembles pleomorphic adenoma grossly, being encapsulated and lobulated.
- Mainly in parotid.
- Most common intraoral sites are lips and buccal mucosa.
- Predominantly in middle aged people.
- Men : women = 2:3
- Presents as a slow growing, mobile or fixed mass, usu. Asymptomatic but pain and tenderness may be seen in about 1/3 of patients.
- Facial muscle weakness may be seen.





Acinic cell carcinoma – firm discrete submucosal mass of the left upper lip



Histologic features :

- Usu. Surrounded by a thin capsule.
- Exhibits four growth patterns –

✓ *solid*

✓ *papillary-cystic*

✓ *follicular*

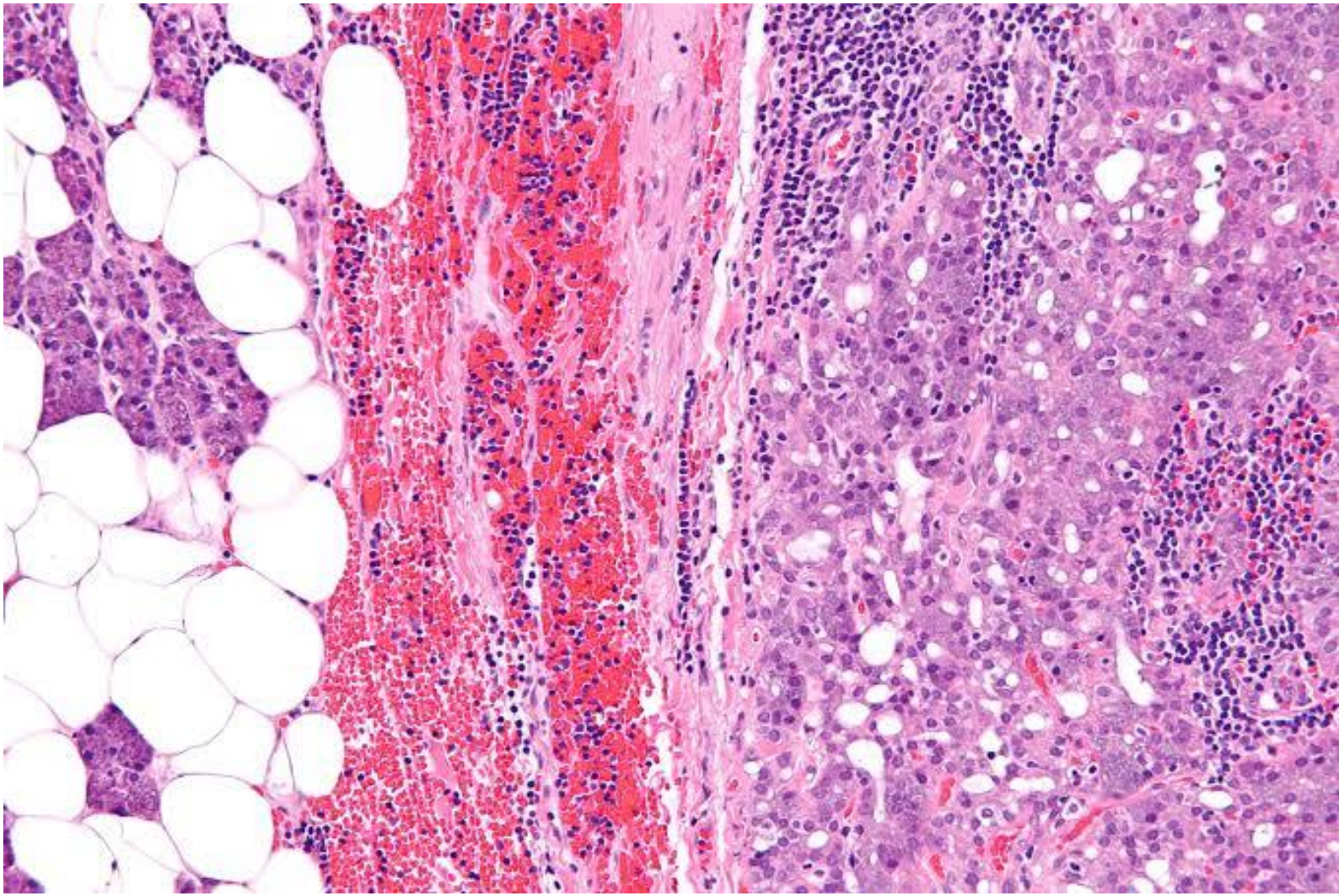
✓ *micro cystic*

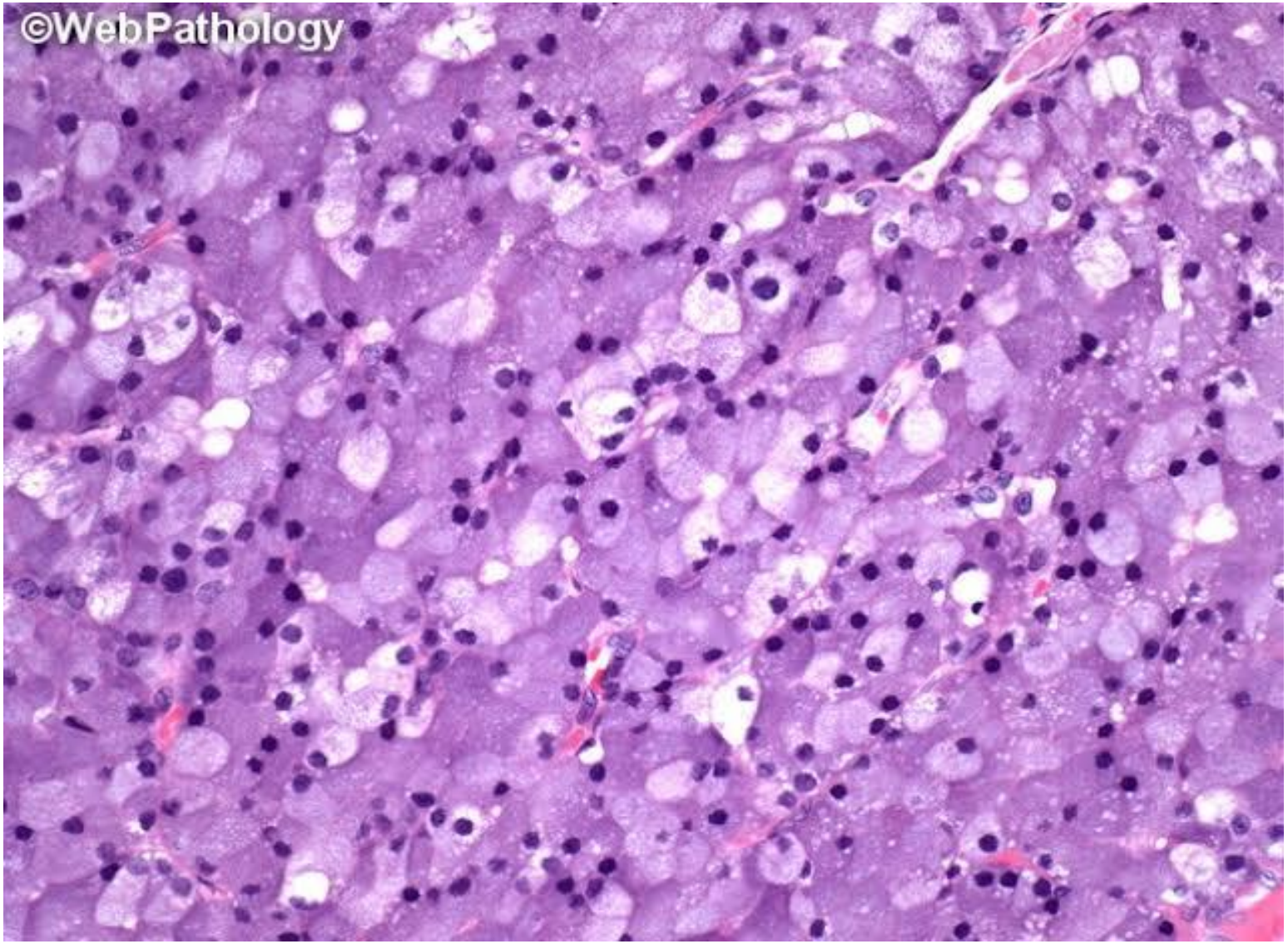
- The most characteristic cell seen has the features of the **serous acinar cells**, with abundant granular basophilic cytoplasm and a round dark stained eccentric nucleus.

- Other cells seen are the **intercalated duct like cells**, which are smaller and the **vacuolated cells** which seem to be unique to this tumor.

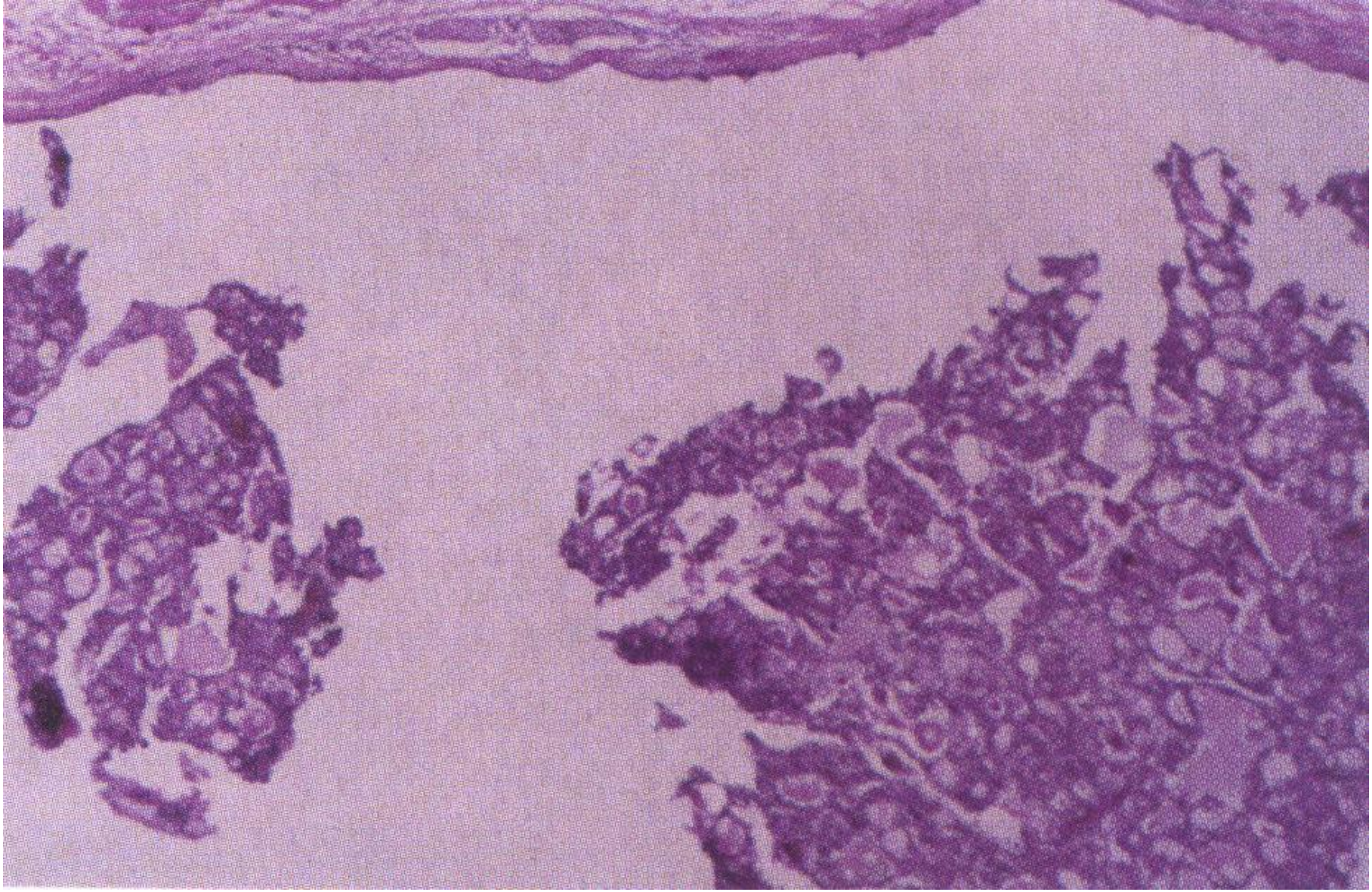
- C.t. stroma is delicately fibrovascular collagenous tissue

- Lymphoid elements are commonly found in the parotid tumors, a feature helpful in the diagnosis. Apparently this tumor can arise from embryologically entrapped salivary gland tissue in lymph nodes, in or near the parotid.

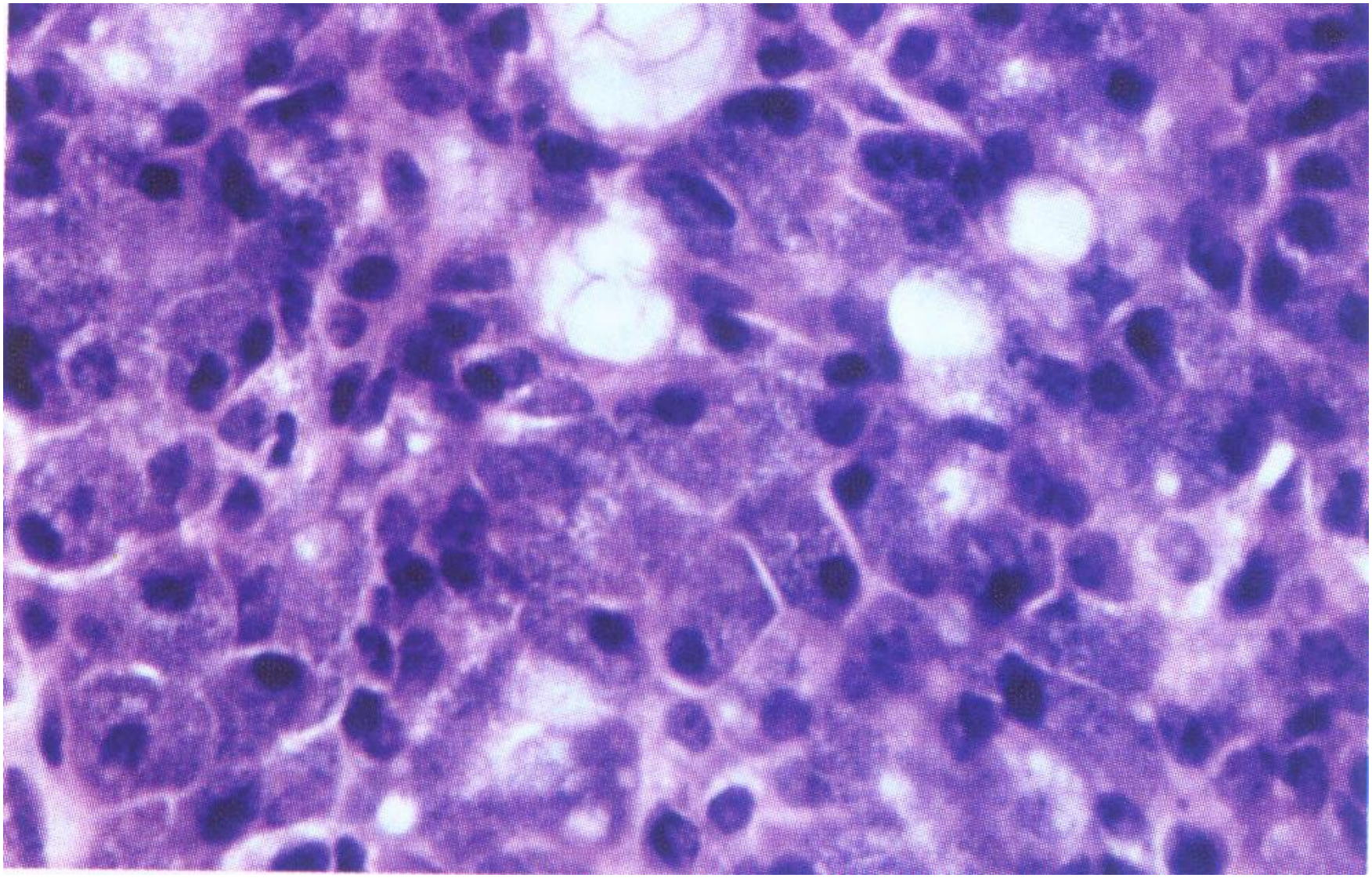




Acinic cell carcinoma – parotid tumor showing sheets of granular serous acinar cells along with clear cells.



Acinic cell carcinoma – papillary-cystic variant showing proliferation of tumor cells into a large cystic space.



Acinic cell carcinoma – high power view of serous cells with basophilic granular cytoplasm

Treatment :

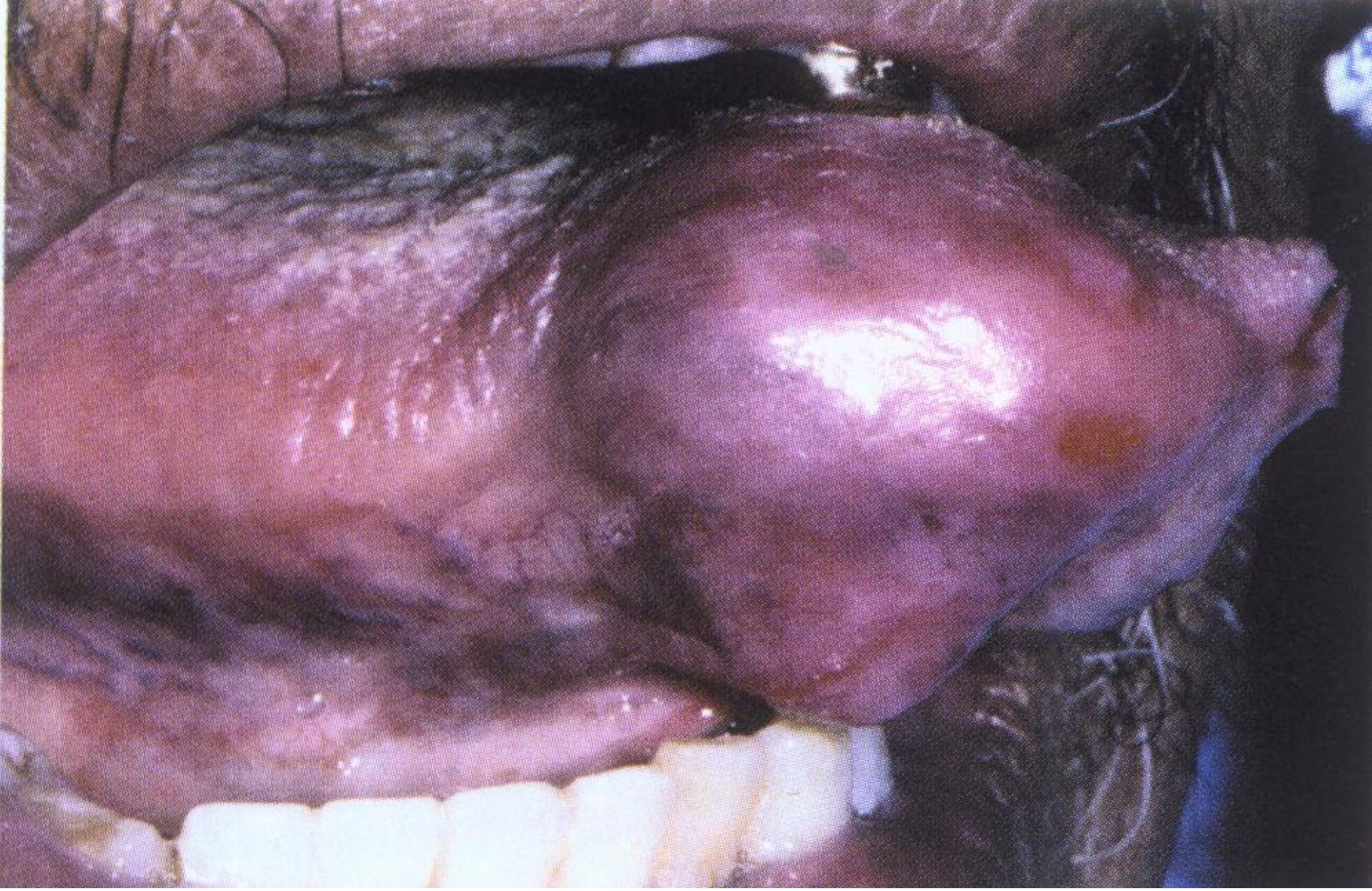
- Total excision of the parotid gland tumors with preservation of the facial nerve unless it is involved.
- Lymph node dissection is indicated only in the presence of clinical involvement.
- Radiation therapy is not helpful.

Mucoepidermoid carcinoma

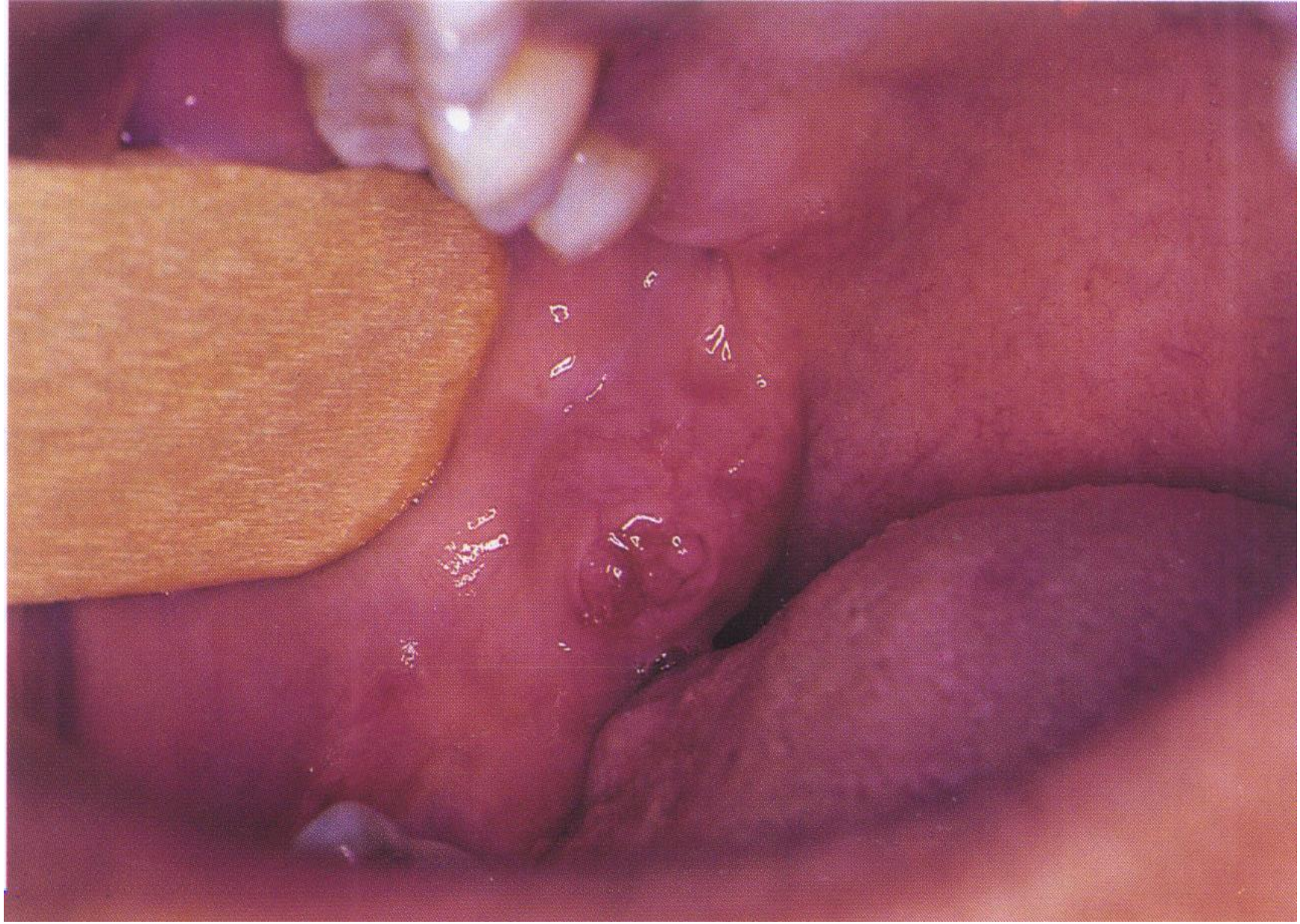
- Most common malignant neoplasm of both major and minor salivary glands.
- Contains both mucous secreting cells and epidermoid type cells
- Columnar and clear cells are also seen, and often demonstrate prominent cystic growth.
- Parotid is the most common site. Intraorally palate is the most common.

Clinical features

- Female predilection.
- Occurs primarily in the 3rd to 5th decade.
- Most common malignant salivary gland tumor in children
- Ionizing radiation exposure may increase the risk of developing MEC.
- The **low grade tumors** are slowly enlarging, painless masses, which simulate the pleomorphic adenoma. They are not completely encapsulated and often contain cystic spcaces which may be filled with a mucoid material. Hence they resemble mucoceles, esp. in the retro molar area.
- The **high grade tumors** grow rapidly and produce pain as an early symptom. Facial nerve palsy is common when parotid is involved. It is not encapsulated, but tends to infiltrate the adjacent tissues and metastasize to the regional lymph nodes. Distant metastasis is also common.



Mucoepidermoid carcinoma - mass of the tongue



Mucoepidermoid carcinoma – cystic appearing mass of lateral soft palate and pterygomandibular raphe

Histopathology

- Composed of mucous secreting cells , epidermoid type (squamous) cells and intermediate cells.
- The **mucous cells** are of various shapes and have abundant, pale, foamy cytoplasm that stains positive for mucin stains.
- The **epidermoid cells** are polygonal shaped with prominent intercellular bridges and rarely keratinization.
- A group of basaloid cells referred to as **intermediate cells** are important in recognizing MEC. These cells are larger than the basal cells and smaller than squamous cells & are believed to be the progenitor of epidermoid and mucous cells.

- Occasionally **clear cells** are also seen. These are generally mucin and glycogen free.

- Epidermoid cells, together with intermediate and mucous cells line cystic spaces or form solid masses or cords. Epidermoid and mucous cells may be arranged in a glandular pattern.

Grades of mucoepidermoid carcinoma

- **Low grade-** shows
  - well formed glandular structures
  - prominent mucin filled cystic spaces
  - Minimal cellular atypia and high proportion of mucous cells
- **Intermediate grade**
  - Have solid areas of epidermoid cells with intermediate cells predominating.
  - Cyst formation is less prominent
- **High grade**
  - Cells are present as solid nests and cords of basaloid cells and epidermoid cells
  - Prominent nuclear pleomorphism and mitotic activity
  - Very less cystic component
  - Necrosis and perineural invasion present

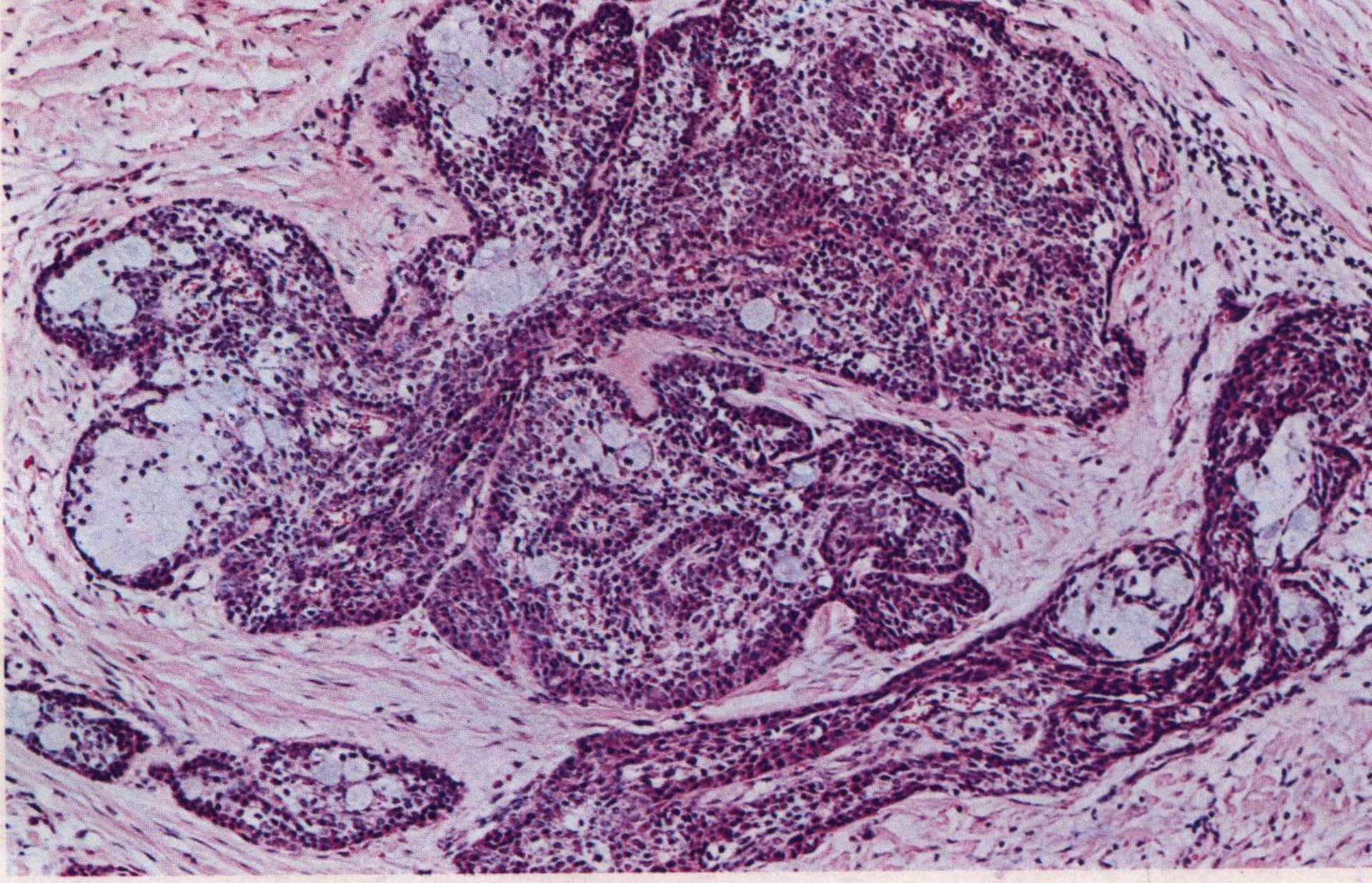
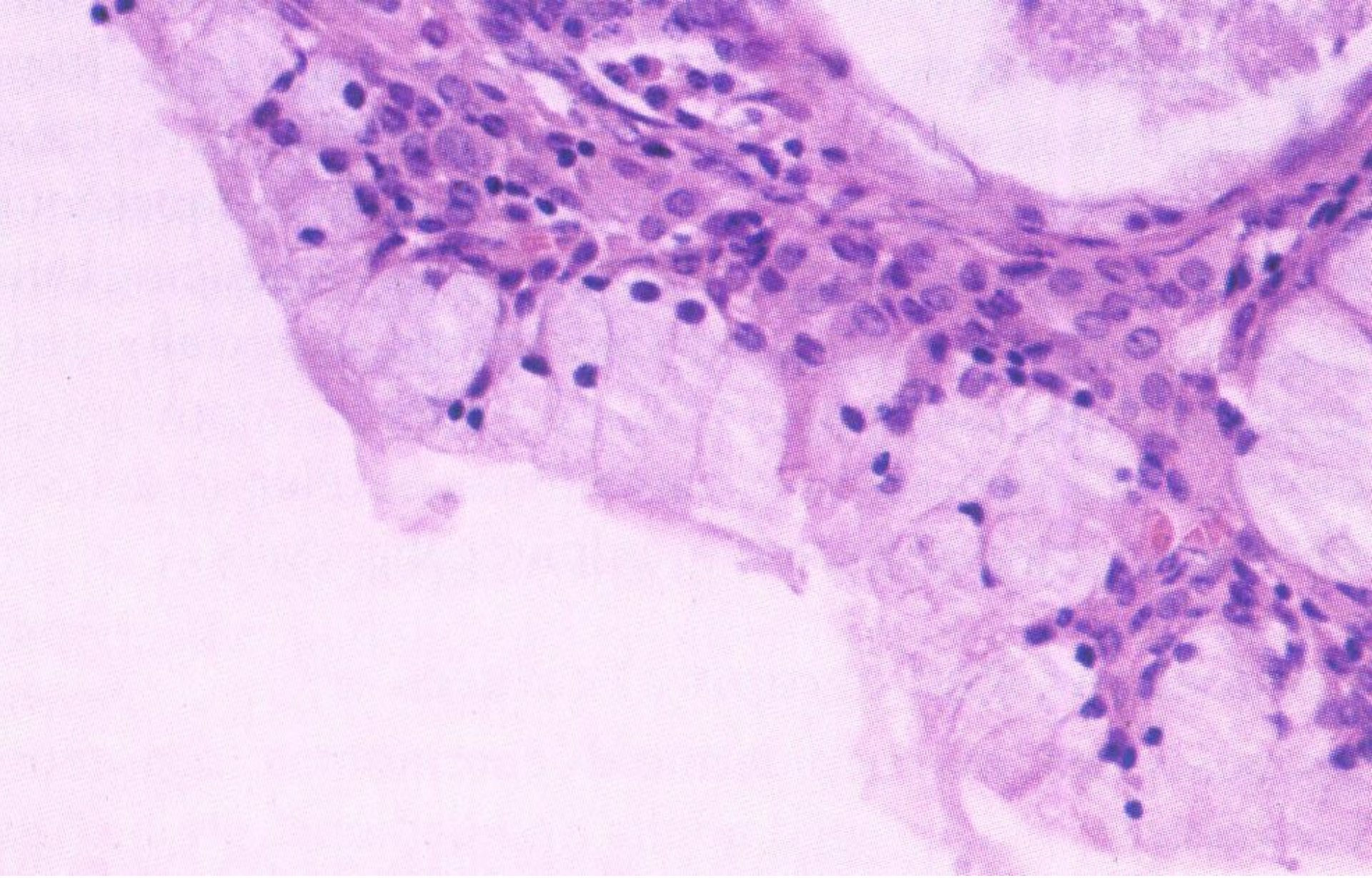
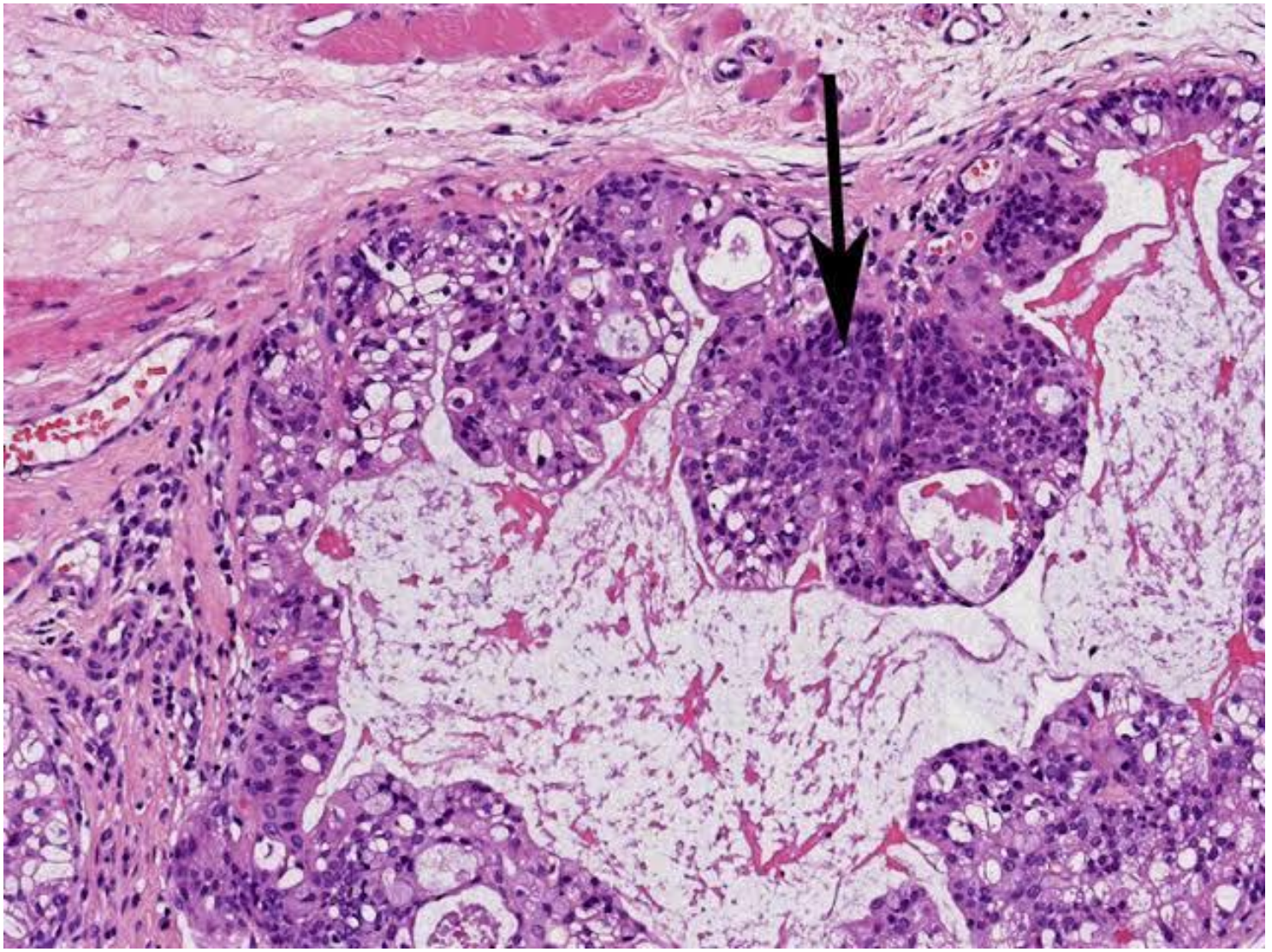


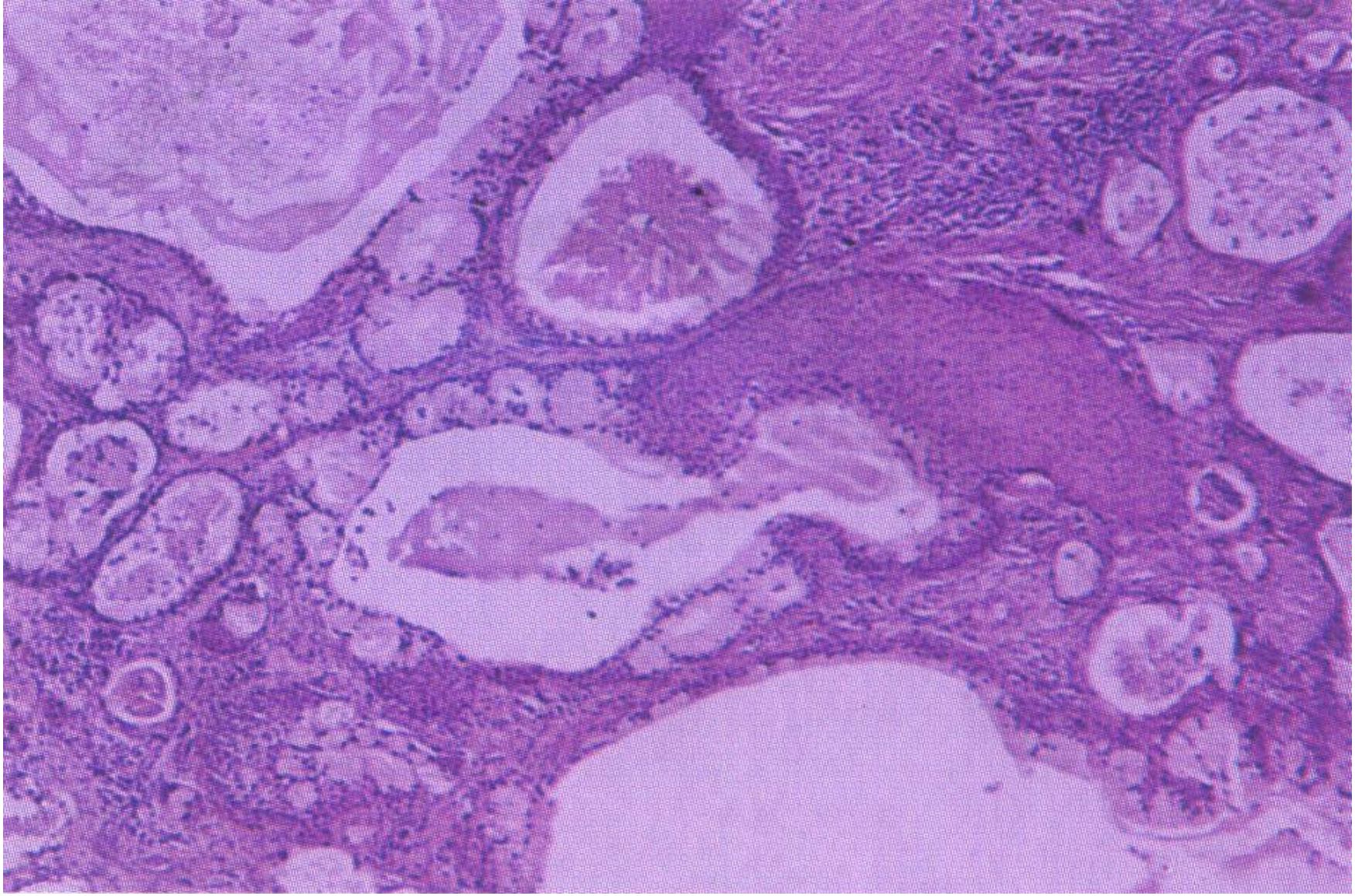
Fig. 17. Mucoepidermoid tumour

Clumps and masses of epidermoid and mucus-secreting cells in a fibrous stroma

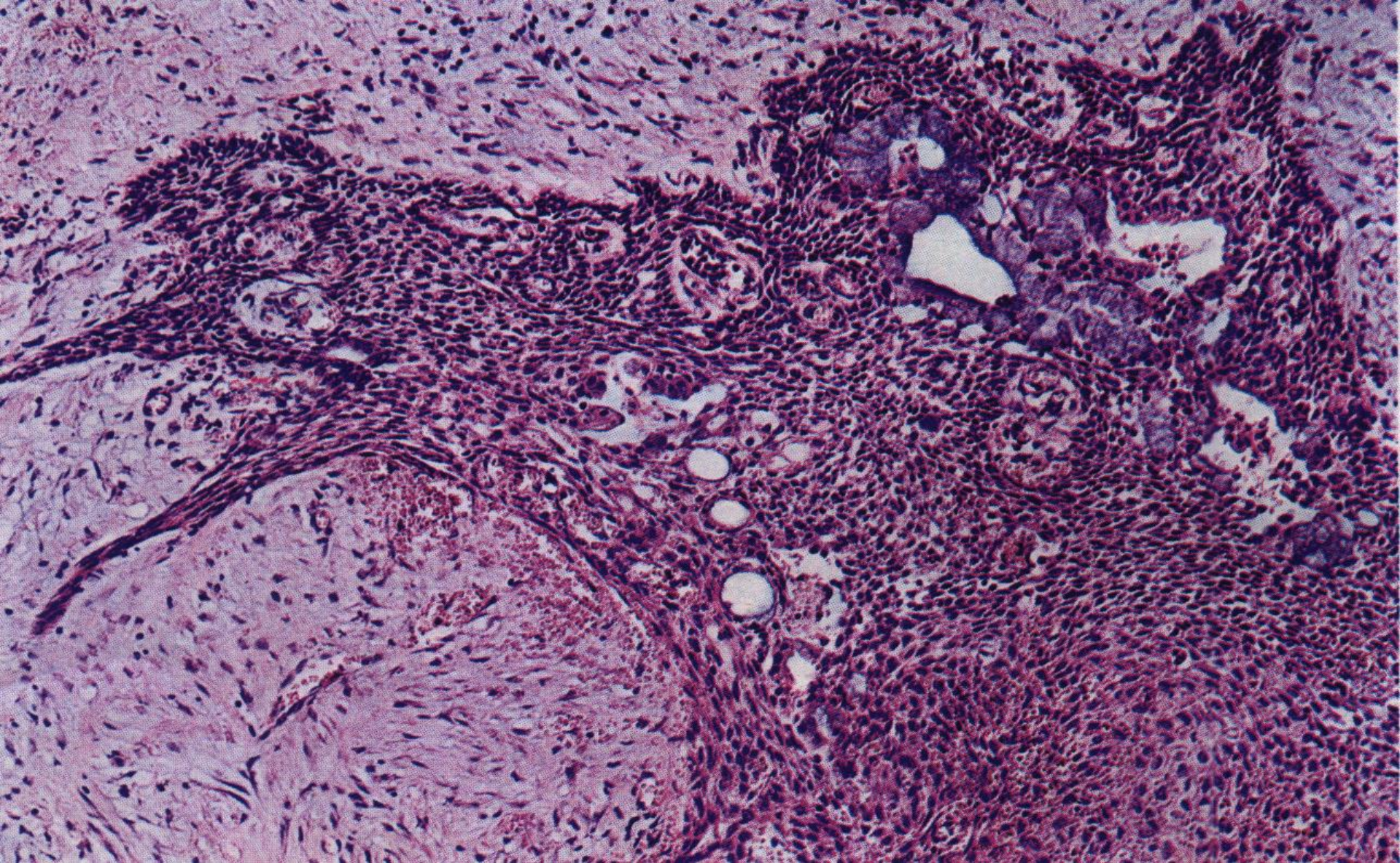


Mucoepidermoid carcinoma - low grade tumor showing numerous large mucous cells surrounding a cystic space.





Mucoepidermoid carcinoma – moderately well differentiated tumor showing ductal and cystic spaces surrounded by mucous and squamous cells.



Mucoepidermoid carcinoma – high grade tumor showing solid tumor mass composed of epidermoid and basaloid cells

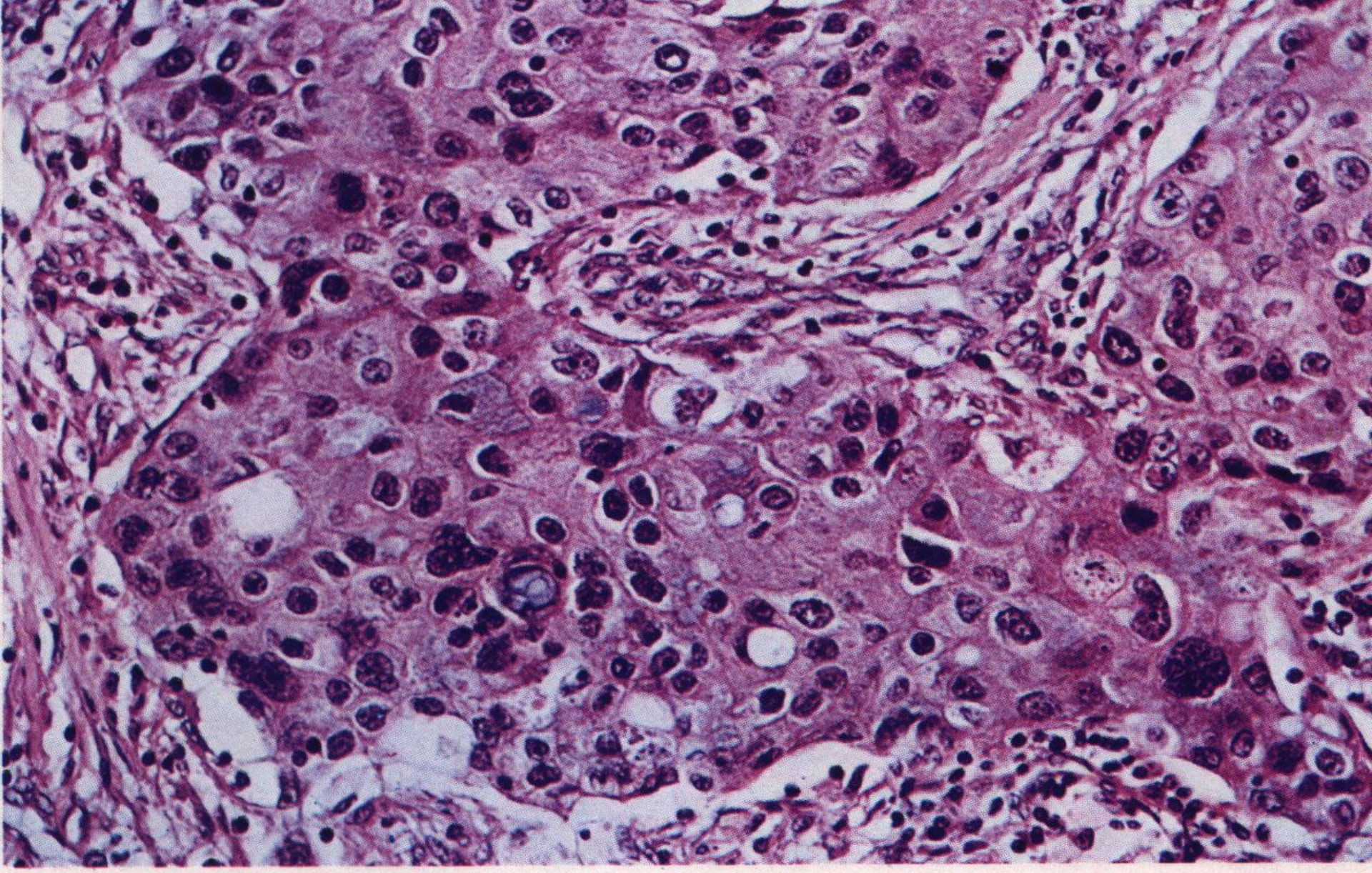
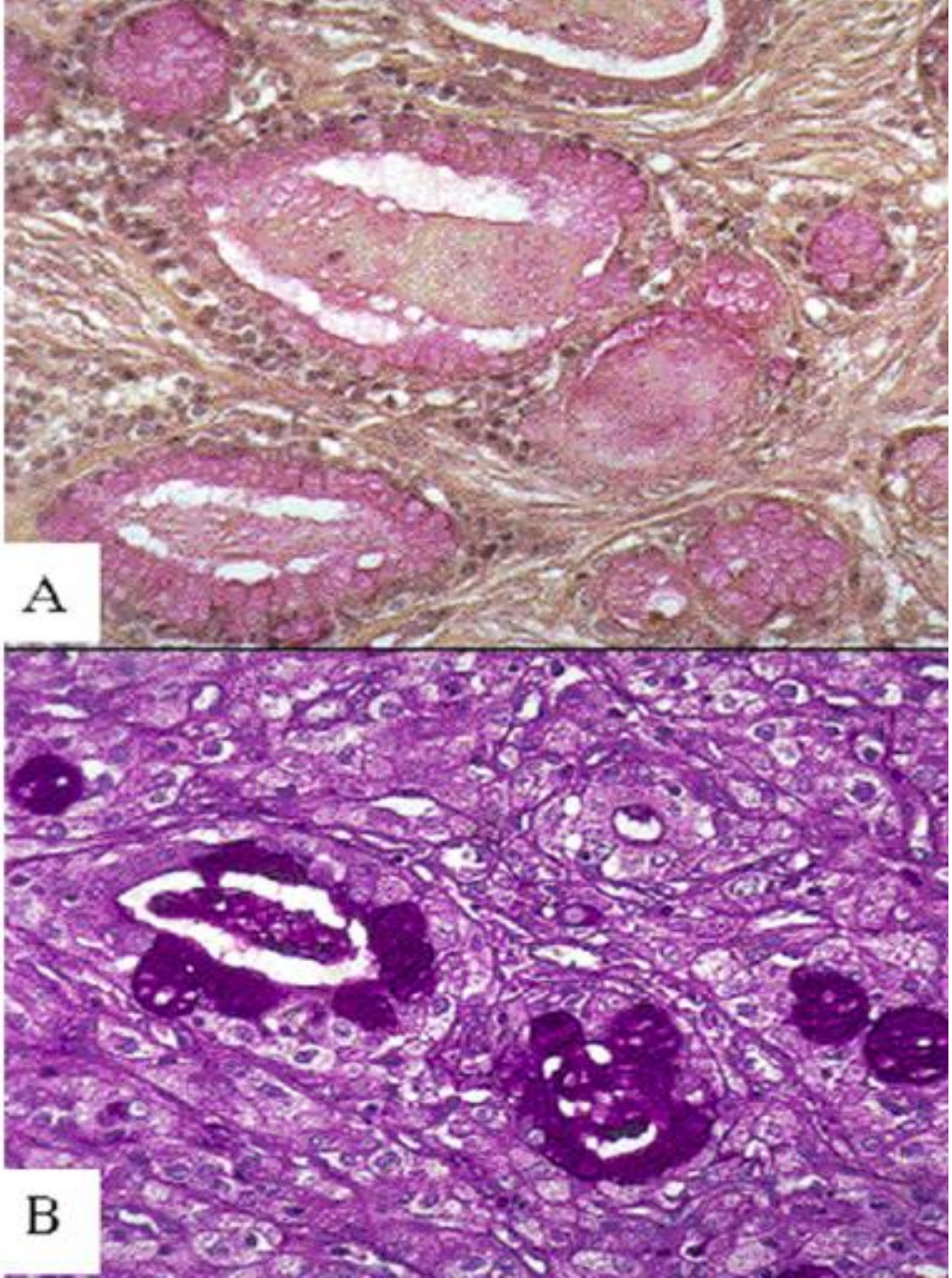


Fig. 23. Mucoepidermoid tumour

Poorly differentiated growth with pleomorphism. Some mucus present



Mucoepidermoid carcinoma

A. Mucicarmine stain
B. PAS stain

The two components of the tumor are large, pale, mucous secreting cells, which typically surround cystic spaces and sheets of epidermoid cells.

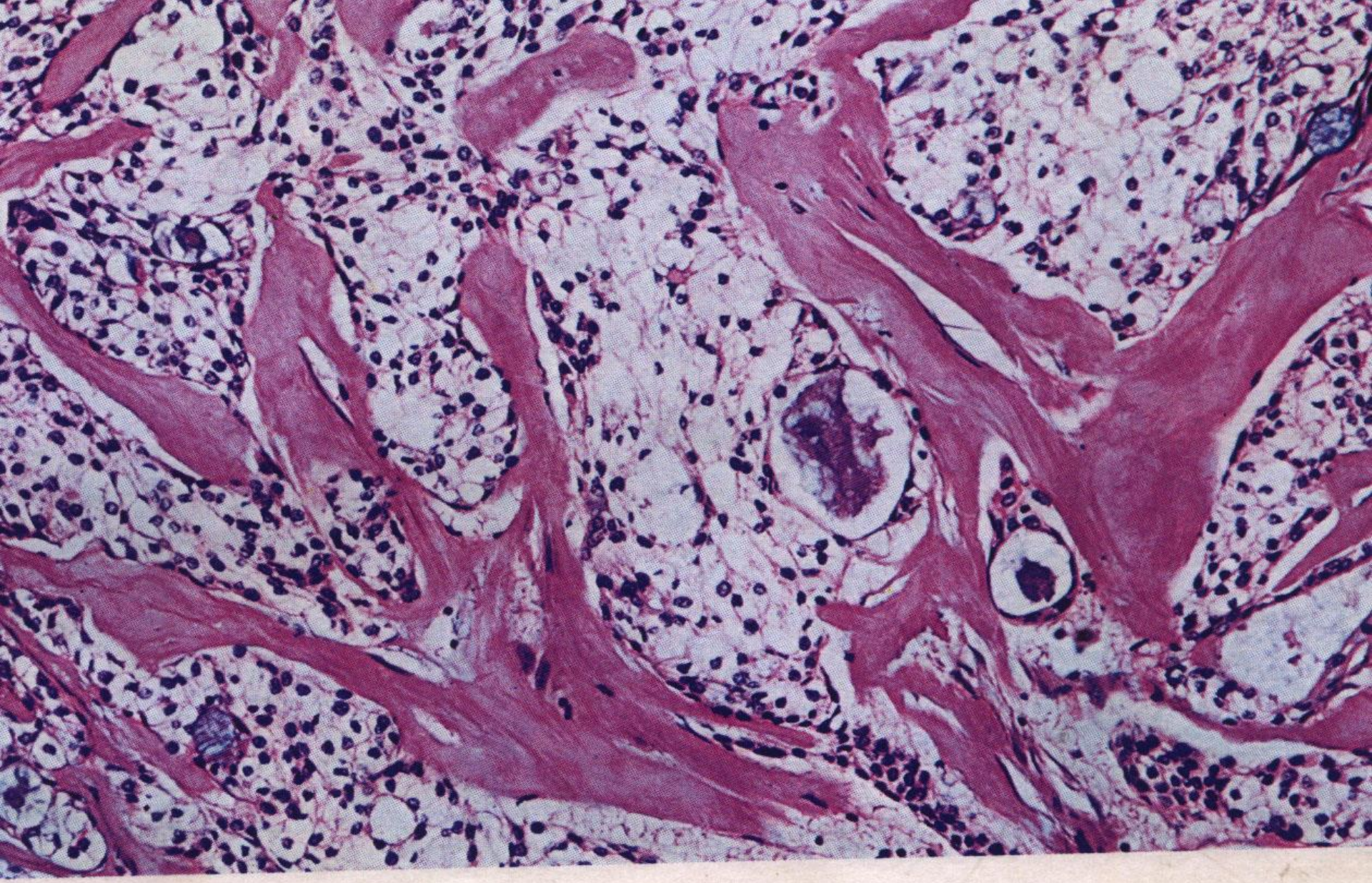


Fig. 22. Mucoepidermoid tumour
Clear-celled type. Some mucus also present

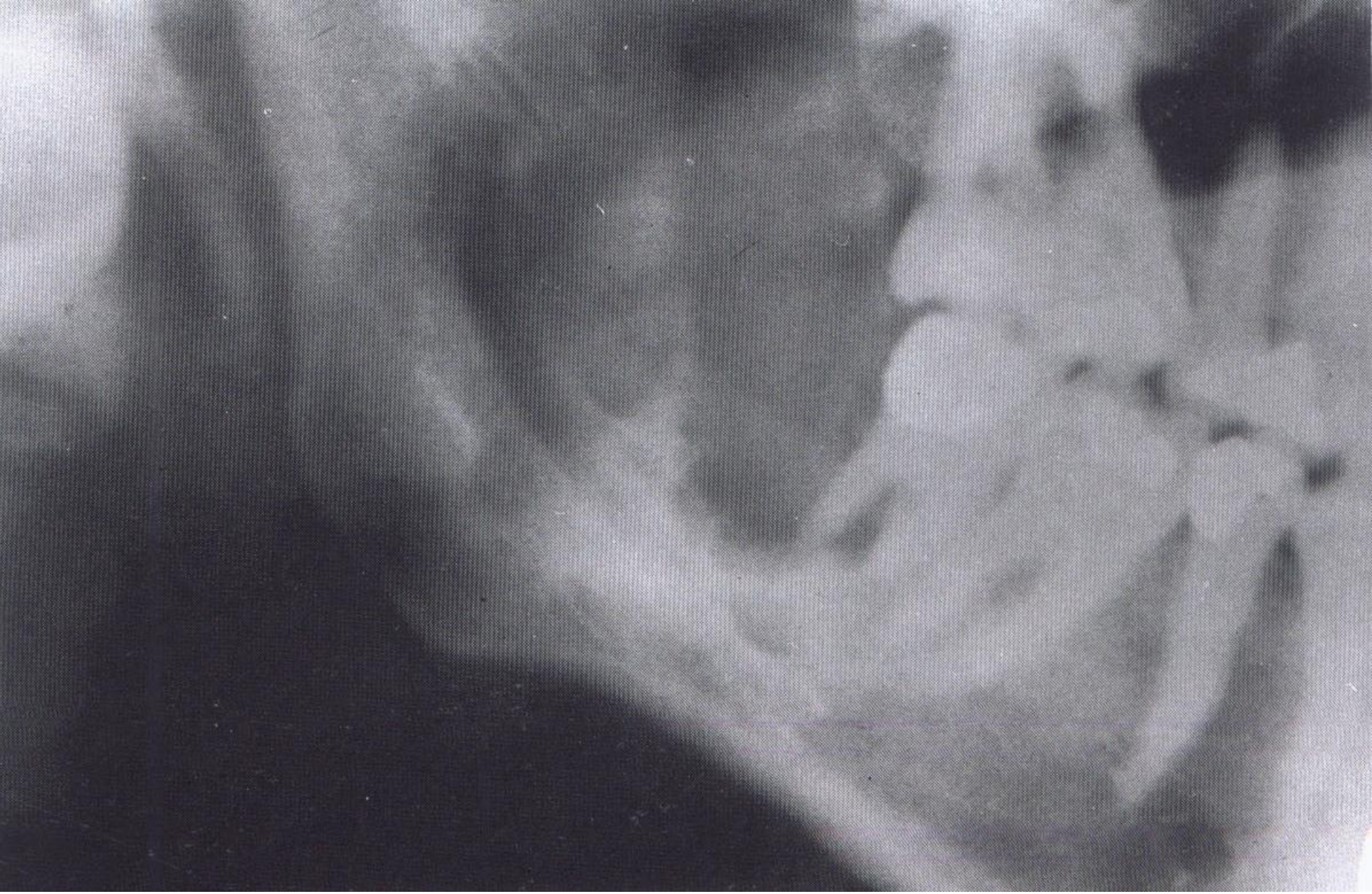
Variants of MEC

❖ Sclerosing mucoepidermoid carcinoma

- This variant is extremely rare, characterized by an intense central sclerosis, usu. With an inflammatory infiltrate at the periphery.
- The sclerosis may obscure the typical morphologic features of these tumors & cause diagnostic difficulties.

❖ Intraosseous mucoepidermoid carcinoma

- When MEC originates within the jaws, it is called intraosseous or central. More common in mandible than maxilla.
- Thought to form by the malignant transformation of the epithelial lining of odontogenic cysts.
- It presents as an asymptomatic radiolucent lesion of the low grade malignancy.



Intraosseous (central) mucoepidermoid carcinoma

ill defined multilocular radiolucency of posterior mandible.

Treatment :

- Conservative excision with preservation of the facial nerve.
- Affected submandibular gland should be removed entirely.
- Concomitant chemotherapy and post-operative irradiation might be helpful.

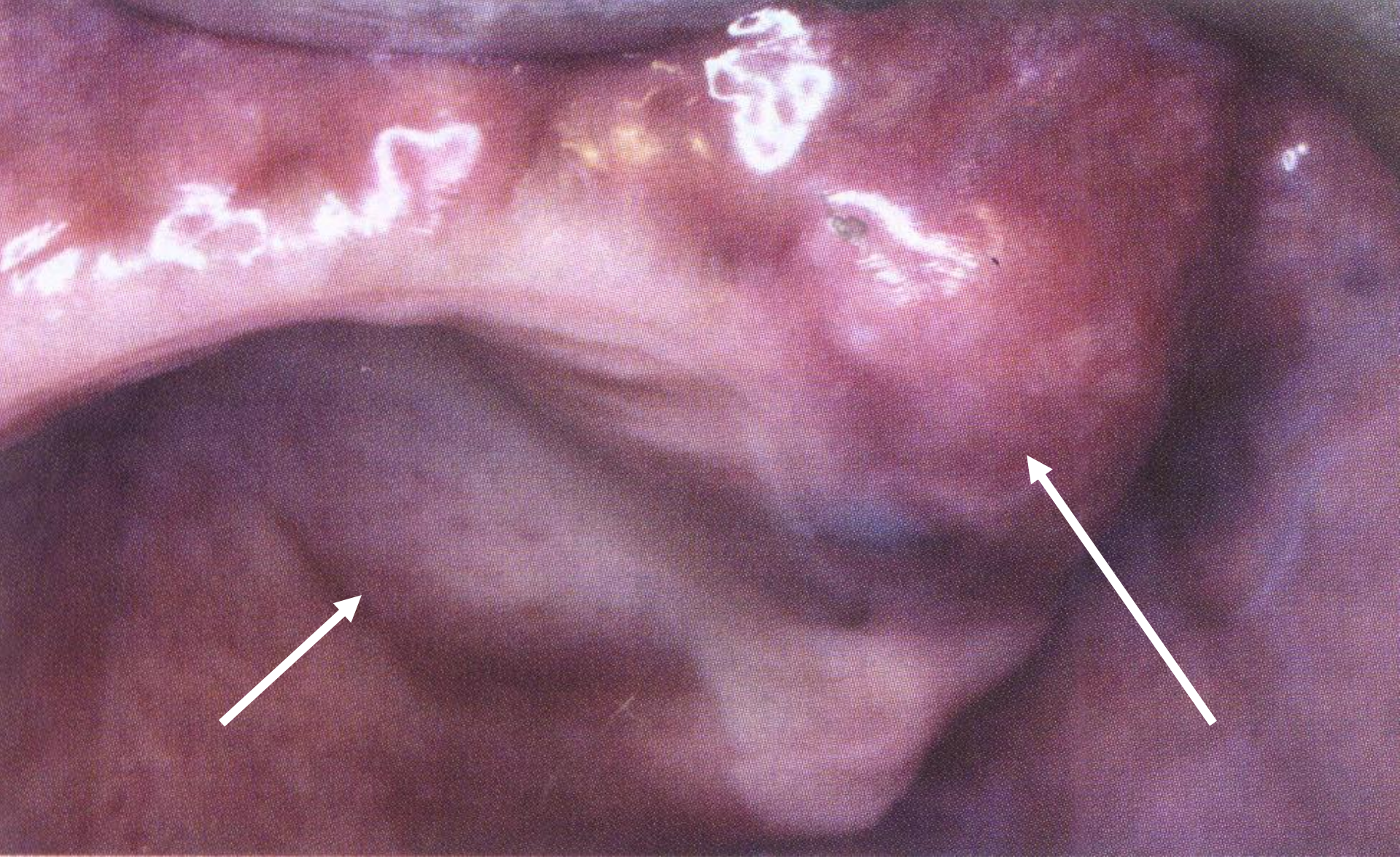
Adenoid cystic carcinoma (cylindroma, basaloid mixed tumor)

- Slow growing but aggressive neoplasm.
- High recurrence rate
- Characterized by proliferation of ductal

(luminal) and myoepithelial cells in various patterns.

Clinical features :

- Parotid, submaxillary and accessory glands in the palate and tongue are the most commonly involved glands.
- Occurs during the 5^{th} and 6^{th} decade of life
- Common in females.
- Early local pain, facial nerve palsy, fixation to deeper structures and local invasion are some of the presenting features.
- Has marked tendency to spread through perineural space and usually invades well beyond the clinically apparent border.



Adenoid cystic carcinoma- painful mass of hard palate and maxillary alveolar ridge.

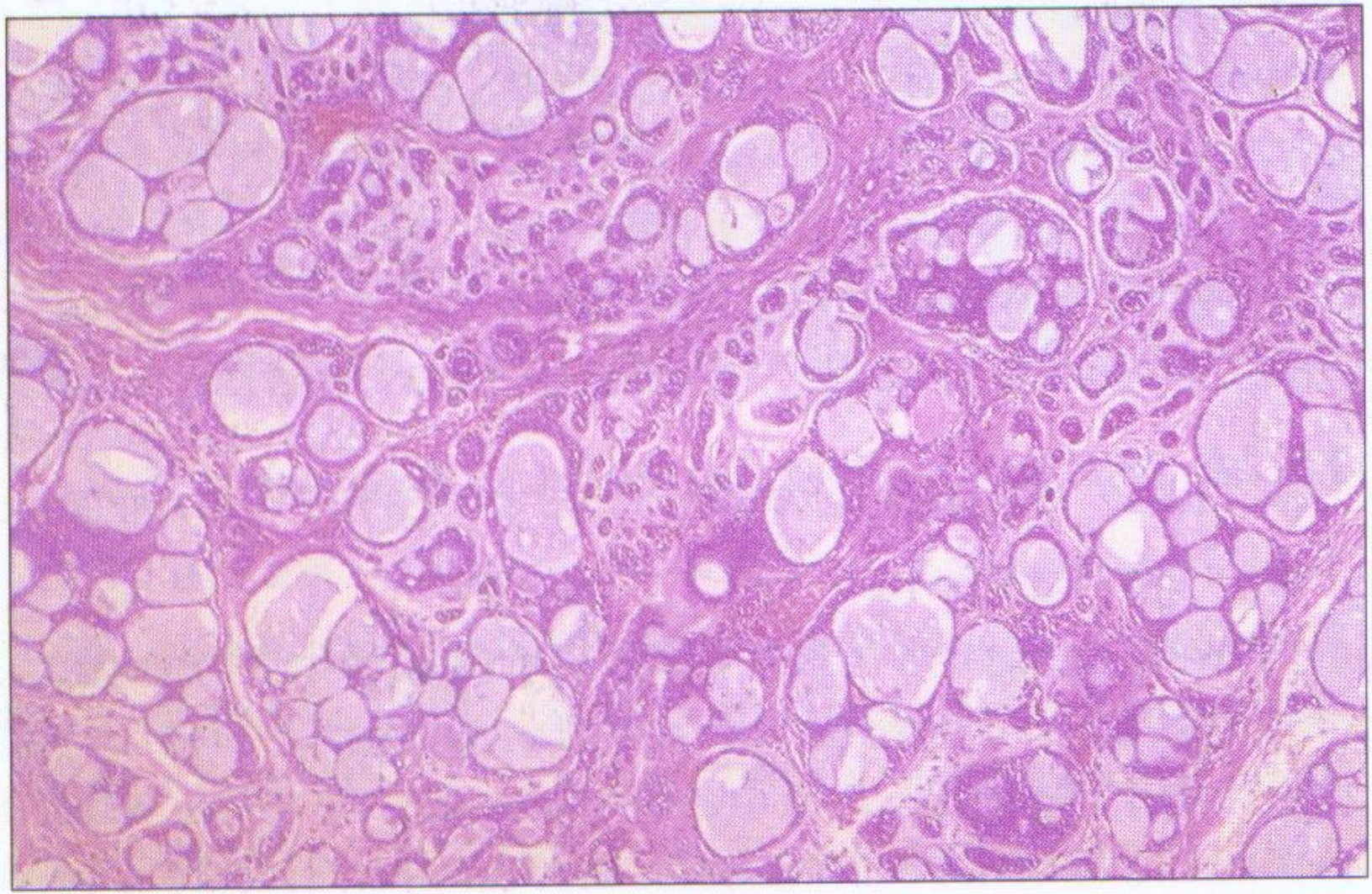
Histological features

- Composed of myoepithelial cells and ductal cells
- 3 growth patterns have been described

✓ **Cribriform pattern (classical)** shows basaloid epithelial cell nests that form multiple cylindrical cyst like patterns resembling a Swiss cheese or honey comb pattern. The lumen contains PAS positive mucopolysaccharide secretion.

✓ **Tubular pattern** shows tubular structures that are lined by stratified cuboidal epithelium.

✓ **Solid pattern** shows solid group of cuboidal cells with little tendency towards duct or cyst formation. It is the least common pattern. It is a high grade lesion with 100 % recurrence rates.



15.39 Adenoid cystic carcinoma.

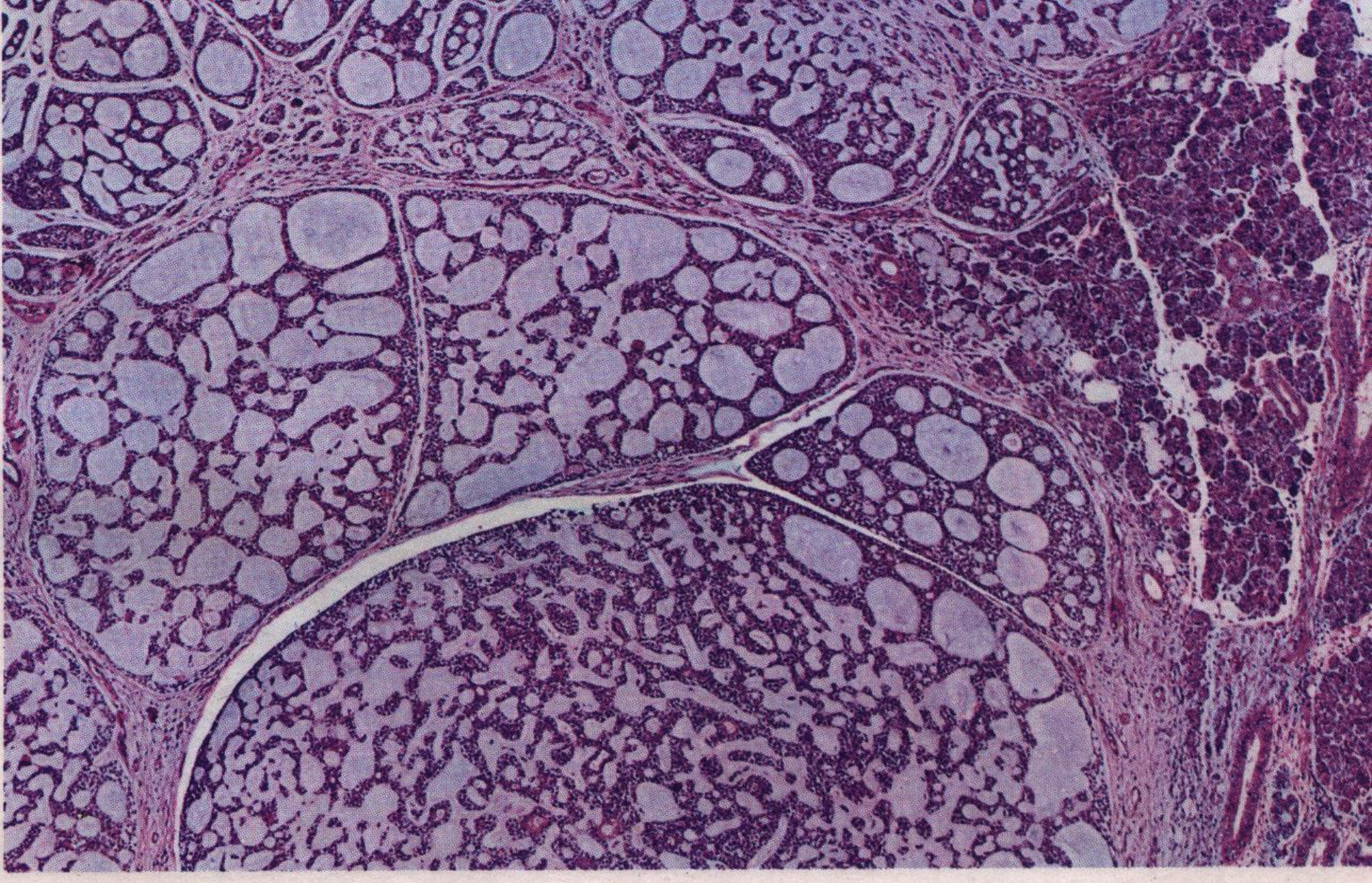
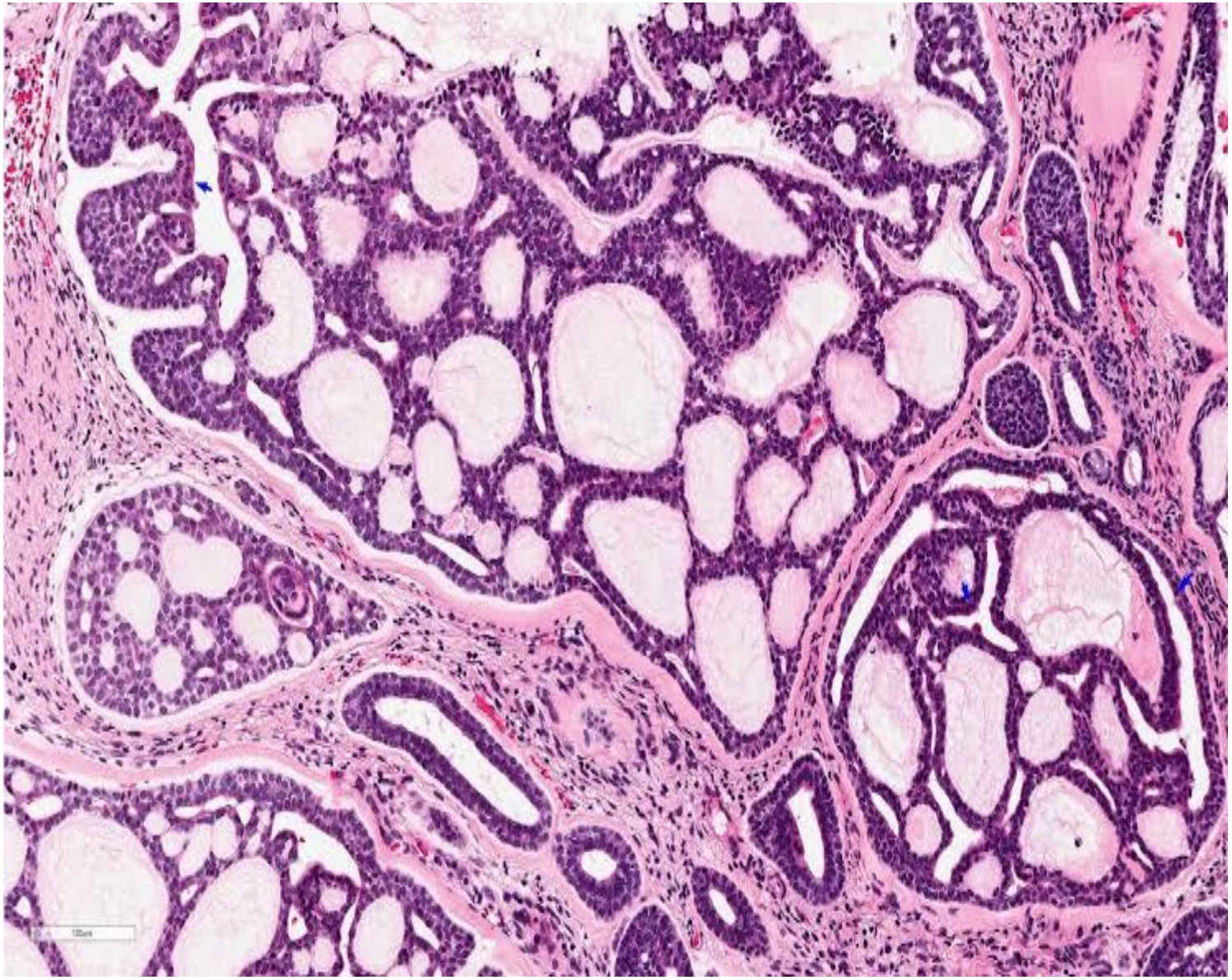
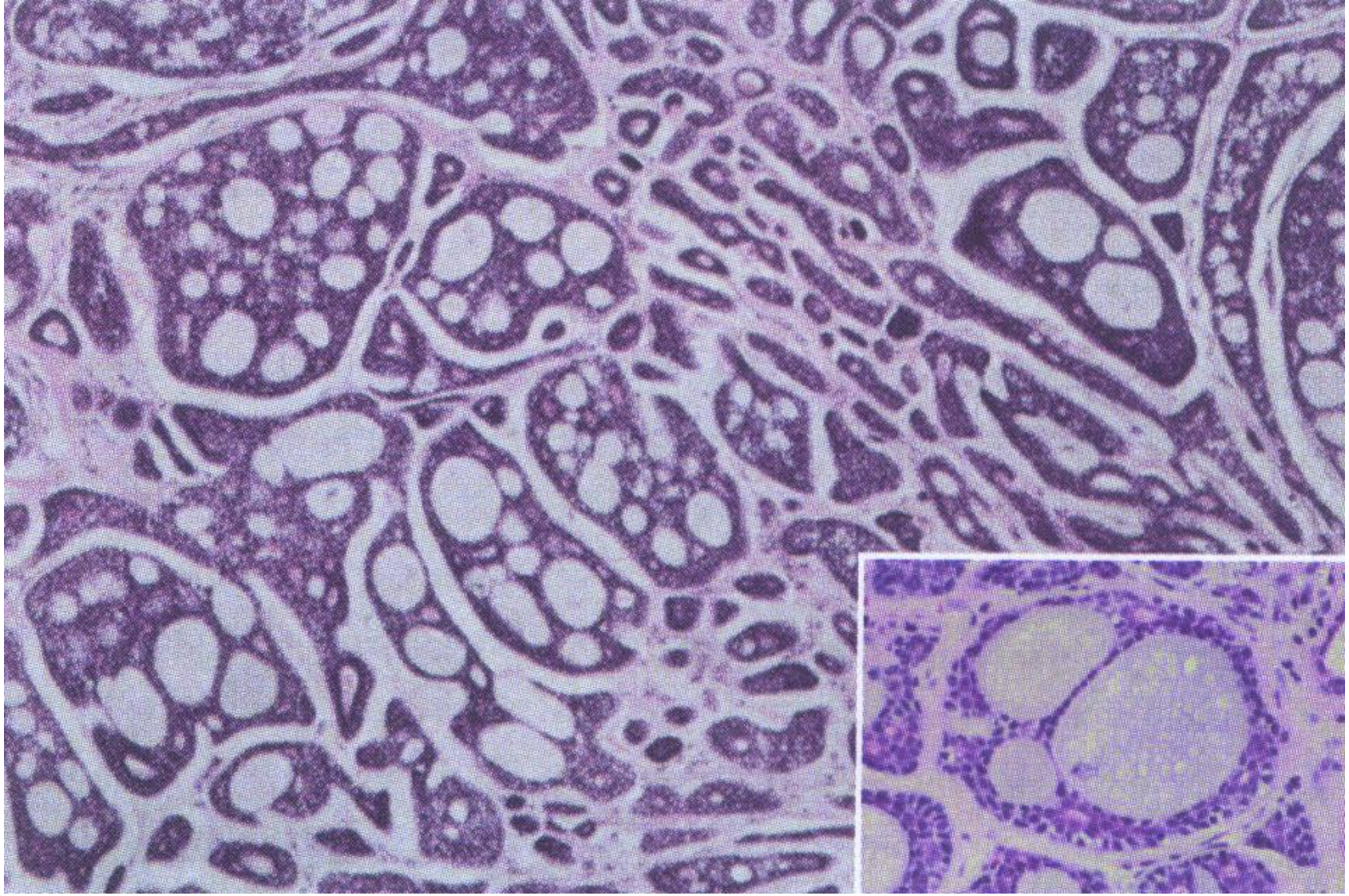
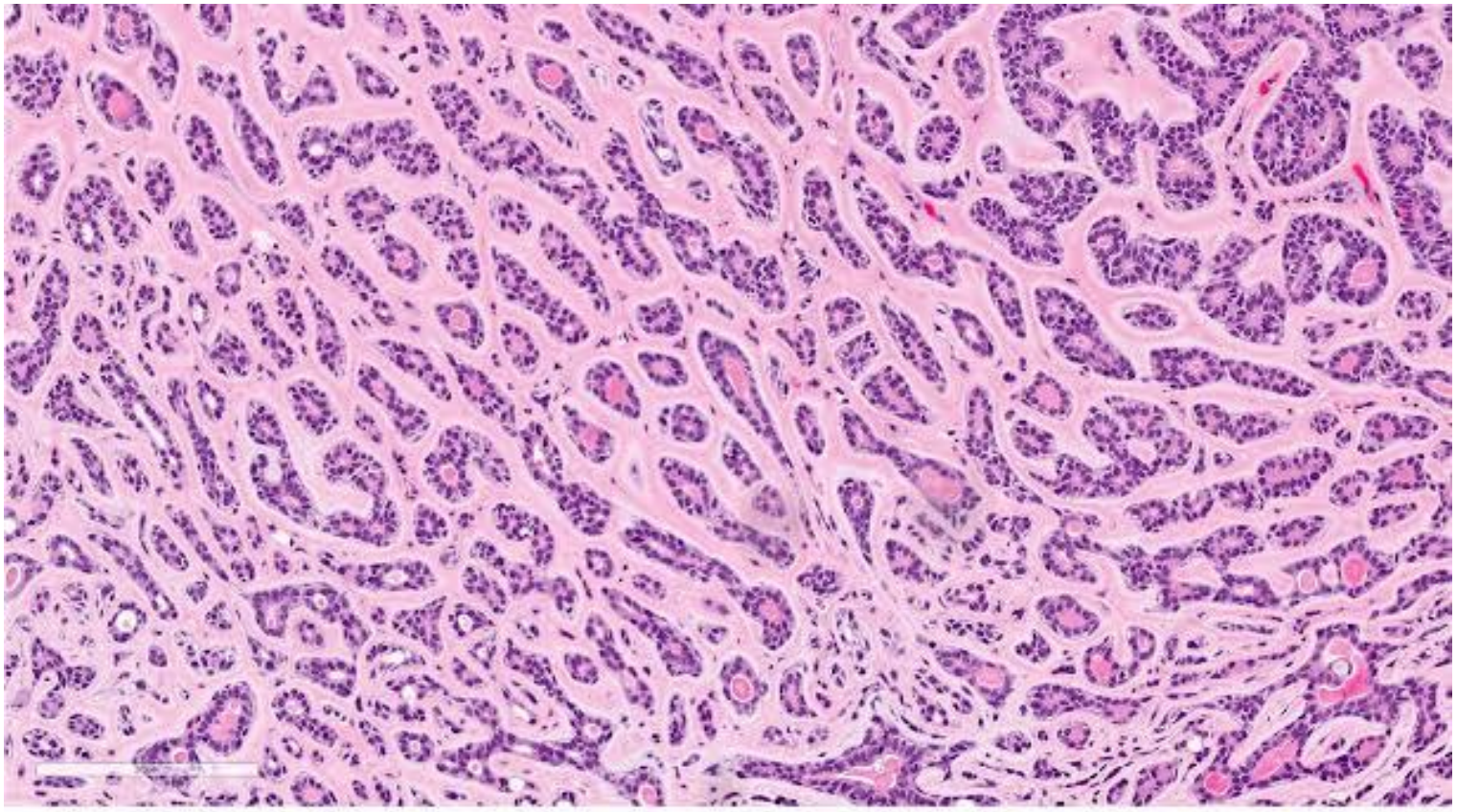


Fig. 30. Adenoid cystic carcinoma
Characteristic cribriform pattern

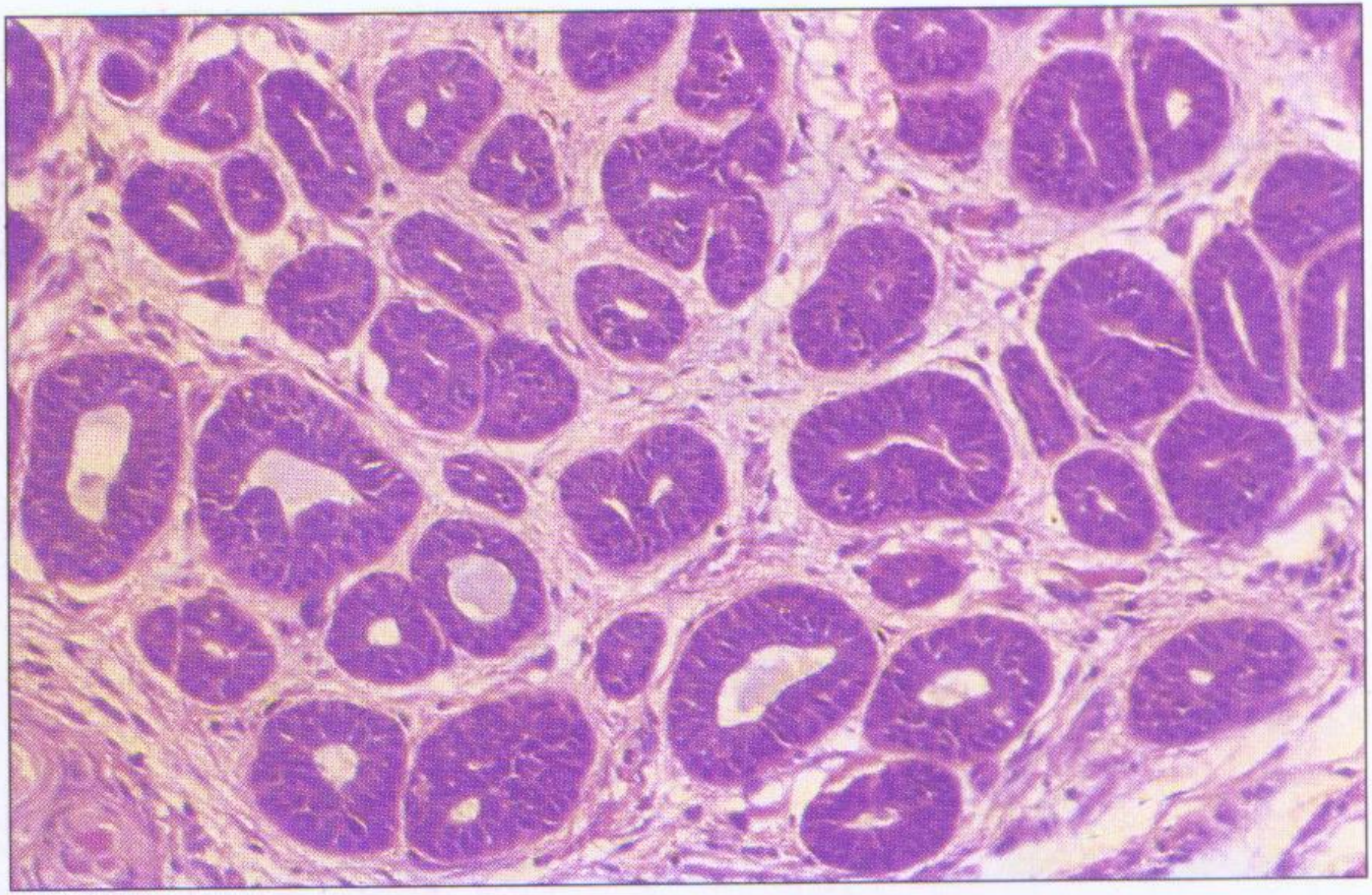




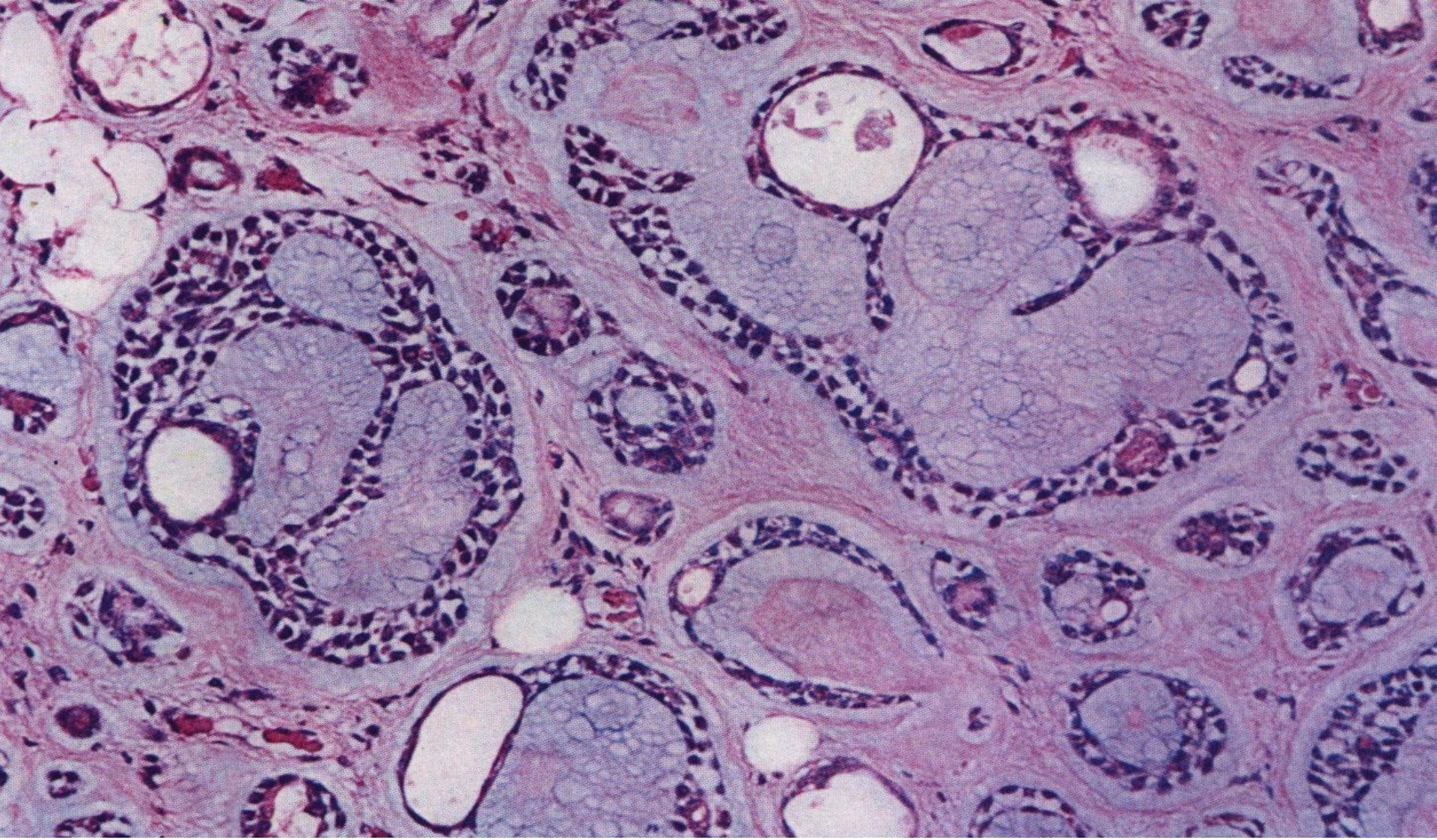
Adenoid cystic carcinoma – islands of hyperchromatic cells forming cribriform & tubular structures. Inset shows a small cribriform island.



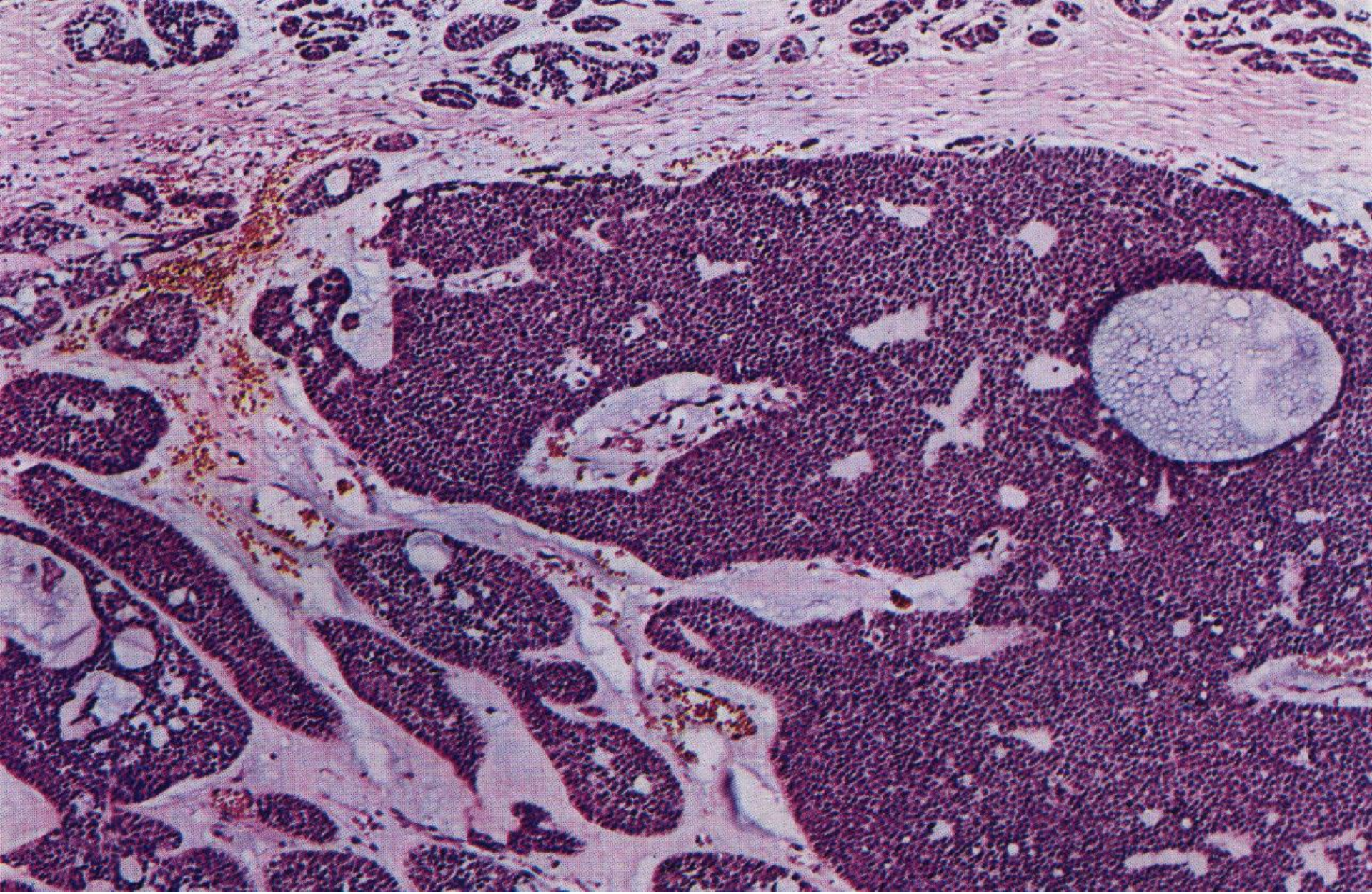
Tubular pattern is composed of inner ductal and outer myoepithelial cells. The ductal cells are cuboidal with eosinophilic cytoplasm. The myoepithelial cells are angulated and basaloid.



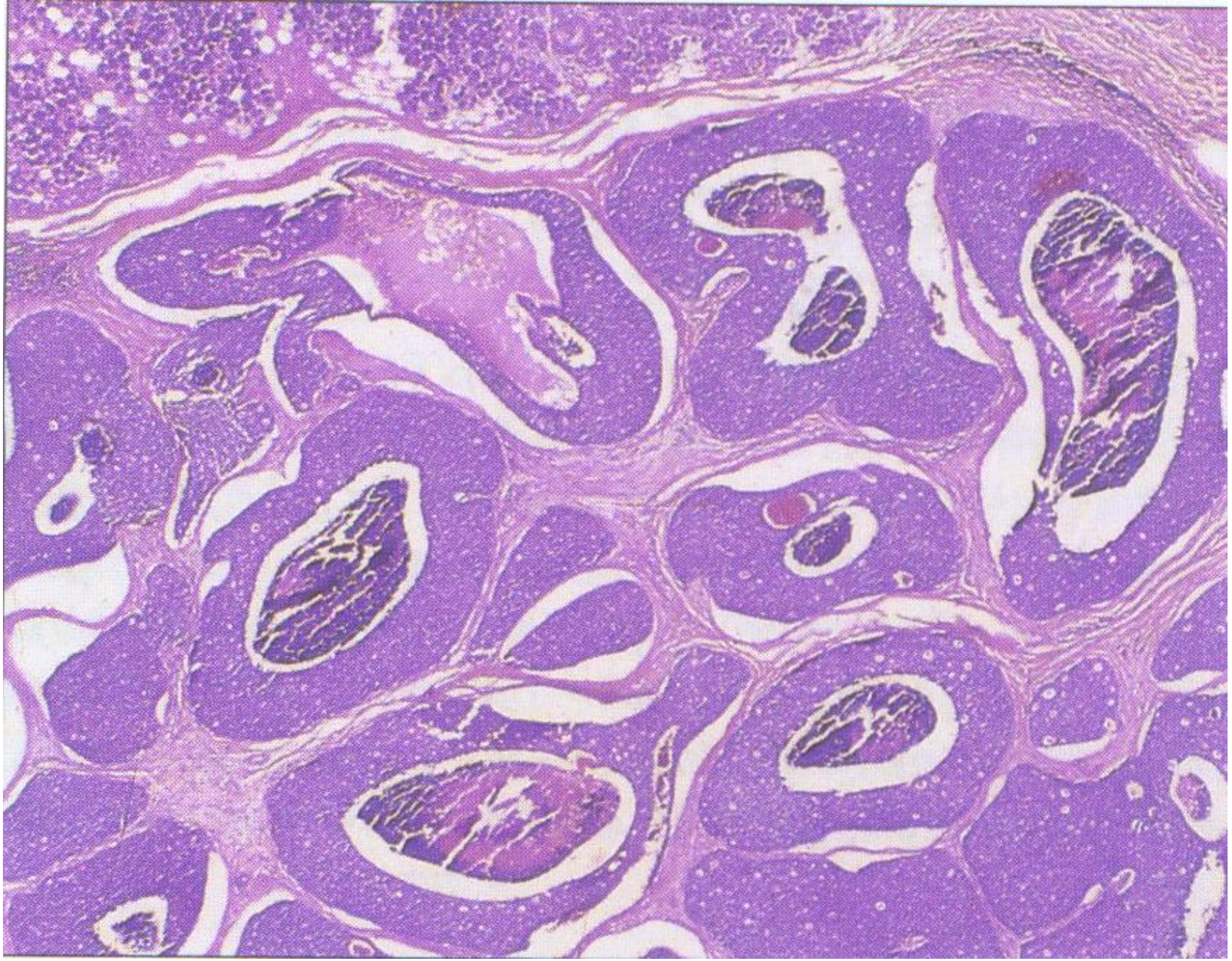
15.41 Adenoid cystic carcinoma — tubular variant.



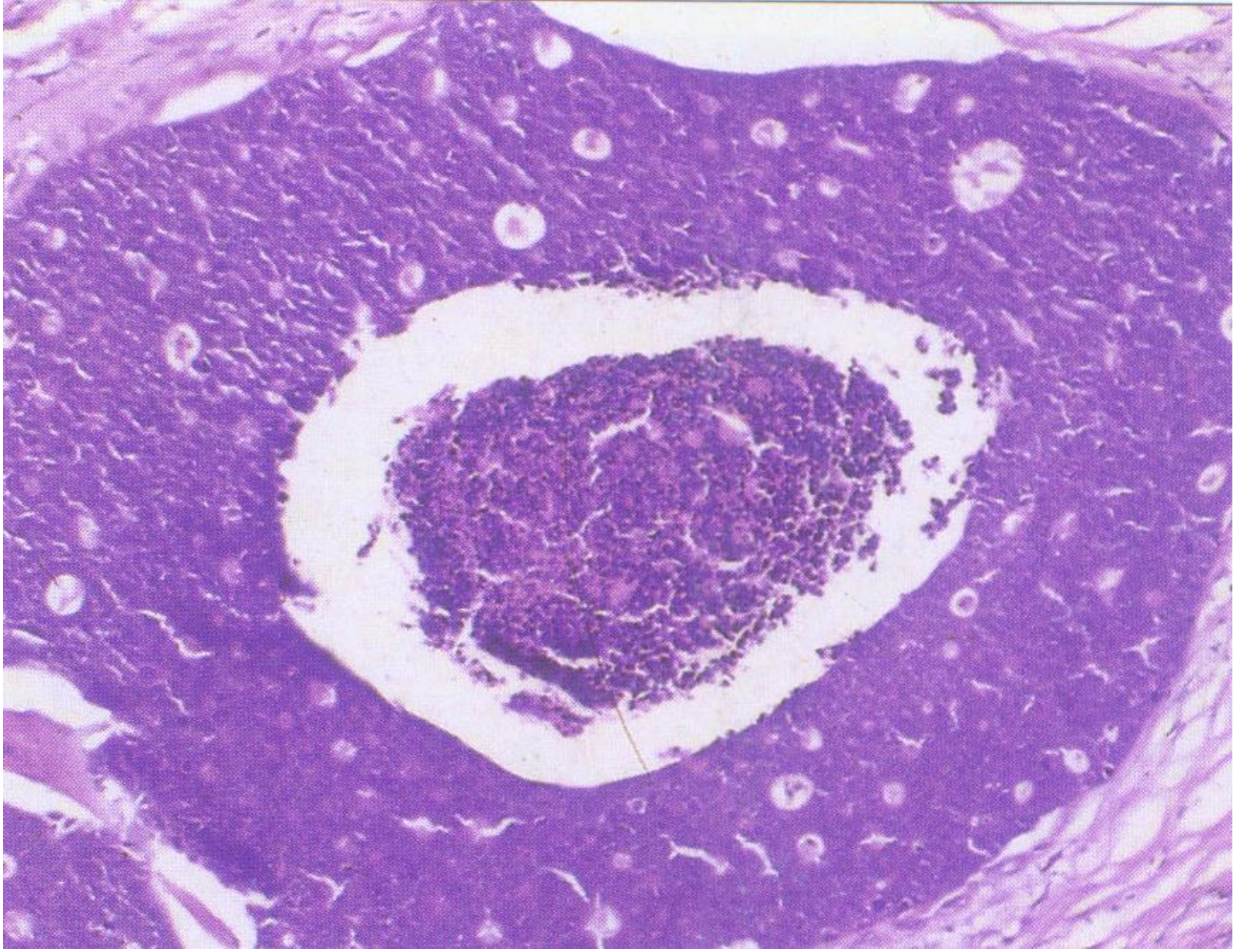
Adenoid cystic carcinoma – myoepithelial cells around dilated ducts and enclosing areas of mucoid and hyaline stroma.



Adenoid cystic carcinoma – a more solid variant.



Adenoid cystic carcinoma – solid variant



Adenoid cystic carcinoma – solid variant (high power)

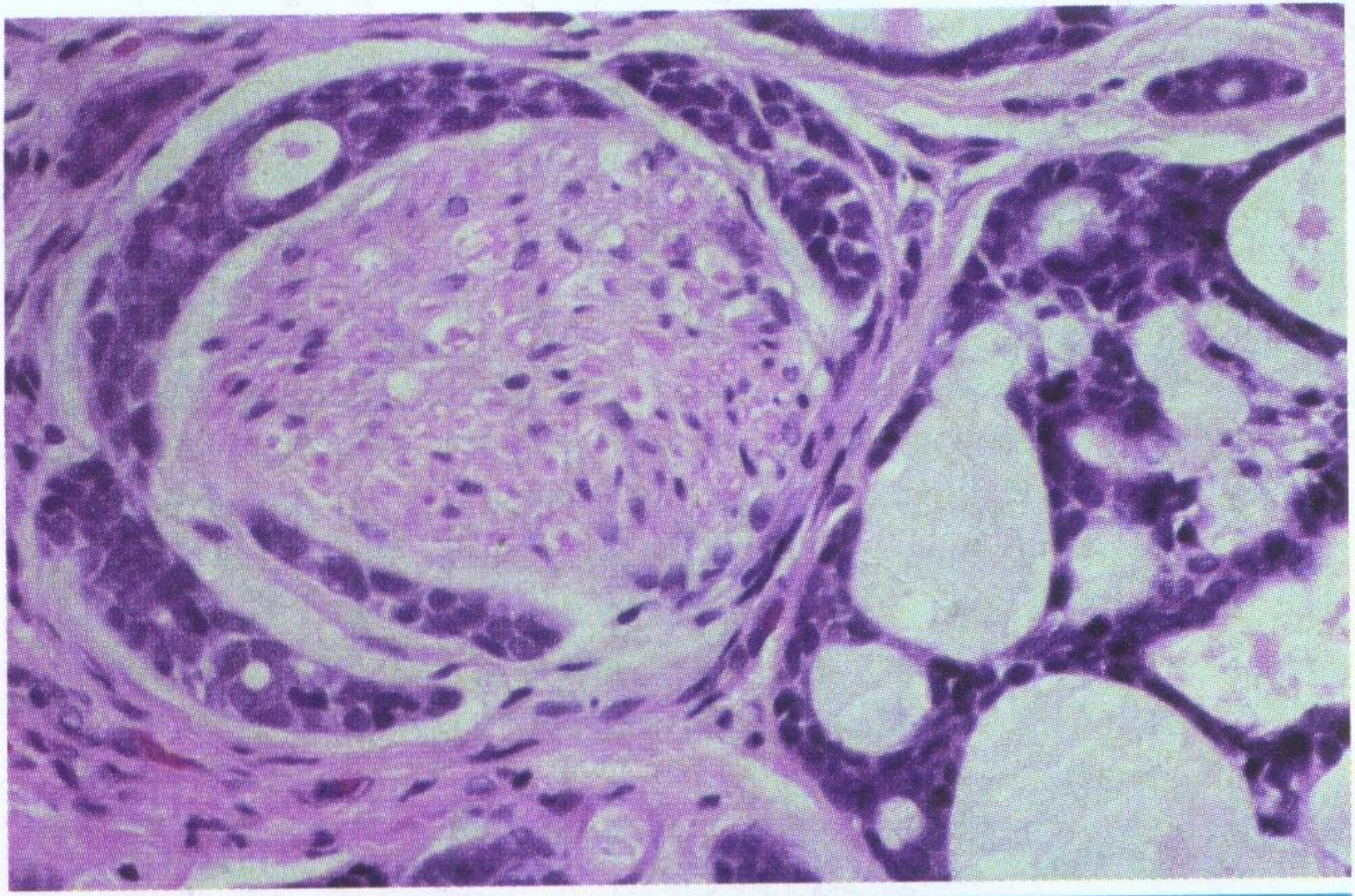
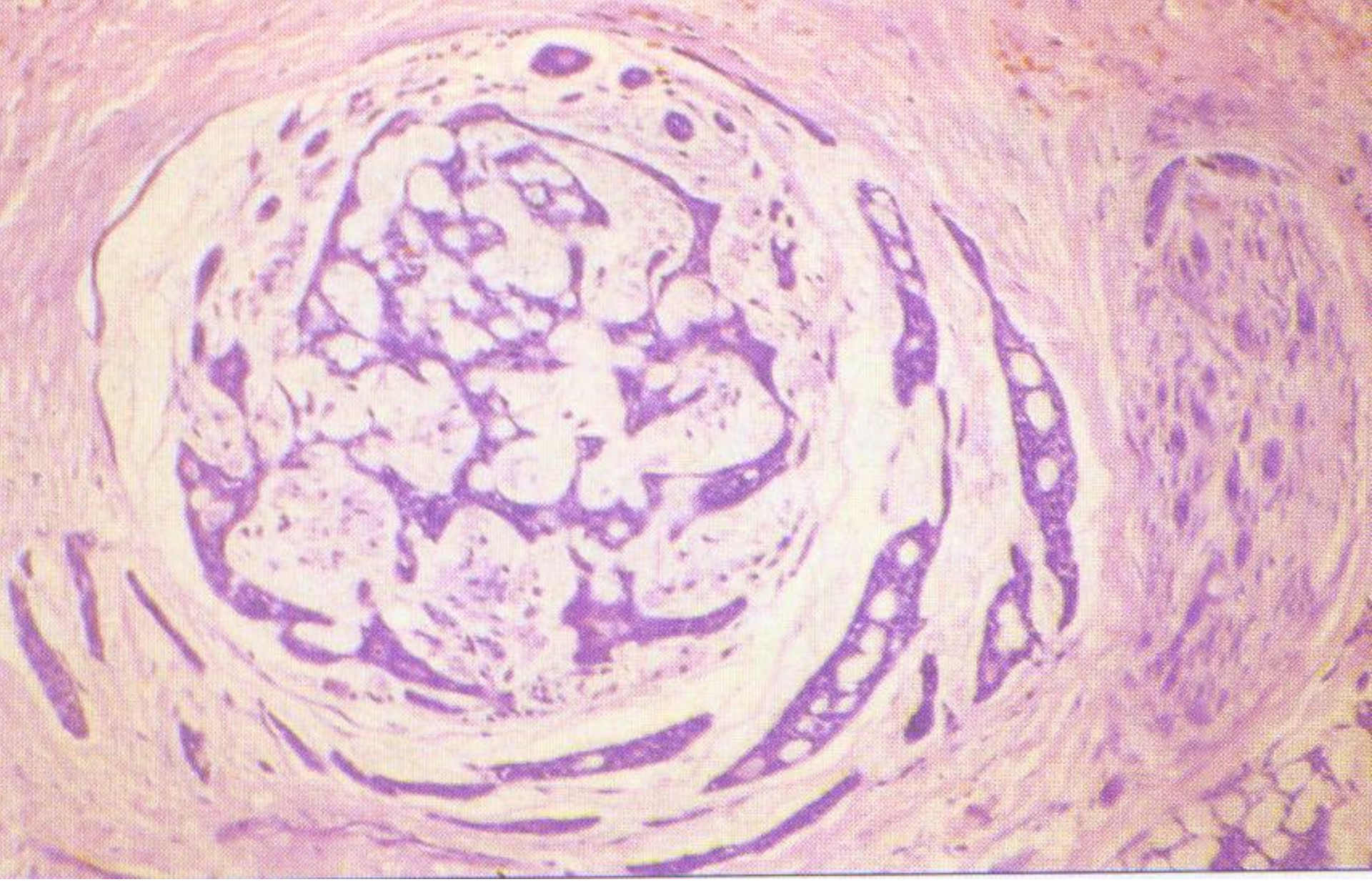


Figure 11-72 ◆ Adenoid cystic carcinoma. Perineural invasion.



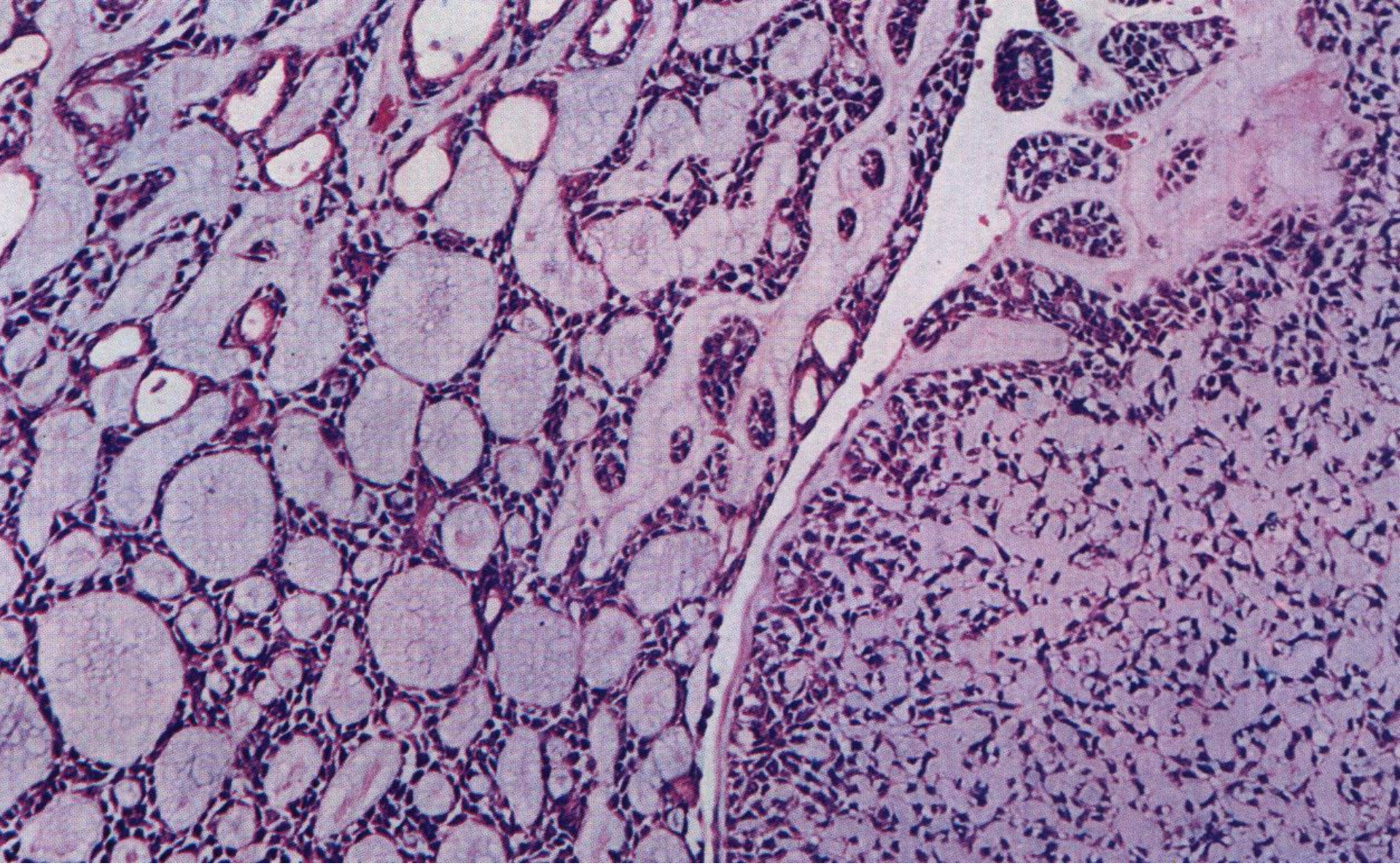
Adenoid cystic carcinoma – showing perineural invasion.

Dedifferentiated adenoid cystic cell carcinoma :

- A rare variant characterized histologically by 2 components –
- ✓ Conventional low grade adenoid cystic carcinoma
- ✓ High grade dedifferentiated carcinoma.
- Because of the frequent recurrence and metastasis, the clinical course is short with a predominant solid growth pattern.
- Histologically the low grade tumor merges gradually with the extensive dedifferentiated component (composed of solid sheets and cords of anaplastic tumor cells with focal gland formation.)

Treatment –

- Chiefly surgical excision, but in some cases coupling with radiotherapy has also proved helpful.
- Overall prognosis is not good.



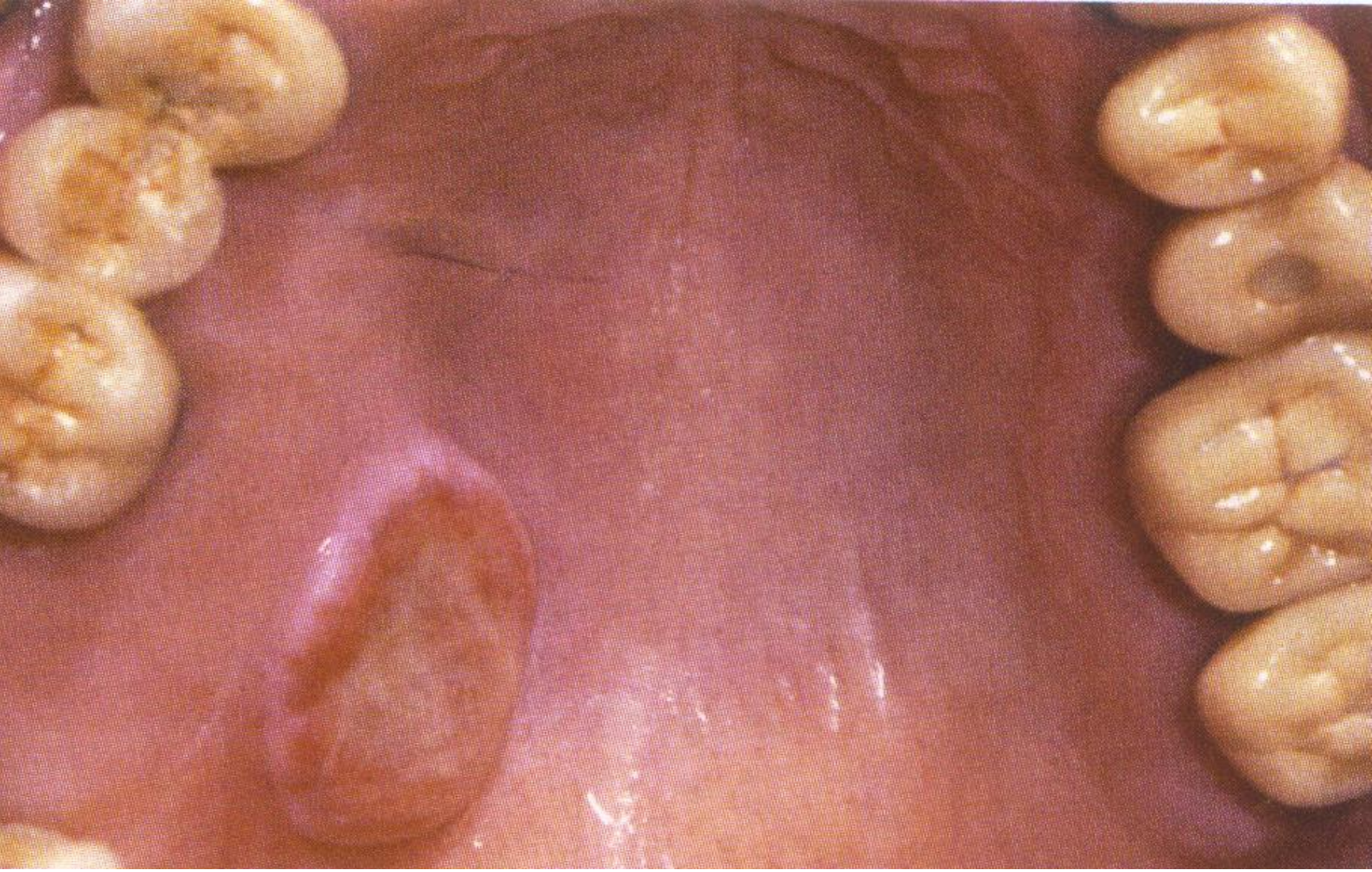
Adenoid cystic carcinoma – the dedifferentiated variant on the right.

Polymorphous low grade adenocarcinoma (PLGA)

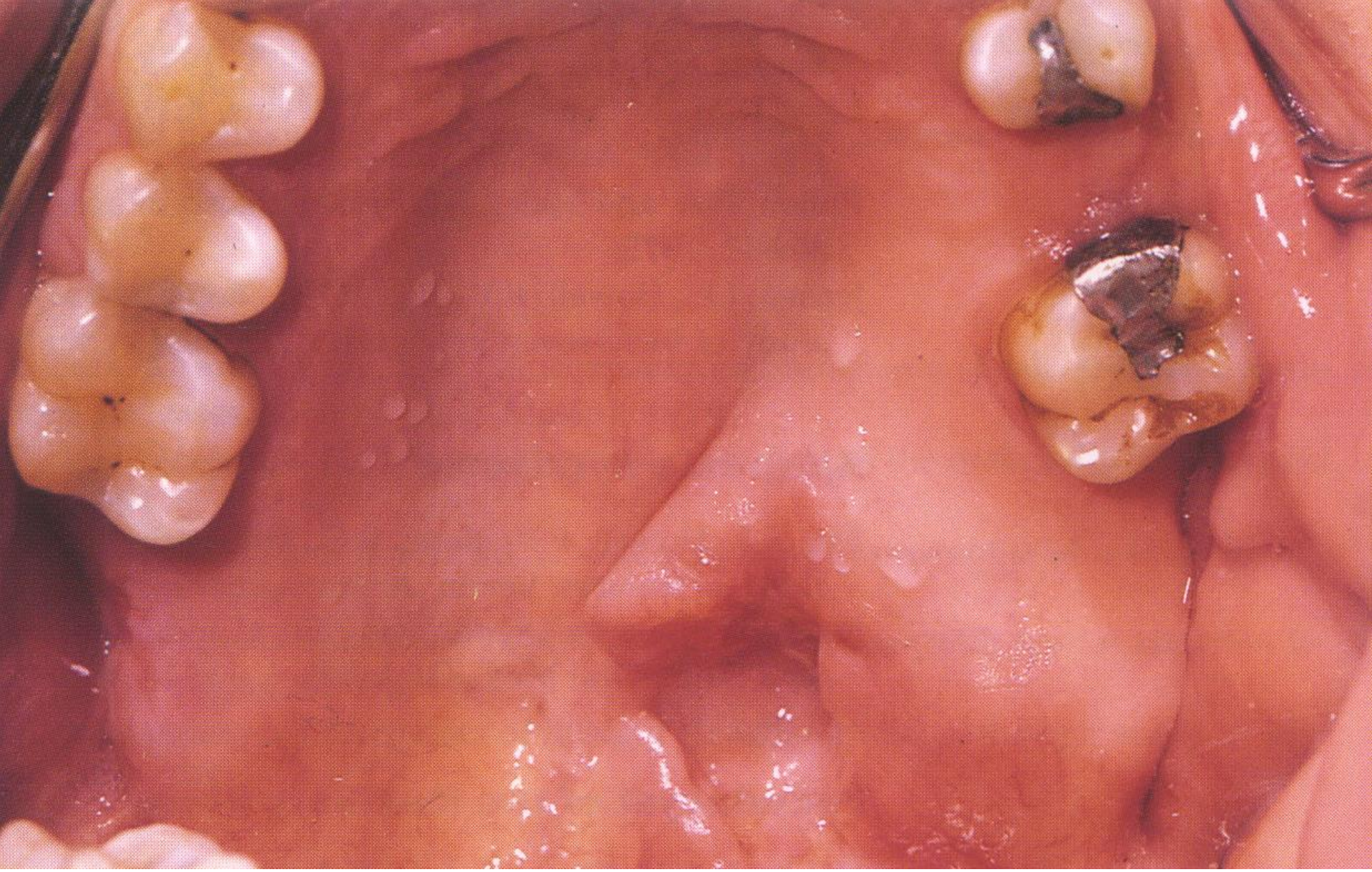
- Limited to minor salivary gland sites.
- Characterized by bland, uniform nuclear features, infiltrative growth and perineural infiltration.

Clinical features :

- Average age 59 years.
- Female : male = 2 :1.
- Typically presents as a firm, non tender swelling involving the mucosa of the cheek, palate or upper lip.



Polymorphous low grade adenocarcinoma – ulcerated mass of the posterior lateral hard palate



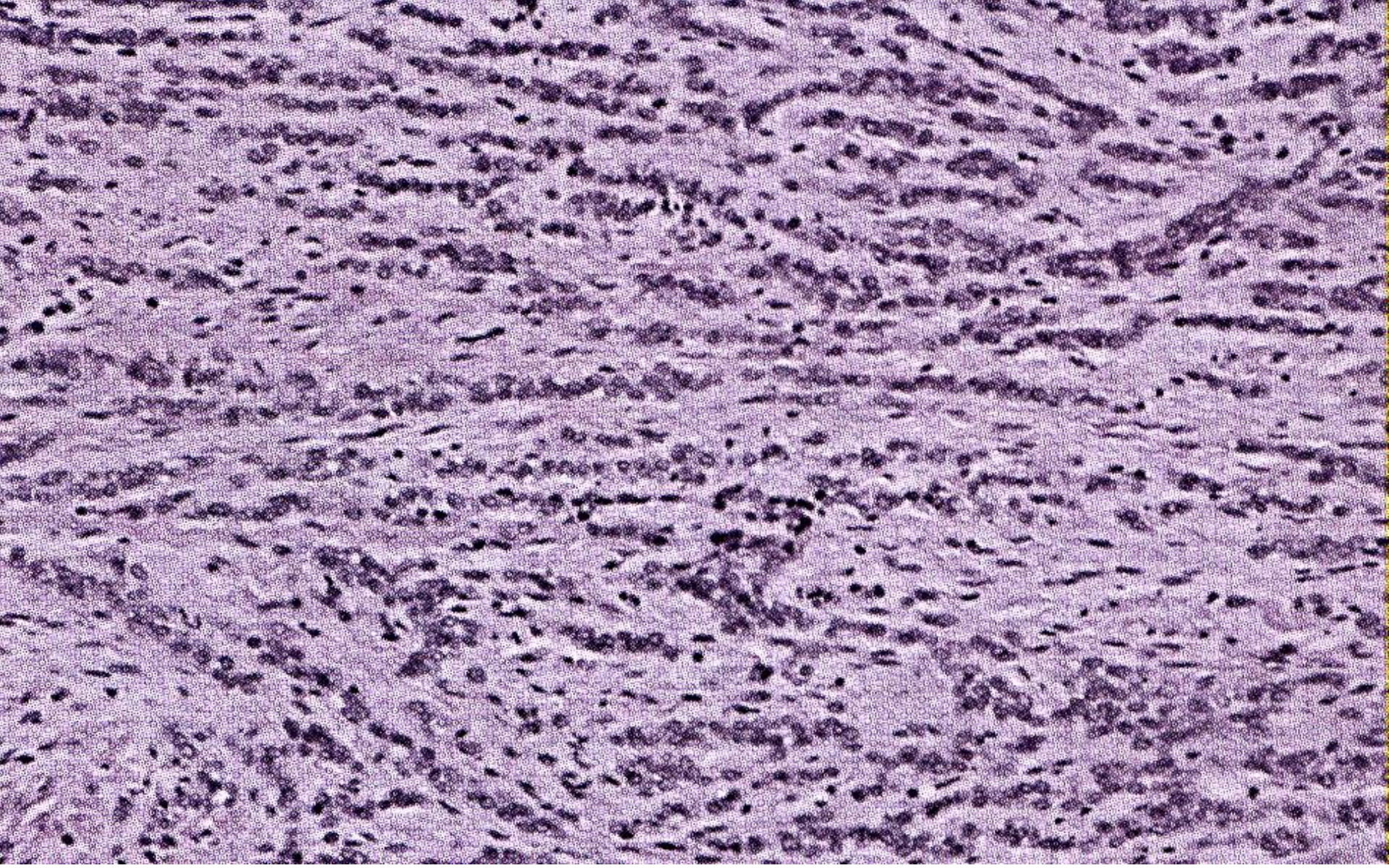
Polymorphous low grade adenocarcinoma
large firm swelling of hard and soft palates.

Histologic features :

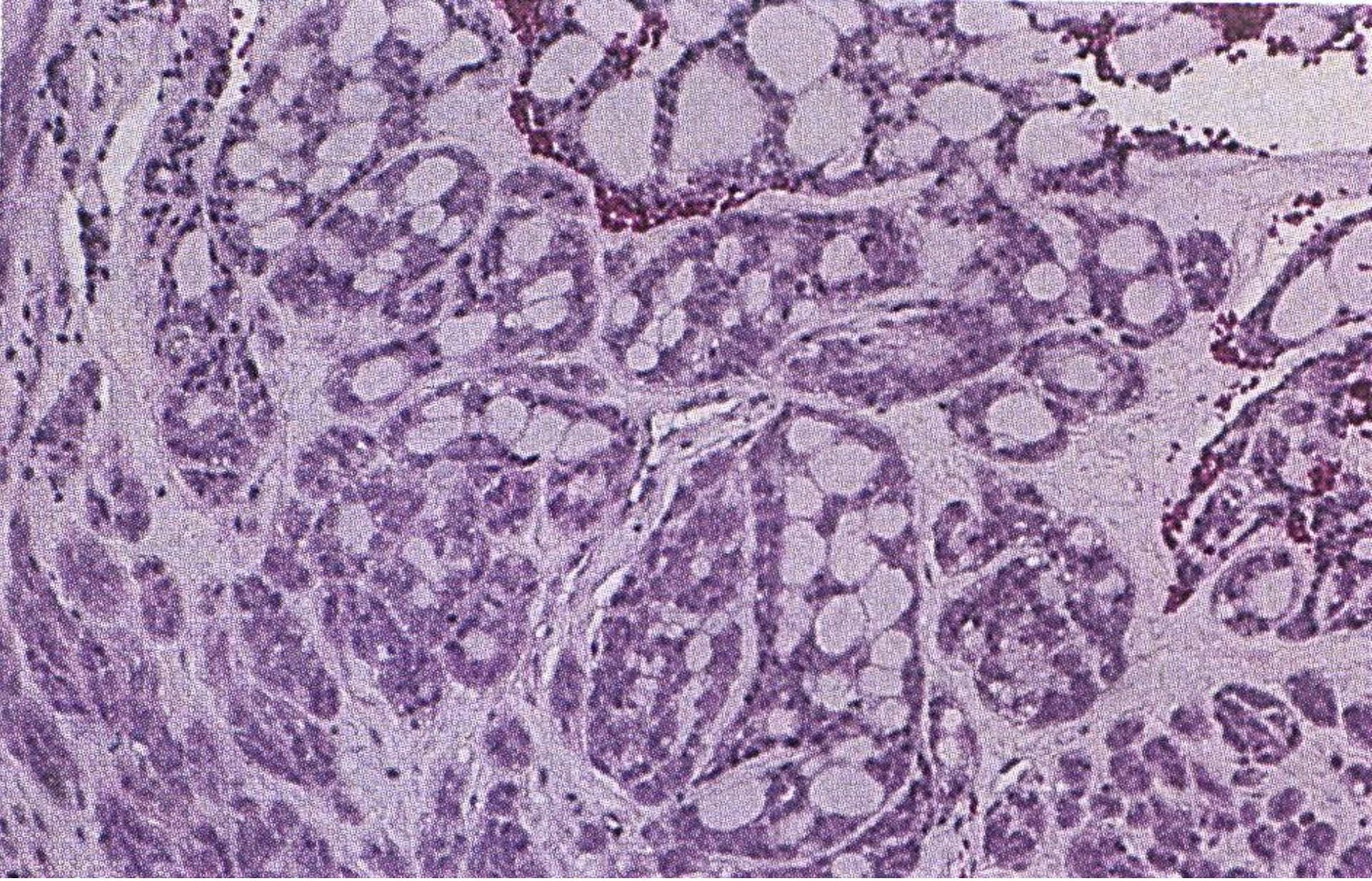
- Well circumscribed but unencapsulated and infiltrate into adjacent structures.
- Four types of growth patterns are seen – solid, ductal, cystic and tubular.
- Sometimes a cribriform pattern is seen, which resembles adenoid cystic carcinoma.
- Tumor is composed of cuboidal to columnar cells that have uniform ovoid to spindle shaped nuclei.
- Stroma varies from mucoid to hyaline, and sometimes tumor nests are separated by fibrovascular stroma.
- Perinuclear invasion is common.

Treatment :

- Conservative surgery. prognosis good.



Polymorphous low grade adenocarcinoma – pale staining cells which infiltrate as single-file cords.



Polymorphous low grade adenocarcinoma – cribriform arrangement of uniform tumor cells with pale staining nuclei.

Epithelial- myoepithelial carcinoma

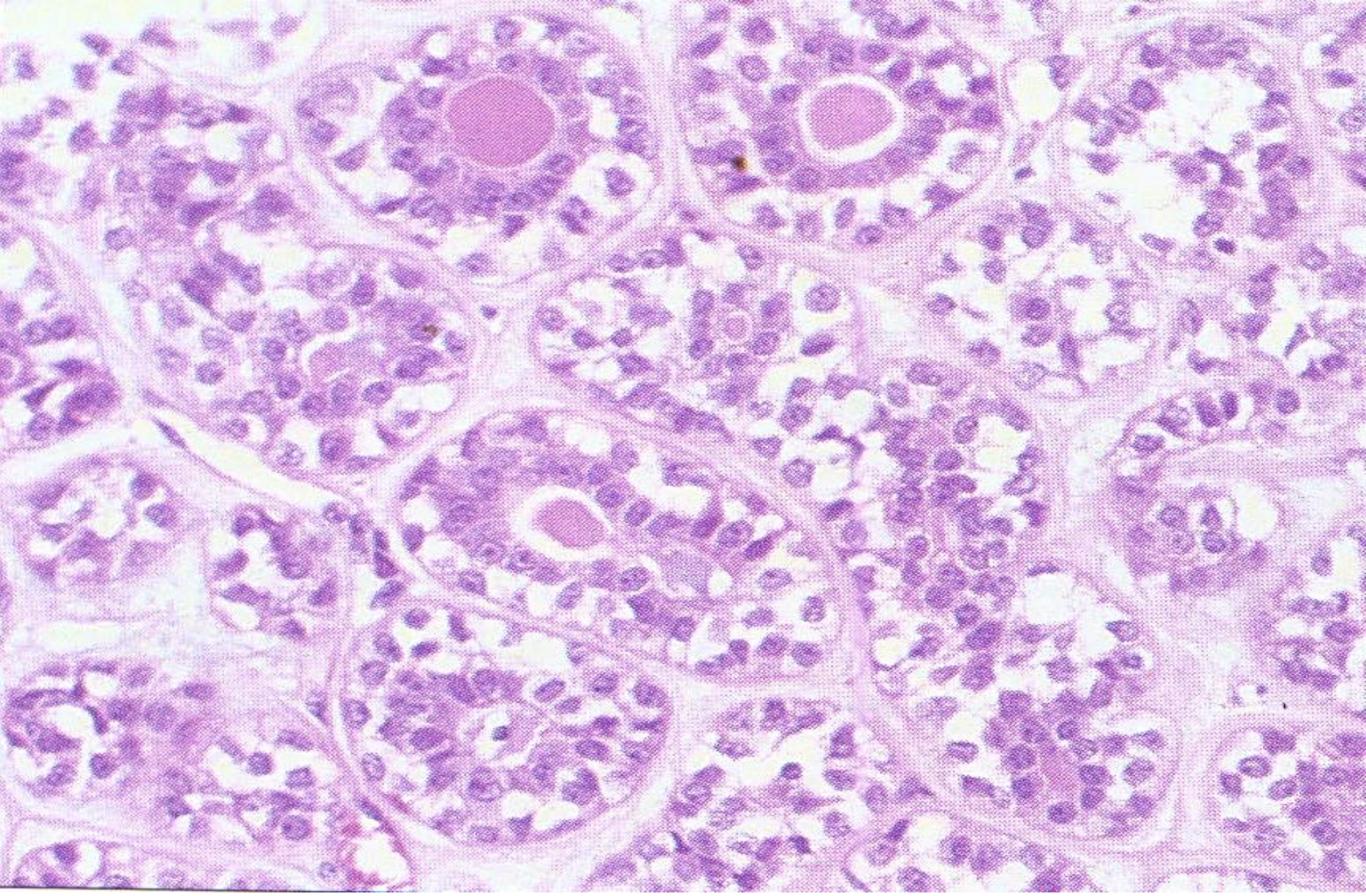
- A biphasic low grade epithelial neoplasm, composed of variable proportions of ductal and large clear staining myoepithelial cells.

Clinical features :

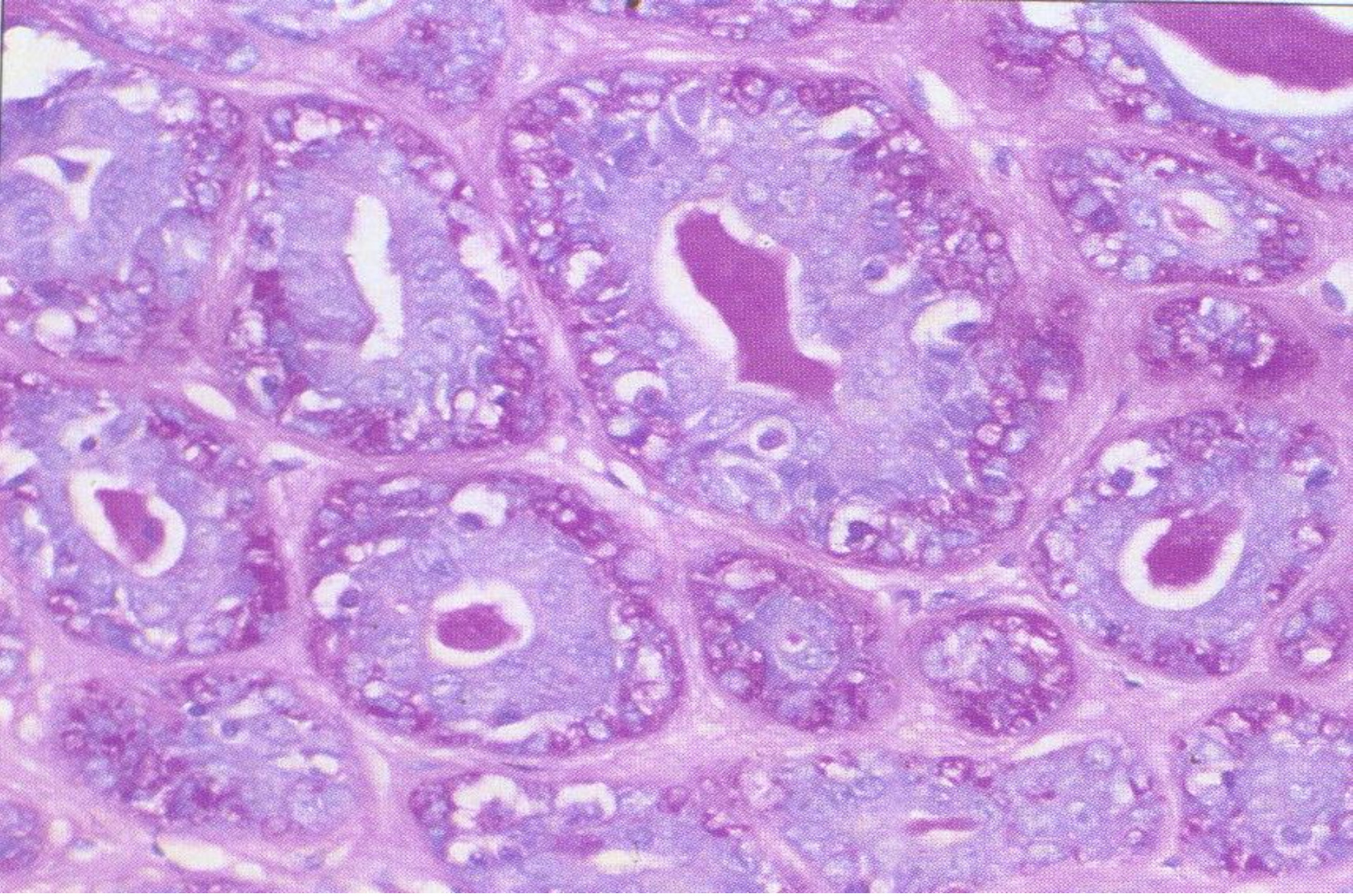
- Mean age- 60 years.
- More in women
- Localized swelling with a steady increase in size.
- May be nasal obstruction and facial deformity.
- Patients with these tumors are at increased risk of a primary second malignancy- either in salivary glands or a separate site (breast or thyroid).

Histologic features :

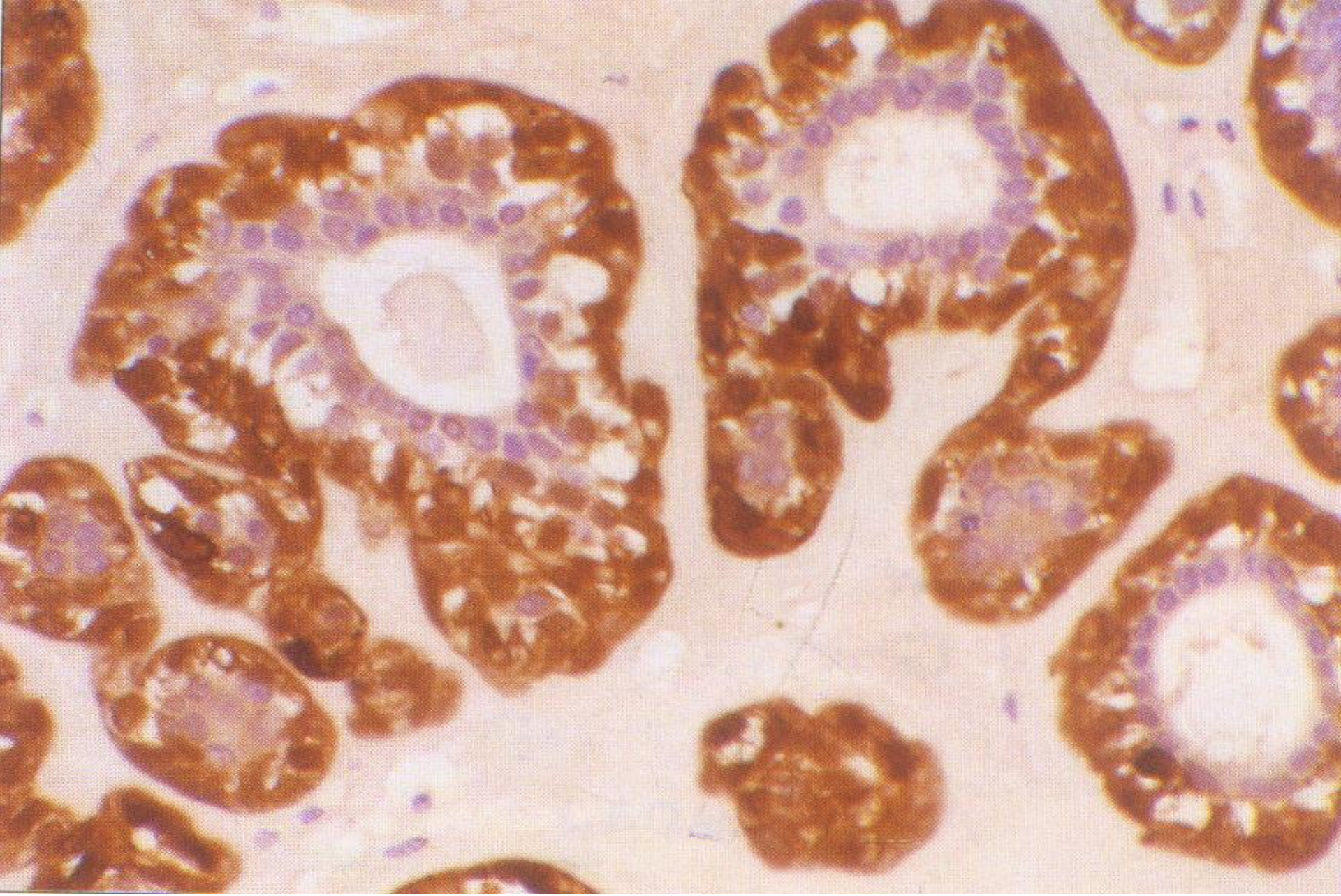
- Vary greatly from solid lobules separated by bands of hyalinized fibrous tissue to irregular, papillary cystic arrangements with tumor cells which partially or completely fill cystic spaces.
- Most tumors show a multinodular growth pattern with islands of tumor cells separated by dense bands of fibrous c.t. These islands are composed of small ducts lined by cuboidal epithelium, surrounded by clear cells which interface with a thickened, hyaline like basement membrane.
- The inner luminal cuboidal cells have finely granular eosinophilic cytoplasm & centrally or basally located nucleus.
- The outer clear myoepithelial cells vary in shape from columnar to ovoid & have a vesicular nucleus located towards the basement membrane.



Epithelial- myoepithelial carcinoma



Epithelial- myoepithelial carcinoma - PAS stain.



Epithelial- myoepithelial carcinoma – S100 stain.

Treatment :

Even with complete surgical resection, recurrences and distant metastases remain a concern.

Basal cell adenocarcinoma

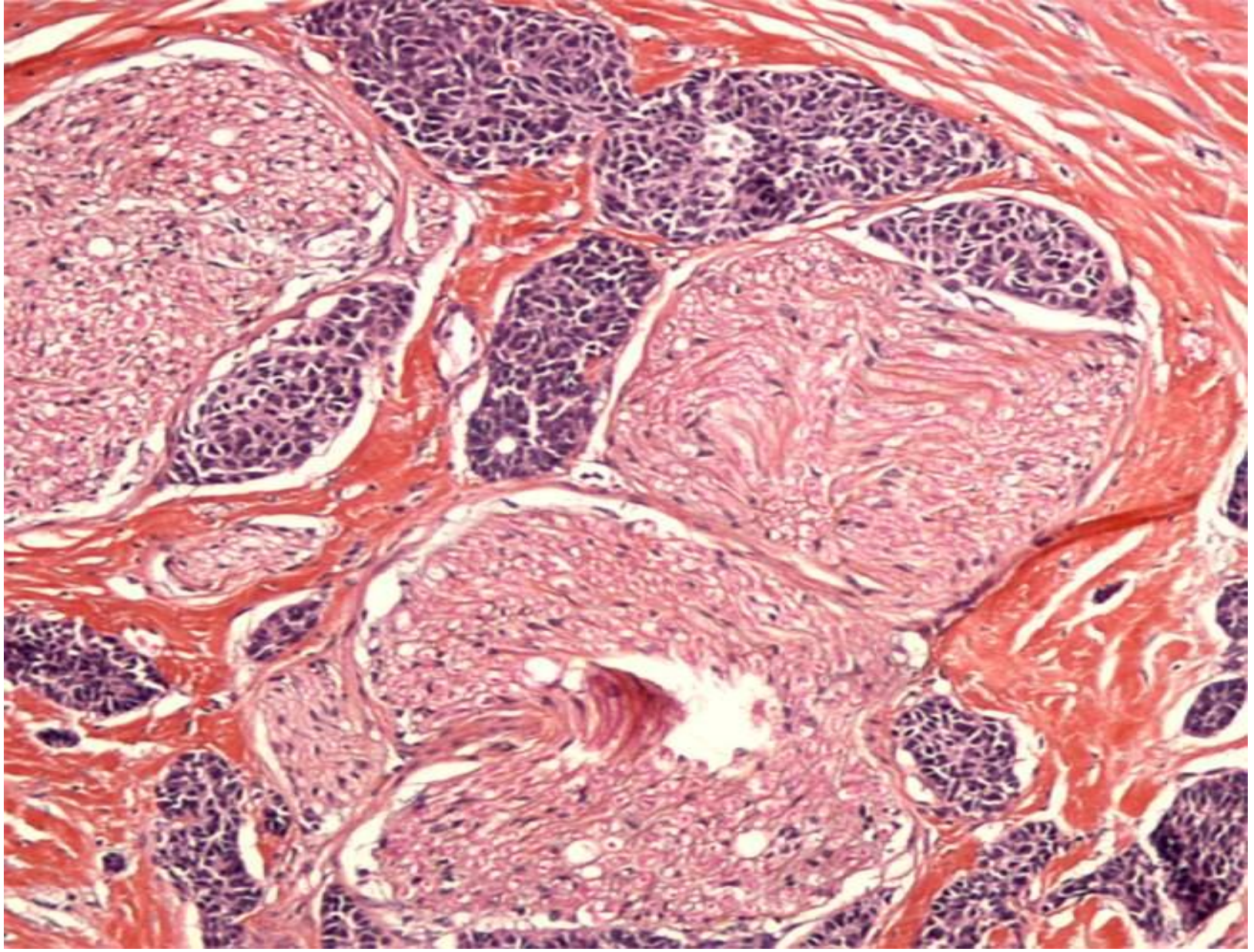
- A low grade malignant neoplasm, cytologically similar to basal cell adenoma, but is infiltrative & has a small potential for metastasis.

Clinical features :

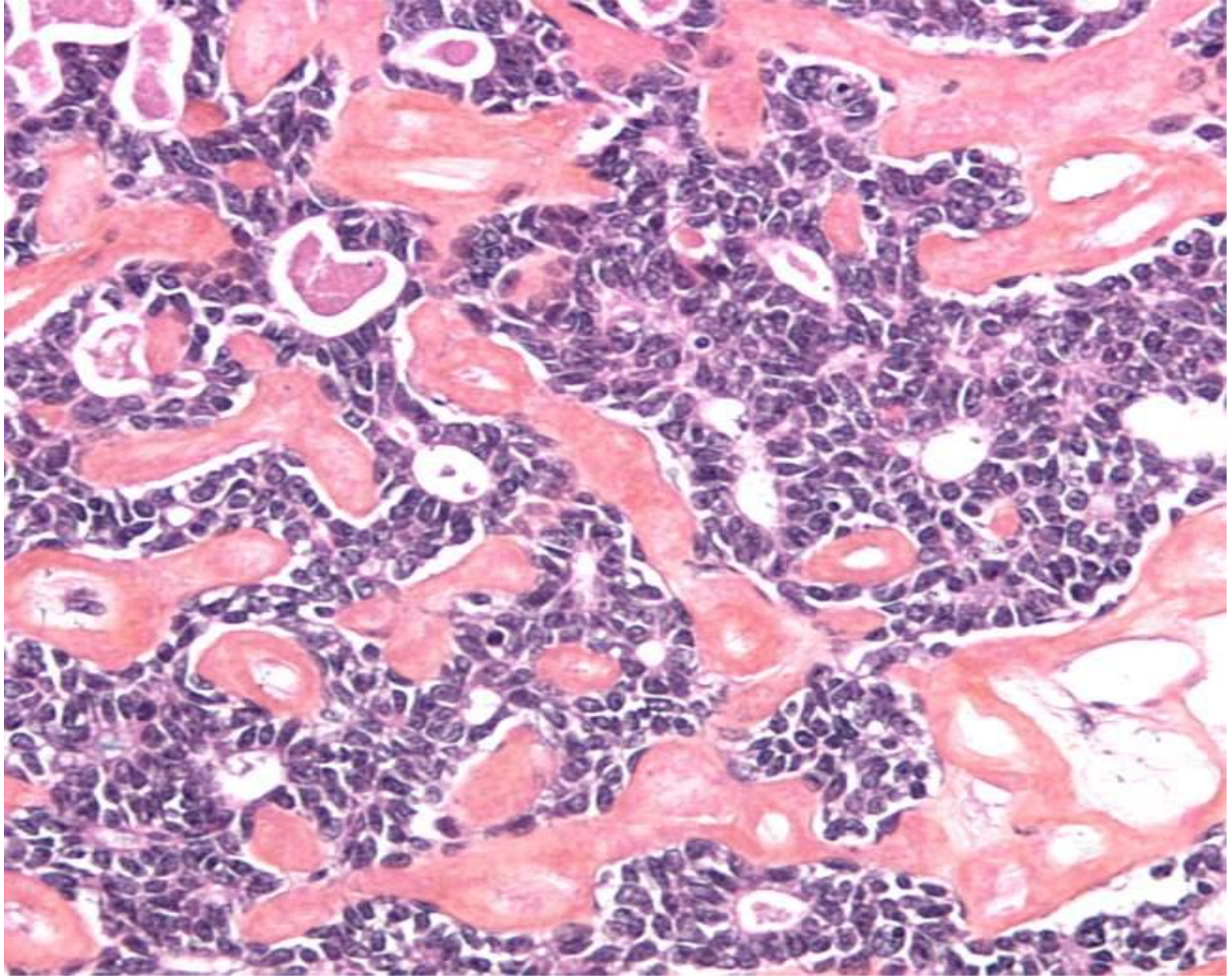
- In major salivary glands, chiefly parotid.
- Mean age – 60 years.
- Just like other salivary tumors, swelling is the only sign or symptom experienced.

Histologic features :

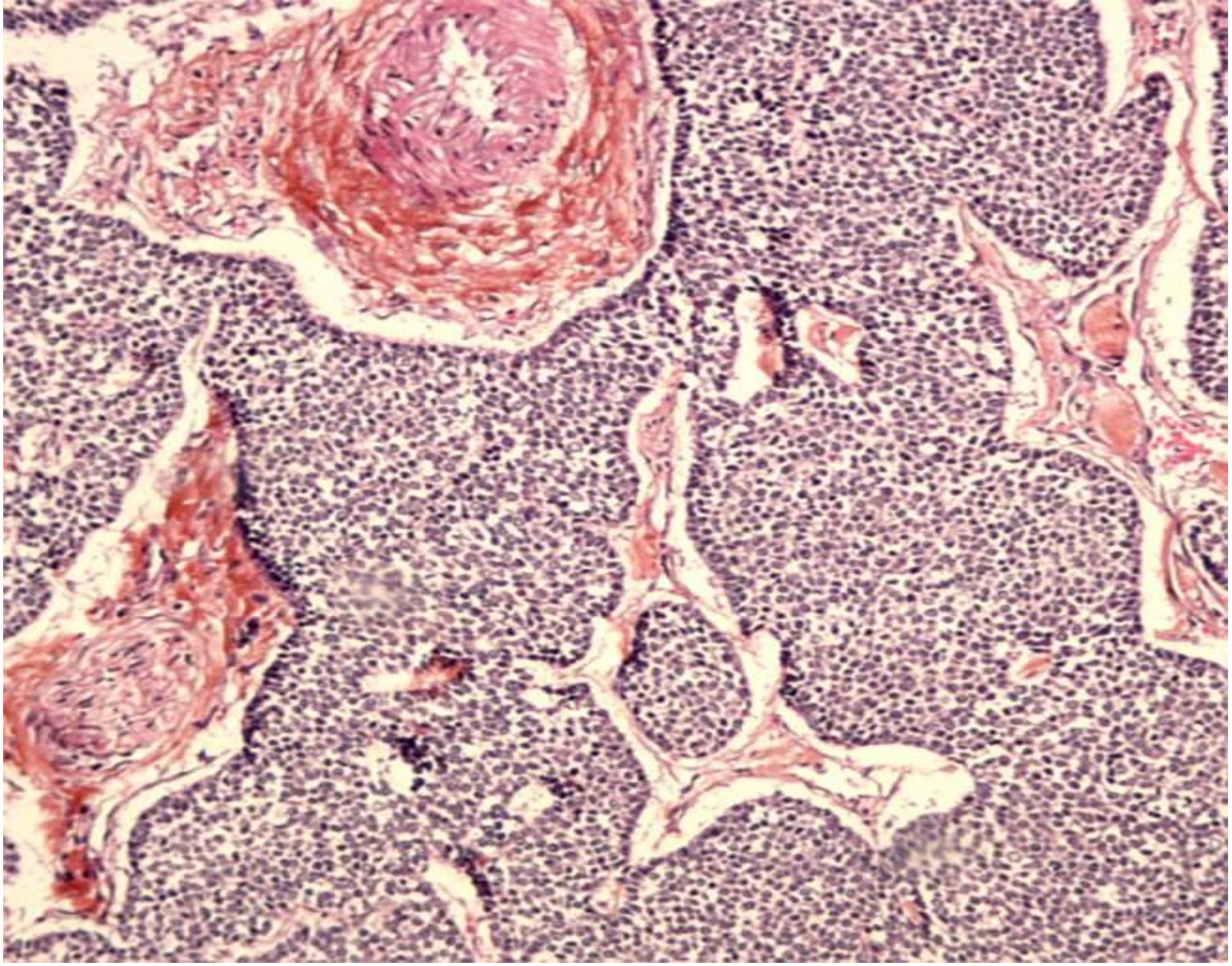
- Divided into four subtypes –
  - Solid
  - Ductal
  - Trabecular
  - Membranous
- The prevalent pattern is solid neoplastic aggregates with a peripheral palisading arrangement, frequently delineated by basement membrane like material.
- The neoplastic clusters are formed by two cell populations – (a) small dark cell – predominant. (b) large pale cell. Generally the small dark cells are present peripherally to the large paler cells.
- Tumor extends into the surrounding tissues by local infiltration as nodules, nests and cords.
- Perinuclear and vascular invasion may be seen.



Basal cell adenocarcinoma



Basal cell adenocarcinoma



Basal cell adenocarcinoma

Treatment :

- They are low grade tumors which are infiltrative, locally destructive, tend to recur and only occasionally metastasize.
- Surgical excision with a wide margin is the primary treatment.
- Overall prognosis is good.

Sebaceous carcinoma

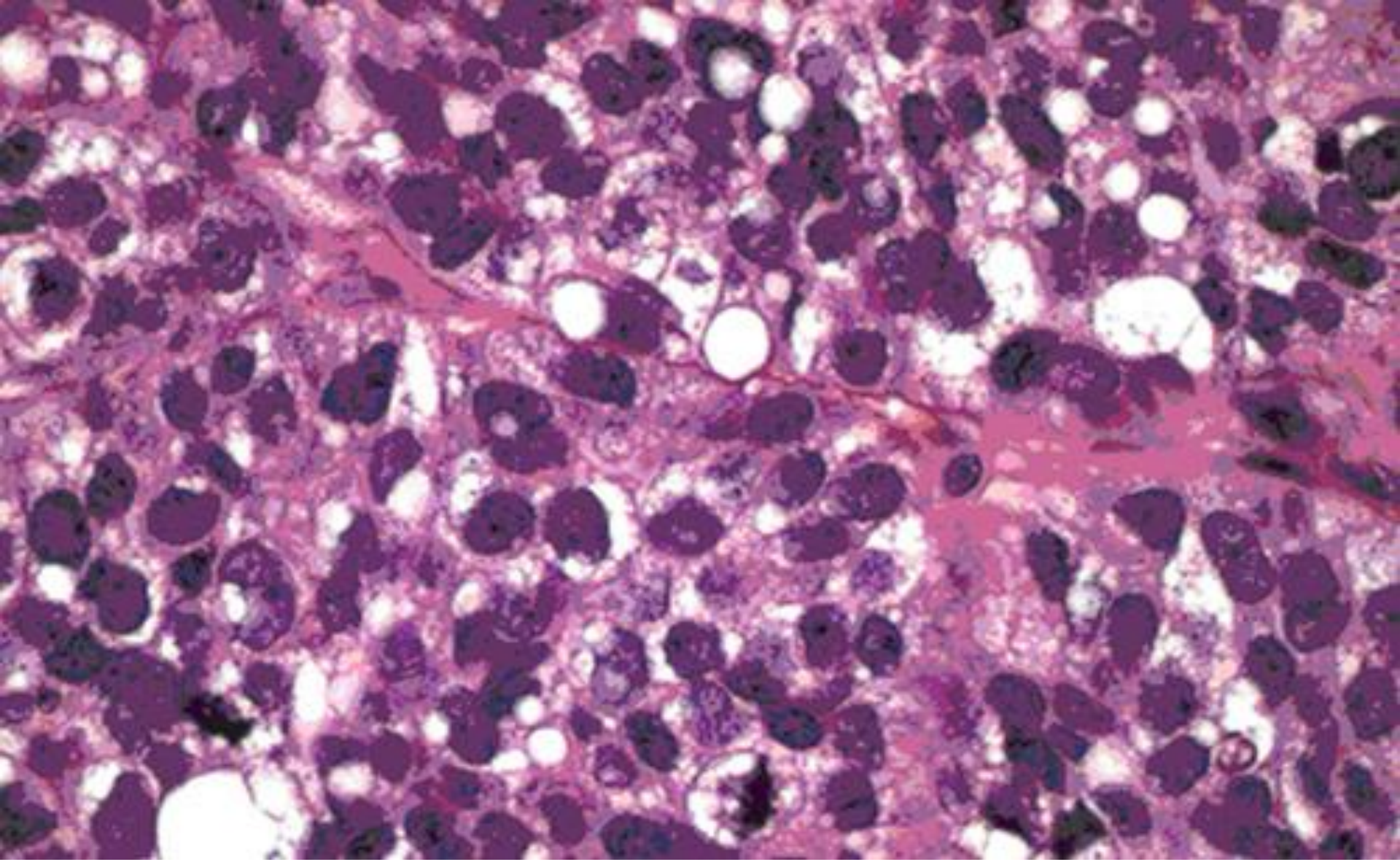
- Consists chiefly of sebaceous cells, arranged in sheet and/or nests with different degrees of pleomorphism, nuclear atypia and invasiveness.

Clinical features :

- Bimodal age distribution; peak incidence in third and seventh decades.
- Male: female = 1:1
- Mostly parotid.
- Chief complaint is a painful mass with varying degrees of facial nerve palsy and occasionally fixation of the skin.

Histologic features :

- Well circumscribed or partially encapsulated with pushing or locally infiltrating margins.
- Tumor cells may be arranged in multiple large foci or sheets & have hyperchromatic nuclei surrounded by clear to eosinophilic cytoplasm.
- Areas of cellular necrosis and fibrosis seen.
- Perineural invasion in more than 20 % cases.
- Vascular invasion is very unusual.



Sebaceous carcinoma – well differentiated tumor composed of an area resembling sebaceous adenoma admixed with sheets of carcinoma cells.

Treatment :

- Varies from local excision and parotidectomy to preoperative and postoperative radiotherapy, with or without chemotherapy.

Papillary cystadenocarcinoma

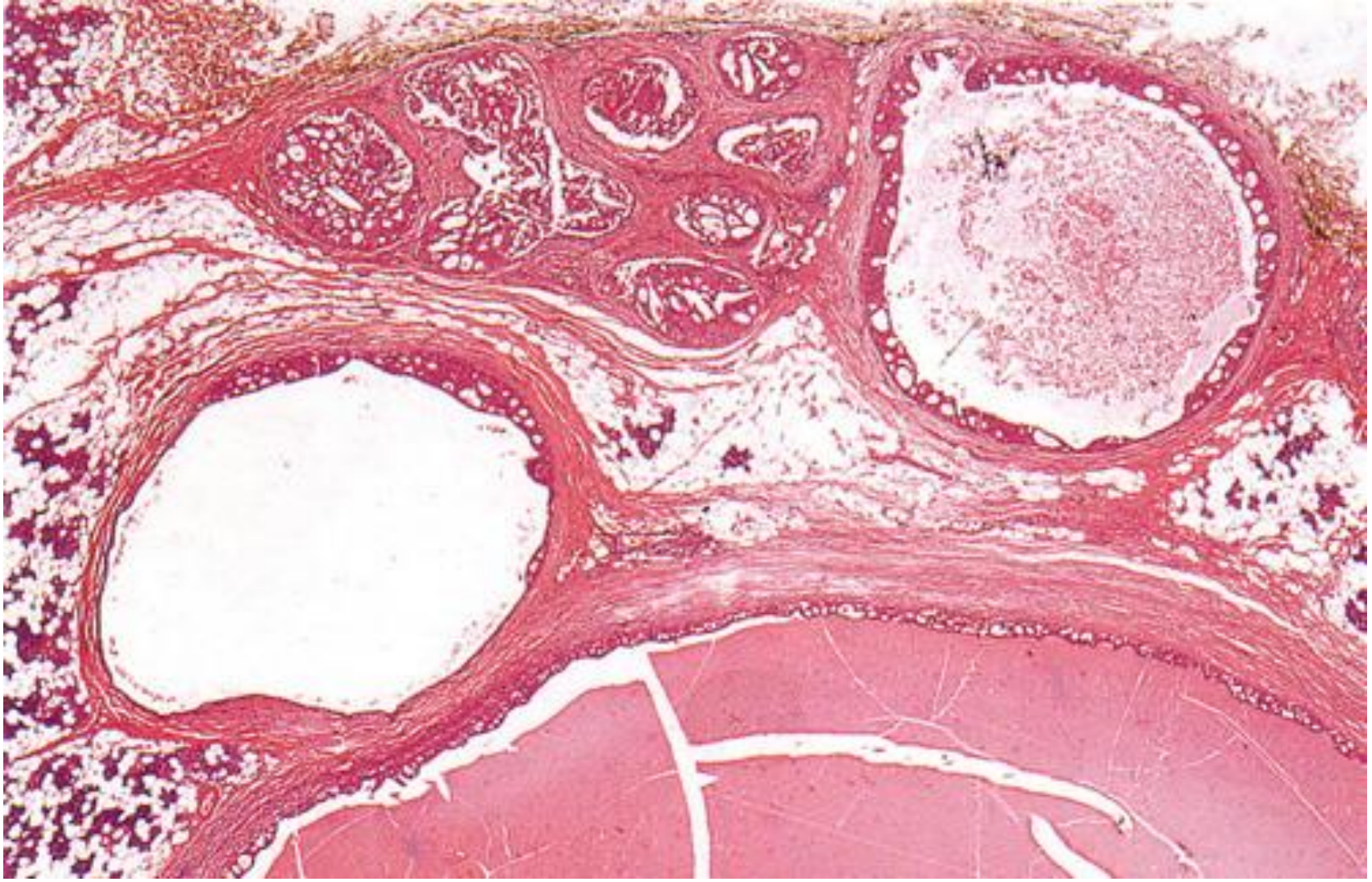
- Characterized histologically by prominent cystic &, frequently, papillary growth but lacking features that characterize cystic variants of several more common salivary gland neoplasms.

Clinical features :

- Low grade neoplasm.
- Chiefly in major salivary glands (parotid).
- Equal in men and women.
- Average age 59 yrs.
- Slow growing asymptomatic mass.

Histologic features :

- A cystic growth pattern must dominate the histologic pattern for the diagnosis to be considered.
- These tumors may appear circumscribed or reveal haphazard growth.
- The lumina are often filled with mucus and hemorrhage, or dystrophic calcifications are sometimes evident focally.
- Lining cells vary from cuboidal to tall columnar, & often a single tumor contains basaloid, oncocytic, clear and mucus cells, that form adenomatous or nodular , solid epithelial areas. These solid areas occupy spaces between the cystic structures.
- Encapsulation is complete and infiltration into salivary gland parenchyma or fibrous or adipose tissue is seen.



Papillary cystadenocarcinoma – cystic neoplasm showing irregular cysts with great variation in size and frequent intraluminal papillary process. Invasion into the parotid parenchyma is noticed.

Treatment :

same as other low grade tumors.

Mucinous adenocarcinoma

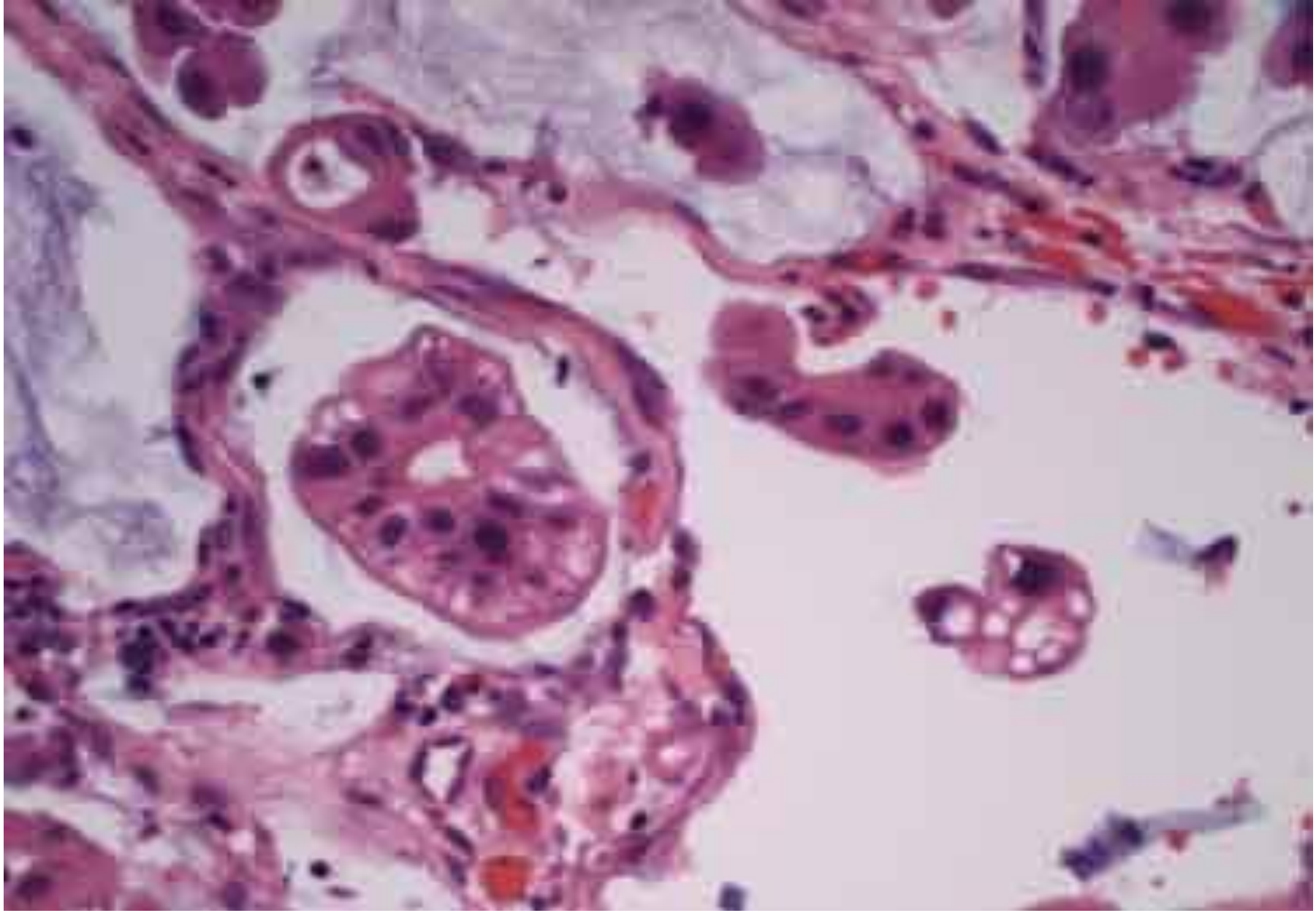
- Characterized by a large amount of extra cellular epithelial mucin that contains cords, nests and solid epithelial cells.

Clinical features :

- In major salivary glands with the submandibular gland as the predominant site.
- Soft, spongy masses that may be thought of as cysts.
- May be associated with dull pain and tenderness.

Histologic features :

- Grossly it is very mucoid, with a slimy texture and may actually ooze mucoid material. They are circumscribed but not encapsulated.
- Islands & cords of tumor cells that appear to be floating within pools of mucin. These pools may be divided into irregular lobules by fibrous c.t. septa.
- Tumor cells are moderately large, cuboidal and polygonal cells with eosinophilic to amphophilic cytoplasm, and may have intracytoplasmic mucin. Nuclei are vesicular, & scattered mitotic figures may be found.
- Tumor islands are surrounded by mucoid substance.



Mucinous adenocarcinoma

Treatment :

Complete excision with care to avoid seeding the surgical site.

Oncocytic carcinoma (oncocytic adenocarcinoma)

Clinical features :

- High grade carcinoma
- Mostly in parotid.
- Average age 63 years.
- Pain or facial paralysis.
- Overlying skin is sometimes discolored or wrinkled.

Histologic features :

- Tumors with a significant oncocytic component include Warthin's tumor, oncocytoma & oncocytic carcinoma.
- Characterized by oncocytes with marked cellular atypia, frequent mitoses, destruction of adjacent structures, perineural or vascular invasion, and lymph node metastasis.

Treatment :

- Aggressive surgery provides a better prognosis.

Salivary duct carcinoma

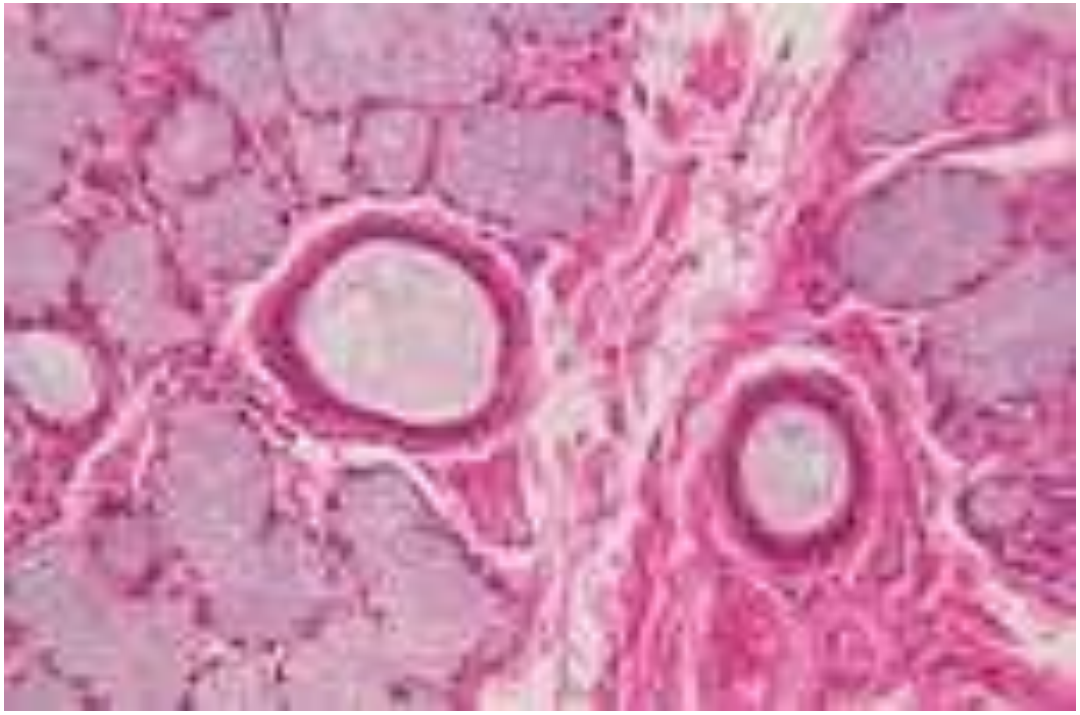
- High grade malignant epithelial neoplasm composed of structures that resemble expanded salivary gland ducts. A low grade variant also exists.

Clinical features :

- Parotid swelling
- Facial nerve dysfunction may be the initial manifestation.
- The high grade variant of this tumor is one of the most aggressive types of salivary gland neoplasias and has a very poor prognosis.

Histologic features :

- Composed of clusters of tumor cells that may have small lumina or cribriform arrangements, but solid irregularly shaped tumor cell aggregates are frequently present.
- Tumor cells are cuboidal & polygonal with a moderate amount of eosinophilic cytoplasm & accompanied by a dense fibrous c.t. that may be hyalinized in some areas.
- Invasion of nerves and blood vessels is frequent, as is infiltration of salivary gland lobules and extra salivary tissues like fat, bone and muscle.



Salivary duct carcinoma

Treatment :

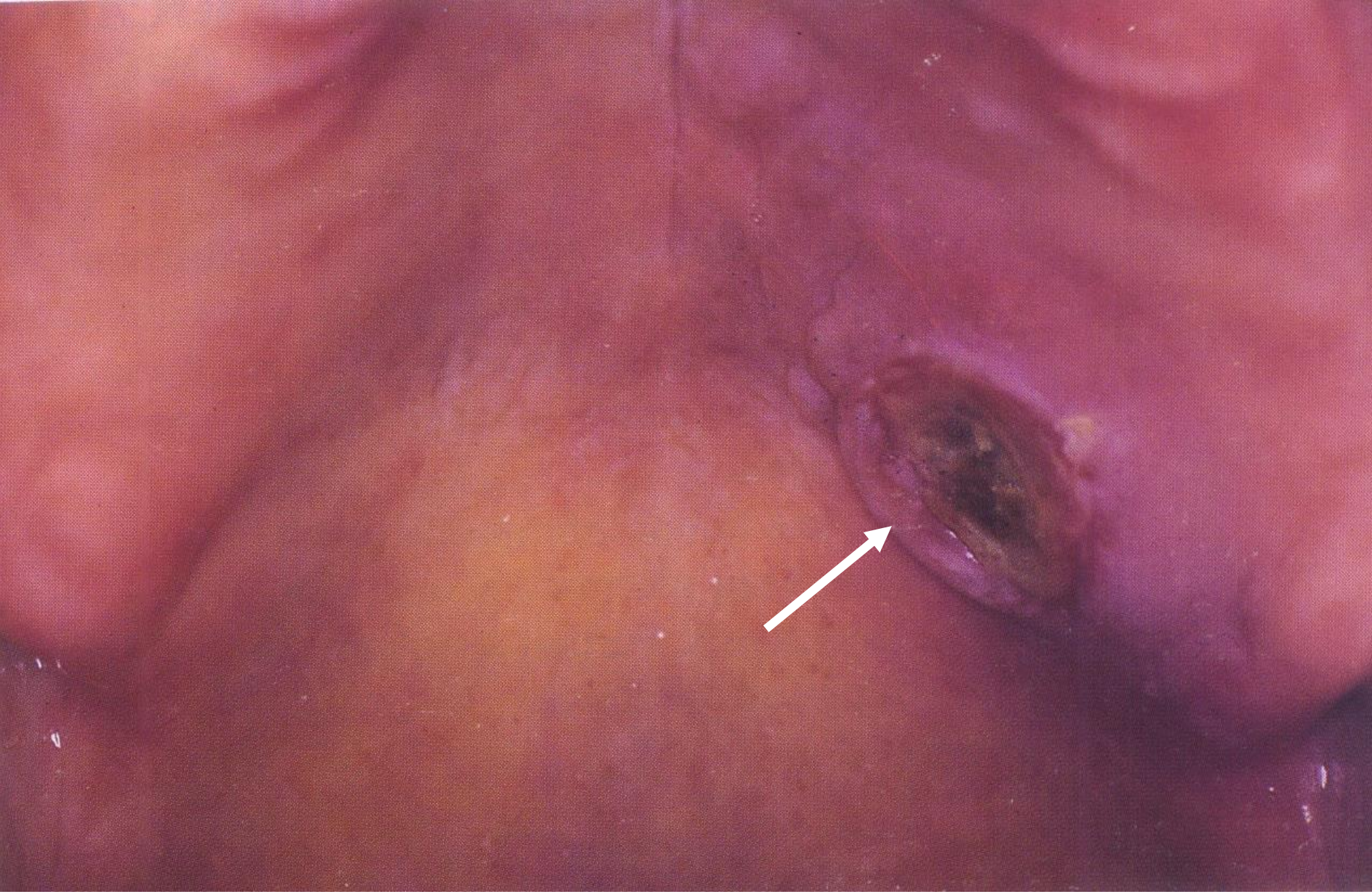
- Complete local excision with radical neck dissection and post-op radiation.

Adenocarcinoma

- Rare but aggressive tumor.

Clinical features :

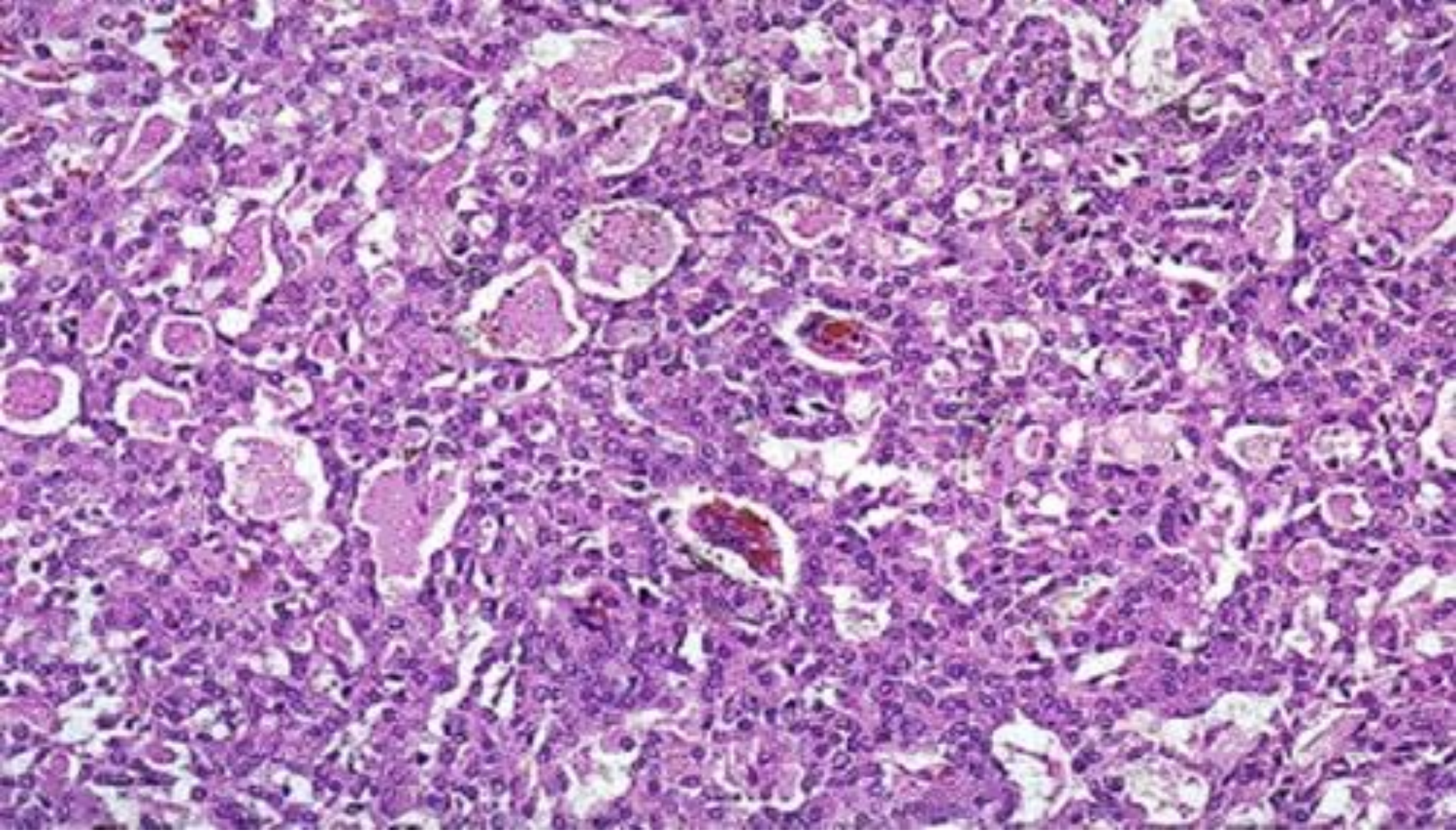
- Over 40 years of age.
- Equally in men and women.
- Parotid and minor salivary glands of palate, lip and tongue.
- Pain or facial weakness at presentation.



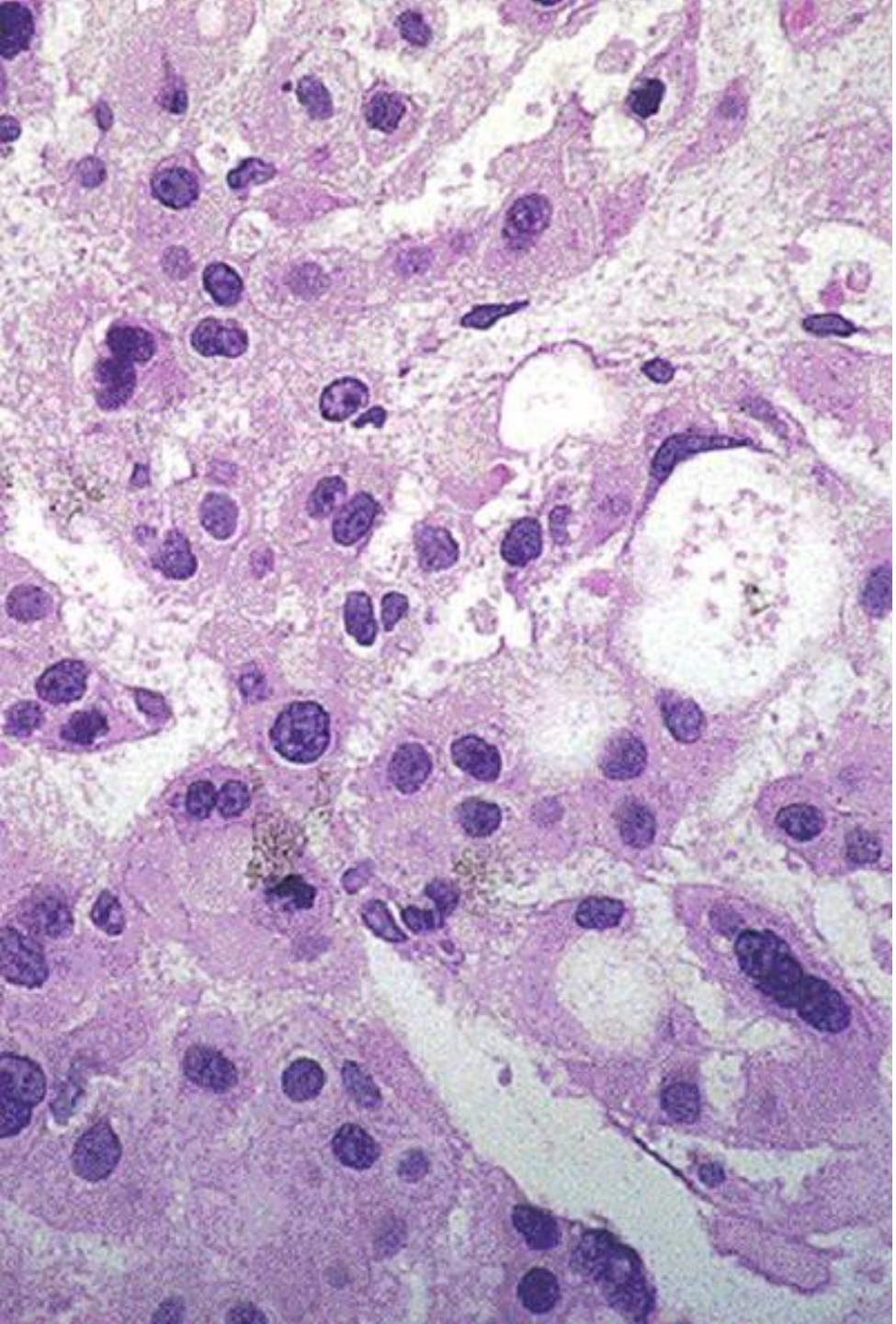
Adenocarcinoma – ulcerated raised mass of palate.

Histologic features :

- Generally a solid tumor without any cystic spaces.
- Show a wide range of growth patterns & hence difficult to classify.
- All of these have in common the formation of glandular strictures, described as grades I, II or III based upon the degree of cellular differentiation.
- Grade I lesions have a well formed ductal structures and grade III have a more solid growth pattern with few glandular characteristics.



Adenocarcinoma – low grade tumor showing morphologically uniform population of cells showing formation of many ductal structures. Mitotic figures are rare which is typical for this group of tumor.



Adenocarcinoma –
high power view showing nuclear atypia.

Treatment :

- Aggressive treatment is needed. Complete local excision with sacrifice of the facial nerve in case of parotid is required.
- In minor salivary glands, a portion of the maxilla or mandible may have to be resected with the tumor.

Malignant myoepithelioma

- A rare malignant tumor in which the tumor cells almost exclusively manifest myoepithelial differentiation

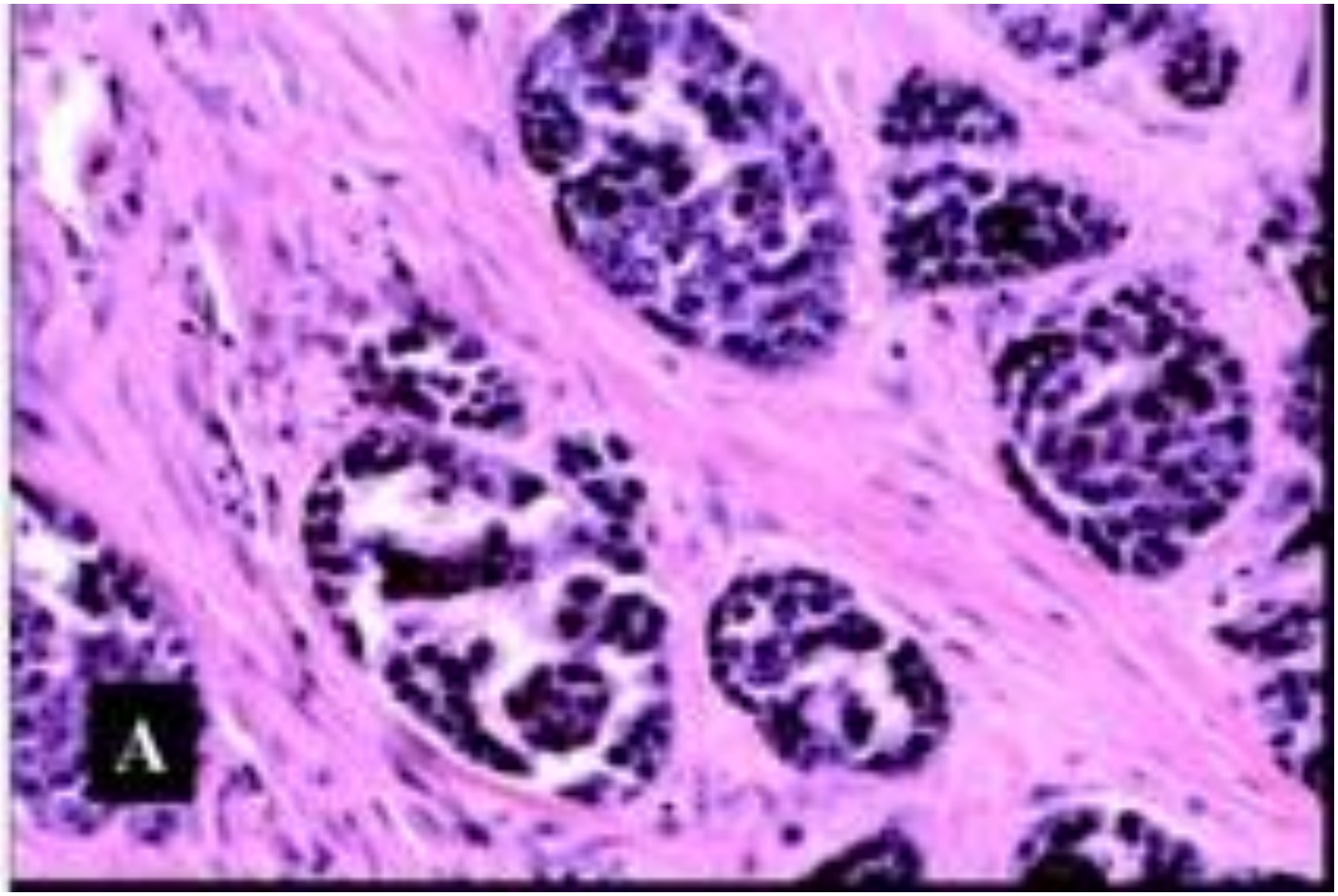
Clinical features :

- Majority in parotid gland
- Mean age 55 years.
- Painless mass
- Histologic grading does not appear to correlate well with clinical behavior.

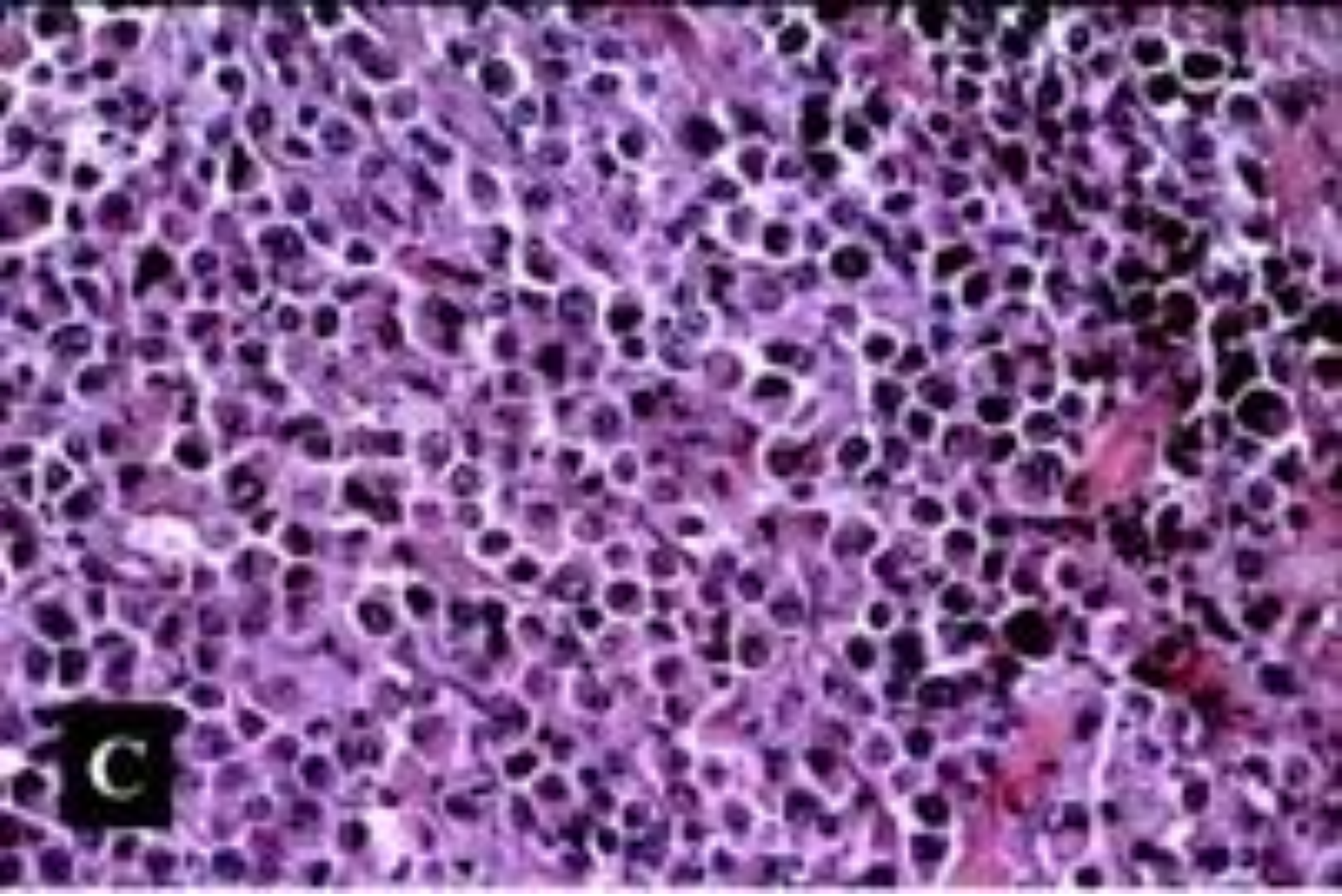
Histologic features :

- Tumor cells may be spindle or plasmacytoid in shape.
- Epithelioid or clear cells may also be present.
- cell types are often intermixed but one type always predominates.
- Tumors may be quite cellular and more suggestive of sarcoma than carcinoma.
- Stroma in other areas may be more conspicuous and myxoid.
- They are distinguished from their benign counterpart by their infiltrative, destructive growth, increased mitotic activity and cellular pleomorphism.

Treatment : wide surgical excision.



Malignant myoepithelioma



Malignant myoepithelioma

Carcinoma in pleomorphic adenoma (malignant mixed tumor)

- Includes 3 distinct clinicopathologic entities :

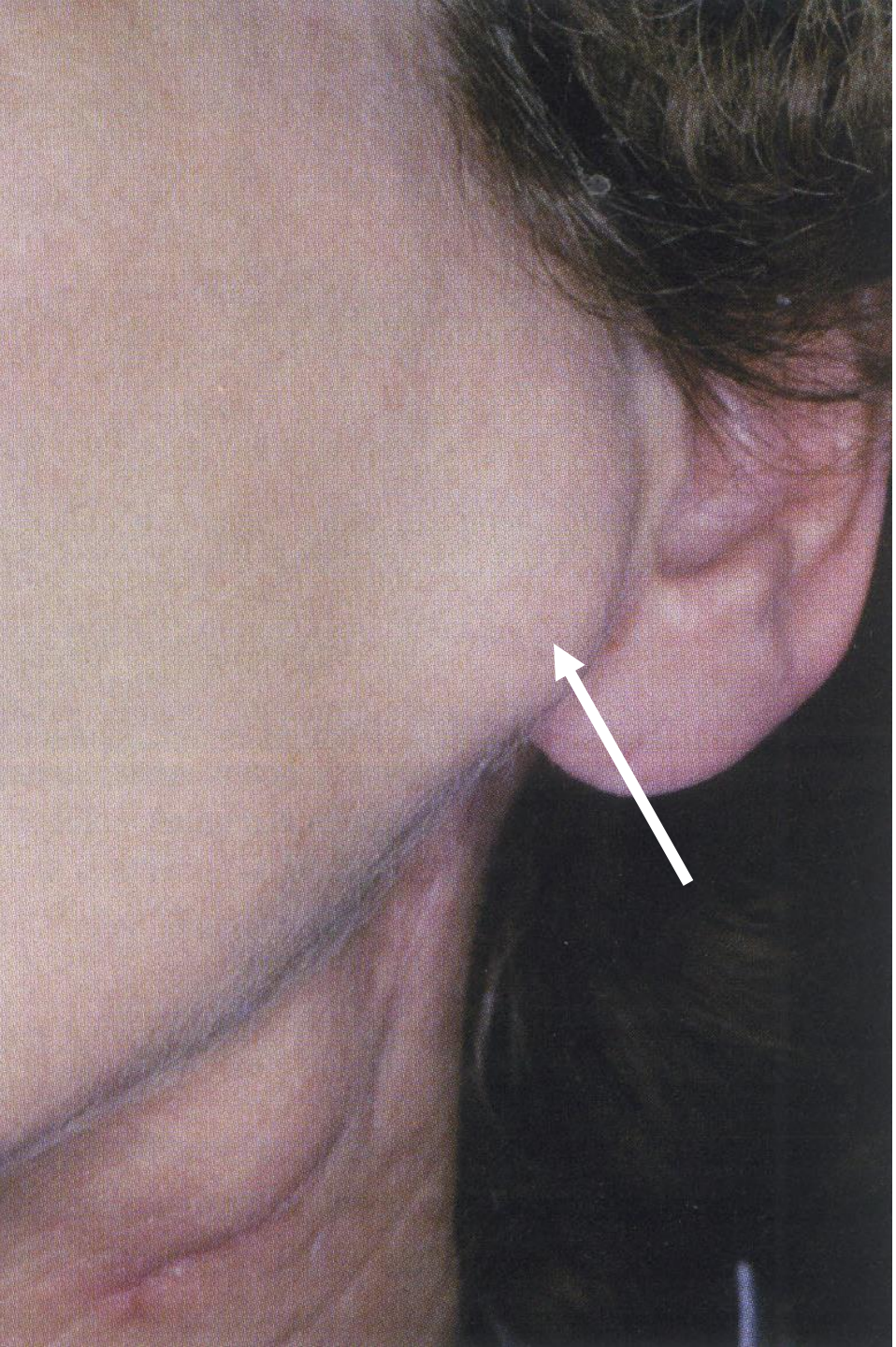
1. Carcinoma ex pleomorphic adenoma
2. Carcinosarcoma
3. Metastasizing mixed tumor

Carcinoma ex pleomorphic adenoma

Most common of the three types. It occurs when a carcinoma develops from the epithelial component of a preexisting PA. diagnosis requires the identification of the benign tumor in the biopsy sample.

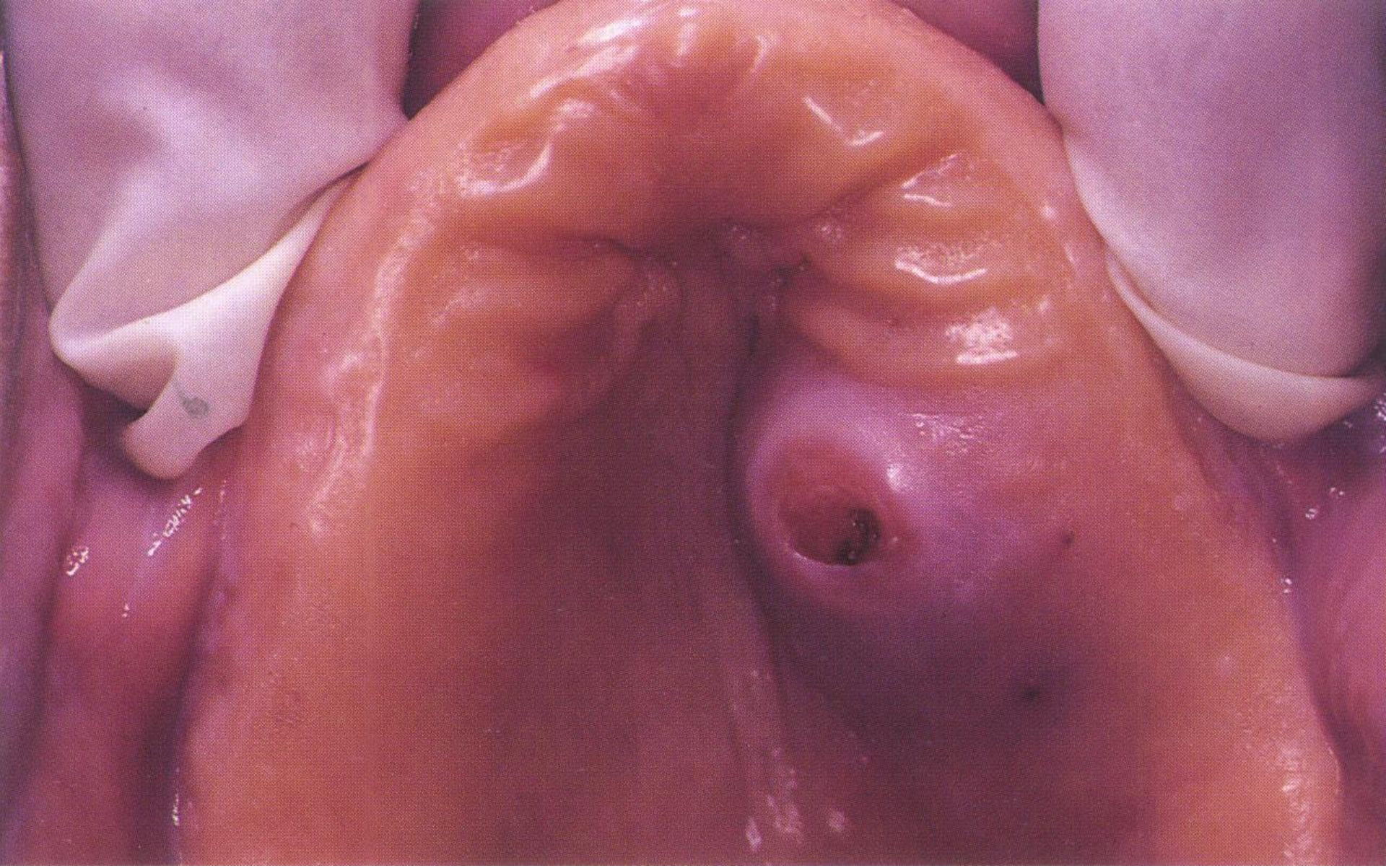
Clinical features :

- In major salivary glands, chiefly parotid.
- In sixth to eighth decades of life with patients averaging 10 yrs older than those with PA.
- Usually presents as a painless mass with recent rapid enlargement of a long standing nodule.
- Patients may experience facial paralysis.



Carcinoma ex-pleomorphic adenoma

Mass of the parotid gland.

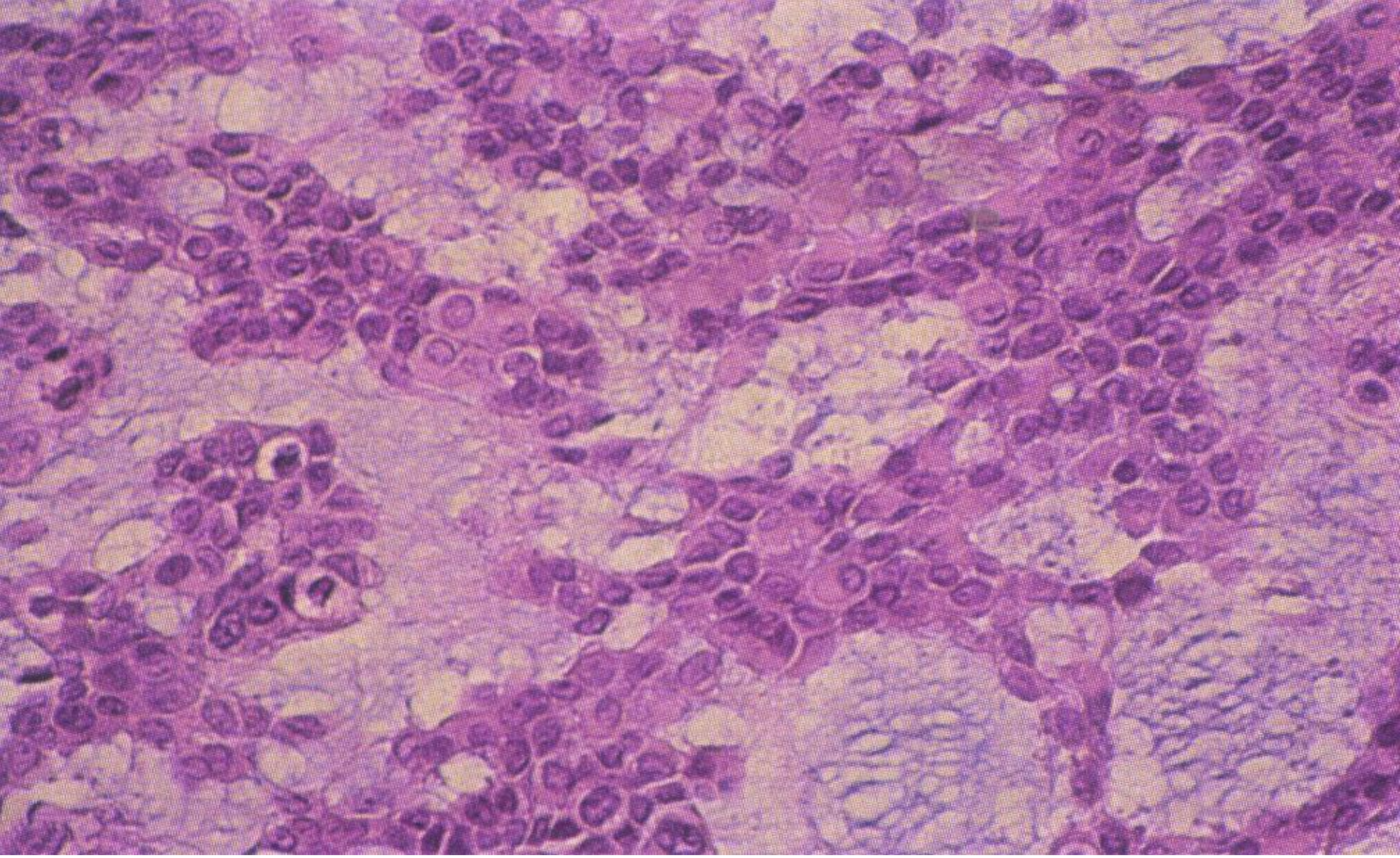


Carcinoma ex pleomorphic adenoma

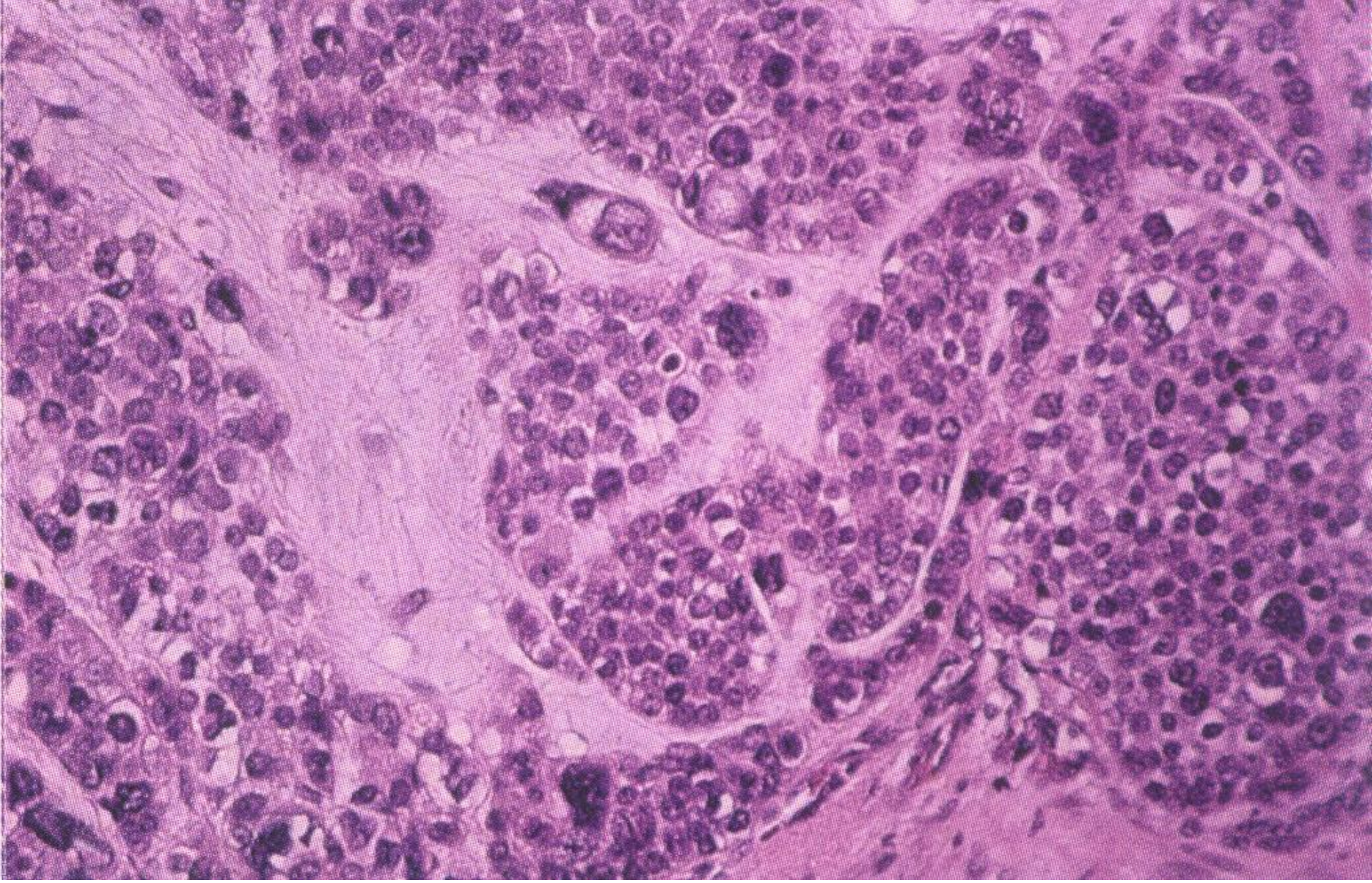
Ulcerated mass of the hard palate.

Histologic features :

- Malignant appearing epithelial cells are present adjacent to a typical appearing PA.
- These cells may take the form of any epithelial malignancy except acinic cell. Most commonly it will be undifferentiated carcinoma, or adenocarcinoma.
- This tumor tends to be more aggressive than other salivary malignancies.
- Almost 25% of these patients will have lymph node metastasis on presentation.



Carcinoma ex pleomorphic adenoma – benign portion of the tumor showing sheets of plasmacytoid myoepithelial cells within a myxoid background.



Carcinoma ex pleomorphic adenoma – malignant portion of the tumor showing epithelial cells with pleomorphic nuclei.

Treatment :

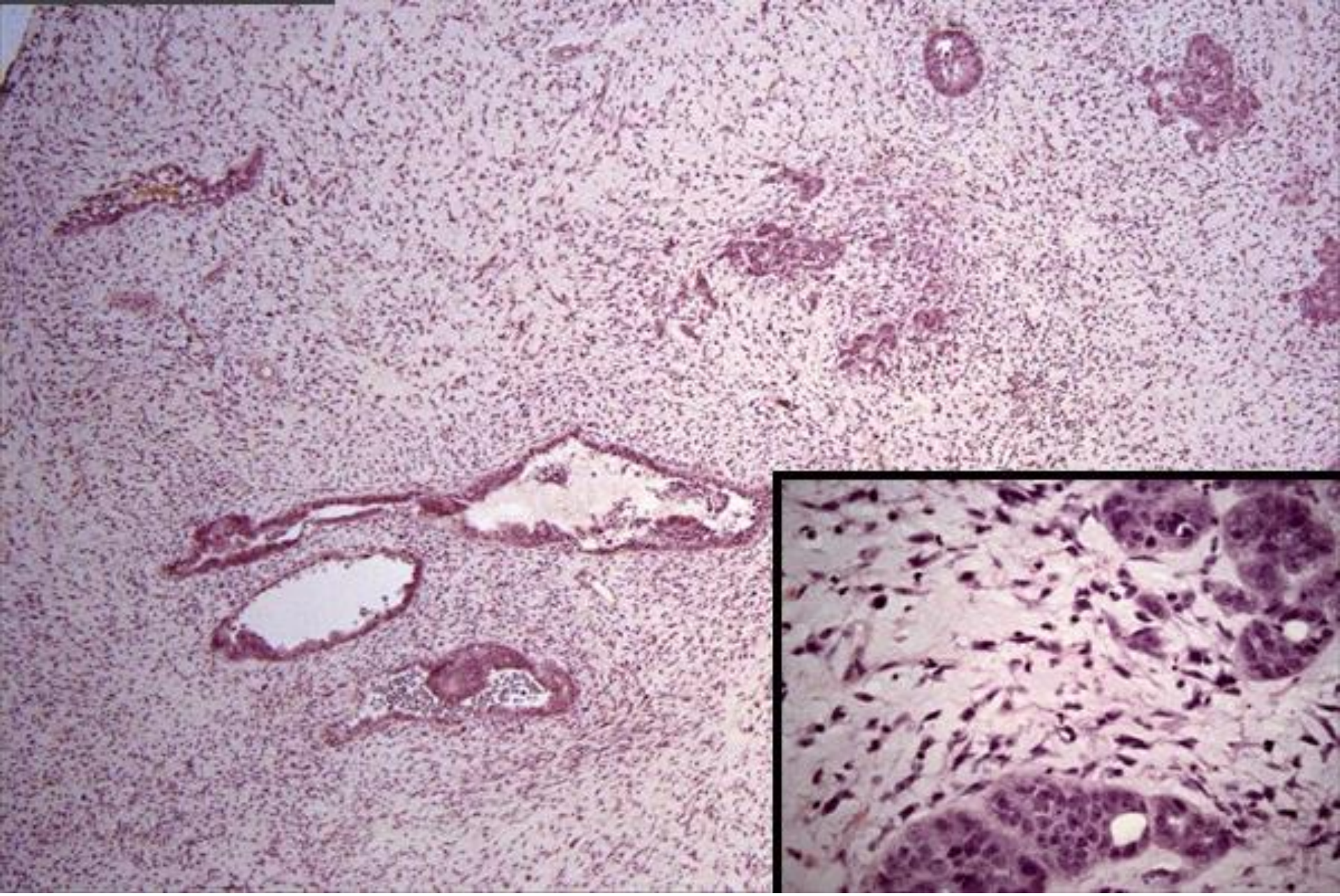
- Radical surgical resection with neck dissection and post-op radiation therapy.

Carcinosarcoma (True malignant mixed tumor)

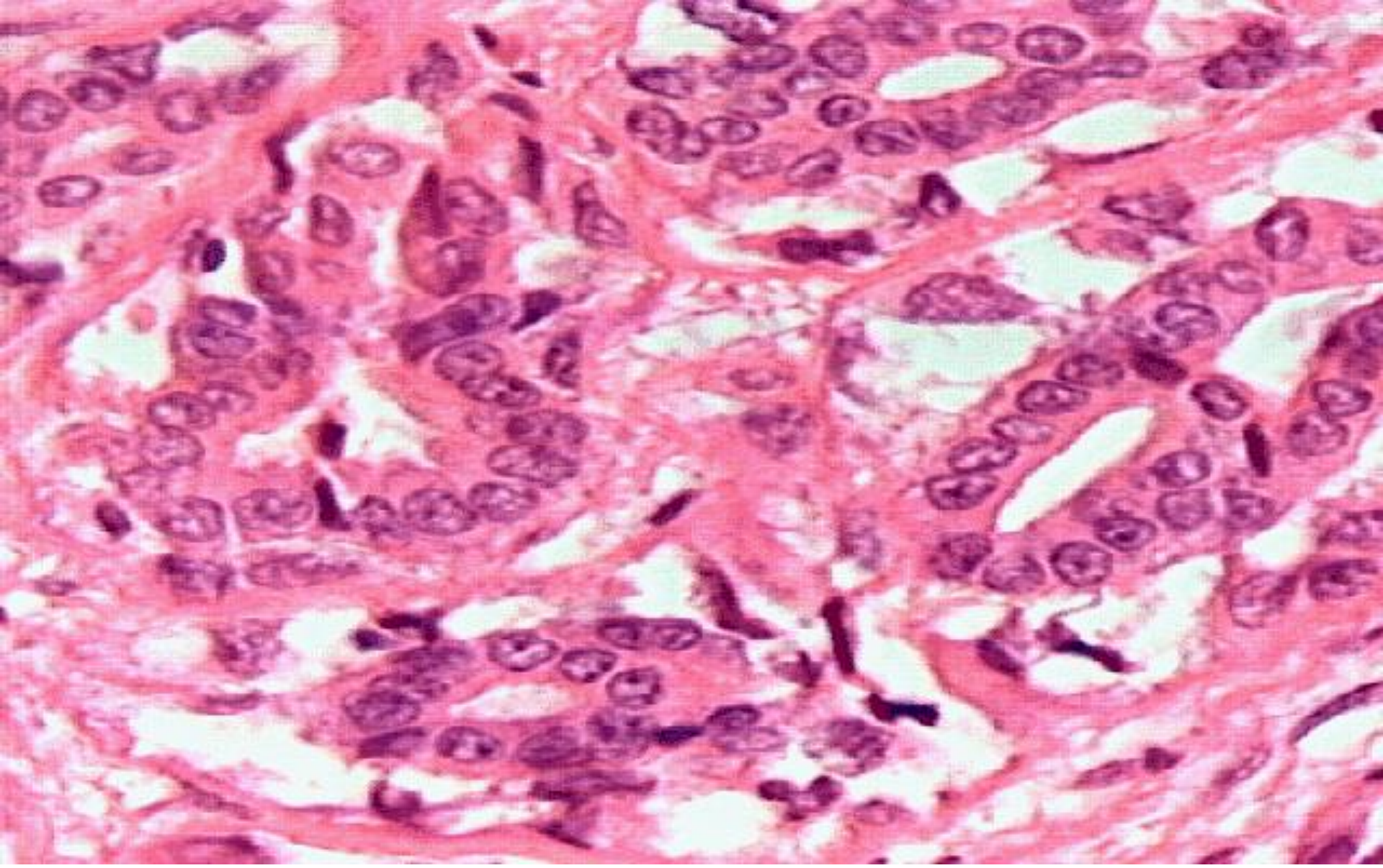
- A rare tumor that contains both carcinoma and sarcoma components.
- The metastatic lesions contain both stromal and epithelial elements.
- Some of these lesions develop *de novo* while others develop in association with benign mixed tumor.
- In major salivary glands, chiefly parotid.
- Average age 60 yrs.
- Men and women are equally affected.
- Swelling, pain, nerve palsy and ulceration are frequent findings.

Histologic features :

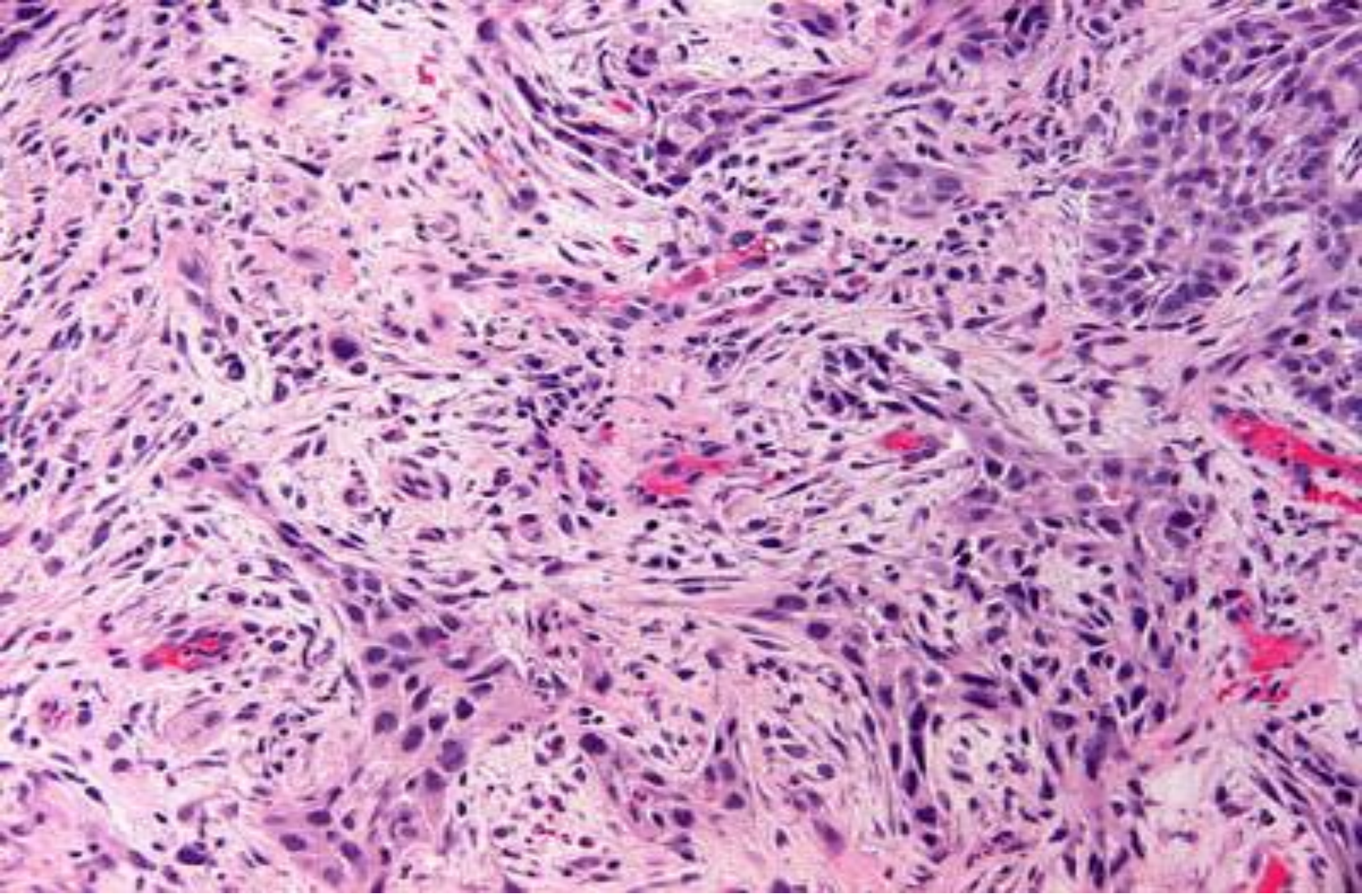
- In the majority, sarcoma is the dominating component and chondrosarcoma is the most common cell type.
- Carcinoma element is usually an undifferentiated or high grade ductal adenocarcinoma.



Carcinosarcoma



Carcinosarcoma



Carcinosarcoma

Treatment :

- Radical surgery, neck dissection and post- op radiotherapy.
- An aggressive tumor which usually presents with distant metastasis on presentation.

Metastasizing mixed tumor

- It is an otherwise benign acting PA that develops metastatic deposit.
- There is often a very long interval between the diagnosis of the primary tumor and the metastasis.
- In major salivary glands
- Histologic features are within the spectrum of the PA.

Squamous cell carcinoma

- A malignant epithelial neoplasm of the major salivary glands composed of squamous cells.
- This diagnosis is not made in minor glands since distinction from the more common mucosal SCC is not possible.
- Primary SCC of these glands is so rare that MEC, metastatic SCC to the gland or intraglandular nodes & direct extension of a SCC must be first excluded.

Clinical features :

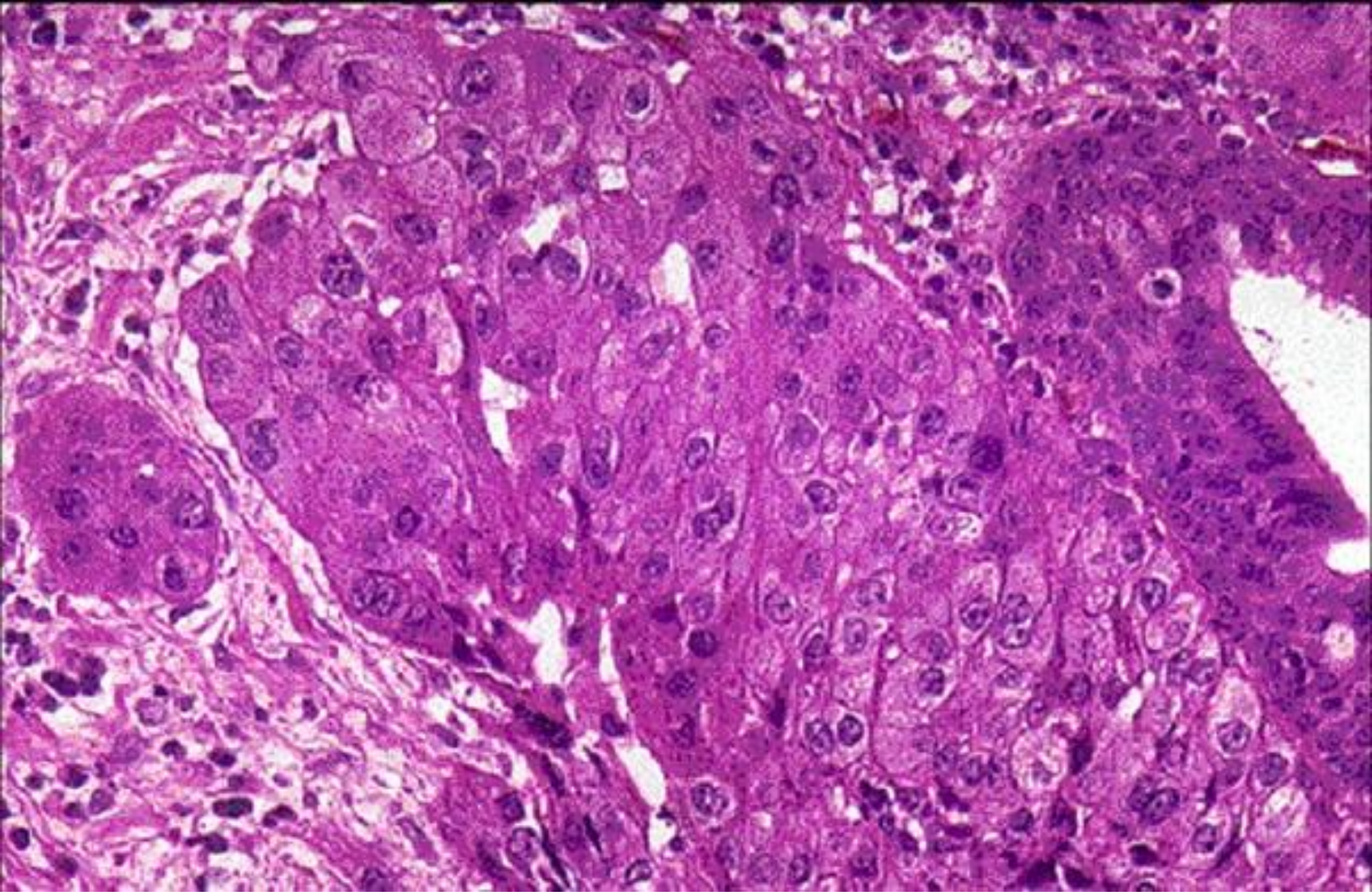
- Male : female = 2:1
- Usually over 60 yrs of age.
- Previous exposure to ionizing radiation appears to increase the risk of developing this tumor.
- May be associated with pain or facial weakness.

Histologic features :

- Same as SCC of other sites.
- Displays aggressive behavior.

Treatment :

- Surgical resection, neck dissection and post-op radiation
- Prognosis poor.



Primary Squamous cell carcinoma of salivary glands
(high power view).

Small cell carcinoma

- High grade malignant tumor
- Subdivided into neuroendocrine and ductal types.

Histologic features :

- Tumor cells have oval, hyperchromatic nuclei and scant cytoplasm
- Organized in sheets, strands and nests.
- Most of these exhibit neuroendocrine differentiation which are more frequently found in the minor salivary glands & have a better survival rate than those of the lung.

Treatment :

- Highly aggressive tumors, although prognosis may be better than those for extra-salivary neoplasias.
- Treatment of choice is wide surgical excision, with radiation and/or chemotherapy.

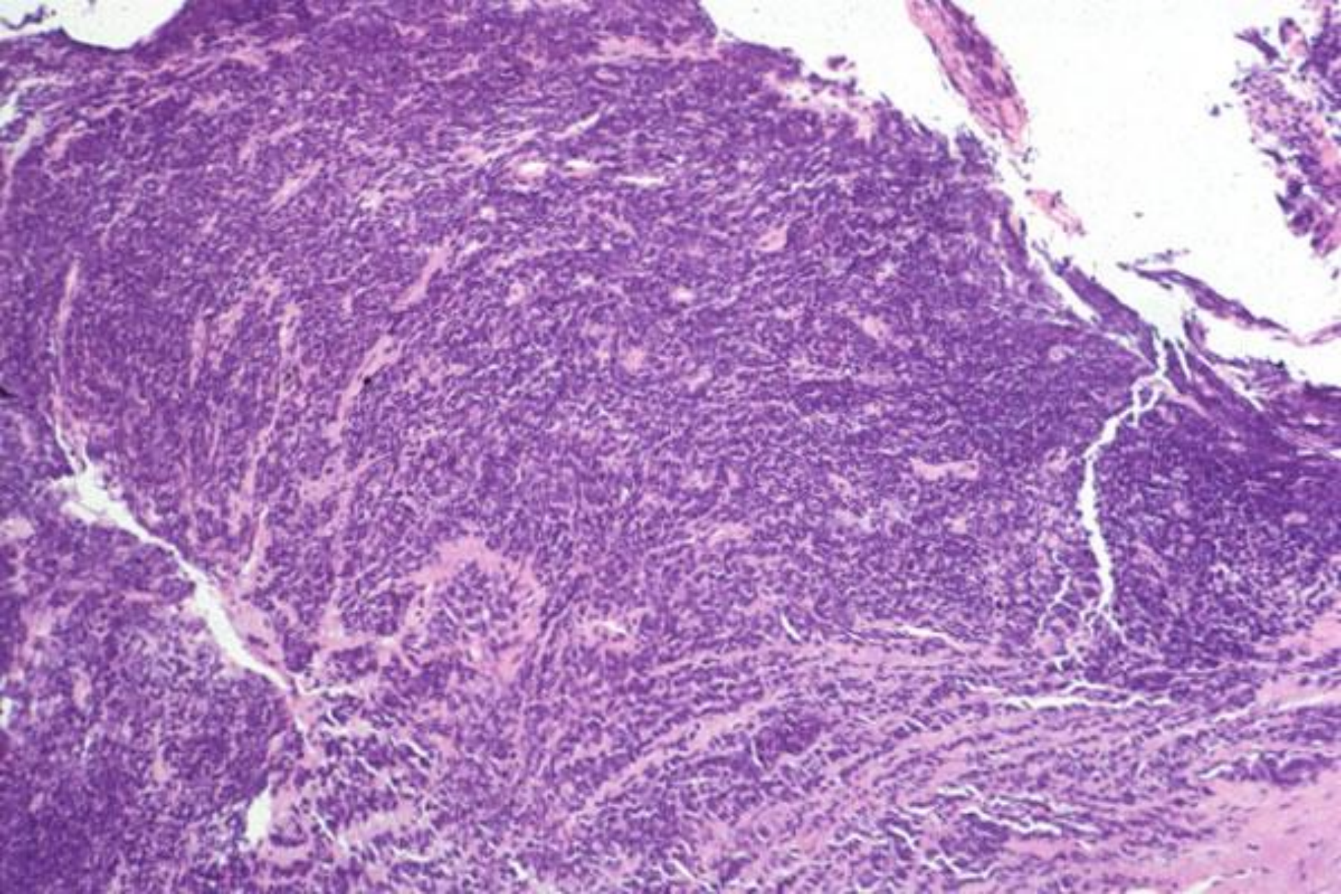
Undifferentiated carcinoma

- Malignant epithelial neoplasms that lack the specific morphologic features of other types of salivary gland carcinomas.
- This group includes –

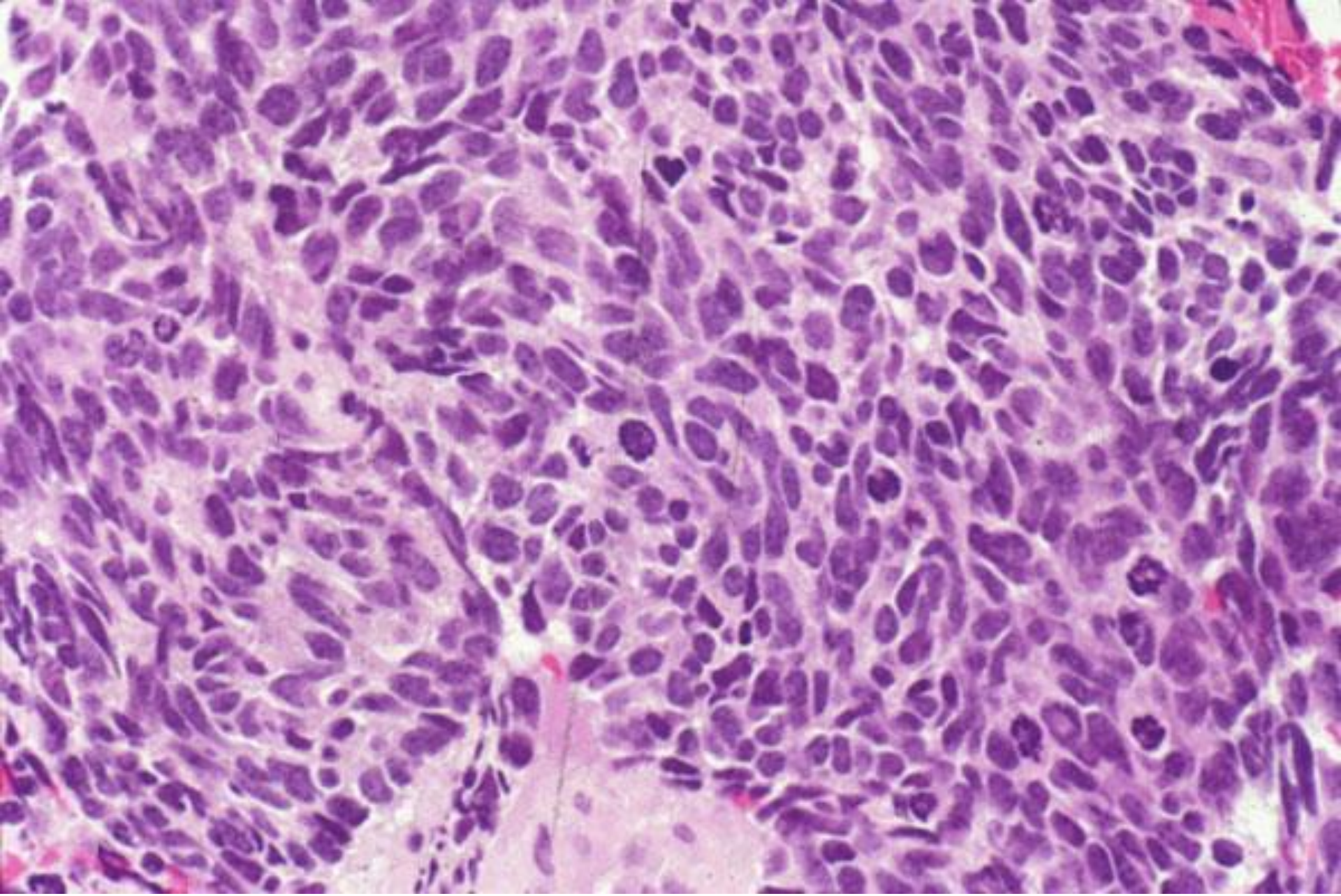
i. Small cell Undifferentiated carcinoma
ii. Large cell Undifferentiated carcinoma
iii. Lymphoepithelial carcinoma

Small cell Undifferentiated carcinoma

- A rare primary malignant tumor.
- Undifferentiated counterpart of an anaplastic small cell carcinoma.



Small cell Undifferentiated carcinoma (low power view)



Small cell Undifferentiated carcinoma (high power view)

Large cell Undifferentiated carcinoma

- Features of acinar , ductal, epidermoid, or myoepithelial differentiation are absent, although sometimes, poorly formed duct-like structures are found.
- Rapid growth of a parotid swelling is the common clinical presentation.
- High grade neoplasm that frequently metastasizes and has a poor prognosis.

Lymphoepithelial carcinoma

- Associated with a dense lymphoid stroma
- Exceptionally high incidence of this tumor in Eskimo and Inuit populations.
- Associated with EBV.
- Mainly in parotid.
- Pain is frequent.
- Sometimes facial nerve palsy.
- Metastasis common.

Treatment :

- Surgery alone or with radiotherapy.

Other carcinomas

Adenosquamous carcinoma

Exhibits histological features of both adenocarcinoma and SCC.

Sebaceous lymphadenocarcinoma

- Malignant counterpart of sebaceous lymphadenoma.
- Low grade tumor that has the ability to recur locally.
- Lymph node metastasis or distant metastasis may develop late in the clinical course.

Nonepithelial tumors

- Pertain to Major salivary glands.
- Benign types include hemangioma, lipoma, and lymphangioma.
- Malignant types include malignant schwannoma, hemangiopericytoma, malignant fibrous histiocytoma, rhabdomyosarcoma, and fibrosarcoma.
- It is important to establish a primary salivary gland origin for these tumors by excluding the possibilities of metastasis and direct extension from other sites. Also salivary gland carcinosarcoma should be excluded.

Malignant lymphomas

- Lymphomas of major salivary glands are characteristically of the Non-Hodgekin's type.

- Patients with Mikulicz's disease are at an increased risk for development of non Hodgekin's disease.

Secondary tumors

Tumors whose origins lie outside the salivary glands may involve the major salivary glands by :

- Direct invasion
- Hematogenous metastasis
- Lymphatic metastasis

Direct invasion is mainly from SCC and BCC of the overlying skin.