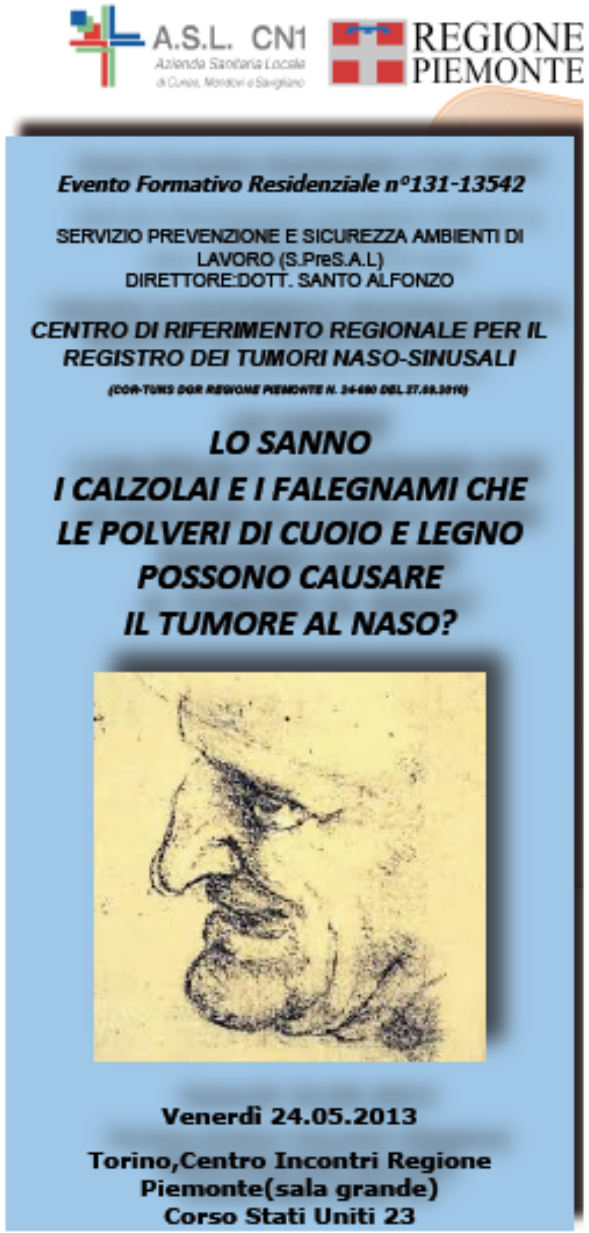

La diagnosi istopatologica delle neoplasie naso sinusali

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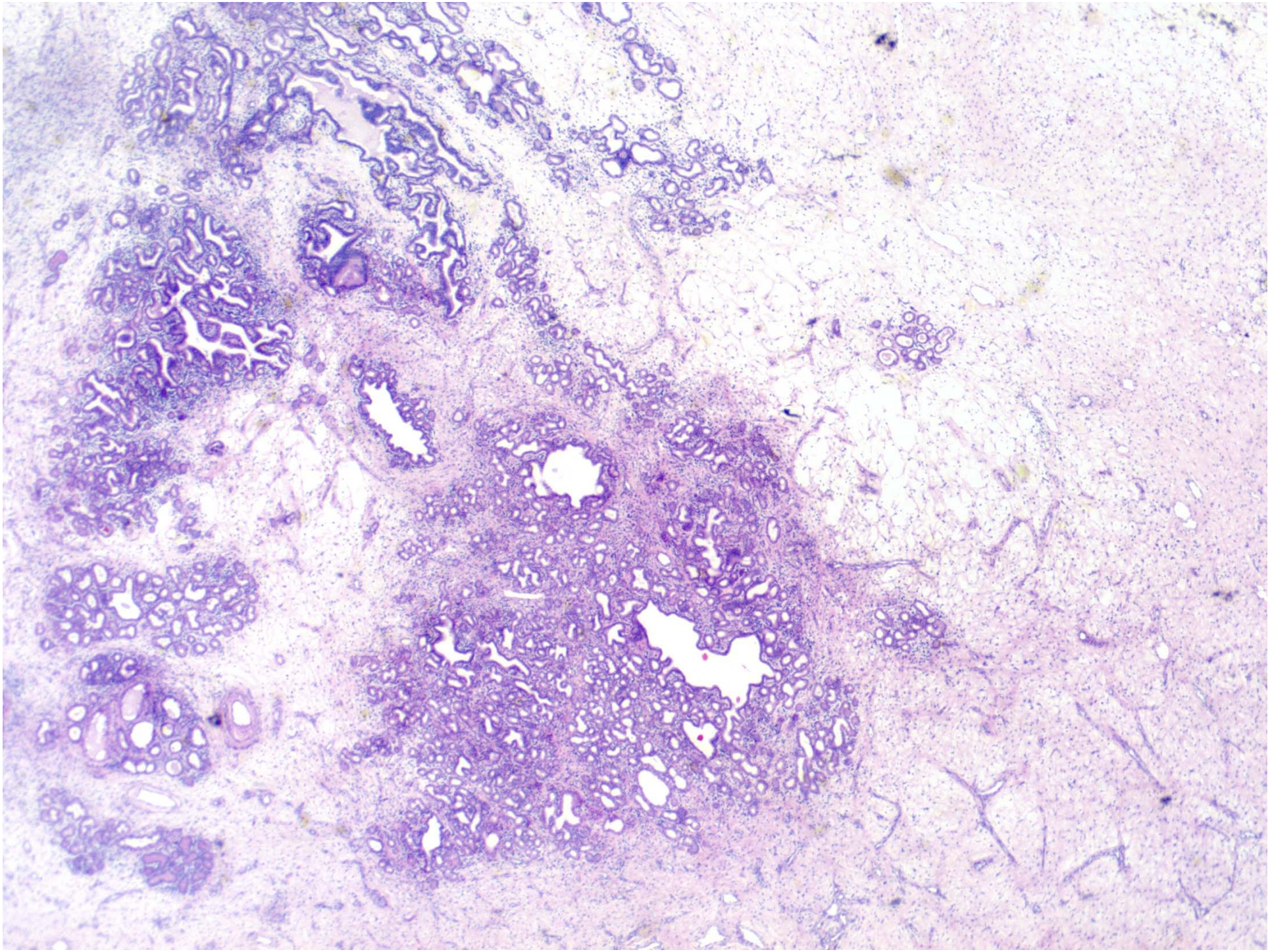
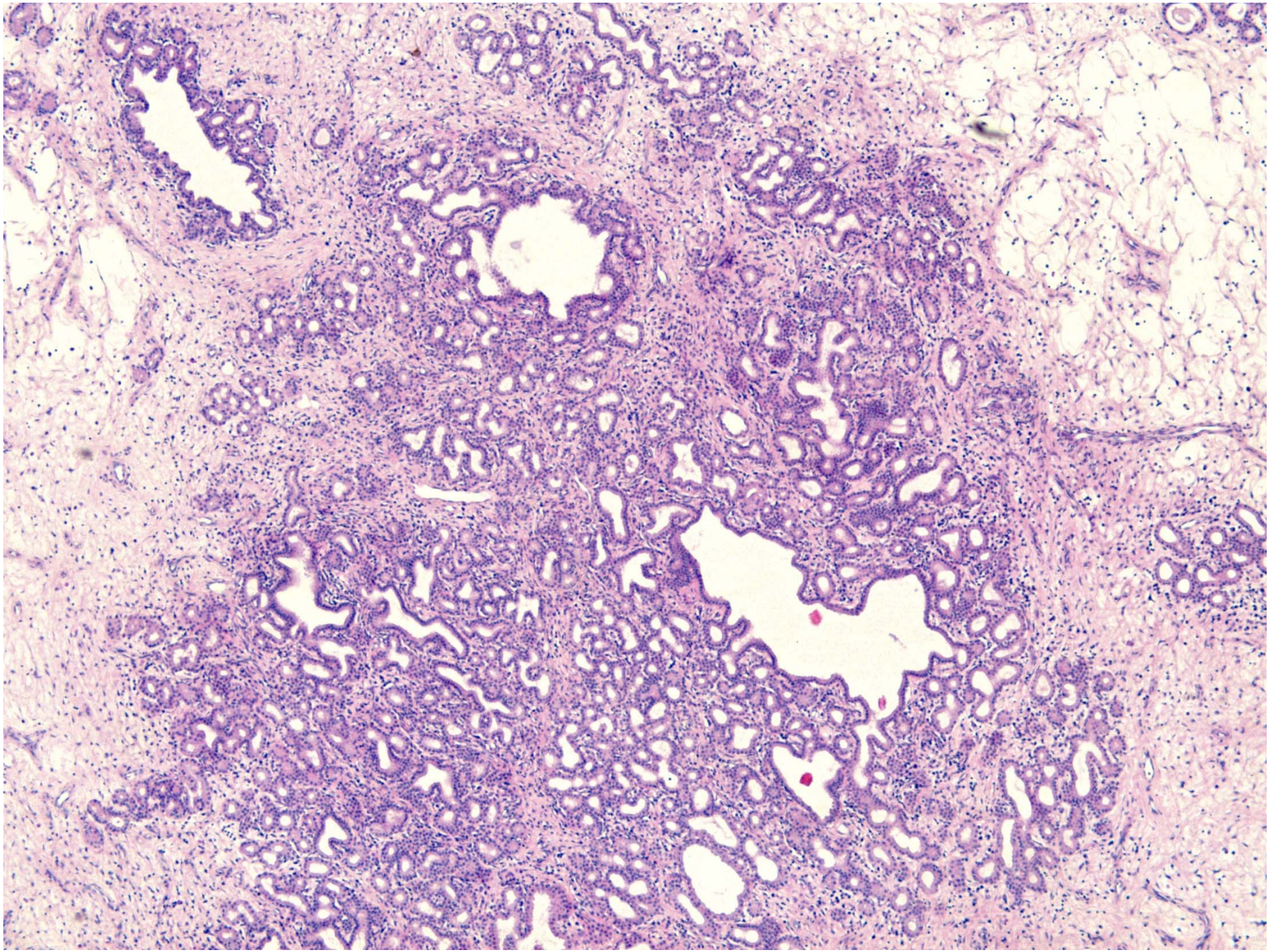
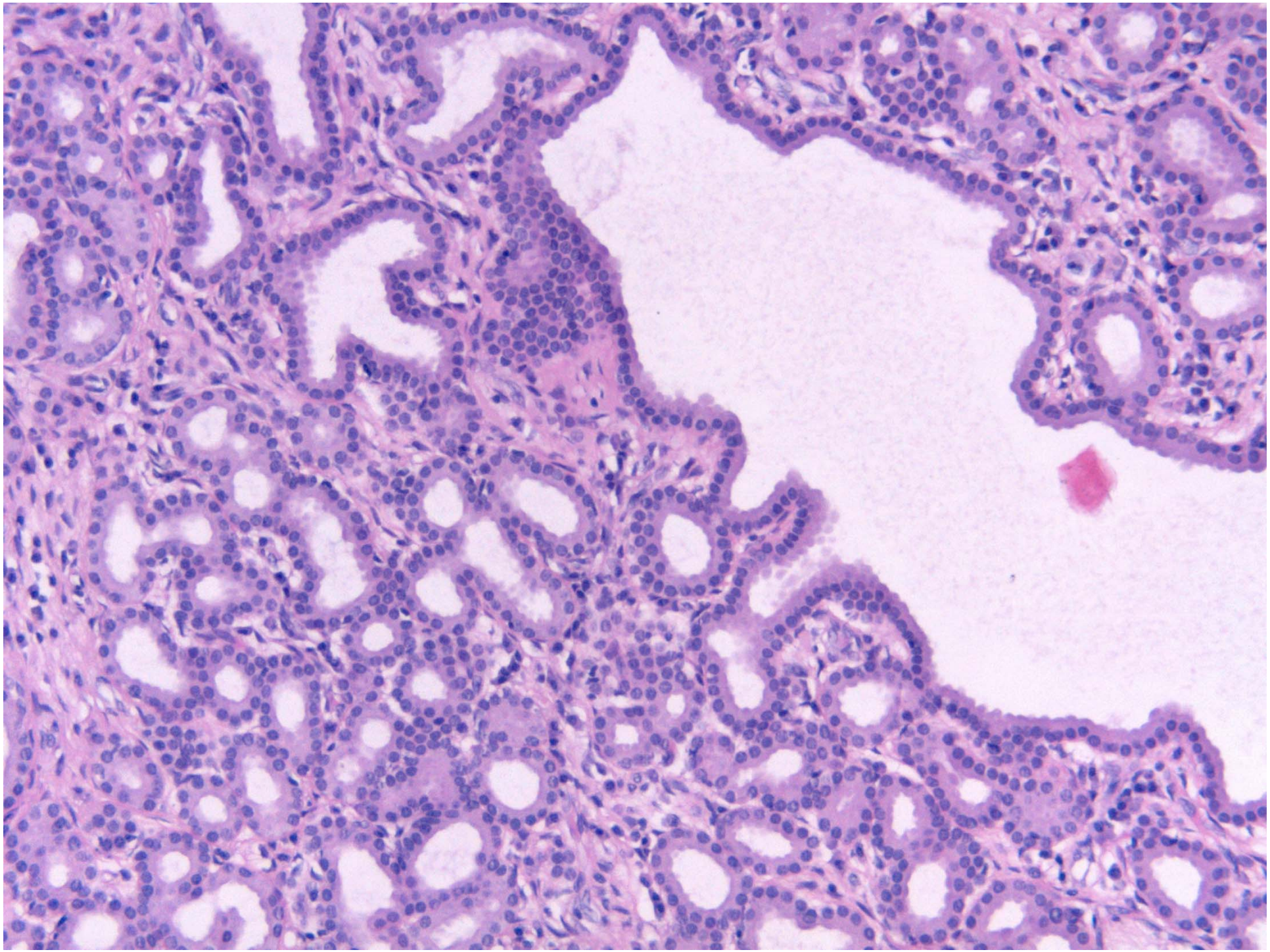
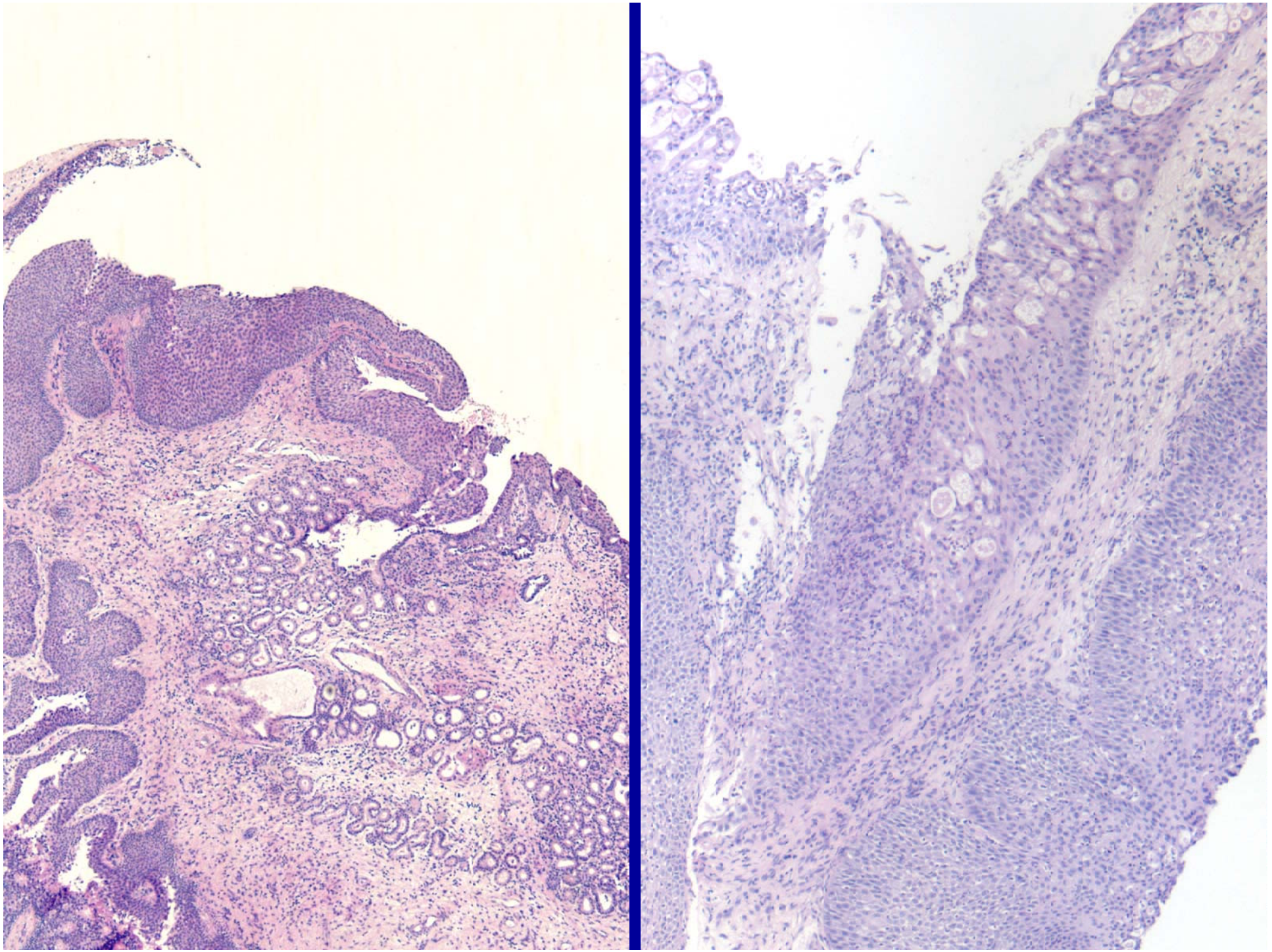
Case 1

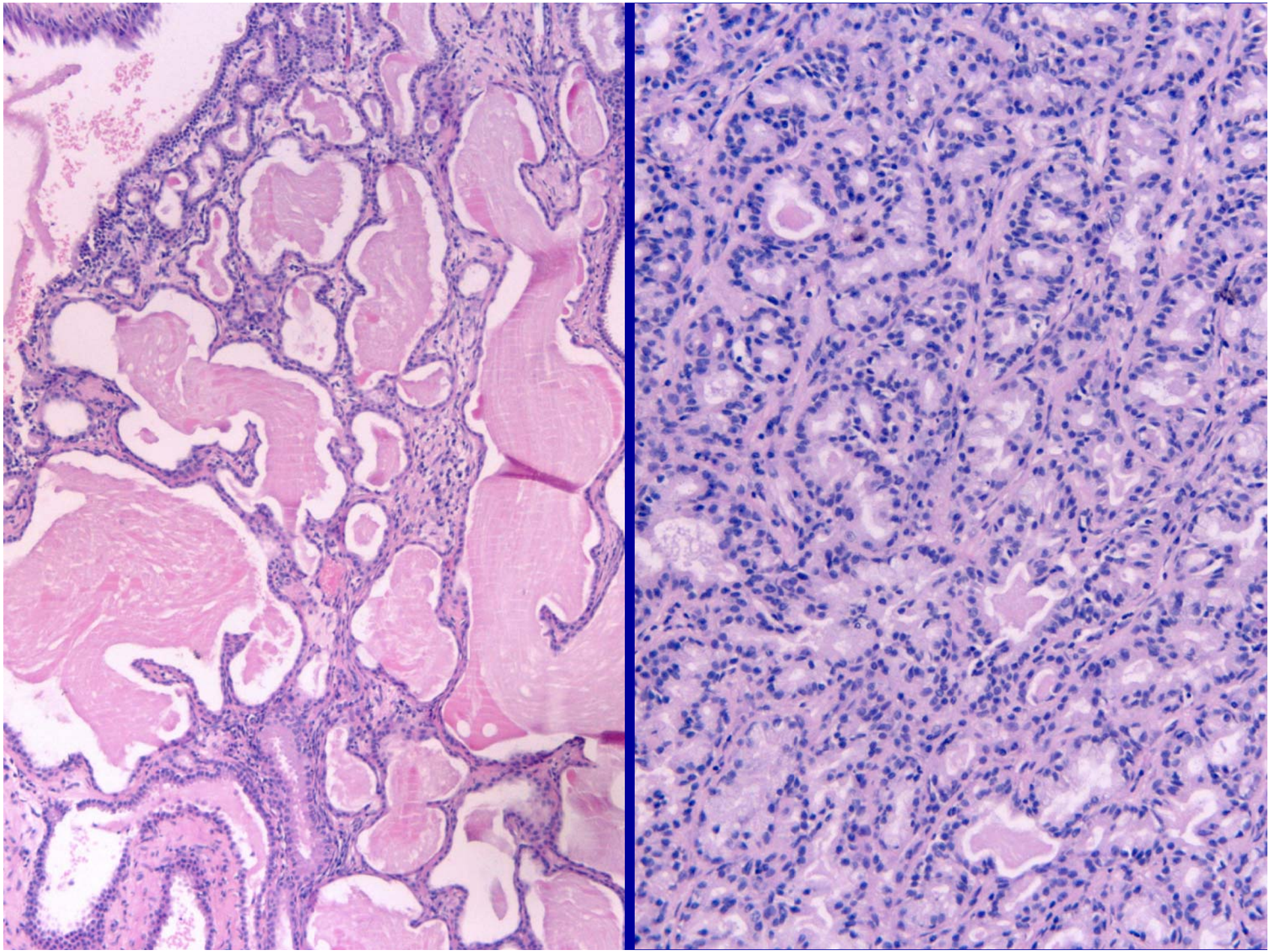
47-yr-old male with a polypoid lesion of the right nasal cavity, focally eroding the skull base. A squamous cell carcinoma of the oral cavity was also removed during the same surgical procedure.

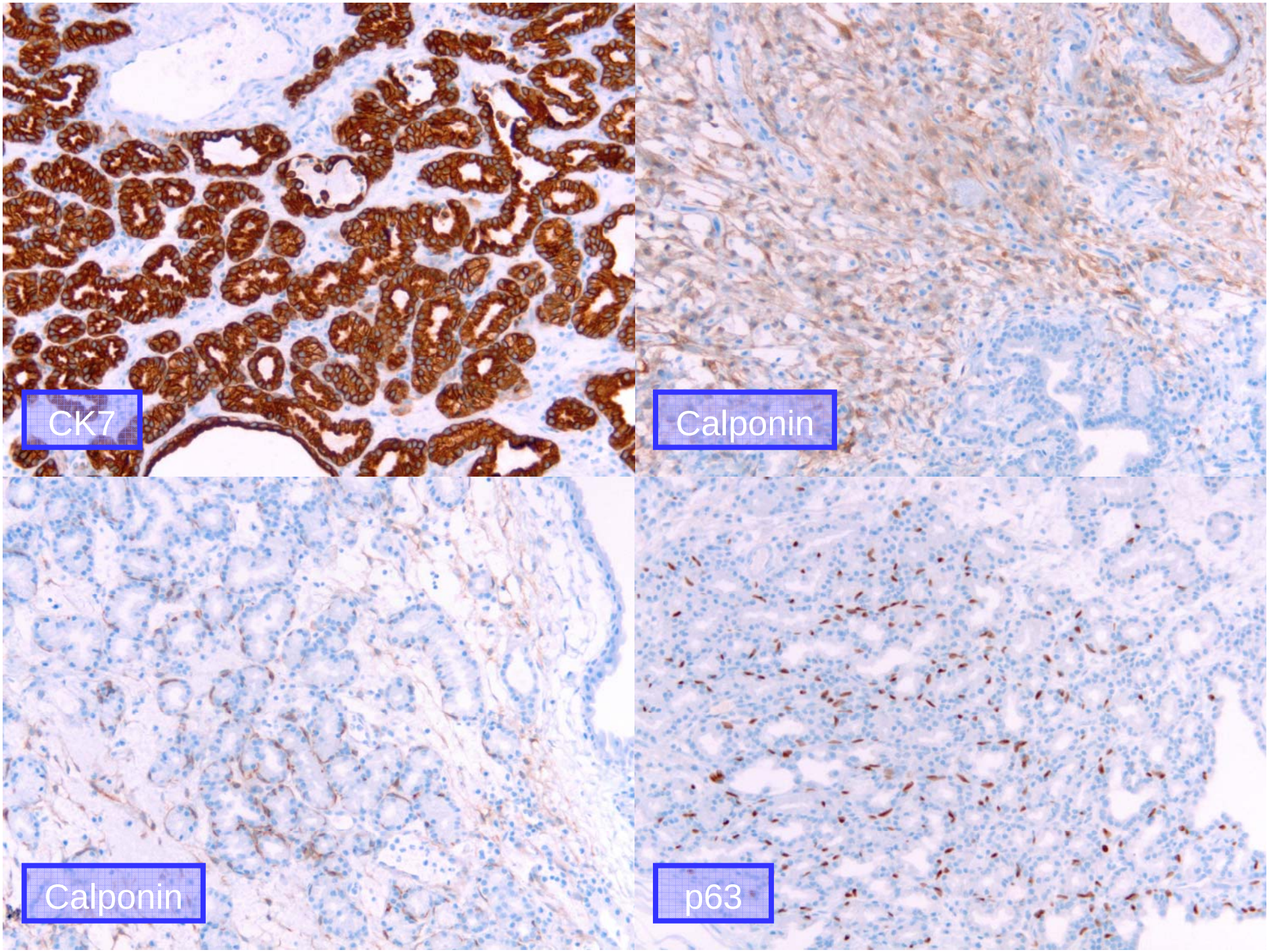











CK7
Calponin
Calponin
p63

Diagnosis

Sinonasal seromucinous hamartoma (microglandular adenosis of the nose)

Seromucinous hamartoma

- Rare benign glandular proliferation of the sinonasal tract and nasopharynx described by Baillie and Batsakis in 1974
- Approximately 25 cases reported
- Polypoid lesions, posterior nasal septum and nasopharynx (80%)>>>lateral nasal wall
- Wide age range (14-85) and slight male predominance (3:2)
- Obstructive symptoms

Seromucinous hamartoma

- Lobular or haphazard growth of small glands and tubules, primarily composed of serous cells with eosinophilic cytoplasm
- Mucinous cells are not a common feature
- The nuclei are small and there is no appreciable mitotic activity or necrosis
- Edematous or fibrous stroma, variable mixed chronic inflammatory infiltrate
- Periglandular hyalinization may be seen

Seromucinous hamartoma

Immunohistochemistry

- Seromucinous hamartomas typically stain for S100 and CK7 and are negative for CK20
- In most cases there is no myoepithelial layer with actin and calponin and also lack the p63 and 34bE12 basal layer

Seromucinous hamartoma

Differential Diagnosis

- Low grade adenocarcinoma:
  - SH does not show the epithelial tufting, micropapillae, haphazard back-to-back growth or cribriforming that can be seen in sinonasal low grade adenocarcinomas
- Inflammatory polyp
- Respiratory Epithelial Adenomatoid Hamartoma (REAH)

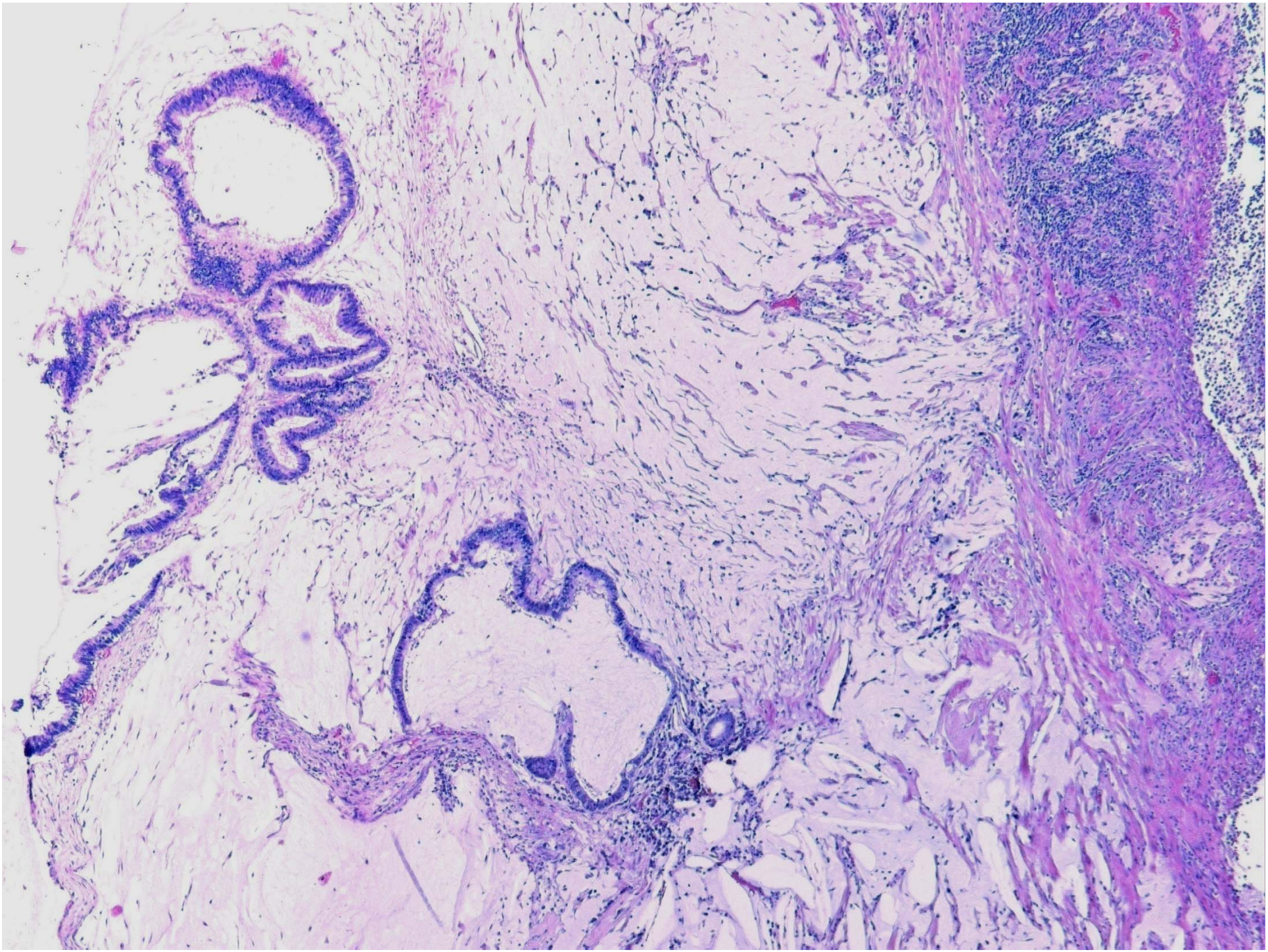
Seromucinous hamartoma

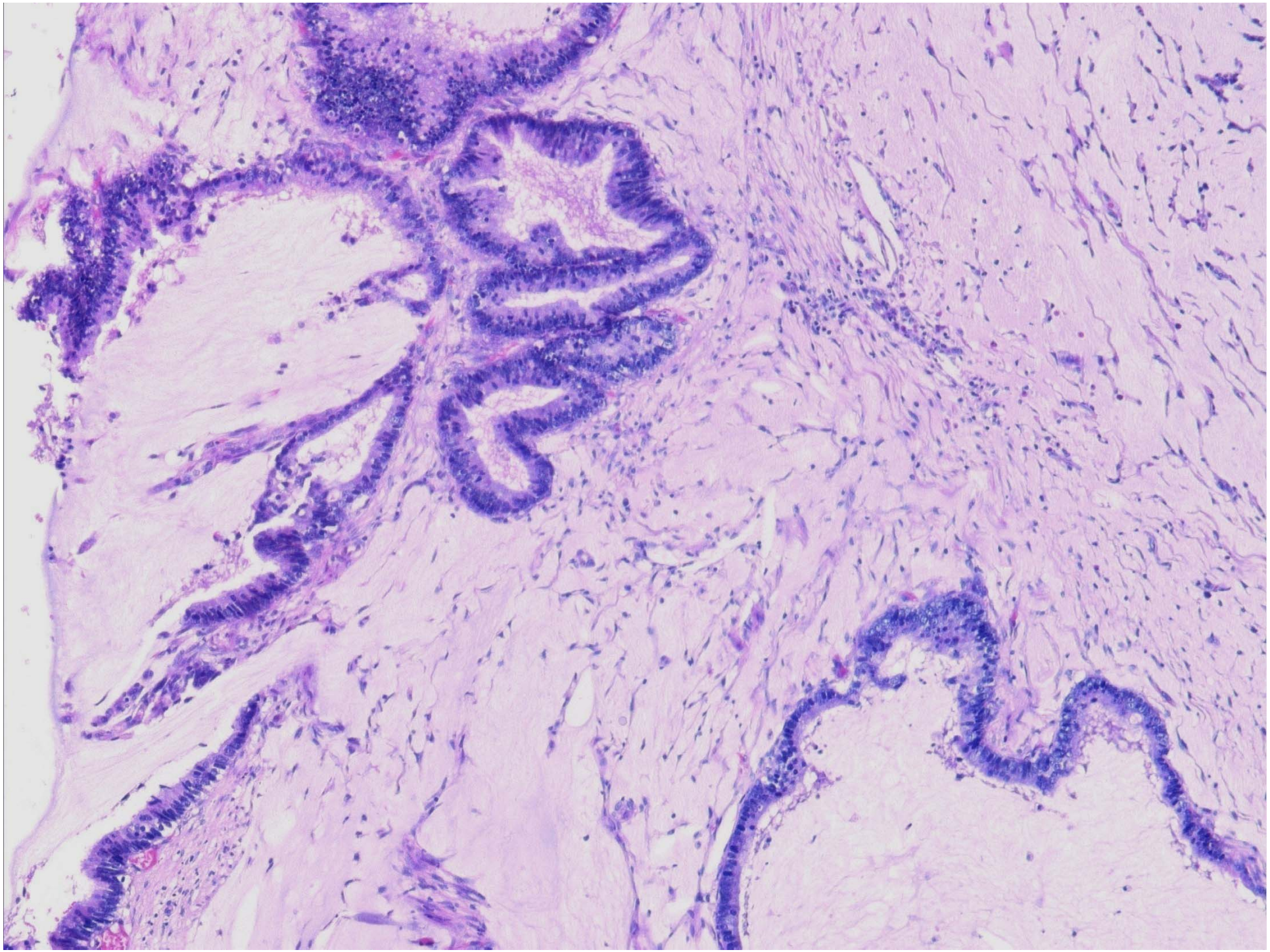
Treatment and Prognosis

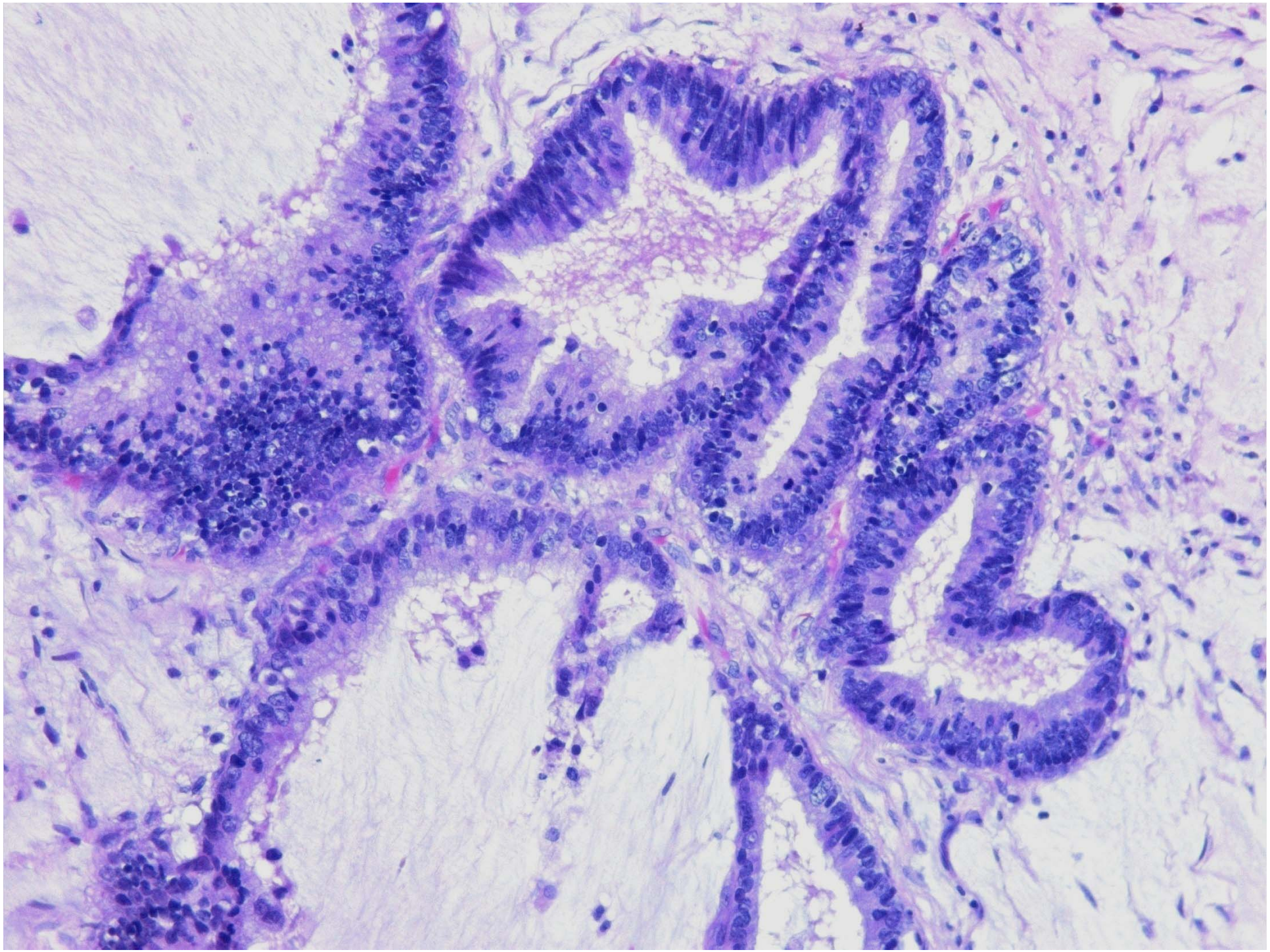
- Complete excision is curative in virtually all cases
- One example with recurrence reported in the literature
- Hamartoma or true neoplasm?

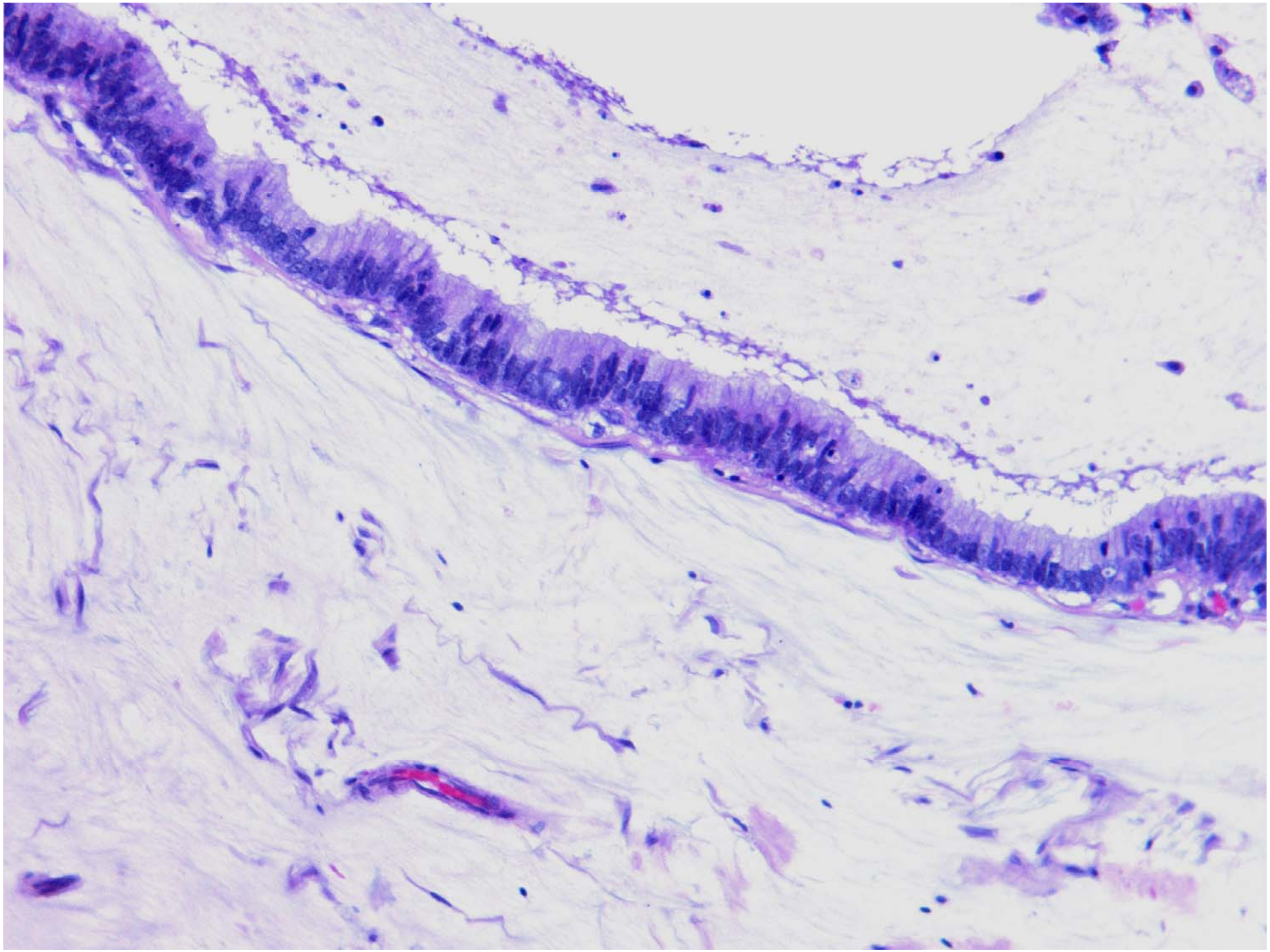
Case 2

A 62 year old male with a tumor involving the left nasal cavity and the ethmoid. The patient had been employed in a leather factory for 40 years.









Diagnosis

Intestinal type adenocarcinoma (mucinous variant)

Intestinal Type Adenocarcinoma

- In our series the most frequent adenocarcinoma
- Association with occupational exposure to wood or leather dust
- Male predominance
- Mean age at diagnosis 58 yrs
- Aggressive tumors often presenting in advanced stage
- Repeated local recurrences (50%), unfrequent lymph node (0-20%) or distant metastases (30%)

Intestinal Type Adenocarcinoma

• Papillary tubular cylinder cell		74%
◦ Well differentiated	18%	
◦ Moderately differentiated	36%	
◦ Poorly differentiated	20%	
• Alveolar goblet cell	13%	Mucinous 26%
• Signet ring cell	3%	
• Transitional	10%	

From: Barnes 1986; Kleinsasser 1988; Franquemont 1991; Franchi 1999

Intestinal Type Adenocarcinoma

Differential Diagnosis

- Metastatic colorectal adenocarcinoma
- Low grade non-intestinal type adenocarcinoma
- Mucocele

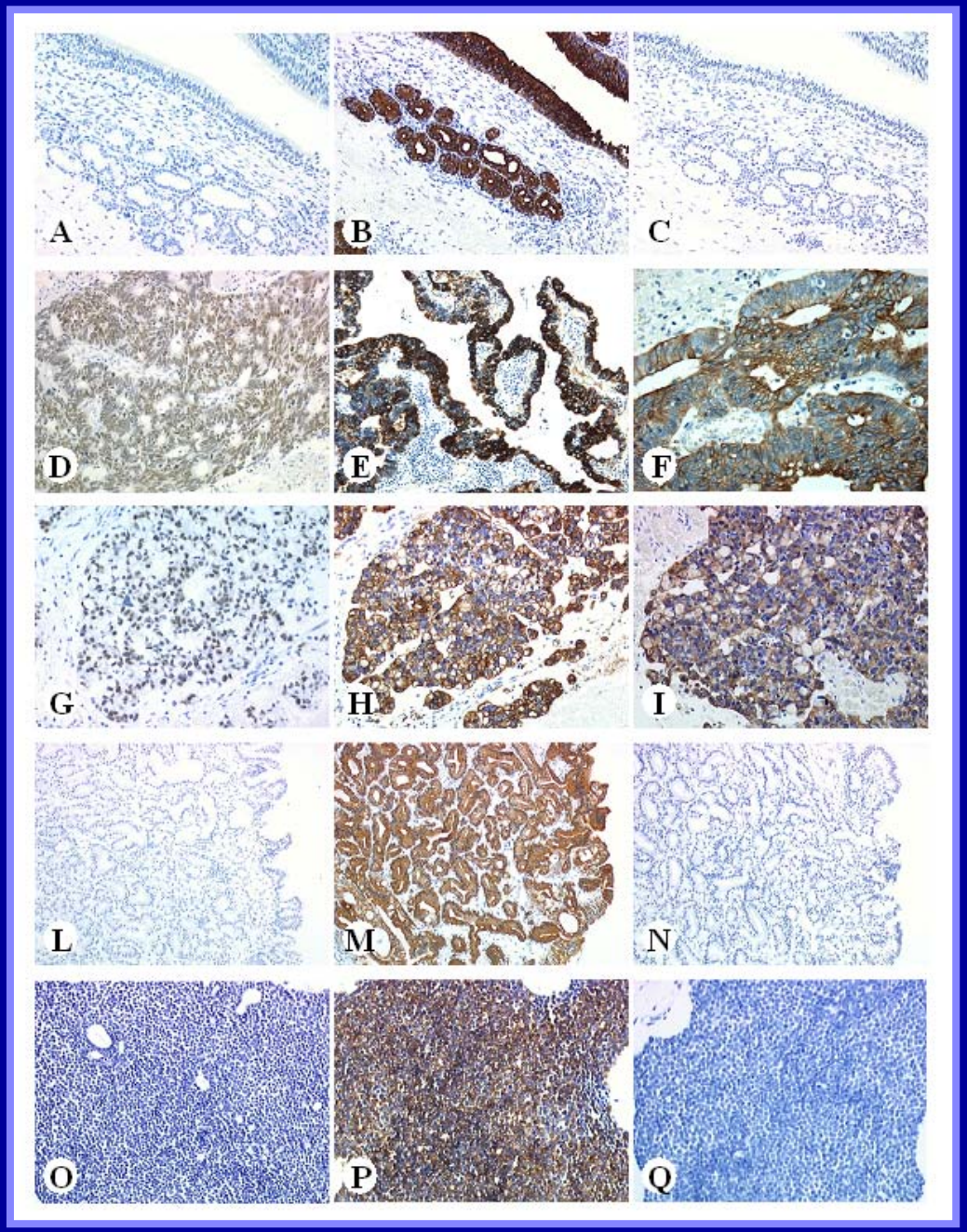
Virchows Arch (2004) 445:63–67
DOI 10.1007/s00428-004-1030-4

ORIGINAL ARTICLE

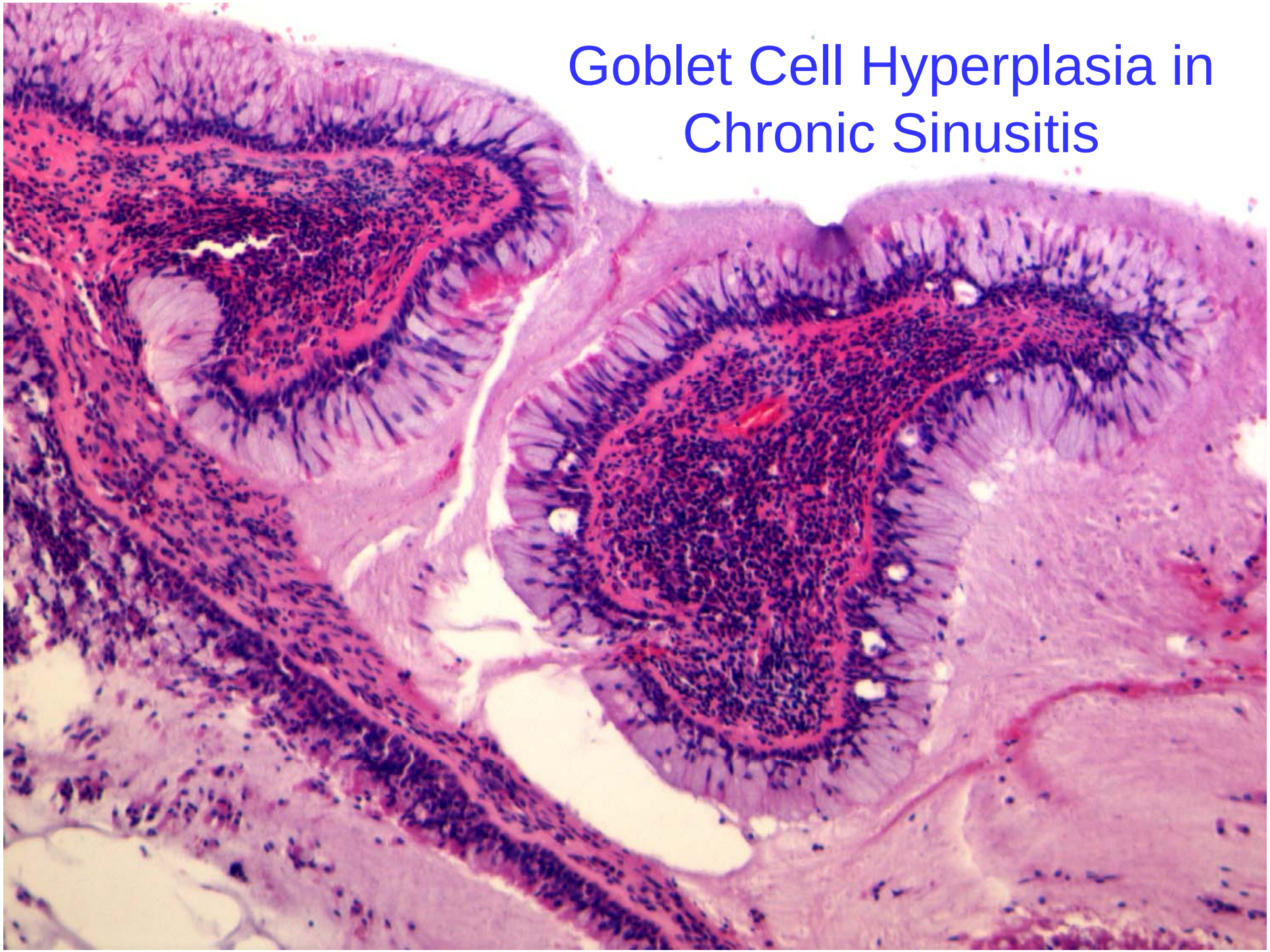
A. Franchi · D. Massi · A. Palomba · M. Biancalani · M. Santucci

CDX-2, cytokeratin 7 and cytokeratin 20 immunohistochemical expression in the differential diagnosis of primary adenocarcinomas of the sinonasal tract

	CDX-2	CK 7	CK 20
Nasal mucosa	A	B	C
ITAC	D	E	F
ITAC, mucinous	G	H	I
Low grade adenocarcinoma	L	M	N
Adenoid cystic carcinoma	O	P	Q

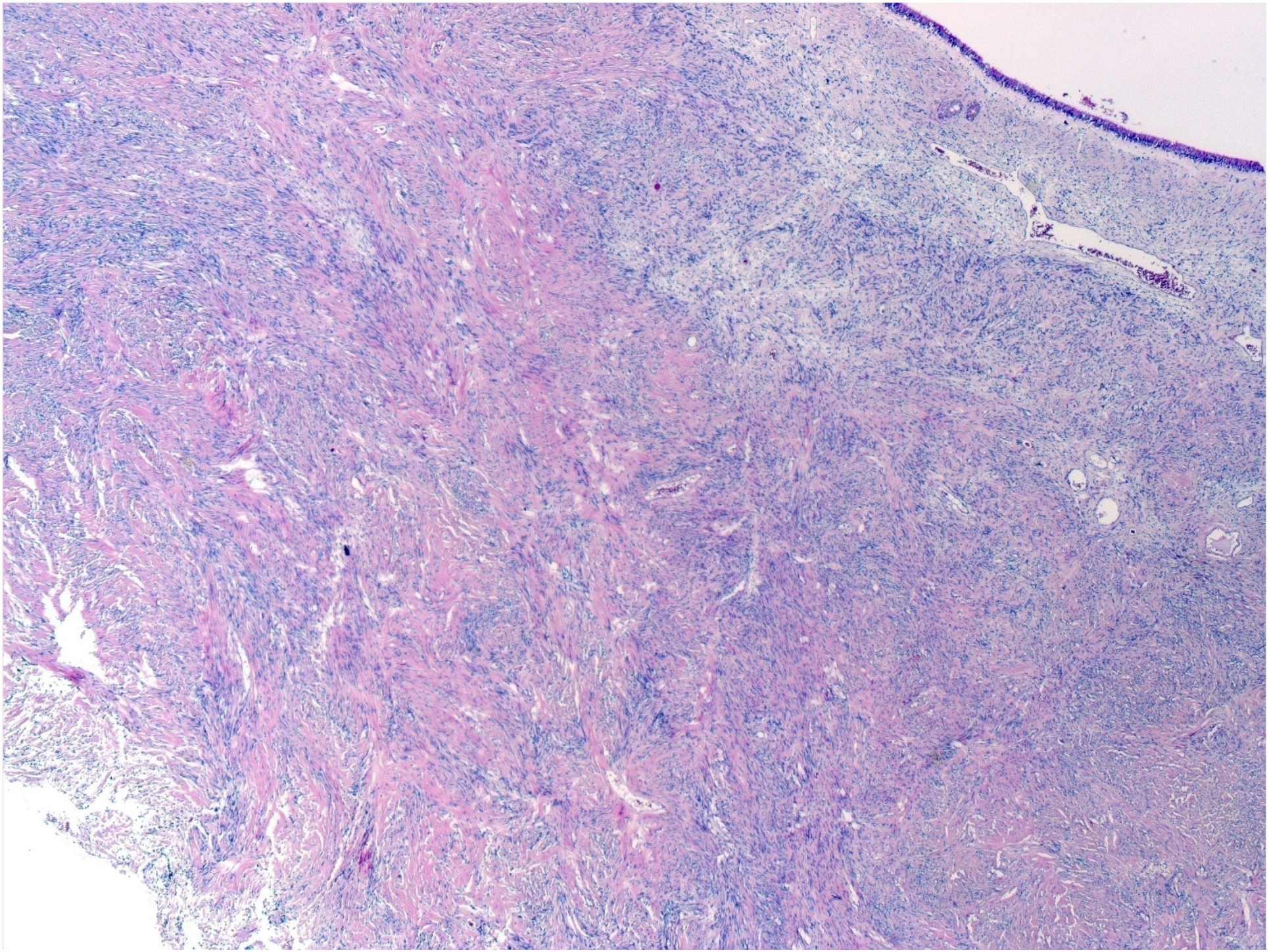


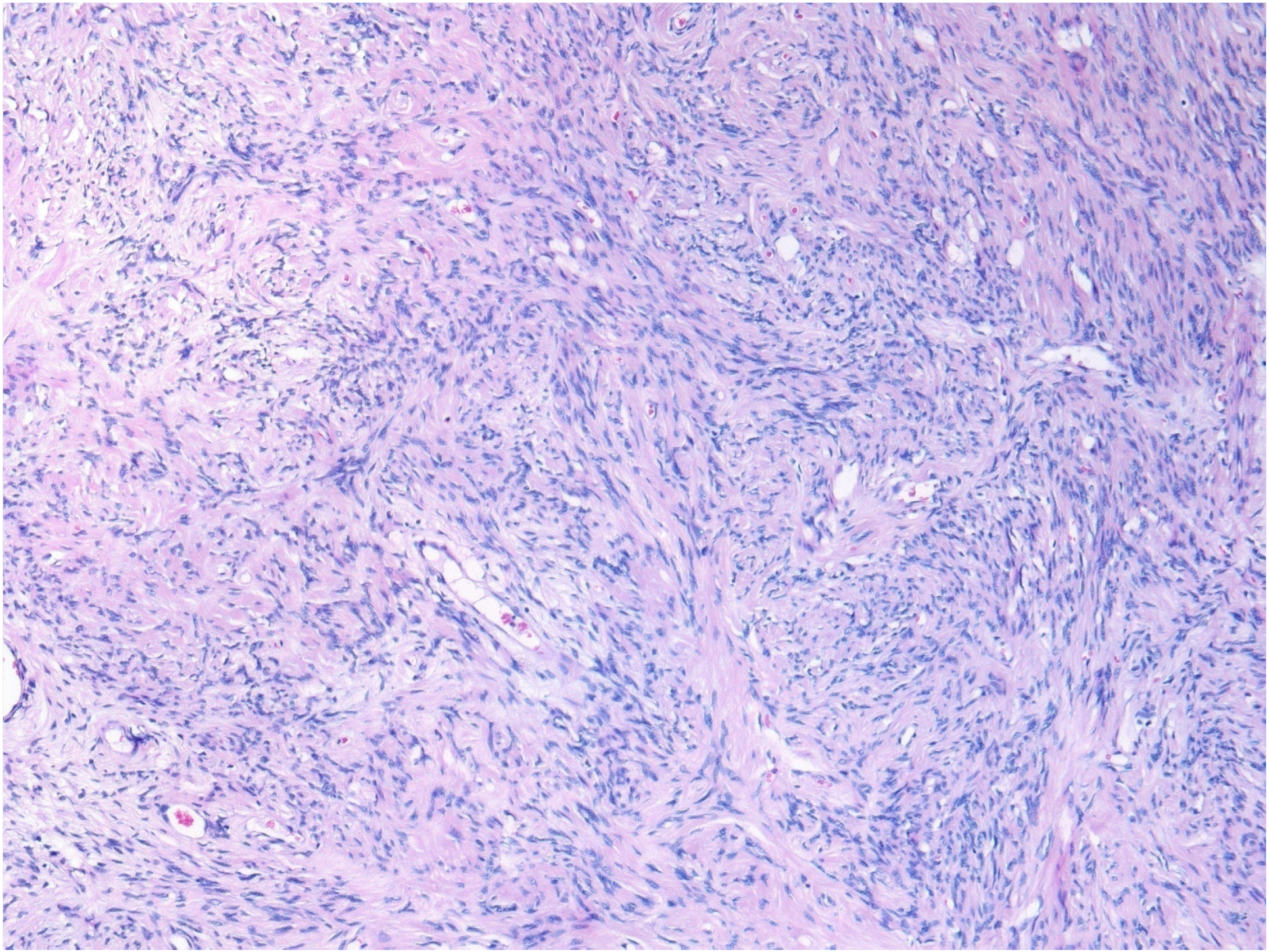
Goblet Cell Hyperplasia in Chronic Sinusitis

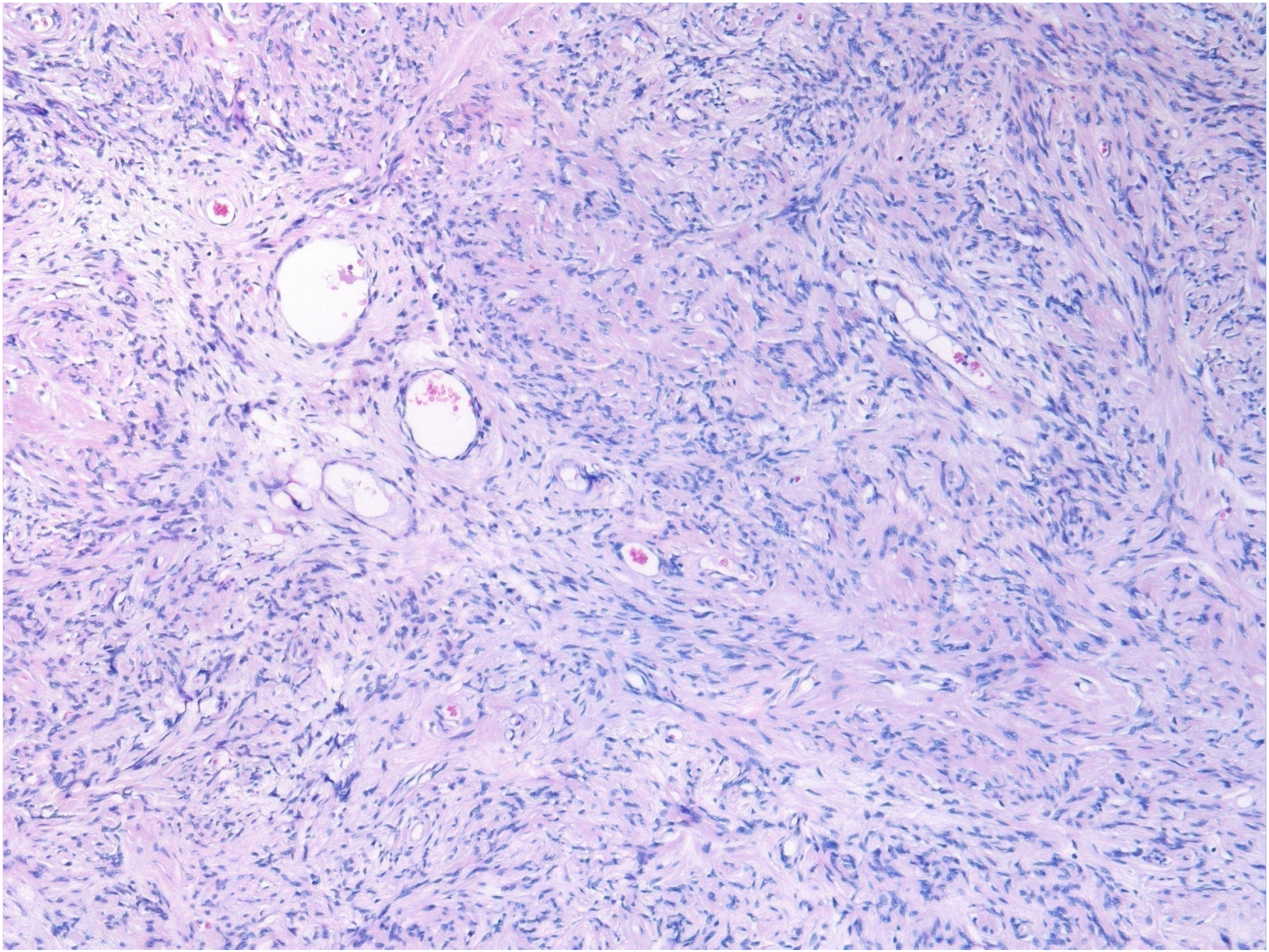


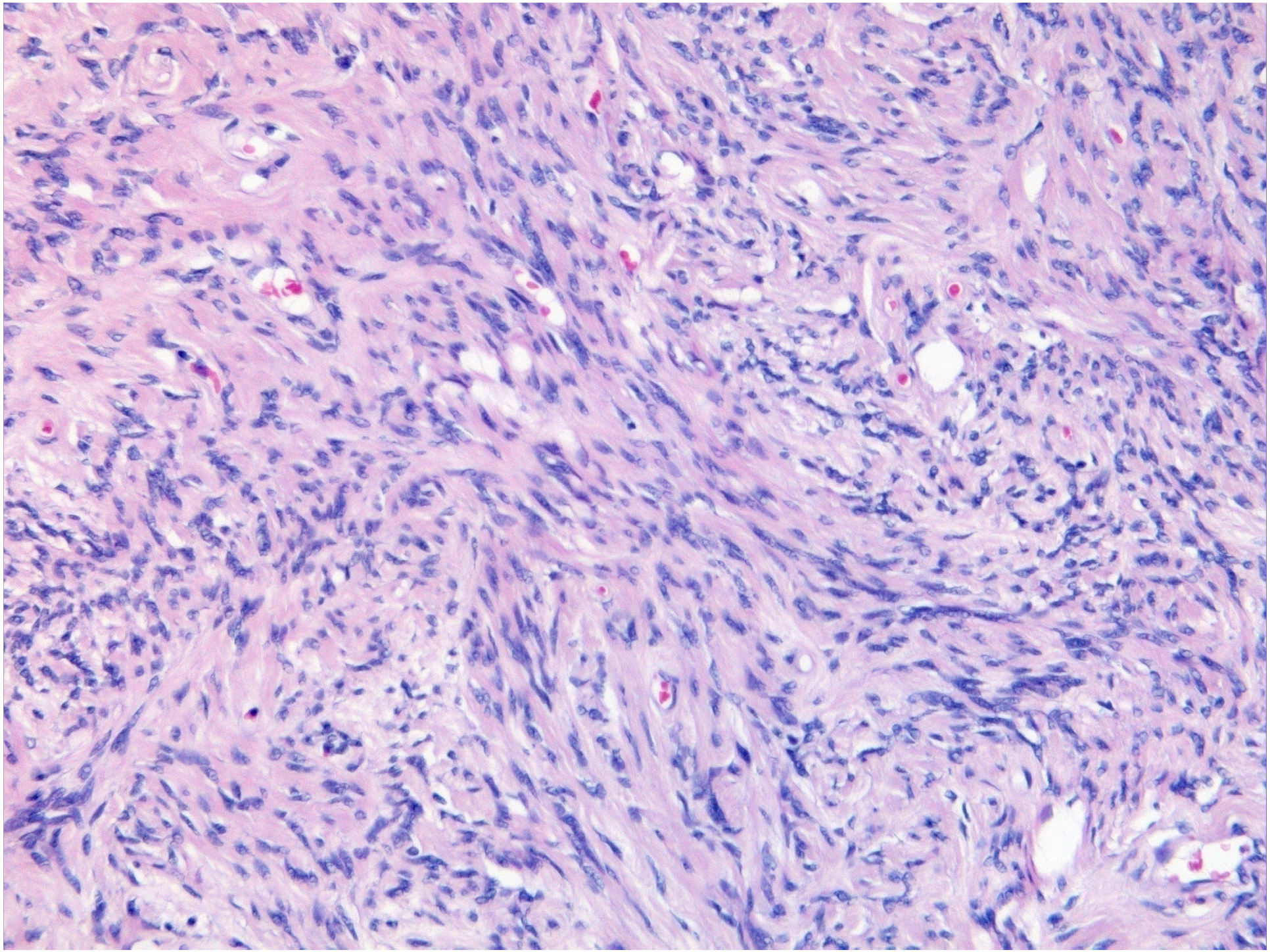
Case 4

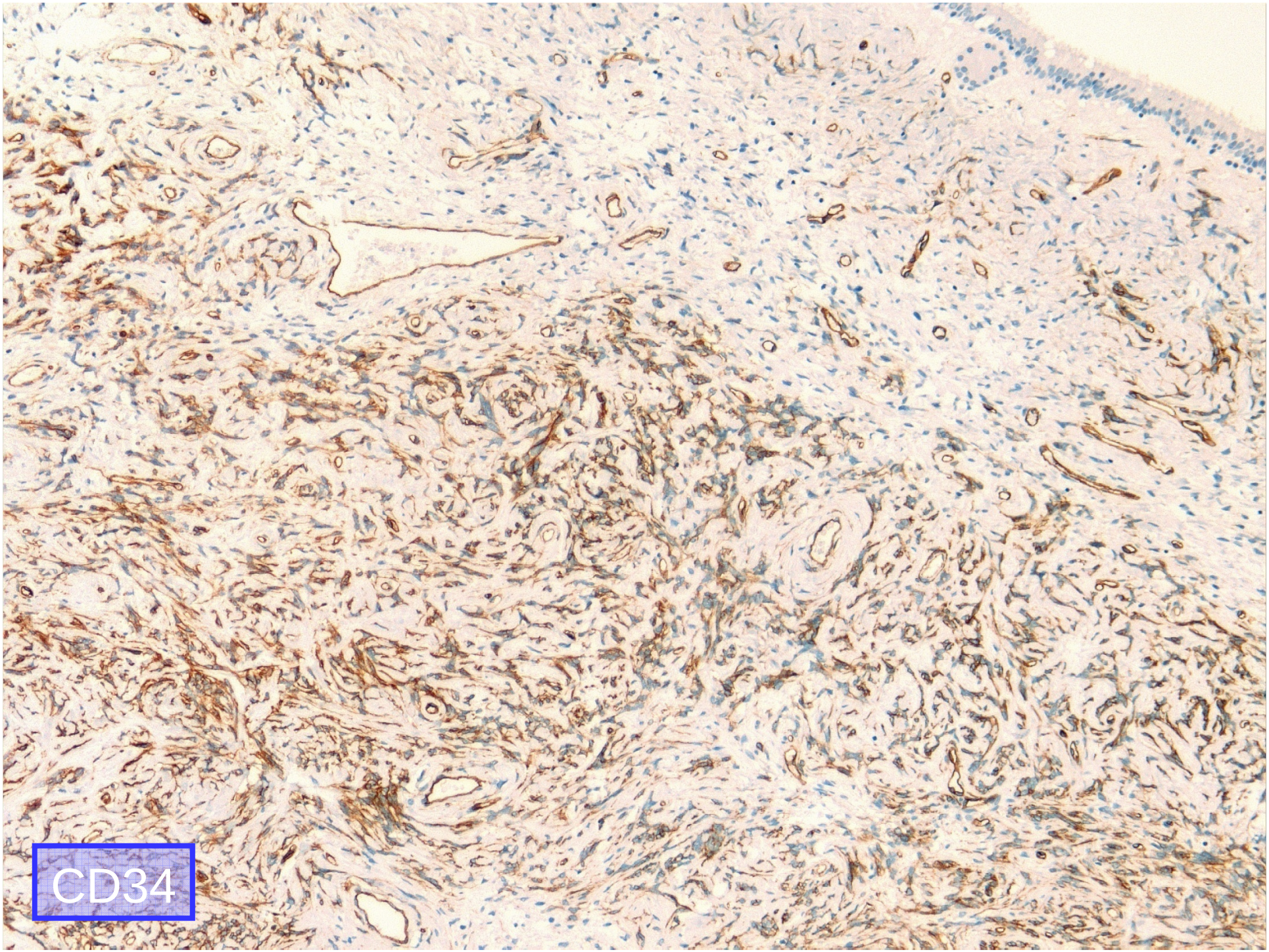
A 38 year old woman with a tumor of the ethmoid sinus, extending in the frontal bone and in the anterior cranial fossa

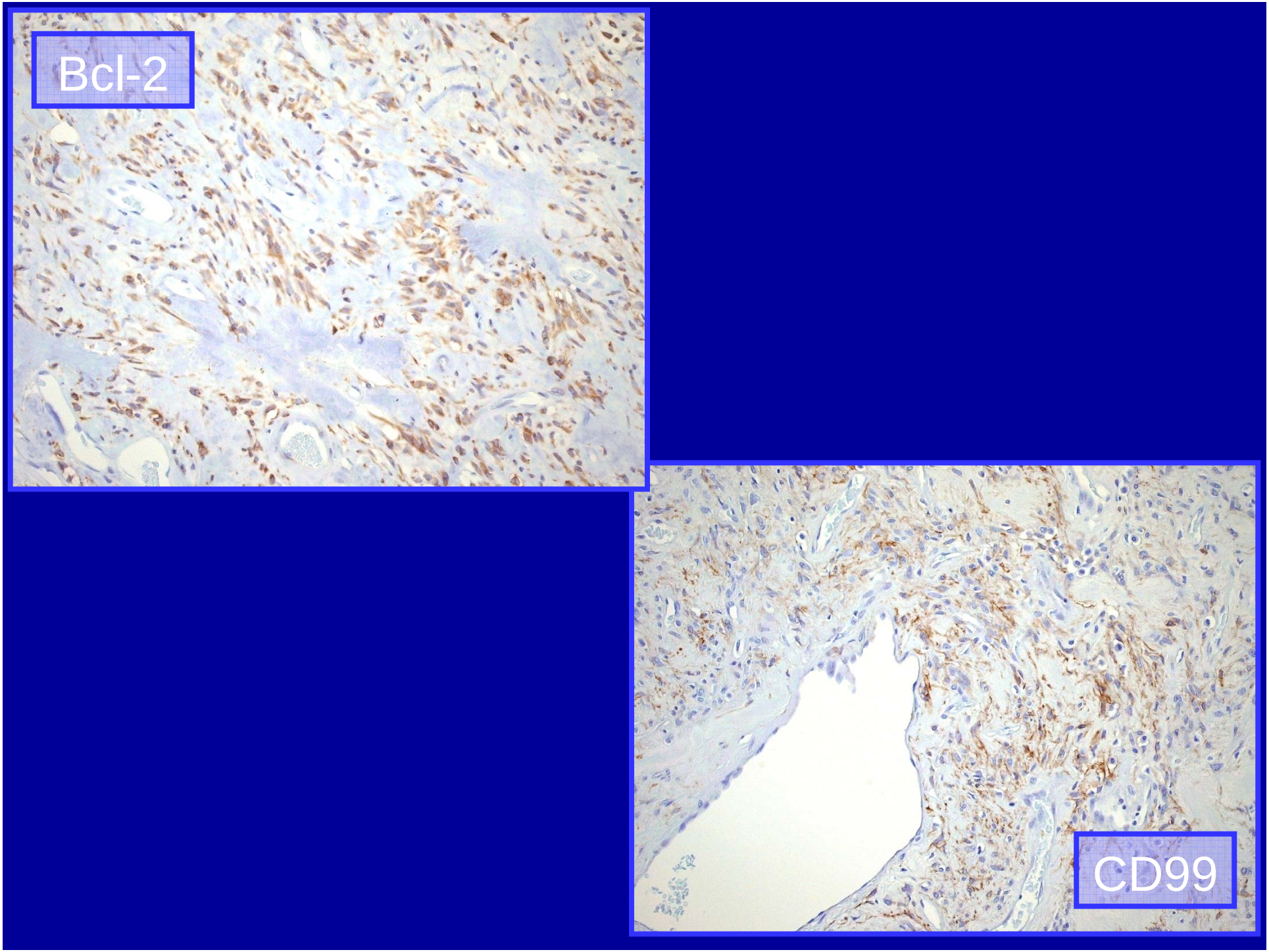









CD34


Bcl-2
CD99

Diagnosis

Solitary fibrous tumour

Solitary fibrous tumour

- Benign fibroblastic proliferation with variable cellularity and vascularity having features identical to those of solitary fibrous tumour of the pleura
- Uncommon in the upper respiratory tract (<0.1% of all neoplasms)
- Polypoid firm intranasal mass in a middle-aged patient; no gender predilection

Solitary fibrous tumour

- Proliferation of bland looking, uniform spindle cells, with no specific architectural arrangement, embedded within abundant collagen matrix
- Prominent vascular component, with interlaced thin-walled dilated capillary vessels

Solitary fibrous tumour

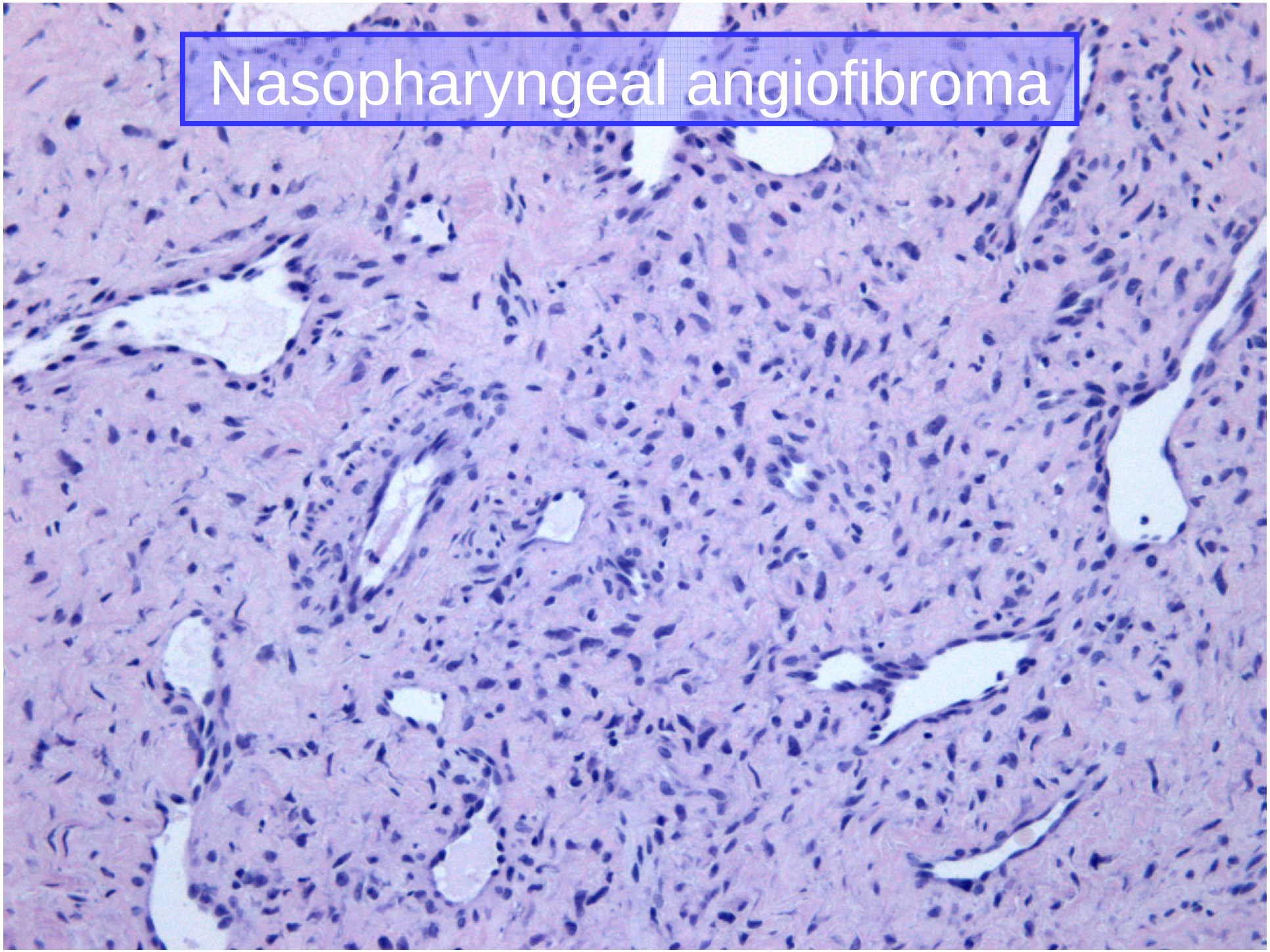
Immunohistochemistry

- Positive for CD34, bcl-2 and CD99
- Negative for EMA, S100 and actins

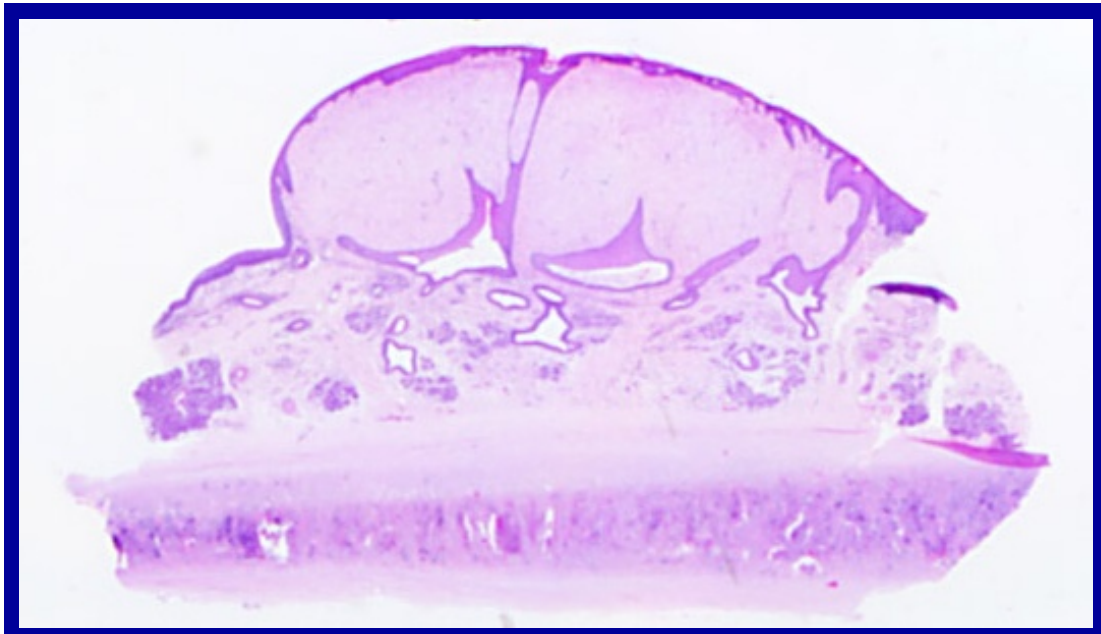
Solitary fibrous tumour

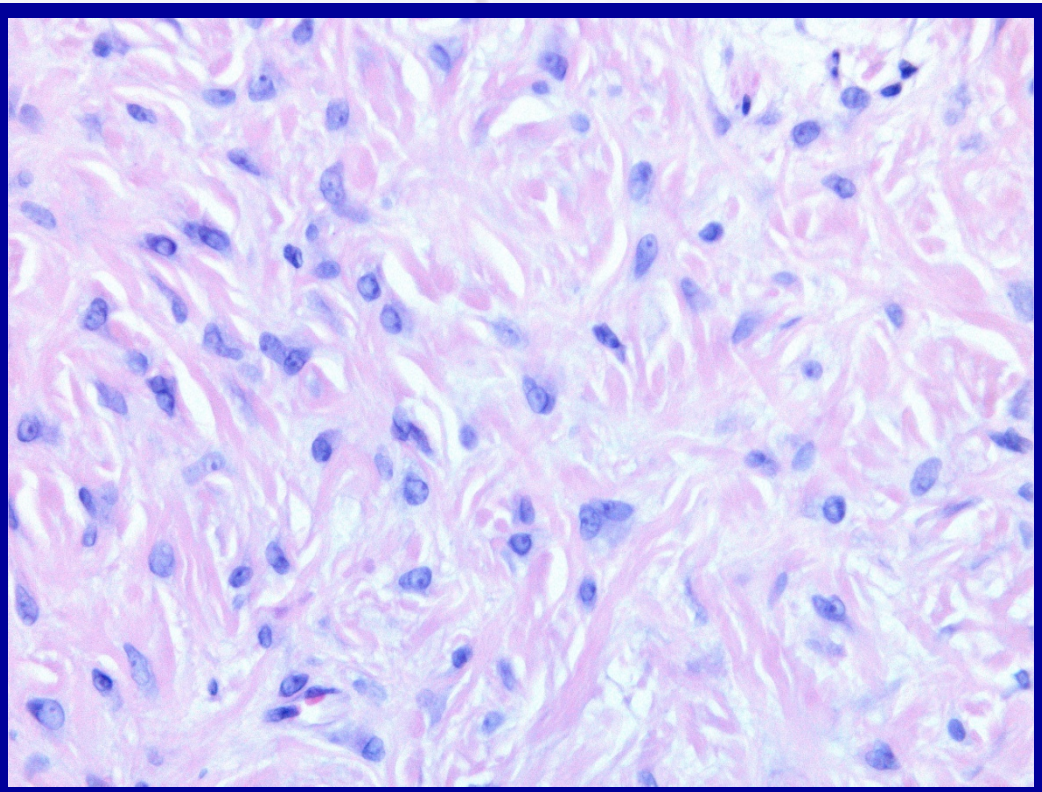
Differential diagnosis

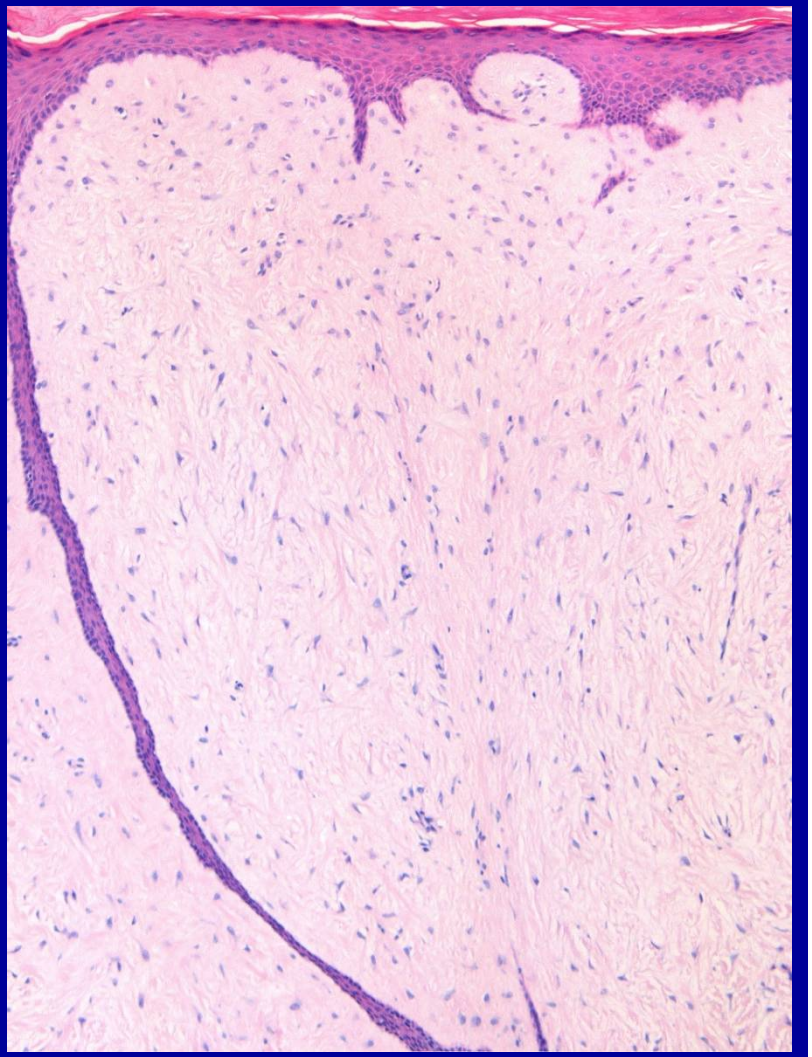
- Hemangiopericytoma
- Angiofibroma
- Nasal fibroma
- Desmoid fibromatosis
- Benign/malignant schwann cell tumours
- Synovial sarcoma
- Fibrosarcoma


Nasopharyngeal angiofibroma

Nasal fibroma







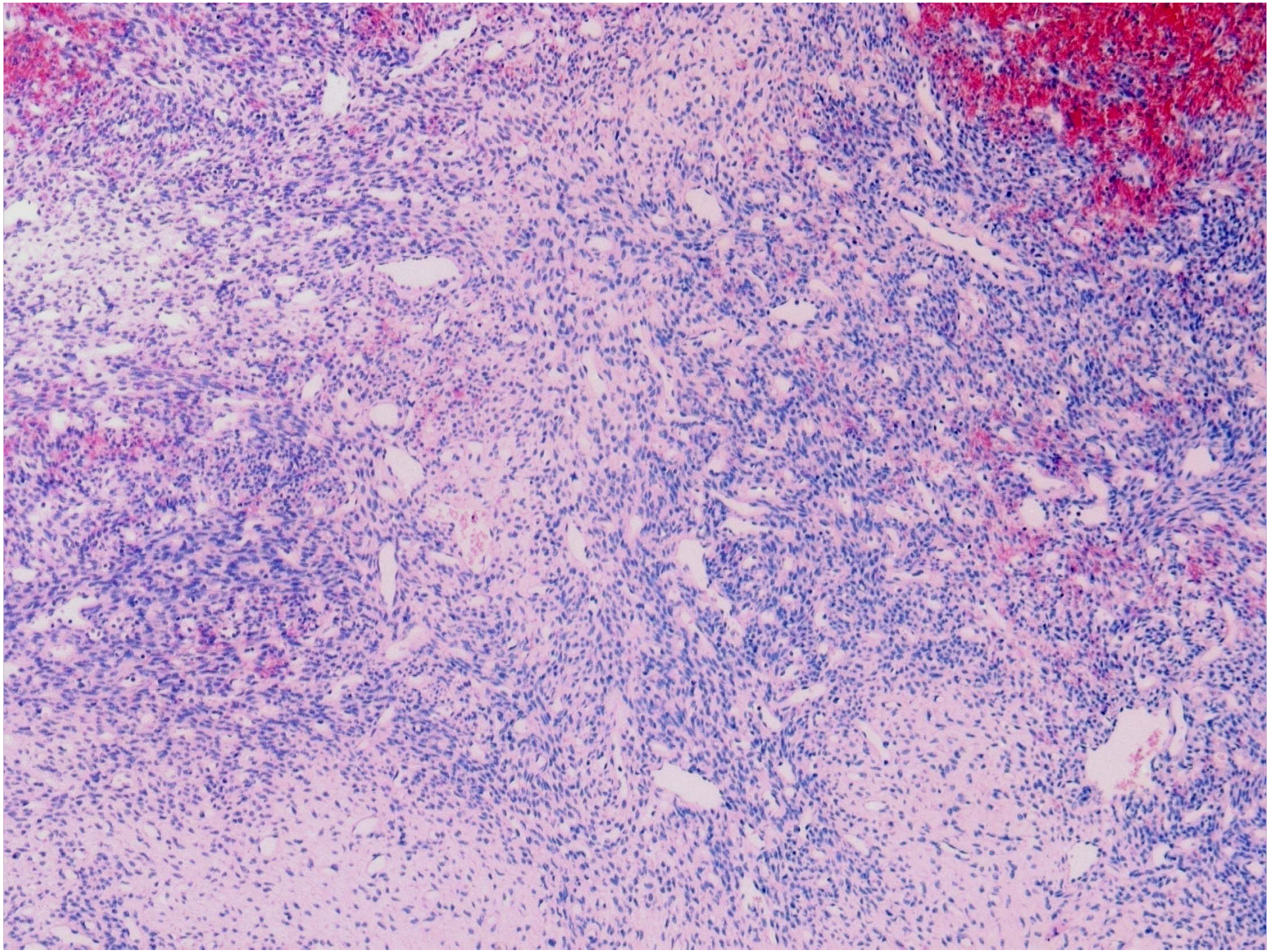
Solitary fibrous tumour

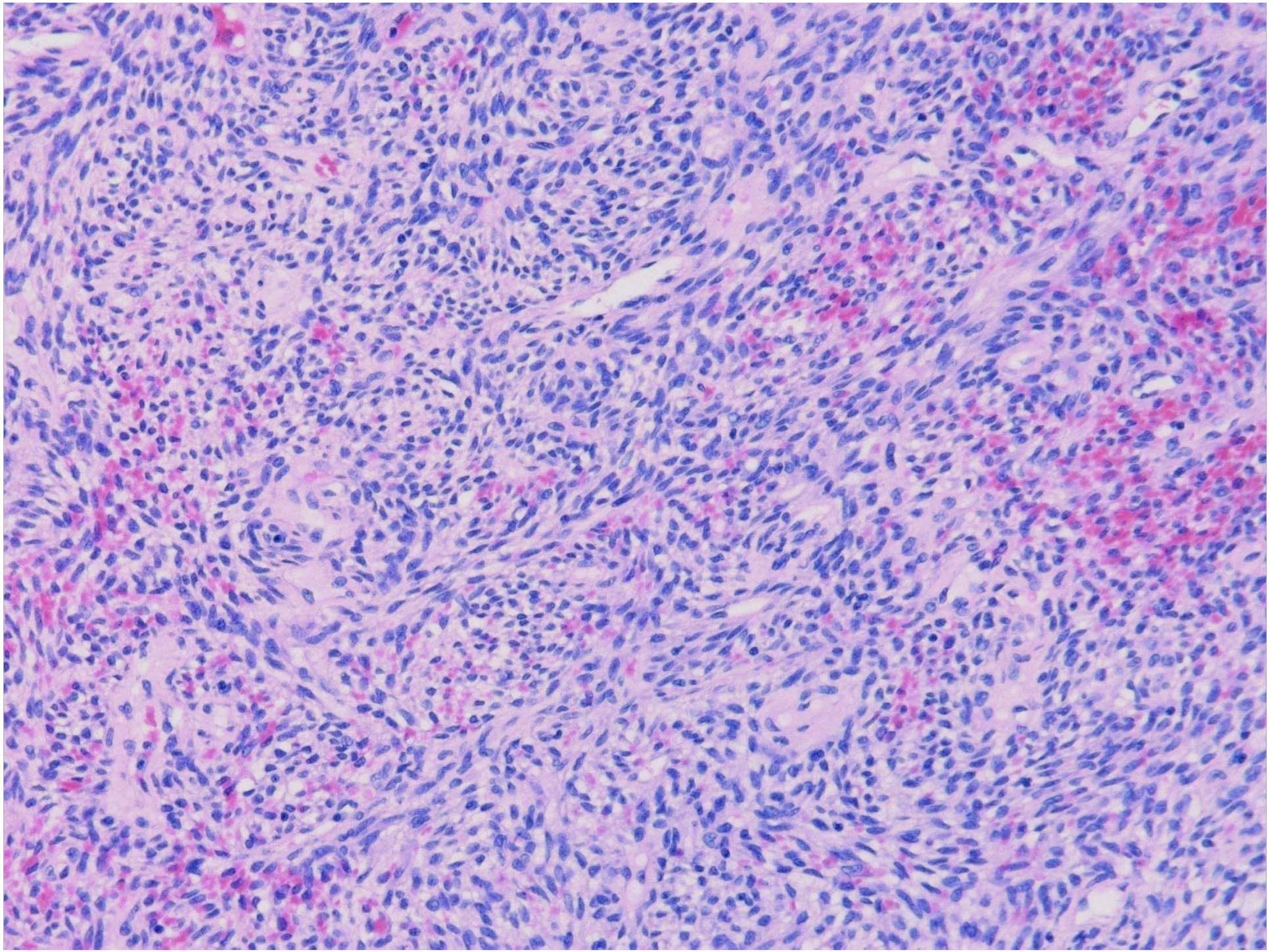
Treatment and prognosis

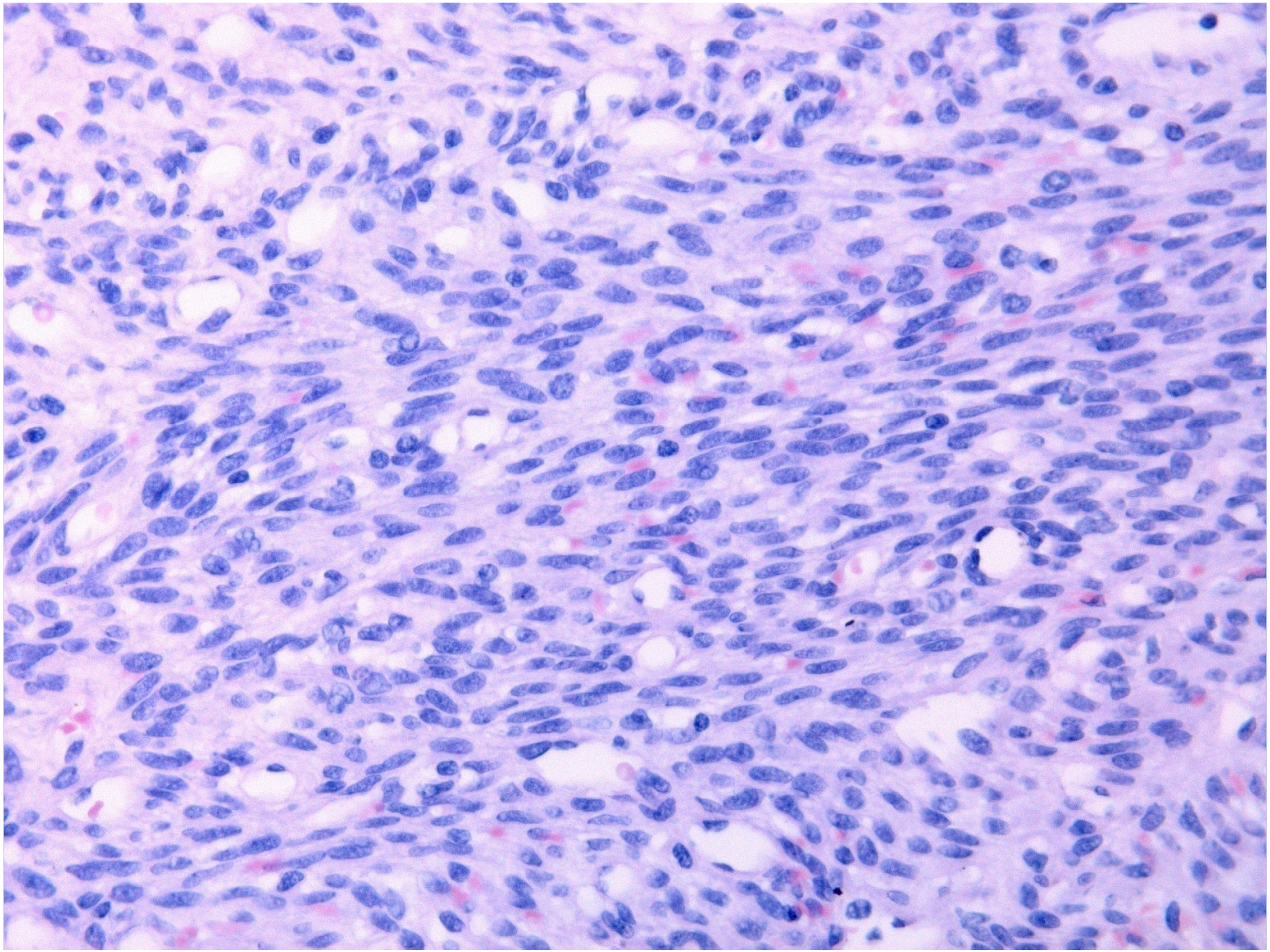
- Complete surgical removal is the treatment of choice
- Nasal solitary fibrous tumour has a benign behaviour, although cases with infiltration of the ethmoid sinuses, extension to the nasopharynx or to the anterior cranial fossa have been described
- So far, no nasal solitary fibrous tumour has been reported to recur or metastasize

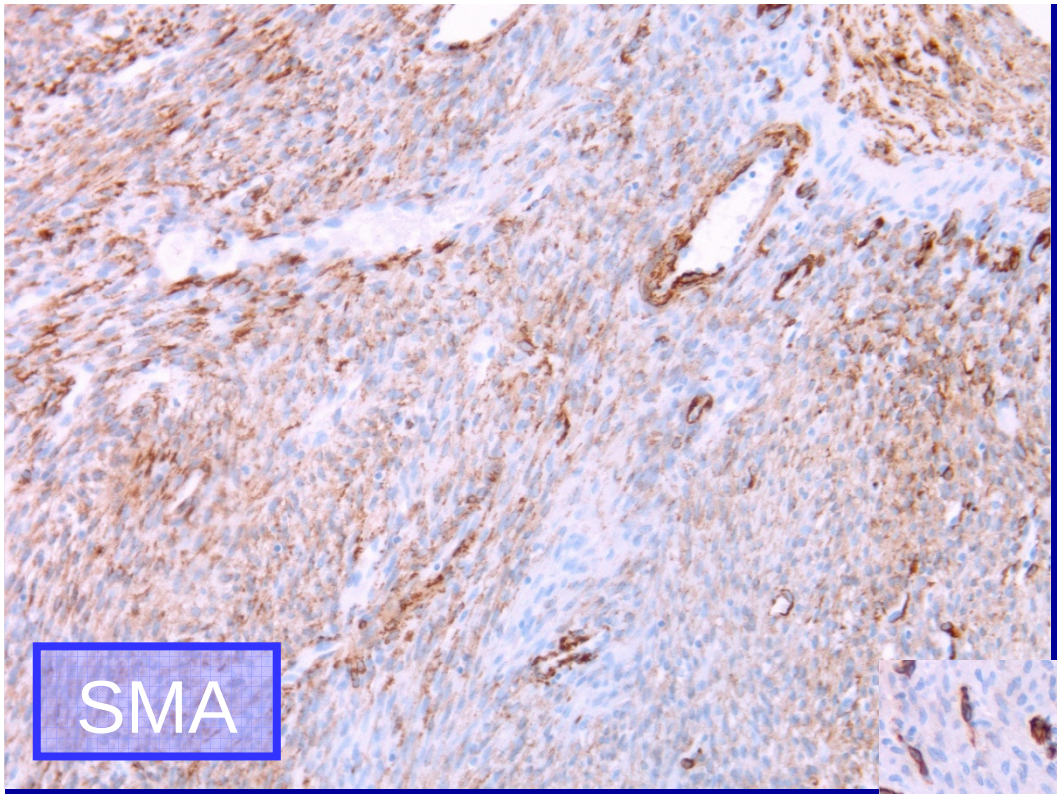
Case 5

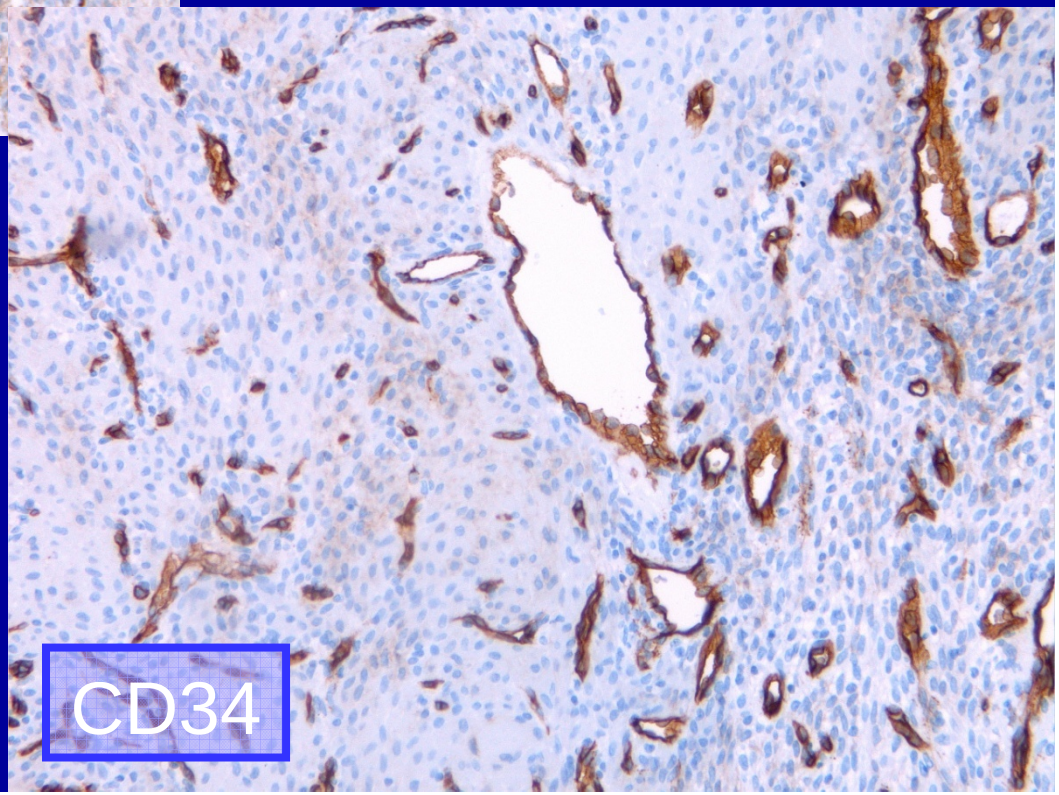
A 38 year old woman with a tumor of the ethmoid sinus, extending in the frontal bone and in the anterior cranial fossa








SMA


CD34

Diagnosis

Sinonasal-type hemangiopericytoma

Sinonasal-type hemangiopericytoma

- A sinonasal tumour demonstrating perivascular myoid phenotype
- <0.5% of all sinonasal neoplasms
- Very slight female predominance
- All ages can be affected with a peak in the 7th decade
- Tumours most frequently arise unilaterally in the nasal cavity alone, although extension into paranasal sinuses can occur

Sinonasal-type hemangiopericytoma

- Subepithelial well-delineated but unencapsulated cellular tumour effacing or surrounding the normal structures
- Closely packed cells, forming short fascicles
- Prominent vascularity in the form of capillary-sized to large spaces that may have a “staghorn” or “antler-like” configuration
- Peritheliomatous hyalinization is characteristic

Sinonasal-type hemangiopericytoma

- Neoplastic cells are uniform, elongated to oval, and possess vesicular to hyperchromatic, round to oval to spindle- shaped nuclei, and lightly eosinophilic cytoplasm
- Mild nuclear pleomorphism and occasional mitotic figures may be present, but necrosis is not found
- Extravasated erythrocytes, mast cells, and eosinophils are nearly ubiquitously present
- Occasionally, tumour giant cells, fibrosis or myxoid degeneration may be seen

Sinonasal-type hemangiopericytoma

Immunohistochemistry

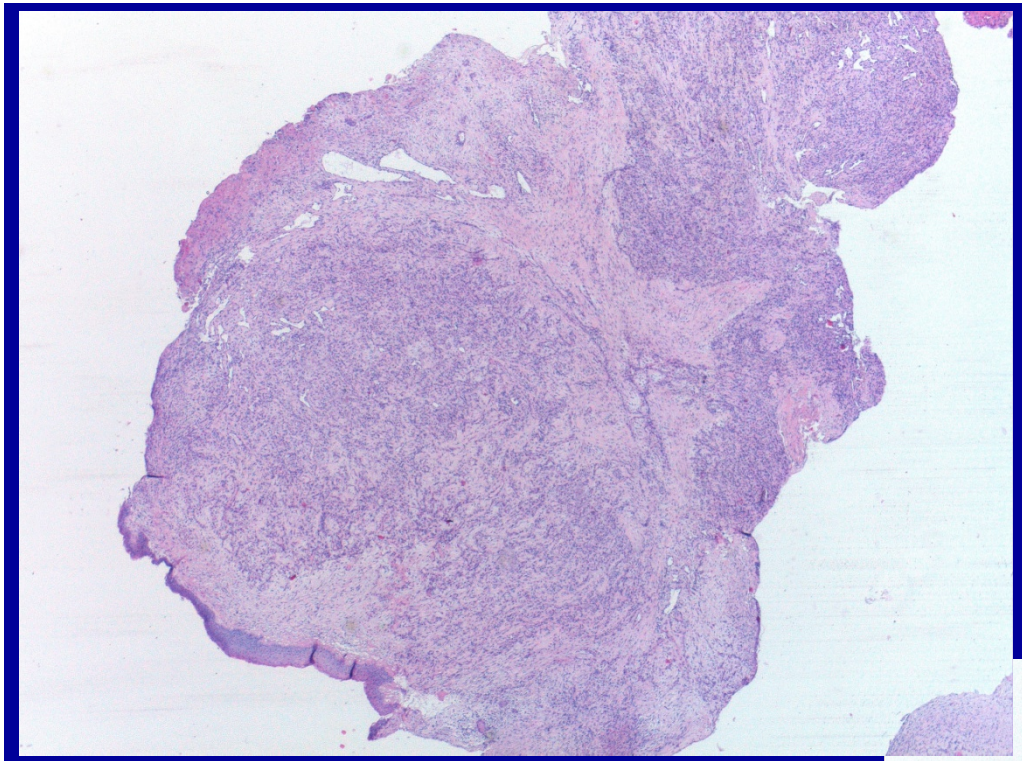
- Positive for actins, factor XIIIA and vimentin
- Negative for CD34, Bcl-2, FVIII-R Ag, CD99 and CD117

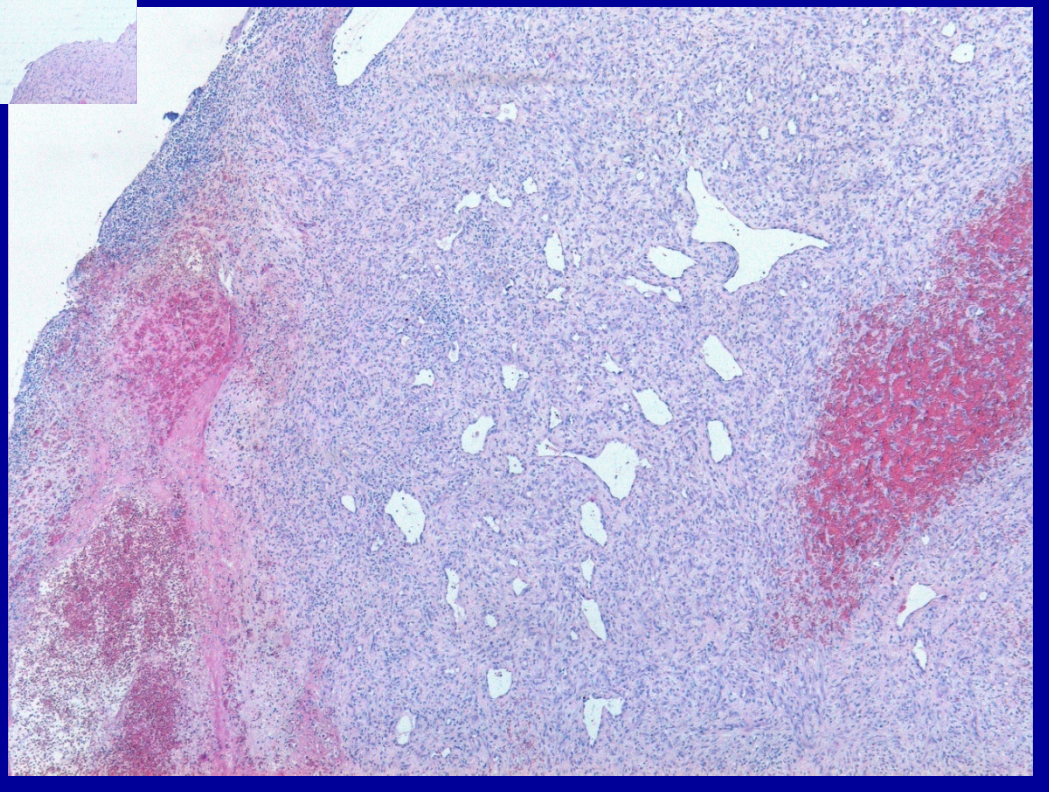
Sinonasal-type hemangiopericytoma

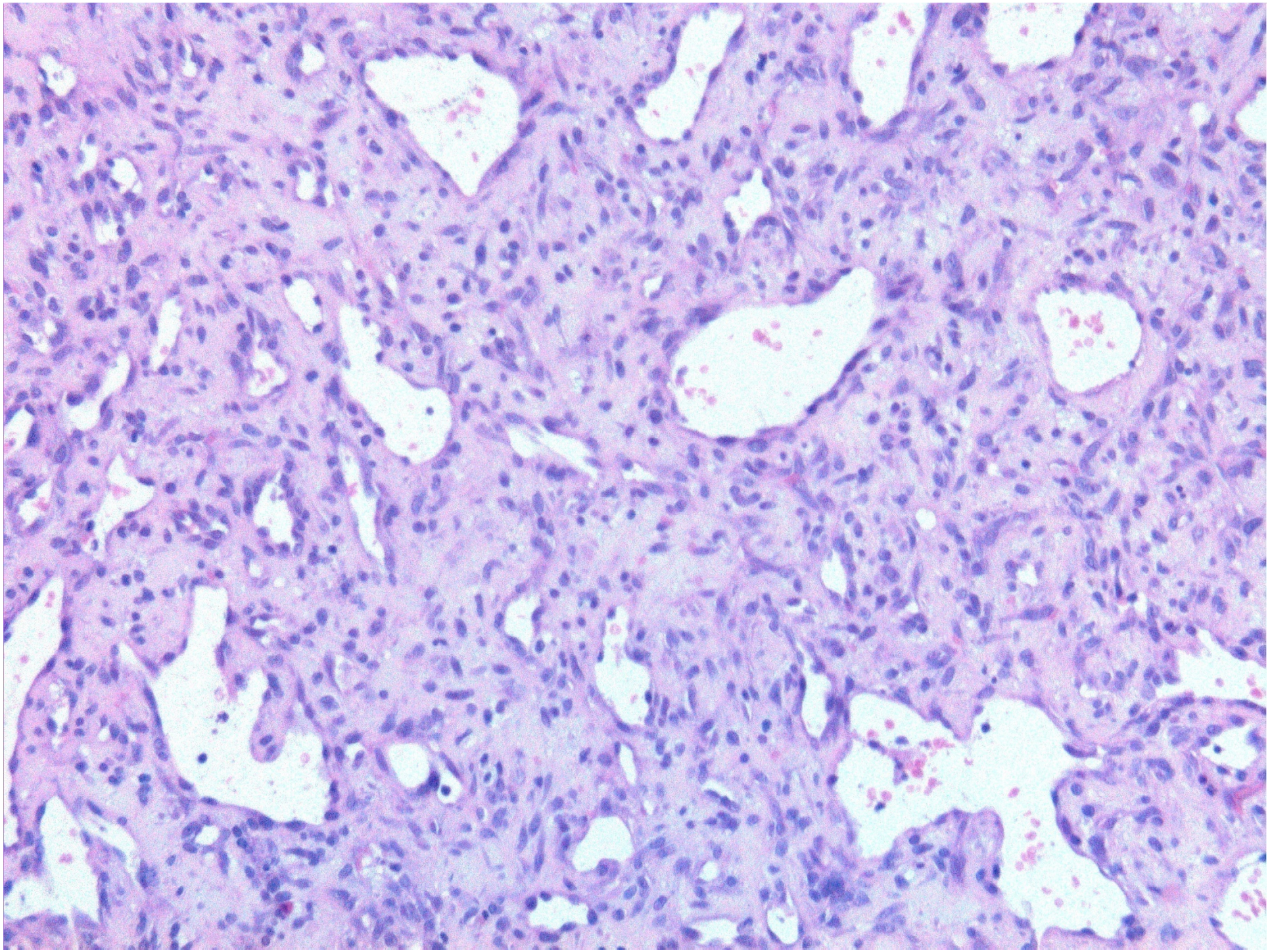
Differential diagnosis

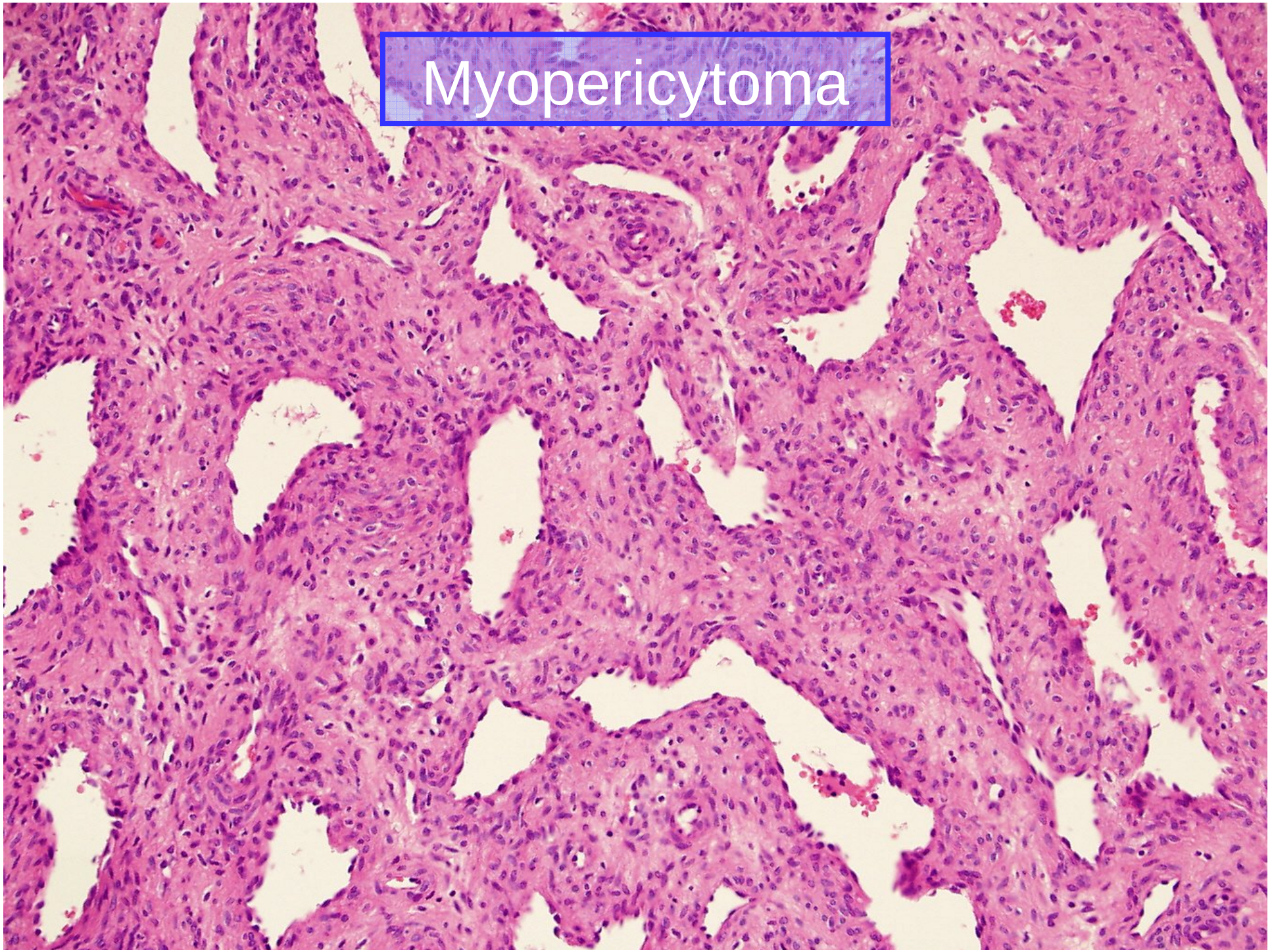
- Lobular capillary hemangioma (pyogenic granuloma)
- Solitary fibrous tumour
- Myopericytoma
- Glomangioma
- Leiomyoma and leiomyosarcoma
- Synovial sarcoma

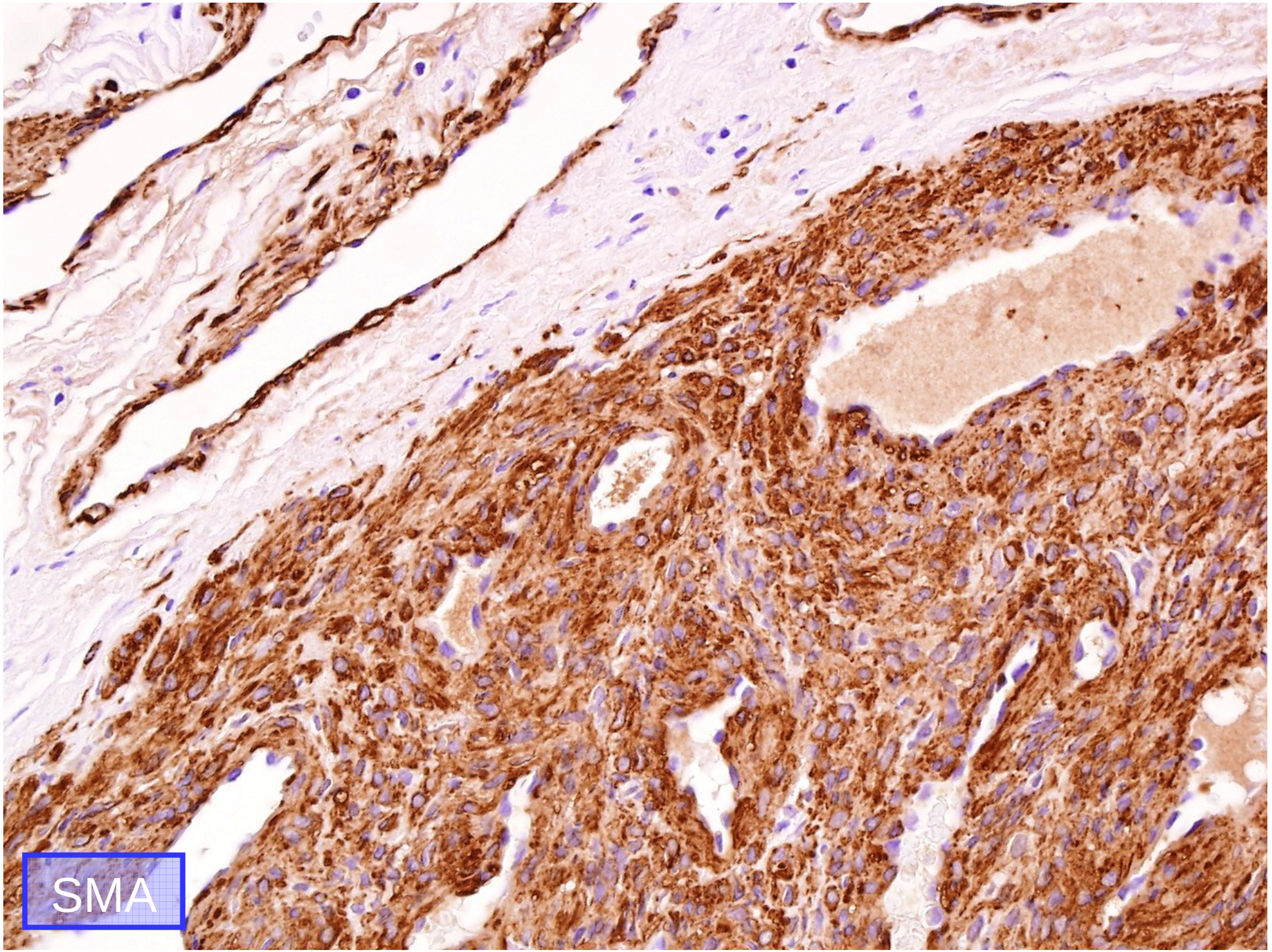
Lobular capillary hemangioma








Myopericytoma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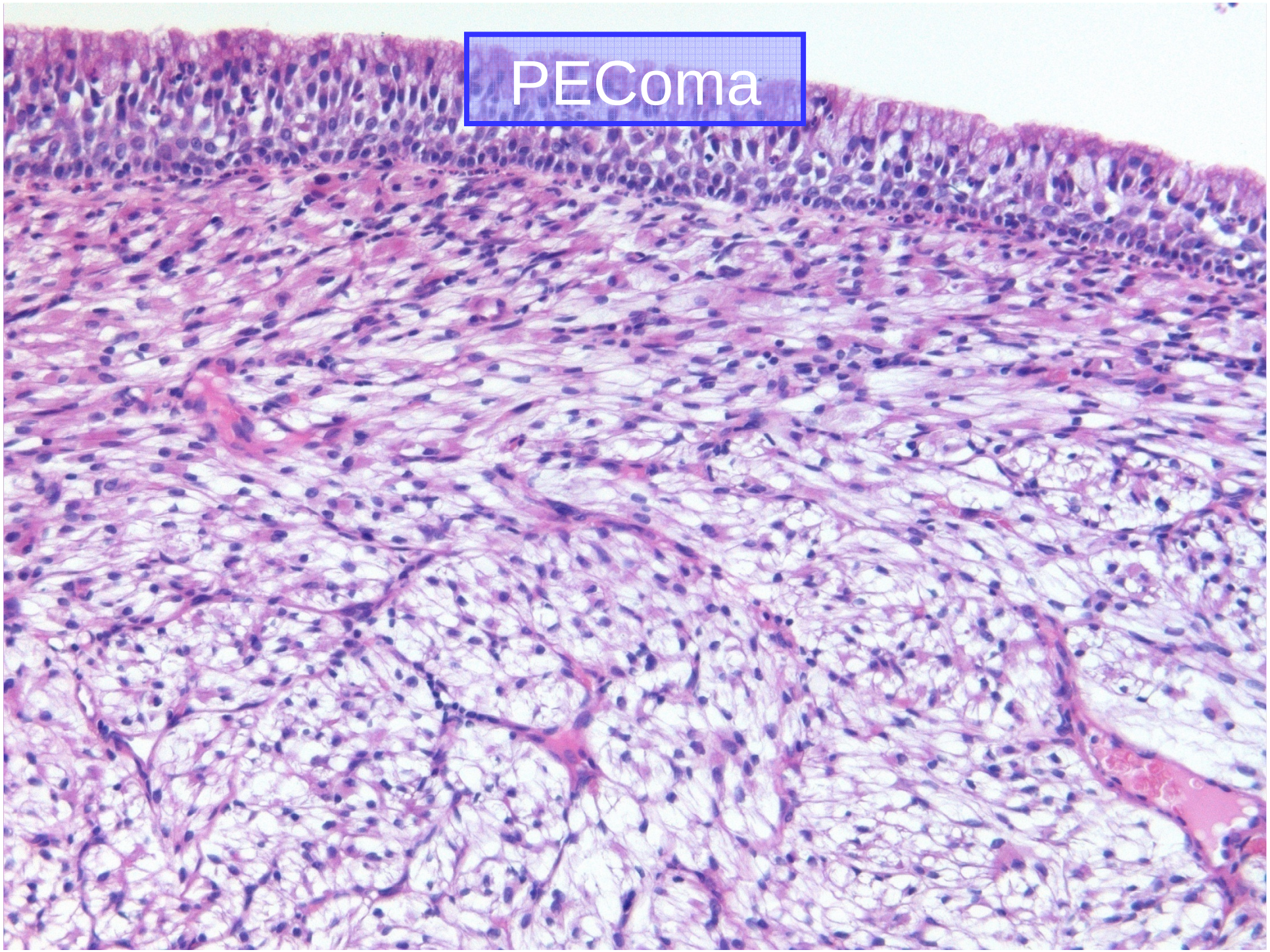
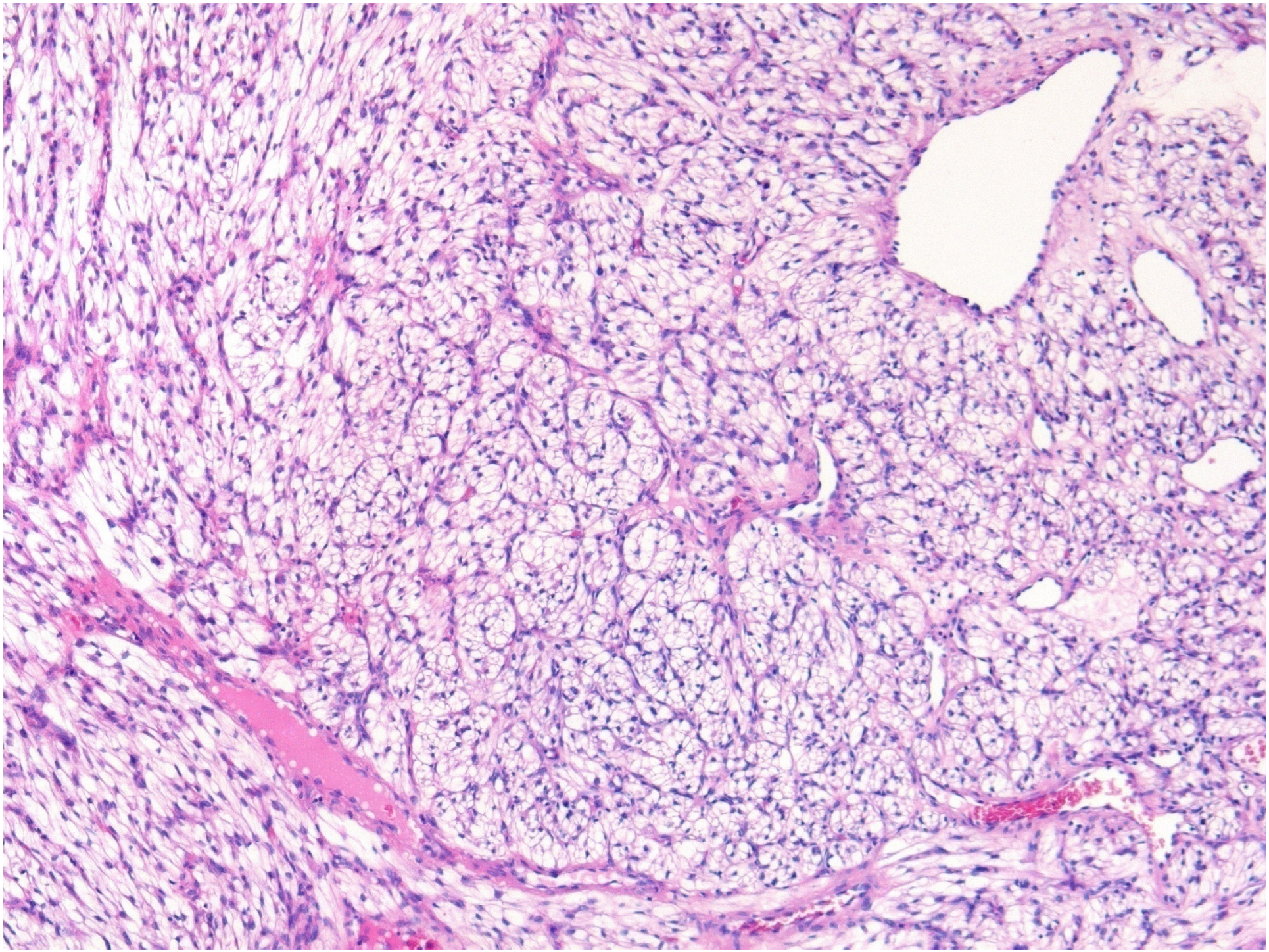
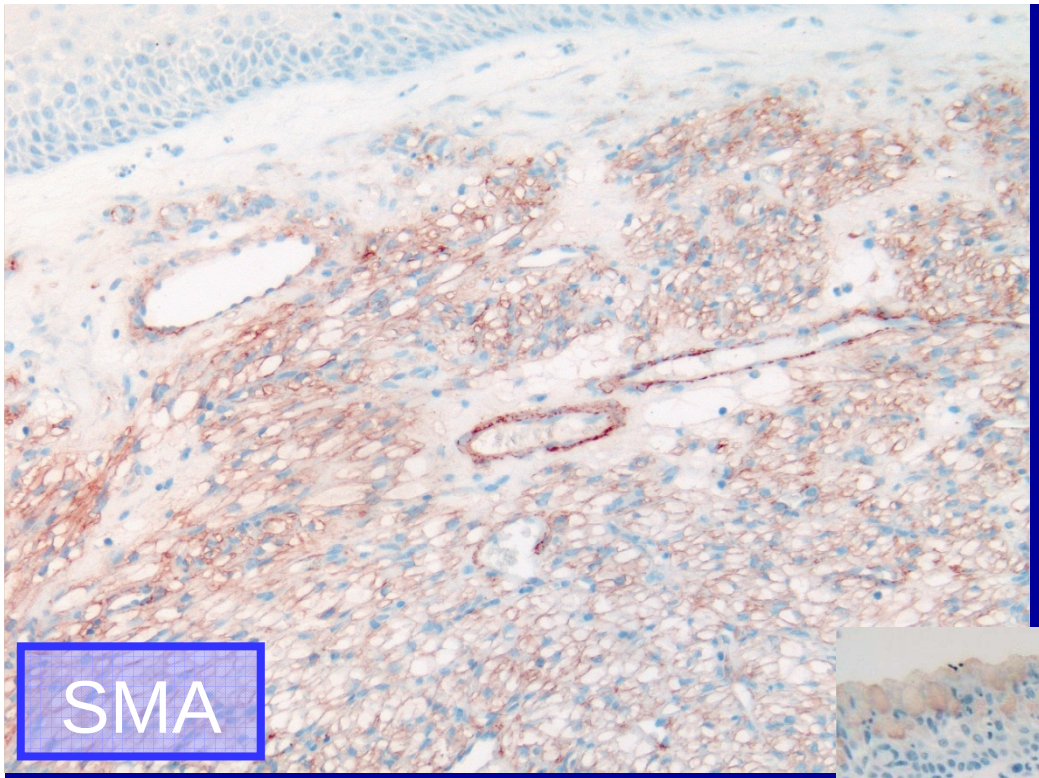

PEComa





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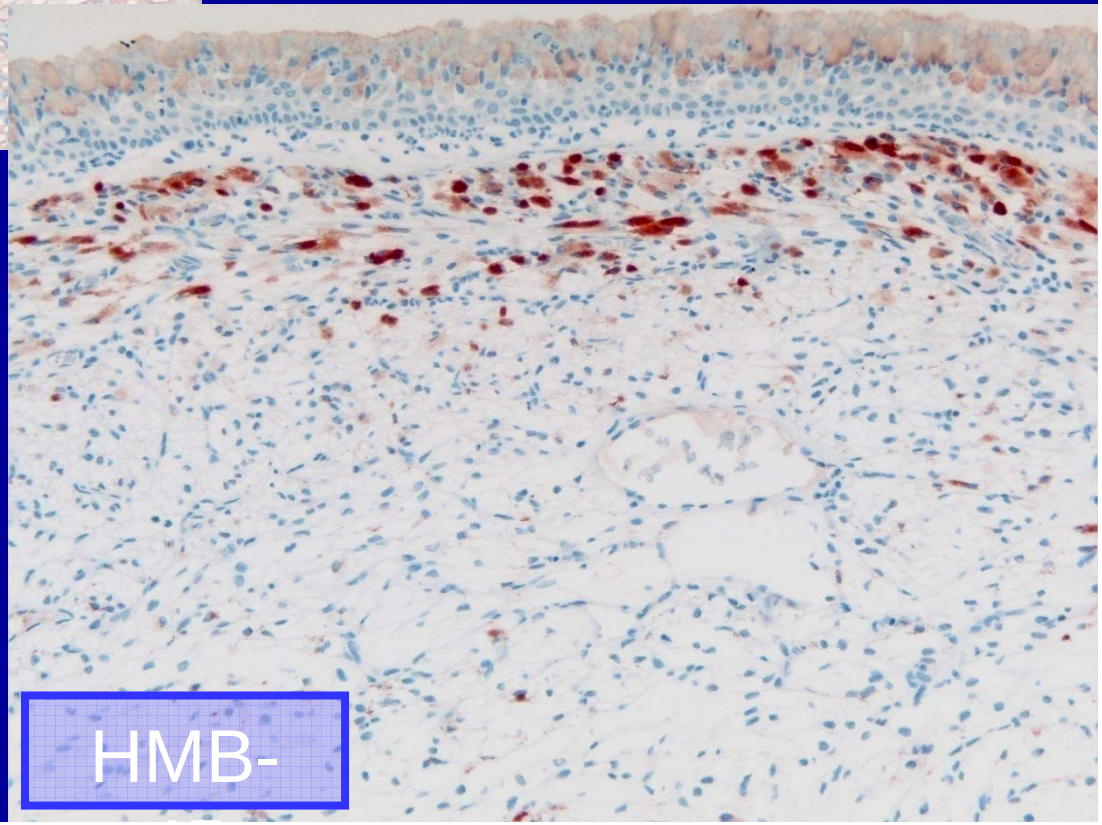
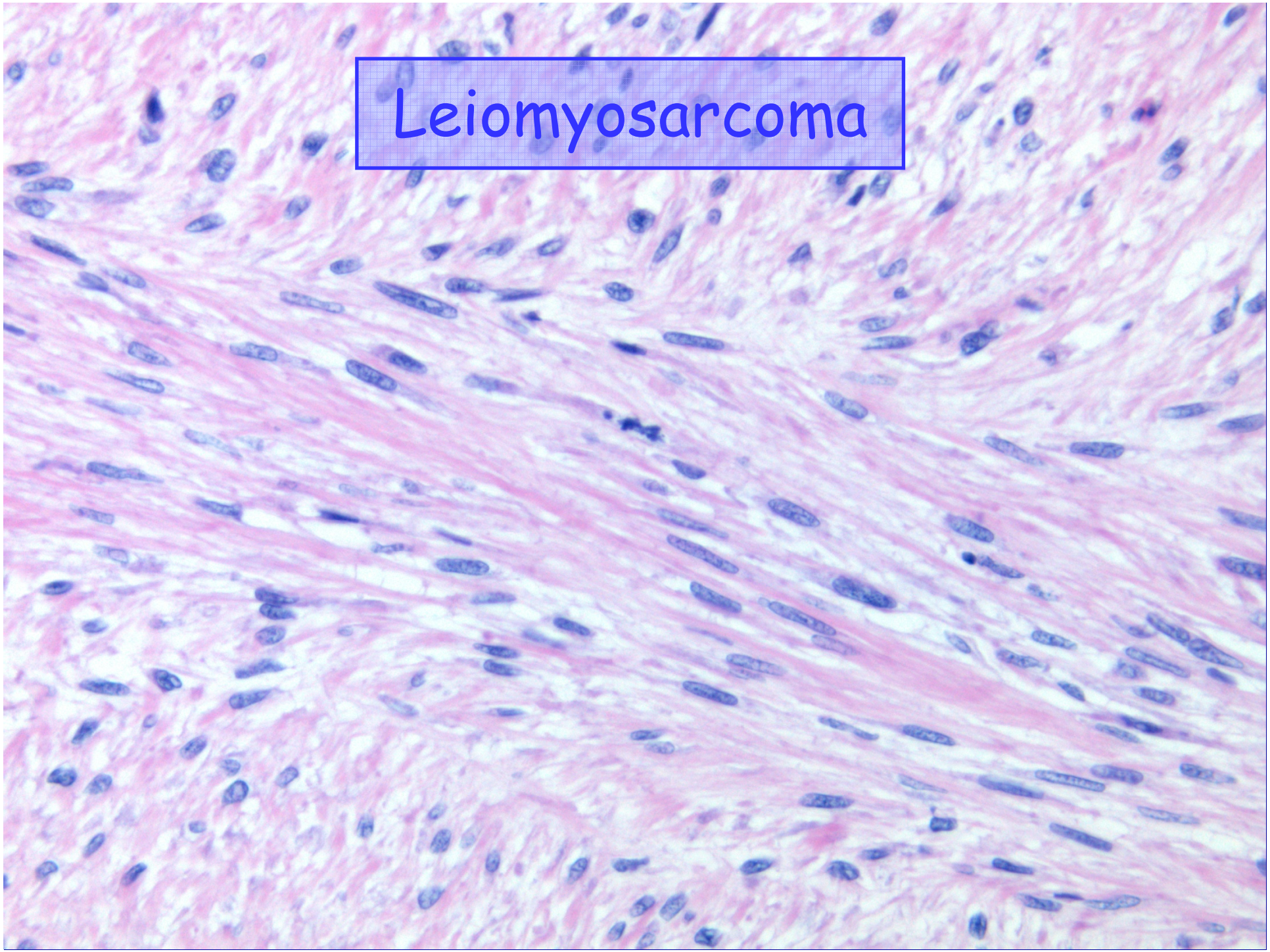


HMB-

Sinonasal tumours of contractile pericytic cells

- Hemangiopericytoma
- Miopericytoma
- Glomangioma


Leiomyosarcoma

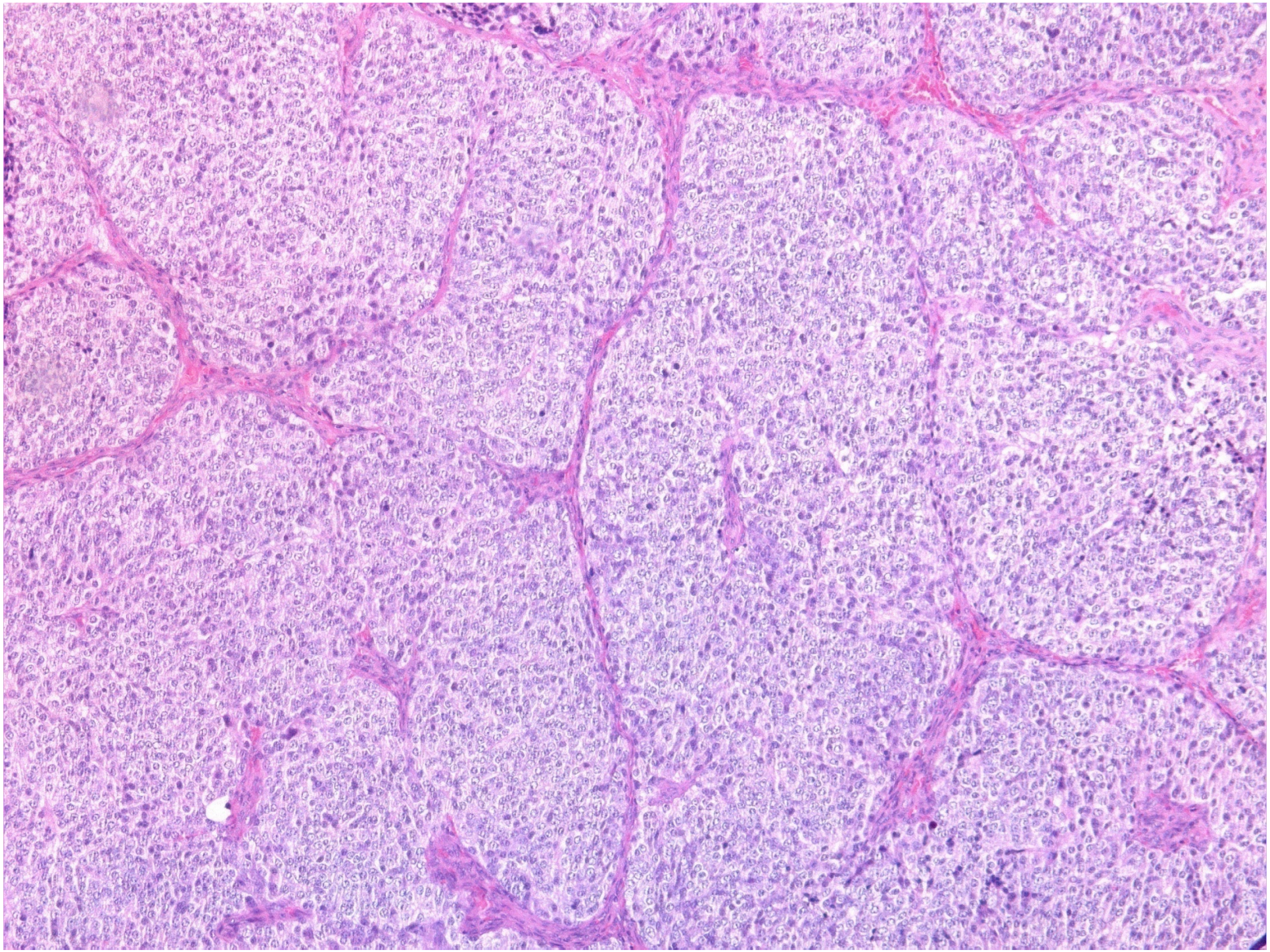
Sinonasal-type hemangiopericytoma

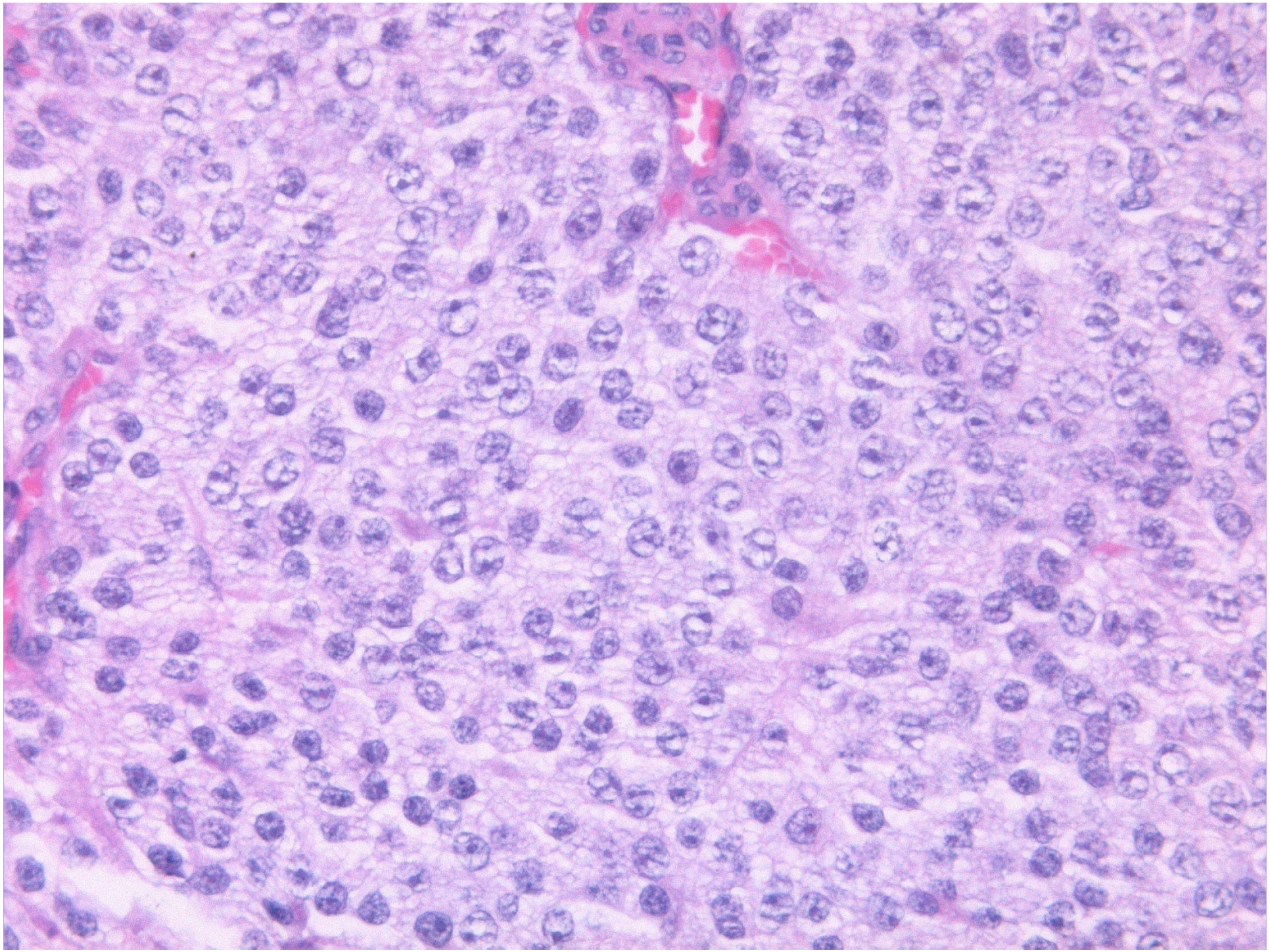
Treatment and Prognosis

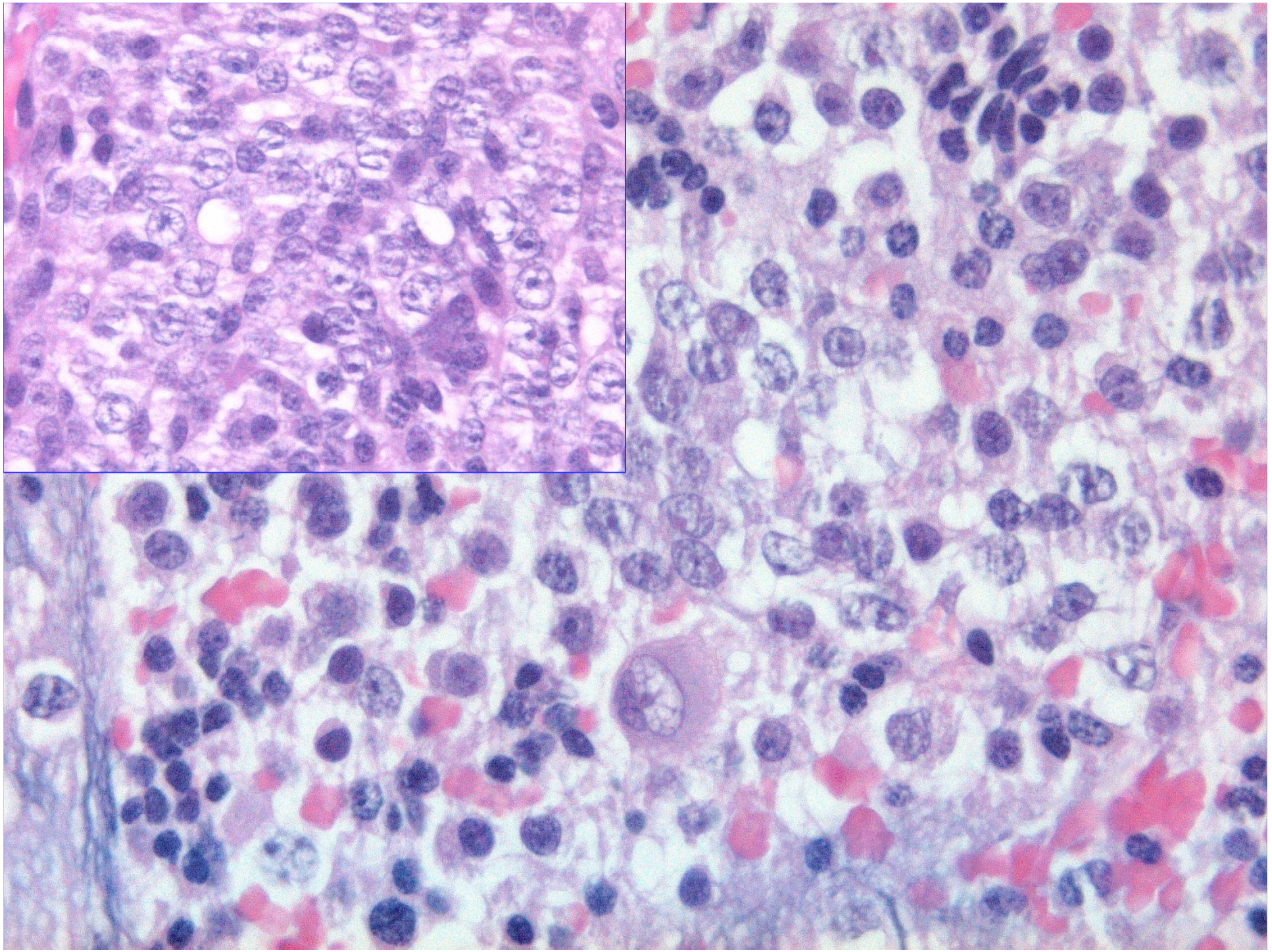
- Surgery is the treatment of choice varying from simple polypectomy without extended resection to wide excision with tumour-free margins
- Overall it is an indolent tumour with a 5-year-survival rate >90%
- Local recurrence develops in 20-40% of cases, even several years after diagnosis
- Aggressive behaviour is rare; associated with larger tumour dimensions (>5 cm), bone invasion, nuclear pleomorphism, brisk mitotic activity, and necrosis

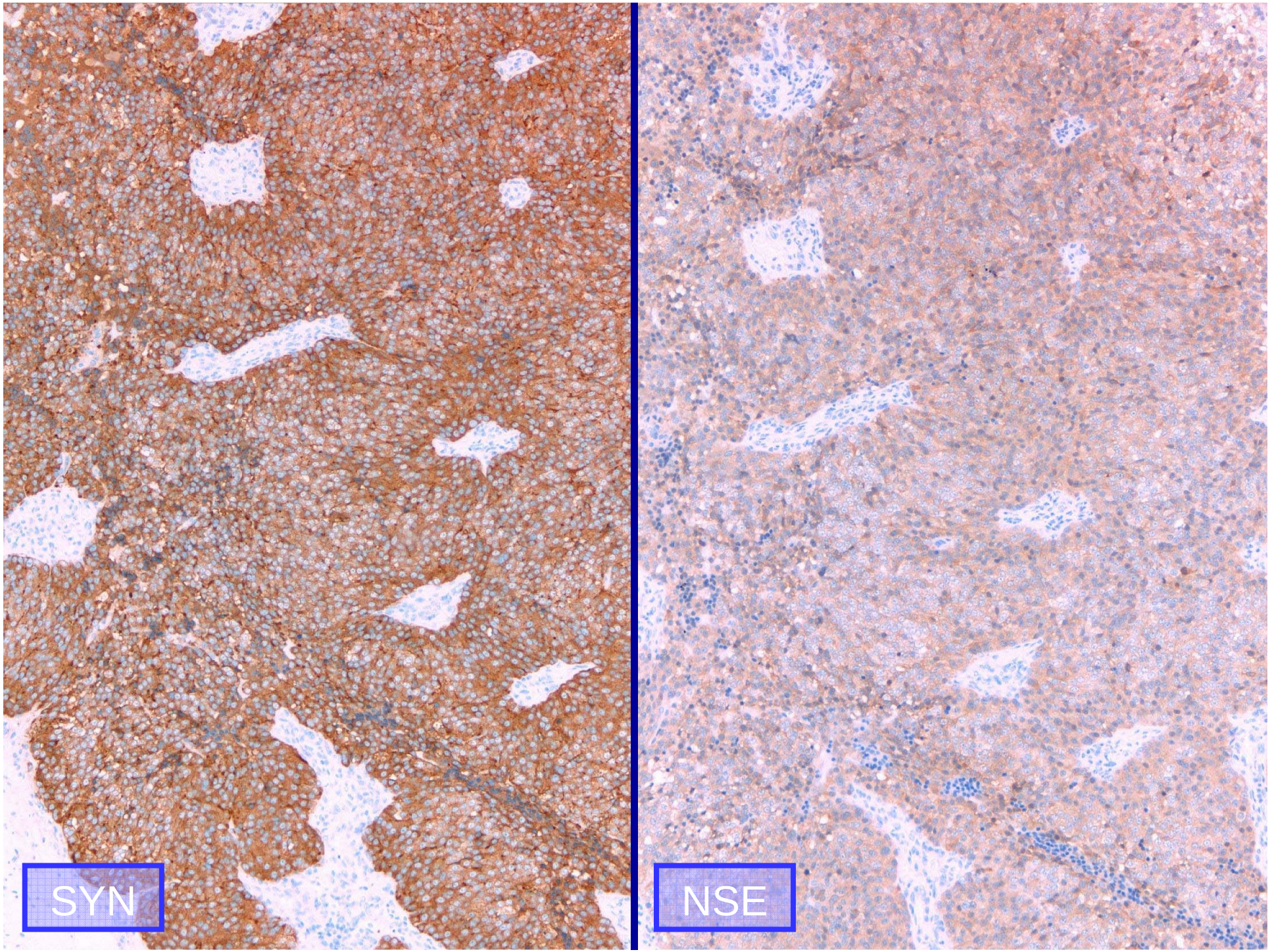
Case 6

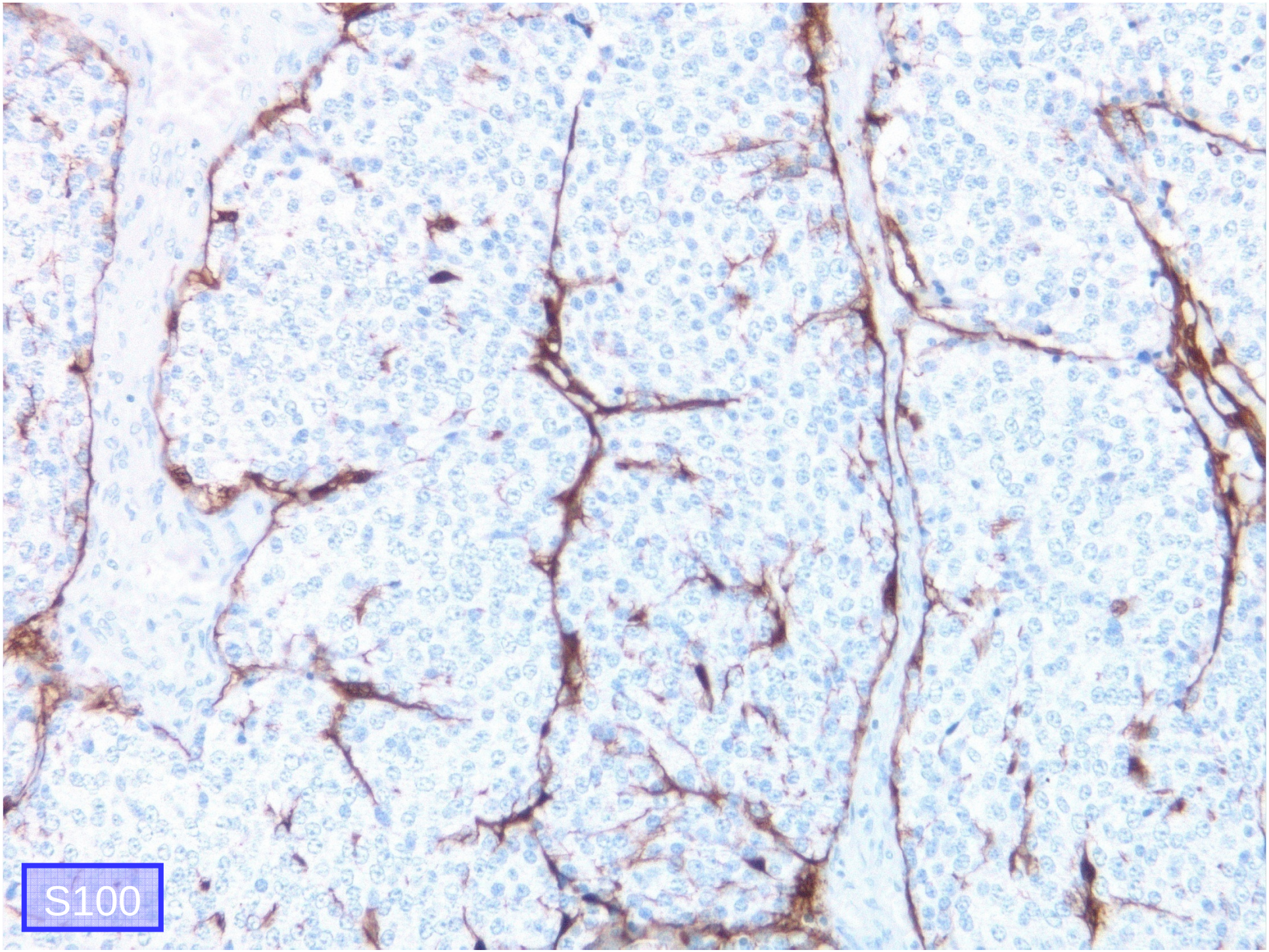
A 70 year old man with a tumor of the vault of the right nasal cavity extending in the anterior cranial fossa








SYN
NSE


S100

Diagnosis

Olfactory neuroblastoma

Olfactory neuroblastoma

- A malignant neuroectodermal tumour thought to originate from the olfactory membrane of the sinonasal tract
- Uncommon neoplasm representing approximately 2-3% of sinonasal tract tumours
- Age: 2 years to 90 years, bimodal incidence peaks at 15 and 55 years
- Both genders are affected equally

Olfactory neuroblastoma

- The most common site of origin is in the upper nasal cavity in the region of the cribriform plate
- “Ectopic” origin in lower nasal cavity or within one of the paranasal sinuses (e.g., maxillary sinus) may occur
- May on occasion present as an intracranial (frontal lobe) mass with involvement of the superior aspect of the cribriform plate or rarely, occur intracranially with no intranasal component

Olfactory neuroblastoma

- Circumscribed lobules or nests separated by a richly vascularized fibrous stroma
- Neoplastic cells have uniform, small round nuclei with scant cytoplasm, dispersed (“salt and pepper”) coarse to fine nuclear chromatin and inconspicuous nucleoli
- Nuclear pleomorphism, mitotic activity and necrosis are usually absent, except for high-grade tumours

Olfactory neuroblastoma

- The cells do not have distinct borders and are surrounded by a neurofibrillary matrix, which corresponds to tangles of neuronal cell processes
- Rosettes of the Homer-Wright type (pseudorosettes) and Flexner-Wintersteiner type (true neural rosettes) identified in up to 30% and less than 5% of tumours, respectively

Olfactory neuroblastoma

Uncommon findings

- Stromal calcifications
- Ganglion cells
- Melanin-containing cells
- Divergent differentiation
  - glandular (adenocarcinoma-like)
  - squamous
  - teratomatous
  - rhabdomyoblastic

Olfactory neuroblastoma

Histologic Grading (Hyams)

Microscopic Features	Grade 1	Grade 2	Grade 3	Grade 4
Architecture	Lobular	Lobular	±Lobular	±Lobular
Pleomorphism	Absent to Slight	Present	Prominent	Marked
NF matrix	Prominent	Present	May be present	Absent
Rosettes	Present*	Present*	May be present**	May be present**
Mitoses	Absent	Present	Prominent	Marked
Necrosis	Absent	Absent	Present	Prominent
Glands	May be present	May be present	May be present	May be present
Calcification	Variable	Variable	Absent	Absent

NF-neurofibrillary; *Homer Wright rosettes (pseudorosettes); **Flexner-Wintersteiner rosettes (true neural rosettes)

Olfactory neuroblastoma

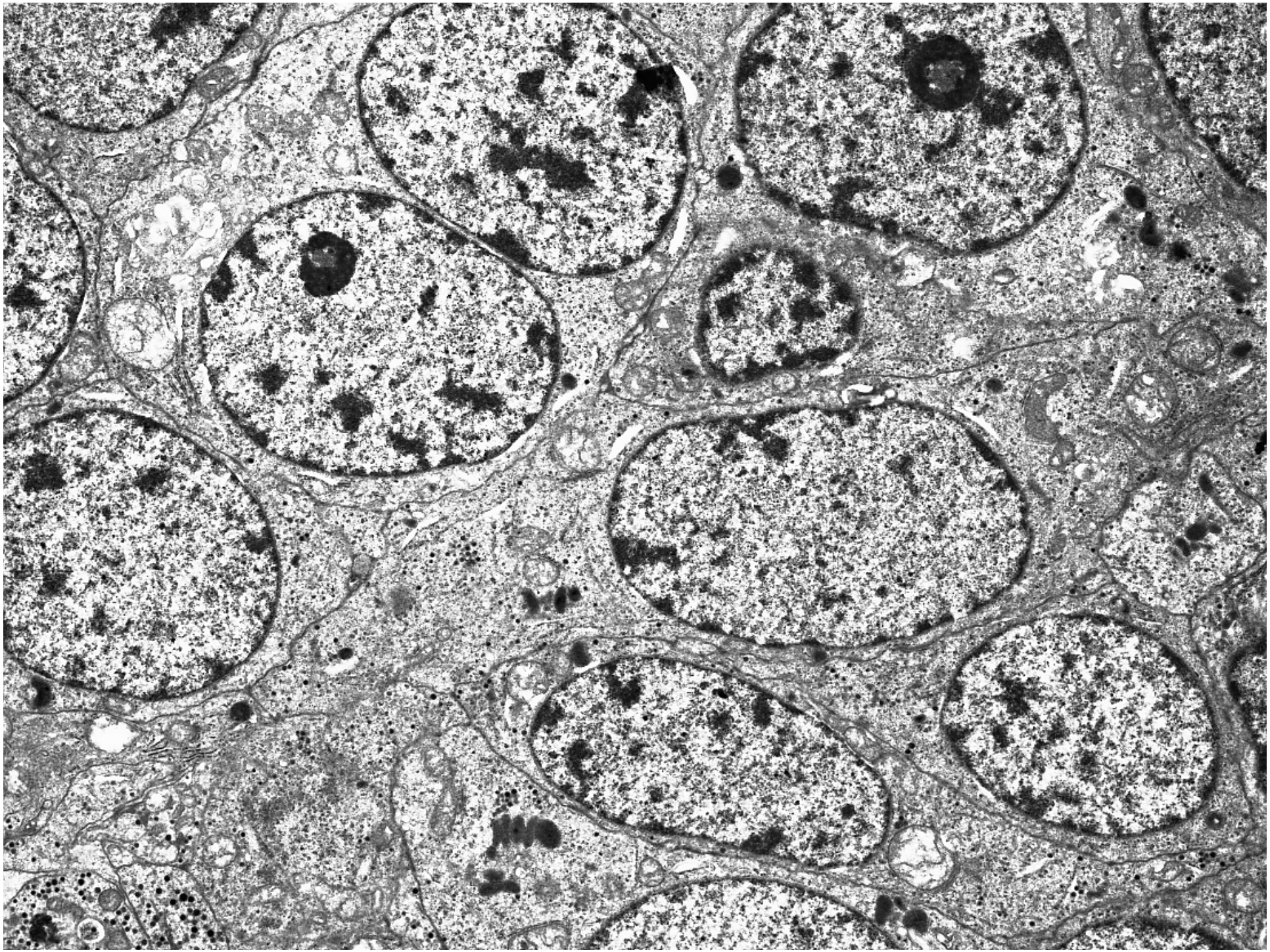
Staging (Kadish)

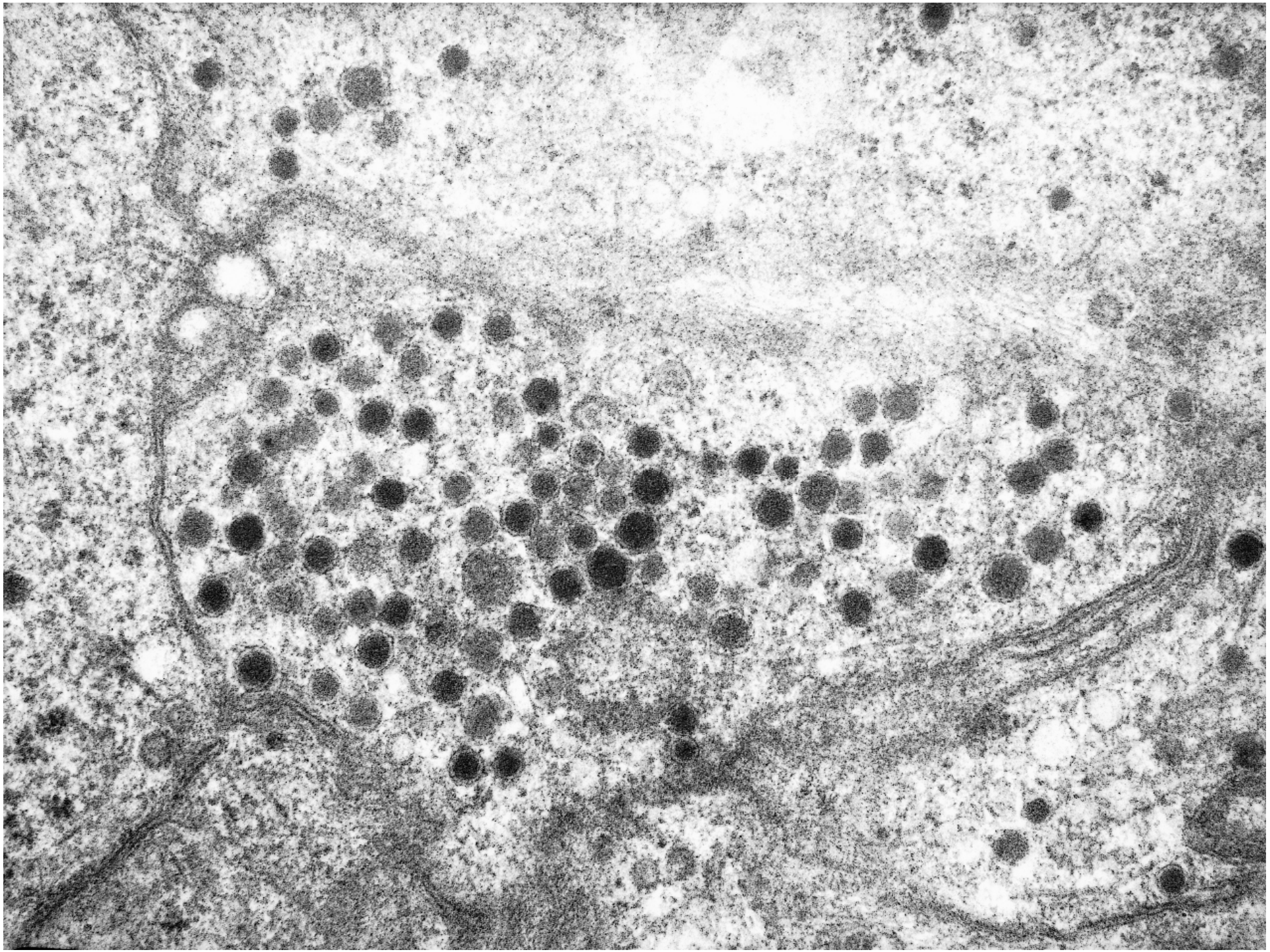
Stage	Extent of Tumour	5-Year survival
A	Tumour confined to the nasal cavity	75-91%
B	Tumour involves the nasal cavity plus one or more paranasal sinuses	68-71%
C	Extension of tumour beyond the sinonasal cavities	41-47%

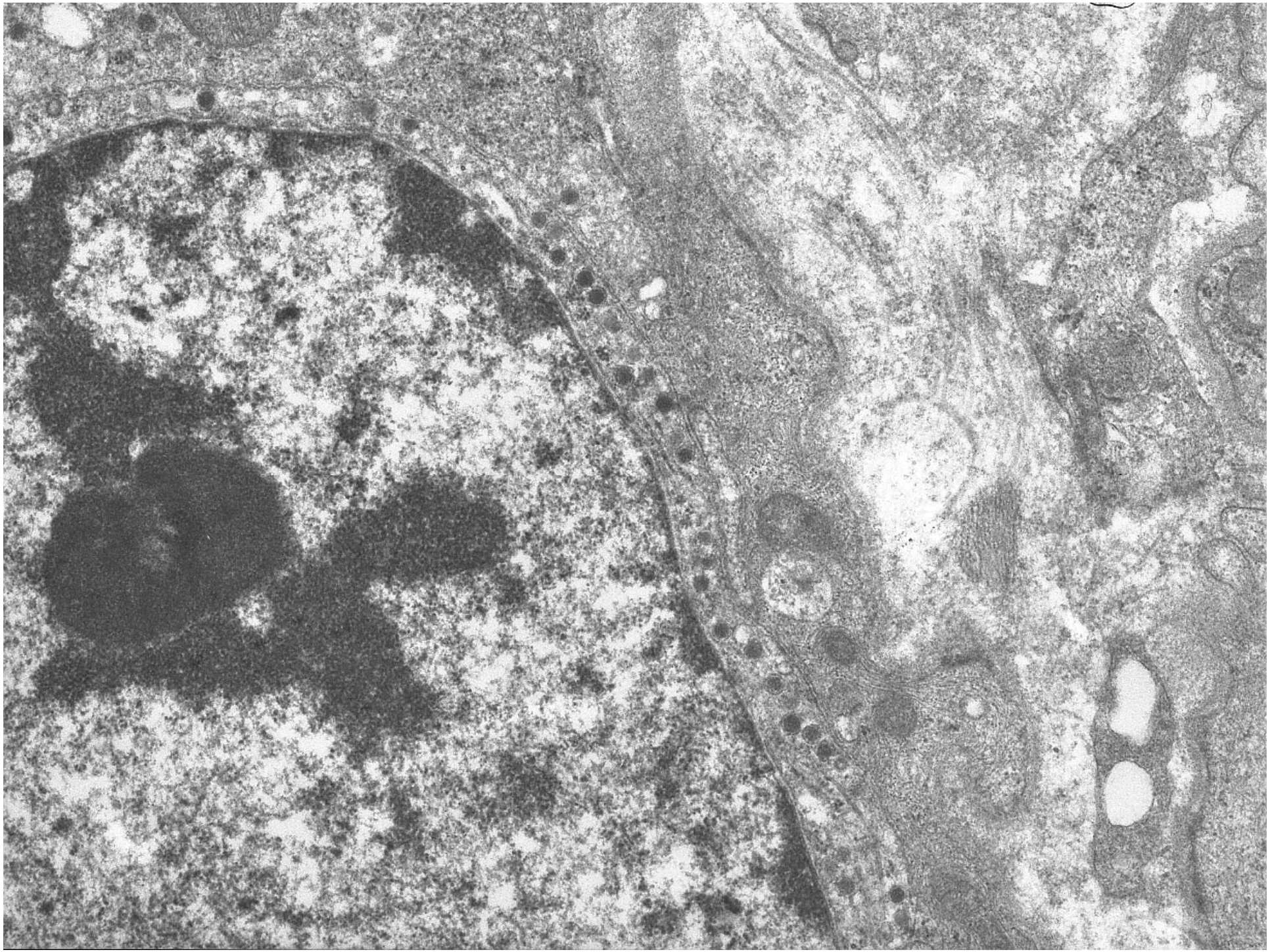
Olfactory neuroblastoma

Immunoprofile

- NSE
- Synaptophysin
- Neurofilament protein (NFP)
- Class III beta-tubulin
- Microtubule-associated protein
- Chromogranin
- Leu-7
- Cytokeratin is usually negative, but some cases can show focal positivity
- S-100 positive in sustentacular cells
- GFAP







Olfactory neuroblastoma

Differential Diagnosis

- SCCNET
- SNUC
- Carcinoid
- Paraganglioma
- Pituitary adenoma
- Melanoma
- Lymphoma
- PNET/Ewing sarcoma
- Metastatic neuroblast.
- Rhabdomyosarcoma

Misdiagnosis of olfactory neuroblastoma

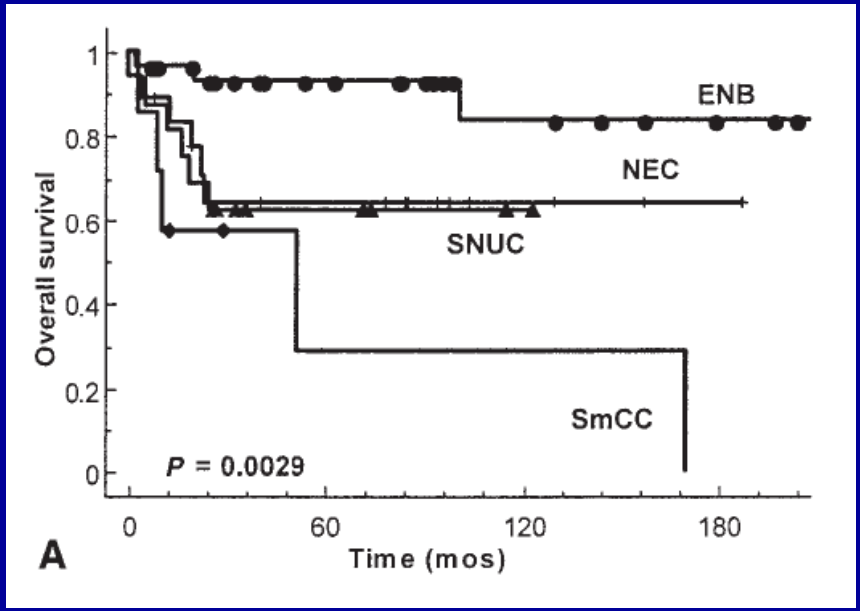
- Twelve patients referred to MD Anderson Cancer Center with diagnosis of ON
- Only in two the diagnosis was confirmed
- There were two cases of melanoma, three cases of SCCNET, three cases of pituitary adenoma and two cases of SNUC

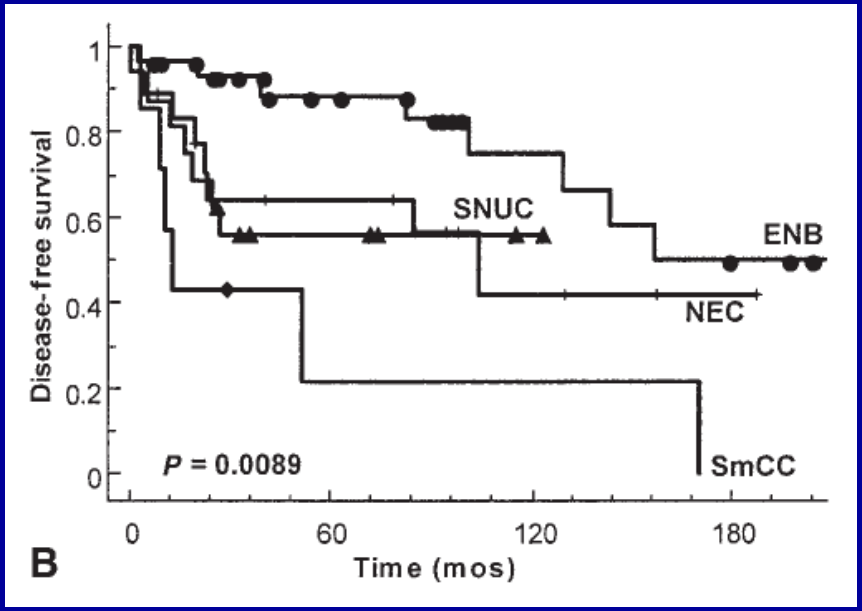
Cohen ZR et al. 2002

Sinonasal malignancies with neuroendocrine differentiation

- 72 patients treated for primary sinonasal neuroendocrine tumors
  - 31 with esthesioneuroblastoma
  - 16 with sinonasal undifferentiated carcinoma
  - 18 with neuroendocrine carcinoma
  - 7 with small cell neuroendocrine carcinoma

Rosenthal et al. Cancer 2004





Rosenthal et al. Cancer 2004

Summary: Survival and Patterns of Failure in Patients with Sinonasal Carcinomas with Neuroendocrine Differentiation

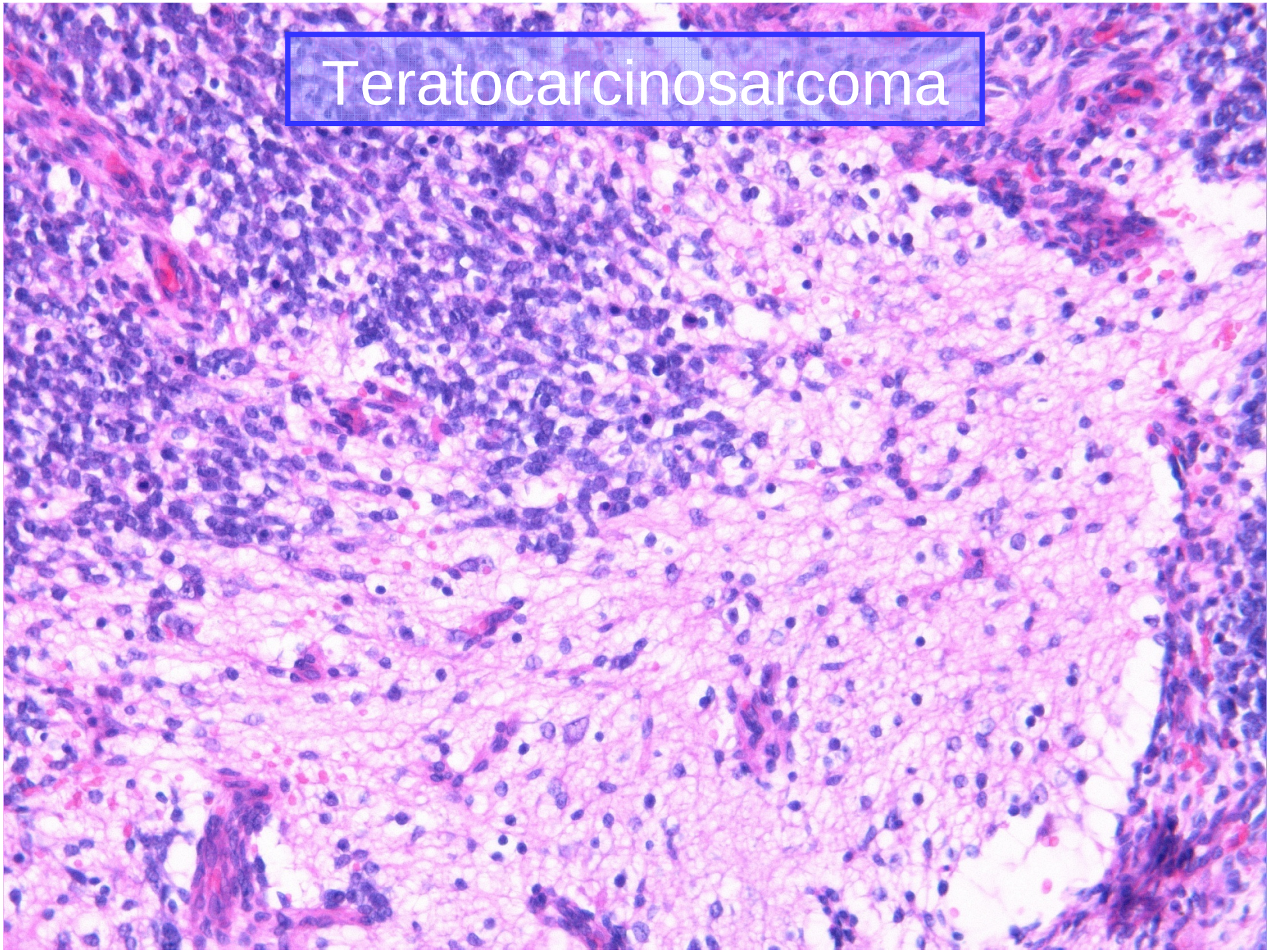
	Five-yr rates (%)			
Histology	OS	LC	RF	DM
ENB	93.1	96.2	8.7	0.0
NEC	64.2	72.6	12.9	12.3
SNUC	62.5	78.6	15.6	25.4
SmCC	28.6	66.7	44.4	75.0

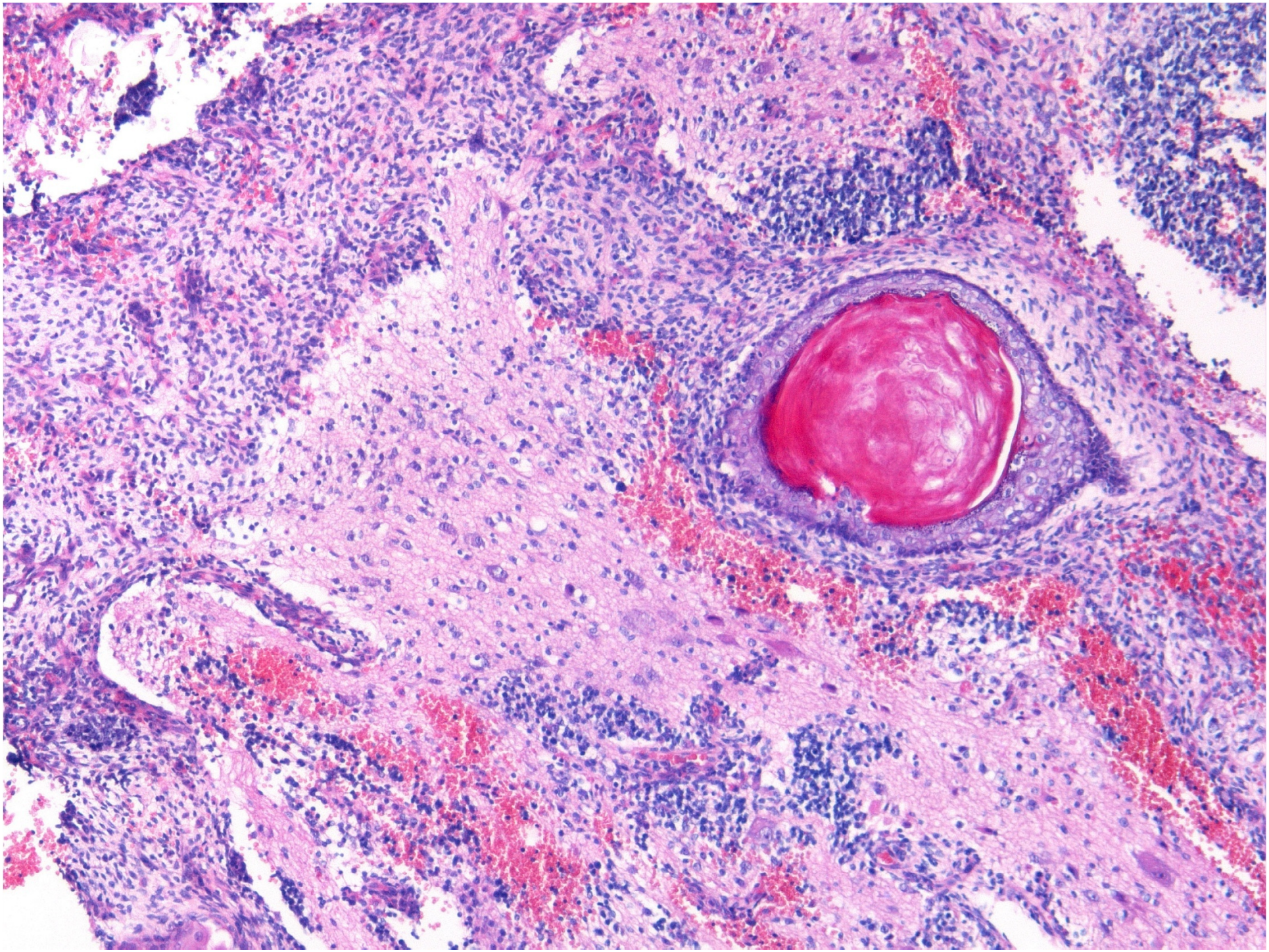
OS: overall survival; LC: local control; RF: recurrence-free; DM: distant metastasis; ENB: esthesioneuroblastoma; NEC: neuroendocrine carcinoma; SNUC: sinonasal undifferentiated carcinoma; SmCC: small cell carcinoma.

Sinonasal malignancies with neuroendocrine differentiation

- There appears to be a divergent natural history which is divided macroscopically into ENB and non-ENB categories
- Patients who have tumors with ENB histology have excellent survival, local control, and distant control rates with local treatment only
- Patients who have tumors with non-ENB histologies demonstrate poorer rates of survival and should be preferentially treated with combined-modality therapy

Rosenthal et al. Cancer 2004

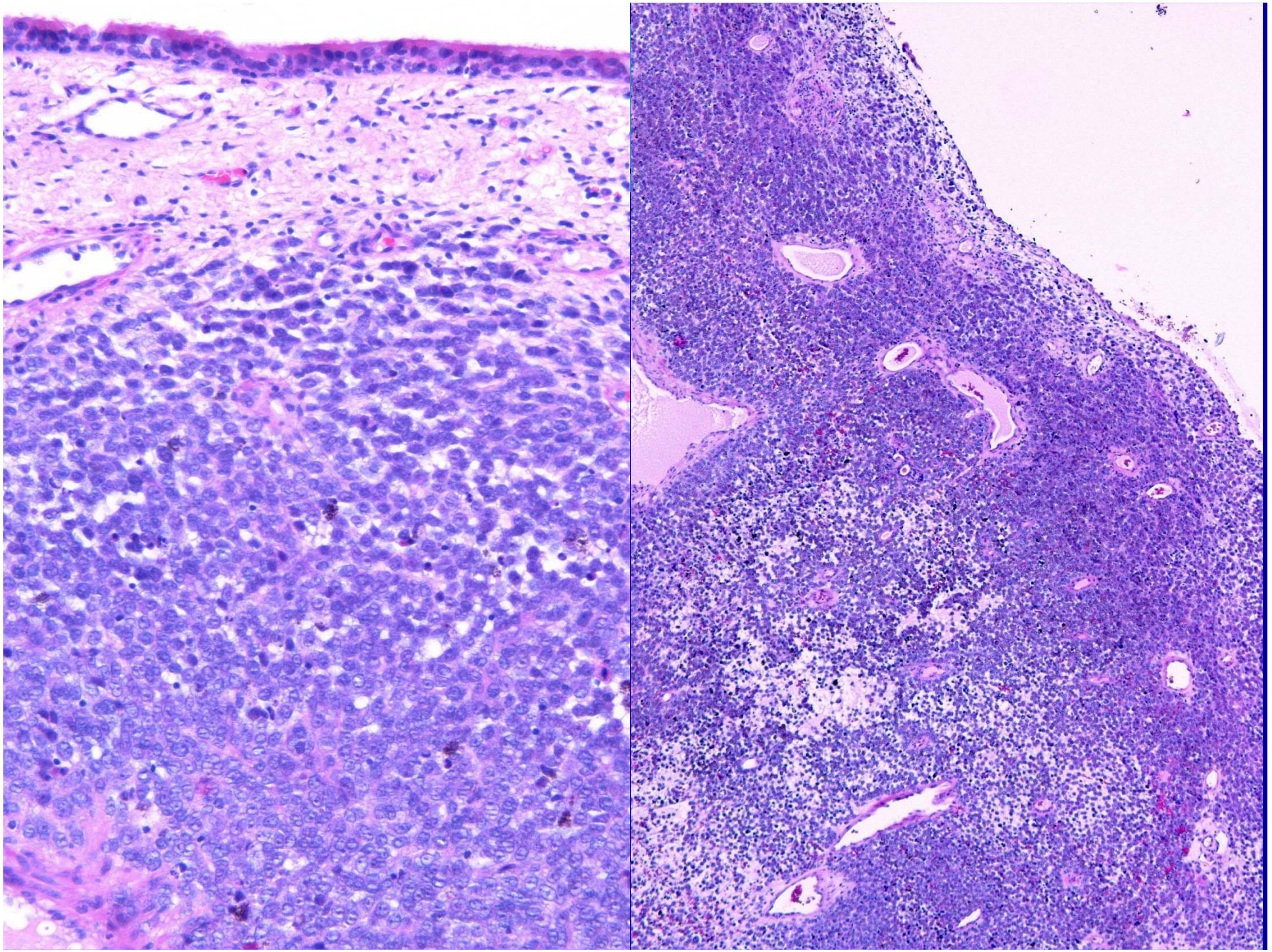

Teratocarcinosarcoma

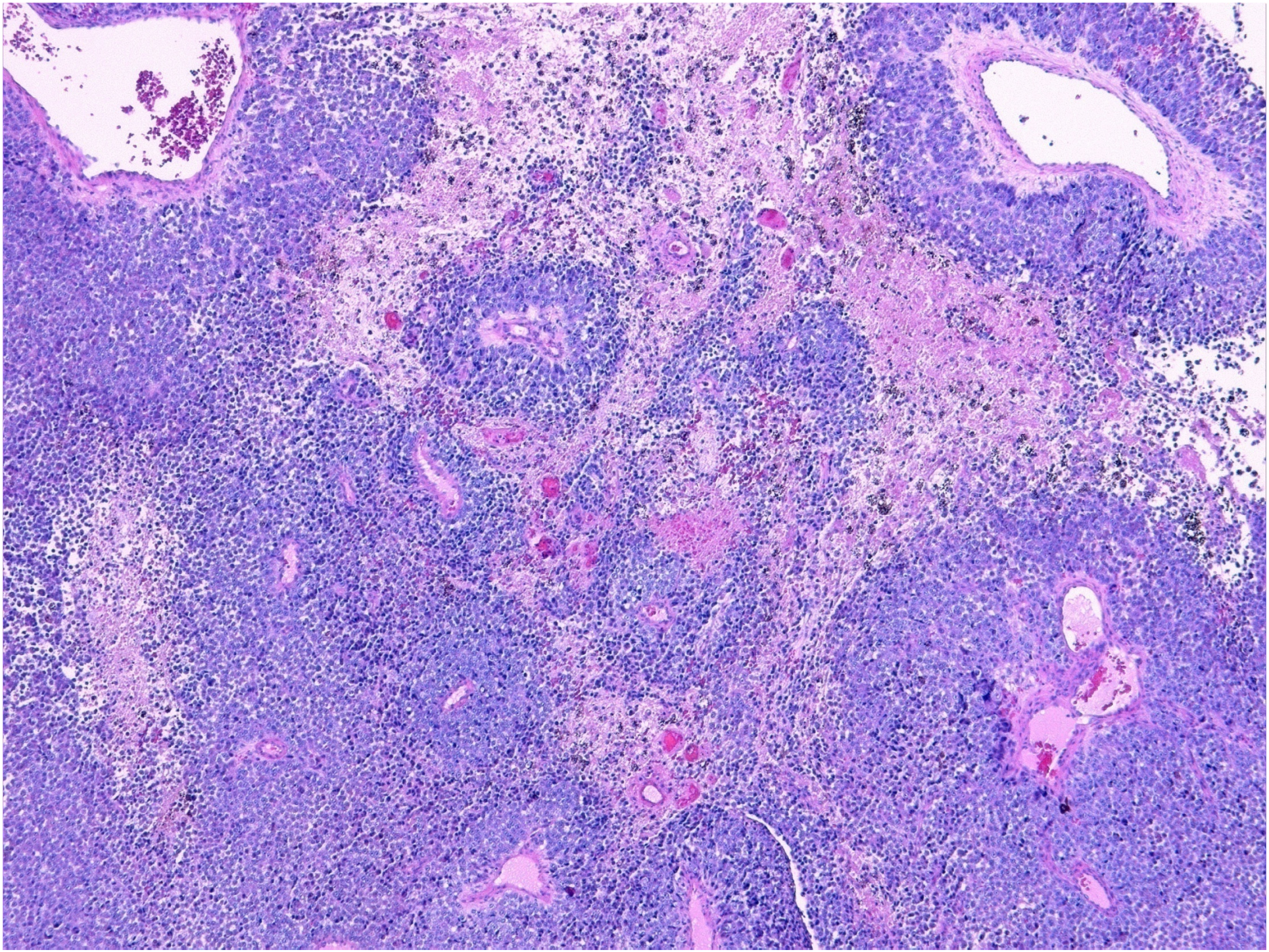


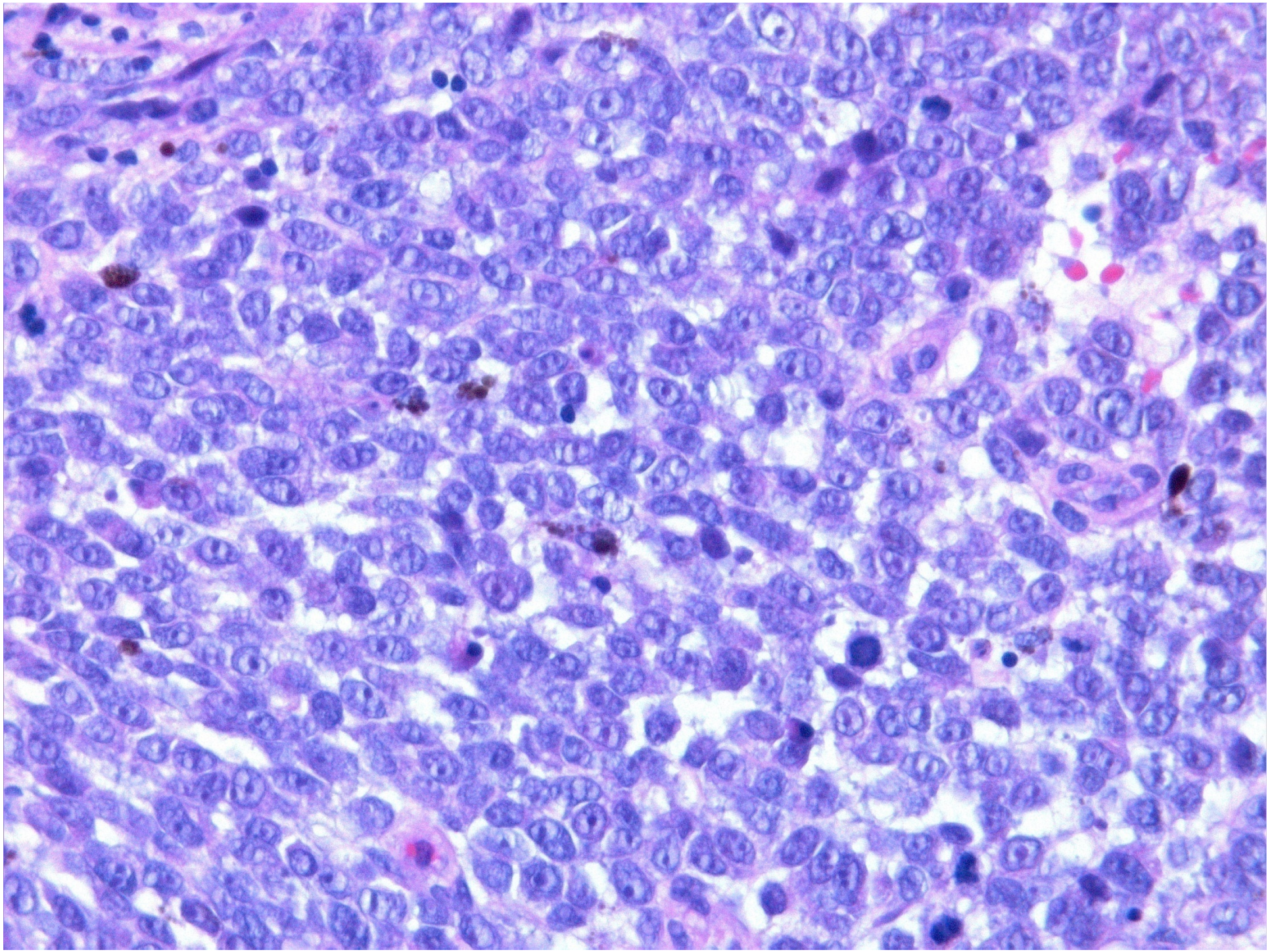

costruzioni.net

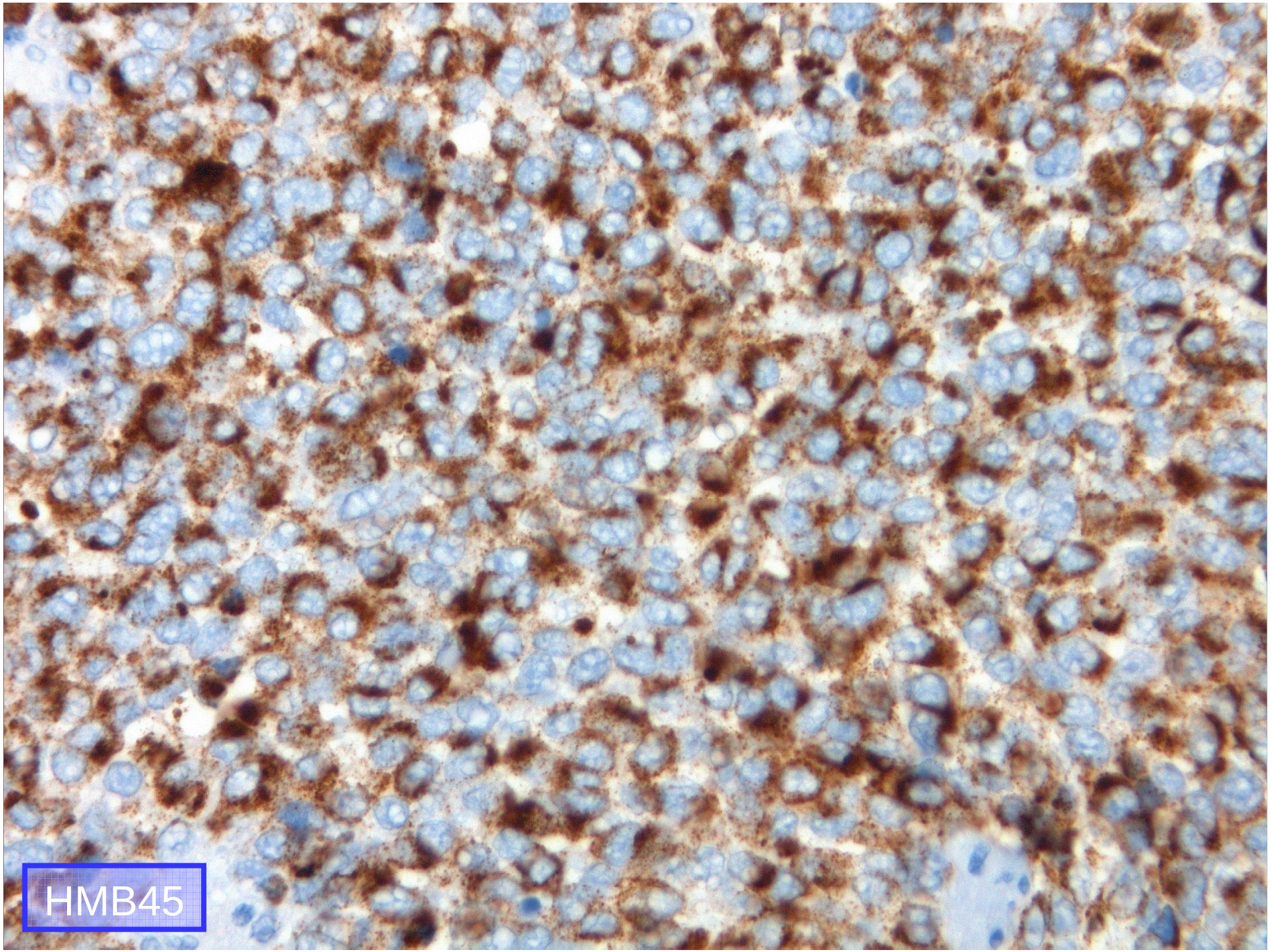
Case 7

A 77 year old woman with a large destructive tumor involving the left nasal cavity and the left maxillary sinus








HMB45

Diagnosis

Sinonasal melanoma

Sinonasal melanoma

- Sinonasal melanomas represent between 0.5 and 1.5% of all melanomas and between 3 and 20% of sinonasal malignant neoplasms
- They most frequently develop after the fifth decade of life, no definite sex predilection
- Supposed origin from melanocytes present in the mucosa of the upper respiratory tract
- Grossly either pigmented (black-brown) or non-pigmented (pink-tan) lesions
- Anterior portion of the septum or within sinuses

Sinonasal melanoma

- Metastatic disease to be ruled out
- Primary melanomas may show junctional activity, but this is usually lost in advanced stages of the disease, when ulceration is present
- Solid, loosely cohesive, storiform, pseudo-alveolar or organoid patterns

Sinonasal melanoma

- Medium to large size cells that may be polyhedral, round, fusiform, pleomorphic, microcytic, or a mixture of them
- Finely granular cytoplasm and nuclei with one or more eosinophilic nucleoli, prominent mitotic activity
- Vascular invasion and neurotropism may be identified in up to 40% of cases; pigment recognized in 2/3
- Osteocartilaginous differentiation has also been observed

Sinonasal melanoma

Immunohistochemistry

- Positive for vimentin, S-100 protein, HMB-45, anti-tyrosinase, melan-A and microphthalmia transcription factor
- Occasionally positive for NSE, CD117, CD99, synaptophysin, CD56, and CD57
- Negative for cytokeratin, EMA, muscle markers, CD45

Sinonasal melanoma

Differential diagnosis

- Carcinoma
- Lymphoma
- Sarcoma

Sinonasal melanoma

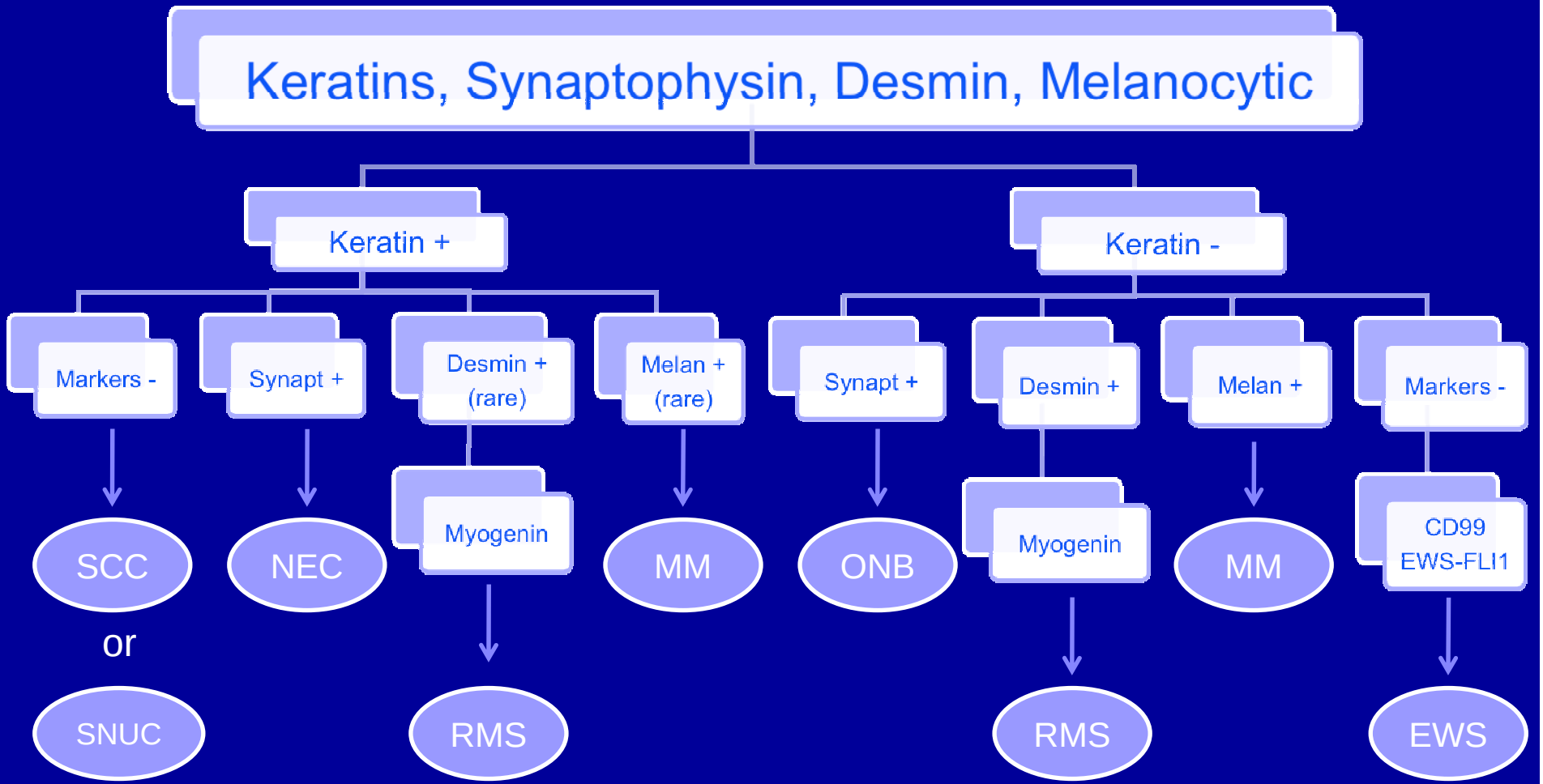
Treatment and prognosis

- Surgery is the treatment of choice; radiotherapy for unresectable cases
- The prognostic significance of the level of local invasion does not apply to mucosal melanomas because of the absence of histological landmarks analogous to the papillary and reticular dermis; nevertheless, invasion deeper than 0.5 mm is associated with decreased survival

Sinonasal melanoma

- At presentation, 70-80% of cases are localized, 10-20% have regional lymph node and <10% have distant metastasis
- High recurrence rate often related to the multicentricity of the tumours
- Five year survival lower than 35%

Diagnostic Algorithm for Undifferentiated Sinonasal Tumours



Thanks for your attention!