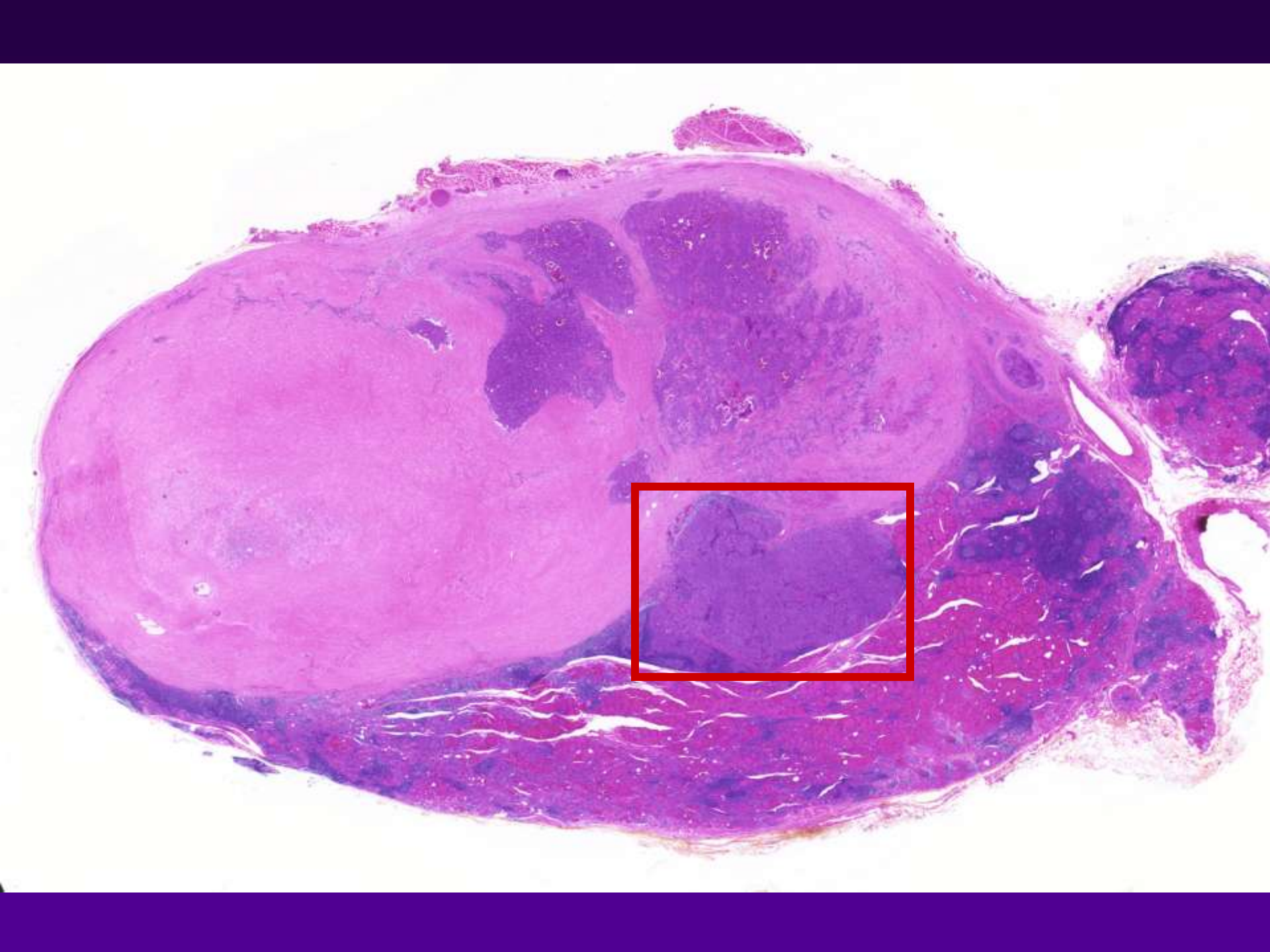
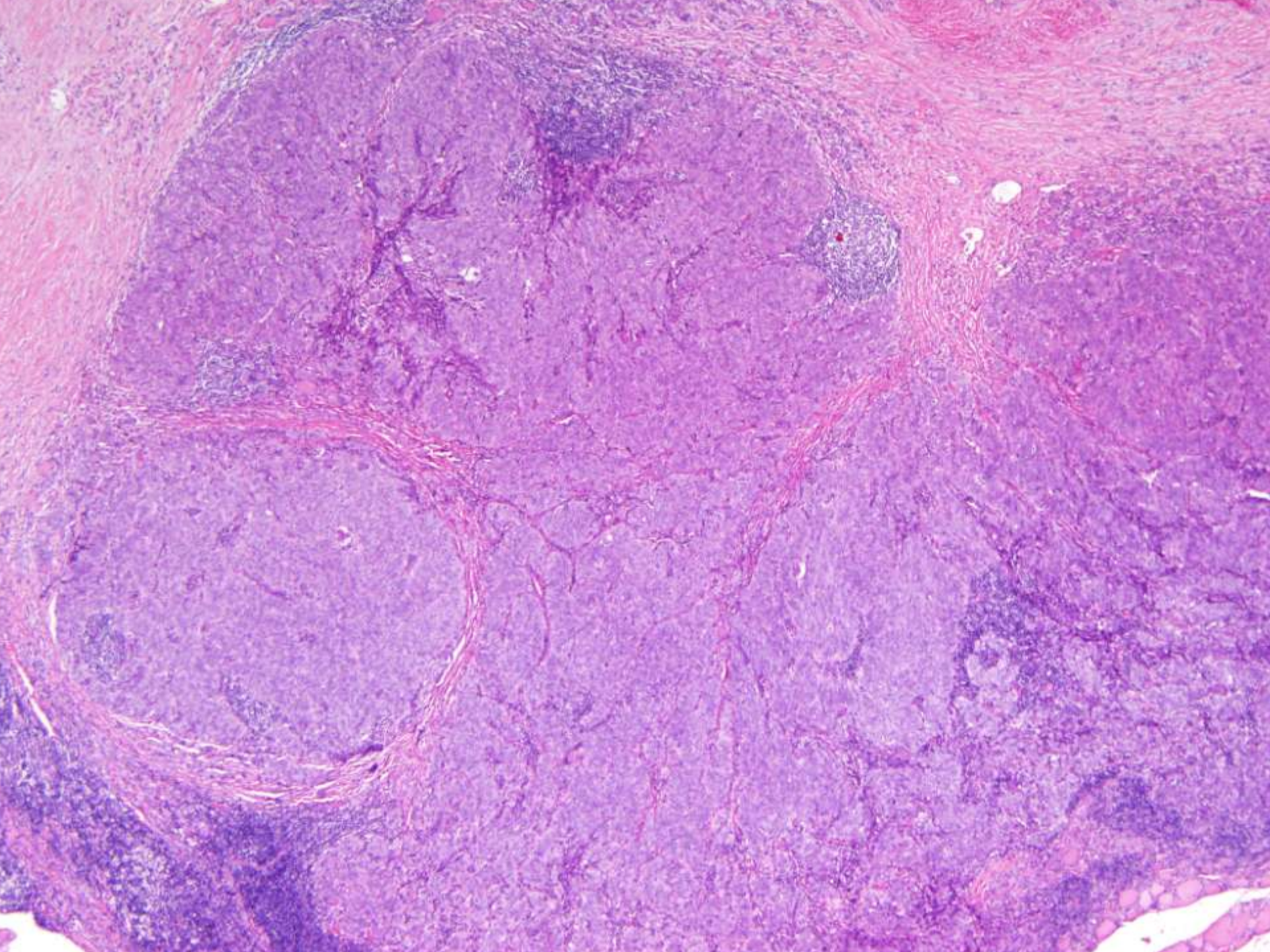
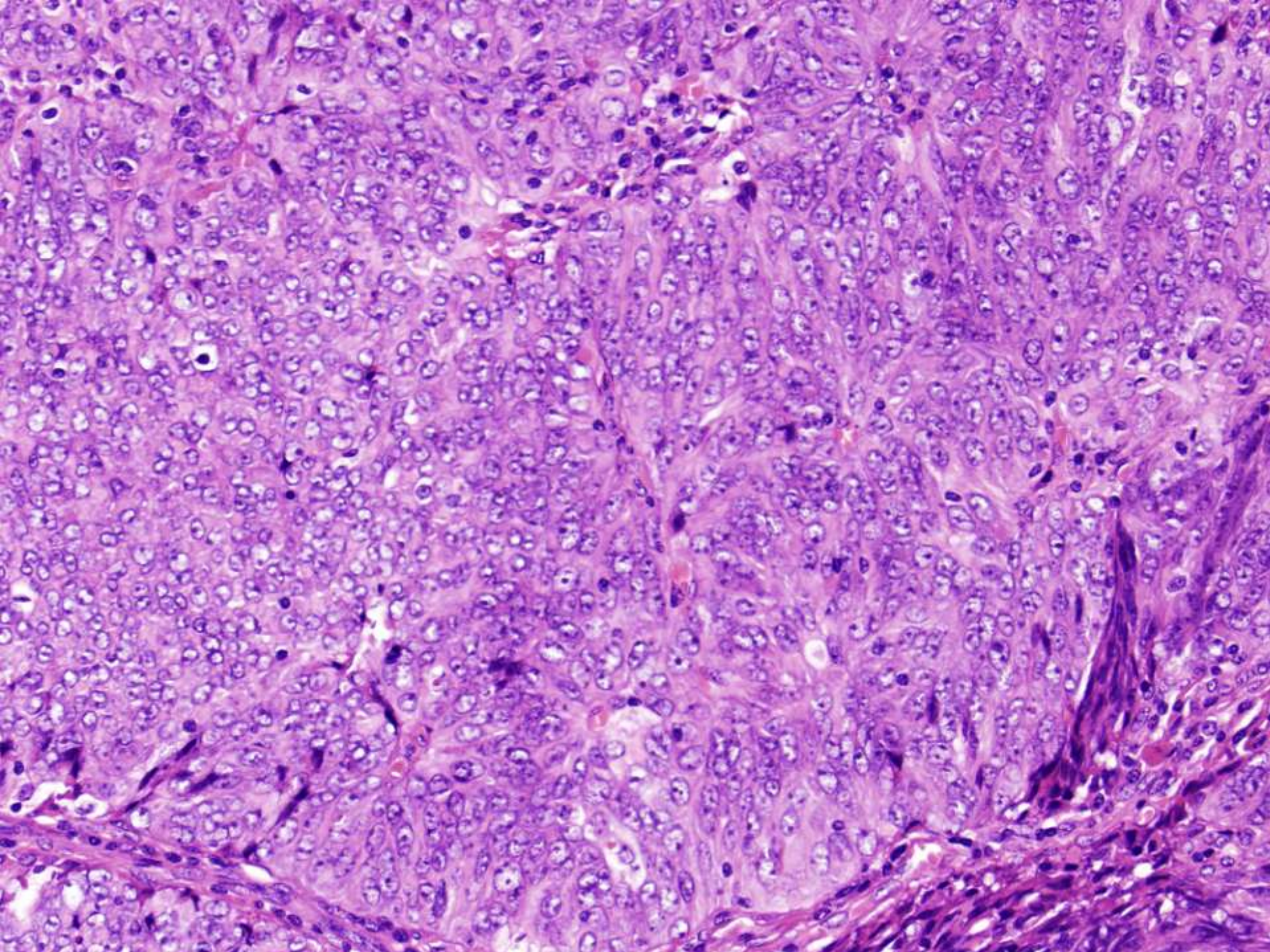


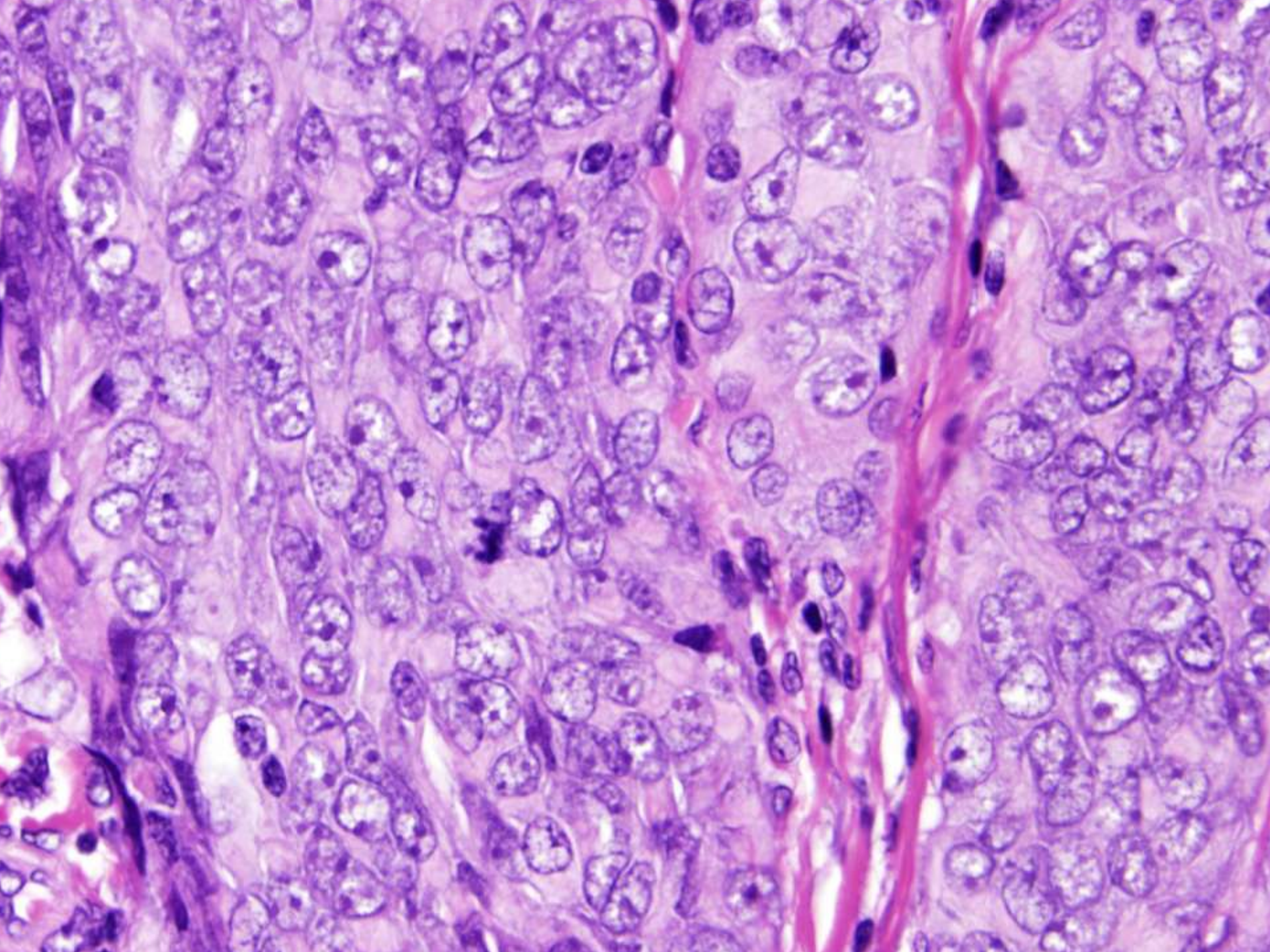
Chan - Case 1

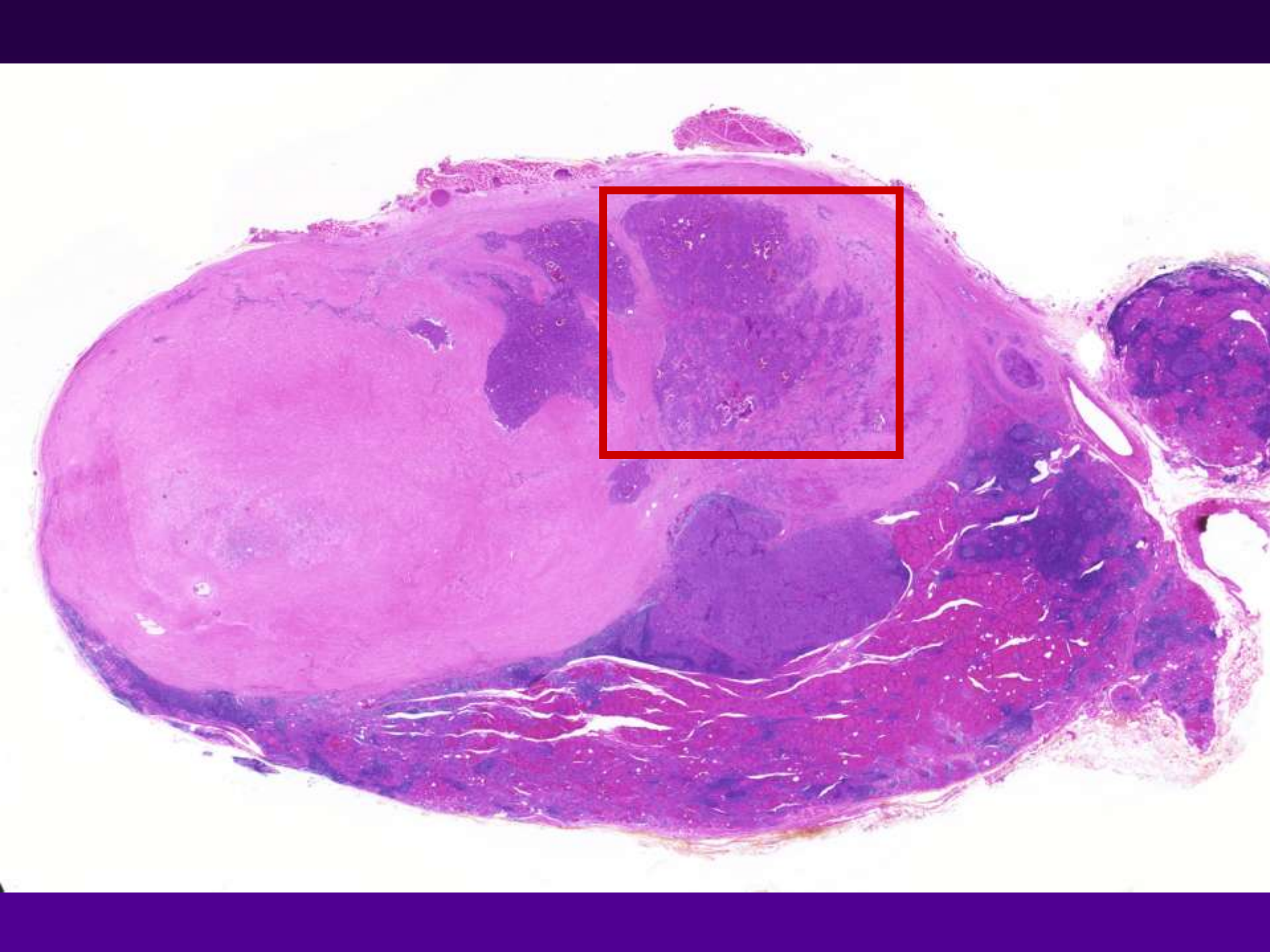
- F/27
- Presented with right neck swelling
- Fine needle aspiration of thyroid: malignant neoplasm
- Total thyroidectomy performed, revealing a 2 cm hard nodule

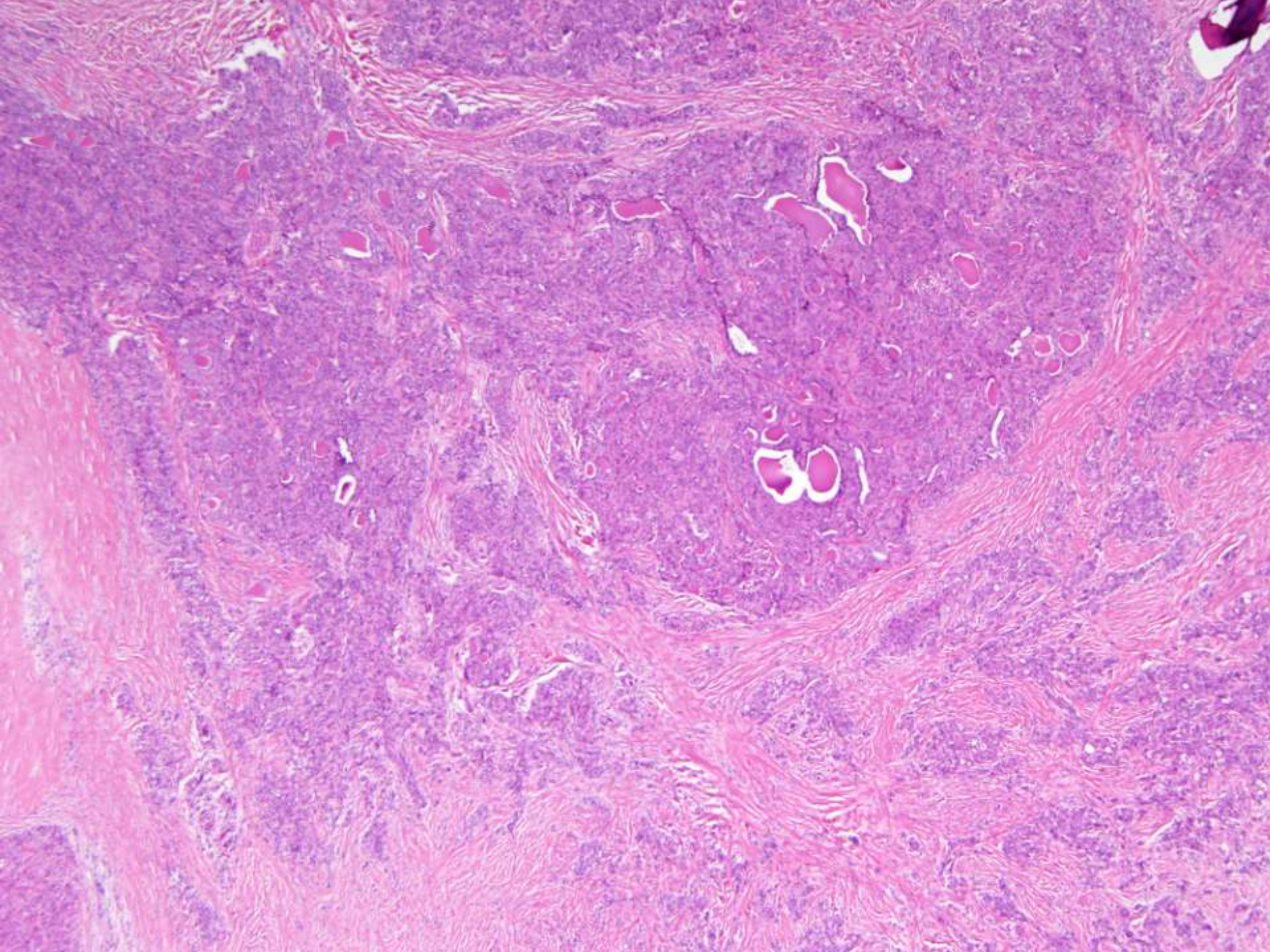


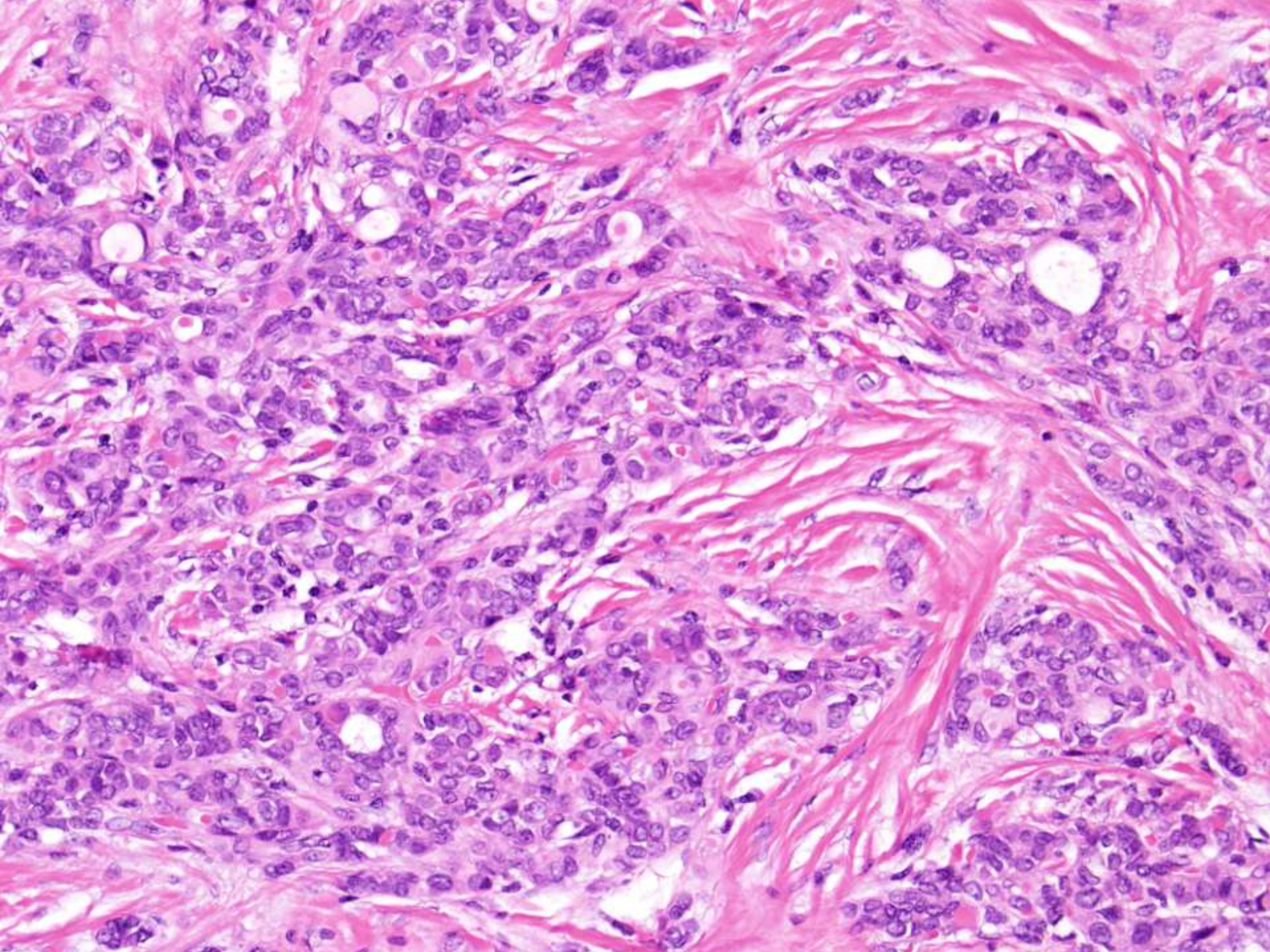


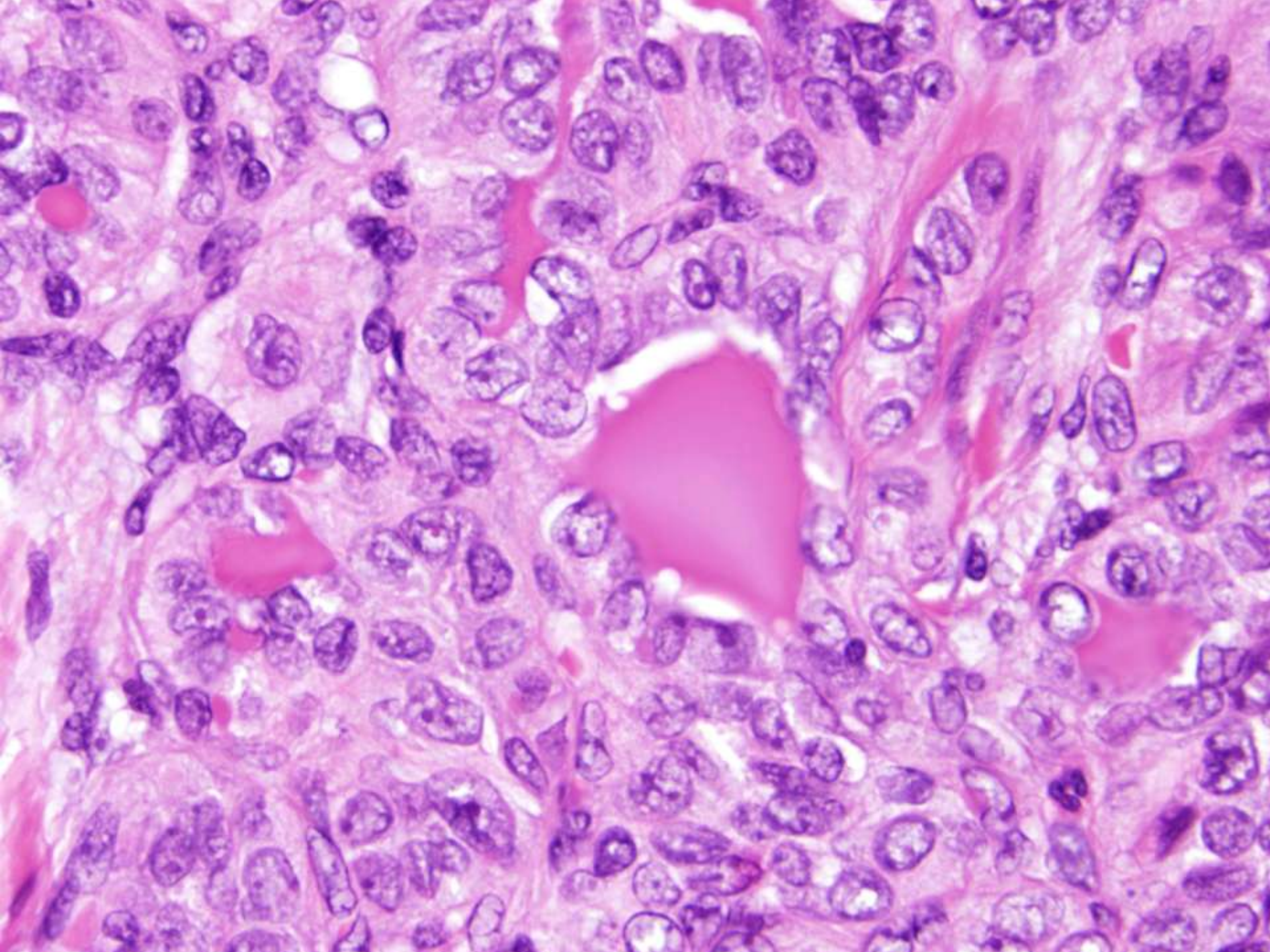


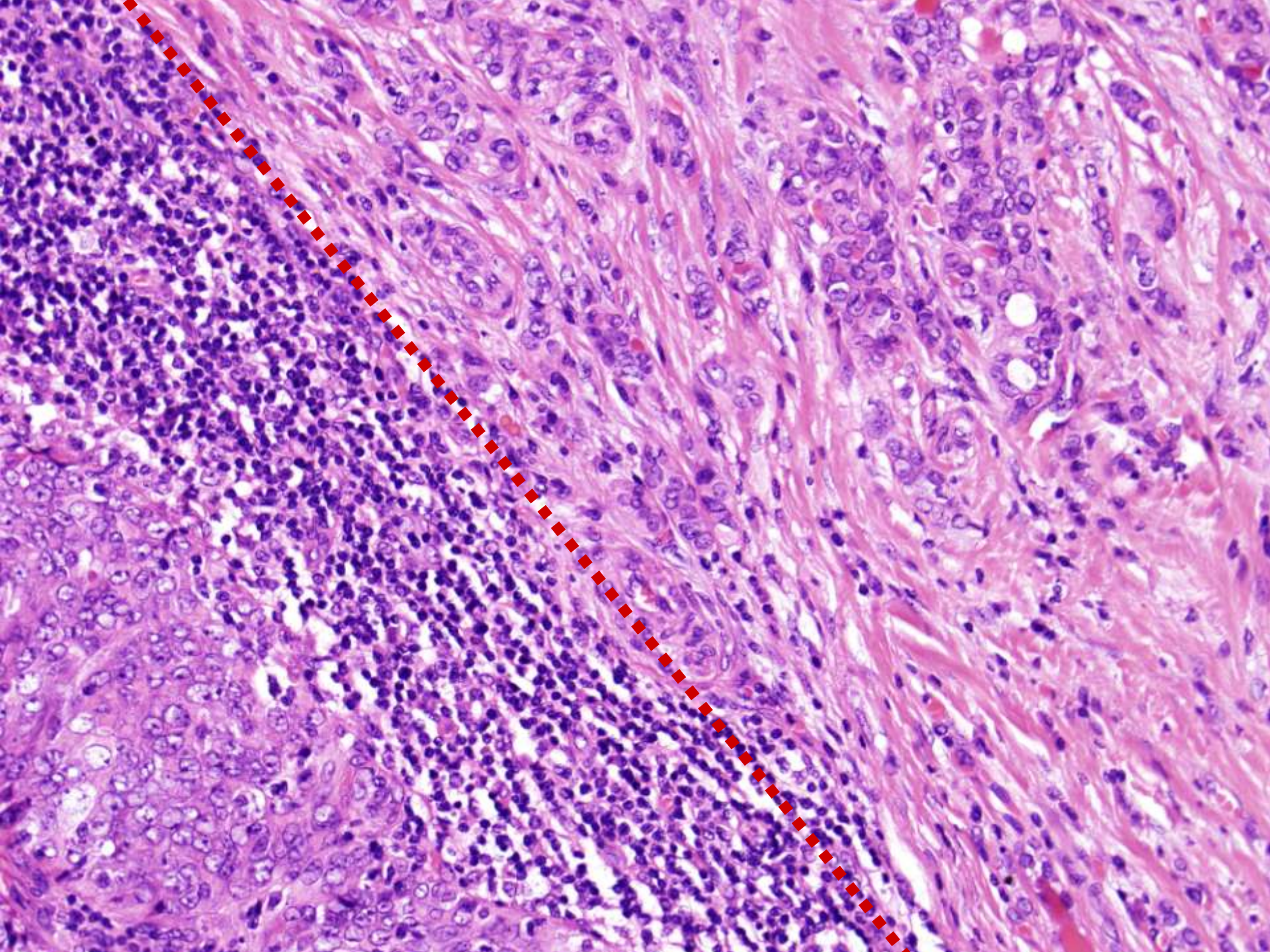












Analysis

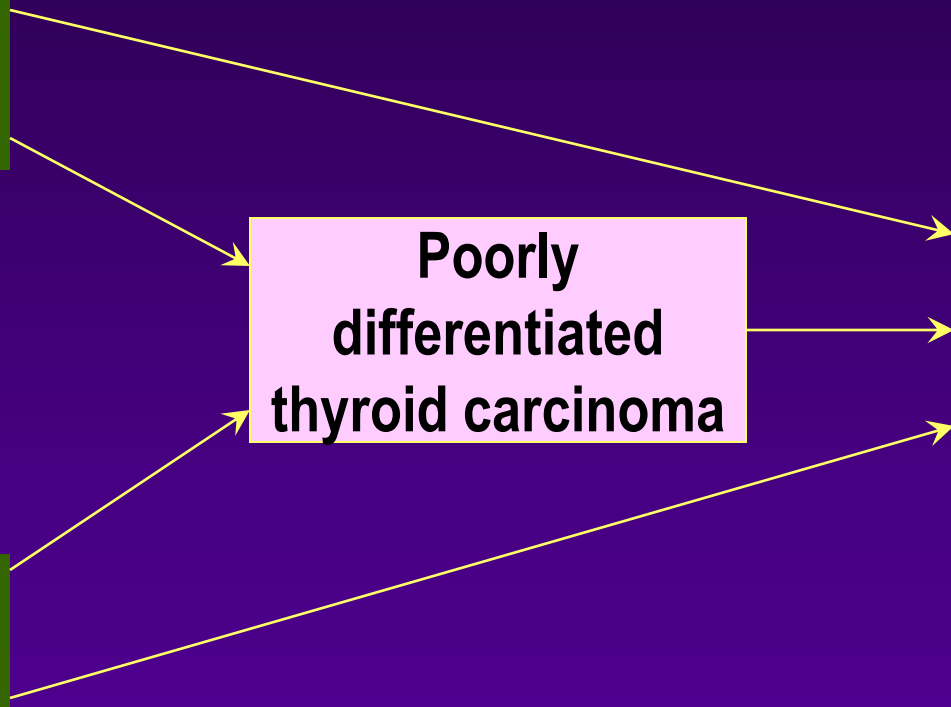
- Definite component of PTC present (follicular/solid variant)
- There is another morphologically different carcinoma with larger nuclei and mitotic activity
 - ~~Still papillary carcinoma (solid variant)?~~
 - Poorly differentiated thyroid carcinoma?
 - Undifferentiated carcinoma?

**Papillary
carcinoma**

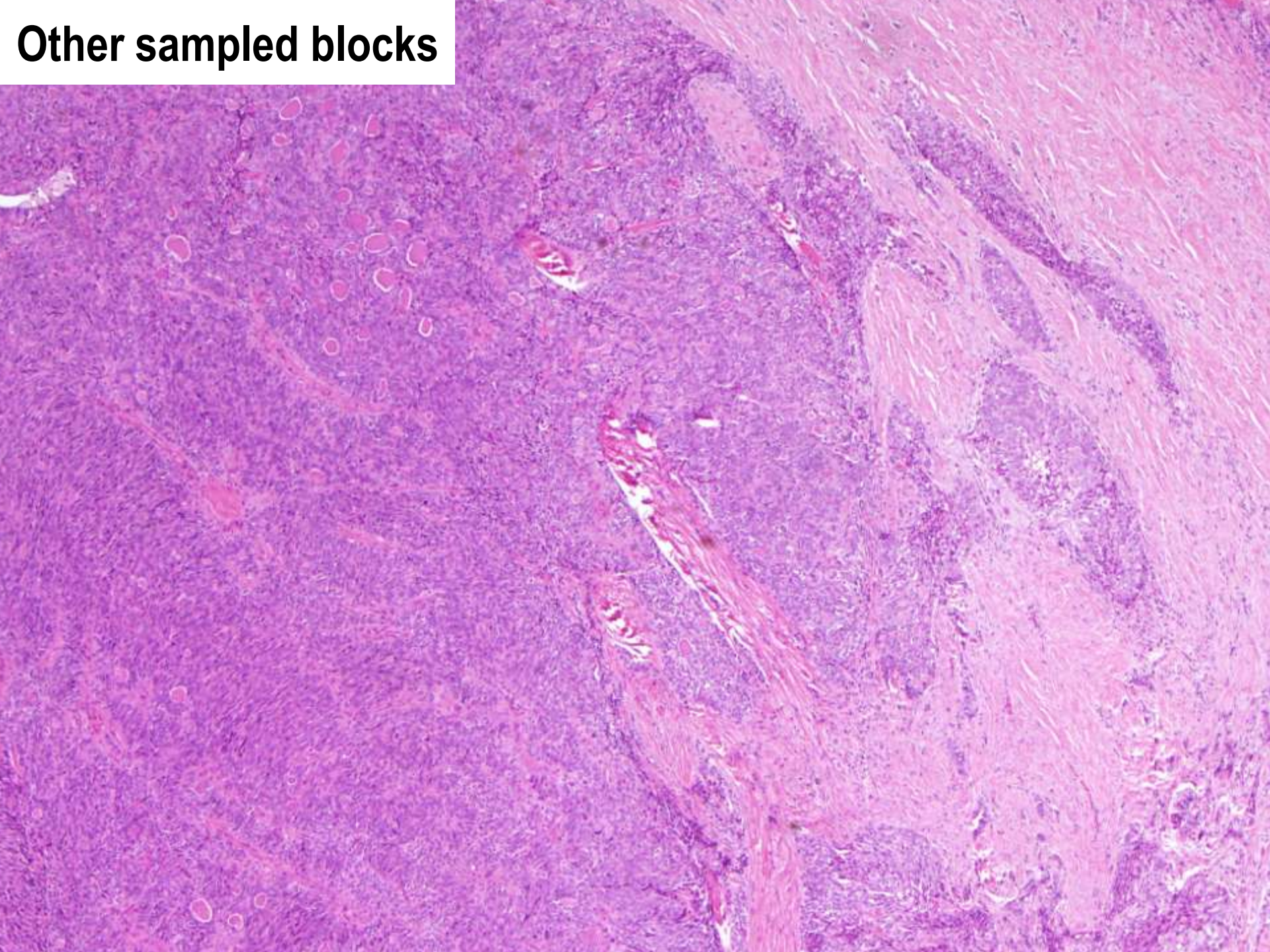
**Poorly
differentiated
thyroid carcinoma**

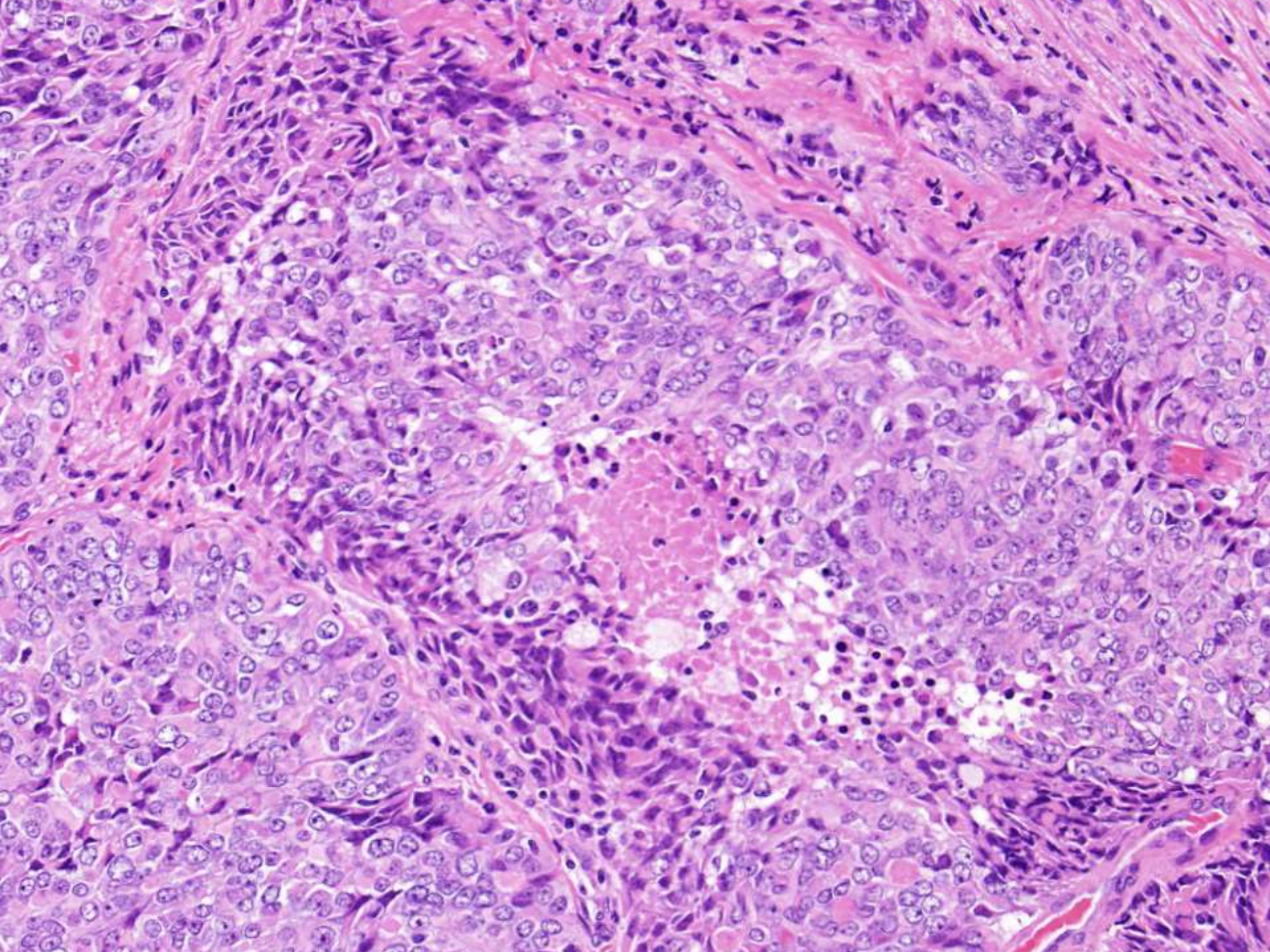
**Undifferentiated
carcinoma**

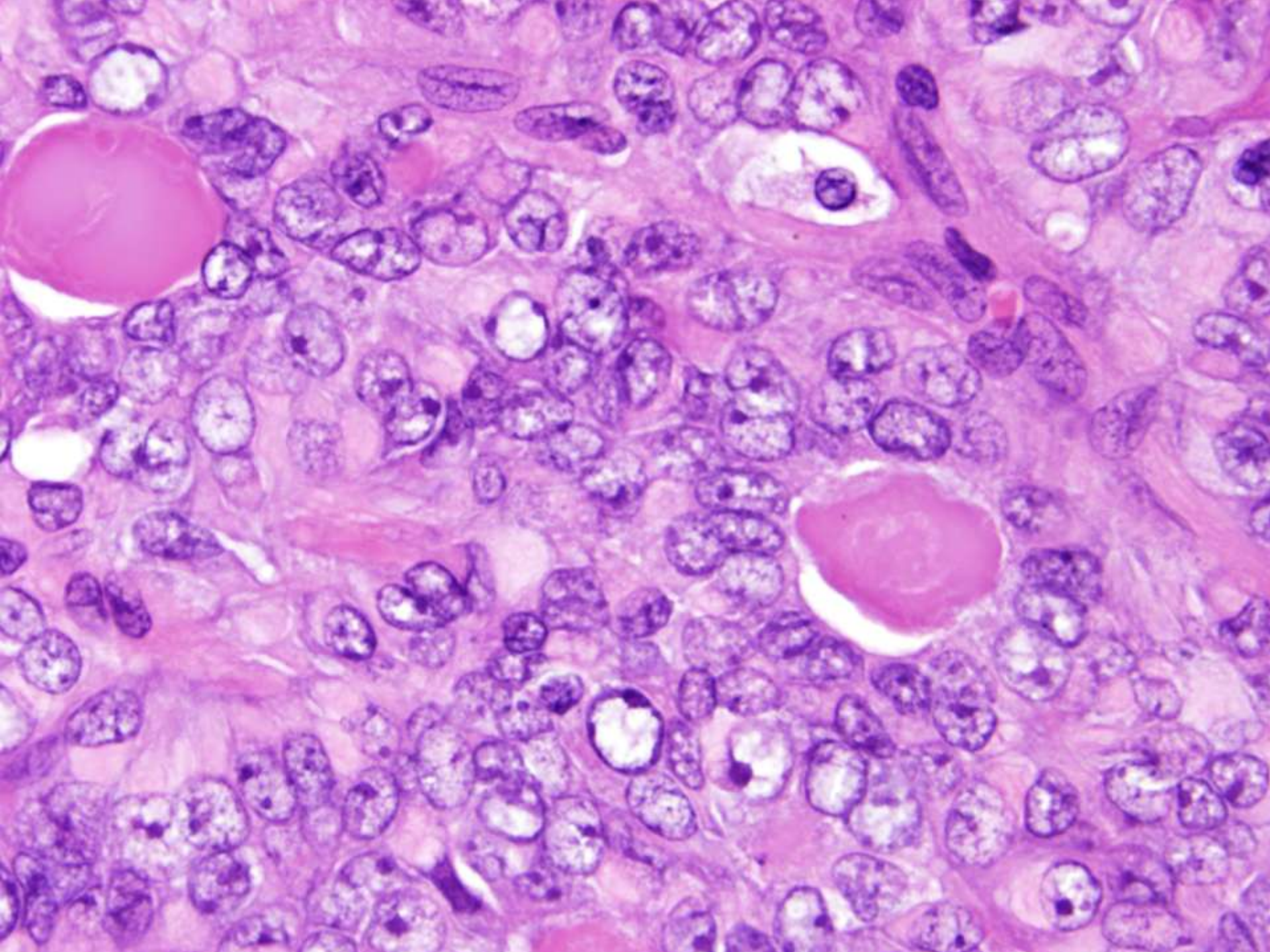
**Follicular
carcinoma**



Other sampled blocks



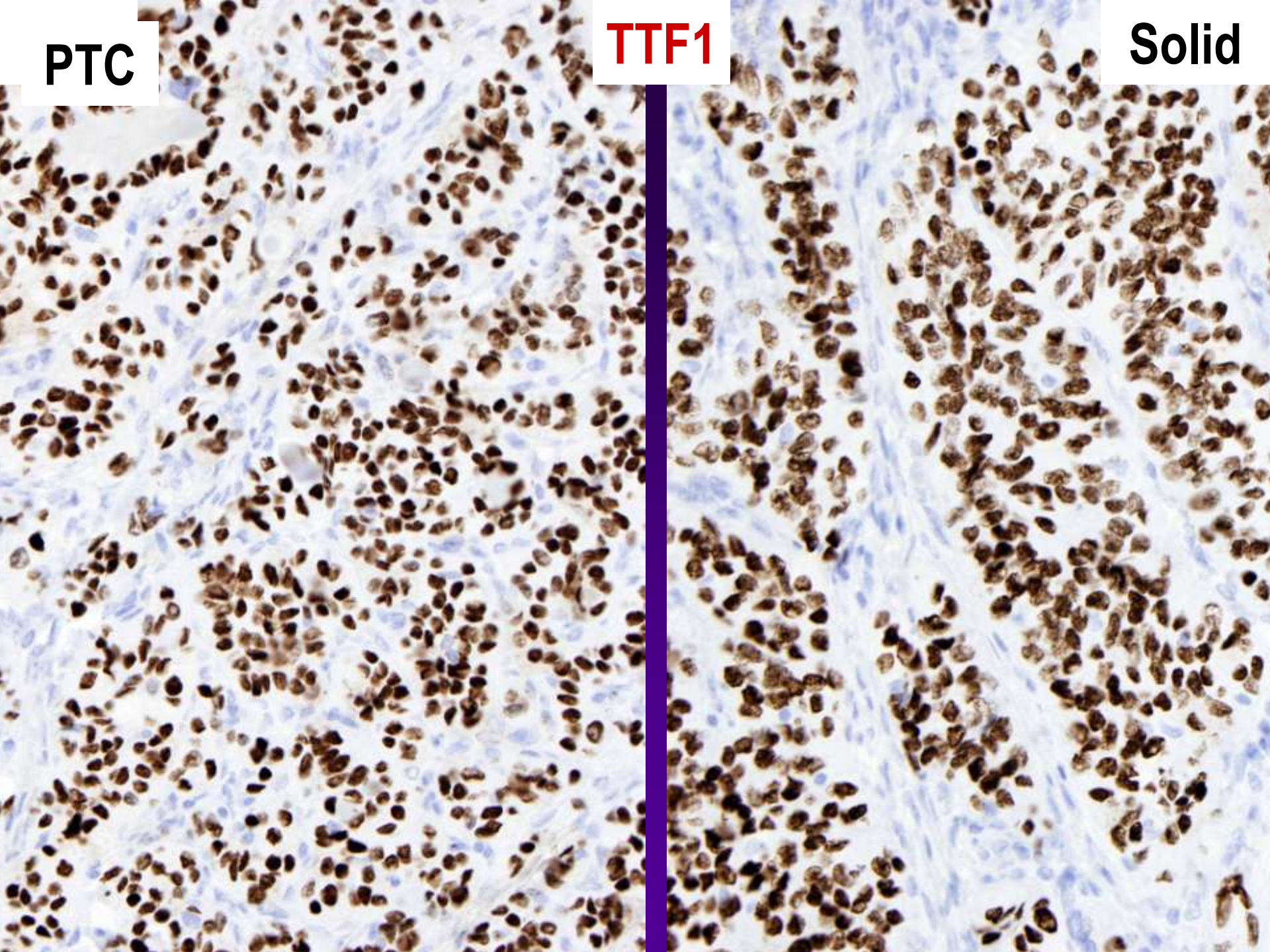




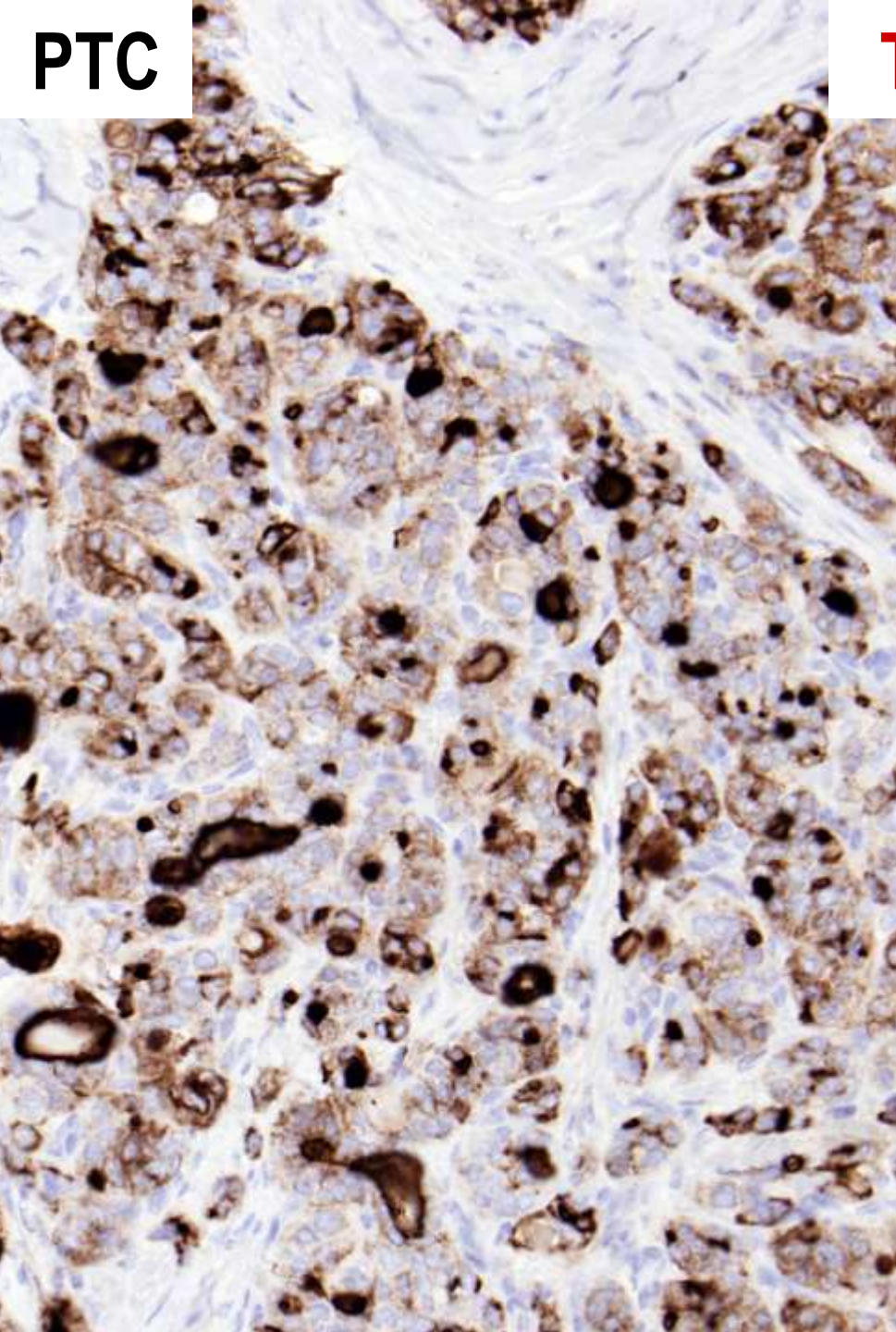
PTC

TTF1

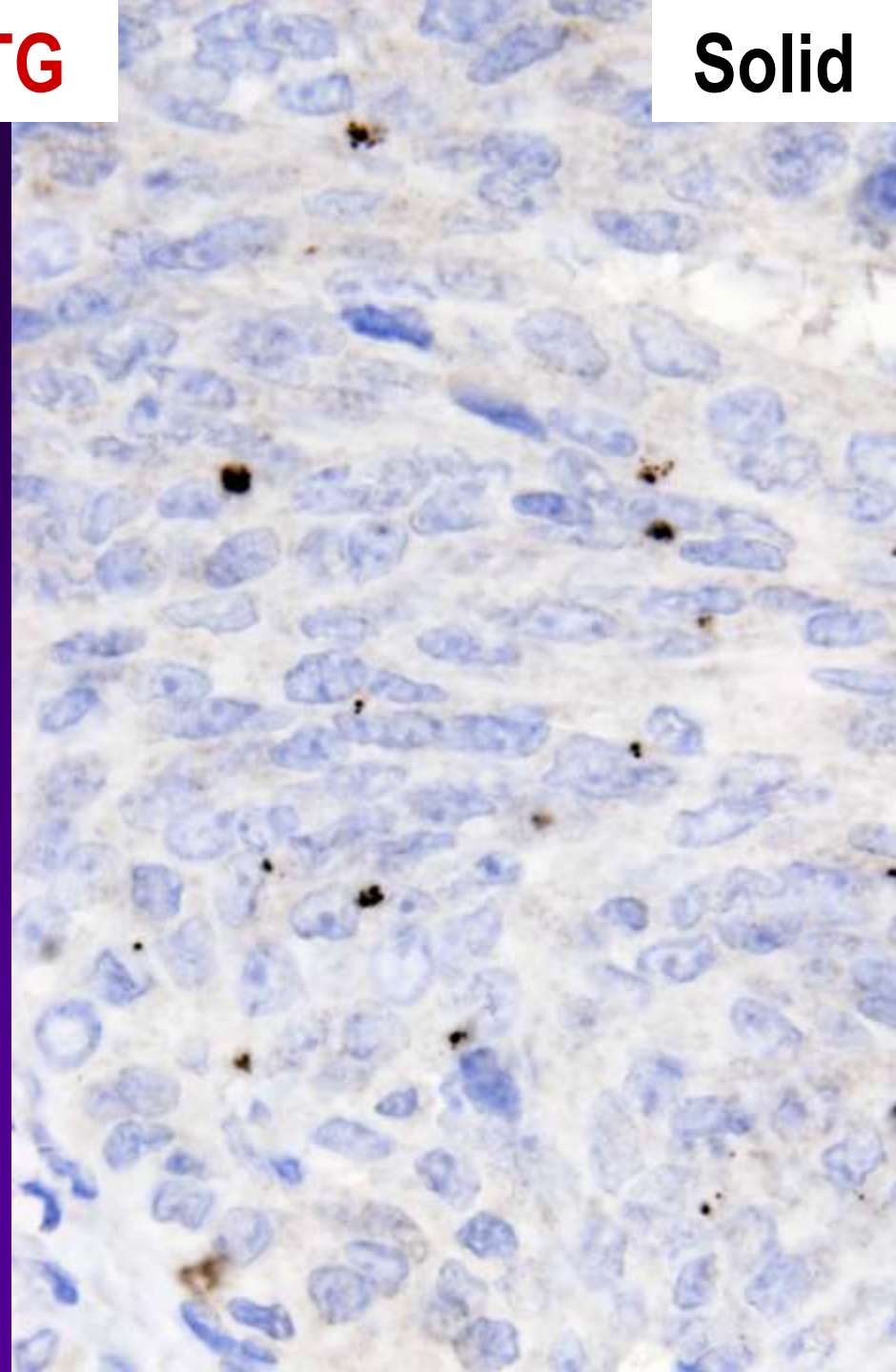
Solid



PTC



TG

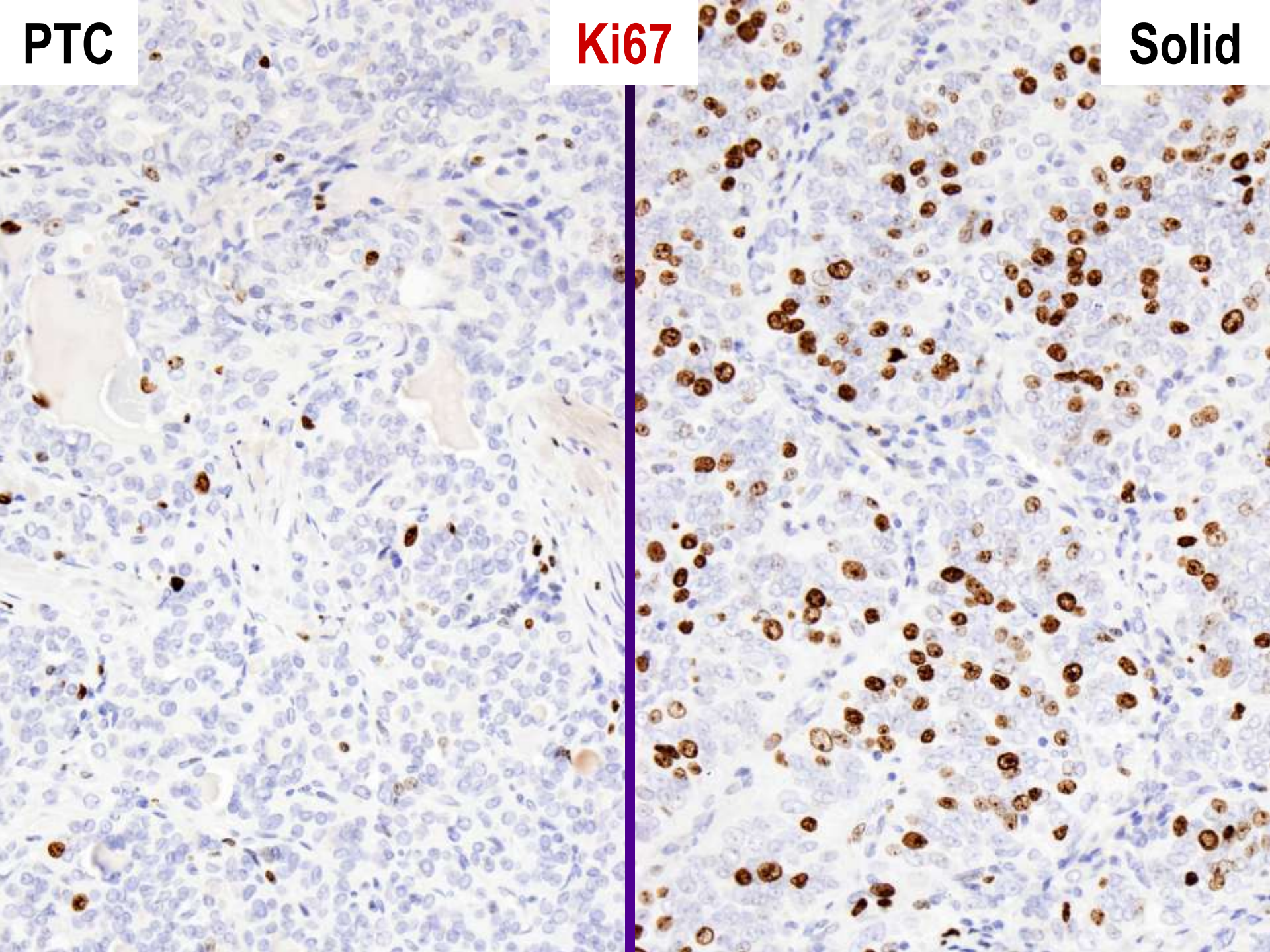


Solid

PTC

Ki67

Solid



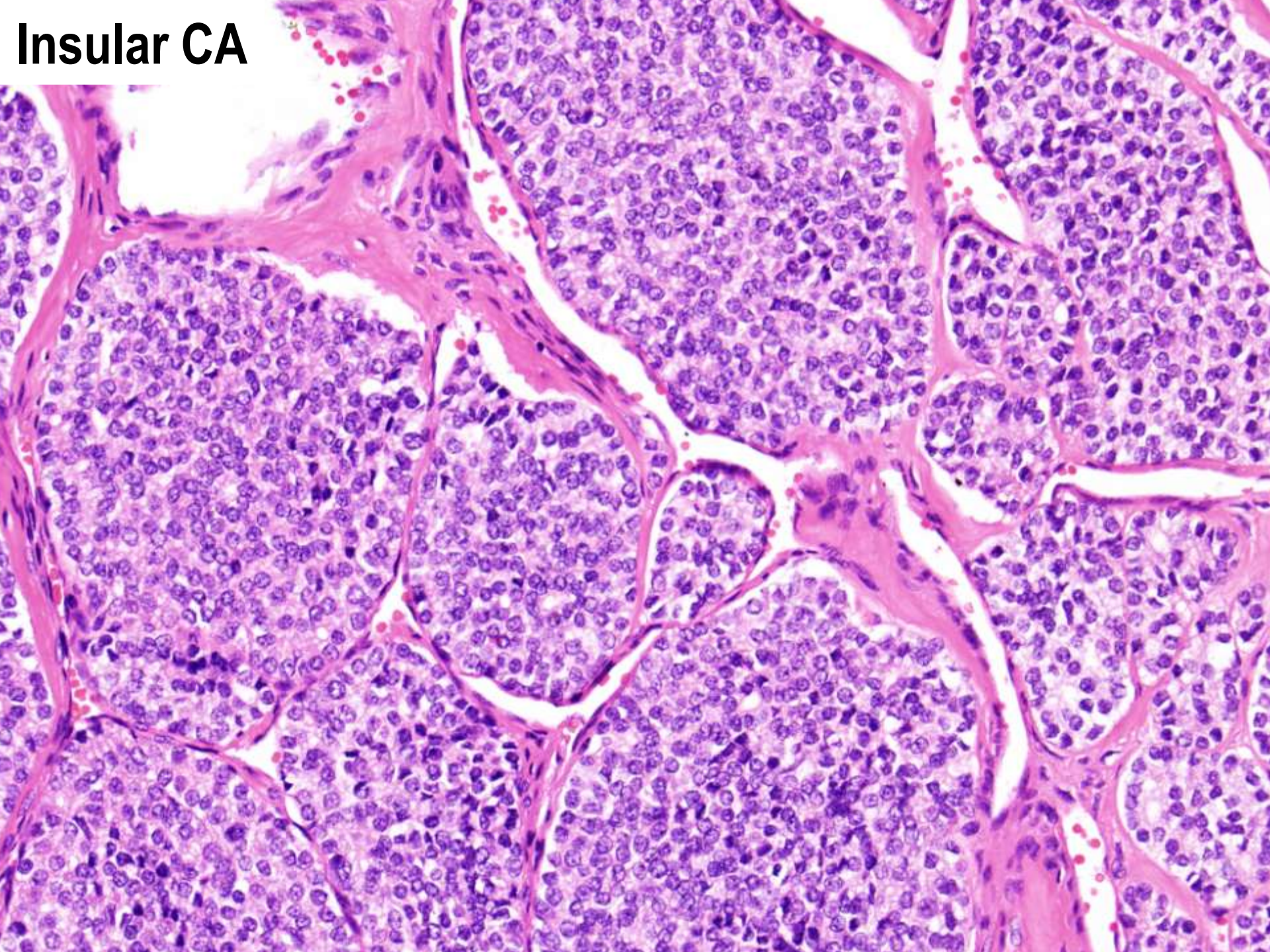
Diagnosis

Thyroid –

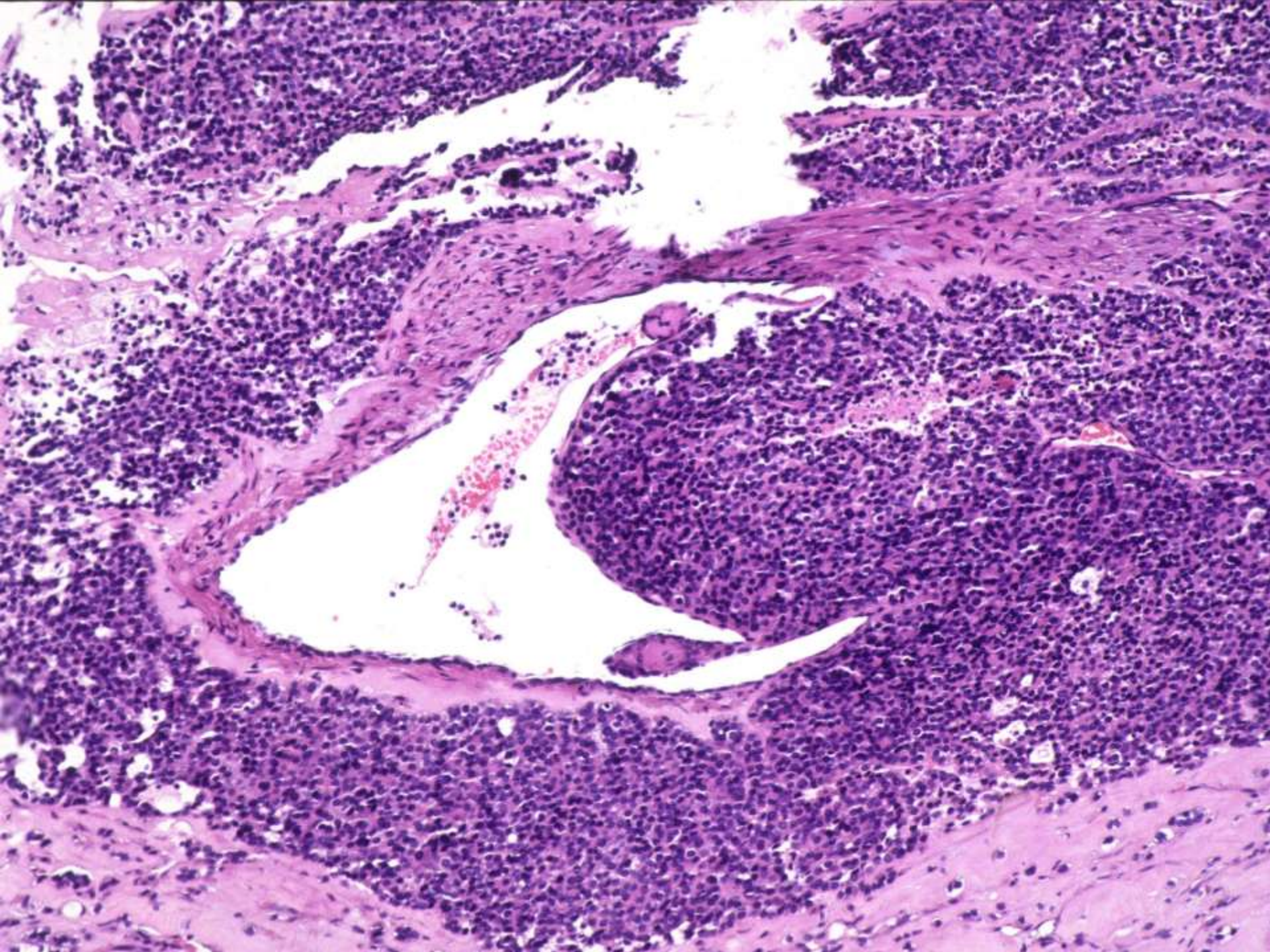
Poorly differentiated thyroid carcinoma,
with coexistent papillary carcinoma

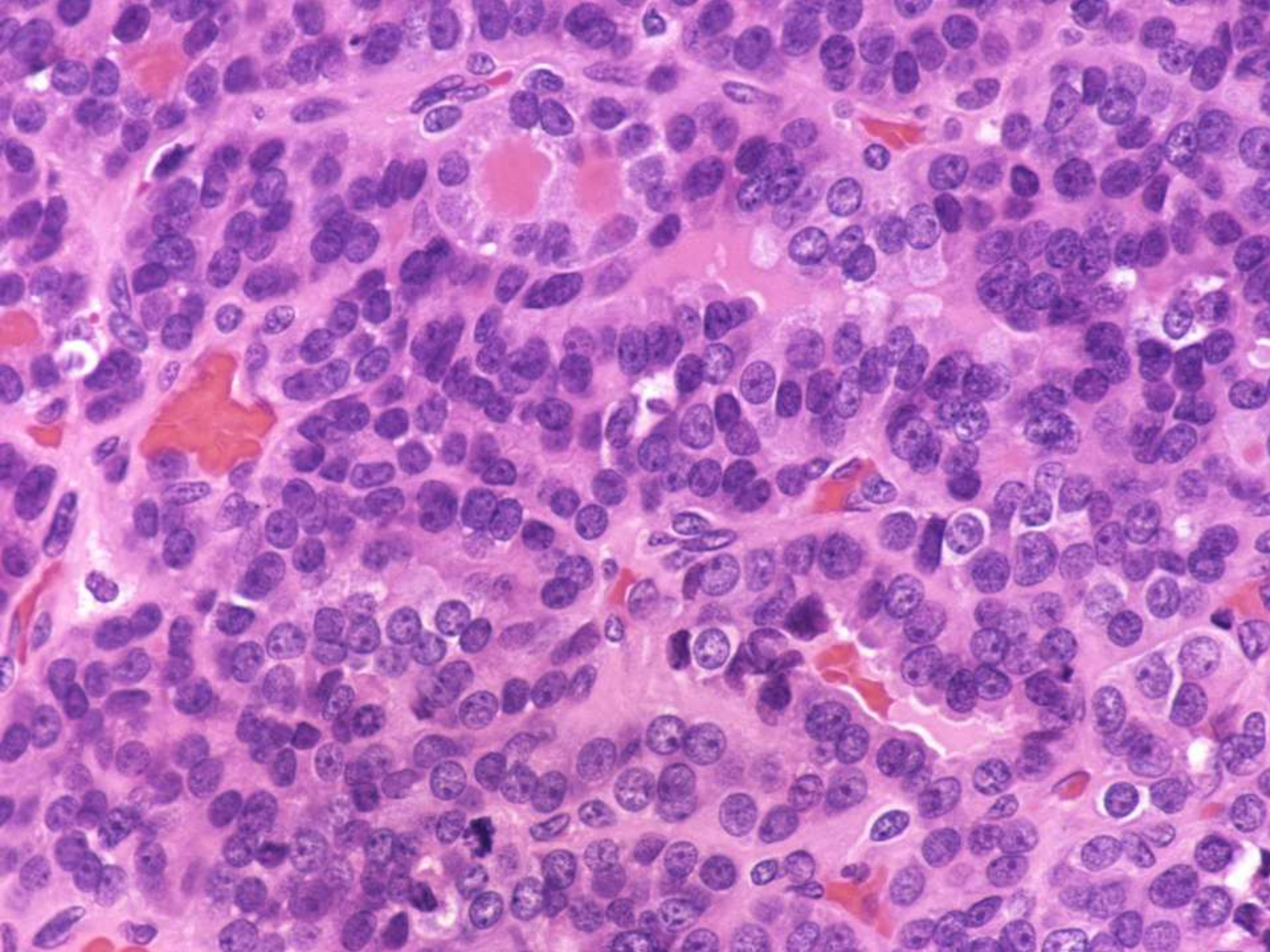
POORLY DIFFERENTIATED THYROID CARCINOMA

- Tumor with morphology, biology and behavior intermediate between well differentiated thyroid carcinoma and undifferentiated carcinoma
- Lack of uniformity of diagnostic criteria
- Insular carcinoma (*Carcangiu et al*) emphasizes insular growth, necrosis, small hyperchromatic nuclei and mitoses
- *Sakamoto et al* rely on solid, trabecular or scirrhous growth
- Still others have expanded the morphologic spectrum

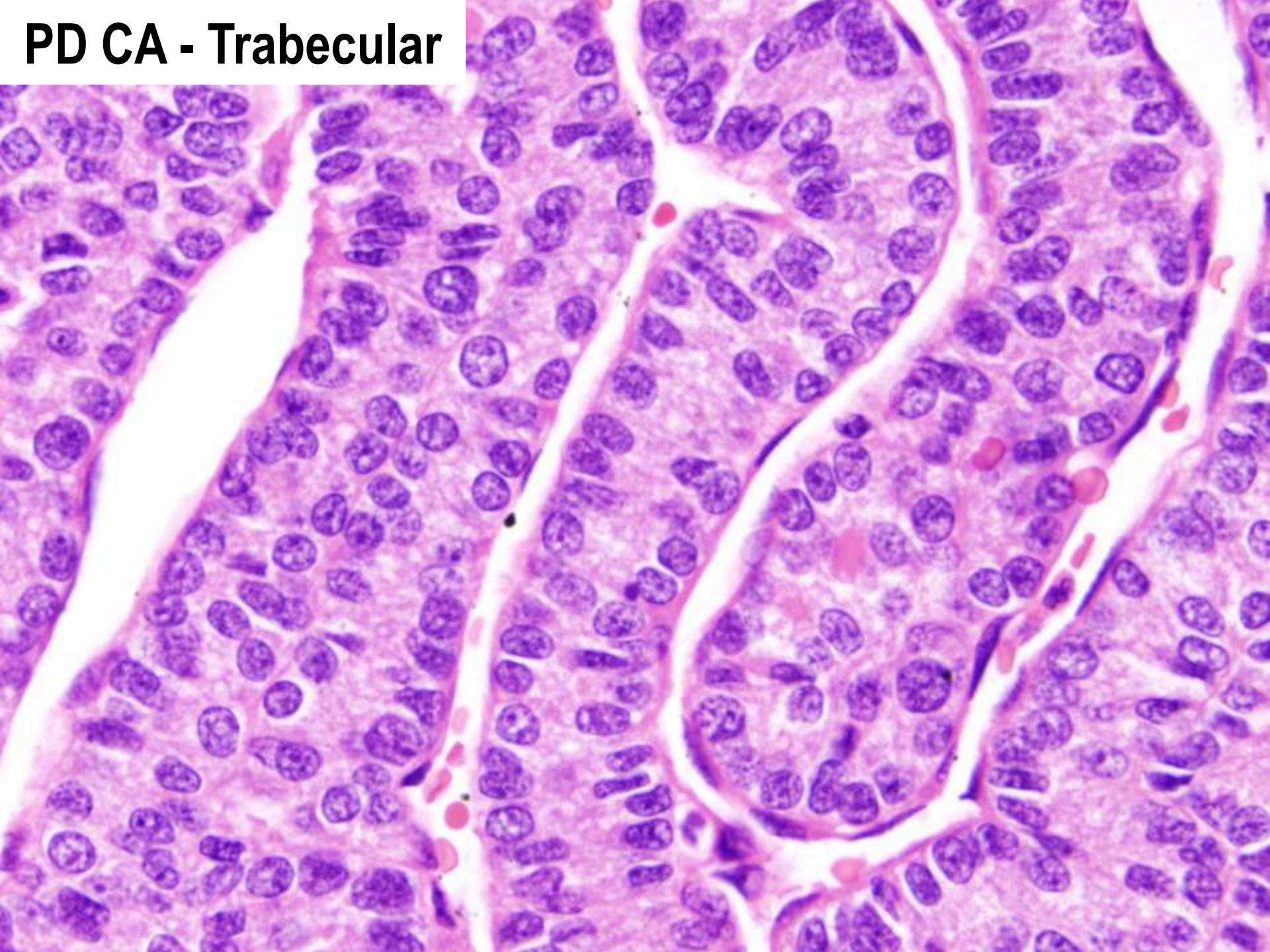


Insular CA

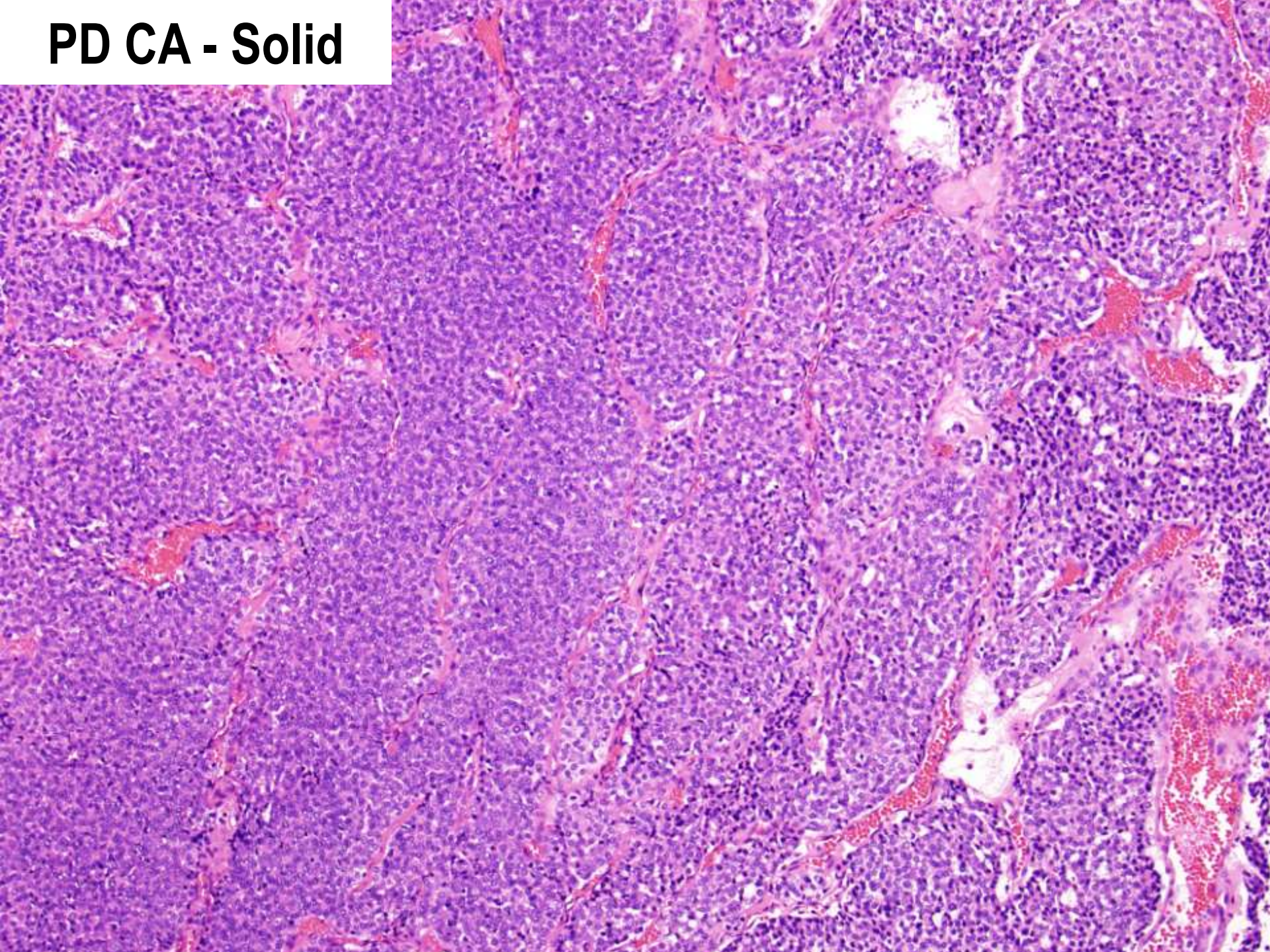




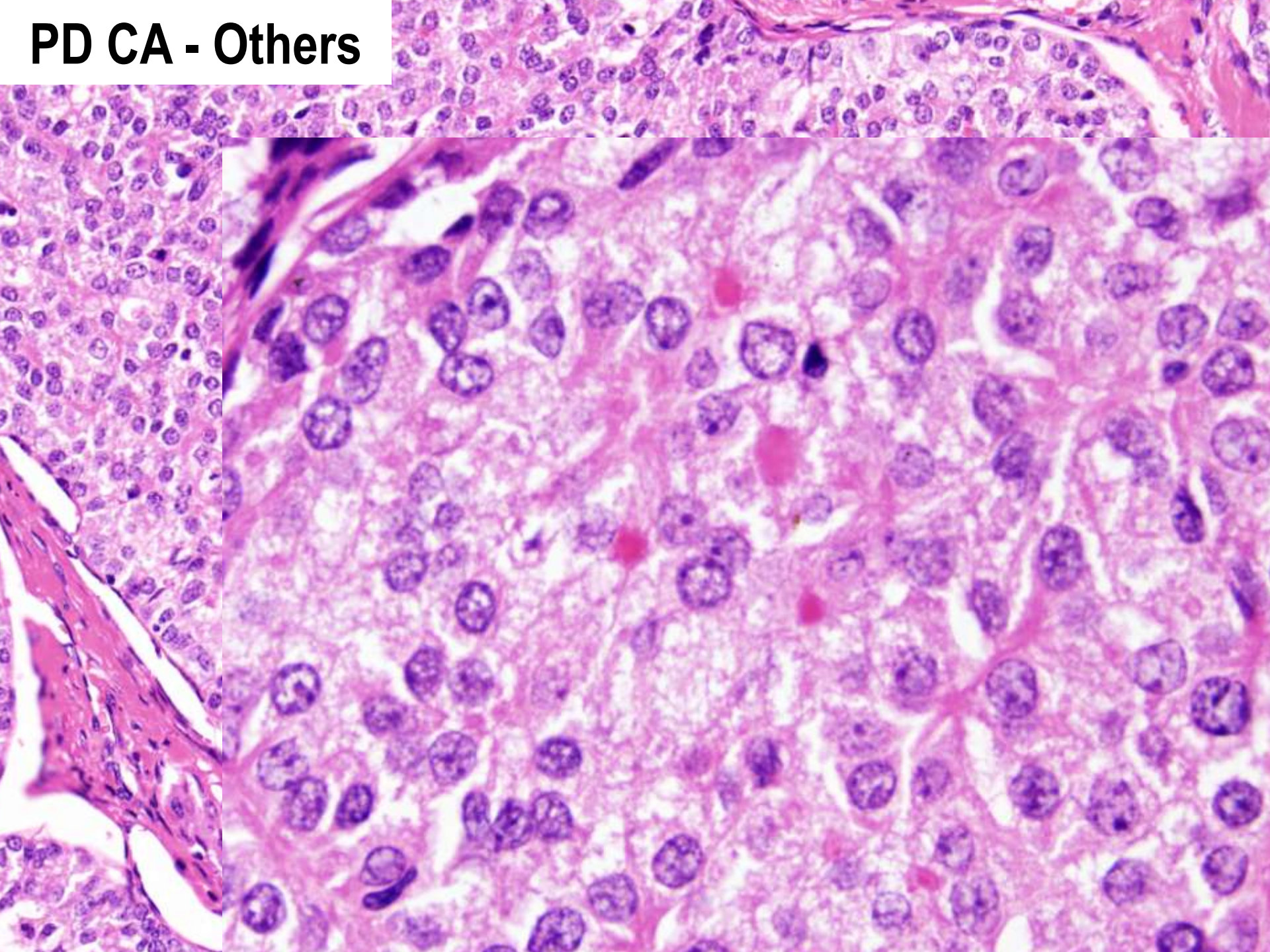
PD CA - Trabecular



PD CA - Solid



PD CA - Others



Turin proposal: Diagnostic criteria of poorly differentiated thyroid carcinoma

- Presence of solid, trabecular or insular growth pattern
- Absence of conventional nuclear features of PTC
- Presence of ≥ 1 of the following:
 - Convoluted nuclei
 - Mitoses ≥ 3 per 10 HPF
 - Tumor necrosis

Turin proposal: Diagnostic criteria of poorly differentiated thyroid carcinoma

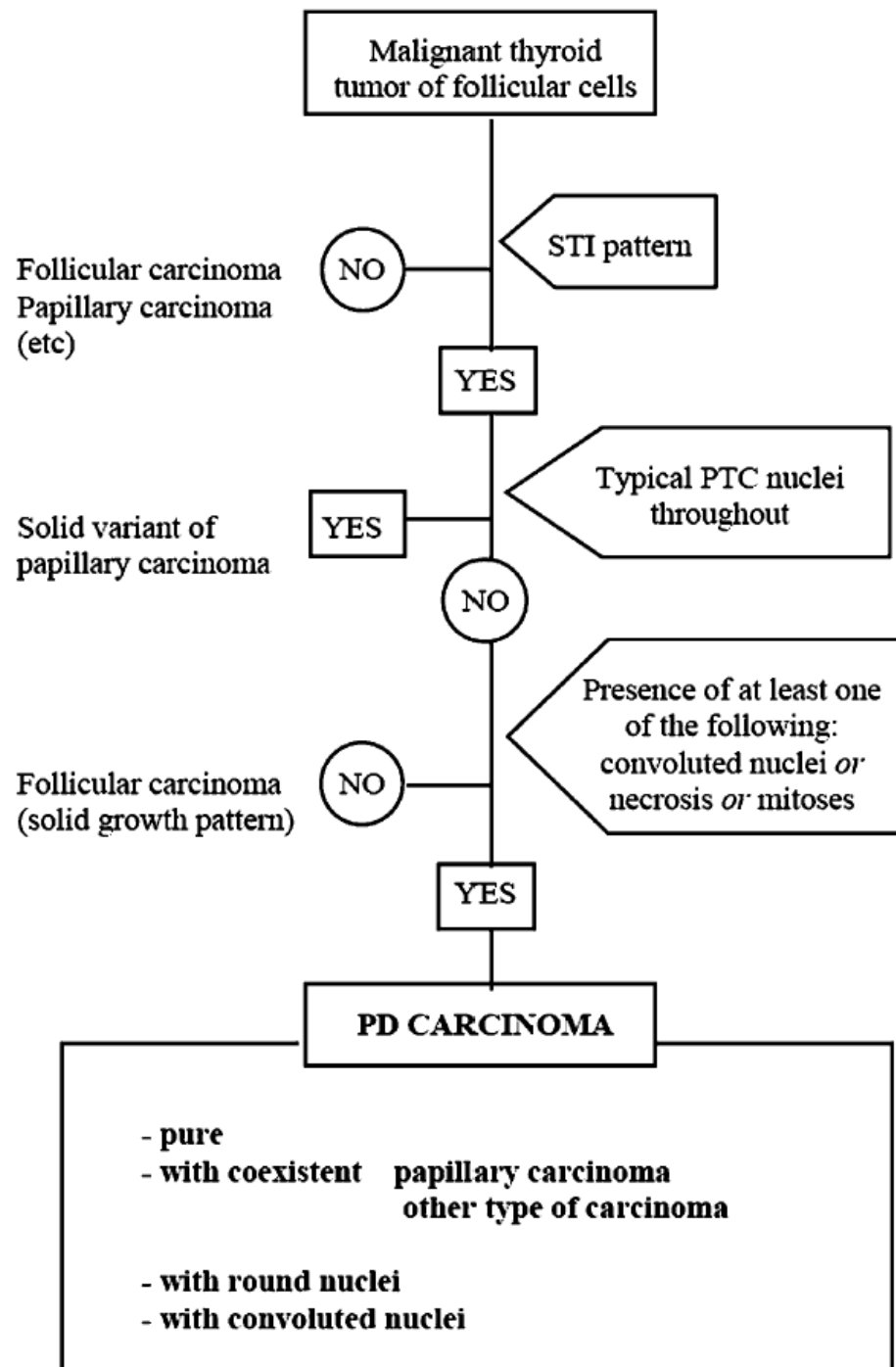
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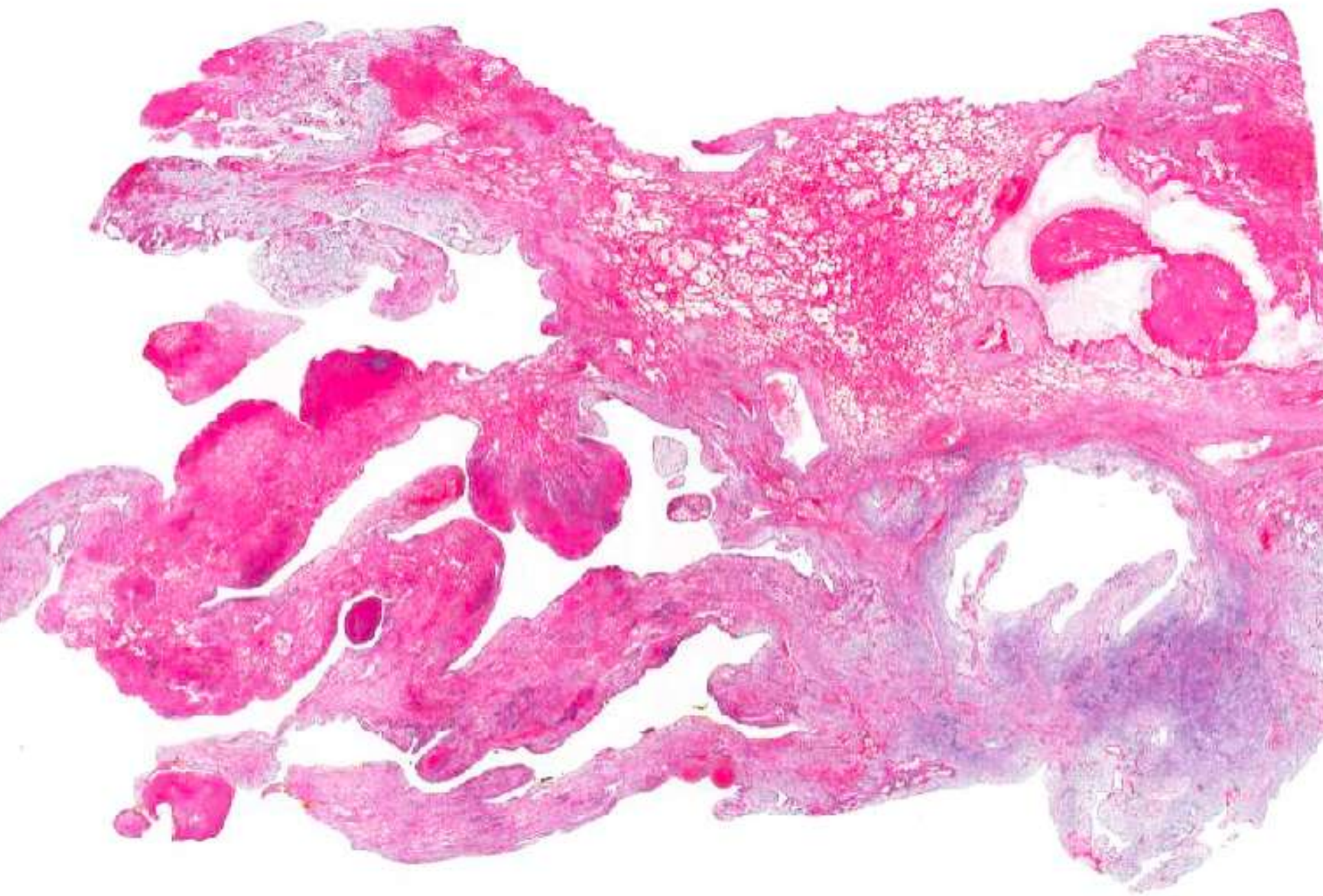


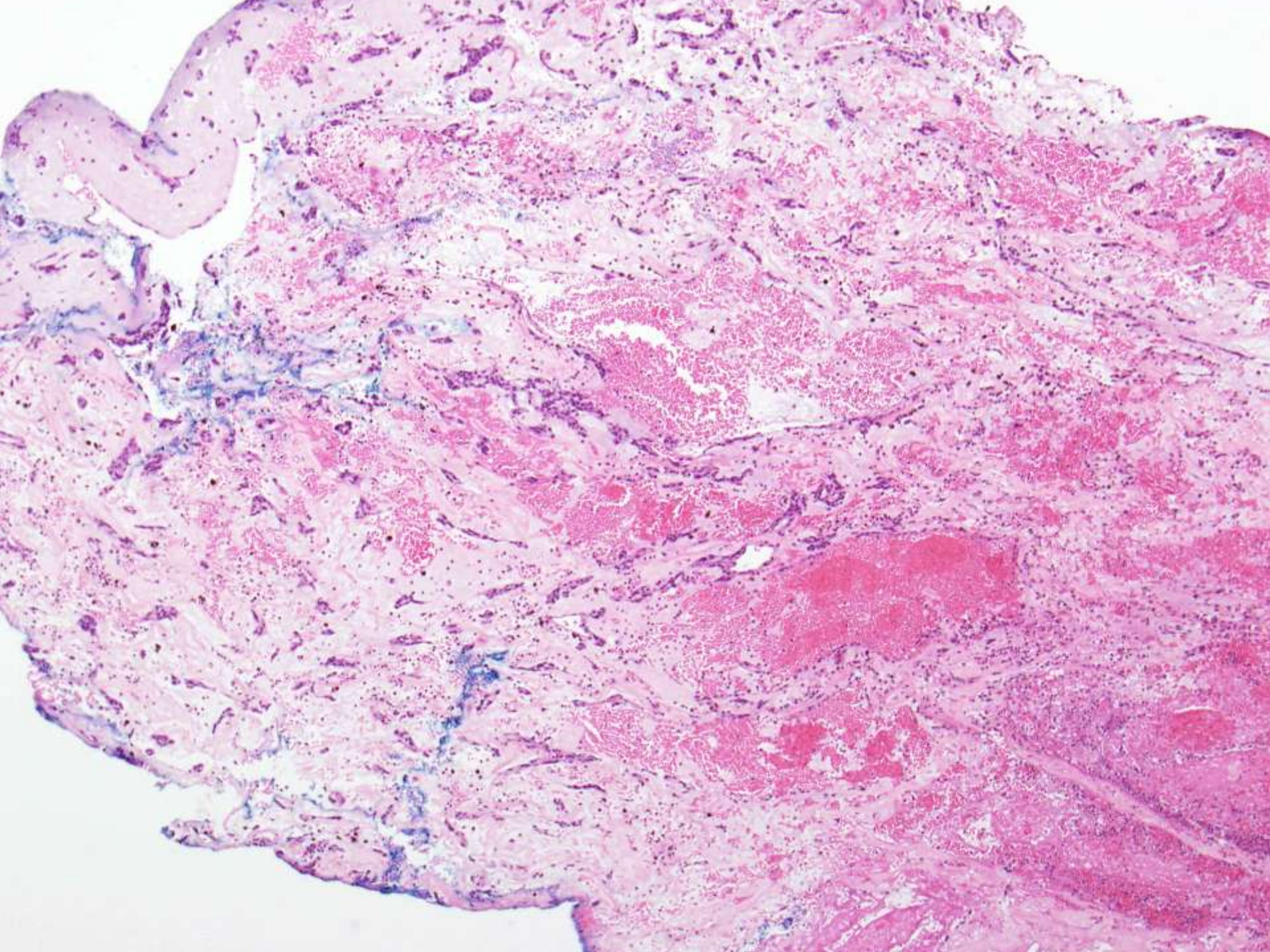
Clinical features of poorly differentiated thyroid carcinoma diagnosed according to Turin proposal (*Asioli et al 2010*)

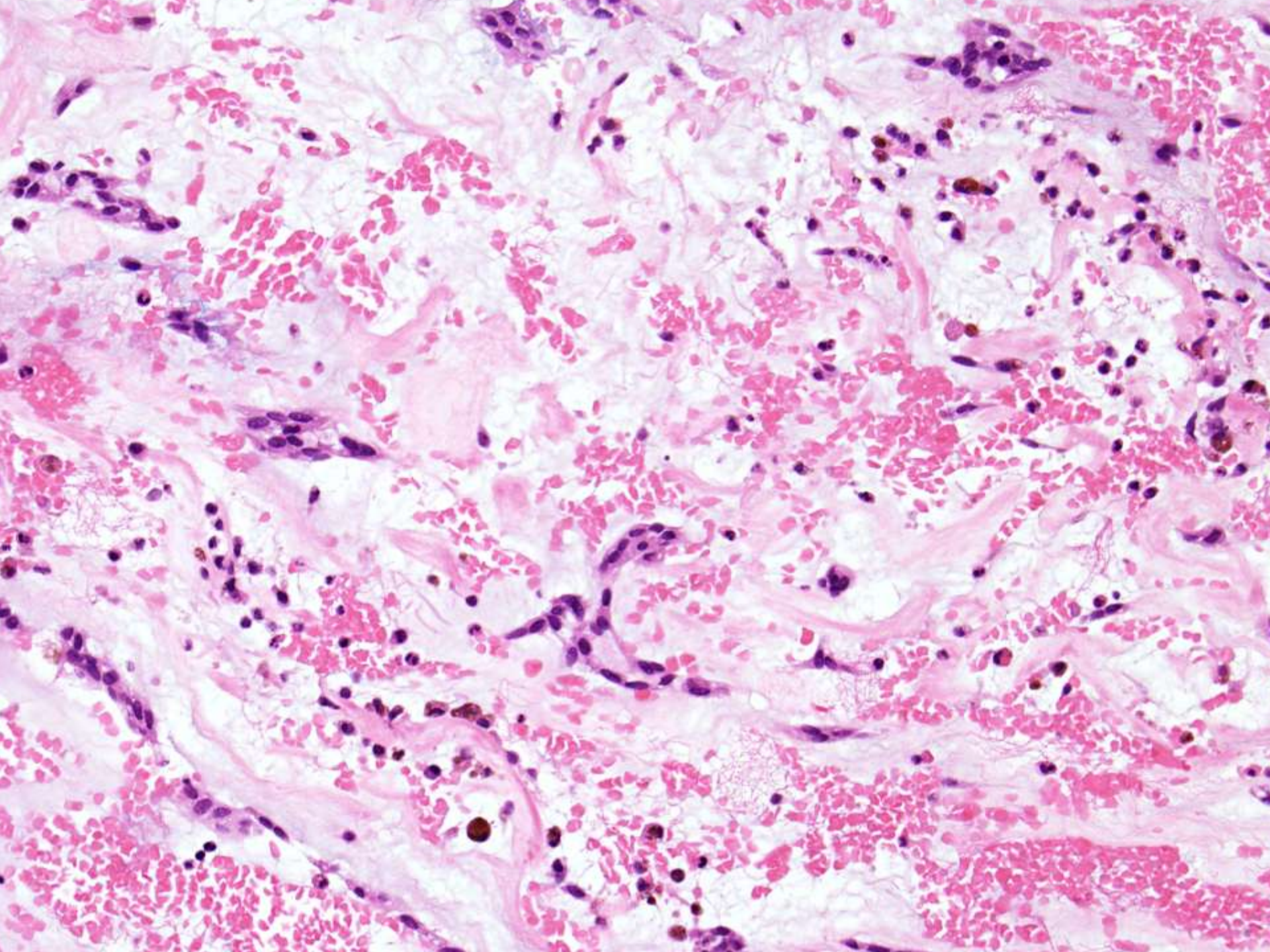
- Prevalence: 1.8% in USA, 6.7% in Northern Italy
- Age: 14-90 (mean 60.6 years)
- PTC component 11%, follicular carcinoma component in 24%
- Lymph node metastasis: 15%
- Distant metastasis: 38%
- Local recurrence: 13%
- 5-yr overall survival: 72%
- 10-yr overall survival: 46%

Chan - Case 2

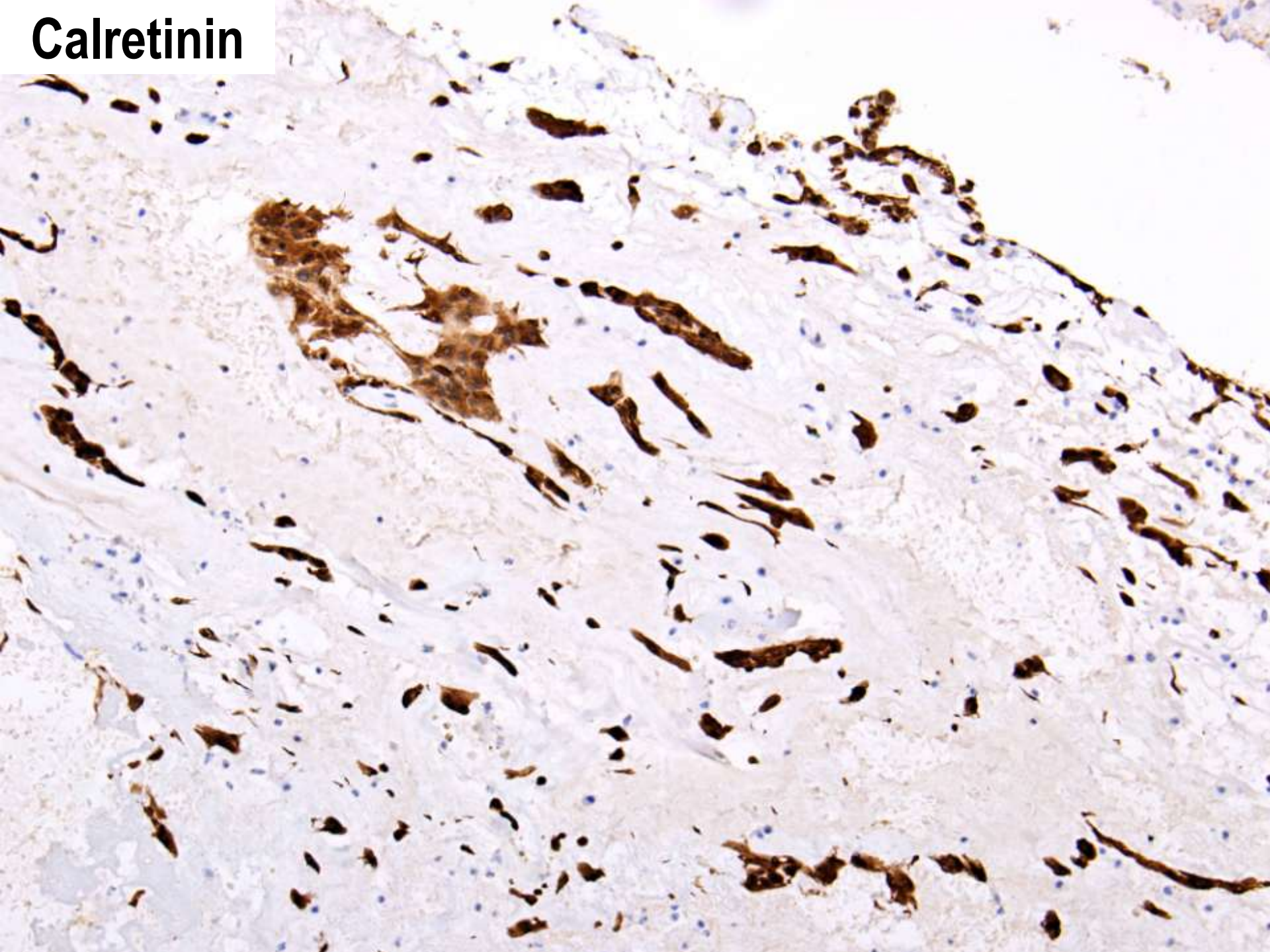
- F/70
- Had history of hypertension and diabetes mellitus
- Presented with cardiogenic shock, bradycardia, acute renal failure and ischemic stroke
- Echocardiogram: large left atrial mass causing inflow obstruction of mitral valve
- Mass was excized





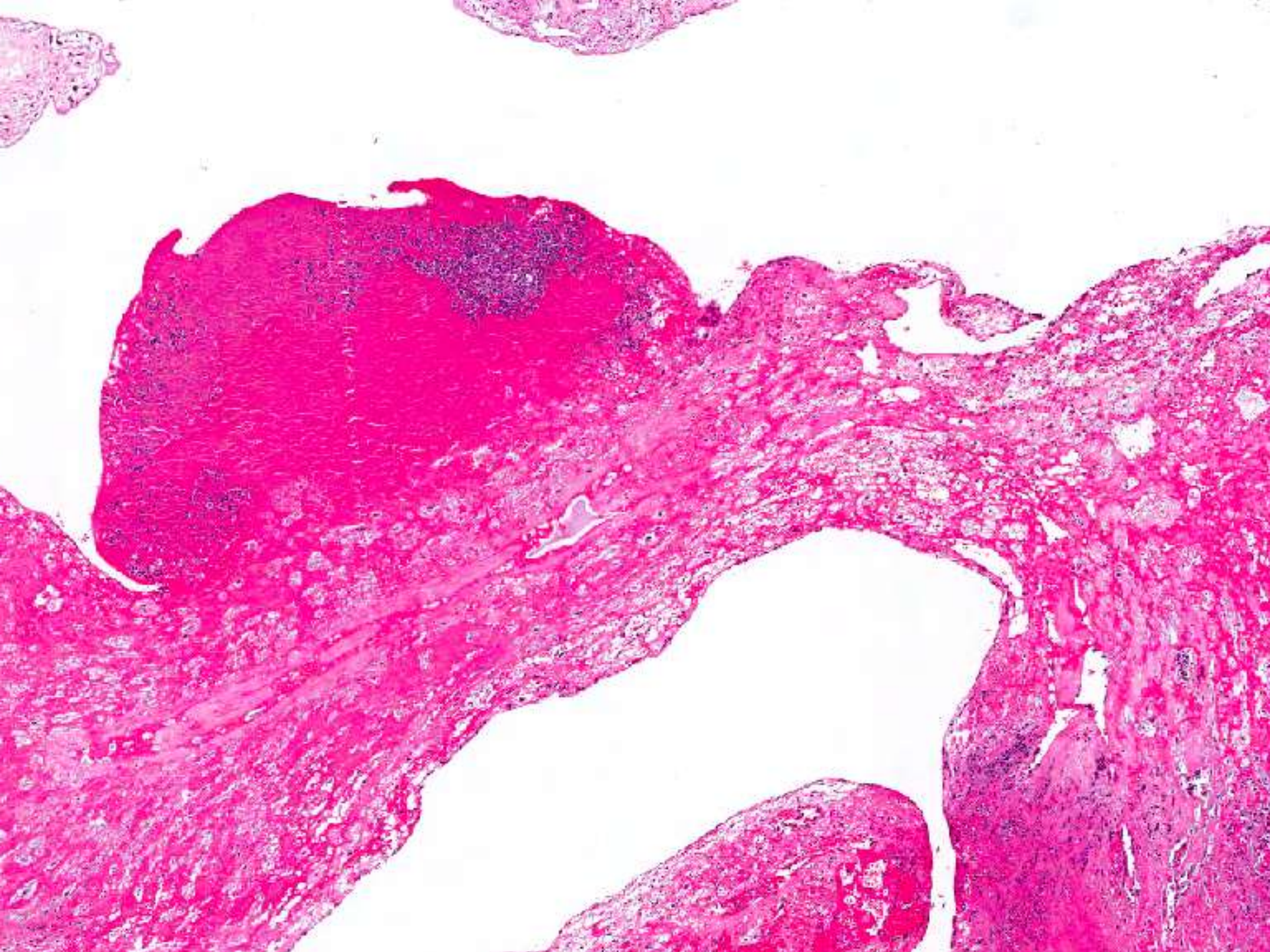


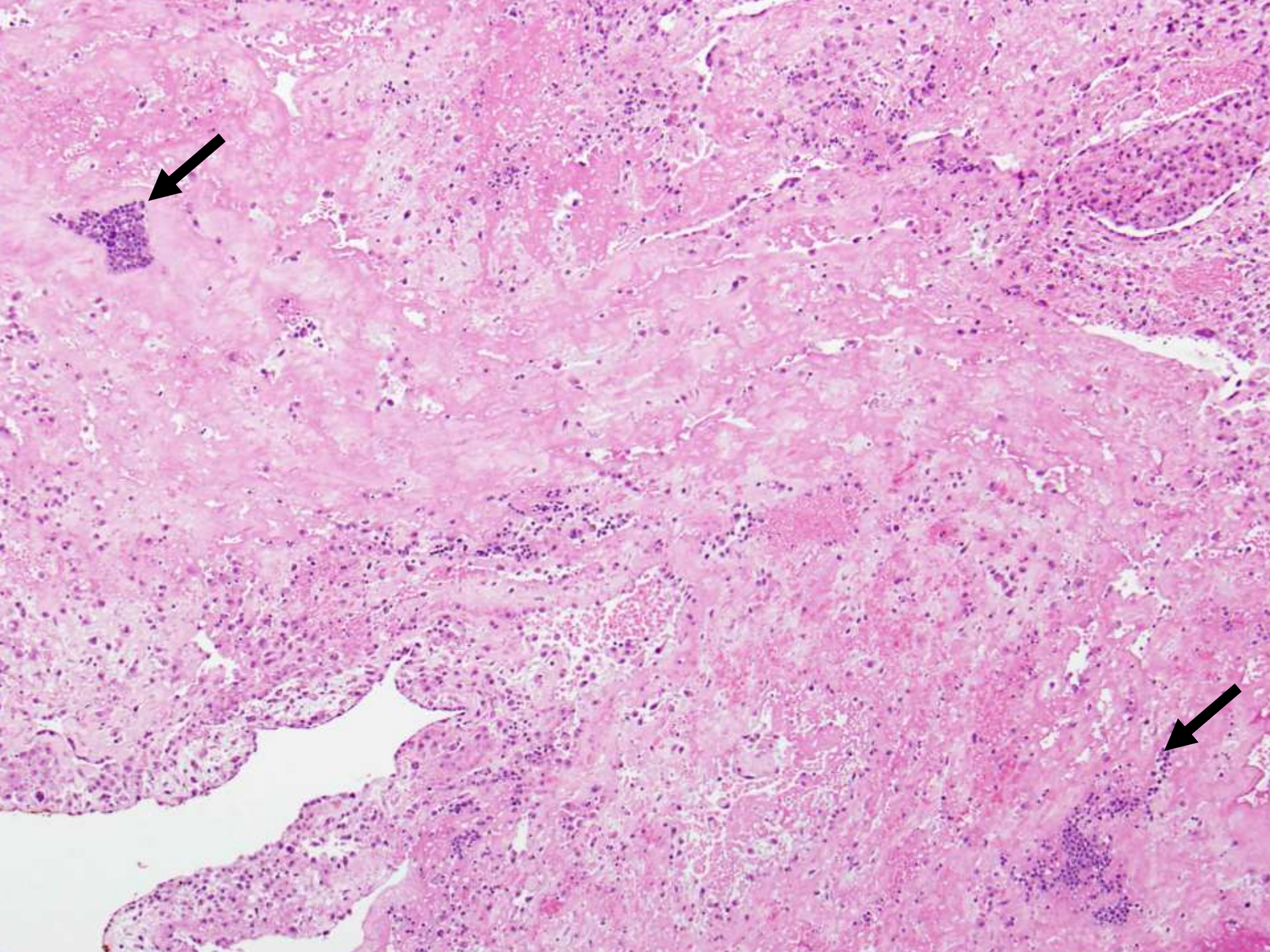
Calretinin

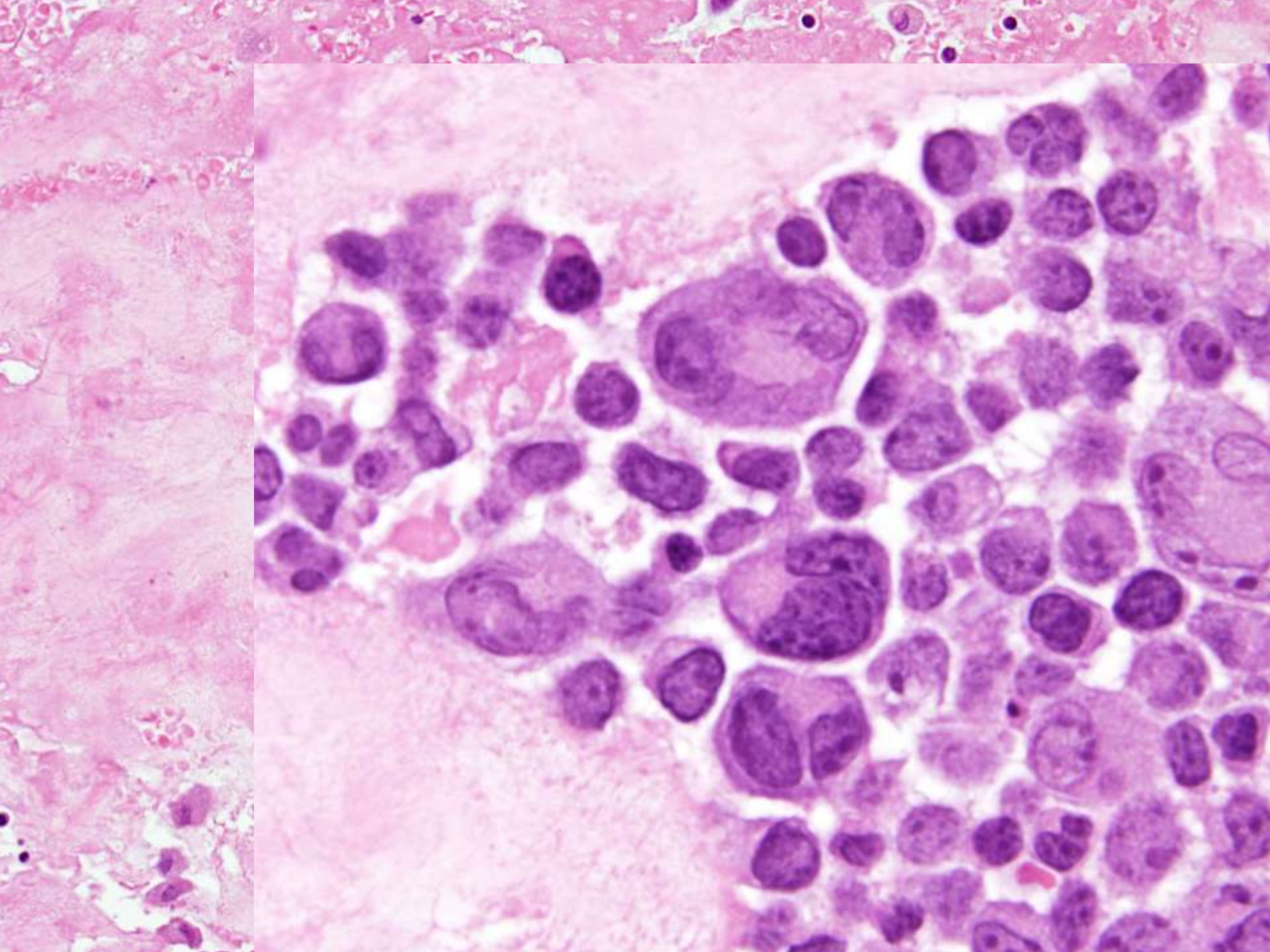


There is no doubt an atrial myxoma

But

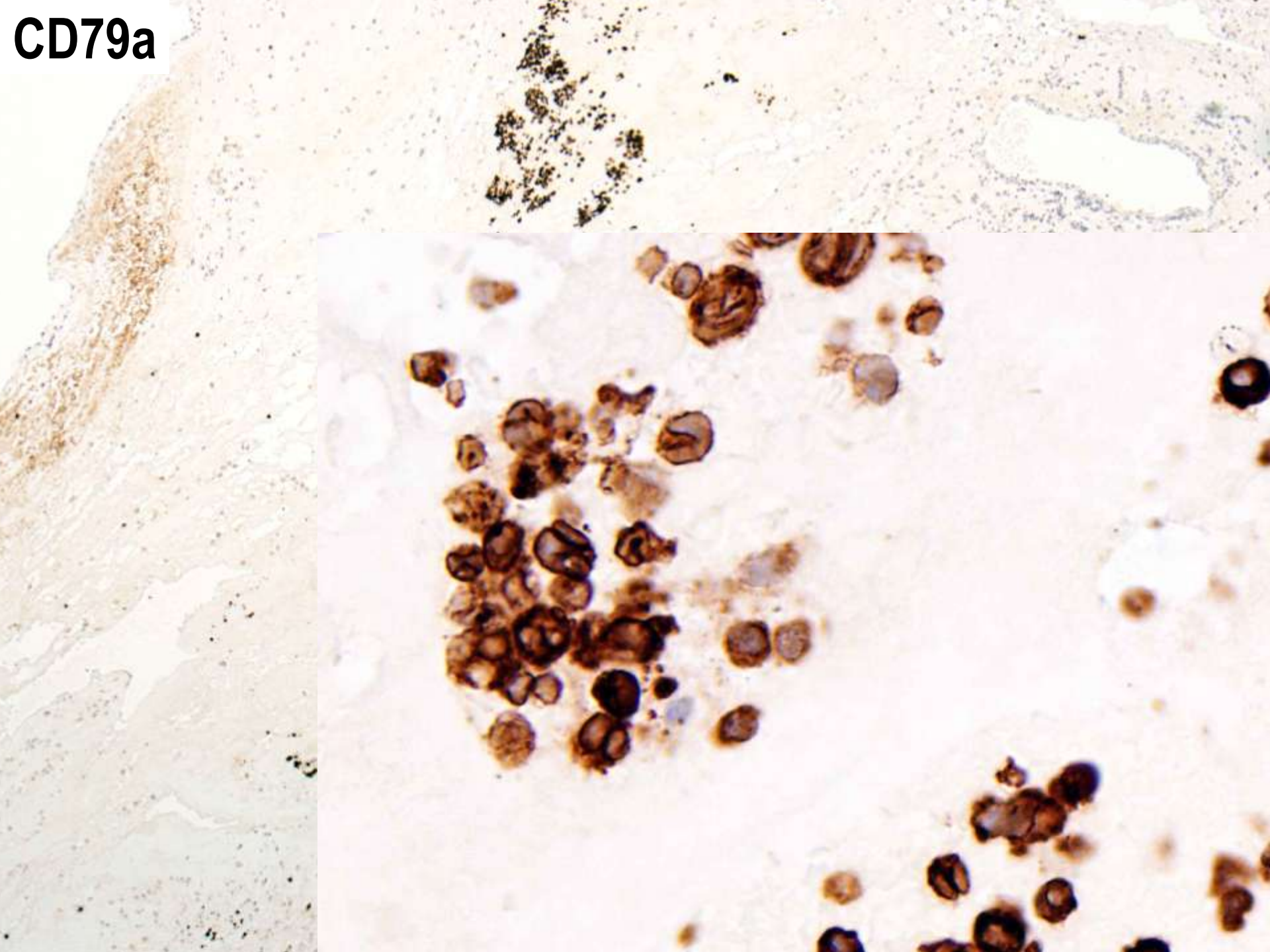




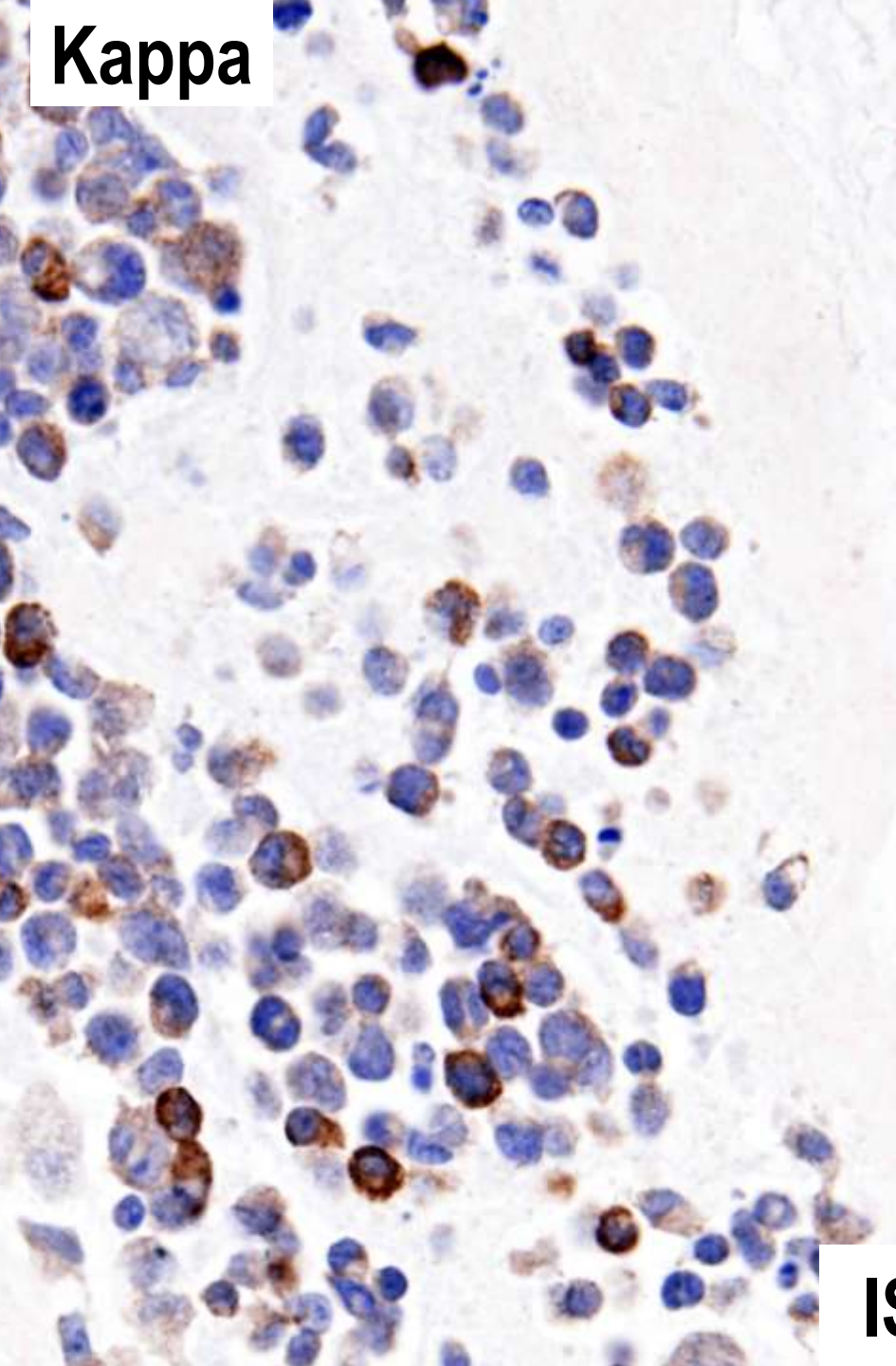


Reactive lymphoid cells?
Lymphoma cells?

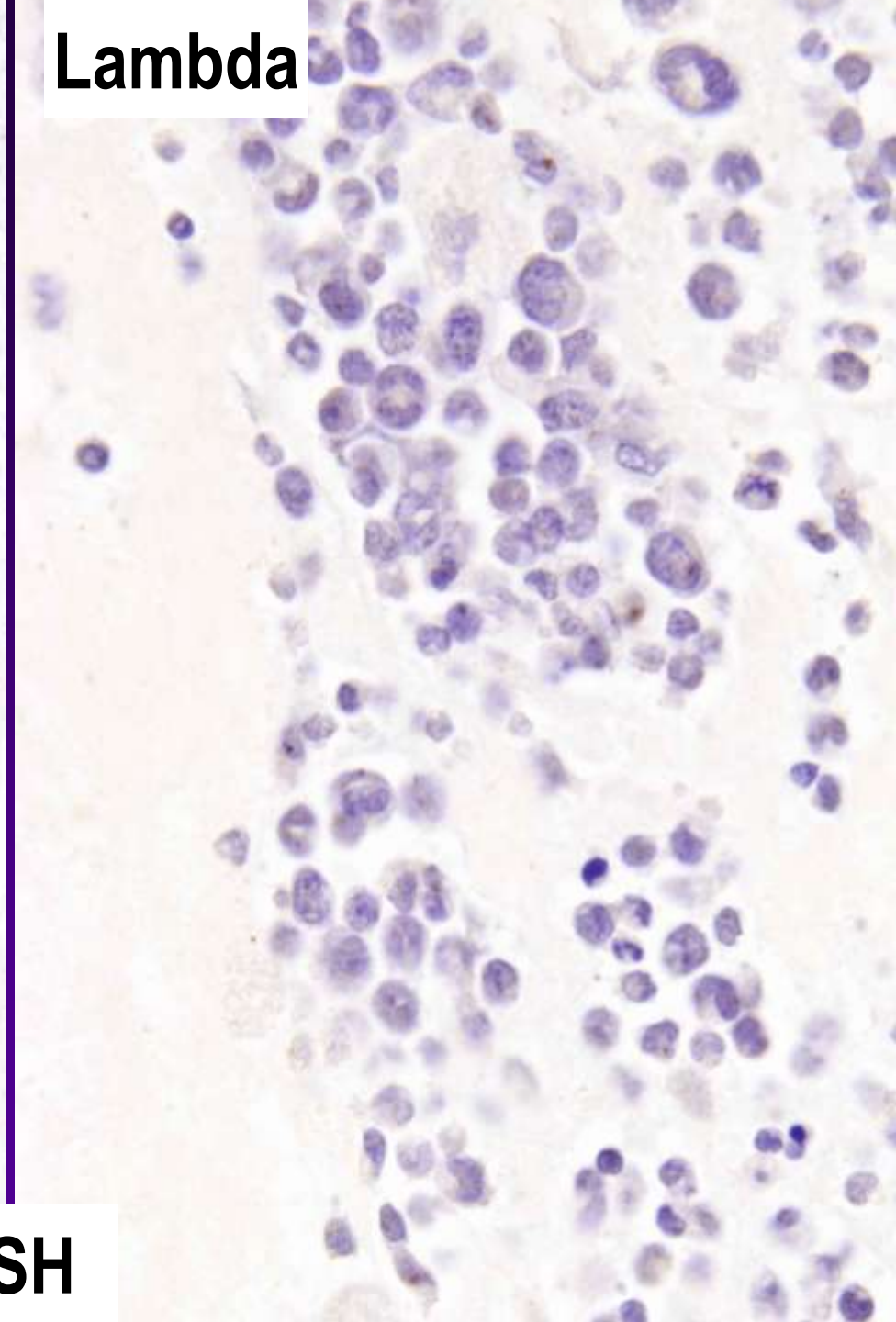
CD79a



Kappa

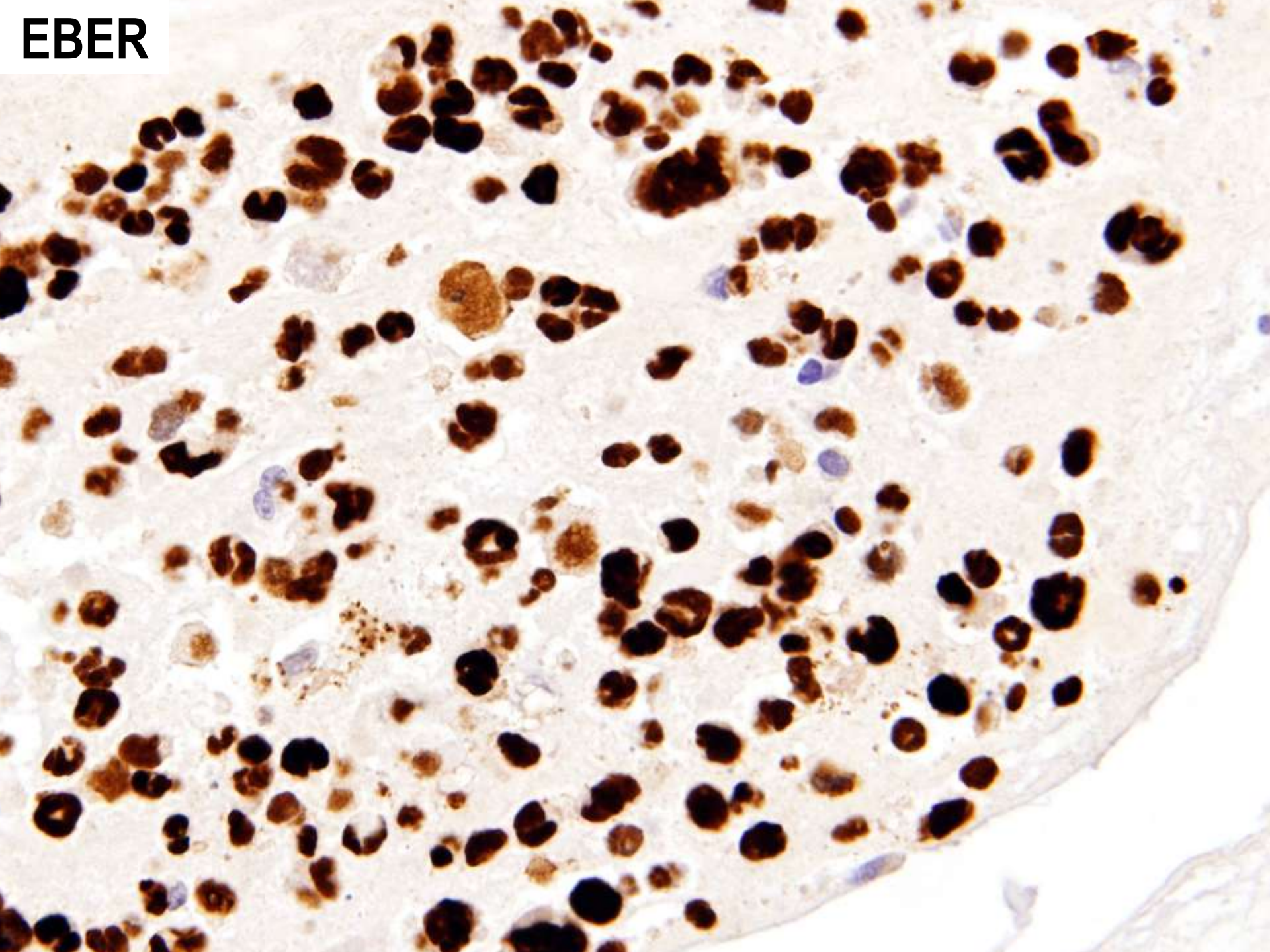


Lambda



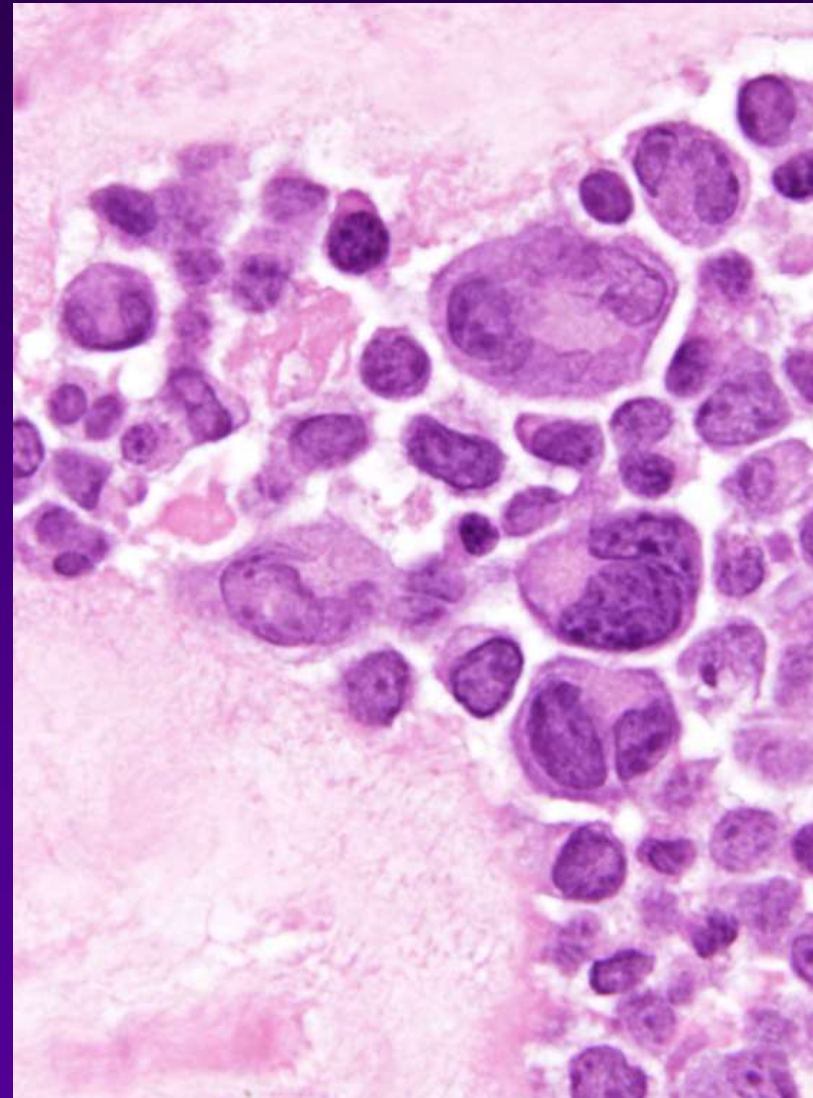
ISH

EBER



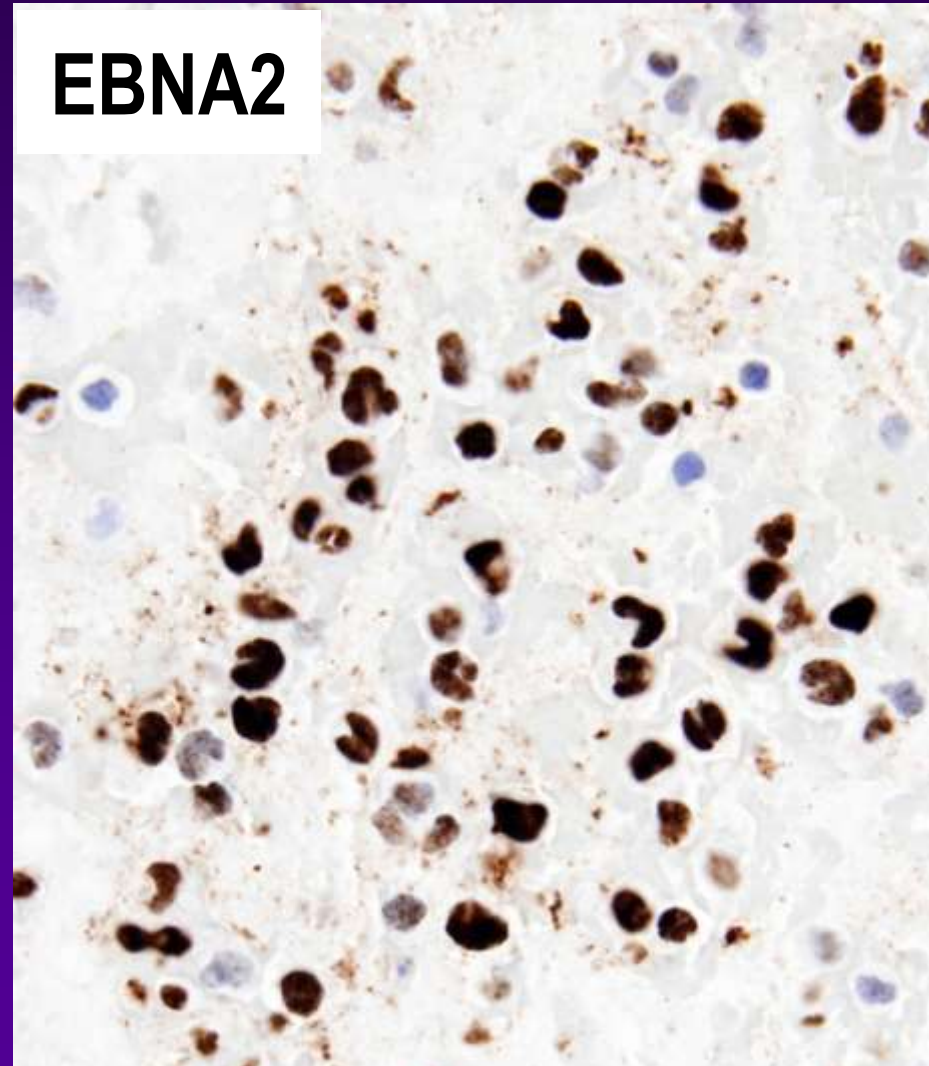
Features supporting diagnosis of lymphoma

- Definite cytologic atypia
- All cells are of B lineage
- Monotypic (ISH for Ig mRNA)
- Clonal *IGH* gene rearrangement
- EBV positive



How to classify this large B-cell lymphoma?

- EBNA2+
- Occurrence in a special enclosed environment (atrial myxoma) known to be able to produce systemic inflammatory symptoms



Diagnosis

Heart – Atrial myxoma, harboring
incidental diffuse large B-cell lymphoma
associated with chronic inflammation

Outcome of patient

- Patient gradually recovered with persistent right hemiplegia postoperatively
- Subsequent CT staging revealed no other tumors; marrow negative
- Four cycles of chemotherapy (R-CEOP) given
- Unfortunately died from complications of chemotherapy at 5 months

Overtreated?

Diffuse large B-cell lymphoma (DLBCL) associated with chronic inflammation

- Recognized as a distinct lymphoma entity in the 2008 WHO Classification
- Definition: DLBCL occurring in the context of long-standing chronic inflammation, and showing EBV association

Diffuse large B-cell lymphoma associated with chronic inflammation

- Most cases involve enclosed spaces. Reported scenarios:
 - Pyothorax-associated lymphoma (the prototype)
 - Chronic osteomyelitis (medullary cavity of bone)
 - Metallic implant (joint space, space between prosthesis and bone)
 - Surgical mesh (space between soft tissue and mesh)
 - Chronic skin ulcer

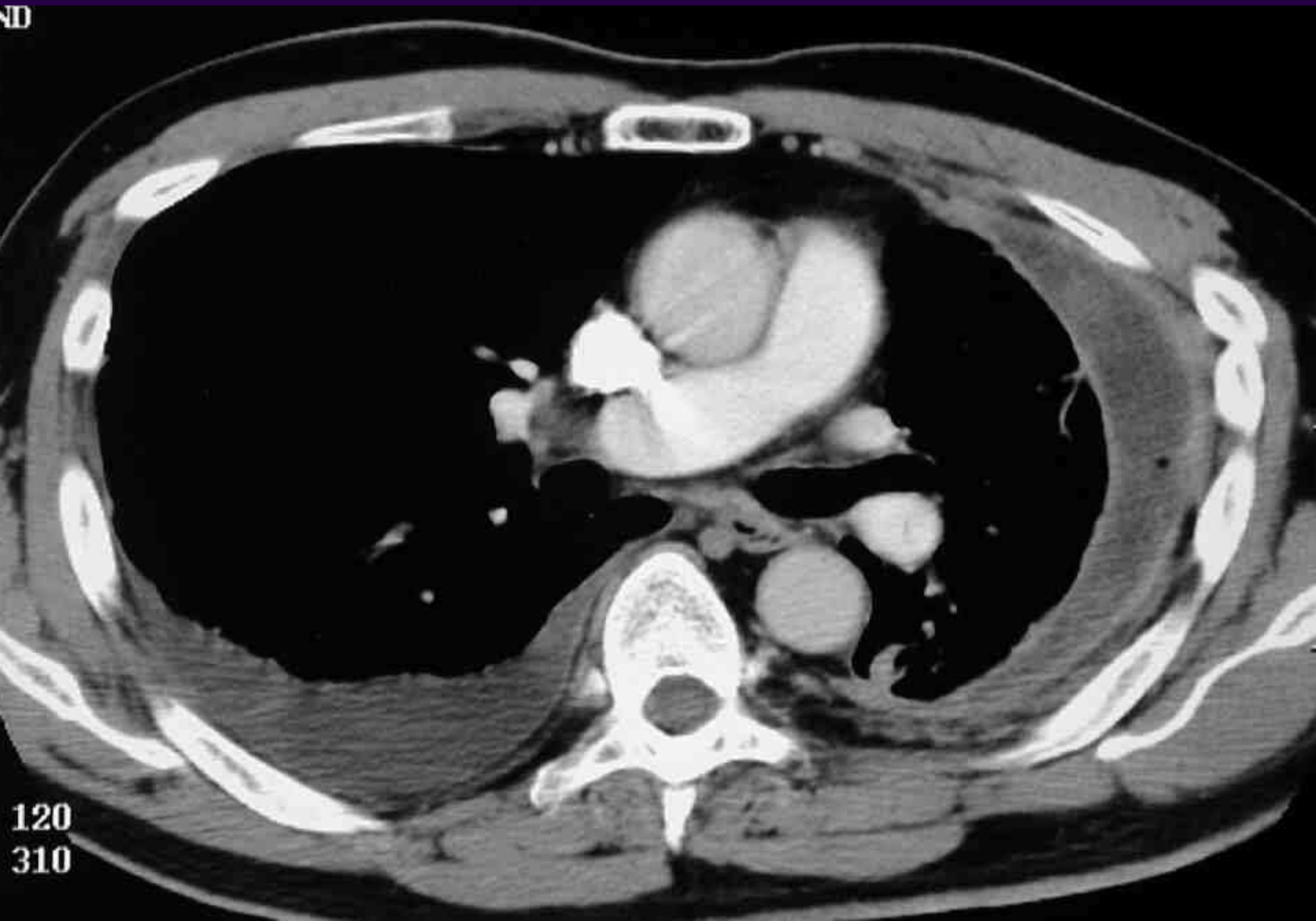
Diffuse large B-cell lymphoma associated with chronic inflammation: Characteristic features

- Long latency period between onset of inflammation/ irritation and development of lymphoma (usually > 10 years)
- CD20+ diffuse large B-cell lymphoma
- EBV positive; HHV8 negative

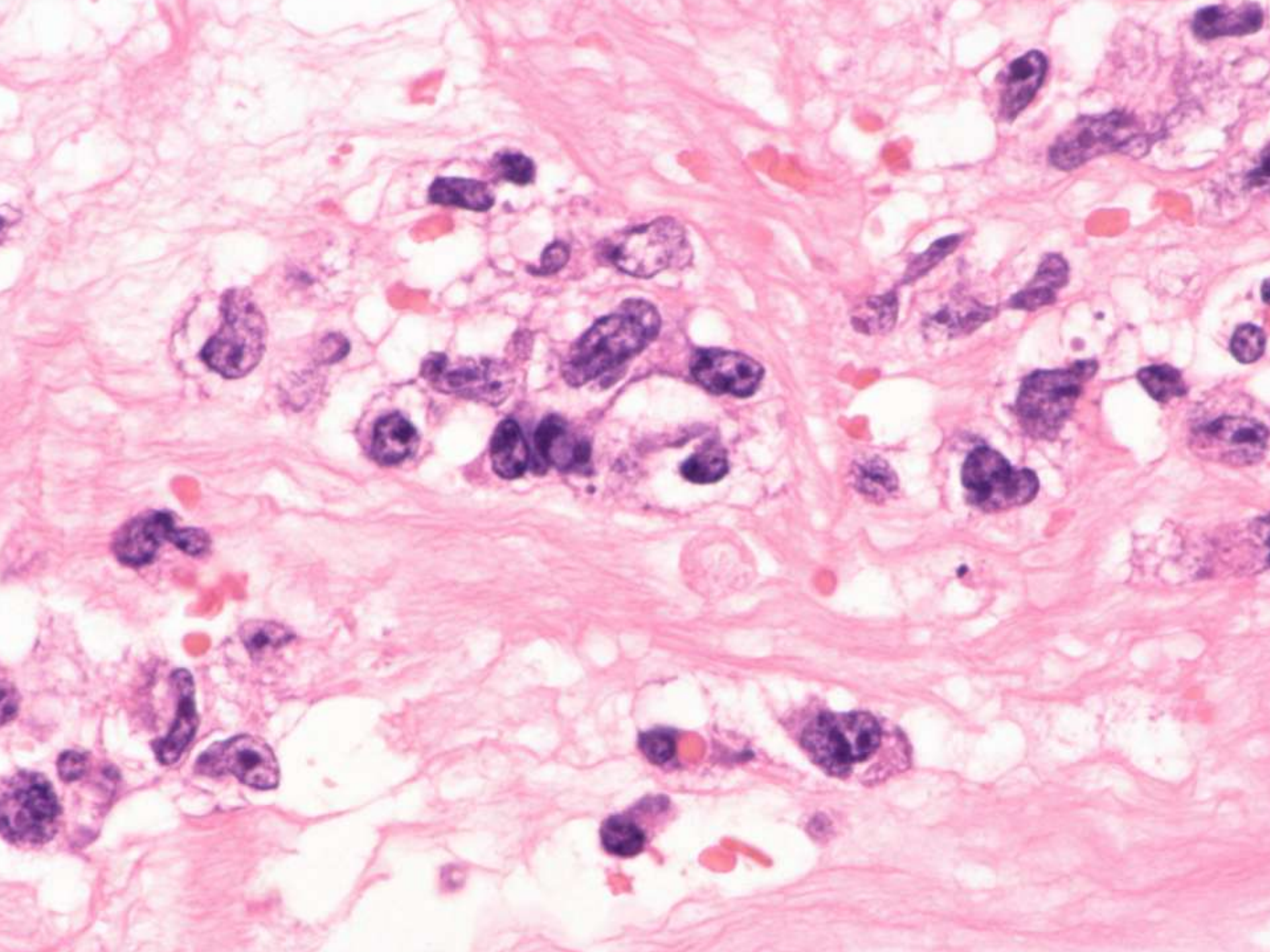
Pyothorax-associated lymphoma

- Rare, reported mostly in Japanese; but also recognized in western countries
- Complicates longstanding pyothorax resulting from artificial pneumothorax for treatment of pulmonary TB or TB pleuritis
- Lymphoma develops 20-50 years after onset of TB

ND



120
310



DLBCL associated with chronic inflammation: Pathogenesis

- Presence of 'local immunodeficiency' in the enclosed space (supporting evidence: EBNA2 expression)
- Cytokines derived from chronic inflammatory cells can build up to high levels in enclosed spaces, e.g. IL-10 (immunosuppressive) → permitting emergence of EBV+ B-cell clone

EBV latency in tumors

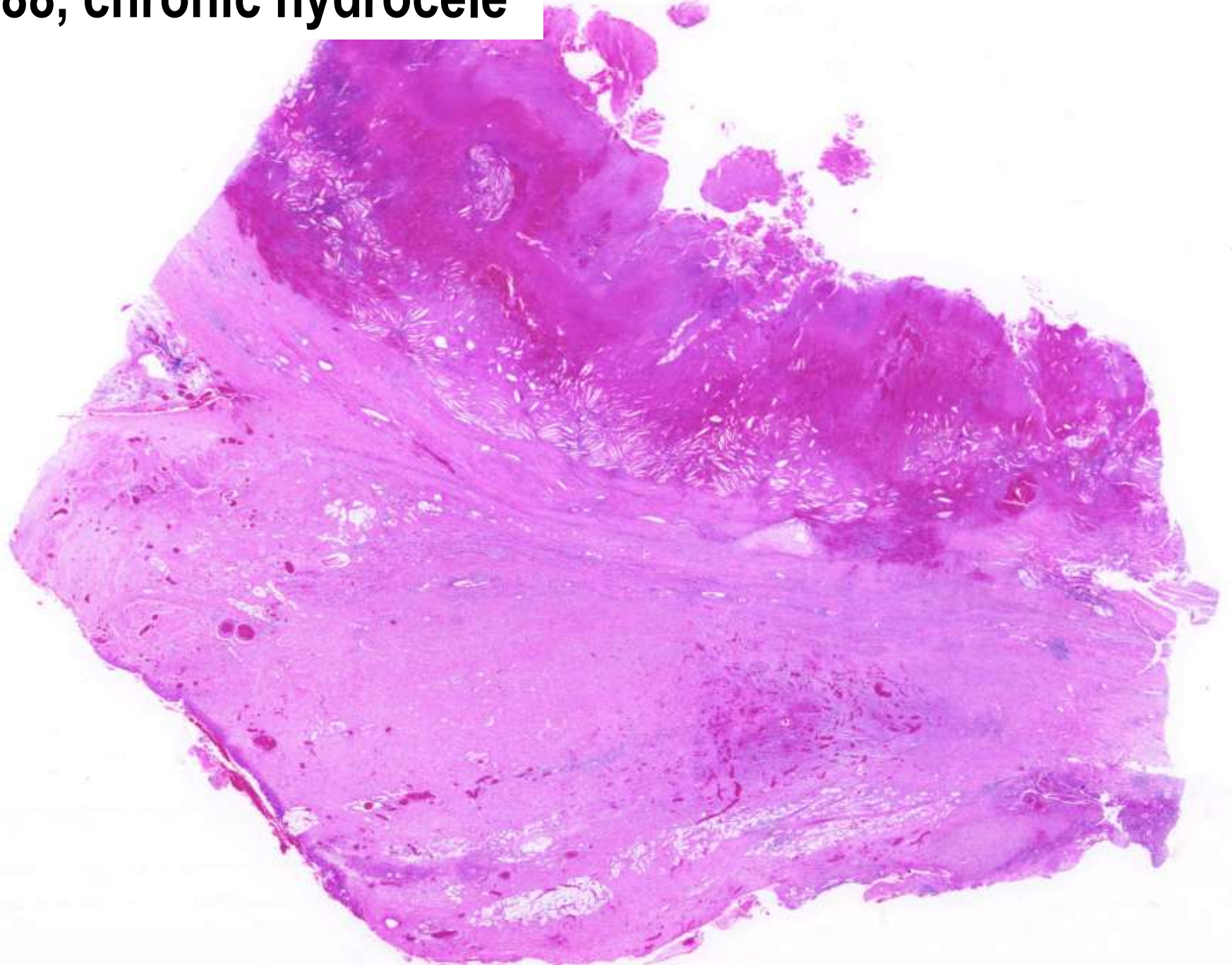
	Type I	Type II	Type III
Expressed genes	EBNA1	EBNA1 LMP1	EBNA1 LMP1 EBNA2 (highly immunogenic)
Examples	Burkitt lymphoma	Hodgkin lymphoma T or NK lymphoma Nasopharyngeal CA	PTLD

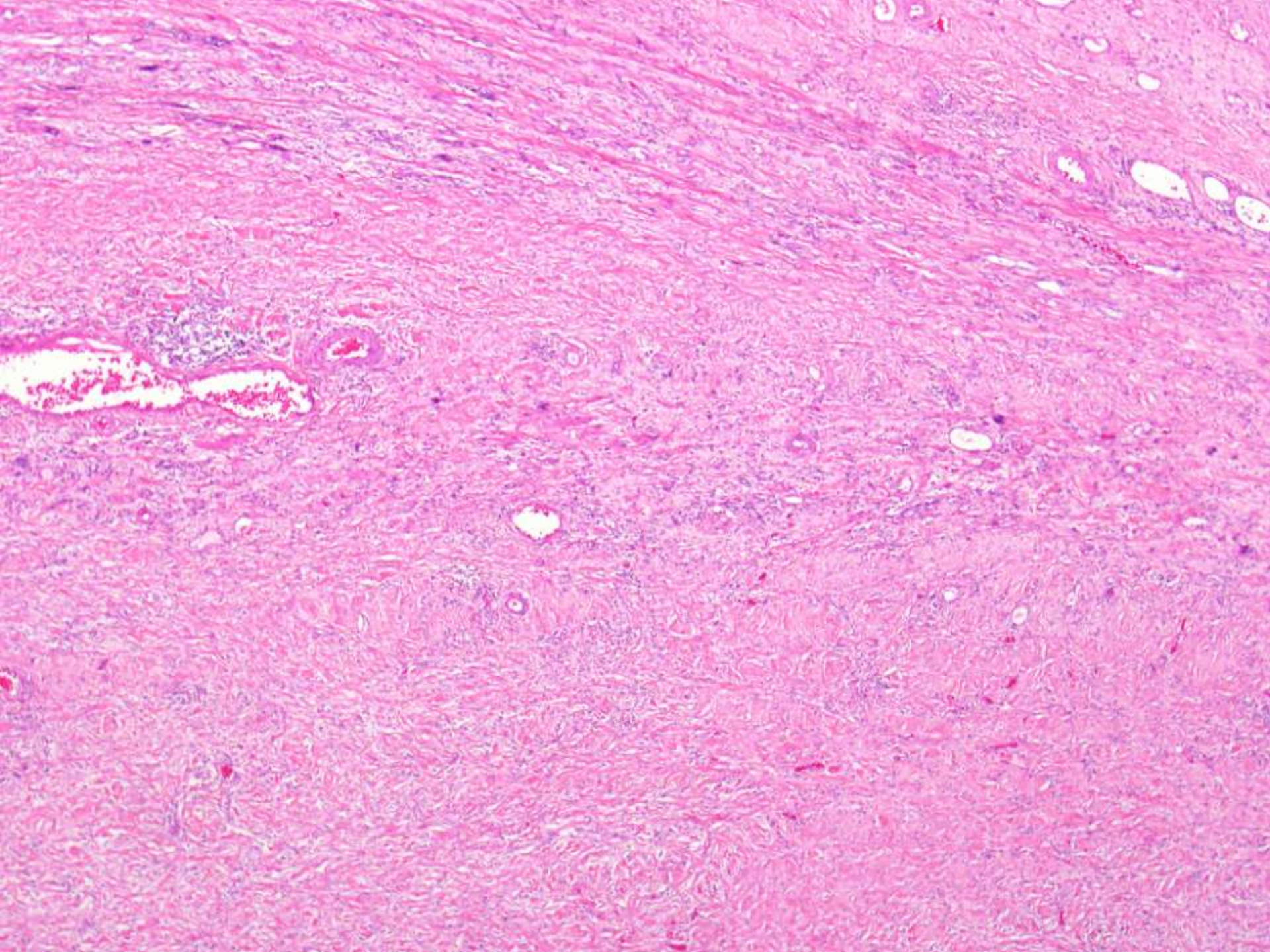
DLBCL associated with chronic inflammation: new scenarios

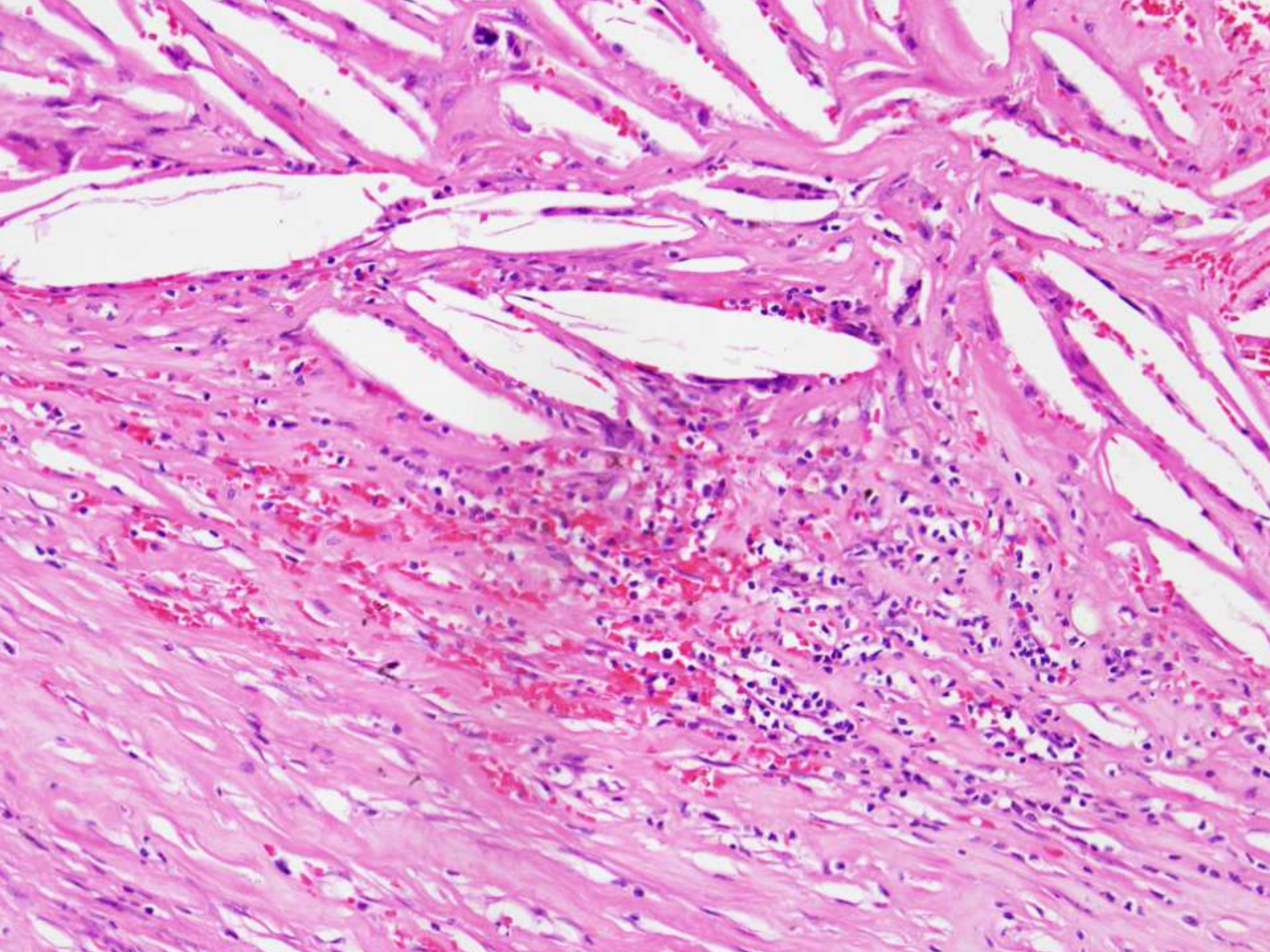
Incidental findings

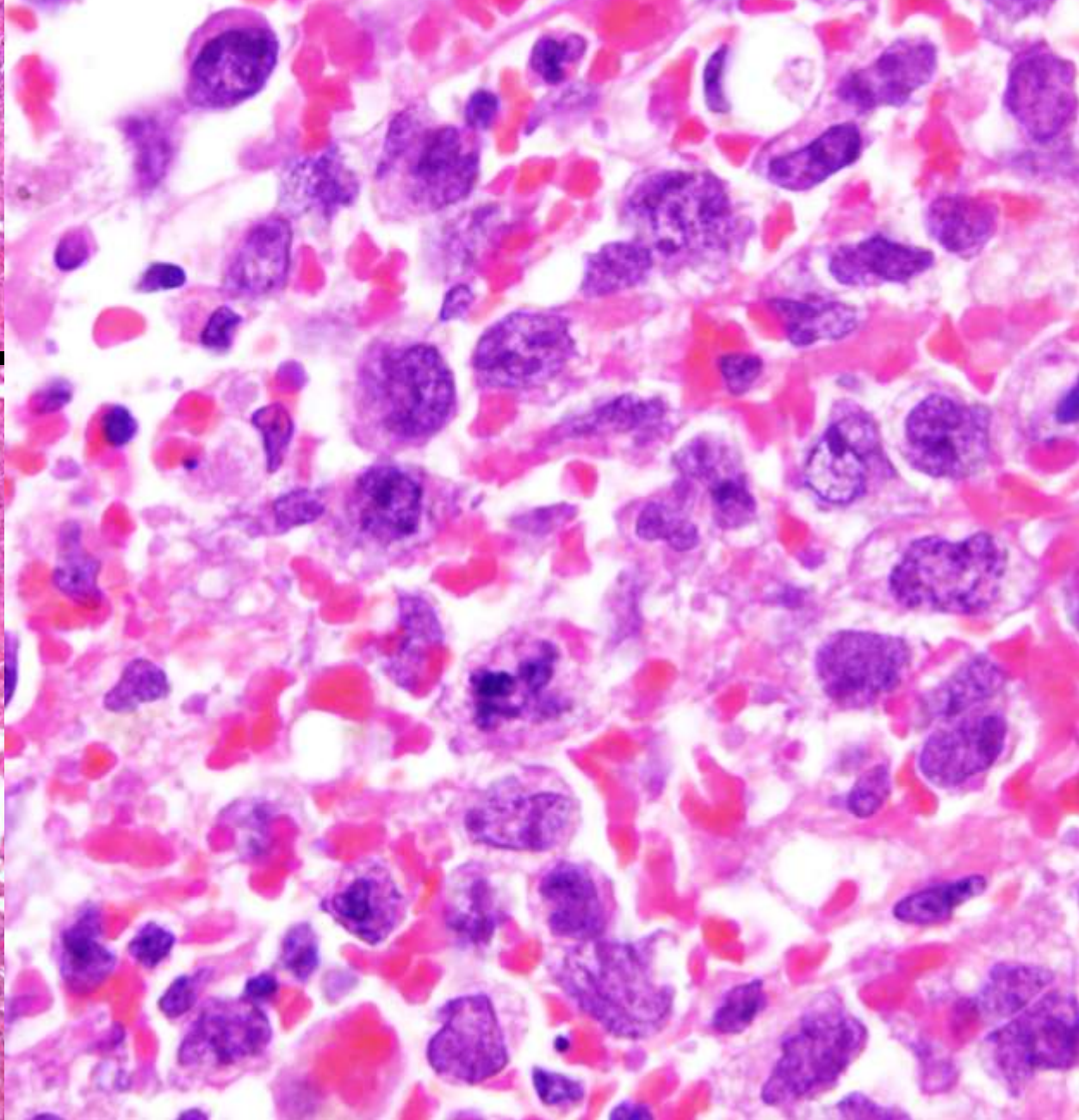
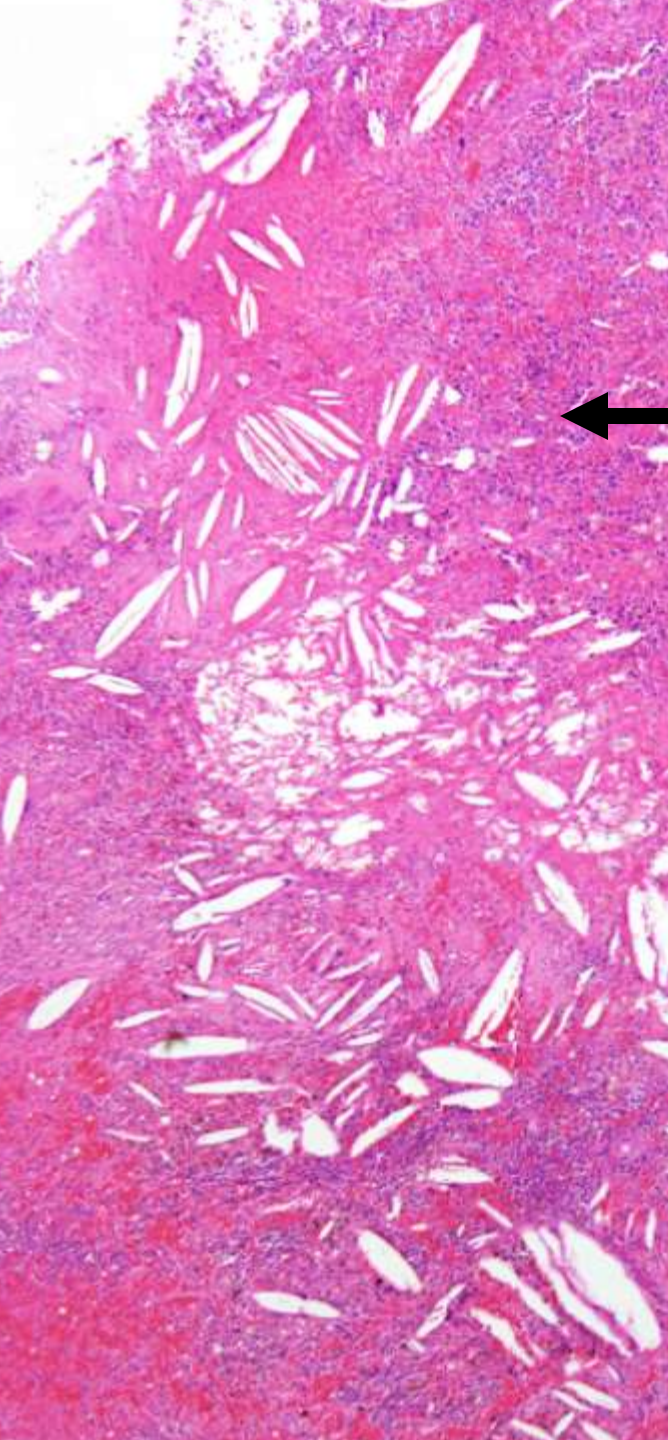
- Within atrial myxoma
- Splenic false cyst (pseudocyst)
- Long-standing hydrocele

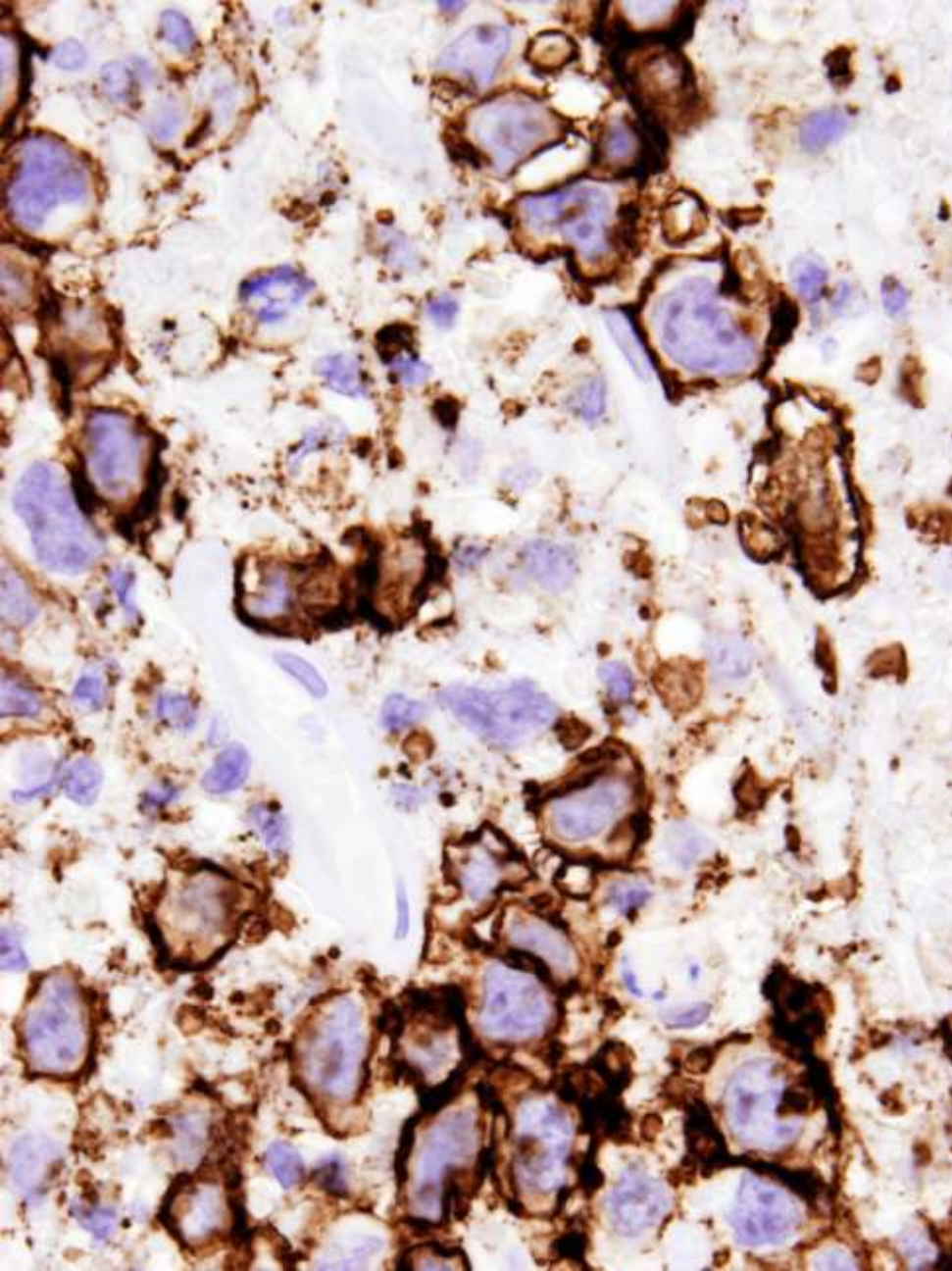
M/88, chronic hydrocele



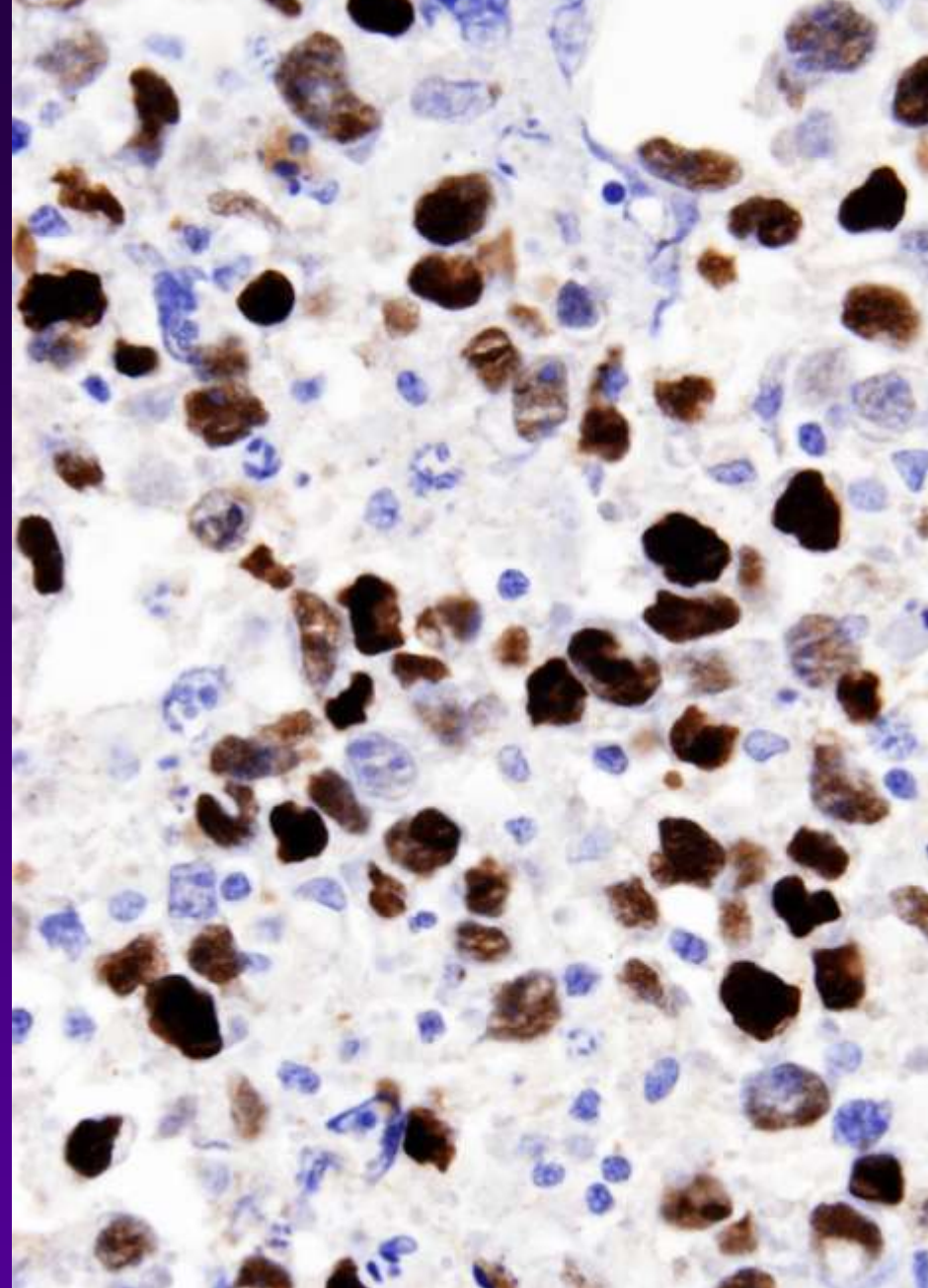








CD20



EBER

DLBCL of chronic inflammation: new scenarios

Possible scenarios that may be encountered in future:

- In pancreatic pseudocyst
- In long-standing ovarian cyst
- In long-standing thyroid degenerate cyst

DLBCL of chronic inflammation: new scenarios

- How should these incidental cases of DLBCL be treated?
- Would surgery be adequate? The surgery might have removed the lymphoma already together with the preexisting lesion