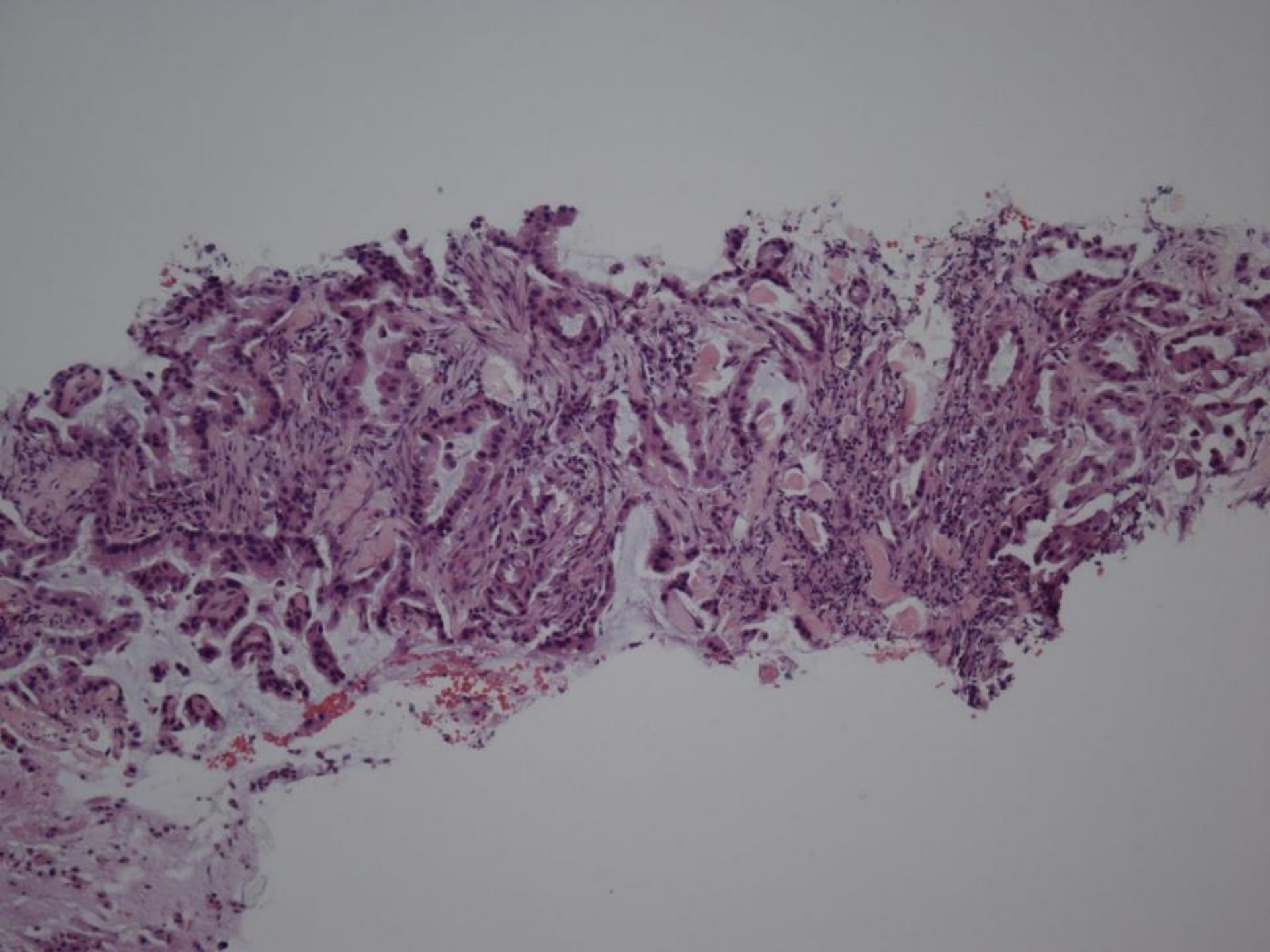
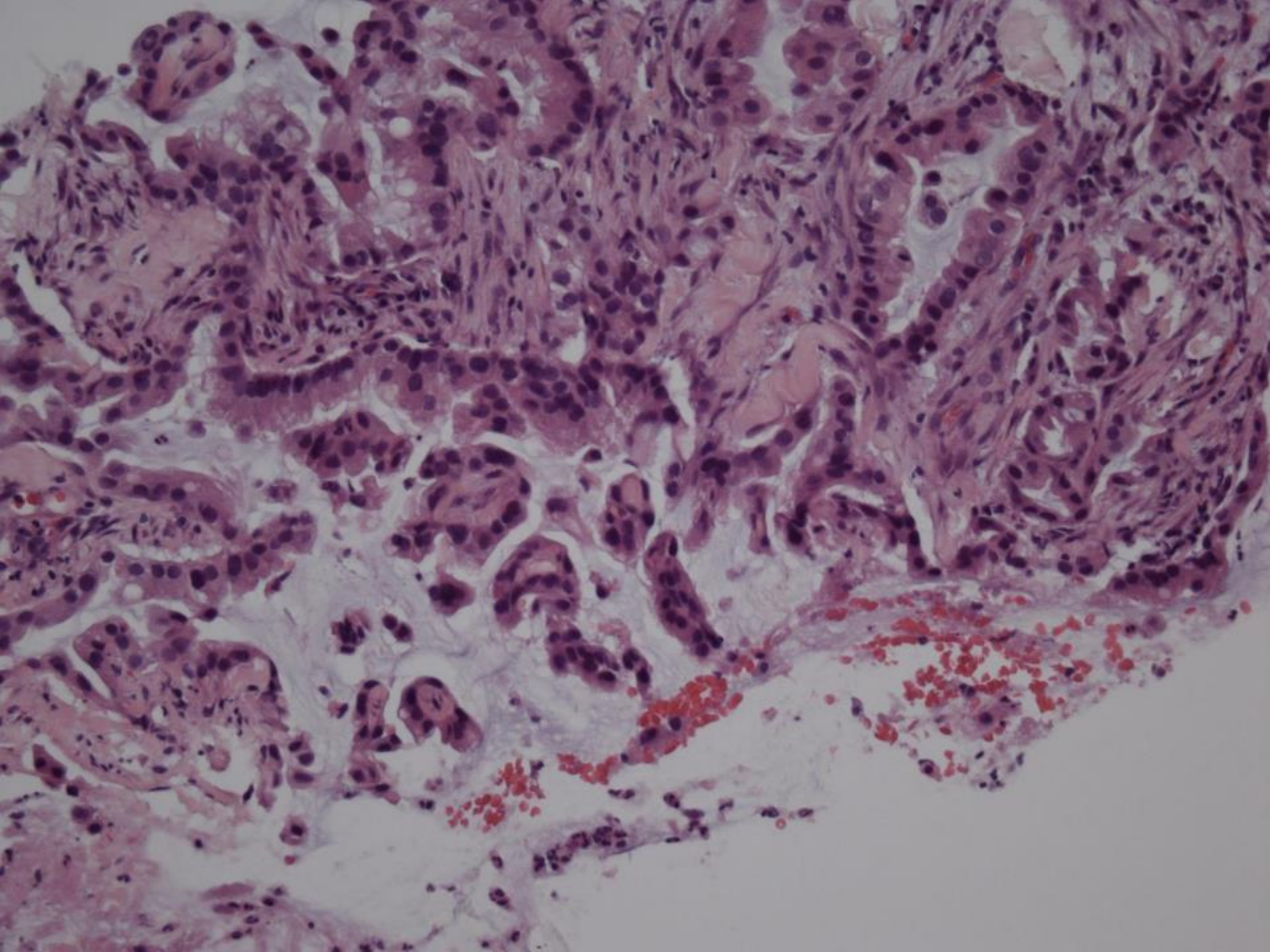
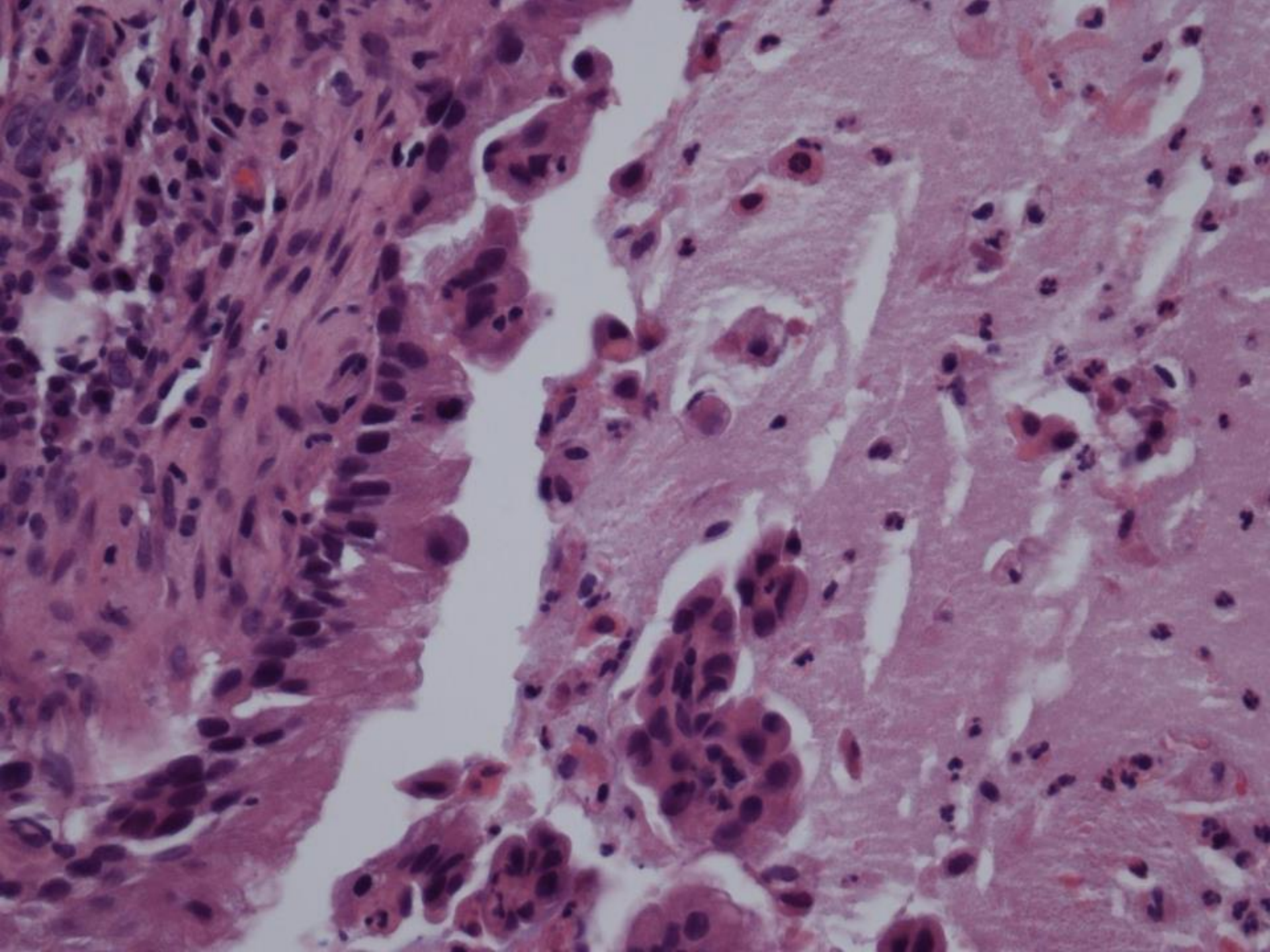
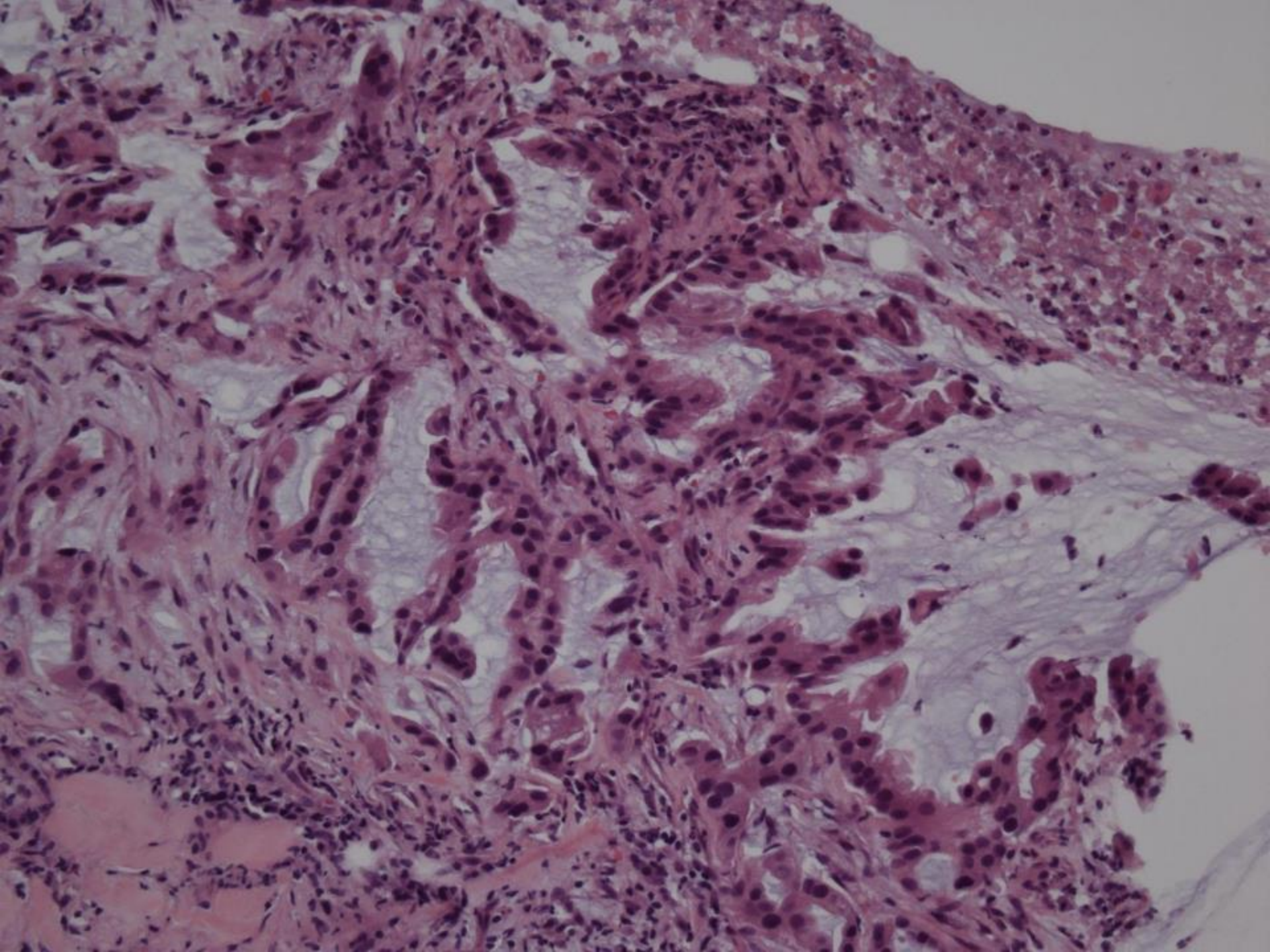
Case 4 History

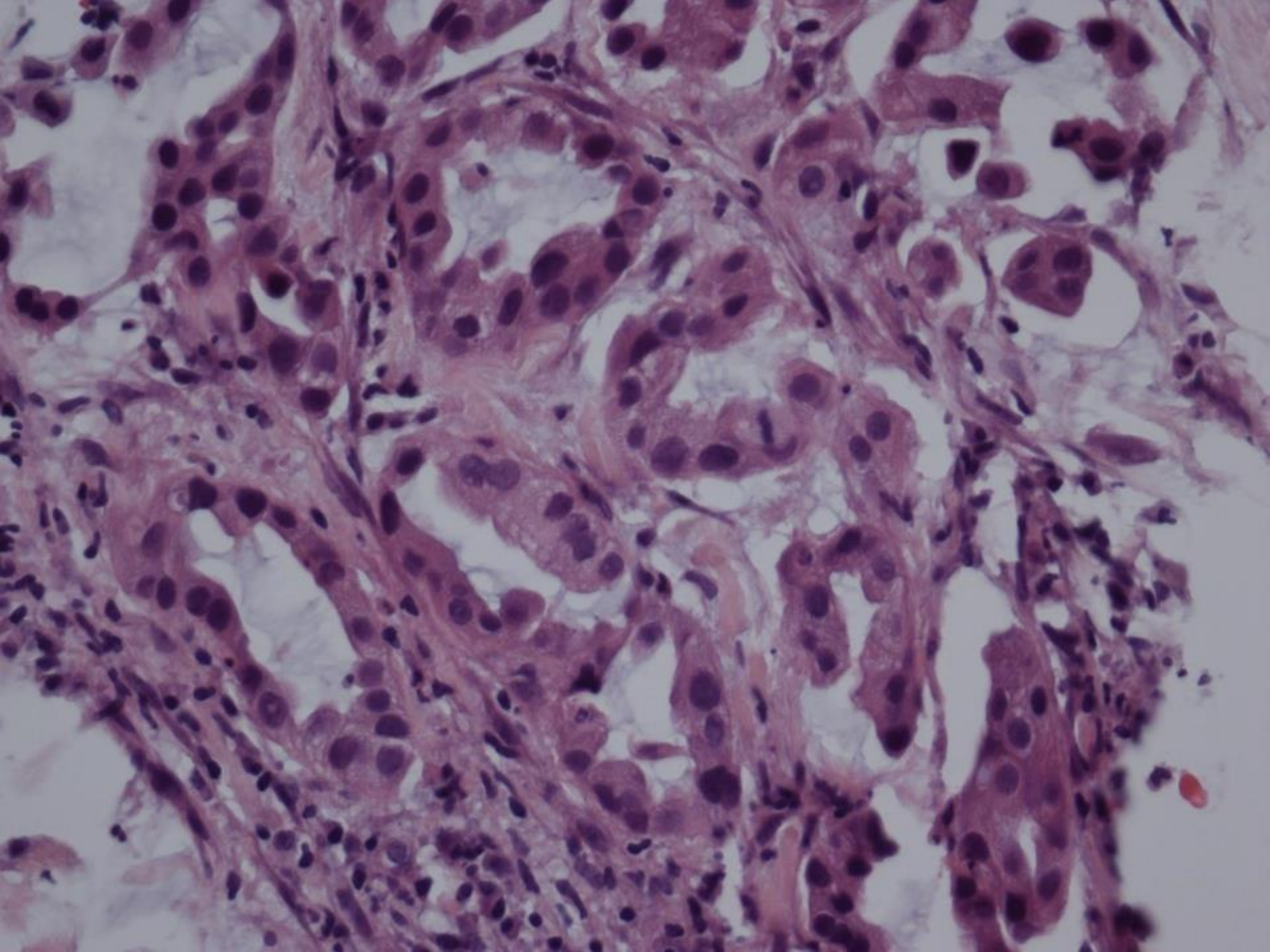
- 64 year old woman
- Breast mass
- Core biopsy

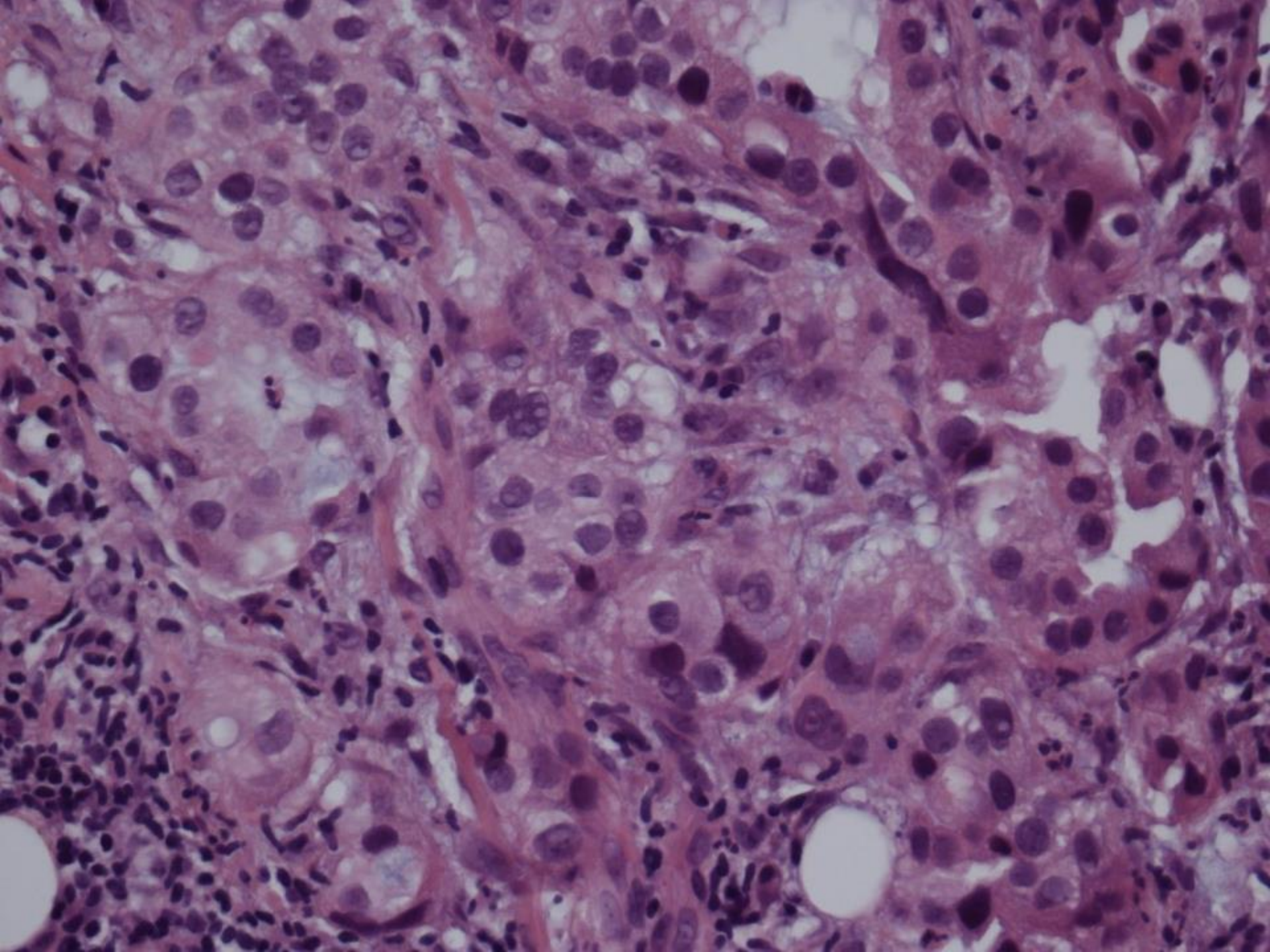










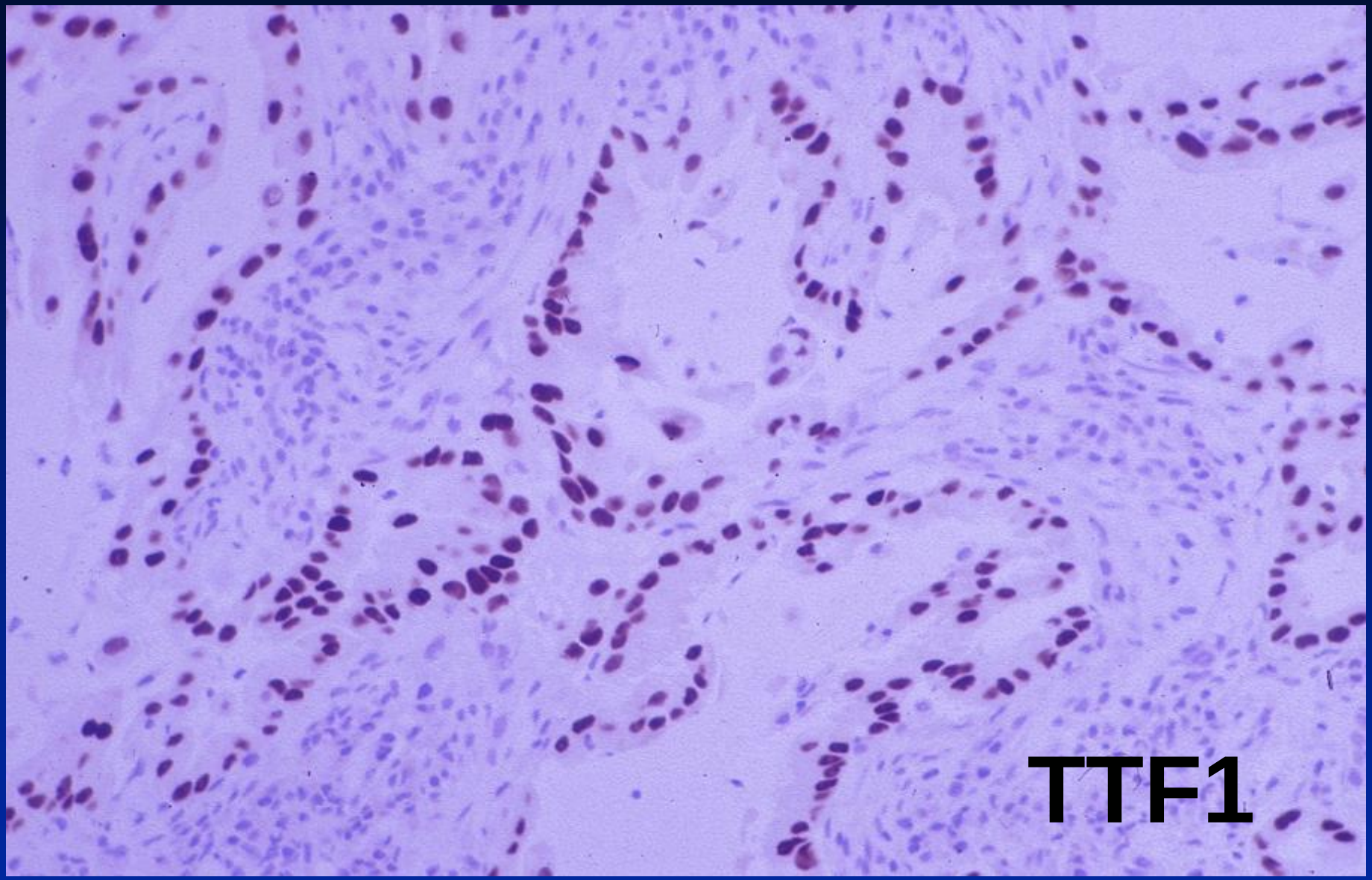


Histological features

- Invasive adenocarcinoma
- Irregularly shaped glands
- Columnar and cuboidal cells
- Mucinous
- Not typical of mammary origin

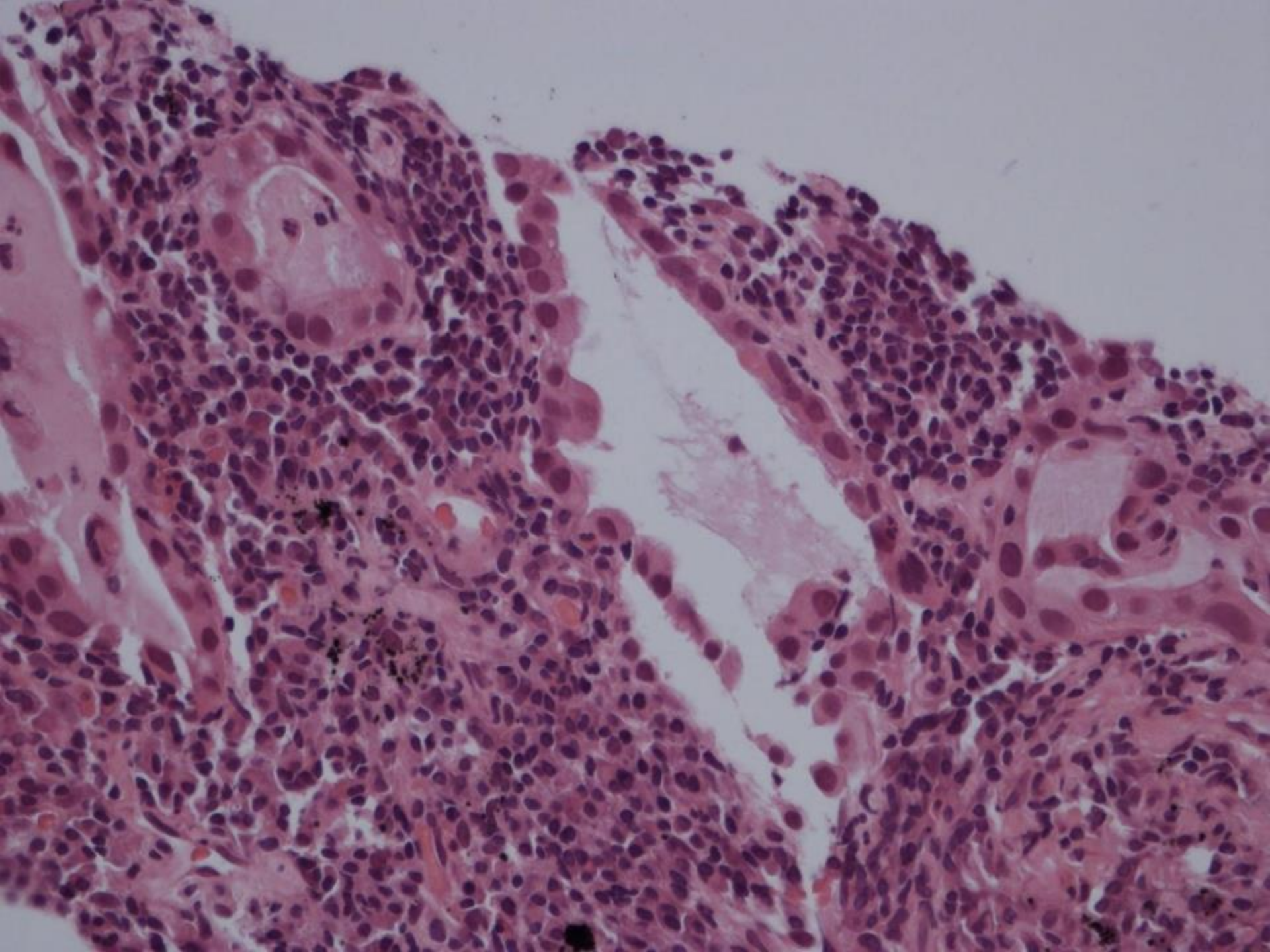
Responses

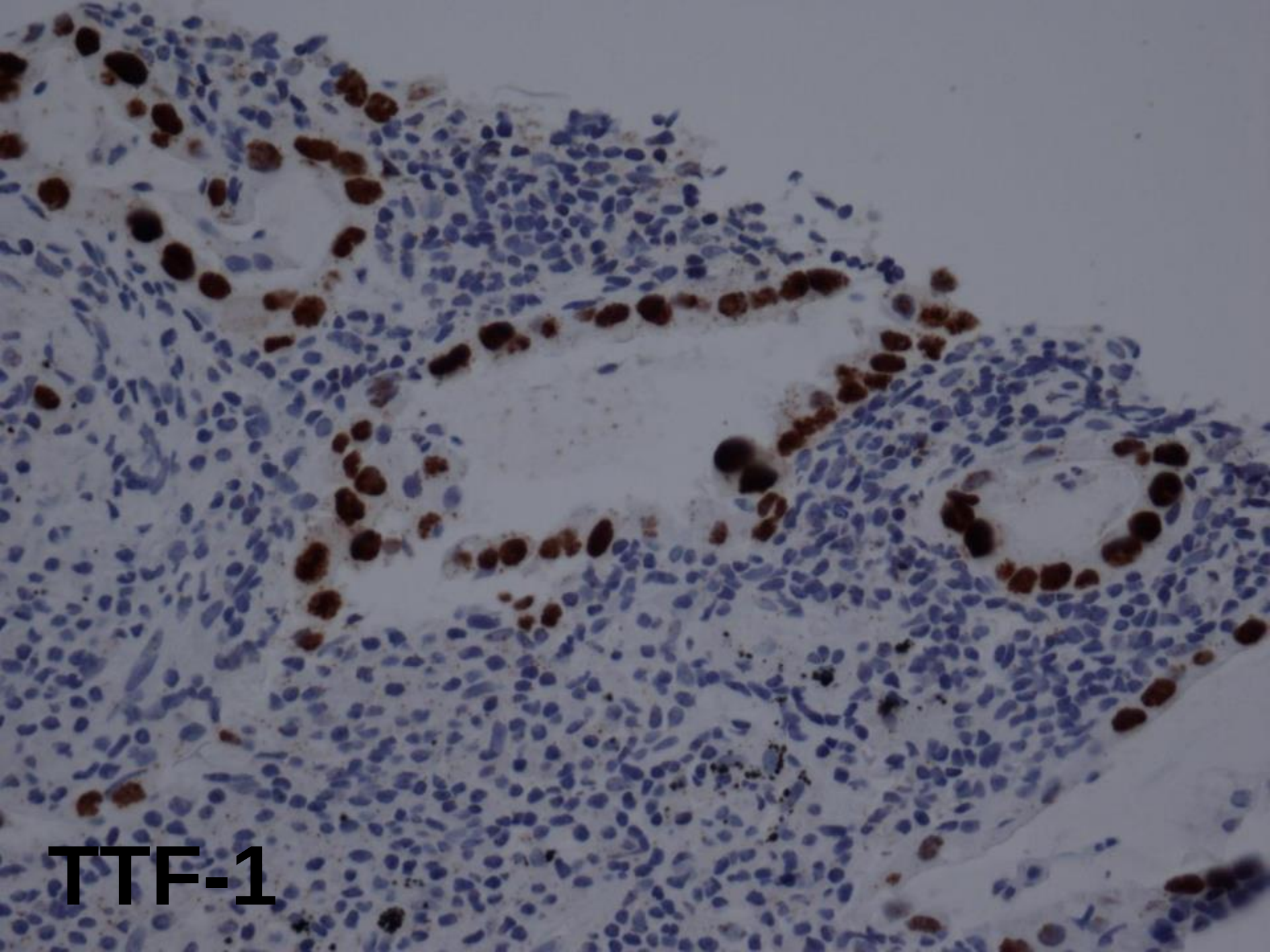
Mucinous carcinoma	13
Mucinous + NST	4
Primary mucinous carcinoma	1
Secretory carcinoma	2
Papillary DCIS ?intracystic	1
Mucinous carcinoma primary v secondary (GI, ovarian or pancreas)	14
Metastatic mucinous carcinoma	1

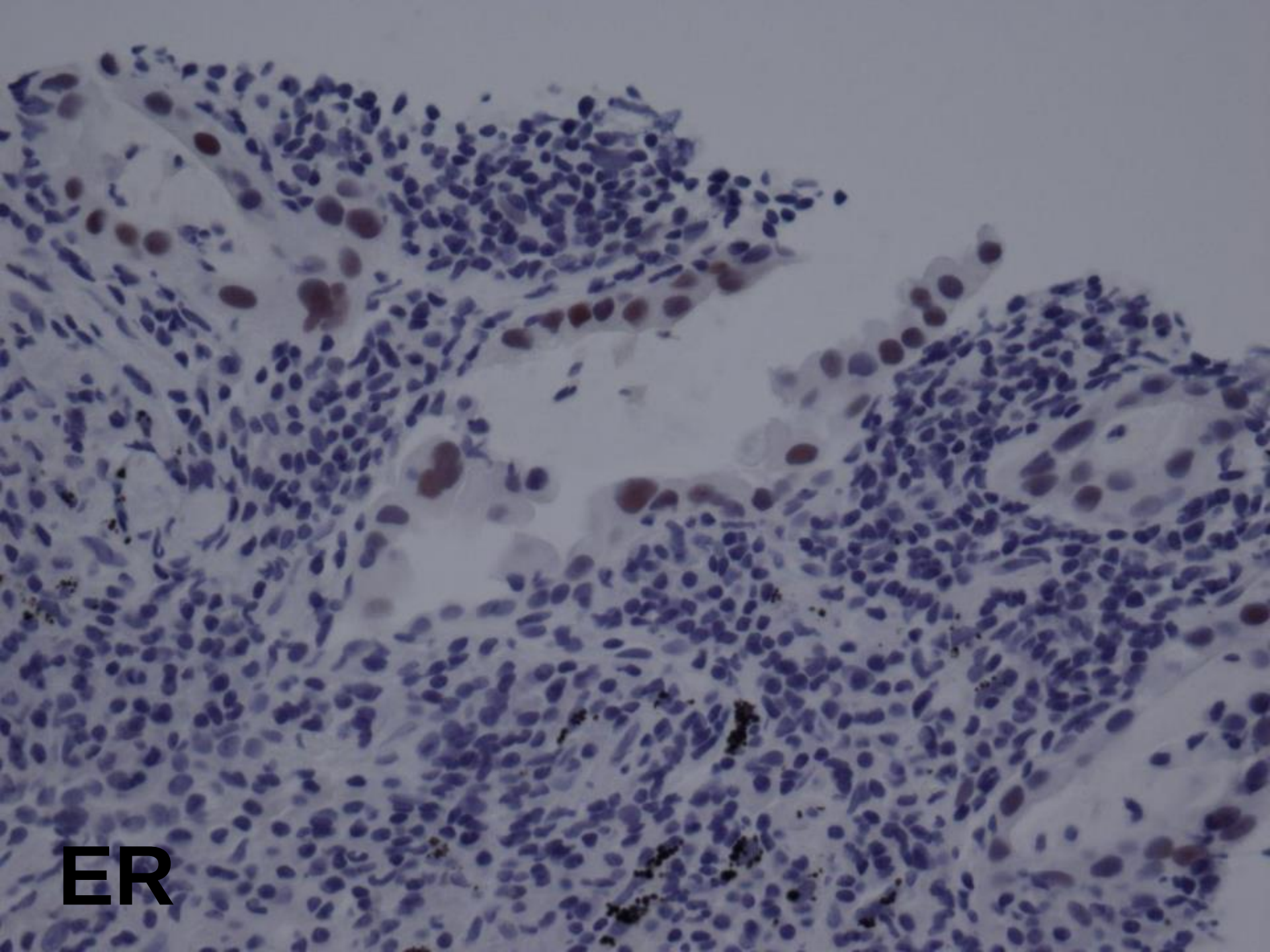

TTF1

Previous history

- 4 months before
- Lung mass




TTF-1


ER

Pulmonary adenocarcinoma

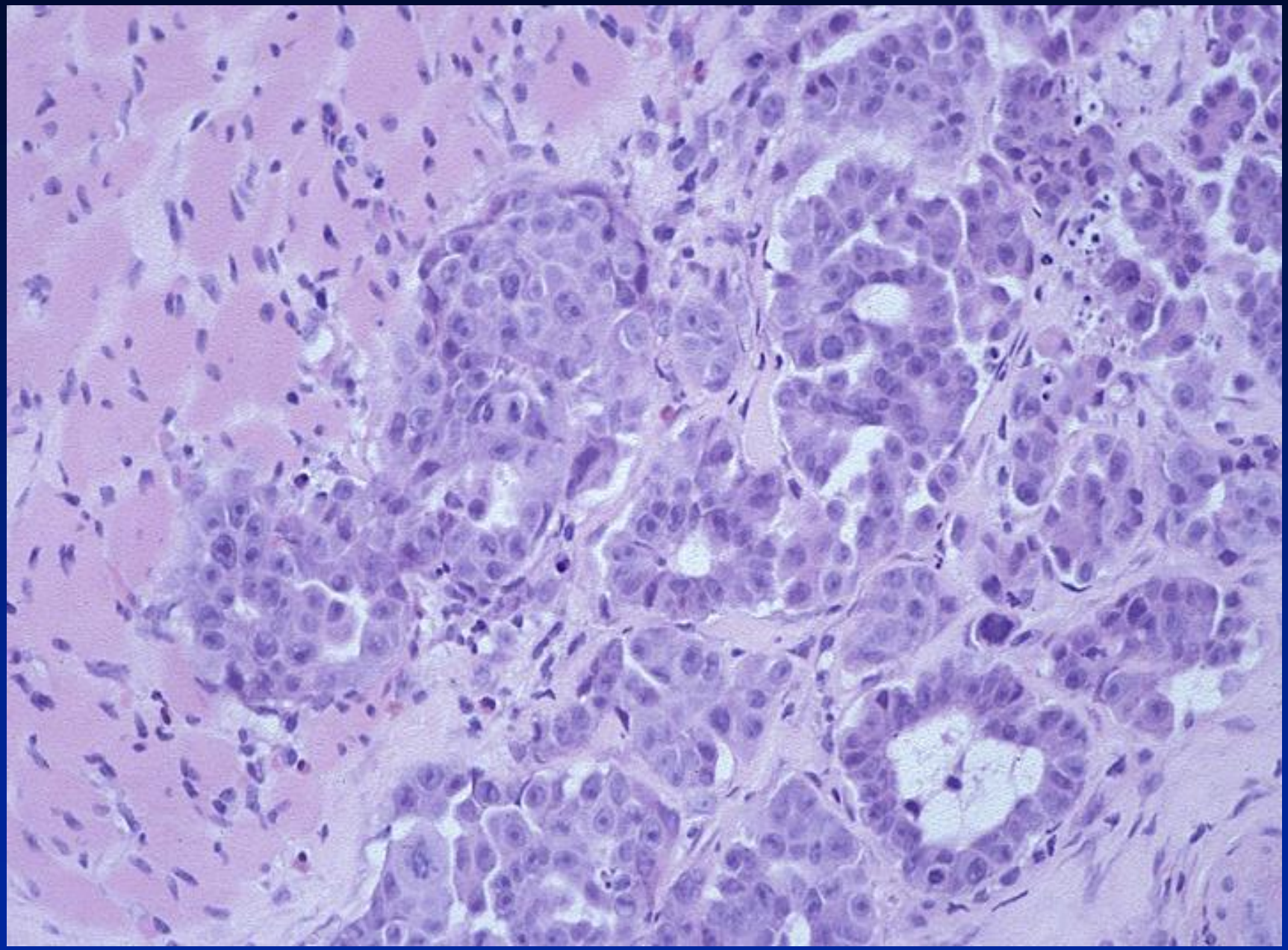
- TTF-1 positive
- CK7 positive
- CK20 weakly positive
- ER weakly positive

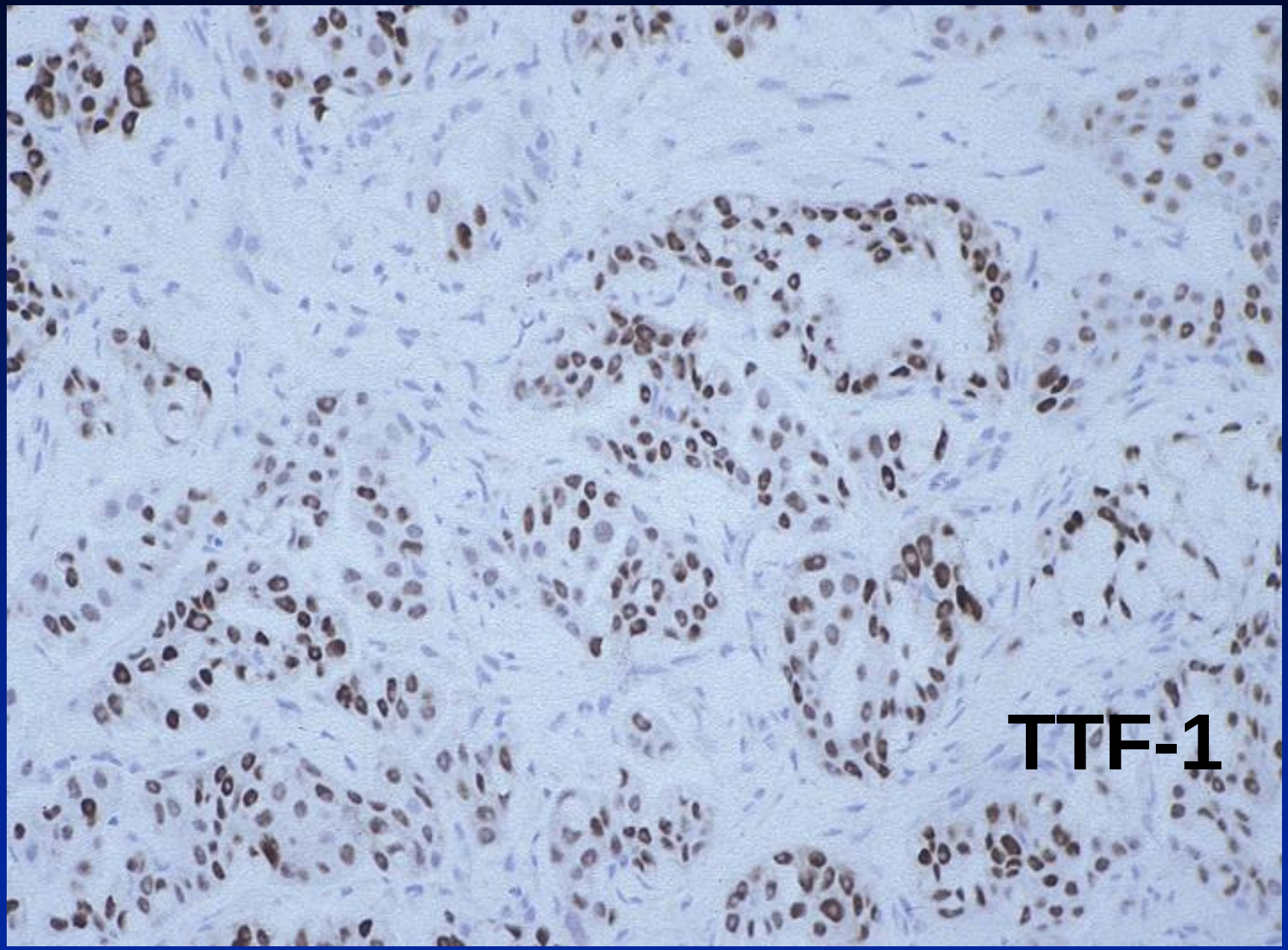
Diagnosis

Metastatic pulmonary adenocarcinoma

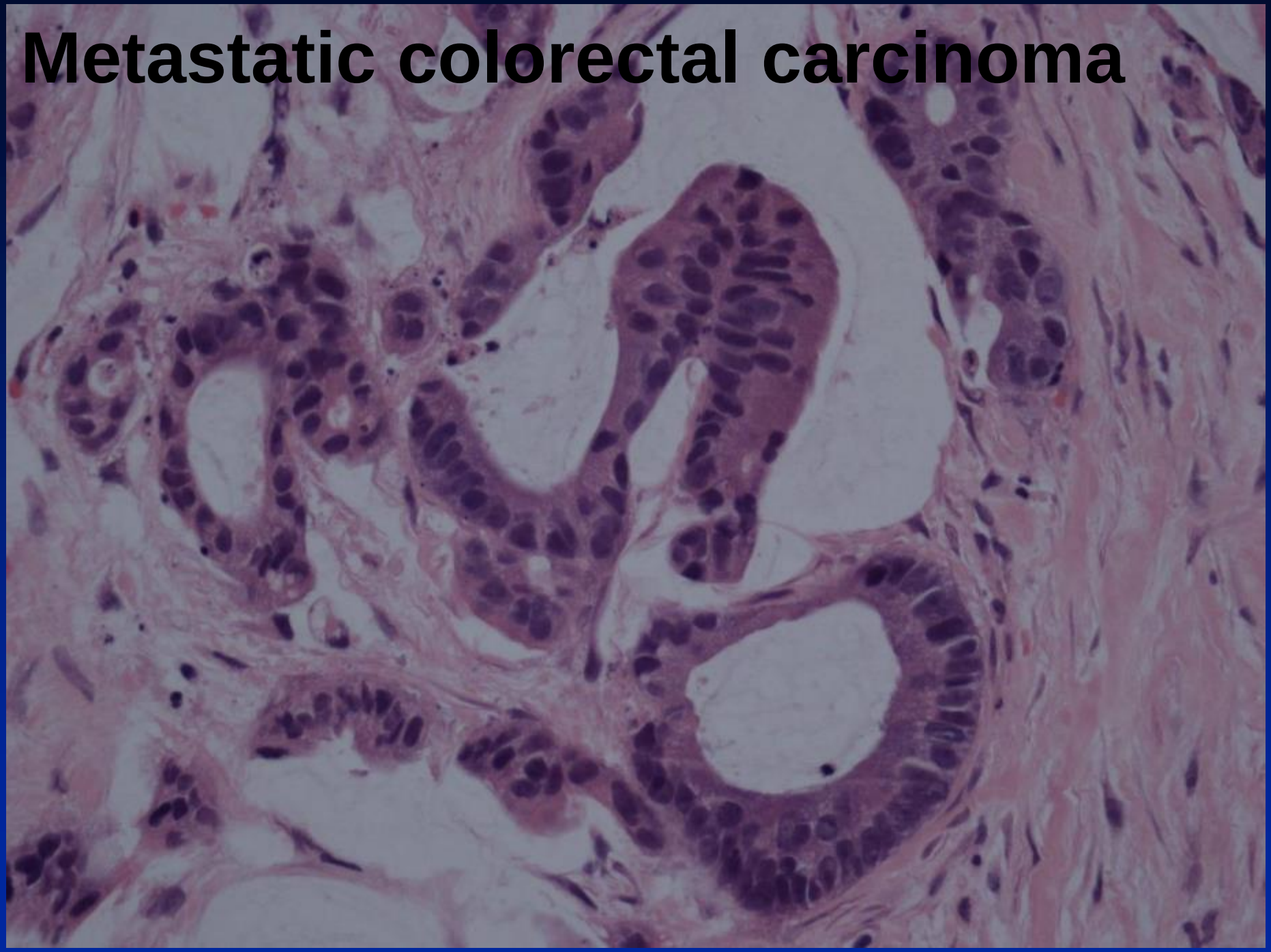
Thyroid transcription factor-1

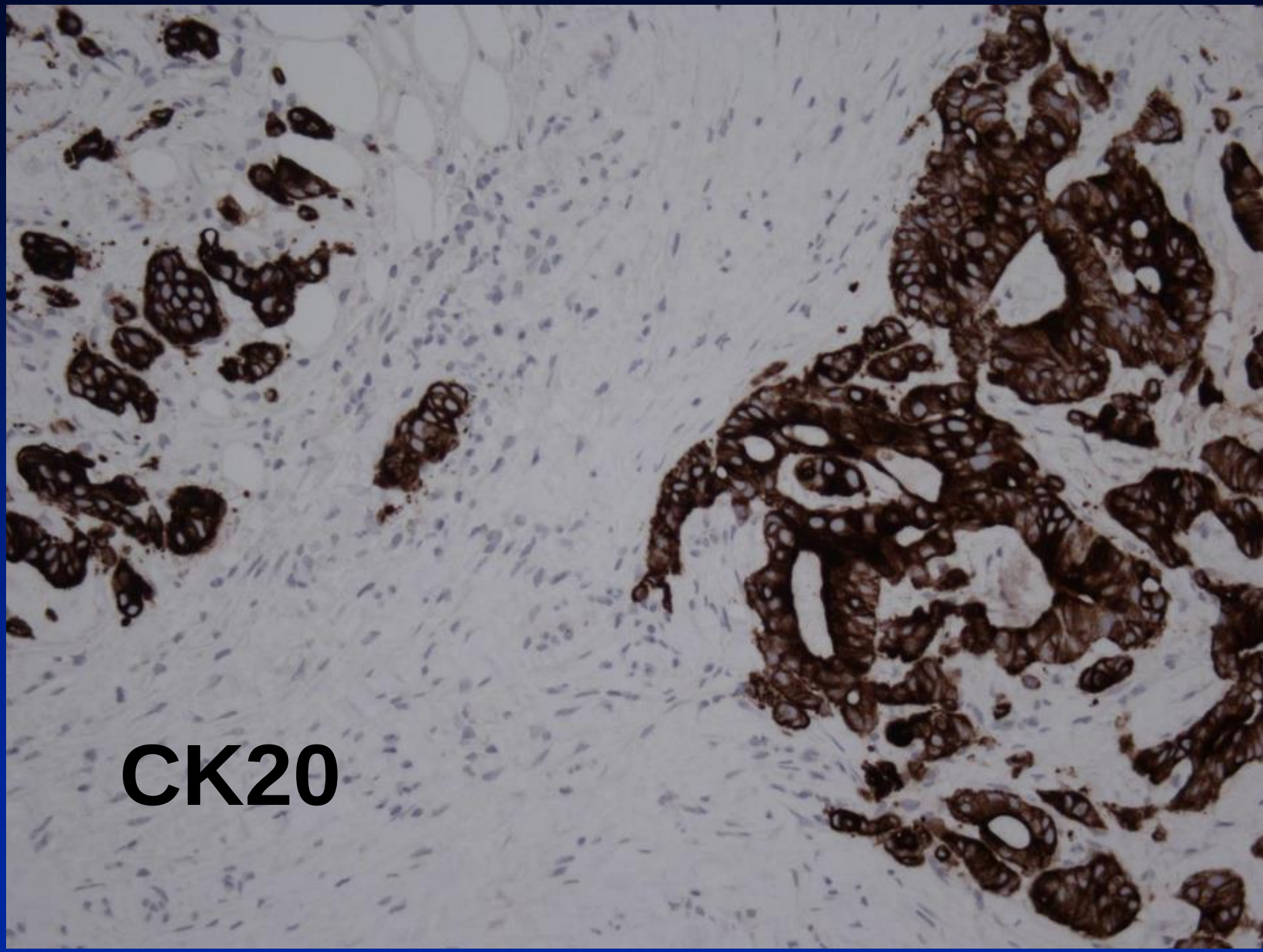
Lung	Adenocarcinoma	75%
	Squamous	0 - 40%
	Large cell	0 - 25%
	Small cell	90%
Extrapulmonary small cell		up to 80%
Thyroid (follicular & papillary)		majority
Breast		rare
Other carcinomas		rare




TTF-1

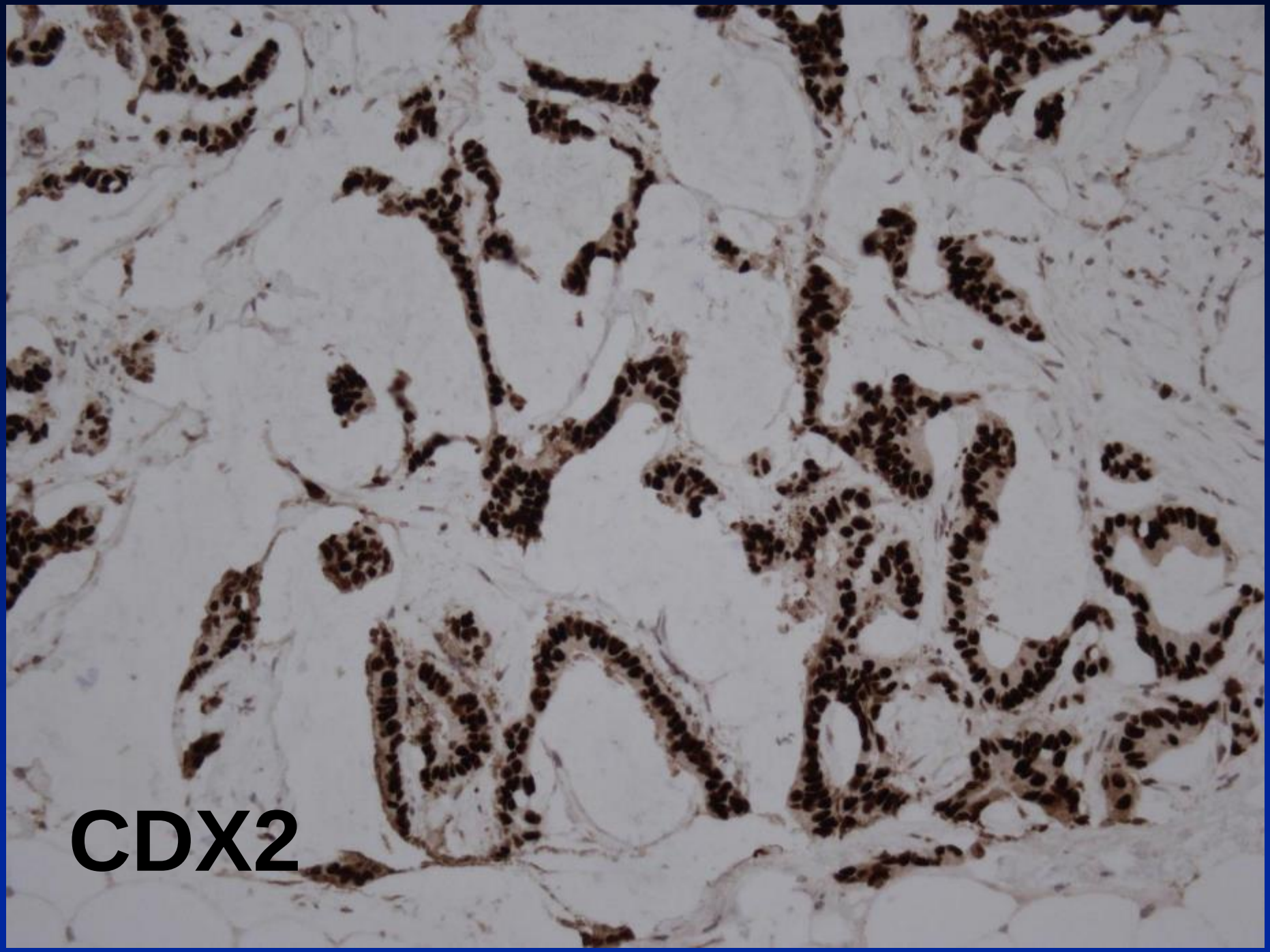
Metastatic colorectal carcinoma




CK20

CK7/CK20

CK7+/CK20-	Breast
	Non-mucinous ovary
	Lung adenocarcinoma
	Endometrium, Mesothelioma
	Thyroid, Oesophagus adenoca
	Salivary gland
CK7-/CK20+	Colorectal
CK7+/-CK20+	Gastric
CK7+/CK20+	Pancreas/biliary
	Mucinous ovary
	Transitional cell carcinoma
CK7-/CK20-	Prostate, Renal clear cell carcinoma
	Hepatocellular
	Pulmonary squamous


CDX2

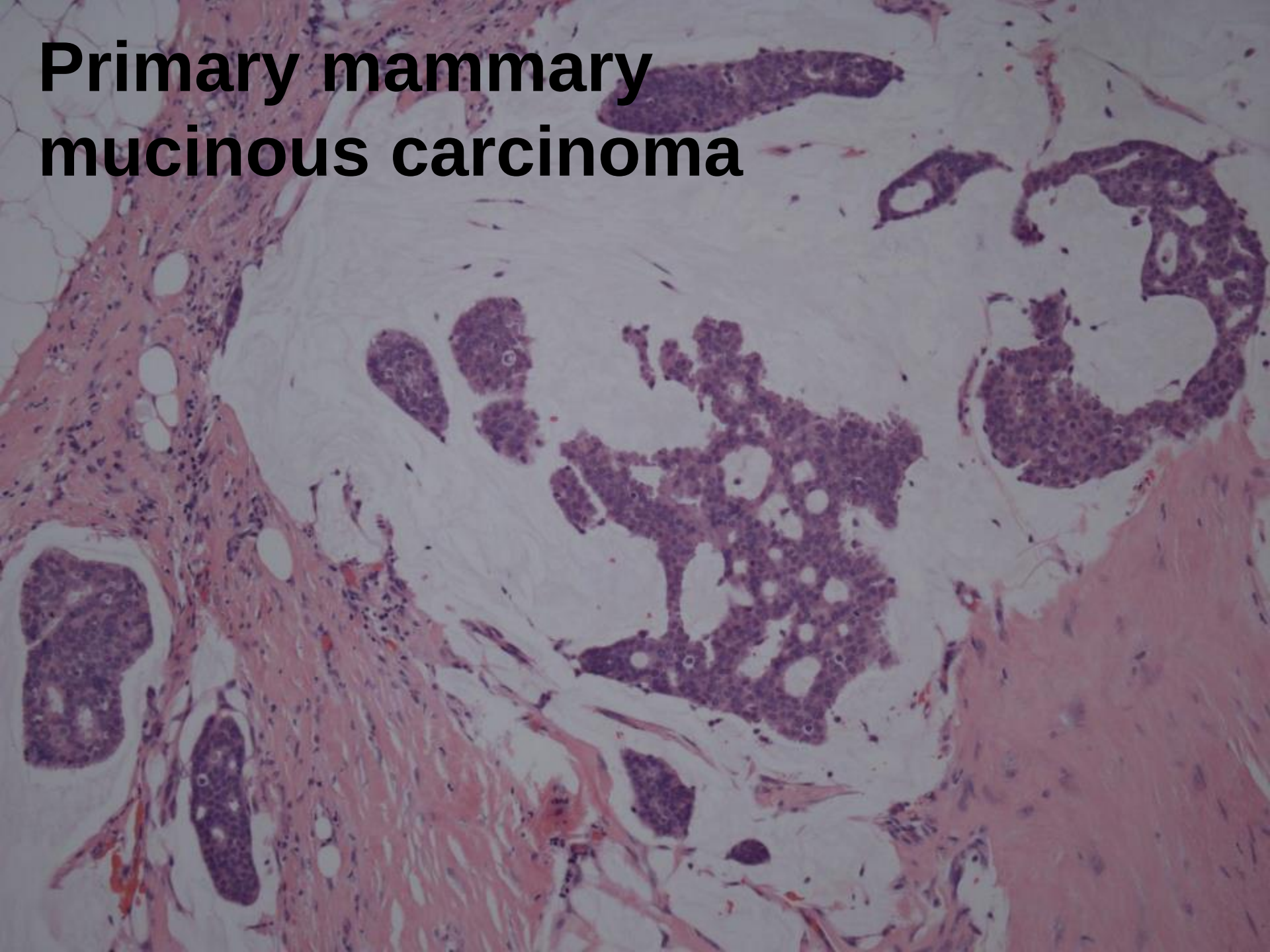
CDX-2

Expressed by carcinoma of

- **Oesophagus**
- **Stomach**
- **Small & large bowel**
- **Mucinous ovary**
- **Bladder adenocarcinoma**

Breast - rare

Primary mammary mucinous carcinoma



Mucinous adenocarcinoma

Chu et al. Determining the site of origin of mucinous adenocarcinoma: an immunohistochemical study of 175 cases. Am J Surg Pathol 2011;35:1830

Mucinous adenocarcinoma

CK7 positive: breast, gynae, lung

- **focal positive:** rectum, upper GI, bladder
- **negative:** colon

CK20 diffuse positive: colorectal

- **focal positive:** upper GI, bladder, ovary, lung
- **negative:** breast, cervix, endometrium

CDX2 homogeneous pos: colorectal

- **heterogeneous:** upper GI, ovary, lung
- **negative:** breast, cervix, endometrium

Mucinous adenocarcinoma

ER positive: breast, endometrium, cervix

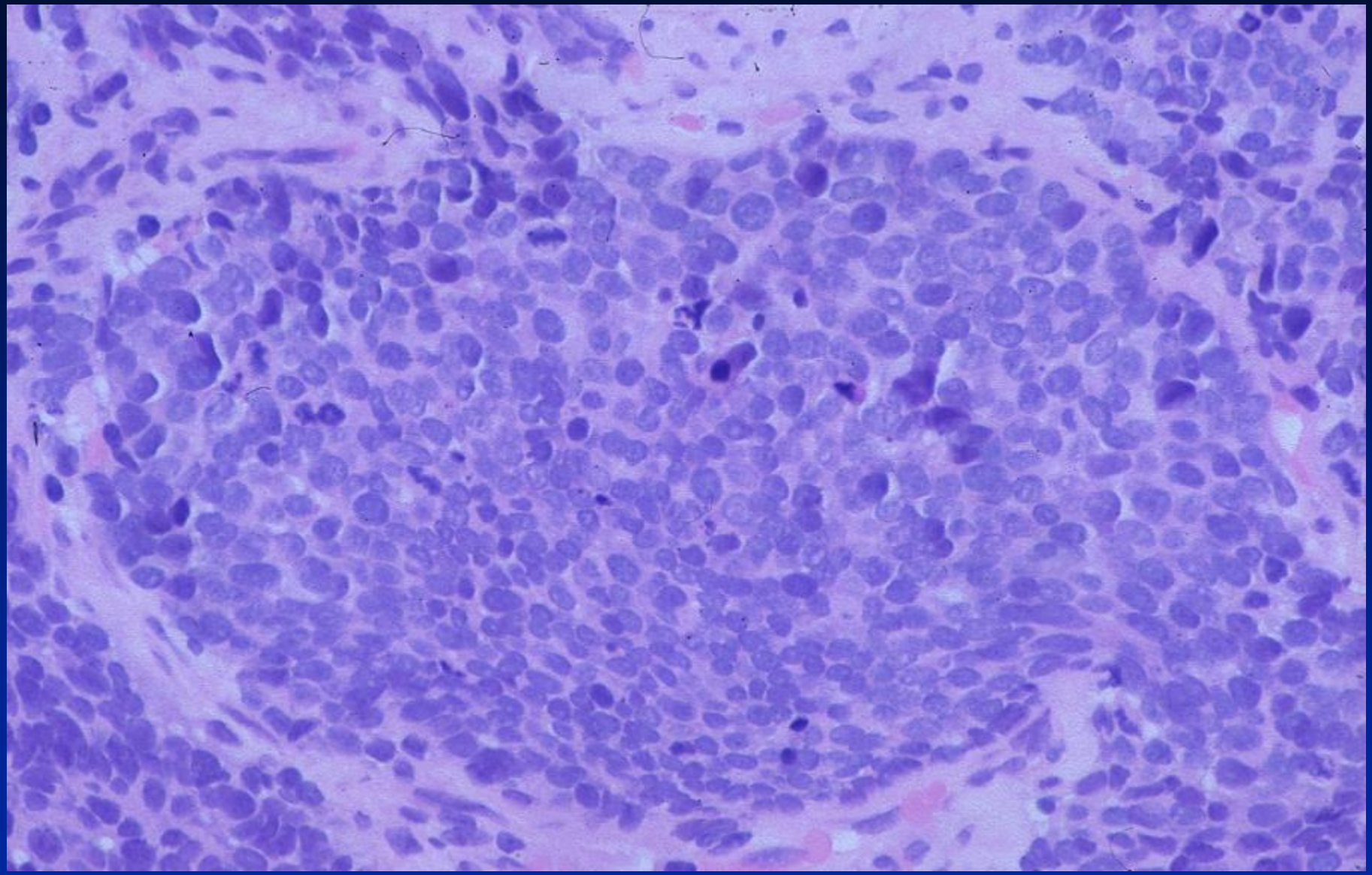
negative: ovary

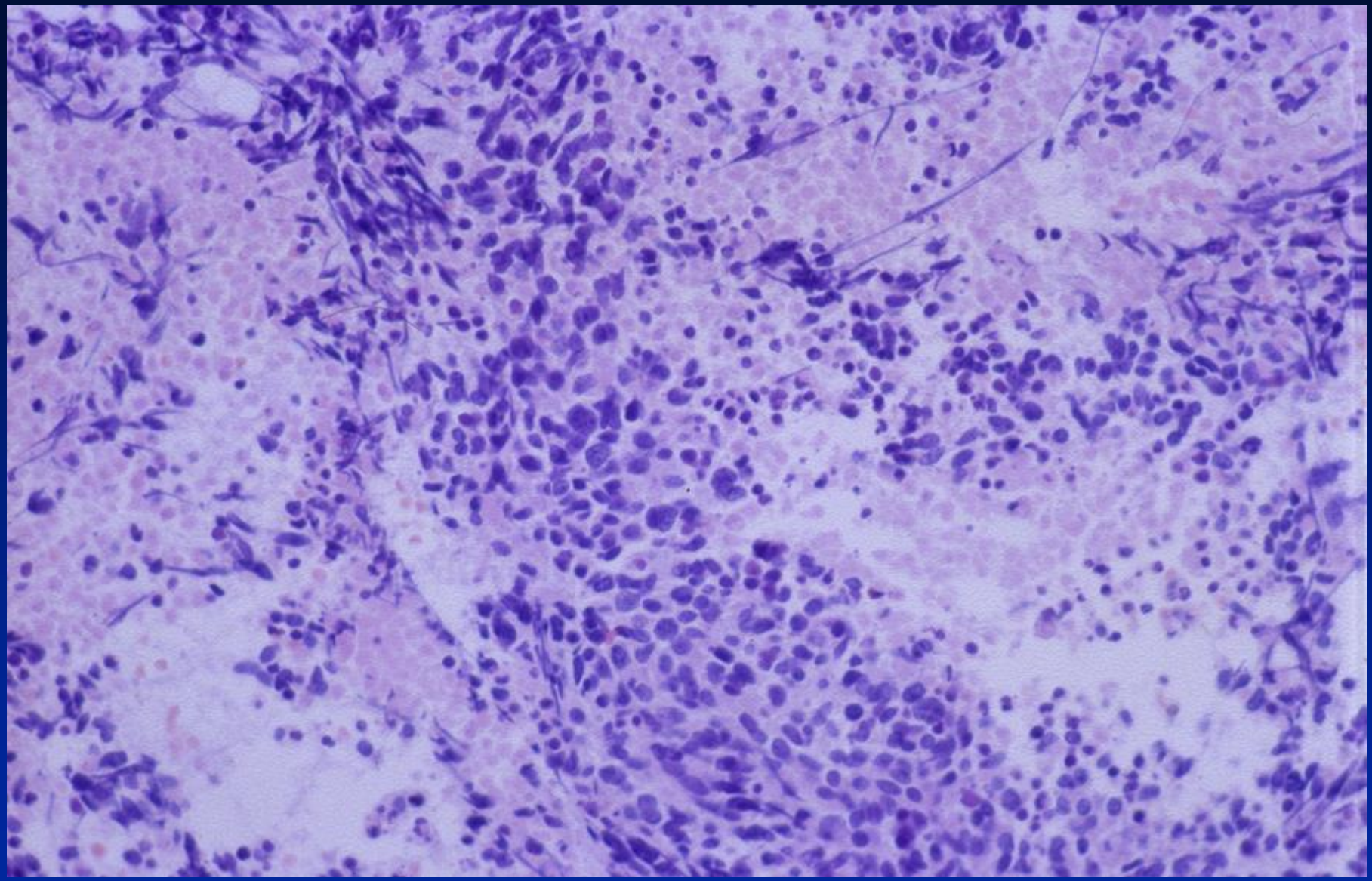
WT1 positive: breast

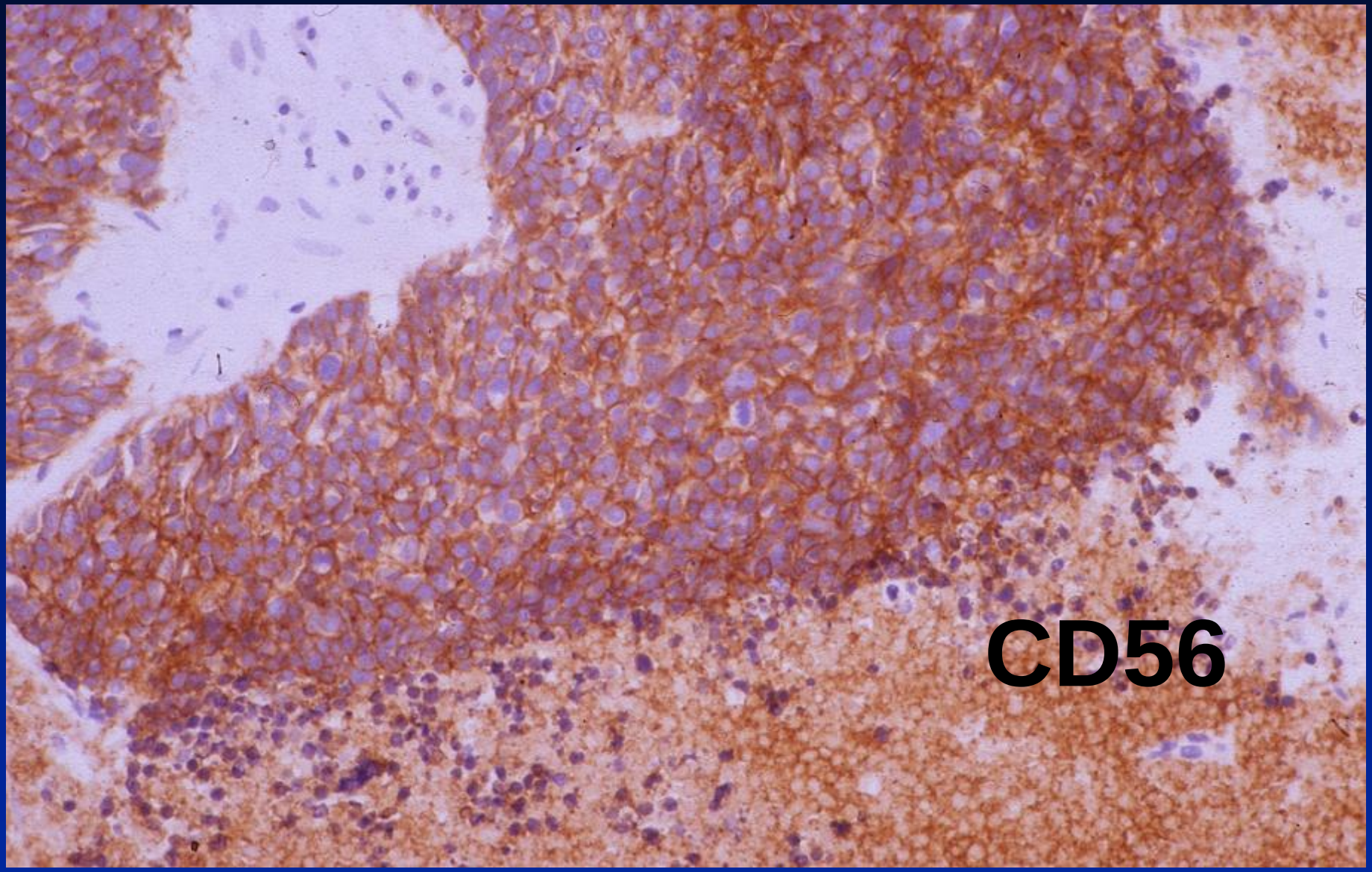
negative: lung, GI, ovary etc

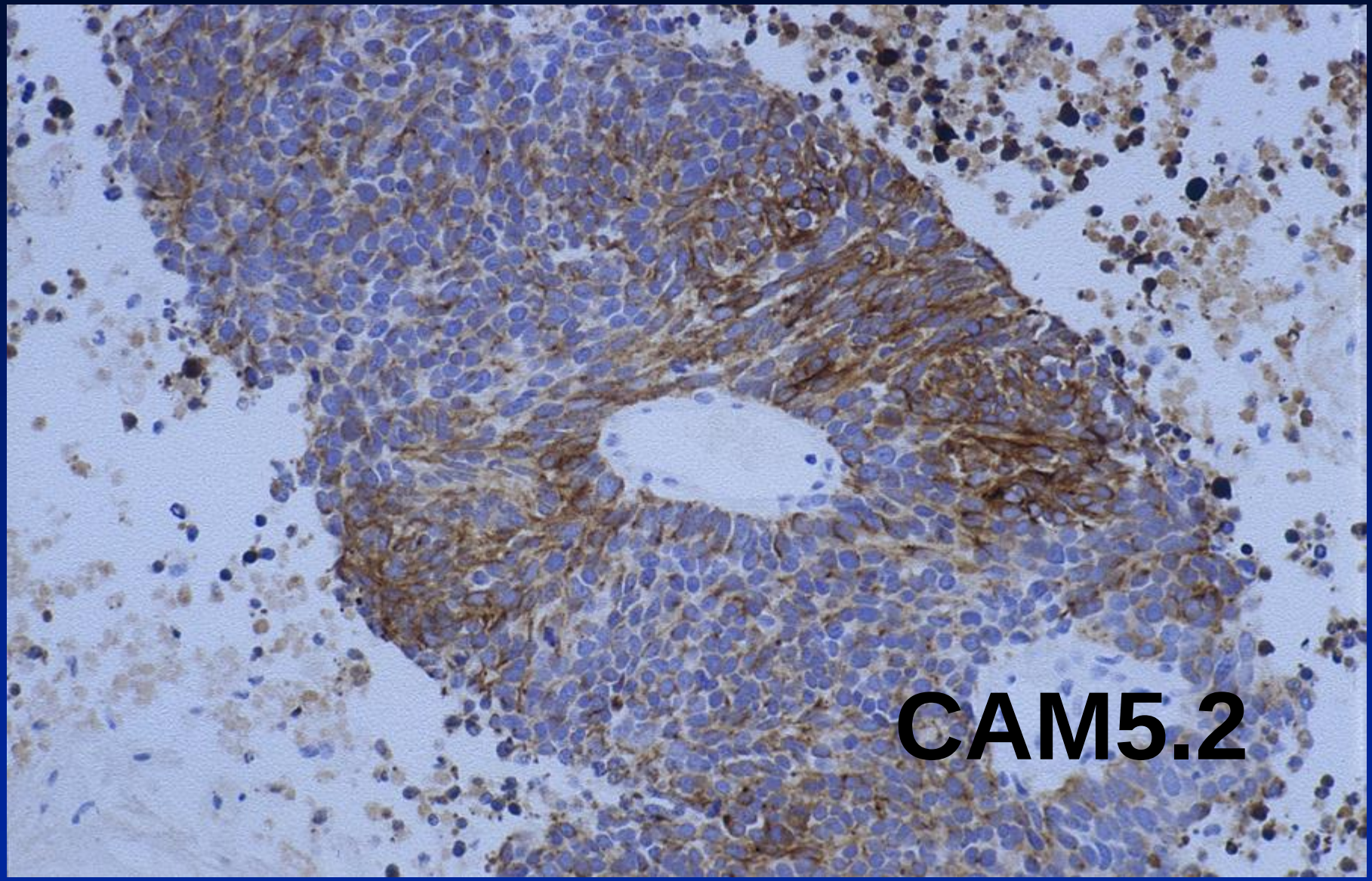
PAX8 positive: ovary, endometrium

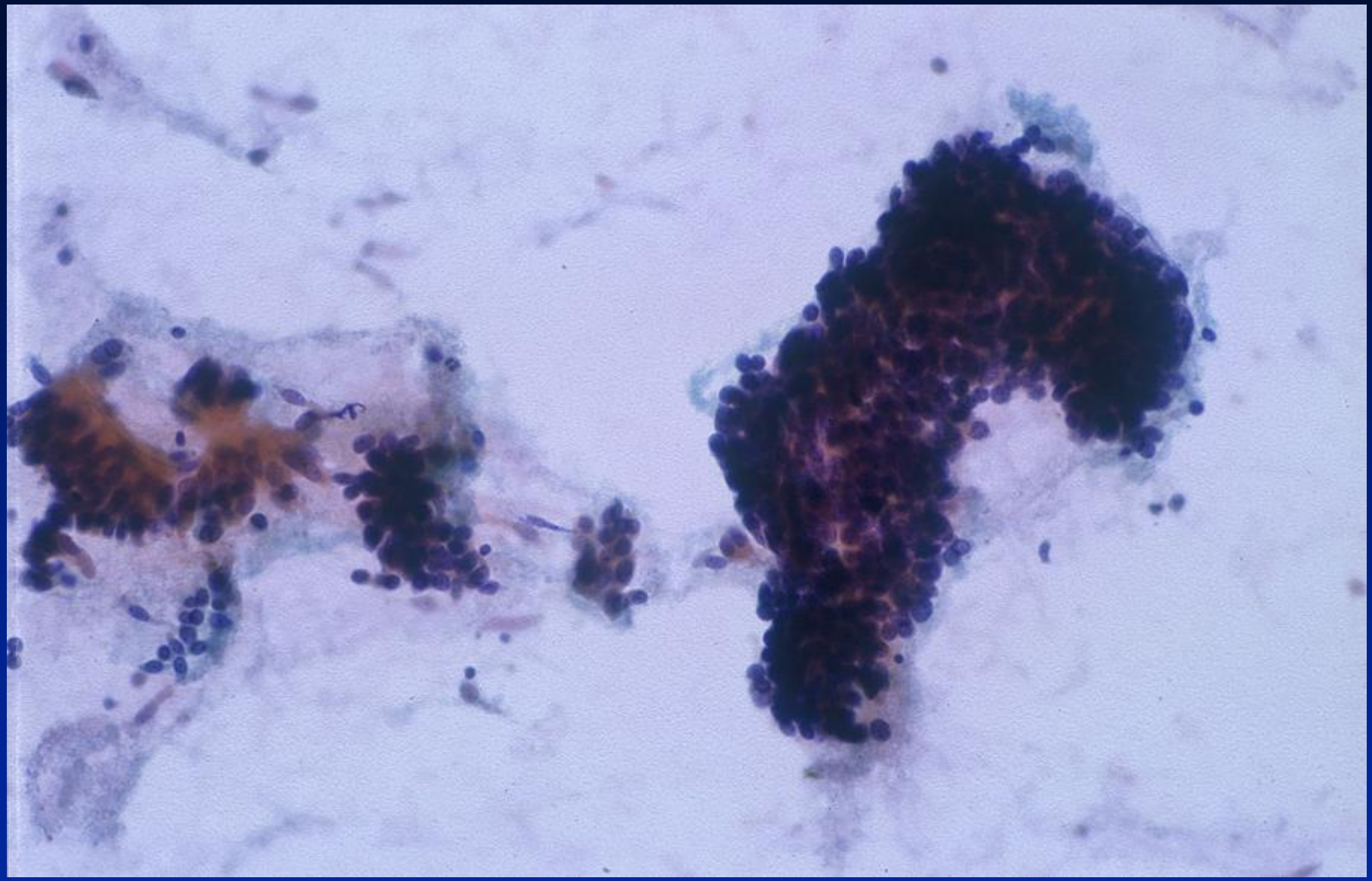
negative: breast, lung, GI etc

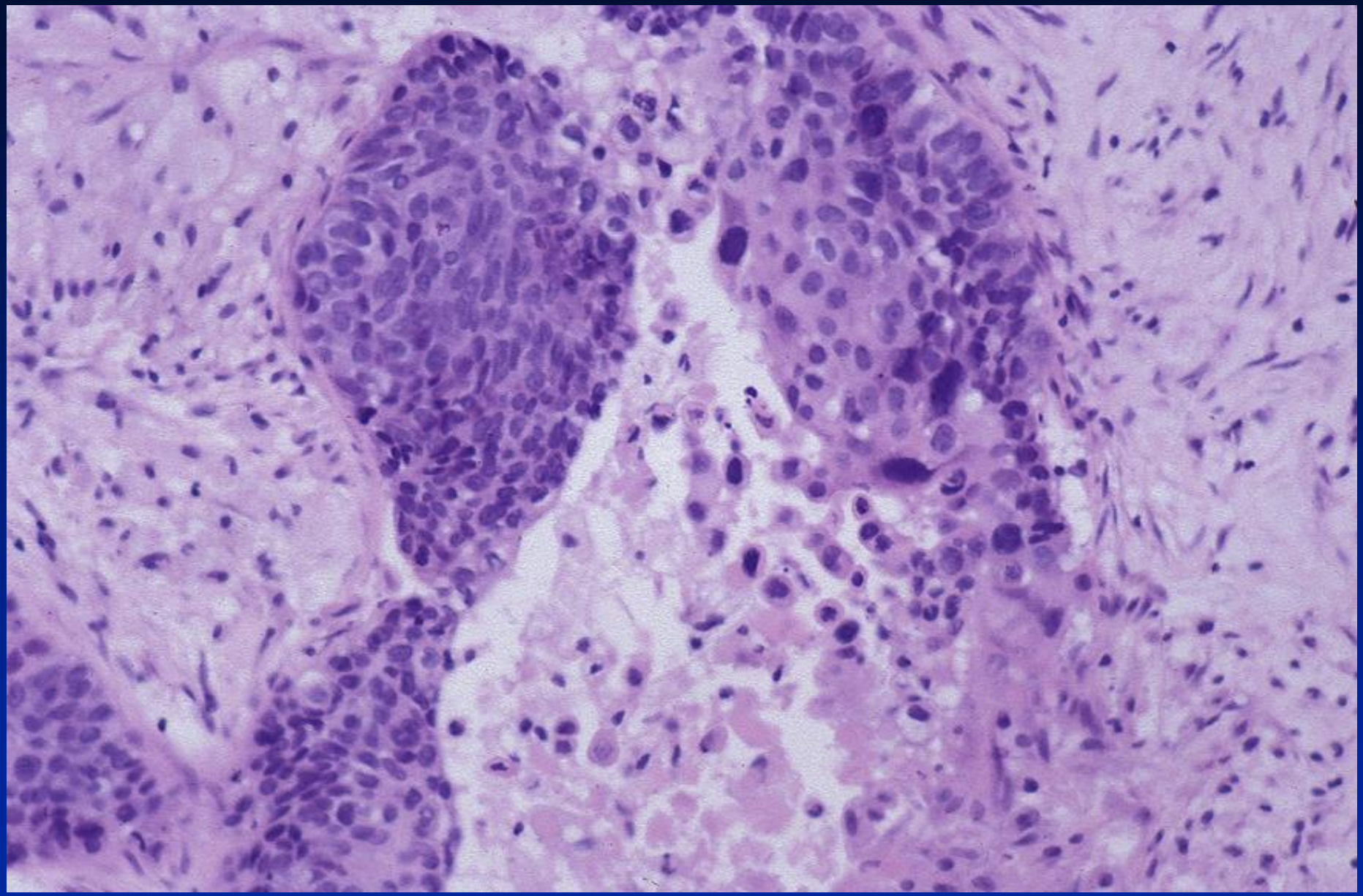


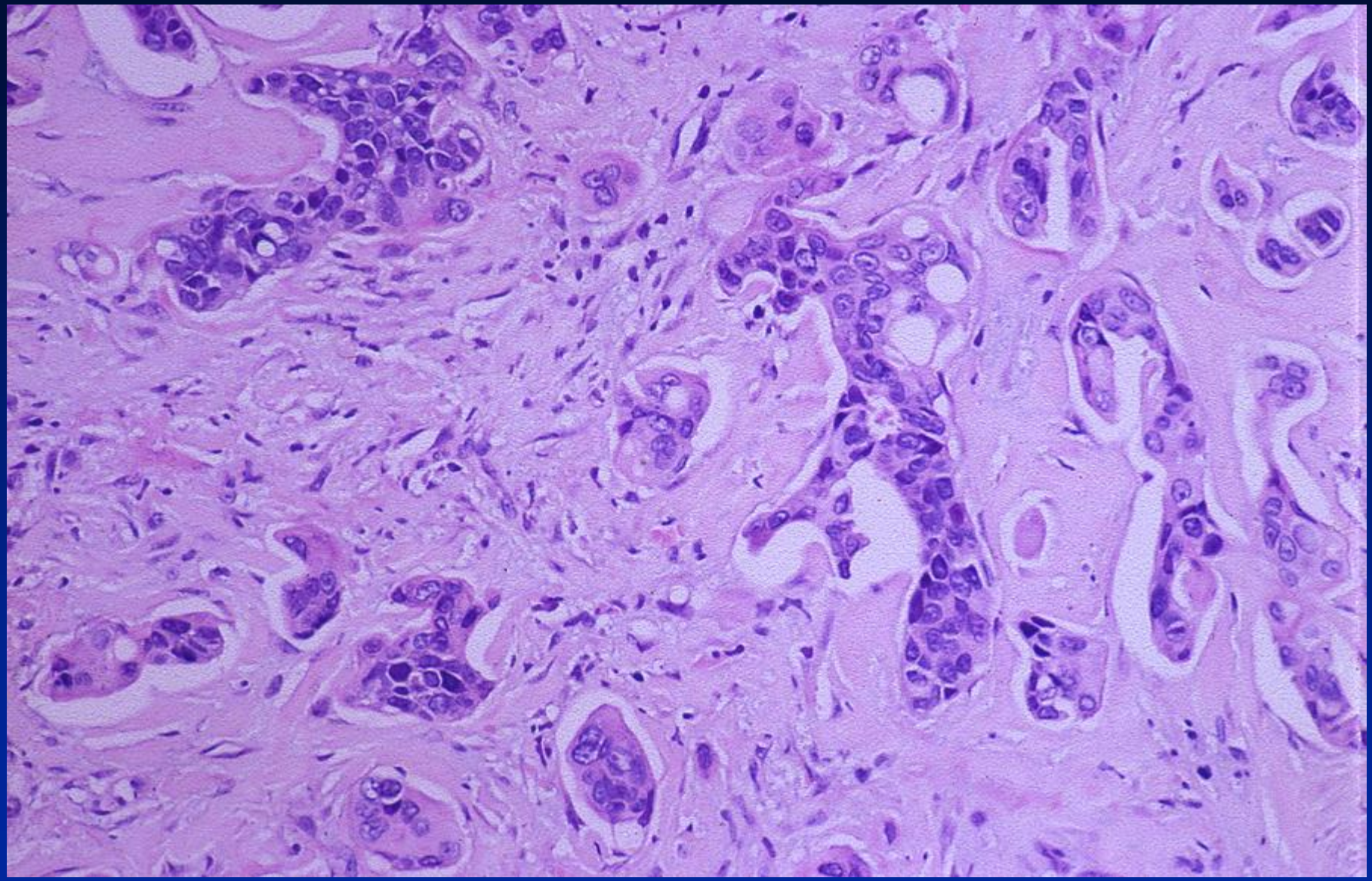


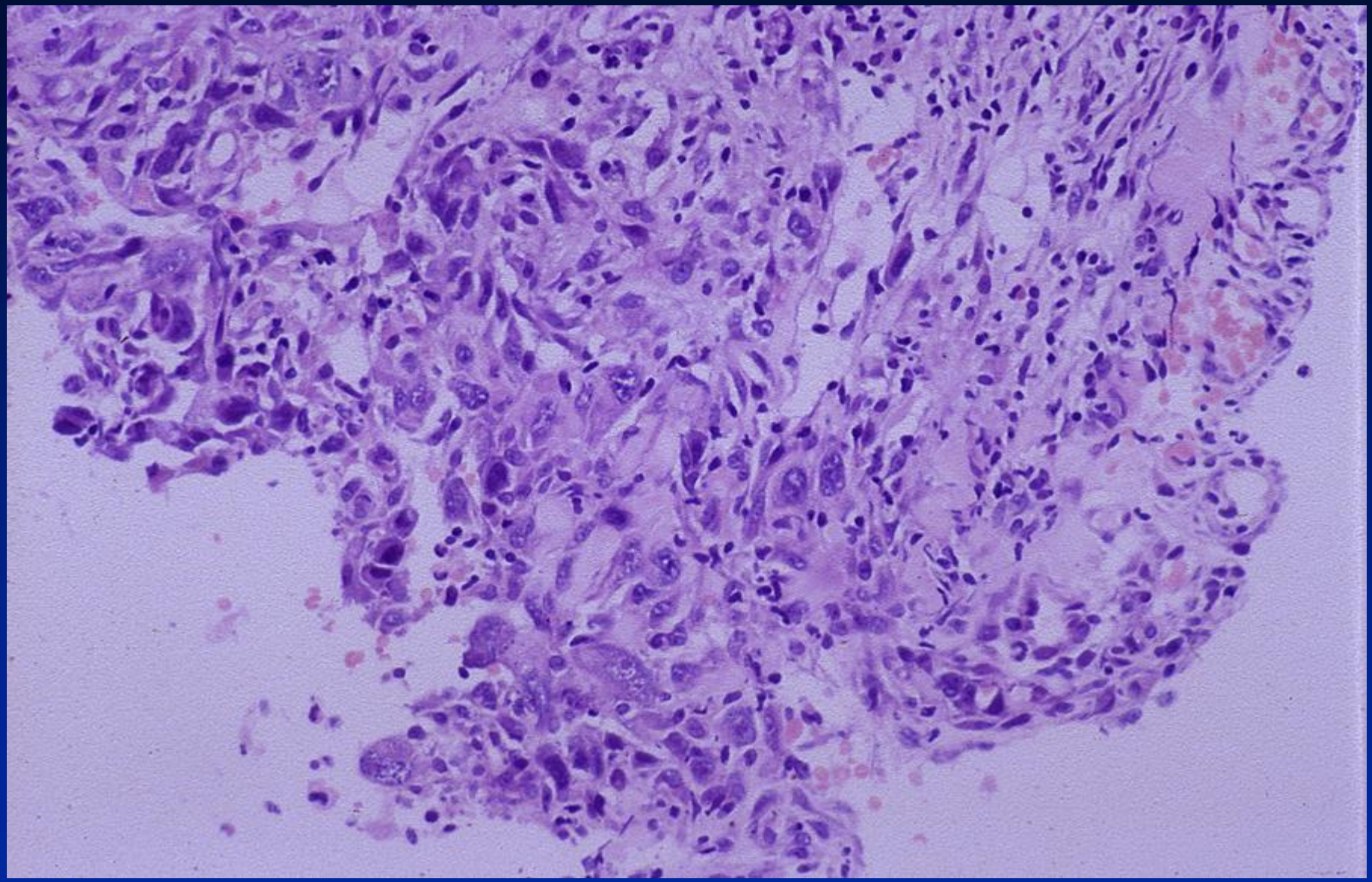

CD56


CAM5.2









Metastases from pulmonary carcinomas

- Morphology may give clues
- Squamous, oat cell, unusual adenocarcinoma
- History often vital
- TTF-1 useful in adenocarcinoma
- ER, GCDFP-15 favour breast

Gross cystic disease fluid protein-15

Breast	70%
Salivary gland	20%
Skin adnexal	
Prostate	10%
Others	Uncommon (<10%)

Gross cystic disease fluid protein-(GCDFP-15): expression in primary lung adenocarcinoma.

Am J Surg Pathol. 2008;32:426-32

- GCDFP-15 expression in 11/211 (5%)
- Distinctive morphology
- Mixed acinar and papillary
- Abundant extracellular mucin
- Abundant eosinophilic granular cytoplasm
- All 11 were ER-, PR-
- 81% TTF-1+

Metastases to Breast

- Usually manifestation of disseminated disease
- Average interval from primary to breast secondary about 2 years (can be much longer e.g. melanoma and ovary)
- Breast lesion is initial sign of tumour in about 25%
- Generally poor prognosis: majority die within a year

Metastases to Breast

- Usually systemic treatment or palliative care more appropriate than surgery
- Accurate non-operative diagnosis can therefore prevent unnecessary surgery
- Frequency about 0.5% compared with primary mammary carcinoma

Metastases to breast

Clinical features

Radiological features

- Usually not helpful
- Except for history of extramammary malignancy

Metastases to breast - common sites of origin

- Malignant melanoma 87
- Lung 78
- Ovary 50
- Prostate 39
- Kidney 24
- Stomach 15
- Ileum 13

Alva & Shetty-Alva 1999

Lymphoma
(Breast)

Histological features on core biopsy

	Primary mammary	Metastasis to breast
DCIS	32 – 40%	0%
Lobular neoplasia	3%	0%
Elastosis	51%	0%
Calcification	19%	17%*
Vascular inv	3%	0%

*serous papillary carcinoma of ovary

J Clin Pathol 2007;60:1333

Common histological types of invasive carcinoma

- Ductal
- Lobular
- Tubular
- Cribriform
- Mucinous
- Medullary
- Micropapillary
- Metaplastic
- Mixed

Histological features of metastases to breast on core biopsy

- About two-thirds show features not typical of primary mammary carcinoma eg clear cell carcinoma, small cell carcinoma
- About one third show features consistent with primary mammary carcinoma (history essential)

J Clin Pathol 2007;60:1333

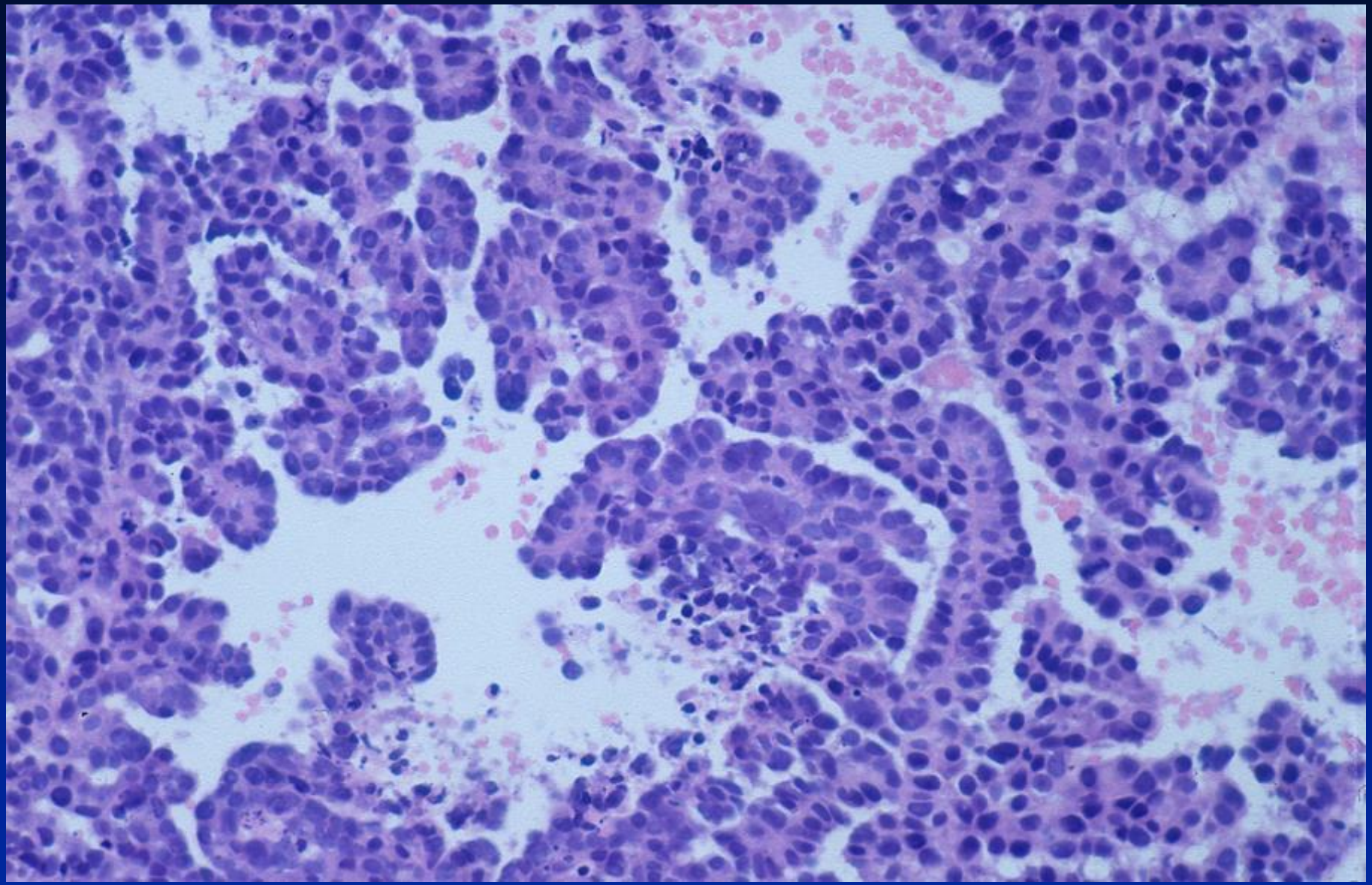
Histological diagnosis

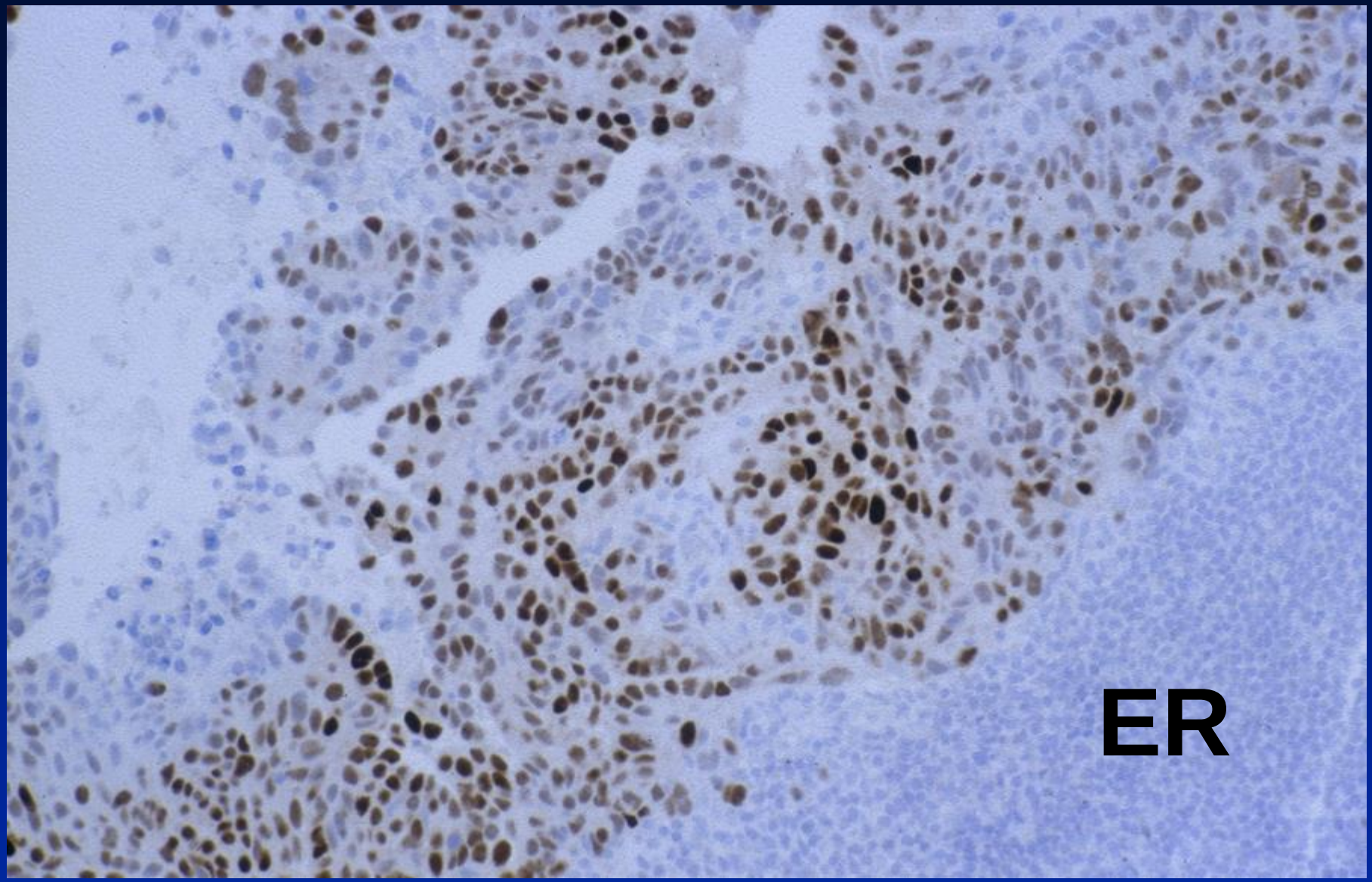
Most useful information:

- **Clinical history**
- **Morphology on H&E sections**
- **Comparison with previous histology**

Immunohistochemistry

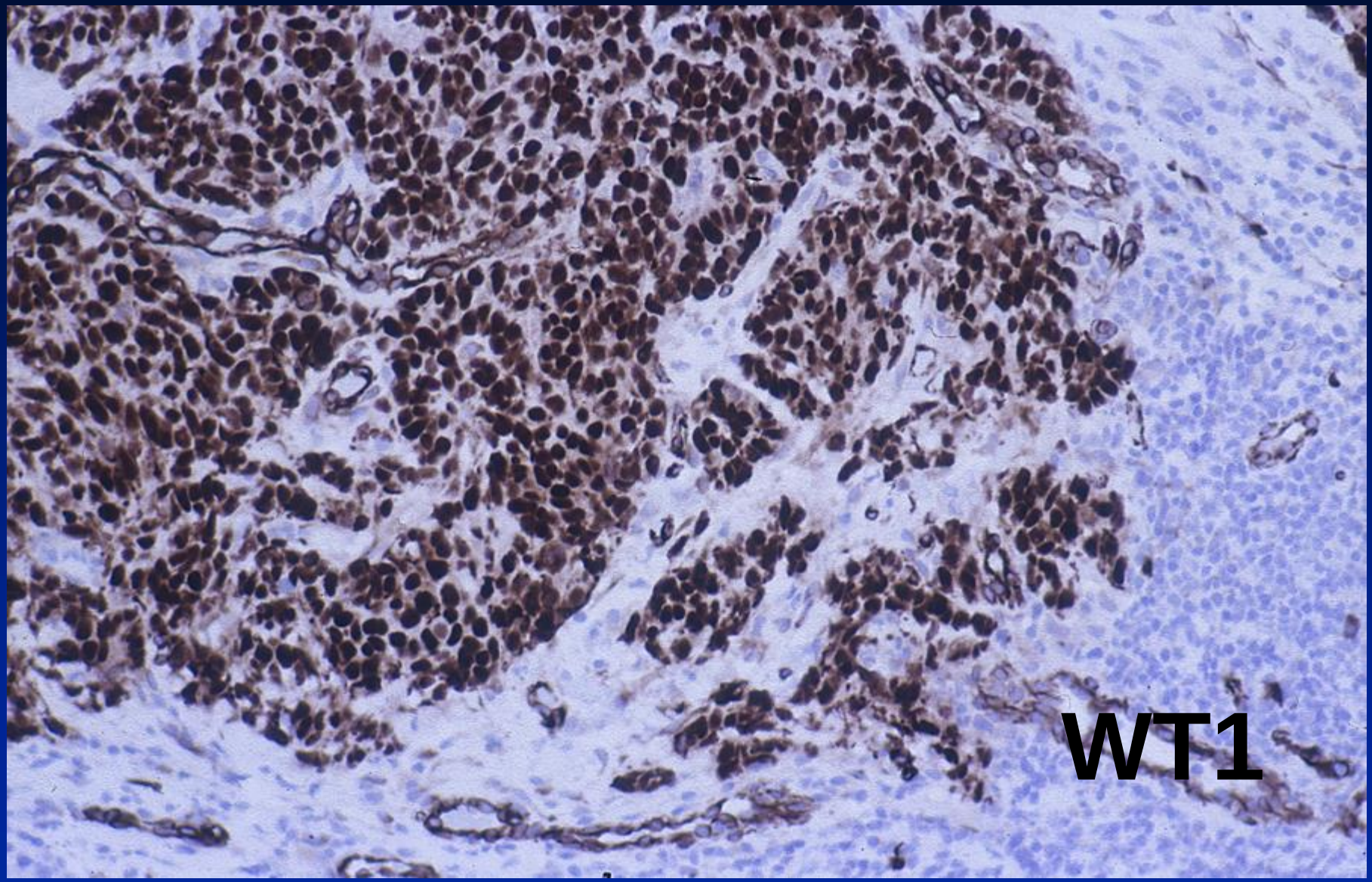
- Supplementary to H&E and clinical
- Could extramammary tumour be metastasis from the breast?
- Compare with extramammary tumour (may be occasional discordance especially in small biopsies)
- No marker 100% sensitive or specific
- Use panels of antibodies
- Interpret literature with care (variable techniques and criteria)




ER

Oestrogen receptor

- Strong staining largely confined to breast, ovarian and endometrial carcinomas
- Occasional tumours from other sites express ER, but almost always weak and focal

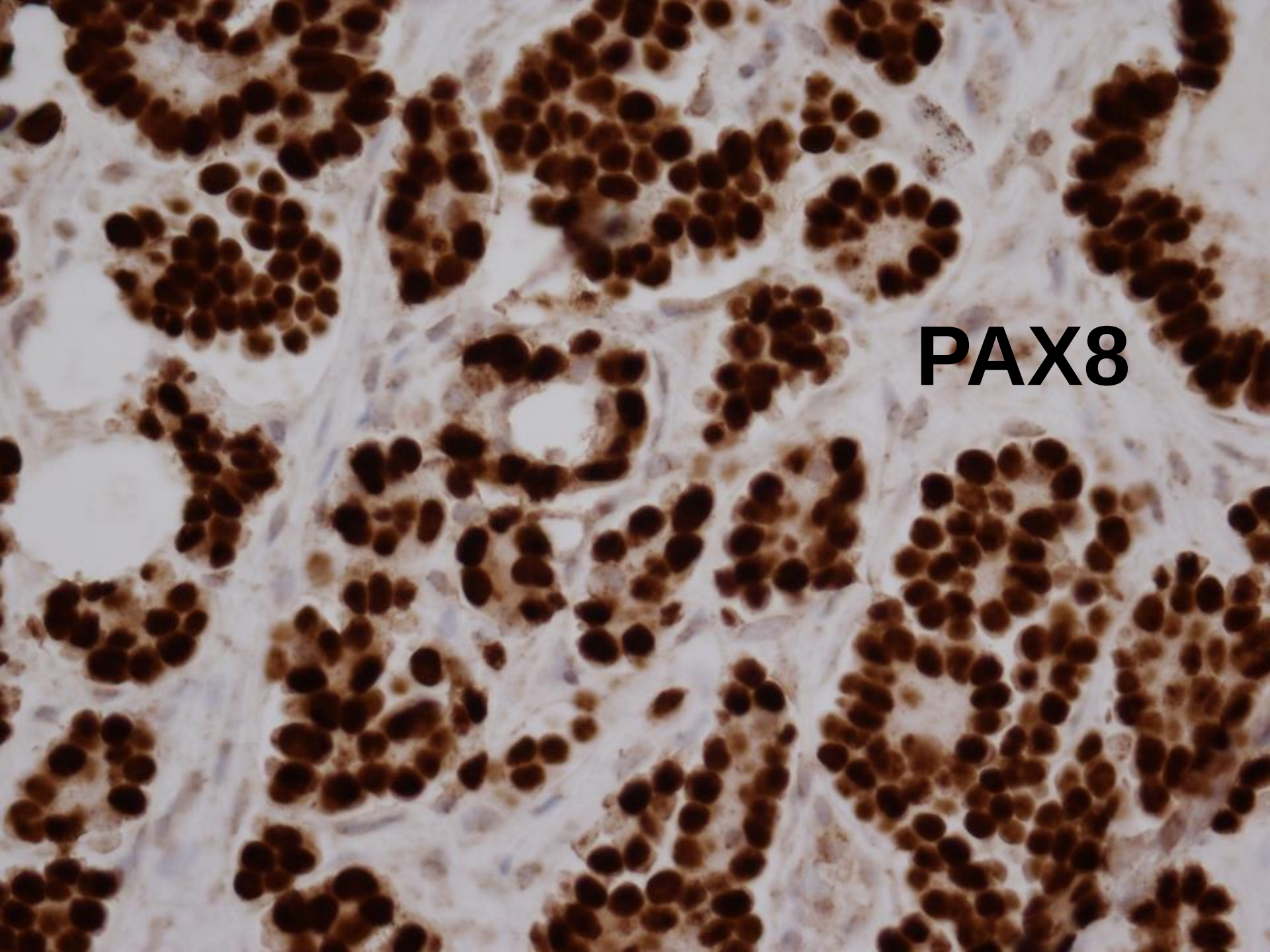

WT1

WT1

Ovary	70%
Serous	95%
Breast	0 - 7%
pure mucinous	66%*
mixed mucinous	33%*
micropapillary	3 – 6%**
Mesothelioma	70 - 95%
Other	usually negative

*Domfeh et al. Mod Pathol 2008

**Lee Histopathology 2007, Moritani Mod Pathol 2008


PAX8

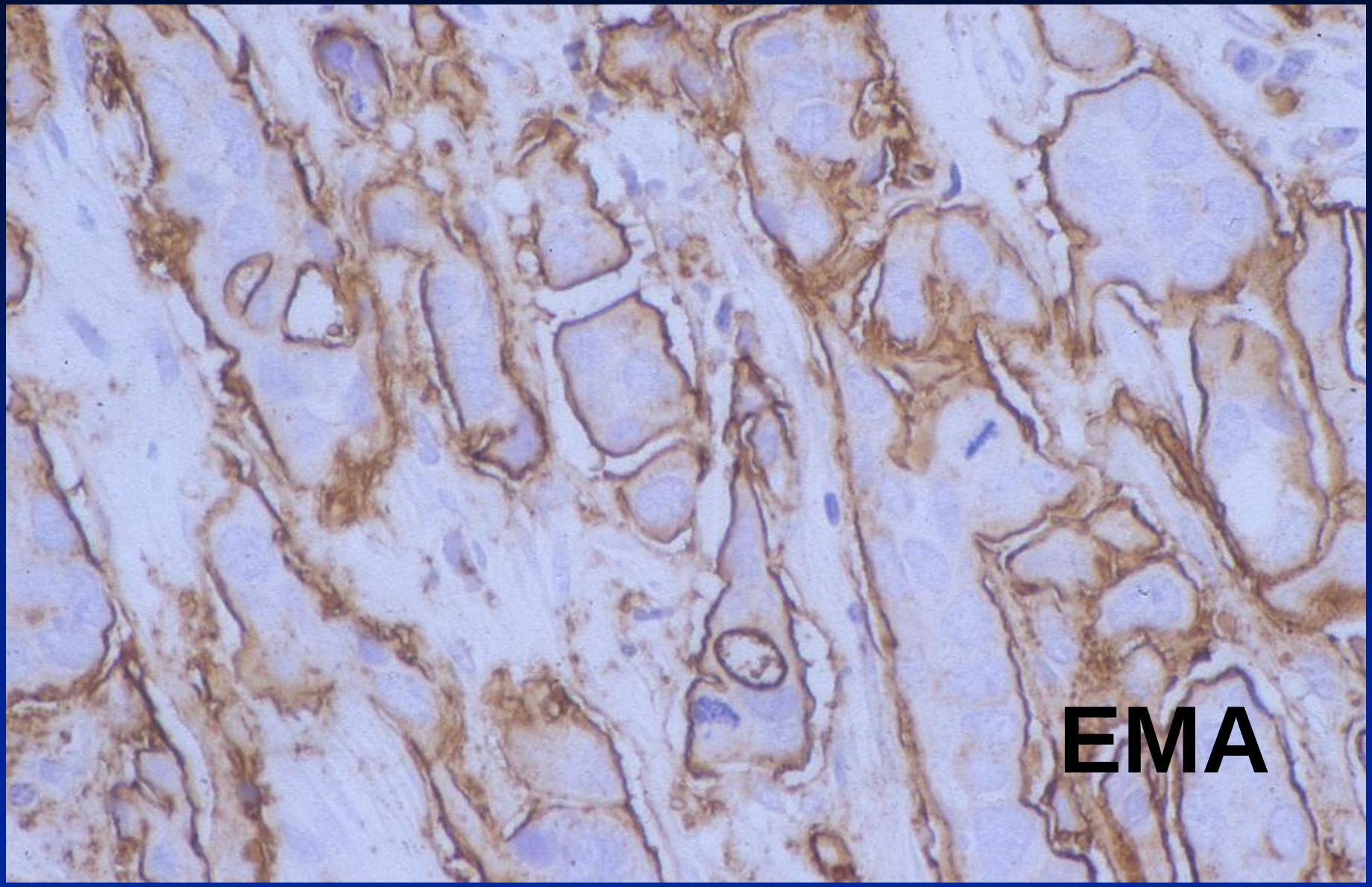
Pax8

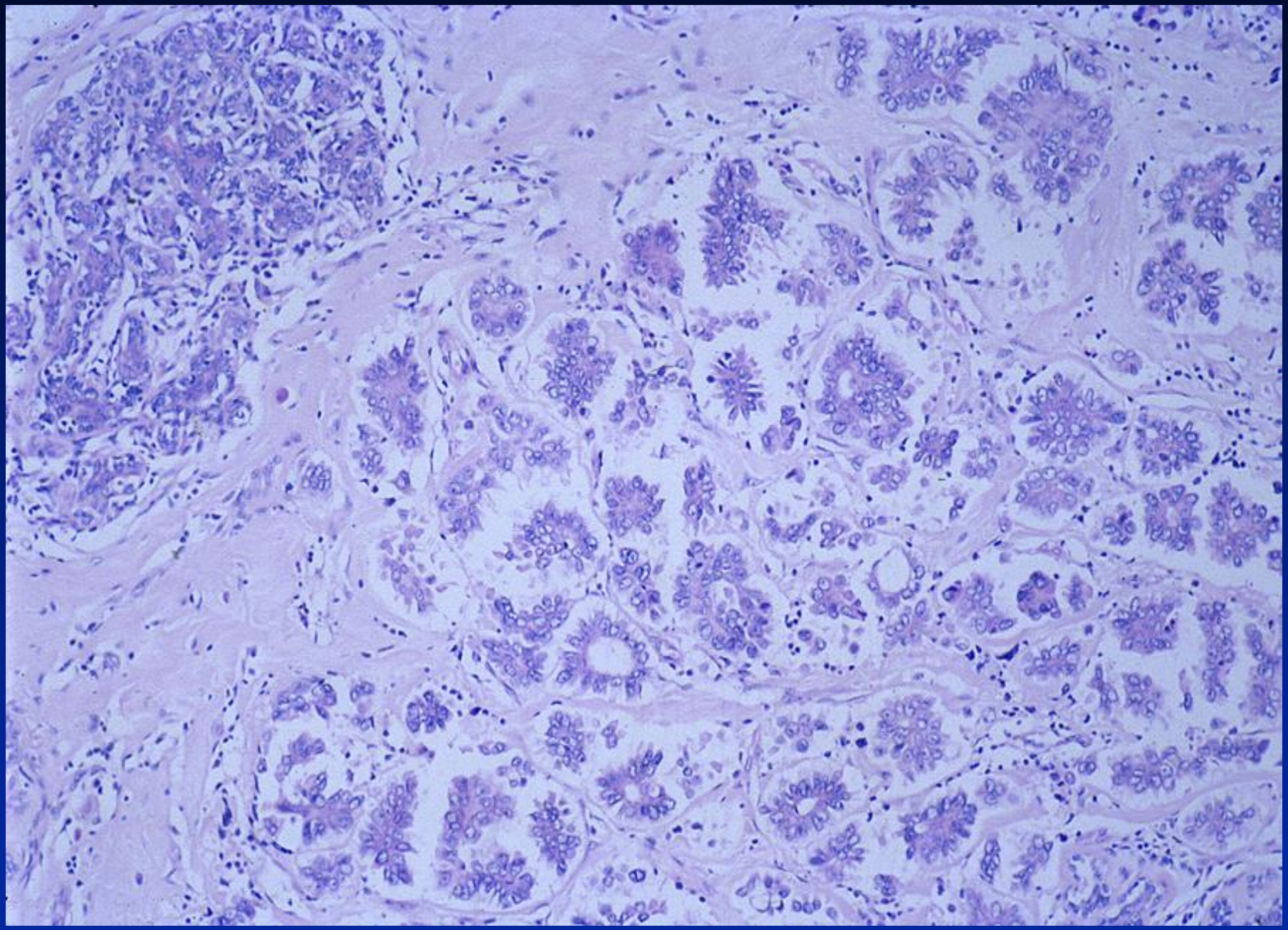
- Transcription factor
- Organogenesis of thyroid, kidney, & Müllerian system
- Regulates WT1

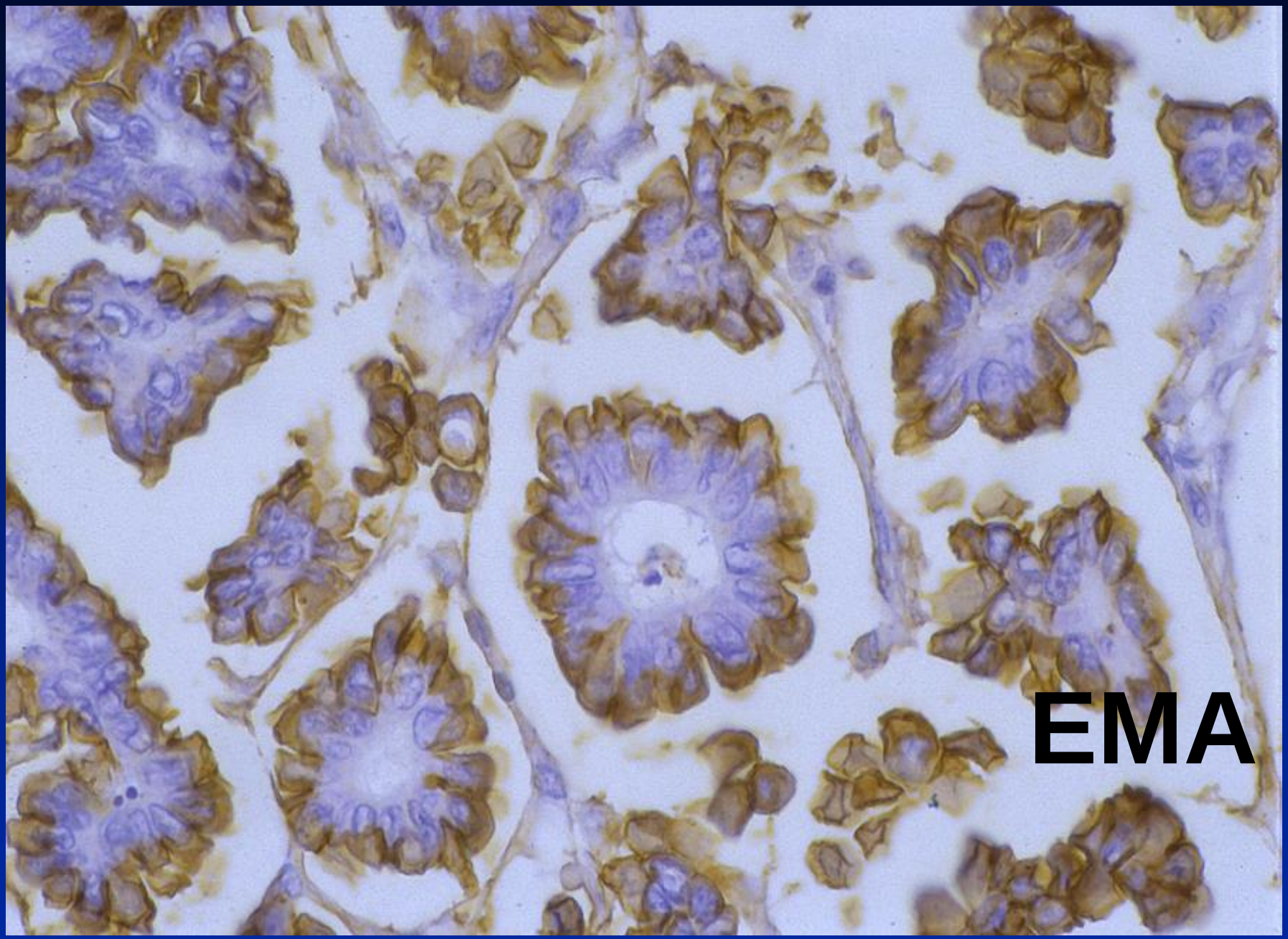
Pax8

• Serous papillary ca ovary	80 - 99%
• Non-serous ovarian ca	68 - 71%
• Cervical carcinoma	91%
• Endometrial carcinoma	85 - 98%
• Renal cell carcinoma	90%
• Thyroid carcinoma	91%
• Breast carcinoma	0%
• Upper GI & pancreas	0%
• Pulmonary carcinoma	rare

Laury et al. Am J Surg Pathol 2011
Woodard et al. Am J Clin Pathol 2011
Nonaka et al. Am J Surg Pathol 2008


EMA

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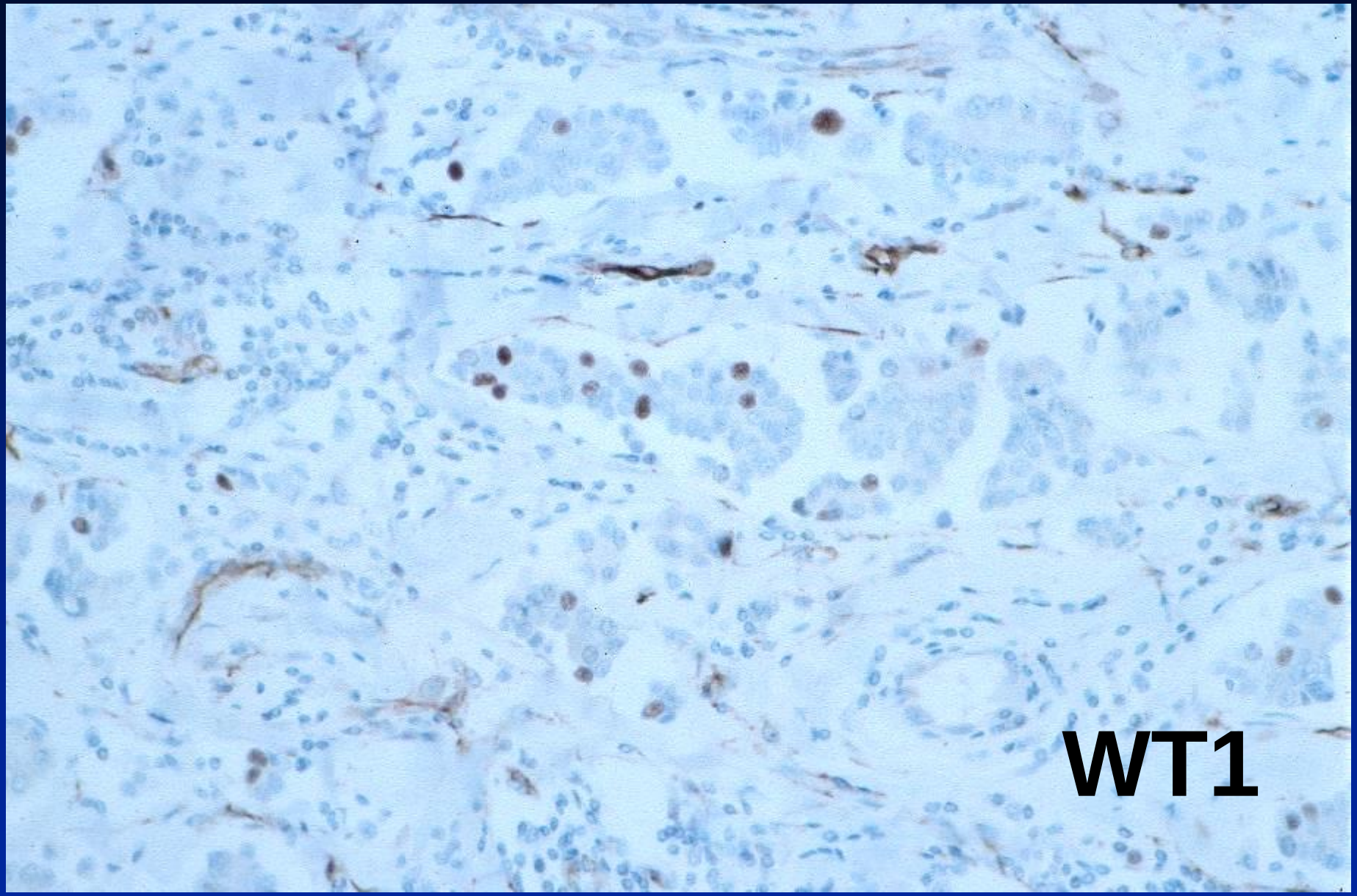
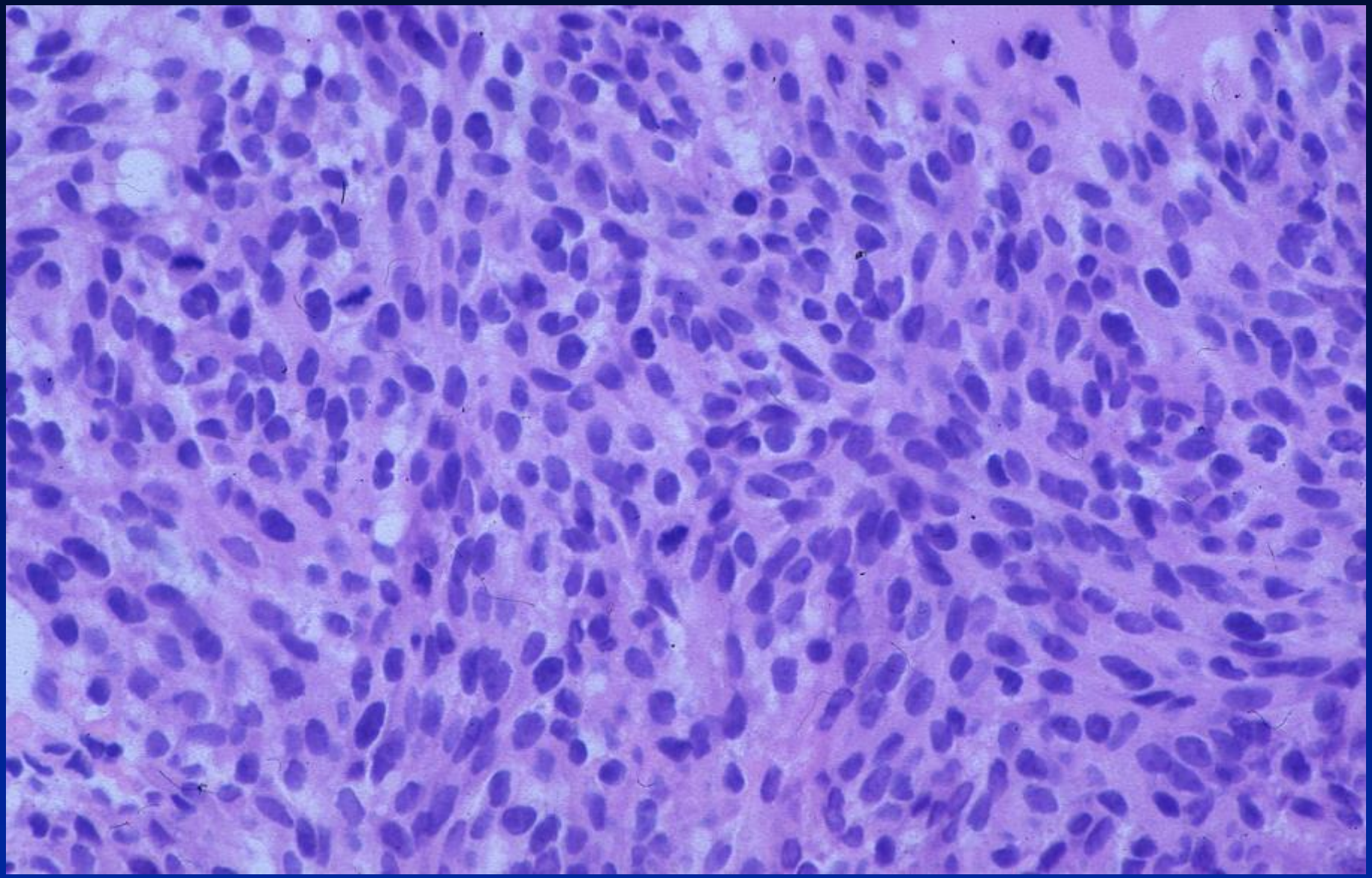
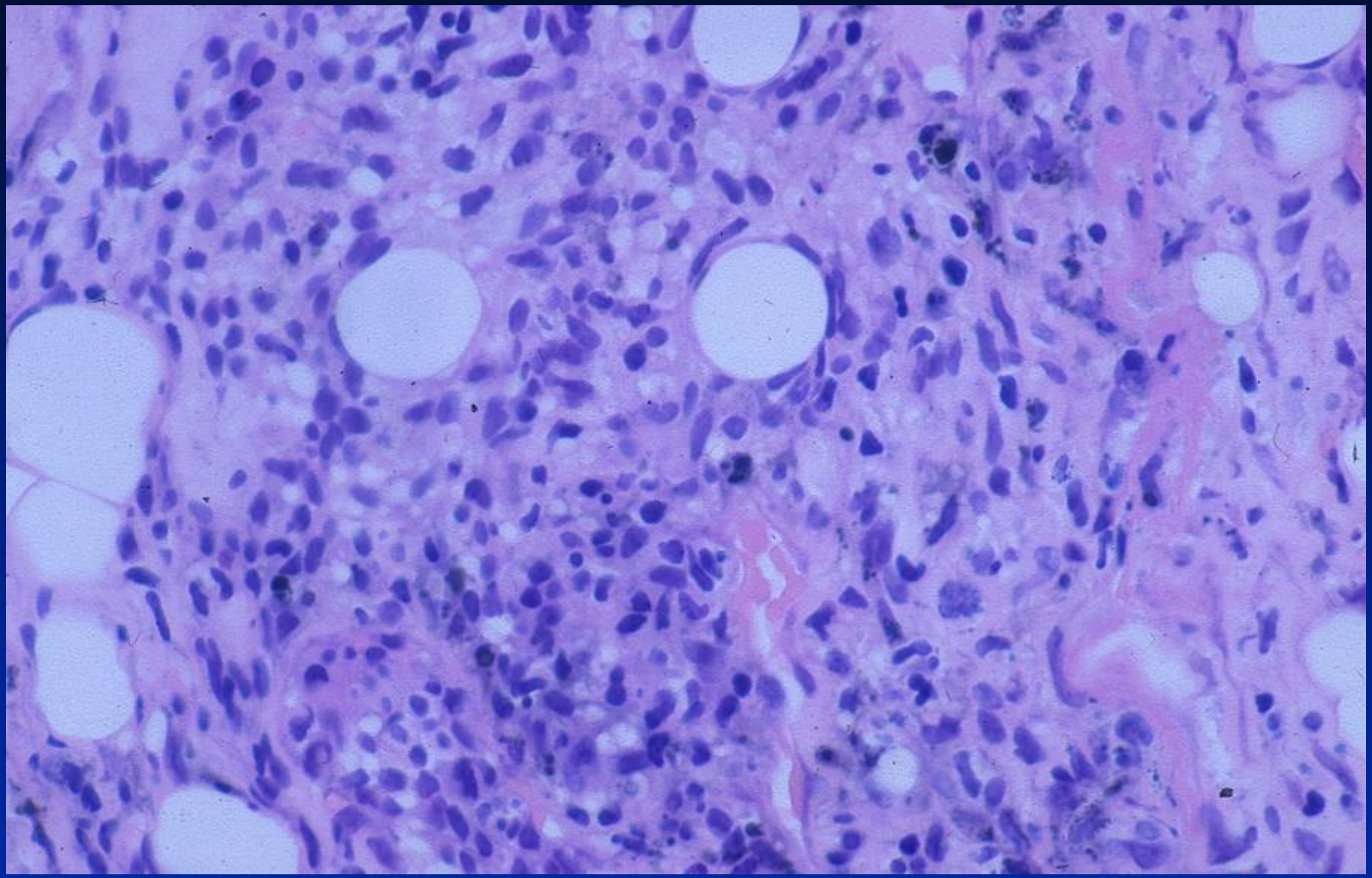
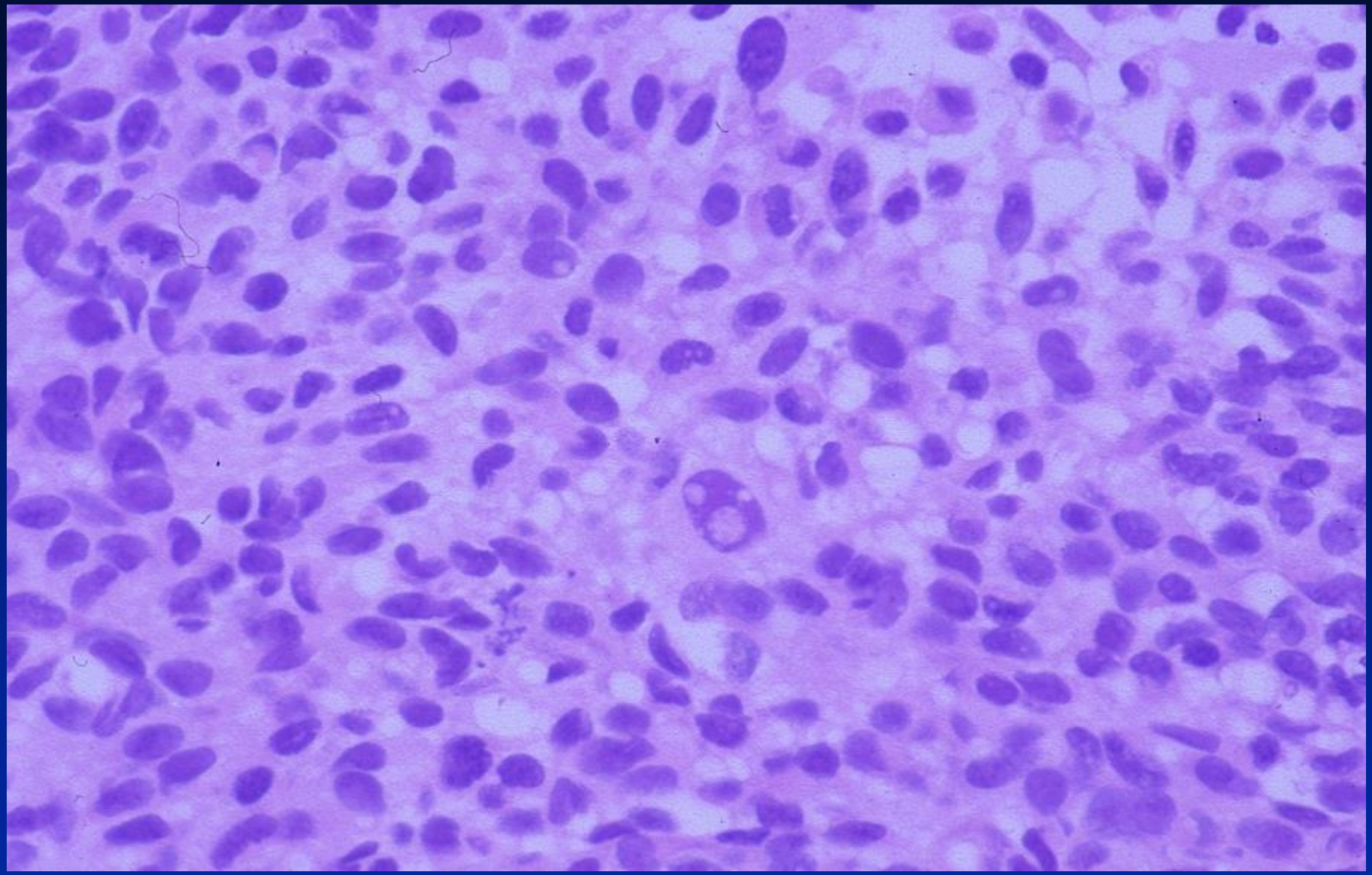

WT1

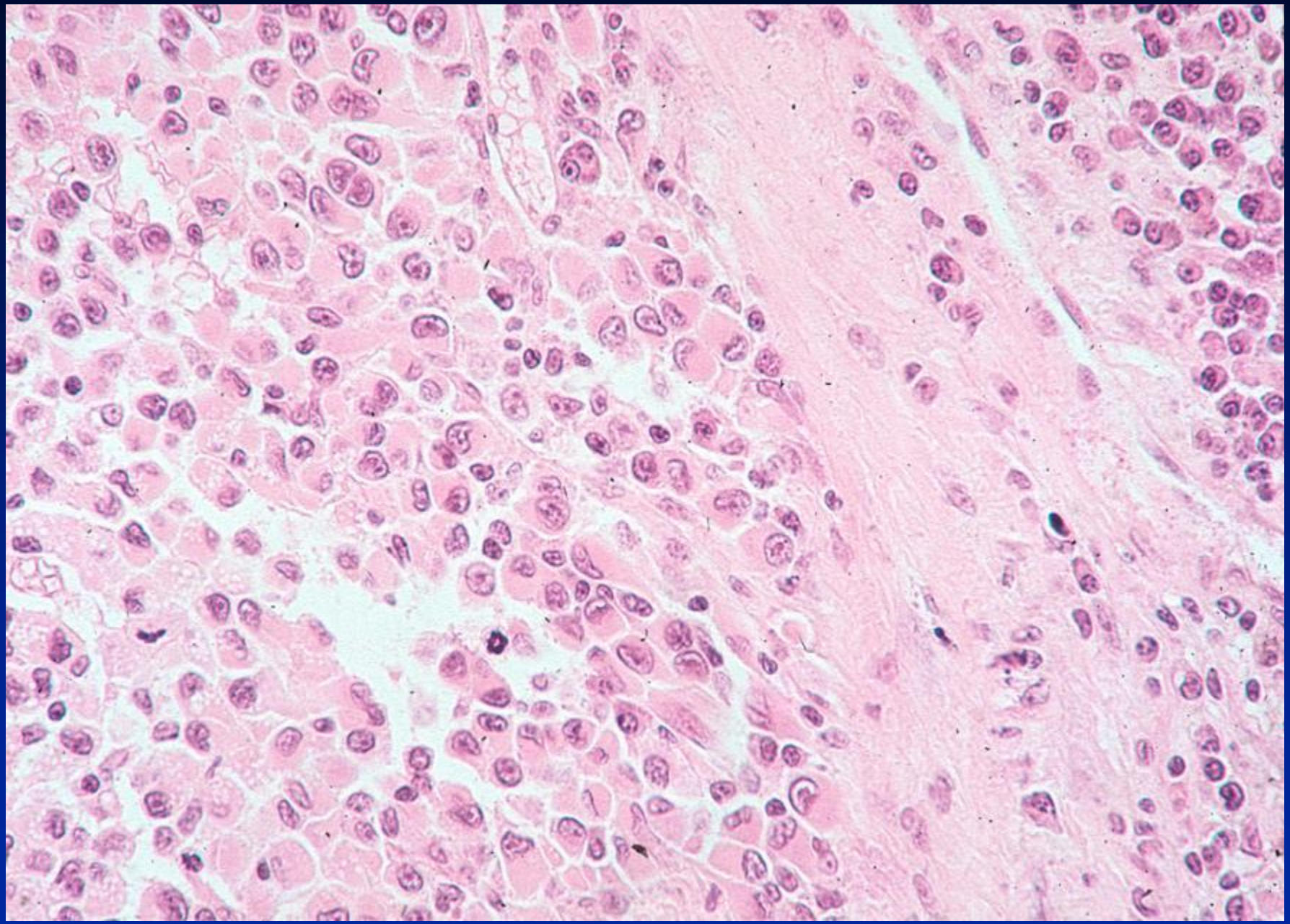
Ovarian carcinoma

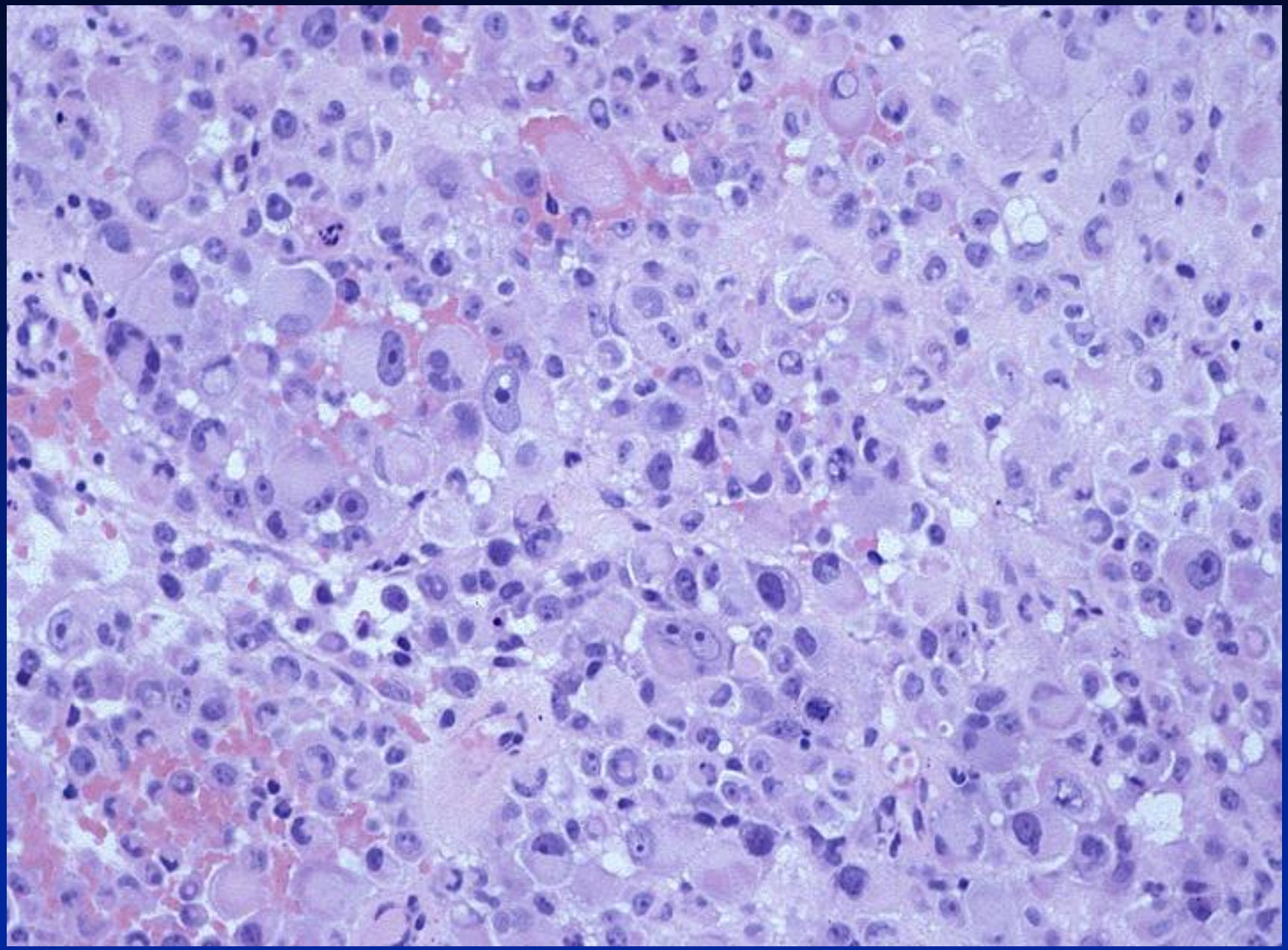
- Serous papillary commonest type to metastasise to breast
- Clue: papillary architecture
- Calcification
- EMA pattern
- WT1 and PAX8 favour ovary
- GCDFP-15 favours breast







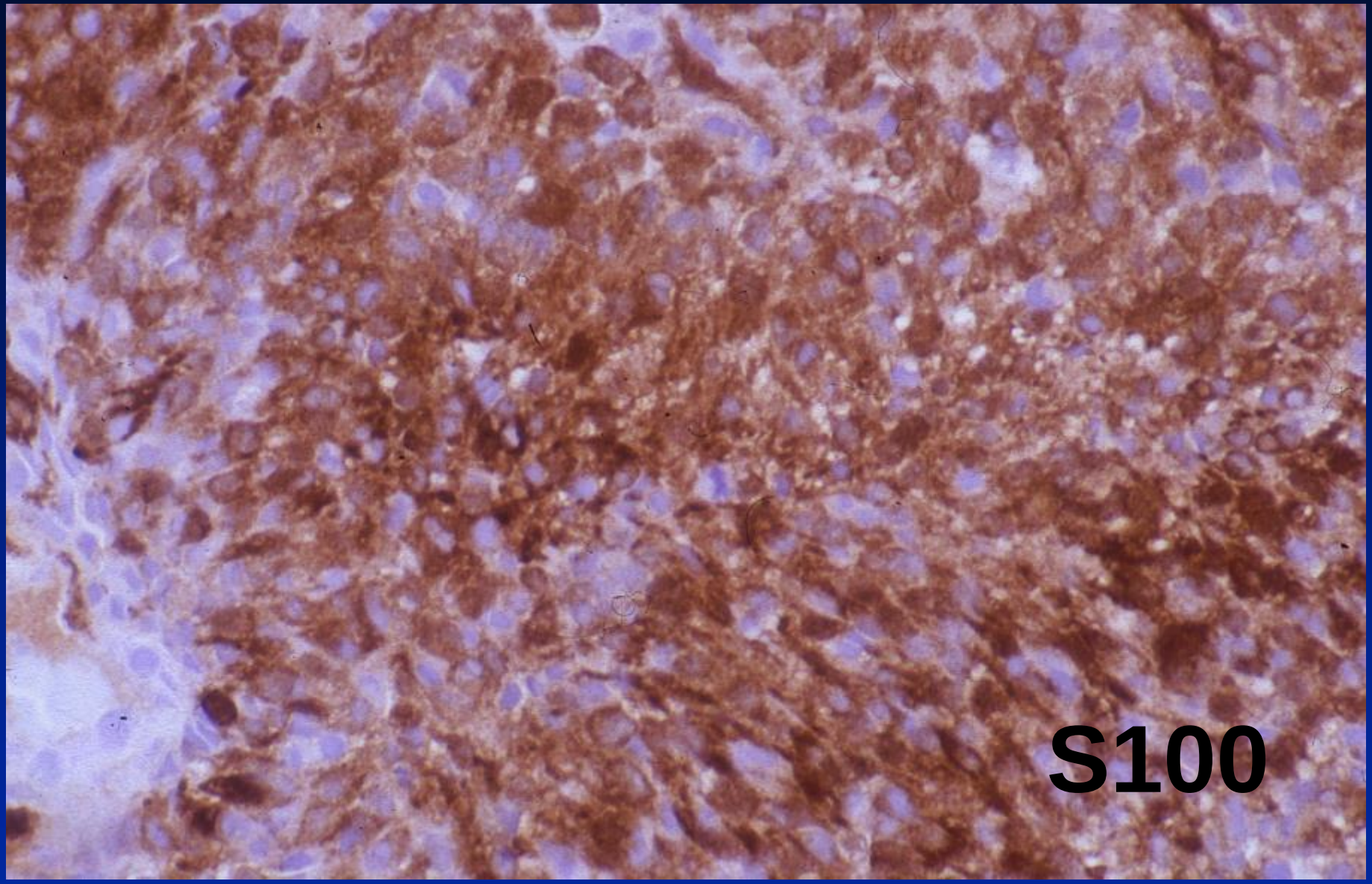


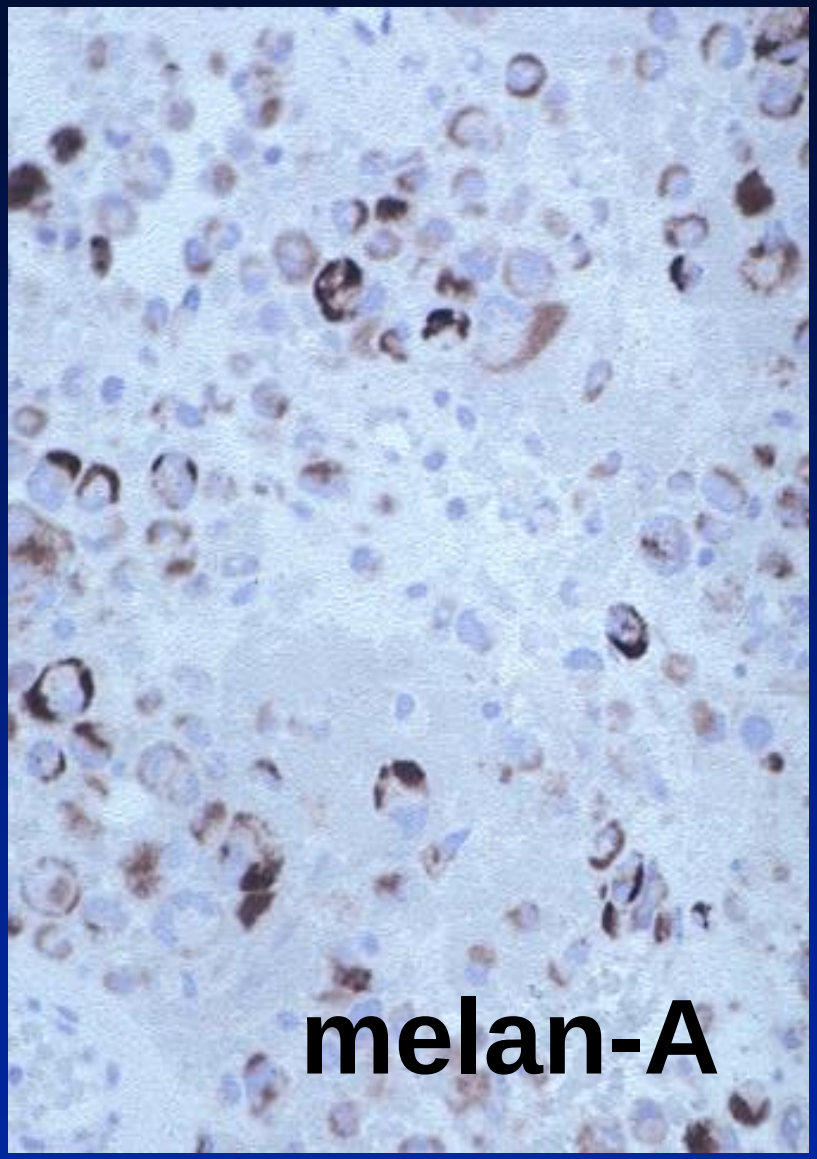


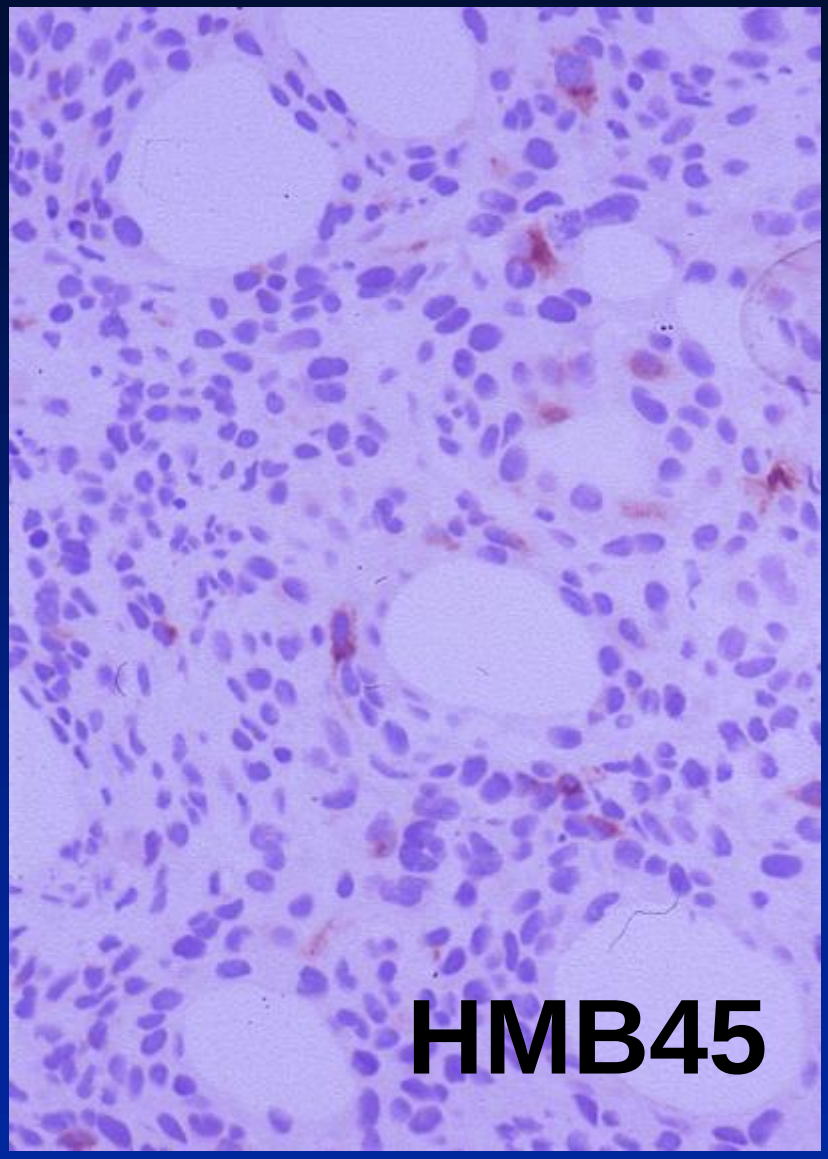
Melanoma

Histological clues

- Spindle cells
- Intranuclear inclusions
- Plasmacytoid
- Epithelioid
- Pigment
- May be similar mammary carcinoma


S100


melan-A

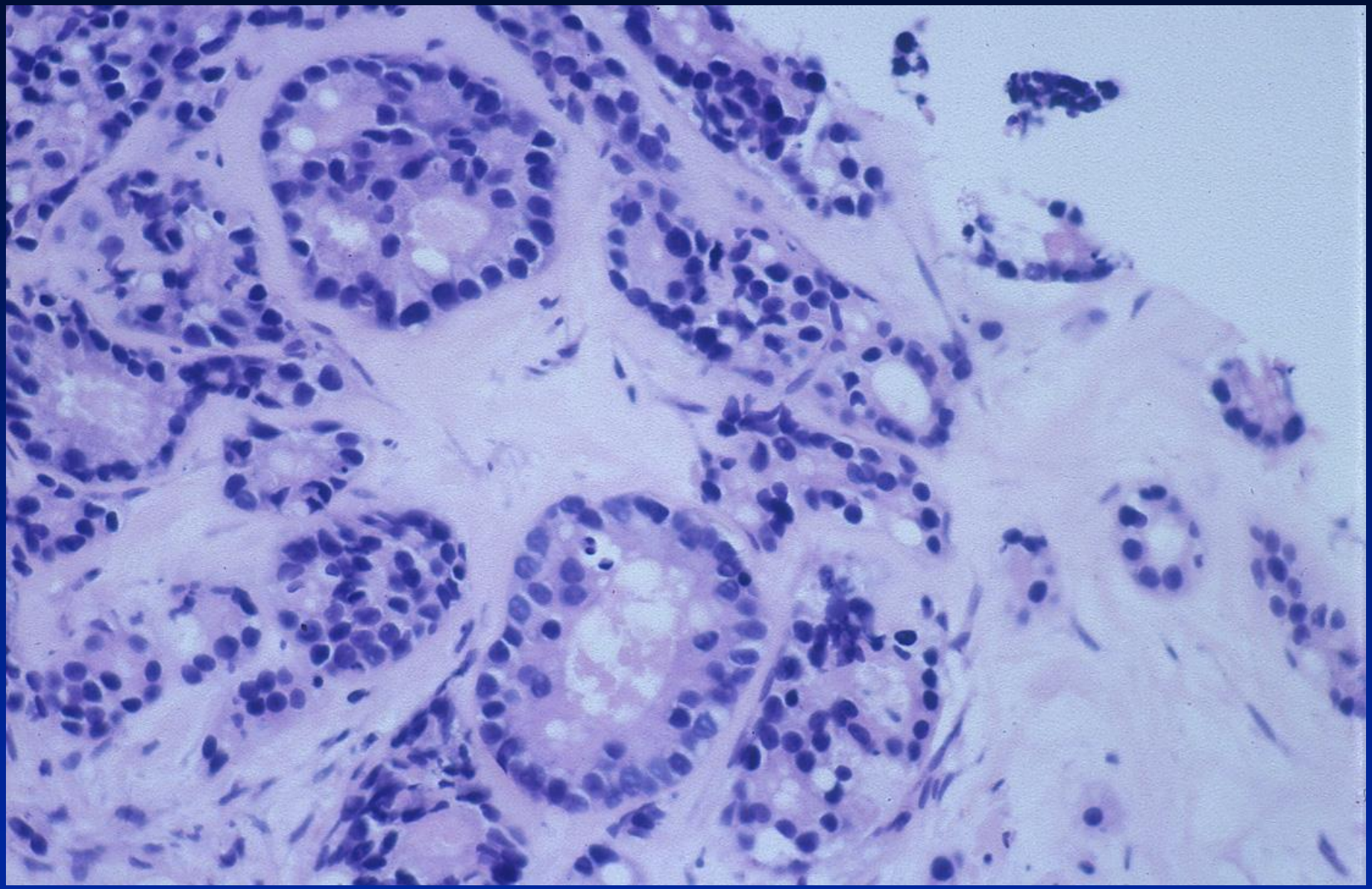

HMB45

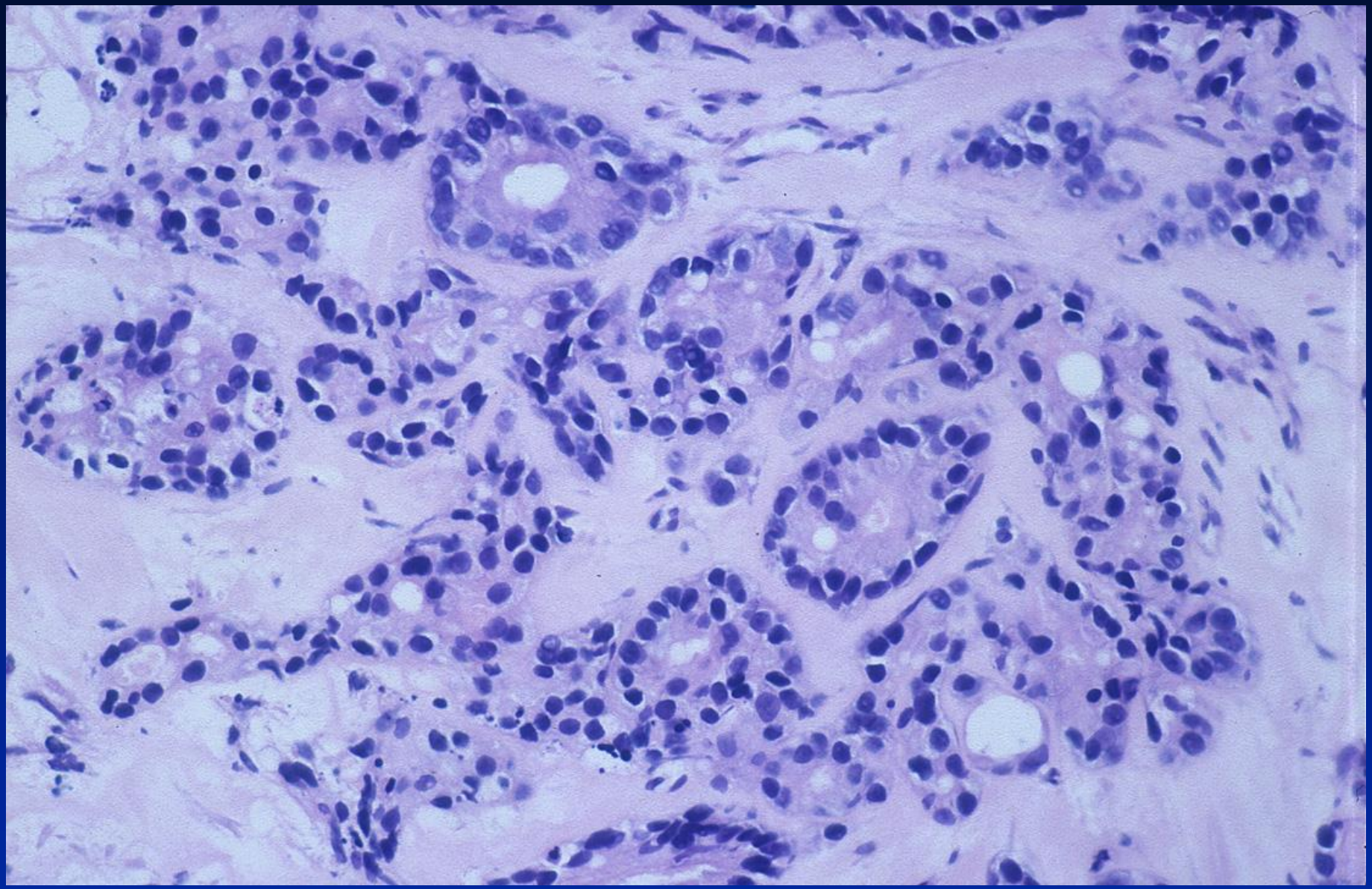
Melanoma

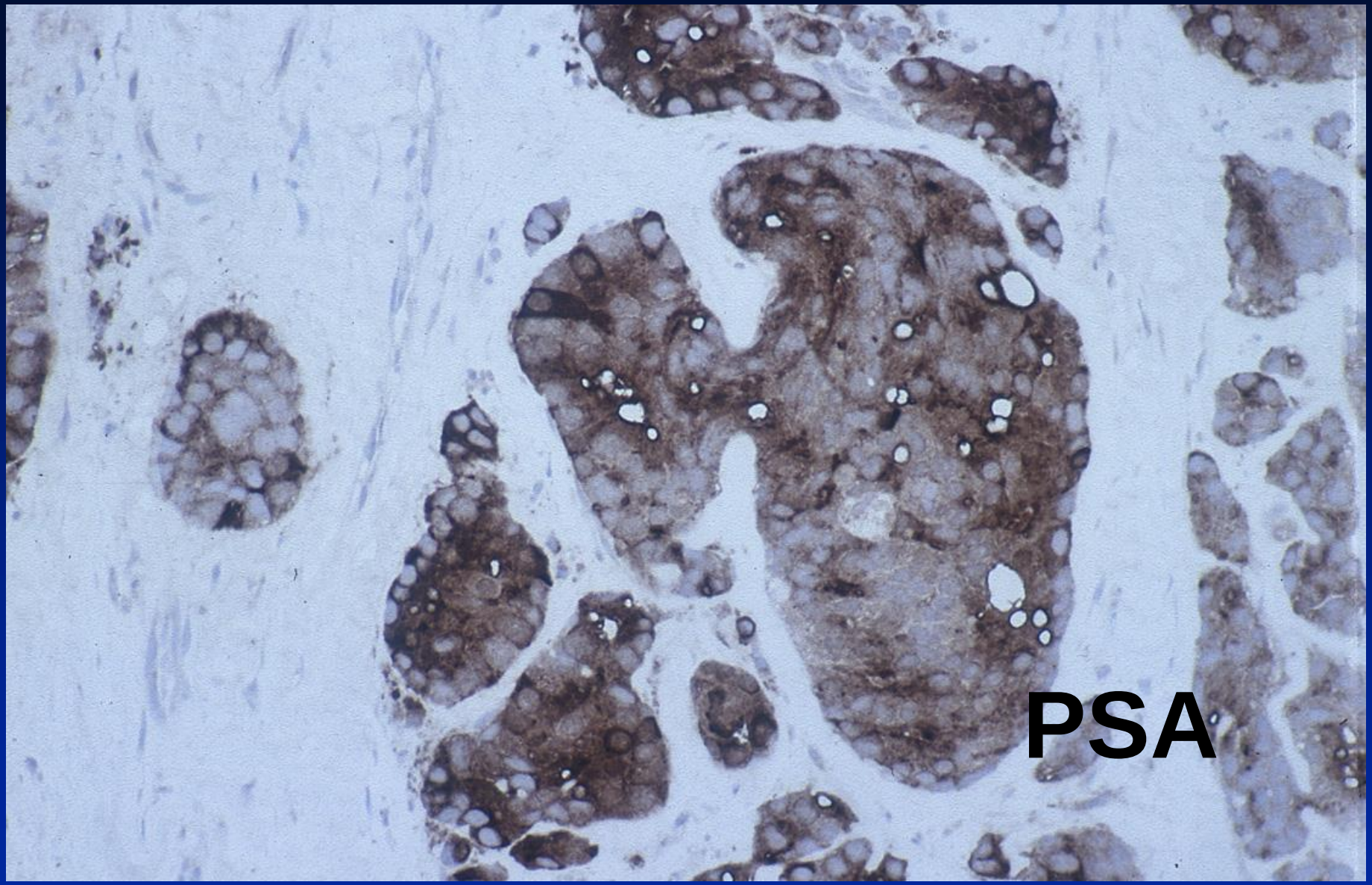
S100	95%+
HMB45	90-100% (primary)
	80% (metastases)
Melan A	80-90%

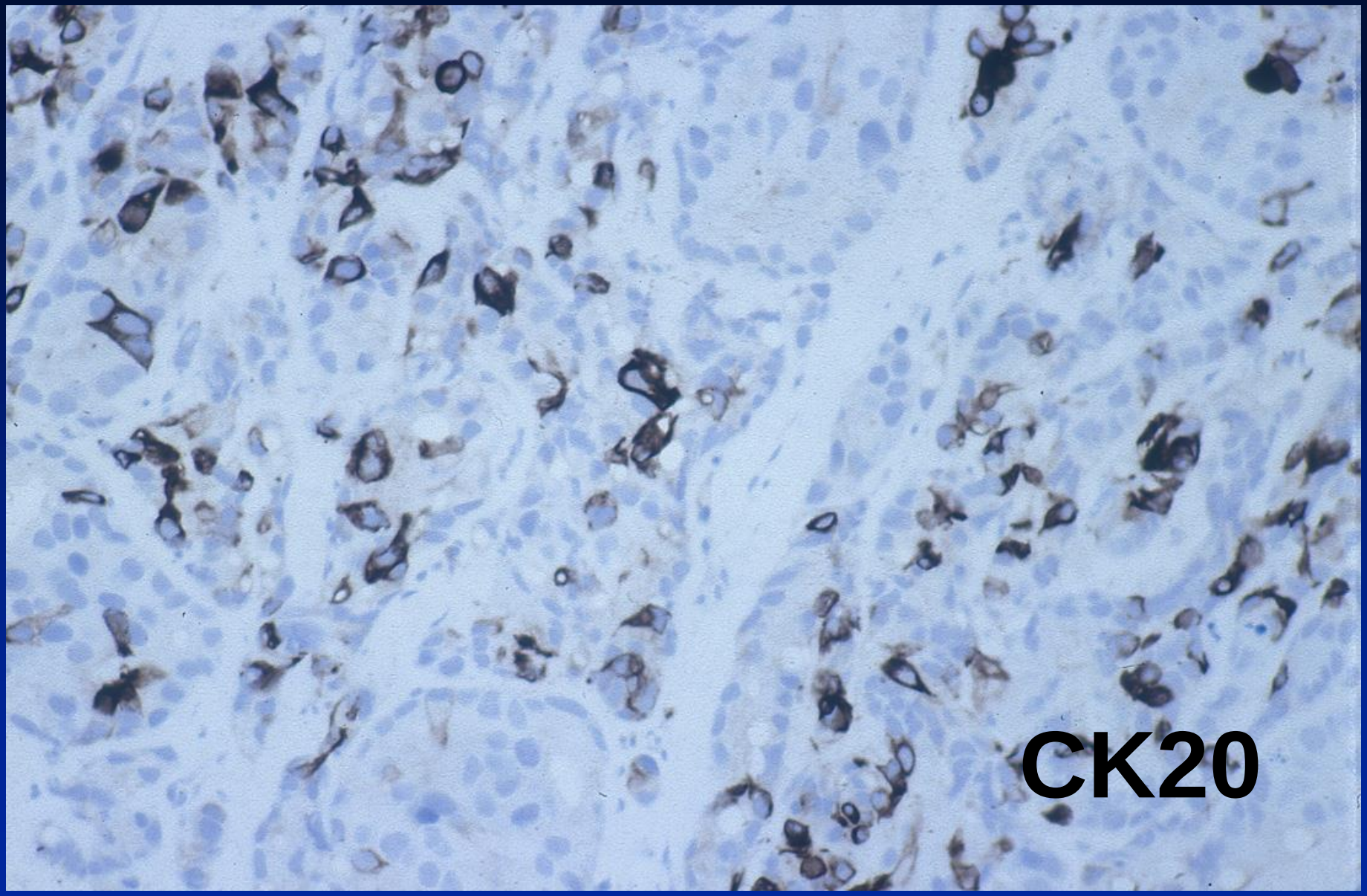
Aberrant expression

- Cytokeratins esp CAM5.2
- EMA
- CD68
- CD38





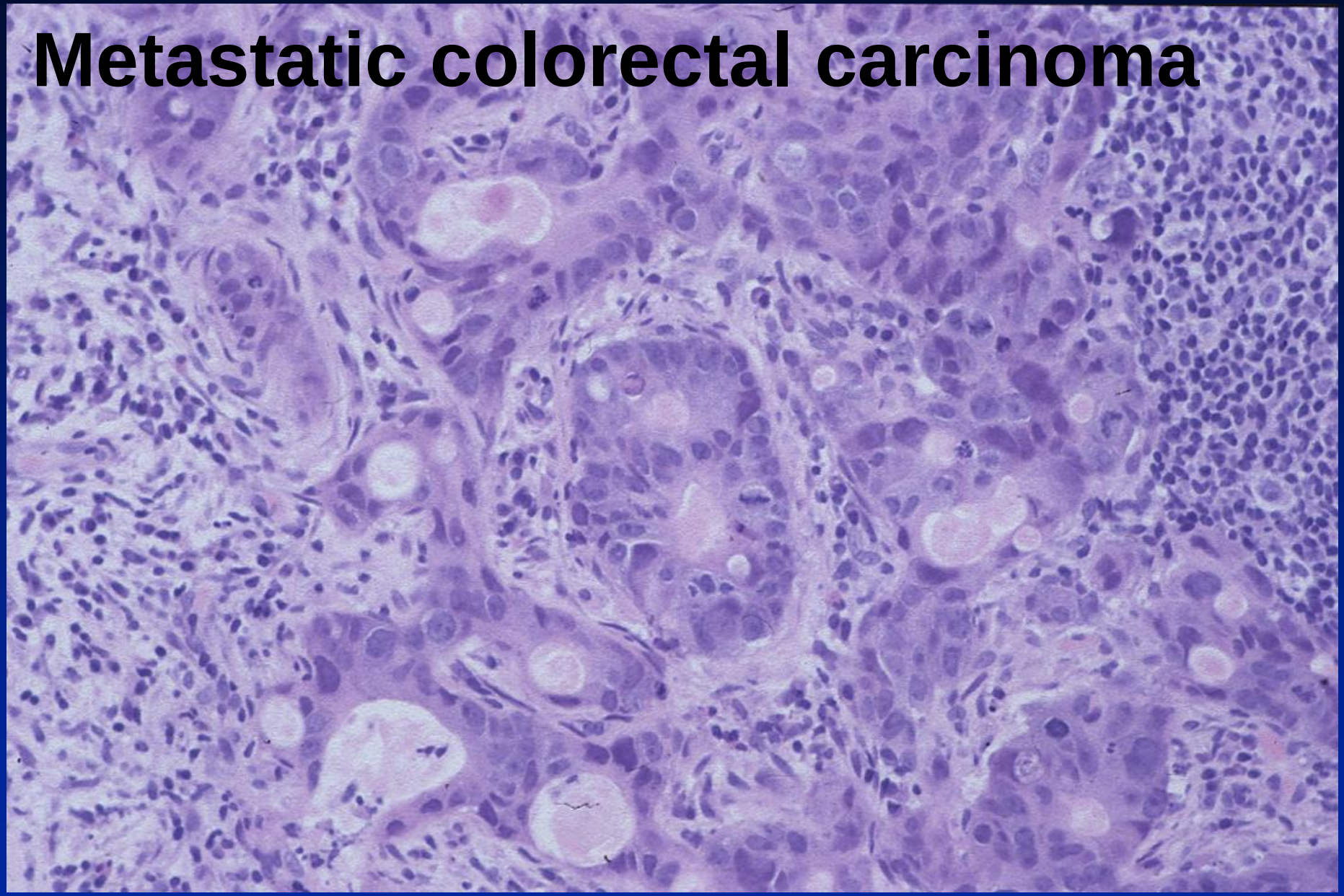

PSA

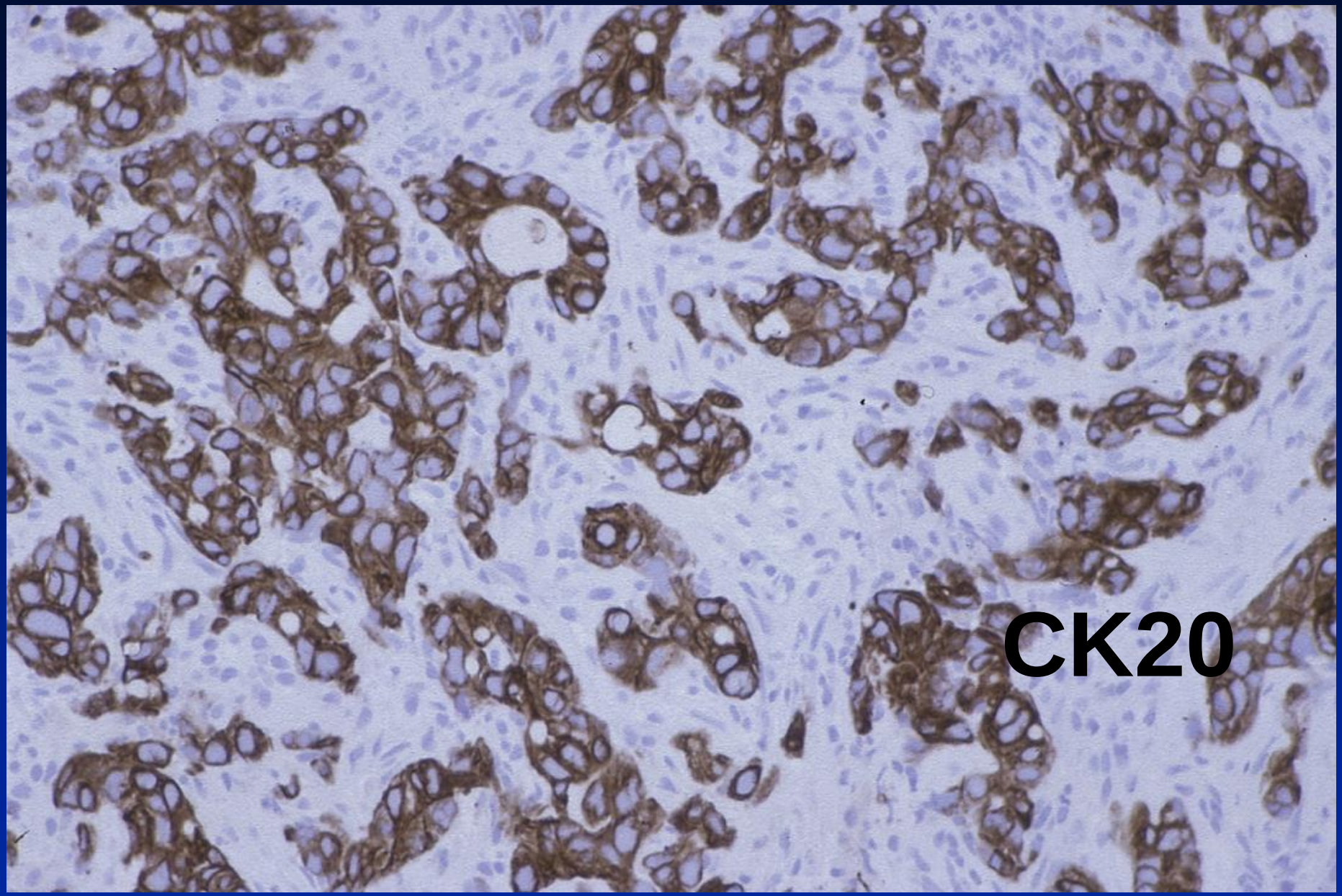

CK20

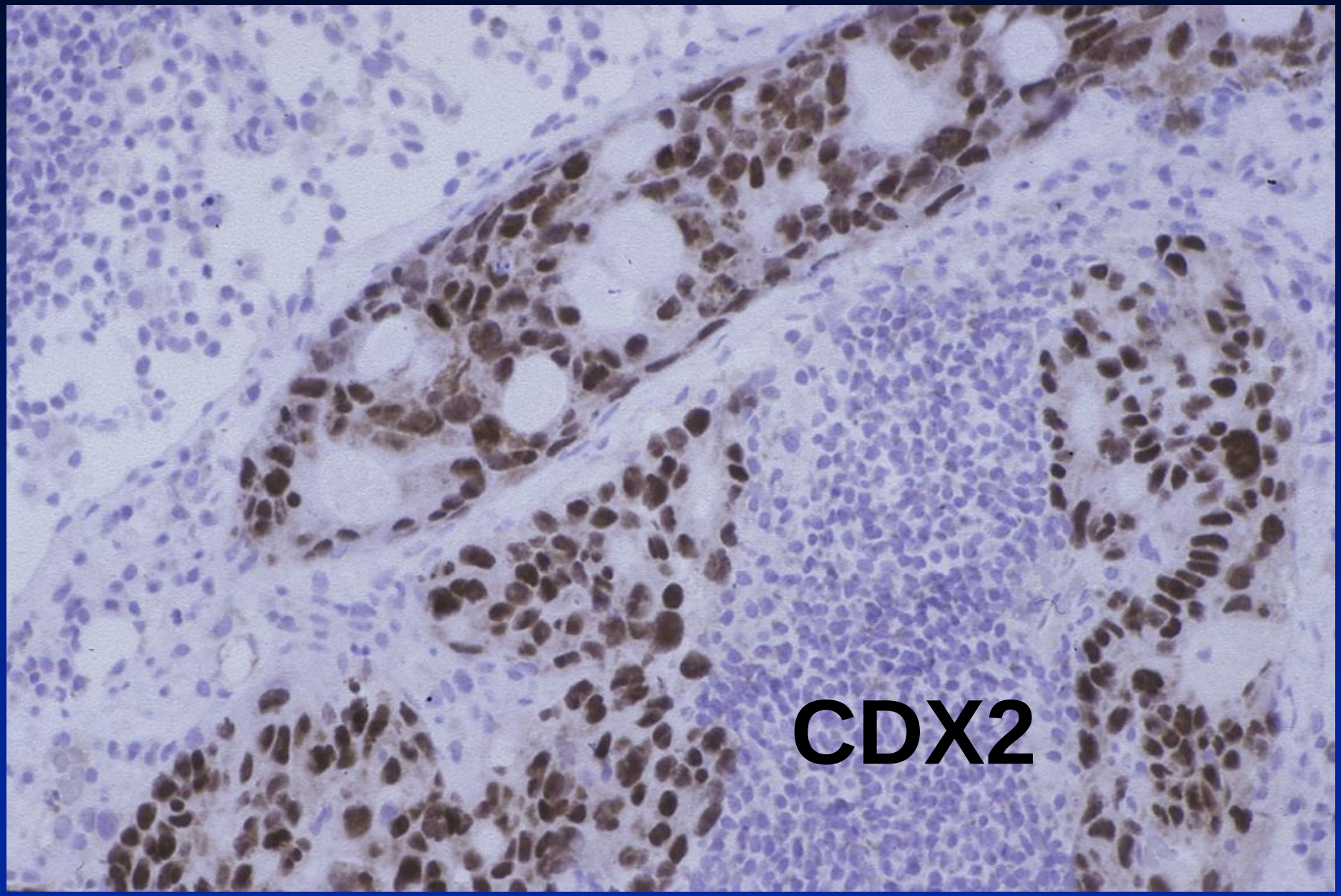
Carcinoma of prostate

- Prostate specific antigen 95 - 100%
  (Male Breast Ca 7/45 (16%))
- Prostatic acid phosphatase up to 100%
  (Male Breast Ca 0/45)
  Can be expressed by salivary gland ca etc
- CK7-/CK20- 60%, CK7-/CK20+ 20%
  ?CK7 & CK20 in male breast cancer
- ER and GCDFP-15 uncommon

Metastatic colorectal carcinoma




CK20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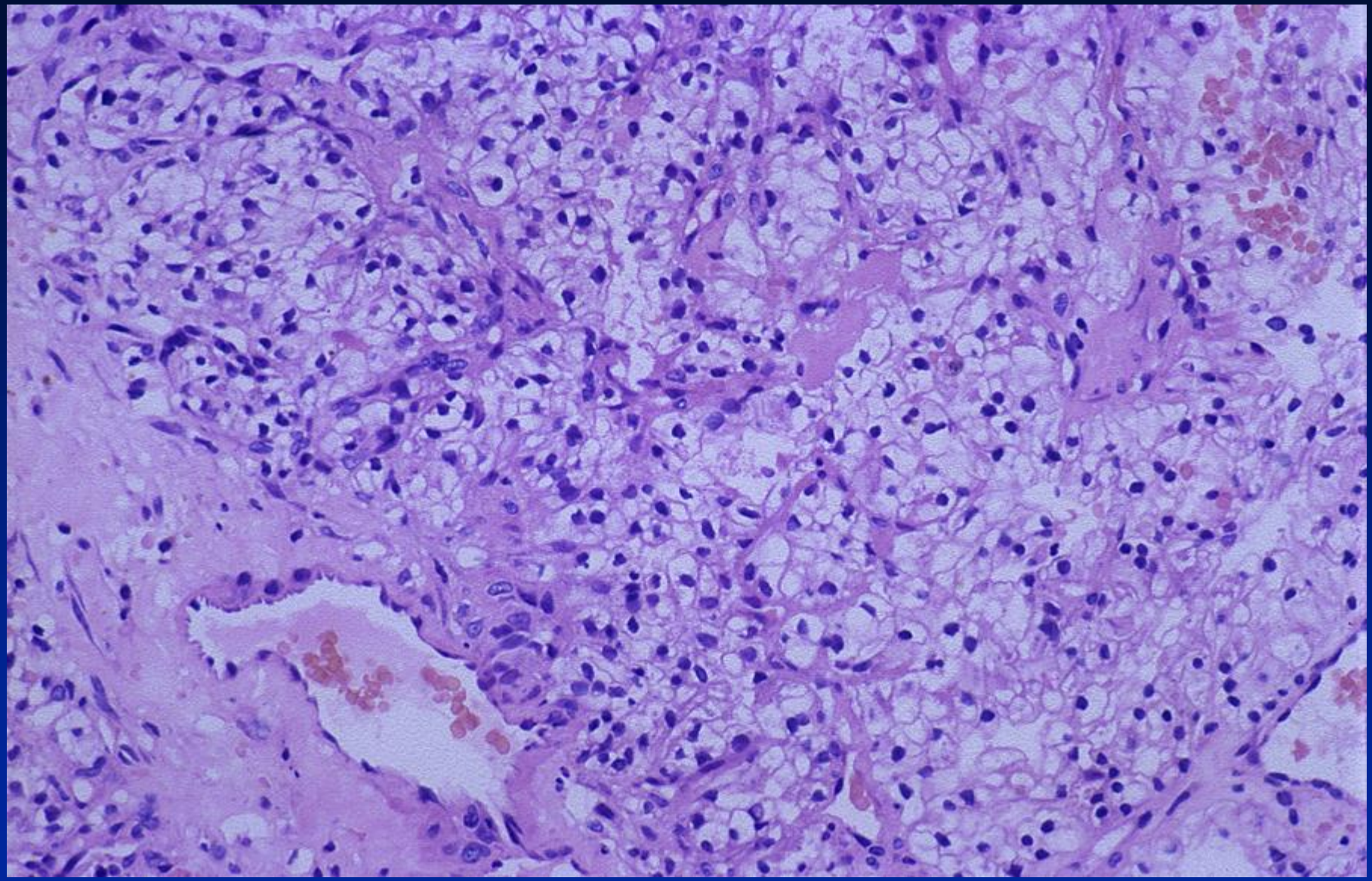

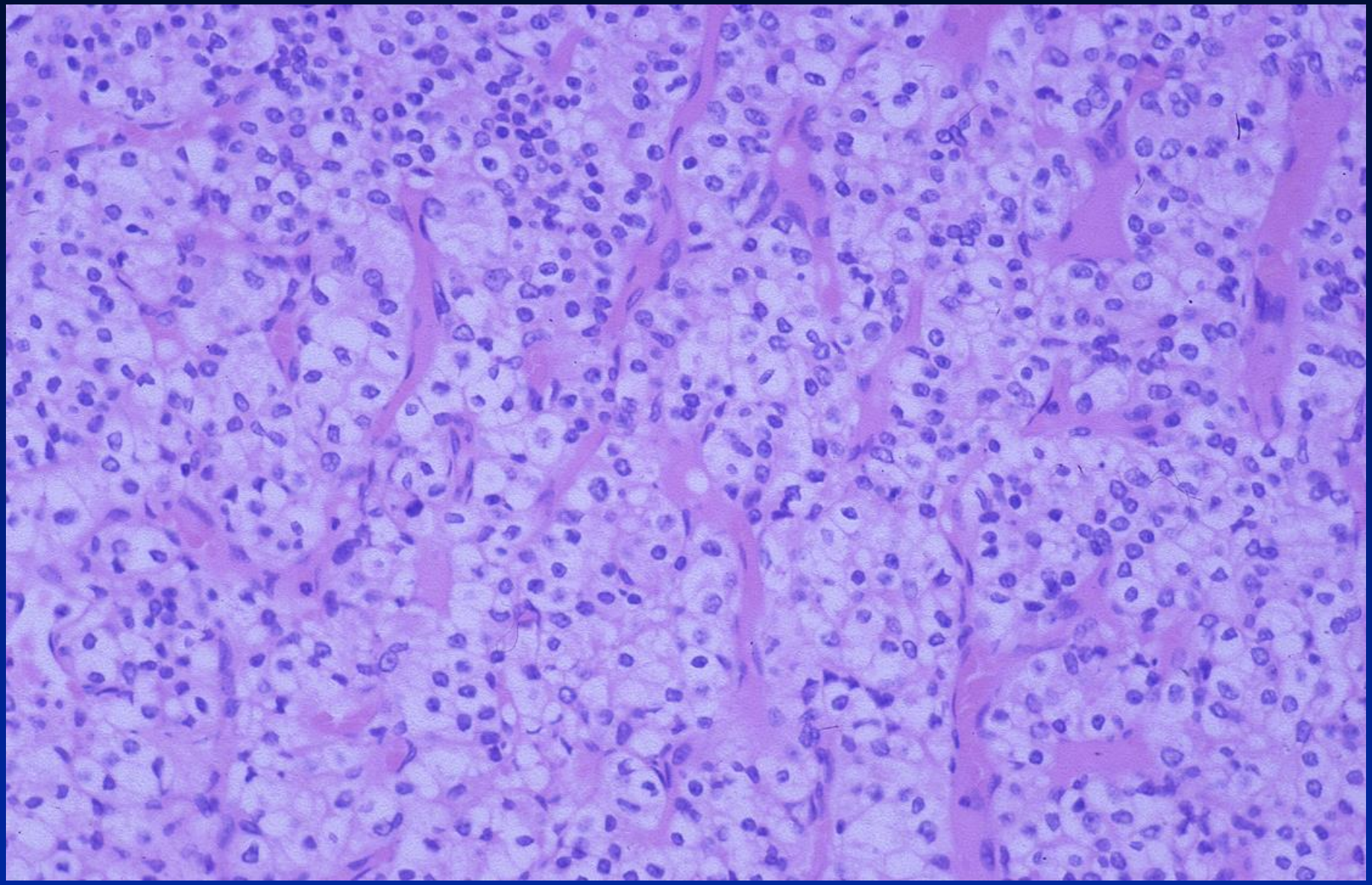

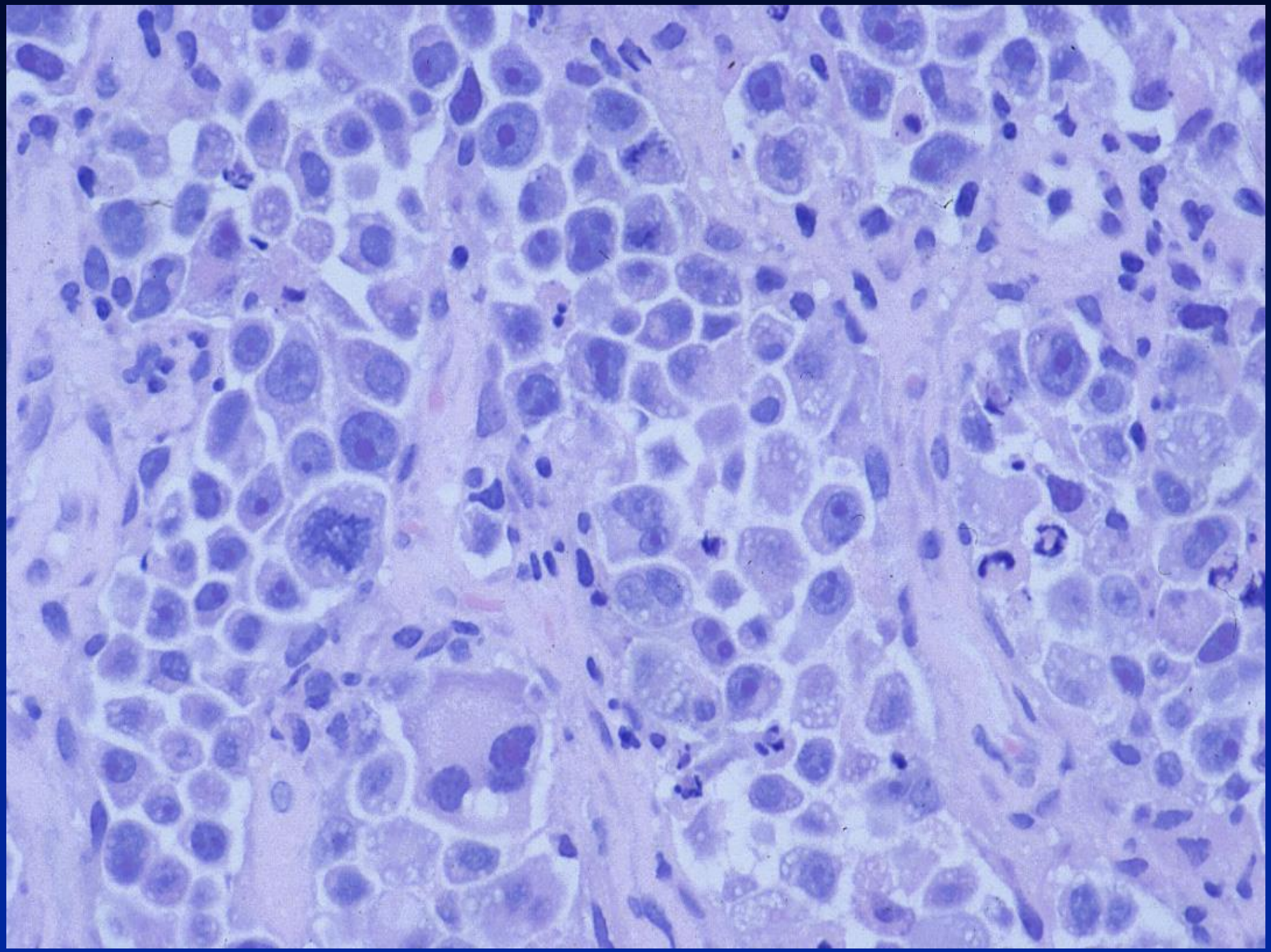

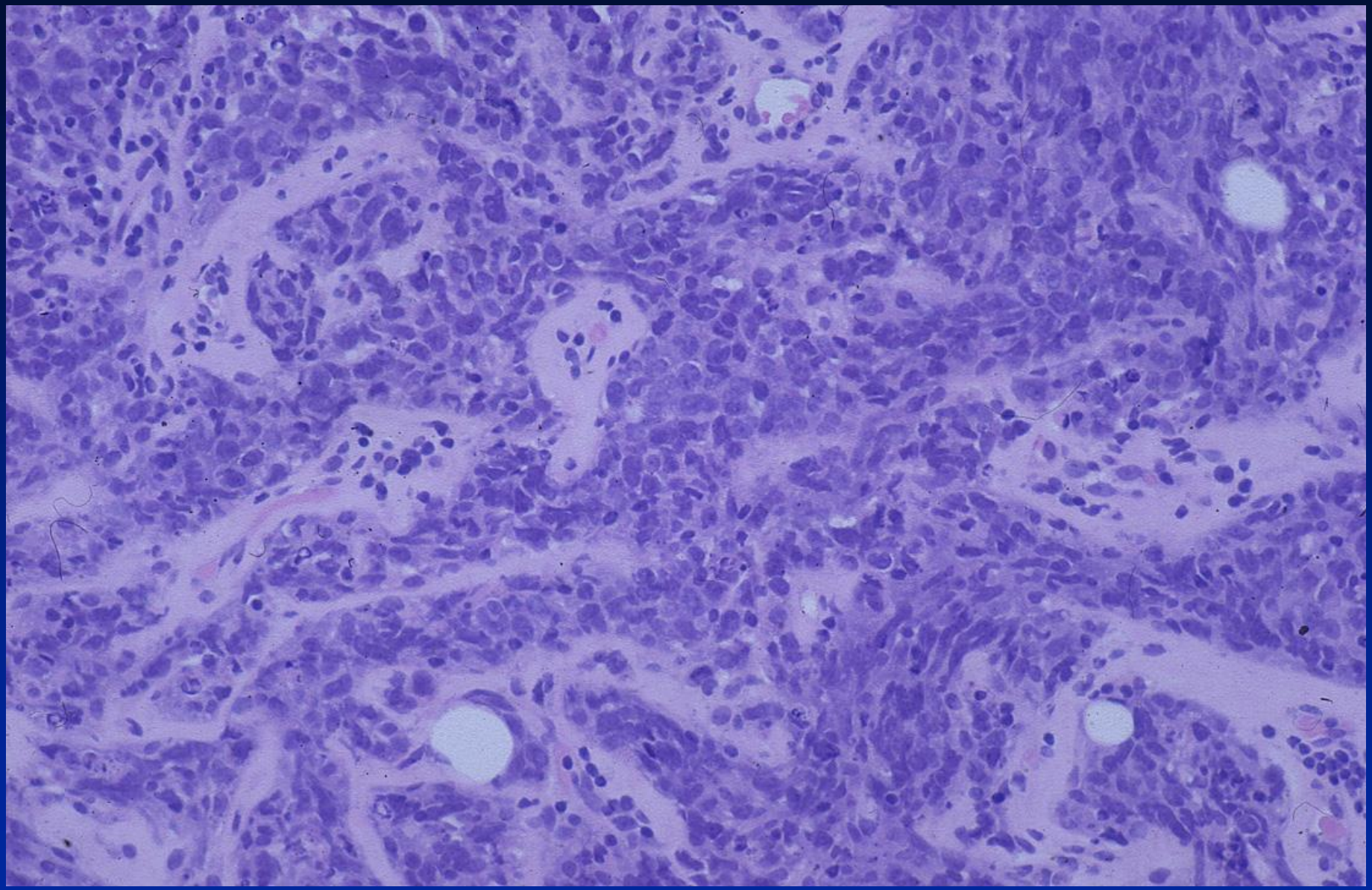

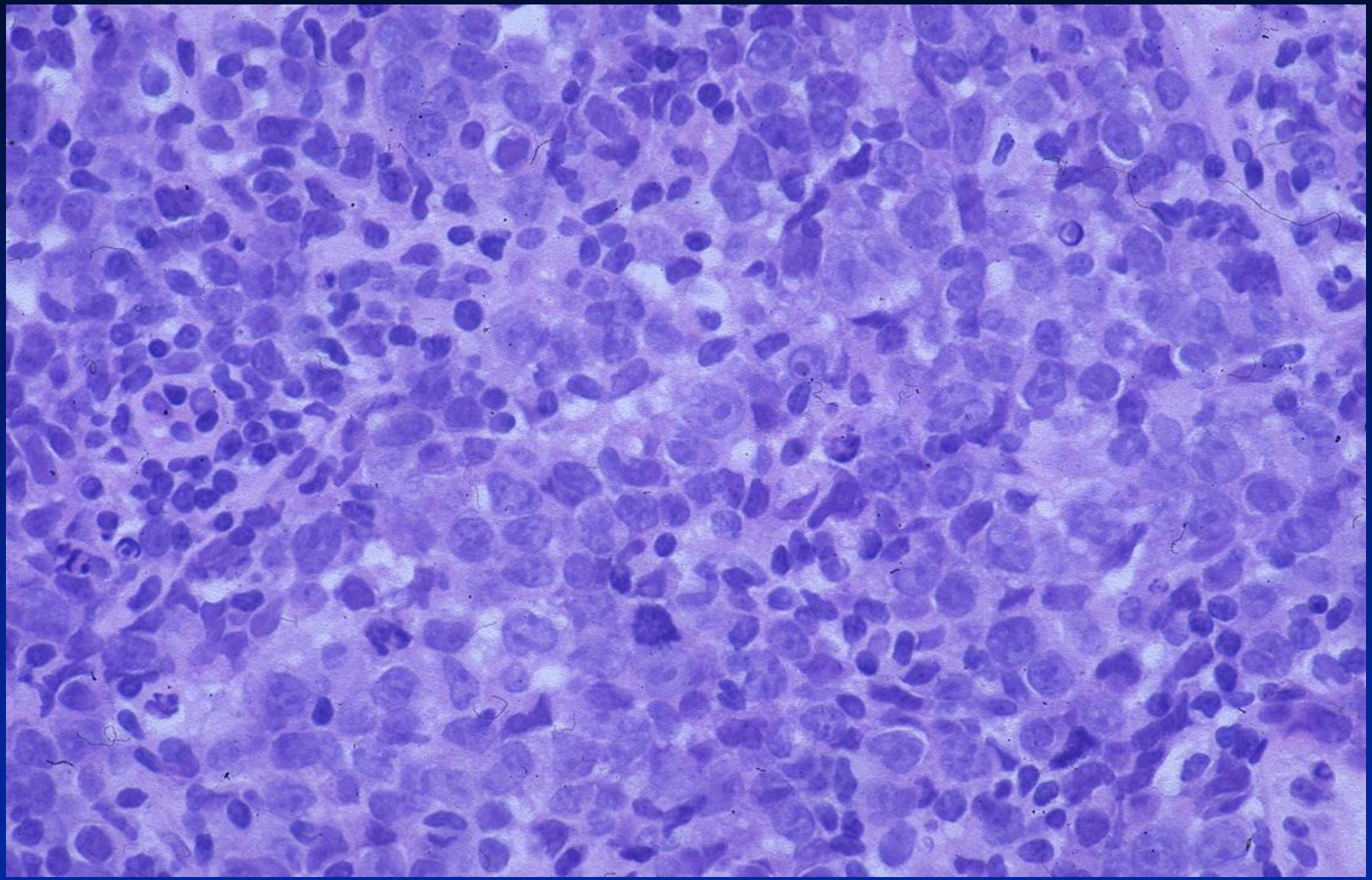

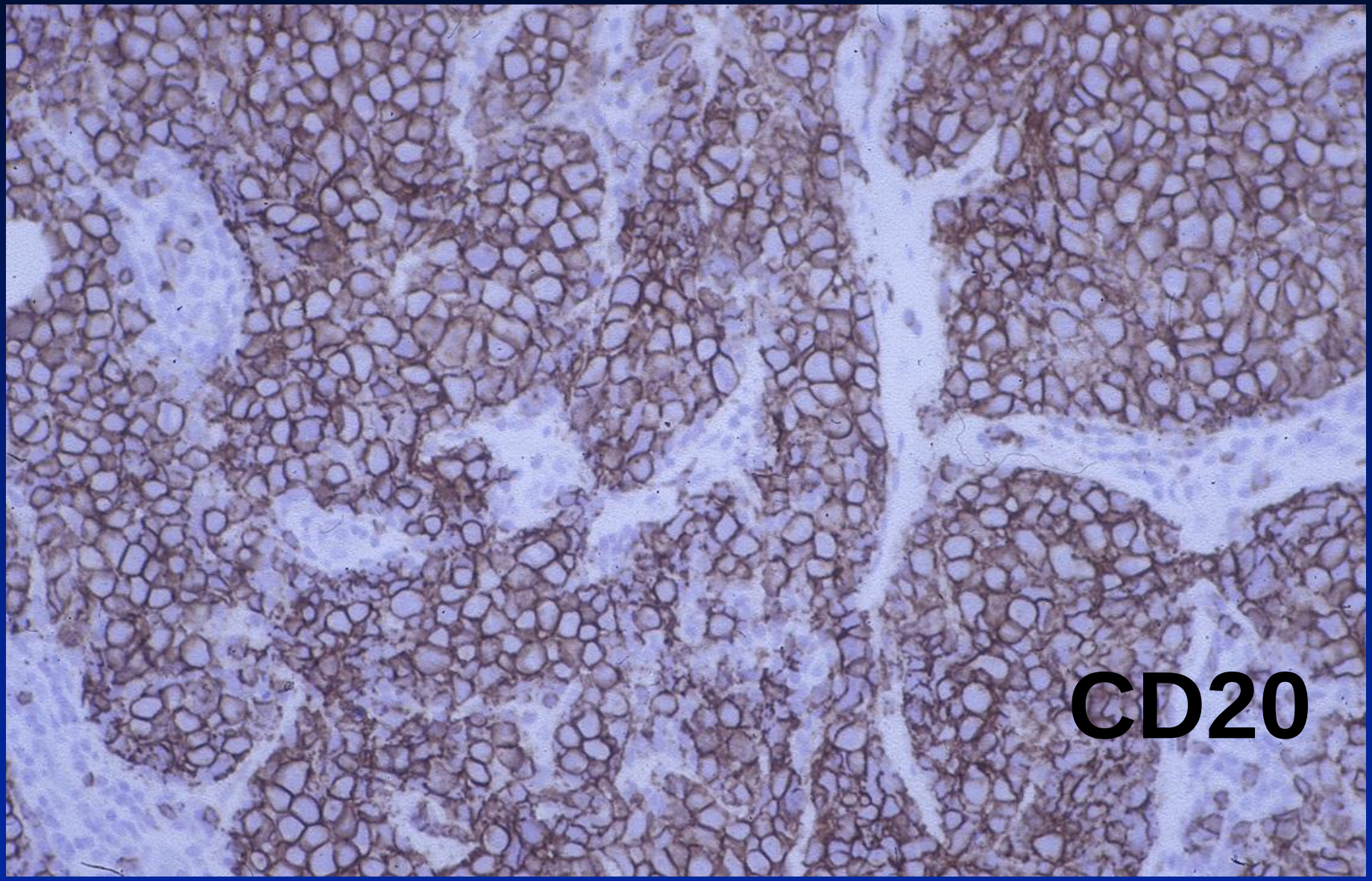
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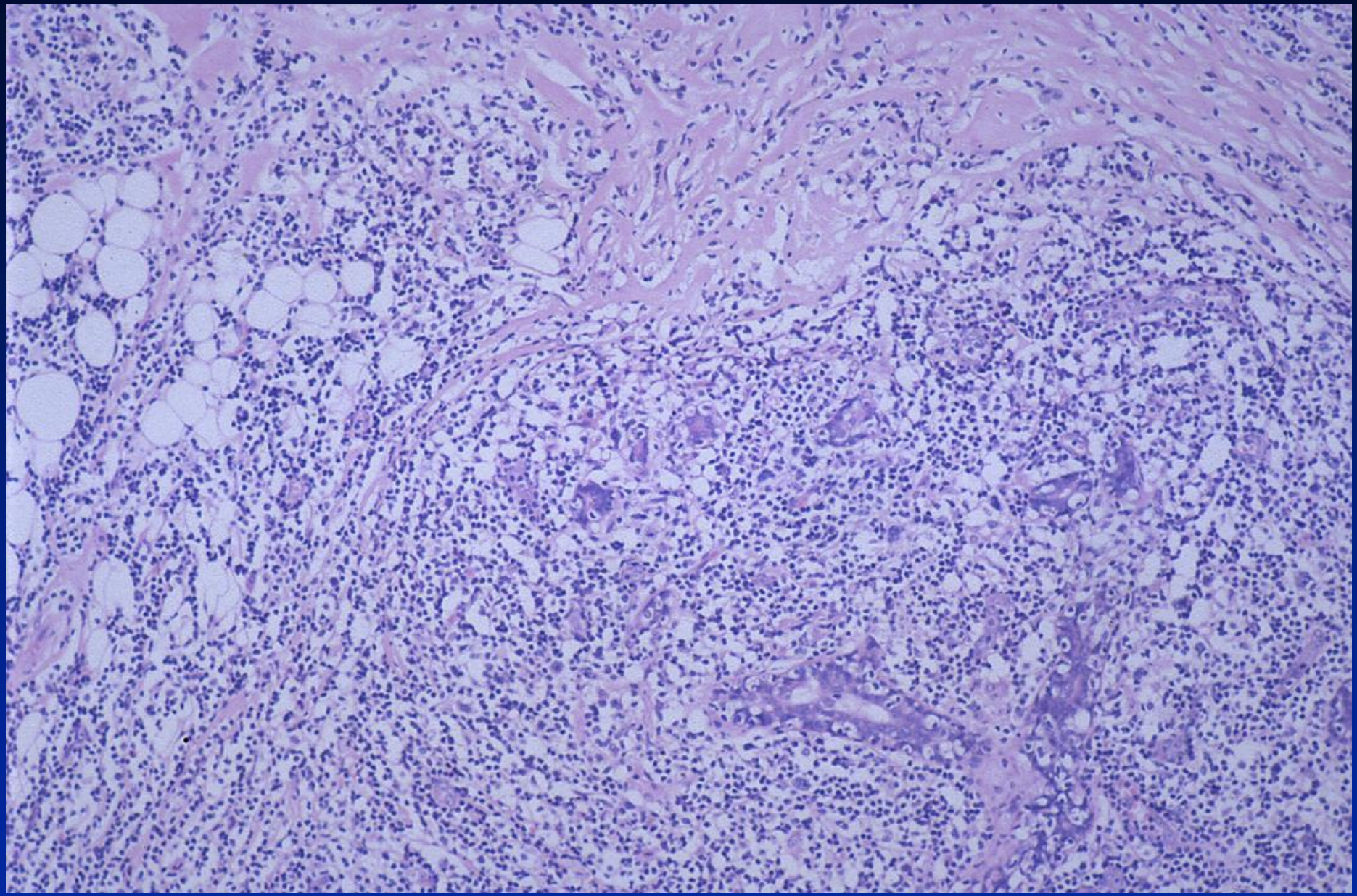

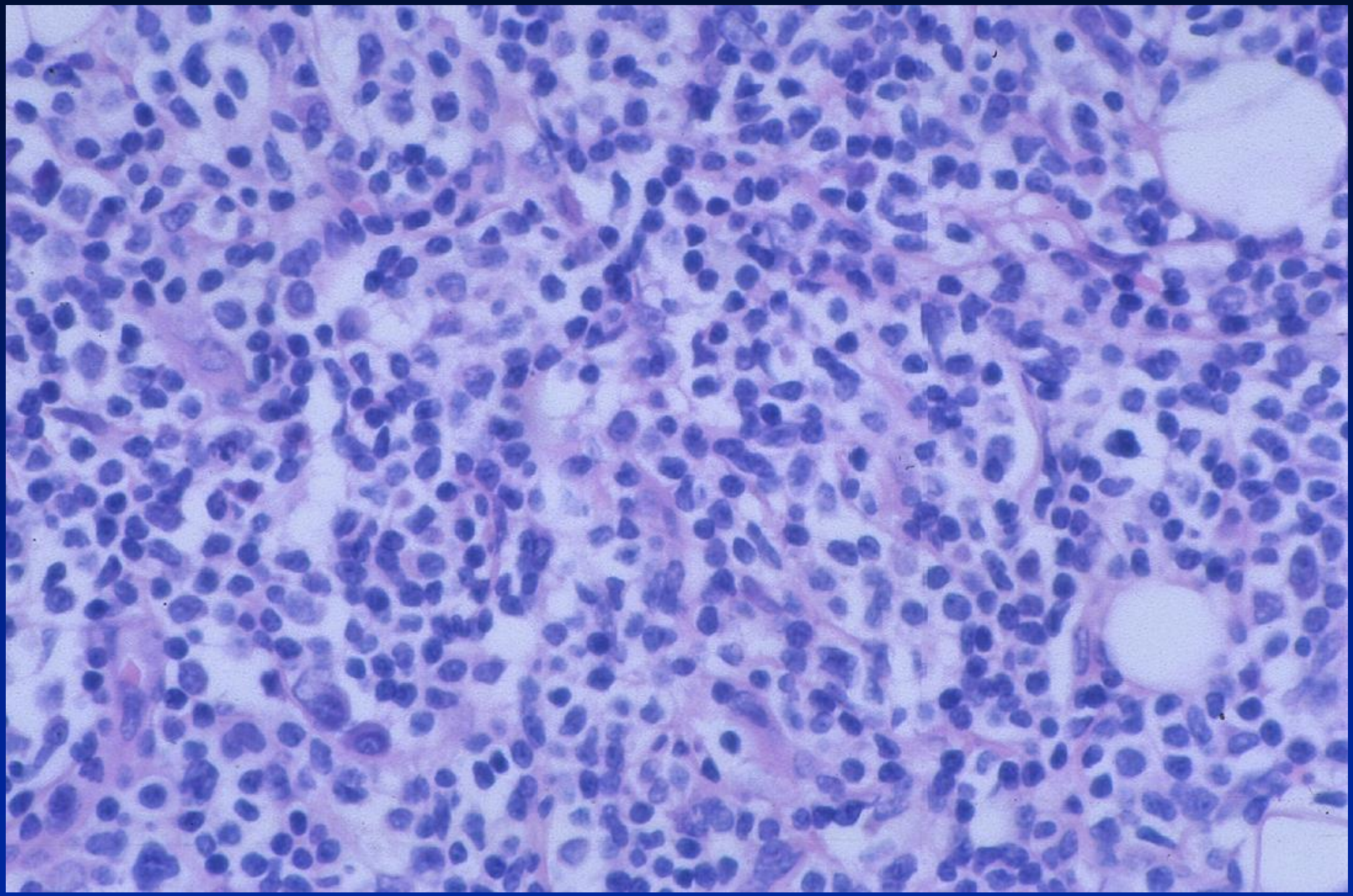

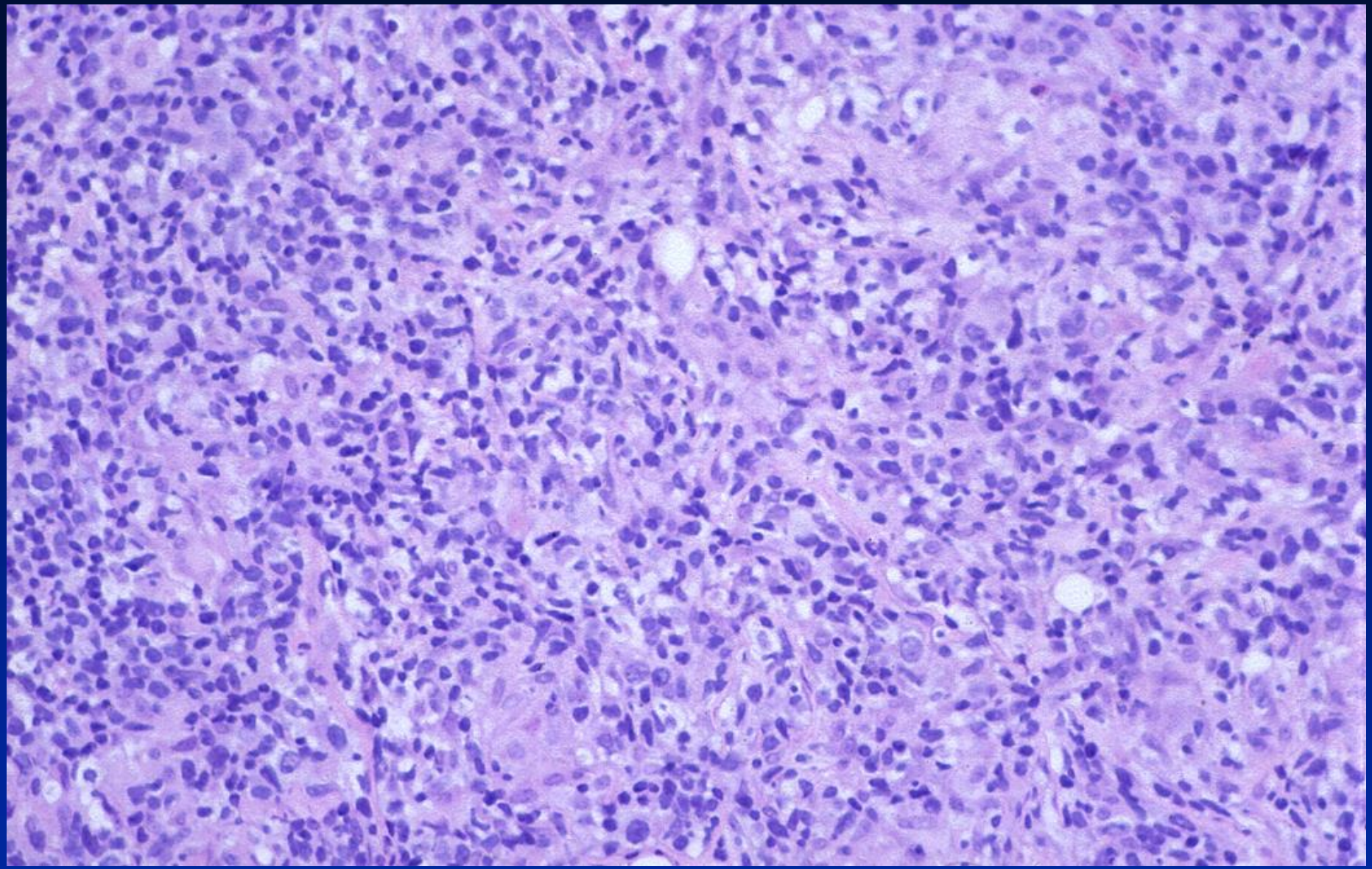

Lymphomas

- Diffuse large B cell
- Follicular
- Marginal zone
- Small lymphocytic/CLL
- T cell
- Distinction of primary and secondary based on clinical features
- Need to consider diagnosis
- Specialist opinion

Metastases to the breast

- Clinical history very helpful
- Important clue is pathology not typical of breast
- Lack of elastosis, calcification and carcinoma in situ
- Compare with primary
- Immunohistochemistry panel
- Clinically important diagnosis