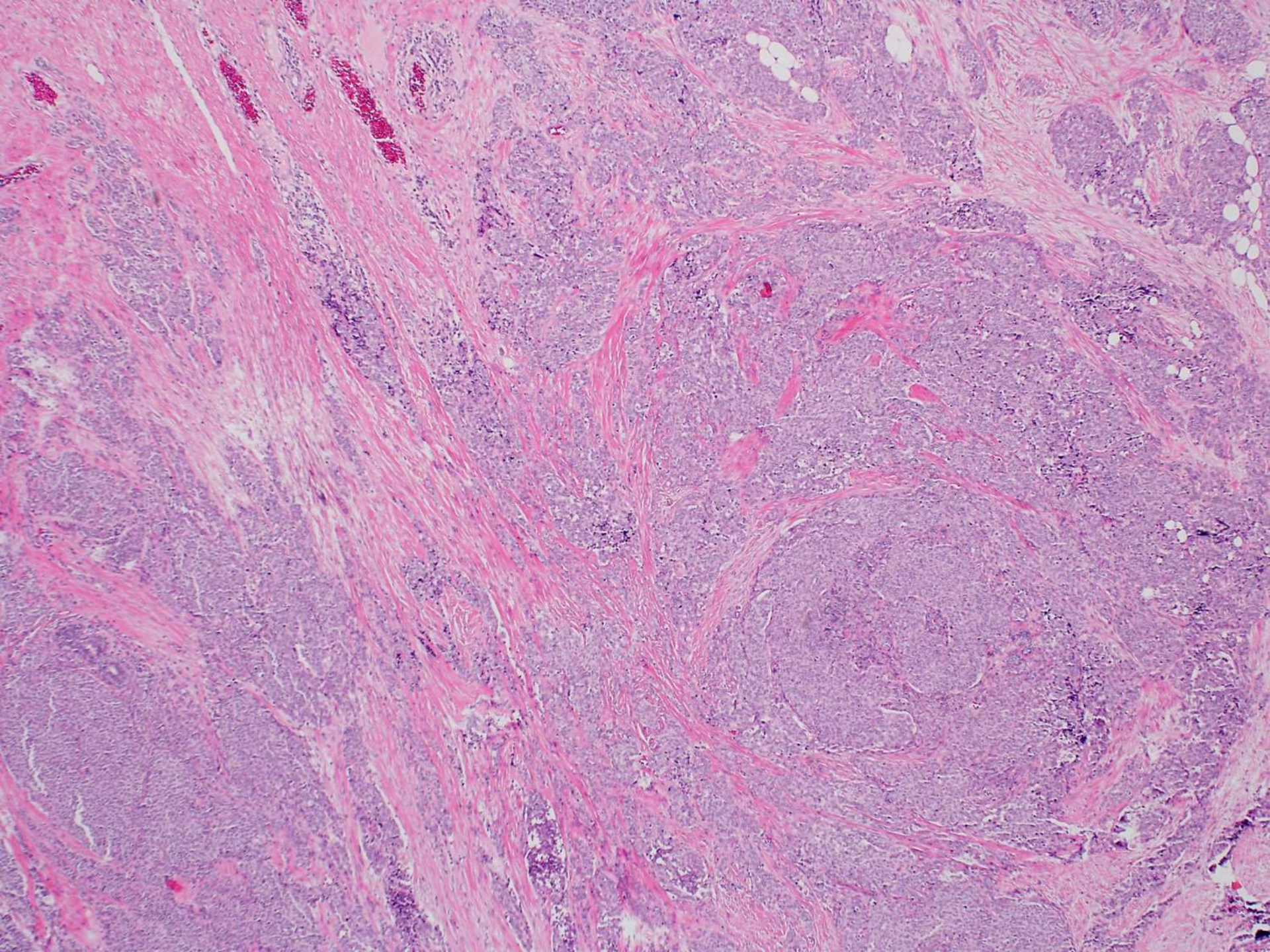
JULY 2021 DIAGNOSIS LIST

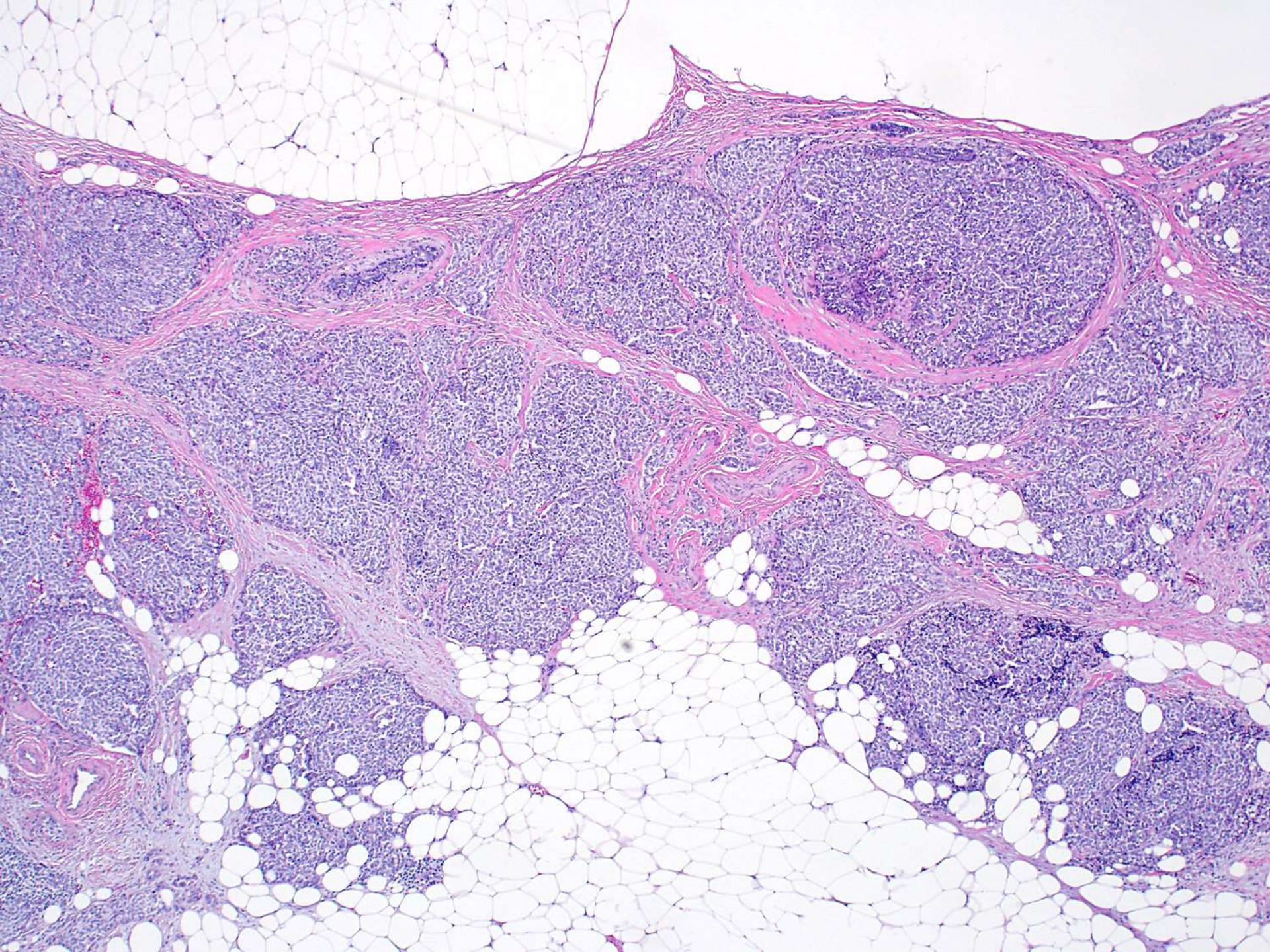
21-0701: metastatic neuroendocrine tumor (ACTH secreting) [breast/breast path]
21-0702: interstitial cystitis with clonal B-cell expansion [bladder/hemepath&GU path]
21-0703: periductal stromal tumor/sarcoma [breast/breast path]
21-0704: clear cell hidradenoma like tumor [lymph node/dermpath& soft tissue path]
21-0705: FSGS, collapsing glomerulopathy, COVID related [kidney/med kidney path]
21-0706: COVID related thrombosis [kidney/med kidney path]
21-0707: metastatic meningioma [liver/GI path]

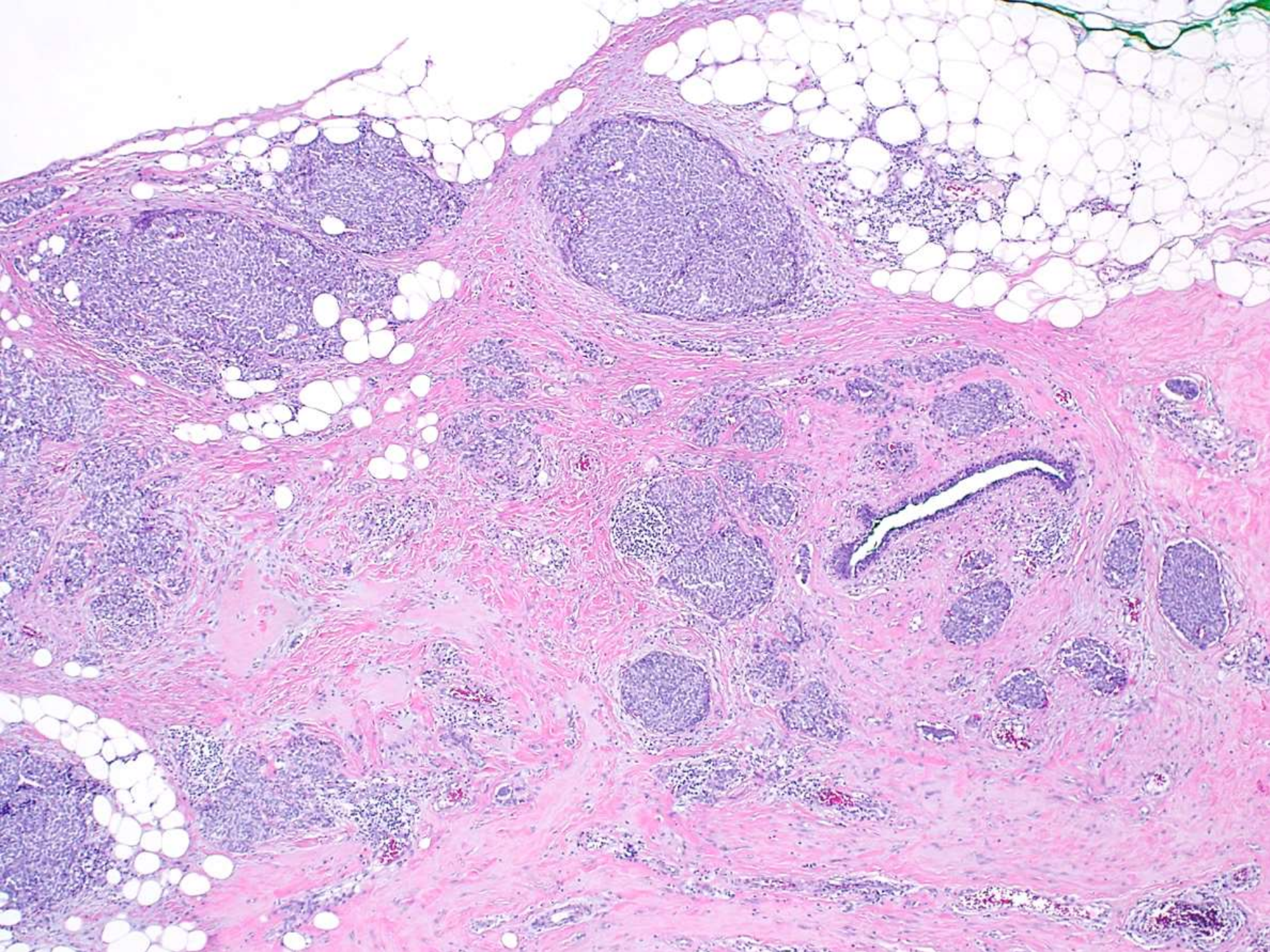
21-0701

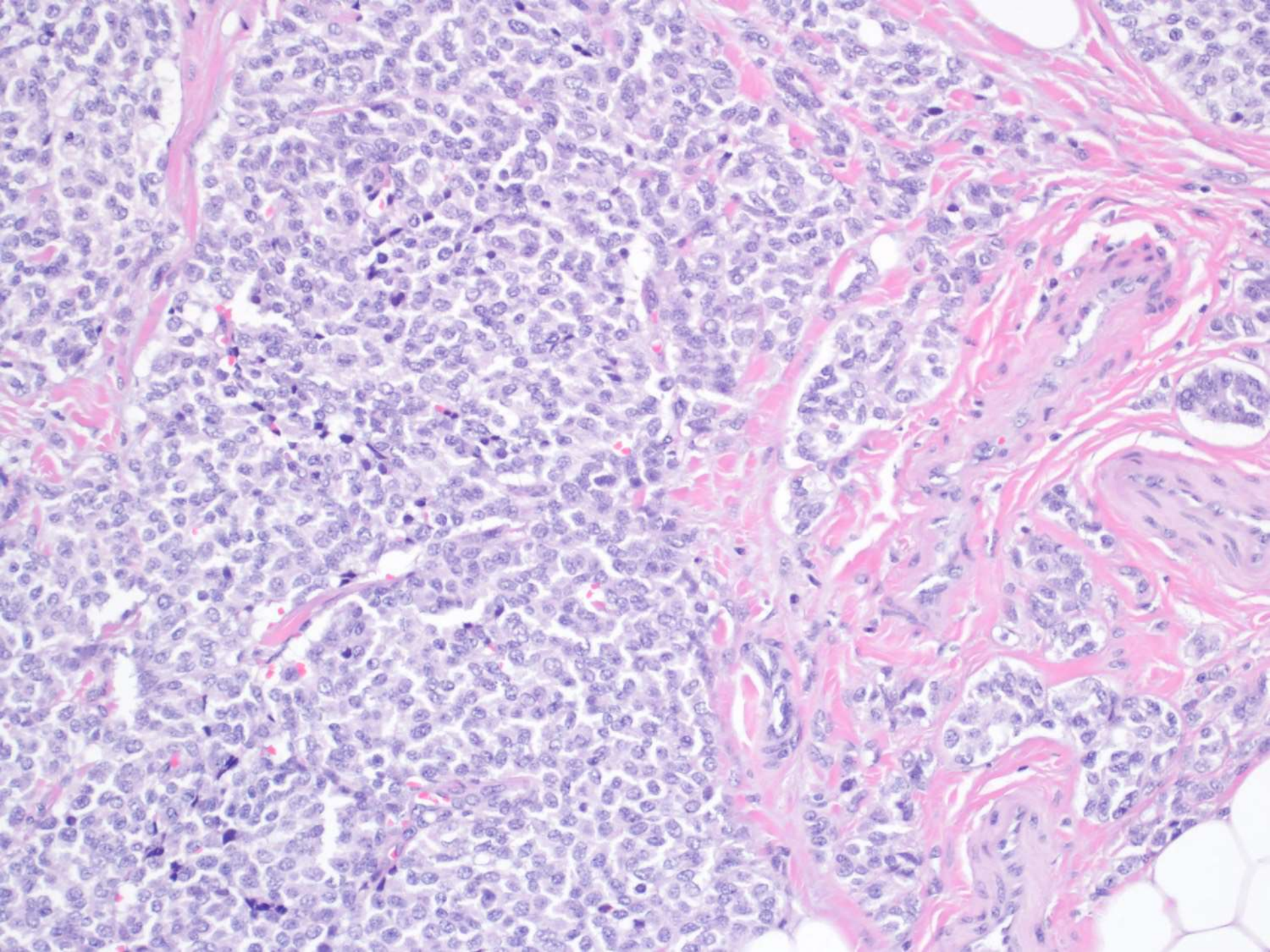
Megan Troxell; Stanford

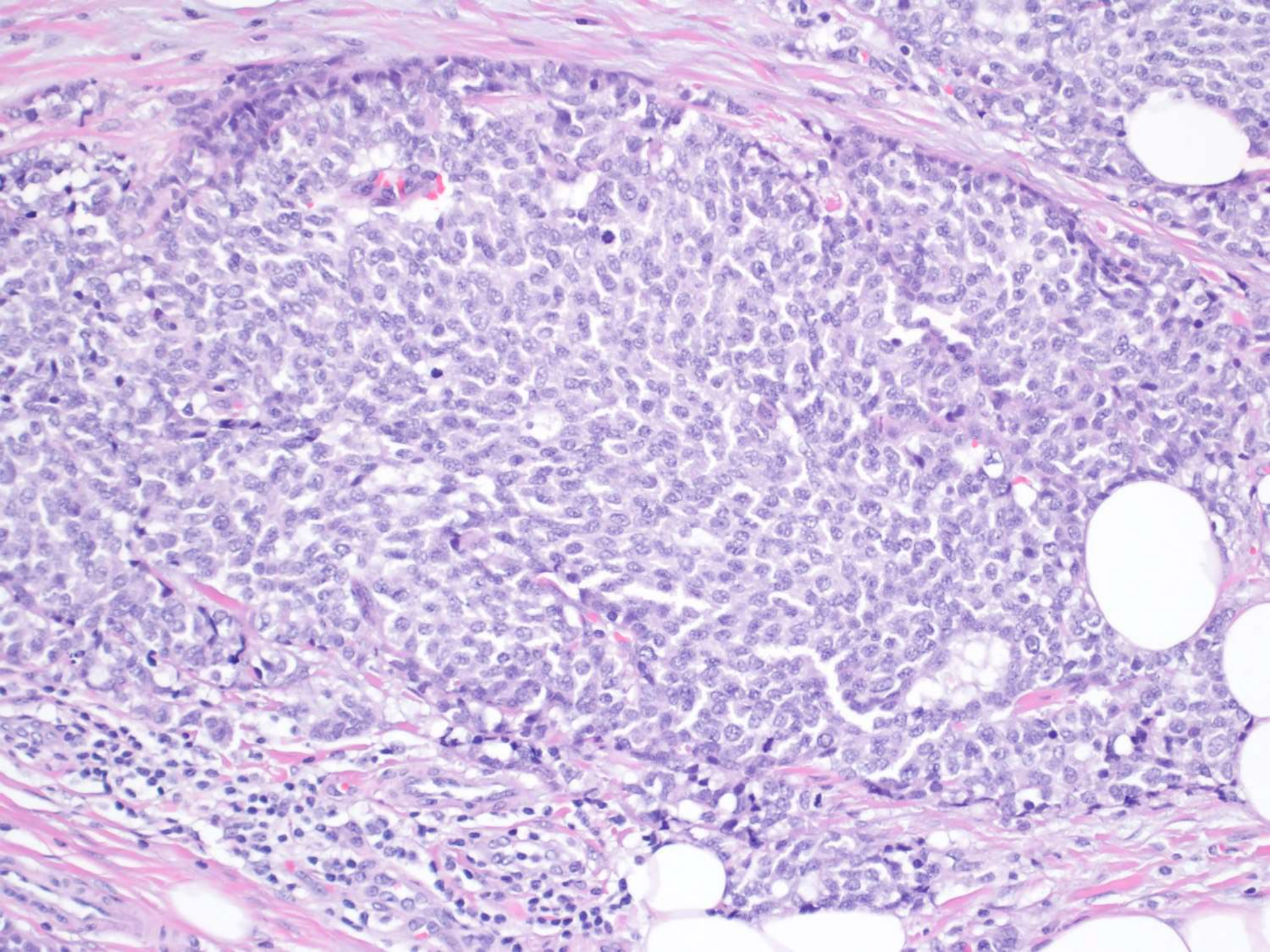
35-year-old F with breast lesion; needle biopsy benign; lumpectomy performed.

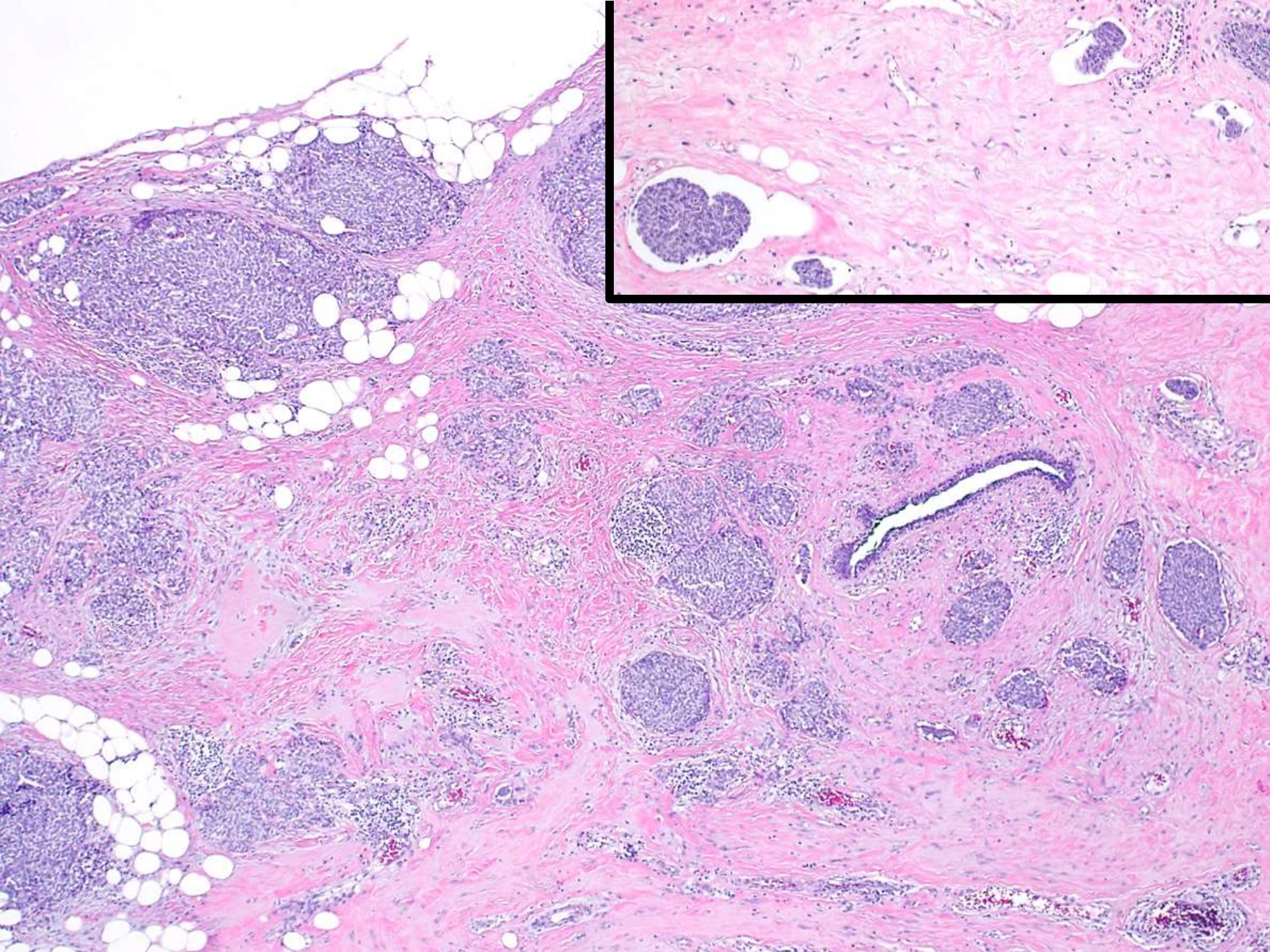




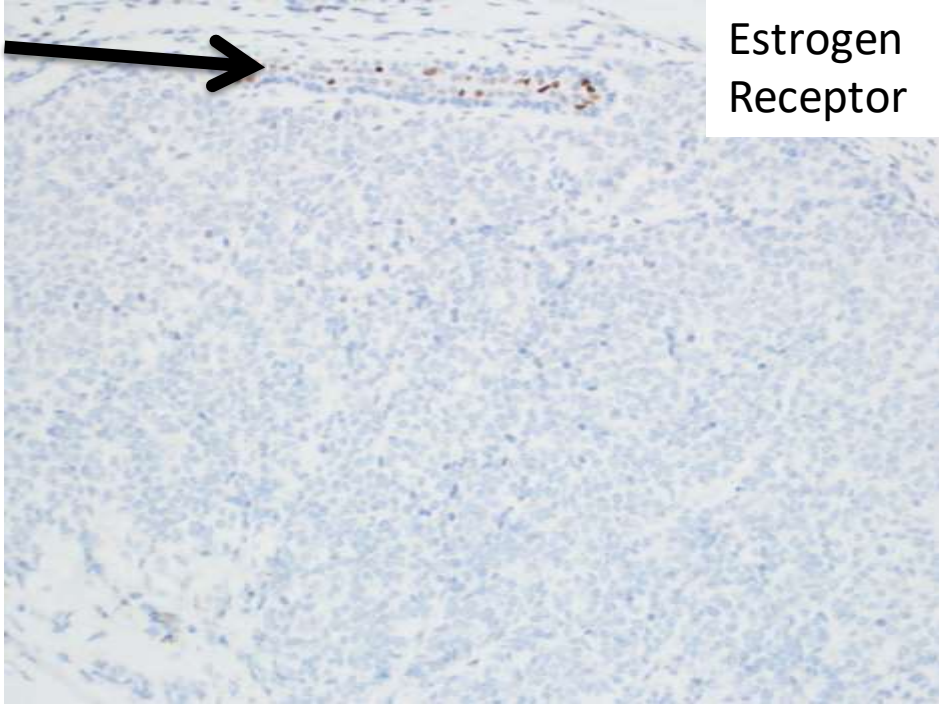


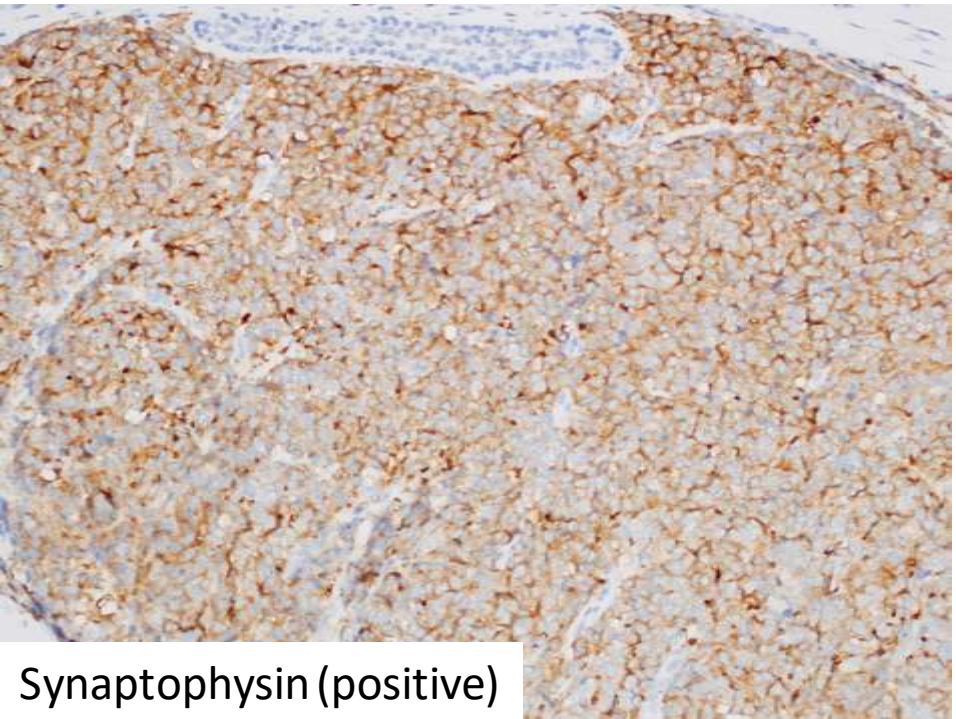


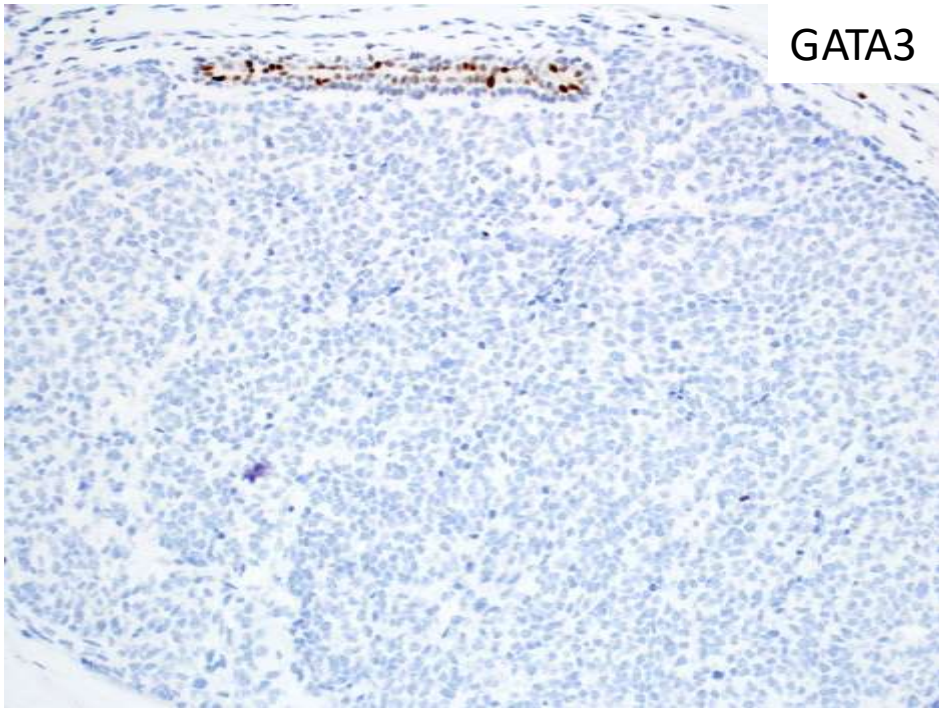




- Negative
  - Breast stains
    - ER, GATA3, BRST2, Mammaglobin
  - TTF-1
  - CDX-2
- Positive
  - ACTH, synapto, chromogranin
  - keratin




Synaptophysin (positive)



The rest of the story…

- 35 year old woman with Cushing's
- Breast lesion discovered in workup for source of ACTH
  - But the pathologist didn't know that
    - started therapy for TNBC
    - Unknown origin; likely lung/mediastinal
  - Clues:
    - Neuroendocrine morphology, r/o metastasis!
    - ER and other breast markers reliable for breast NE
    - Extensive LVI

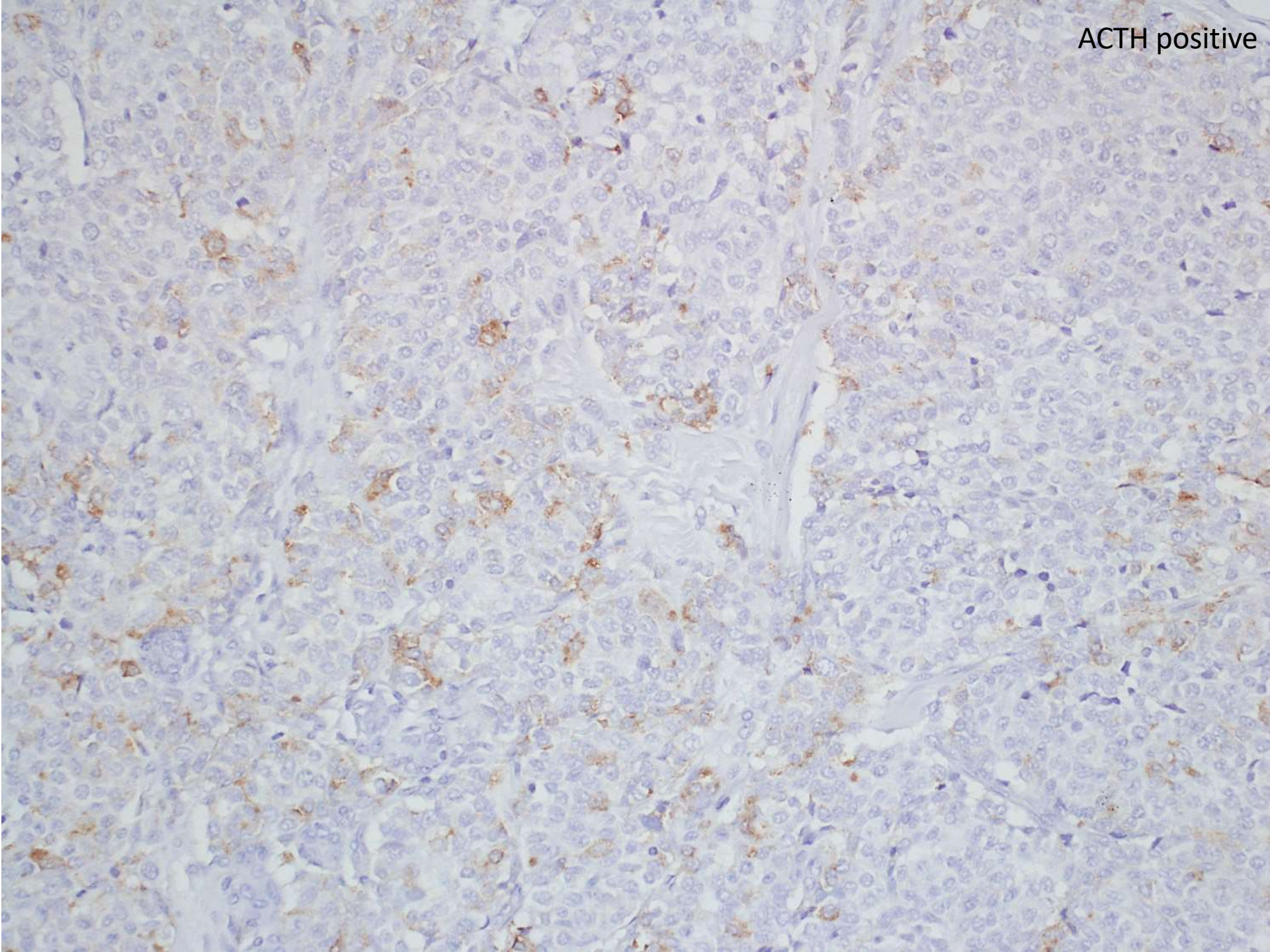

ACTH positive

Table 6
Immunohistochemistry in metastatic well differentiated neuroendocrine carcinoma, versus primary breast carcinoma with neuroendocrine differentiation, compiled from the literature [18,89,102–104].

Stain	Breast primary	Metastatic GI[b]	Metastatic Lung
Estrogen Receptor	88/92 (96%)	2/17 (12%)	2/9 (22%)
Progesterone Receptor	56/78 (82%)	0/17 (0%)	1/9 (11%)
GCDFP – 15	24/56 (43%)	0/10 (0%)	0/5 (0%)
Mammaglobin	26/56 (46%)	0/10 (0%)	0/5 (0%)
GATA3	32/32 (100%)	0/14 (0%)	
CDX2	0/40 (0%)	16/16 (100%)[a]	0/4 (0%)
TTF – 1	0/47 (0%)[c]	0/10 (0%)	6/11 (55%)
CK7	37/49 (92%)	0/10 (0%)	3/5 (60%)
CK20	0/40 (0%)	0/10 (0%)	0/5 (0%)

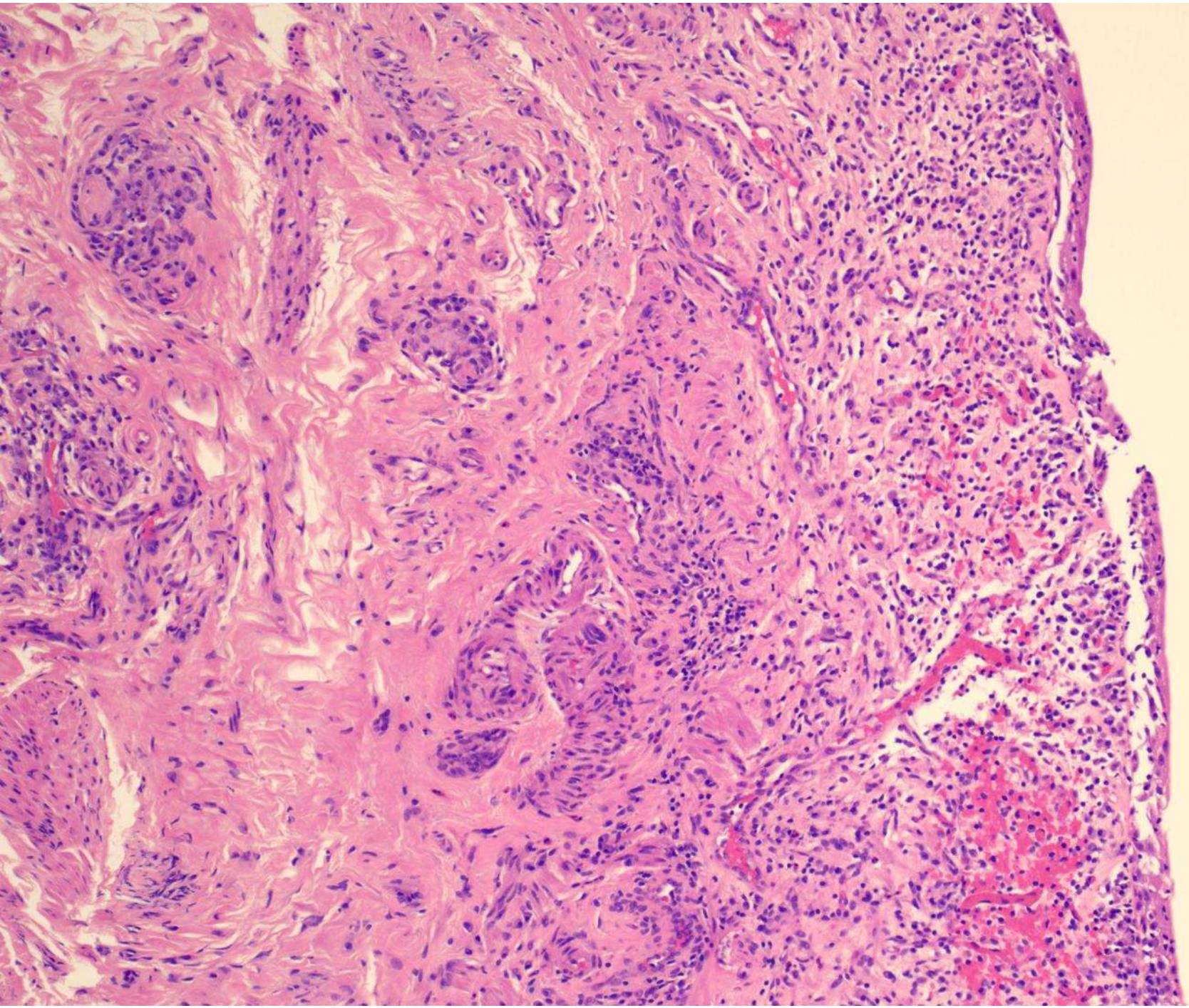
If NE ER+++ I don't necessarily do other markers

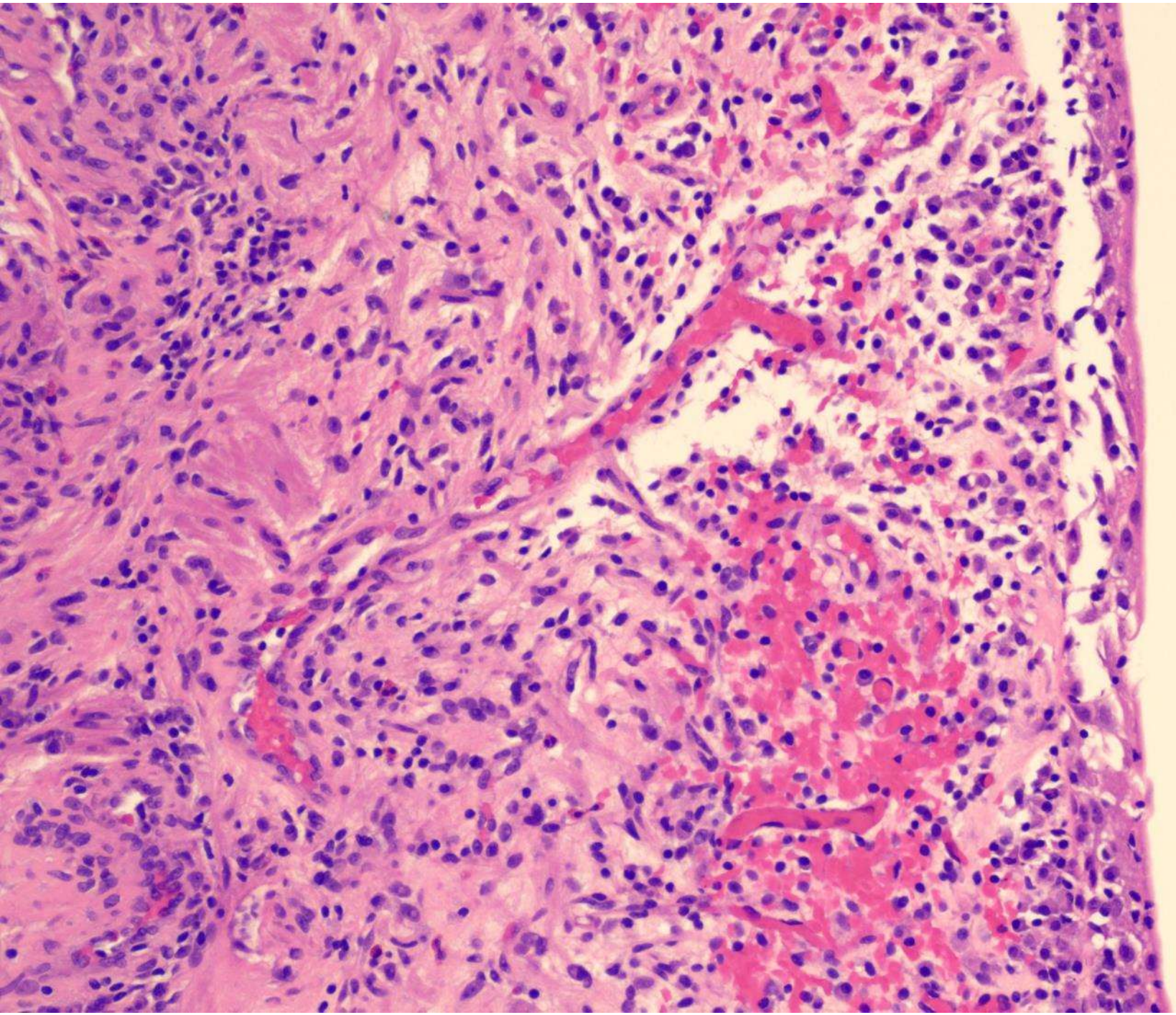
Troxell ML. Seminars in Diagnostic Pathology. 2017;34:479–95

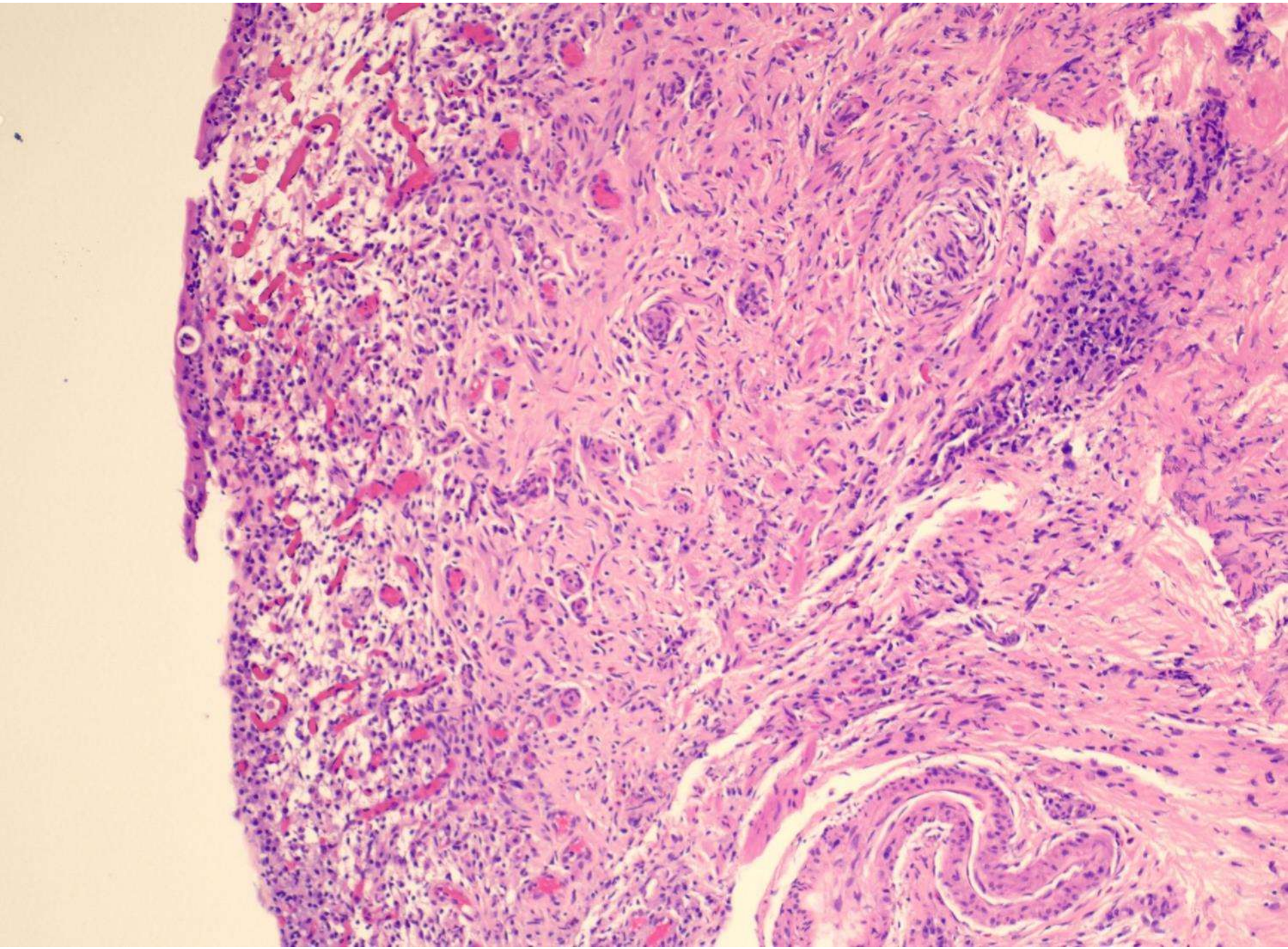
21-0702

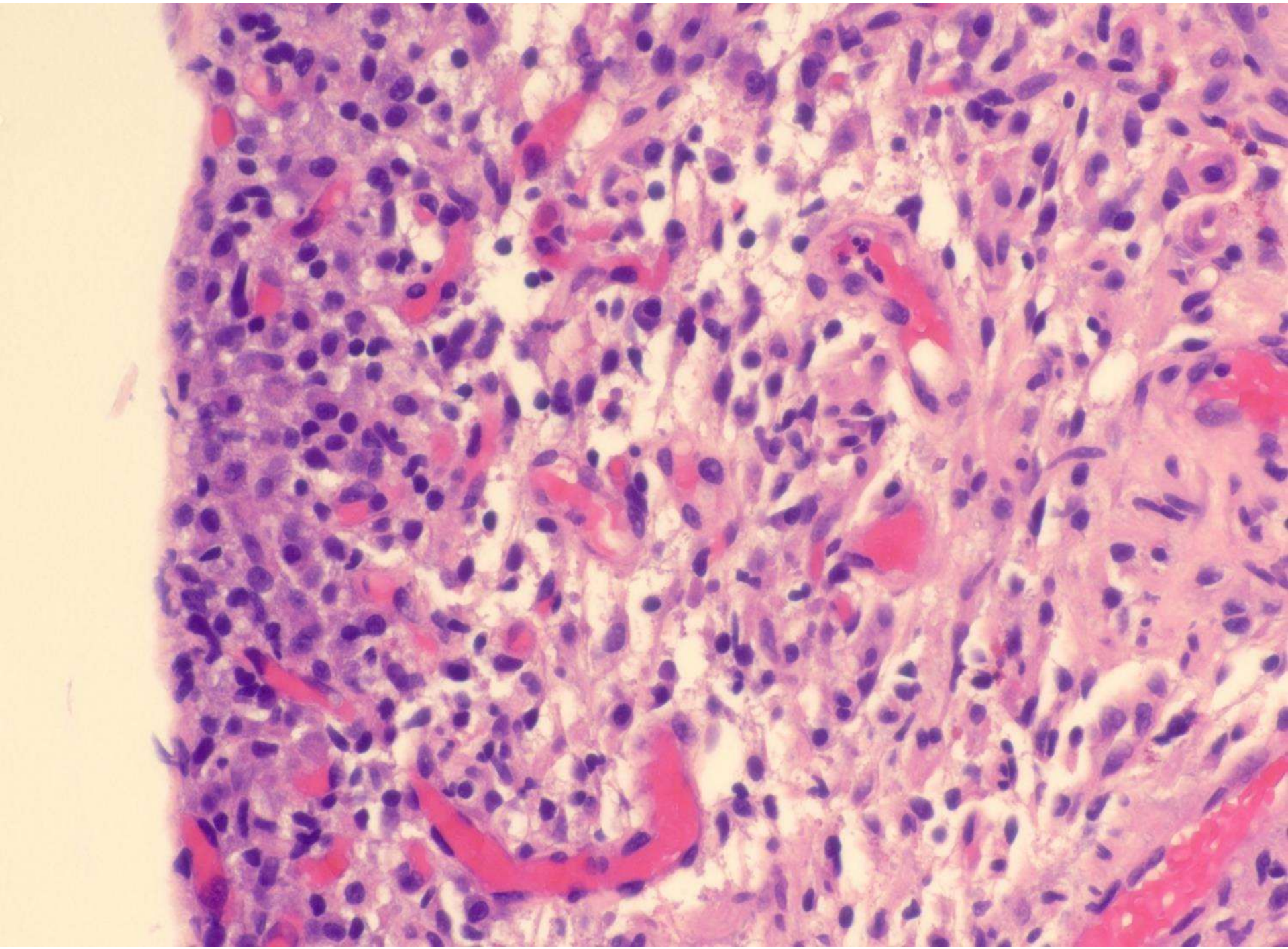
Charles Lombard, El Camino Hospital

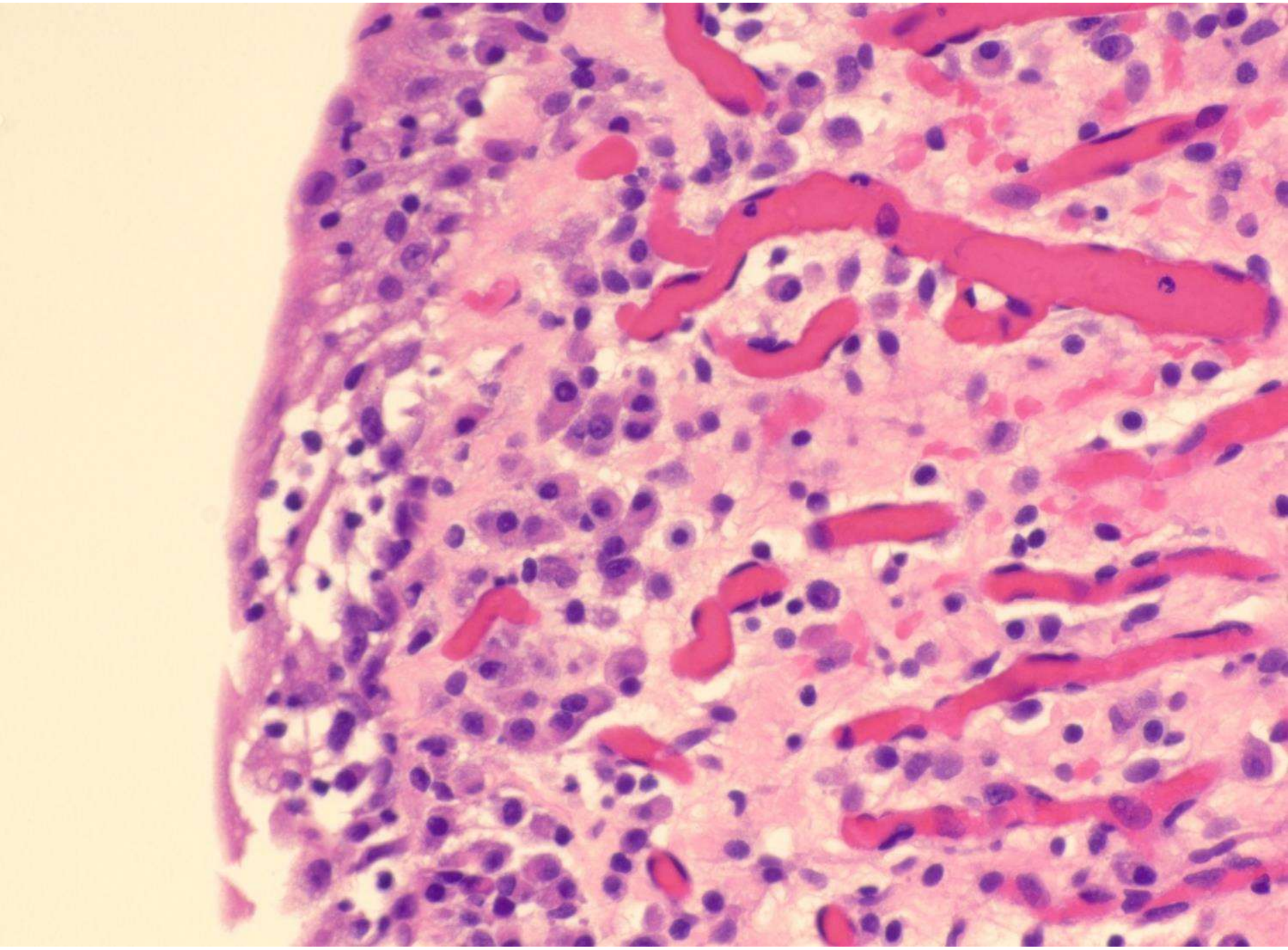
42-year-old M history of Henoch Schönlein Purpura and possible Crohn's disease has persistent urinary discomfort and bladder lesions.

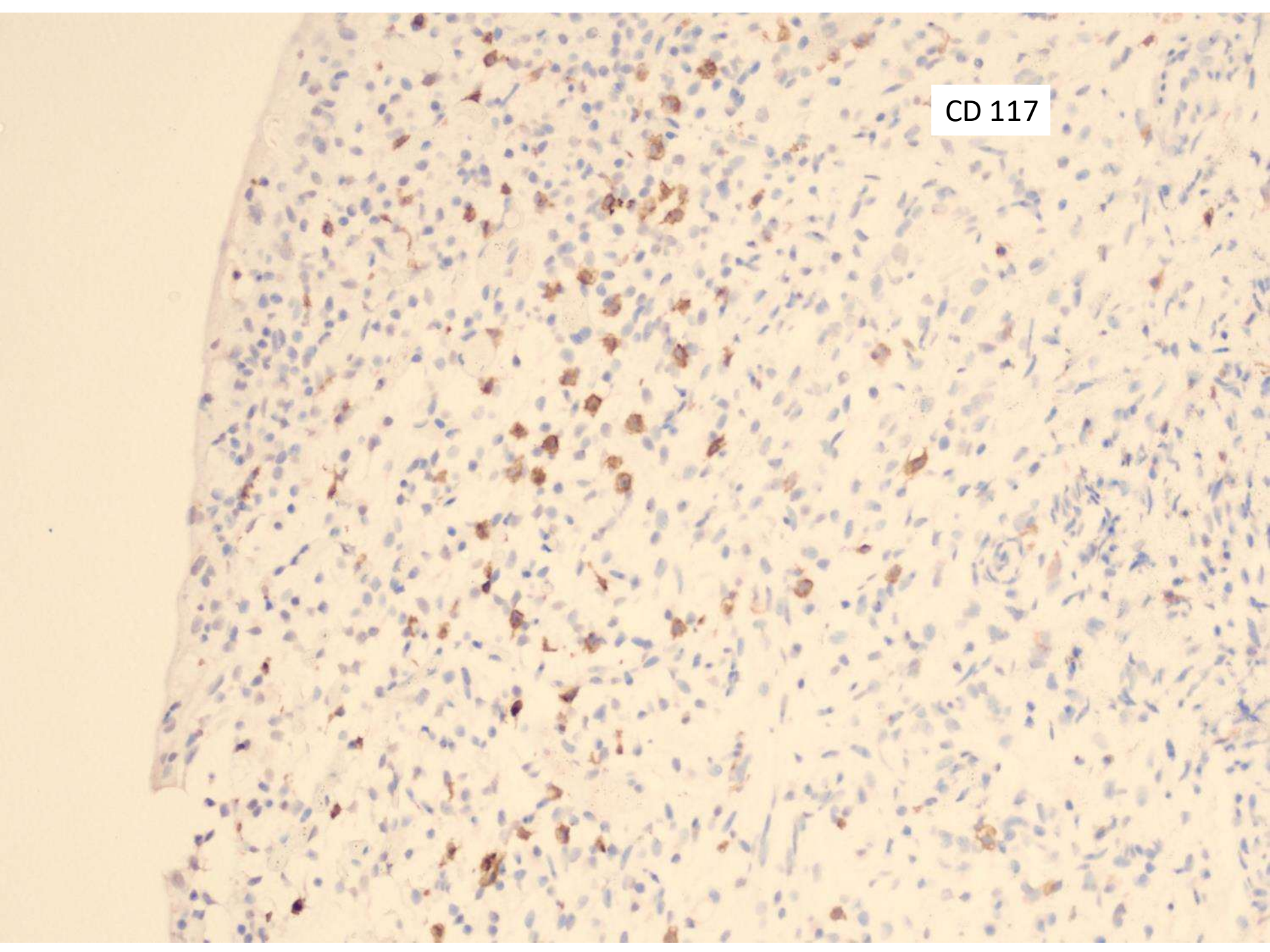


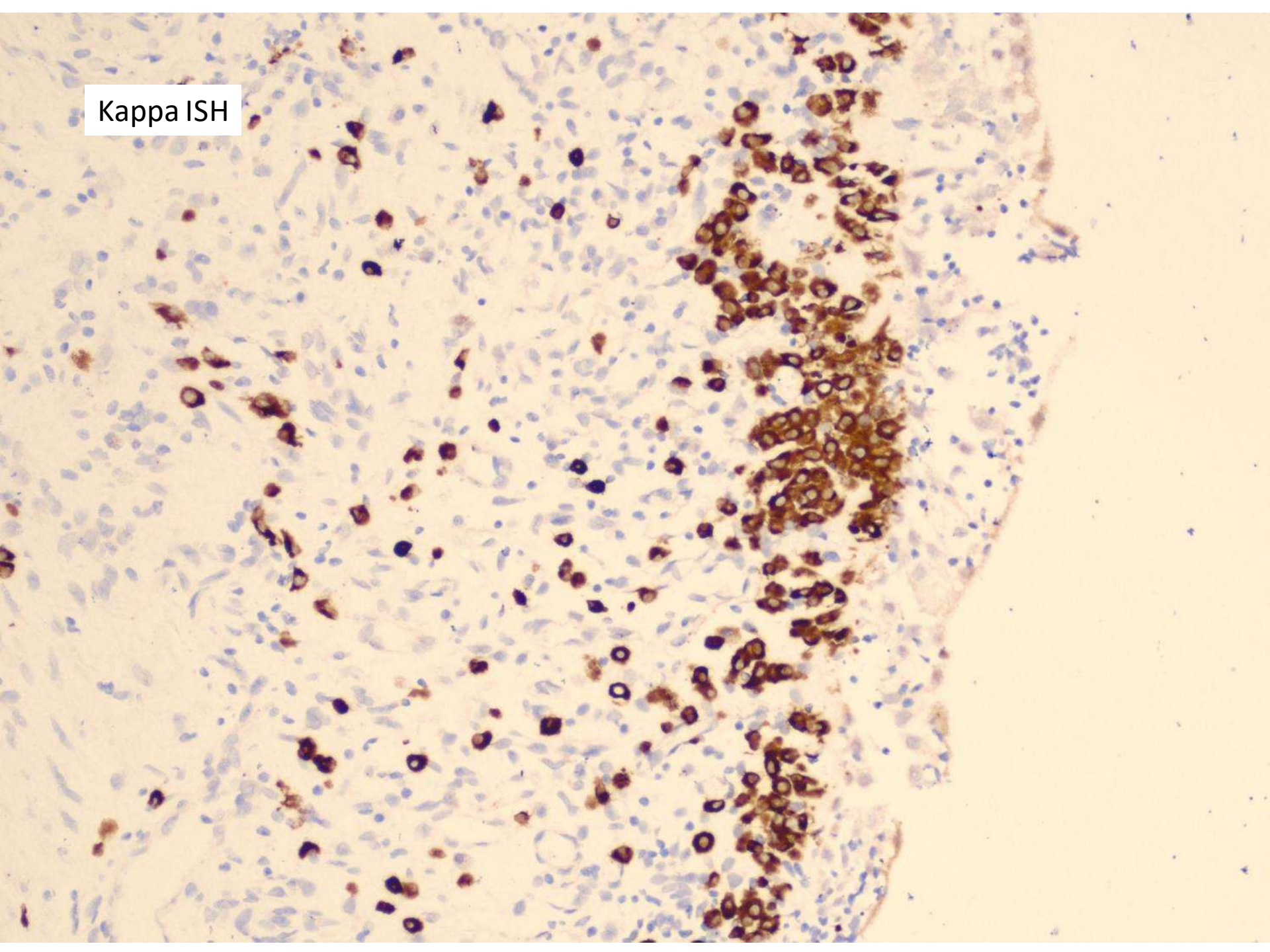


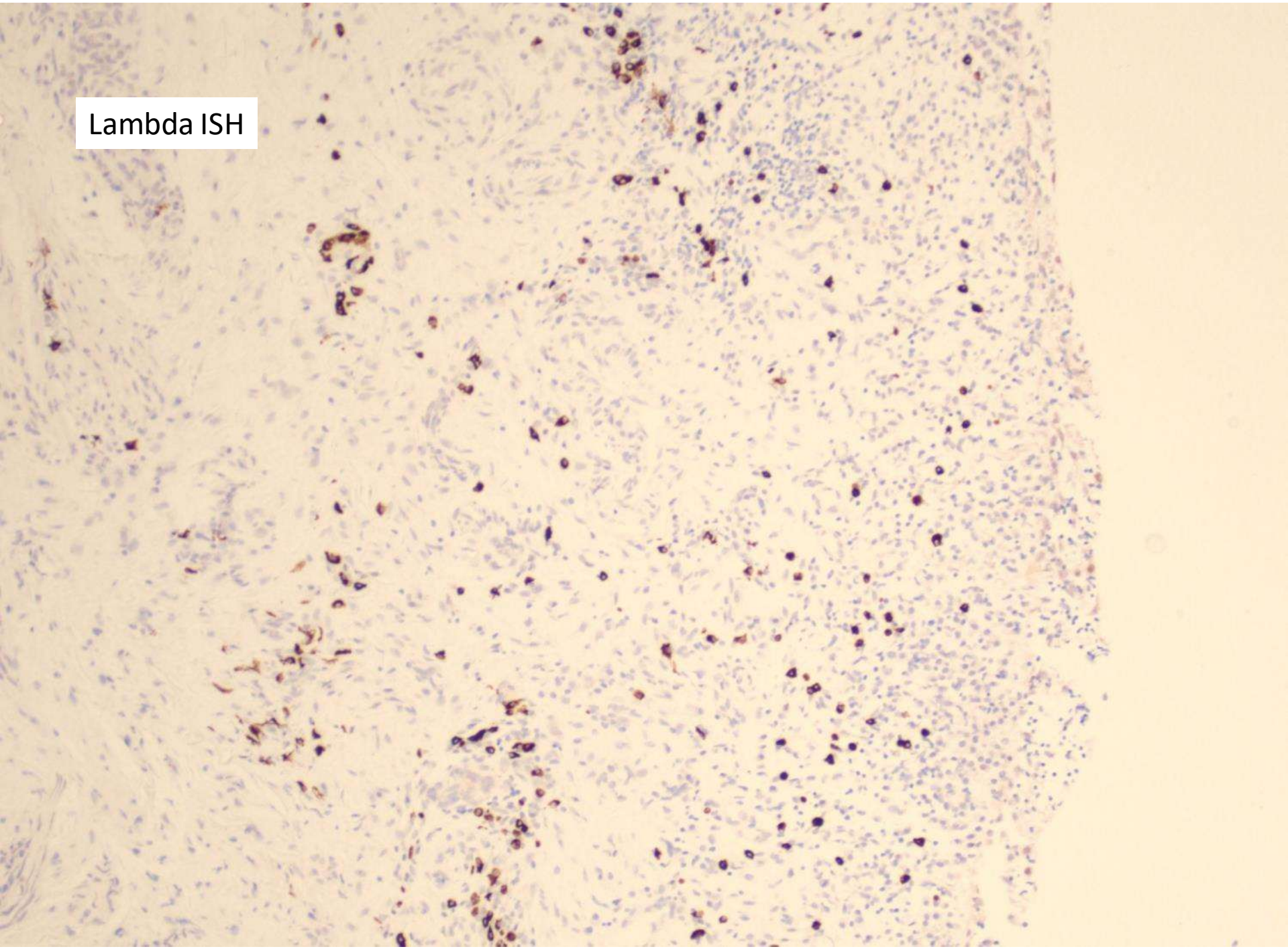







CD 117


Kappa ISH


Lambda ISH

Hunner-type interstitial cystitis with clonal B cell expansion

Reference:

Maeda et al: “Hunner-type (classic) interstitial cystitis: A distinct inflammatory disorder characterized by pancystitis, with frequent expansion of clonal B cells and epithelial denudation.” PLOS one 2015; 10:e0143316.

ORIGINAL ARTICLE

Monotypic Plasma Cell Proliferation of Uncertain Clinical Significance Mimicking Interstitial Cystitis

An Early Lesion of MALT Lymphoma?

Ana Cristina Vargas, PhD, FRCPA,†‡ Ivan Burchett, FRCPA,*§‖ Jennifer Turner, FRCPA,*‖ Warick Delprado, FRCPA,* Ross Brookwell, PhD, AFRCPA,¶ Venu Chalasani MD,‡ Anthony J. Gill, MD, FRCPA,†‡# and Fiona M. Maclean, FRCPA*†‖*

AJSP 2021;45(6):841-53

Interstitial cystitis

- Term introduced by Dr. Alexander Skene in 1887
- Dr. Guy Hunner described the symptom complex of bladder pain and the cystoscopic “Hunner ulcer” in 1915.
- Currently interstitial cystitis/bladder pain syndrome is regarded as a disease complex with varying etiologies/pathogenesis.

Hunner type (classic) interstitial cystitis Japanese series

- This is the only clinically relevant and proven phenotype and is regarded as a distinct entity
  - Lymphoplasmacytic inflammation
    - Up to 30% with monotypic plasma cells
      - 15 males; 11 females. Avg age: 73
    - Up to 10% with IgG4 phenotype
  - Increased numbers of mast cells
  - Hypervascularity
  - Epithelial denudation

AJSP Series from Australia

- Urinary bladder biopsies in which MALT was in ddx:
  - 22 cases of Monotypic plasma cell proliferation of uncertain significance IgA+ 64%, IgM+ 23%
    - 6 with amyloid deposits
  - No mass lesions; No systemic lymphoma
  - No evidence of progressive disease
  - Symptoms mimick interstitial cystitis/bladder pain syndrome
  - Males 73%; median age 73
- ?? Early form of plasma cell neoplasm vs MALT vs clonal expansion of plasma cells in chronic inflammatory background

IC has a strong link to autoimmunity

- At least 50% of patients with IC can are found to have a variety of autoantibodies.
- IC is associated with a variety of other autoimmune diseases
  - Sjogren's syndrome, RA, SLE, autoimmune thyroiditis.
  - 2-3% with Crohns's disease or UC
- IC has been successfully treated with a variety of treatments used for autoimmune disorders
  - Cyclosporine and corticosteroids
  - Certoizumab

Models of disease

- Animal models of IC have been reported by inducing autoimmune reactions to the urothelial mucosa through a variety of techniques

Clonal expansion of plasma cells

- On pathologic/histologic grounds difficult to r/o an early MALT lymphoma
- There are arguments against this interpretation:
  - There is no epidemiologic evidence to suggest an association between IC and lymphoma
  - Evolution to MALT lymphoma has not been seen in large clinics following these patients
  - It is thought to represent a local immune reaction with selection of a specific clone of B cells.

Other examples of clonal expansions

- Synovium of pts with RA
- Liver in pt with IgG4 associated cholangitis
- Salivary gland myoepithelial sialadenitis
- CSF in MS patients
- Gastric helicobacter infections
- EBV associated disease

Chronic inflammatory conditions and clonal expansions

- Chronic inflammation whether from chronic autoimmune disease or chronic viral infections could amplify B cell activation processes by inhibiting apoptotic activity thereby leading to longer survival of B cell subsets.
- Understanding how B cell receptor activation is maintained and which check points are at risk for being deregulated thereby leading to persistent activation may be important in understanding why some of these expansions become malignant.

- Reference: Ferracccioli and Tolusso: "Infections, B cell receptor activation and autoimmunity". Autoimunity Reviews 2007;7: 109-113.

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

NEJM 2021;384: 2039-52.
May 27, 2021

Dan L. Longo, M.D., *Editor*

Somatic Mutations in "Benign" Disease

Satu Mustjoki, M.D., and Neal S. Young, M.D.

Somatic mutations in benign disease

- Mutations arise throughout life from embryogenesis through adult life
- Clonality is a feature of cancer, but…
- Clonality is also common in healthy organs.
  - CHIP (mutations are ubiquitous in young; clones tiny)
  - MPN driver mutations (JAK2 V617F,DNMT3A, and TET2) may arise in first several post-zygotic divisions
  - Clonal expansion/organization of Colonic crypts, esophagus
  - Clones with cancer driver mutations in normal skin, endometrium, pancreas, bronchial epithelium, bladder and prostate
- Clones expand in adaptation to the environment

Summary

- Current thinking underestimates the role of somatic mutations in human disease
- The pathophysiology of these mutations can inform diagnosis, classification, and monitoring of many nonmalignant diseases.
- Identification of these mutations and the conditions that lead to their expansion can lead to new therapies.

21-0703

Ben Dulken/Gregory Bean; Stanford

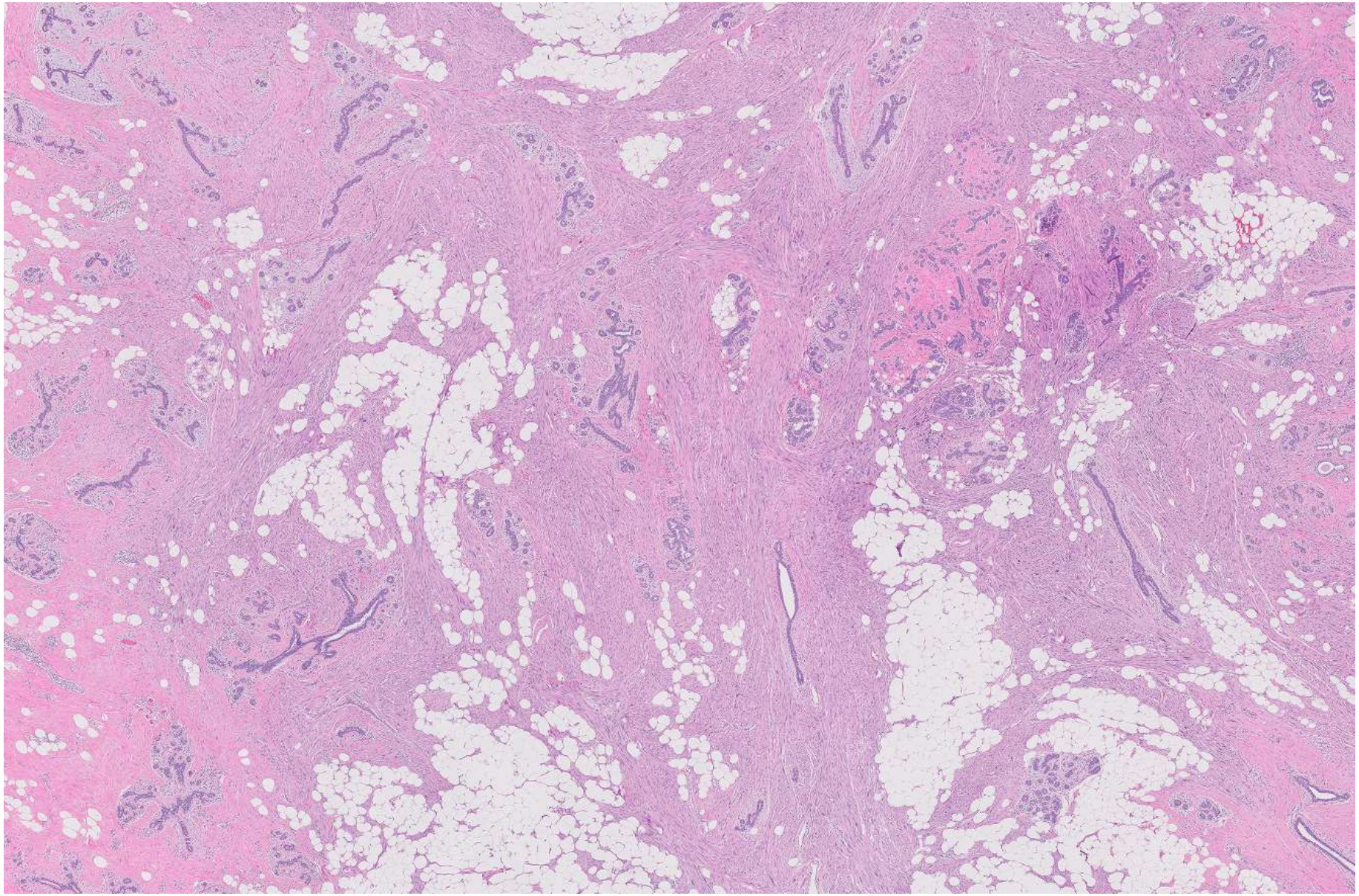
20-year-old F with Li-Fraumeni syndrome, with history of borderline phyllodes tumor and DCIS.

History

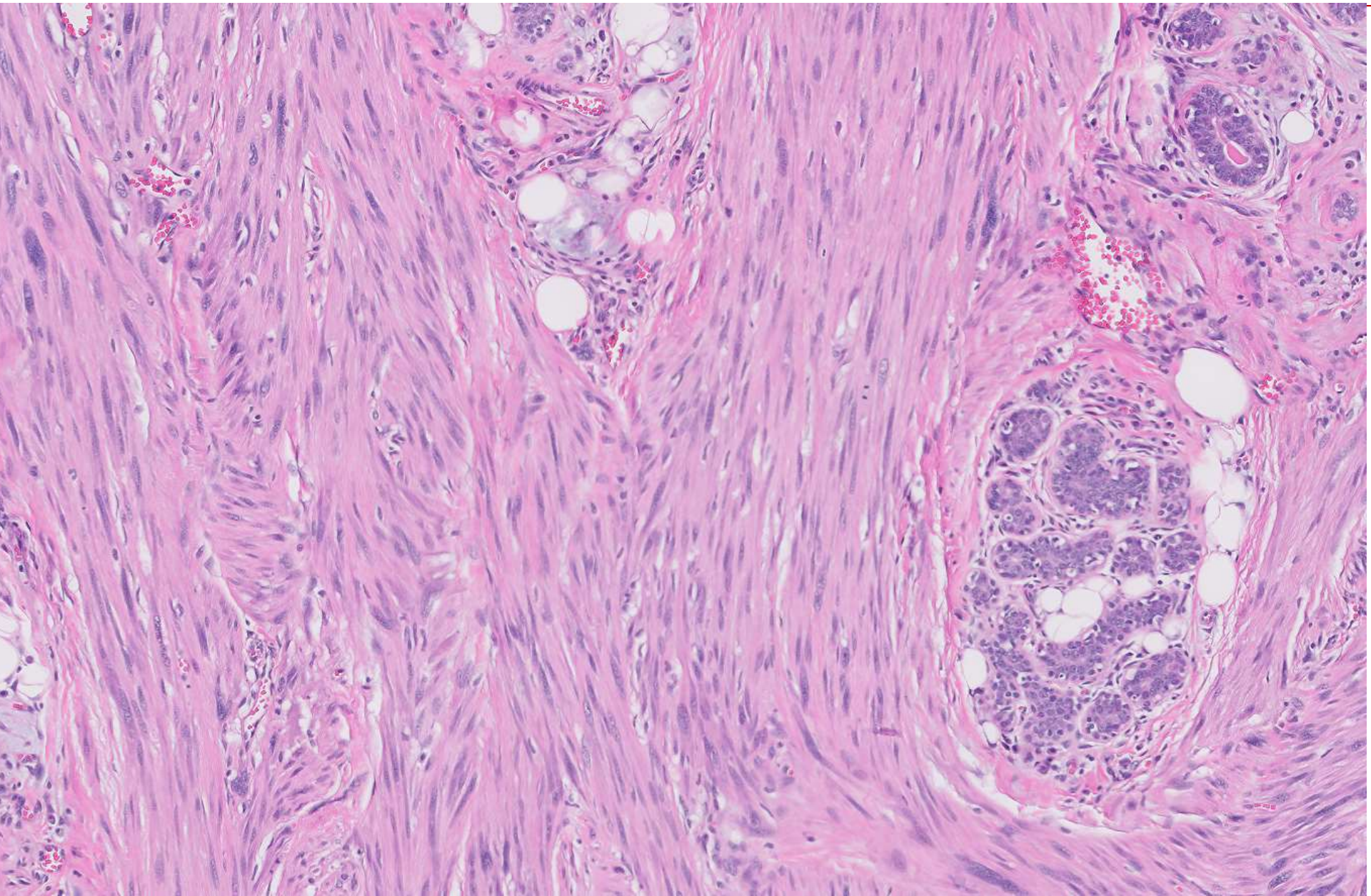
- 20Y female
- History of excision of borderline phyllodes tumor with small focus of DCIS.
- History of osteosarcoma of the humerus s/p resection and radiation at age 13.

- Undergoing bilateral mastectomy.
- Several targeted lesions in bilateral breasts by imaging.

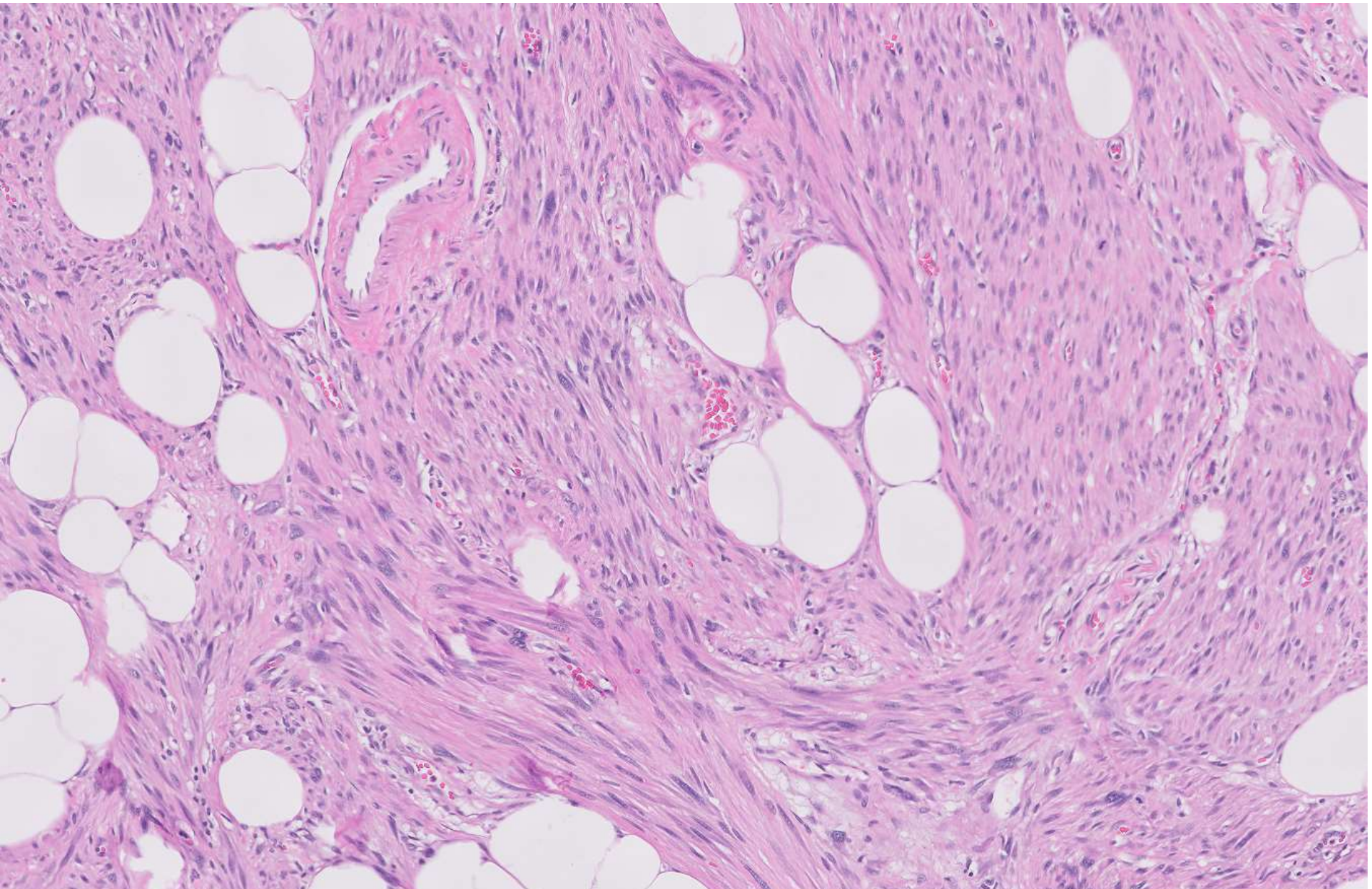
Infiltrative lesion in the left breast

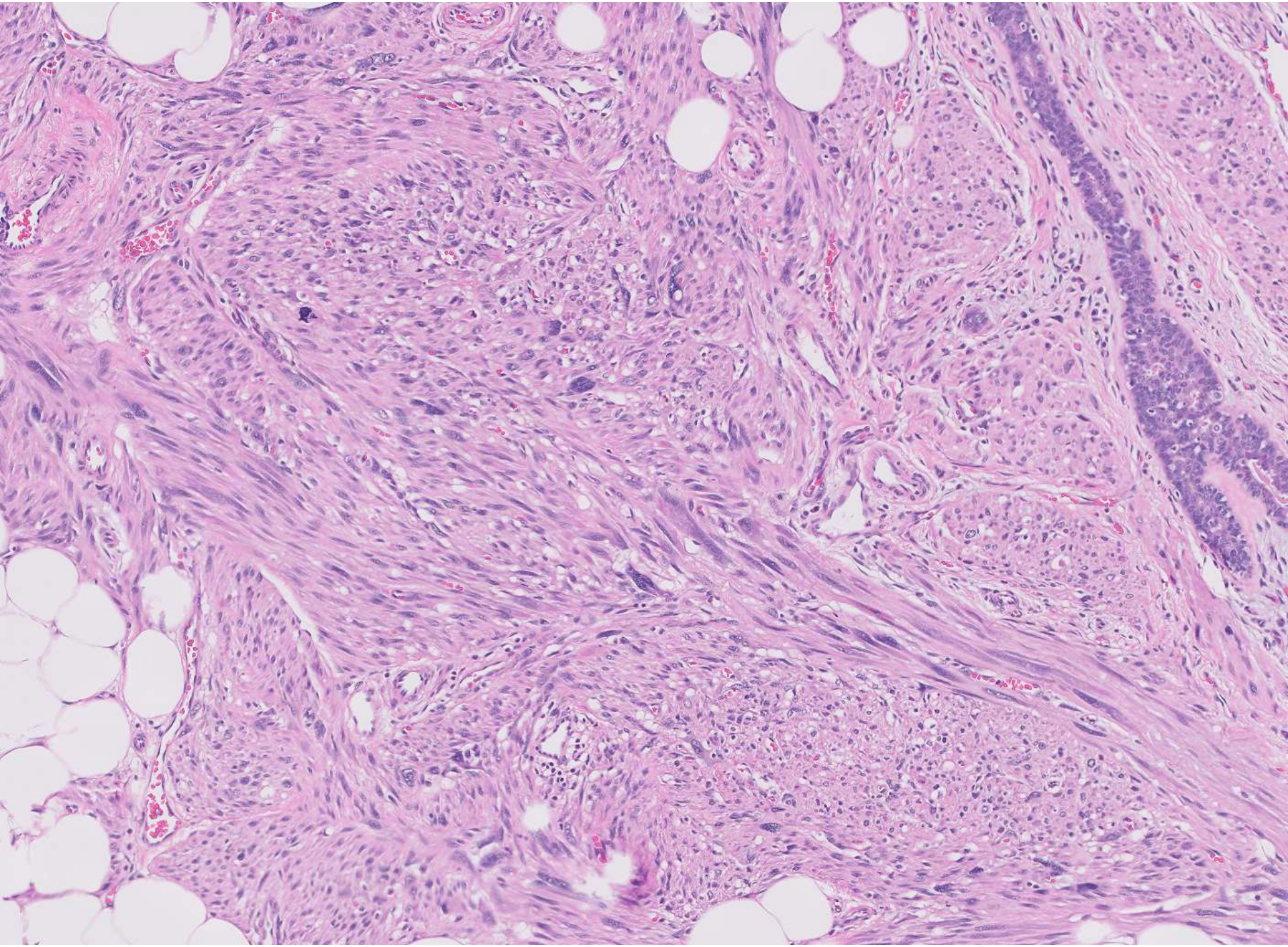


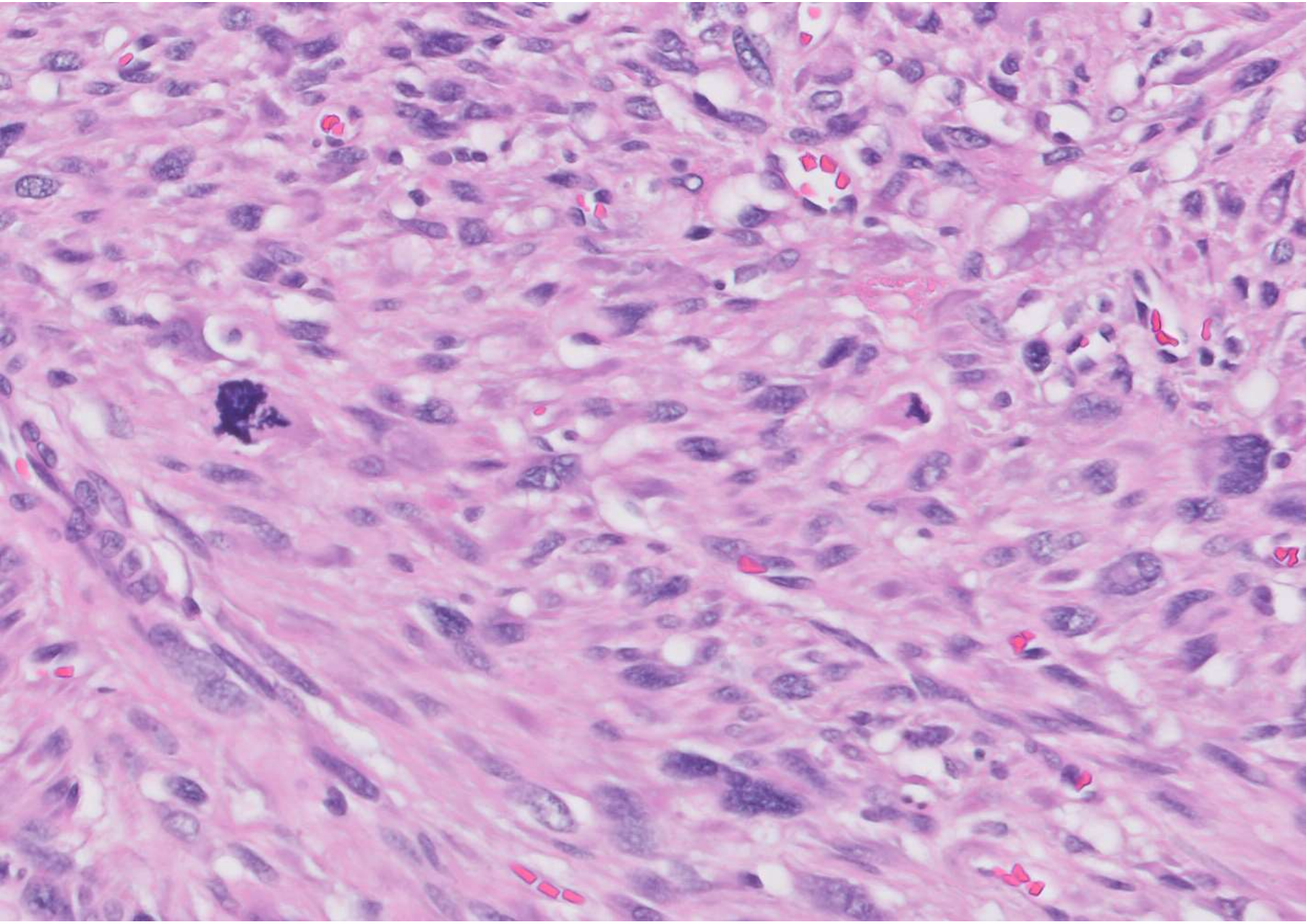
Infiltrative lesion in the left breast



Infiltrative lesion in the left breast





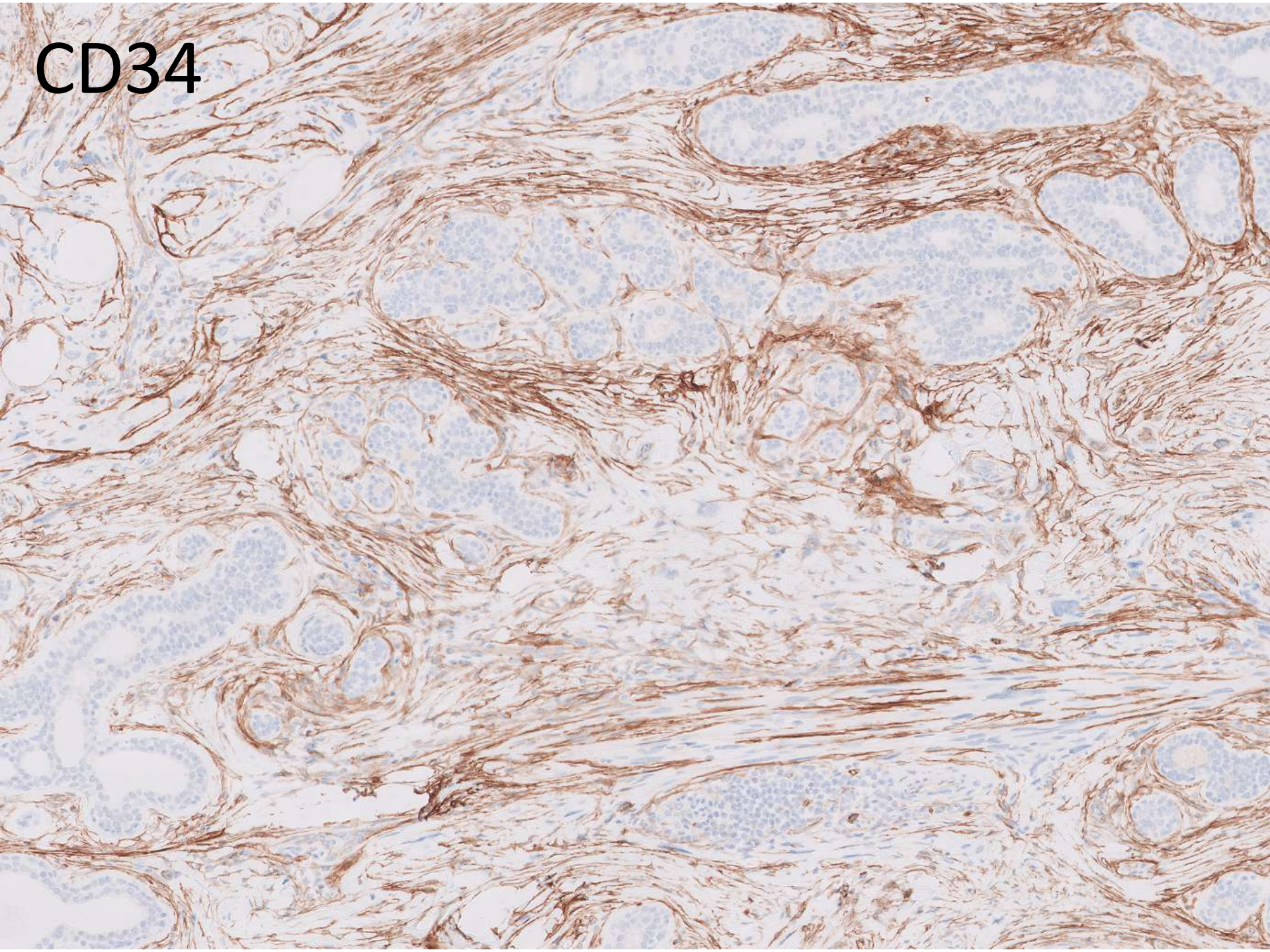


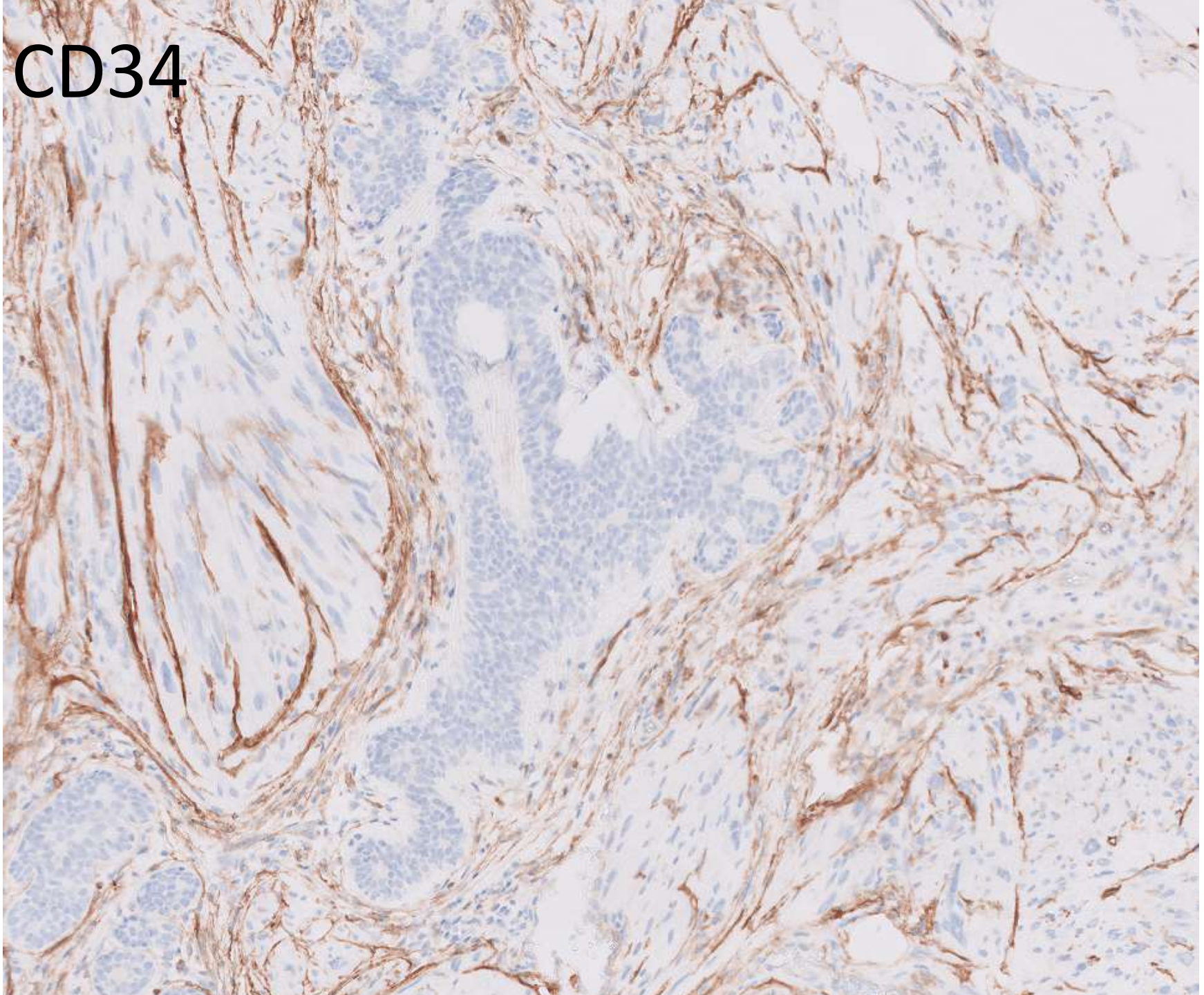
Differential Diagnosis

- Phyllodes tumor
- Periductal stromal tumor
- Metaplastic carcinoma

Less likely:

- Inflammatory myofibroblastic tumor
- Rhabdomyosarcoma
- Malignant peripheral nerve sheath tumor
- Leiomyosarcoma
- Solitary fibrous tumor
- Fibromatosis


CD34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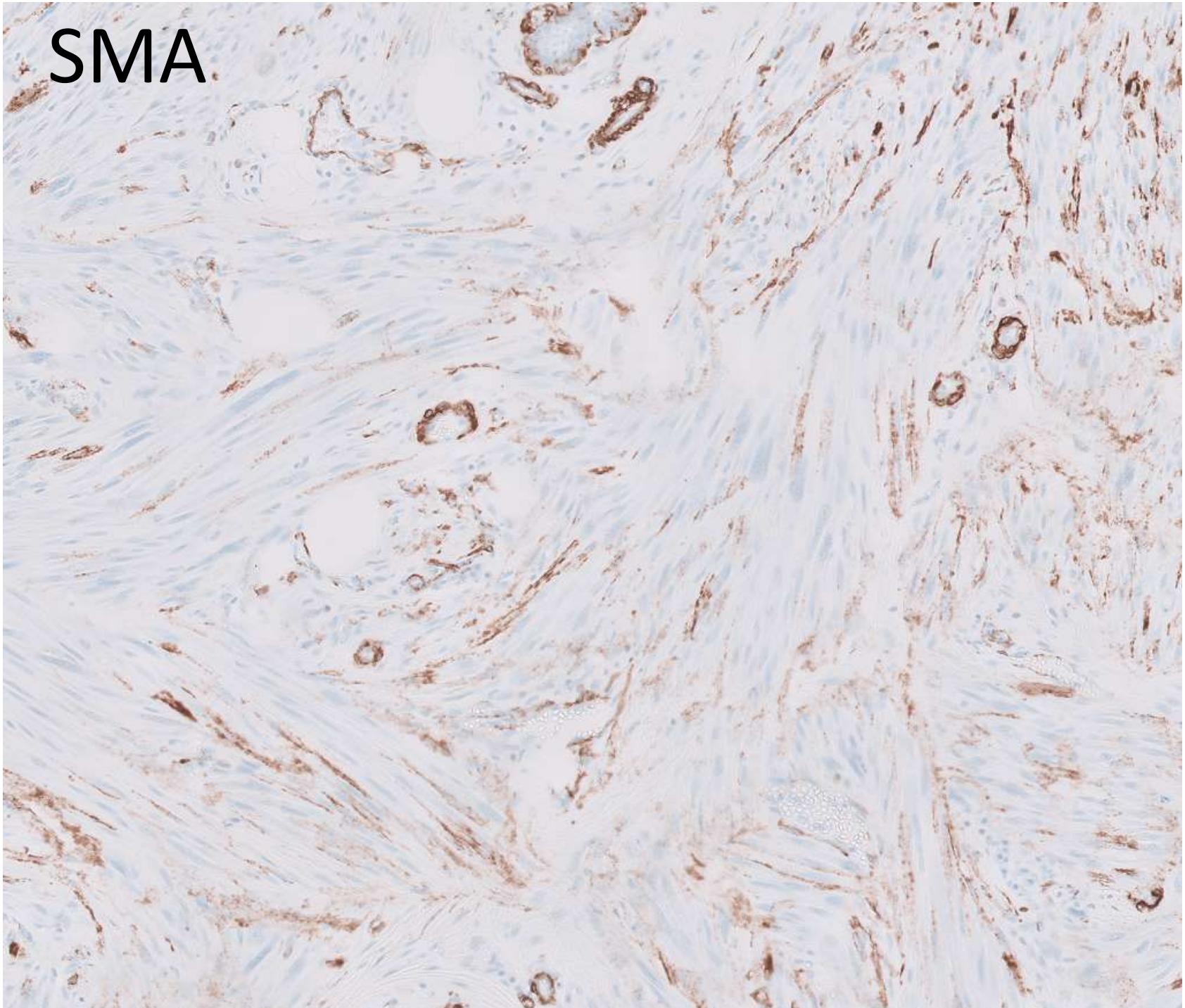
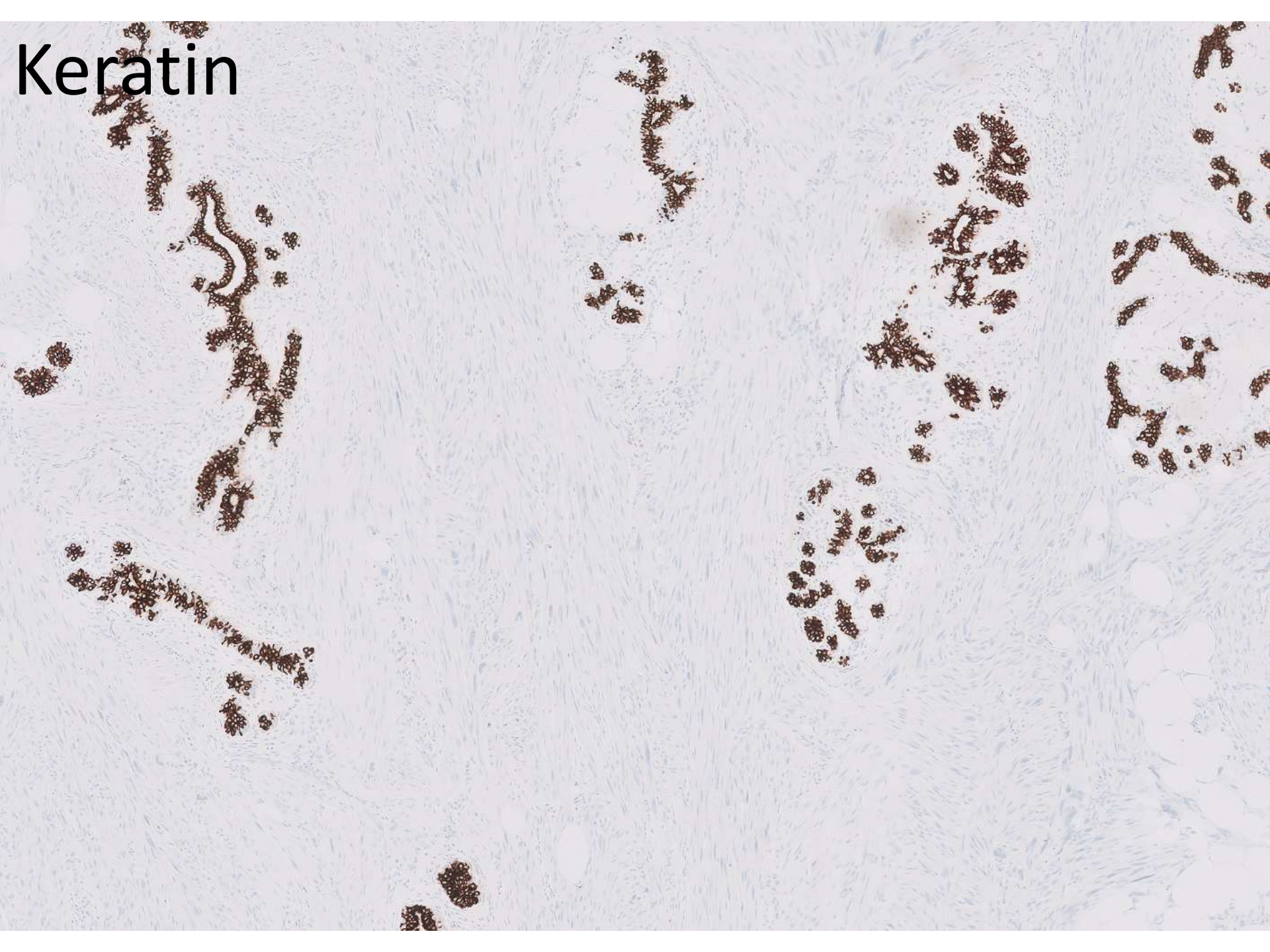
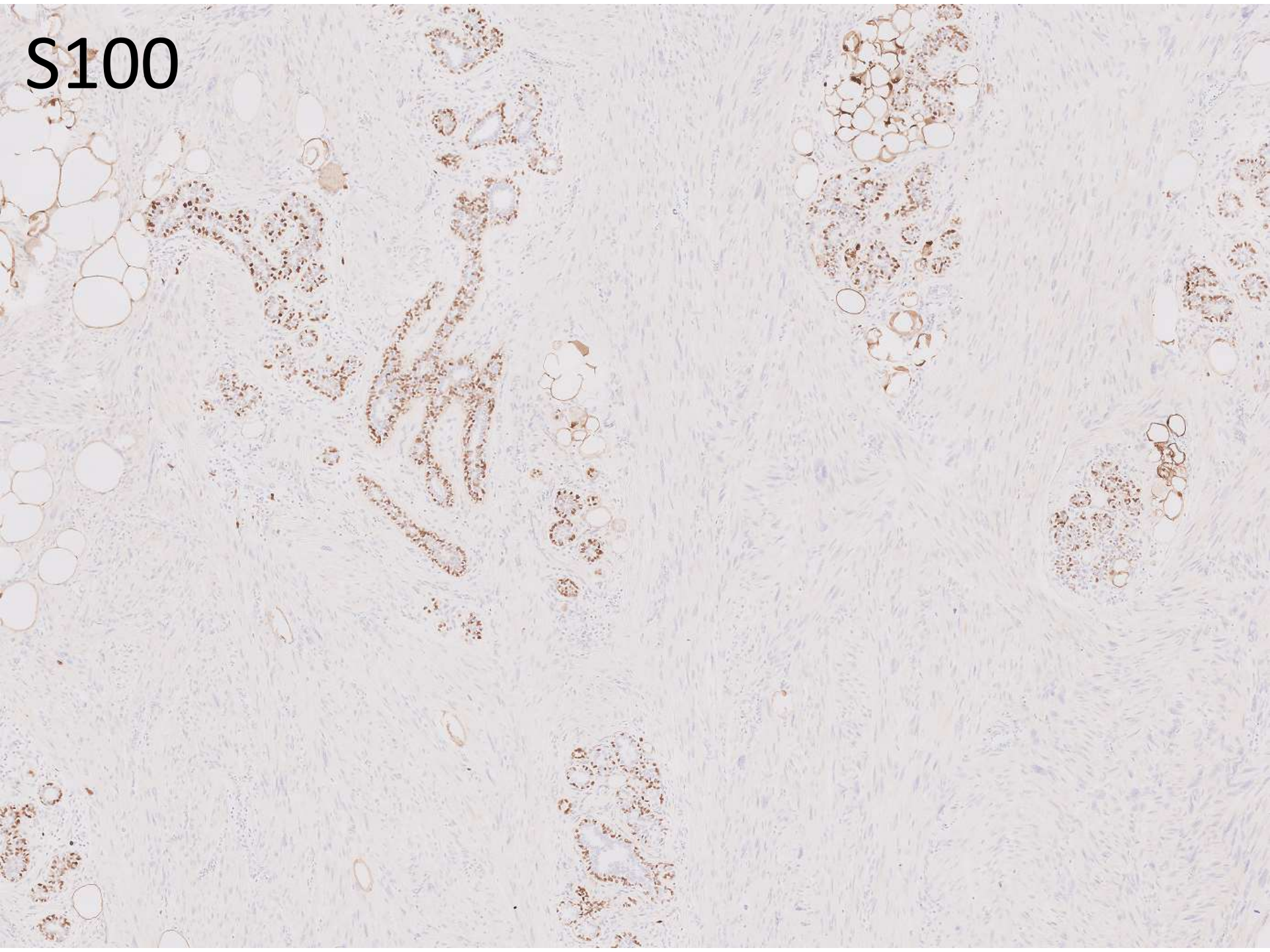
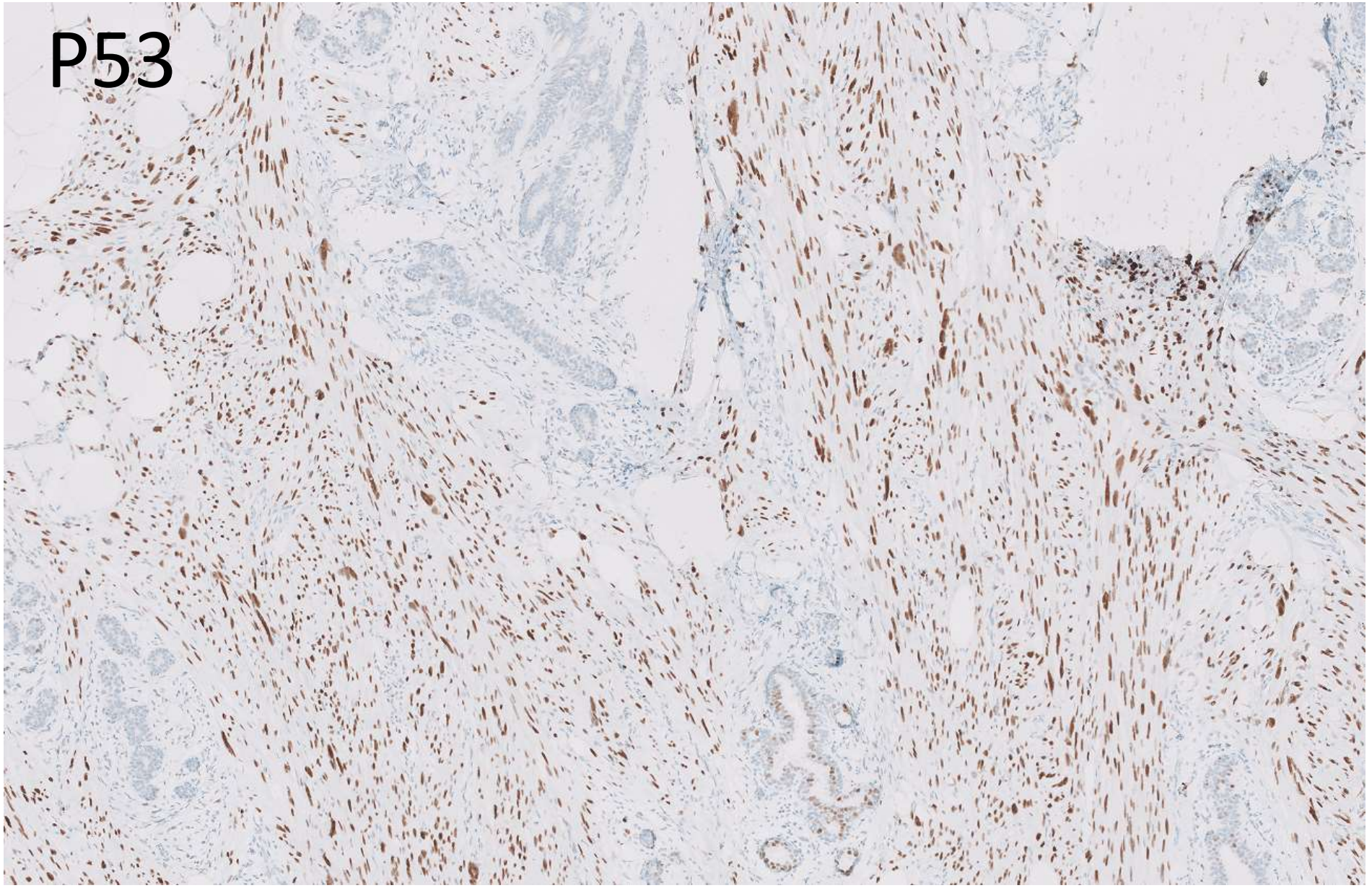

SMA


Keratin


S100


P53

Complete Immunohistochemical Profile

- CD34 (patchy positive)
- SMA - patchy positive, desmin and caldesmon show only focal positivity.
- Cathepsin-K negative, Ckmix-, CK34betaE12-, CK5/6-, p63-, myogenin-, PAX7-, S100-, ALK- and STAT6-

Periductal stromal tumor (formerly sarcoma)

- The term periductal stromal tumor/sarcoma was defined in 2003 by Burga, et al. as:
  1) A predominantly spindle cell stromal proliferation of variable cellularity and atypia around open tubules and ducts devoid of a phyllodes pattern
  2) One or more often multiple nodules separated by adipose tissue
  3) Stromal mitotic activity of ≥3/10 high power fields
  4) Stromal infiltration into surrounding breast tissue
- 20 patients were studied by Burga, et al. and 1 had metastasis to the lungs of an angiosarcoma derived from the underlying periductal stromal tumor.
  - Otherwise the patients had similar outcomes to Phyllodes tumor (though with limited follow up).
- In 2012, WHO revised the name from sarcoma -> tumor to reflect the comparatively less ominous nature of this diagnosis.
- In 2019, WHO further revised this diagnosis to consider PST a variant of phyllodes tumor and not a distinct entity.
- The prognosis and clinical behavior of this tumor are not well studied.

[1] Burga AM, Tavassoli FA. Periductal stromal tumor: a rare lesion with low-grade sarcomatous behavior. Am J Surg Pathol. 2003; 27(3):343-8.
[2] Tse G, Koo JS, Thike AA. Phyllodes tumor. In: WHO classification of tumours: Breast tumours, 5th edition. Lyon, France: International Agency for Research on Cancer, 2019. pp 172-176.

Final Diagnosis

1) A predominantly spindle cell stromal proliferation of variable cellularity and atypia around open tubules and ducts devoid of a phyllodes pattern

2) One or more often multiple nodules separated by adipose tissue

3) Stromal mitotic activity of ≥3/10 high power fields **(10/10 HPF in this tumor)**

4) Stromal infiltration into surrounding breast tissue

Final Diagnosis:

PERIDUTAL STROMAL TUMOR/SARCOMA, 1.8CM, EXCISED (SEE COMMENT AND TABLE)

Other considerations in the differential diagnosis

- Differentiation from Phyllodes tumor is primarily based on architecture, and can be difficult or impossible in a biopsy.
- Phyllodes tumors and fibroadenomas tend to occur in slightly younger patients (Median age 45 vs. 55.3)
- CD117 has been proposed as a marker, though studies have also shown positivity in malignant Phyllodes tumor.

Tumor type	CD34	CD117	HHF35	Dominant growth pattern
Fibroadenoma	4/4	0/4	2/4* (1)	Intracanalicular
Phyllodes tumor	3/3	0/3	2/3	Intracanalicular & leaf-like processes
Periductal stromal sarcoma	13/15† (4)	6/15† (2)	2/15	Pericanalicular
MPT (Chen et al.)†	3/12	8/12	10/12	

* Focal in the number of cases in parentheses.
† Data retrieved from Chen et al. (*J Surg Res*, 2000).
MPT, malignant phyllodes tumor; FA, fibroadenoma; PT, phyllodes tumor; PDSS, periductal stromal sarcoma.

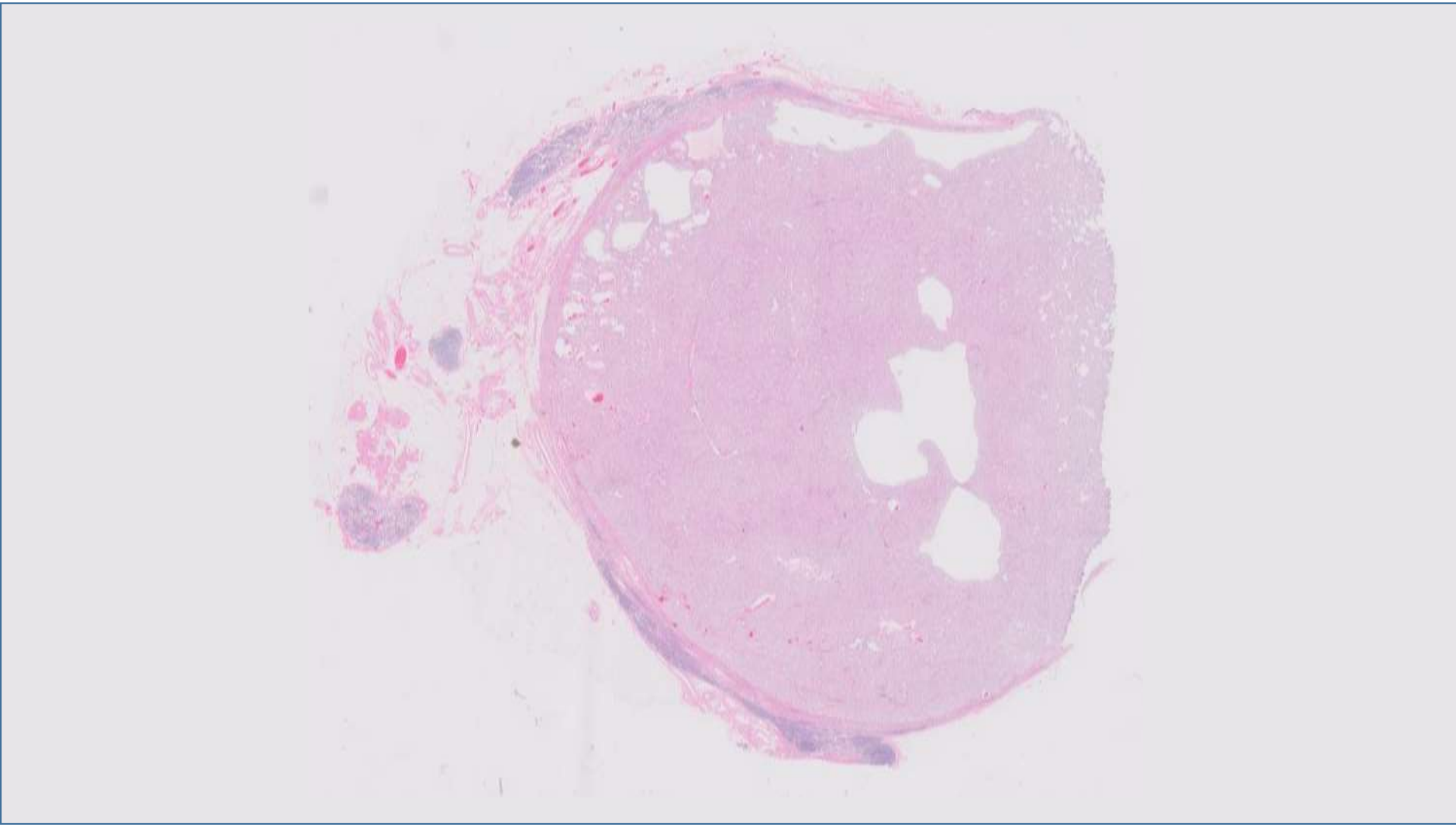
- Differentiated from periductal stromal hyperplasia by mitotic activity and nuclear atypia.
- The prognosis has not been shown to be significantly different from Phyllodes tumor and excision with wide margins is the recommended treatment.

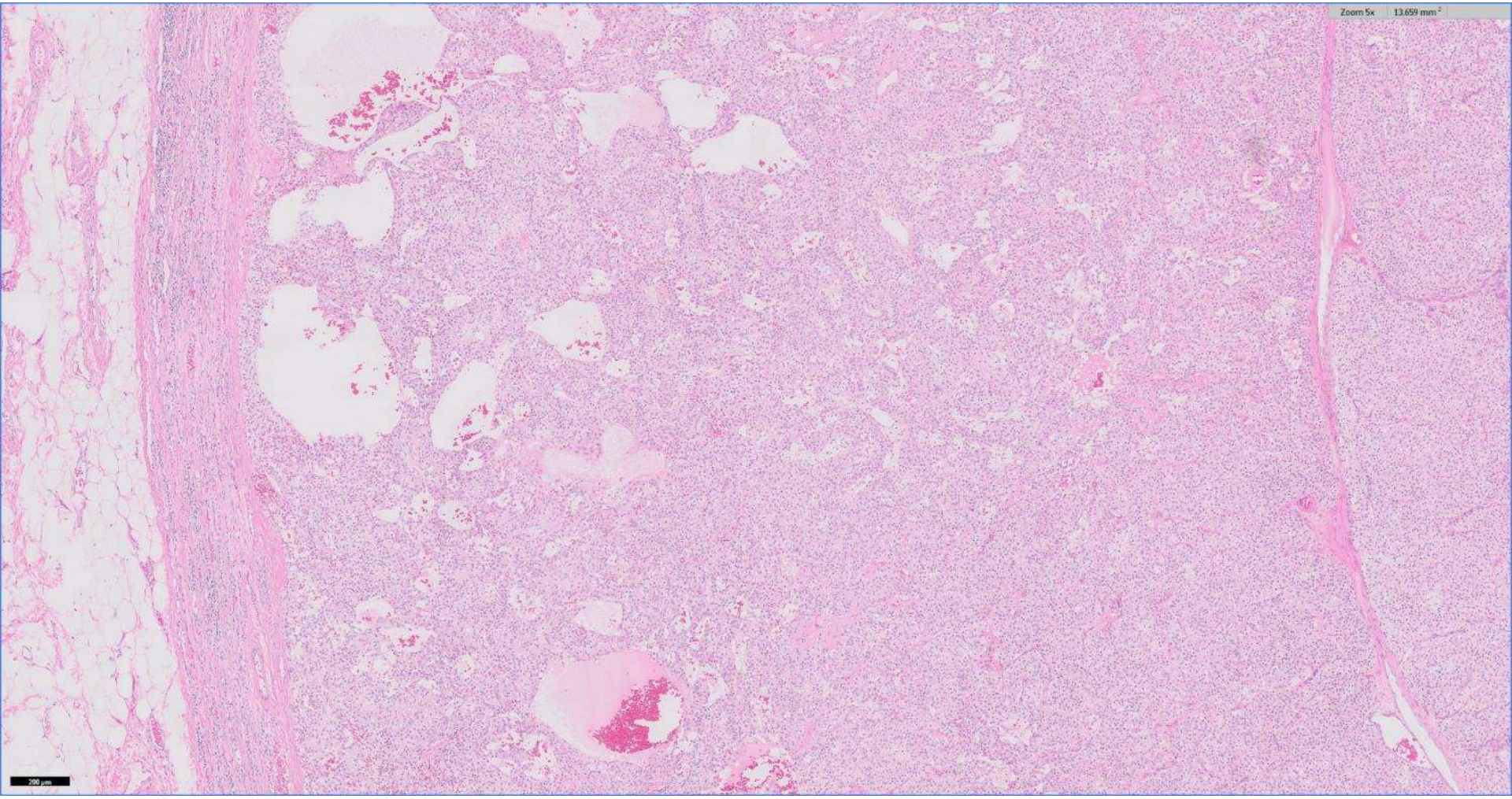
[1] Burga AM, Tavassoli FA. Periductal stromal tumor: a rare lesion with low-grade sarcomatous behavior. Am J Surg Pathol. 2003; 27(3):343-8.
[2] Tse G, Koo JS, Thike AA. Phyllodes tumor. In: WHO classification of tumours: Breast tumours, 5th edition. Lyon, France: International Agency for Research on Cancer, 2019. pp 172-176.

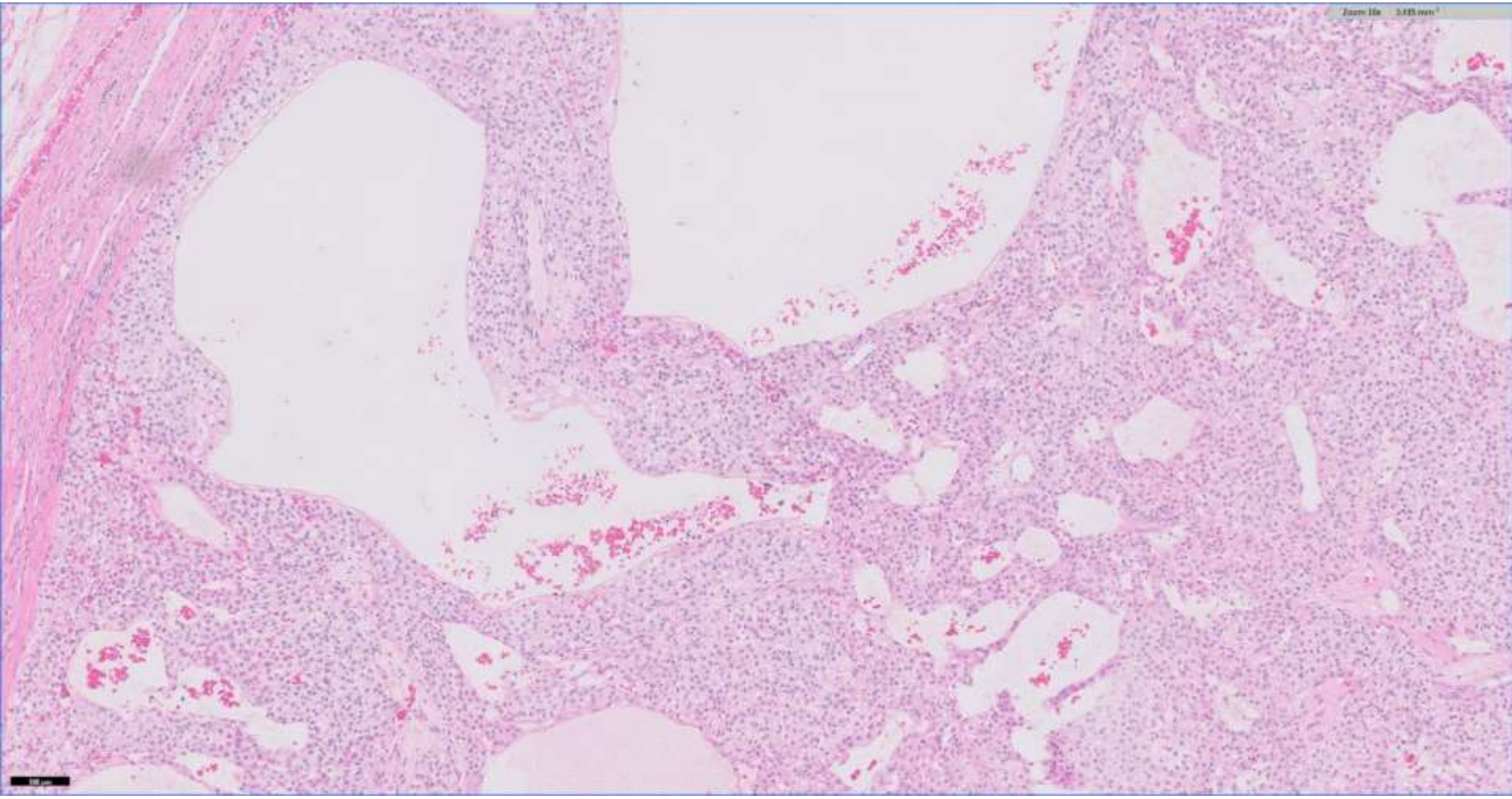
21-0704

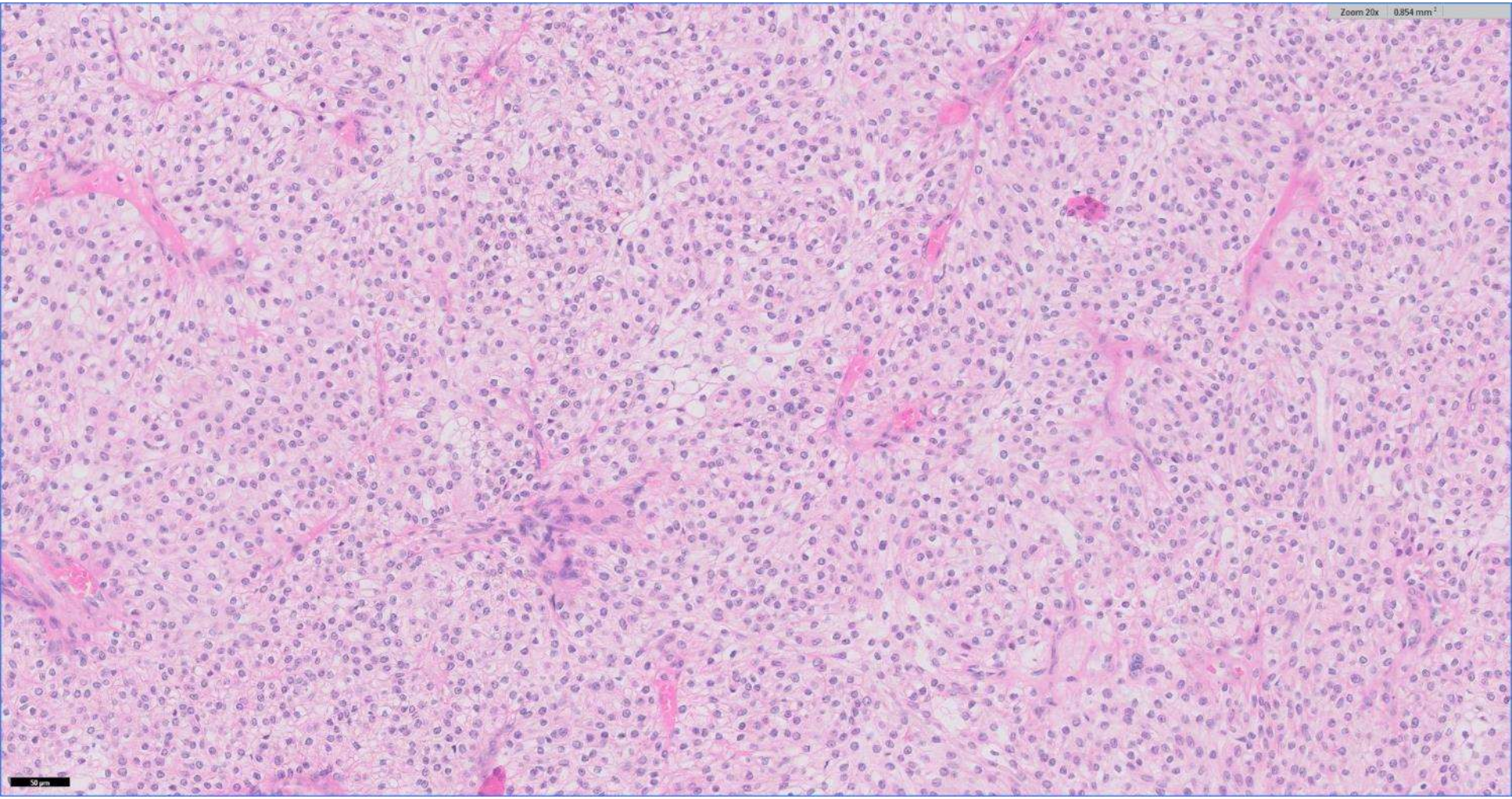
Nicholas Ladwig; UCSF

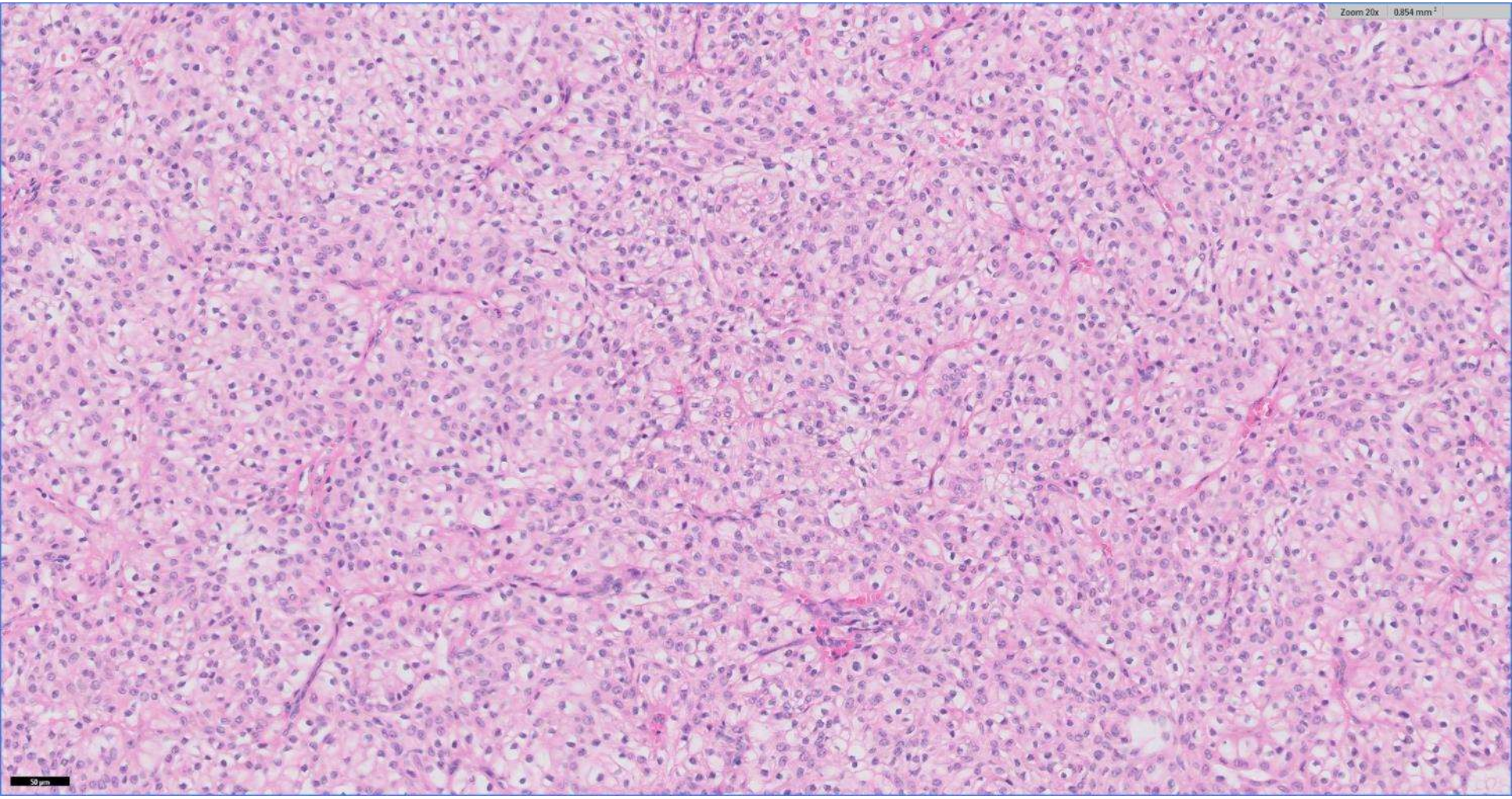
31-year-old F with tender right inguinal mass. Full-body PET scan showed low-level metabolism in a right inguinal lymph node (2.2 cm) with no other sites of hypermetabolism

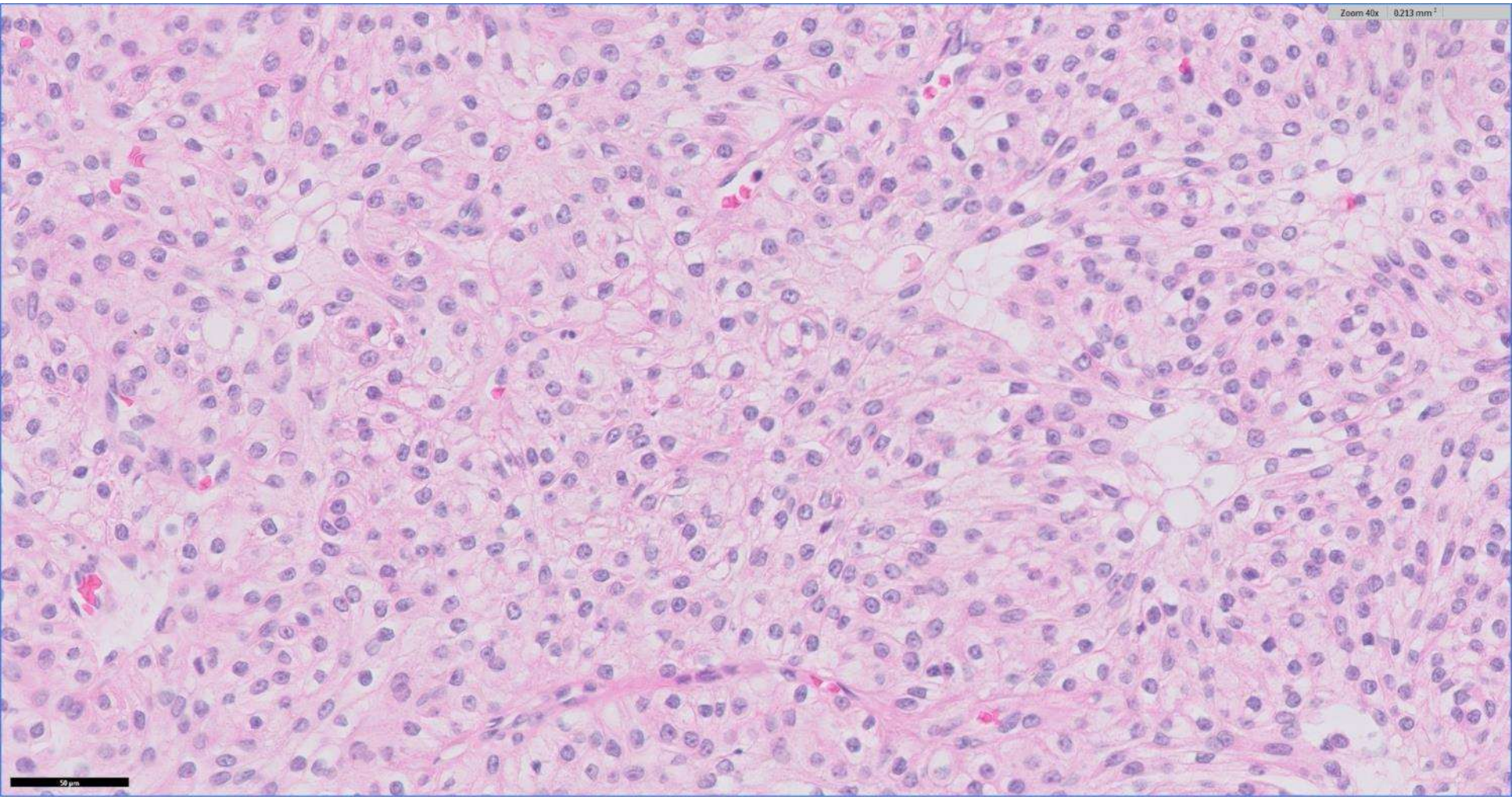


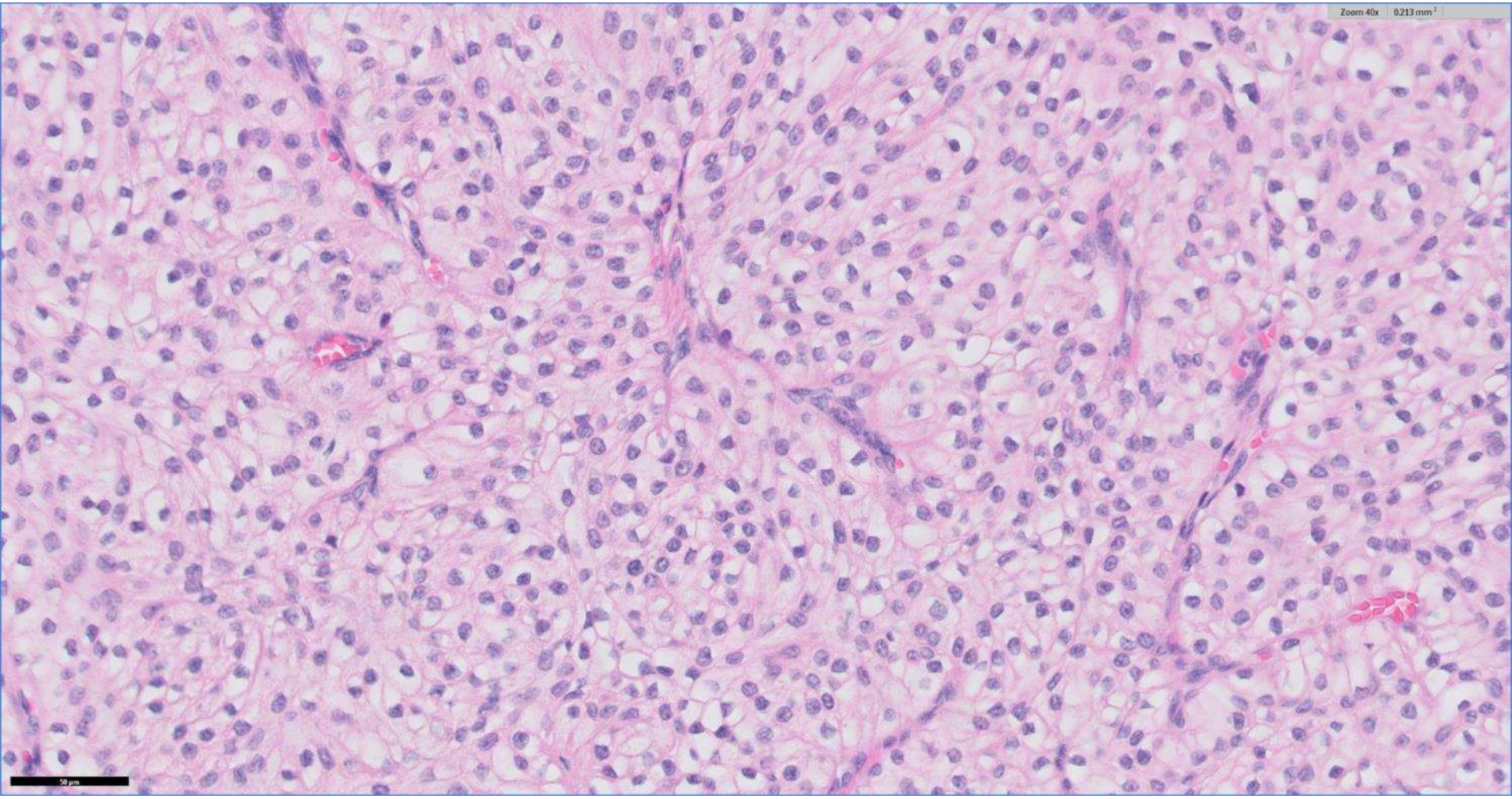

Zoom 5x
13.659 mm²
200 µm



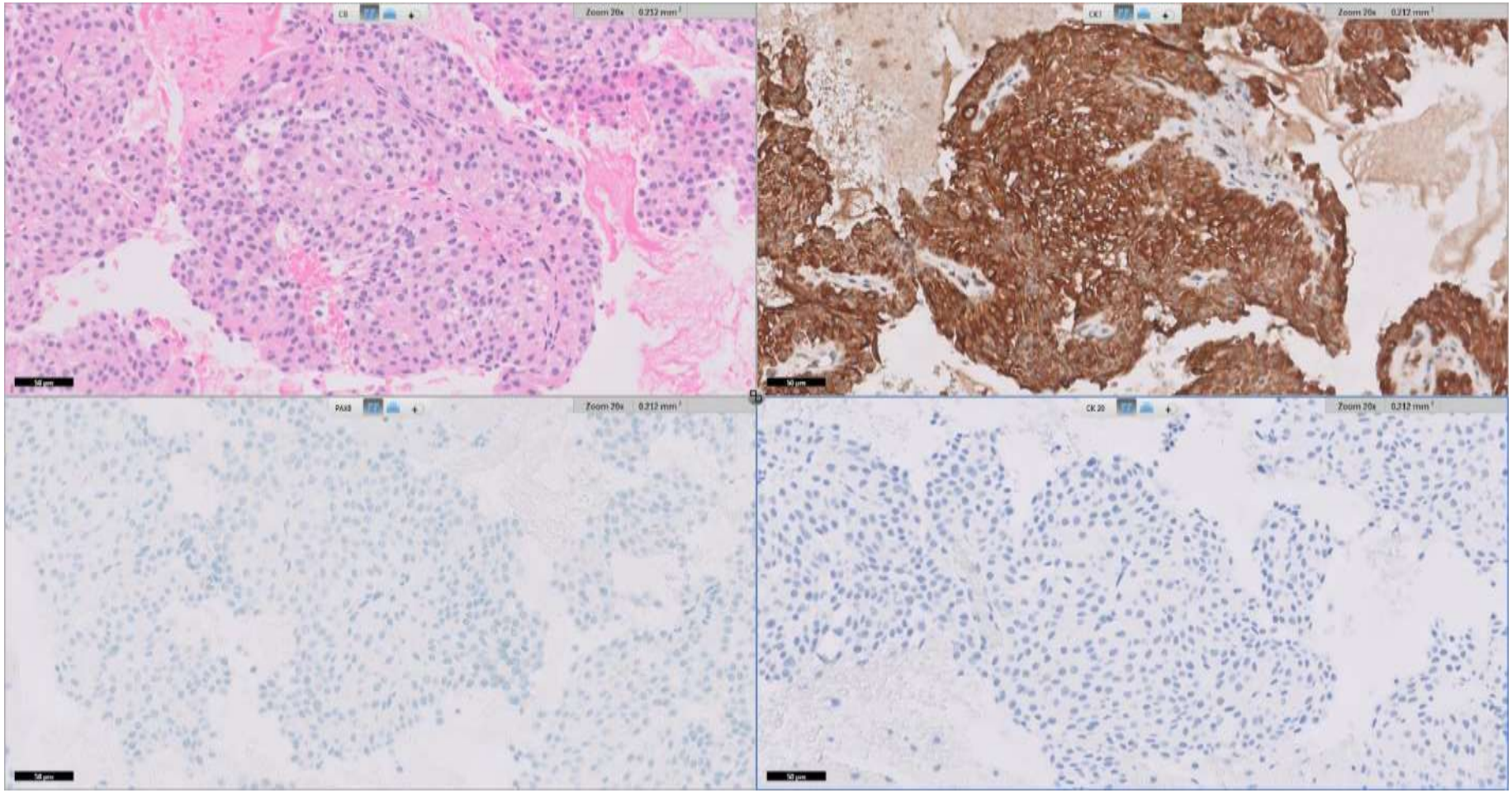

Zoom 20x
0.854 mm²
50 µm


Zoom 20x
0.854 mm²
50 µm

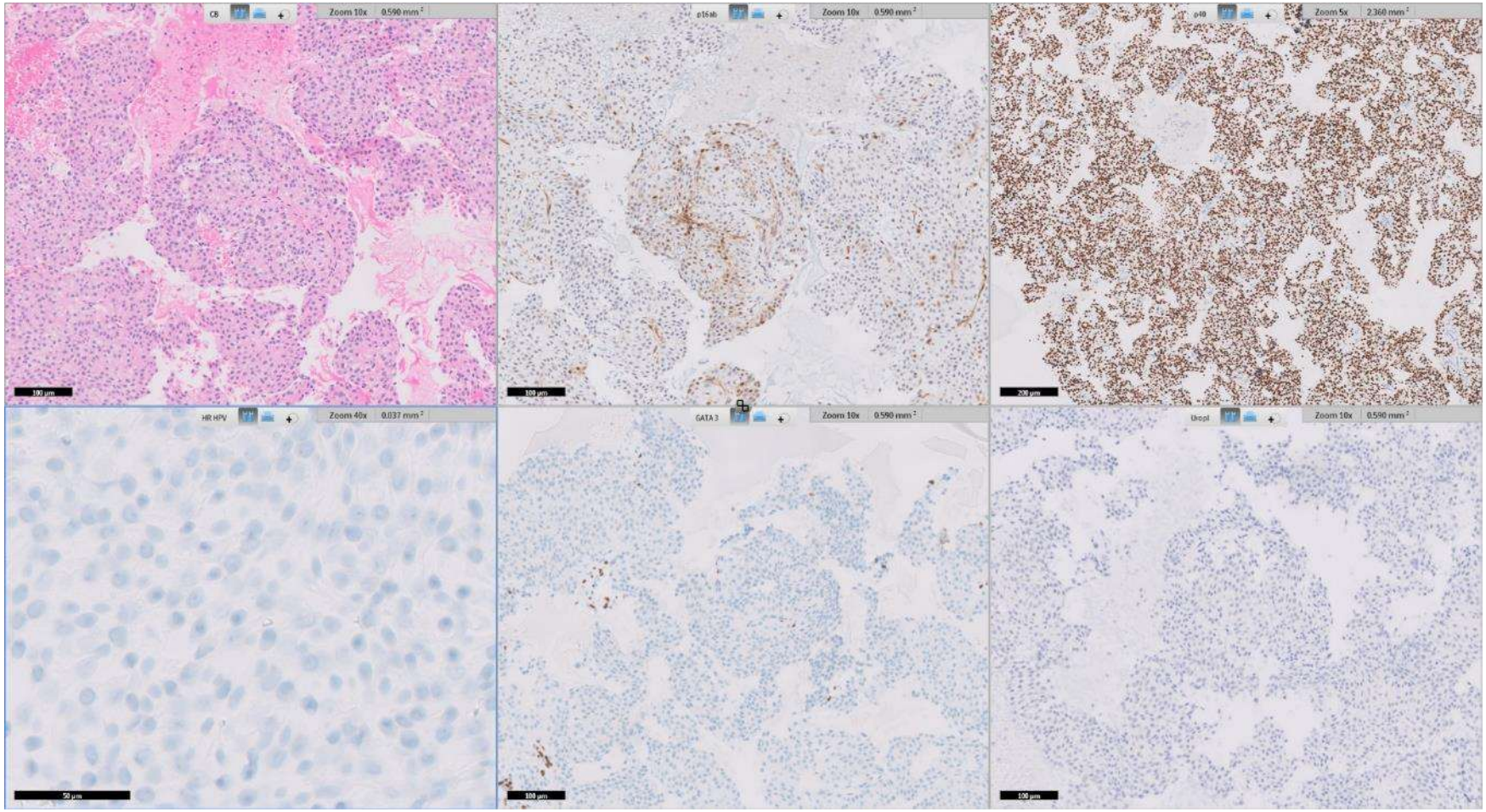

Zoom 40x
0.213 mm⁻¹
50 µm


Zoom 40x
0.213 mm²
50 µm

Immunohistochemistry



Immunohistochemistry



Diagnosis:

Intranodal Clear Cell Hidradenoma-Like Tumor

Clear Cell Hidradenoma vs Hidradenocarcinoma

Clear Cell Hidradenoma

- Benign cutaneous adnexal neoplasm
- Typically solitary cutaneous nodules in adult patients
- Well-circumscribed, non-encapsulated
- Polygonal/fusiform cells with clear-to-eosinophilic cytoplasm
- Duct-like/cystic spaces
- Variable fibrosis

Clear Cell Hidradenocarcinoma

- Suggested Criteria
  - Infiltrative margins / deep infiltration
  - Necrosis
  - Nuclear pleomorphism
  - >4 mitotic figures / 10 HPF
  - Ki67 > 11% -or- PHH3 > 0.7%
  - LVI / PNI

> Am J Dermatopathol. 2021 Jun 1;43(6):e76-e79. doi: 10.1097/DAD.0000000000001886.

Three Cases of Clear Cell Hidradenoma With "Benign" Lymph Node Involvement

Guillermo Gonzalez-Lopez [1], Maria C Garrido-Ruiz [1], Juan J Rios-Martin [2], Jose L Rodriguez-Peralto [1]

Affiliations + expand

PMID: 33464750 DOI: 10.1097/DAD.0000000000001886

FROM THE INTERNATIONAL SOCIETY OF DERMATOPATHOLOGY

Clear Cell Nodular Hidradenoma Metastatic to a Lymph Node: Do "Benign" Metastases Exist?

Stefanato, Catherine M.; Chaudry, Iskander H.; Calonje, Eduardo J. **Author Information**

The American Journal of Dermatopathology: June 2006 - Volume 28 - Issue 3 - p 228

Review > J Cutan Pathol. 2016 Aug;43(8):702-6. doi: 10.1111/cup.12720. Epub 2016 May 17.

Lymph node location of a clear cell hidradenoma: report of a patient and review of literature

Claire Tingaud [1], Valérie Costes [1], Eric Frouin [2], Christophe Delfour [1], Bernard Cribier [3], Bernard Guillot [4], Vanessa Szablewski [1]

Affiliations + expand

PMID: 27080562 DOI: 10.1111/cup.12720

Intranodal CCH-Like Tumor – Clinical Data

TABLE 1. - Clinical Features

	Sex	Age, yr	Duration	Presentation	Treatment	Follow-Up
Case 1	F	29	6 mo	Inguinal lymphadenopathy	Resection of involved lymph node	4 mo
Case 2	M	32	NA	Inguinal lymphadenopathy	Ipsilateral inguinal lymph node dissection	7 yrs
Case 3	M	51	NA	Lower limb nodule with concurrent inguinal lymphadenopathy	Resection of cutaneous lesion and involved lymph node	7 yrs

F, female; M, male; NA, not available.

Intranodal CCH-Like Tumor – Clinical Data

TABLE 2. - Summary of Reported Cases of CCH With Lymph Node Involvement

Reference	Age, Gender, y	Cutaneous Lesion	Involved Lymph Node*	Further Treatment Beyond Resection of Cutaneous Lesion and Involved Lymph Node	Follow-Up†
Stefanato et al[5]	30 F	Thigh	Inguinal	No	6 yrs
Stefanato et al[5]	42 F	Axilla	Axillary	No	11 yrs
Stefanato et al[5]	57 M	None	Axillary	Axillary lymphadenectomy	2 yrs
Tingaud et al[8]	48 M	None	Inguinal	No	18 mo
Au et al[7]	36 F	Groin	Inguinal	No	Not specified

*A single lymph node was involved in all cases.
†Follow-up was reported to be uneventful in all cases.
F, female; M, male.

Clear Cell Hidradenoma – MAML2 Fusions

Frequent fusion of the *CRTC1* and *MAML2* genes in clear cell variants of cutaneous hidradenomas

Marta Winnes, Lena Mölne, Mart Suurküla, Ywonne Andrén, Fredrik Persson, Fredrik Enlund, Göran Stenman

First published: 02 March 2007 | https://doi.org/10.1002/gcc.20440 | Citations: 48

UC-eLinks

- t(11;19)(q21;p13)translocation results in a fusion of the N-terminal cyclic AMP response element binding protein (CREB) of the cAMP coactivator TORC1 (also called CRTC1) to MAML2.

- ***Intranodal tumors have yet to be tested for MAML2 Fusion

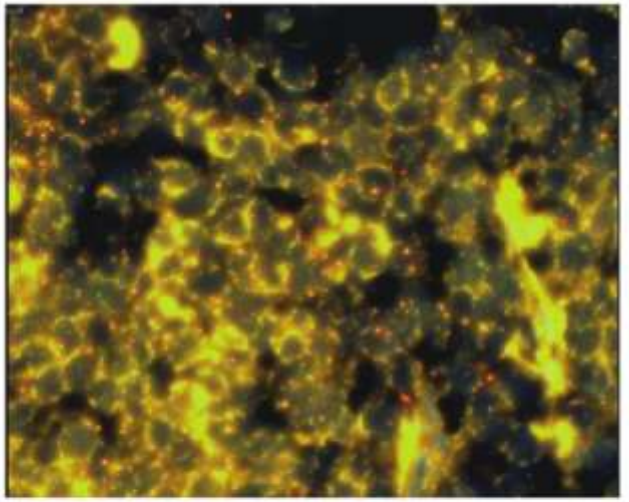


Fig. 3. MAML2 gene fluorescence *in situ* hybridization (FISH) analysis: separation of the red and green signals showing the *MAML2* gene rearrangement, in replacement of the usual yellow spot produced by the colocalisation of the red and green signals indicating an intact locus.

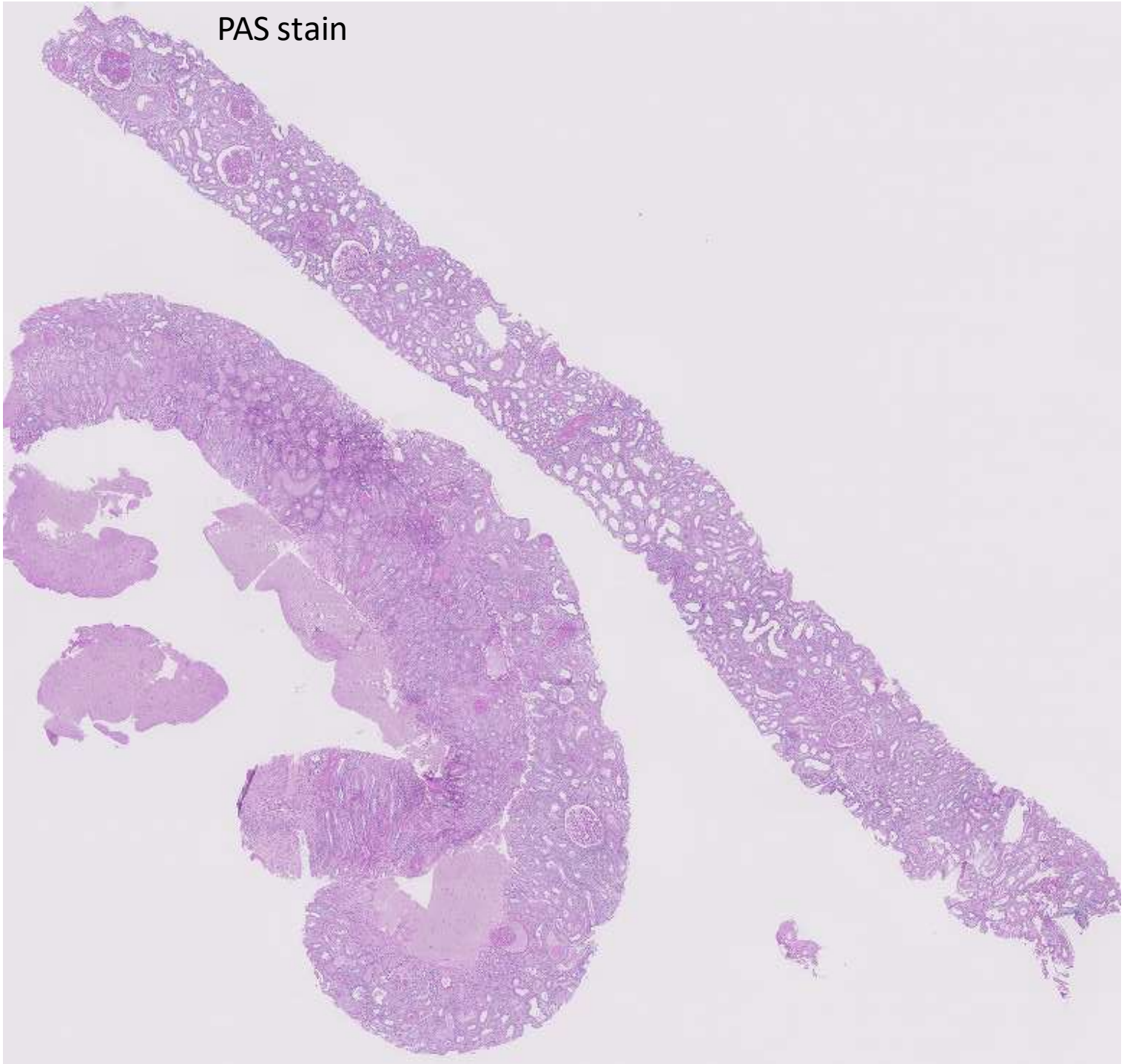
Summary

- Clear cell hidradenoma is a benign cutaneous adnexal tumor that may present as an isolated intranodal tumor ("Intranodal CCH-like tumor")
- Most common in inguinal/axillary lymph nodes and may or may not have concurrent cutaneous tumor
  - Low-malignant potential –vs– "benign" metastasis –vs– synchronous primary
  - Excellent outcomes in cases of intranodal tumor
- Bland, polygonal tumor cells with squamoid features and abundant eosinophilic-to-clear cytoplasm
- Benign cytomorphology without malignant features argues against hidradenocarcinoma
- *MAML2* FISH testing is confirmatory, but only (+) in ~50% and not tested in intranodal tumors

21-0705

Paul Miller/Megan Troxell; Stanford

21-year-old African American man with recent COVID infection, pneumonia, flank pain. Rising creatinine and 11 gram/day proteinuria.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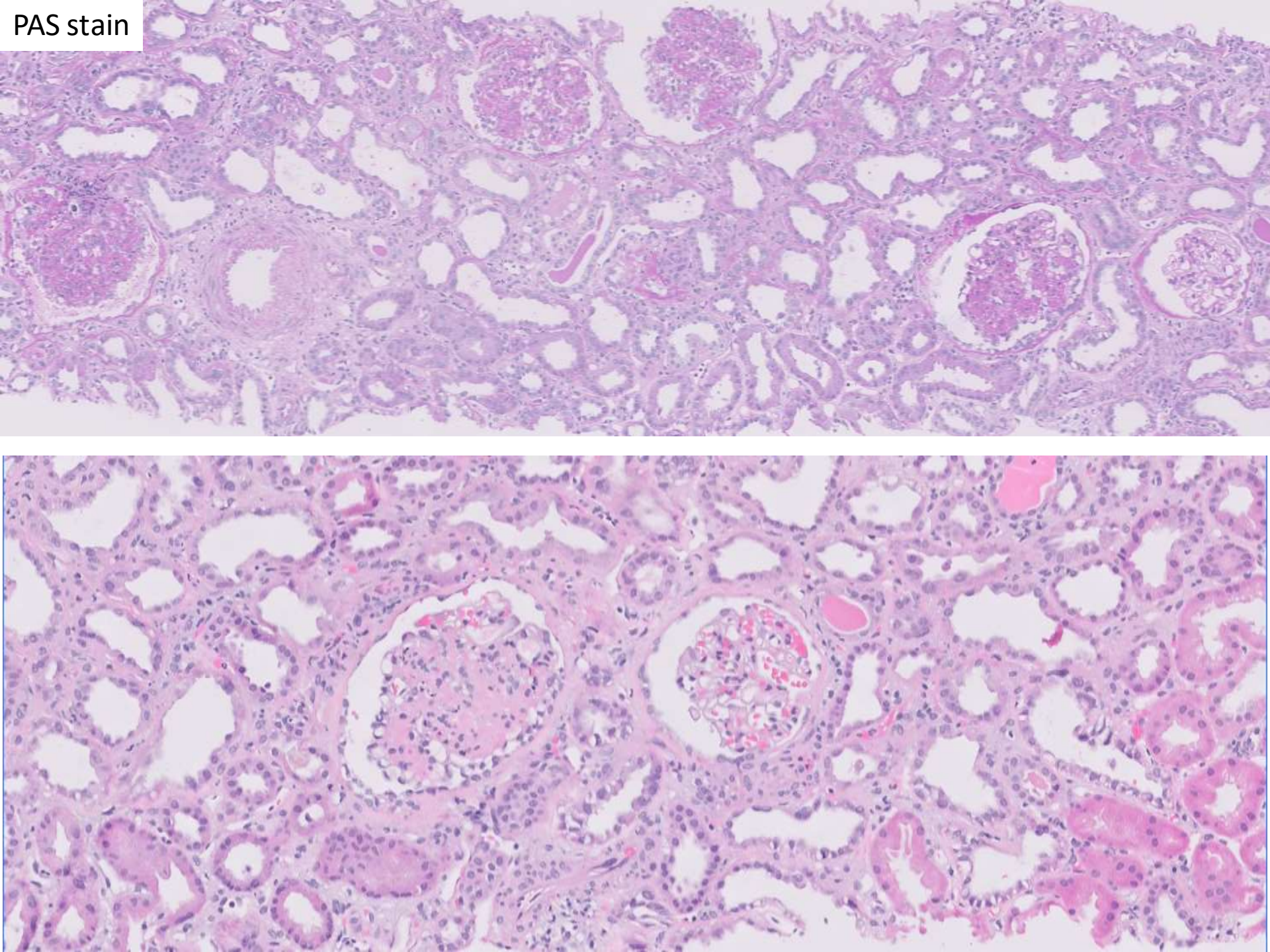
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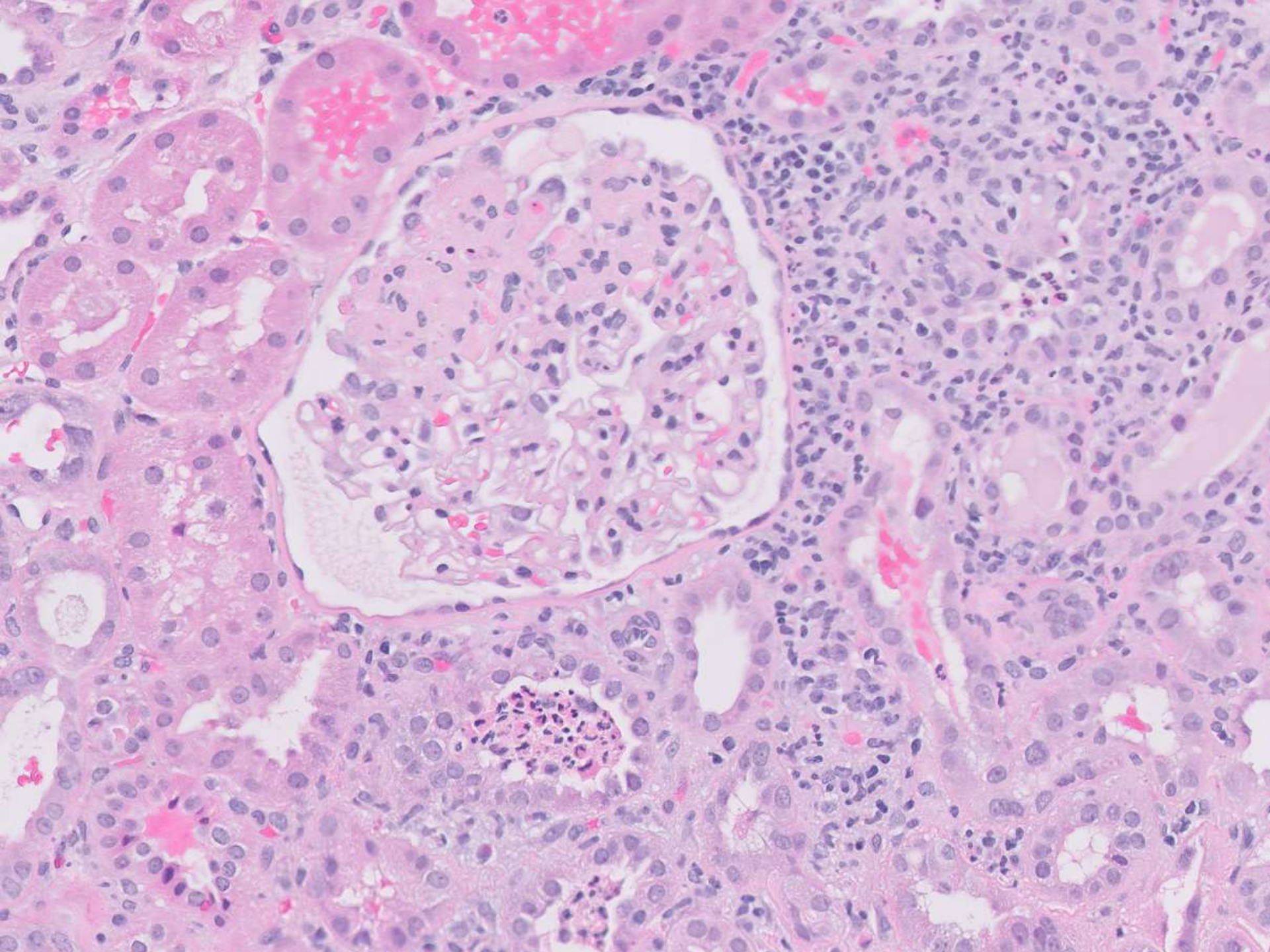

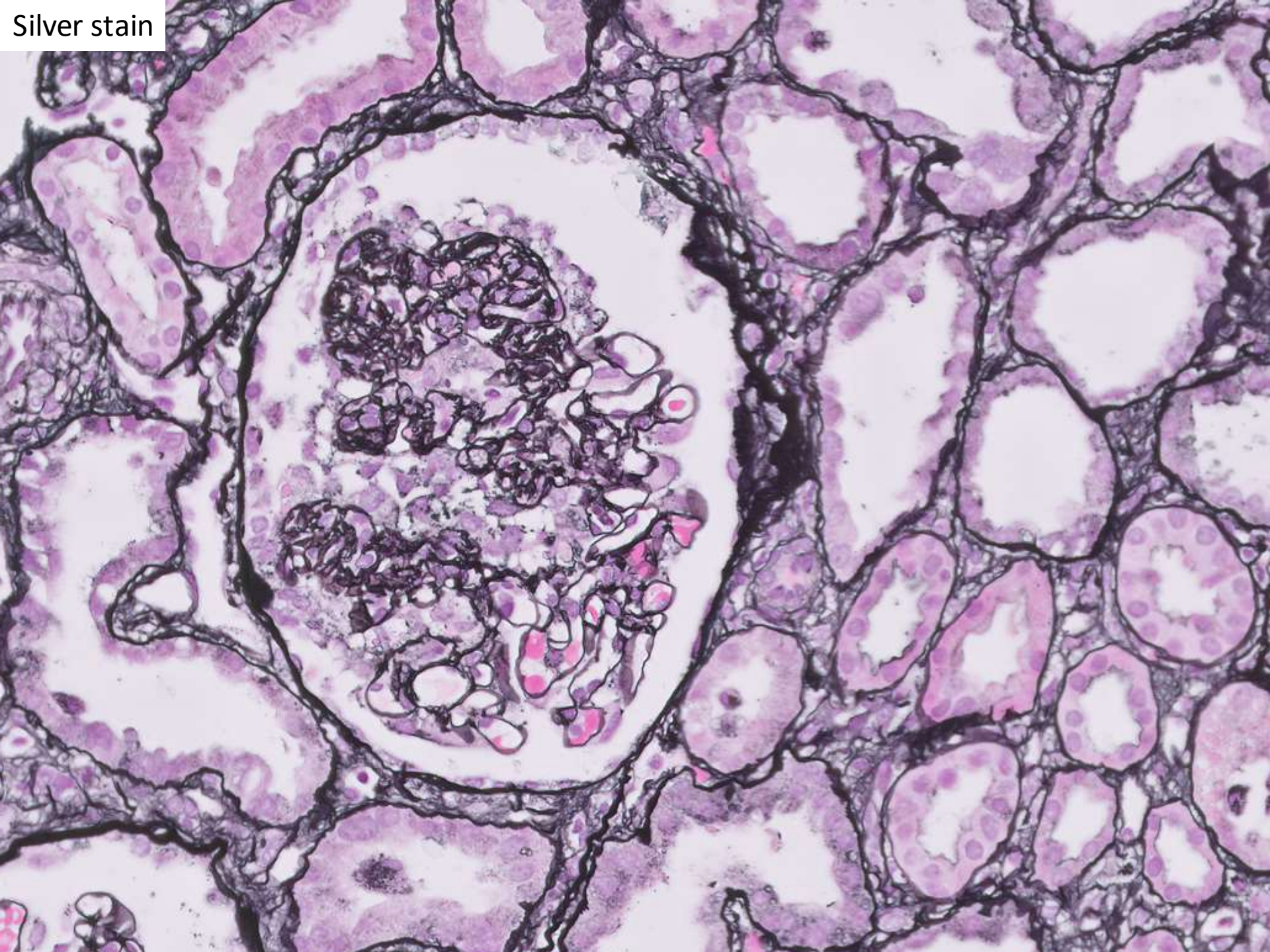
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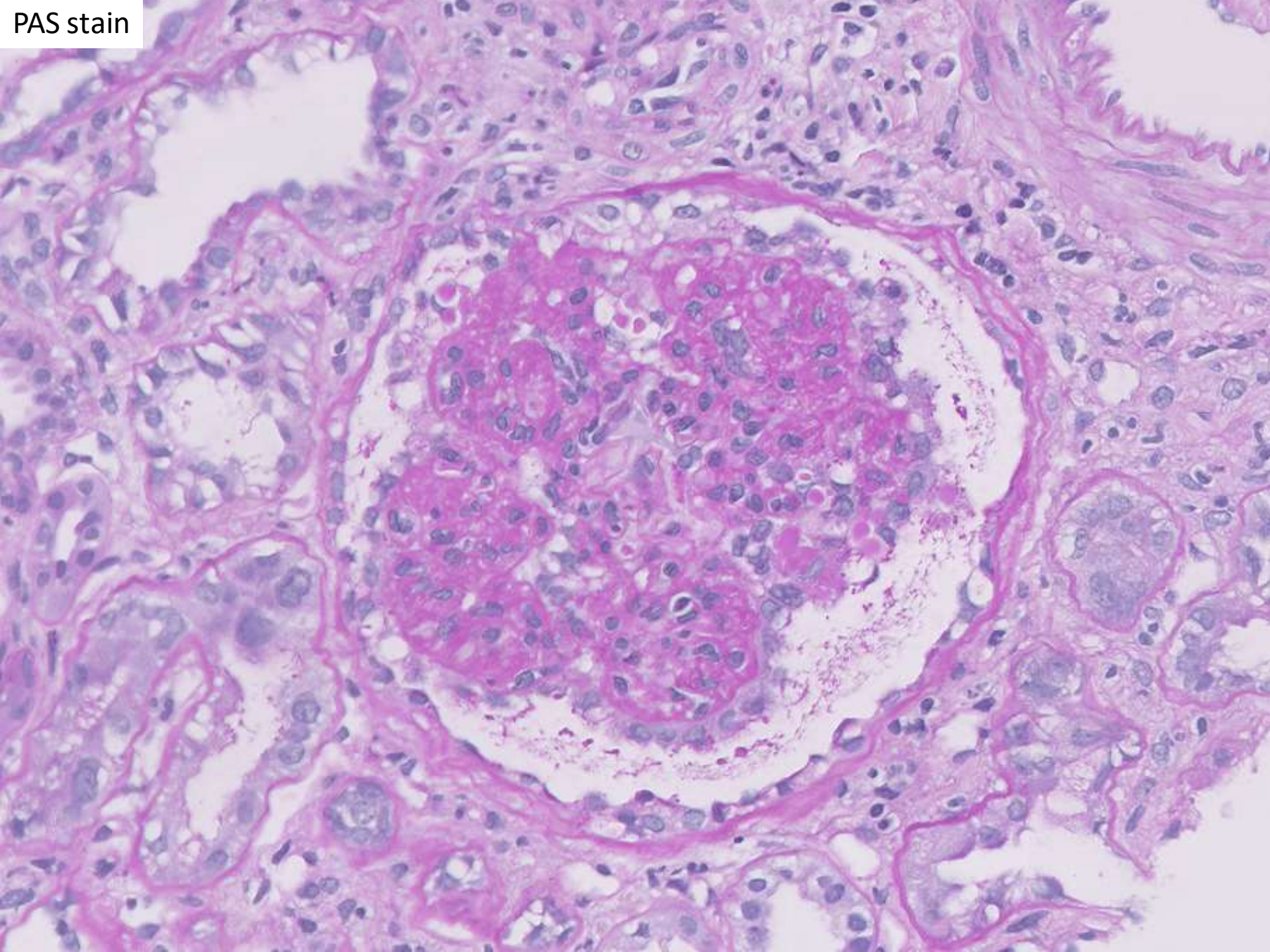
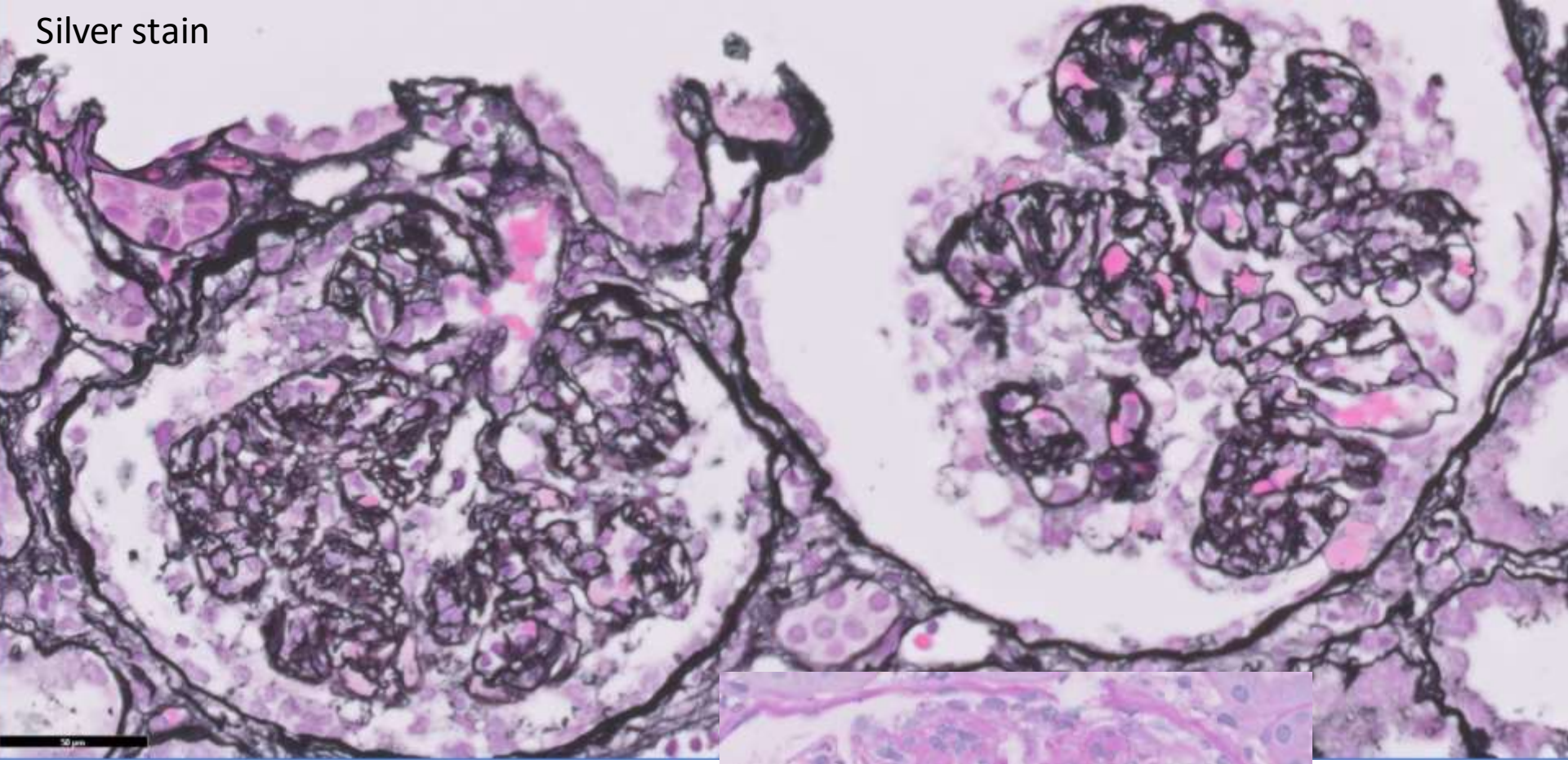
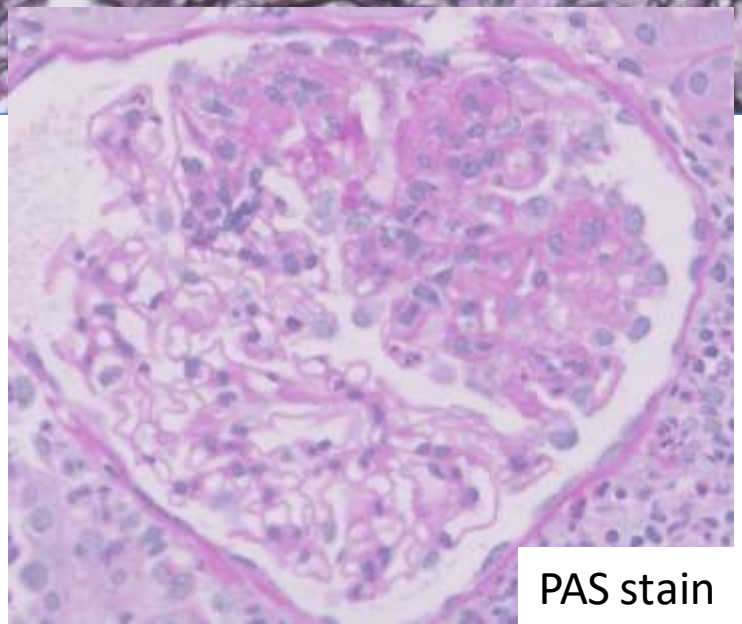

PAS stain

Silver stain





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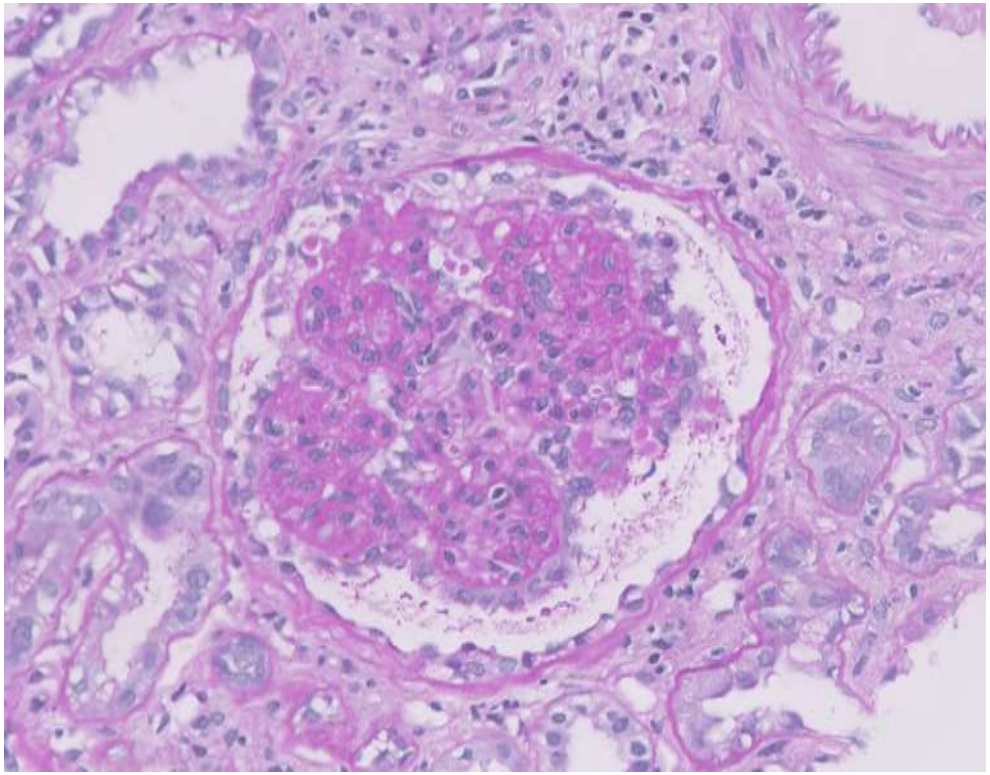
Histologic Findings Collapsing Glomerulopathy

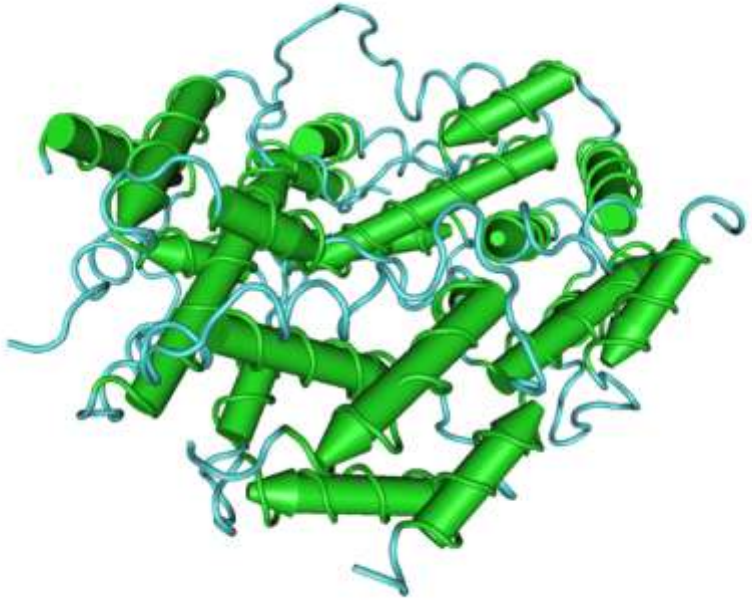


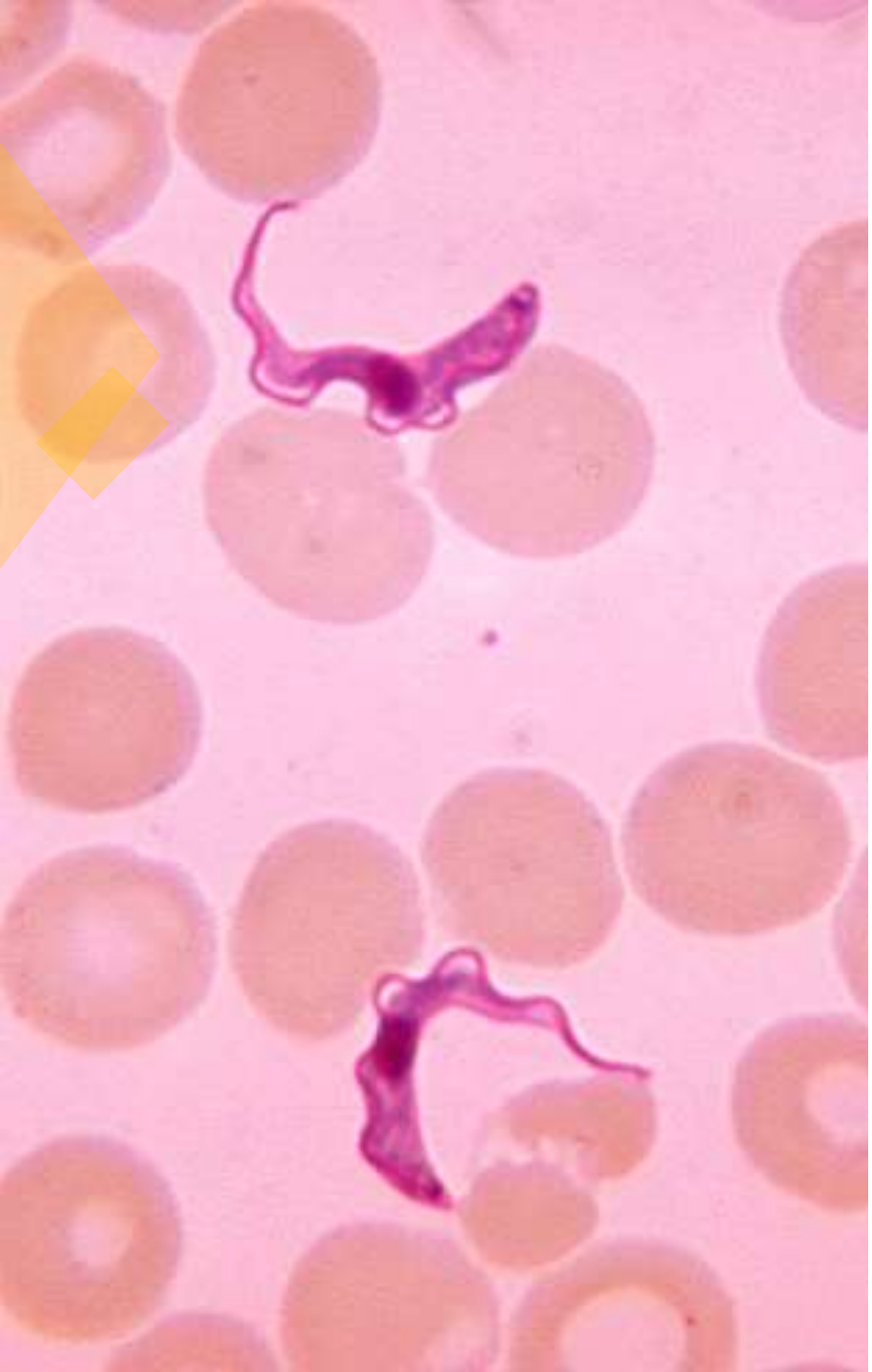
- At least one glomerulus with segmental or global collapse of the glomerular tuft with epithelial cell hypertrophy/hyperplasia
- Tubulointerstitial scarring and interstitial acute/chronic inflammation are common
- Microcystic tubular dilatation is characteristic
- IF: Negative or non-specific staining of C3/IgM
- EM: Diffuse podocyte foot process effacement. TRIs are commonly seen.

Collapsing Glomerulopathy Associations

- Infections
  - **HIV (e.g HIVAN), COVID-19**, CMV Parvovirus B19, EBV
- Systemic disease
  - SLE, HLH, transplant
- Drugs
  - Interferons, bisphosphonates
- Vascular diseases
  - Atheroembolic disease, TMA, CNI-associated

?





APOL1, Trypanosomes, and Kidney Disease

- APOL1 G1 and G2 mutations
  - Evolved approximately 10,000 years ago in the west African population as a defense against select Typanosoma subspecies
- Approximately 14% of the African American population are homozygous for the risk allele.
- APOL1 G1 and G2 have been associated with an increased risk of a spectrum of kidney disease (including collapsing GN) in the African population
  - The mechanism is not well understood but likely involves disrupted endosomal/lysosomal trafficking in the podocytes

COVID and Collapsing GN

- Recent case series of 6 patients with COVID and collapsing GN:
  - All 6 patients were African American with high risk APOL1 genotypes
- COVID infection has been shown to cause a strong interferon response
- There is no definitive evidence that COVID can directly infect the kidney (PCR, EM, and IHC are negative)

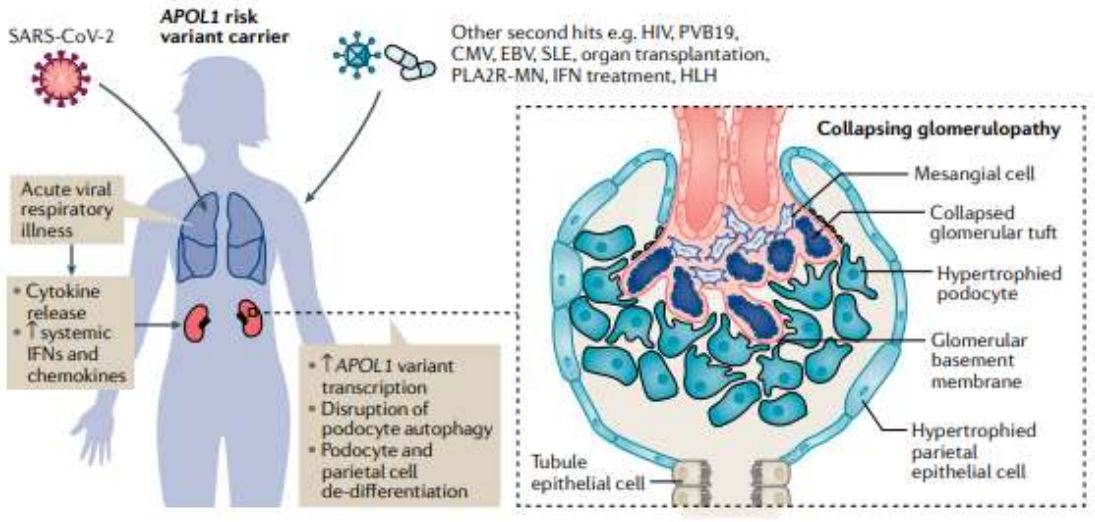


Table 1. Clinical information of six patients with COVID-19, AKI, and nephrotic-range proteinuria

Patient Identifier	Age (y)	Sex	Race	APOL1 Risk Variants	Serum Creatinine(mg/dl)		Urine					Hgb (mg/dl)	WBC (/ul)	Platelet (/ul)	Albumin (g/dl)	Ferritin (ng/ml)	Final Disposition
					Baseline	At Biopsy	Dipstick Protein	Blood (cells/hpf)	WBC (cells/hpf)	UPCR (g/g)	Urine Sediment Microscopy						
1	63	M	B	G1/G1	1.3	4.9	3+	1–3	0–5	12.7	Abundant waxy and muddy brown granular casts	15.6	8.8	244	2.1	2147	Discharged dependent on dialysis
2	64	F	B	G2/G2	1.5	4.2	3+	Negative	Negative	4.6	Some waxy and coarse granular casts	8.8	7.4	421	2.4	6875	Discharged home with improving serum creatinine, did not need dialysis
3	65	F	B	G1/G1	1.3	2.9	3+	Negative	Negative	13.6	Many coarse granular and some muddy brown granular casts	8.3	16.6	299	2.6	4934	Needed dialysis, died with suspected pulmonary embolus
4	44	M	B	G1/G1	1.4	11.4	3+	>100	0–5	25	NP	8.1	4.1	241	2.5	443	Discharged dependent on dialysis
5	37	M	B	G1/G2	1	9	3+	0–2	11–20	NP	NP	11.7	8	64	3	1450	Needed dialysis; then died of ventricular arrhythmia
6	56	M	B	G1/G1	1.2	6.7	3+	50–100	5–10	3.6	NP	13	7	113	2.9	1620	Needed dialysis; discharged off dialysis

Patients 1–3 were part of a 161-patient cohort of AKI in COVID-19[5] and patient 4 was previously reported individually.[7] WBC, white blood cell; UPCR, urine protein-creatinine ratio; Hgb, hemoglobin; M, male; B, black; F, female; NP, not performed.

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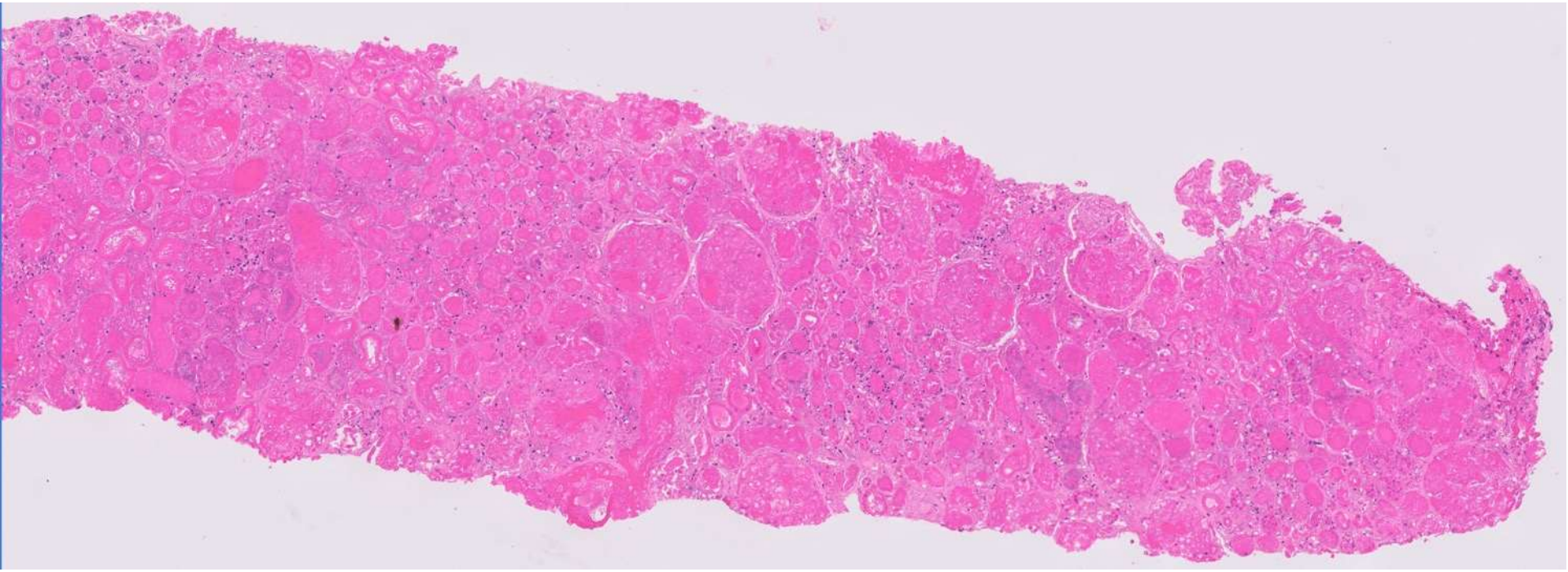
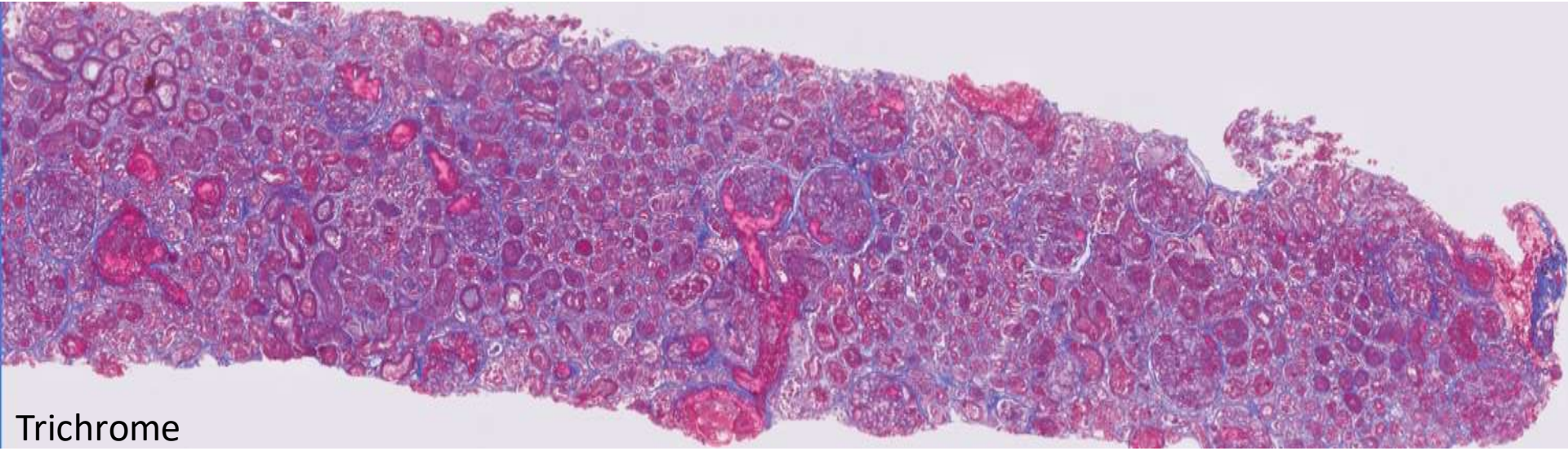
2. Velez JCQ, Caza T, Larsen CP. COVAN is the new HIVAN: the re-emergence of collapsing glomerulopathy with COVID-19. Nat Rev Nephrol. 2020 Oct;16(10):565-567. doi: 10.1038/s41581-020-0332-3. Erratum in: Nat Rev Nephrol. 2020 Aug 11;: PMID: 32753739; PMCID: PMC7400750.

21-0706

Megan Troxell; Stanford

6-year-old boy with Shiga toxin positive bloody diarrhea and thrombocytopenia, complicated by covid and Multisystem Infammatory Syndrome in Children (MIS-C). Renal biopsy during prolonged hospitalization.

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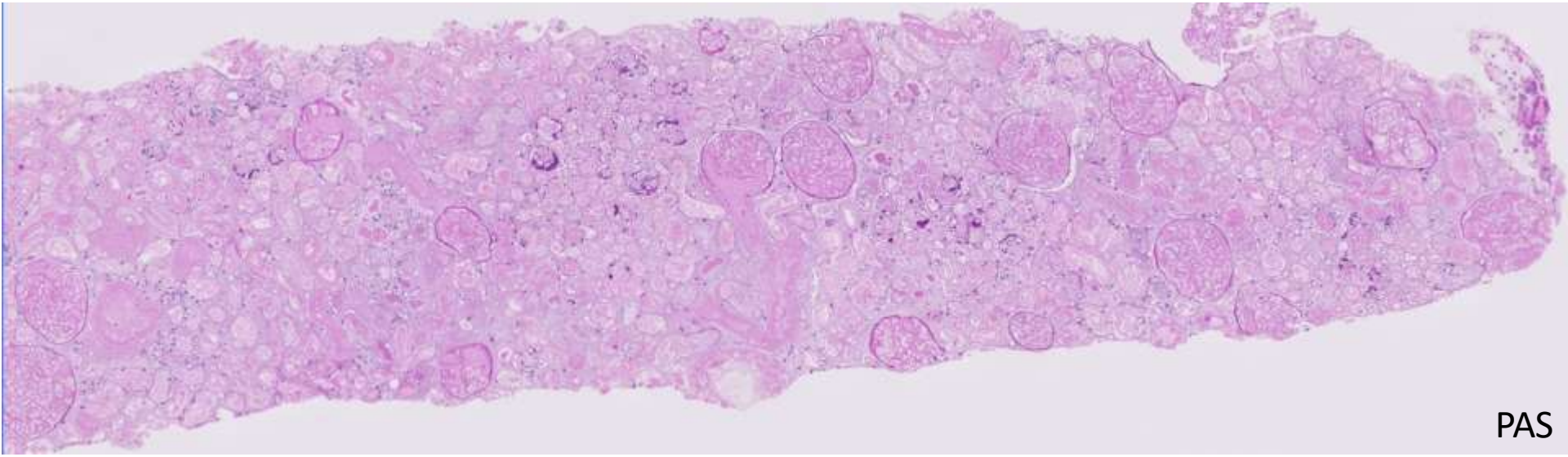
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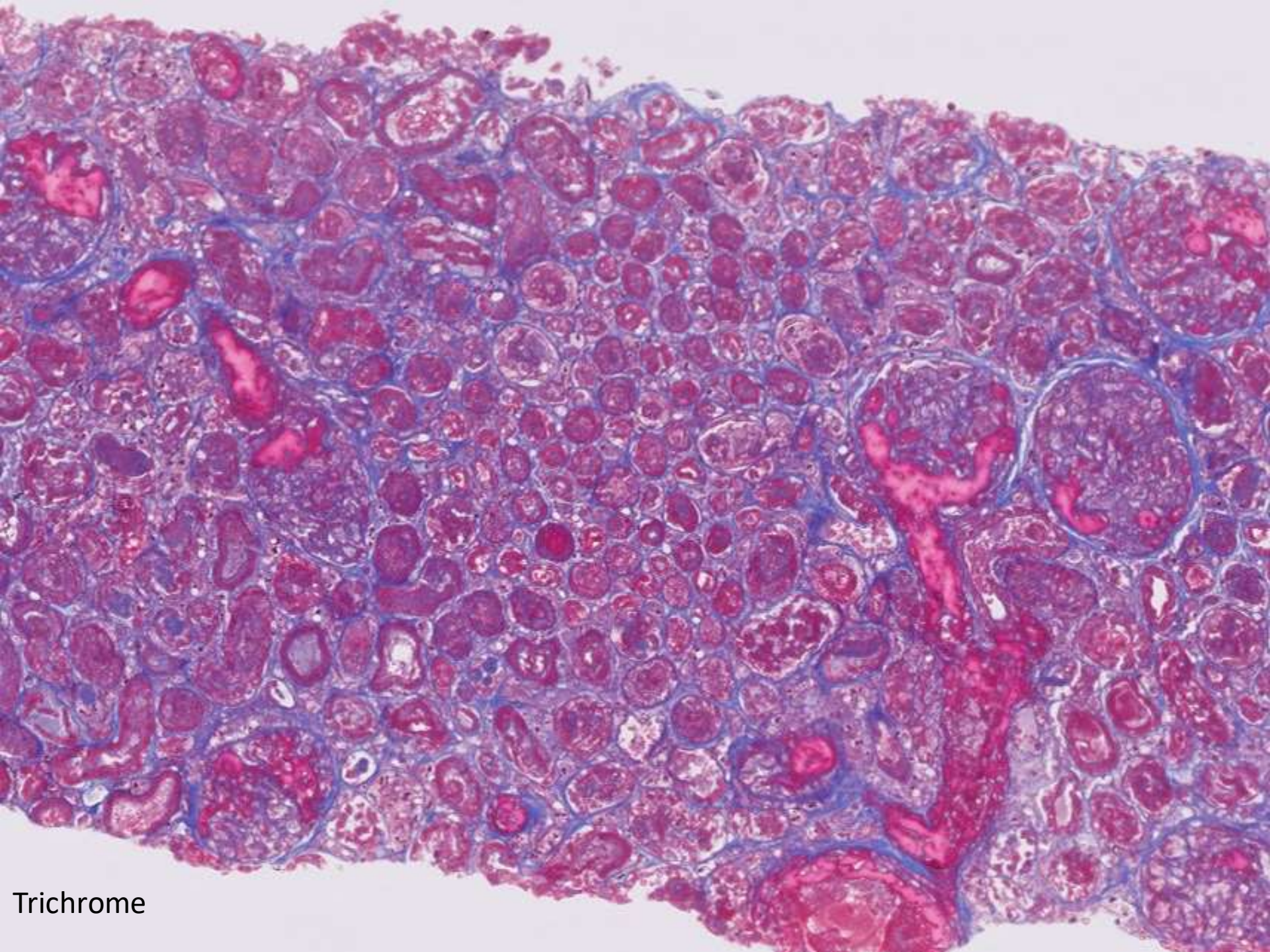

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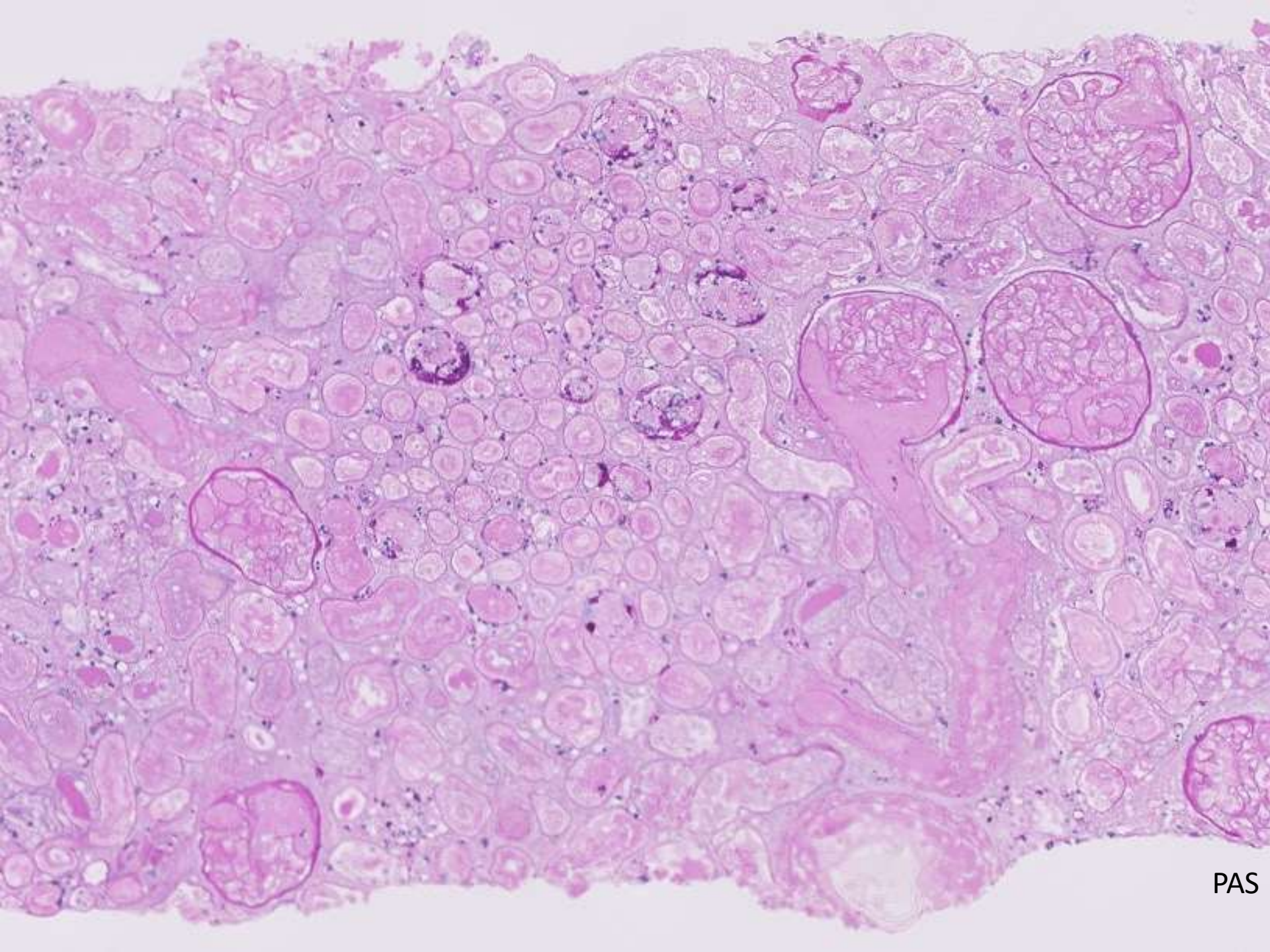
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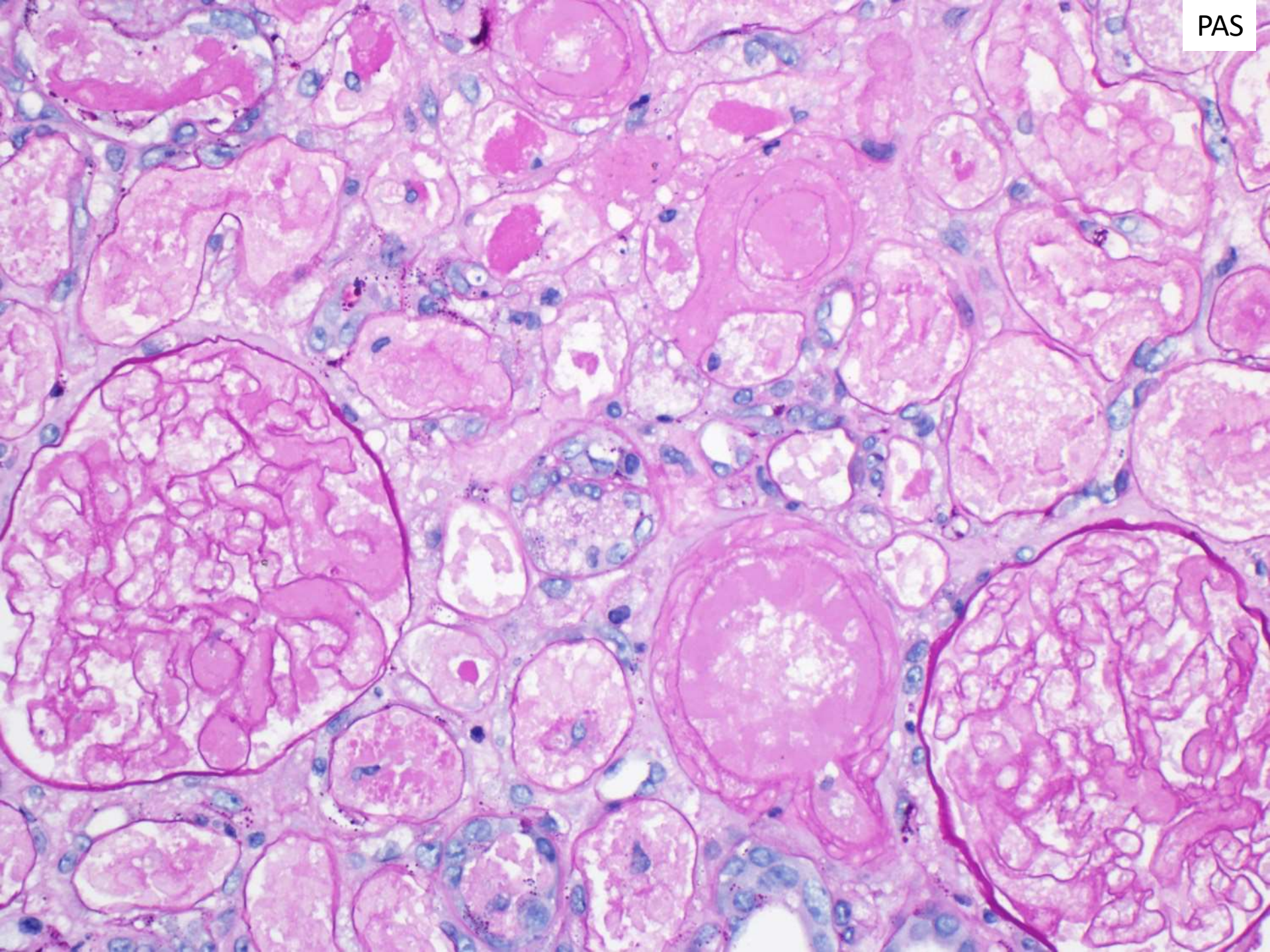
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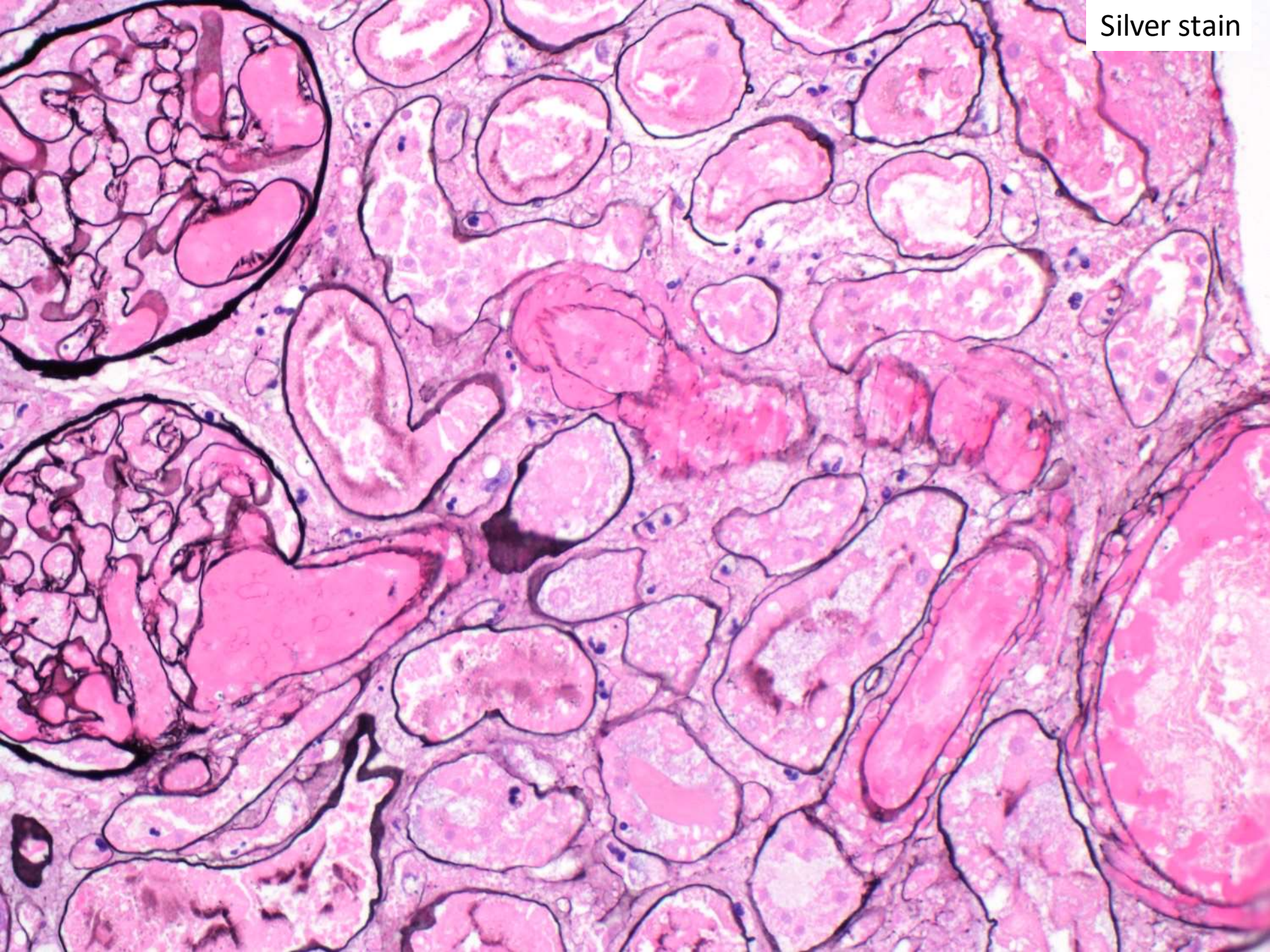
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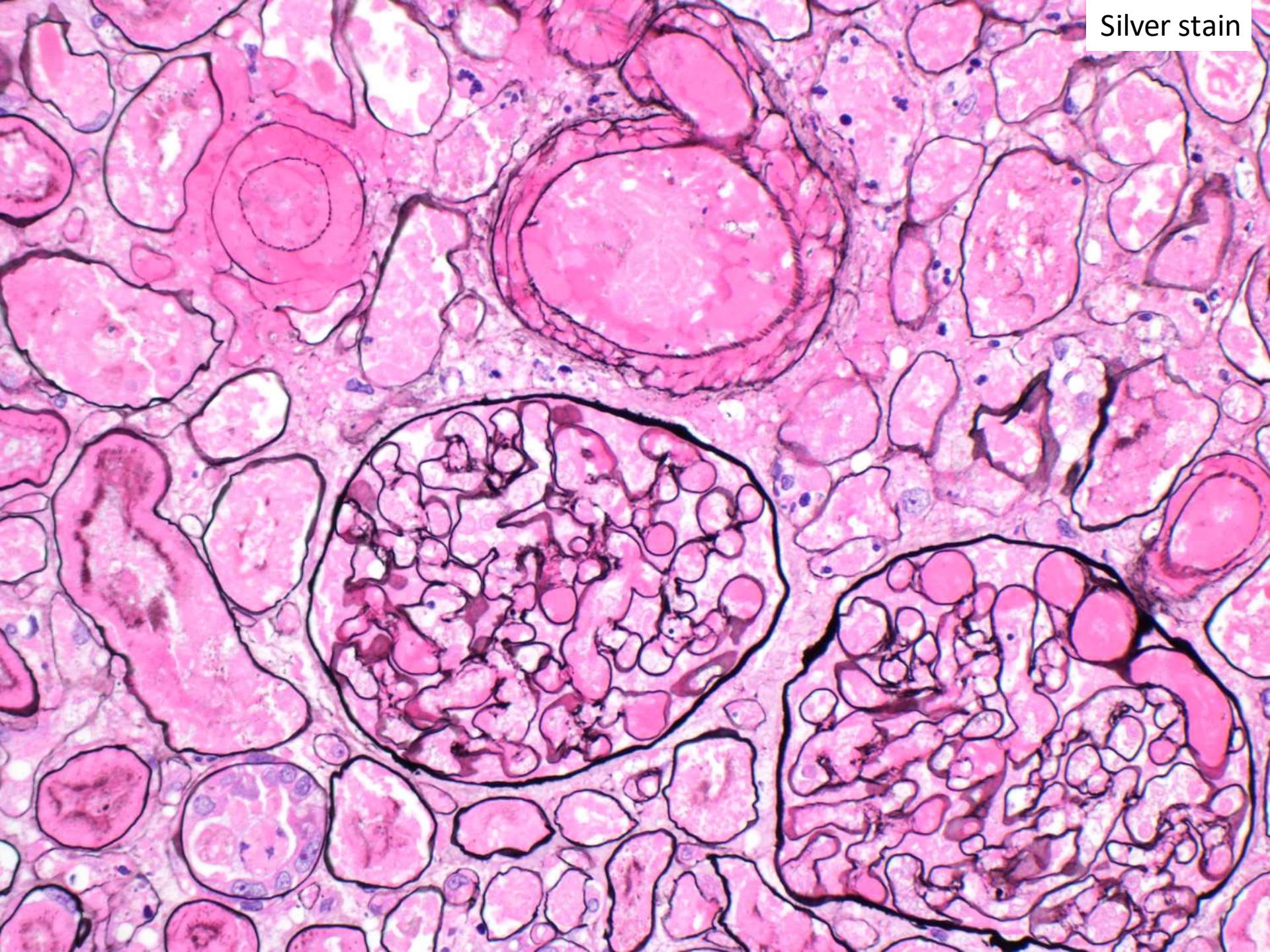
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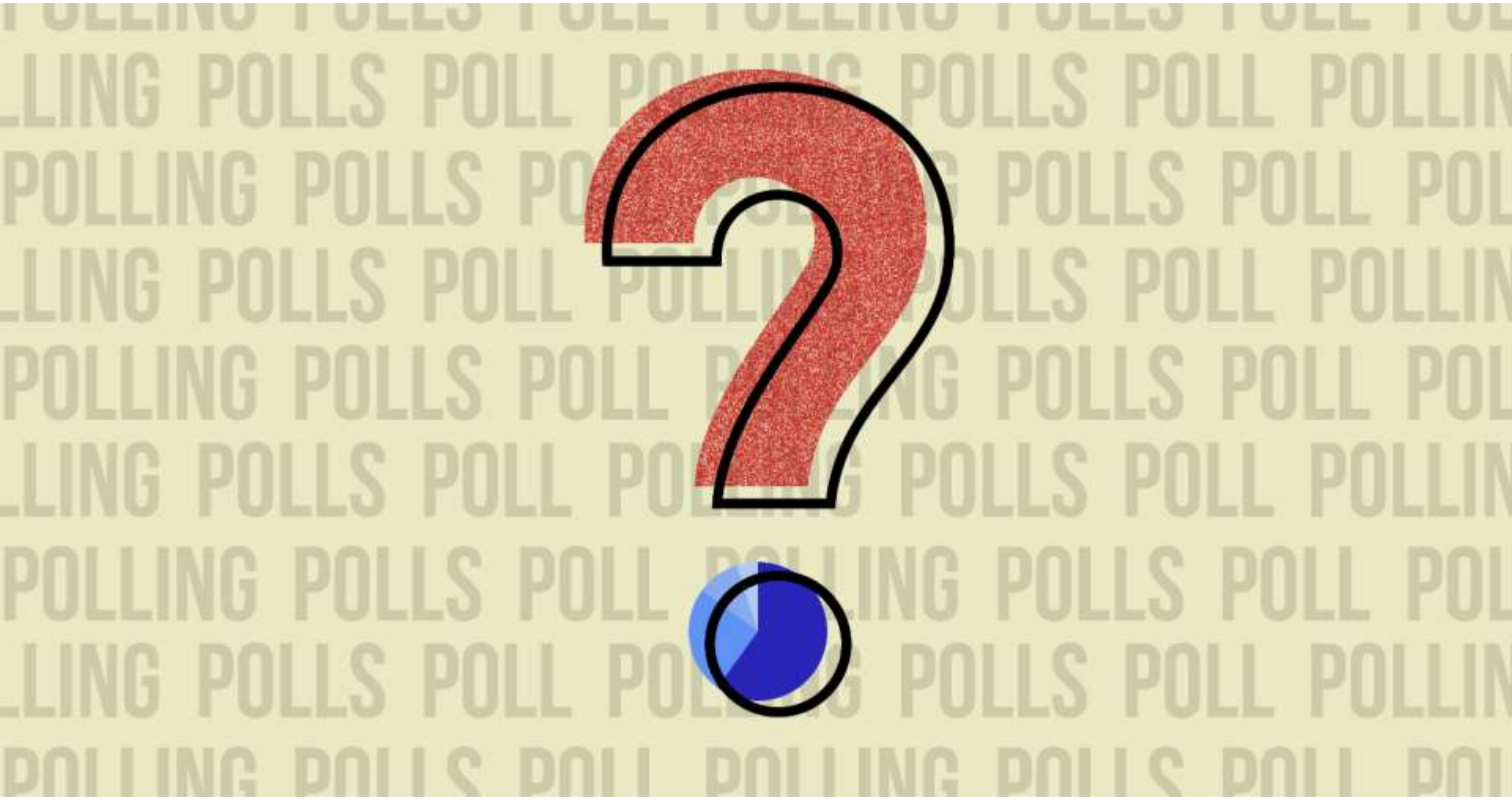
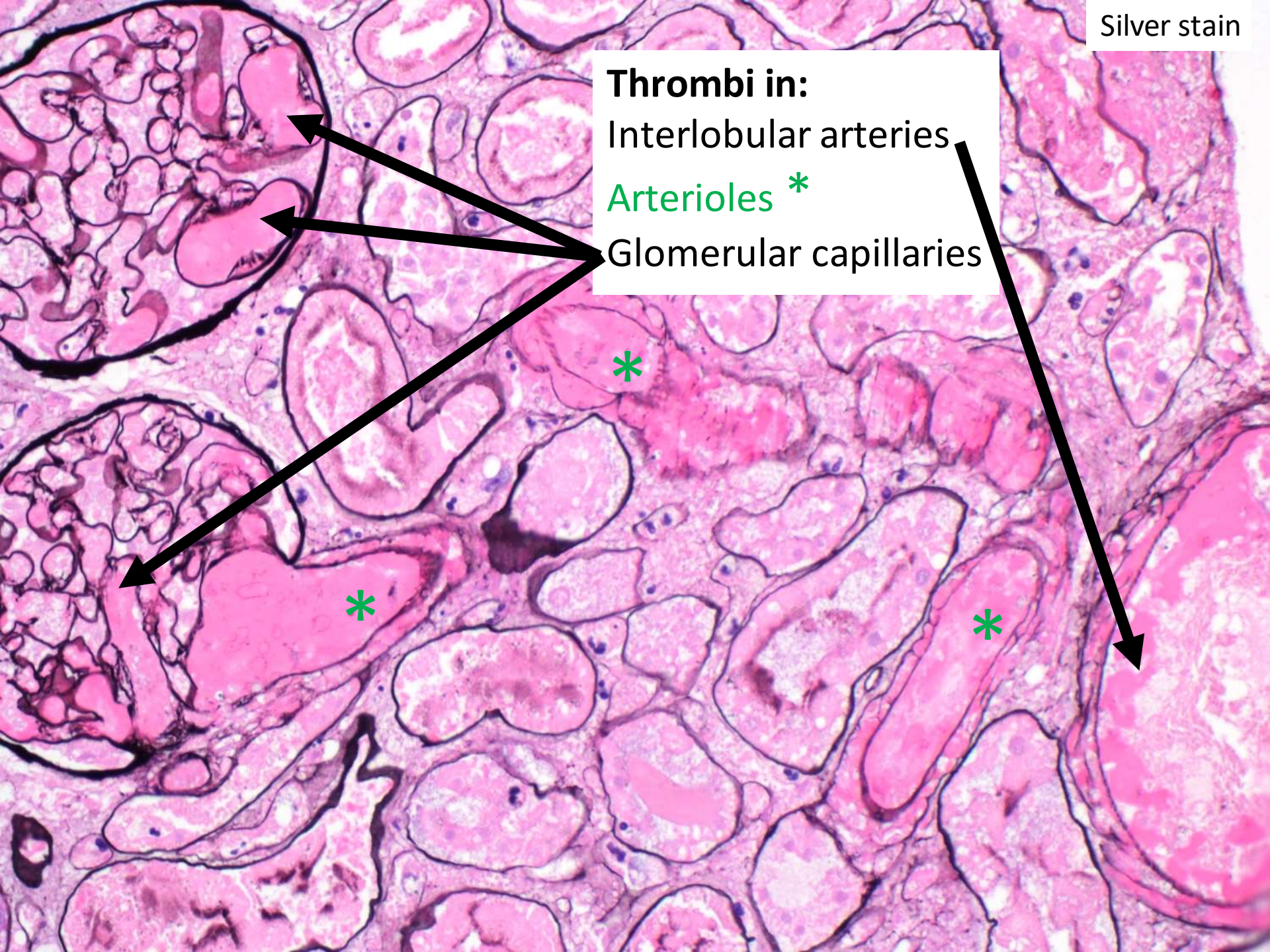
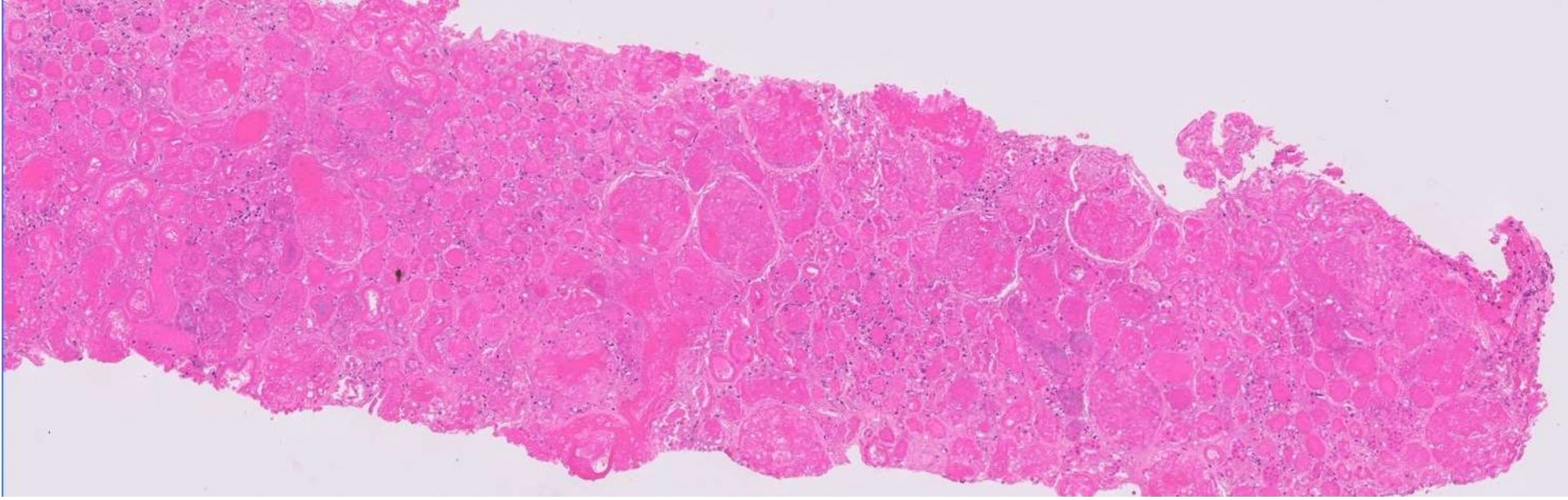

POLLING POLLS POLL

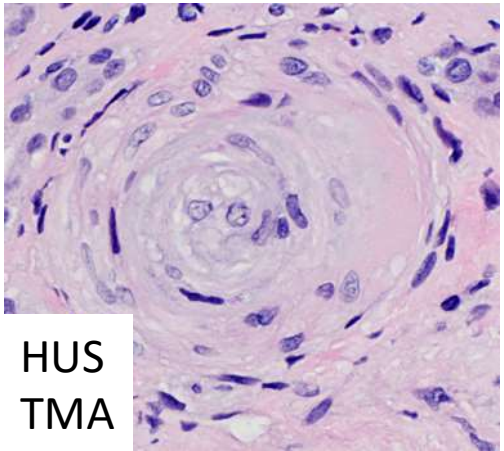

Silver stain
Thrombi in:
Interlobular arteries
Arterioles *
Glomerular capillaries
*
*
*



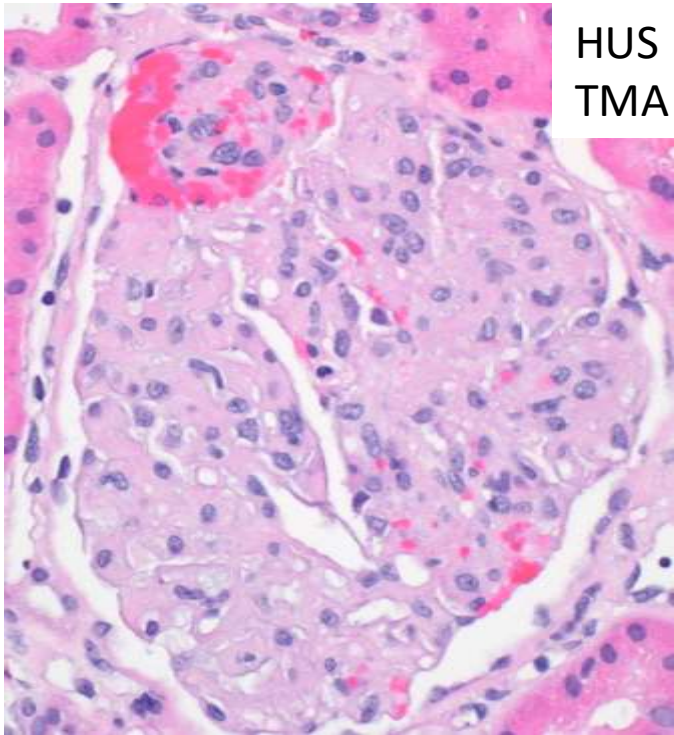
Infarcted kidney at South Bay? Ddx:

- Shiga toxin associated HUS
- Covid associated thrombosis
- Covid associated TMA
- Combination

- Outcome:
  - ESKD/transplant



HUS
TMA

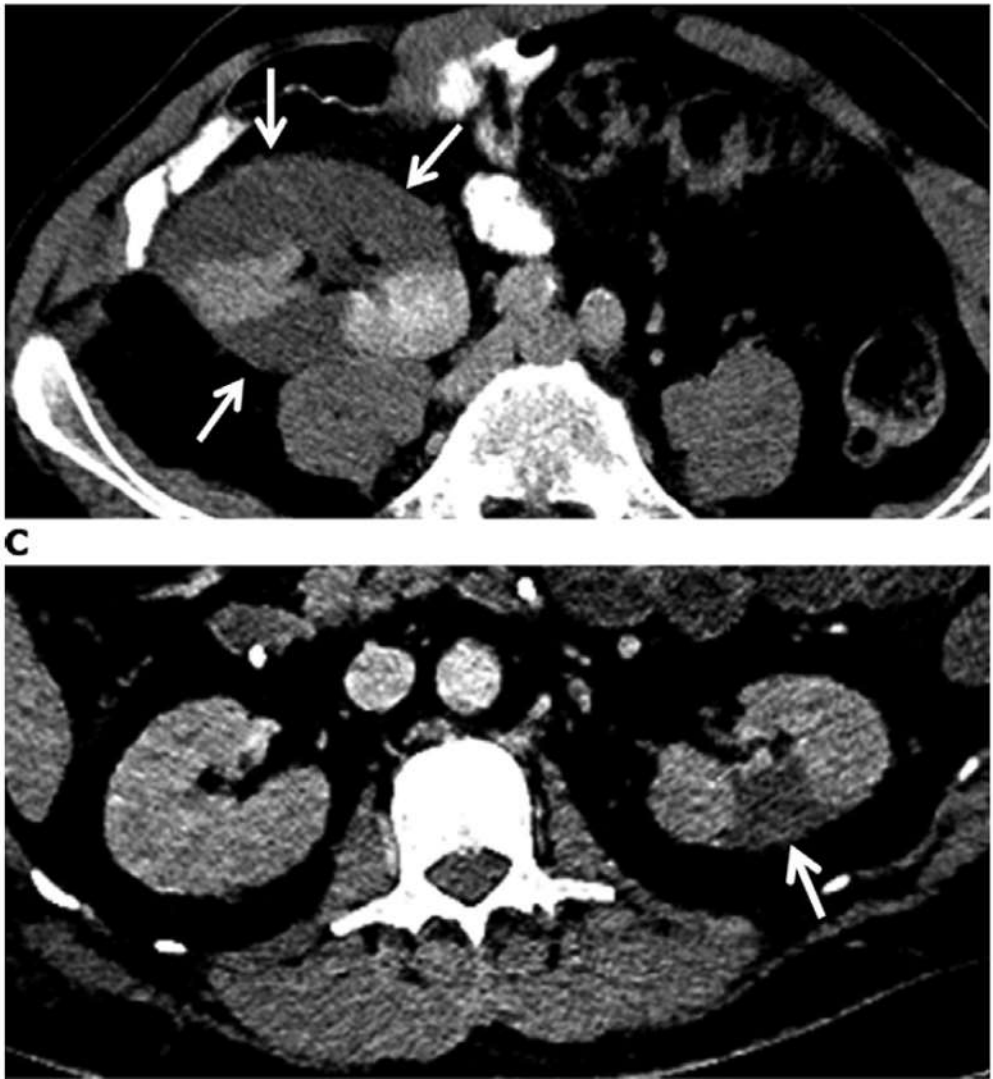


HUS
TMA

Covid coagulopathy

- Thrombocytopenia, elevated D-dimer
- Thromboembolism covid ICU 30-50%
- Stroke, MI (2.5%?)
- Pulmonary microvascular thrombi 9x influenza at autopsy

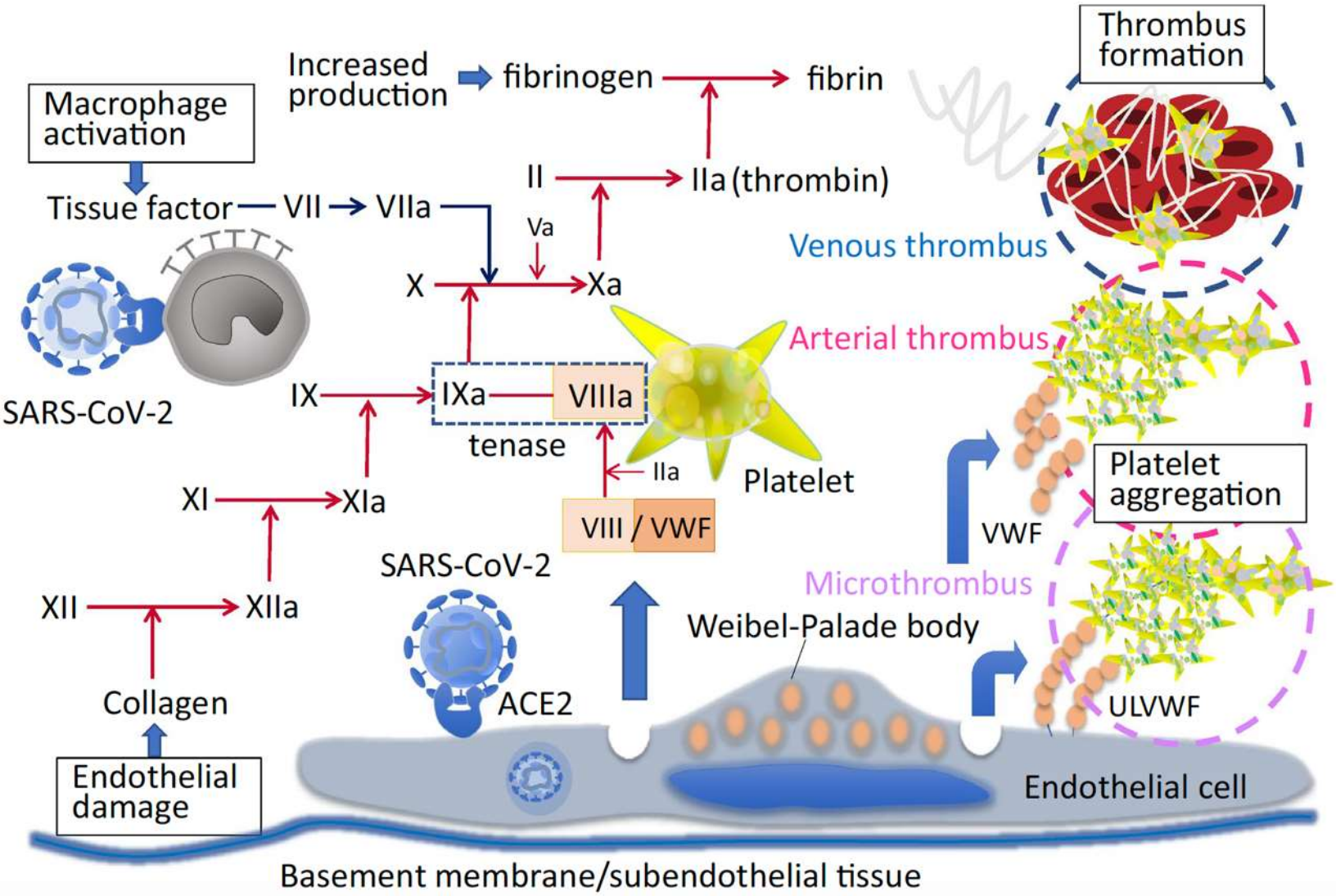
Kidney Infarcts Post. AJKD 2020



The coagulopathy, endotheliopathy, and vasculitis of COVID-19

Toshiaki Iba[1] · Jean Marie Connors[2] · Jerrold H. Levy[3]

Inflammation Research
https://doi.org/10.1007/s00011-020-01401-6



Also:
Innate imm
Complement
Cytokines
NETosis
Anti-phospho-lipid

MIS-C

- Older children after covid infection
- GI symptoms but CV danger

Box 1 Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19 [38] Preliminary case definition [a]

Children and adolescents 0–19 years of age with fever ≥3 days.

AND two of the following:

1. Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet).
2. Hypotension or shock.
3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

AND.

Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.

AND.

No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.

AND.

Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

Radia. Paediatric Respiratory Reviews 2021;38:51–57

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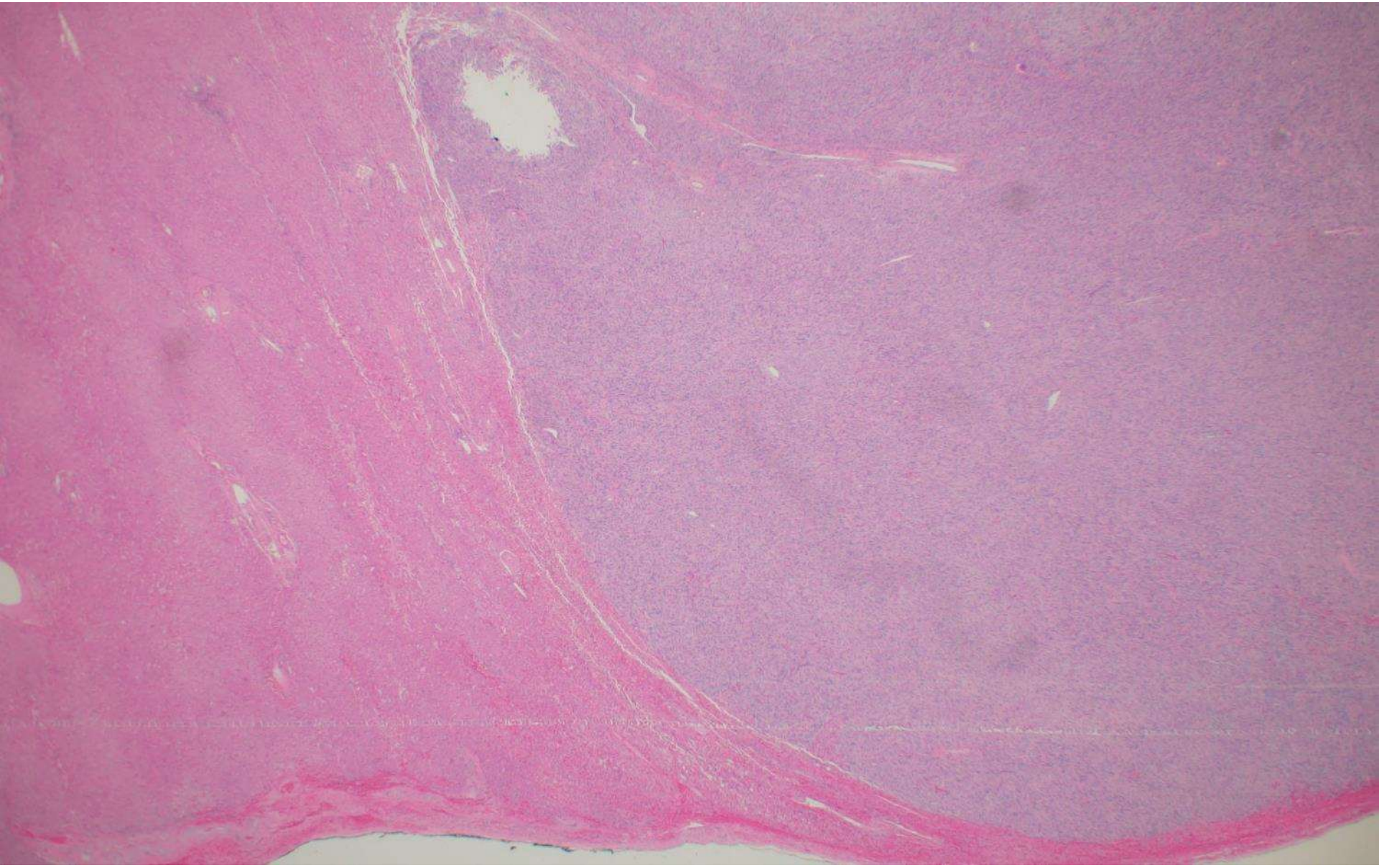
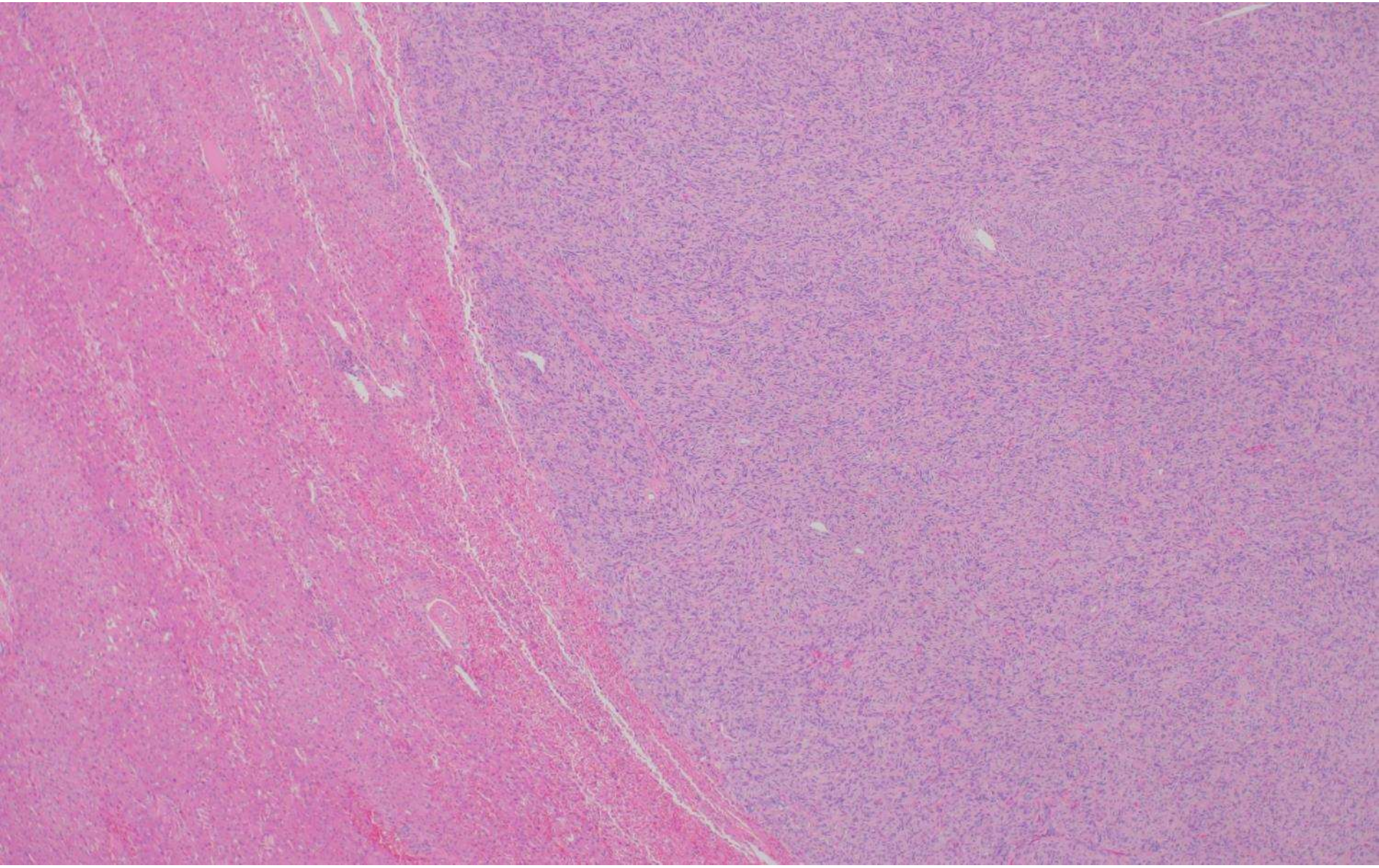
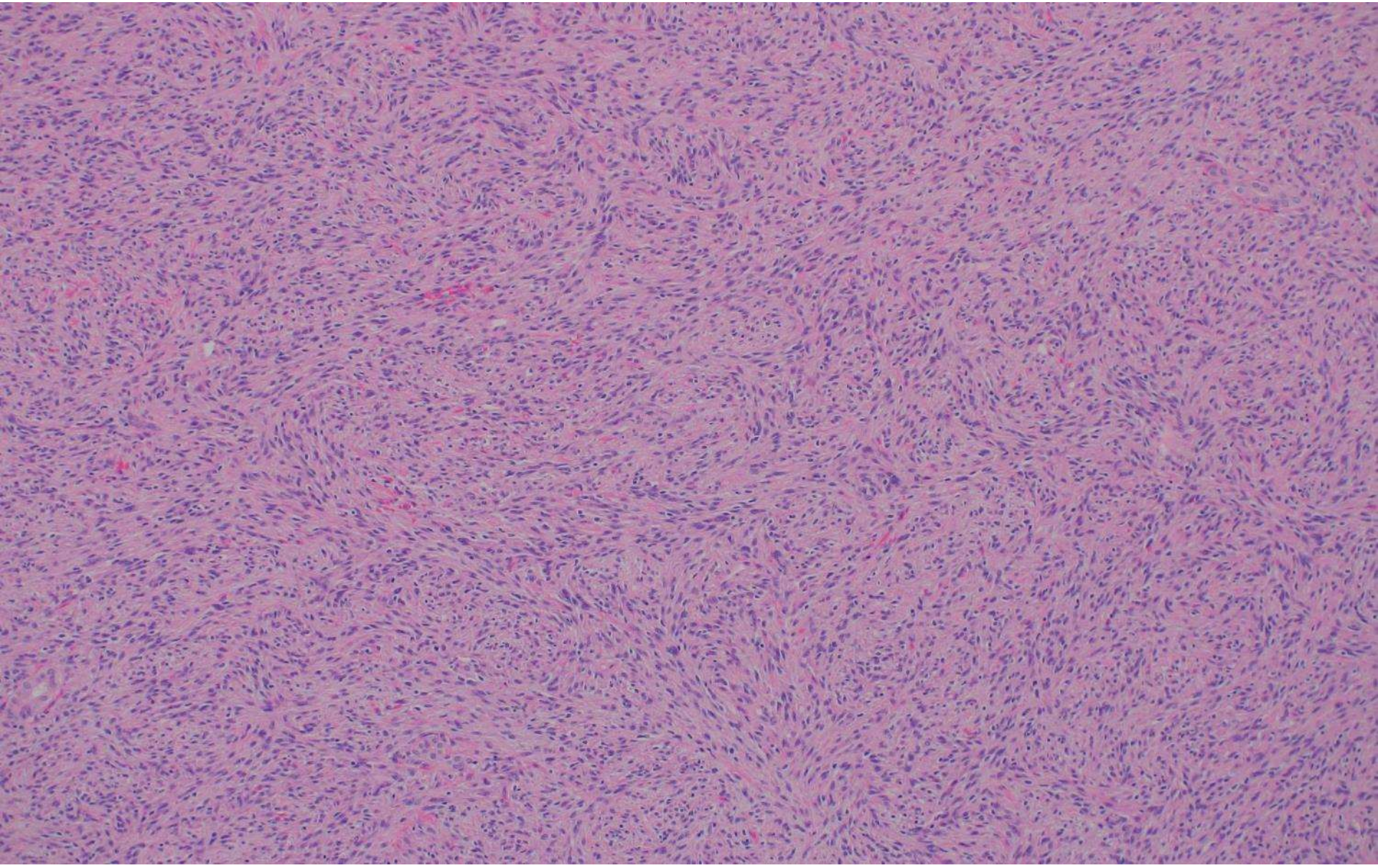
21-0707

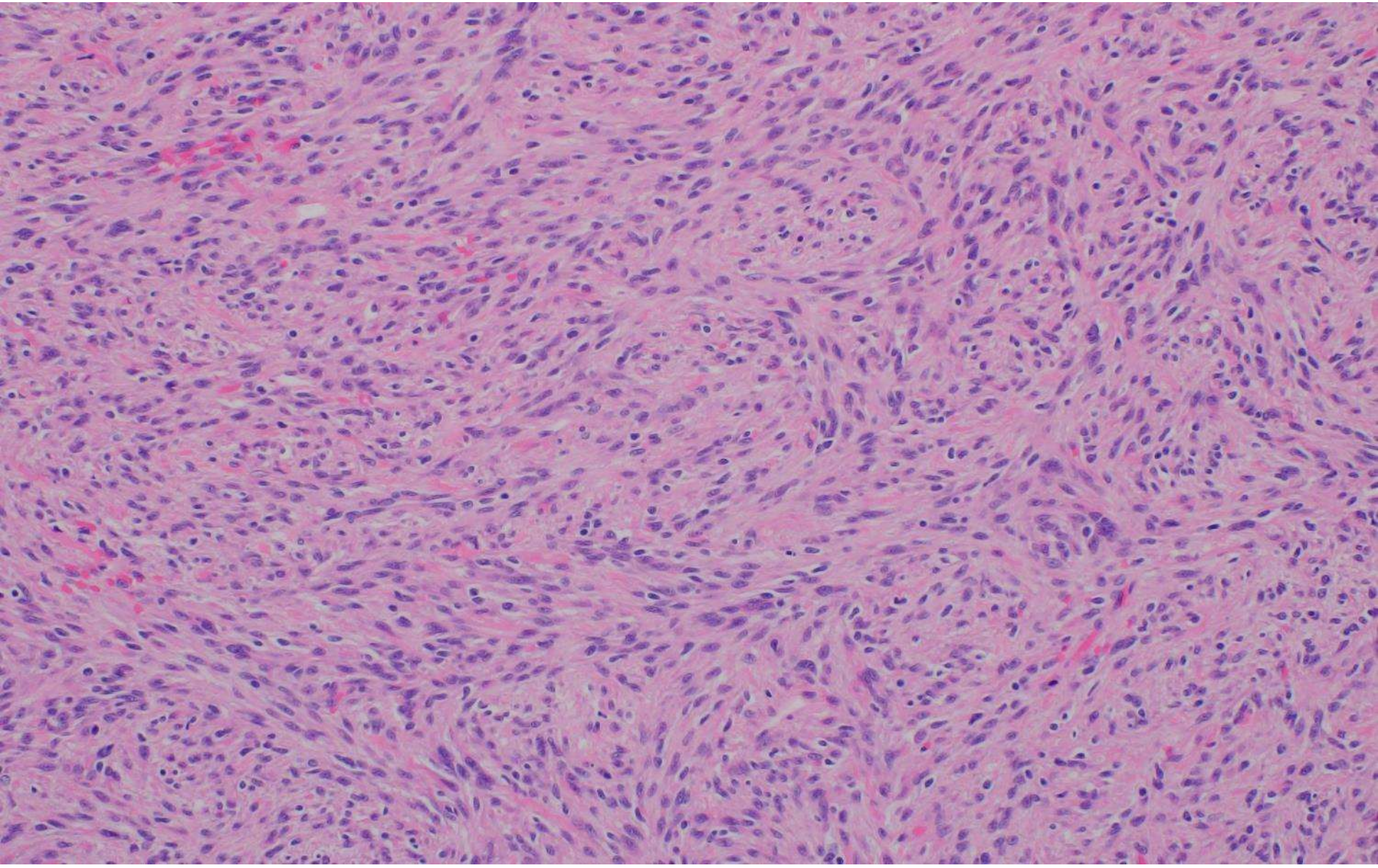
David Bingham; Stanford

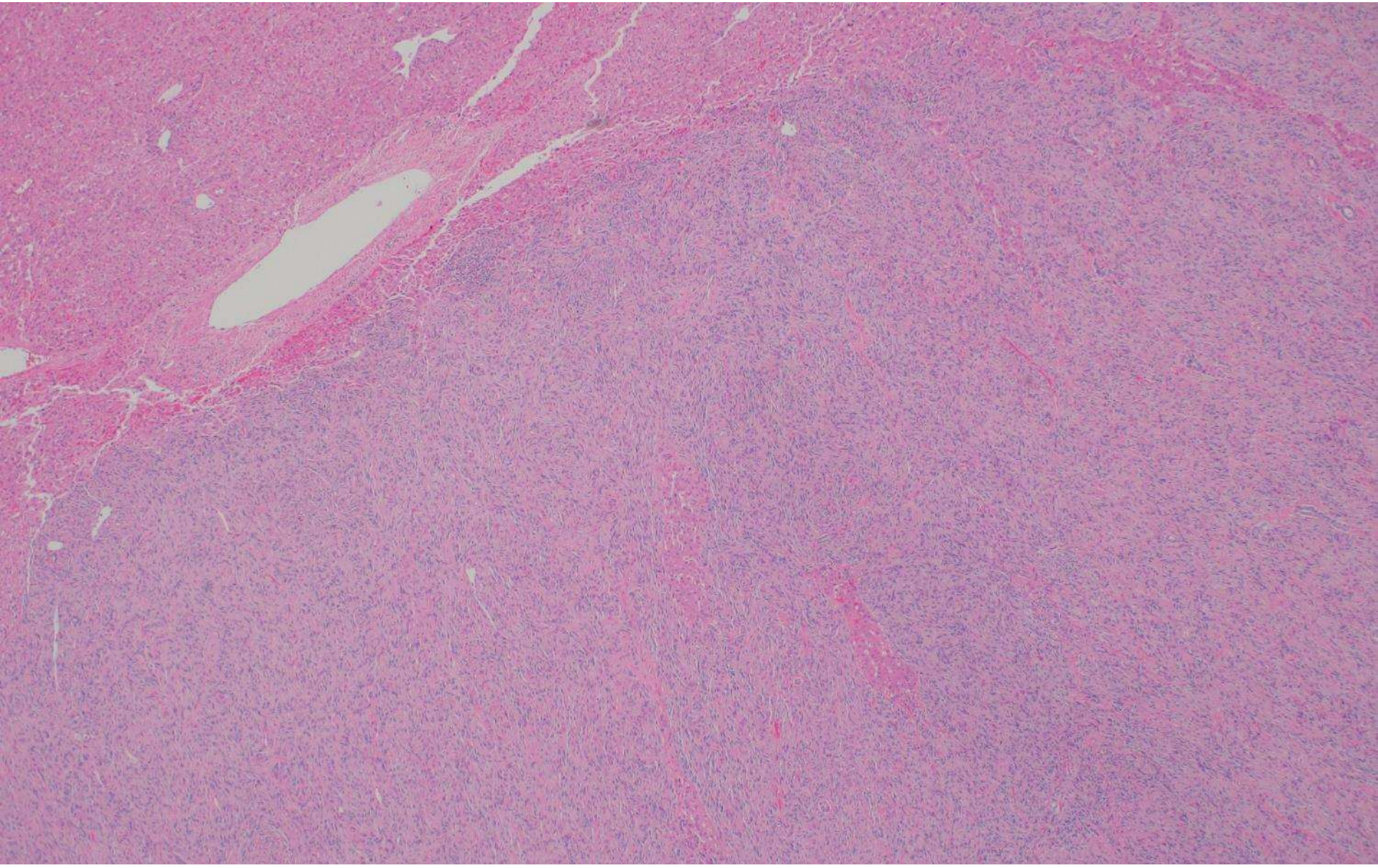
50-year-old F with liver mass.

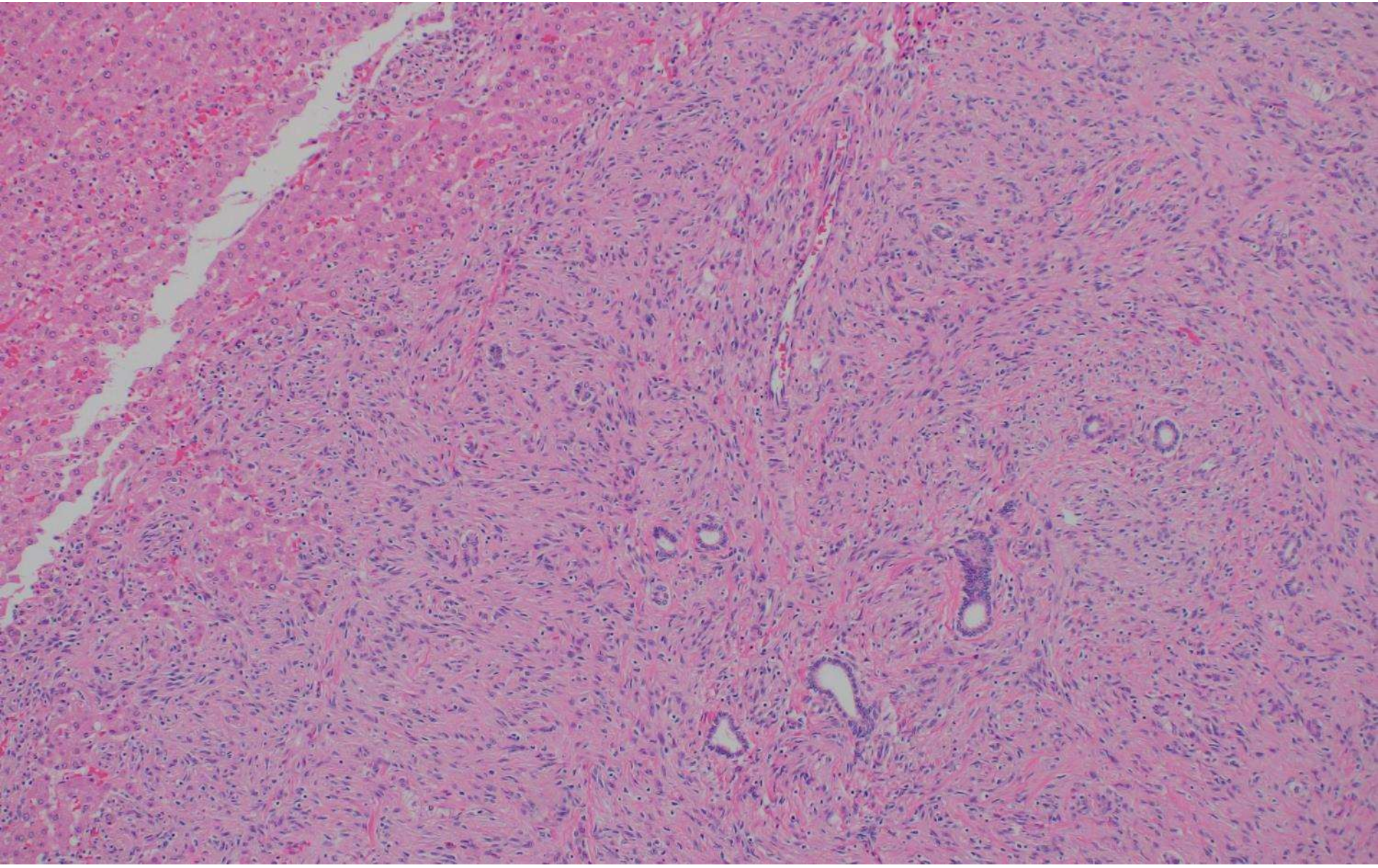


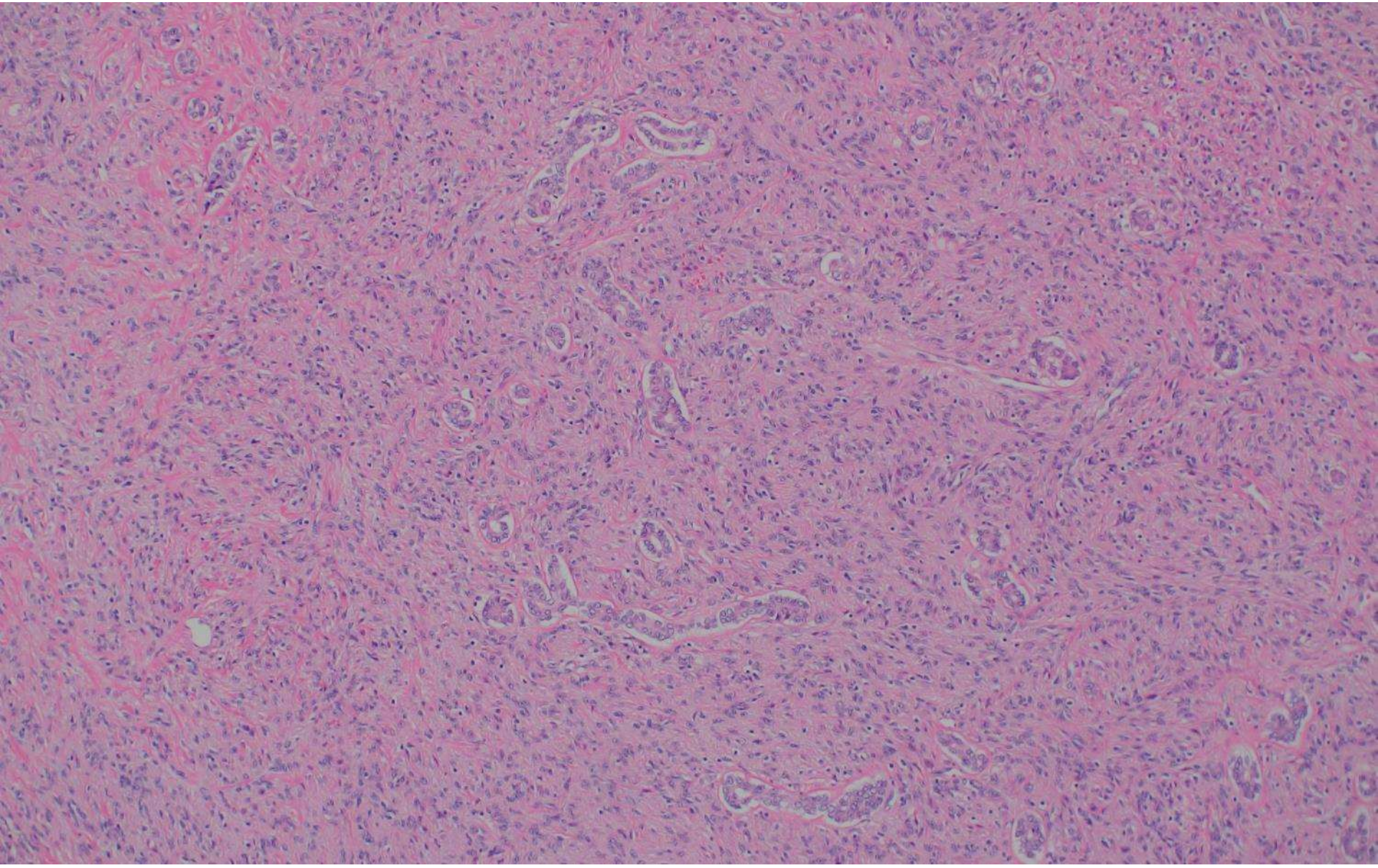


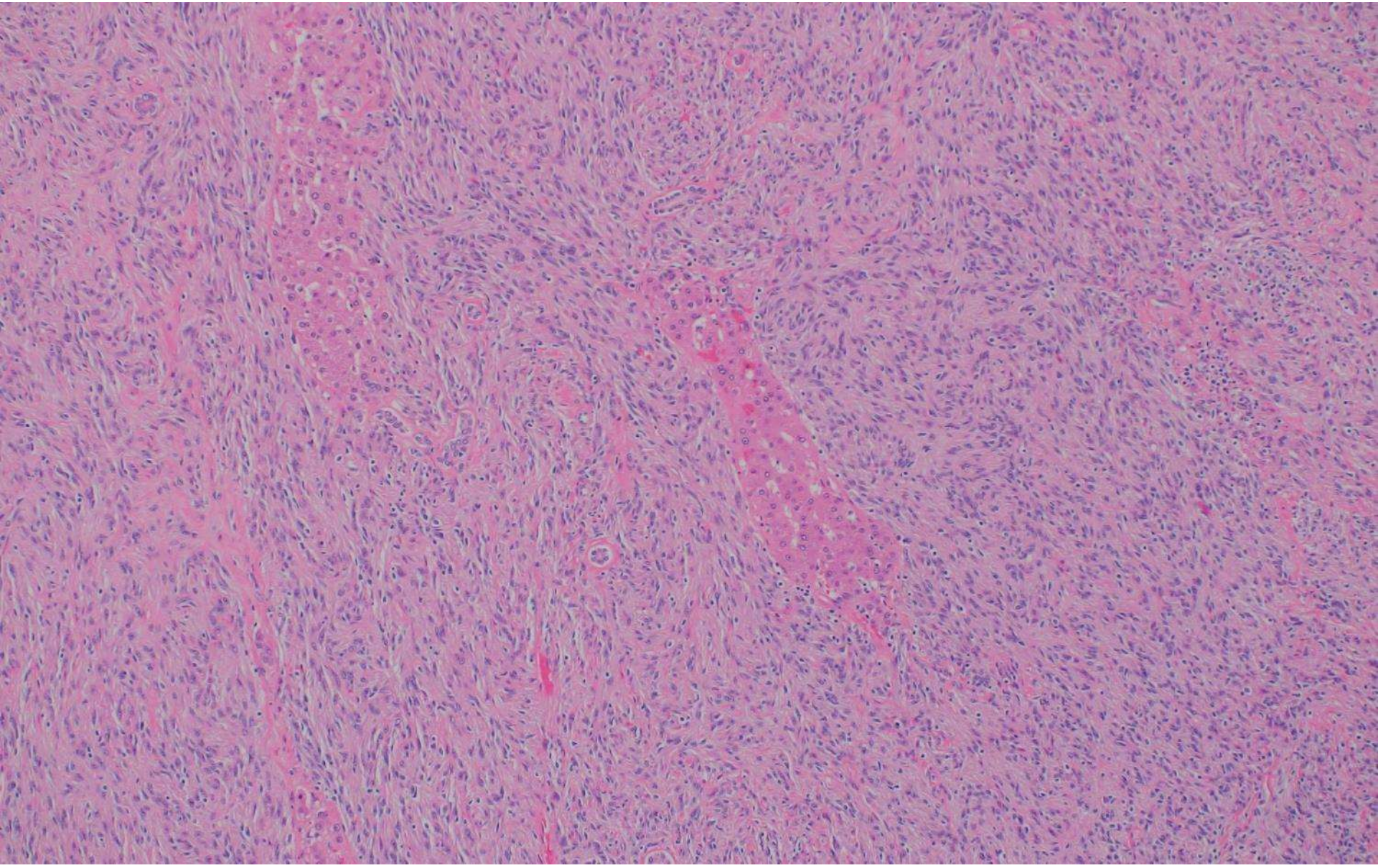


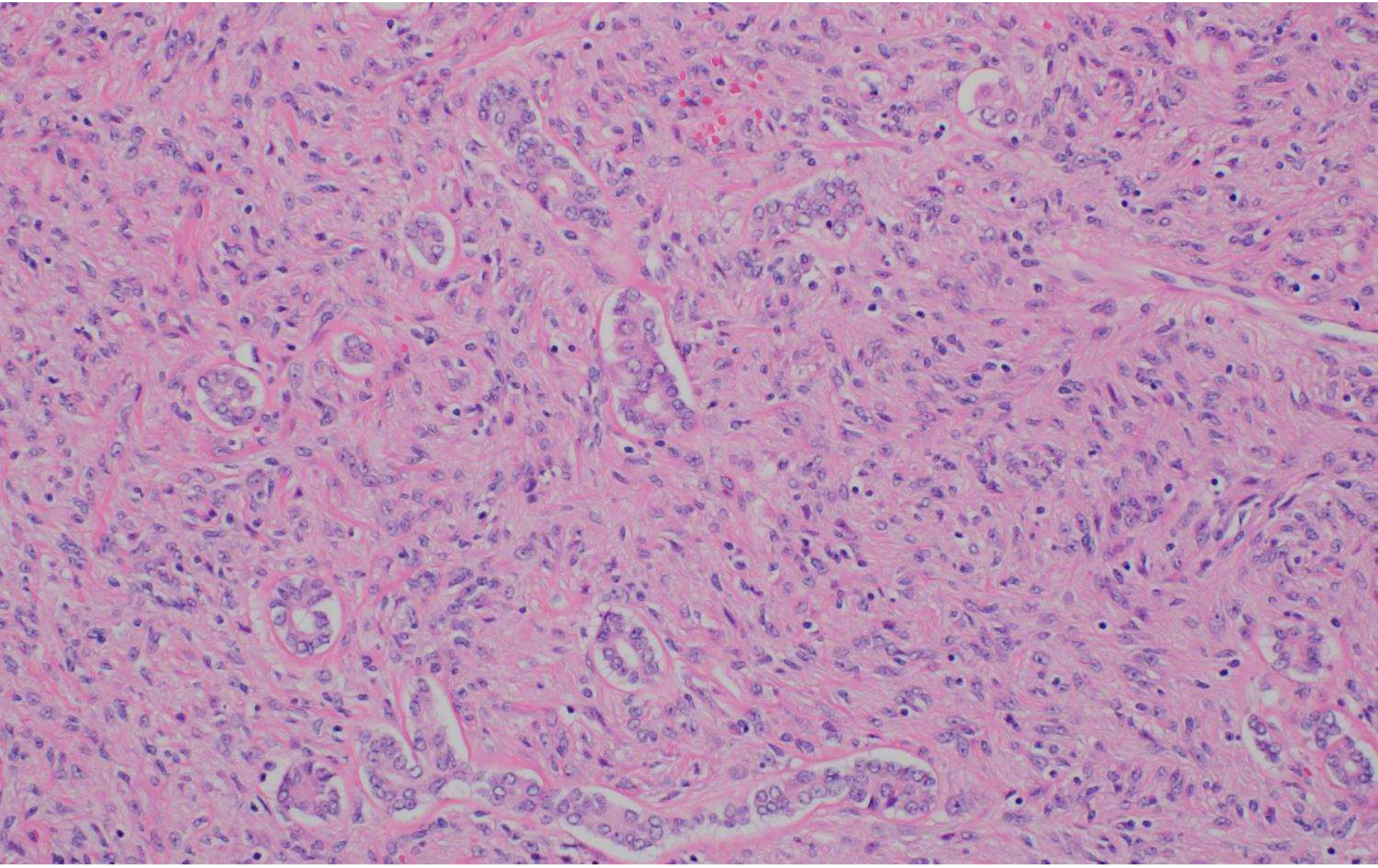




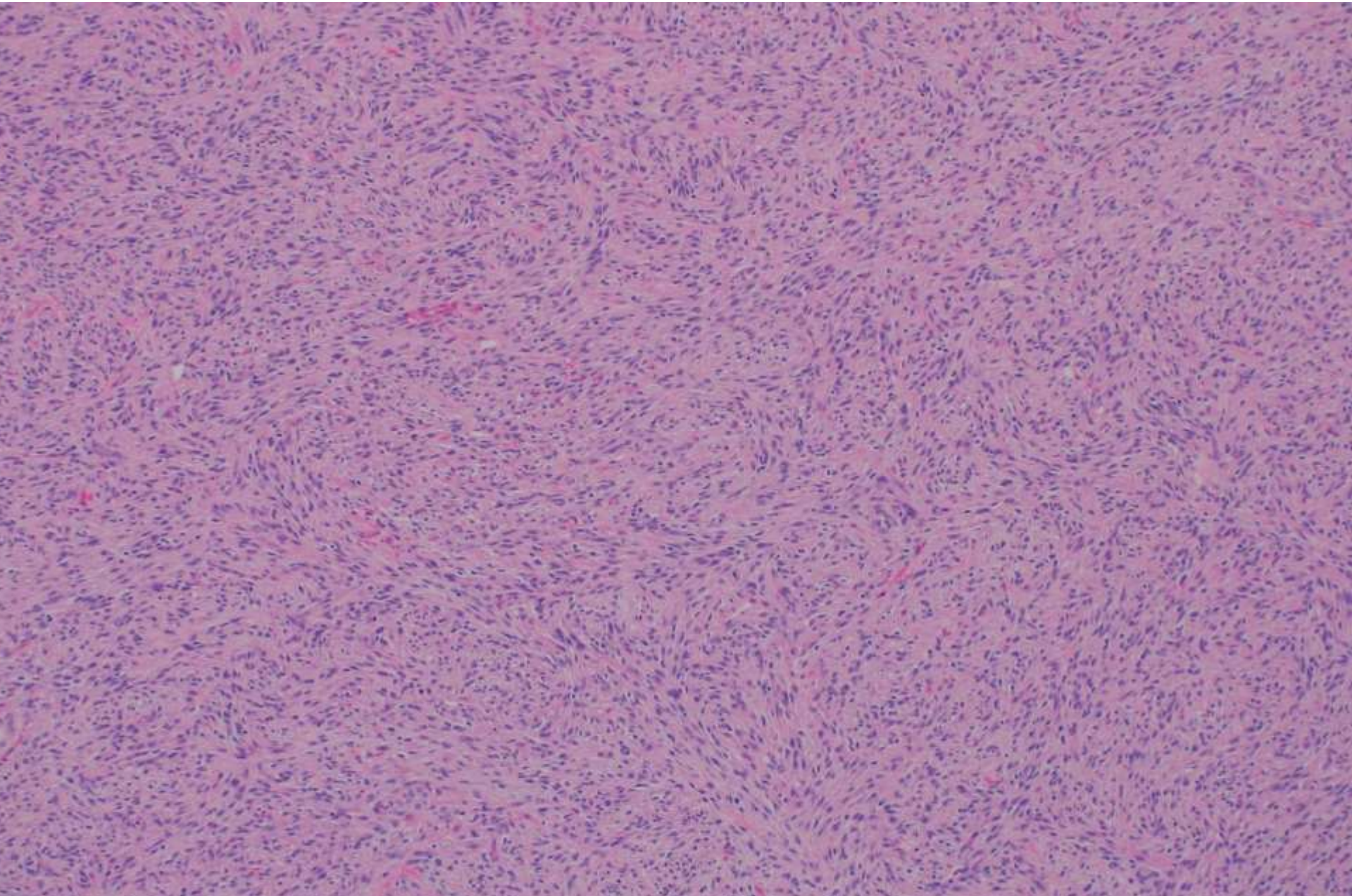








Metastatic Meningioma



Additional history

- Right frontal primary transitional meningioma, WHO grade 1, resected in 2004 with recurrence in 2013
- Incidental chronic HBV with growing liver mass led clinicians to think HCC

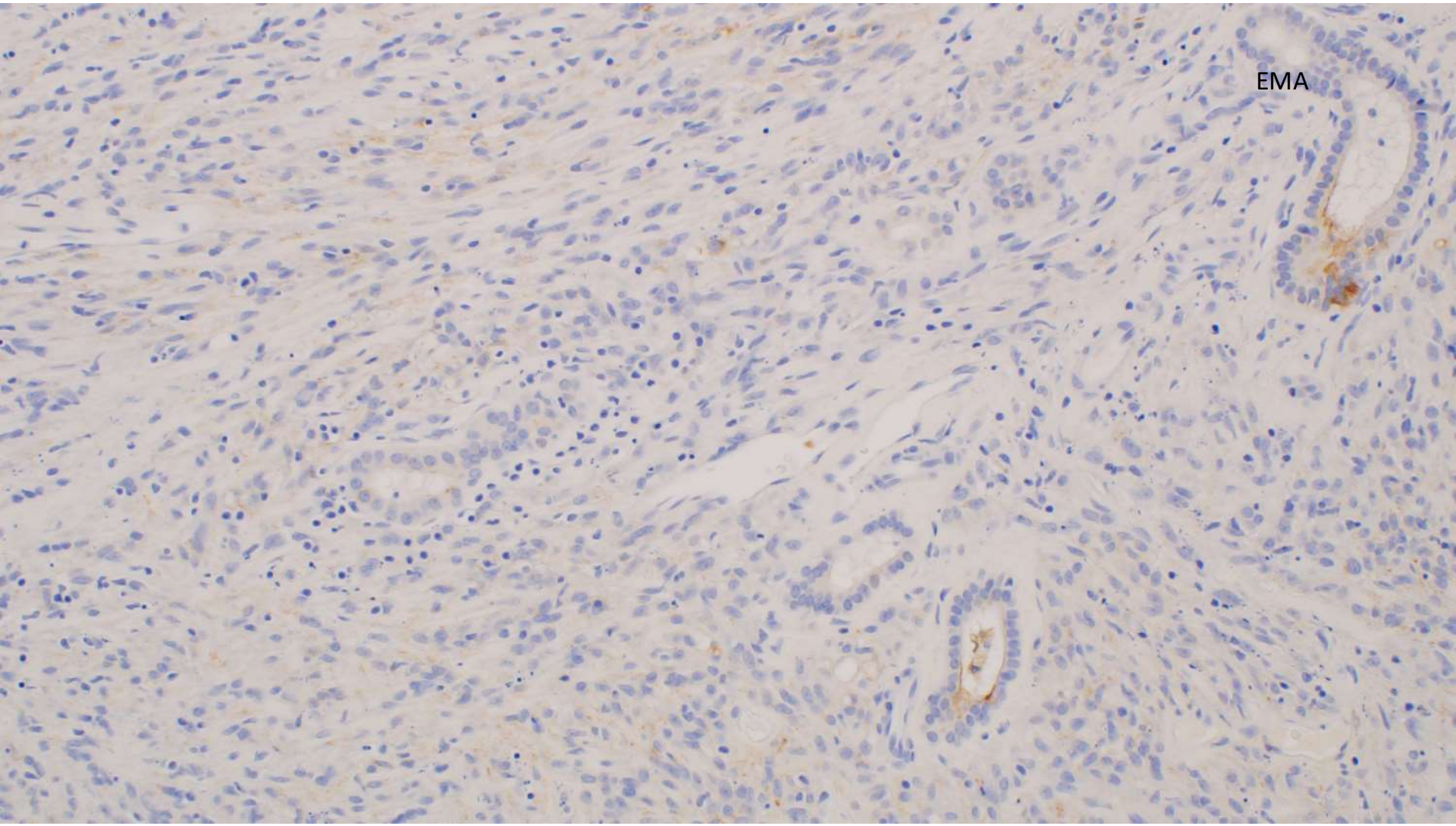
Differential Diagnosis

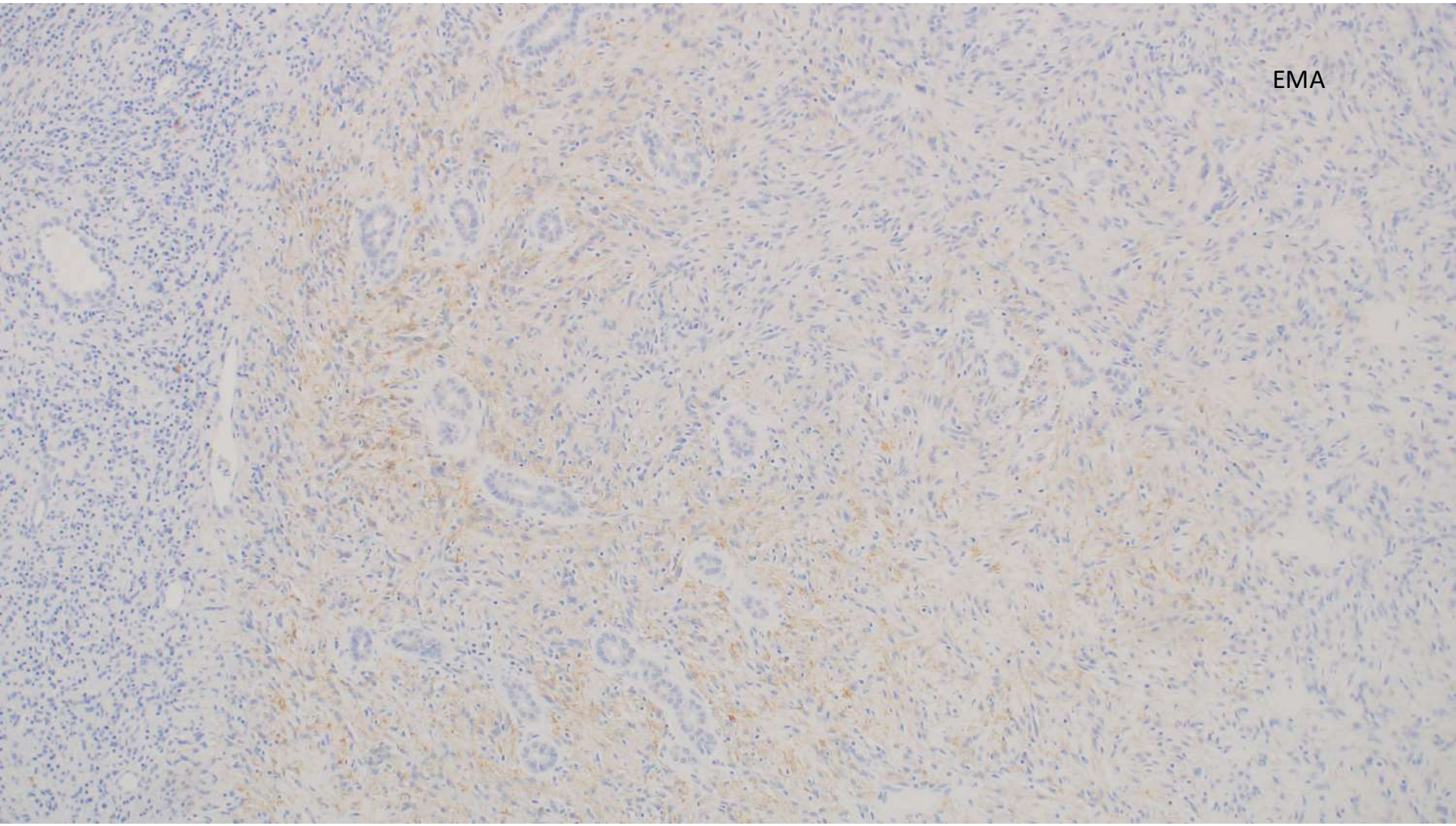
- Hepatocellular carcinoma
- Spindled cell carcinoma
- Metastatic GIST
- Solitary fibrous tumor
- Melanoma
- Vascular neoplasm

IPOX

NEGATIVE for DOG1, CD117, CKmix, desmin, caldesmon, S100, STAT6, HMB-45, HEP-PAR1, ERG, CD31, CD21, ALK, CD34, ActS, CD10 and EBV in situ

EMA faint weakly positive


EMA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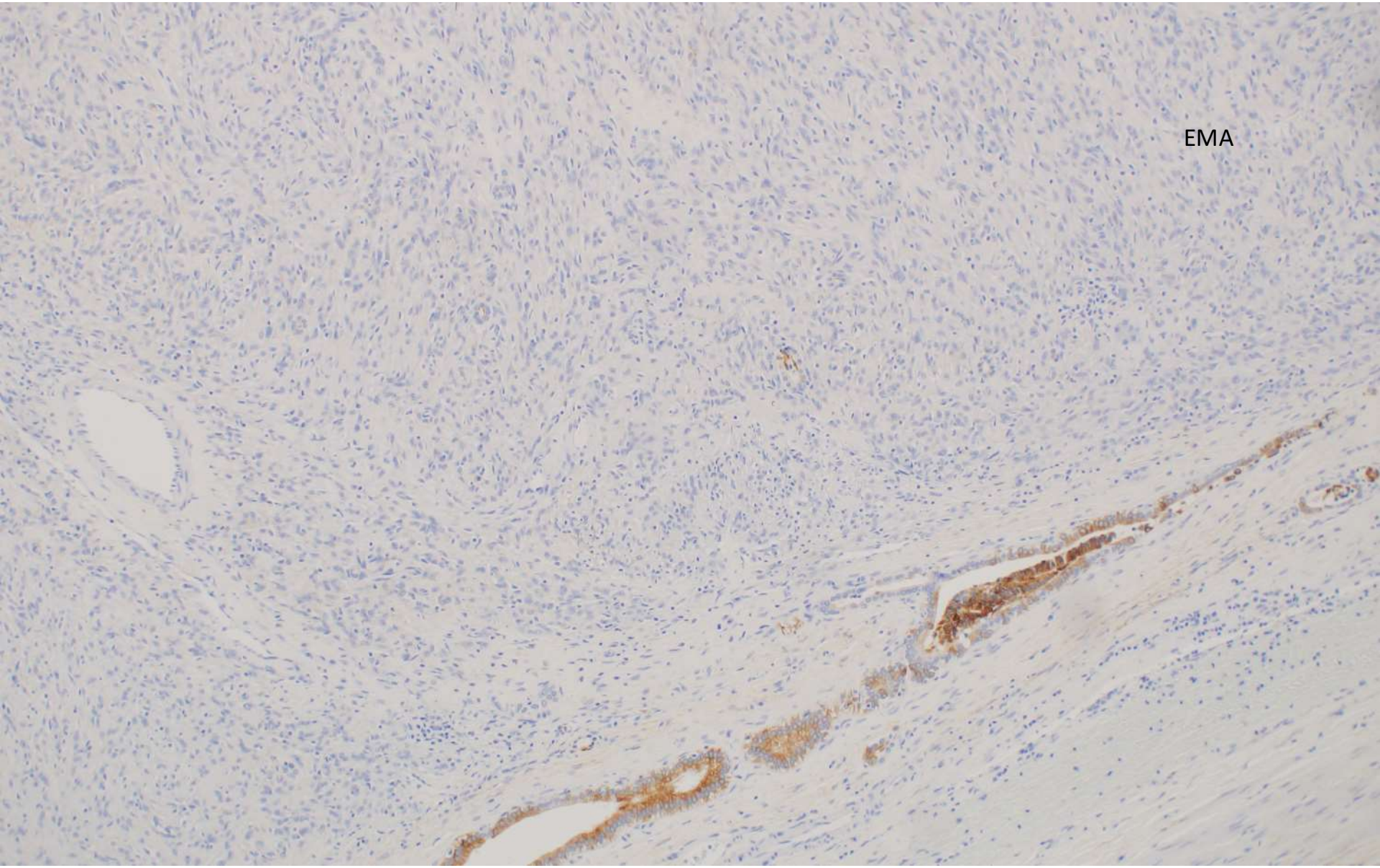
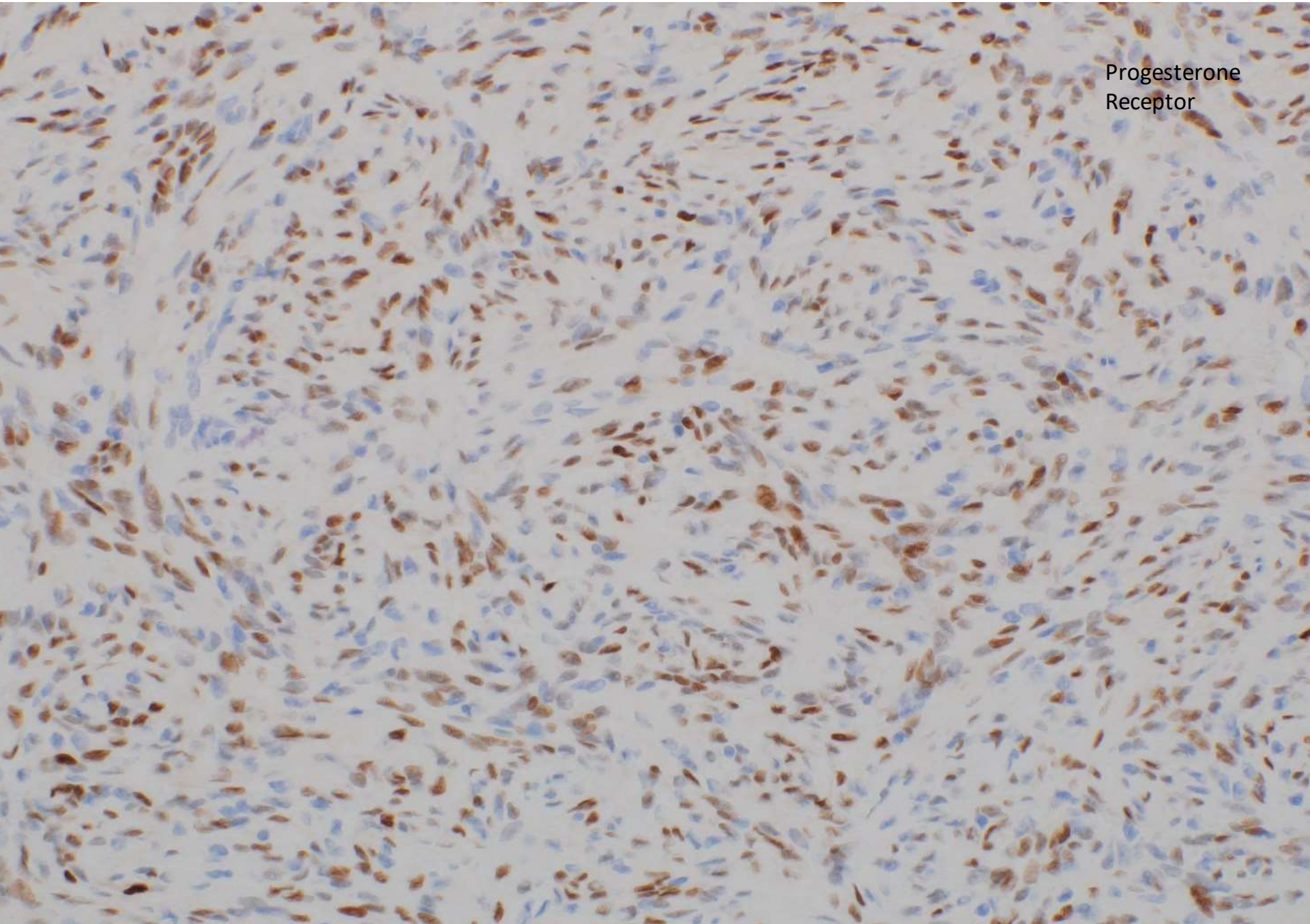
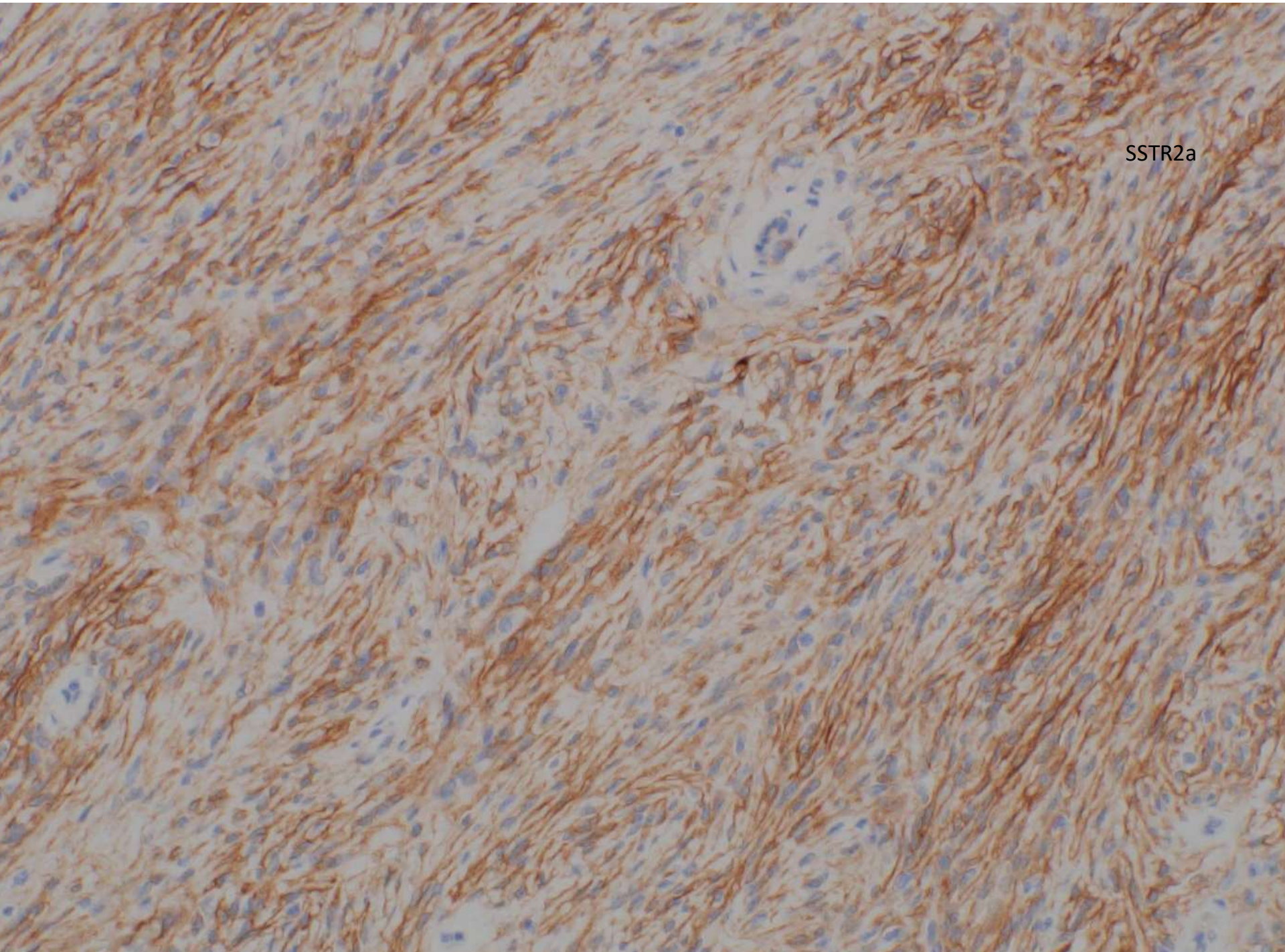

EMA

IPOX

- POSITIVE for PR and SSTR2A (Somatostatin receptor 2a)


Progesterone
Receptor


SSTR2a

SSTR2a (Somatostatin receptor 2a)

- Mediates effects of somatostatin by inhibiting calcium channels
- Present in wide variety of human tissues
- SSTR2A most sensitive (95%) and specific (92%) marker of meningiomas.

References:

- Schnitt SJ, Vogel H (1986) Meningiomas. Diagnostic value of immunoperoxidase staining for epithelial membrane antigen. Am J Surg Pathol 10:640–649

- Menke JR, Raleigh DR, Gown AM, Thomas S, Perry A, Tihan T. Somatostatin receptor 2a is a more sensitive diagnostic marker of meningioma than epithelial membrane antigen. Acta Neuropathol. 2015 Sep;130(3):441-3.

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