South Bay Pathology Society
November 2025

Disclosures
November 3, 2025

Dr. G. Charville has disclosed an active financial relationship with Cartography Biosciences (consultant). South Bay Pathology Society has determined that this relationship is not relevant to the clinical diagnostic case being discussed. The activity planners and faculty listed below have no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

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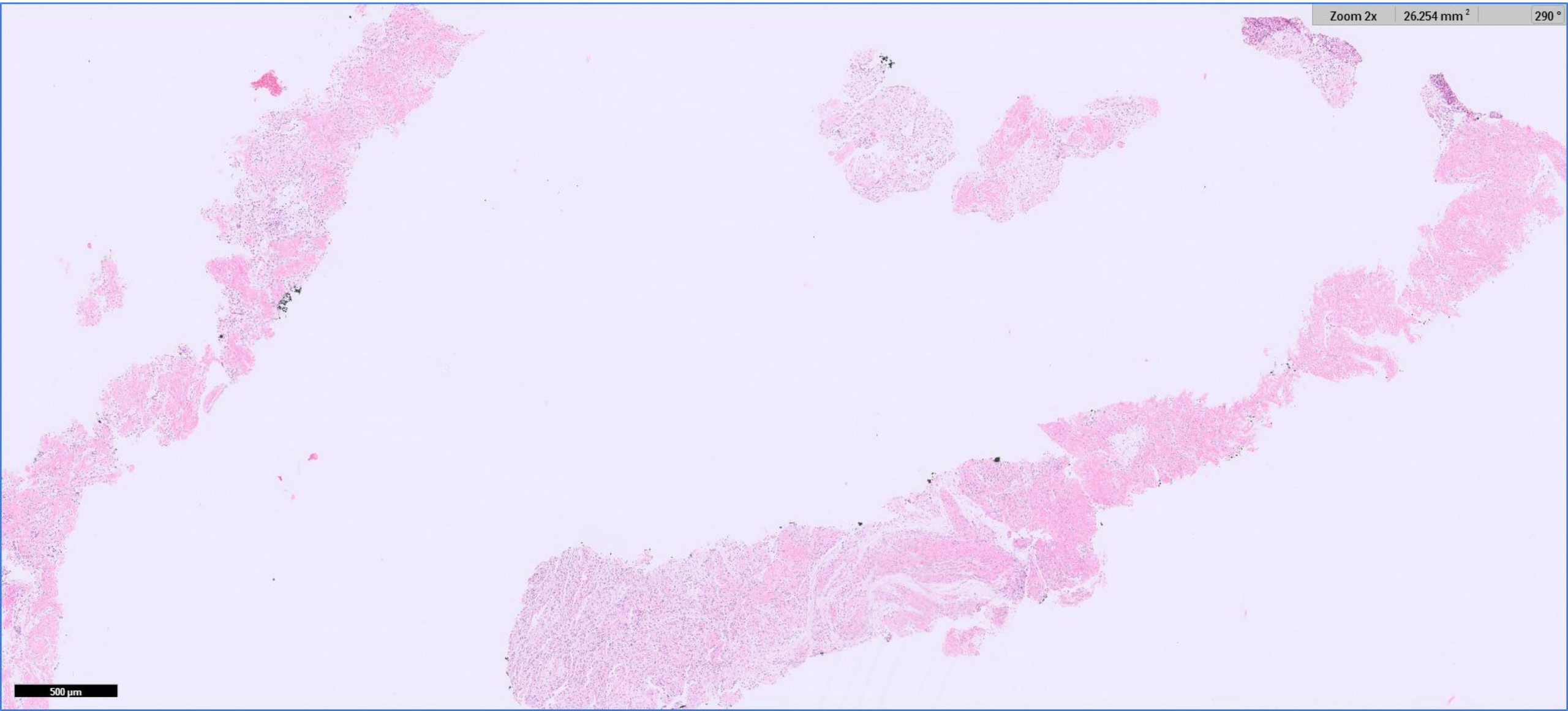
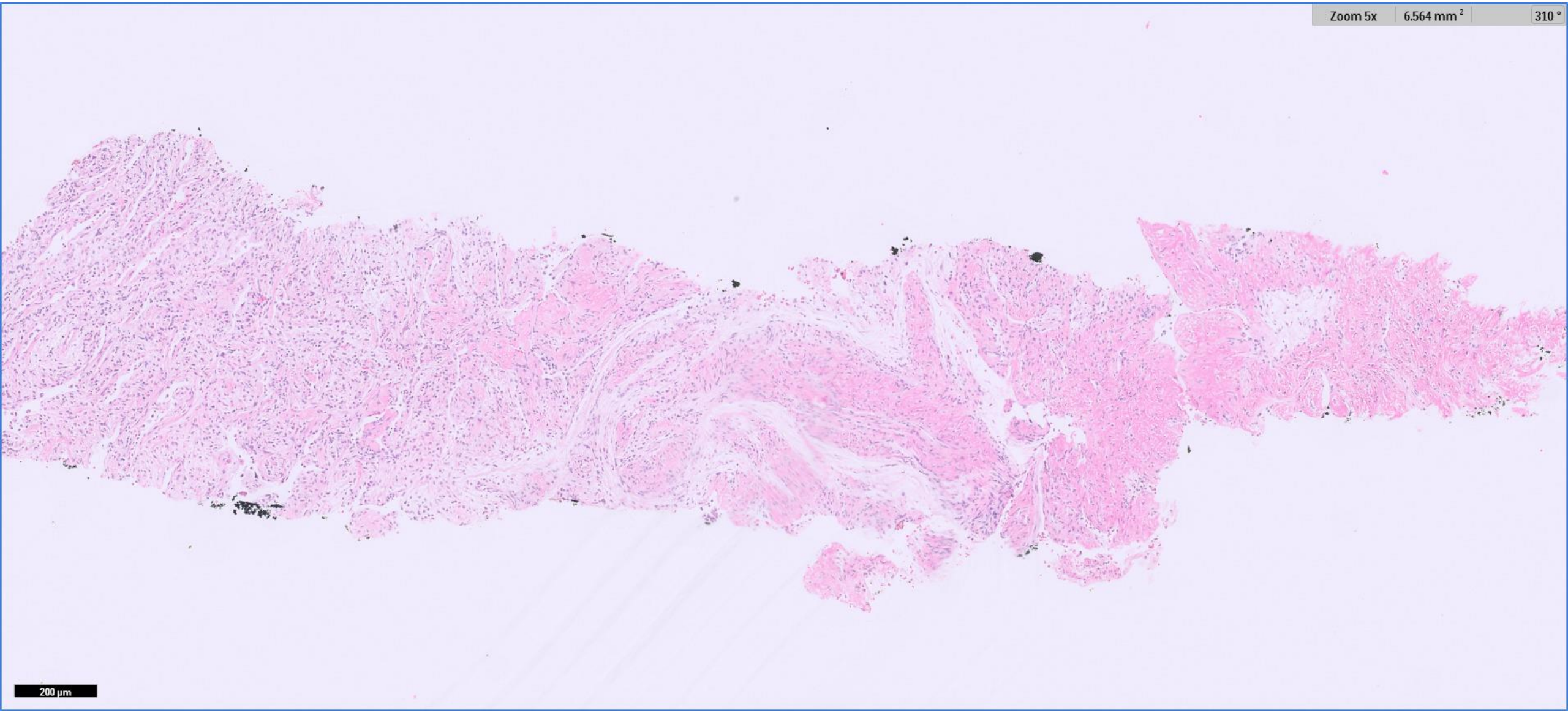
25-1101

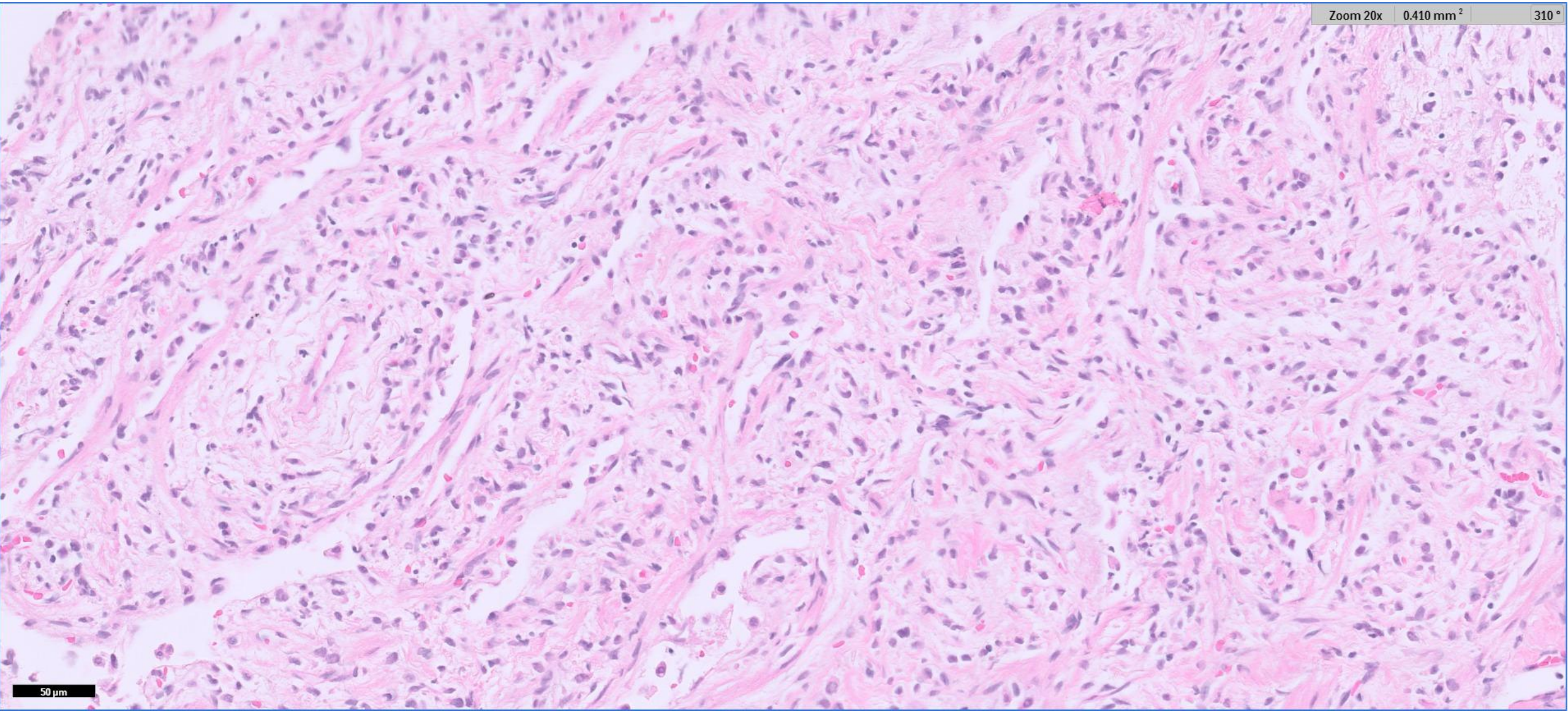
Andrew Xiao and Greg Charville; Stanford

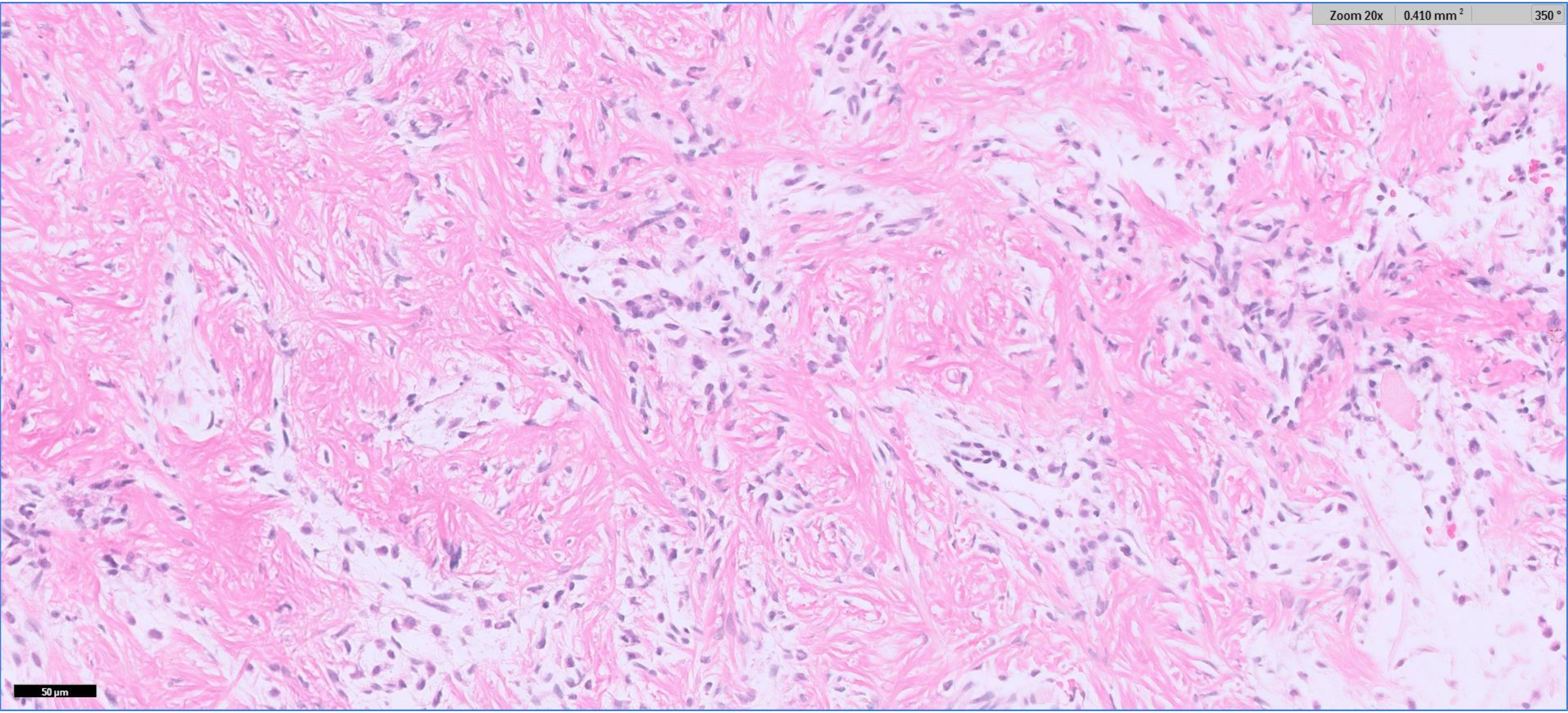
70-ish female with history of lung mass now with a new humerus mass. She undergoes intralesional excision.

Prior lung mass

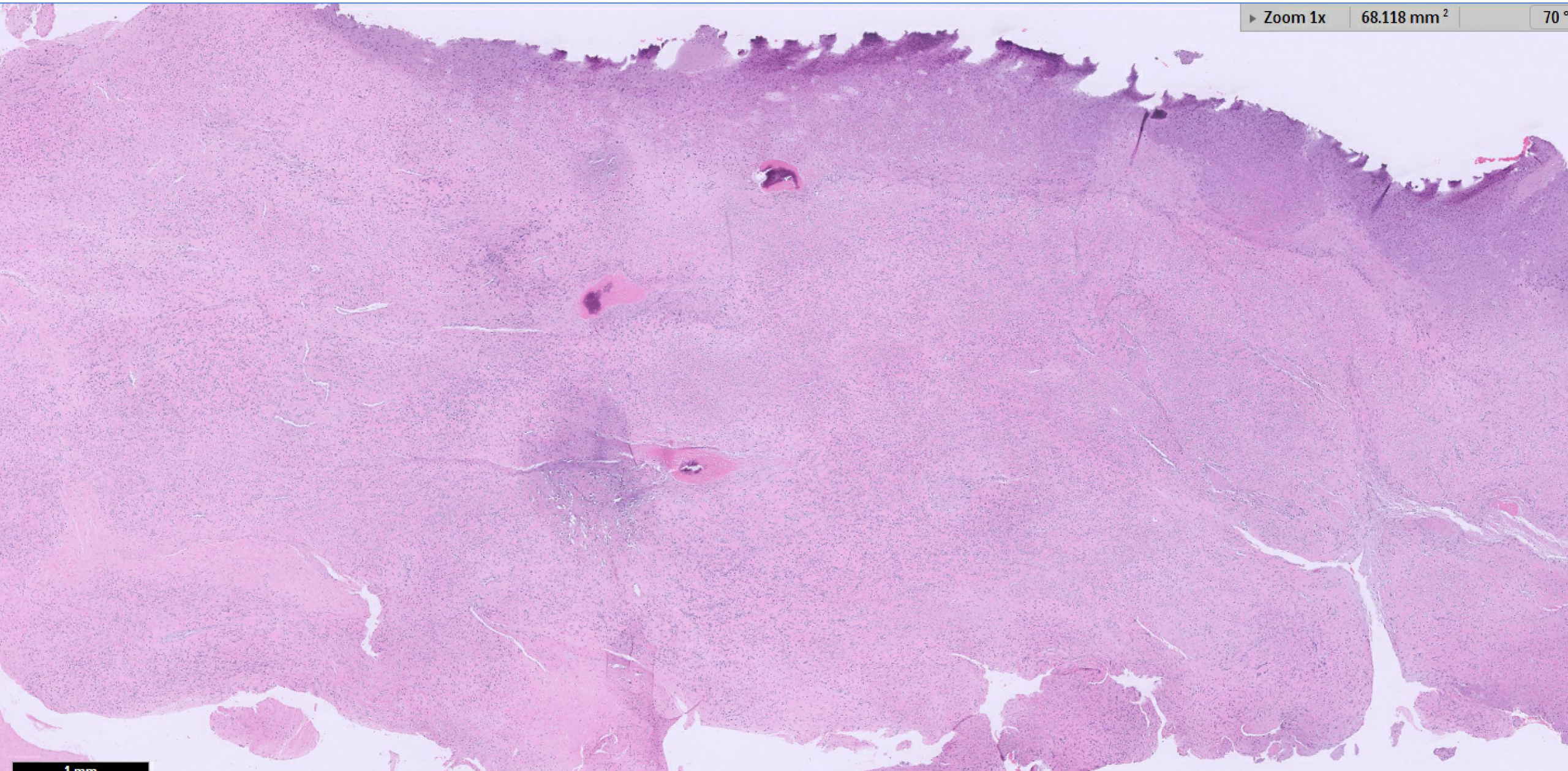


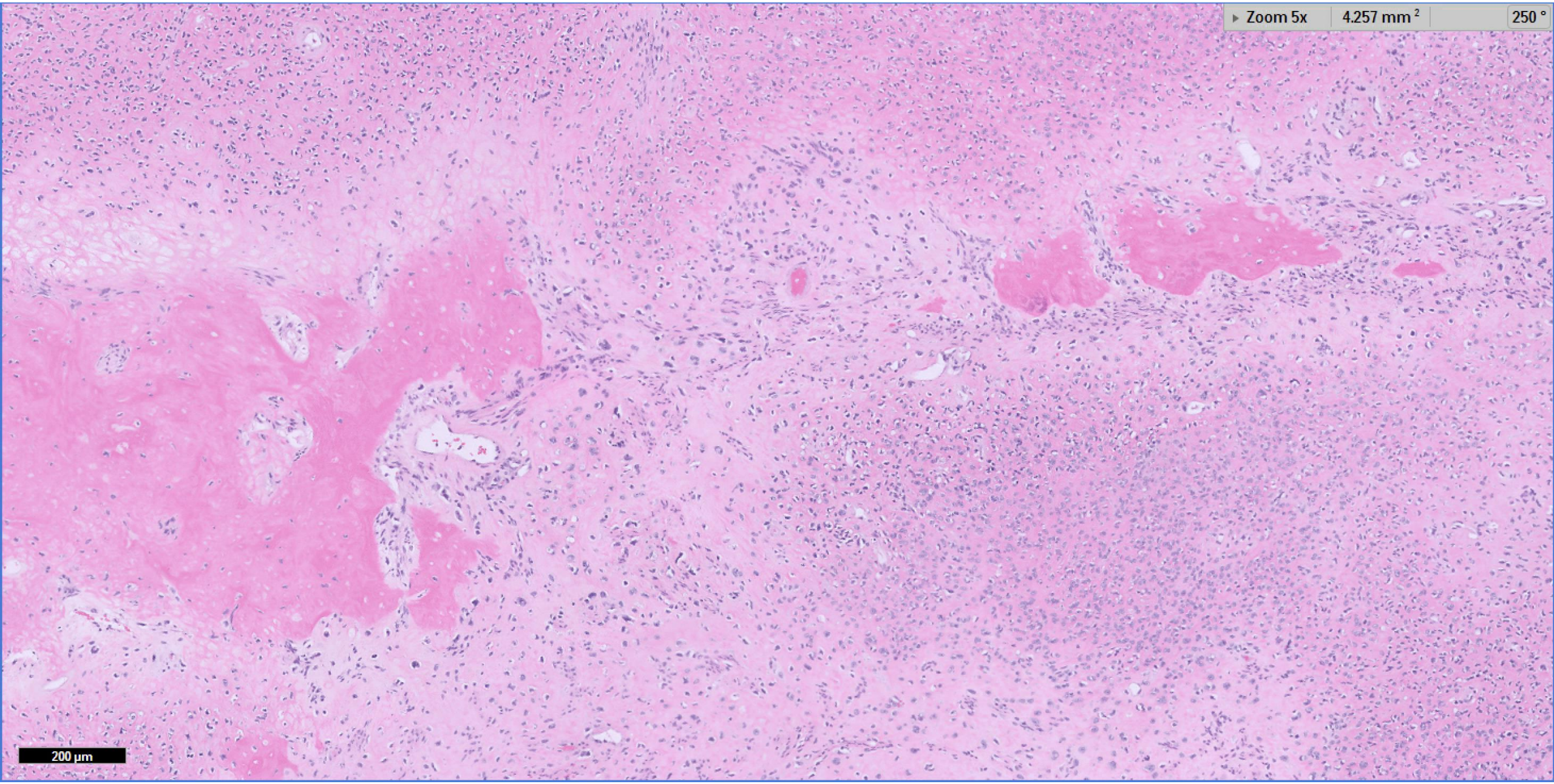

Zoom 5x
6.564 mm ²
310 °
200 µm


Zoom 20x
0.410 mm ²
310 °
50 µm


Zoom 20x
0.410 mm ²
350 °
50 µm

Current humerus mass

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4.257 mm ²
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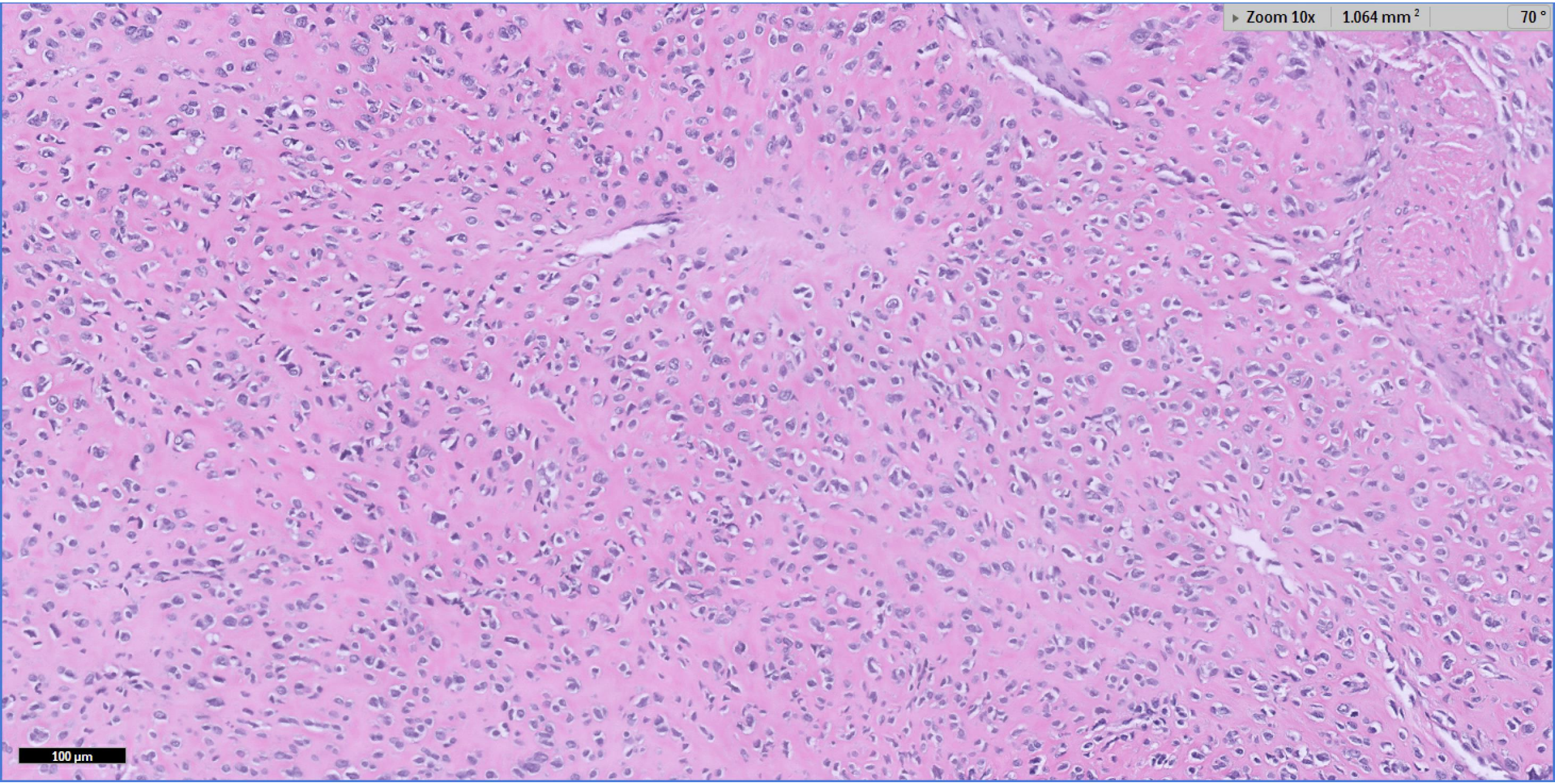
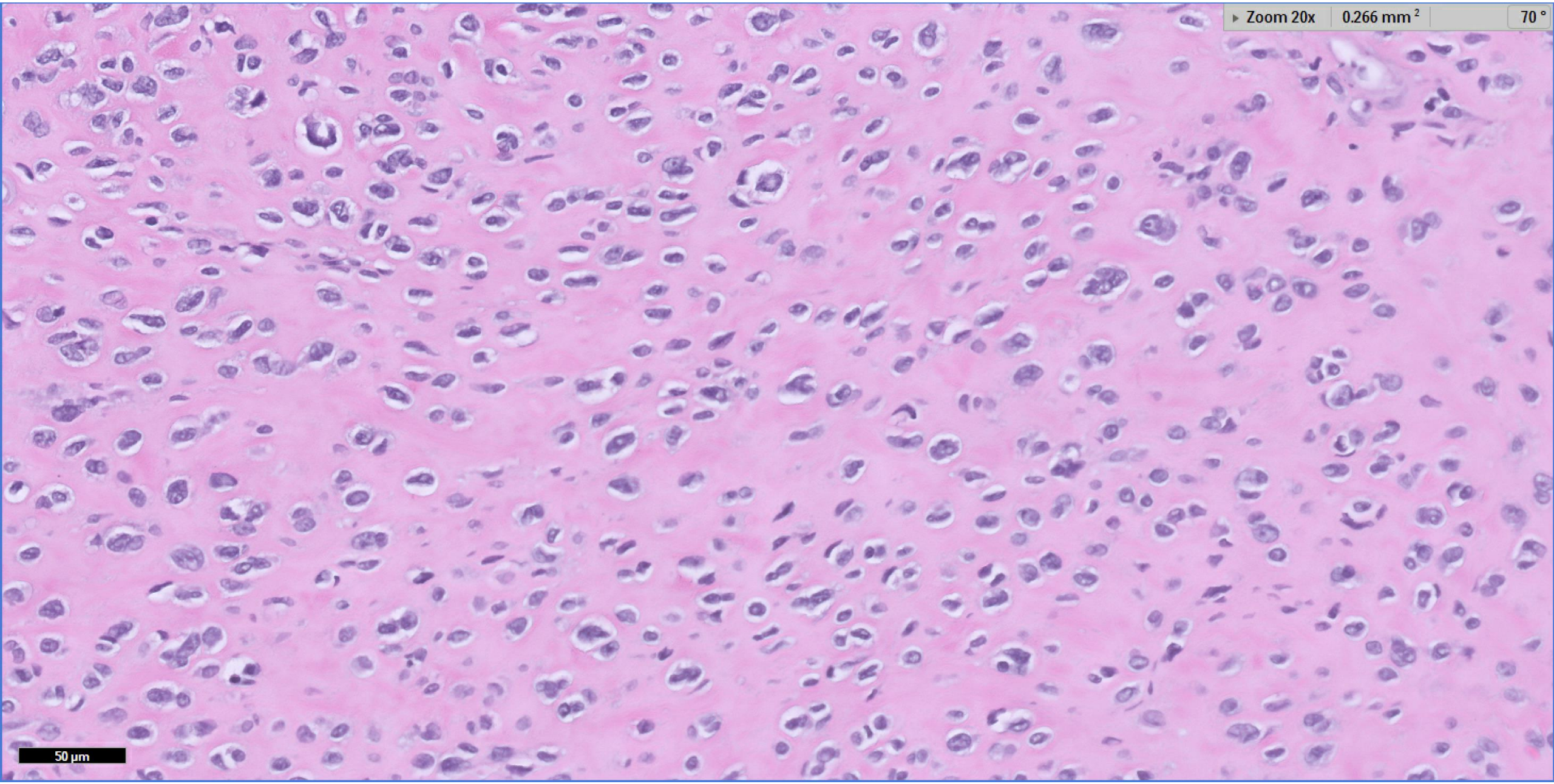
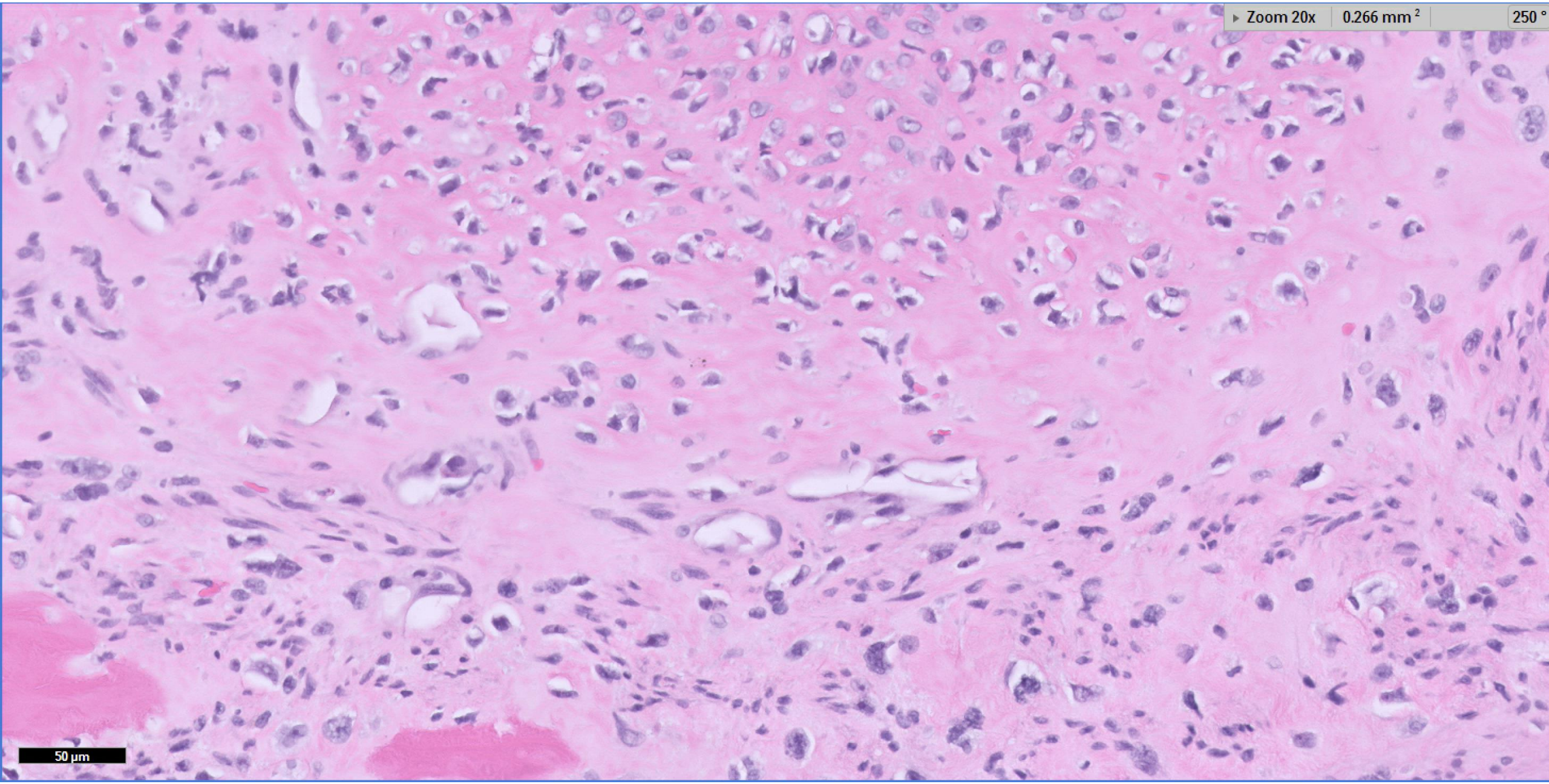
200 µm


Zoom 10x
1.064 mm ²
70 °
100 µm


Zoom 20x
0.266 mm ²
70 °
50 µm


Zoom 20x
0.266 mm ²
250 °
50 µm

DIAGNOSIS?

Recap

- Lung
  - Bland spindle cells with indistinct cytoplasm
  - Hypocellular fibrocollagenous and cellular myxoid areas
  - Fascicular and whorling architecture
  - Thin-walled vessels
- Humerus
  - Individual cells and cords of small to medium-sized epithelioid cells
  - Perinuclear clearing
  - Densely hyalinized, sclerotic matrix
  - Reactive host bone

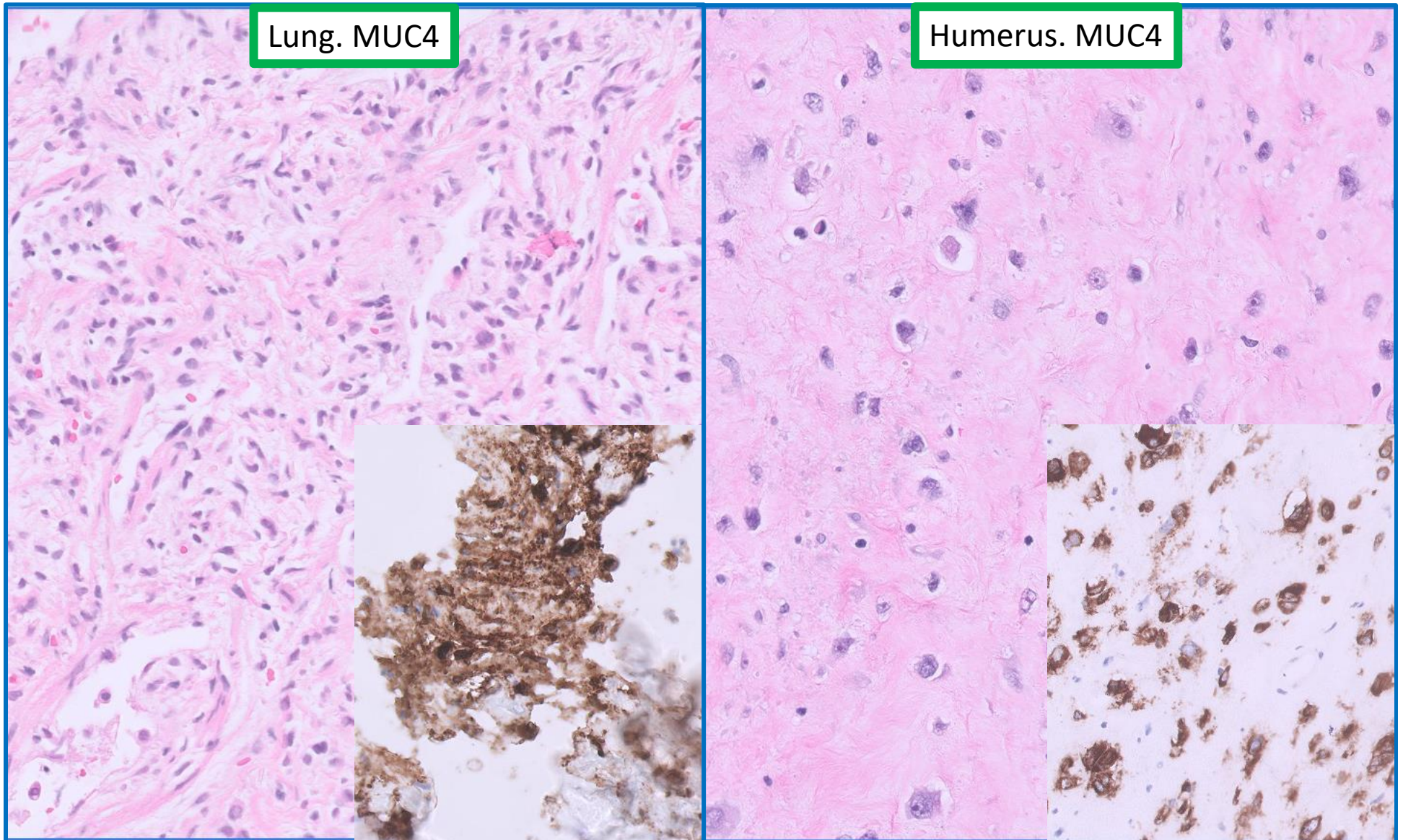
Differential Diagnoses (Lung)

- Perineuroma
- Desmoid fibromatosis
- Myxofibrosarcoma
- Low-grade fibromyxoid sarcoma
- Neurofibroma

Differential Diagnoses (Humerus)

- Osteosarcoma
- PEComa
- Metastatic carcinoma
- Ossifying fibromyxoid tumor
- Myoepithelial carcinoma
- Sclerosing epithelioid fibrosarcoma
- Sclerosing variant of rhabdomyosarcoma

IHC Results



Diagnosis

- Sclerosing epithelioid fibrosarcoma (SEF) arising in context of a pulmonary low-grade fibromyxoid sarcoma (LGFMS)

Fusion-Targeted RNA Sequencing

Result

Positive: Alteration(s) detected

Fusion 1

EWSR1::CREB3L1

A EWSR1::CREB3L1 gene rearrangement is identified that joins exon 11 of EWSR1
exon 6 of CREB3L1 (NM_052854.3) in frame. EWSR1, EWS RNA binding protein 1, is
FET family of DNA/RNA-binding proteins (PMID: 30962207) and is involved in mul
functions including gene expression and RNA processing (PMID: 21816343). EWSR1
multiple gene partners, are frequently observed in sarcomas (PMID: 23329308, P
PMID: 32134119, PMID: 32039736). An EWSR1::TFE3 fusion has been observed in re

Sclerosing Epithelioid Fibrosarcoma (SEF)

- Clinical Features
  - Slight male predominance (59%)
  - Median age: 45 years
  - Most common anatomic distribution
    - Lower extremity
    - Abdomen
    - Visceral organs
    - Limb girdle
    - Trunk
    - Bone

Warmke LM, Yu W, Meis JM. Sclerosing Epithelioid Fibrosarcoma. *Surg Pathol Clin*. 2024;17(1):119-139. doi:10.1016/j.path.2023.06.009

SEF & LGFMS

- SEF related to but distinct from LGFMS
  - Previously thought of as a SEF-LGFMS spectrum
  - Hybrid SEF-LGFMS tumors
  - LGFMS can undergo local or distance transformation into SEF

1. Arbajian E, Puls F, Magnusson L, et al. Recurrent EWSR1-CREB3L1 gene fusions in sclerosing epithelioid fibrosarcoma. *Am J Surg Pathol*. 2014;38(6):801-808. doi:10.1097/PAS.0000000000000158
2. Warmke LM, Yu W, Meis JM. Sclerosing Epithelioid Fibrosarcoma. *Surg Pathol Clin*. 2024;17(1):119-139. doi:10.1016/j.path.2023.06.009

SEF & LGFMS

- SEF related to but distinct from LGFMS
  - MUC4-positive in both SEF & LGFMS
  - Distinct fusion genes

Diagnosis	Most Common Fusion Genes	Less Common Fusion Genes
Sclerosing epithelioid fibrosarcoma	*EWSR1::CREB3L1*	*EWSR1::CREB3L2, FUS::CREB3L2, FUS::CREM, PAX5::CREB3L1, EWSR1::CREB3L3, YAP1::KMT2A HEY1::NCOA2, PRRX1::KMT2D*
Low-grade fibromyxoid sarcoma	*FUS::CREB3L2*	*FUS::CREB3L1, EWSR1::CREB3L1*

1. Arbajian E, Puls F, Magnusson L, et al. Recurrent EWSR1-CREB3L1 gene fusions in sclerosing epithelioid fibrosarcoma. *Am J Surg Pathol*. 2014;38(6):801-808. doi:10.1097/PAS.0000000000000158
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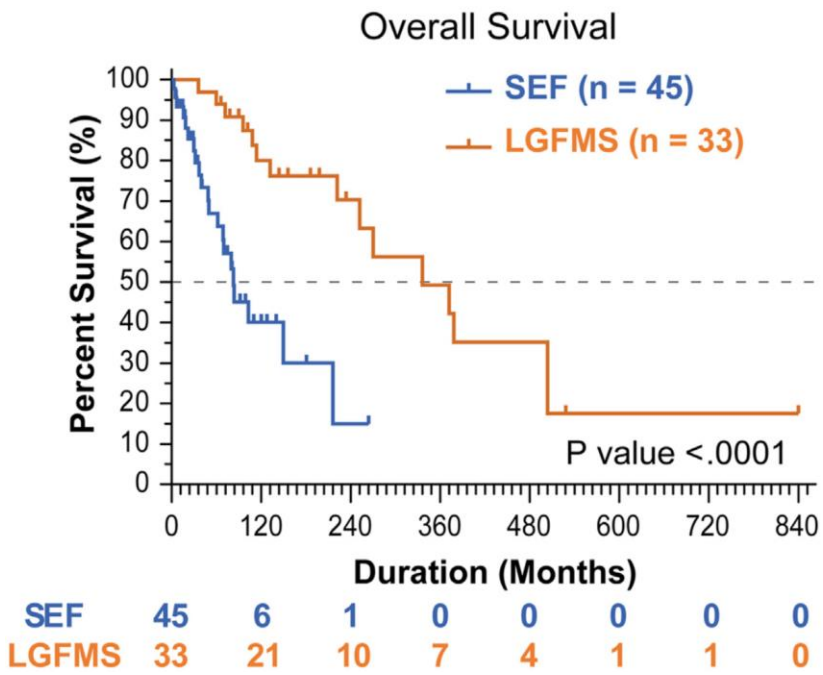
SEF & LGFMS

- "Pure" SEF
  - More aggressive clinically (speed & extent) vs LGFMS
  - Higher metastatic rate
- Key histologic distinction:
  - Sclerotic lesion
  - Epithelioid morphology
  - Cytologic atypia



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“MUC4-negative SEF”

- Now considered a distinct entity
- SEF with *YAP1::KMT2A* or *PRRX1::KMT2D* fusion
- Fibroblastic tumor with SEF-like morphology and *KMT2A* gene rearrangement

Warmke LM, Yu W, Meis JM. Sclerosing Epithelioid Fibrosarcoma. *Surg Pathol Clin*. 2024;17(1):119-139. doi:10.1016/j.path.2023.06.009

SEF Management

- Surgical
  - Early intervention with wide surgical resection
  - Re-excision is recommended for positive margins
- Therapy: recalcitrant to chemoradiation

Warmke LM, Yu W, Meis JM. Sclerosing Epithelioid Fibrosarcoma. *Surg Pathol Clin*. 2024;17(1):119-139. doi:10.1016/j.path.2023.06.009

Key Points

- Osteoid-like foci distinct challenge when in bone
- Integrating histology, immunohistochemistry, and molecular testing
- LGFMS can transform into SEF

Questions?

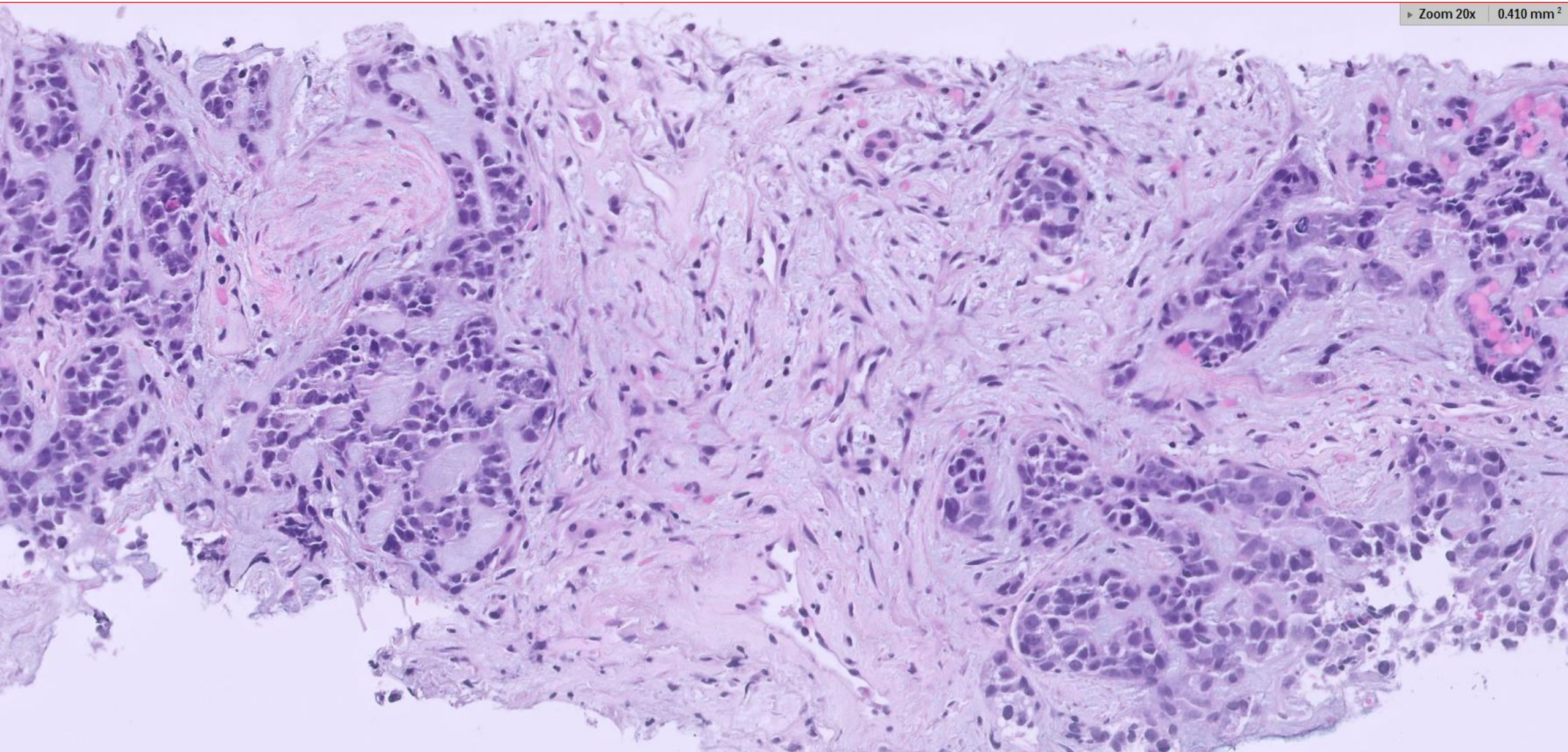
- Thank you, Dr. Charville!

25-1102

Iain Miller, Cansu Karakas; Stanford

60’s-year-old female with history of right breast triple negative invasive ductal carcinoma (per report, 2024) status post neoadjuvant chemotherapy, lumpectomy (ypT1cN0(sn)), and radiation therapy now presenting with an enlarging right lung nodule. Core biopsy of right lung nodule was obtained.

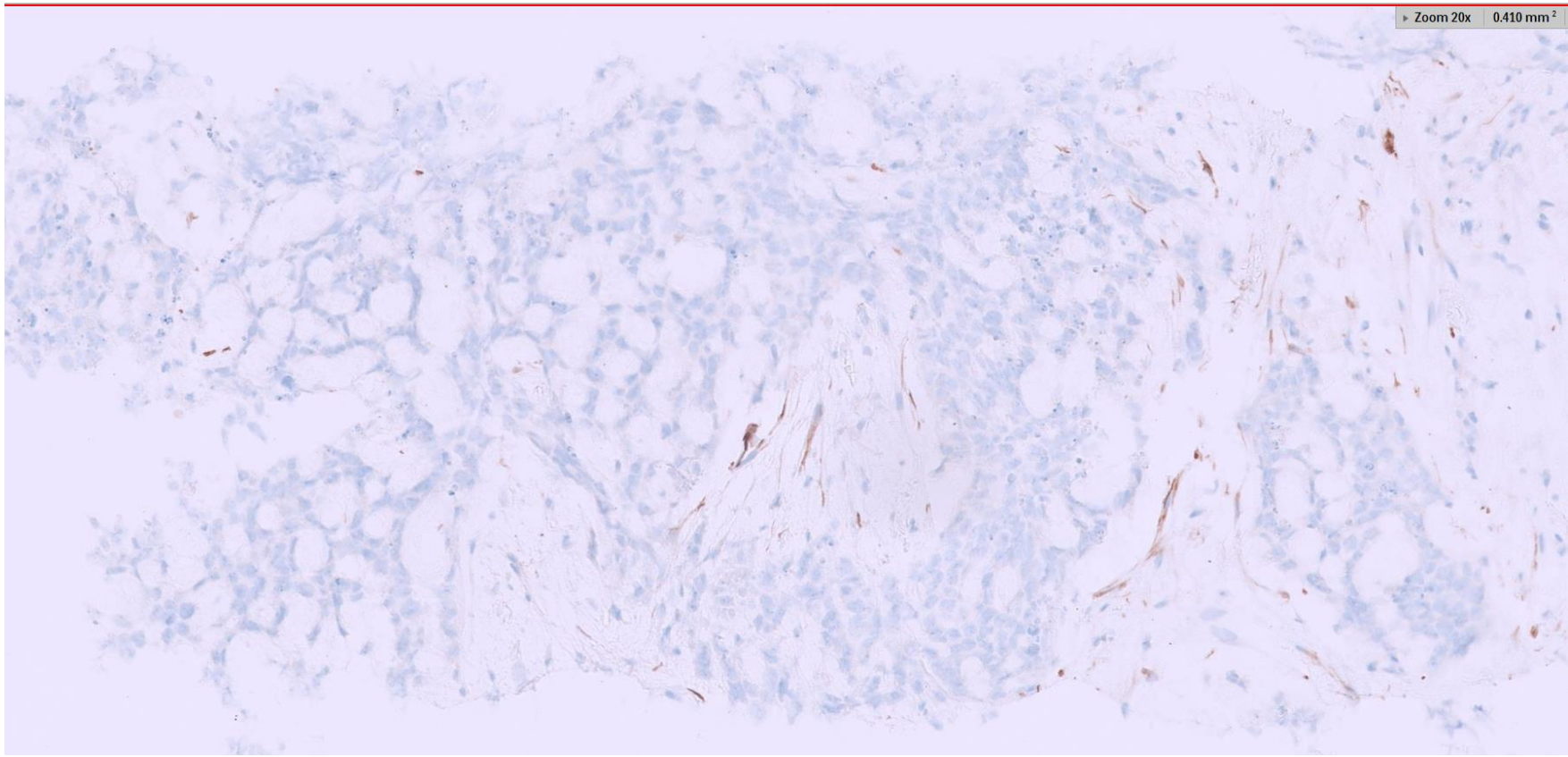
Right lung nodule core biopsy



Immunohistochemistry stains performed

IHC

Stain	Result
• CDX2	Negative
• CK20	Negative
• **CK7**	**Focal positive**
• GATA3	Focal positive
• TTF-1	Negative
• Ki67	50-60%
• P63	Positive
• HER2	Negative (1+)
• CD117	Positive



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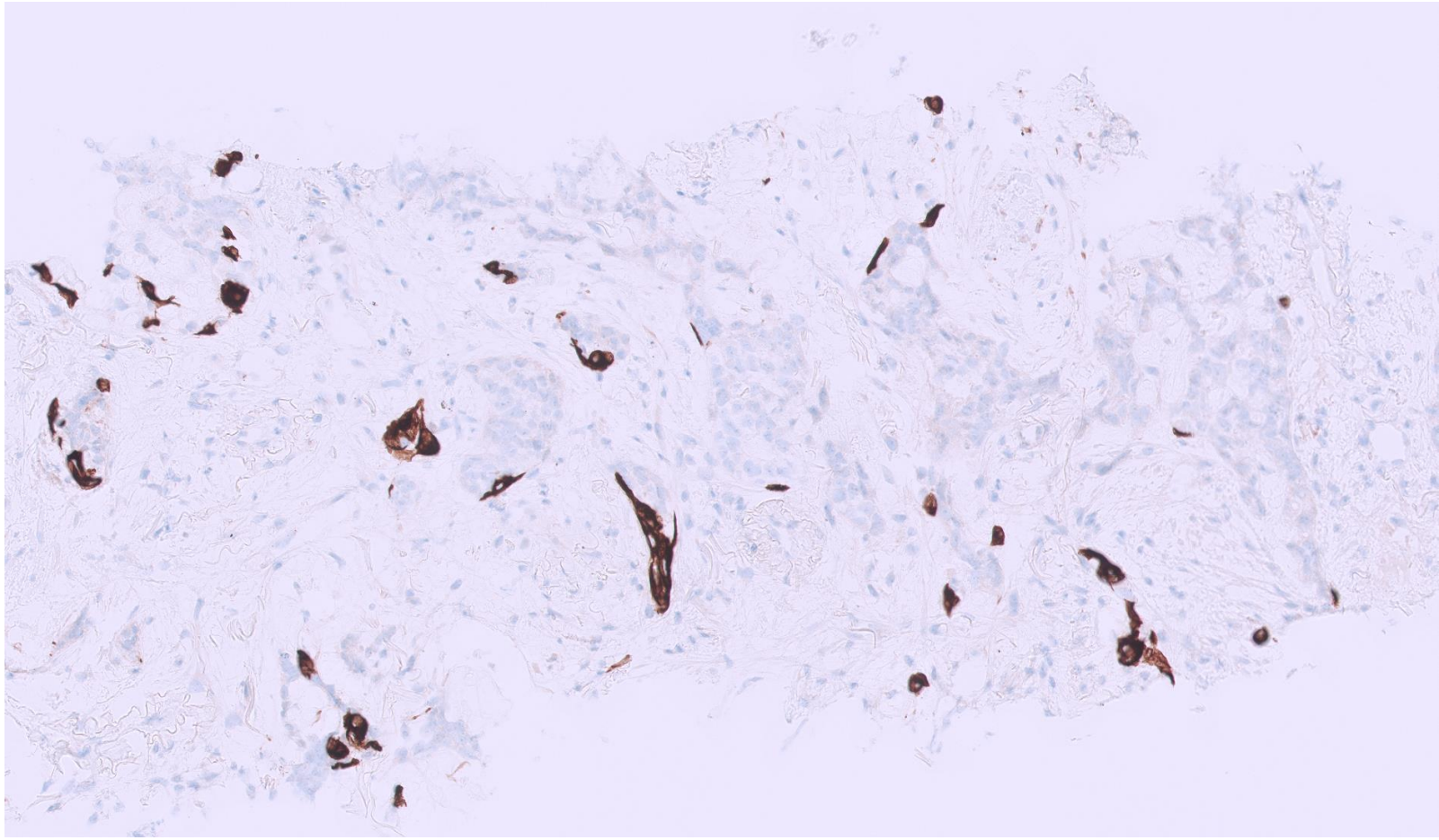

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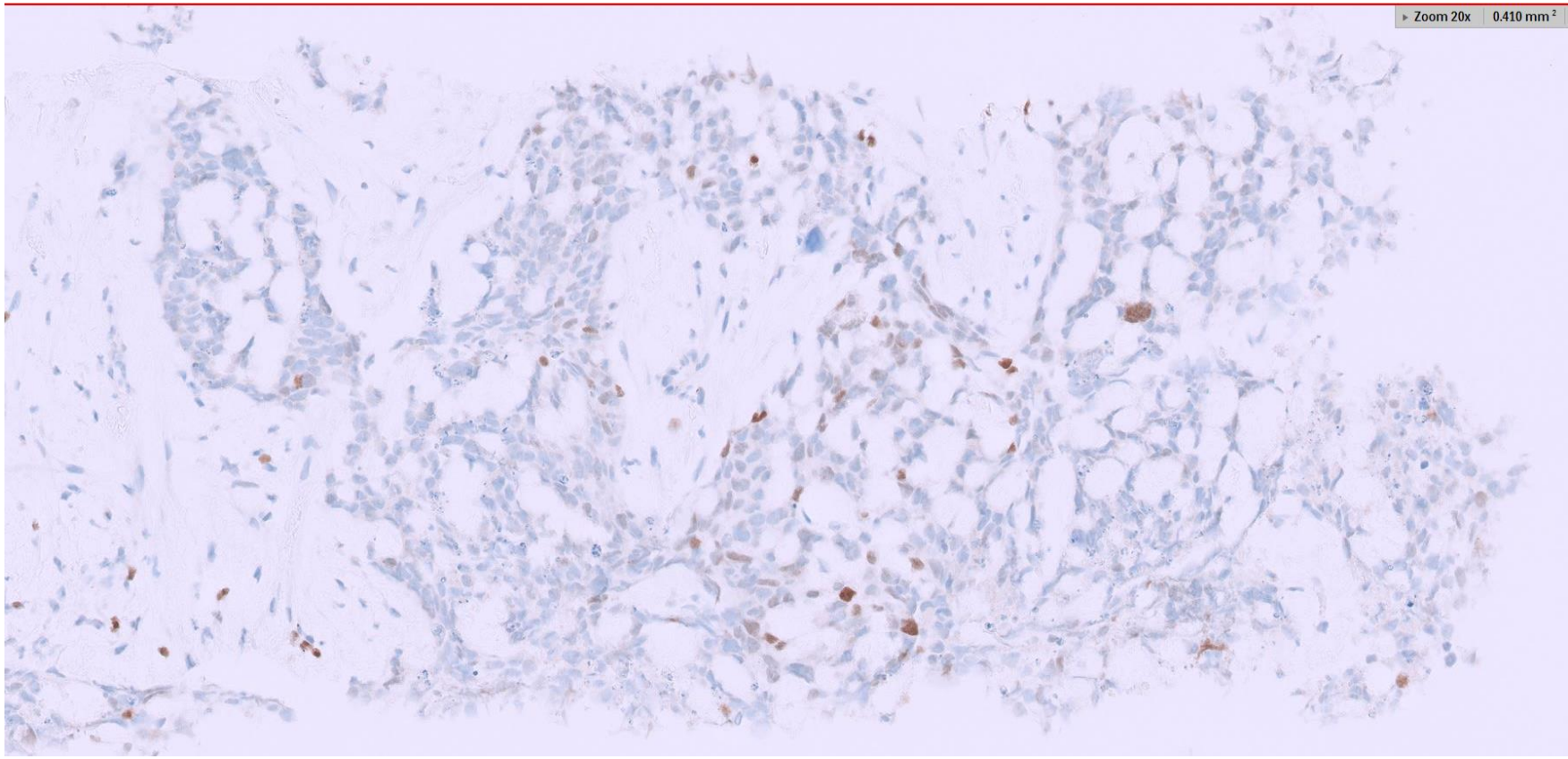

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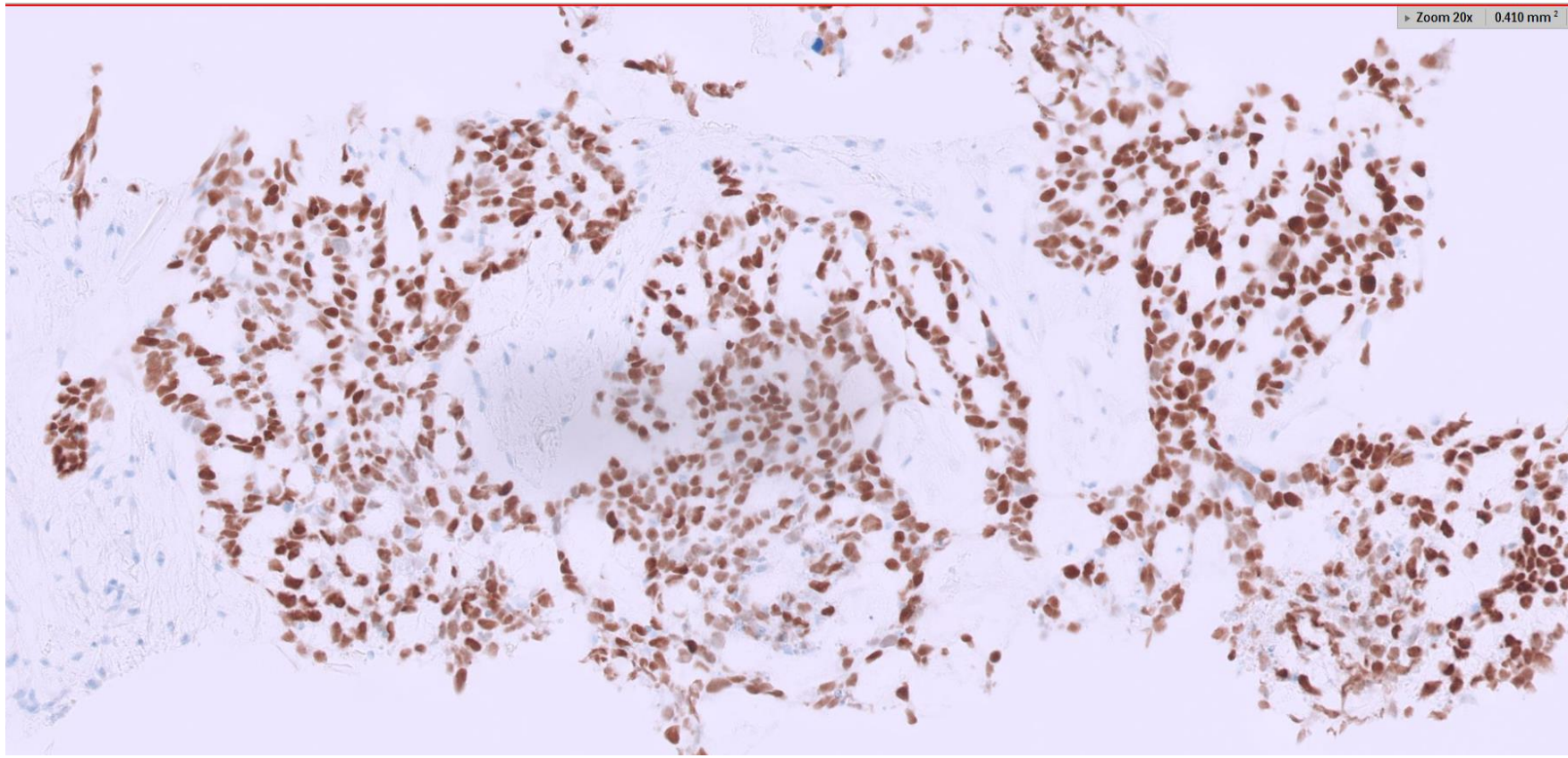

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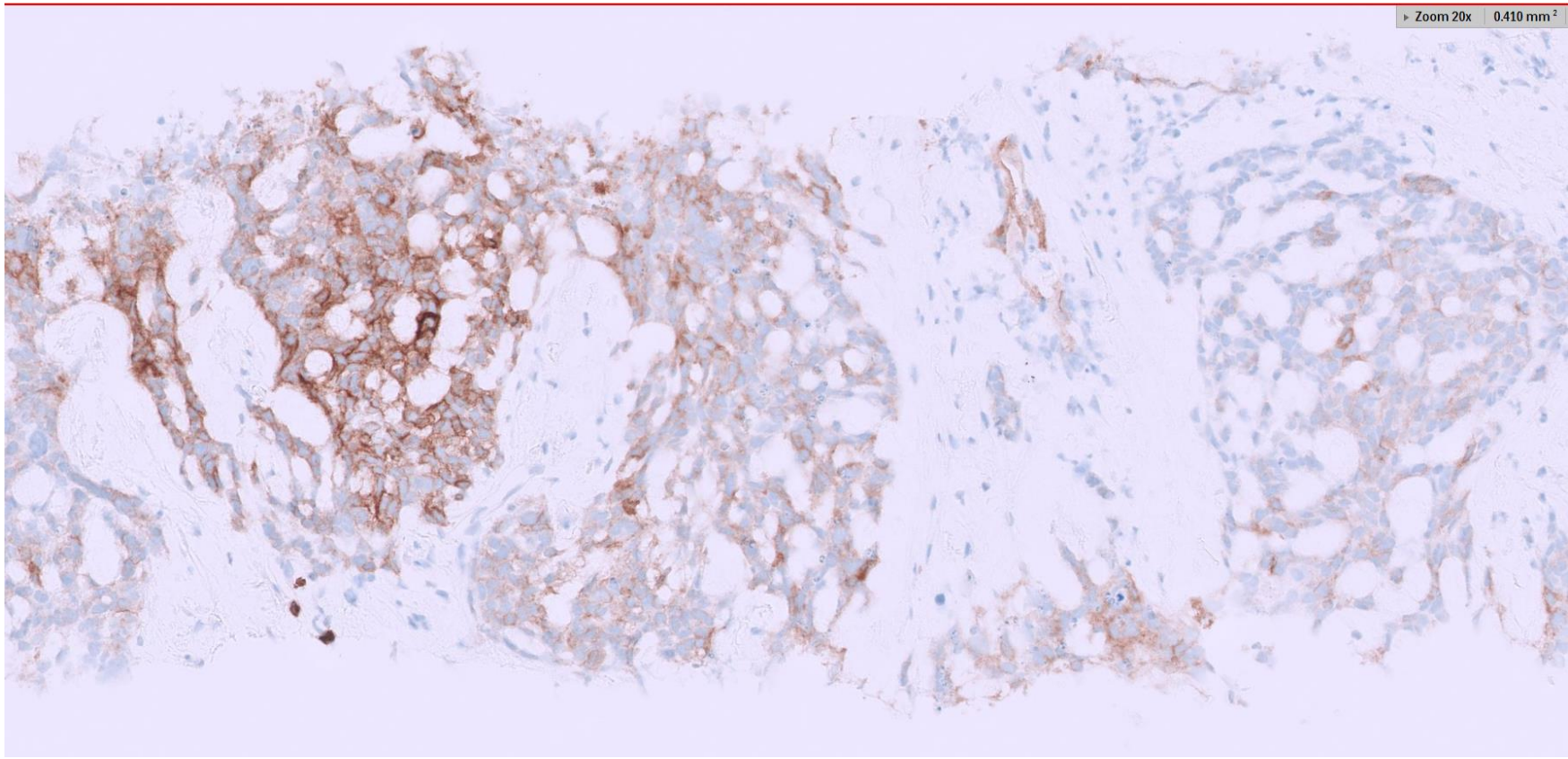
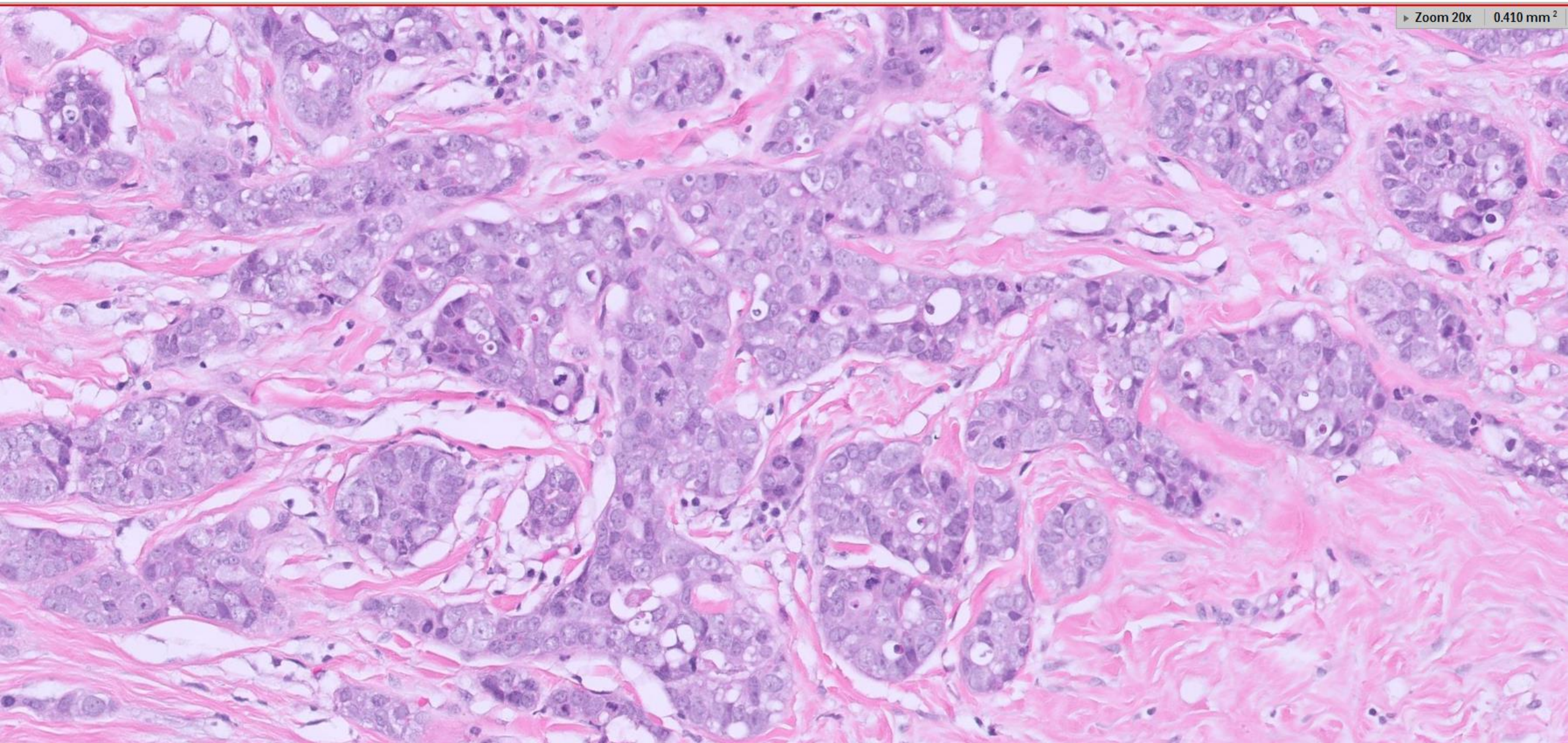


Re-review of prior lumpectomy case



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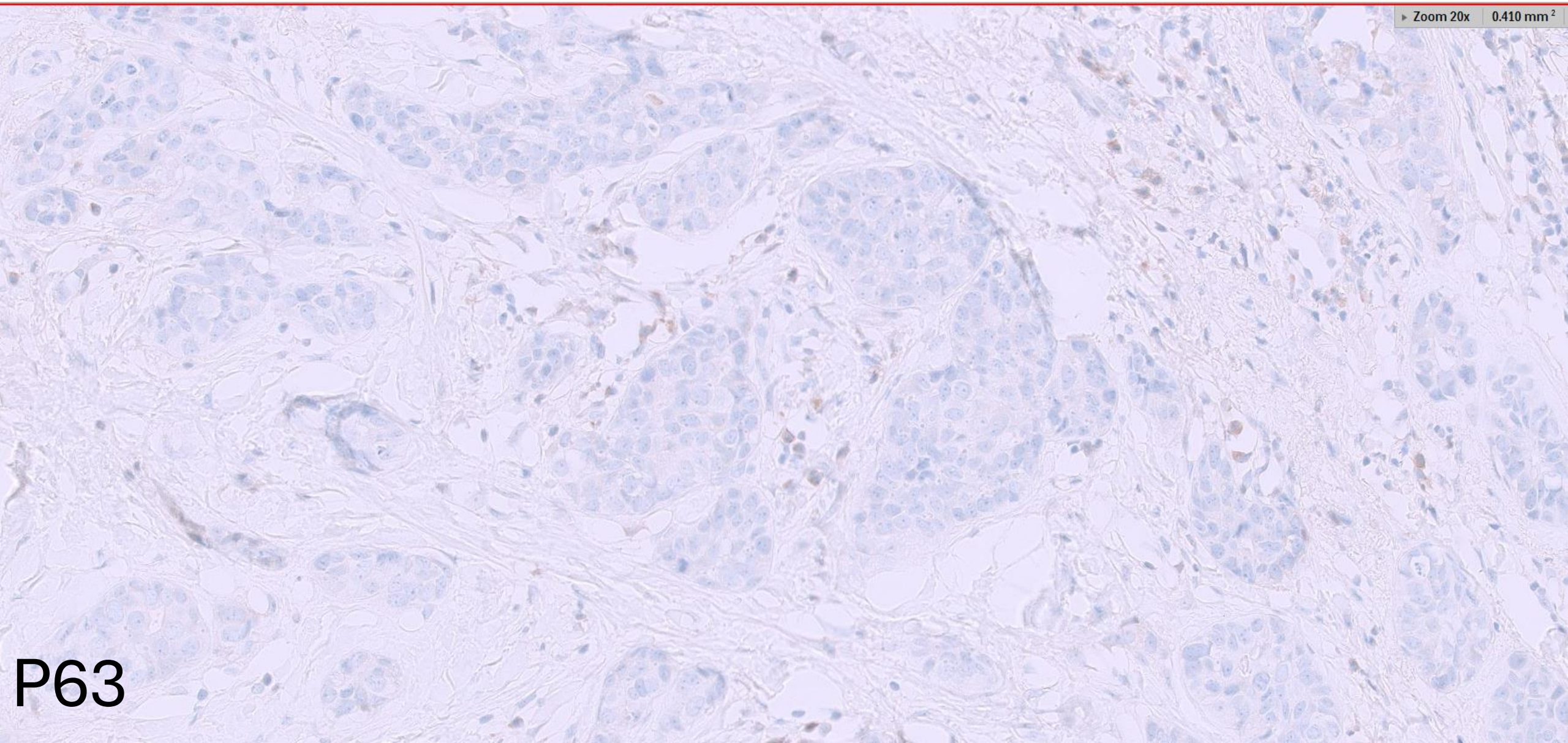

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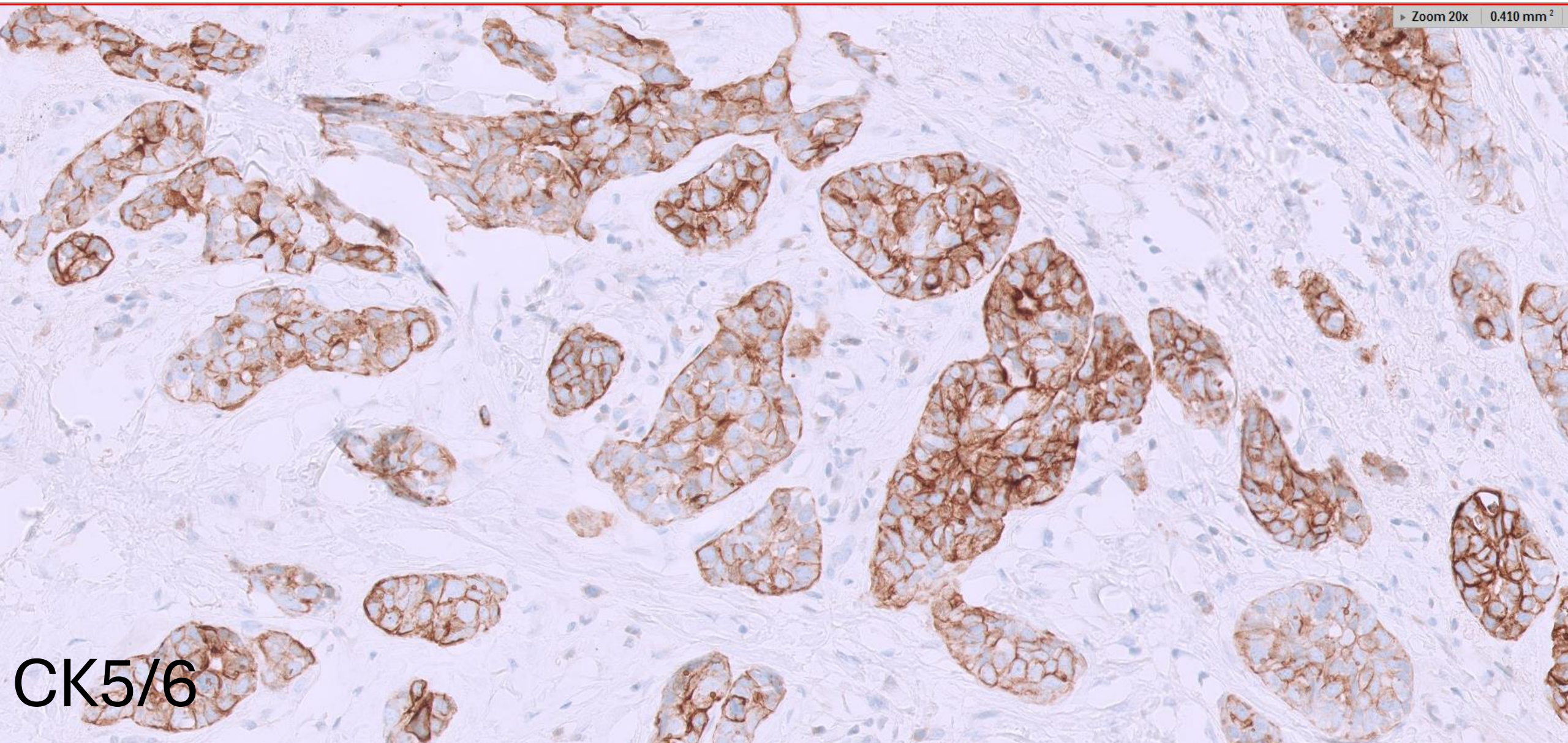

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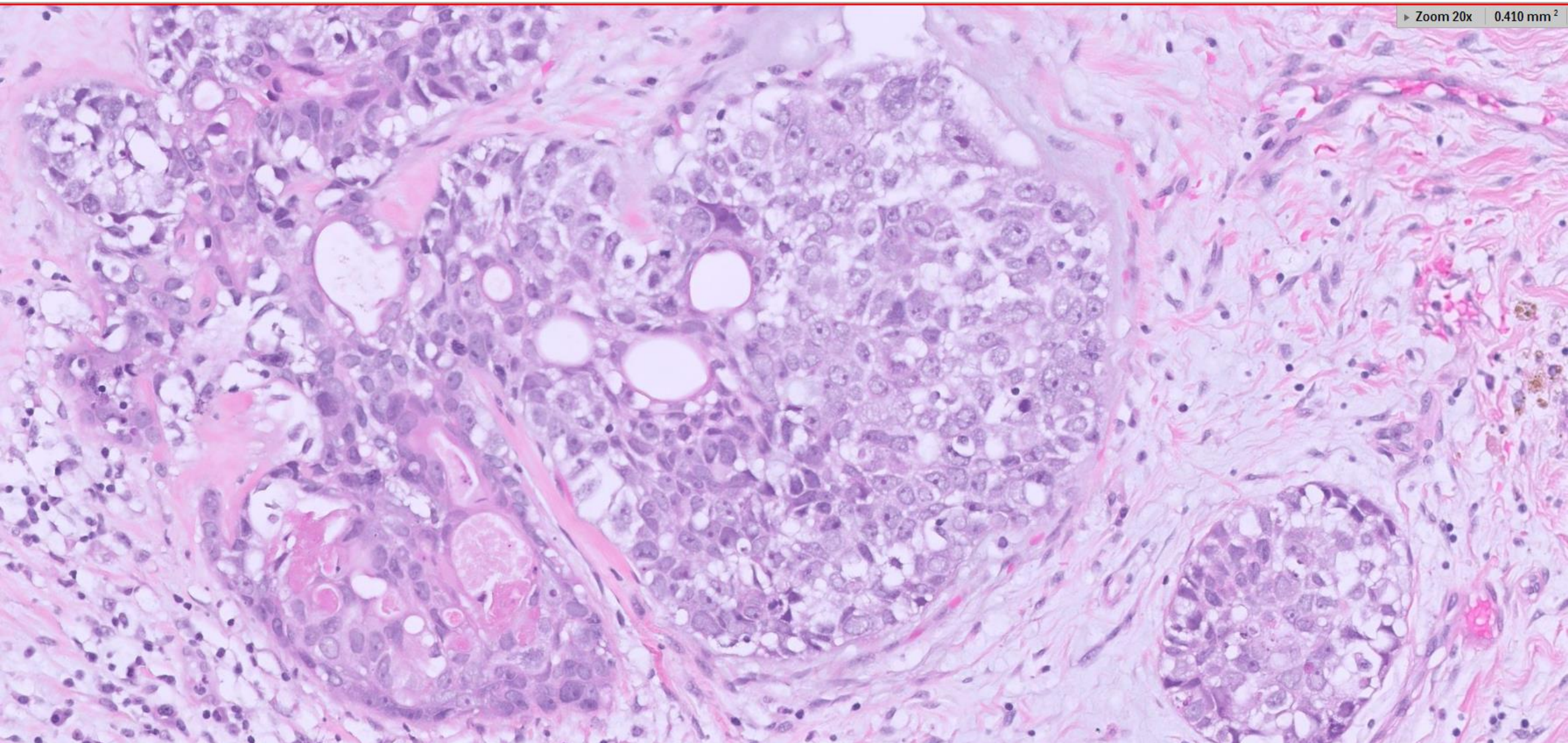

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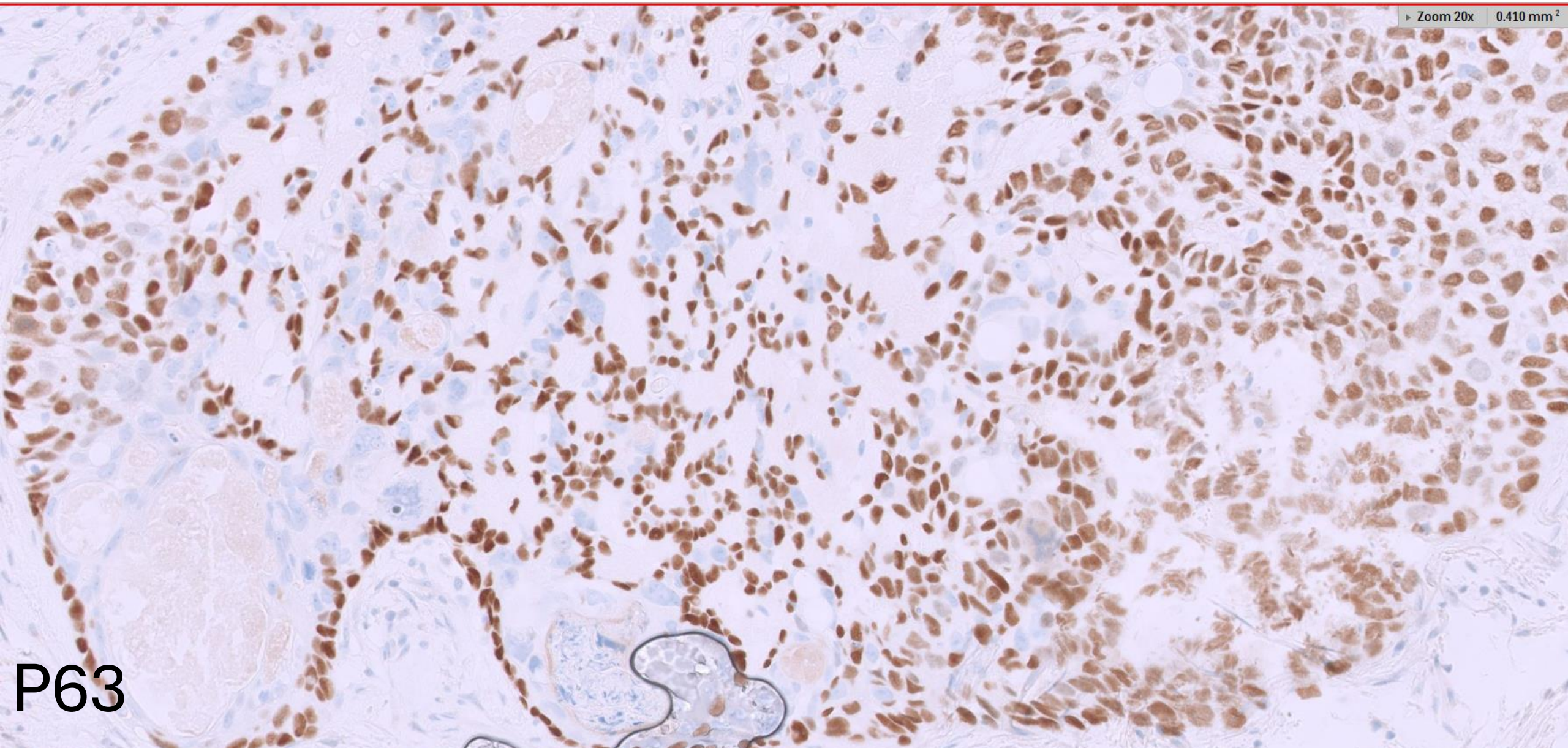

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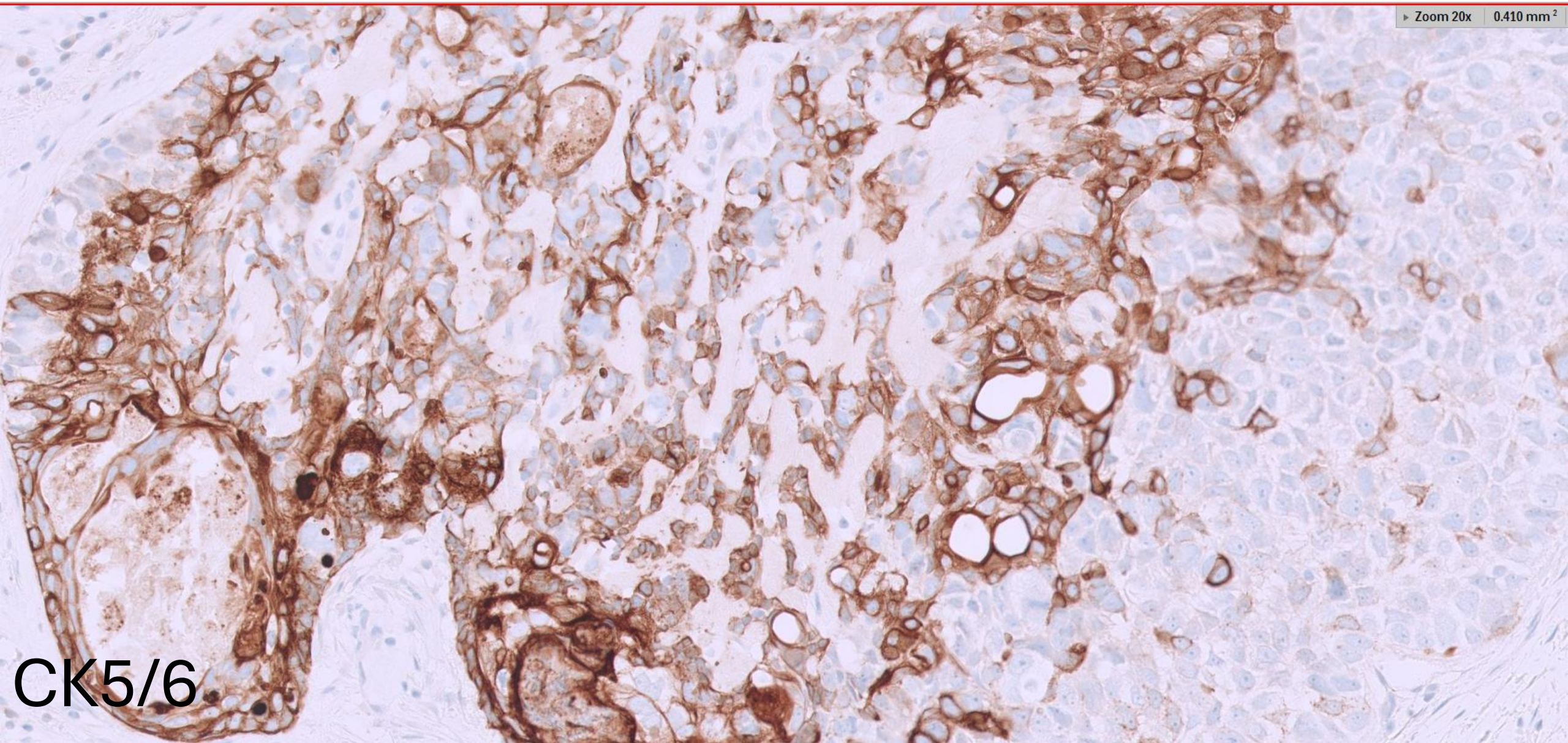
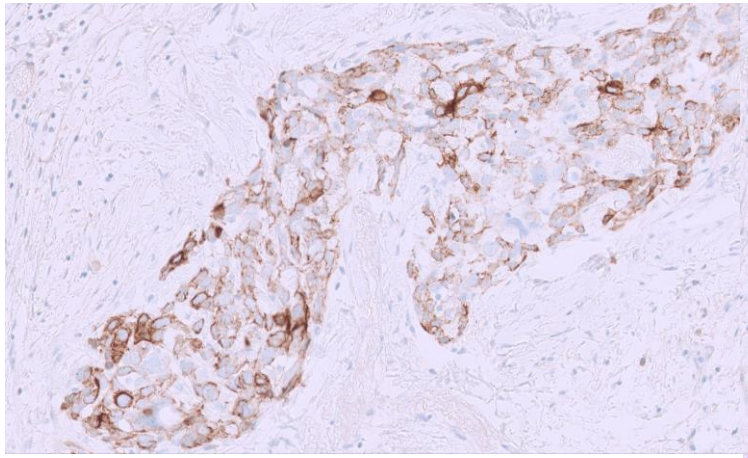


Lumpectomy immunohistochemistry stains

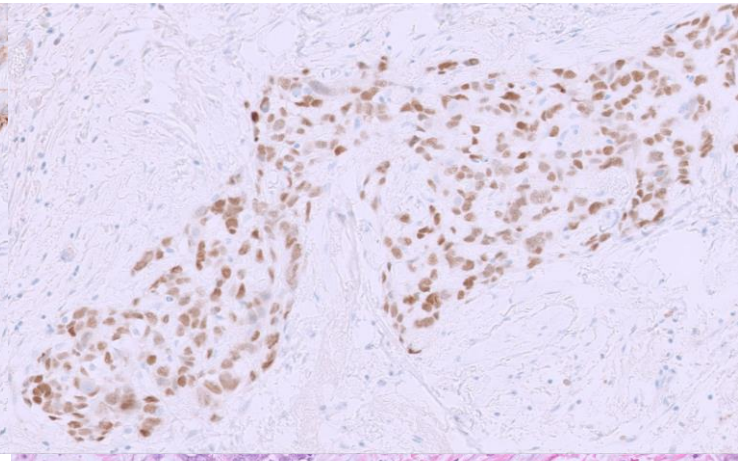
IHC

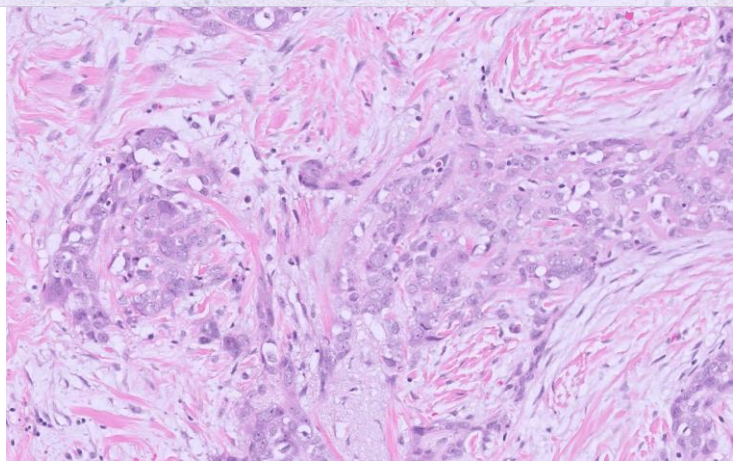
Stain	Result
• ER	Negative (0%)
• PR	Negative (0%)
• HER2	Negative (1+)
• Ki67	50%
• **P63**	**Subset positive**
• **CK5/6**	**Subset positive**
• E-cad	Membranous
• P120	Membranous
• Pan-CK	Positive

CK5/6



P63 positive in one invasive gland





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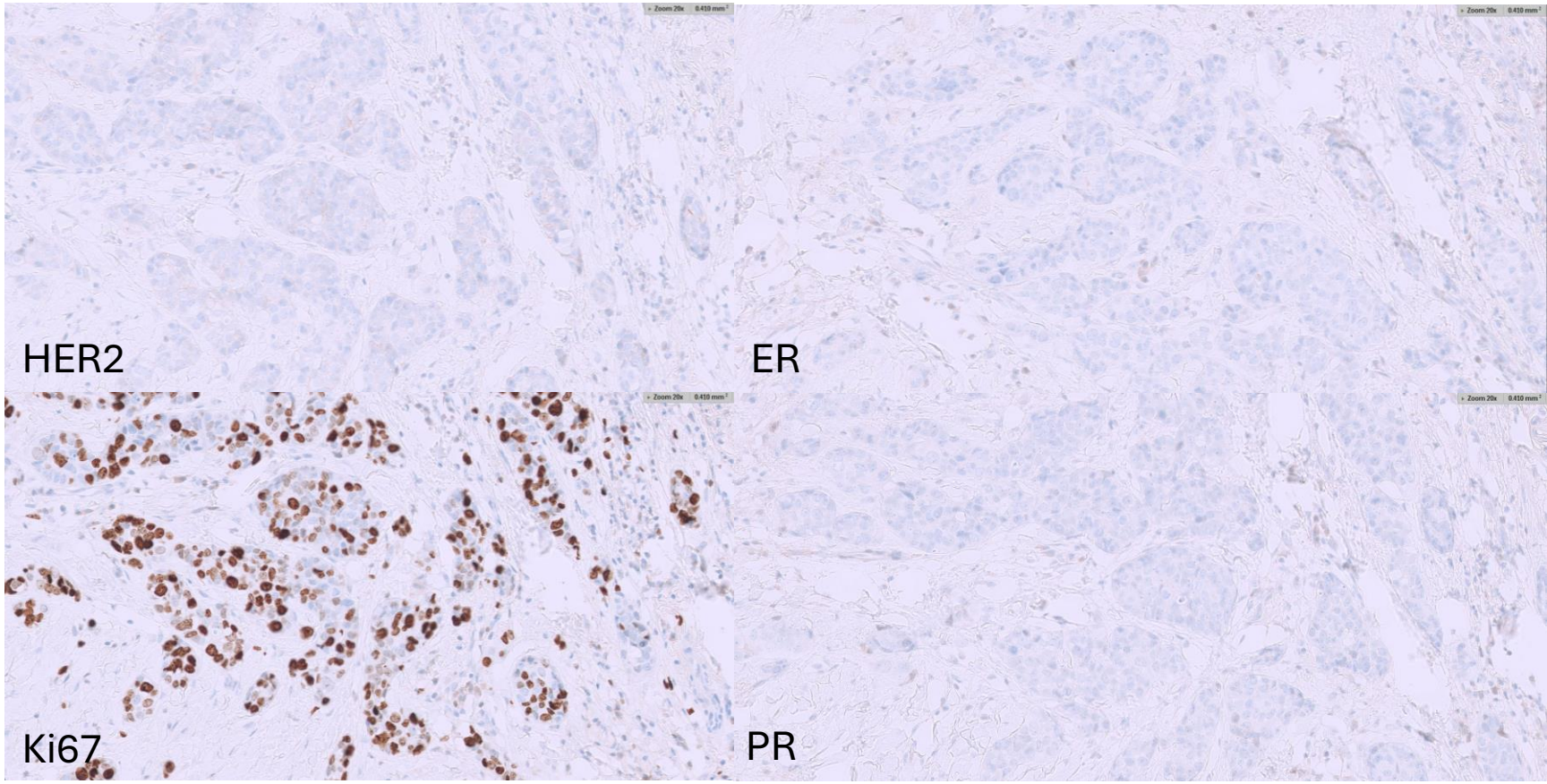


DIAGNOSIS?

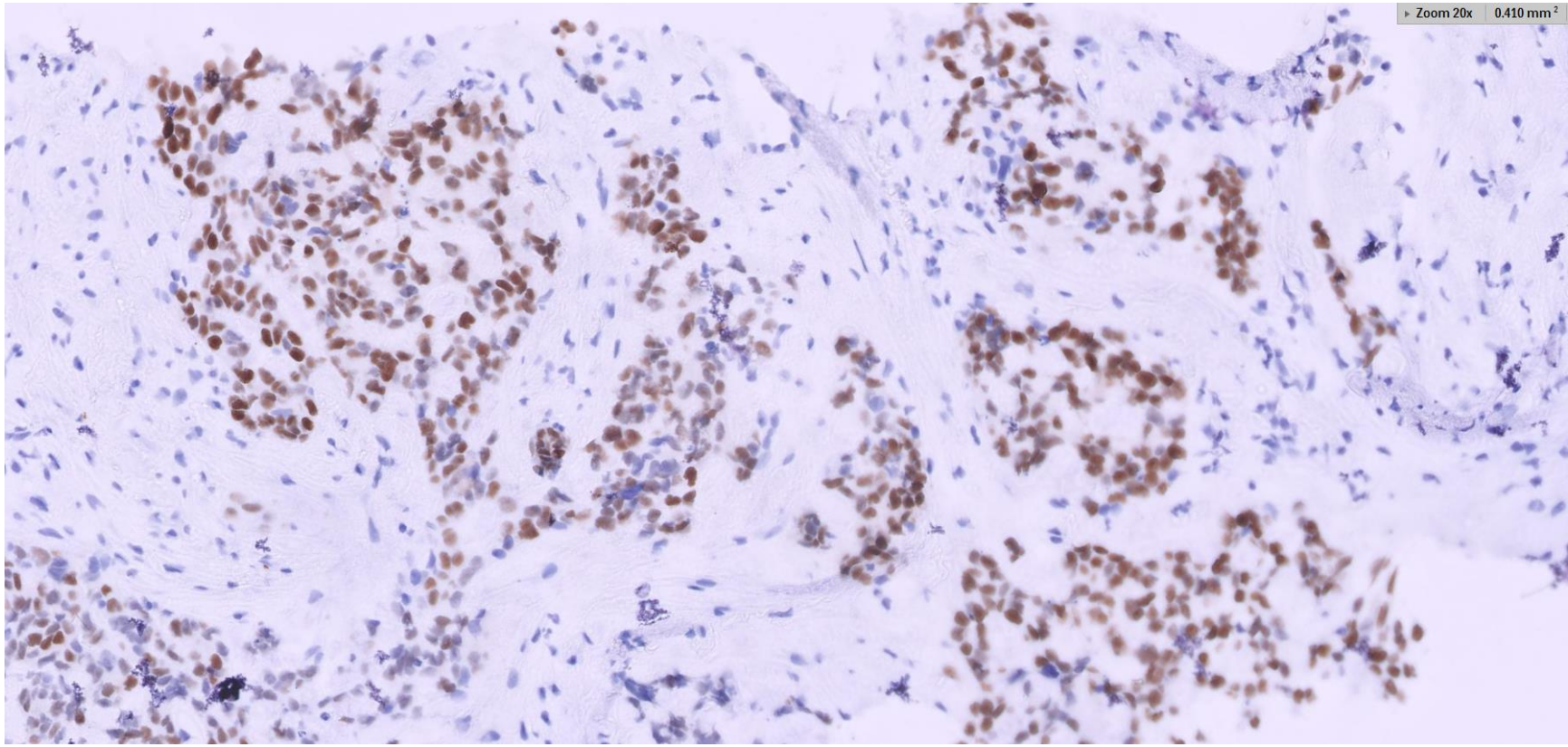
Additional Southbay Slides

Differential Diagnosis:

- Basaloid TNBC
- Metaplastic Carcinoma
- SB-AdCC

Additional IHC on Lung Lesion

IHC Stain	Result
CDX2	Negative
CK20	Negative
CK7	Focal positive
GATA3	Focal positive
TTF-1	Negative
Ki67	50-60%
P63	Positive
HER2	Negative (1+)
CD117	Positive
SOX10	**Positive**
TRPS	Positive
MYB-ISH	Positive



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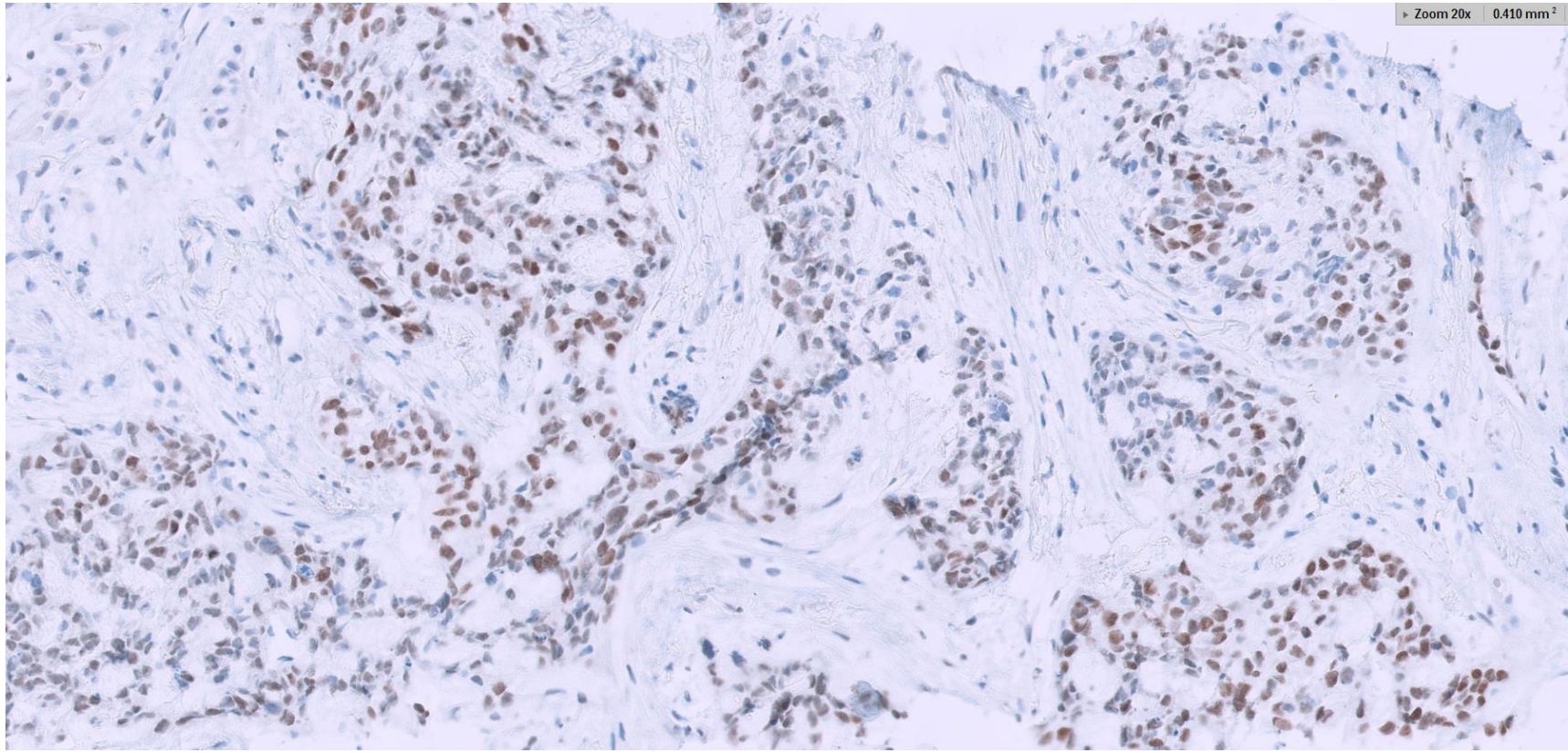
• **TRPS**	**Positive**
• MYB-ISH	Positive



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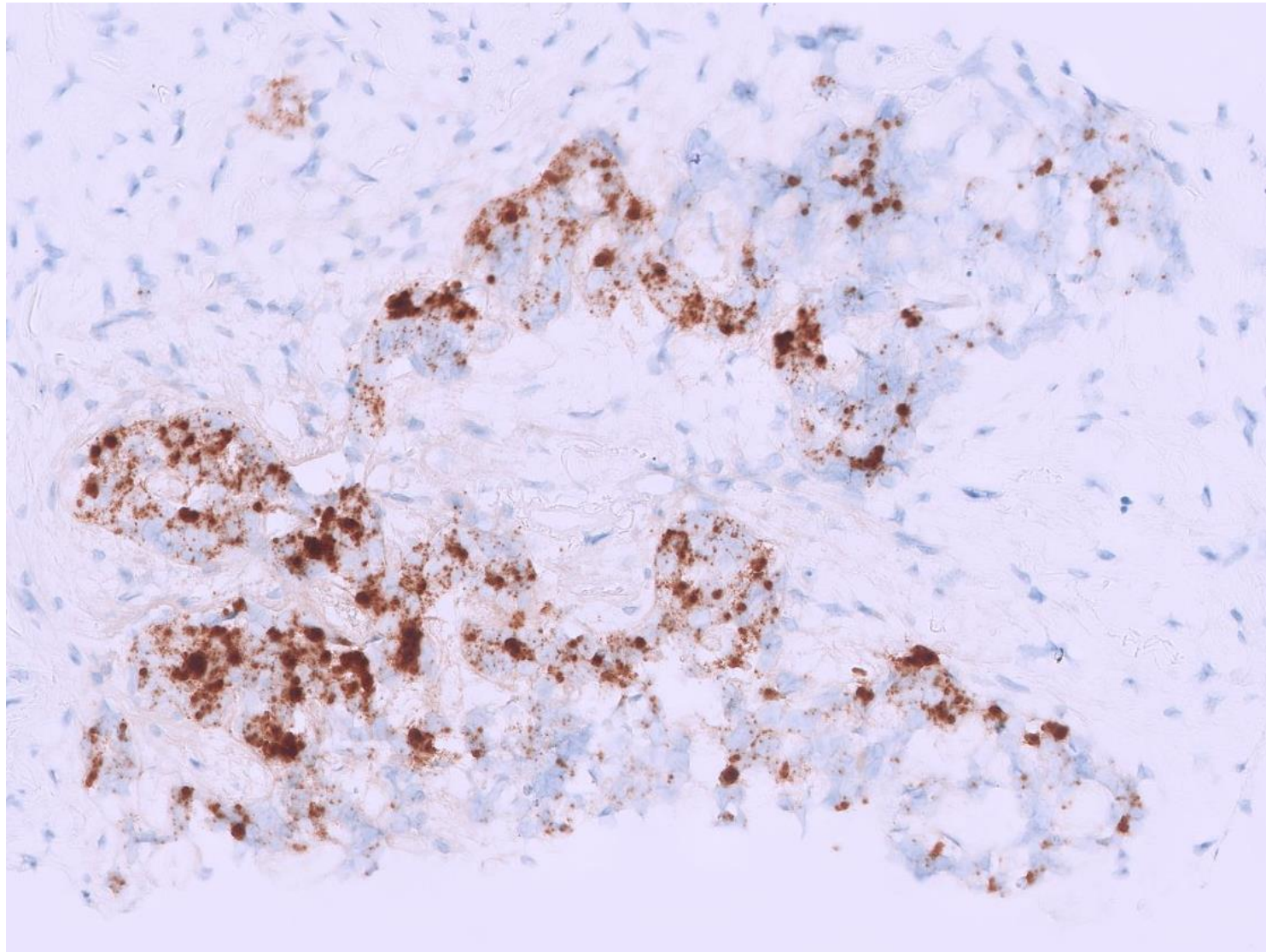
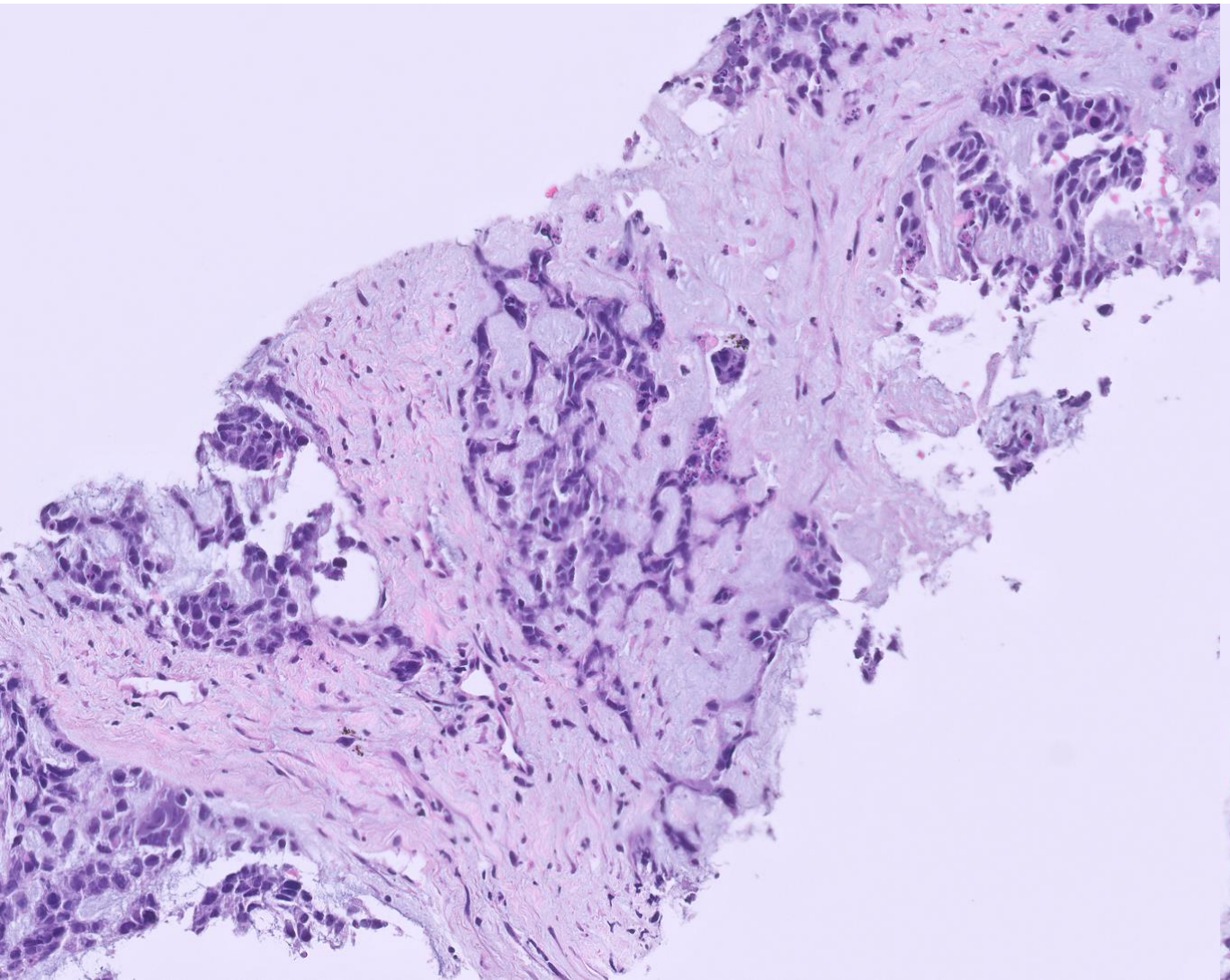
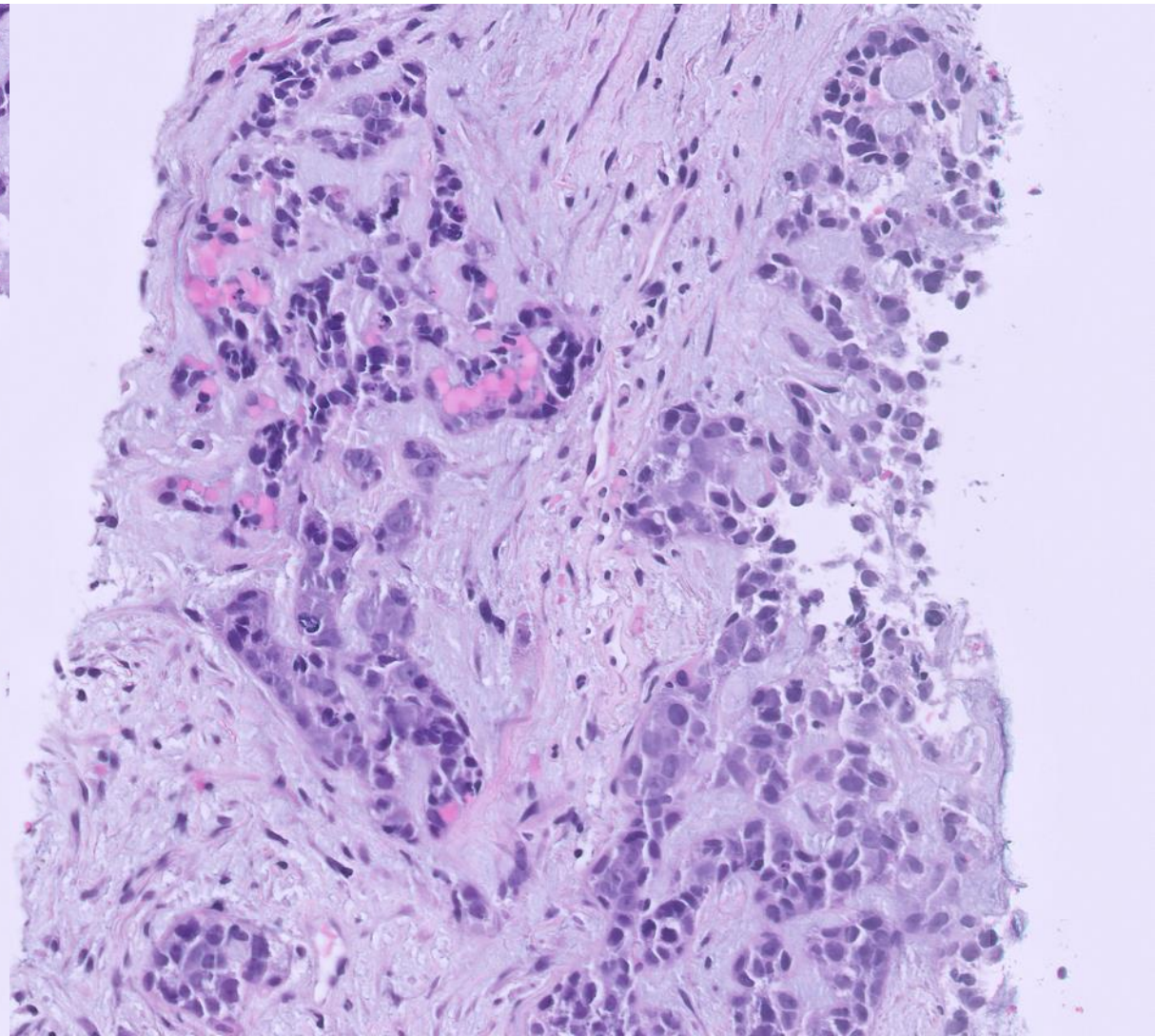


Re-cut H&E on Lung Lesion

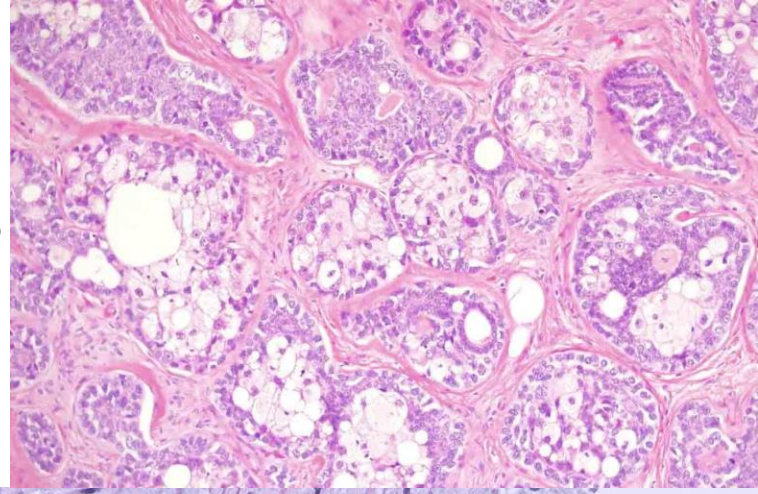
Chondromyxoid stroma



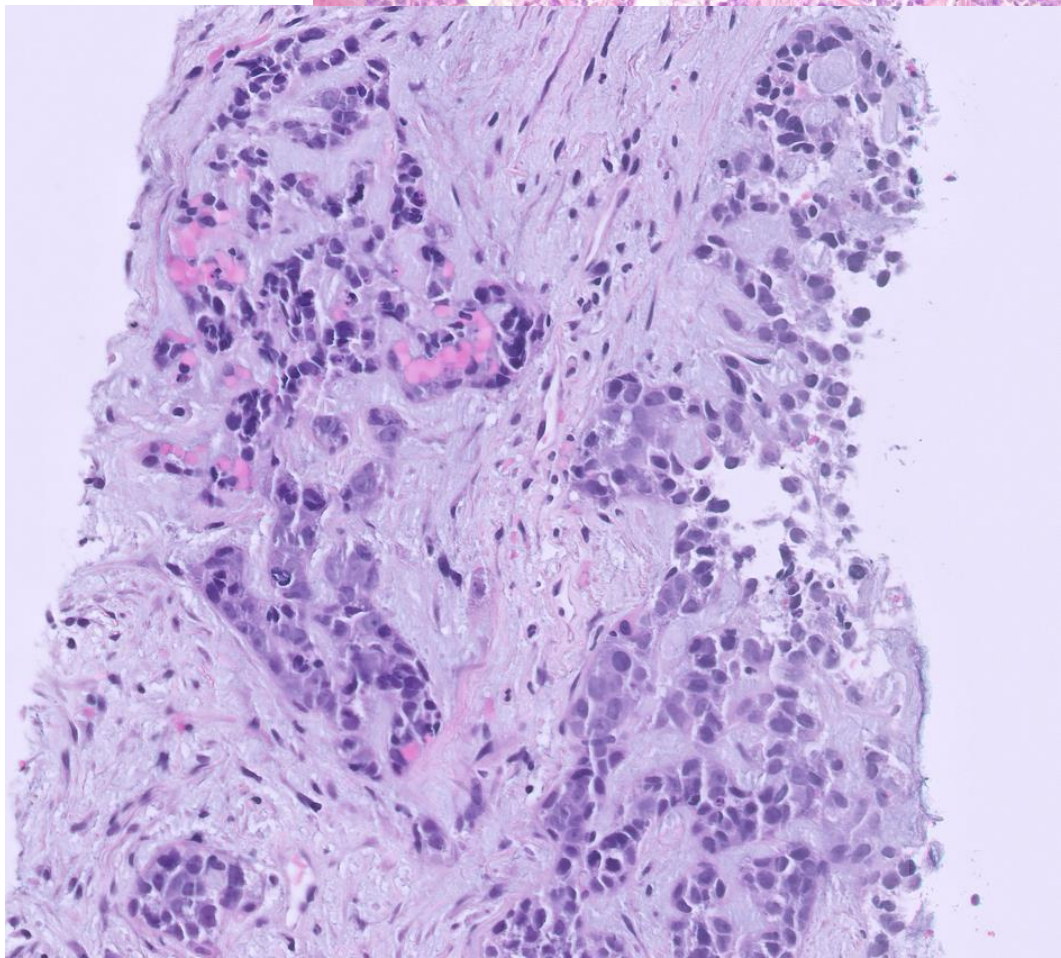
Focal eosinophilic (BM like) material



Lung Biopsy Diagnosis

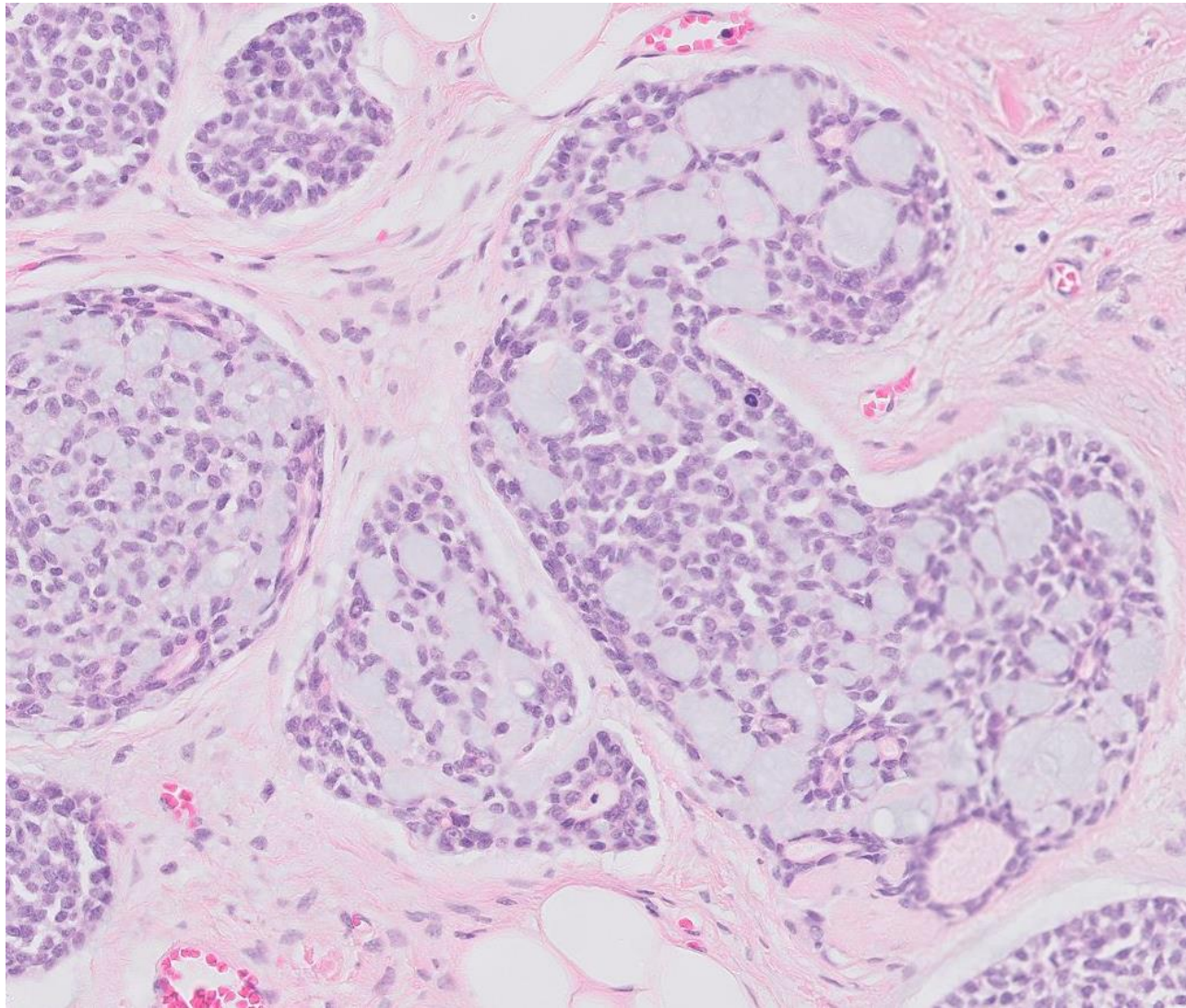


- Solid basaloid variant of adenoid cystic carcinoma, originating from breast primary
- Predominantly solid growth, increased mitotic rate ⟹ Aggressive course
  - Consists predominantly of myoepithelial cells with only sparse luminal cells
    - Myoepithelial cells have scant cytoplasm and hyperchromatic nuclei, conferring the **basaloid appearance**
    - Less frequent basement membrane-like material than classic AdCC
    - SB-AdCC often have aberrations in Notch pathway (~30-60%), alterations in *CREBBP*



Classic-adenoid cystic carcinoma

- Breast AdCC shows the same morphological spectrum observed in salivary gland AdCC
  - Classic AdCC: ~ 70-90% have the *MYB::NFIB* gene rearrangement
    - Central cribriform area surrounded by a peripheral area with predominant tubular architecture
      - Epithelial and myoepithelial cells
        - Epithelial-type cells produce mucins
        - Stroma infiltrates among the myoepithelial cells creating pseudo-lumina



Differential Diagnosis

- Basaloid TNBC
  - Two distinct populations are not present
  - Can be weakly C117 (~50%)and weakly MYB positive (~25-65% of TNBC)
- Metaplastic Carcinoma
  - Particularly HG Adenosquamous carcinoma
    - SB-AdCC can have focal squamous differentiation
    - CD117 negative, MYB negative, and SOX10 negative stains are helpful
- SB-AdCC
  - 2 neoplastic cell populations are present
  - MYB positive (~ 65-95%), CD117 positive, SOX10 positive

Treatment for TNBC

- NeoAdjuvant Chemotherapy ➔ Surgery ➔ +/-Adjuvant Chemotherapy ➔ Radiation
  - For triple negative tumors, generally KEYNOTE-522
    - Weekly Taxol/carboplatin x 12 ➔ AC every 3 weeks x 4 cycles with concurrent pembrolizumab every 3 weeks

- No treatment differences for TNBC at the current time but SCARLET Trial is ongoing
  - (Shorter Anthracycline-Free Chemo-Immunotherapy Adapted to Pathological Response in Early Triple Negative Breast Cancer)
    - Estimated completion date is December 2029

- SB-AdCC has a higher local recurrence and metastatic rates with a ~ 40% death rate
  - Axillary lymph node metastasis (~ 15-30%) and distant metastasis (~ 45-65%) are frequent
  - Most common metastatic site is lung; also reported to bone, liver, brain, and kidney
  - Shorter time to distant metastasis (median: 22 months) compared to C-AdCC (84 months)

Citations

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- Nakai T, Ichihara S, Kada A, Ito N, Moritani S, Kawasaki T, Uchiyama T, Itami H, Morita K, Takano M, Takeda M, Hatakeyama K, Ohbayashi C. The unique luminal staining pattern of cytokeratin 5/6 in adenoid cystic carcinoma of the breast may aid in differentiating it from its mimickers. Virchows Arch. 2016 Aug;469(2):213-22. doi: 10.1007/s00428-016-1963-4. Epub 2016 May 30. PMID: 27240462.
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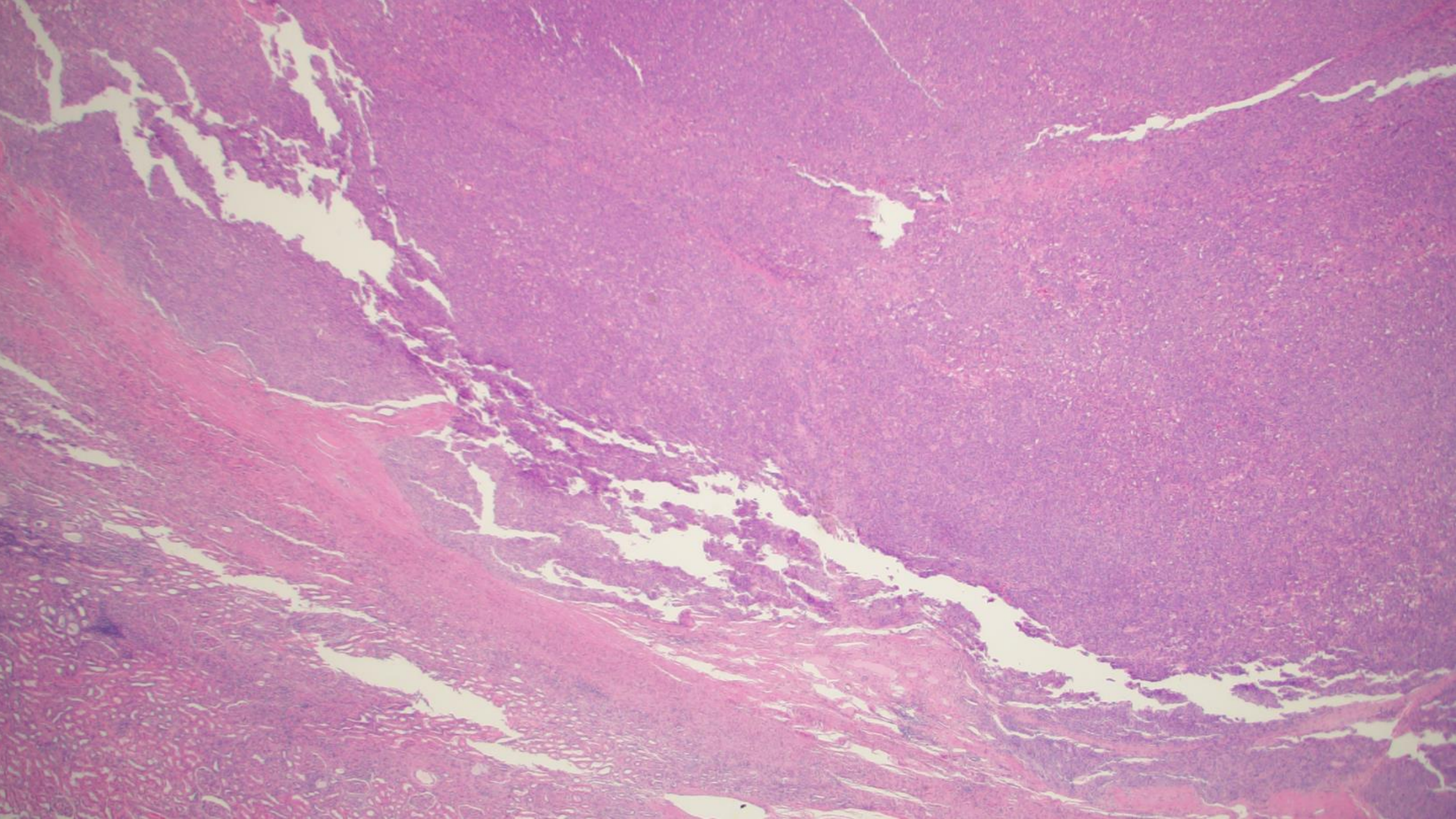
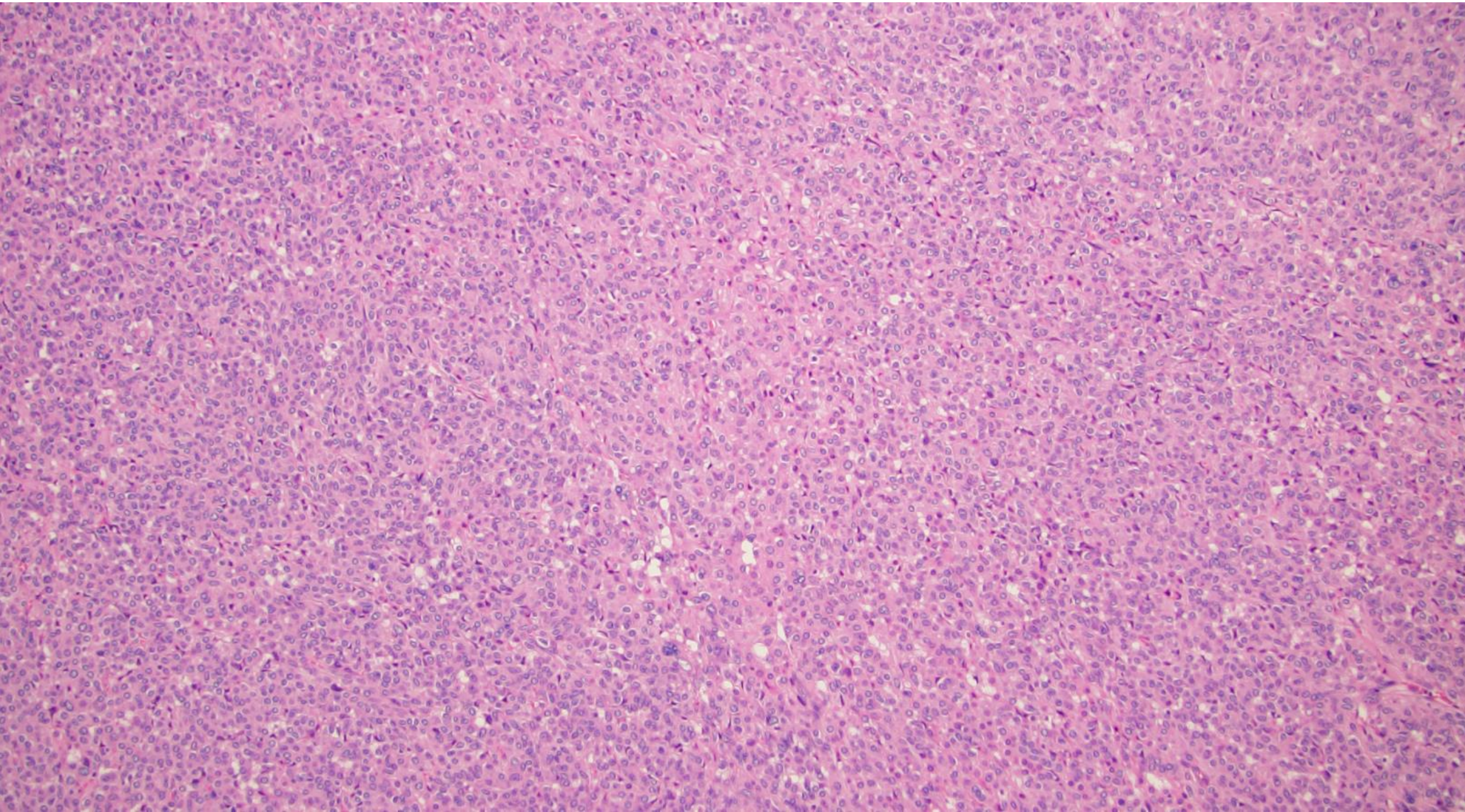
- Mastropasqua MG, Maiorano E, Pruneri G, Orvieto E, Mazzarol G, Vento AR, Viale G. Immunoreactivity for c-kit and p63 as an adjunct in the diagnosis of adenoid cystic carcinoma of the breast. Mod Pathol. 2005 Oct;18(10):1277-82. doi: 10.1038/modpathol.3800423. PMID: 15846389.

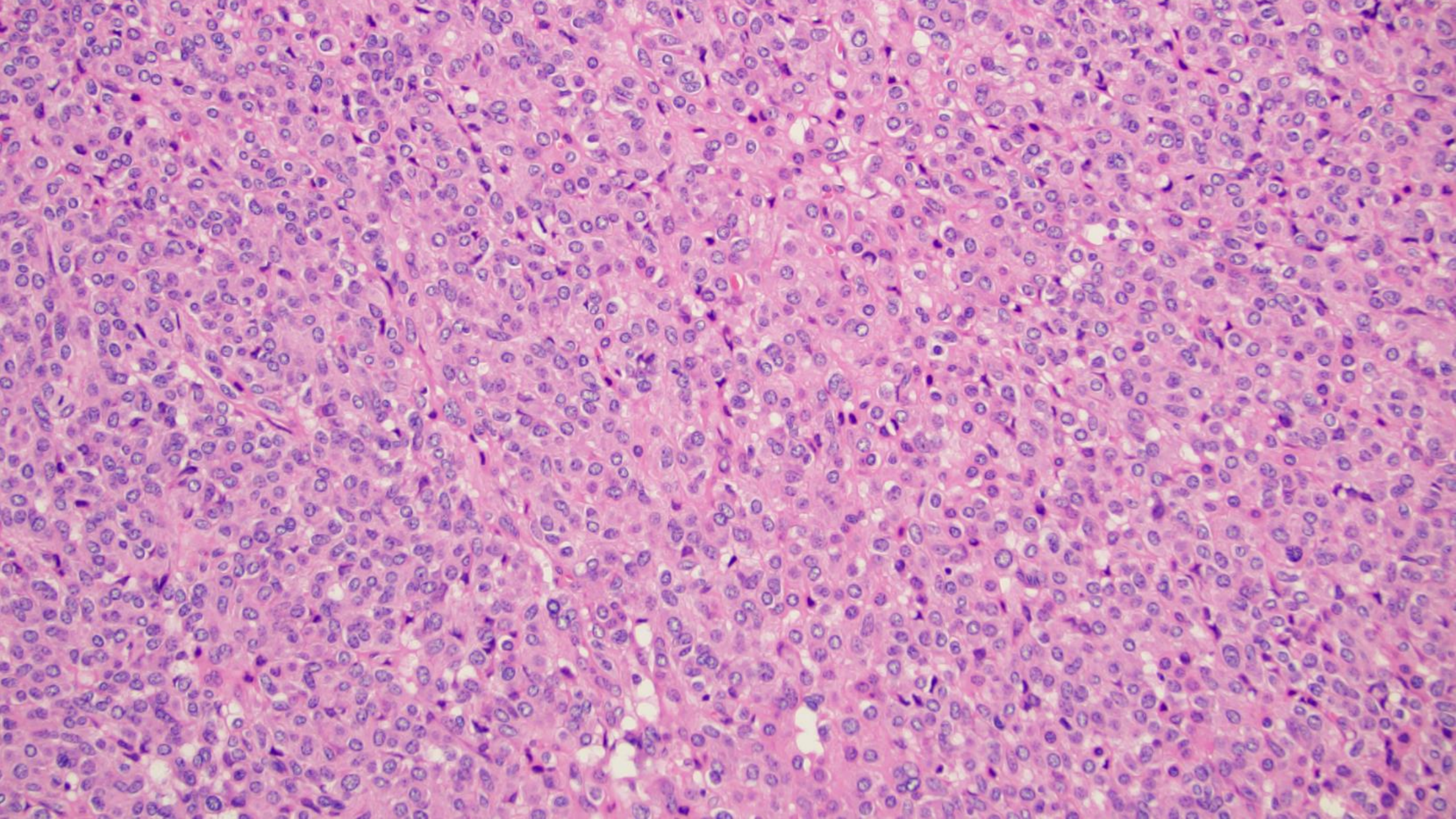
25-1103

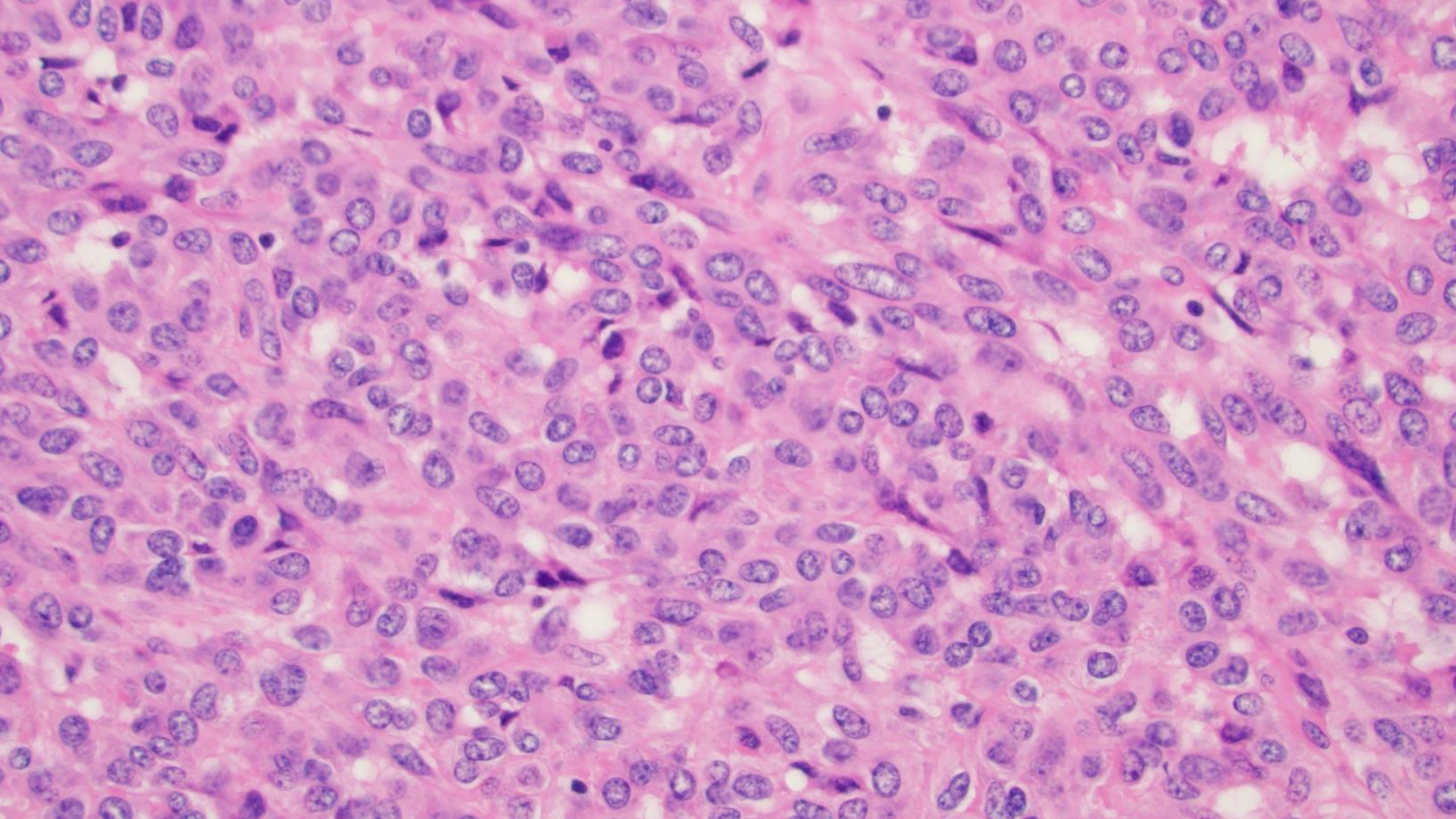
James Mathews (case from Kaiser San Francisco)

30ish year-old woman with a 3.5 cm right kidney mass







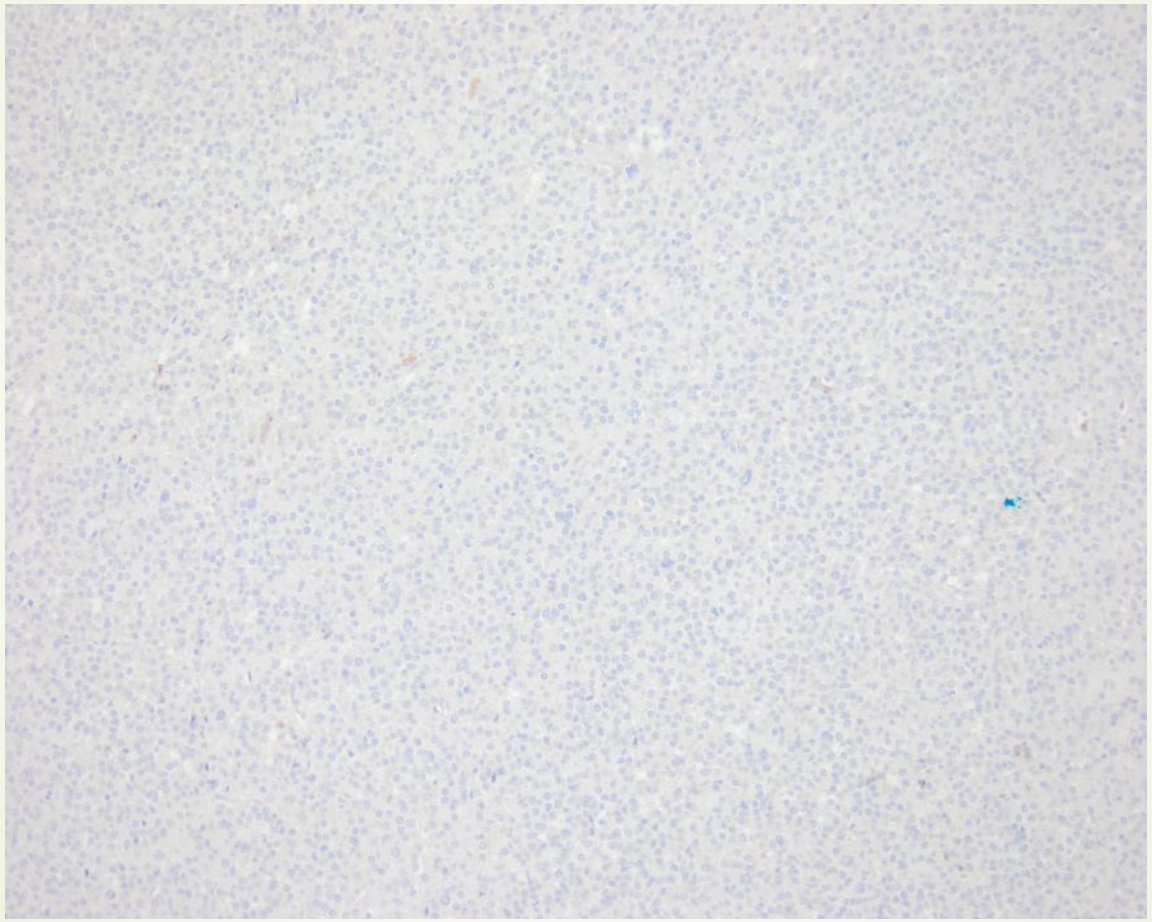


DIAGNOSIS?

H&E Differential Diagnosis:

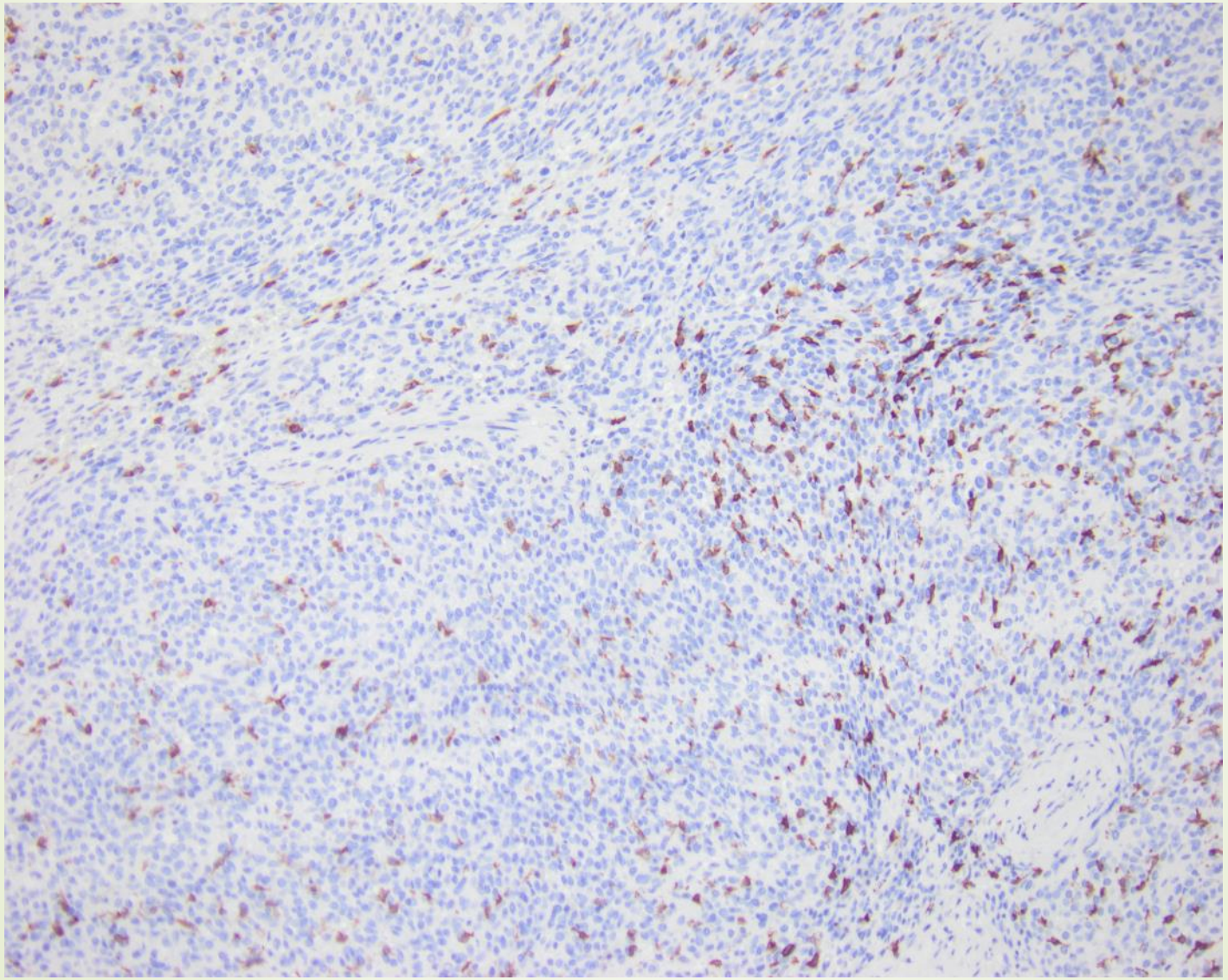
- Glomus Tumor (SMA +, CD34 – or weak)
- Juxtaglomerular cell tumor (CD34 strong+, Renin+)
- Solitary Fibrous Tumor (CD34+, STAT6+)
- Angiomyolipoma (HMB45+)
- Low-grade urothelial carcinoma (GATA3+, keratin+)
- A less common subtype of Renal Cell Carcinoma (PAX8+):
  - Papillary RCC with solid architecture
  - Collecting duct carcinoma

PAX8

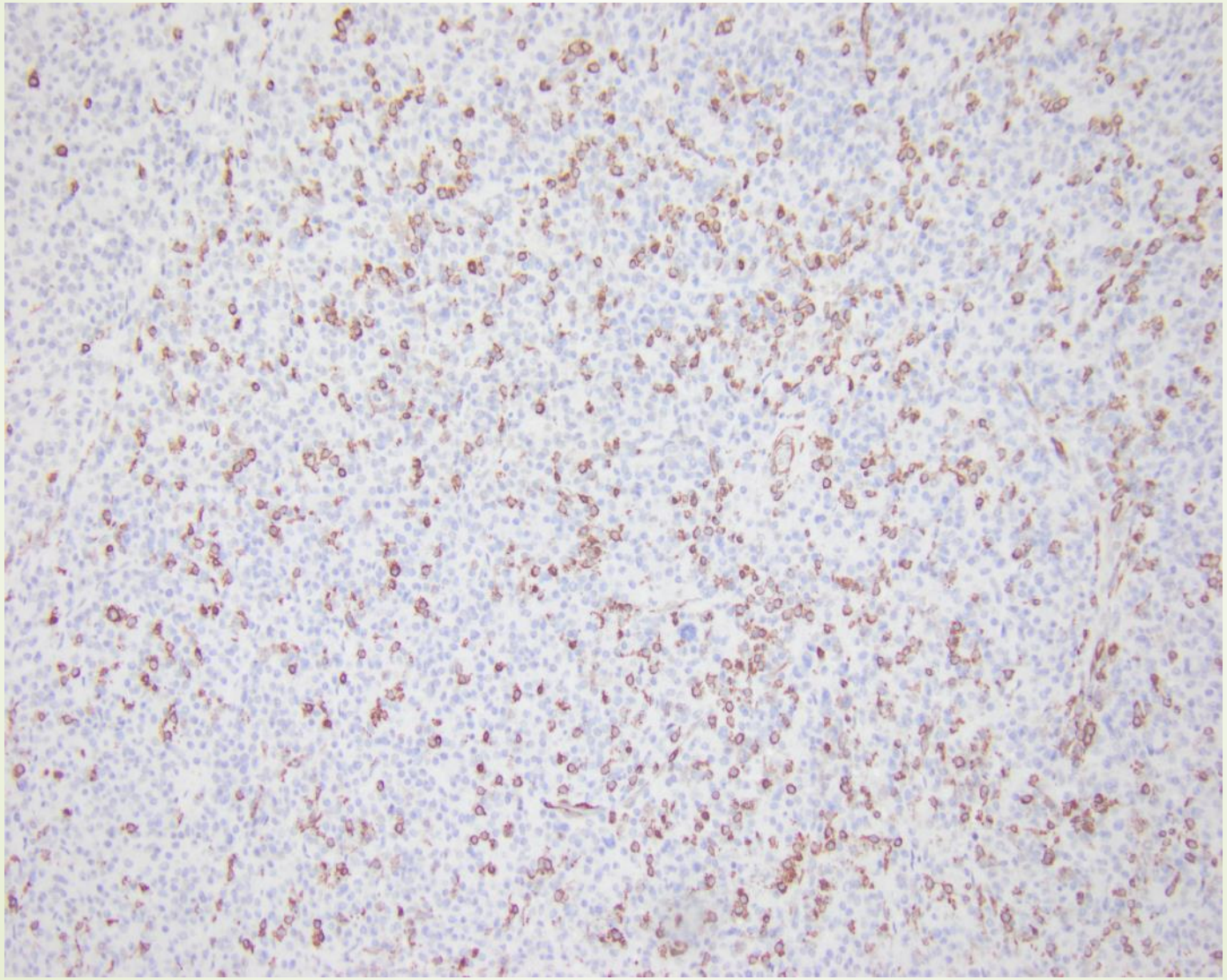


Pancytokeratin: Negative

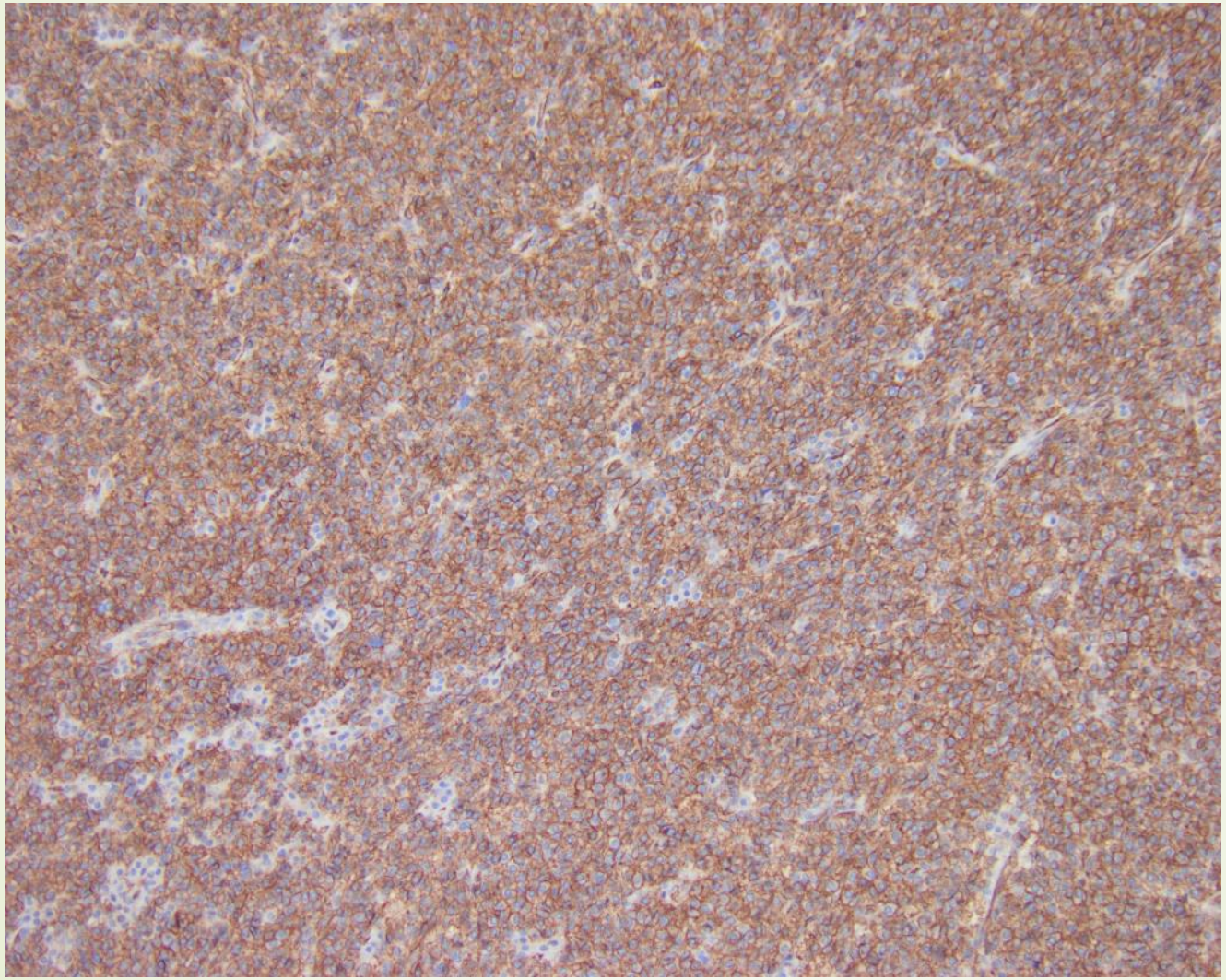
CD117



SMA



CD34

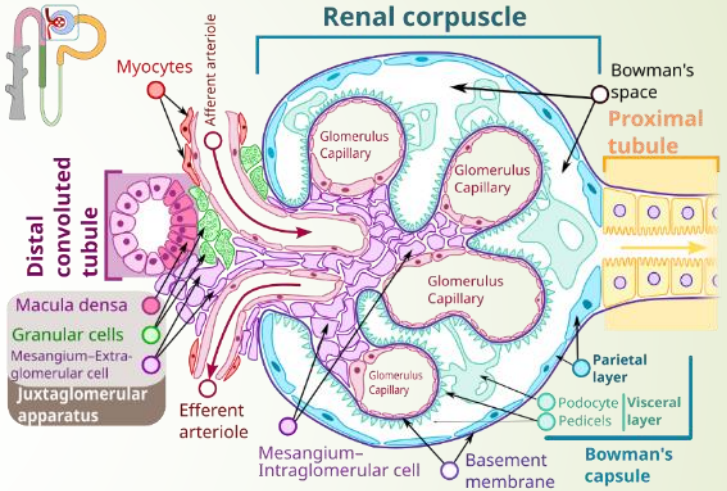


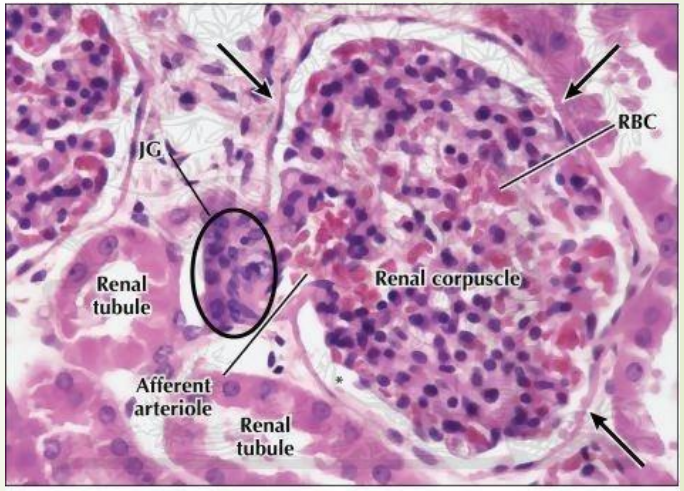
Additional Clinical History

- Taking Lisinopril for hypertension
- Hyperaldosteronism
- Increased plasma renin activity

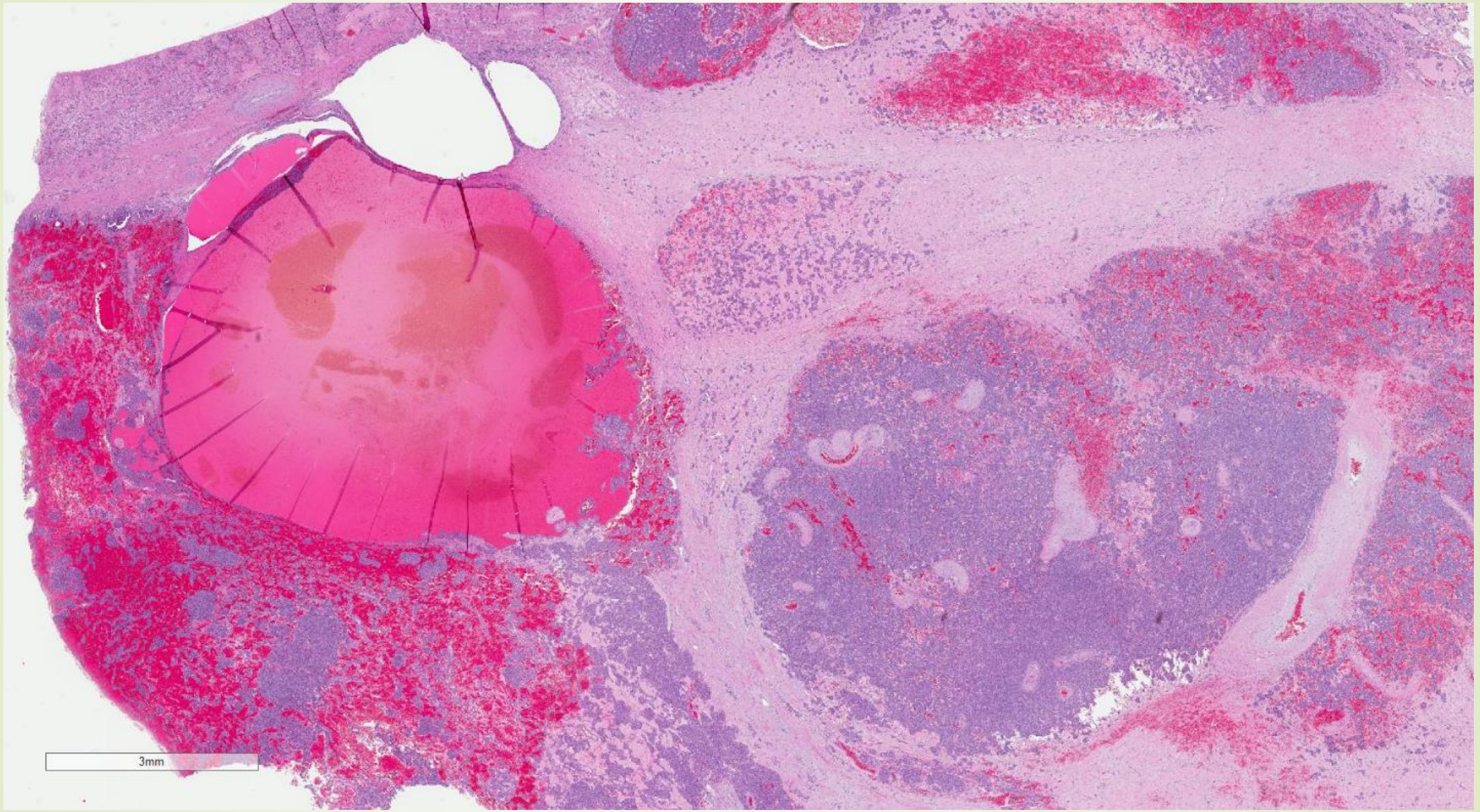
Diagnosis: Juxtaglomerular cell tumor

- Benign* tumor arising from renin producing cells of the juxtaglomerular apparatus
- Female predominance
- Second or third decades of life (range 6 to 80)
- Clinical categories:
  - Typical: hypertension, hyperaldosteronism, hypokalemia
  - Atypical: hypertension and normal potassium
  - Nonfunctioning

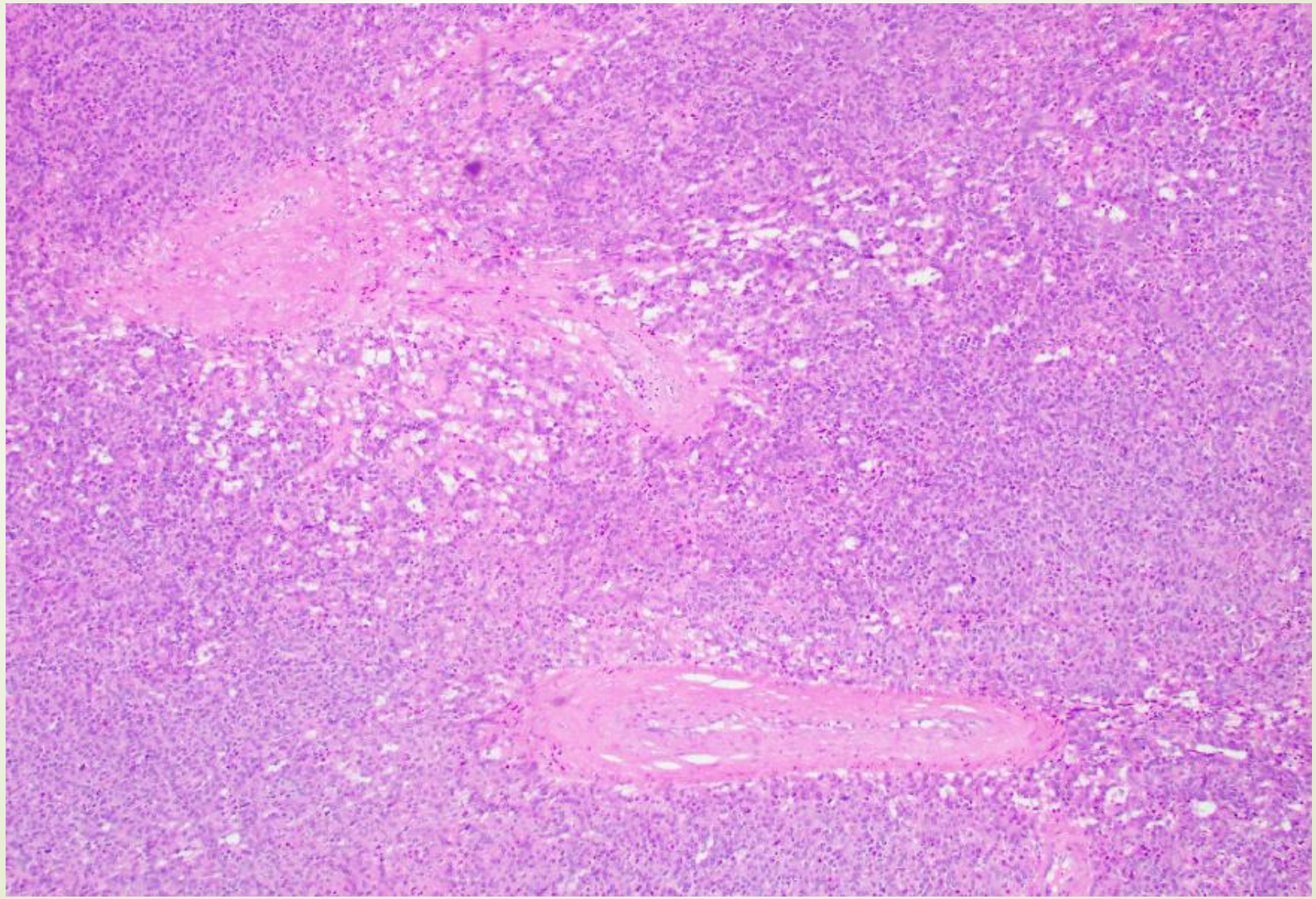




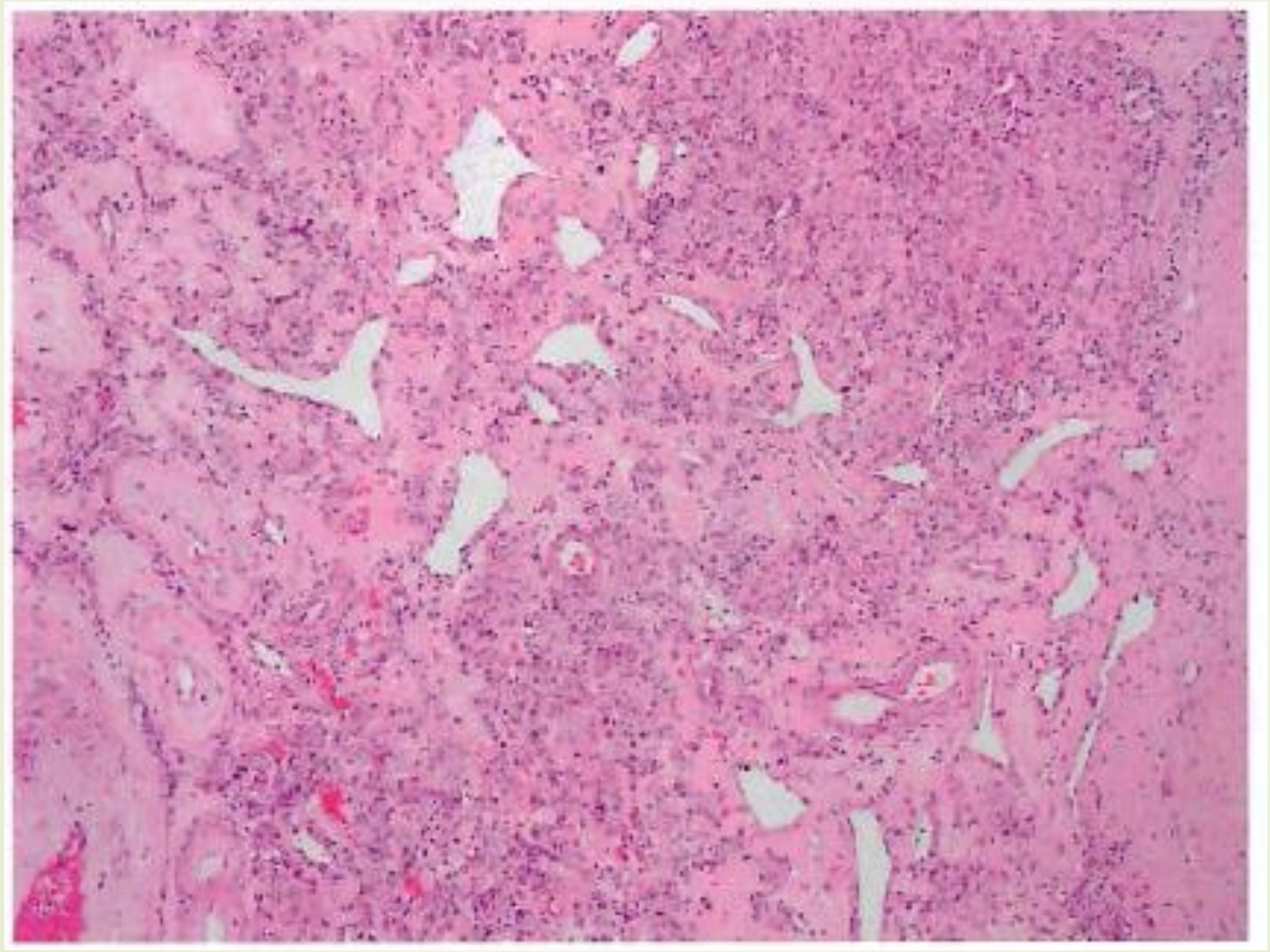
* Rare reports of metastasis


3mm

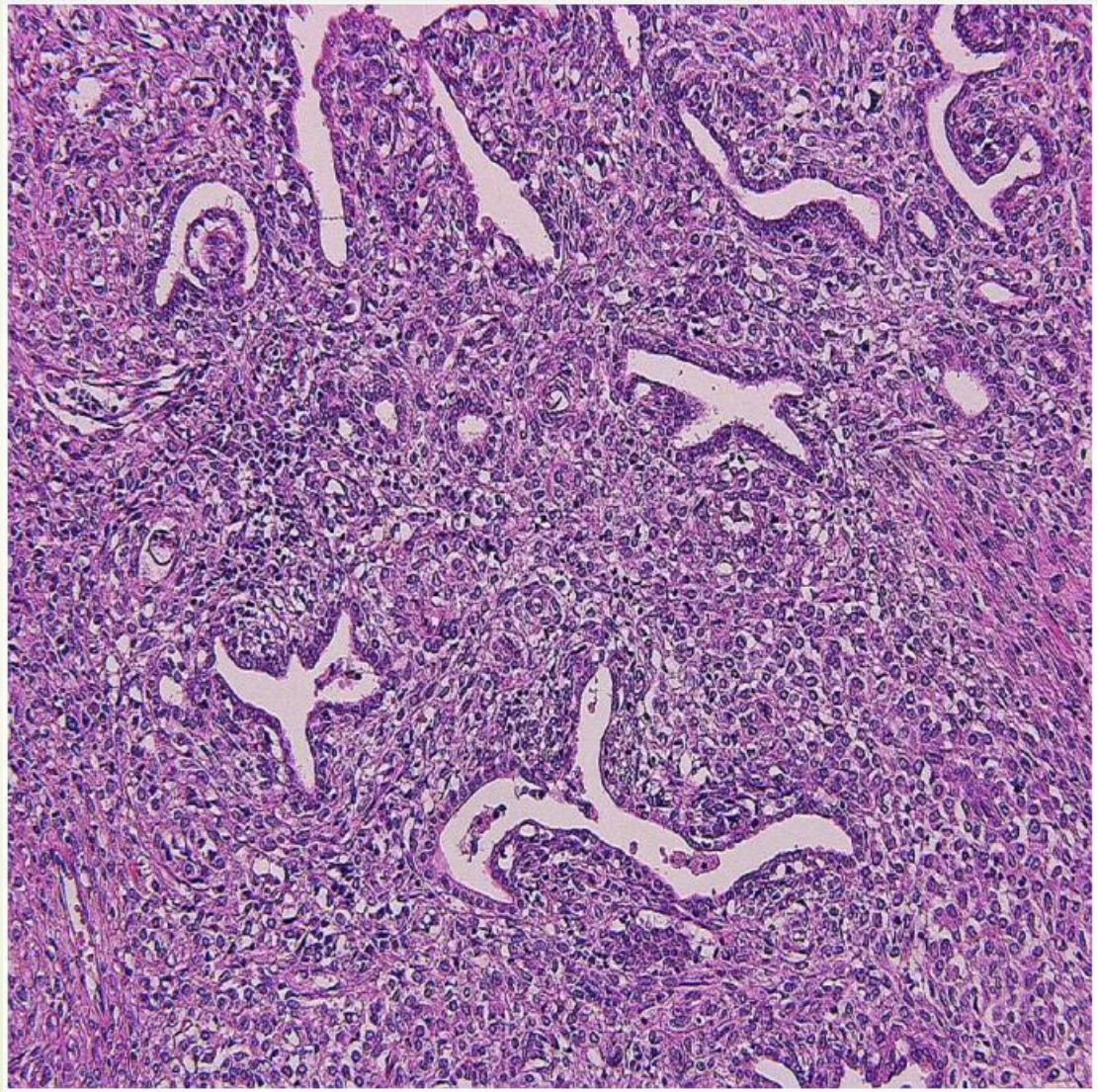
Thick Walled Blood Vessels

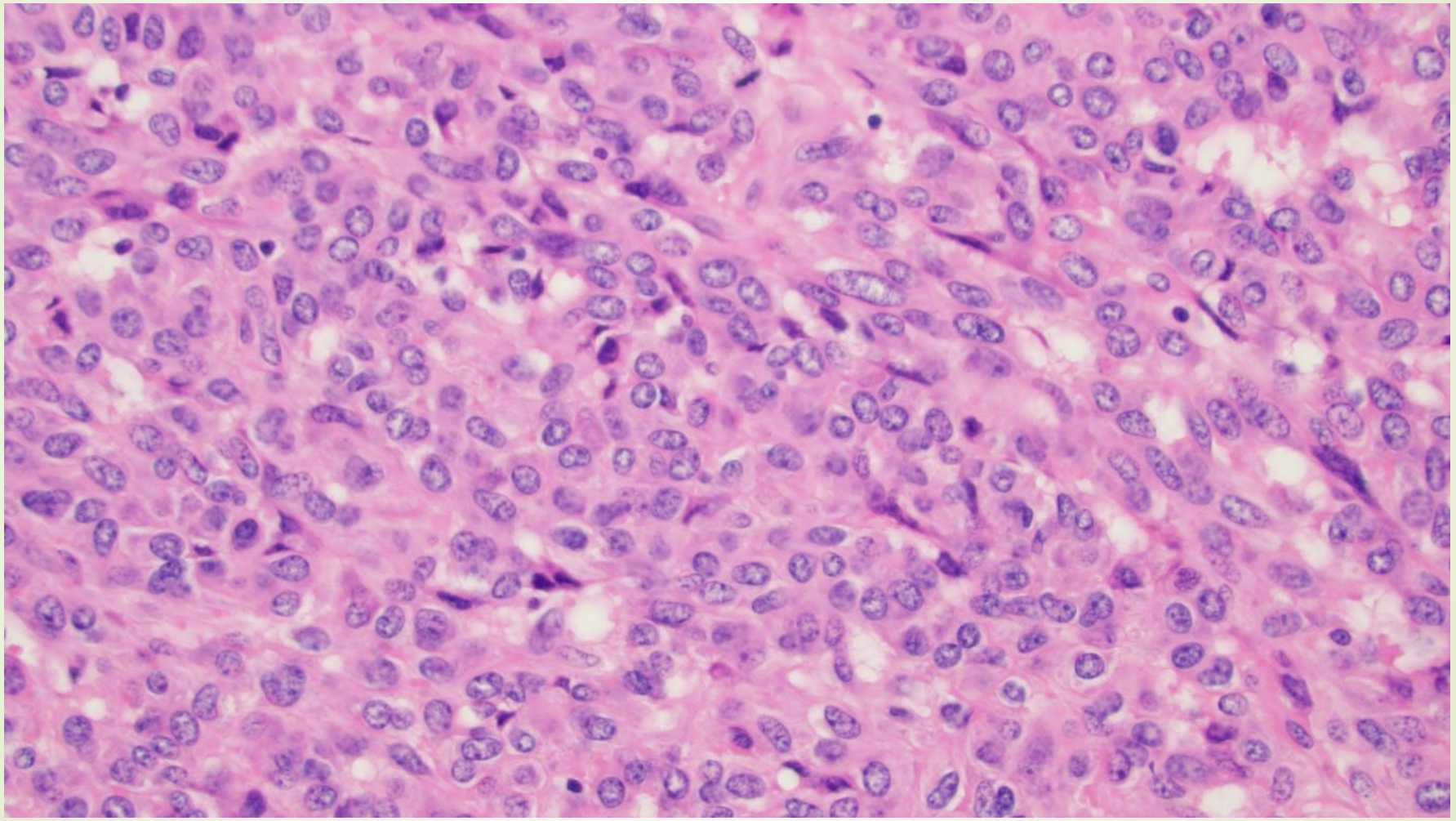


Staghorn Vessels



Entrapped tubules





Notes about the histology

- Mitotic activity, necrosis and pleomorphism are uncommon
- May show renal capsular or vascular invasion

Immunohistochemistry

Positive Stains

- Renin
- CD34
- CD117
- SMA, caldesmon: variable

Negative Stains

- Cytokeratins
- PAX8
- HMB45
- S100
- Desmin
- Chromogranin, Synaptophysin

Molecular

- No characteristic molecular findings

Good Prognosis

- Hypertension resolves with surgical excision in most cases
- Unlikely to recur after resection
- Rare report of metastasis
- Rare deaths due to hypertension

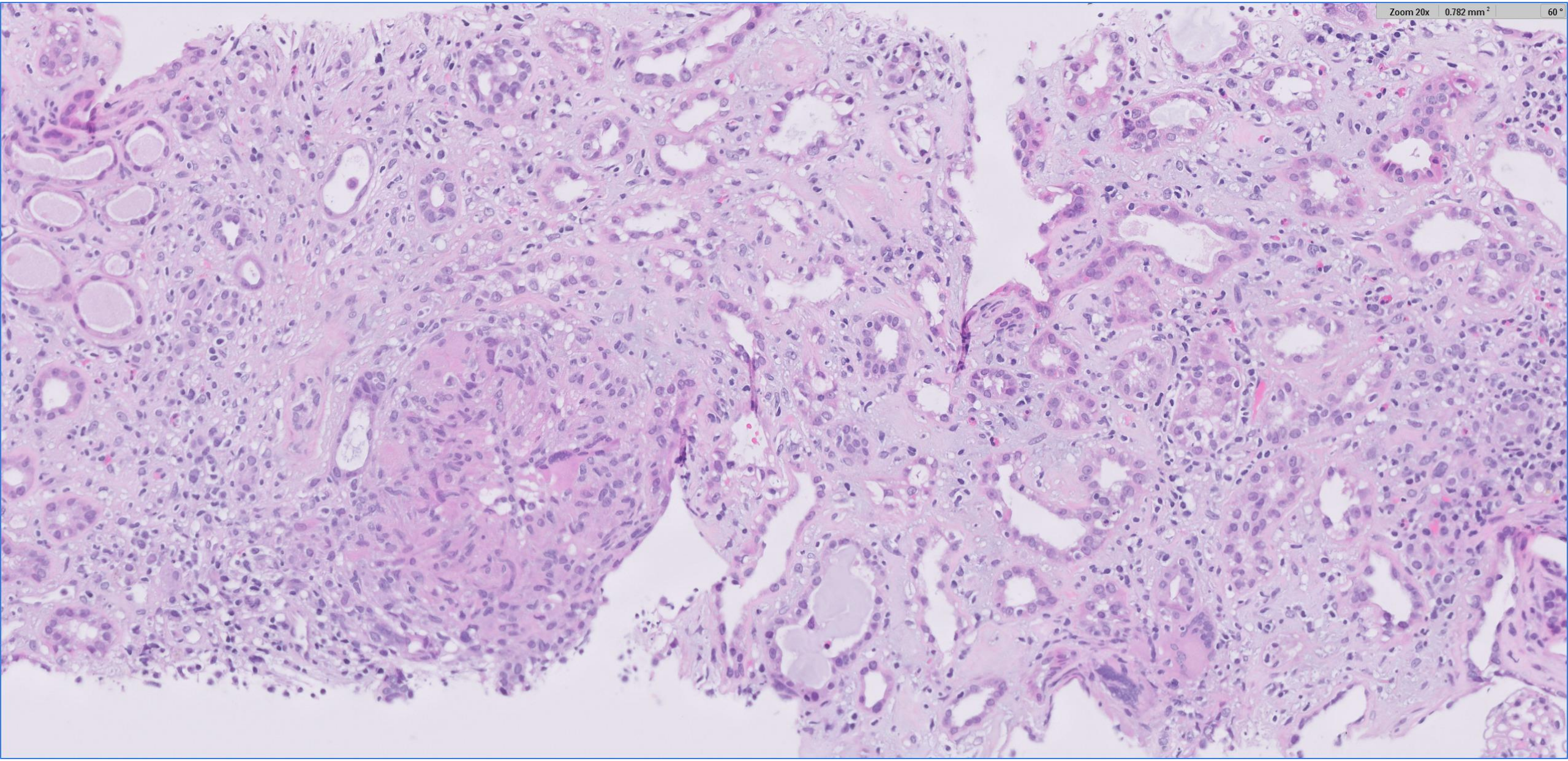
25-1104

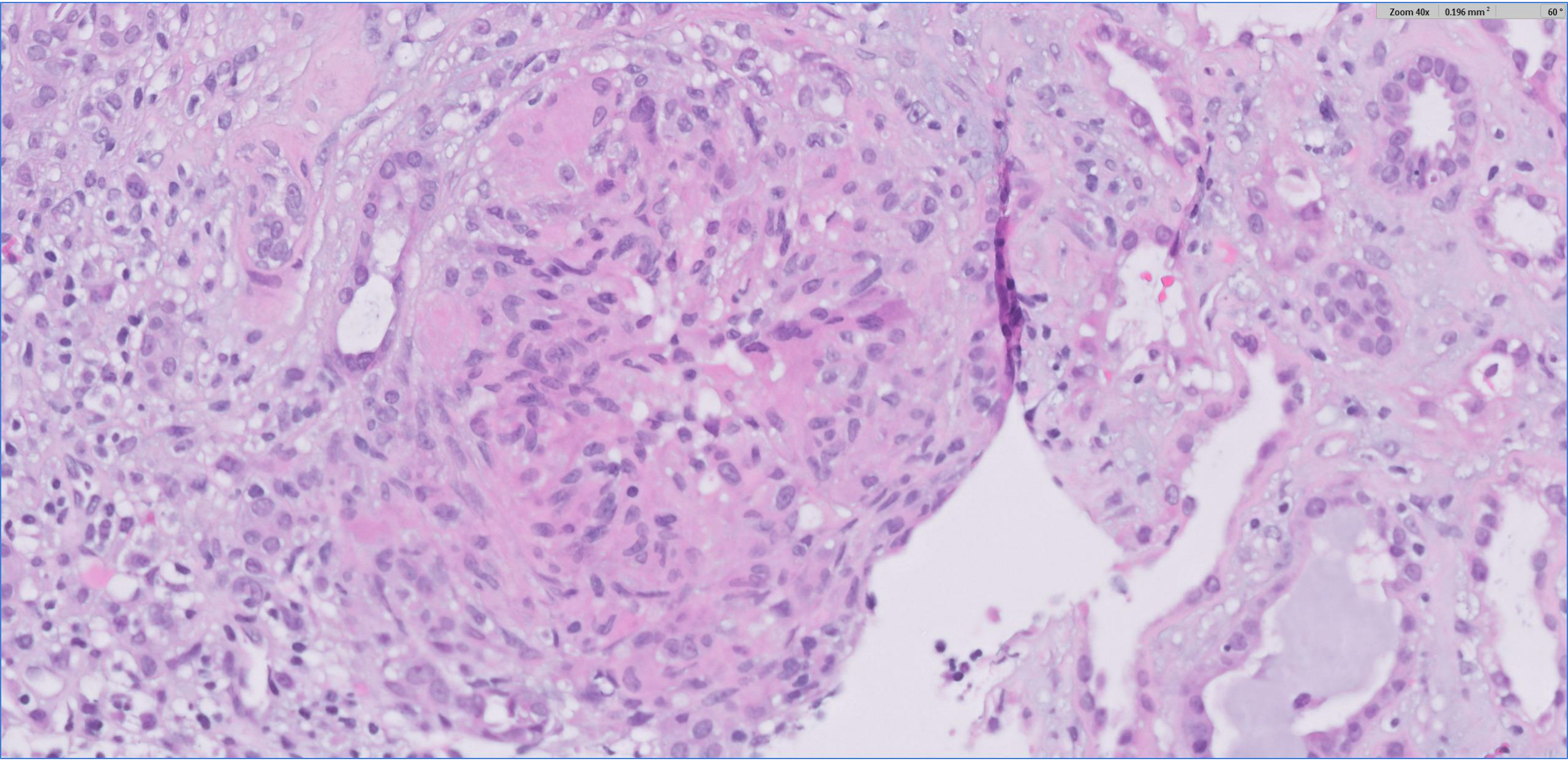
Megan Troxell; Stanford

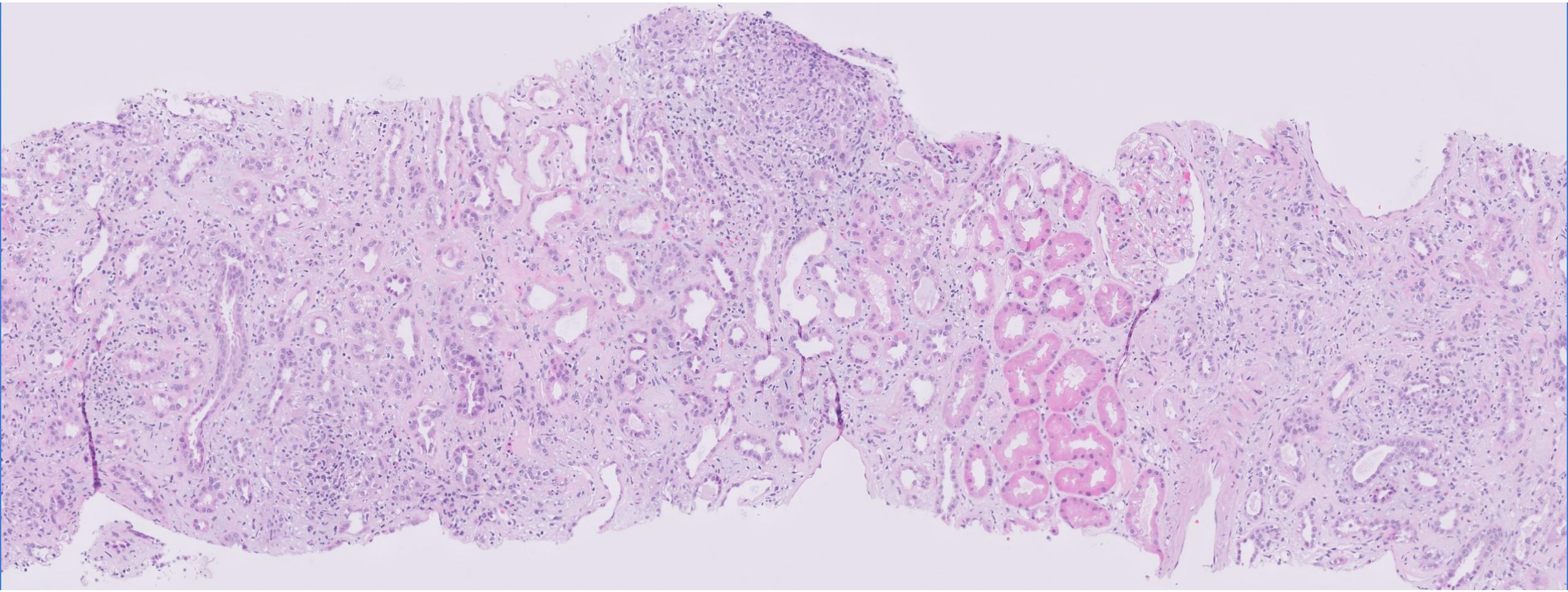
Elderly man with diabetes, hypertension, CKD

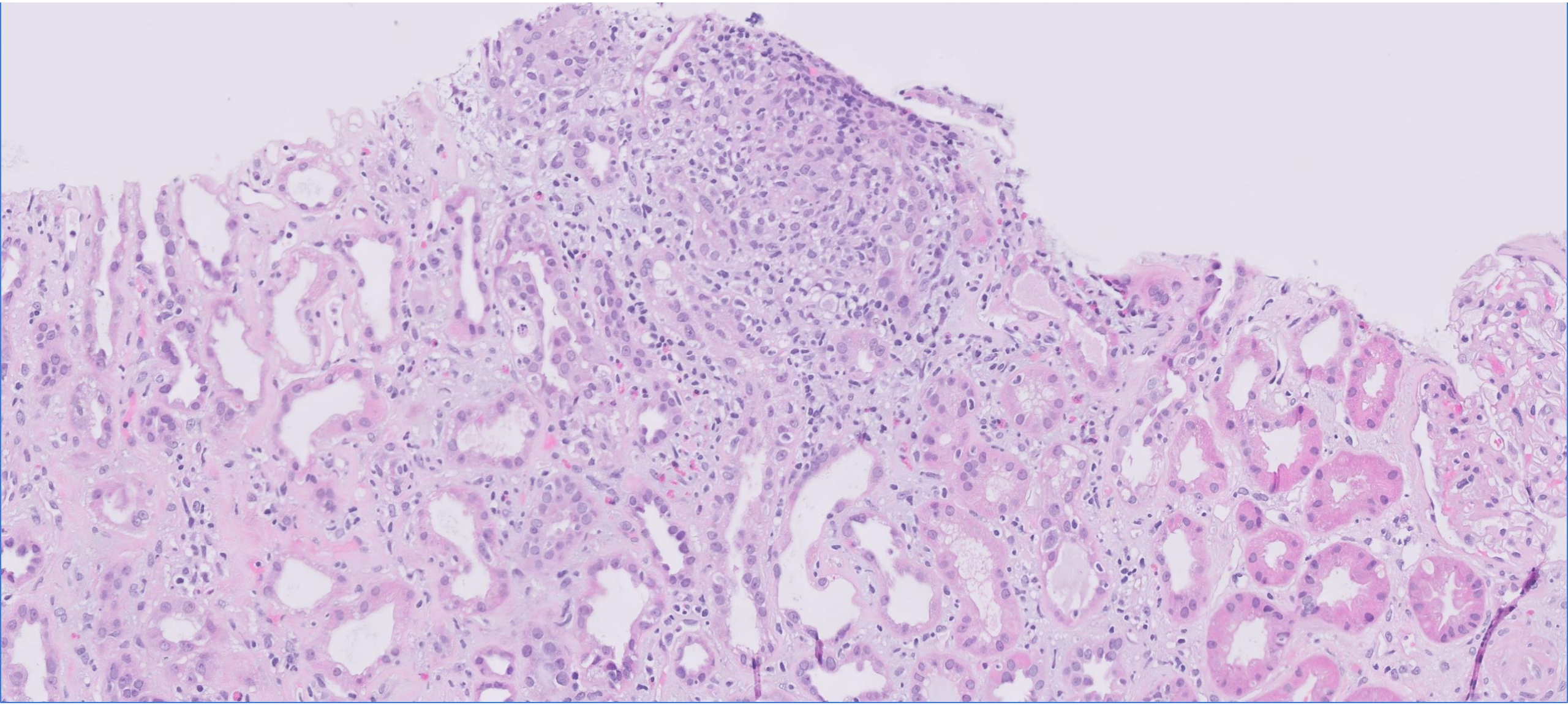
sudden worsening of renal function with creatinine of 2.7–3.4 mg/DL (baseline 1.8). Not improved with d/c several medications

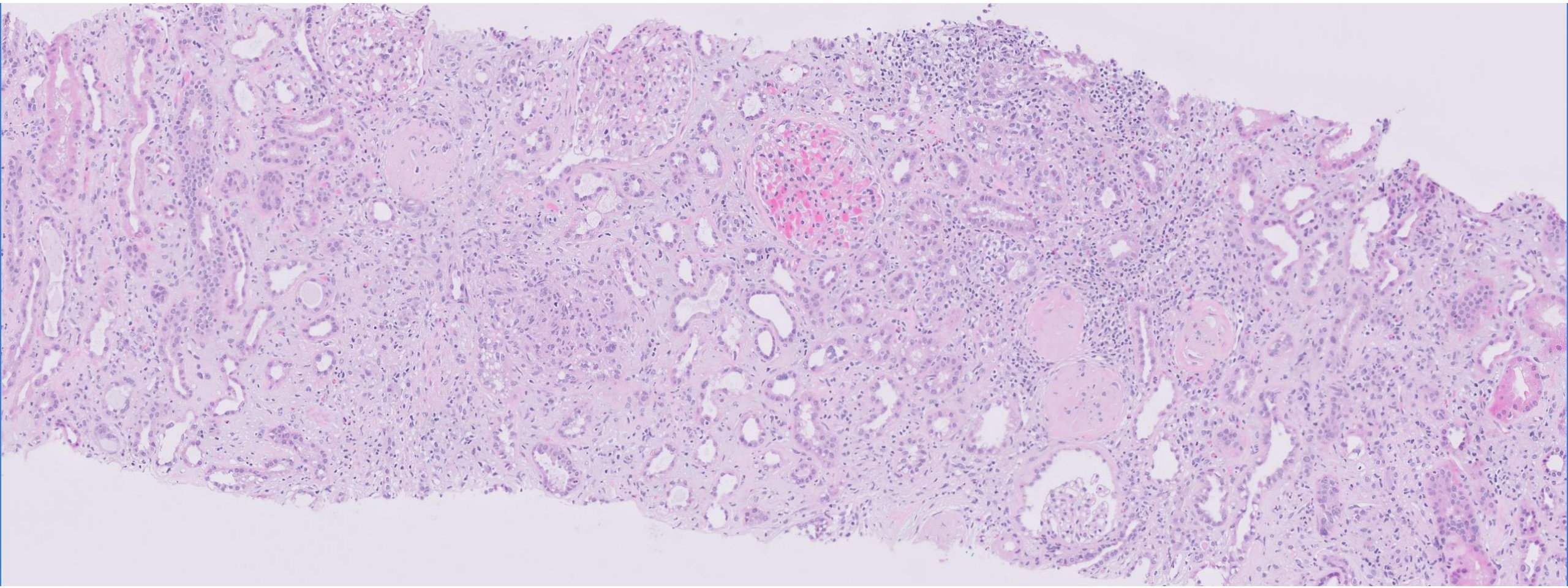
Urine positive for leukocyte esterase, moderate bacteria, with >100 WBC, 1+ protein and 1+ blood. History of bladder cancer (20 years ago), BPH

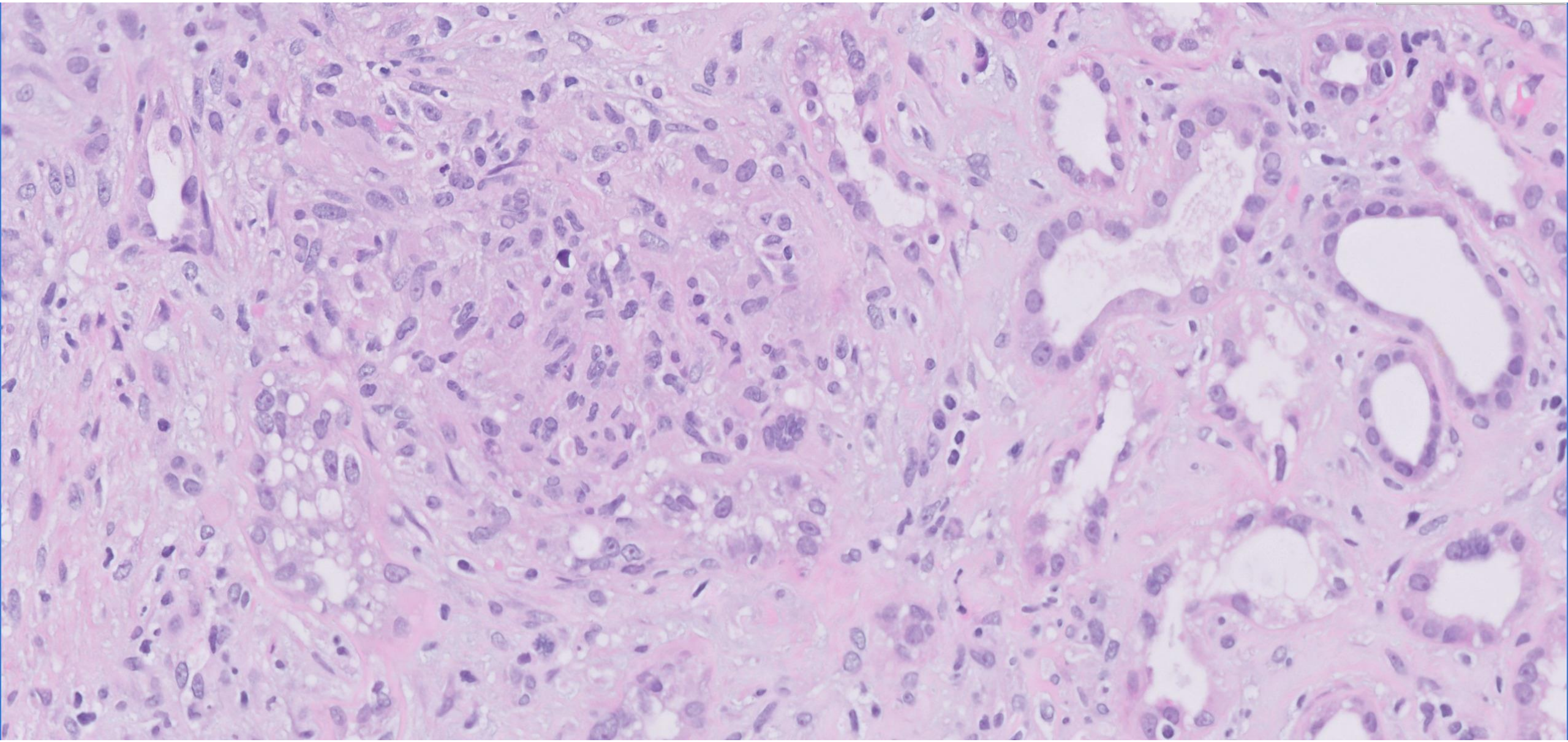

Zoom 20x
0.782 mm ²
60 °


Zoom 40x
0.196 mm ²
60 °

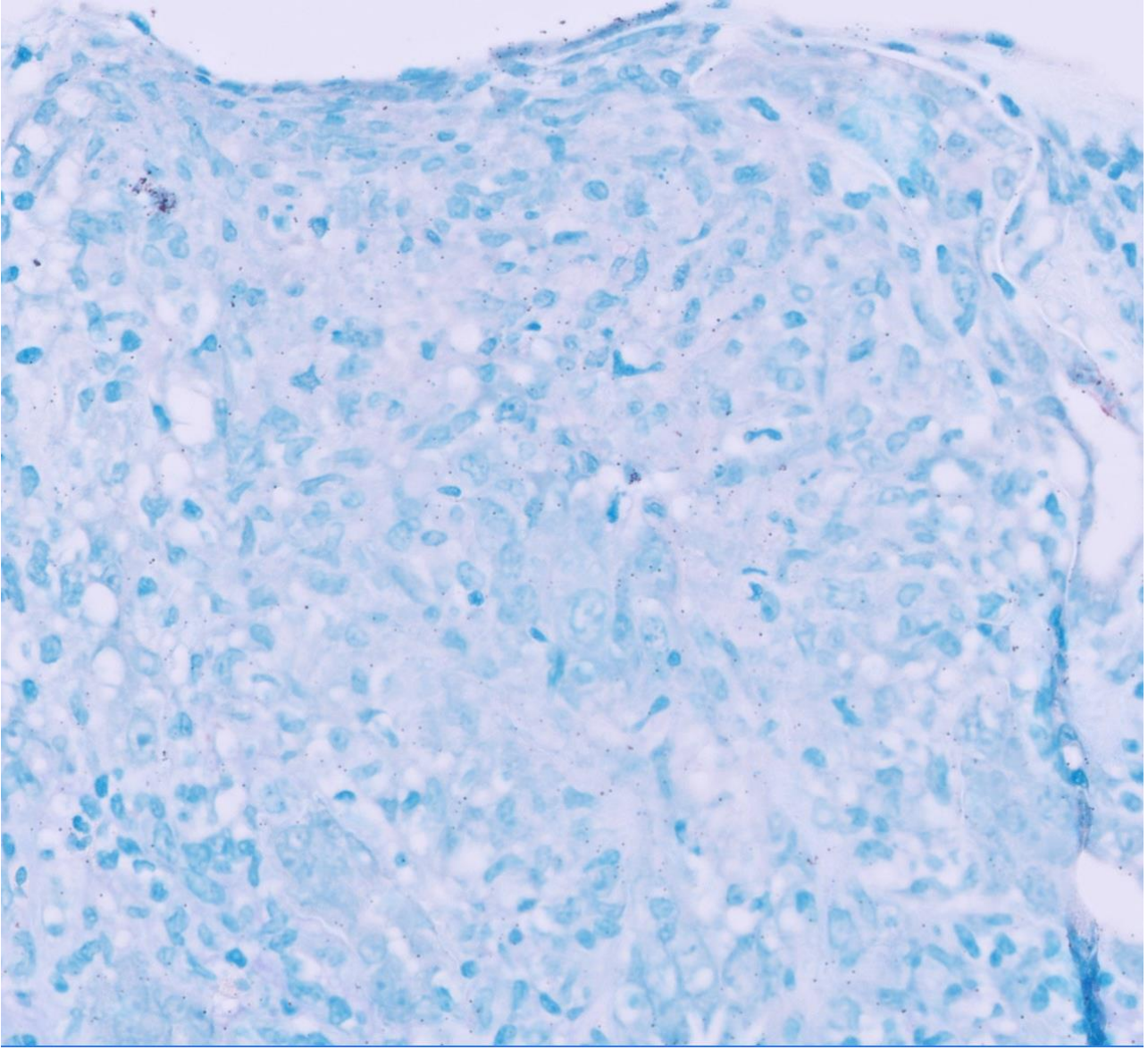




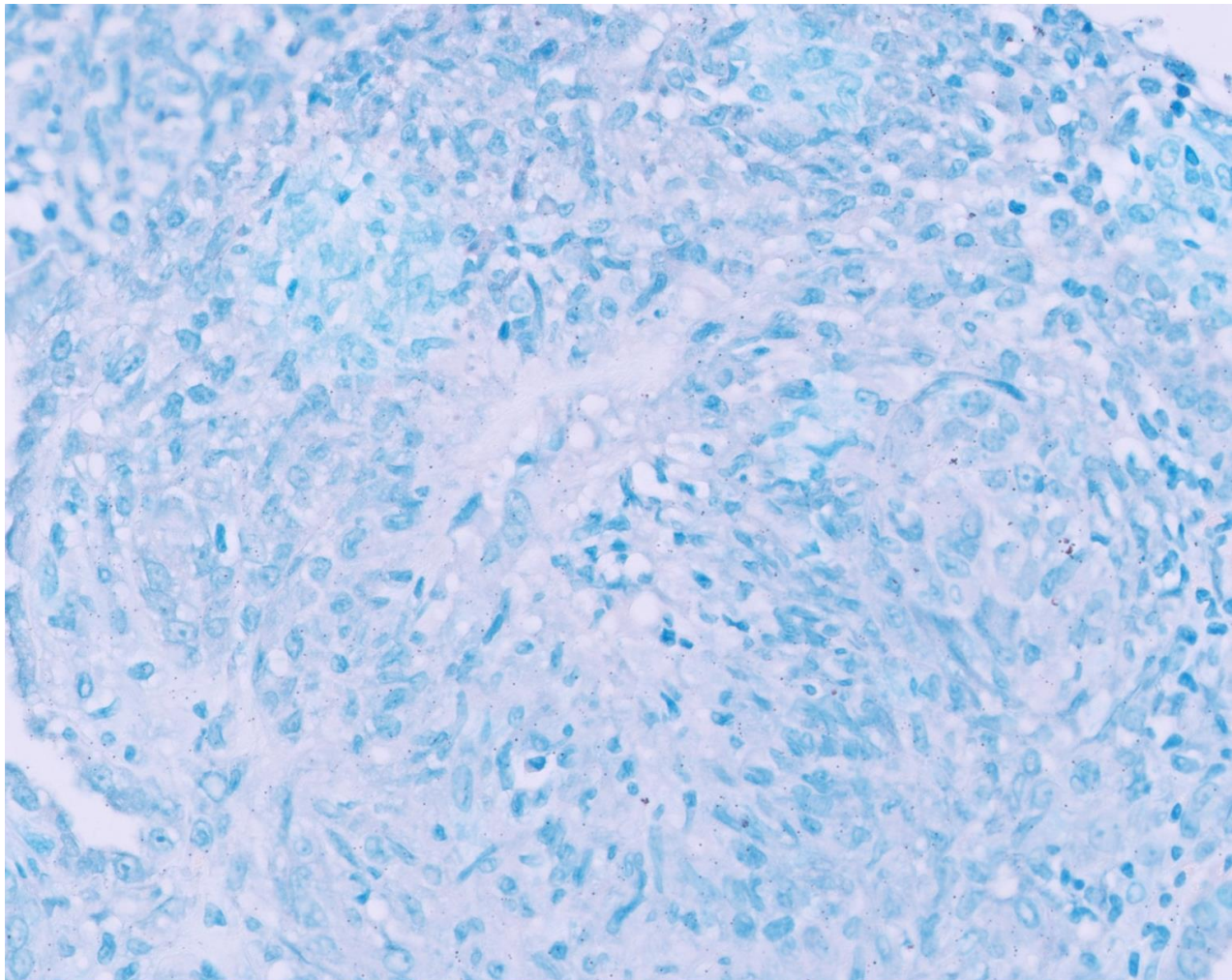




DIAGNOSIS?



FITE negative



Diagnosis

- **Acute interstitial nephritis with granulomas**
- **Arteriosclerosis**
  - …necrosis as well as white blood cell casts raises the possibility of an infection, particularly an ascending infection (pyelonephritis).
  - Other entities on the differential diagnosis include autoimmune disease such as vasculitis, ANCA disease, and sarcoidosis, as well as tubular rupture.
  - The history of bladder cancer is noted; BCG therapy can rarely result in granulomatous kidney involvement, yet BCG exposure was very distant in time.

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  - Other entities on the differential diagnosis include autoimmune disease such as vasculitis, ANCA disease, and sarcoidosis, as well as tubular rupture.
  - The history of bladder cancer is noted; **BCG therapy can rarely result in granulomatous kidney involvement, yet BCG exposure was very distant in time.**
    - **Well, more like 5 years prior than 20**

The rest of the story

- Quantiferon positive
- AFB+ and myobacterium culture+ urine
- MTB PCR+
- ID consult: likely BCG related, though available results cannot distinguish between MTB and M. Bovis (BCG).
  - Later confirmed M. Bovis by CPDH
  - Recommend 9 months INH and Rifampin
  - Also as per County Public Health Depart. “active infectious disease”
- Bladder specimens also w/ necrotizing granulomatous inflame
- sCr 2.2-2.6 ~ 2 year post bx; urine many RBC and WBC

Bacillus Calmette-Guérin (BCG) Infection Following Intravesical BCG Administration as Adjunctive Therapy For Bladder Cancer

Incidence, Risk Factors, and Outcome in a Single-Institution Series and Review of the Literature

Maria Asuncion Perez-Jacoiste Asin *Medicine 2014;93: 236–54*

0022-5347/92/1473-0596$03.00/0
THE JOURNAL OF UROLOGY
Vol. 147, 596–600, March 1992
Printed in U.S.A.

INCIDENCE AND TREATMENT OF COMPLICATIONS OF BACILLUS CALMETTE-GUERIN INTRAVESICAL THERAPY IN SUPERFICIAL BLADDER CANCER

DONALD L. LAMM, AD P. M. VAN DER MEIJDEN, ALVARO MORALES, STANLEY A. BROSMAN, WILLIAM J. CATALONA, HARRY W. HERR, MARK S. SOLOWAY, ADOLPHE STEG AND FRANS M. J. DEBRUYNE

- BCG: attenuated live strain of Mycobacterium bovis
  - FDA approved in 1990
- Systemic granulomas: hypersensitivity vs active infection?
- Risk factors: traumatic instillation; age? Immunosuppression?

Lamm n=2602 treated

- Overall
  - 0.4% sepsis
  - 1% granulomatous prostatitis
  - <1% PNA/hepatitis

Complication	N=282 review	Select details
Disseminated infection	34%	Includes miliary TB
Osteomuscular	20%	Prosthetic Joint infection 2%
Vascular	7%	Mycotic aneurysm
Hepatitis	6%	
Localized GU	23%	Bladder 6%, Prostate 3.5% **Kidney parenchymal 3.5%**

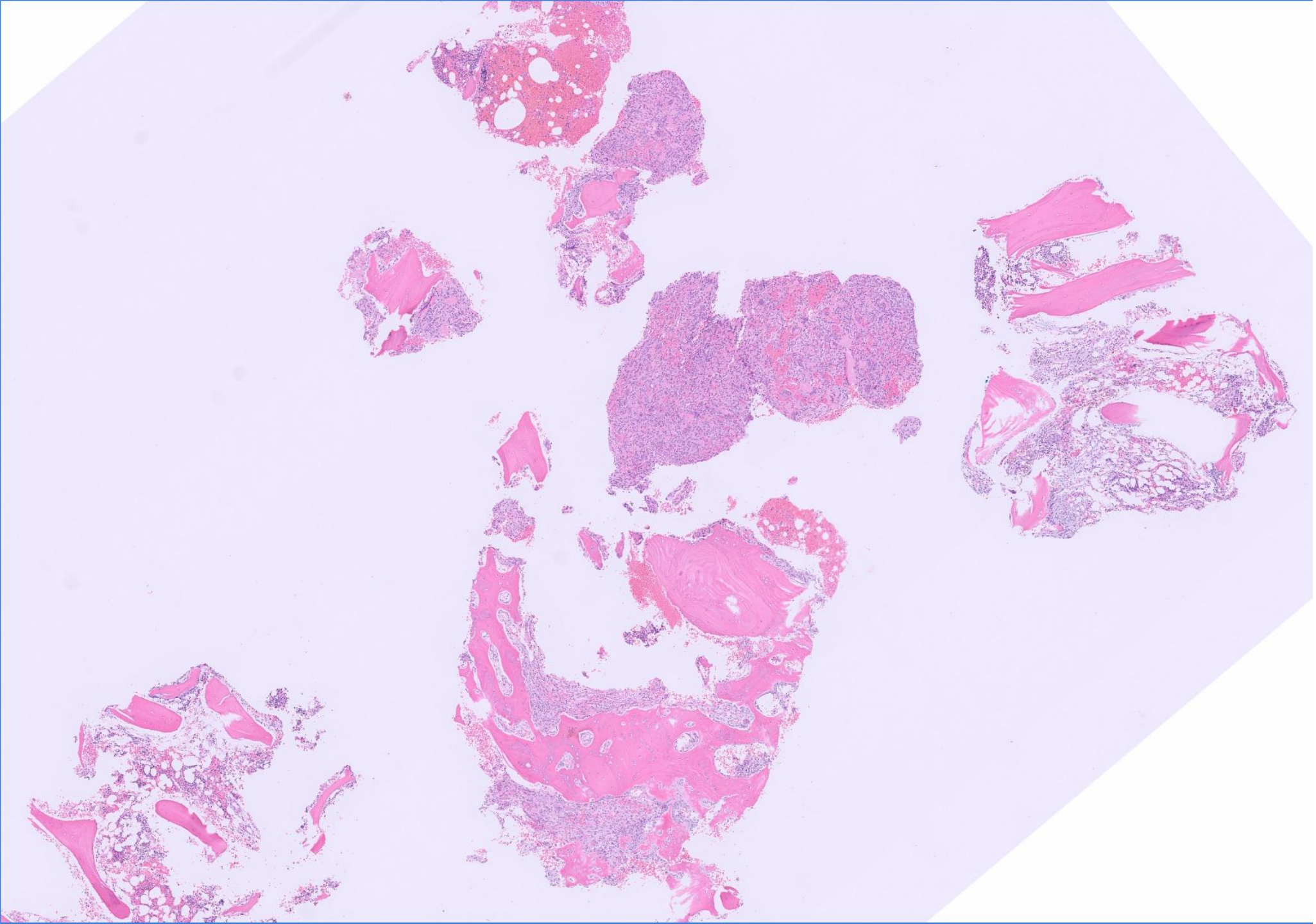
80% treated w/ TB Rx; 5.4% BCG attributable mortality

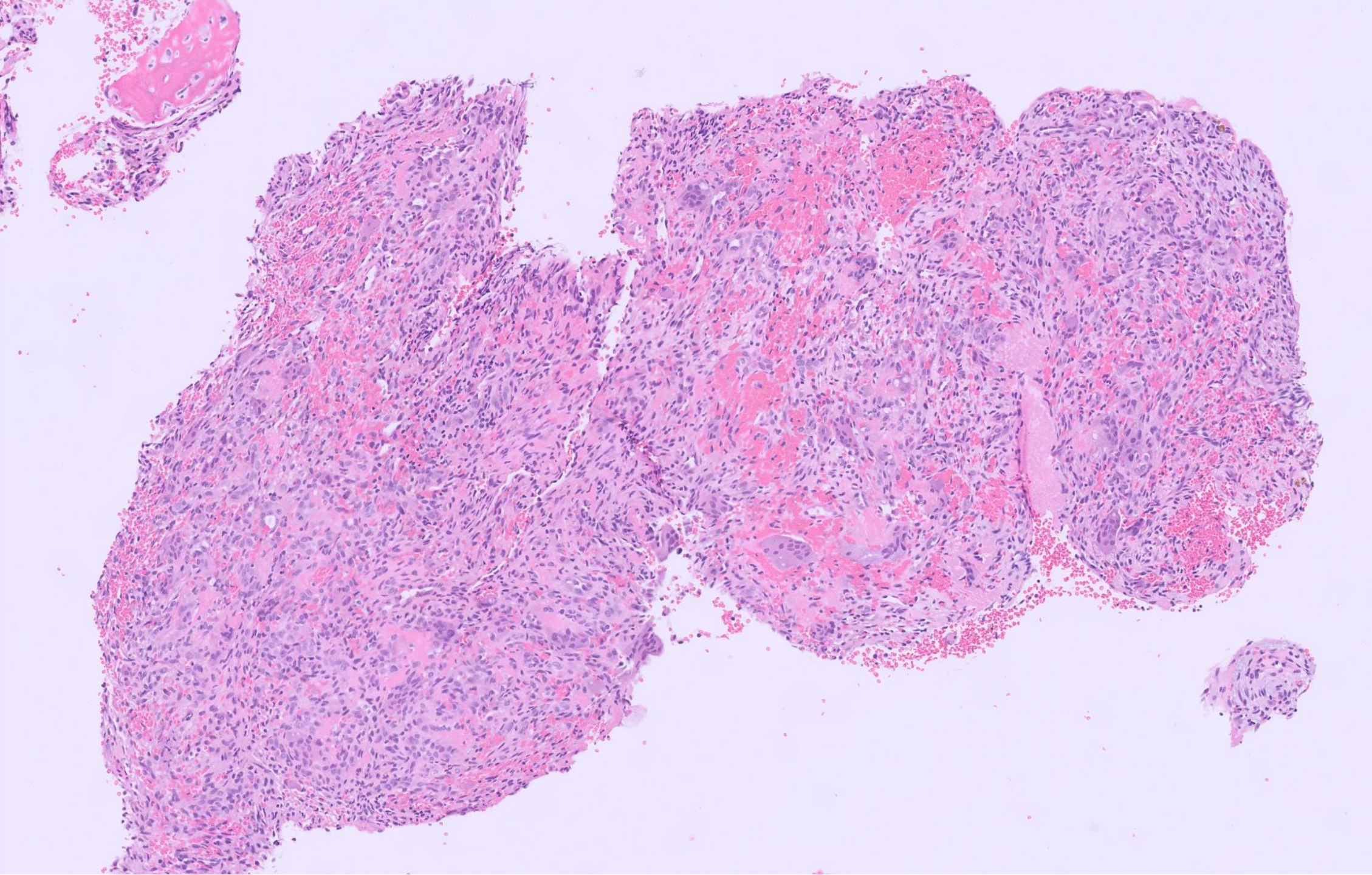
Micro Dx	N=282 review
Overall+	48%
Stain positive	25%
Culture positive	41%
PCR-based	42%
Tissue biopsy +	66%

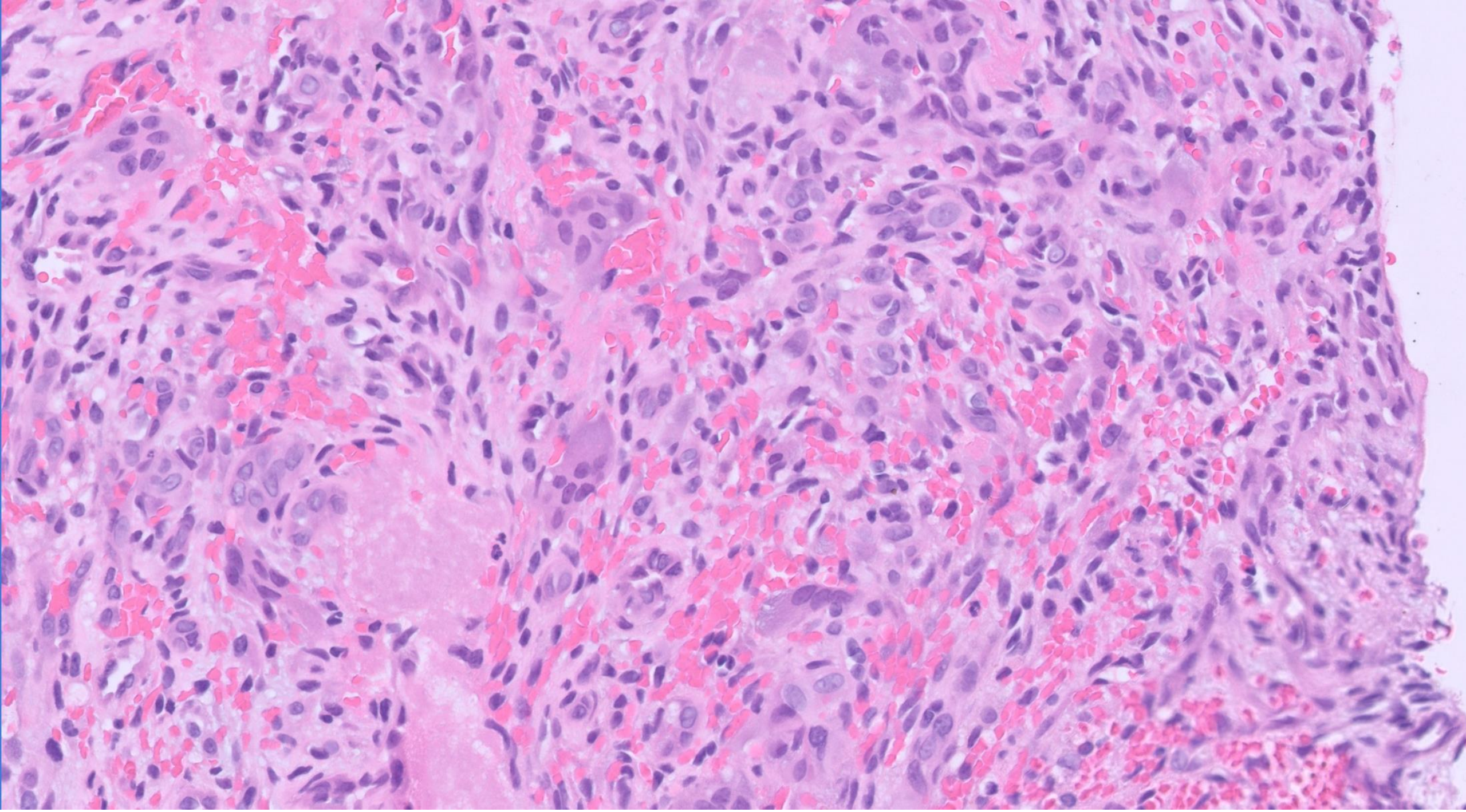
25-1105

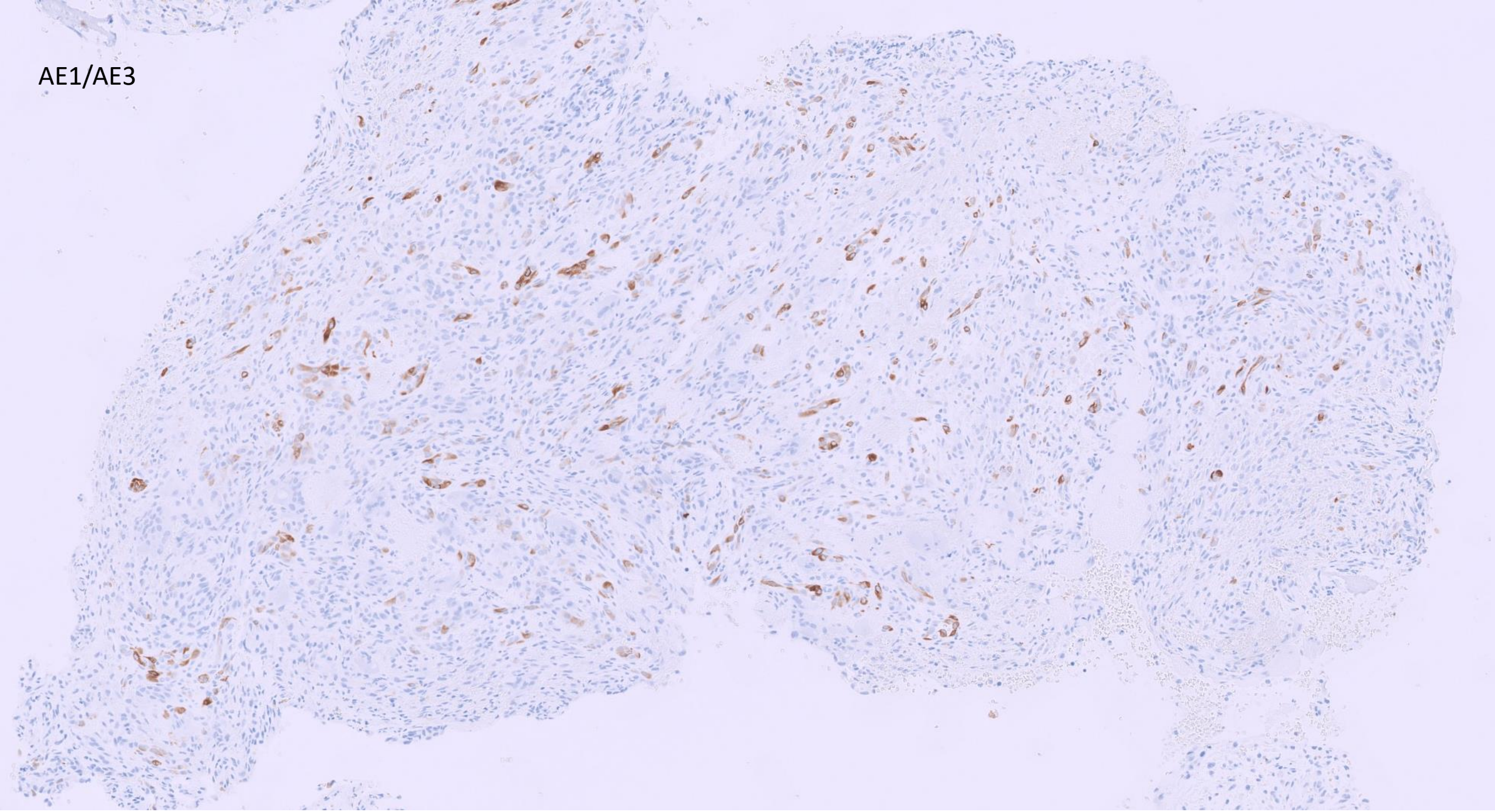
Megan Troxell; Stanford

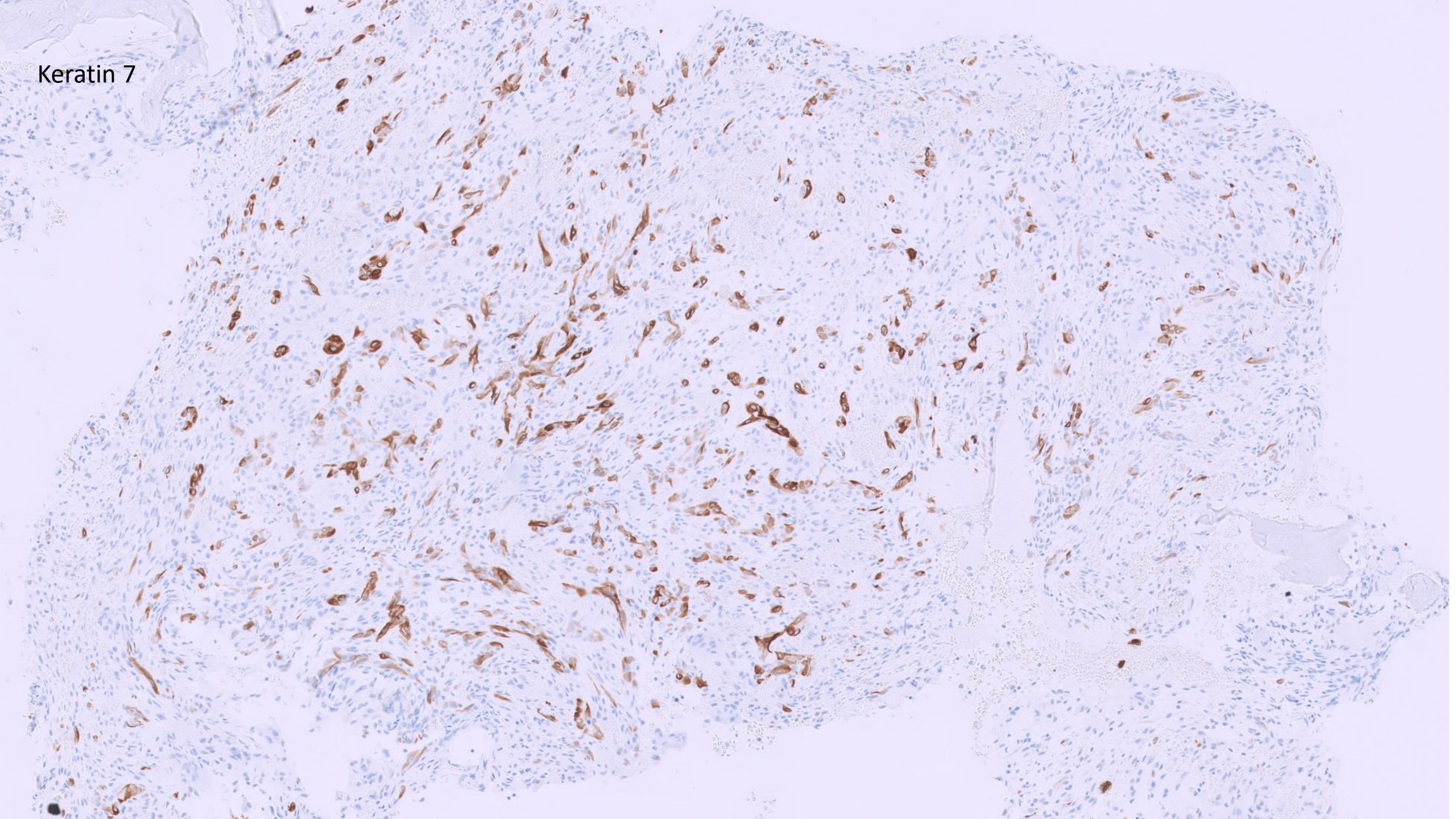
50-ish year-old female with a BRCA1 mutation and a history of high grade carcinoma of the endometrium s/p hysterectomy, adjuvant chemotherapy, right breast grade 3 invasive ductal carcinoma, right mastectomy, adjuvant chemotherapy >10 years ago. Chest wall recurrence followed by resections and adjuvant chemotherapy and radiation ~4 years ago. Now with solitary L3 bone lesion biopsied.





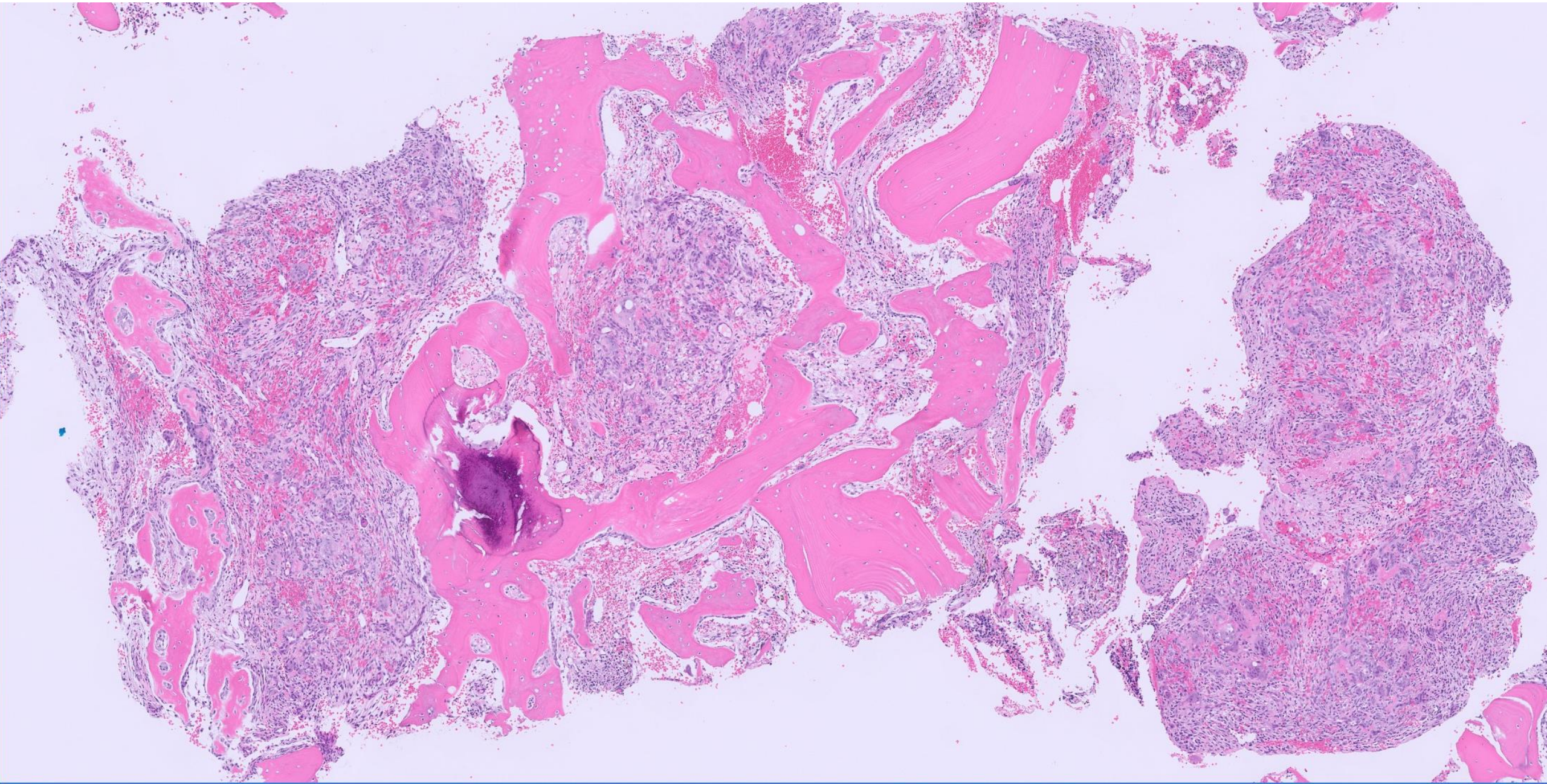


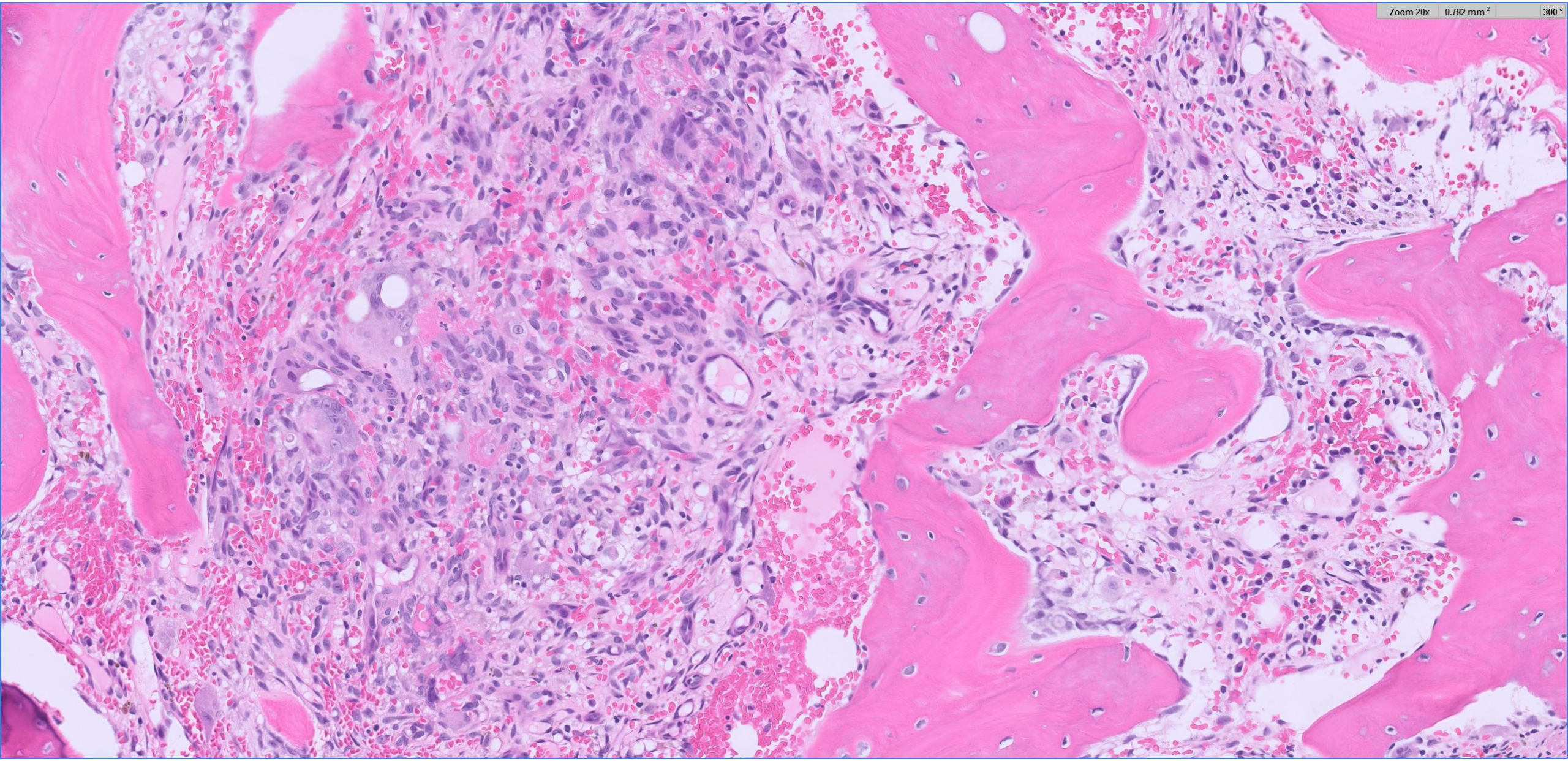

AE1/AE3


Keratin 7

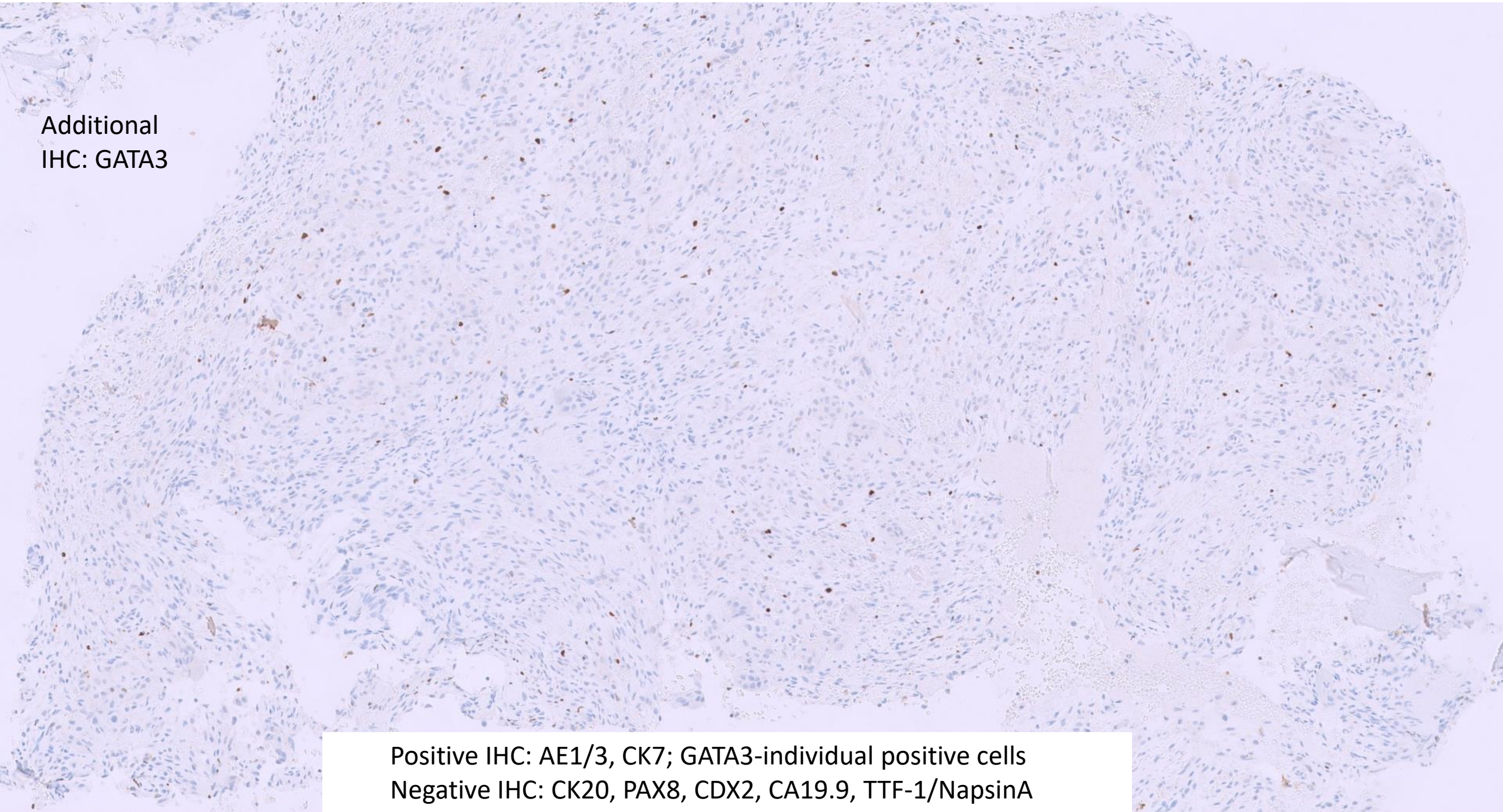
DIAGNOSIS?

Deeper in the block



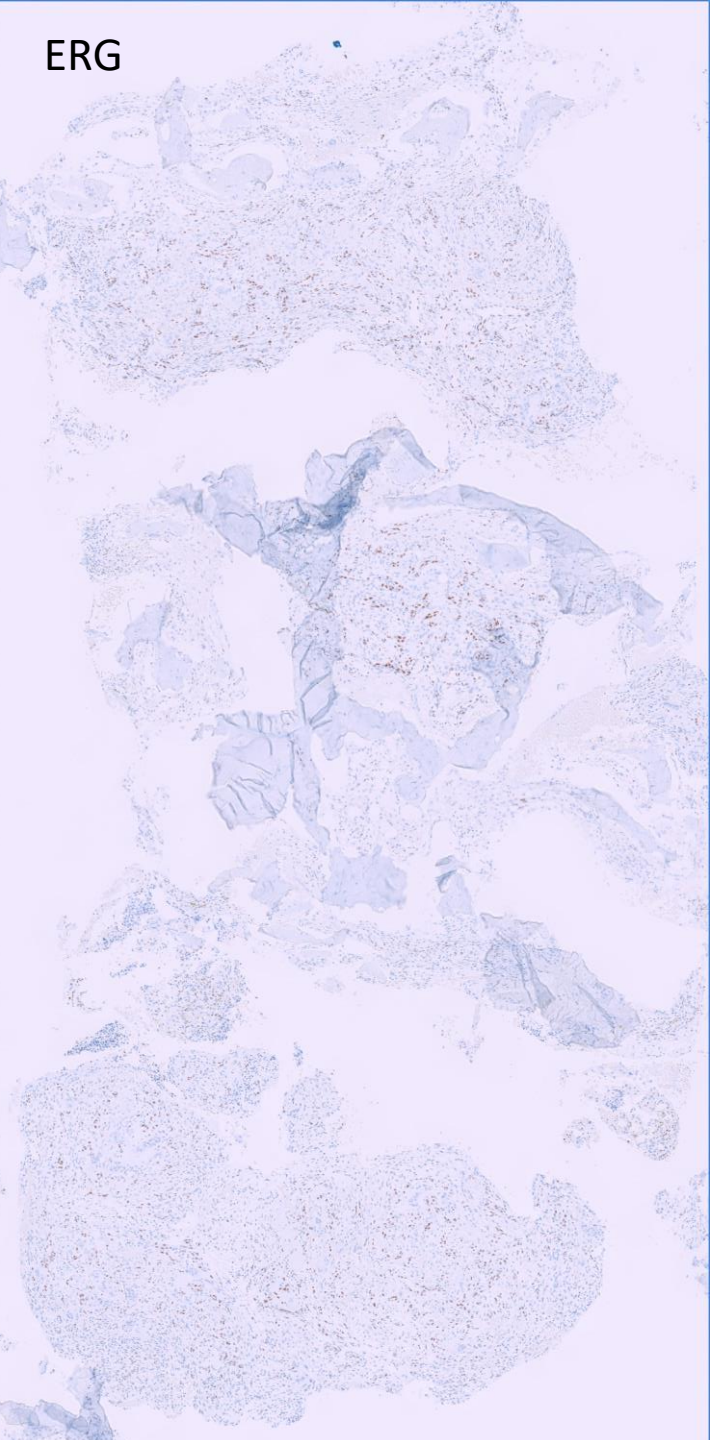

Zoom 20x
0.782 mm ²
300 °

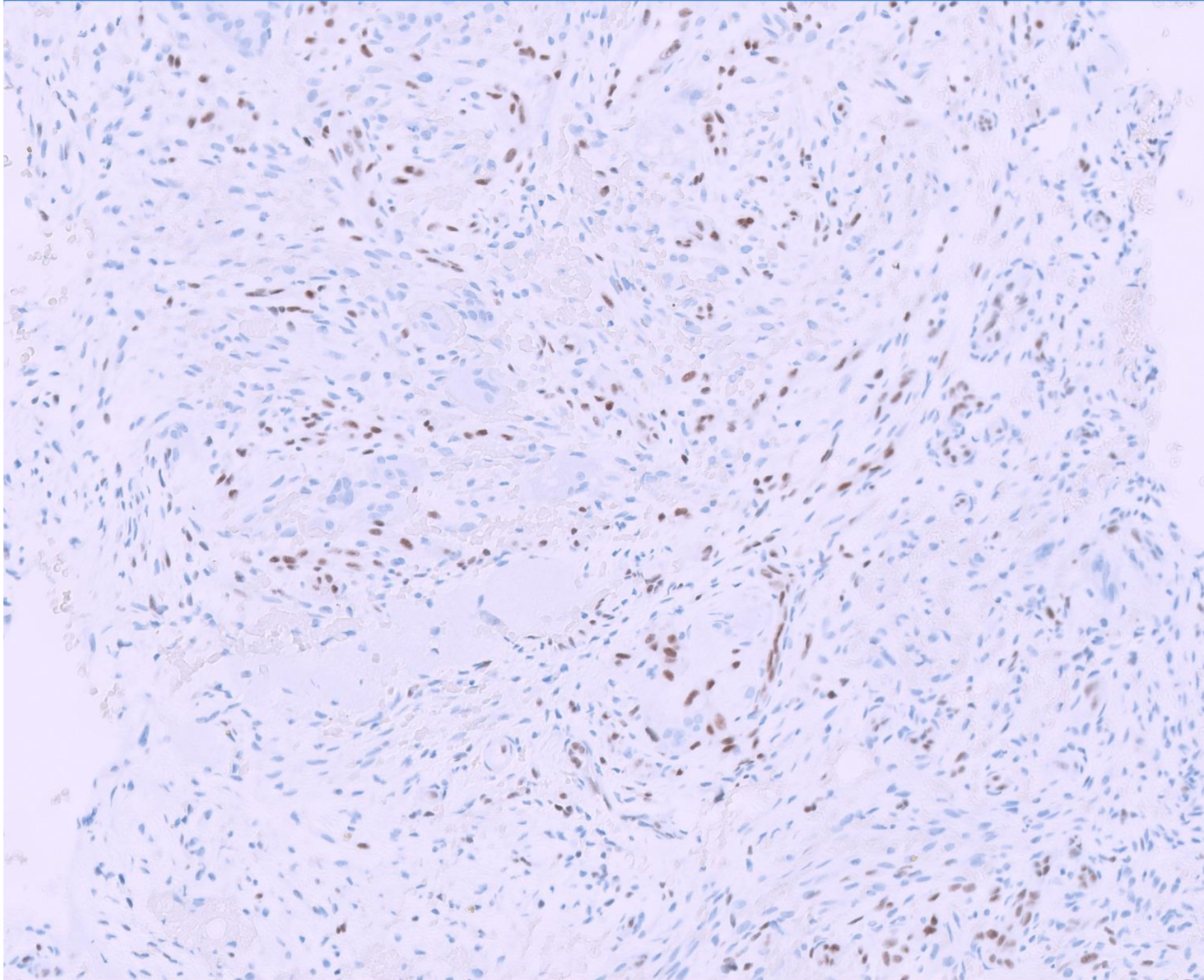
Additional
IHC: GATA3

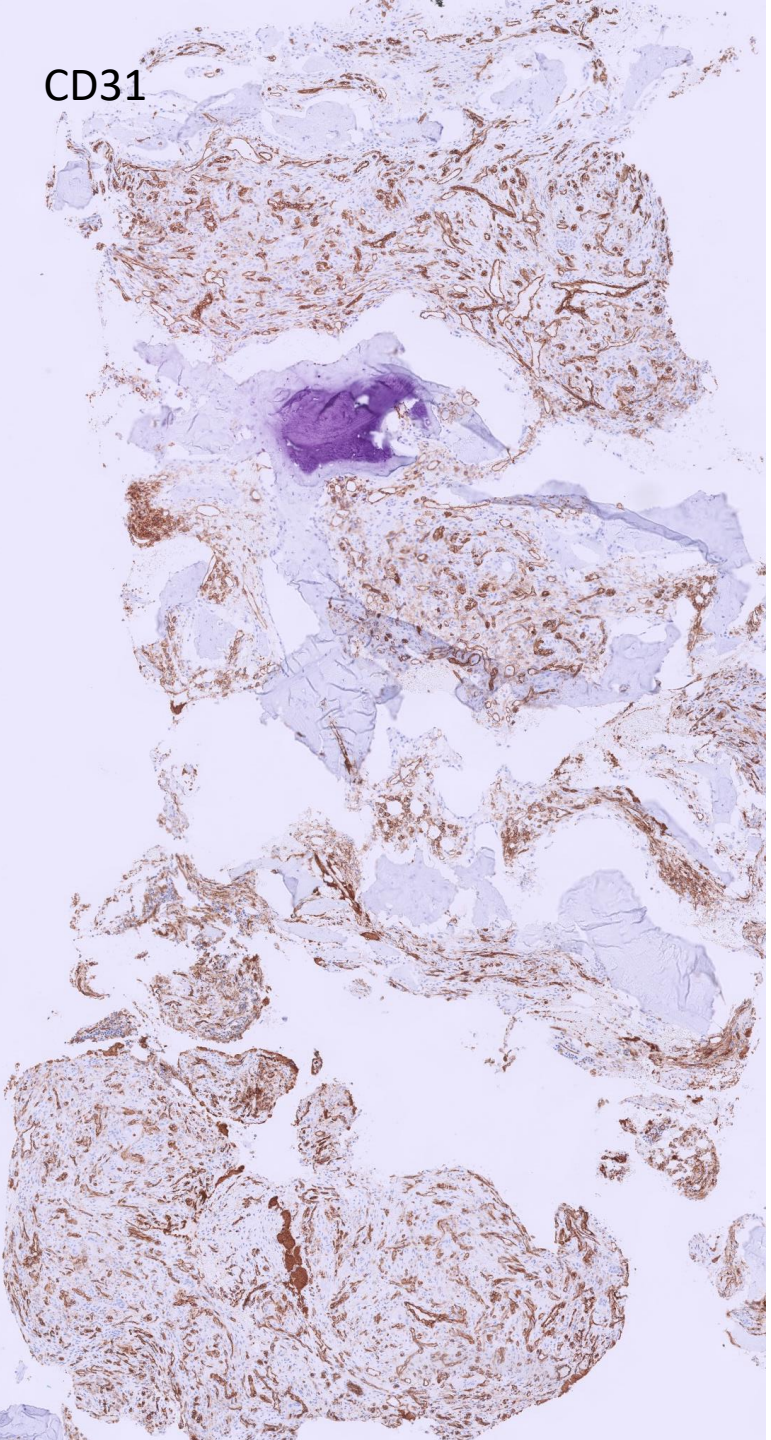


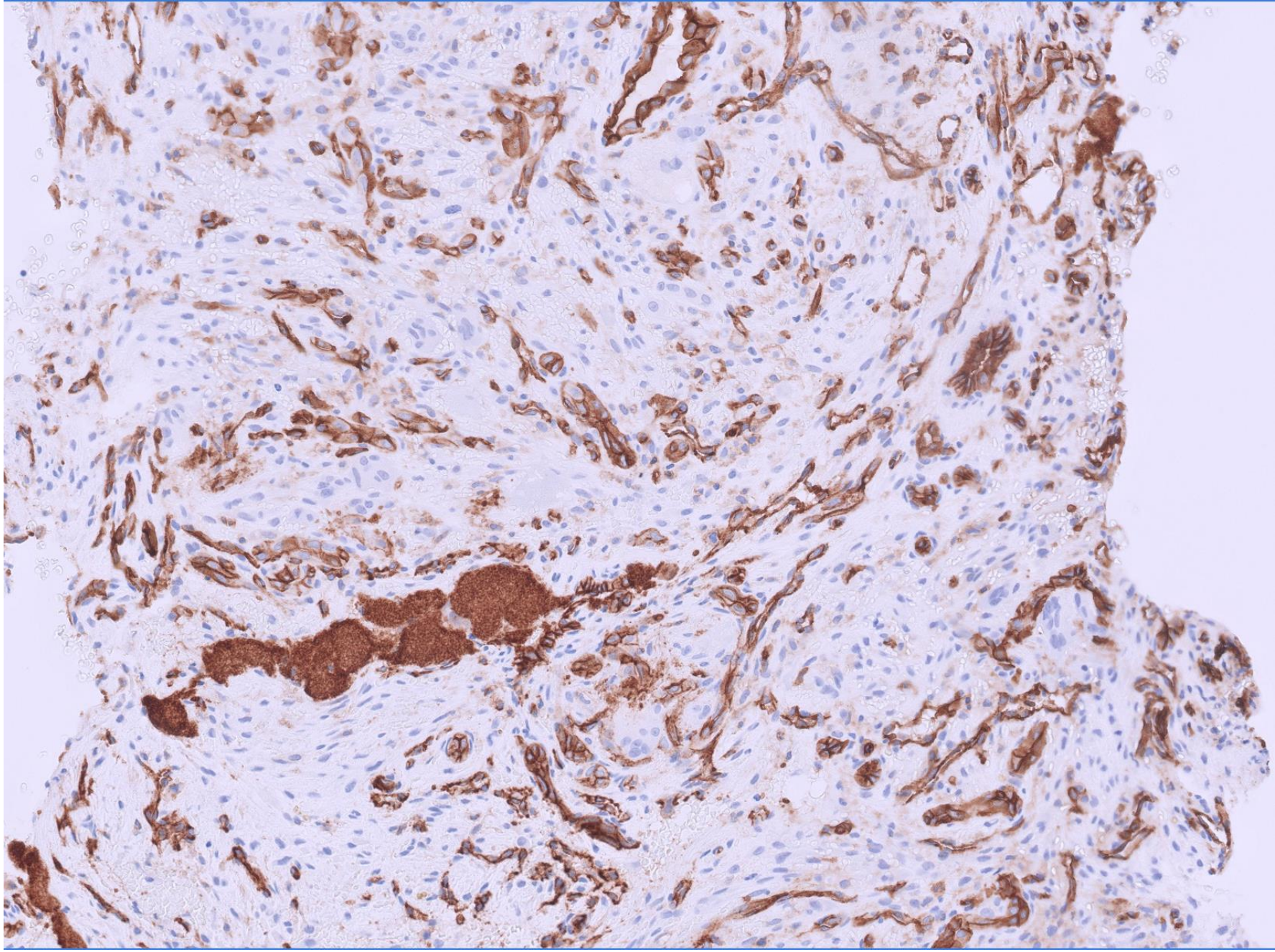
Positive IHC: AE1/3, CK7; GATA3-individual positive cells
Negative IHC: CK20, PAX8, CDX2, CA19.9, TTF-1/NapsinA

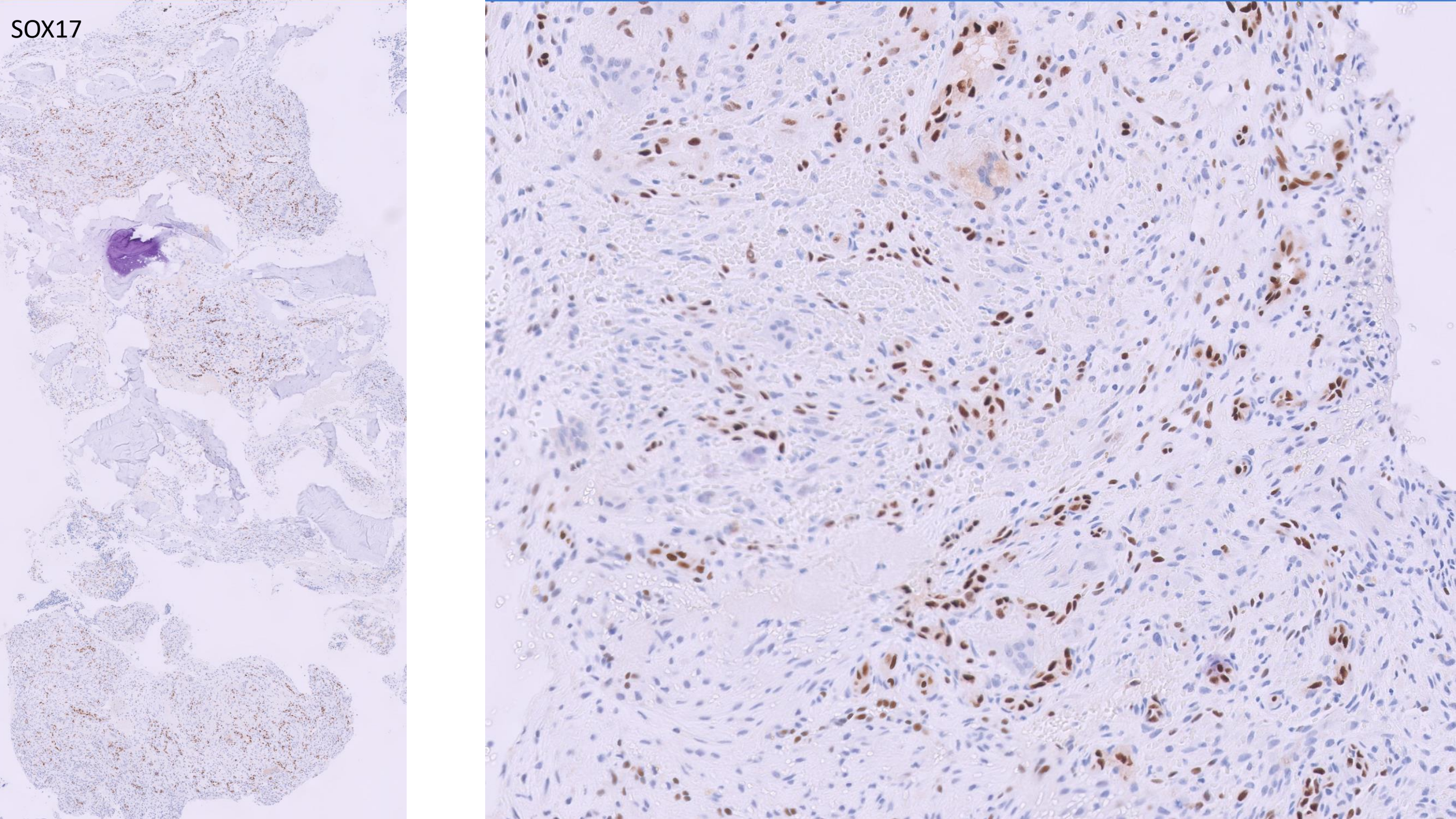
ERG

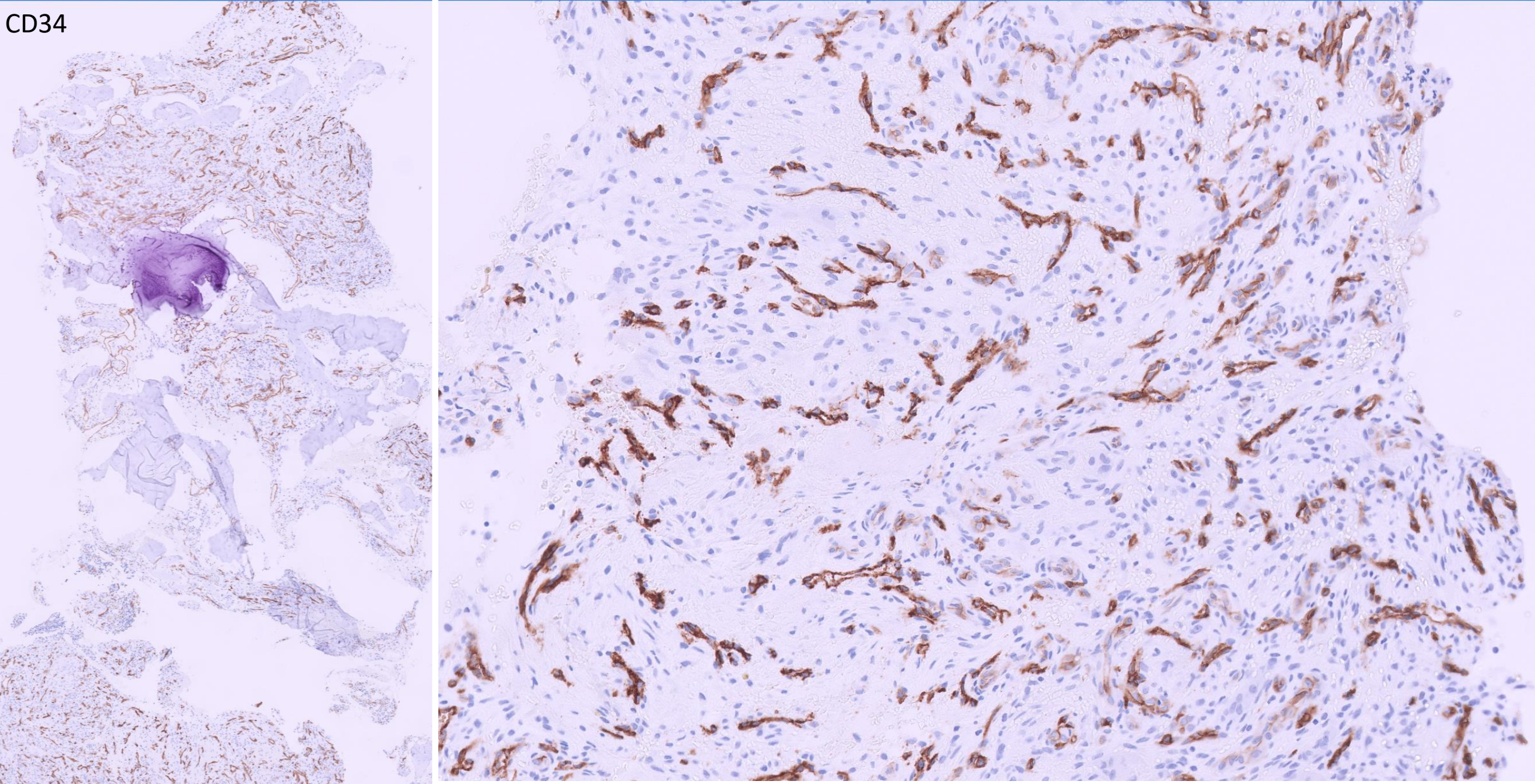





CD31



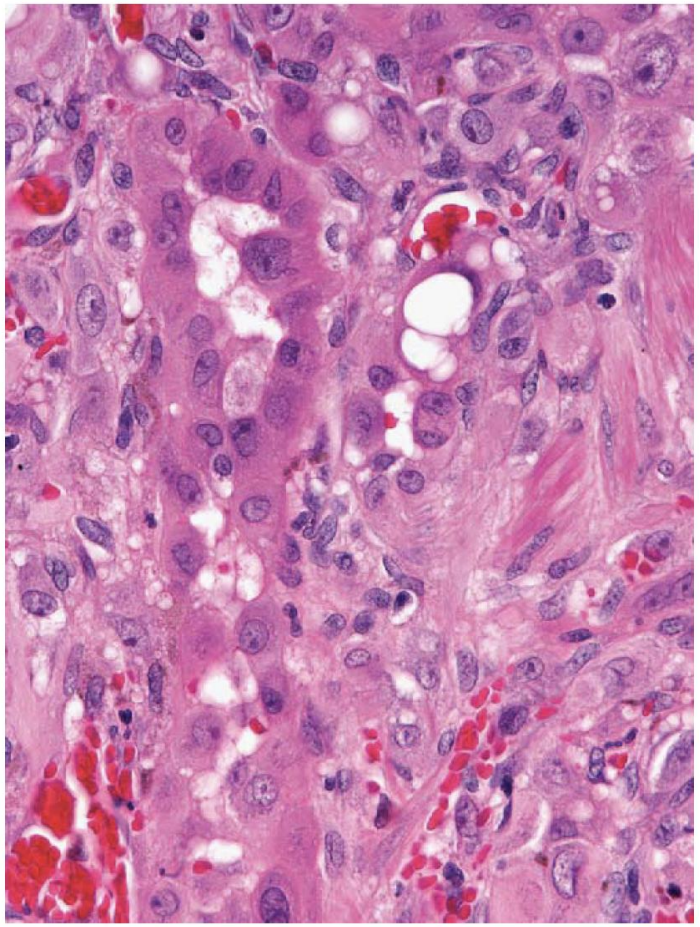

SOX17

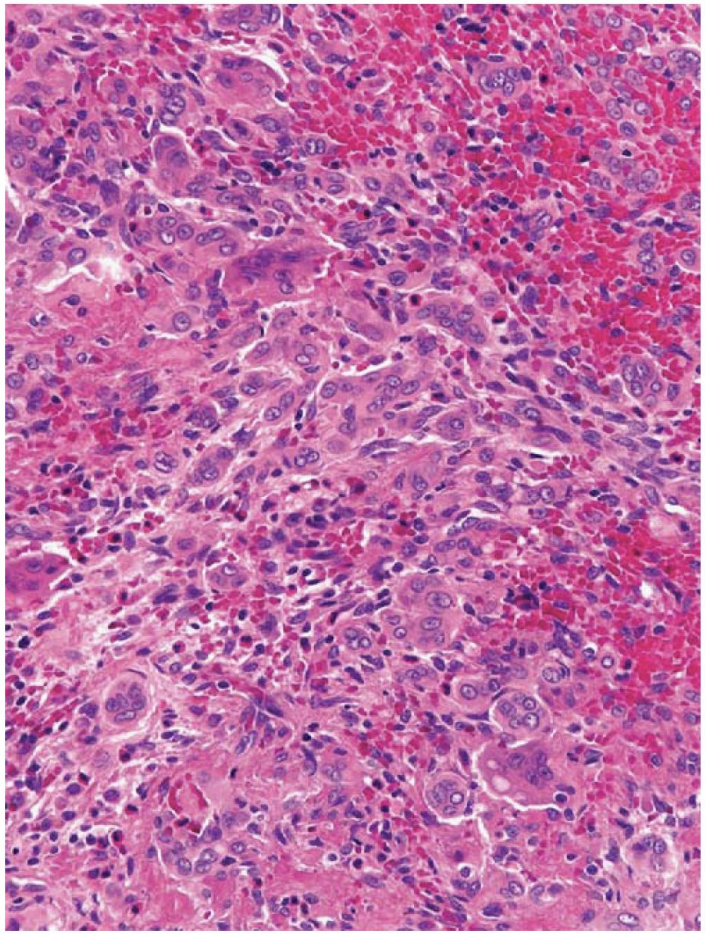


Negative: HHV8, H3.3G34W

Diagnosis

- Vascular proliferation, most consistent with epithelioid hemangioma
- Negative for metastatic carcinoma



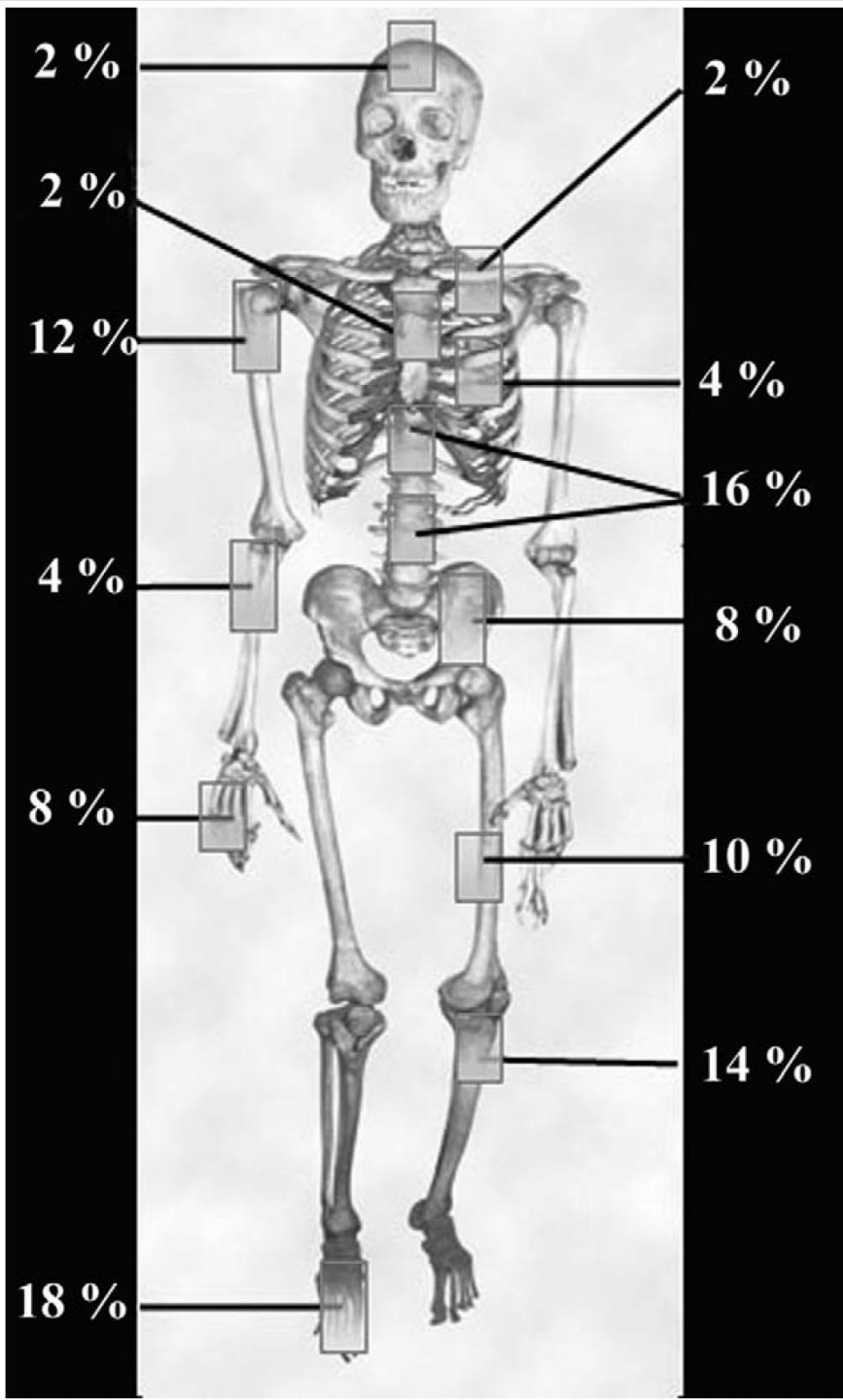


Epithelioid Hemangioma of Bone Revisited

A Study of 50 Cases

G. Petur Nielsen, MD, Amitabh Srivastava, MD,† Susan Kattapuram, MD,‡ Vikram Deshpande, MD,* John X. O'Connell, MD,§ Chas D. Mangham, MD,‖ and Andrew E. Rosenberg, MD**

Am J Surg Pathol 2009;33:270–277



Distribution of Keratins in Normal Endothelial Cells and a Spectrum of Vascular Tumors: Implications in Tumor Diagnosis

HUM PATHOL 200;31:1062-1067.

MARKKU MIETTINEN, MD, AND JOHN F. FETSCH, MD

TABLE 2. Summary of the Expression of Simple Epithelial Keratins 7, 8, 18, and 19 in Vascular Tumors

	K7	K8	K18	K19	EMA
Capillary hemangioma	1/22*	0/20	1/18*	0/26	
Cavernous hemangioma	1/8**	0/4	0/4	0/8	
Venous hemangioma	6/13*	0/13	3/13*	0/13	
Lymphangioma	6/7	0/7	2/7*	0/7	
Spindle-cell hemangioma	0/10	0/10	6/10*	0/10	7/7
Epithelioid hemangioendothelioma	10/20	2/20*	17/17	0/19	2/19
Epithelioid angiosarcoma	6/17	7/18	9/14	1/17	4/16
Angiosarcoma, nonepithelioid	2/48*	4/51*	10/48	0/52	17/48
Kaposi's sarcoma	0/6	0/6	0/6	0/6	0/6

* Denotes focal if any immunoreactivity.

Angiosarcoma & keratin IHC

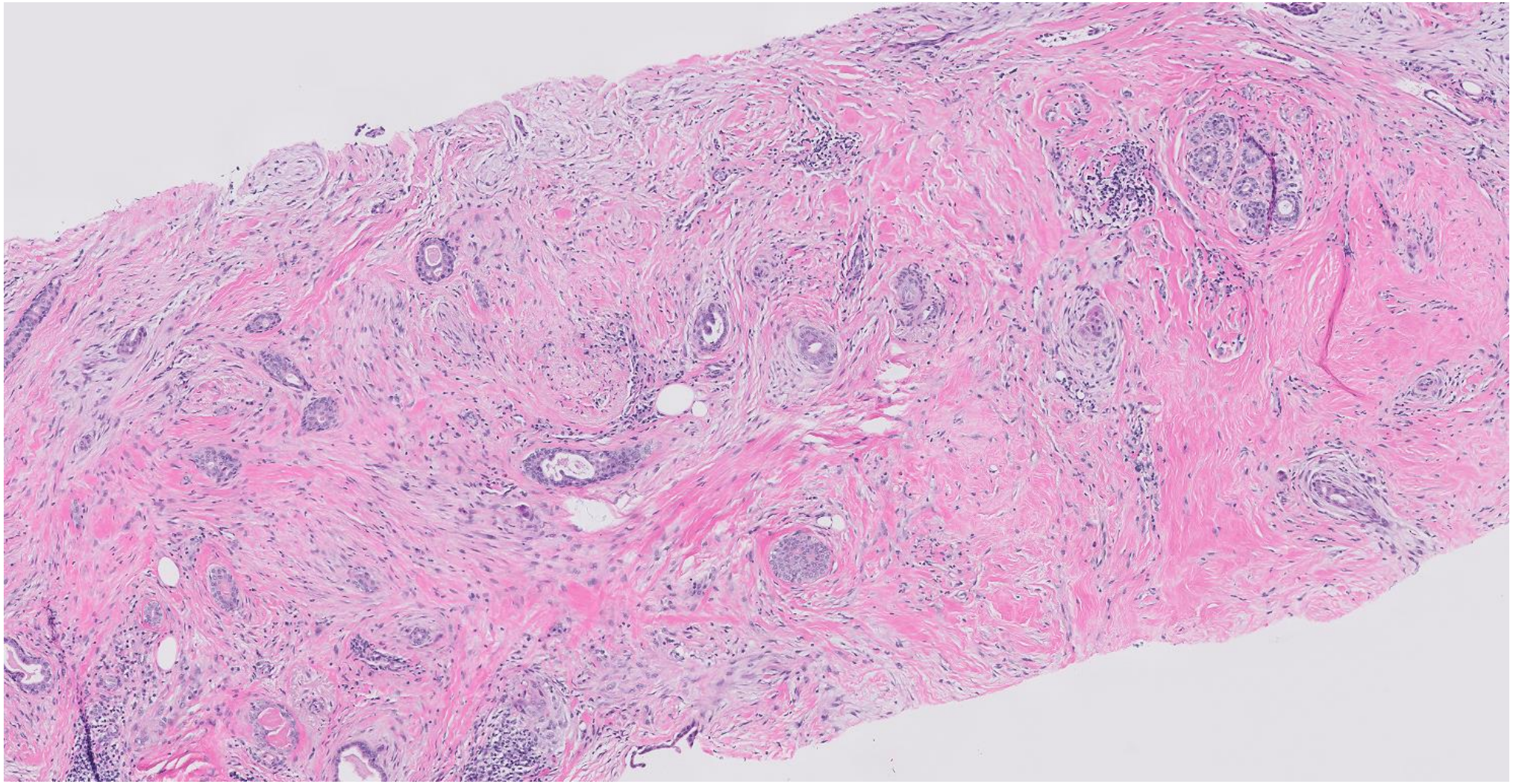
- Angiosarcoma: A Tissue Microarray Study With Diagnostic Implications. Rao. Am J Dermatopathol 2013;35:432–437
  - 4/8 (50%) epithelioid showed keratin expression.
  - 3/32 (9%) nonepithelioid cases also expressed keratins
- Distinct histological features characterize primary angiosarcoma of bone. Verbeke. Histopathology 2011;58:254–264.
  - 27/39 (69%) keratin AE1AE3+

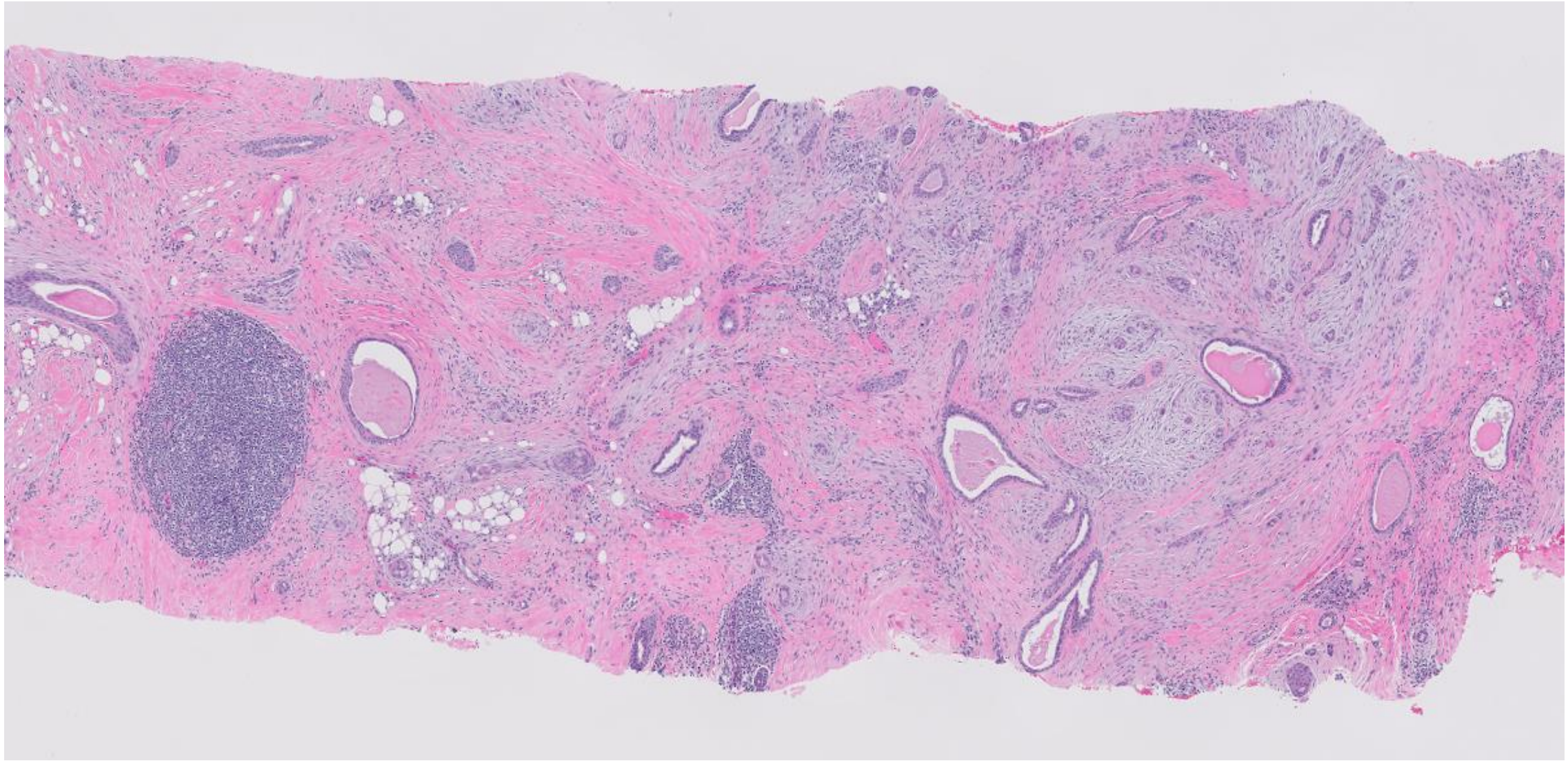
- **Vascular lesions frequently keratin +. Pitfall !!**

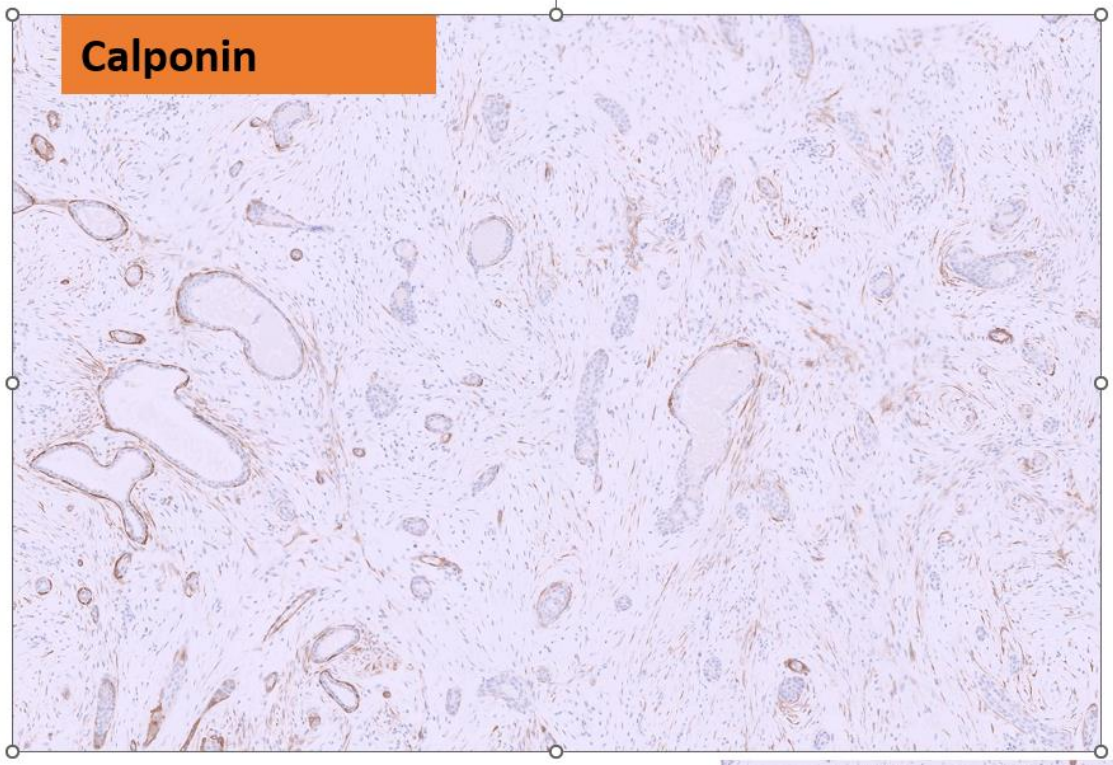
25-1106

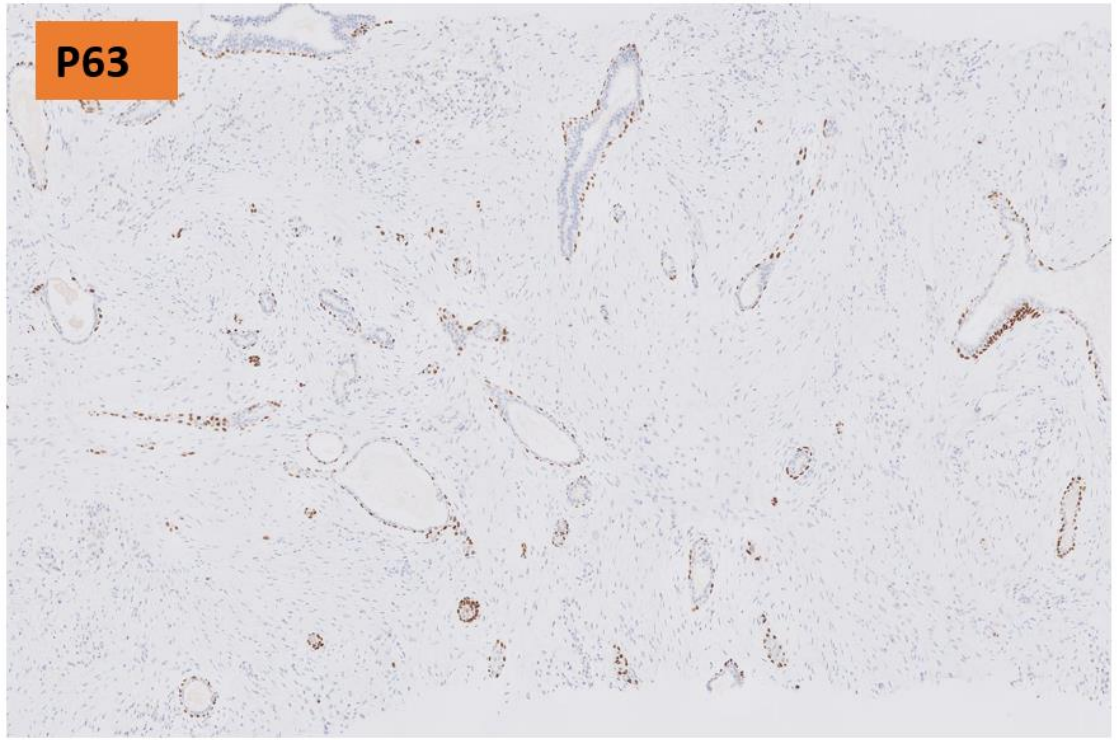
Sheren Younes, Megan Troxell; Stanford

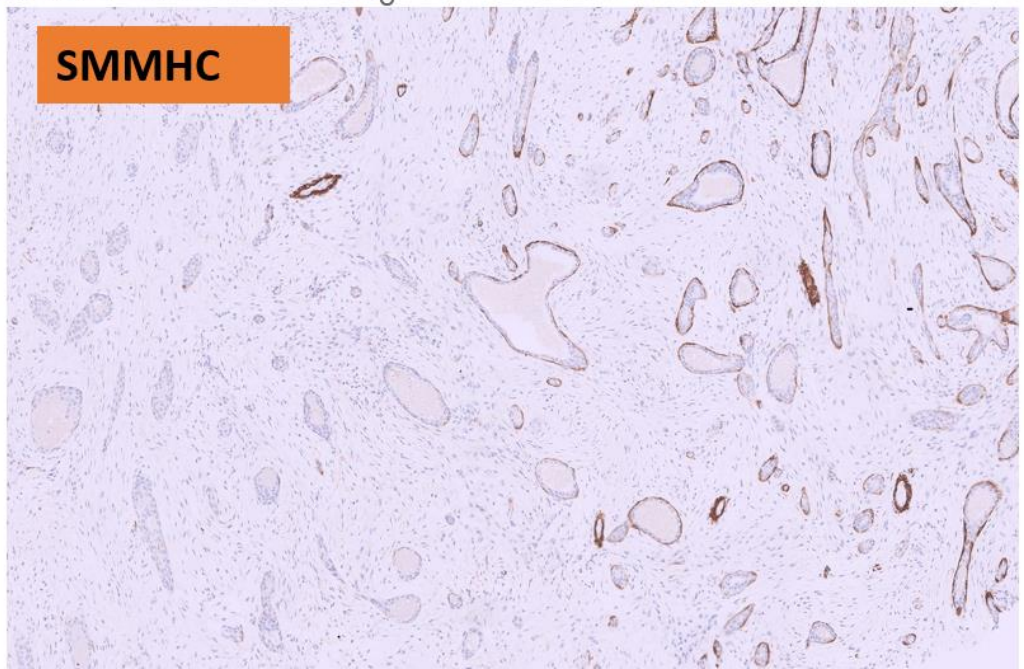
67 year old with right breast mass, 10 o'clock, 6 cm from the nipple, measuring 1.5 cm, core biopsy



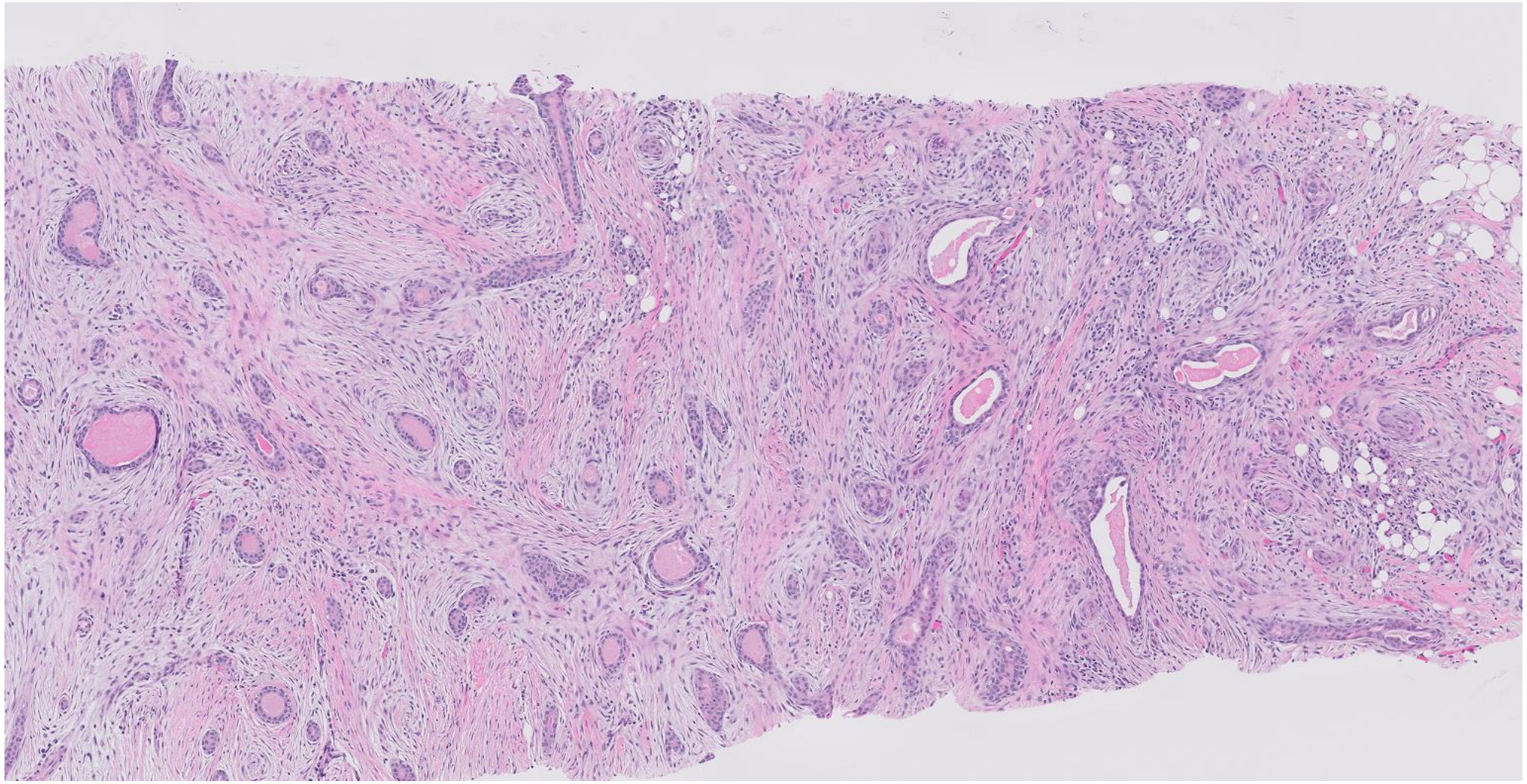


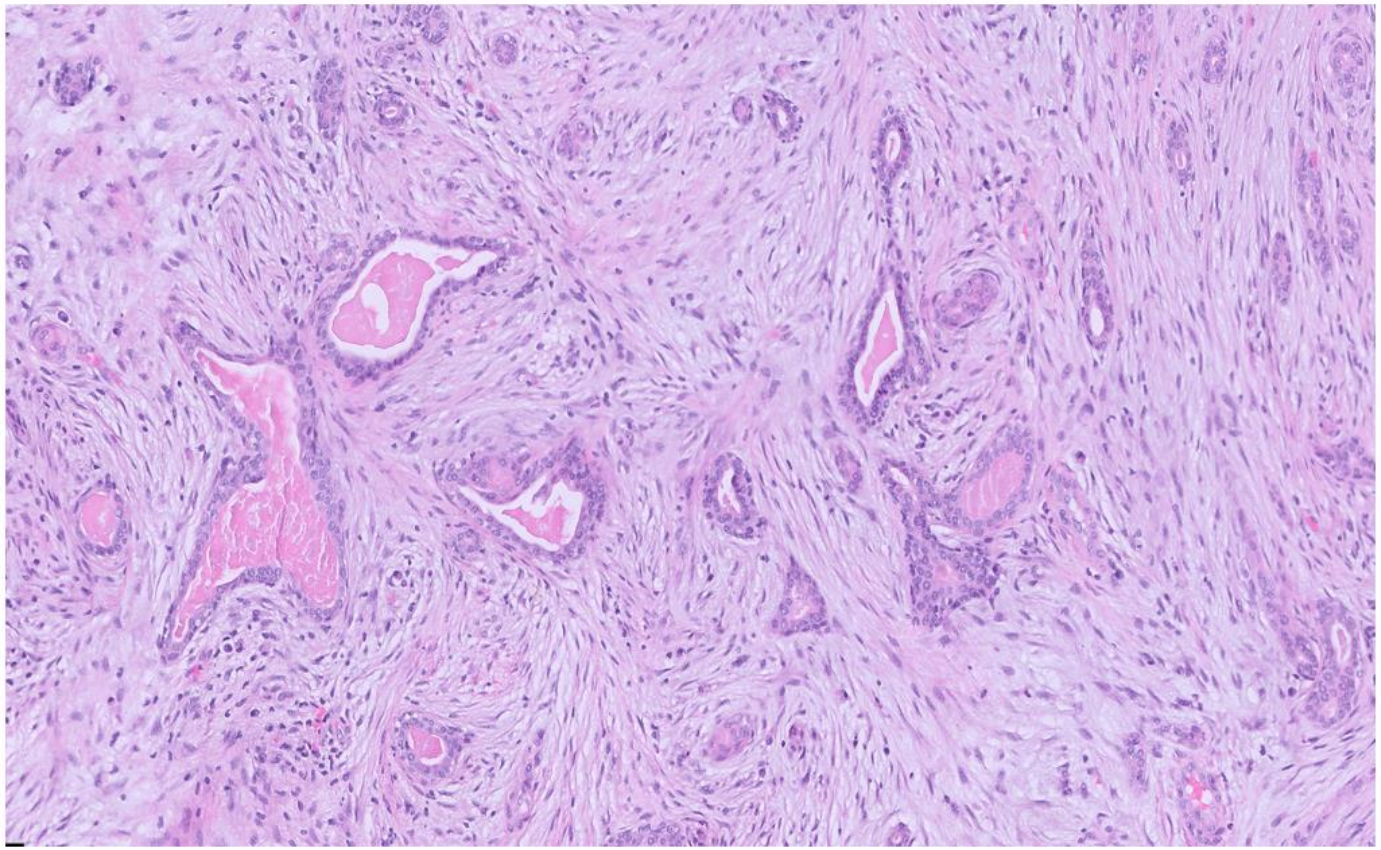

Calponin

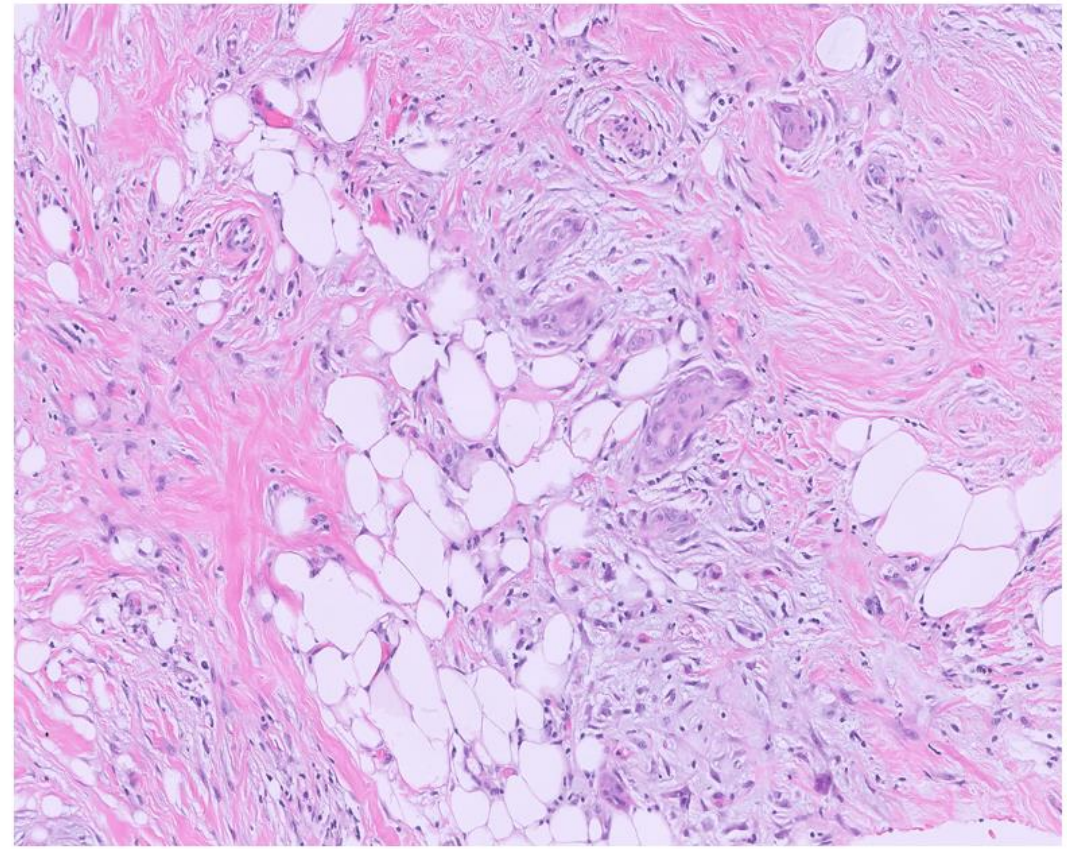

P63

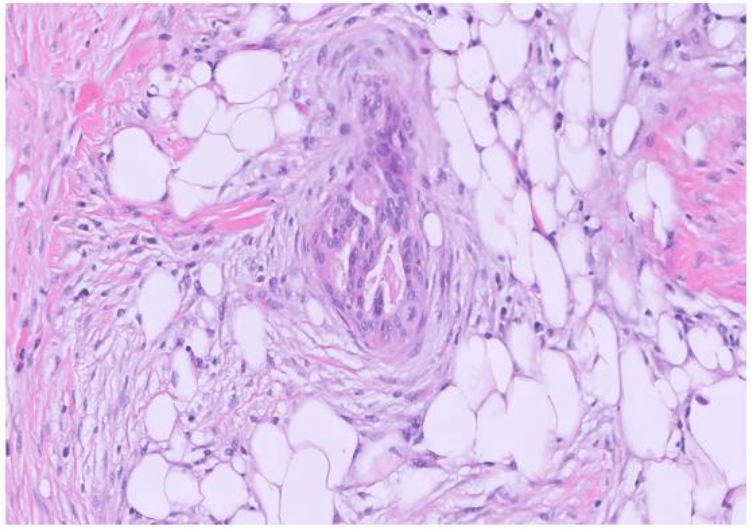

SMMHC

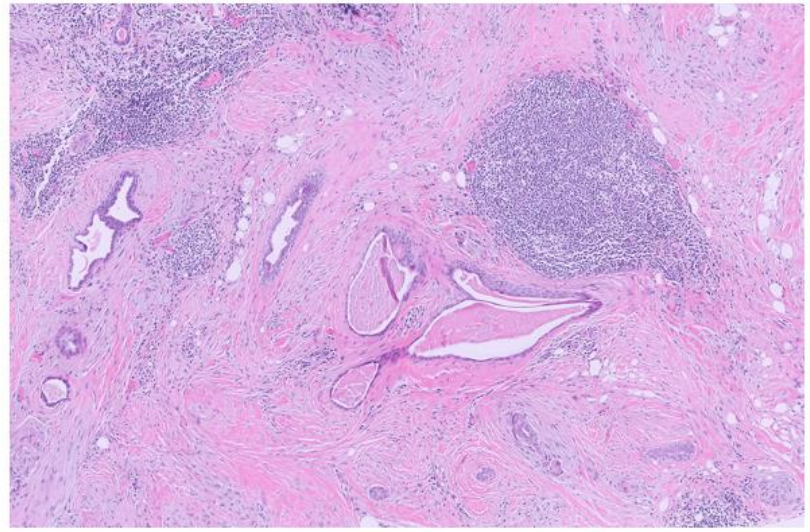
DIAGNOSIS?

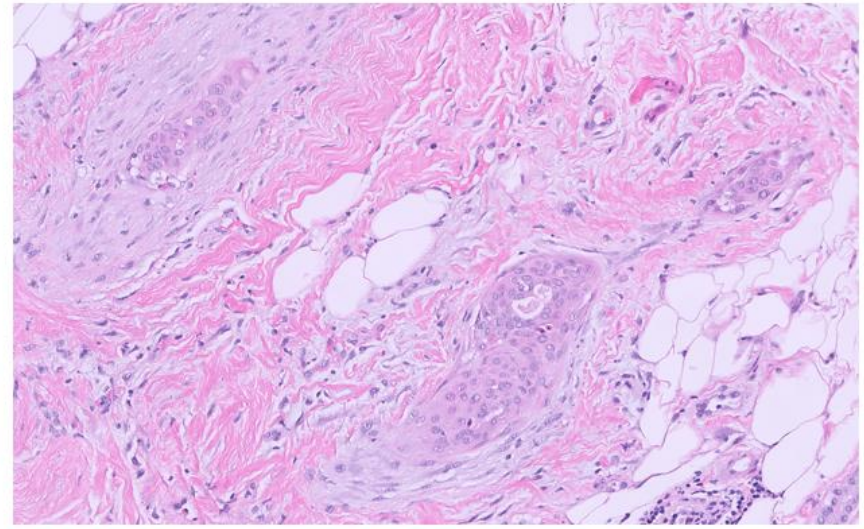


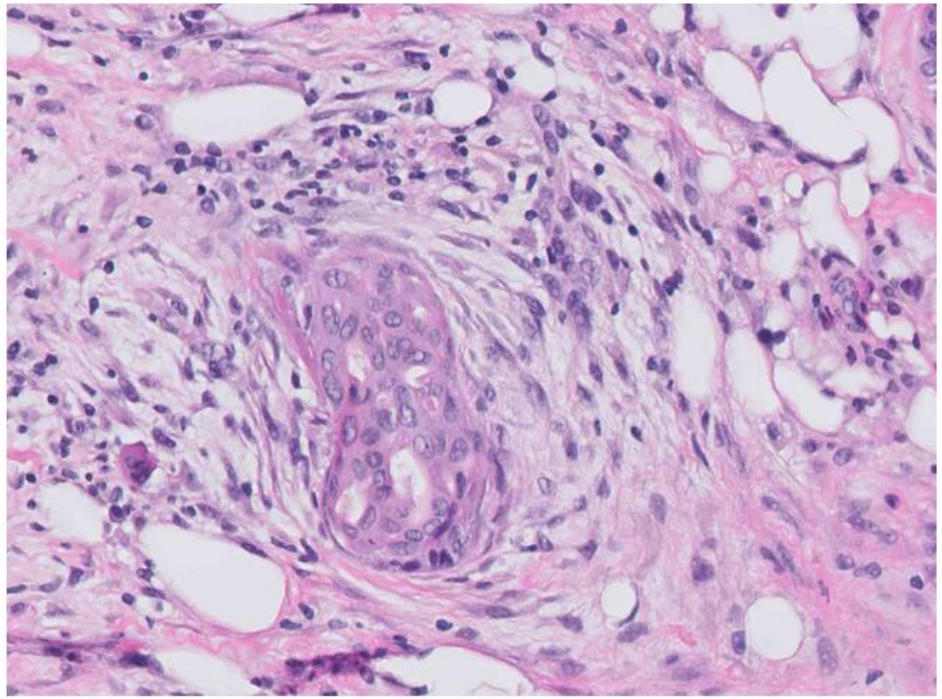


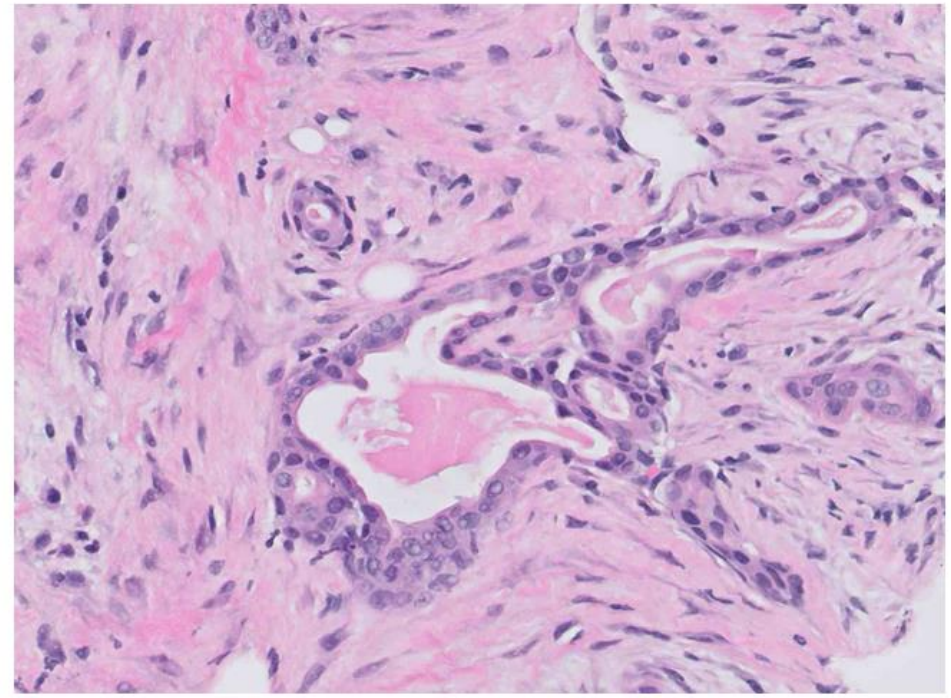


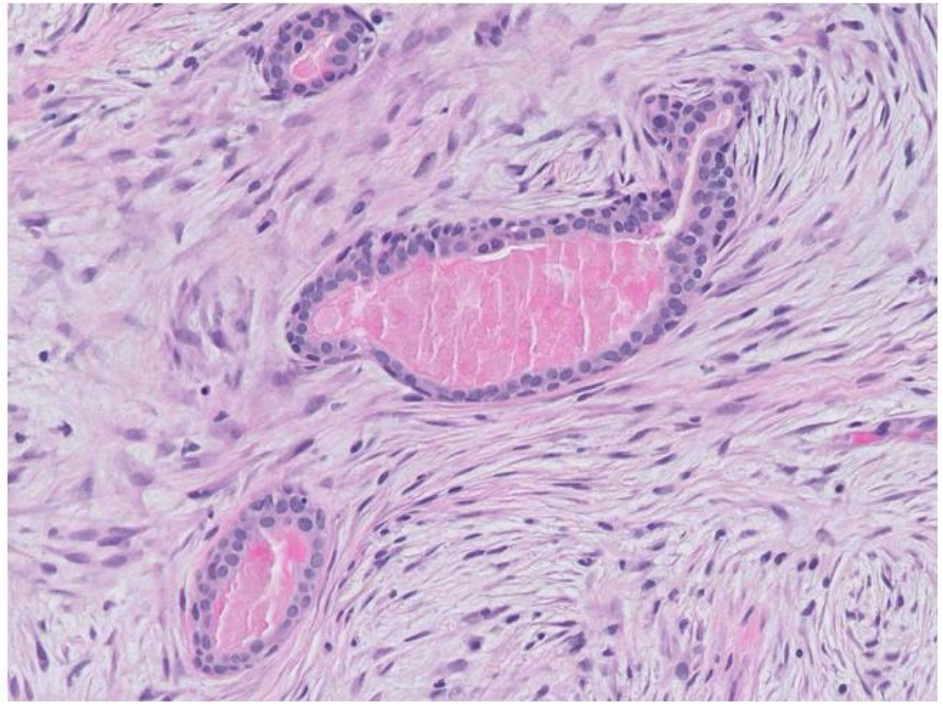


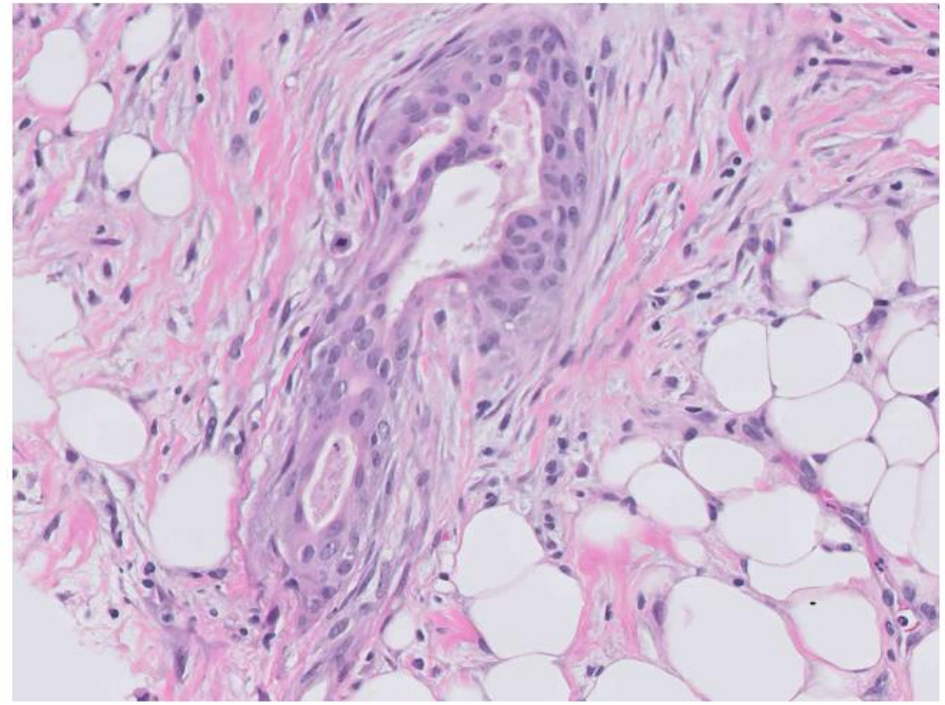




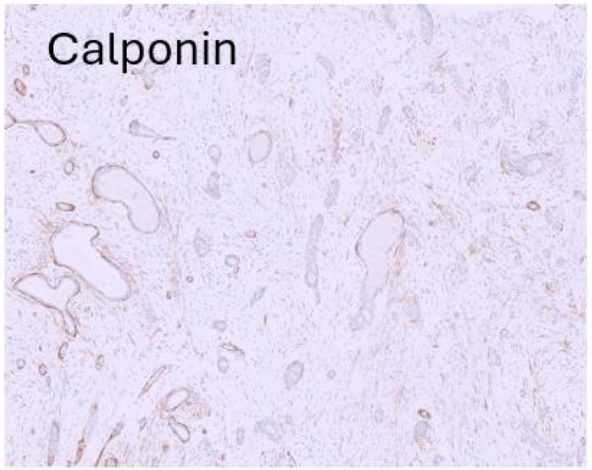


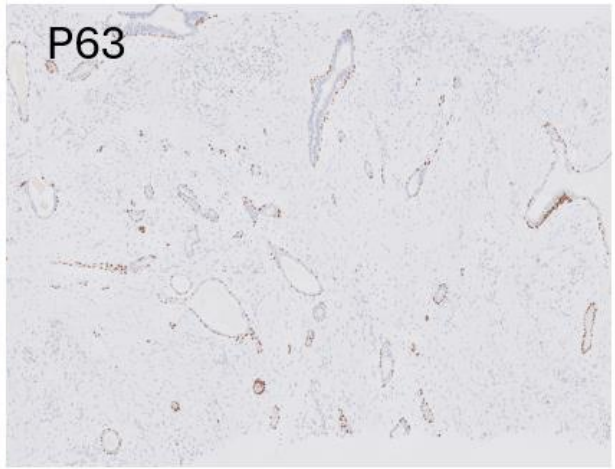


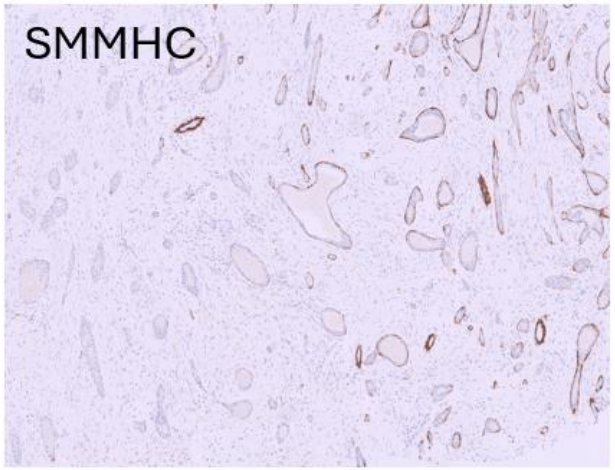


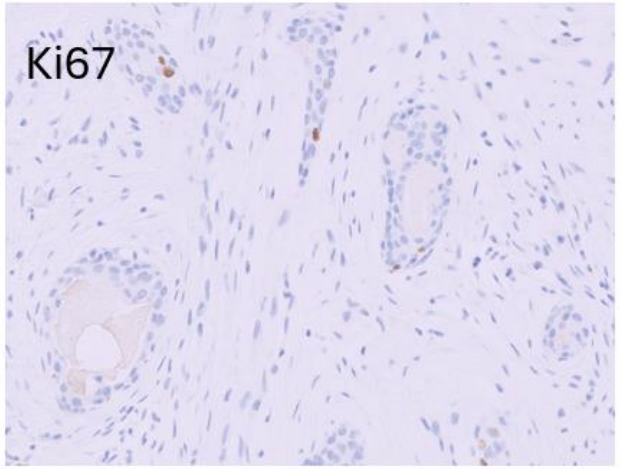


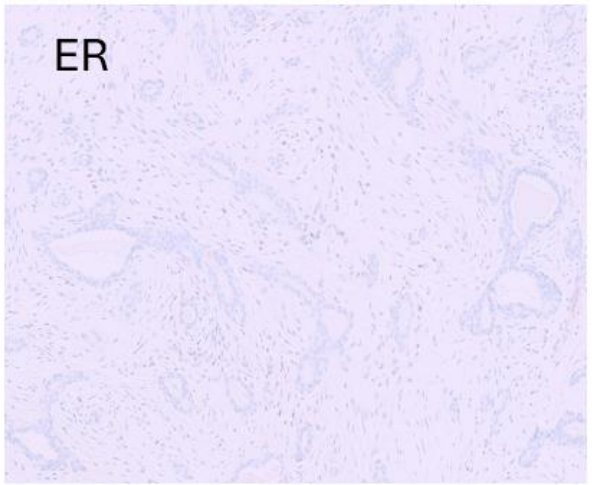
Immunohistochemistry

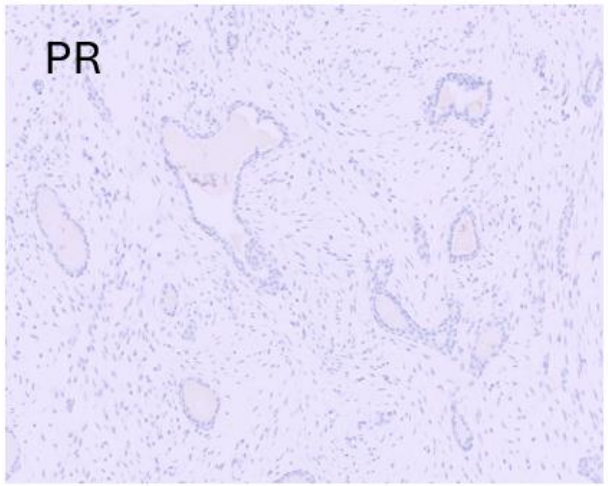


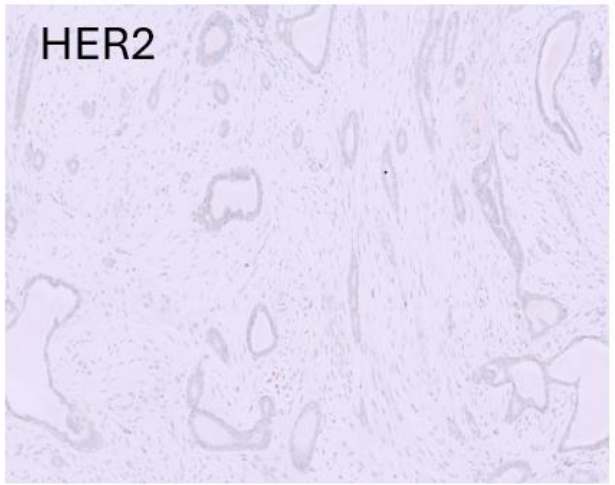


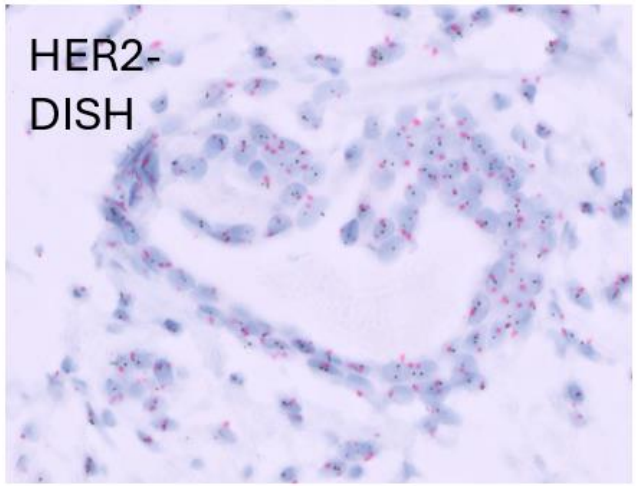










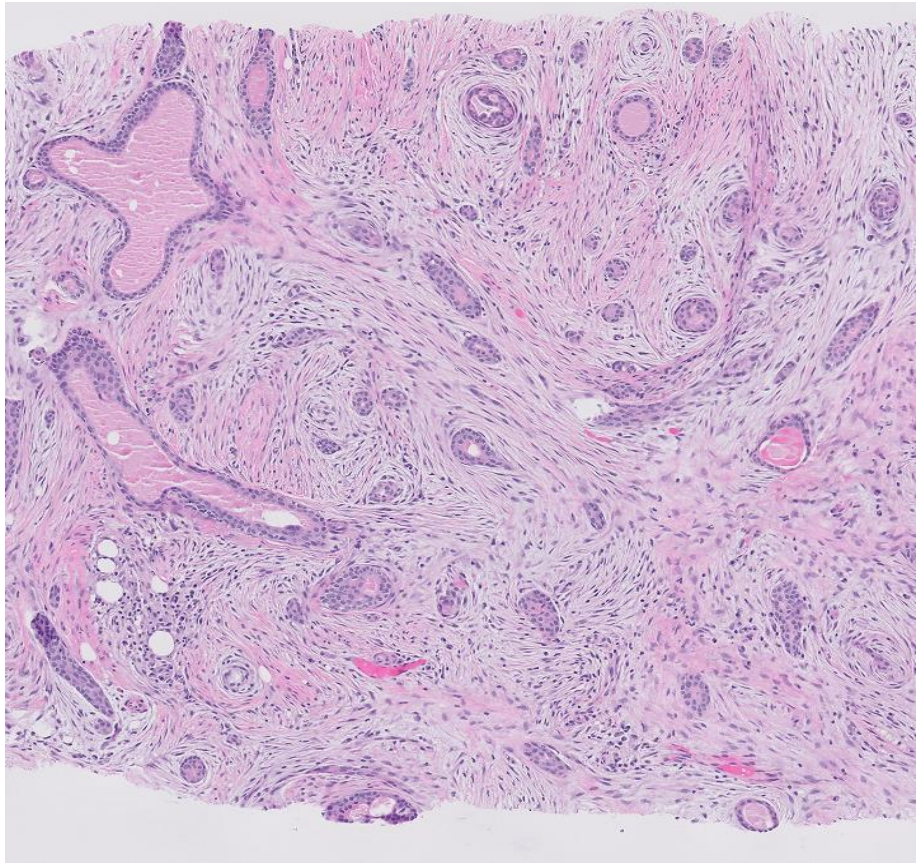


Diagnosis

Low grade adenosquamous carcinoma

Morphology

- Infiltrative nature
- Adenocarcinomatous component; small, rounded and angulated glands, forming slender extensions, insinuating between intact ducts and lobules.
- These glands display varying degrees of squamous differentiation, characterized by pavement-like architecture, prominent intercellular bridges and, to a lesser extent, keratin formation
- Luminal keratin debris
- Stroma ranges from collagenous paucicellular to sclerotic.
- Infrequent epithelial and stromal mitoses
- A prominent lymphocytic reaction may be present at the periphery of the lesion
- May be associated with benign lesions



Immunohistochemistry

- Myoepithelial cells: consistently inconsistent staining pattern, Variable degrees of circumferential complete, discontinuous and absent myoepithelial cell markers, P63, SMMHC and calponin.
- Luminal cells show varying immunoreactivity for p63 (highlighting squamous differentiation) (74%)
- Distinctive stromal lamellar staining pattern, frequently seen with SMMHC and calponin
- Triple negative, ER, PR and HER2

Am J Surg Pathol 2012

Molecular alterations

MODERN PATHOLOGY (2010) 23, 951–960

Genomic and immunohistochemical analysis of adenosquamous carcinoma of the breast

Felipe C Geyer[1], Maryou BK Lambros[1], Rachael Natrajan[1], Rutika Mehta[2], Alan Mackay[1], Kay Savage[1], Suzanne Parry[1], Alan Ashworth[1], Sunil Badve[2] and Jorge S Reis-Filho[1]

[1]*The Breakthrough Breast Cancer Research Centre, Institute of Cancer Research, London, UK and* [2]*Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis, IN, USA*

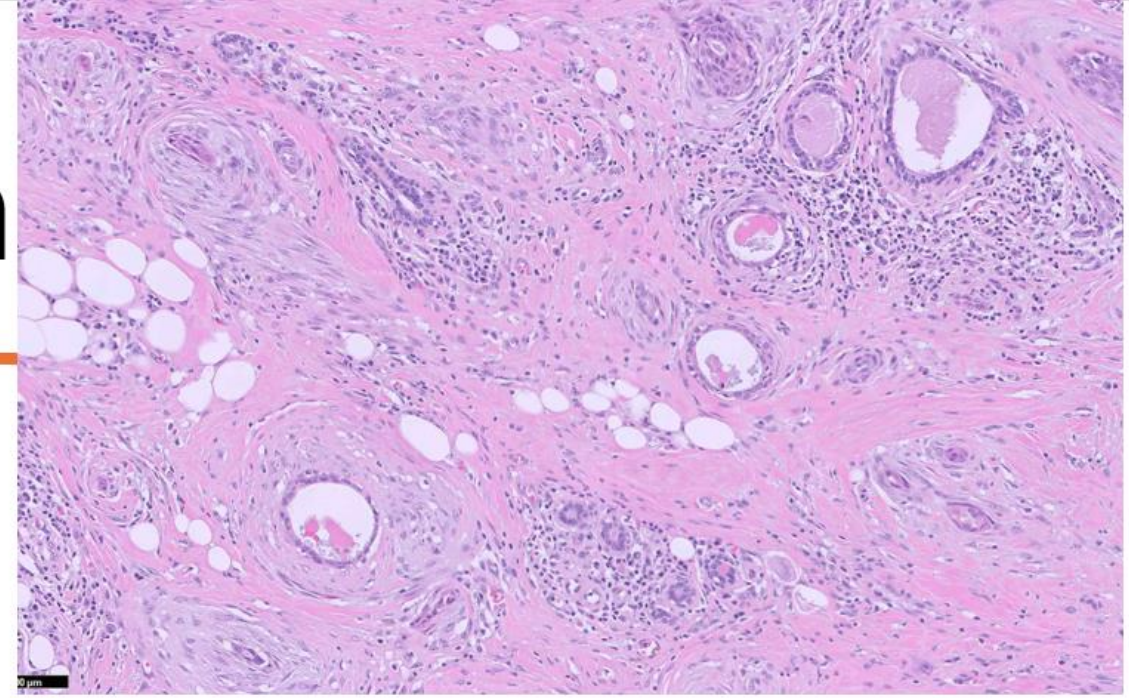
- Mutations
  - PIK3CA mutations in ~ 50%
  - No TP53 mutations reported
- Copy number alterations
  - 2 LGASCs analyzed showed complex copy number changes, including amplifications
  - EGFR amplification reported in a single case
- Direct molecular evidence that a minority of the spindle cells of the stromal component are derived from the epithelial cells, suggesting that some form of EMT may take place

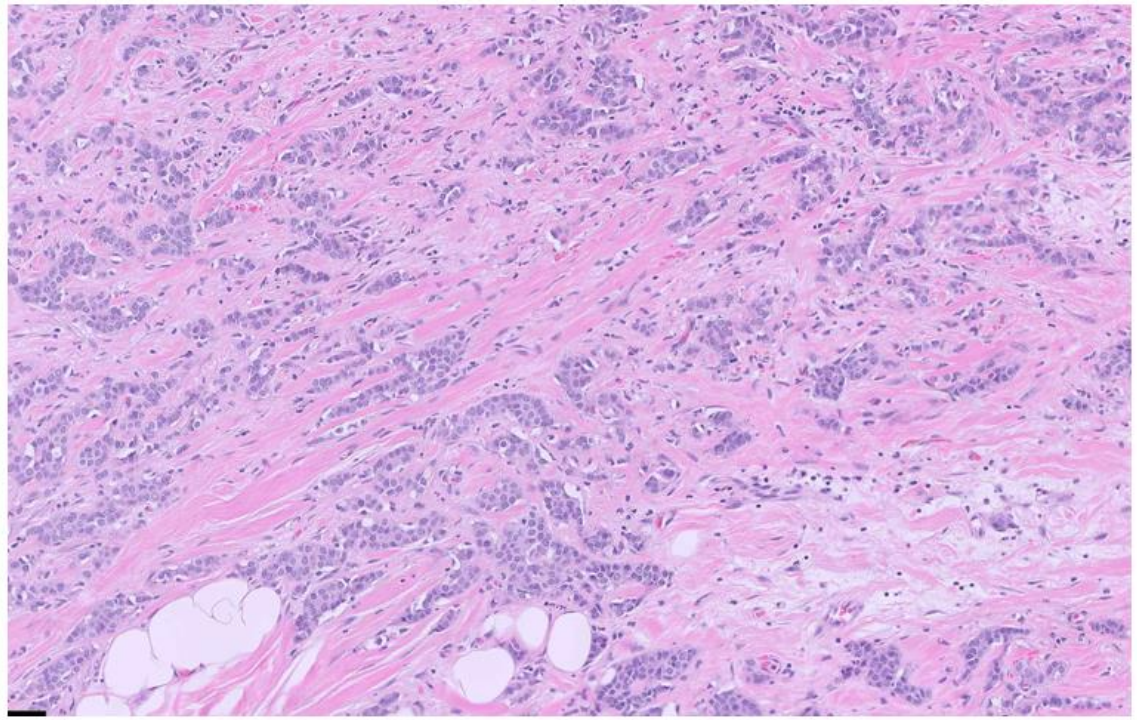
Differential diagnosis

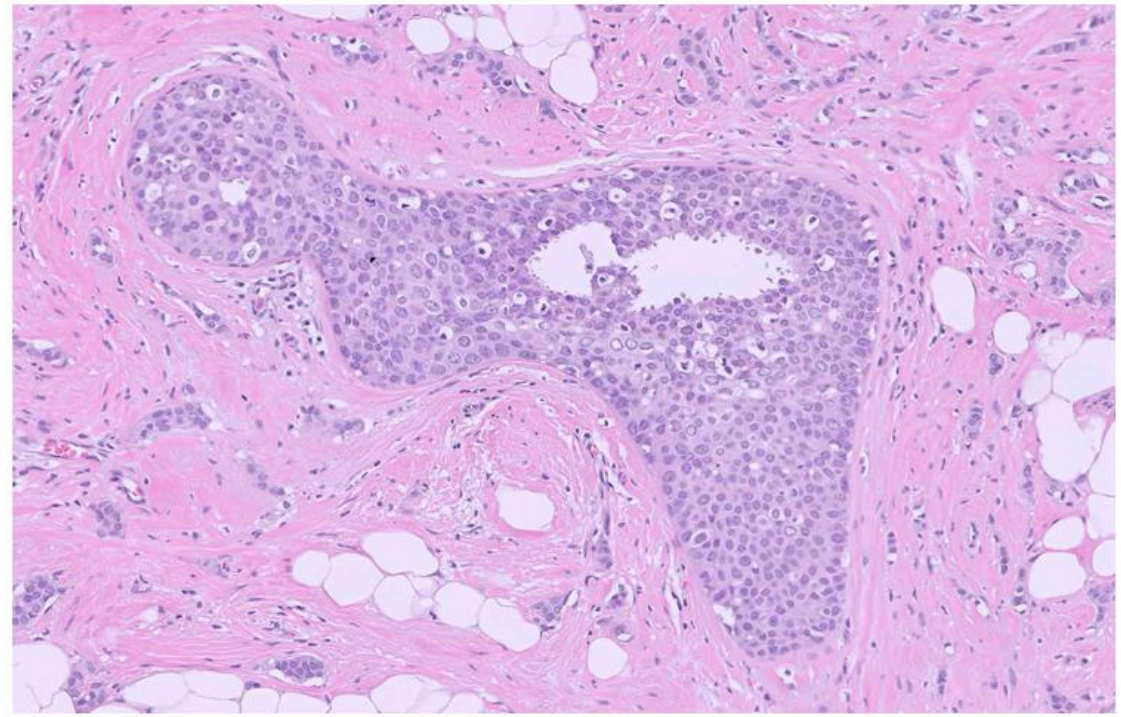
- Tubular carcinoma
  - ER, PR positive
  - Negative myoepithelial markers
  - No squamous differentiation
- Radial scar with squamous metaplasia
  - Heterogenous ER
- Syringomatous adenoma
  - More superficial
- High grade adenosquamous carcinoma
  - Malignant glandular and squamous components

Resection specimen

- R1, R2
- Adenosquamous carcinoma
- Invasive ductal carcinoma and DCIS







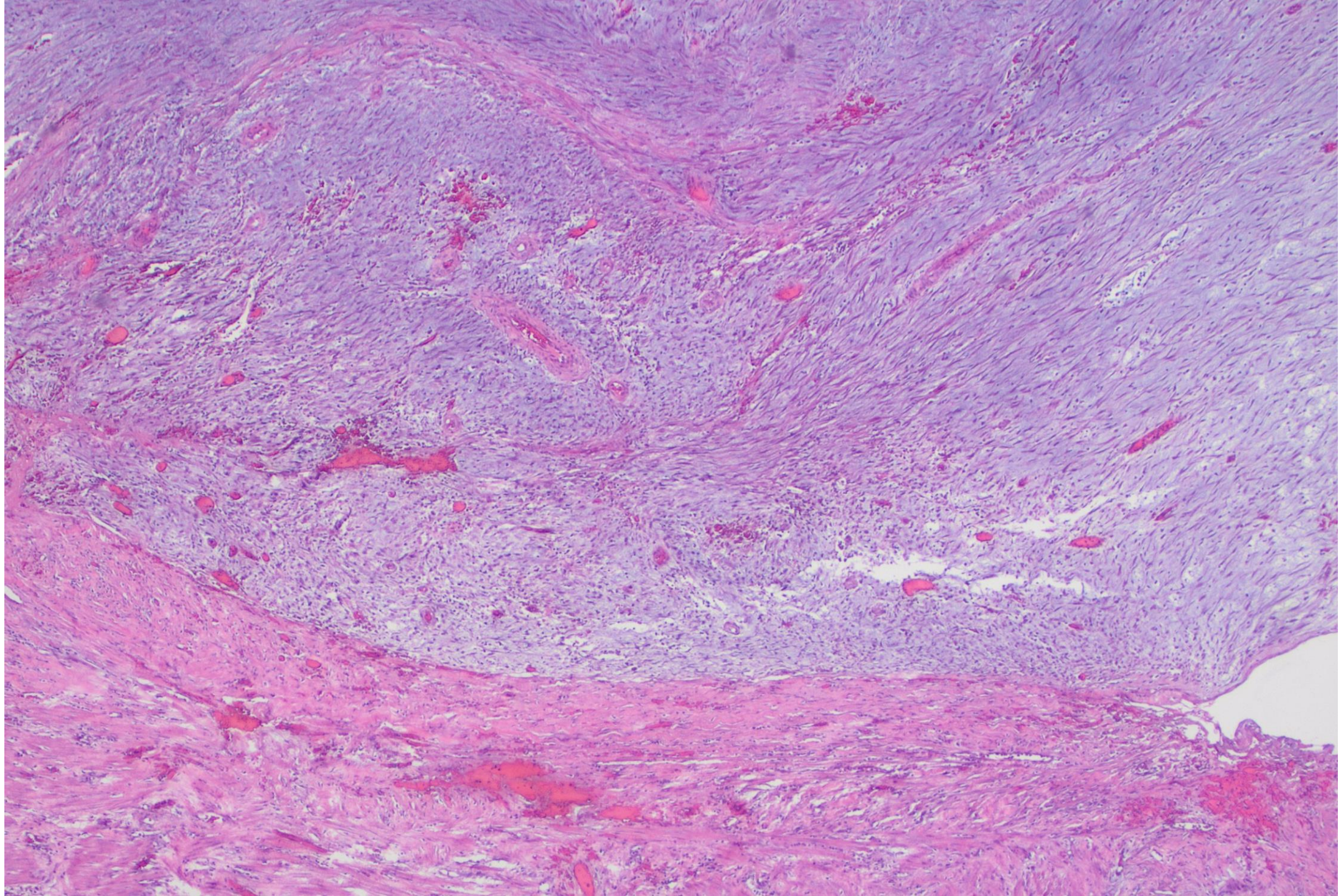
Take home message

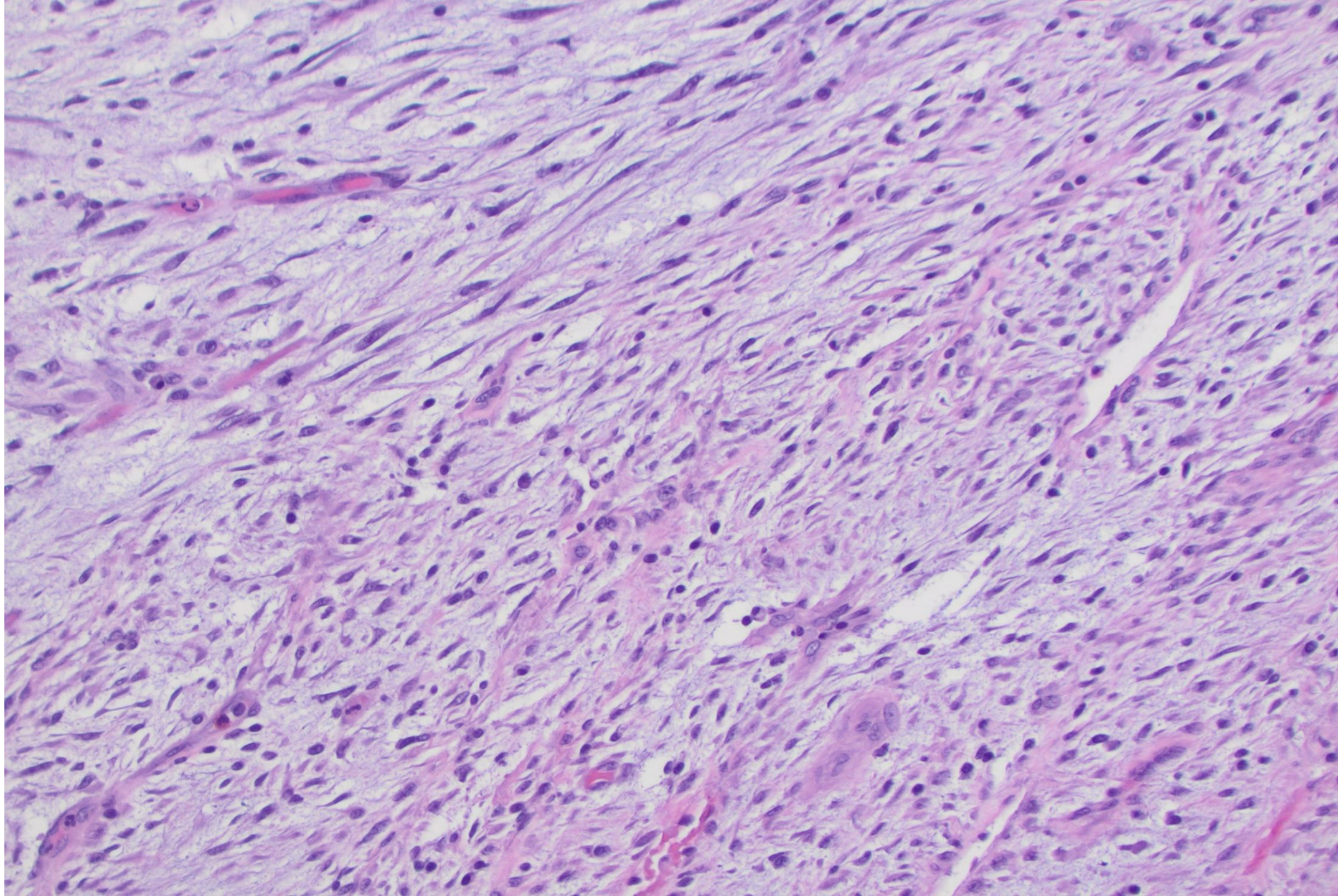
- LGASC is a rare but important entity in the differential diagnosis of small glandular proliferations.
- It has some unique but not entirely specific histopathological features makes the diagnosis confounding.
- LGASC has an indolent behavior and is important to recognize.

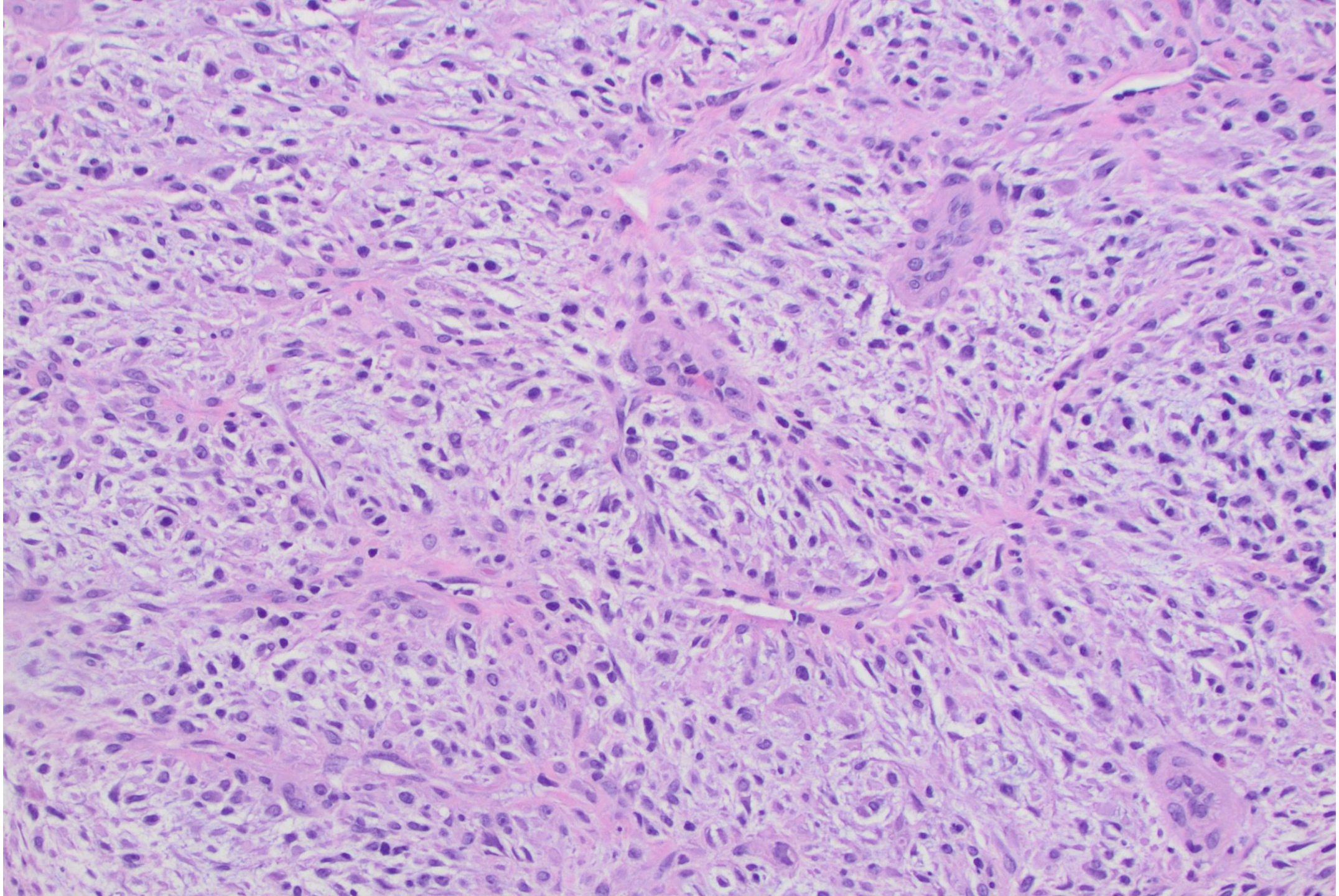
25-1107

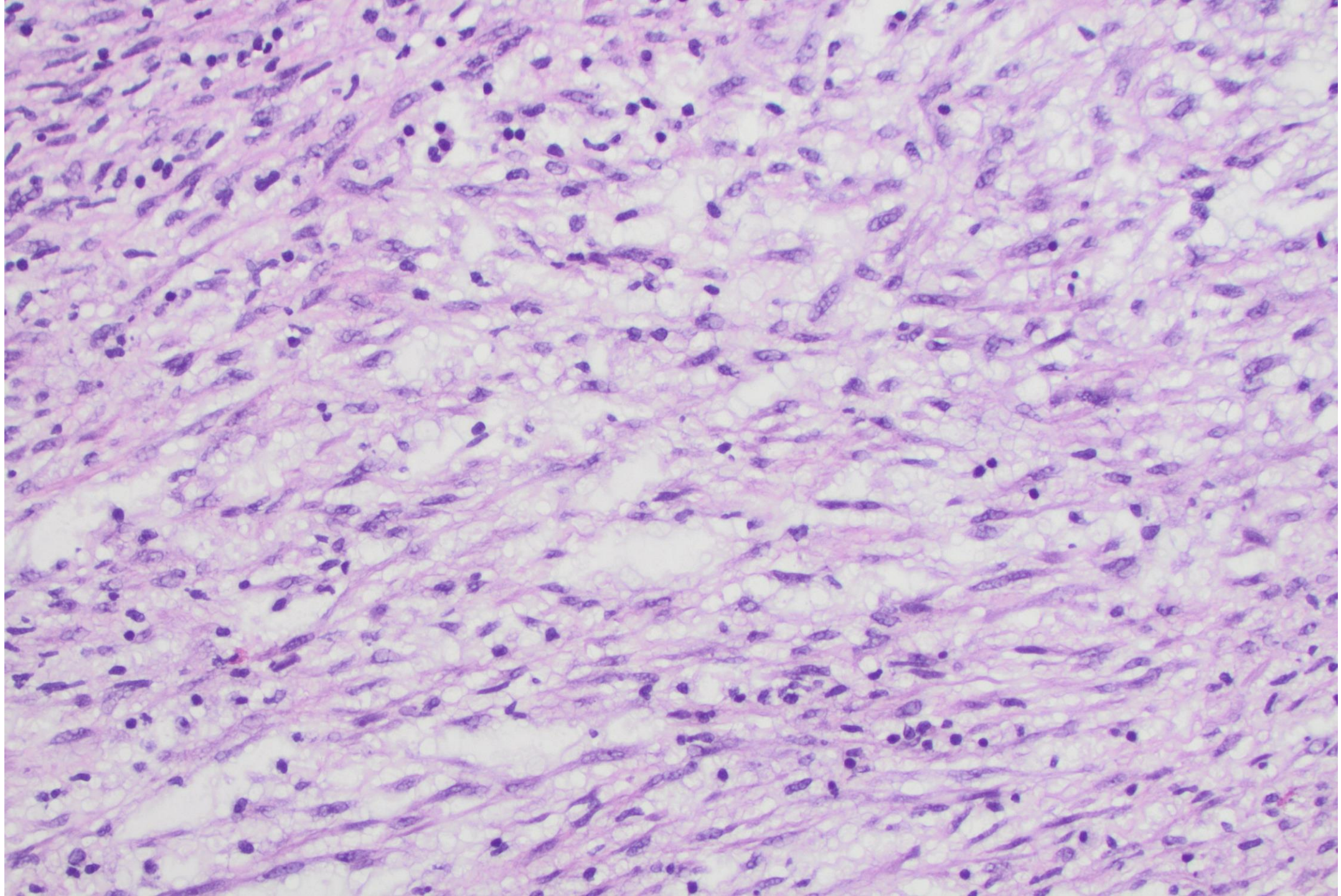
Greg Rumore; Kaiser Permanente

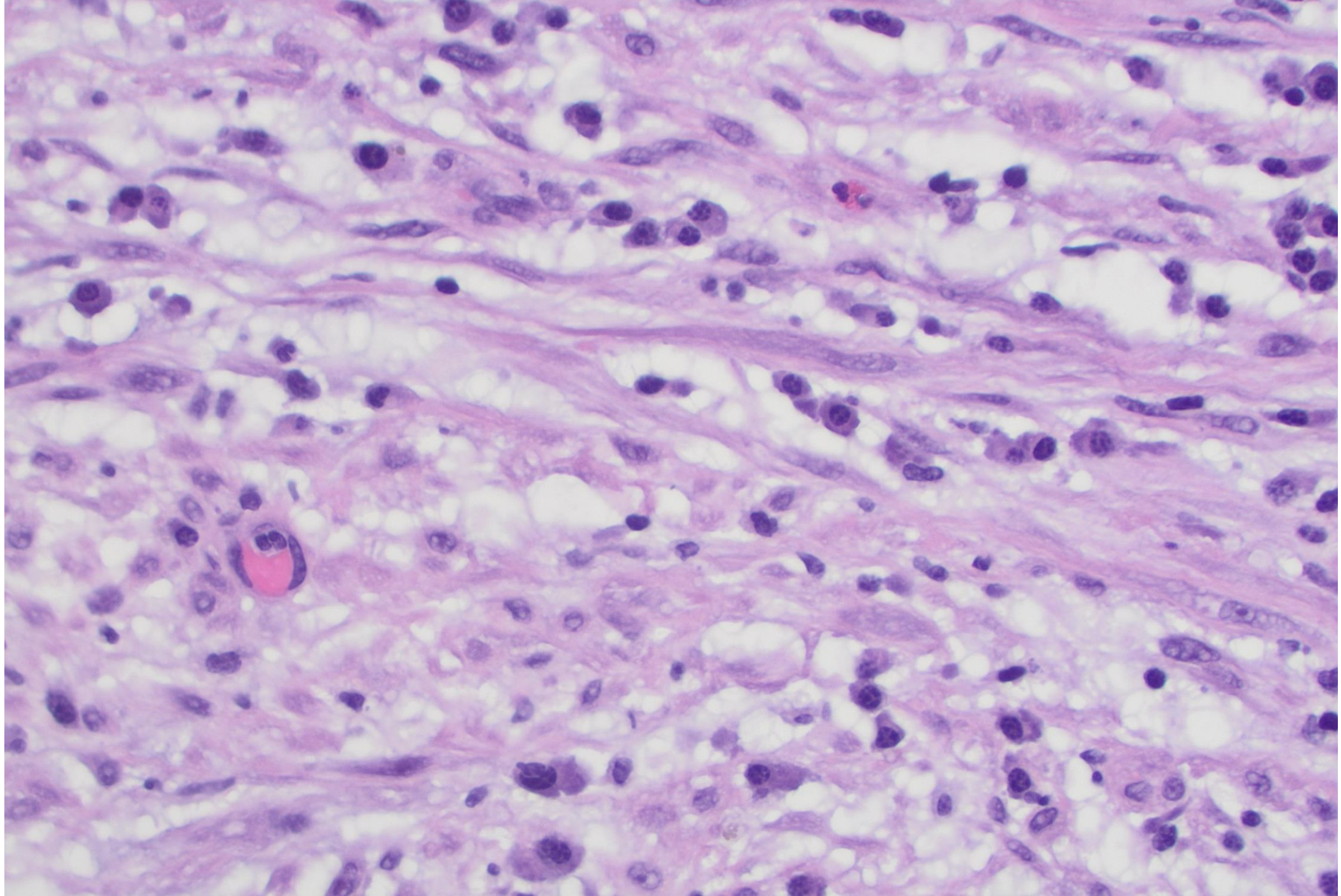
30’s female underwent hysterectomy for AUB and fibroids

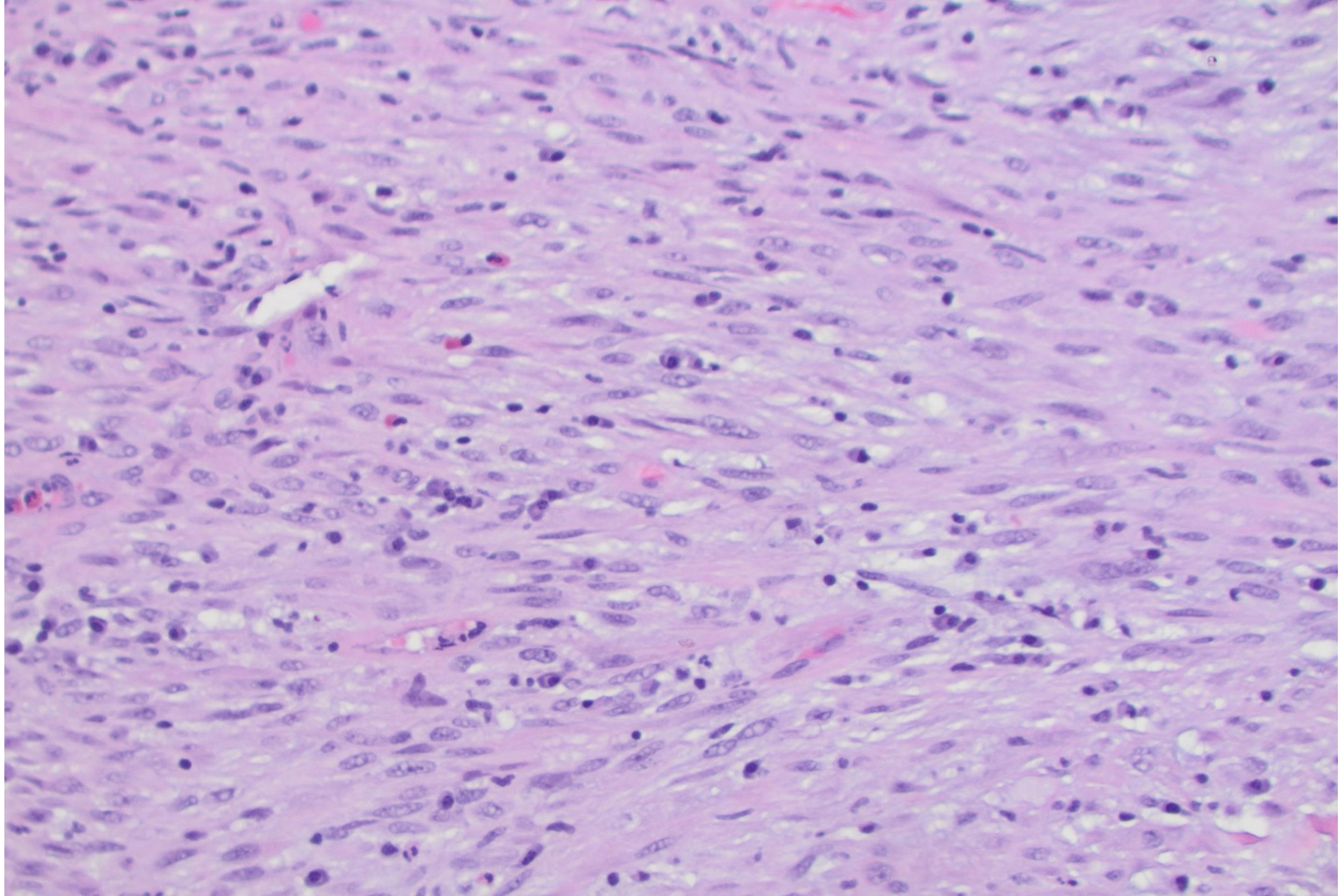


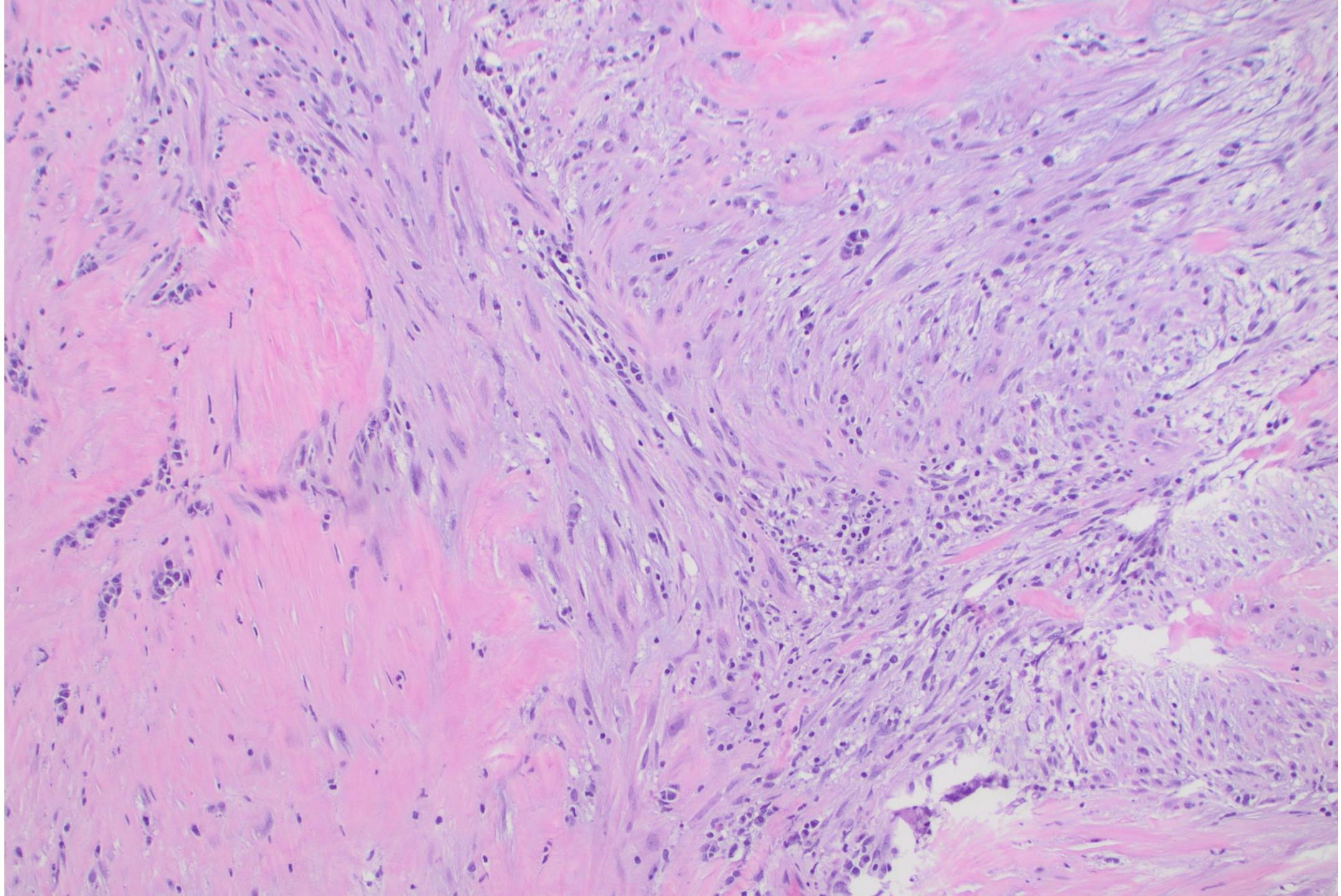


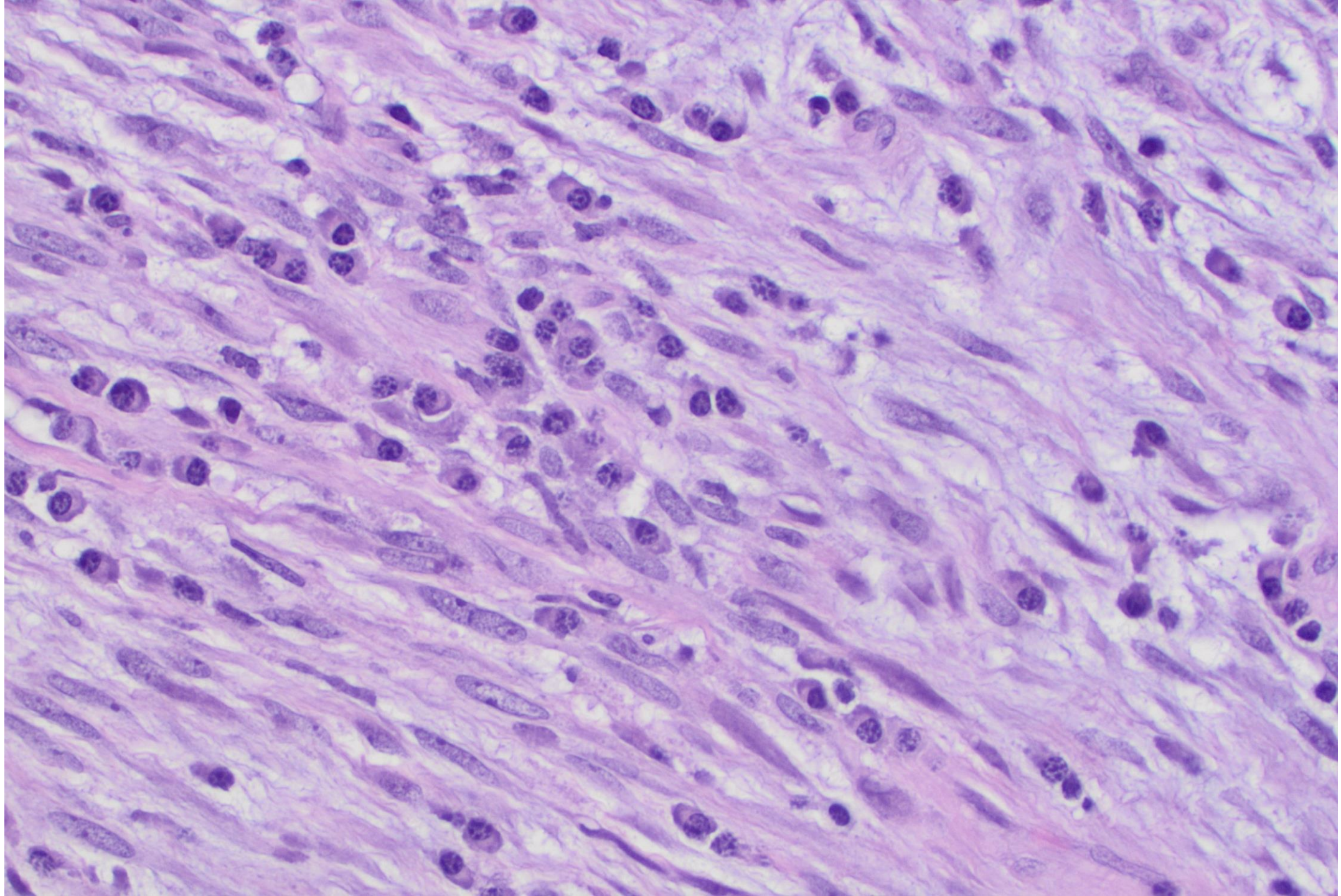


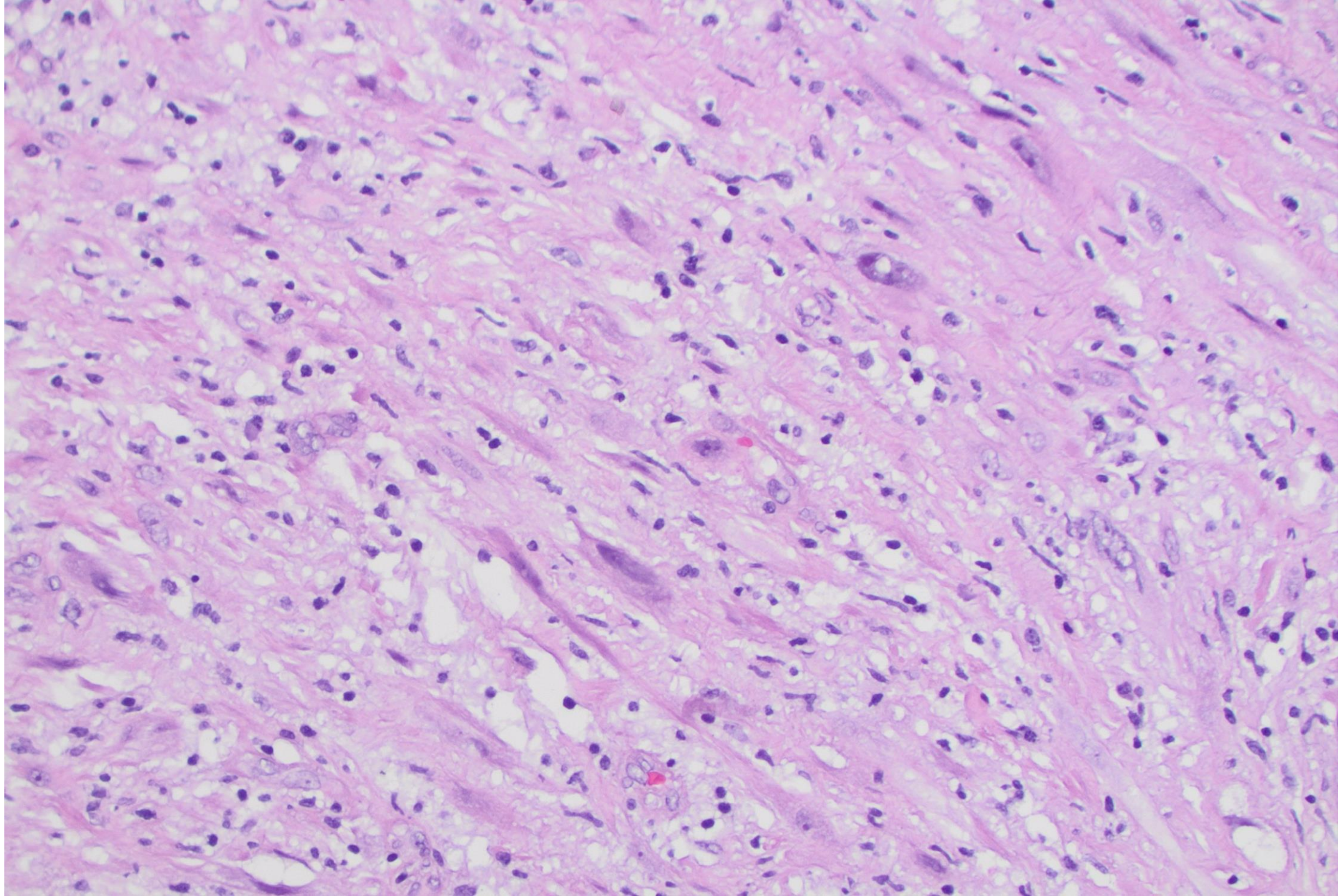


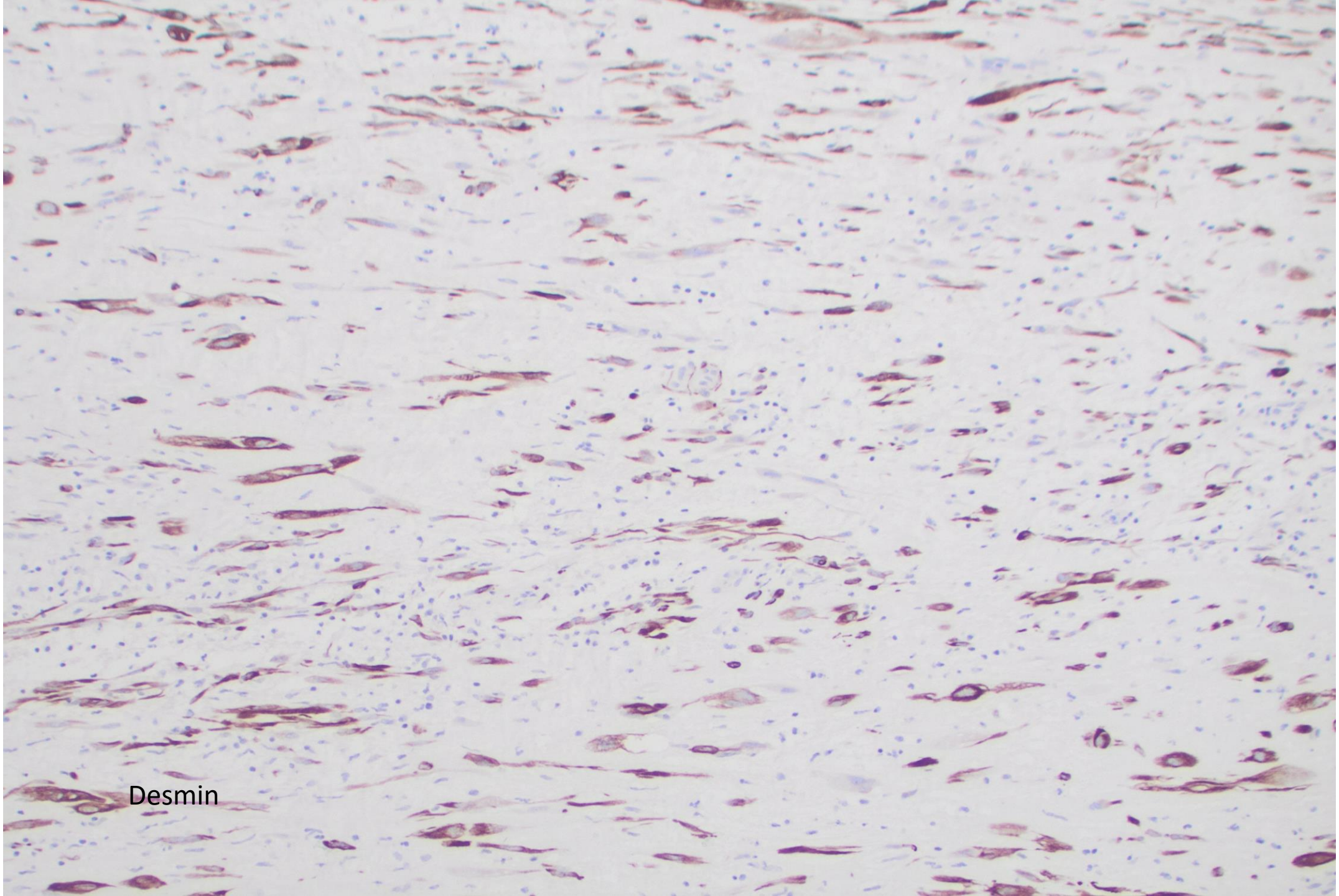








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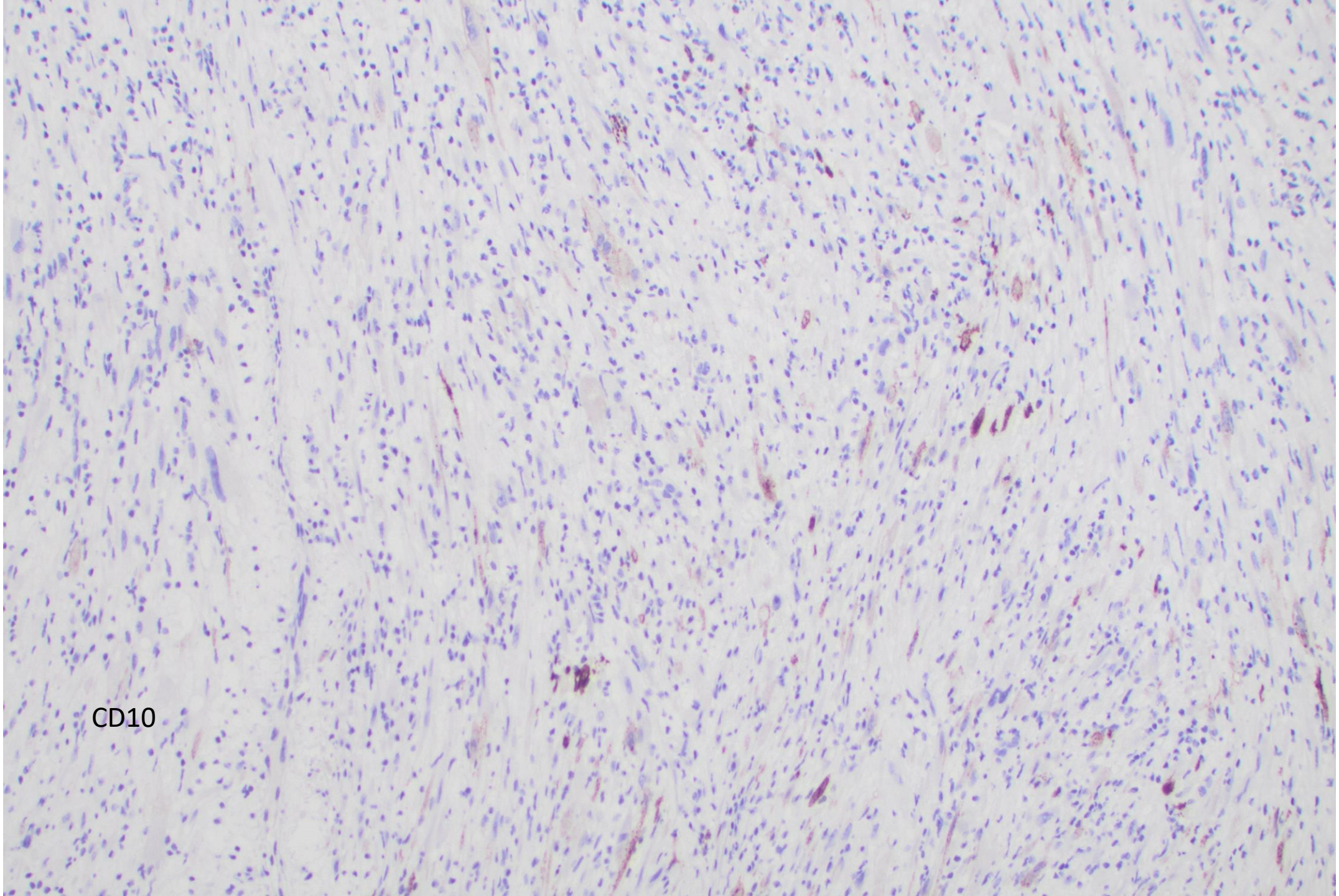
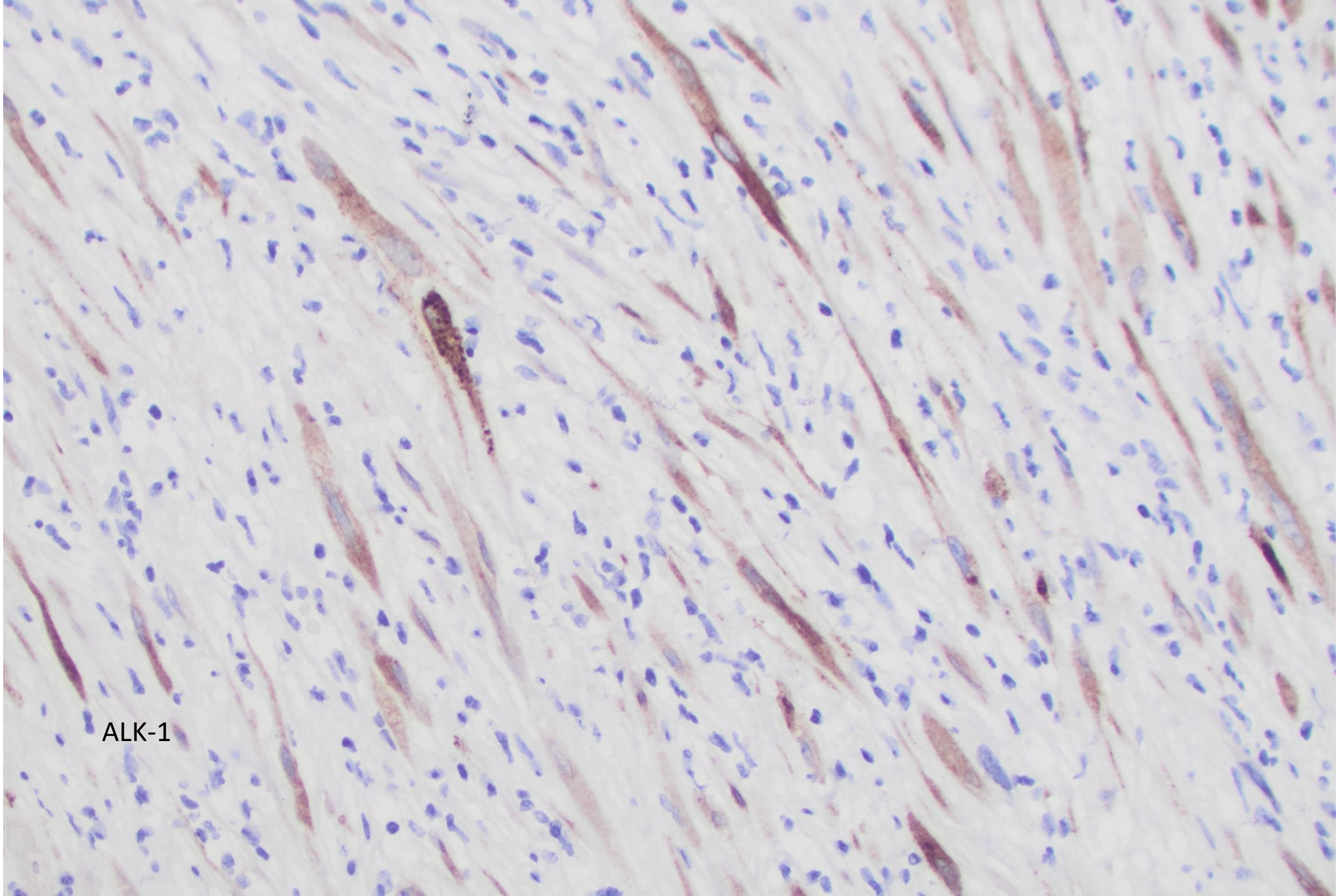
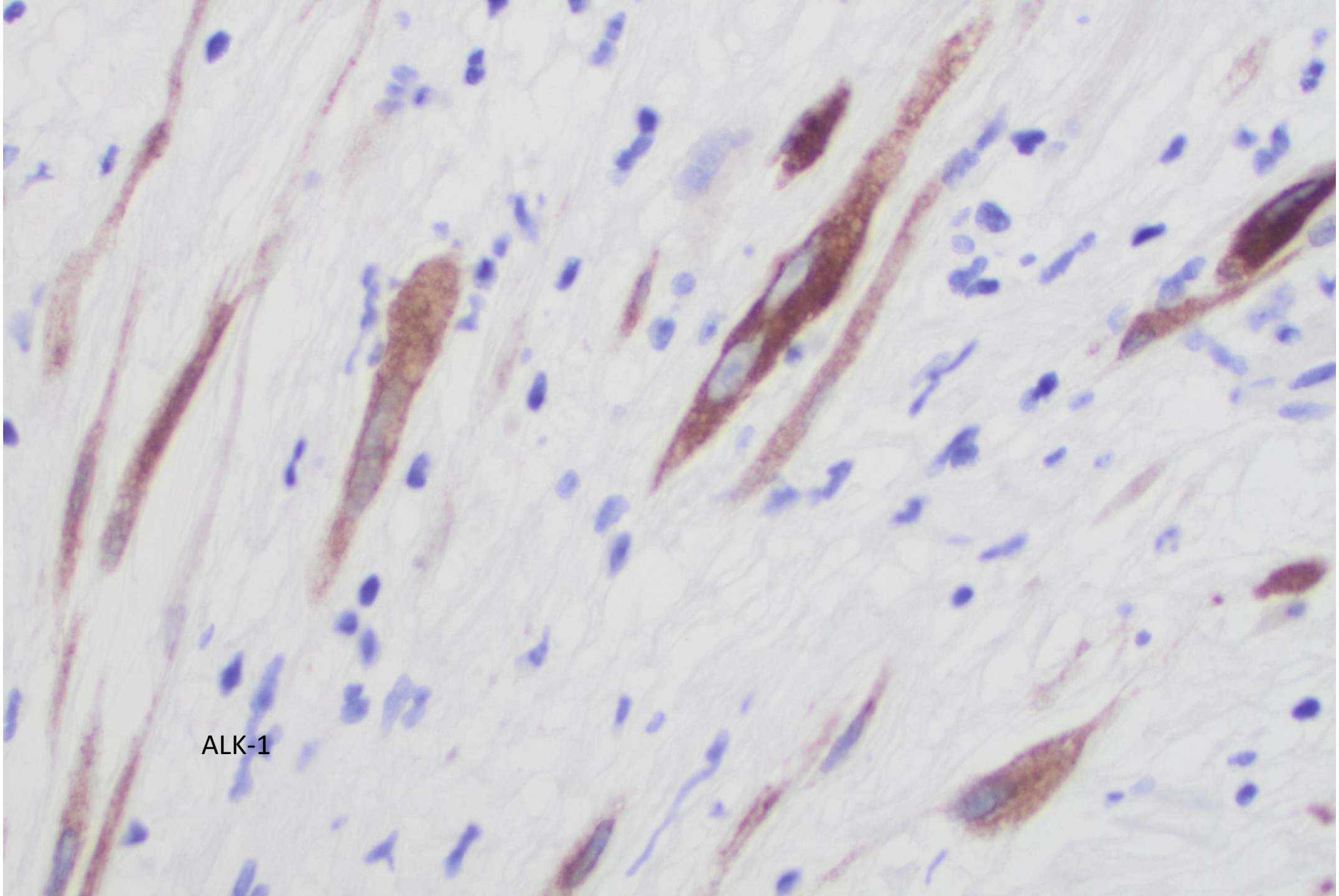

CD10

DIAGNOSIS?


ALK-1


ALK-1

Inflammatory Myofibroblastic Tumor (IMT)

- Rare in uterus (<100 cases reported)
- Usually premenopausal women (median age=38)
- Bleeding, Abdominal discomfort, malaise, fever are common
- >95% + for ALK IHC
- Correlates with alterations in ALK gene
- ALK rearrangements by FISH in 75%

Pathology

- Mean size=7.5 cm.
- Usually intramural-well circumscribed or pushing borders
- 3 main patterns: myxoid, fasicular, hyalinized
- Atypia usually minimal but may be present, =/- mitoses
- Lymphoplasmacytic infiltrate
- DDX- Leiomyoma, myxoid smooth muscle tumors, Leiomyosarcoma

IHC

- Frequently positive for SMA, Desmin, Caldesmon, CD10
- Negative for Keratin, S100, CD34, Ckit
- Wild-type p53
- Granular cytoplasmic positivity for ALK is highly sensitive and specific

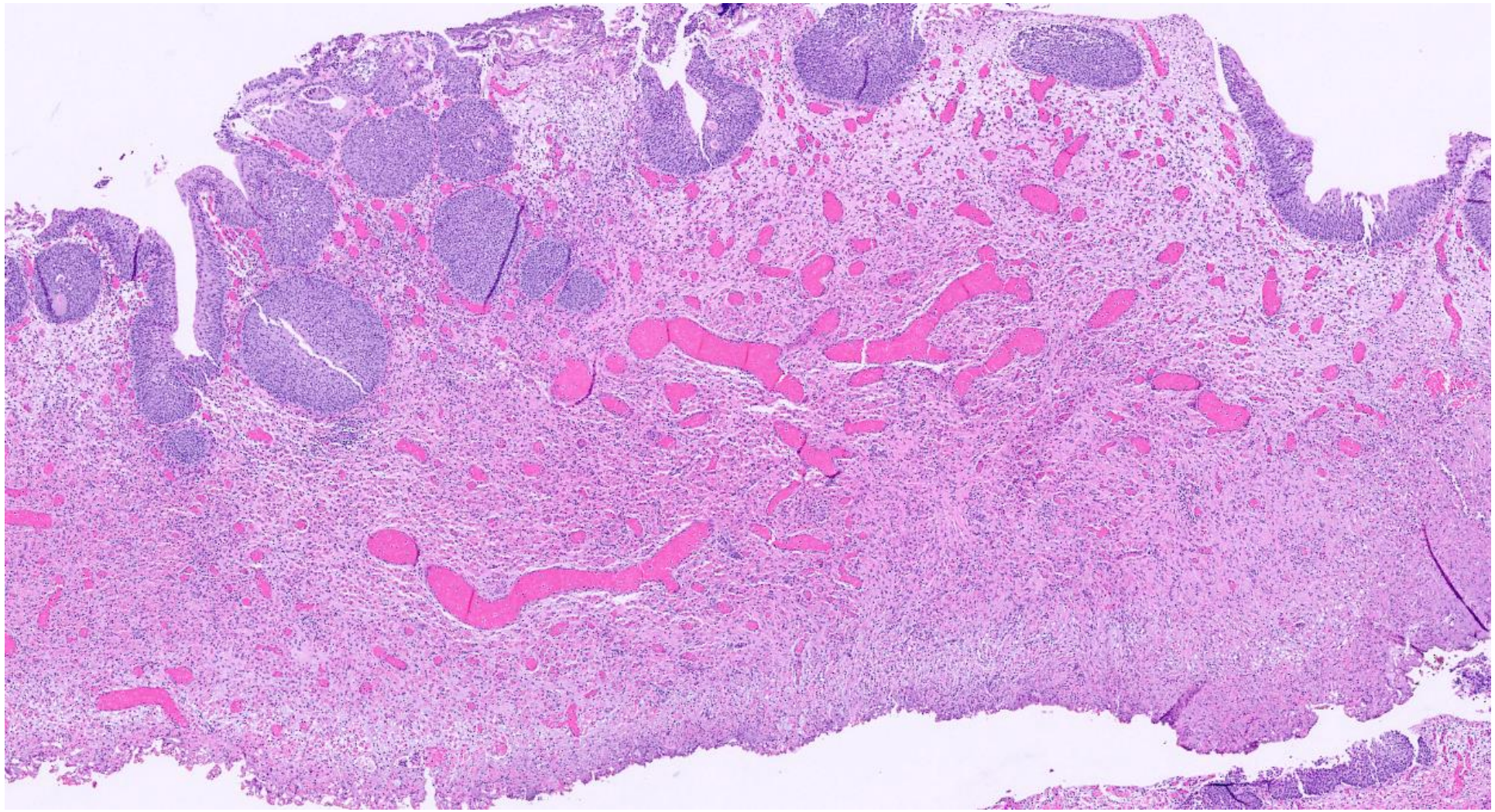
Prognosis

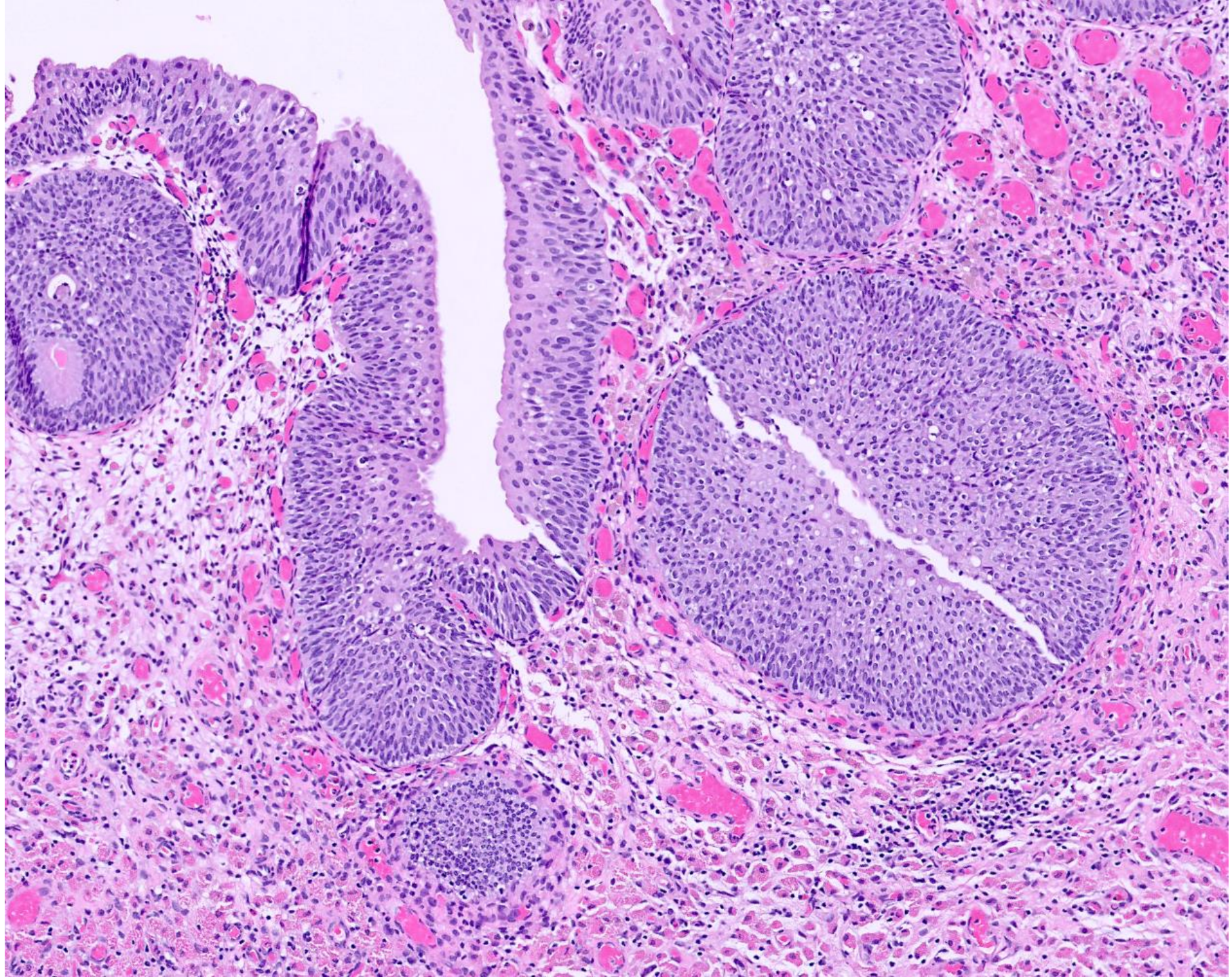
- Most are benign-confined to uterus
- Rarely recurrence or extrauterine spread
- Necrosis, size >7cm, mod-severe atypia, high mitotic rate, LVI have been associated with more aggressive clinical course
- ALK rearrangements may respond to TKI

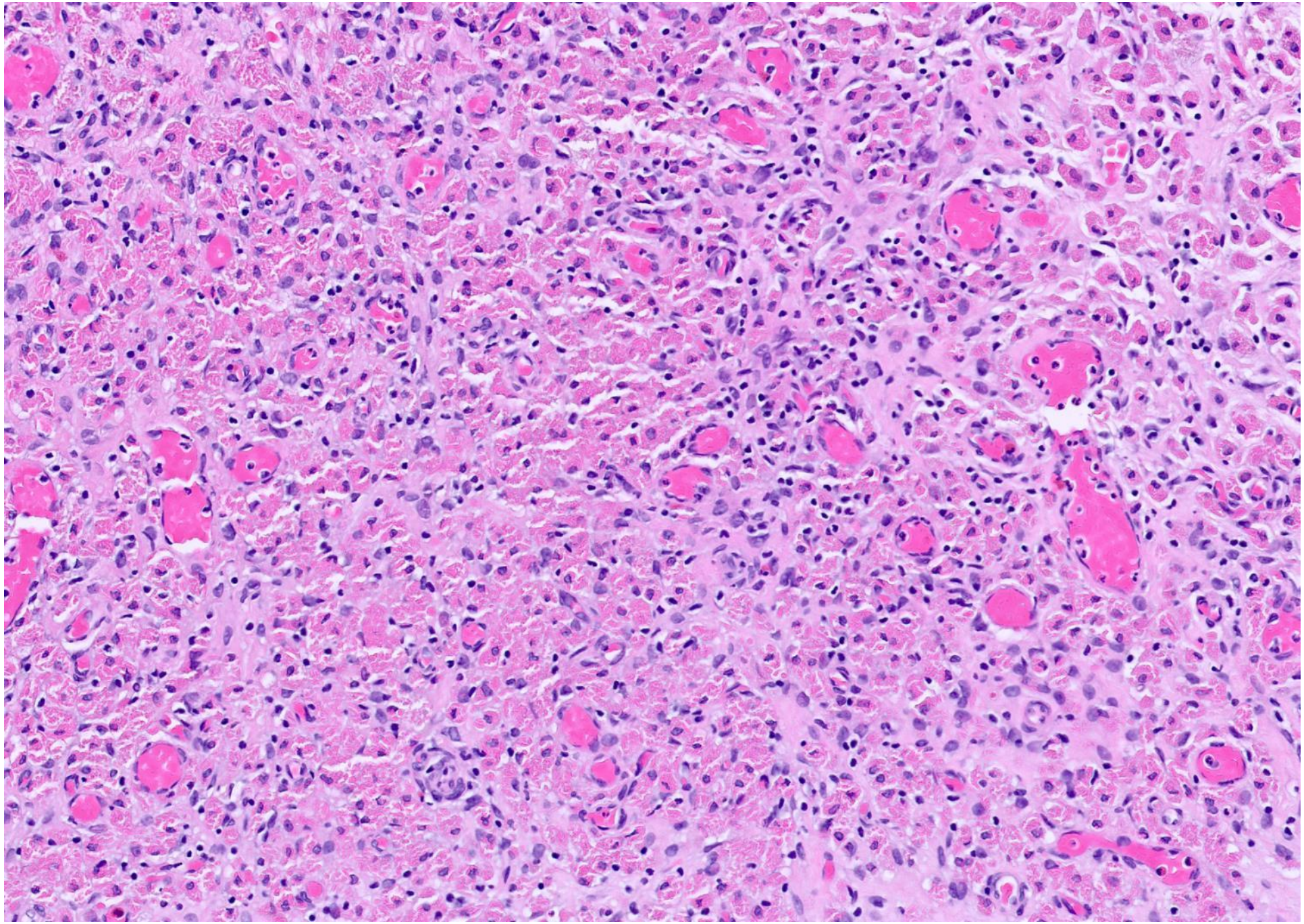
25-1108

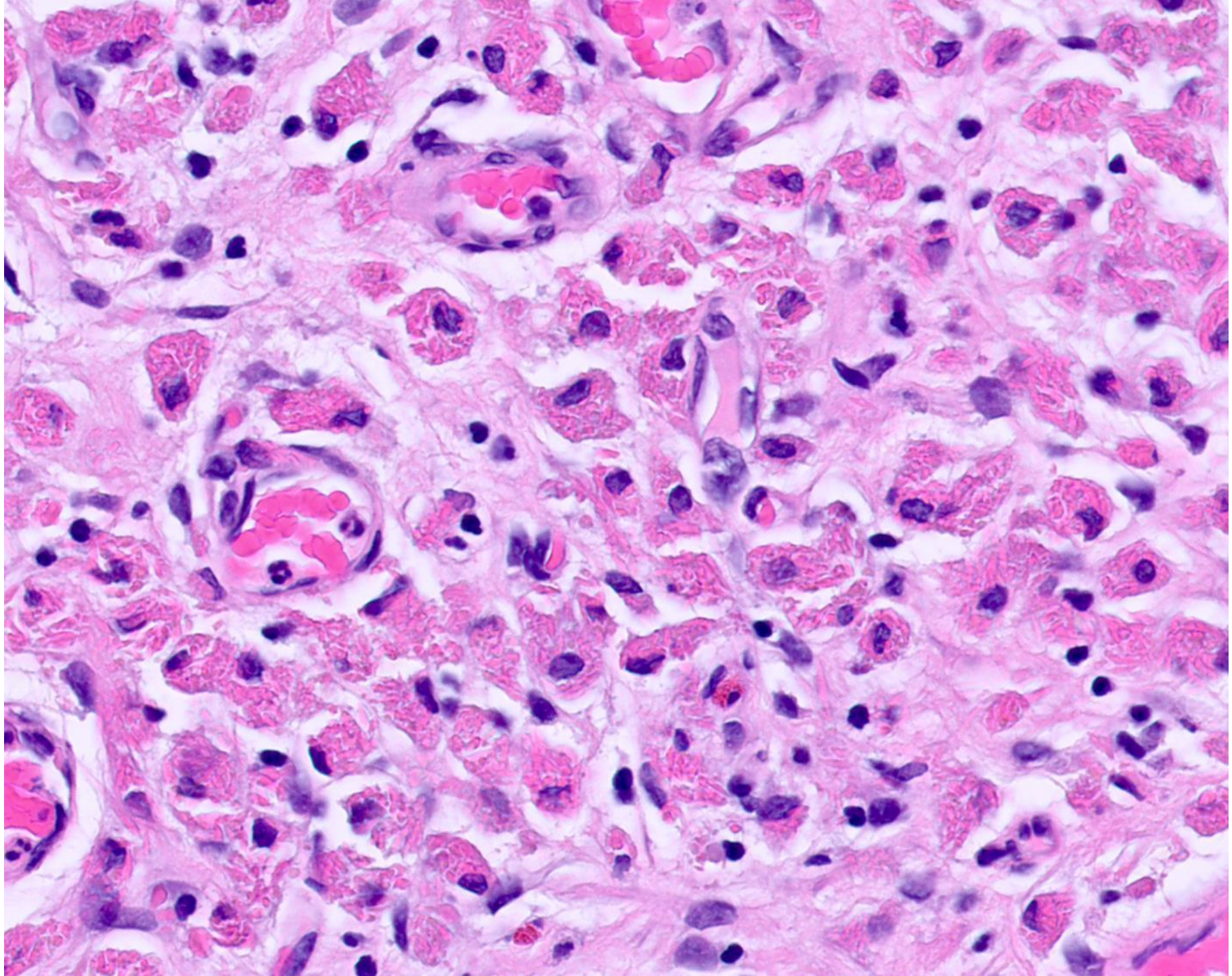
Salima Ali, Emily Chan; Stanford

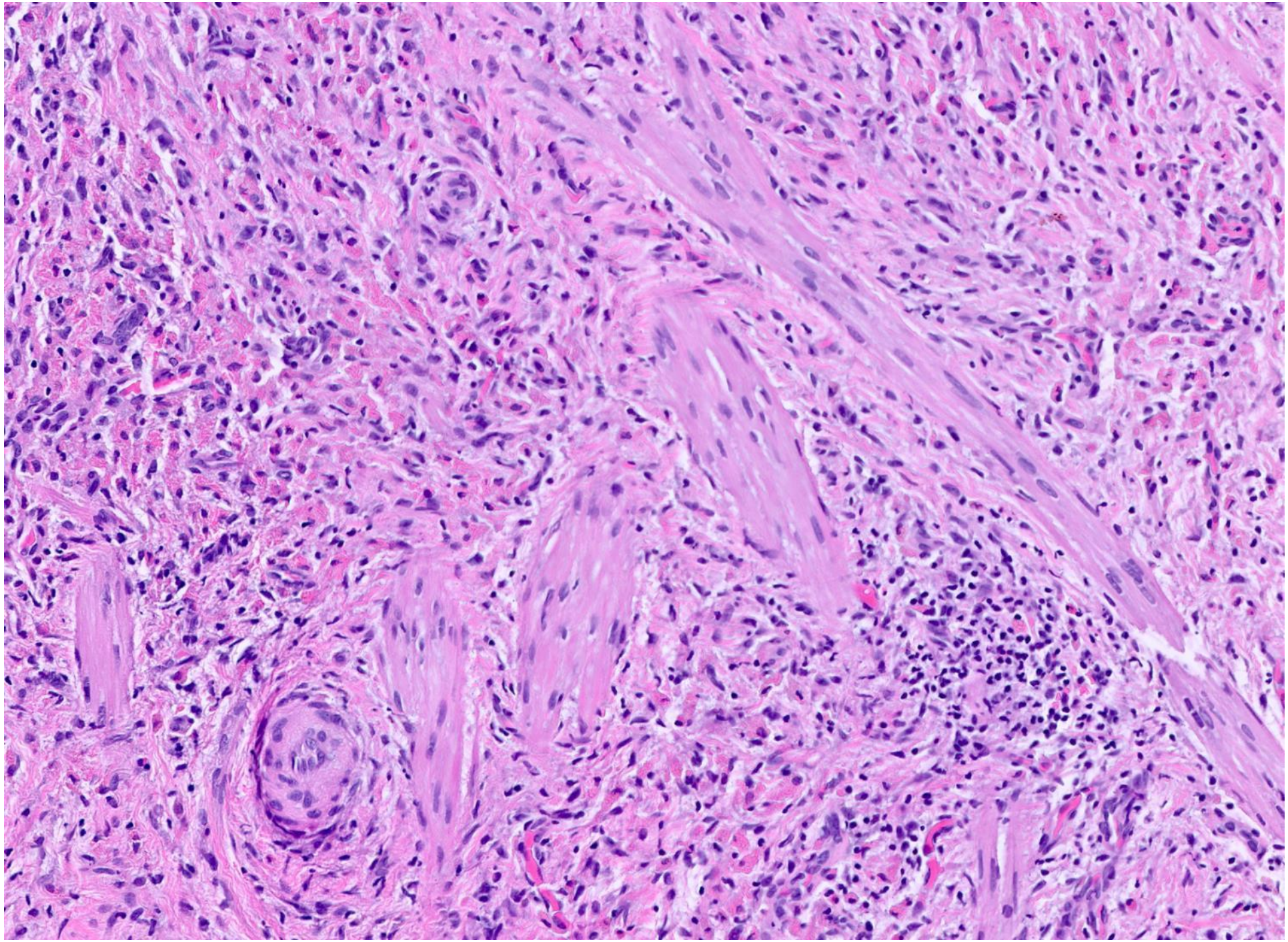
60s-year-old man with hematuria and multiple low-lying elevated tumors on the right and left lateral walls and dome, up to 4 cm, TURBT

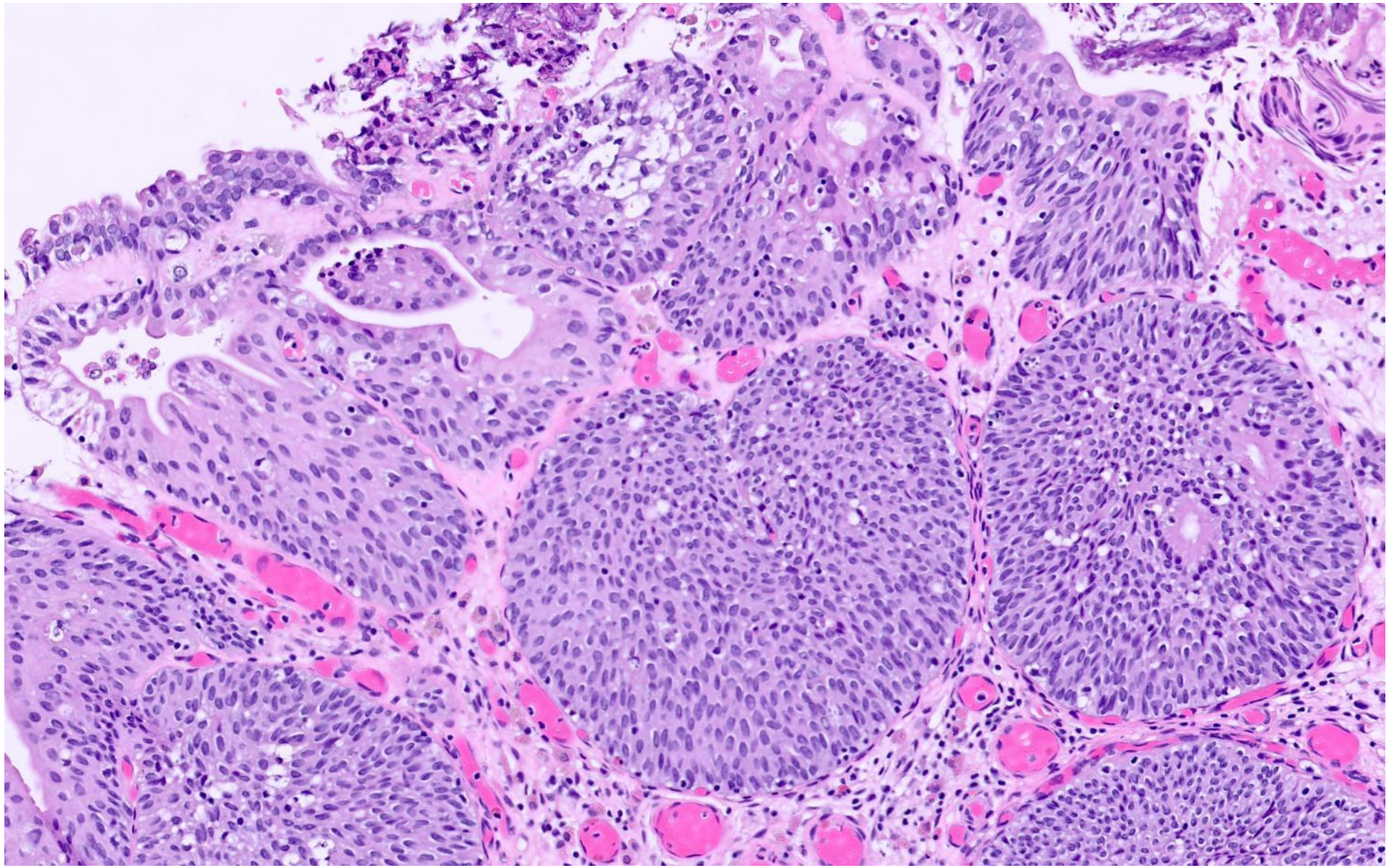


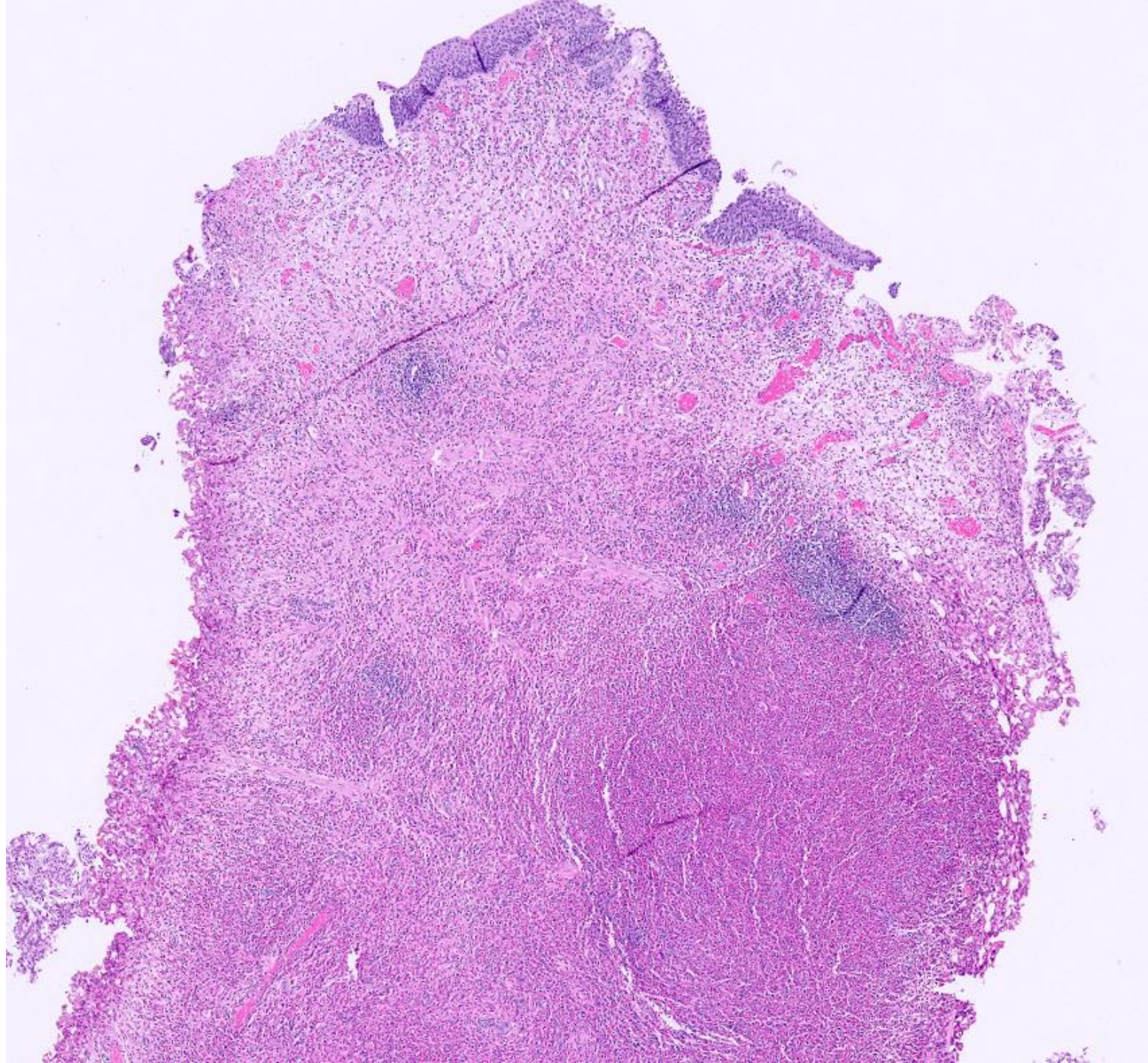


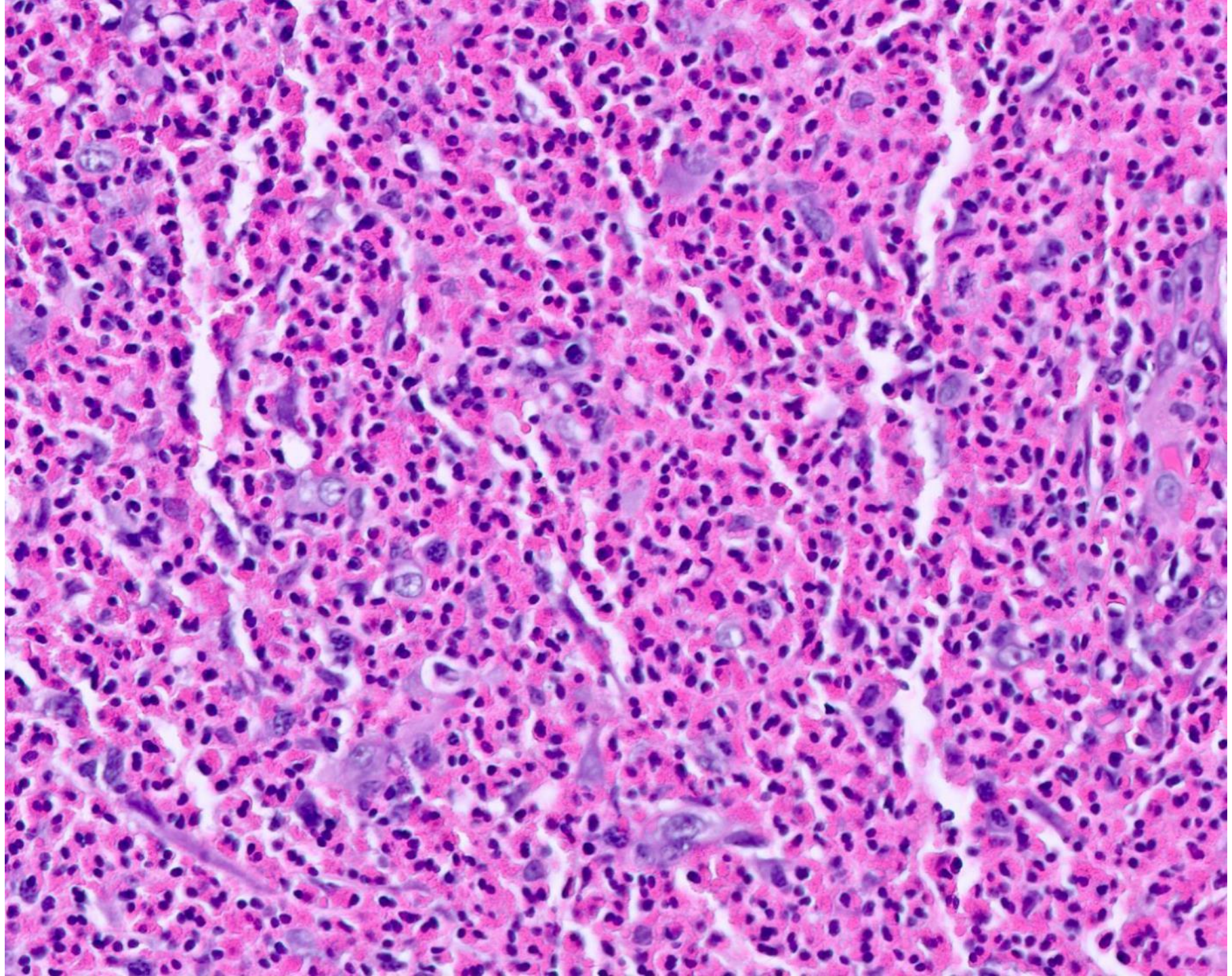




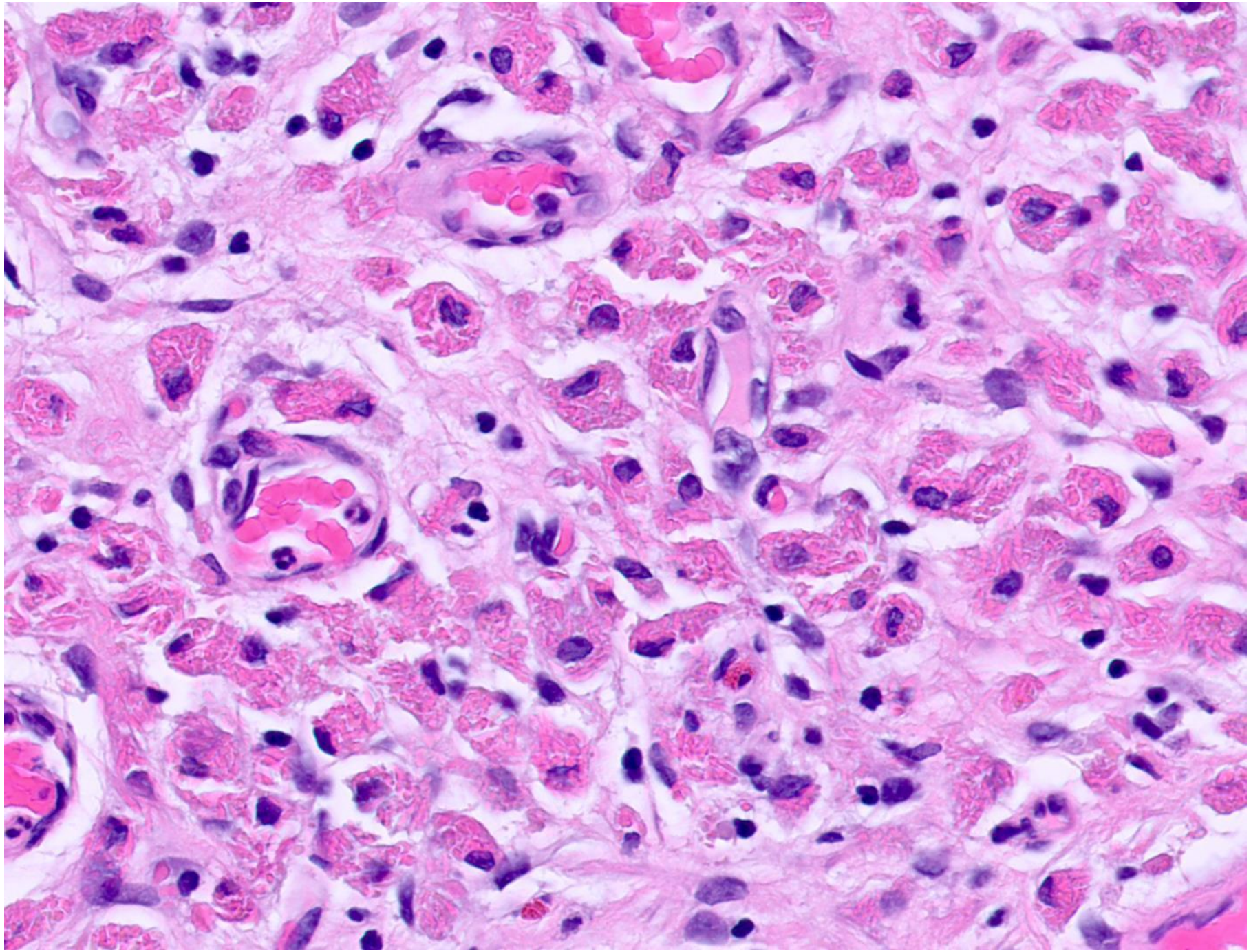








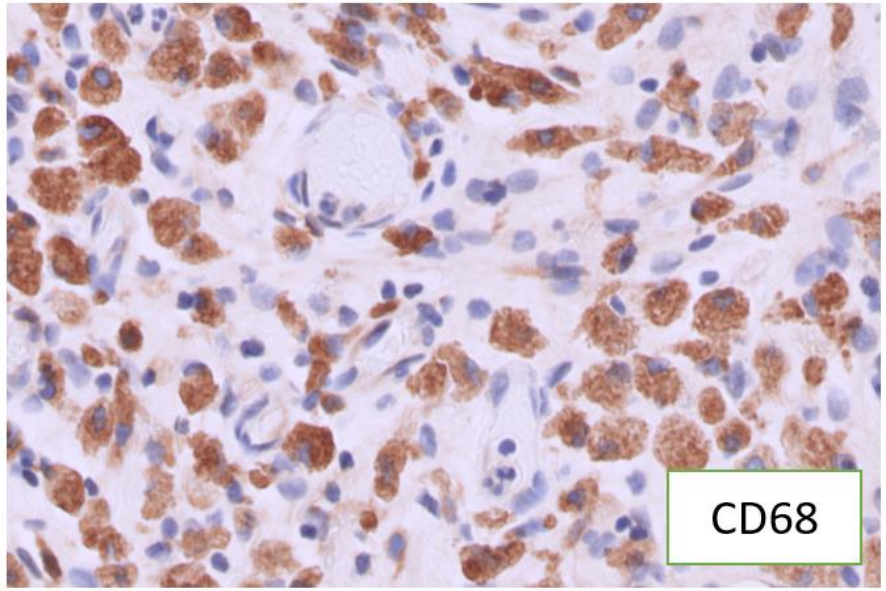
DIAGNOSIS?

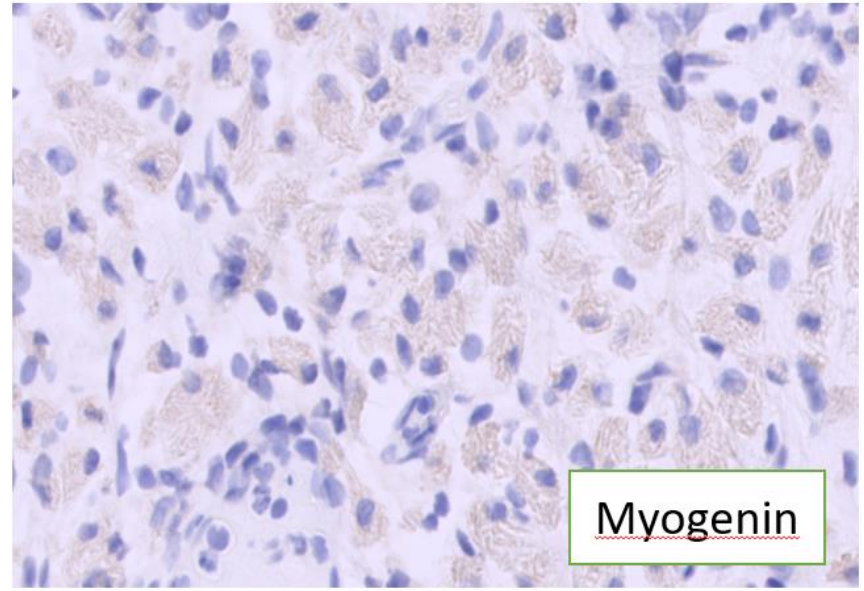


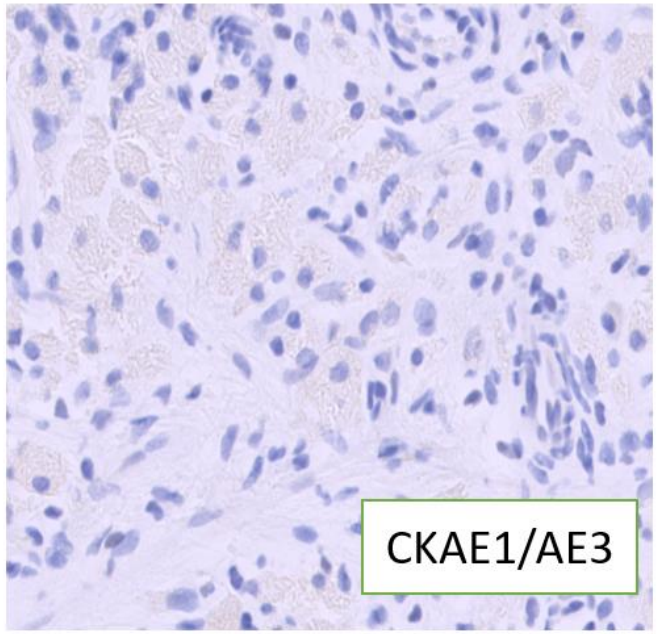
Differential Diagnosis

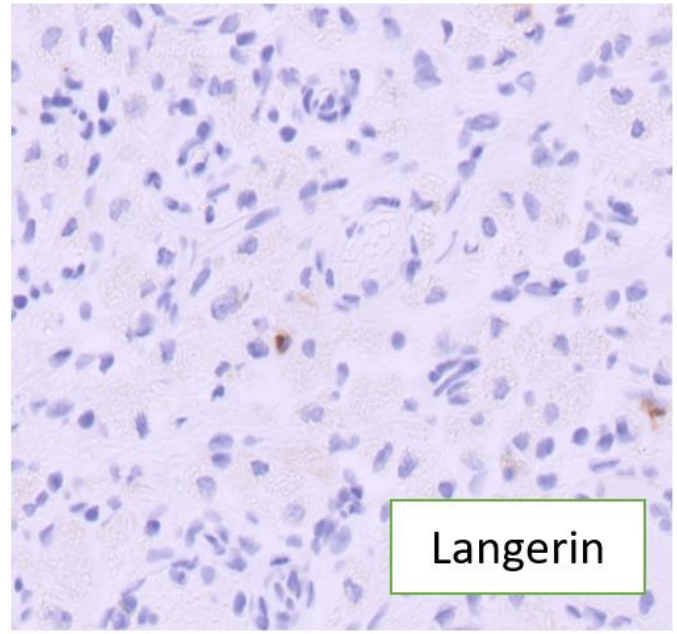
- Langerhan cell histiocytosis
- Rosai Dorfman Disease
- Granular cell tumor
- Rhabdomyoma
- Crystal storing histiocytosis

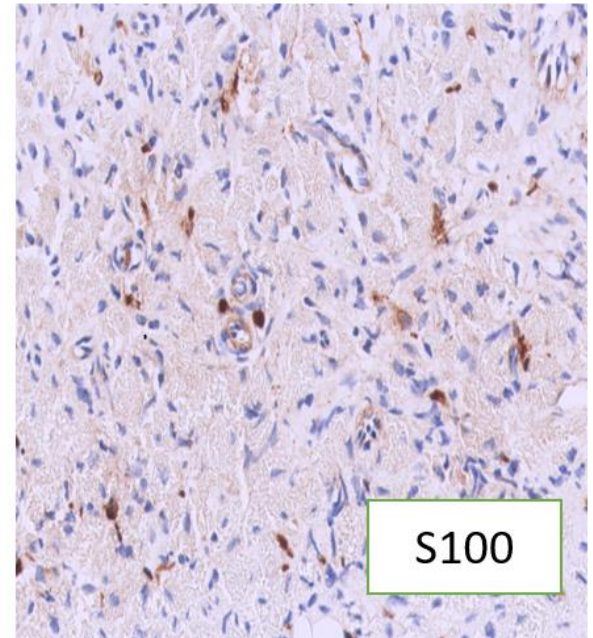
IPOX











Diagnosis

Crystal Storing Histiocytosis (CSH)

Crystal Storing Histiocytosis (CSH)

- Rare lesion composed of histiocytes containing intracellular cytoplasmic crystals.
- Clinical presentation: 24.31% (44/181) incidental finding of a mass or swelling.
- Other symptoms vary depending on organ involved.
- Can be localized and affect one organ or multiple and affect several organs.

Diagnostics (Basel). 2023 Jan 11;13(2):271. doi: 10.3390/diagnostics13020271

Crystal-Storing Histiocytosis: The Iceberg of More Serious Conditions

Mousa Mobarki [1,*], Alexandra Papoudou-Bai [2], Jean Marc Dumollard [3], Abdulaziz H Alhazmi [4], Shaqraa Musawi [5], Mohammed Ali Madkhali [6], Khalid Y Muqri [7], Michel Péoc'h [3], Georgia Karpathiou [3]

Editor: Gustavo Baldassarre

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PMCID: PMC9858286 PMID: 36673081

Conditions associated with CSH

Conditions	Case, *n* (%)
Neoplastic conditions	138
Multiple myeloma	47 (34.06%)
Lymphoma (MZL, LPL, DLBCL, MCL, FL)	62 (44.9%)
MGUS	16 (11.59%)
Waldenström macroglobulinemia	6 (4.35%)
Plasmocytoma	4 (2.90%)
Others	
- Systemic mastocytosis	2 (1.45%)
- Myelodysplastic syndrome	1 (0.72%)

Mobarki M, Papoudou-Bai A, Dumollard JM, Alhazmi AH, Musawi S, Madkhali MA, Muqri KY, Péoc'h M, Karpathiou G. Crystal-Storing Histiocytosis: The Iceberg of More Serious Conditions. Diagnostics (Basel). 2023 Jan 11;13(2):271. doi: 10.3390/diagnostics13020271. PMID: 36673081; PMCID: PMC9858286.

Non-neoplastic conditions	19
Inflammatory - Crohn disease, Plasma cell granuloma, Plasmacytic conjunctivitis	3 (15.7%)
Auto-immune disease -Sjogren's syndrome, Rheumatoid arthritis	6 (31.5%)
Infection - *Helicobacter pylori, strongyloides*	5 (26.3%)
Drug - Clofazimine, Carbamazepine	5 (26.3%)

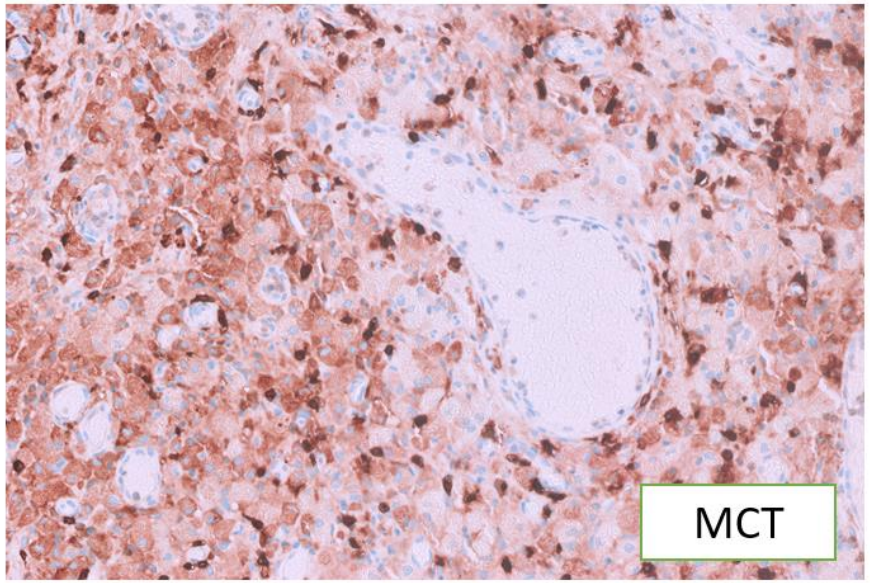
Mobarki M, Papoudou-Bai A, Dumollard JM, Alhazmi AH, Musawi S, Madkhali MA, Muqri KY, Péoc'h M, Karpathiou G. Crystal-Storing Histiocytosis: The Iceberg of More Serious Conditions. Diagnostics (Basel). 2023 Jan 11;13(2):271. doi: 10.3390/diagnostics13020271. PMID: 36673081; PMCID: PMC9858286.

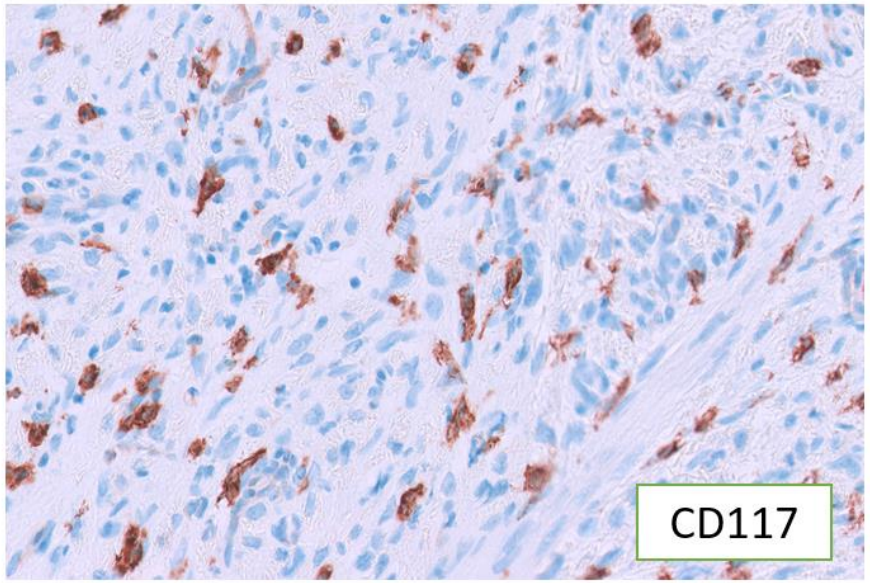
Crystals in CSH

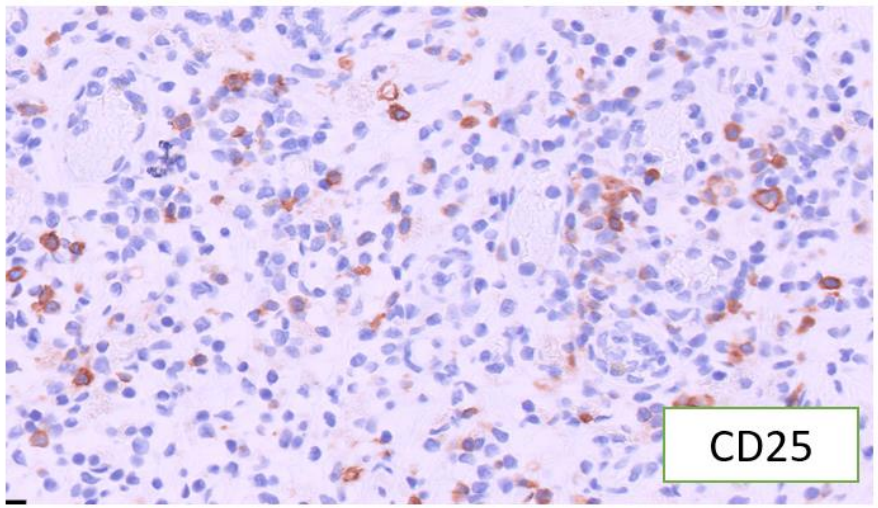
Immunoglobulin deposits	**Case, *n* (%)** **127**
Monoclonal	115 (90.55%)
- Kappa light chain	90 (78.26%)
- Lambda light chain	22 (19.13%)
Polyclonal	12 (9.45%)

Non-immunoglobulin deposits	**9**
Drug	
- Clofazimine, carbamazepine	5 (55.5%)
Environmental foreign particles	
- Silicon, Asbestos	2 (22.22%)
Charcot–Leyden crystals	2 (22.22%)

Etiology/crystal type in our case?







Negative in crystals

Kappa

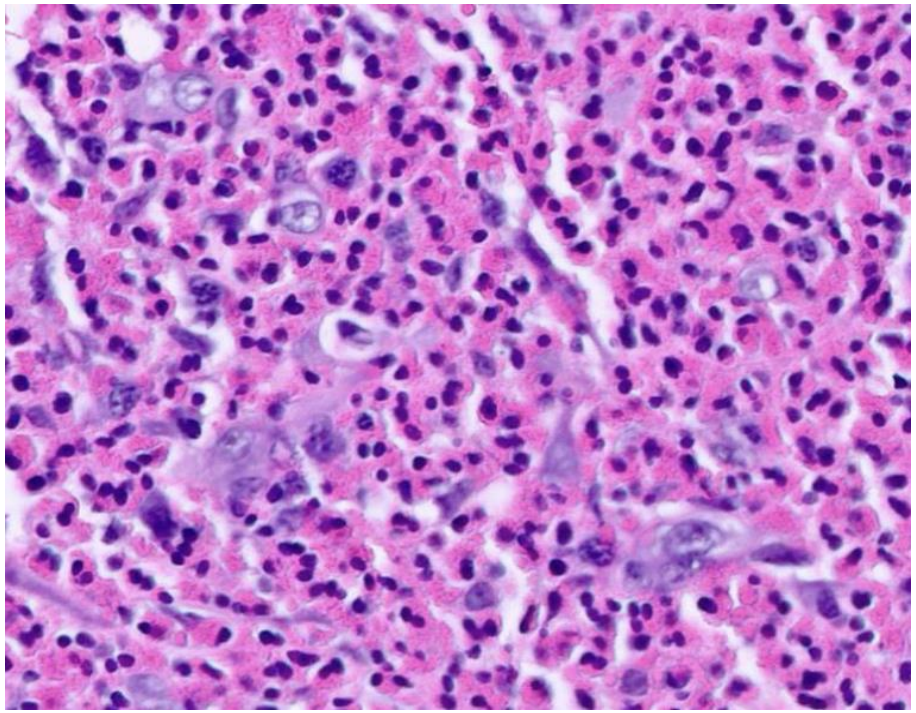
Lambda

IgG

IgM

IgA

- HEME-STAMP NGS: No pathogenic alterations, including no *KIT* alterations.
- Lymphoma workup: Negative



Charcot-leyden type crystals?

Take home points- Crystal Storing Histiocytosis

- Rare lesion
- **Recognition of morphology** (eosinophilic crystals within histiocytes) is key to diagnosis.
- Should **prompt workup** for an associated clonal hematologic disorder.
- **Clinical correlation** to rule out other etiologies (drugs, autoimmune, inflammatory)