# Southbay January 2024

# Disclosures
# January 22, 2024 (“February 2024” meeting)

**Presenters/Faculty:**
Andrew Xiao, MD
Poonam Vohra, MD
Christina Su, MD
Emily Chan, MD
Garrett Chan, MD
Cornelia Ding, MD
Lixia Bai, MD
Megan Troxell, MD, PhD
Natalia Sanchez, MD
Sarah Umetsu, MD
Tyler Jankowski, MD
Ankur Sangoi, MD
Rick Hildebrandt, MD
Yang Hu, MD
David Bingham, MD
Xiaoming Zhang, MD

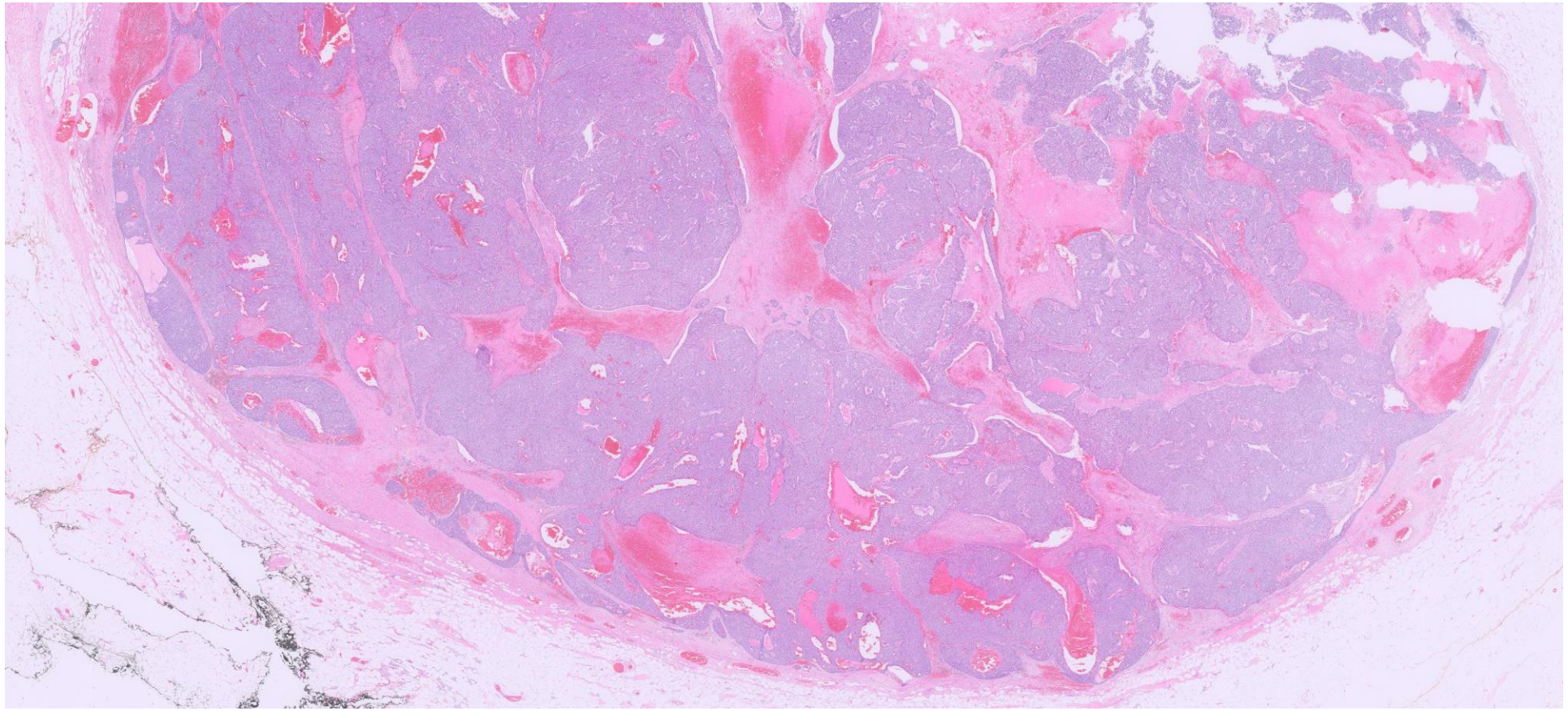
**Activity Planners/Moderator:**
Kristin Jensen, MD
Megan Troxell, MD, PhD
Dave Bingham, MD

24-0101

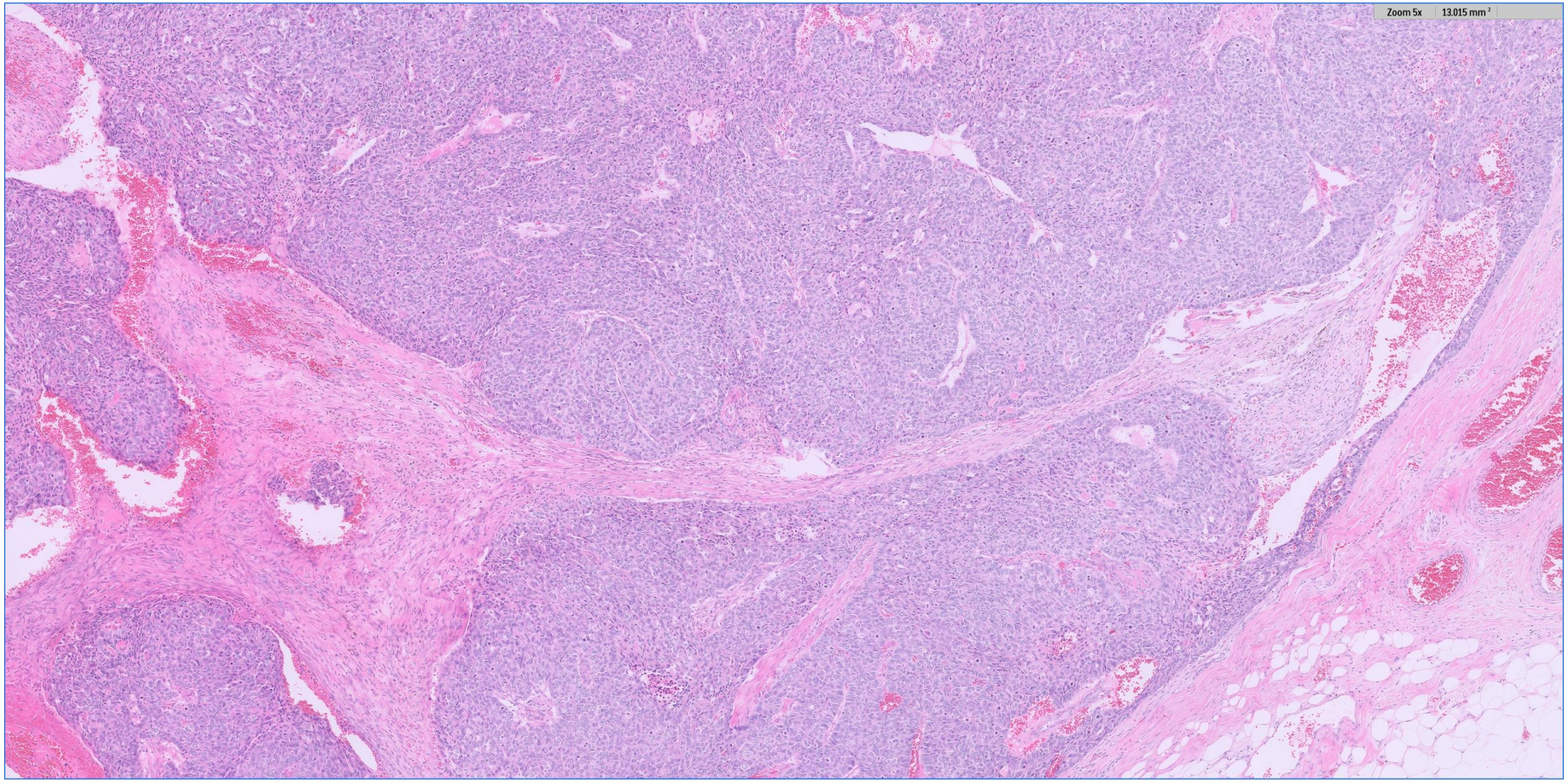
**Andrew Xiao and Poonam Vohra; UCSF**

71 year old female with a well-circumscribed right upper quadrant breast mass found on screening mamography. She had a core biopsy and subsequently underwent right partial mastectomy. Gross evaluation revealed a 27 mm, well-circumscribed, encapsulated, yellow-hemorrhagic, soft and friable mass.

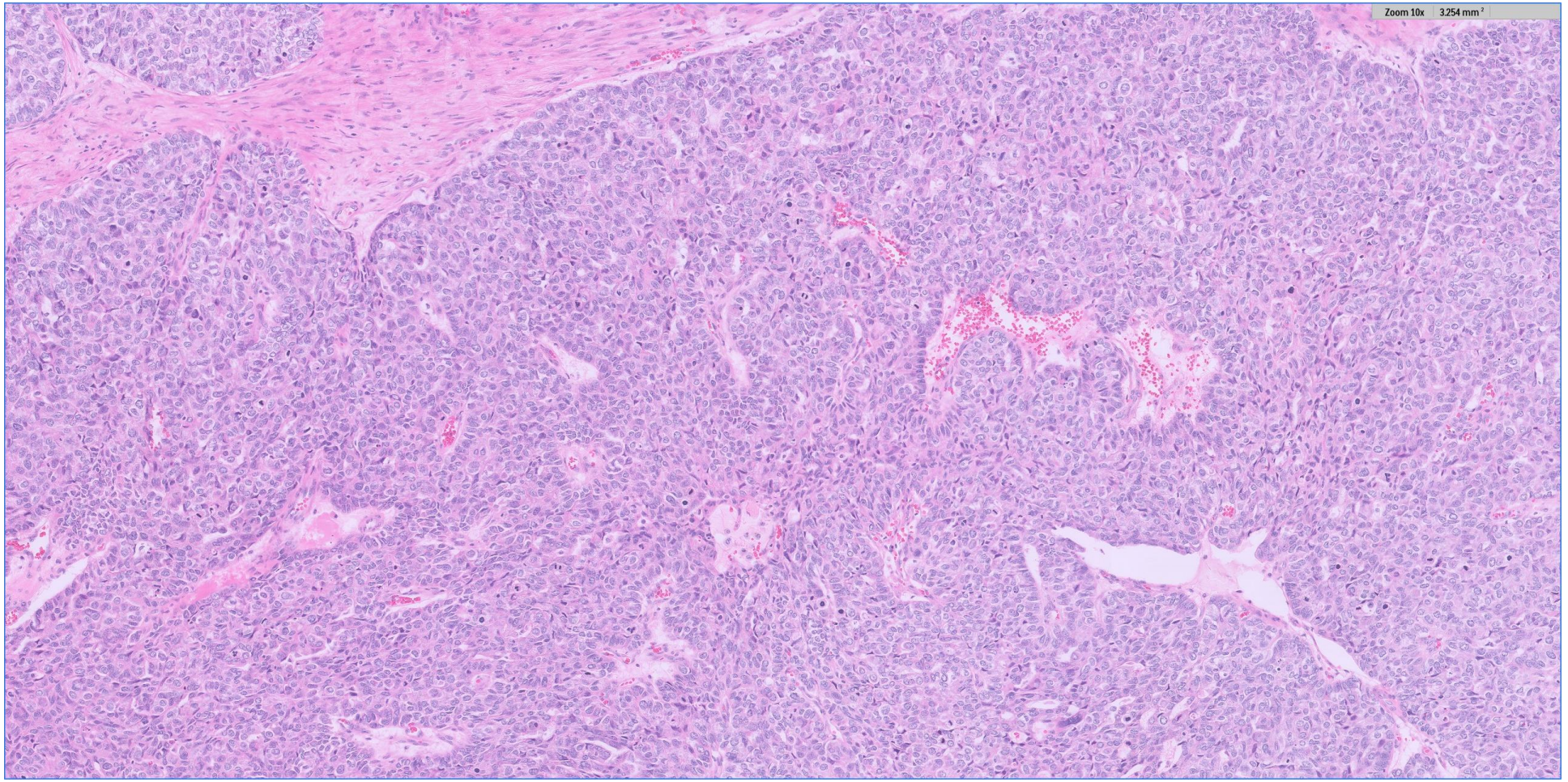
Zoom: 1x



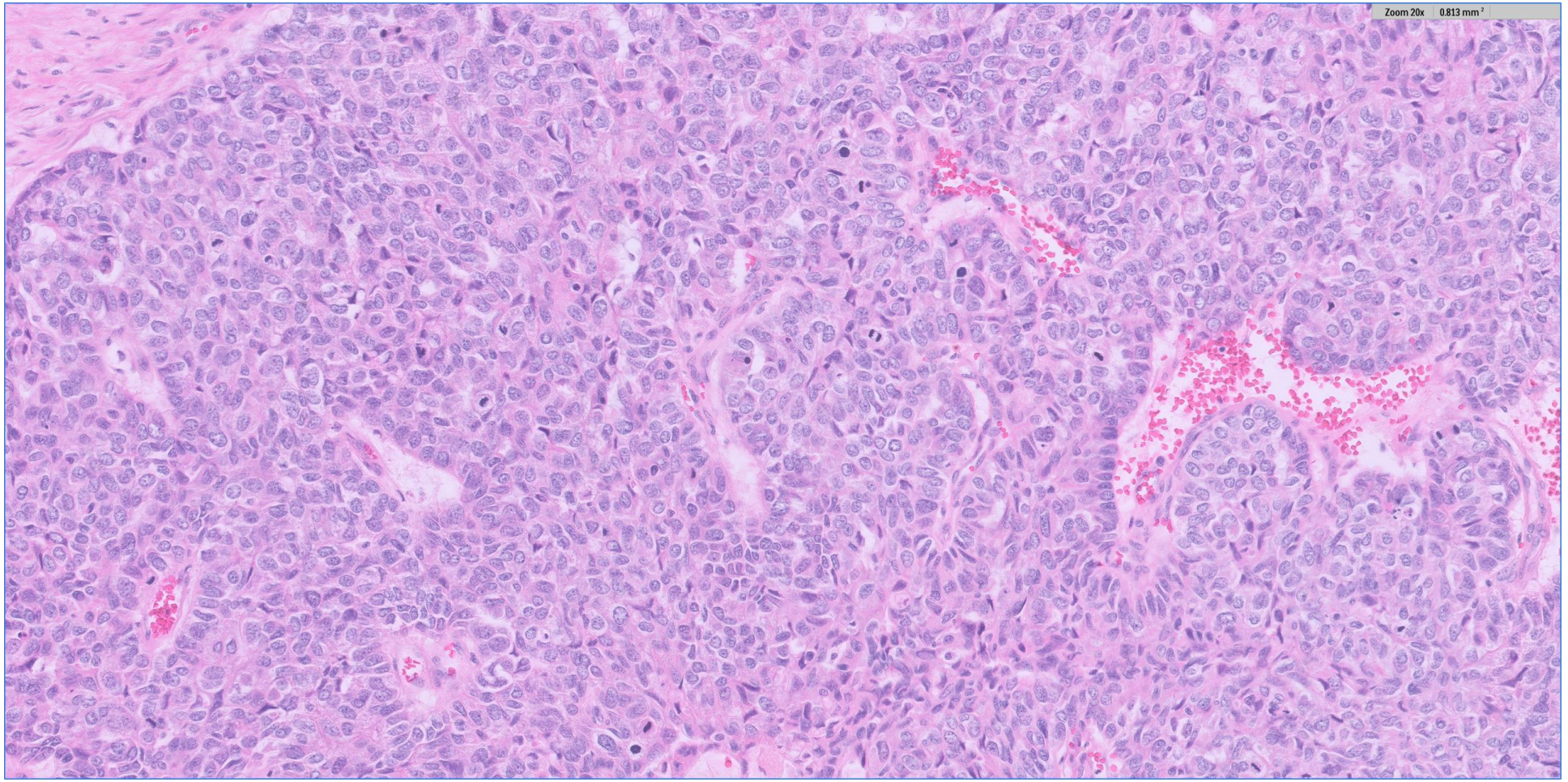
Zoom: 5x



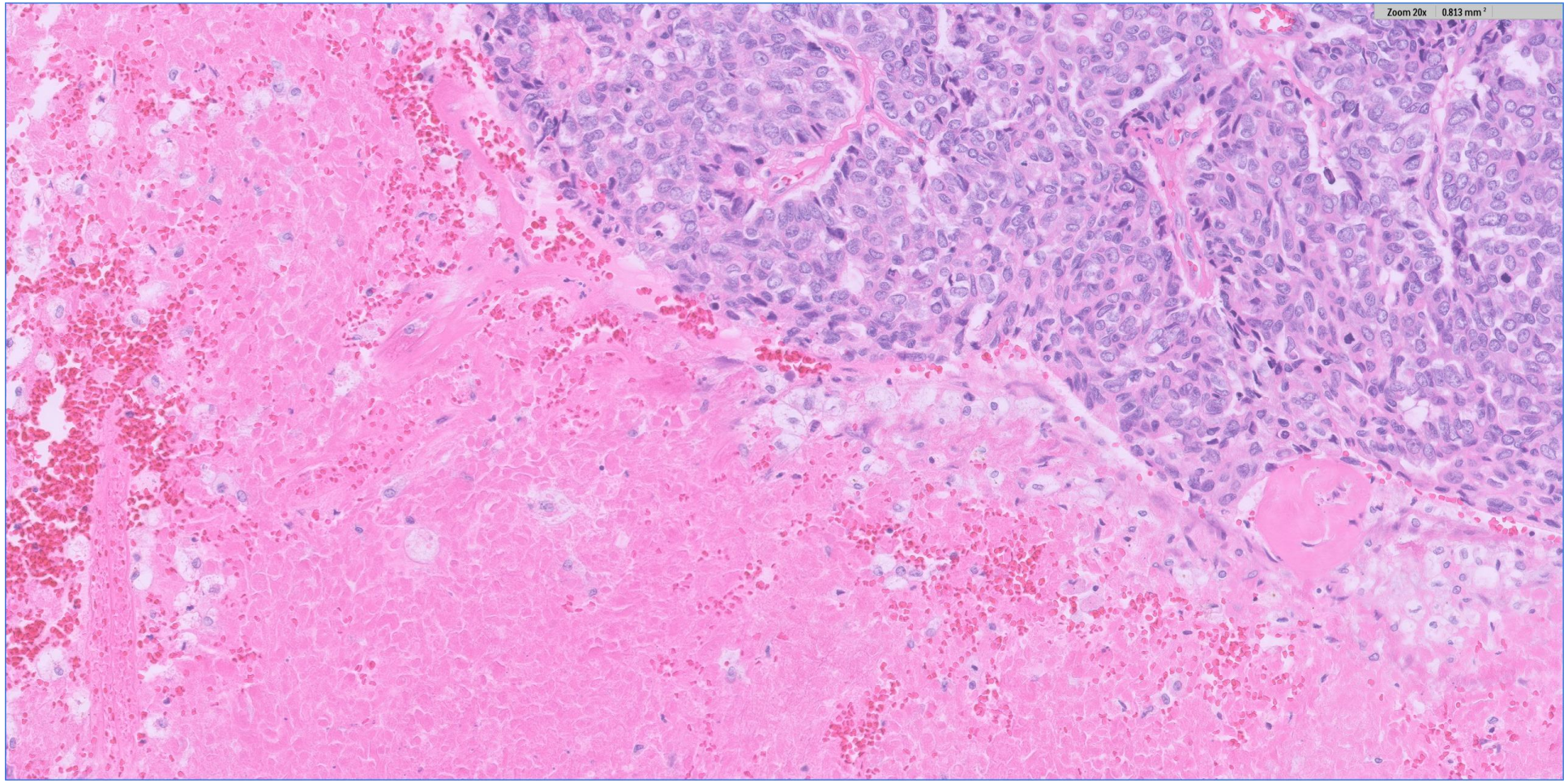
Zoom: 10x



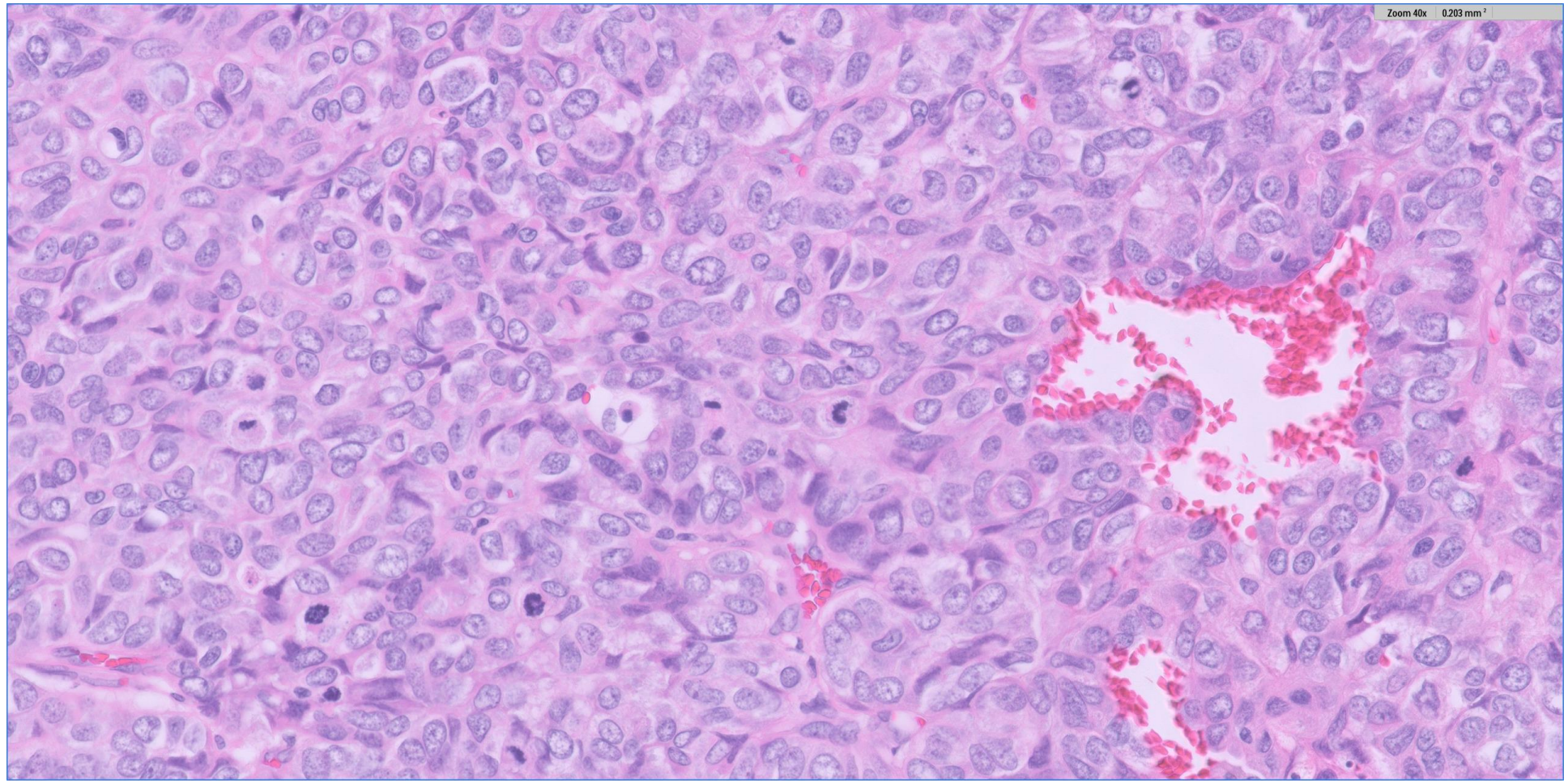
Zoom: 20x



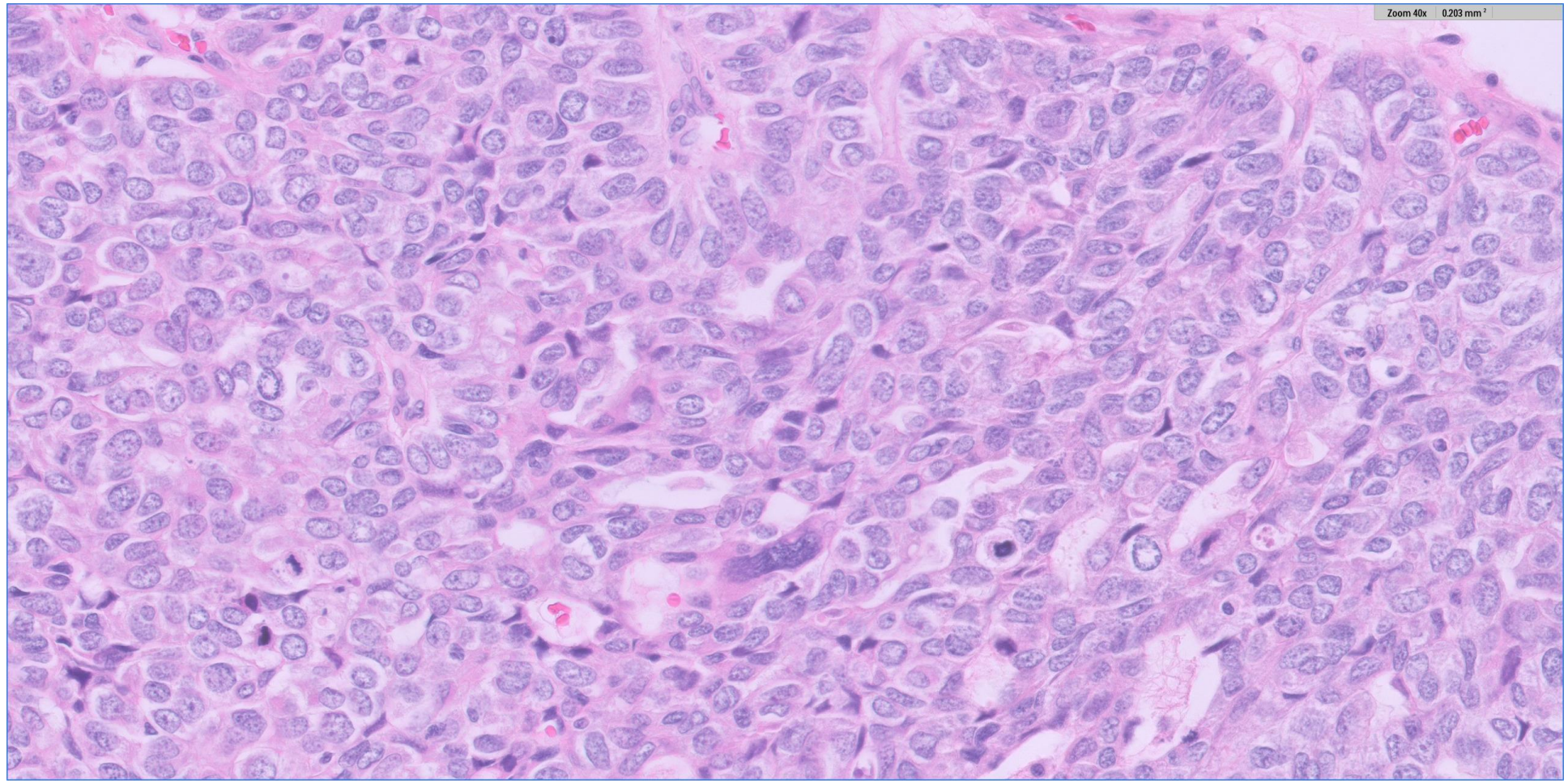
Zoom: 20x



Zoom: 40x



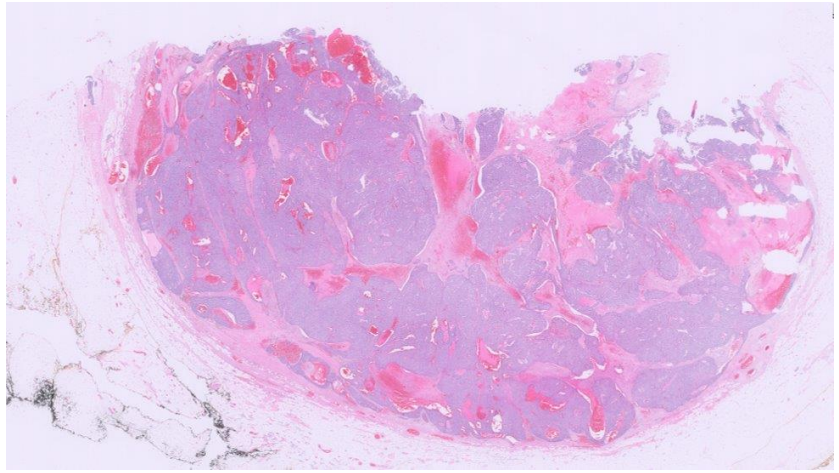
Zoom: 40x



# DIAGNOSIS?

# Histologic Recap

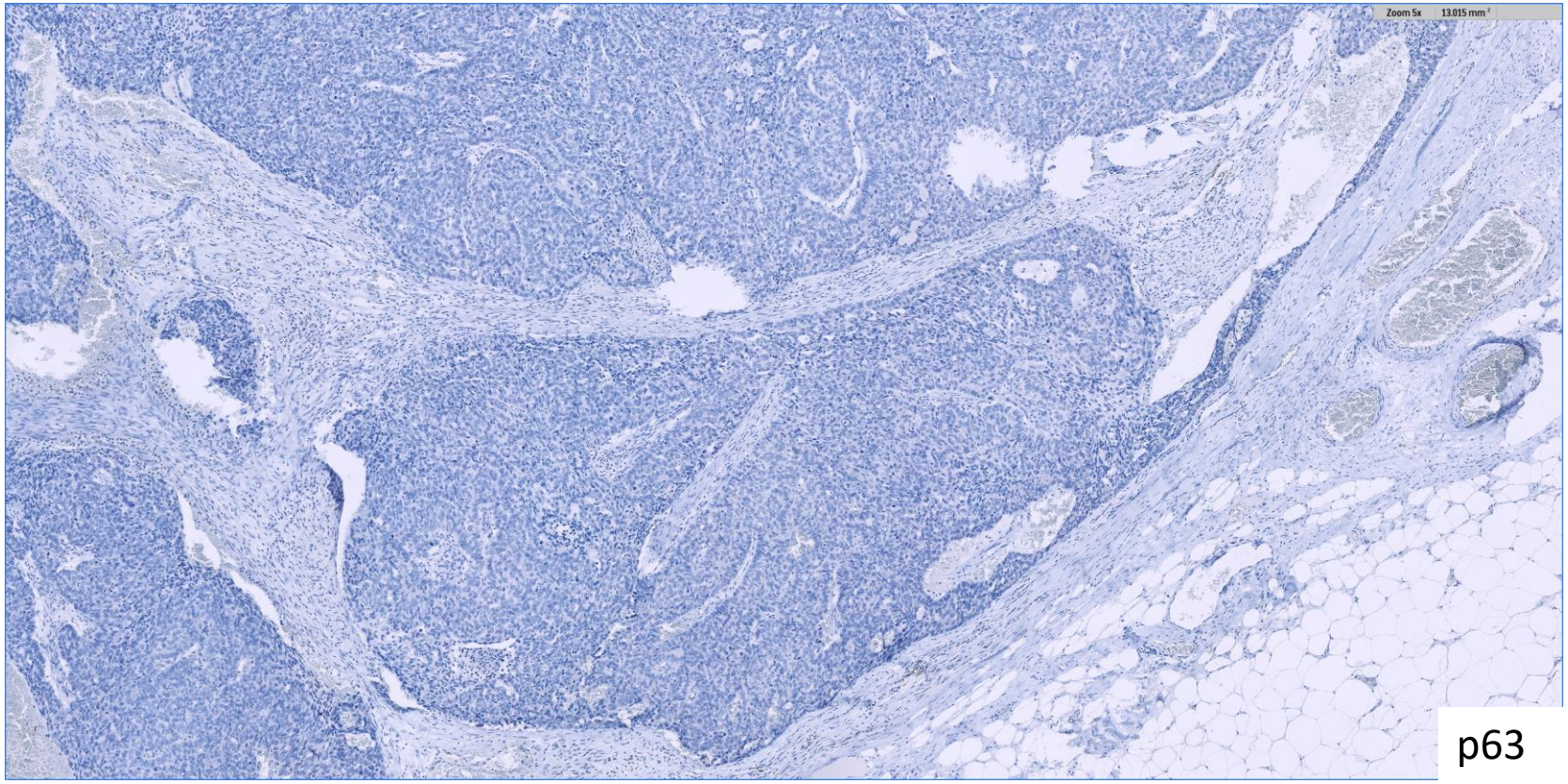
- Singular nodule surrounded by fibrous, well-circumscribed capsule
  - Cystic-appearing space filled with blood and necrosis
  - No frank stromal invasion
- Solid and papillary growth patterns
  - Papillae covered by stratified population of columnar epithelial cells
  - High nuclear grade
  - Increased mitotic rate



# Differential Diagnosis

- Ductal carcinoma in situ, papillary pattern
- Solid papillary carcinoma
- Encapsulated papillary carcinoma (EPC)
- Large duct papilloma

# IHC Results

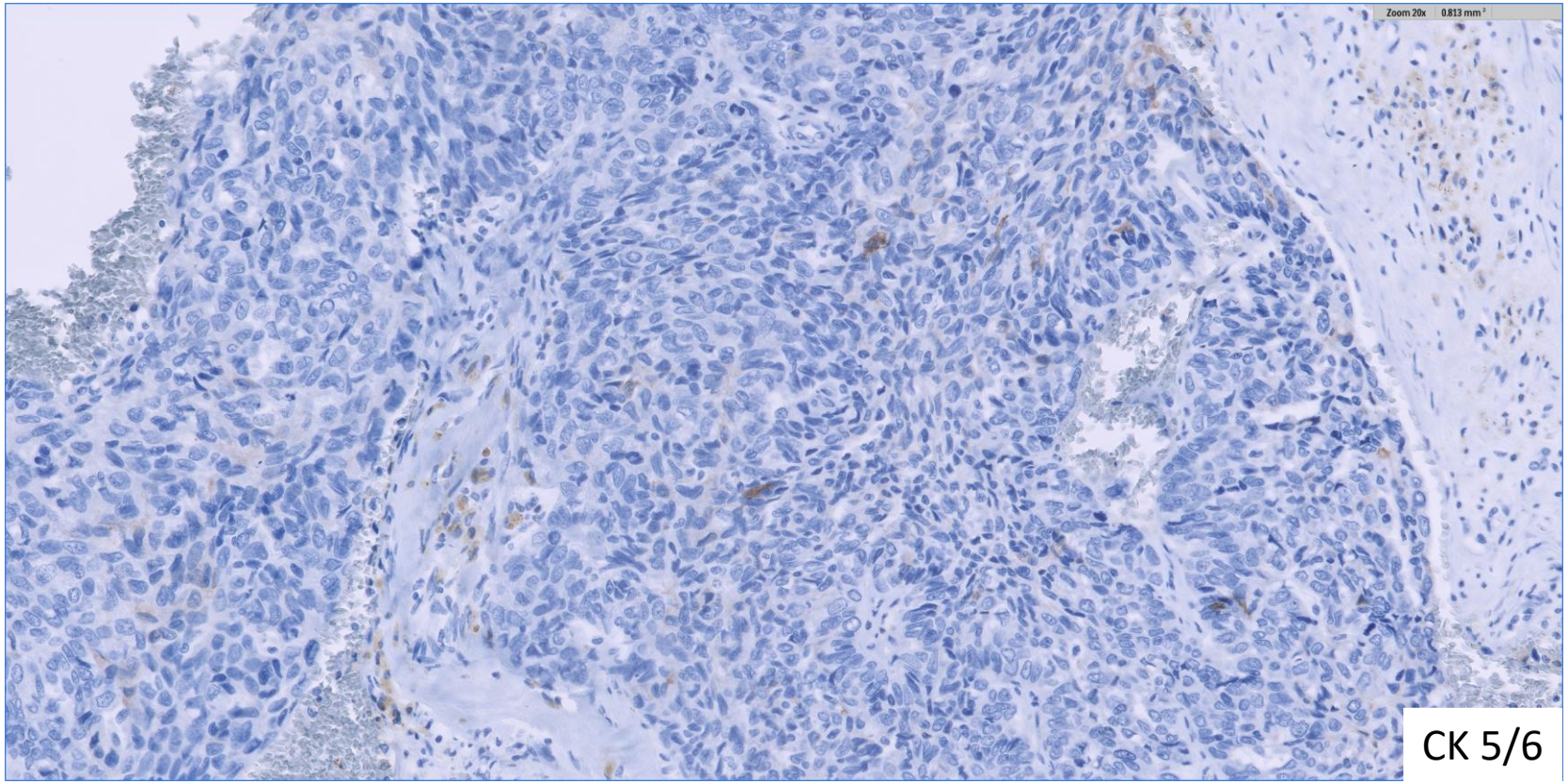



p63

Myoepithelial markers (p63 & SMM):

Negative for myoepithelial cells along papillae and around solid-papillary nodules

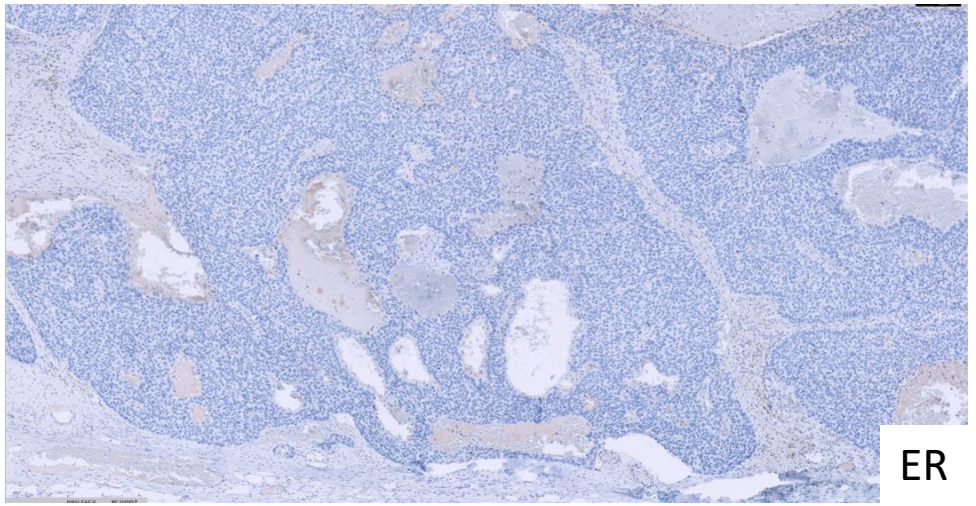
# IHC Results

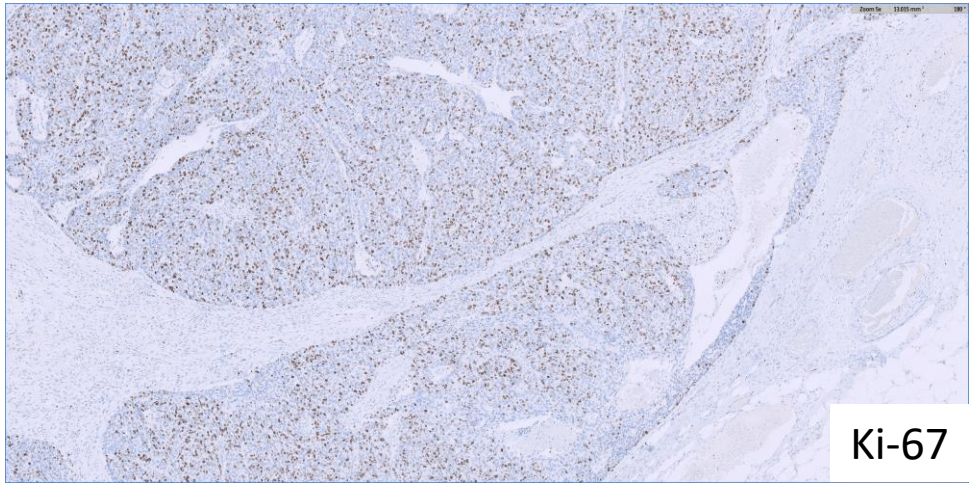



CK 5/6:
Rare staining in tumor cells. Negative along papillae and around solid-papillary nodules.

# Biomarkers

- ER: Negative
- PR: Negative
- HER2: Equivocal; 2+ staining intensity
  - HER2 FISH: Negative
- Ki-67: 40-50%


ER


Ki-67

# Diagnosis

- Invasive carcinoma, solid papillary pattern
  - (High-grade encapsulated papillary carcinoma)

- Let’s discuss EPC first …

# Encapsulated Papillary Carcinoma

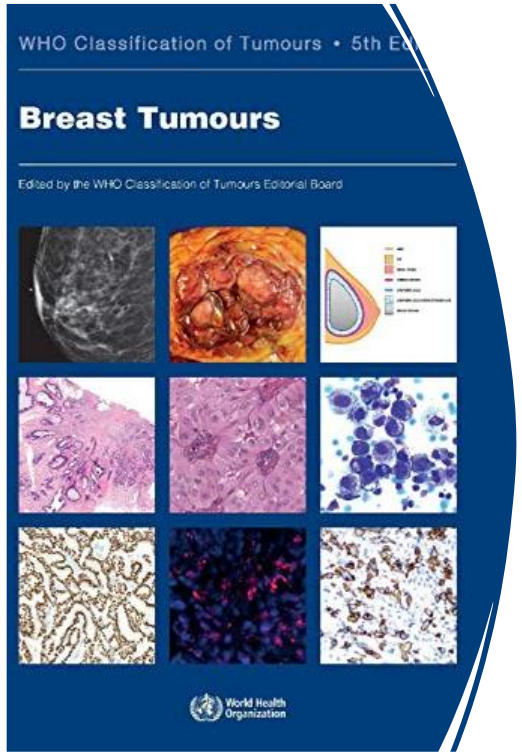
- Delicate papillae covered by **monotonous**, often stratified population of epithelial cells of **low-to-intermediate nuclear grade**

- Almost all are **ER/PR-positive & HER2-negative**

- **Myoepithelial cells absent** both within and surrounding papillary nodule(s), suggestive of an indolent invasive carcinoma

Tay TKY, Tan PH. Mod Pathol. 2021 Jun;34(6):1044-1061.

# WHO Classification of EPC




- Low grade invasive cancer with pushing border
- Indolent behavior and excellent prognosis
  - > 95% 10-year survival in the absence of associated invasive carcinoma
  - Local recurrence possible (7%)
  - Lymph node metastases rare (3%)
- Staged (Tis) and managed as an in-situ lesion (Current consensus)

Rakha EA, et al Histopathology. 2016 Jan;68(1):45-56.
Mulligan AM, O'Malley FP. Int J Surg Pathol. 2007 Apr;15(2):143-7.

Histopathology

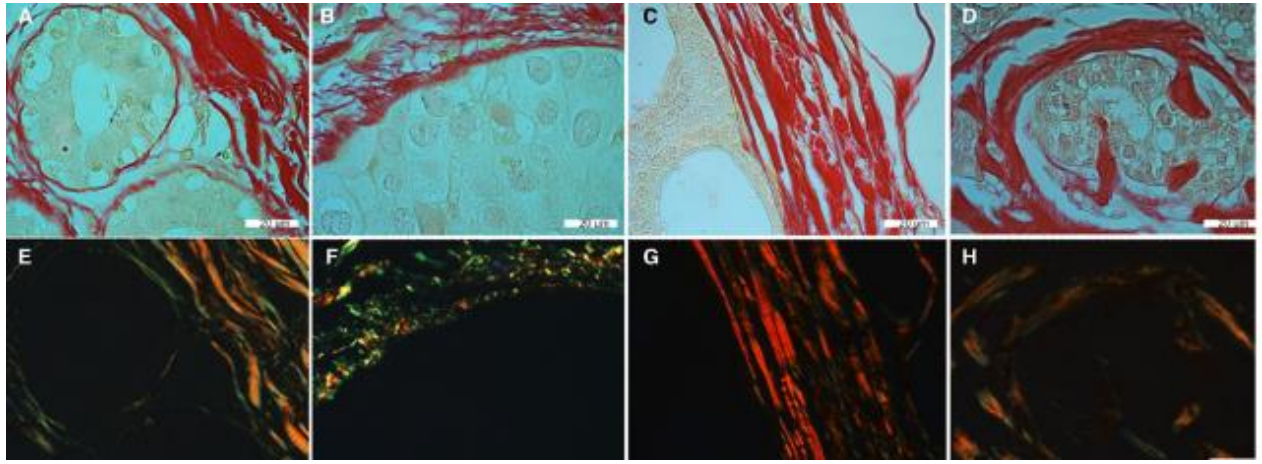
*Histopathology* 2023, **83**, 376–393. DOI: 10.1111/his.14939

**Encapsulated papillary carcinoma of the breast: does it have a native basement membrane?**

Suzan F Ghannam,[1,2,3] Catrin S Rutland,[4] Cinzia Allegrucci,[3,4] Nigel P Mongan[4,5] & Emad Rakha[1,3]

[1]*Division of Cancer and Stem Cells, School of Medicine, The University of Nottingham, Nottingham, UK,* [2]*Department of Histology and Cell Biology, Faculty of Medicine, Suez Canal University, Ismailia, Egypt,* [3]*Nottingham Breast Cancer Research Centre, Biodiscovery Institute, University of Nottingham,* [4]*School of Veterinary Medicine and Sciences, University of Nottingham, Nottingham, UK and* [5]*Department of Pharmacology, Weill Cornell Medicine, New York, NY, USA*

- **Thick, fibrous capsule result from a reactive process**
  - Not an expansion of the native basement membrane material as seen in normal and in-situ lesions
- Supports EPC as **indolent invasive carcinoma**



**Molecular analysis of encapsulated papillary carcinoma of the breast with and without invasion**☆,☆☆

**Christopher J. Schwartz DO**[a], **Amir Momeni Boroujeni MD**[b], **Alireza Khodadadi-Jamayran PhD**[a], **Adriana Heguy PhD**[a], **Matija Snuderl MD**[a], **George Jour MD**[a], **Paolo Cotzia MD**[a], **Farbod Darvishian MD**[a,*]

[a] *New York University Medical Center, New York, NY, 10016, USA*
[b] *Brigham and Women's Hospital, Boston, MA, 02115, USA*

- EPC (irrespective of invasion):
  - Mutations in PIK3CA, KMT2A, CREBBP

- EPC with associated invasive carcinoma:
  - **PIK3CA activating mutations**
  - **Enrichment of 39 stromal genes** implicated in the switch to invasive ductal carcinoma
    - Extracellular matrix regulation
    - Cell adhesion
    - Collagen fibril organization

- Back to high-grade EPC …

Histopathology

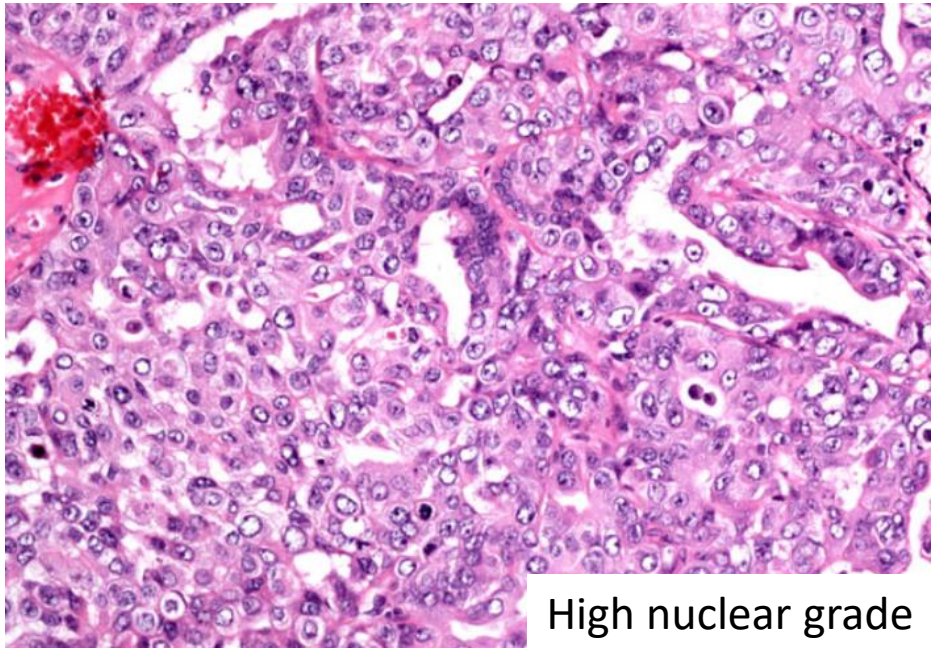
Histopathology 2015, 66, 740–746. DOI: 10.1111/his.12591

# High-grade encapsulated papillary carcinoma of the breast: an under-recognized entity

Emad A Rakha, Zsuzsanna Varga,[1] Somaia Elsheik & Ian O Ellis

*Division of Cancer and Stem Cells, University of Nottingham and Nottingham University Hospitals NHS Trust, City Hospital Campus, Nottingham, UK, and [1]Institute of Surgical Pathology, University Hospital Zurich, Zurich, Switzerland*

- ~3% of EPCs have high-grade features
  - Other studies: 2.5% to 14% (average 6% )
  - **High nuclear grade**
  - **High mitotic activity**
  - **Extensive necrosis**



High nuclear grade

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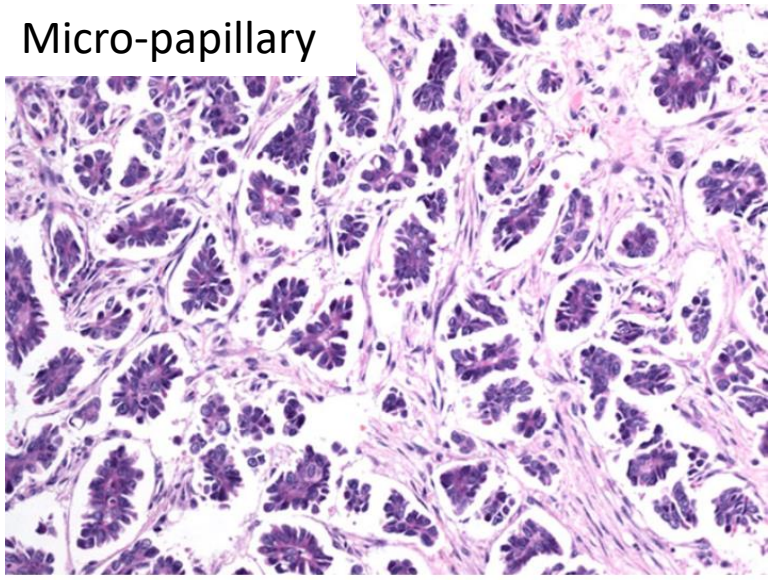
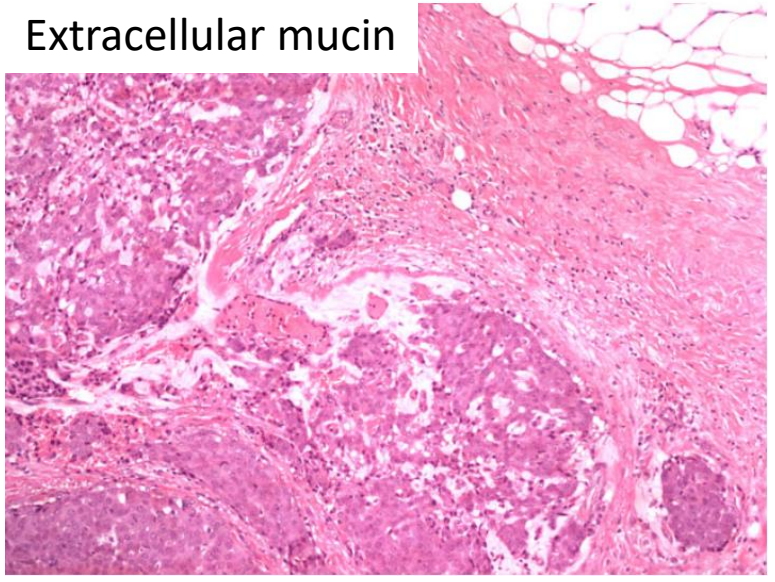
- Rare cases of HG EPC showed:
  - **Focal micro-papillary areas**
  - **Extracellular mucin**

Micro-papillary



Extracellular mucin

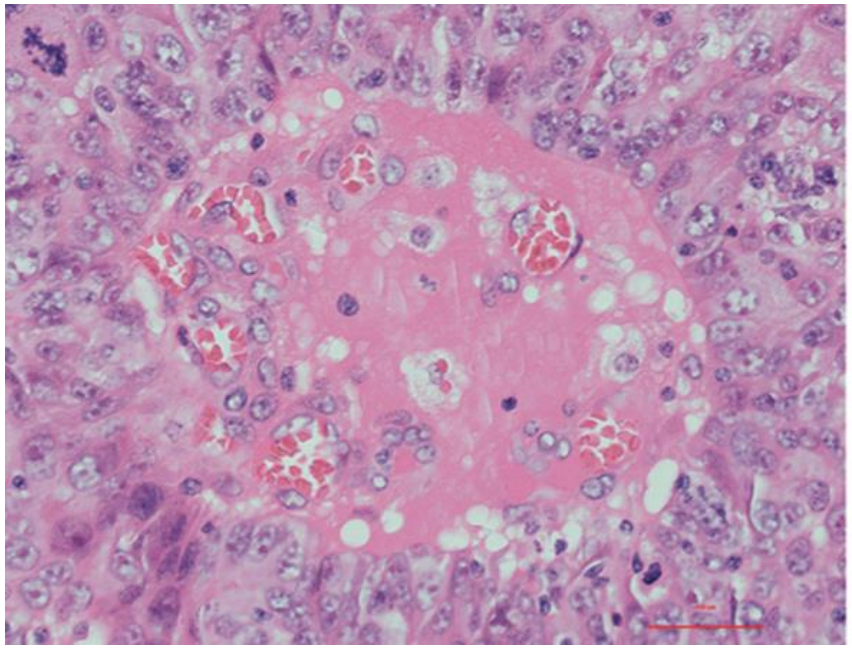


# High-grade encapsulated papillary carcinoma of the breast is clinicopathologically distinct from low/intermediate-grade neoplasms in Chinese patients

**Xuguang Liu[1], Huanwen Wu[1], Lianghong Teng[2], Hui Zhang[1], Junliang Lu[1] and Zhiyong Liang[1]**

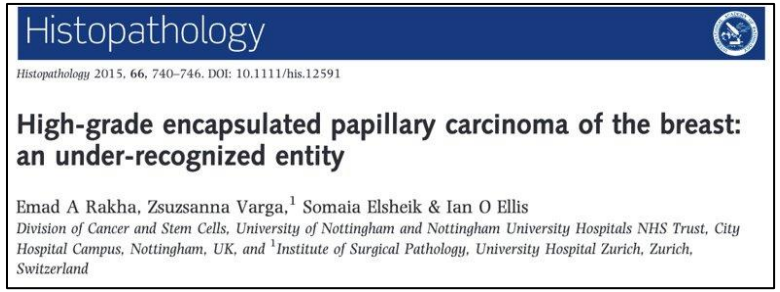
[1]Department of Pathology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College and [2]Department of Pathology, Xuanwu Hospital, Capital Medical University, Beijing, China

- Fibrovascular cores with **multiple enclosed vessels**



# High-grade EPC

- Often triple-negative phenotype (68%)
- Basal type phenotype (50%)
- Higher proportion associated with invasion (up to 57%)
- More aggressive clinical behavior
  - Staged and managed as conventional invasive carcinomas



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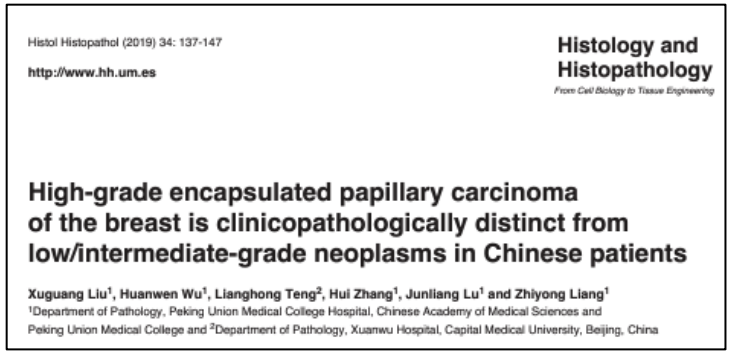

Histol Histopathol (2019) 34: 137-147

http://www.hh.um.es

Histology and Histopathology

From Cell Biology to Tissue Engineering

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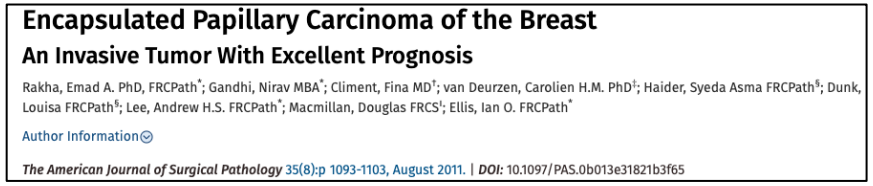

**Encapsulated Papillary Carcinoma of the Breast**

**An Invasive Tumor With Excellent Prognosis**

Rakha, Emad A. PhD, FRCPath*; Gandhi, Nirav MBA*; Climent, Fina MD†; van Deurzen, Carolien H.M. PhD‡; Haider, Syeda Asma FRCPath§; Dunk, Louisa FRCPath§; Lee, Andrew H.S. FRCPath*; Macmillan, Douglas FRCS‖; Ellis, Ian O. FRCPath*

Author Information

*The American Journal of Surgical Pathology* 35(8):p 1093-1103, August 2011. | **DOI:** 10.1097/PAS.0b013e31821b3f65

Esposito NN, Dabbs DJ, Bhargava R. A.Am. J. Clin. Pathol.2009;131; 228–242

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- EPC with associated invasive carcinoma:
  - **PIK3CA activating mutations**
  - **Enrichment of 39 stromal genes** implicated in the switch to invasive ductal carcinoma
    - Extracellular matrix regulation
    - Cell adhesion
    - Collagen fibril organization

# Take Home Points

- Majority of EPCs are low-to-intermediate grade, ER/PR-positive
  - Staged and managed as DCIS (Tis)

- Rare EPCs have high-grade features
  - Staged and managed as conventional IDC

# Questions?

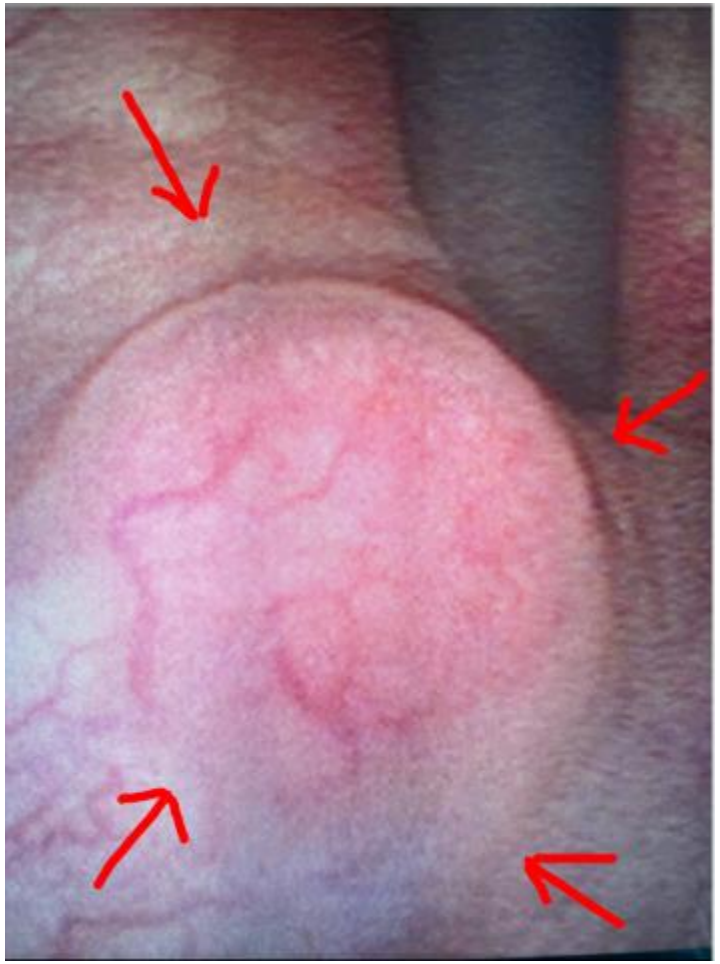
- Thank you, Drs. Poonam Vohra and Yunn-Yi Chen!

24-0102

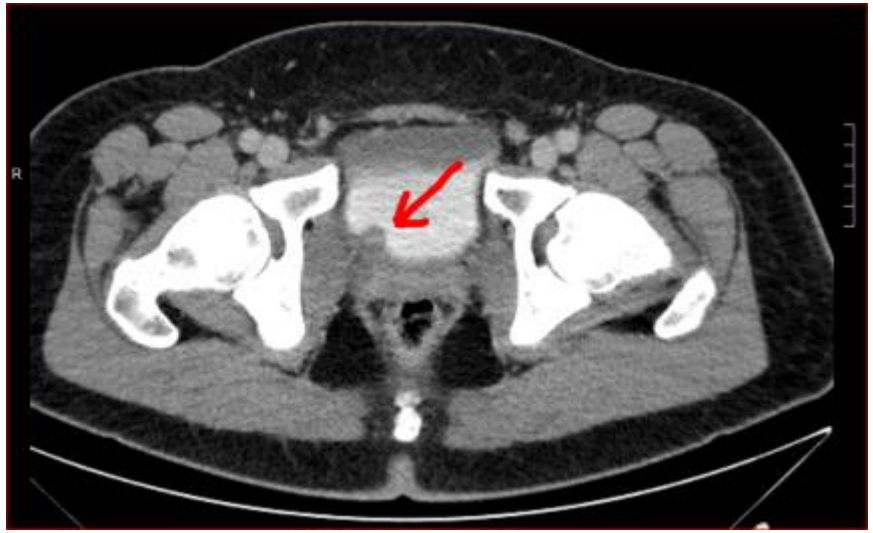
**Christina Su/Emily Chan; Stanford**

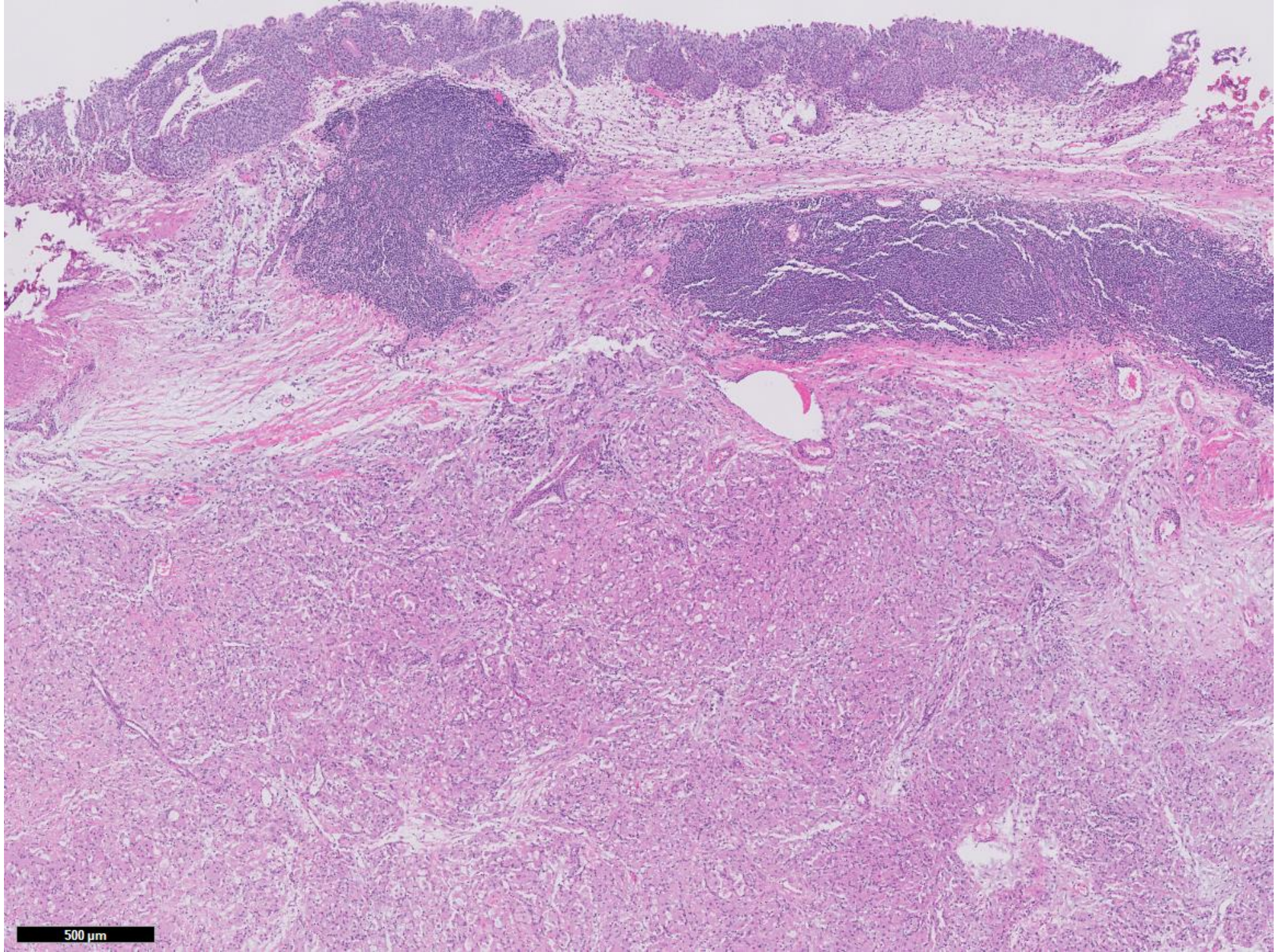
# 32-year-old man with gross hematuria who underwent resection of a 3-4 cm bladder tumor

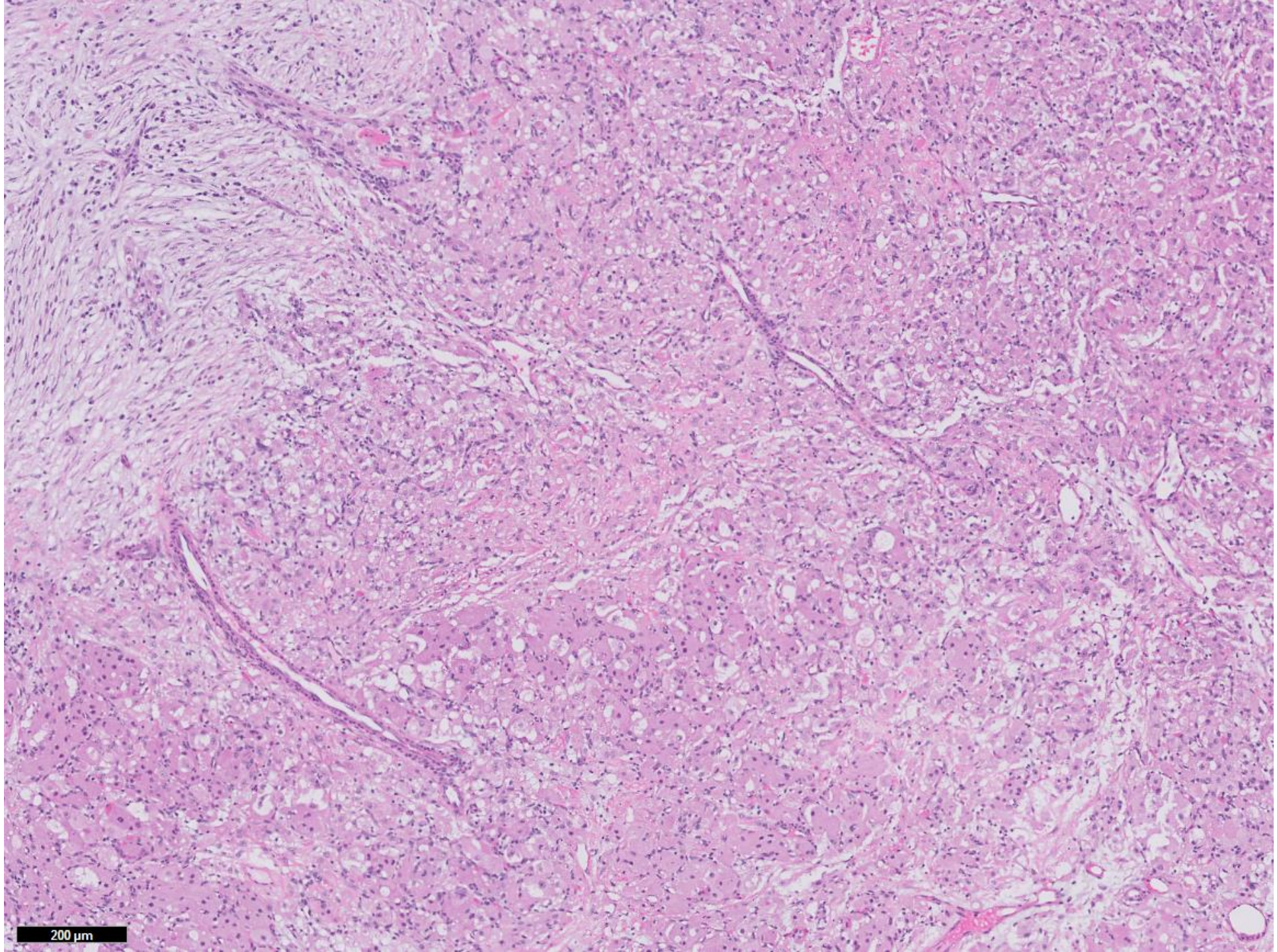
## Cystoscopy

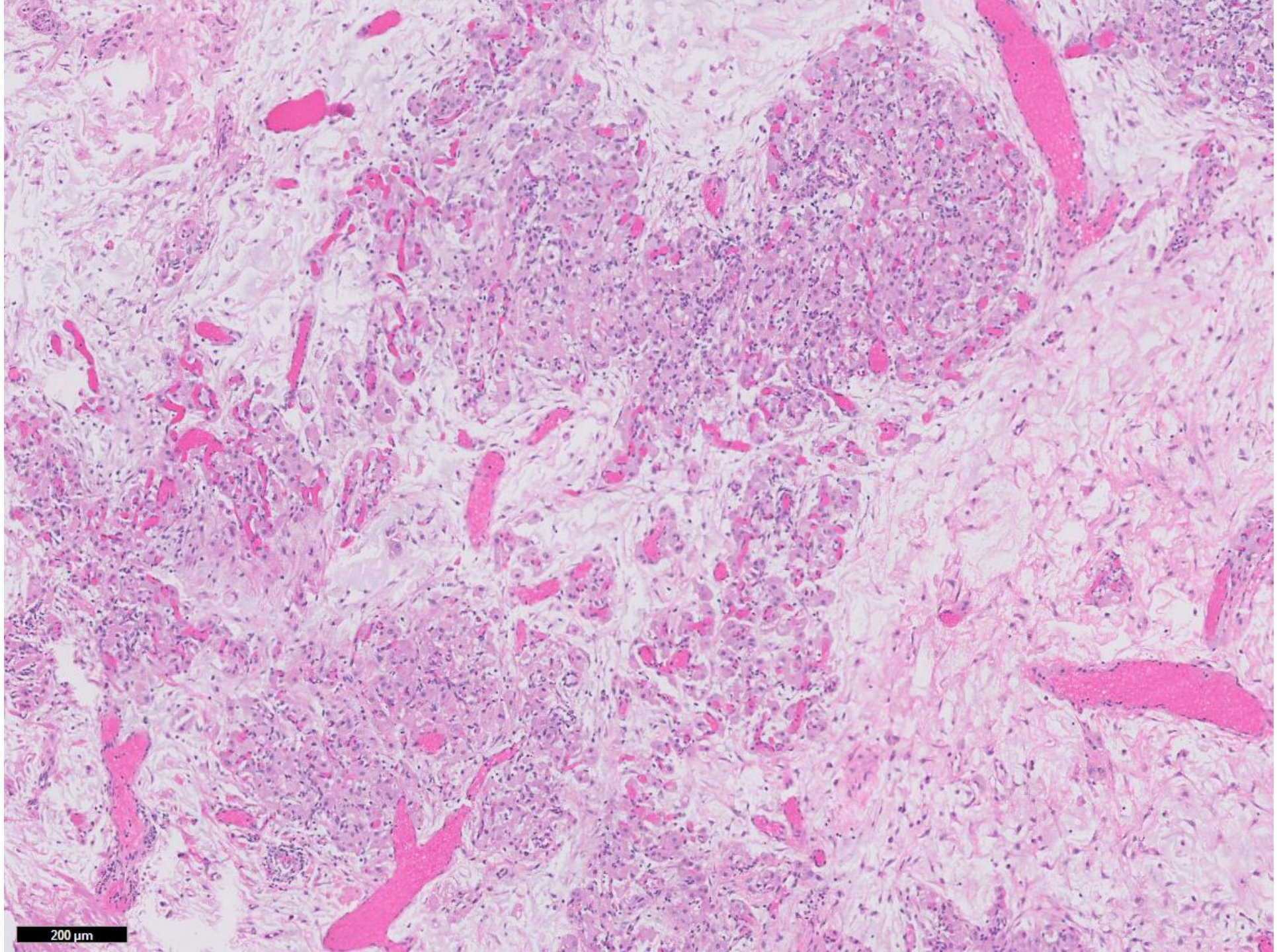


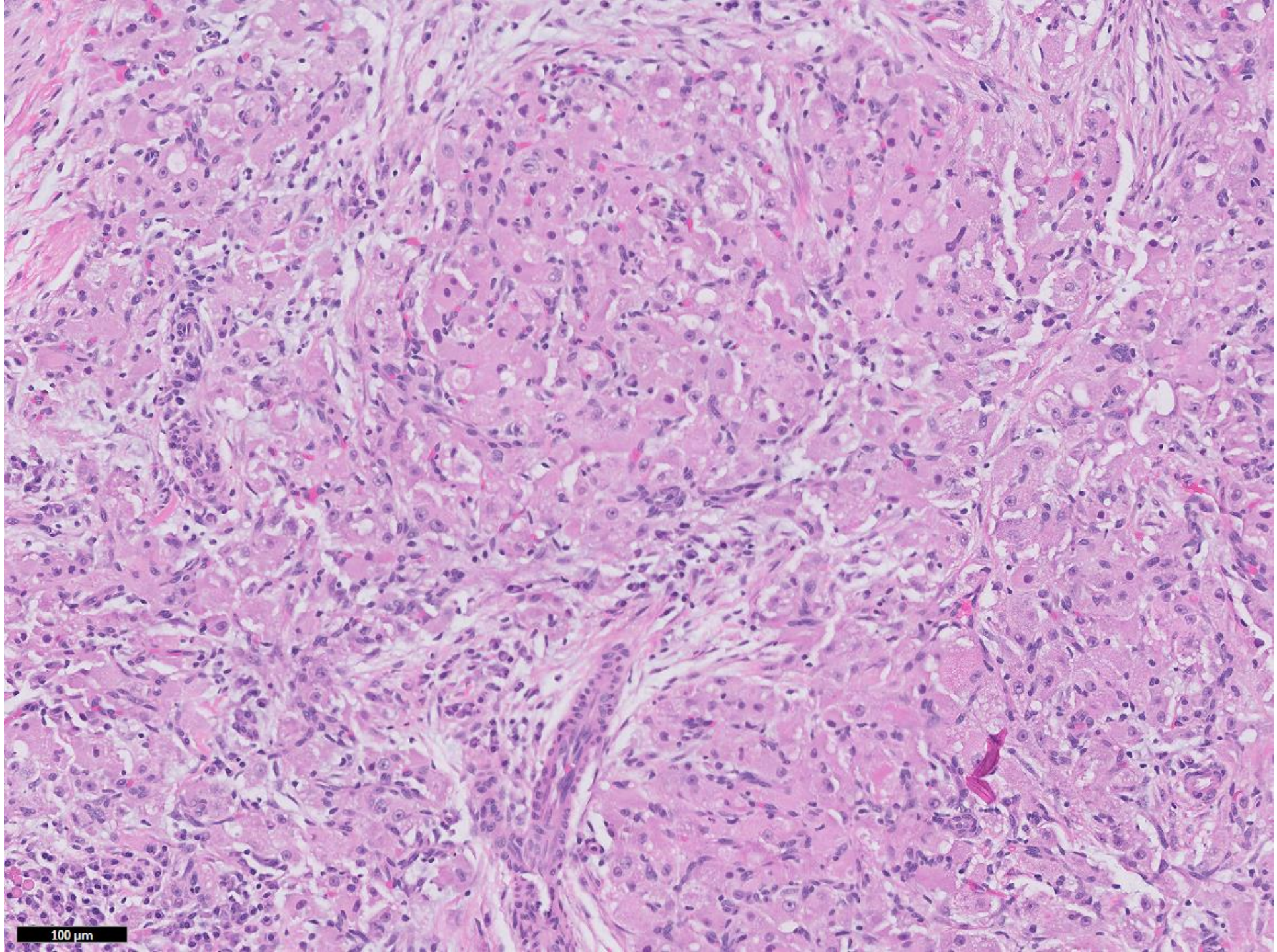
## CT

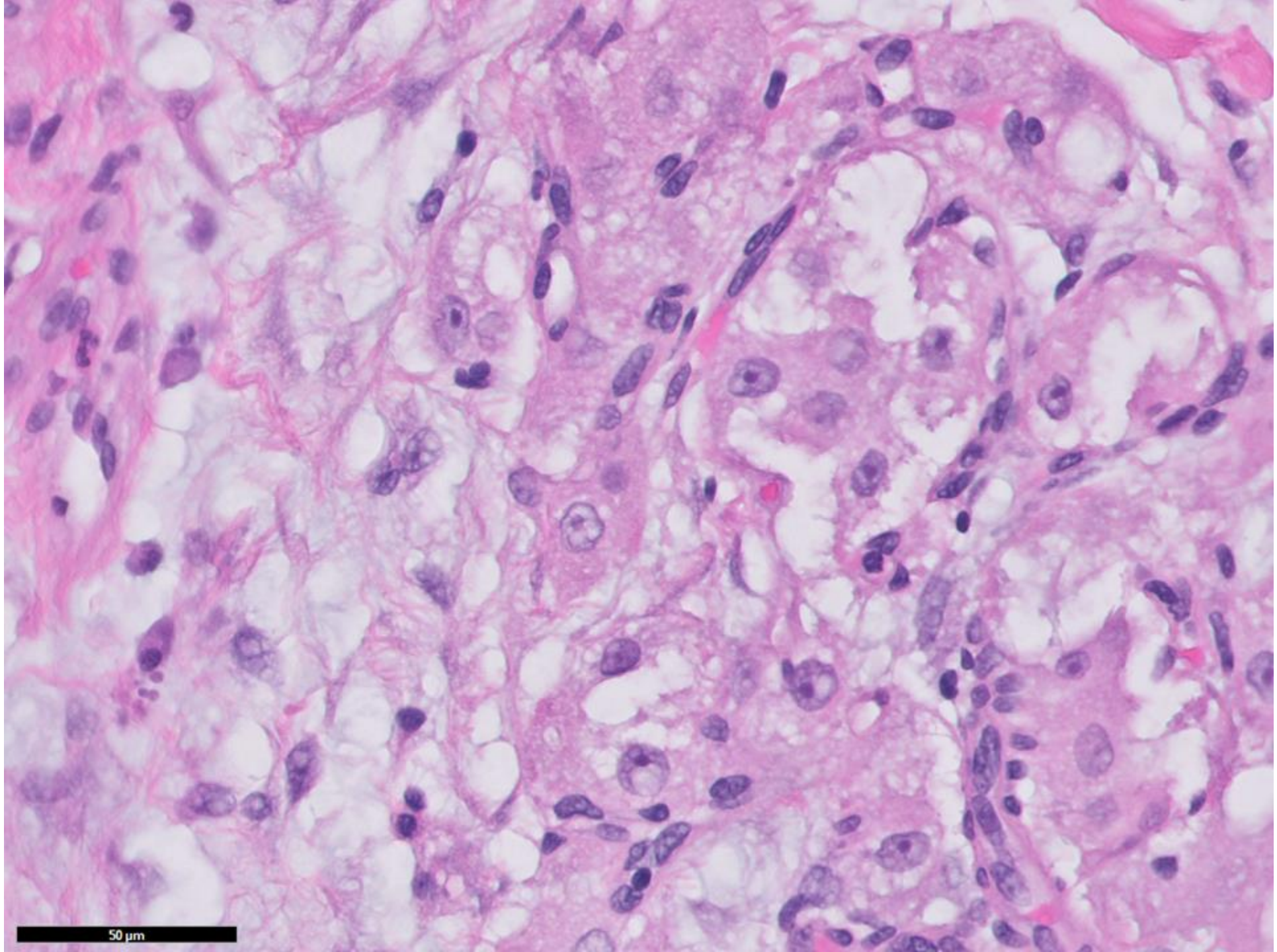


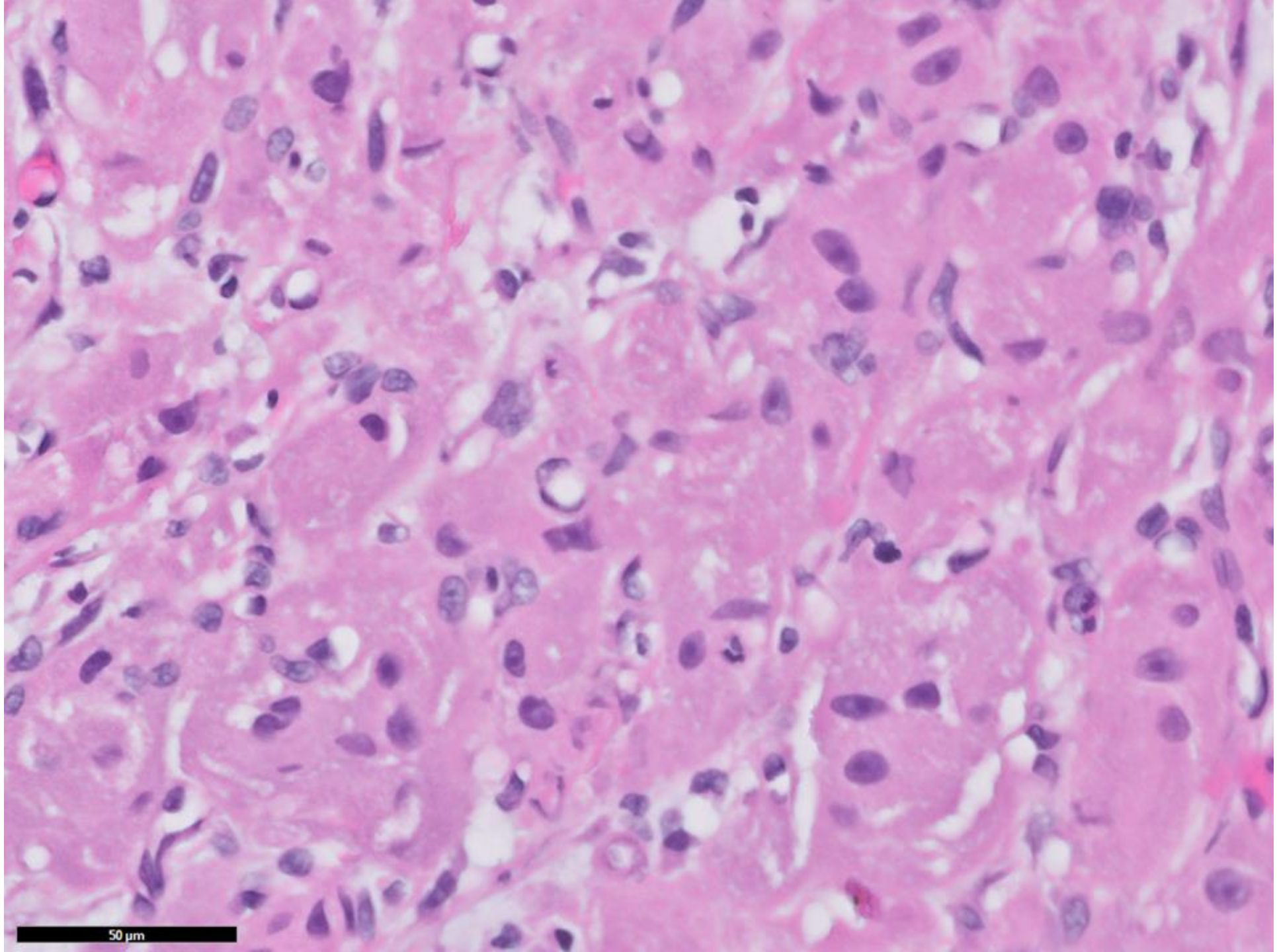

500 µm


200 µm


200 µm


100 µm

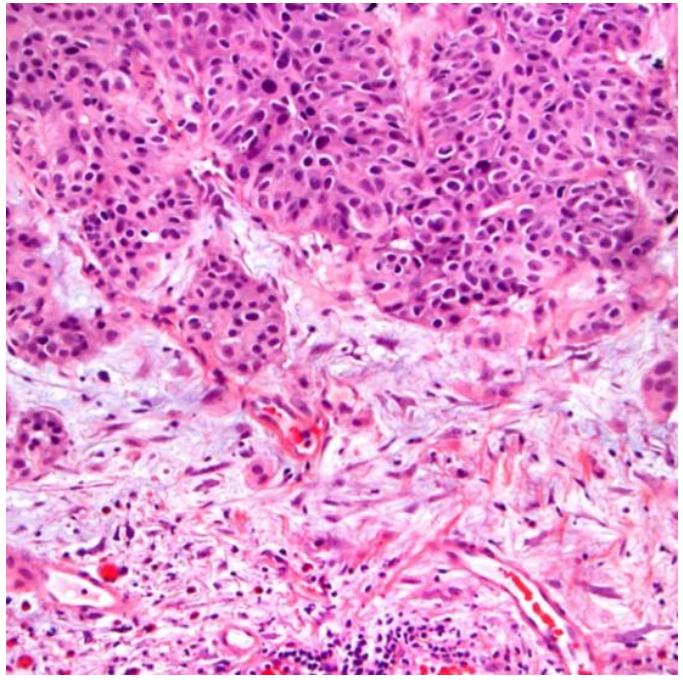

50 µm


50 µm

# DIAGNOSIS?

# Differential Diagnosis

- Urothelial carcinoma

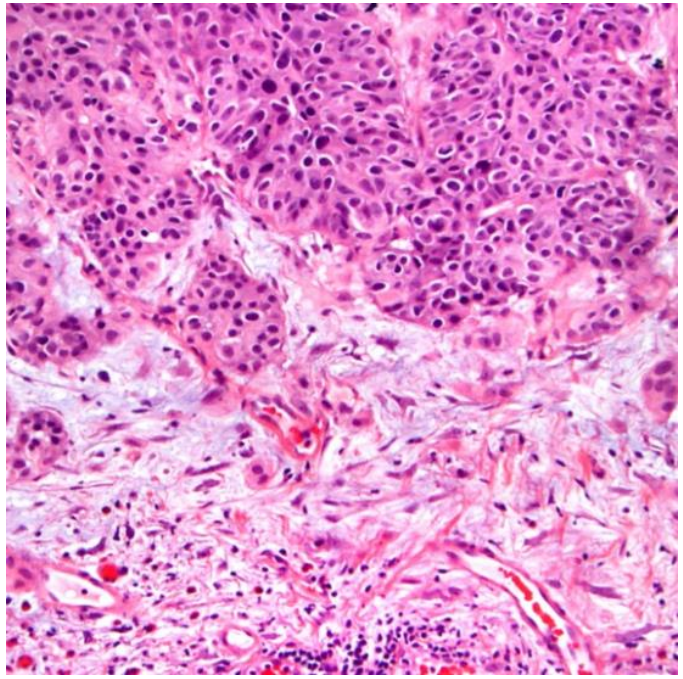


Al-Ahmadie, Invasive Urothelial Carcinoma, *ExpertPath*

# Differential Diagnosis

- ~~Urothelial carcinoma~~

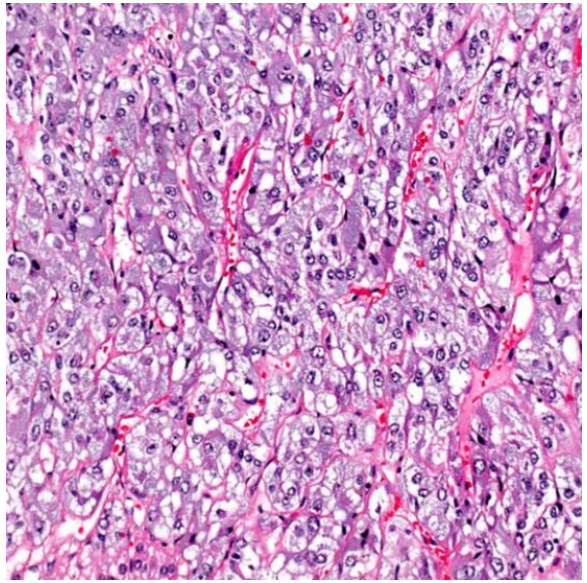
  Submucosal lesion, (-) keratin mix

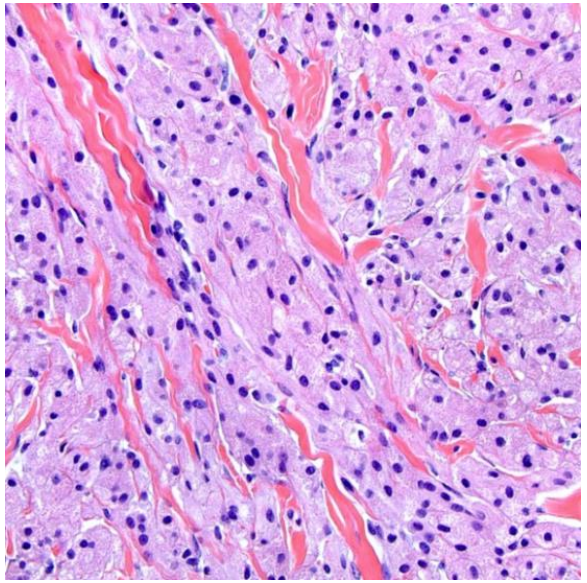


Al-Ahmadie, Invasive Urothelial Carcinoma, *ExpertPath*

# Differential Diagnosis

- ~~Urothelial carcinoma~~
- Paraganglioma
- Granular cell tumor





Smith, Paraganglioma, *ExpertPath*; Lindberg, Granular Cell Tumor, *ExpertPath*

# Differential Diagnosis

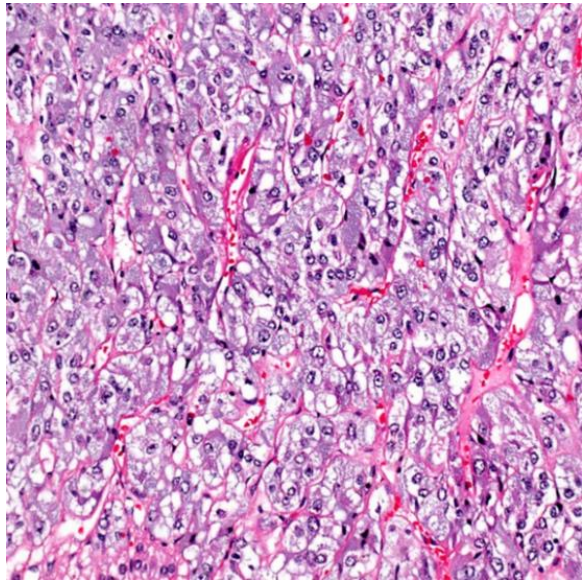
- ~~Urothelial carcinoma~~

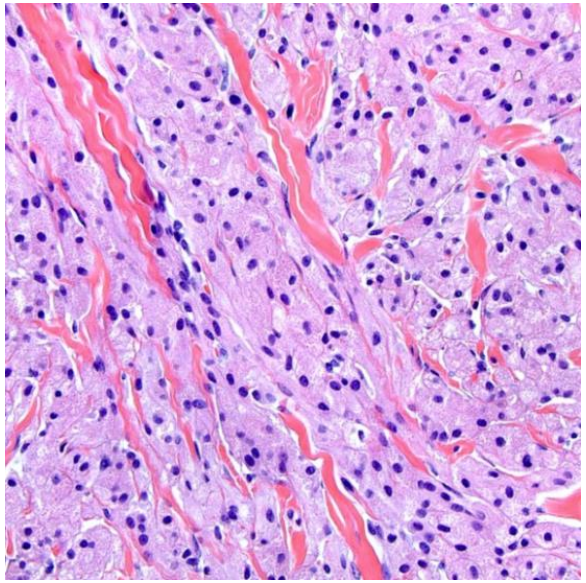
- ~~Paraganglioma~~

  (-) S100, synaptophysin, and chromogranin

- ~~Granular cell tumor~~

  (-) S100

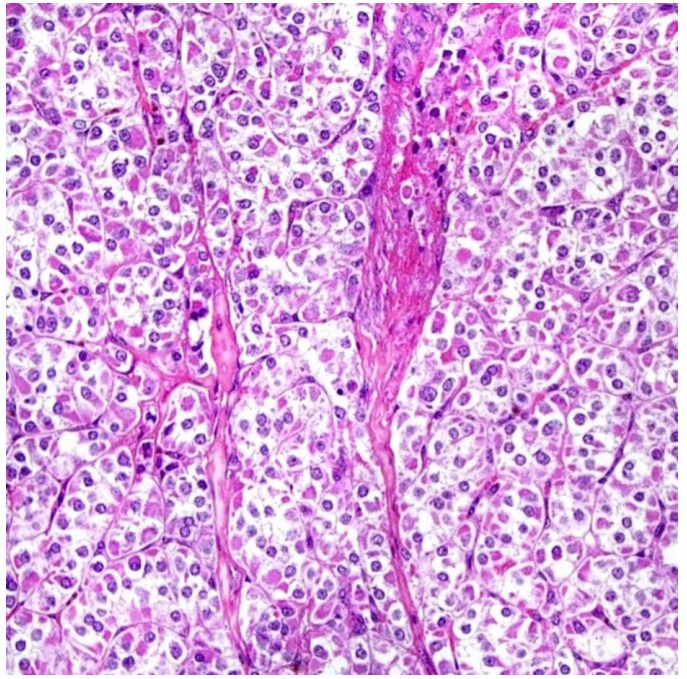




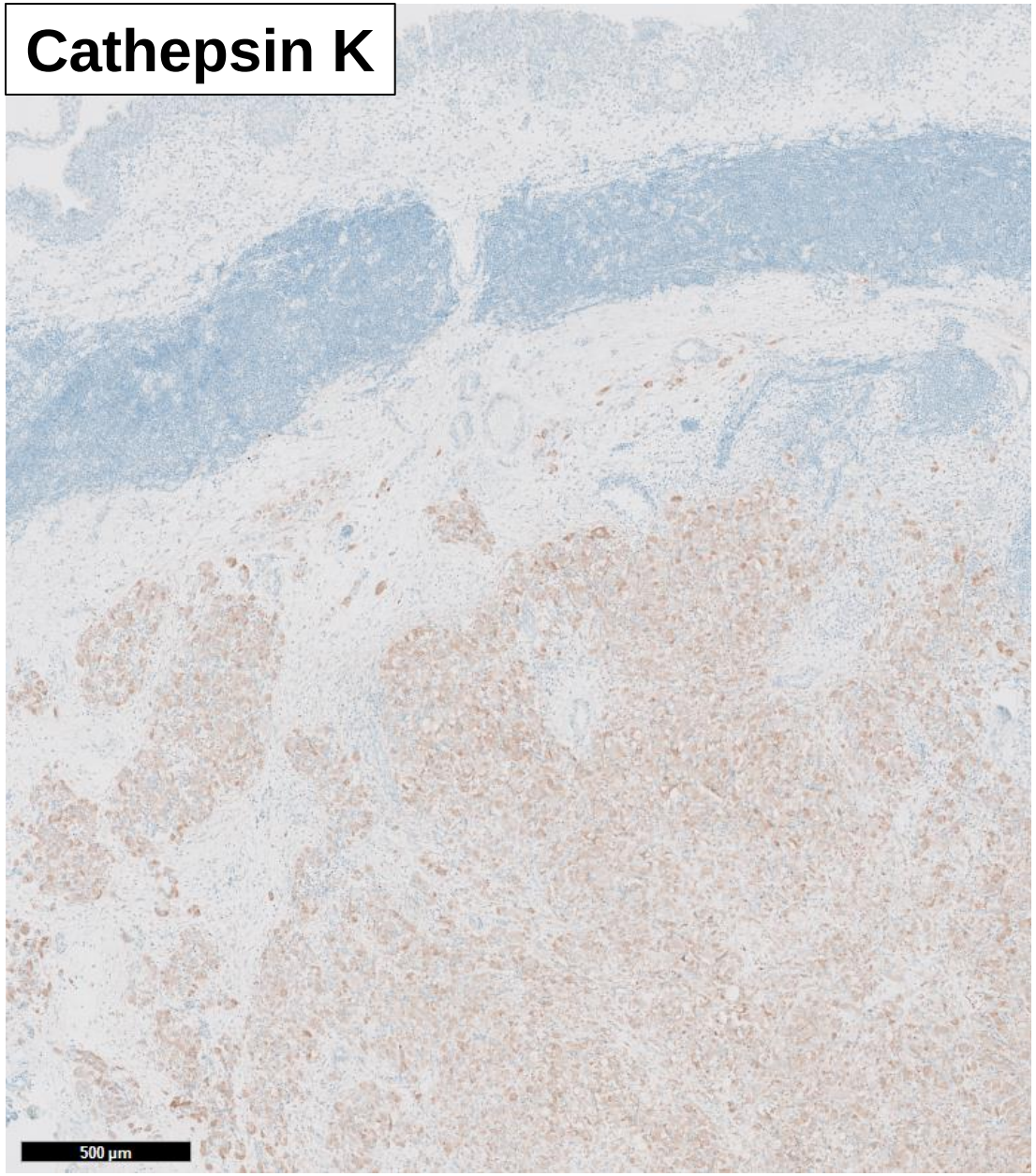
Smith, Paraganglioma, *ExpertPath*; Lindberg, Granular Cell Tumor, *ExpertPath*

# Differential Diagnosis

- ~~Urothelial carcinoma~~
- ~~Paraganglioma~~
- ~~Granular cell tumor~~
- Perivascular epithelioid cell tumor (PEComa)



Lindberg, Perivascular Epithelioid Cell Tumor (PEComa), *ExpertPath*

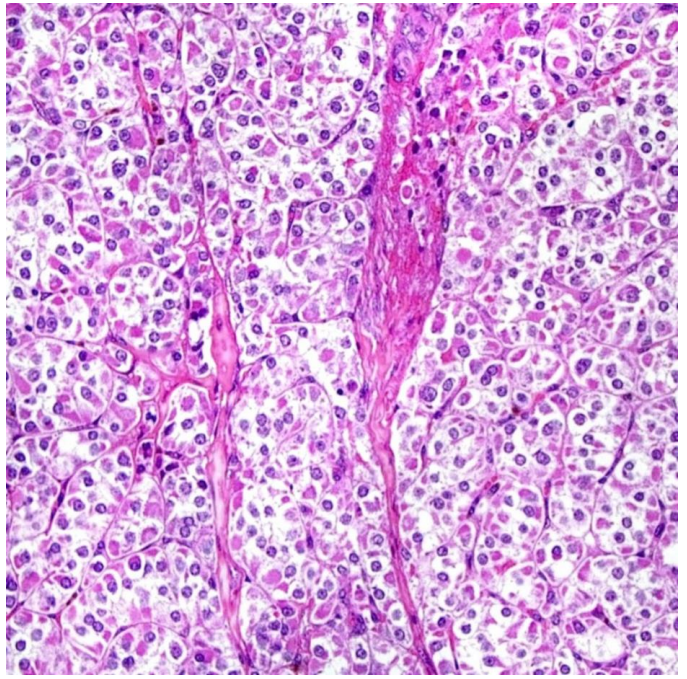



## Negative IHC

- Keratin mix
- Desmin
- Caldesmon
- SMA
- S100
- Synaptophysin
- Chromogranin
- HMB45
- Melan-A
- CD68

# Differential Diagnosis

- ~~Urothelial carcinoma~~
- ~~Paraganglioma~~
- ~~Granular cell tumor~~



- Perivascular epithelioid cell tumor (PEComa)

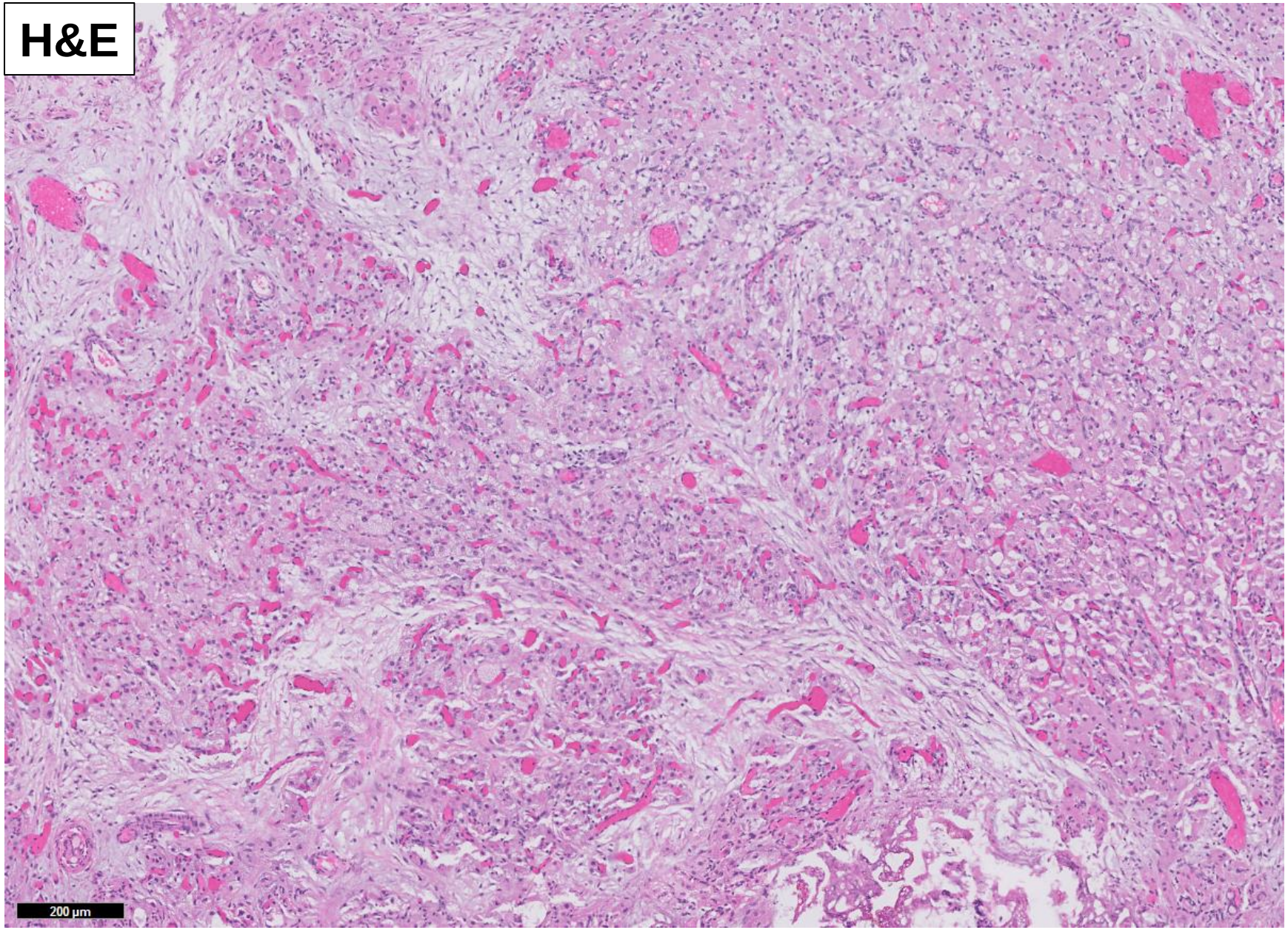
  (+) Cathepsin K; vascularity, (-) HMB45 and Melan-A

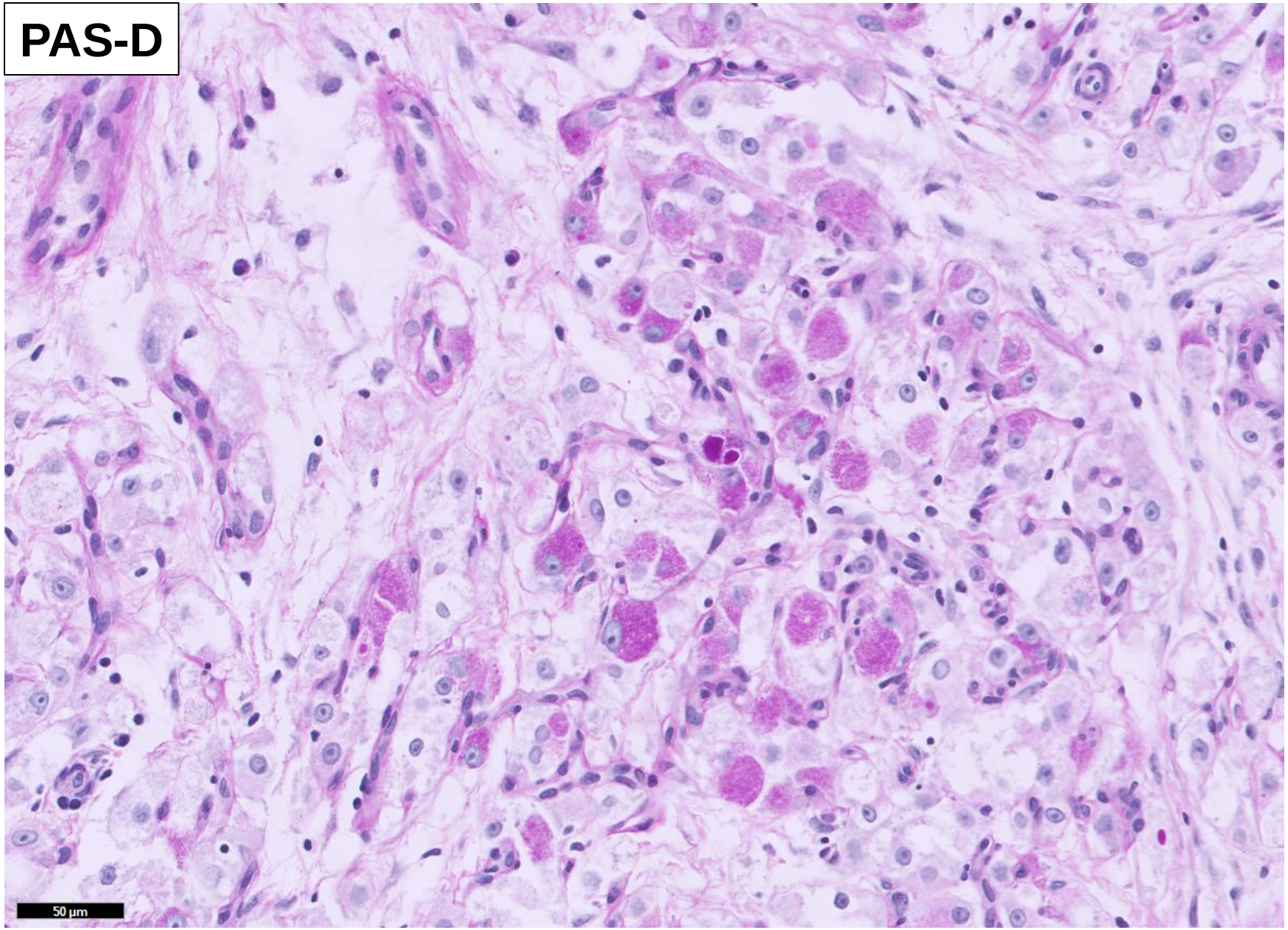
Lindberg, Perivascular Epithelioid Cell Tumor (PEComa), *ExpertPath*

# Differential Diagnosis

- ~~Urothelial carcinoma~~
- ~~Paraganglioma~~
- ~~Granular cell tumor~~
- ~~Perivascular epithelioid cell tumor (PEComa)~~
- Alveolar soft part sarcoma (ASPS)

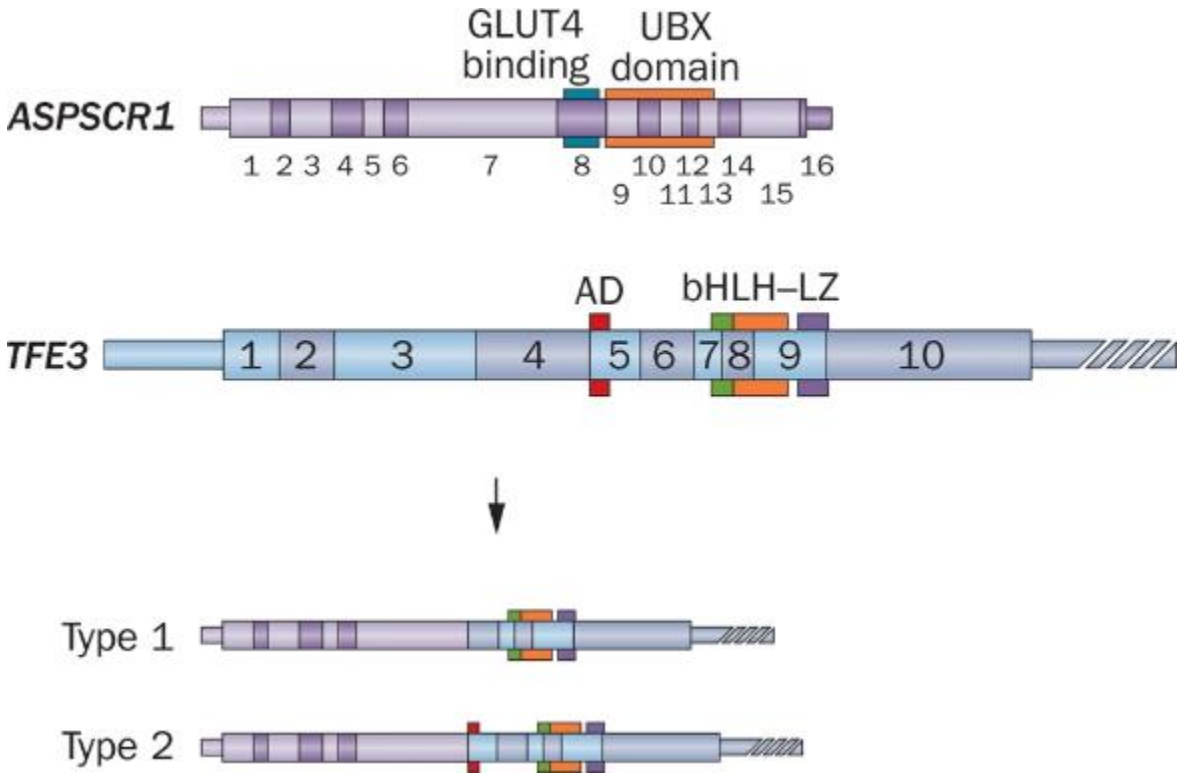
  Morphology, (+) cathepsin K


H&E
200 µm


PAS-D
50 µm

# Molecular Testing

- *ASPSCR1::TFE3* fusion detected by Fusion-STAMP next-generation sequencing panel




Kauffman et al., *Nat. Rev. Urol.*, 11: 465-475 (2014)

# Final Diagnosis

- Alveolar soft part sarcoma with *ASPSCR1::TFE3* fusion identified

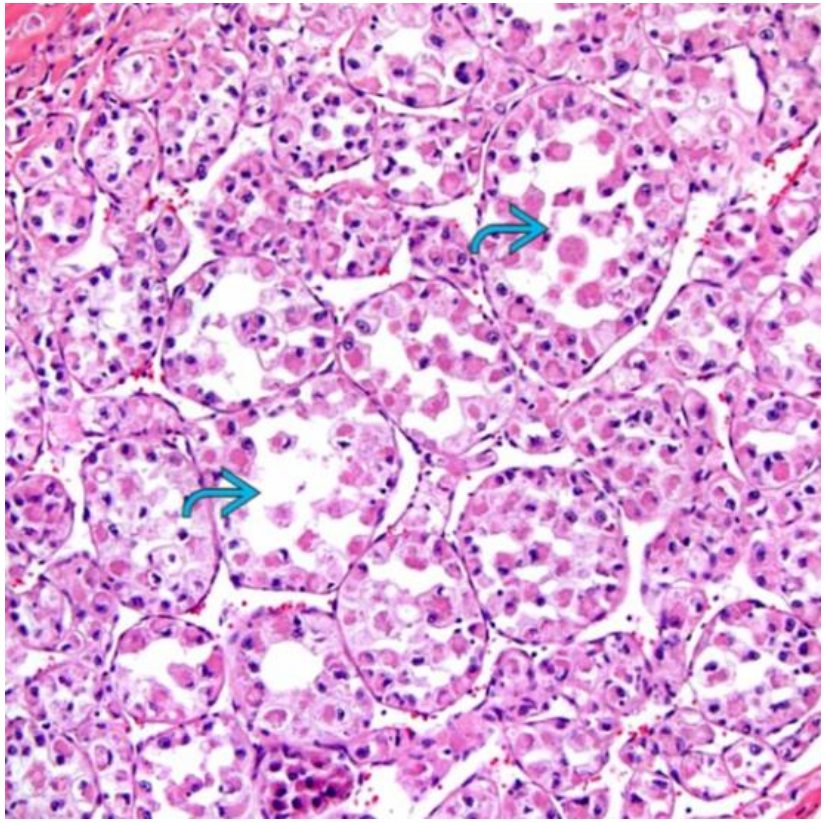
# ASPS: Pathophysiology

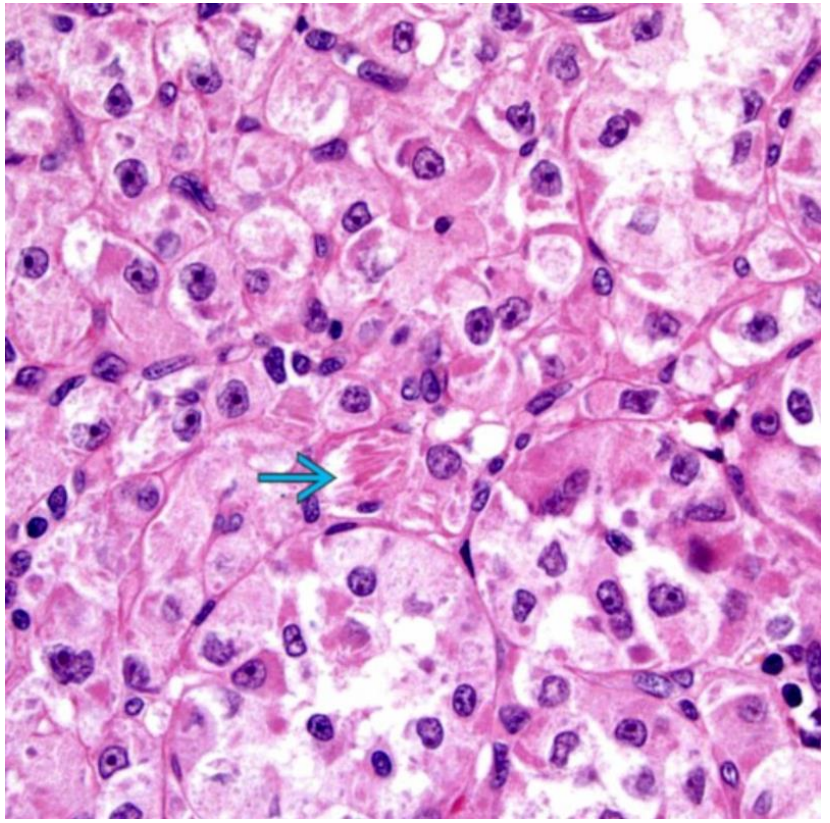
- Rare tumor (<1% of soft tissue sarcomas) of uncertain origin, predominantly in adolescents and young adults

- Typically a slow-growing, painless mass of the lower extremities or trunk, with bladder involvement observed in rare case reports

- Characterized by der(17)t(X;17)(p11.2;q25) translocation producing *ASPSCR1::TFE3* fusion, which causes overexpression of c-Met and activation of c-Met signaling

# ASPS: Diagnosis





- Strong and diffuse nuclear TFE3 staining (ideally with demonstration of *TFE3* rearrangement or *ASPSCR1::TFE3* fusion)

Lindberg, Alveolar Soft Part Sarcoma, *ExpertPath*

# ASPS: Management

- Standard therapy is surgical resection
- 5-year survival rate is 56%, with significantly better outcomes for patients presenting with localized disease
- Radiation and chemotherapy have not demonstrated significant benefit in most studies
- Early clinical trials of targeted therapies, including c-Met inhibitors and tyrosine kinase inhibitors, have shown disease stabilization

# ASPS vs. PEComa: Potential Pitfalls

- Features favoring PEComa
  - Morphology: hyalinized stroma, areas of spindle cells, lack of discohesion, nuclear pleomorphism
  - Immunohistochemistry: (+) for melanocytic markers
  - Molecular: usually *TSC1*/*TSC2* mutations, with subset showing *TFE3* fusions (most commonly with *SFPQ*)

- Rare case reports have documented tumors that show PEComa-like histology but demonstrate the *ASPSCR1::TFE3* fusion

- Rare cases of ASPS with different *TFE3* fusion partners have also been reported

# Summary

- ASPS can occur rarely in the urinary bladder as a submucosal/mesenchymal tumor and should be considered if the morphology fits

- *TFE3*-rearranged neoplasms, including ASPS and PEComa, can overlap significantly in microscopic and molecular findings

- Positive IHC for TFE3 and cathepsin K with negative staining for melanocytic markers, as well as identification of a *TFE3* fusion with appropriate fusion partner, can be helpful in distinguishing ASPS from PEComa

# References

- Thank you to Dr. Greg Charville (Stanford Soft Tissue and Bone Pathology)!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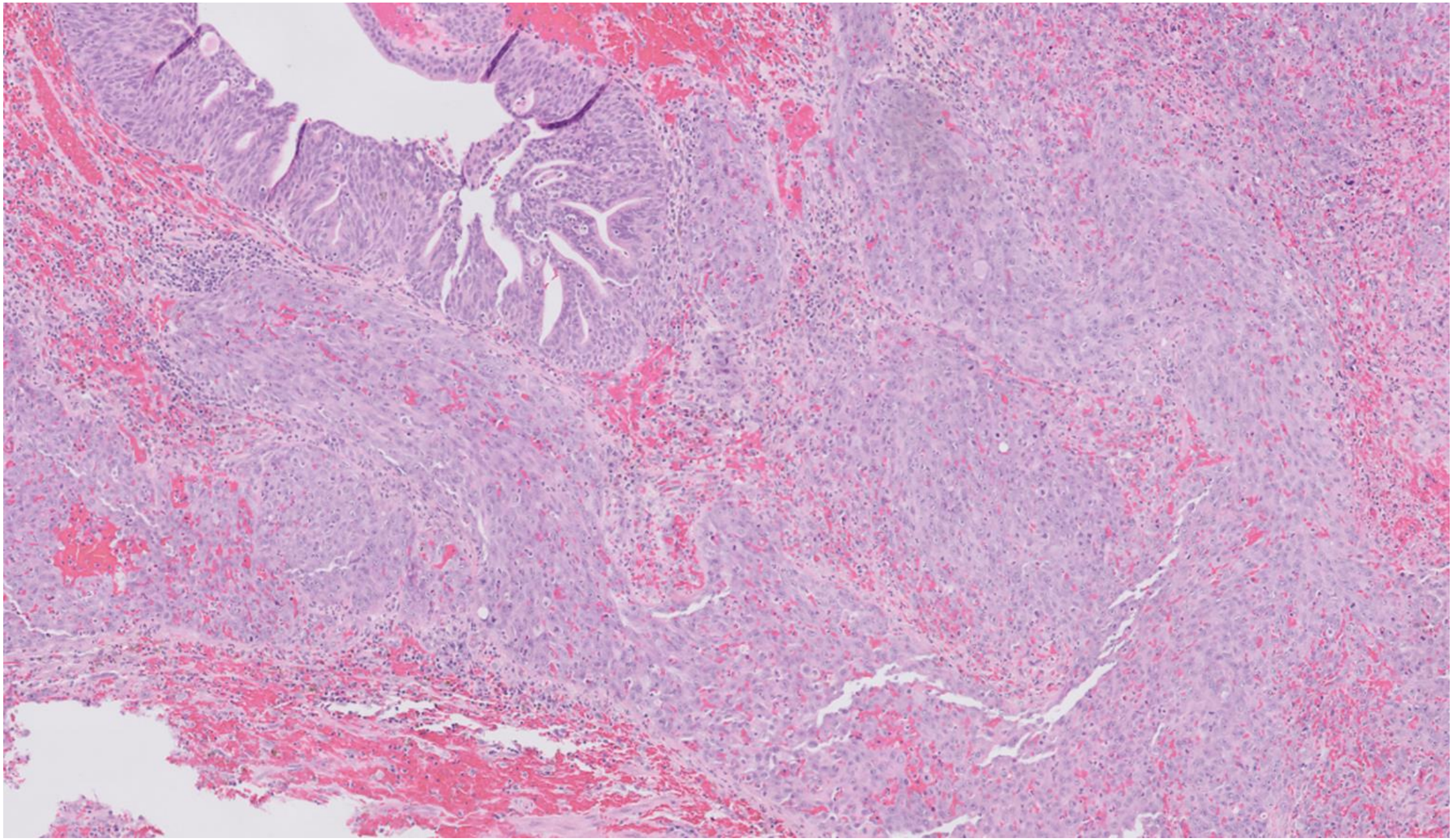
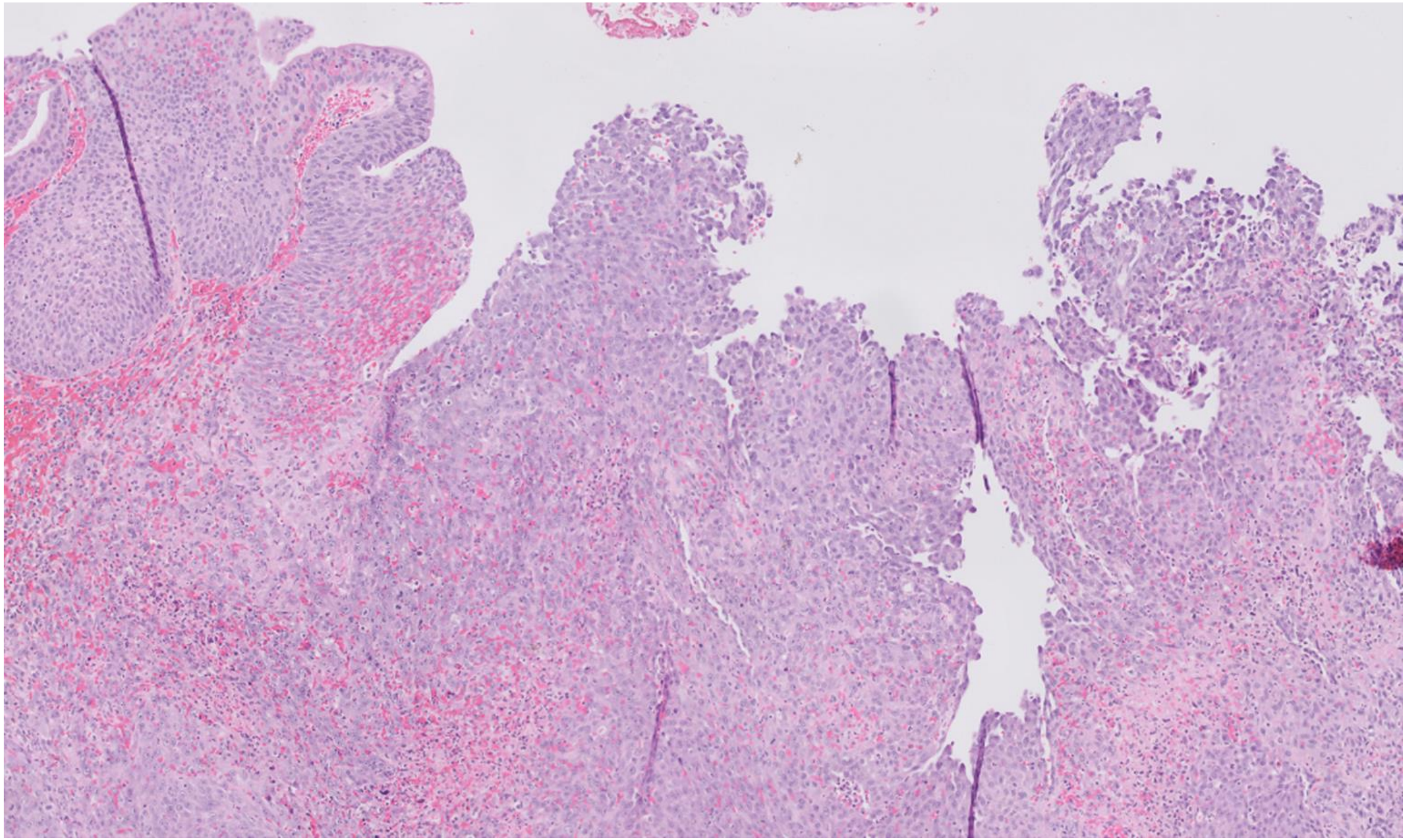
- Zhao M, Huang Y, Yin X, Xu J, Sun Y, Wang J. 2024. PEComa with ASPSCR1::TFE3 fusion: expanding the molecular genetic spectrum of TFE3-rearranged PEComa with an emphasis on overlap with alveolar soft part sarcoma. *Histopathology* 84(3): 482-491. DOI:10.1111/his.15087.

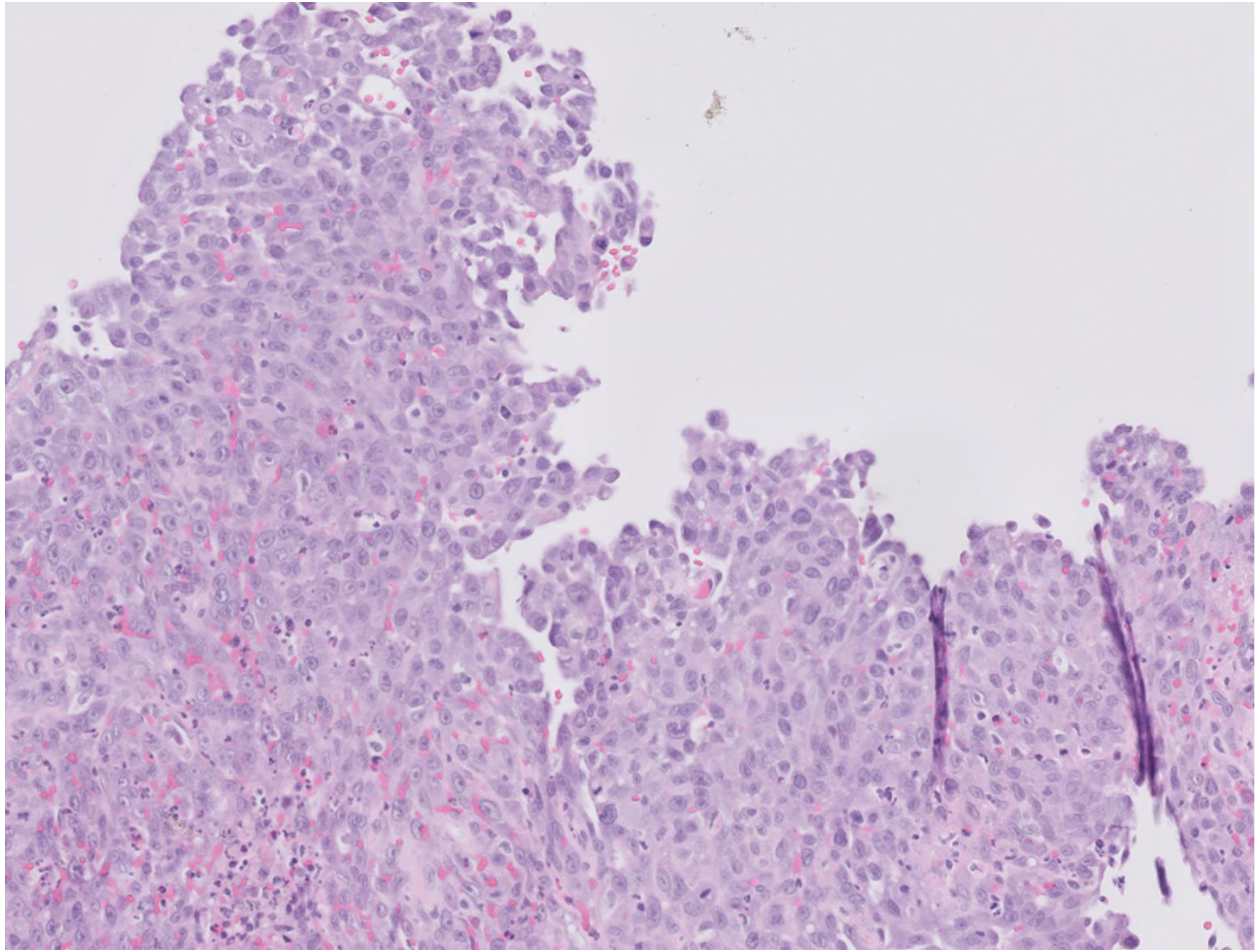
24-0103

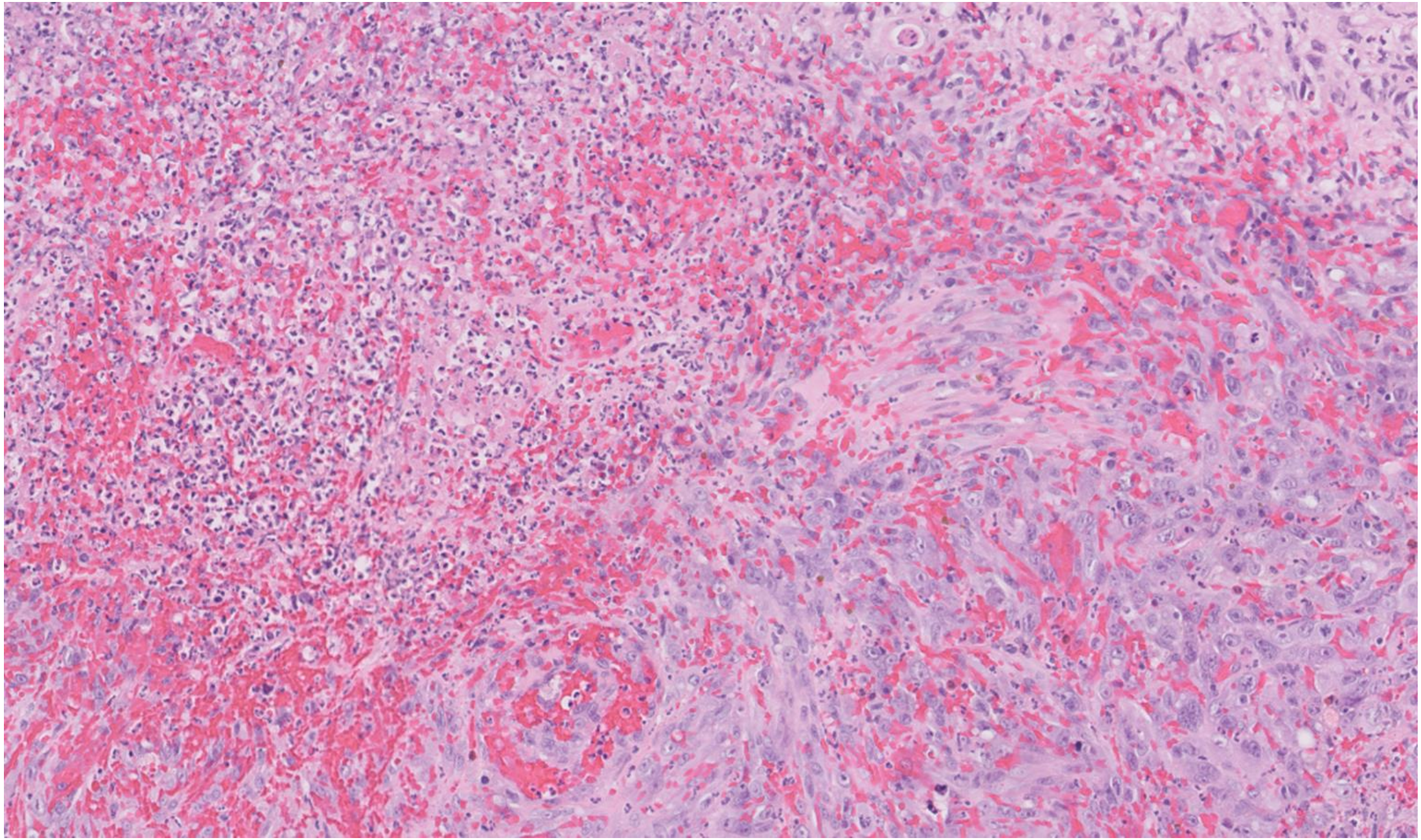
**Garrett Chan and Cornelia Ding; UCSF**

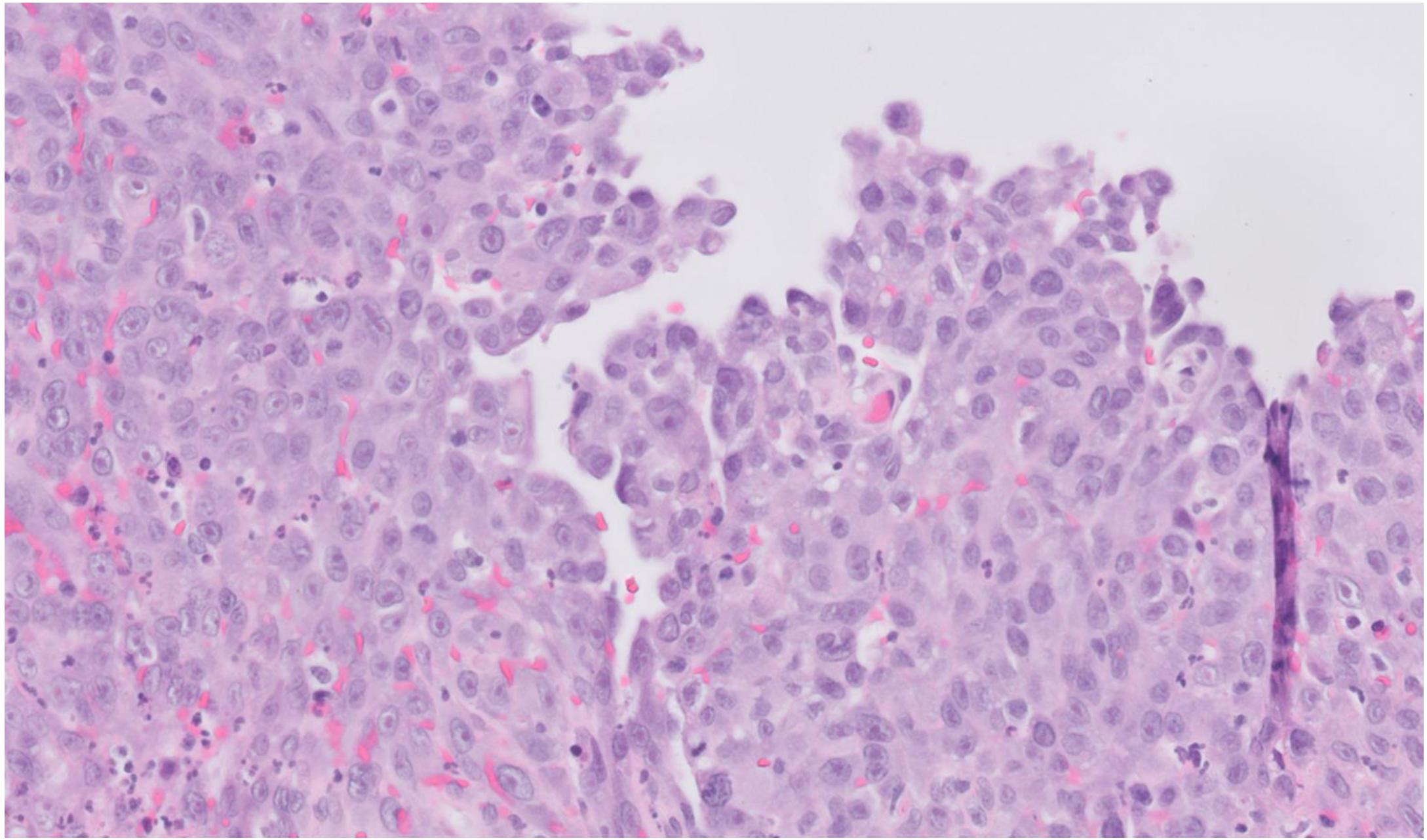
# 62-year-old male presenting with hematuria

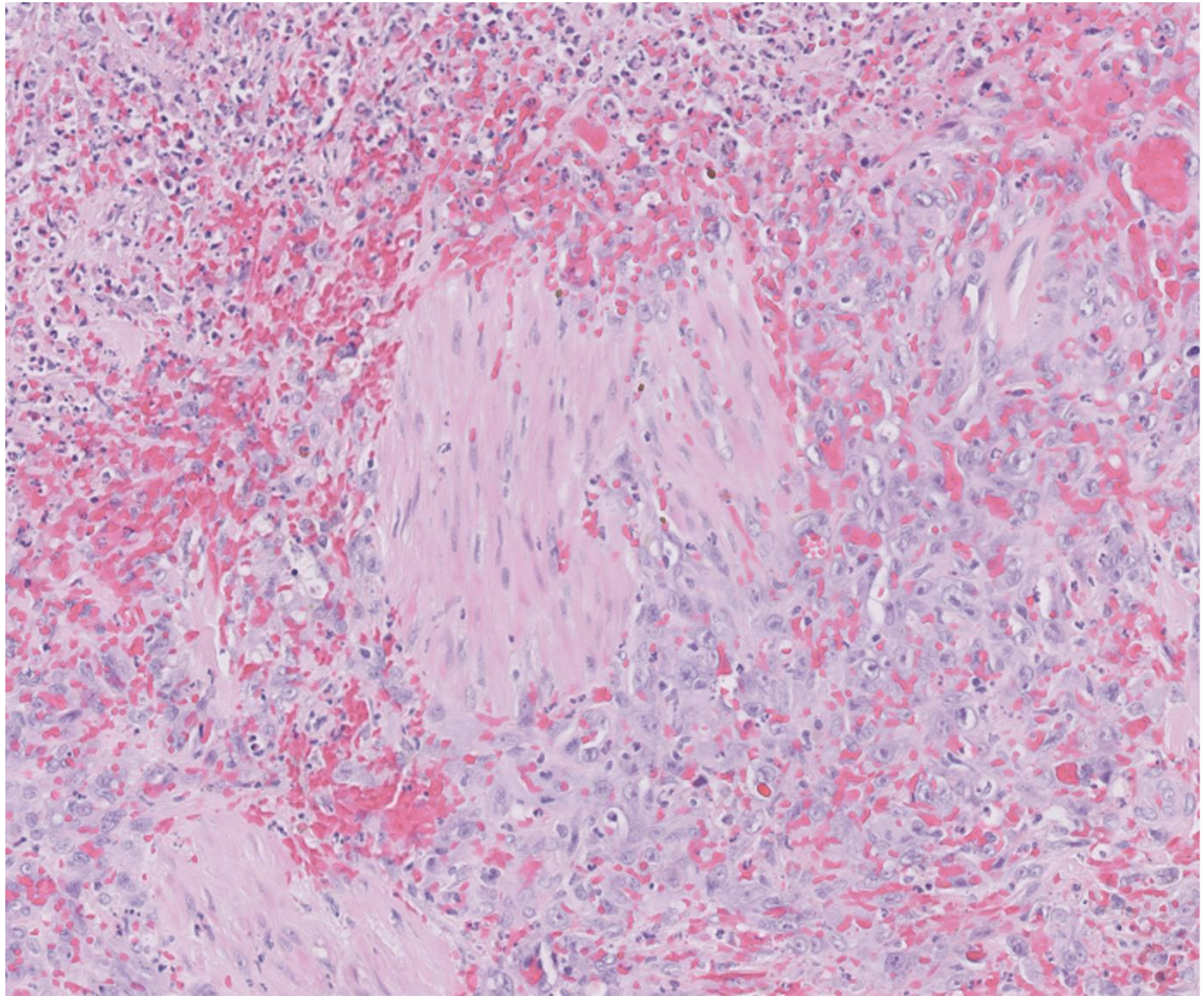












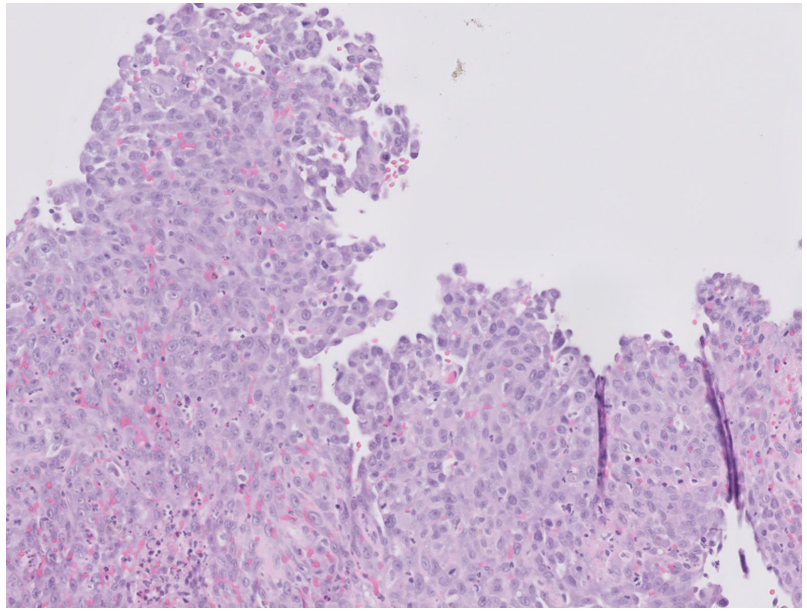
# DIAGNOSIS?

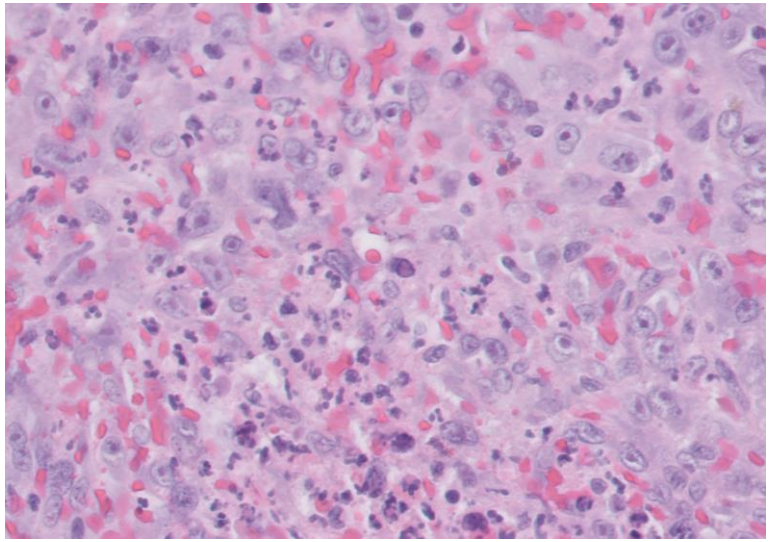
# Patient history

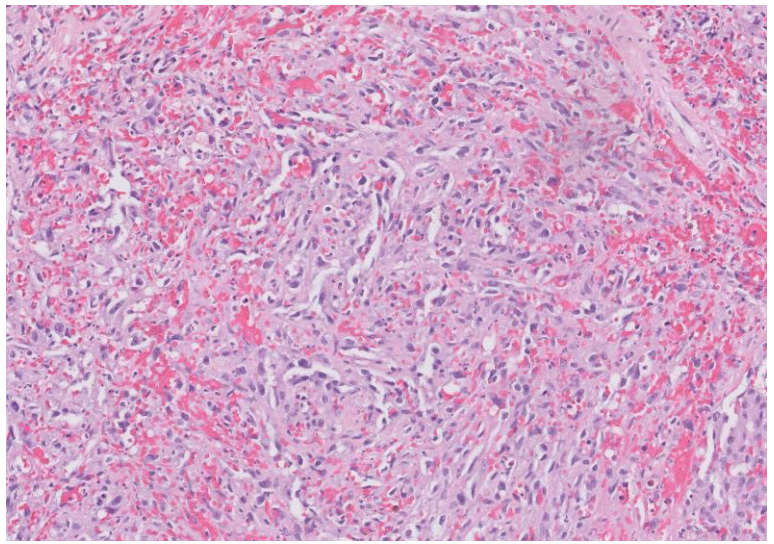
- Presented to outside hospital with hematuria
- Found on cystoscopy to have a mass of the bladder neck encroaching on the right uteral orifice, involving the urethra, bladder neck, and bilateral bladder walls
- Underwent transurethral resection of bladder tumor
- Outside pathology: poorly differentiated tumor, favor angiosarcoma
- Final diagnosis: Malignant epithelioid and vasoformative neoplasm involving bladder wall, consistent with epithelioid angiosarcoma

# Our case

- Atypical spindled to epithelioid cells forming sheets and nests
- Irregular nuclei, vesicular chromatin, and prominent nucleoli
- Vasoformative foci with mixed inflammation
- Intracytoplasmic vacuoles with red blood cells



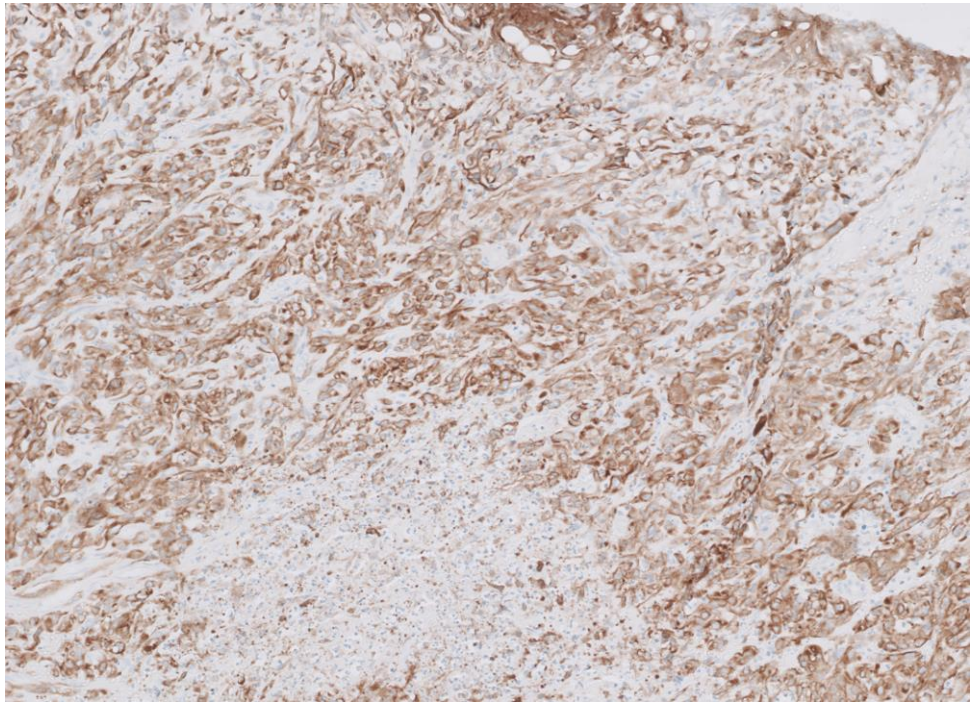




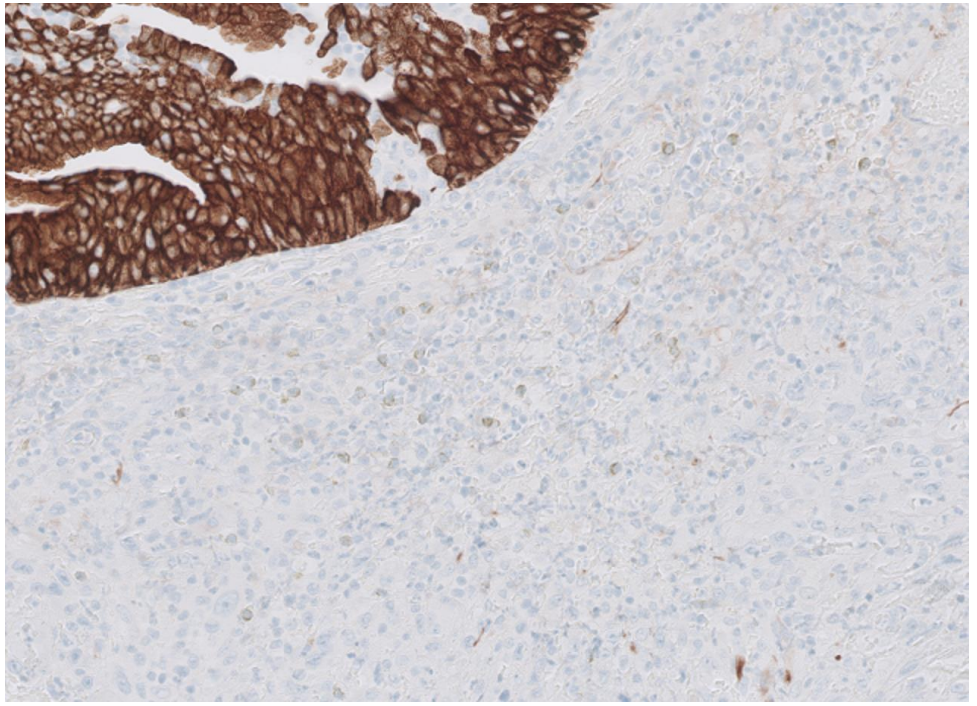
# Differential diagnosis

- Sarcomatoid carcinoma, urothelial or prostatic
- Poorly-differentiated carcinoma
- Epithelioid hemangioendothelioma
- Kaposi sarcoma

# Immunohistochemistry

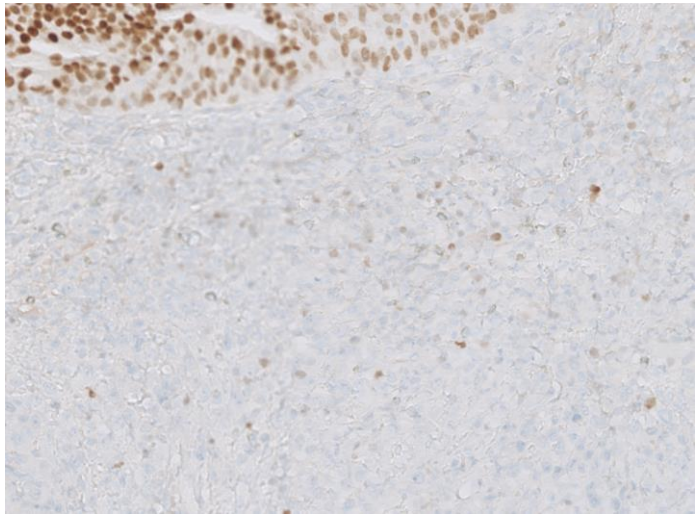


**Pankeratin**

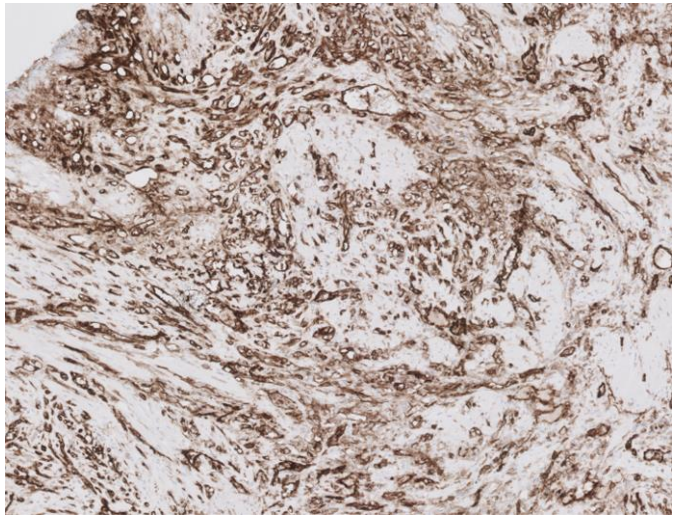


**CK7**

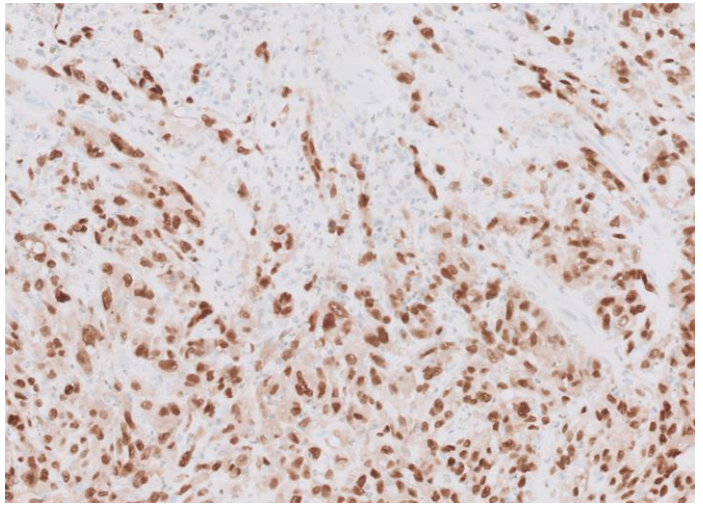
# Immunohistochemistry



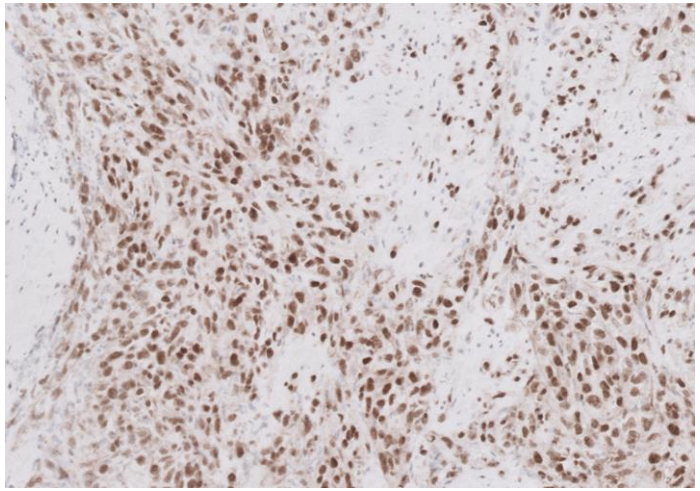
**GATA3**



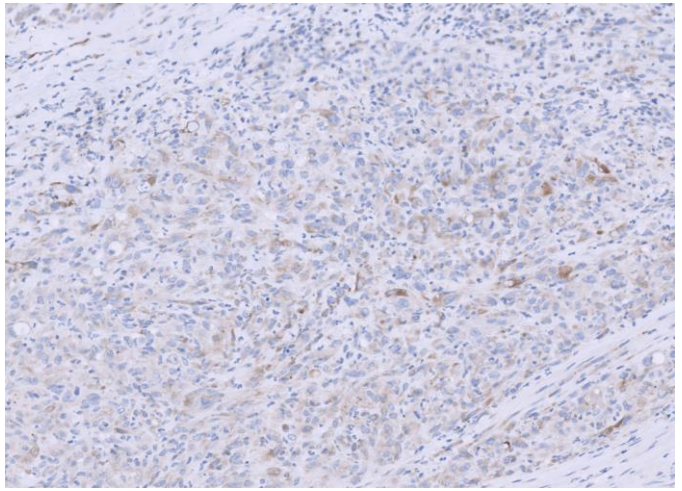
**CD31**



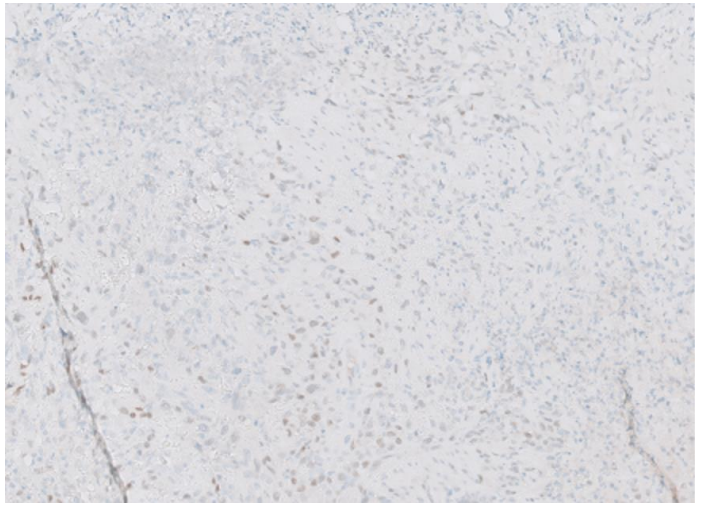
**ERG**



**FLI1**



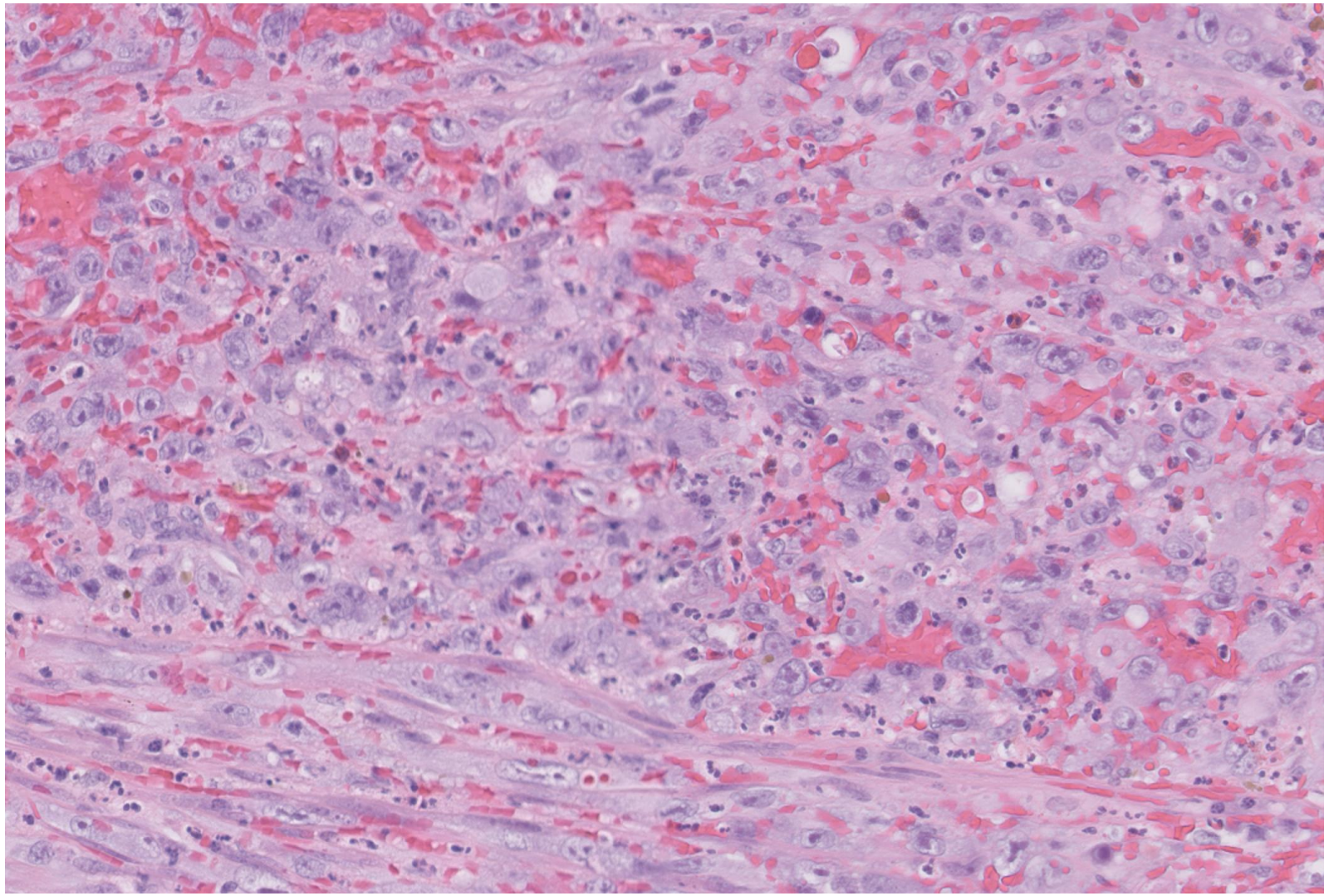
**CAMT**



**cMYC**

# Epithelioid angiosarcoma of the bladder

- Histology: malignant endothelial cells with epithelioid morphology
- Atypical nuclei, hemorrhagic background, occasional intracytoplasmic lumens, and interspersed erythrocytes are helpful
- Positive for at least one endothelial cell marker, urothelial marker negative, but no standard panel
- Our case: CD31+, ERG+, FLI1+, GATA3-



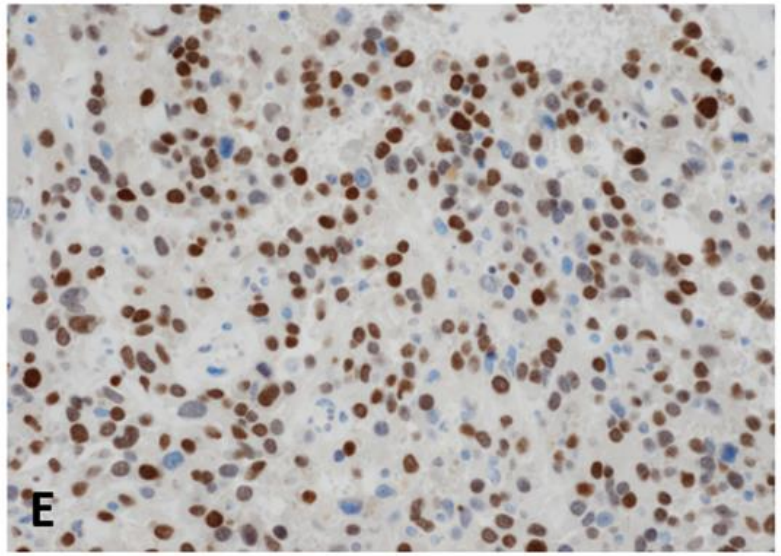
# Epidemiology, clinical features, and risk factors

- Very rare: 2% of genitourinary sarcomas, and sarcomas are only about 2% of all genitourinary malignancies
- Mean age: 65, male predominant
- Average size: 4 cm
- Presentation: hematuria and bladder mass

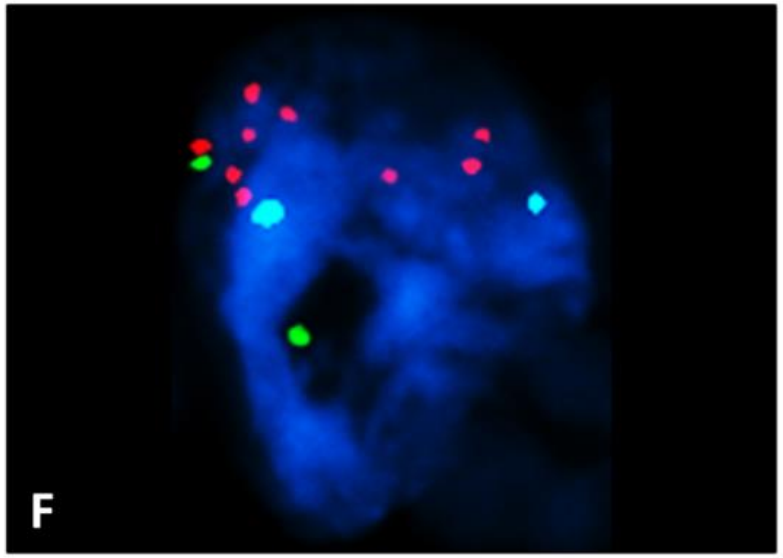
- Exposure to radiation
- Average time between radiotherapy and diagnosis: 11.5 years
- Exposure to smoking, chemicals (arsenic, thorium dioxide, polyvinyl chloride, or chemotherapeutics)
- Patient found to have chemical exposures, worked as a diesel mechanic for Cal Fire

Matoso et al, *Am J of Surg Path*, 2015

# Epithelioid angiosarcoma and *MYC* amplification




**MYC IHC**




**MYC FISH**

- Positive MYC on IHC and *MYC* amplification identified in epithelioid angiosarcoma of bladder
- Proto-oncogene located on 8q24 and involved in cell proliferation and differentiation
- May drive transformation of endothelial cells into angiosarcoma

***MYC* Amplification in Epithelioid Angiosarcoma of the Urinary Bladder and Prostate Following Prostate Radiotherapy: A Case Report with a Novel Molecular Alteration**

Vandana Panwar, MD[1,*], Suzanne J. Tintle, MD, MPH[1,*], Sharon Koorse Germans, MD[1], Prasad Koduru, PhD[1], and Liwei Jia, MD, PhD[1]

Panwar et al, *Int J of Surg Path*, 2022

# Epithelioid angiosarcoma and *MYC* amplification

**Table 1.** Summary of Clinical and Pathological Features of Epithelioid Angiosarcoma of the Urinary Bladder and/or Prostate Associated with Radiation.

| Publications | Age/ Sex | Size (cm) | Years after radiation | MYC status | Outcomes |
|---|---|---|---|---|---|
| Cito, G., *et al* 2021[22] | 78/M | NA | 8 | Positive by IHC Not detected by FISH | Died in the immediate post operative period from peritonitis and septic shock |
| Alessandra, F., *et al* 2020[23] | 65/M | NA | 10 | Positive by IHC FISH not performed | DOD (3 months) |
| Wang, G. *et al* 2016[18] | 79/M | NA | 6 | Positive by IHC FISH not performed | NED (20 months) |
| Rallabandi, H., *et al* 2016[24] | 65/F | NA | 22 | NA | NA |
| Gupta, A., *et al* 2015[25] | 71/M | 6.1 | 8 | NA | LWD with lymph nodes metastases |
| Ojerholm, E., *et al* 2015[26] | 61/M | 3.5 | 7 | NA | NA |
| Kulaga, A., *et al* 2007[27] | 83/F | NA | 14 | NA | DOD (3 months) |
| Chandan, V., *et al* 2003[28] | 77/M | NA | 12 | NA | NA |

M, male; F, female; IHC, Immunohistochemistry; FISH, fluorescence in situ hybridization; NA, not available; DOD, died of disease; NED, no evidence of disease; LWD, live with disease.

- *MYC* amplification identified in other cases
- Associated with radiation- or chronic lymphedema-associated angiosarcomas
- Useful in breast, uncertain prognostic significance in other sites

Panwar et al, *Int J of Surg Path*, 2022

# Take home points

- Epithelioid angiosarcoma is a rare bladder malignancy characterized by malignant endothelial cells with epithelioid morphology, showing vasoformation and atypical cells with intracytoplasmic vacuoles
- Easy to mistake for a carcinoma and for other vascular tumors—consider angiosarcoma in the differential
- Associated with radiation and chemical exposures
- *MYC* amplification may be present but of uncertain significance

# References and acknowledgments

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2. Motaparthi, K., Lauer, S.R., Patel, R.M., Vidal, C.I. and Linos, K., 2021. MYC gene amplification by fluorescence in situ hybridization and MYC protein expression by immunohistochemistry in the diagnosis of cutaneous angiosarcoma: Systematic review and appropriate use criteria. *Journal of Cutaneous Pathology*, *48*(4), pp.578-586.

3. Nizam, A., Paquette, E.L., Wang, B.G. and Aragon-Ching, J.B., 2018. Epithelioid angiosarcoma of the bladder: A case report and review of the literature. *Clinical Genitourinary Cancer*, *16*(6), pp.e1091-e1095.

2. Panwar, V., Tintle, S.J., Koorse Germans, S., Koduru, P. and Jia, L., 2022. MYC amplification in epithelioid angiosarcoma of the urinary bladder and prostate following prostate radiotherapy: a case report with a novel molecular alteration. *International Journal of Surgical Pathology*, *30*(7), pp.792-796.

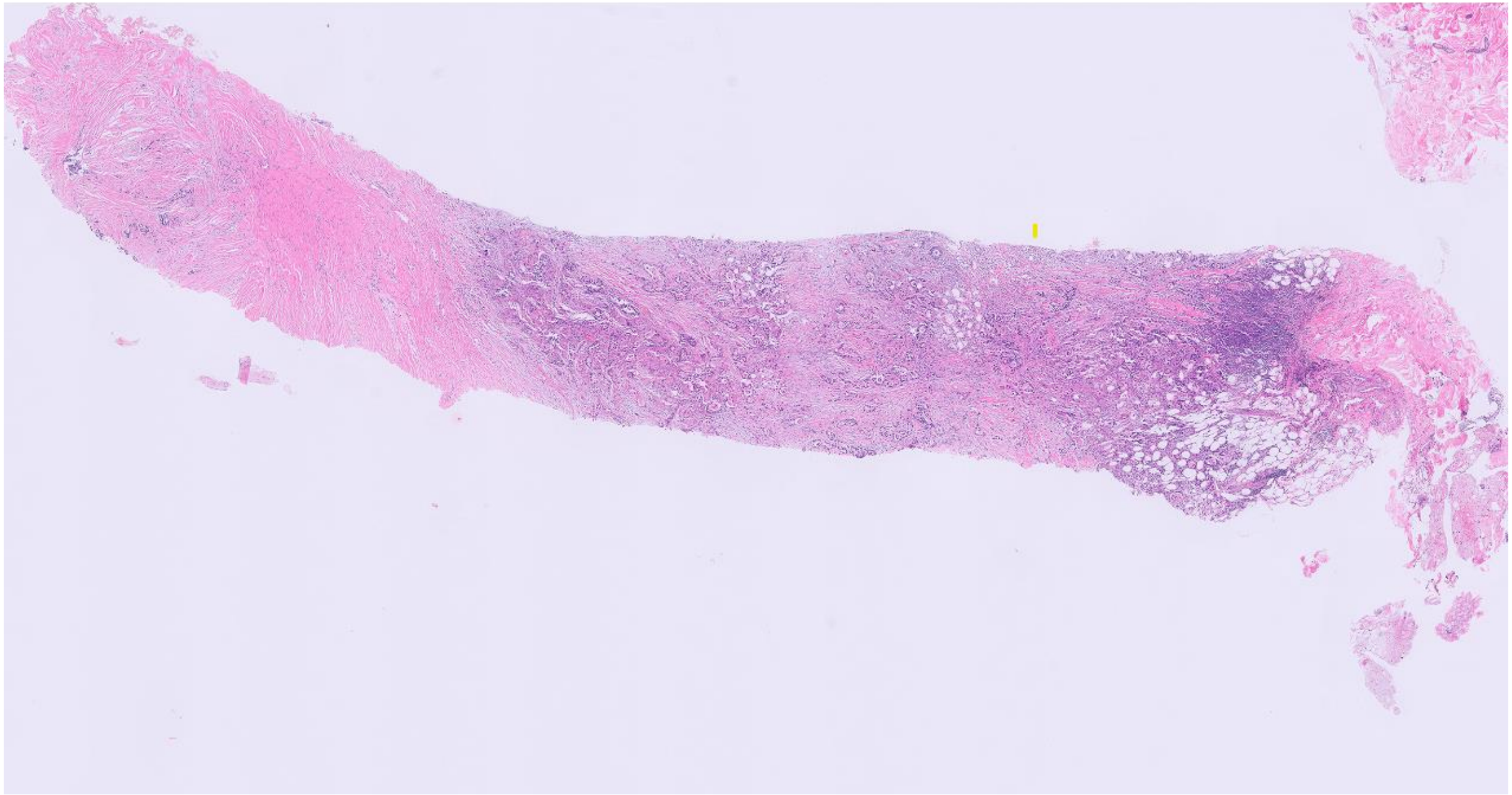
3. Zhang, J., Gong, H., Wang, Y., Zhang, G. and Hou, P., 2022. Angiosarcoma of the visceral organs: A morphological, immunohistochemical, and C-MYC status analysis. *Pathology-Research and Practice*, *238*, p.154118.

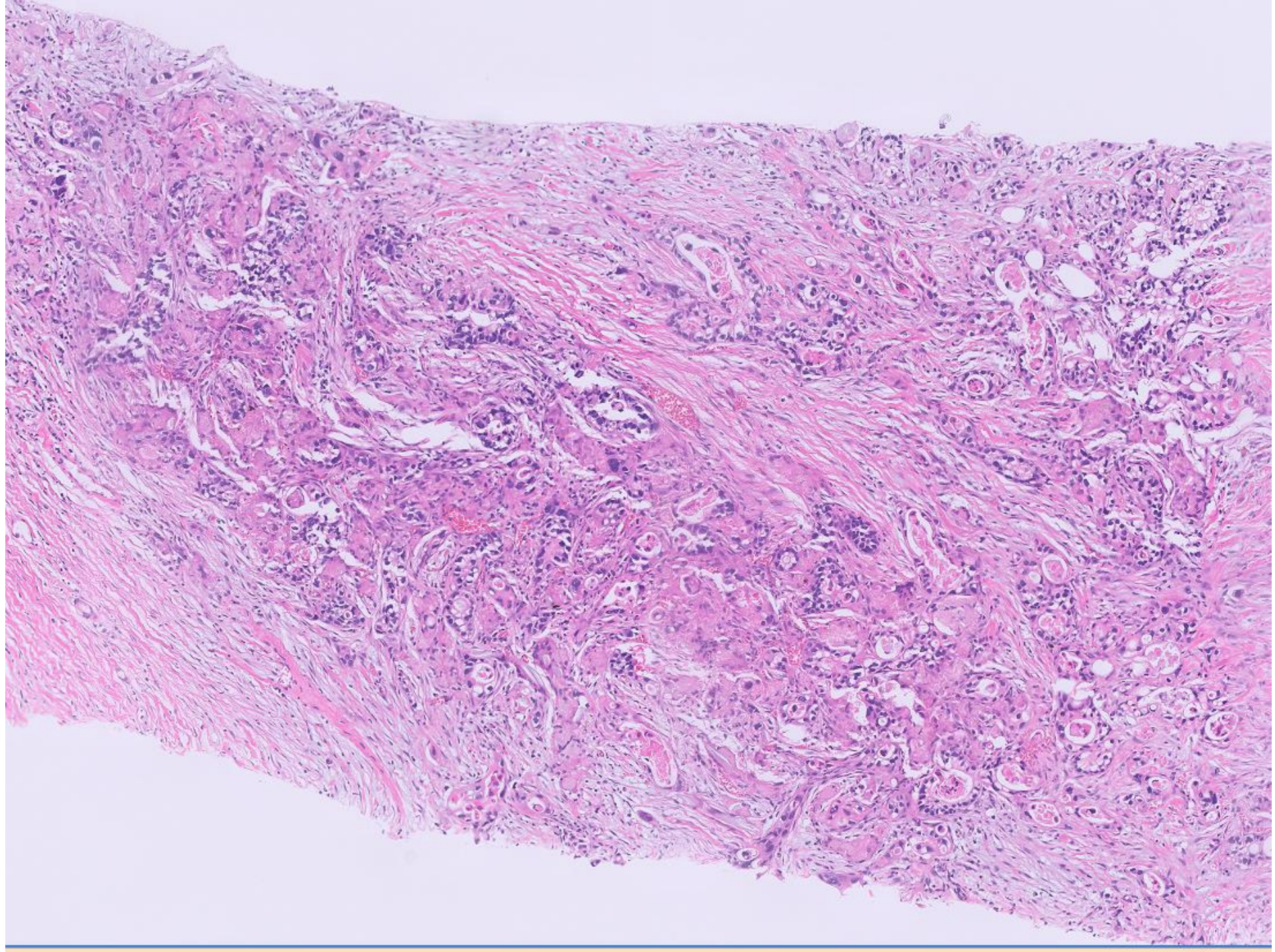
Thank you to Dr. Ding, UCSF Genitourinary Pathology, and the South Bay Pathology Society.
Special thanks to Dr. Rachel Donohue, Providence St. Joseph Medical Center, Eureka, CA.

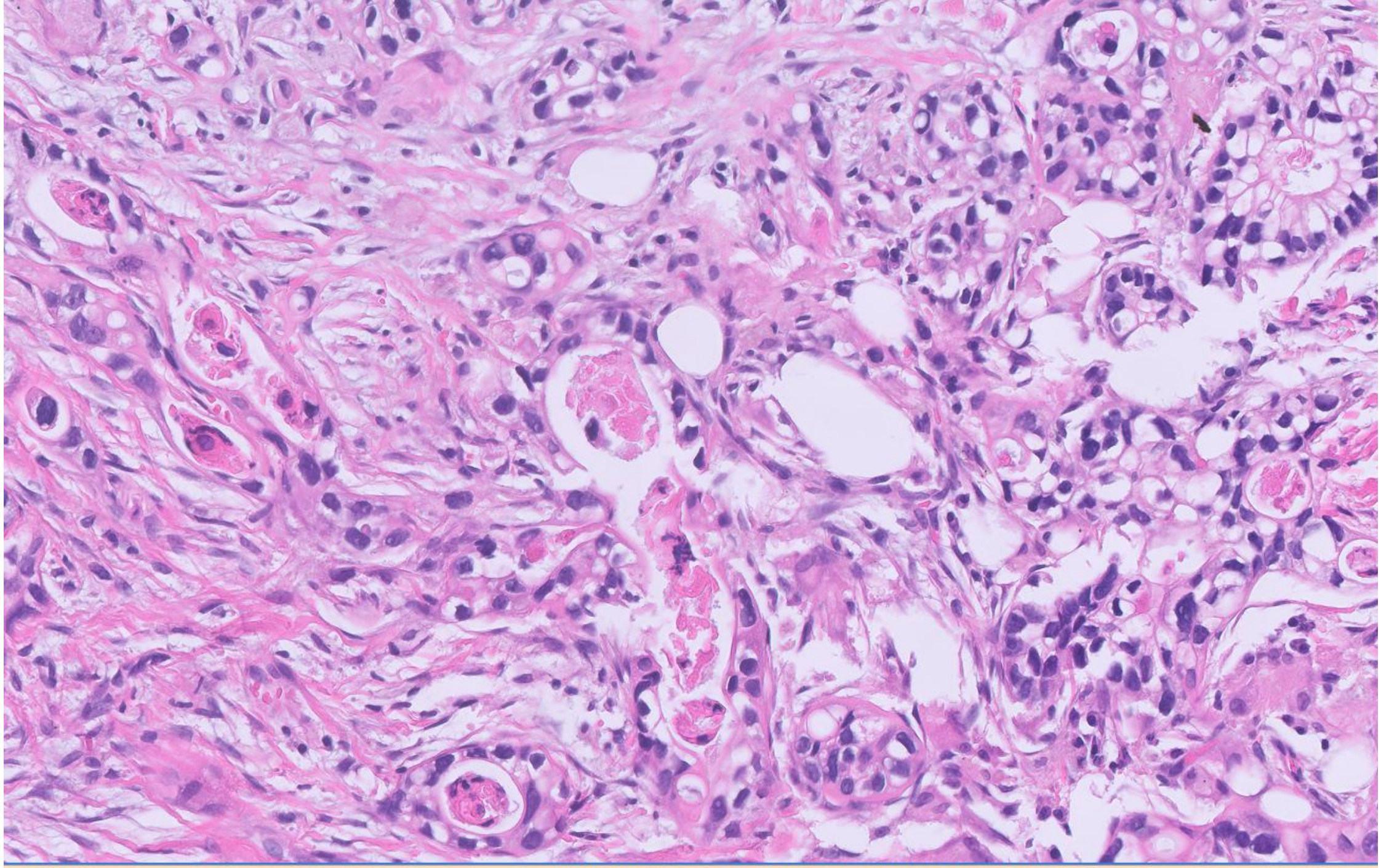
24-0104

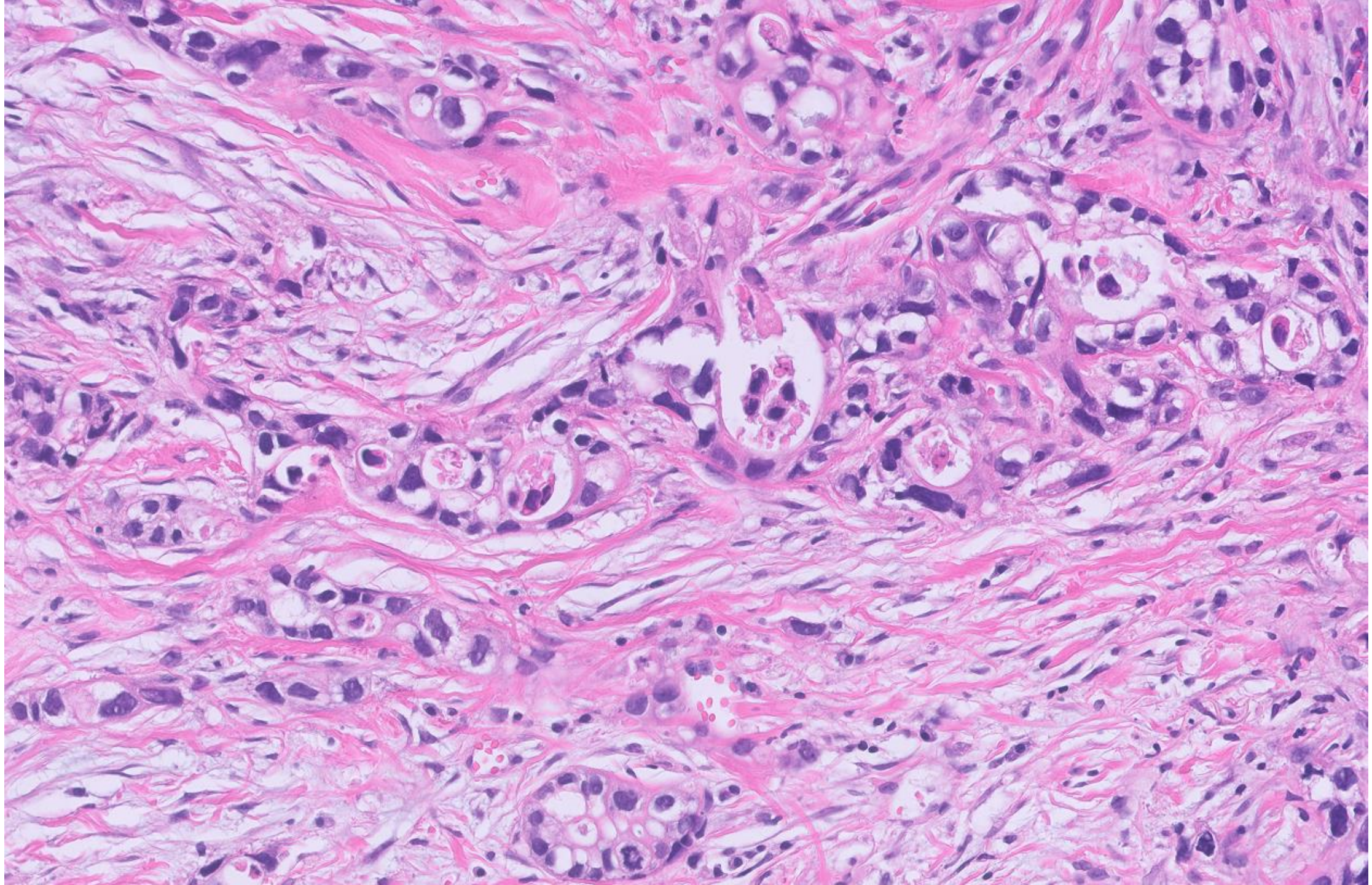
**Lixia Bai MD, PhD  Breast Pathology Fellow and Megan Troxell; Stanford**

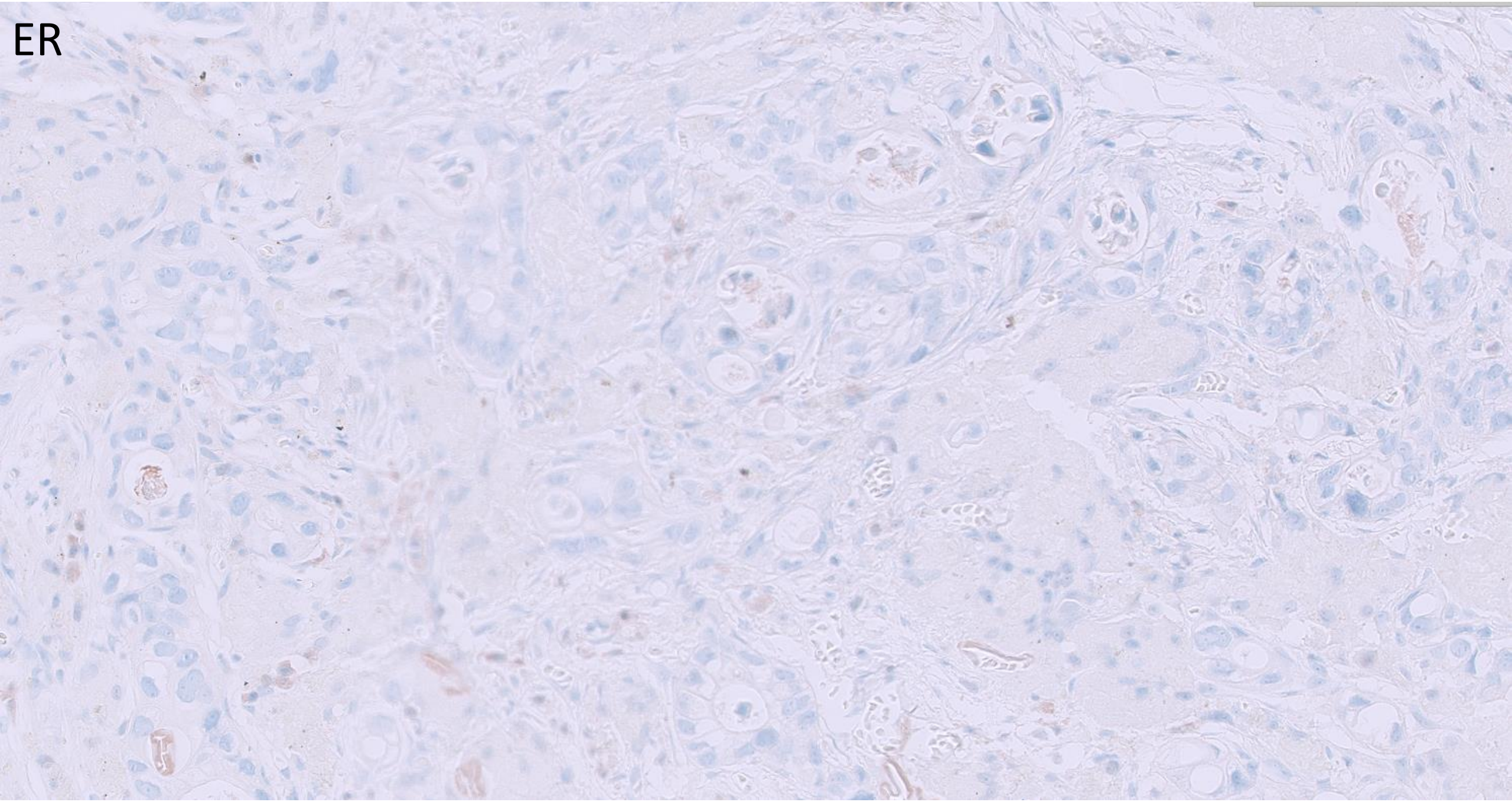
# 90+ years old woman with a 2.9 cm mass in the right breast







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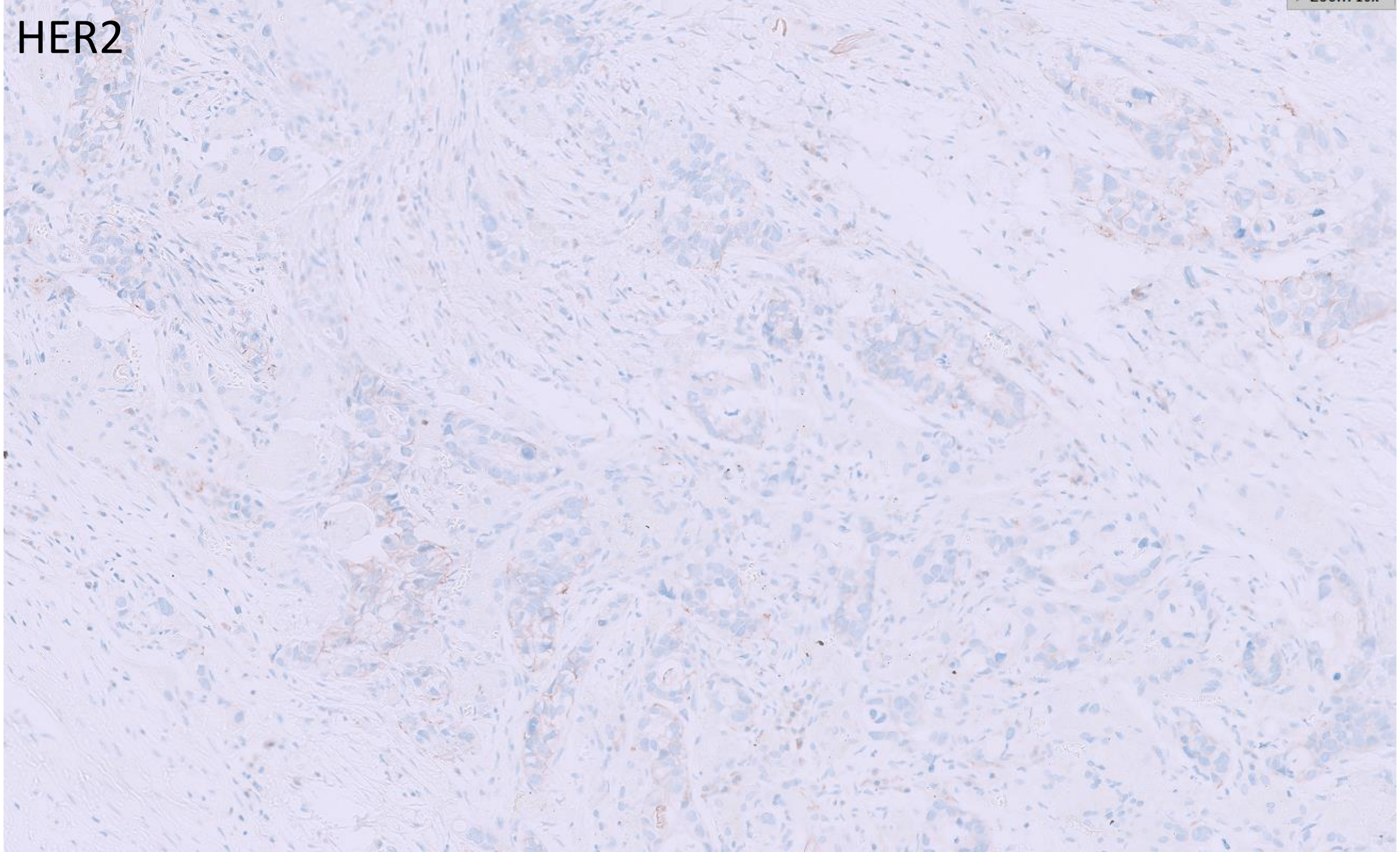
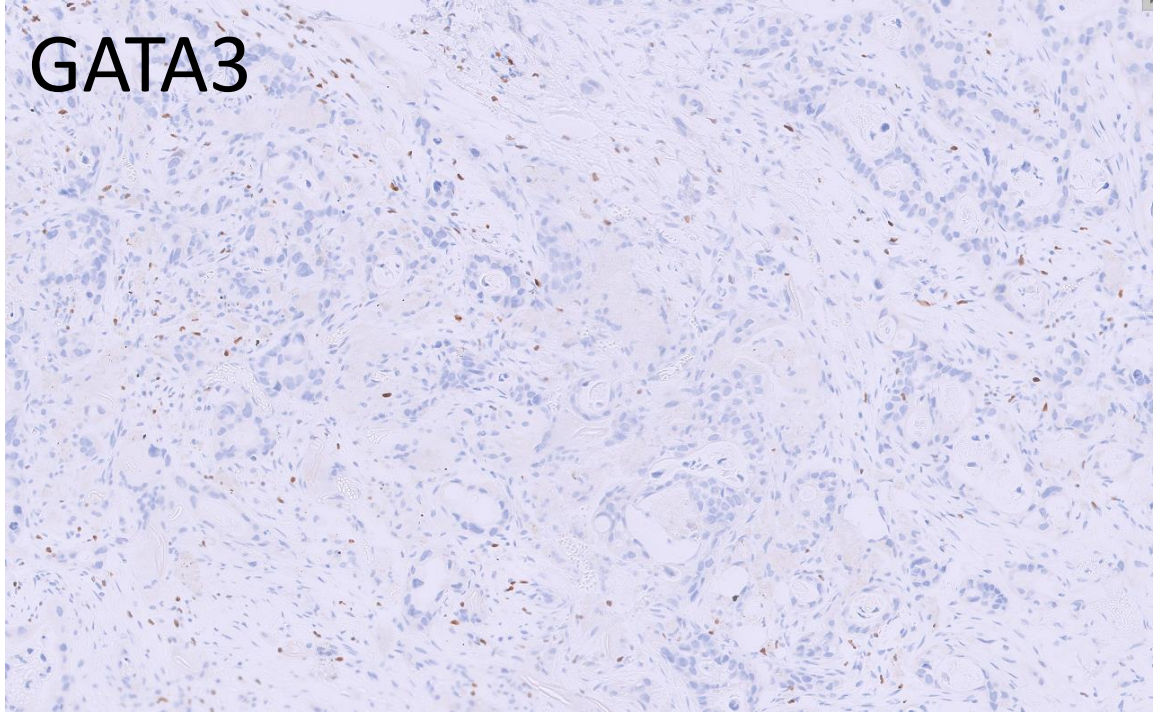
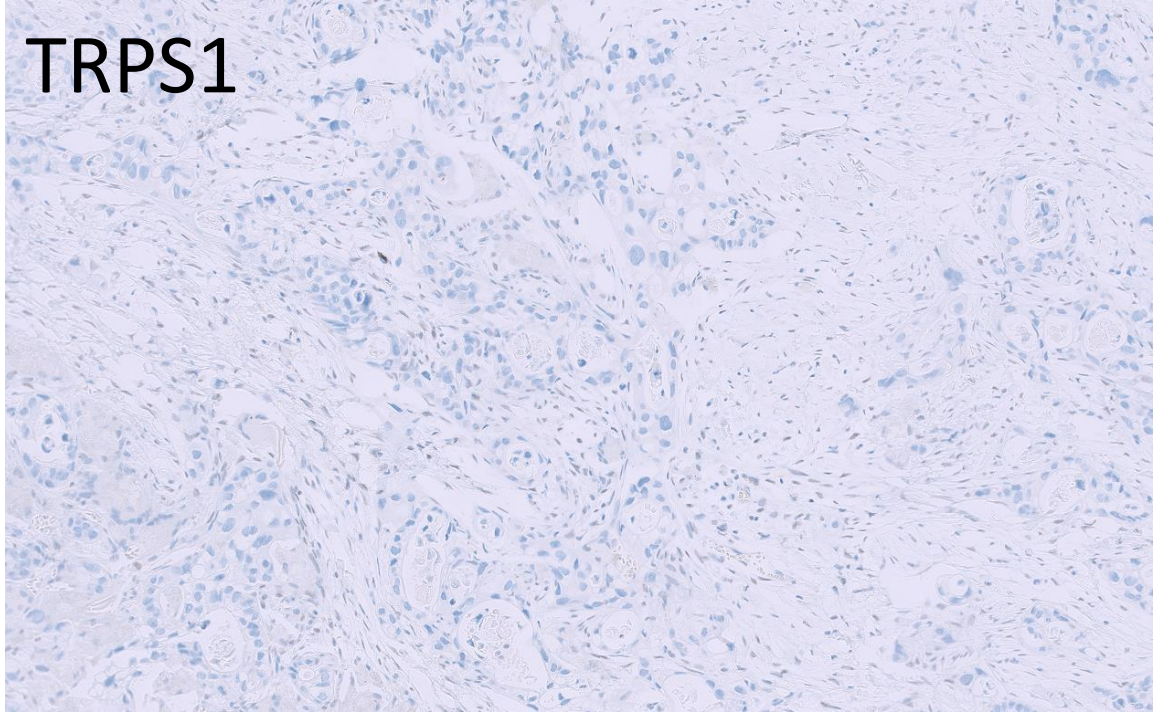

HER2

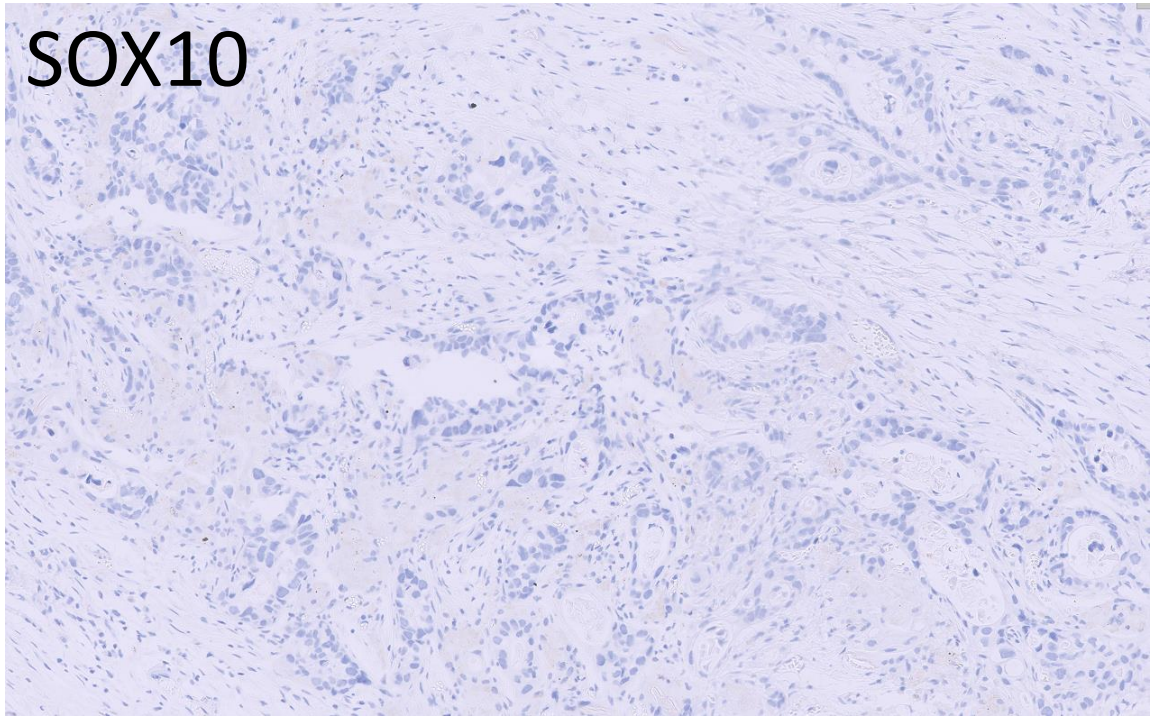
# DIAGNOSIS?

# Differential Diagnosis

- Primary breast cancer
  - Invasive ductal carcinoma
- Metastatic adenocarcinoma

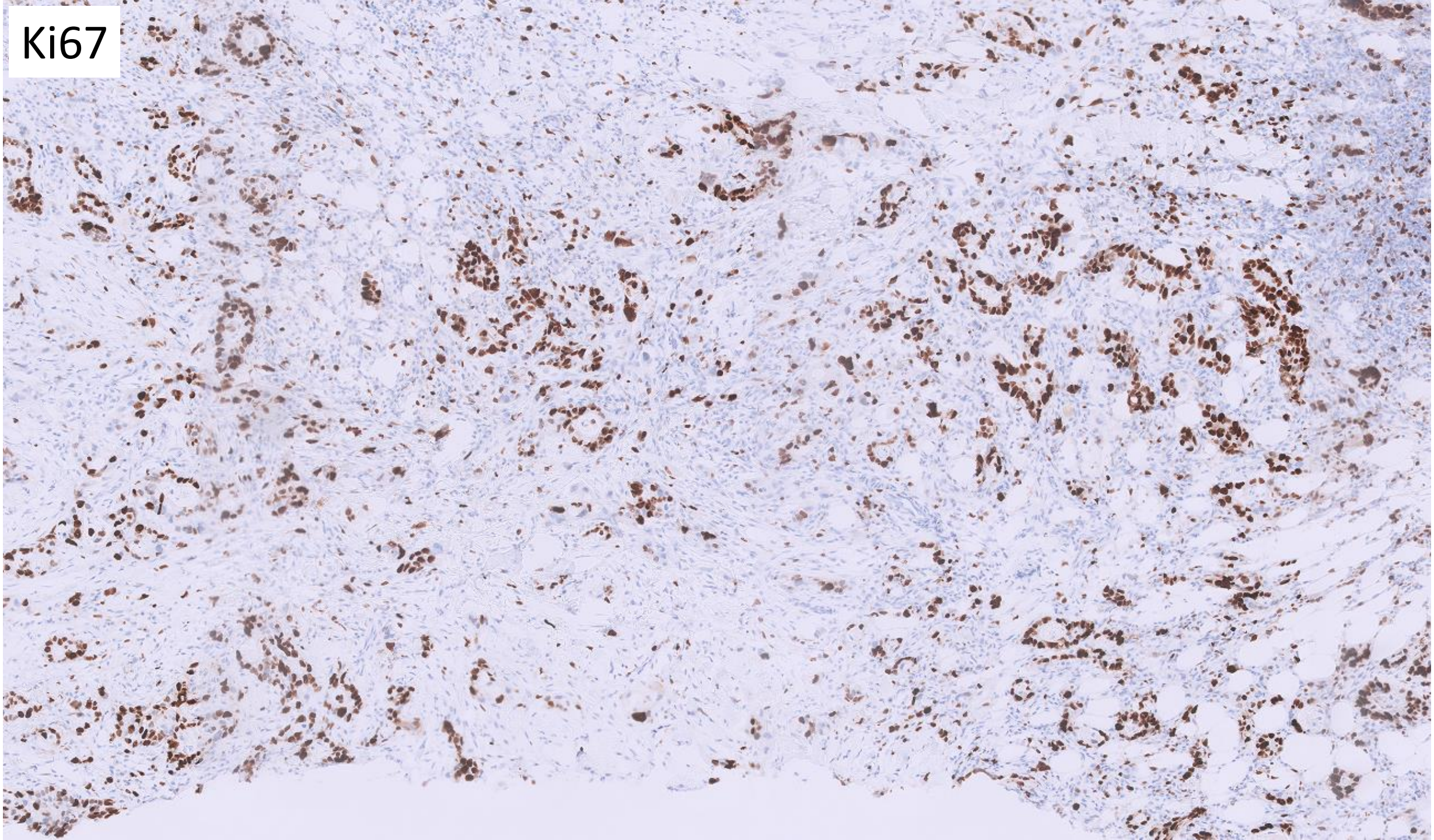


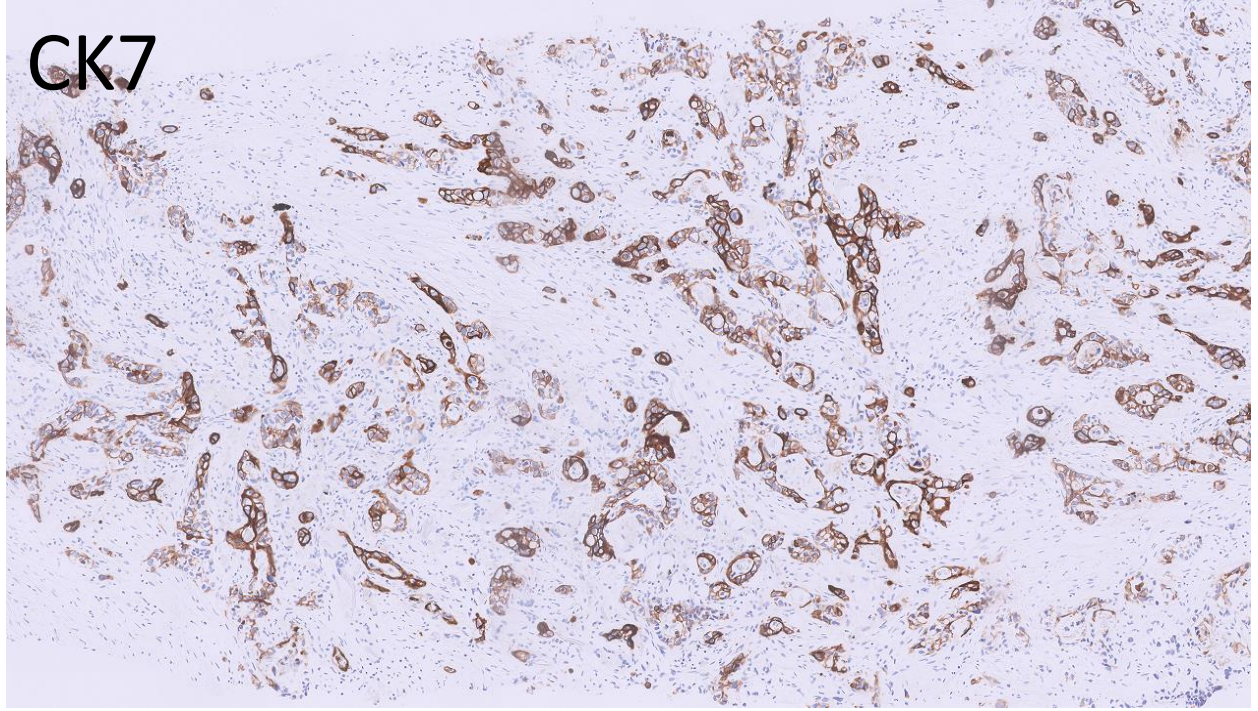



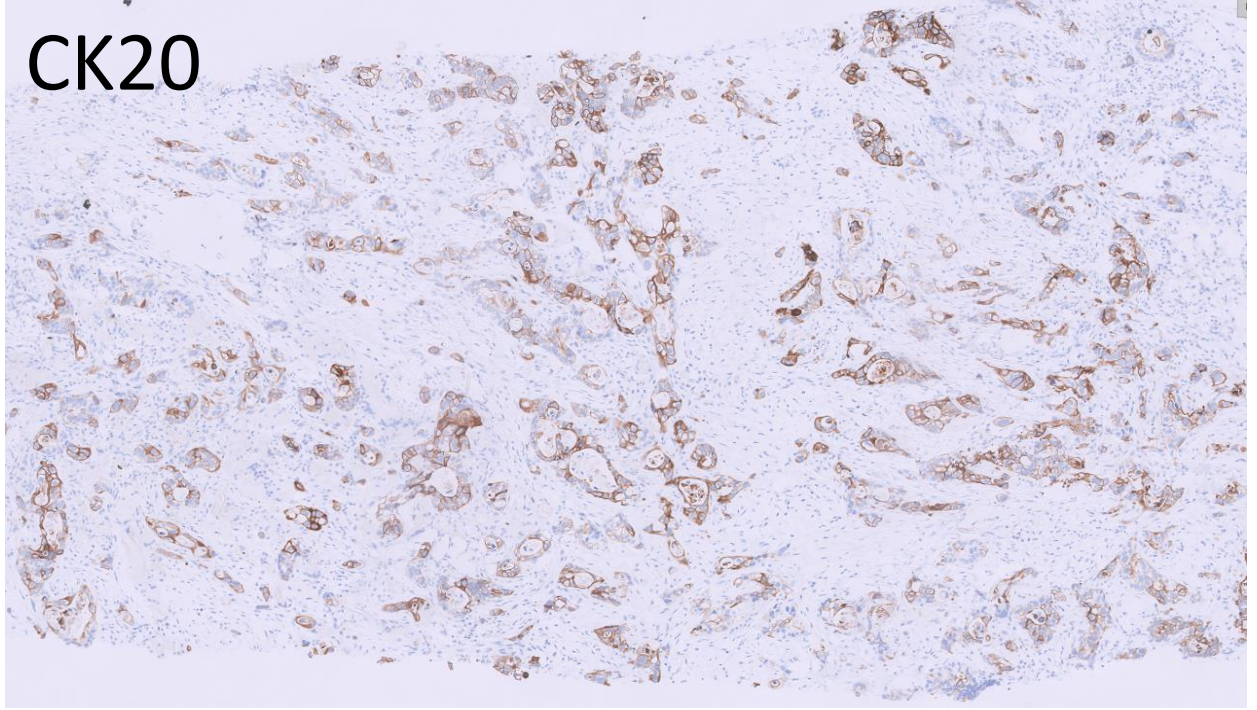



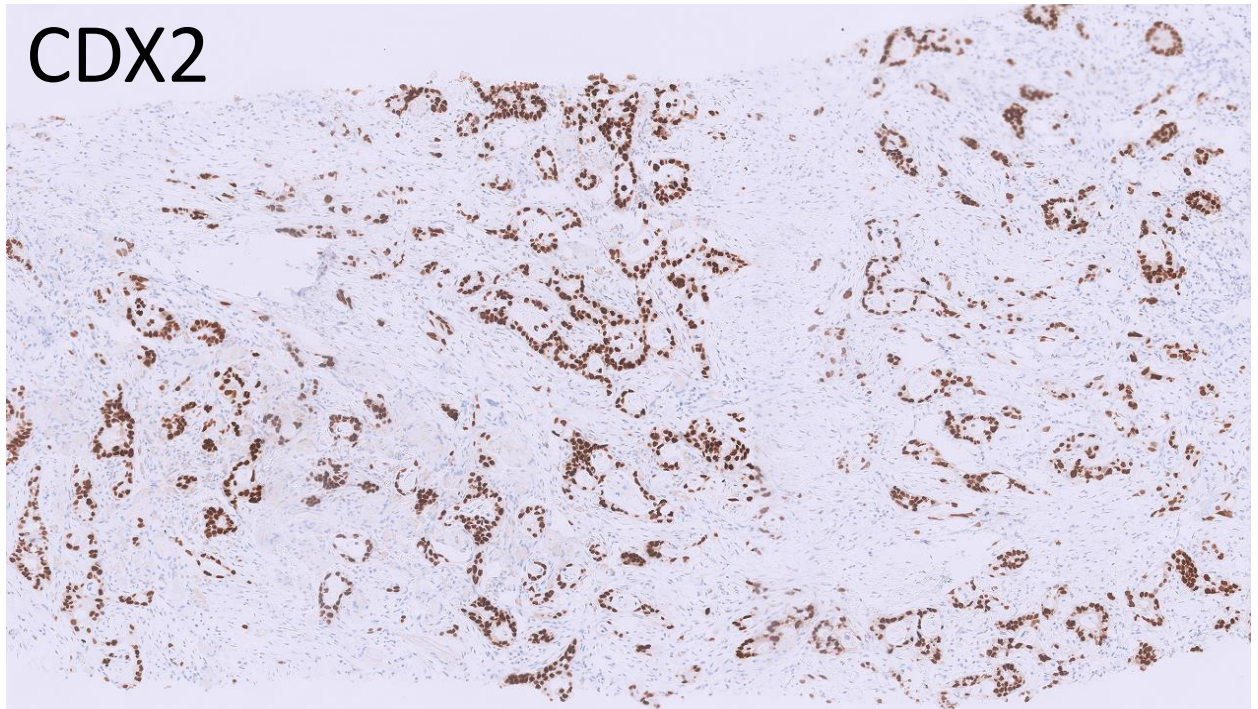

## Biomarkers:

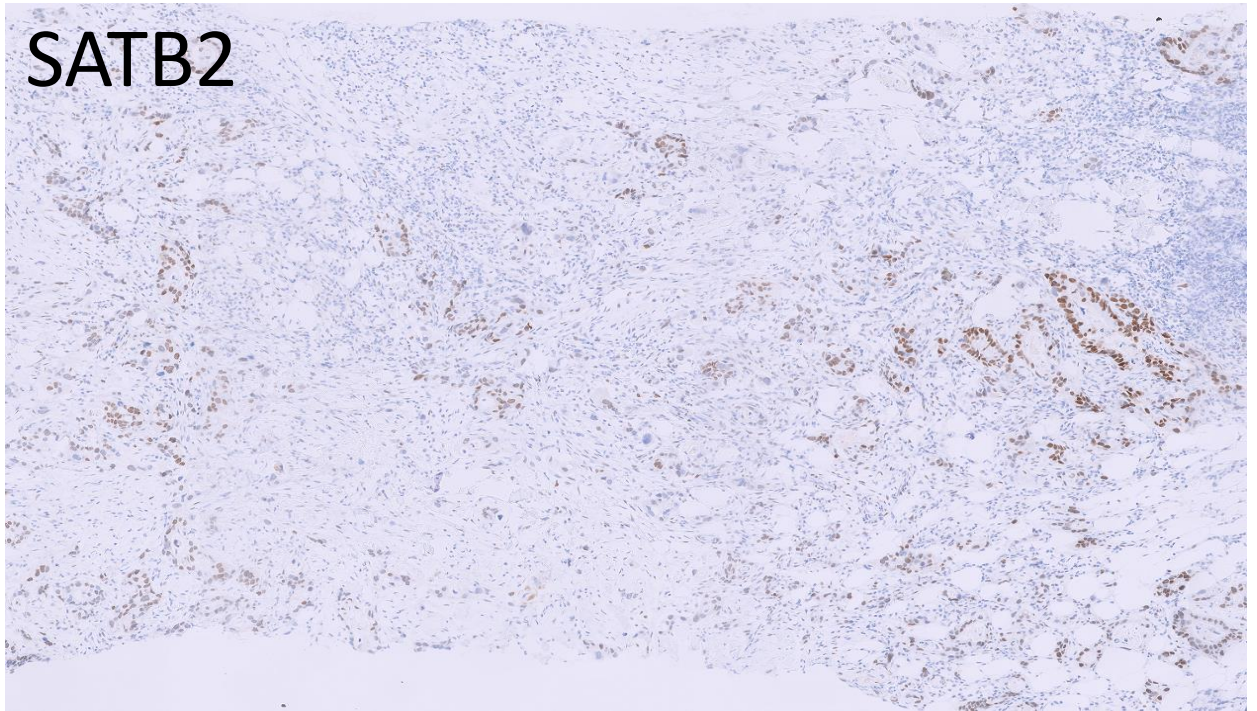
ER negative (0%)
PR negative (0%)
HER2 IHC negative (1+)
HER FISH not performed


Ki67

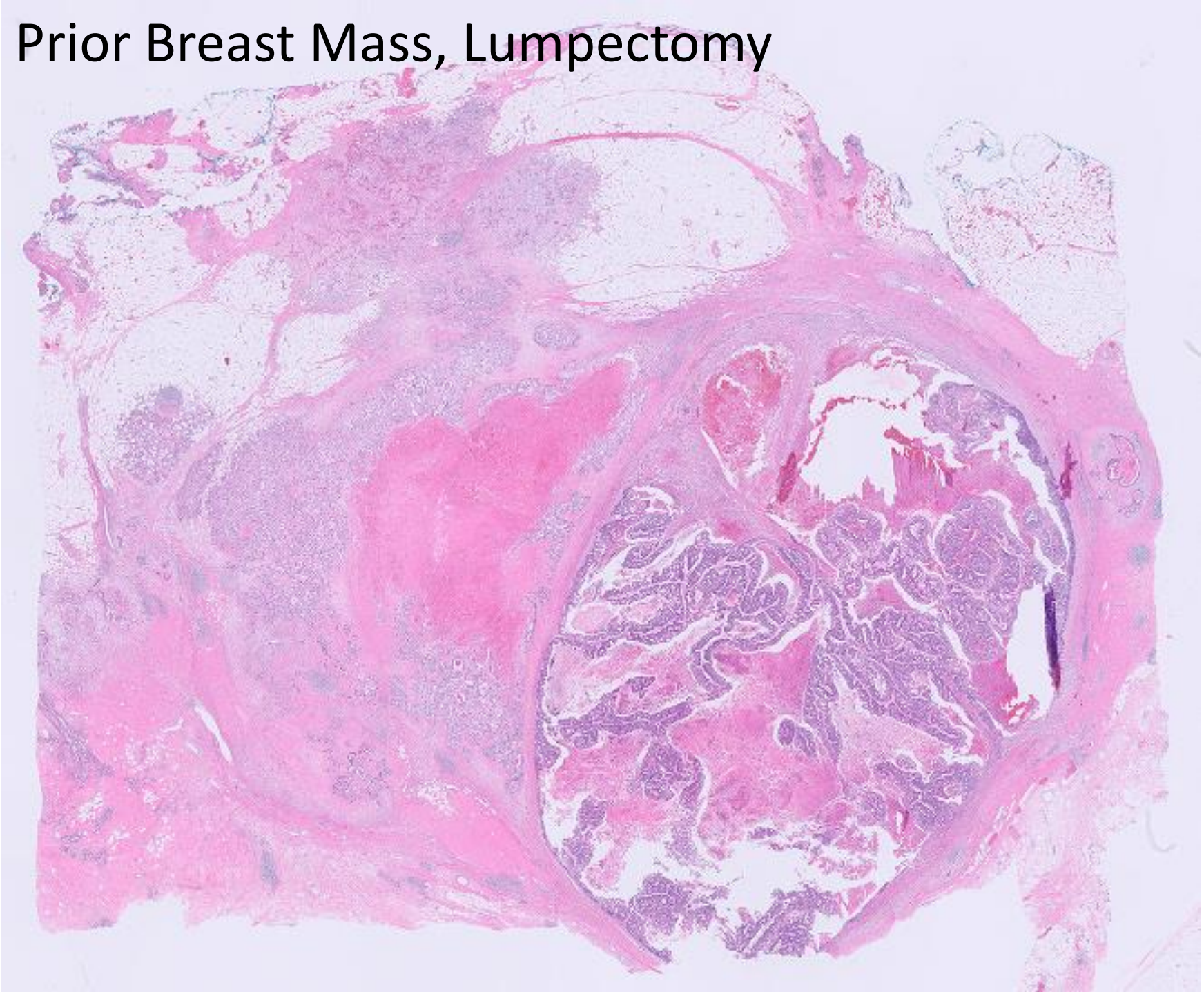

CK7


CK20

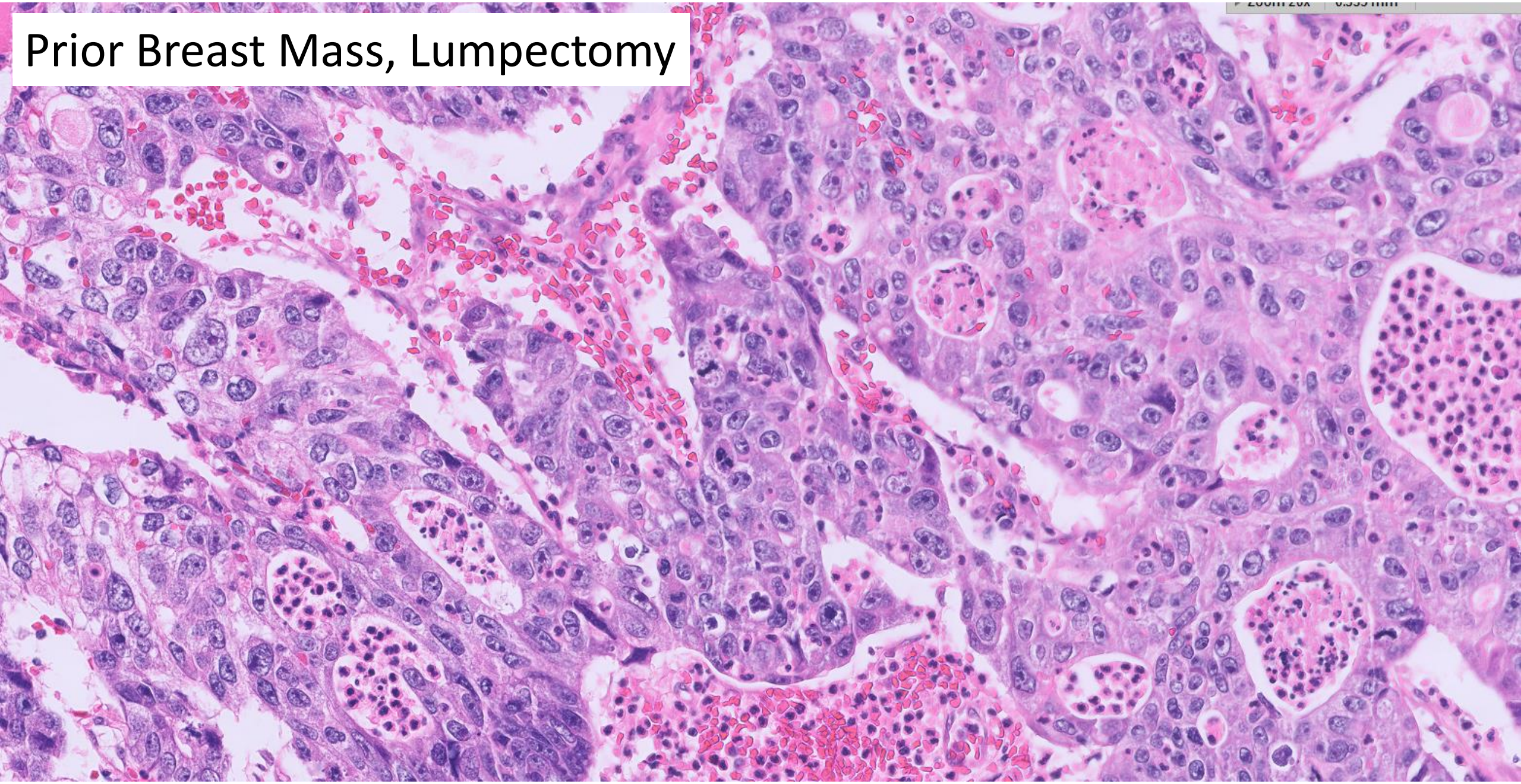

CDX2


SATB2

# Prior Breast Mass, Lumpectomy



# Prior Breast Mass, Lumpectomy



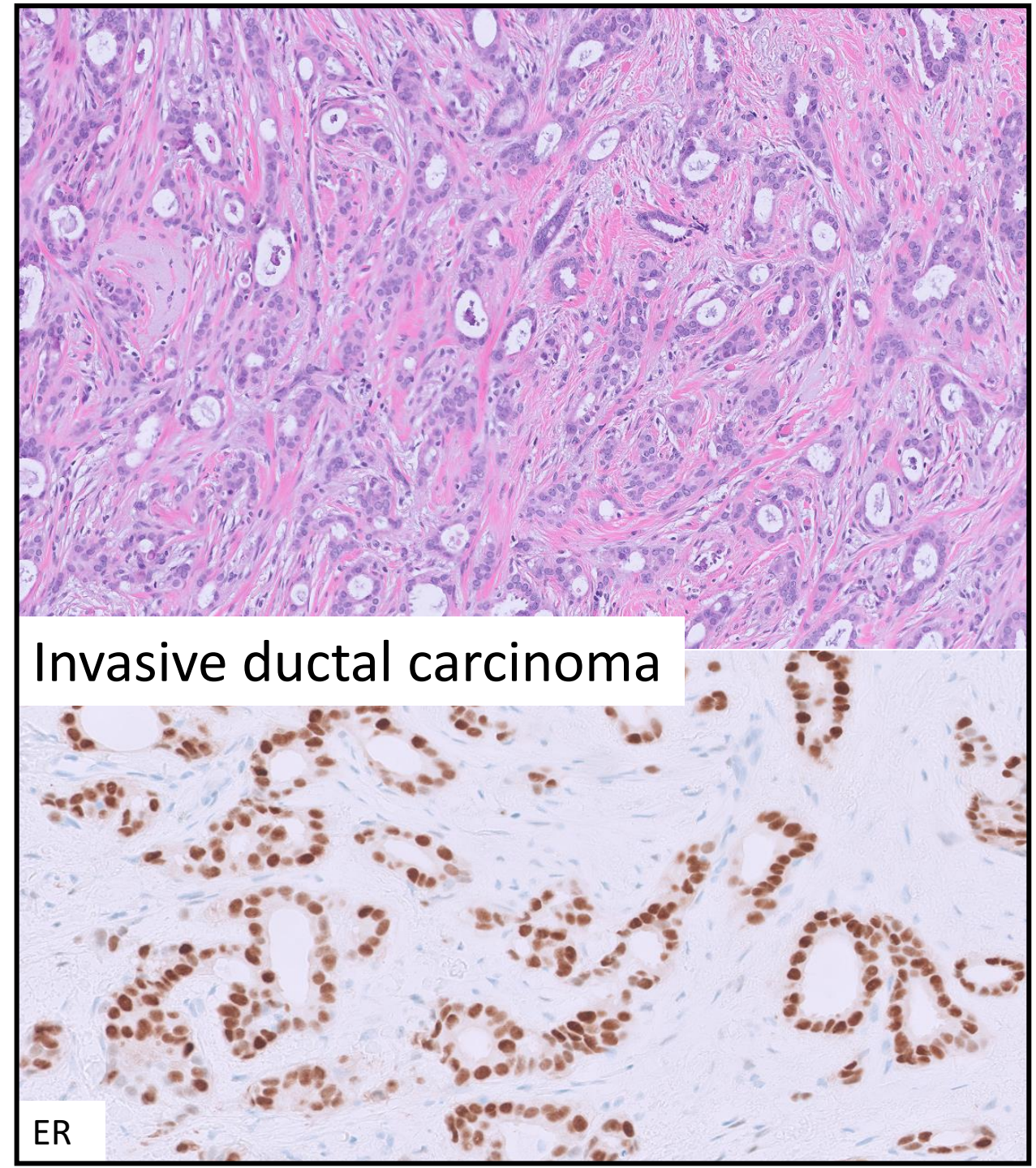
# Prior Breast Mass, Lumpectomy:

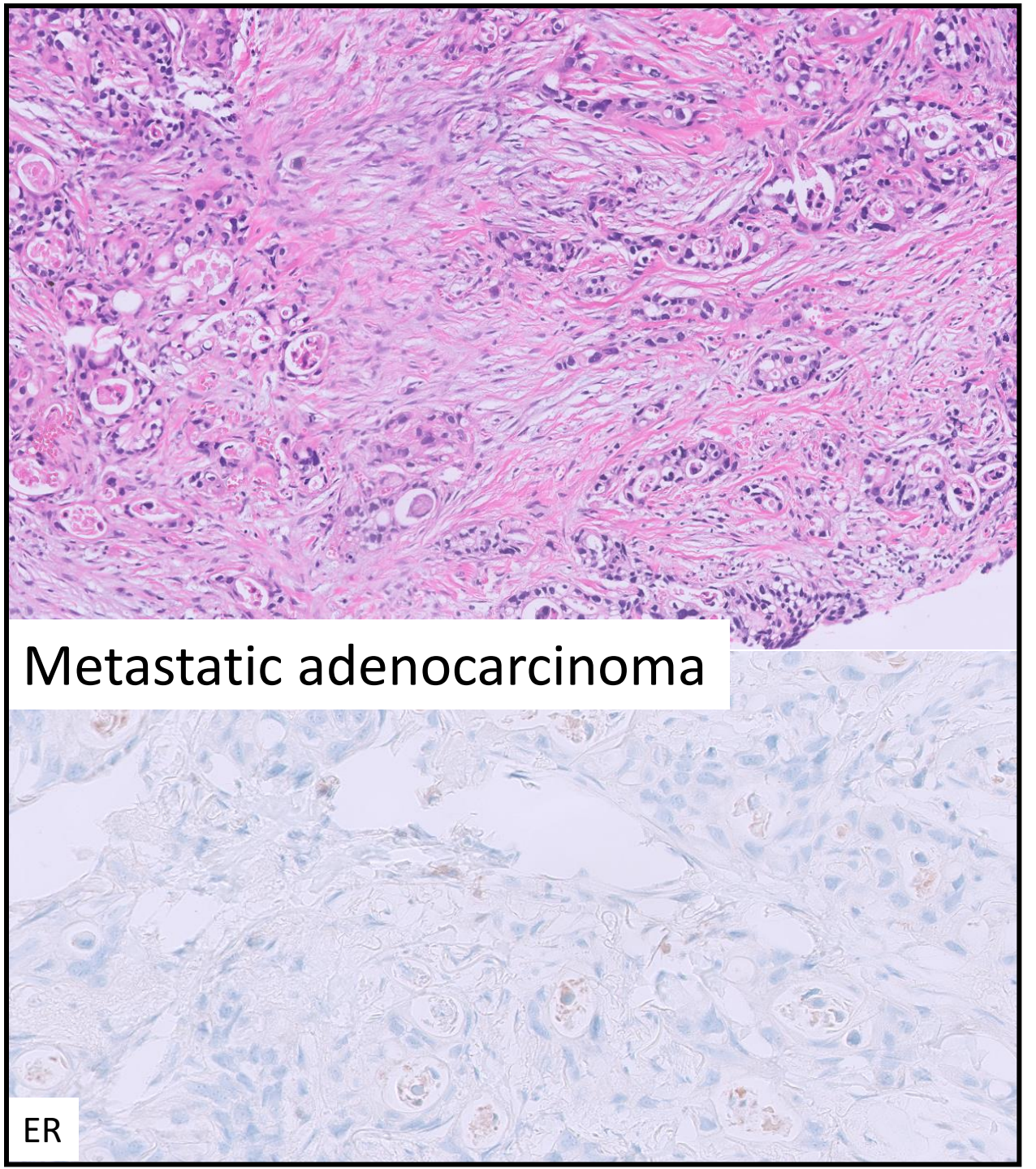
- Positive
  - CK7, CK20, CDX2, SATB2-partial, weak, CA19-9, and CA125-focal
- Negative
  - GATA3, GCDFP-15, P63, PAX-8, WT-1, Napsin A, P16, and Glypican 3

# Right Breast, Core Biopsy

- **Diagnosis**
  - **Moderately to poorly differentiated adenocarcinoma, favor metastatic**

- Comments
  - The morphologic and immunophenotypic features are not characteristic for breast cancer, more compatible with metastatic adenocarcinoma, mostly likely from upper gastrointestinal tract, including pancreatobiliary.
  - Further clinical and radiological correlation, with consideration for endoscopy or dedicated upper GI/pancreatobiliary imaging, is recommended to determine the origin of the carcinoma.


Invasive ductal carcinoma
ER


Metastatic adenocarcinoma
ER

# Take home message

- GI tract malignancy metastasis to the breast is extremely rare.
- The diagnosis of metastasis to the breast should be considered:
  - If the histological and/or immunophenotypic features are not typical of a mammary primary tumor.
  - If there is a history of extramammary malignancy.
- Consultation with colleagues and additional workup are necessary.

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- Ma Y, Liu W, Li J, Xu Y, Wang H. Gastric cancer with breast metastasis: Clinical features and prognostic factors. Oncol Lett. 2018 Nov;16(5):5565-5574.

- Hsieh TC, Hsu CW. Breast metastasis from colorectal cancer treated by multimodal therapy: Case report and literature review. Medicine (Baltimore). 2019 Dec;98(51):e18016.

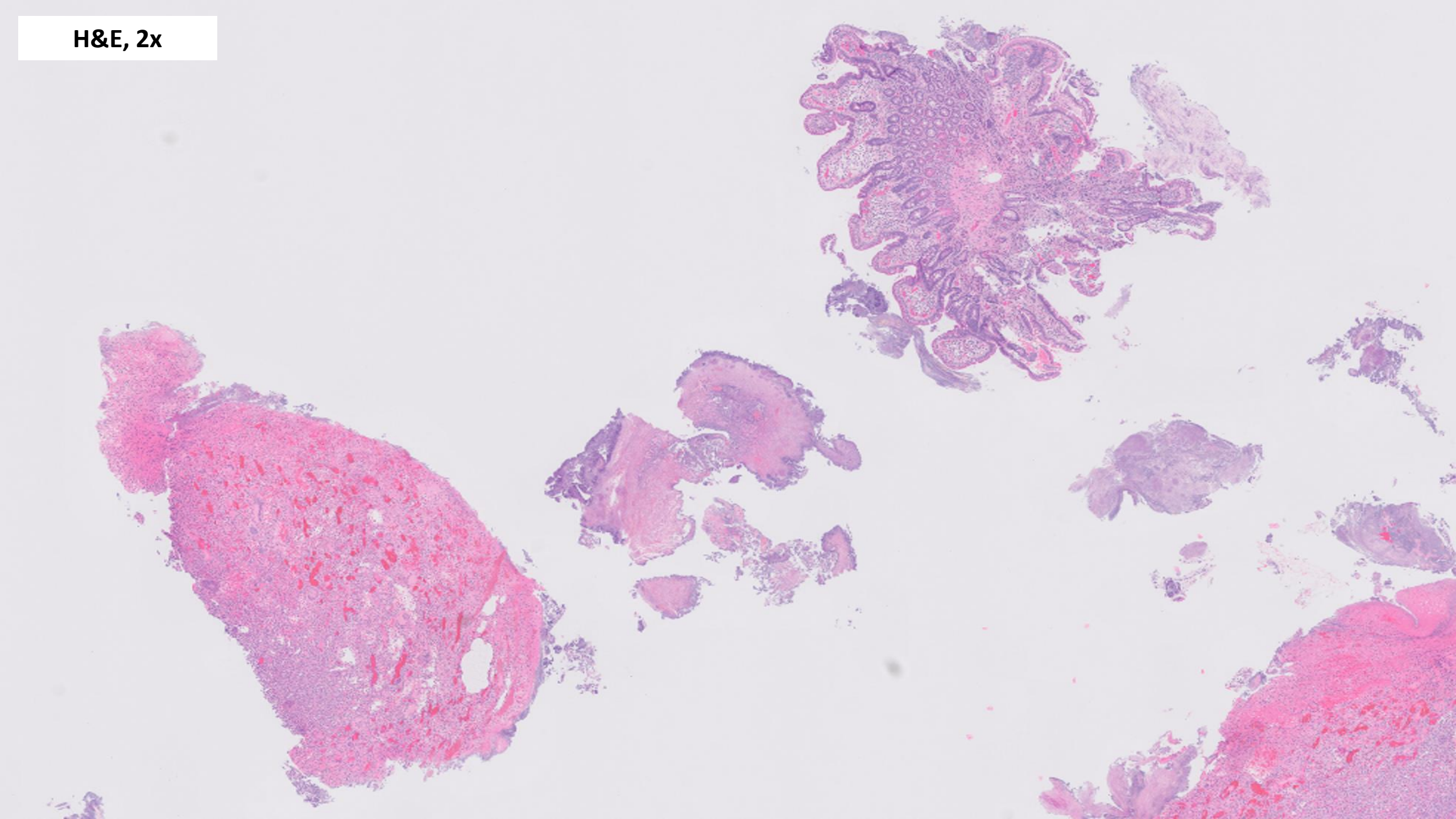
- Lee AHS, Hodi Z, Soomro I, Sovani V, Abbas A, Rakha E, Ellis IO. Histological clues to the diagnosis of metastasis to the breast from extramammary malignancies. Histopathology. 2020 Aug;77(2):303-313.

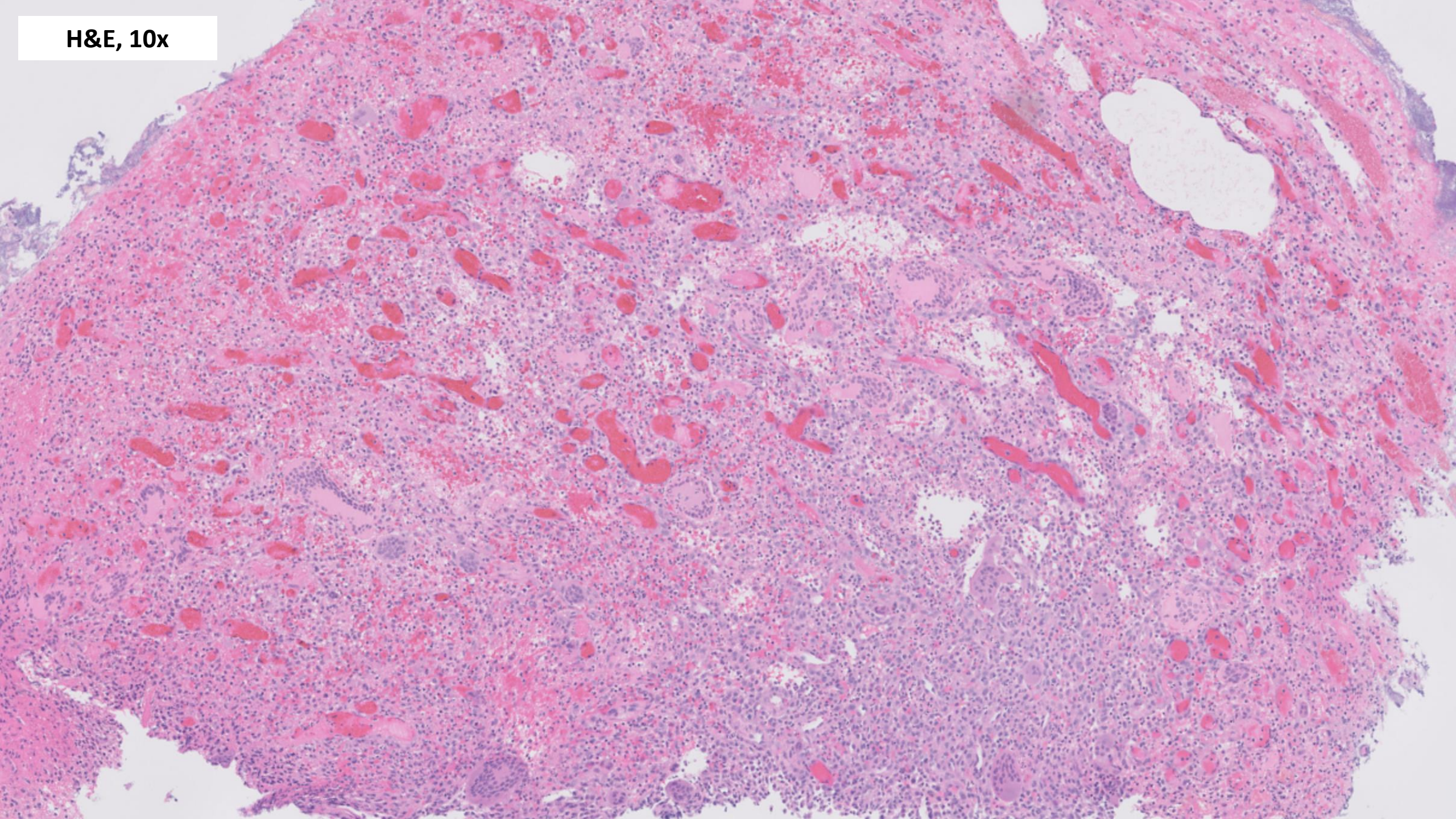
24-0105

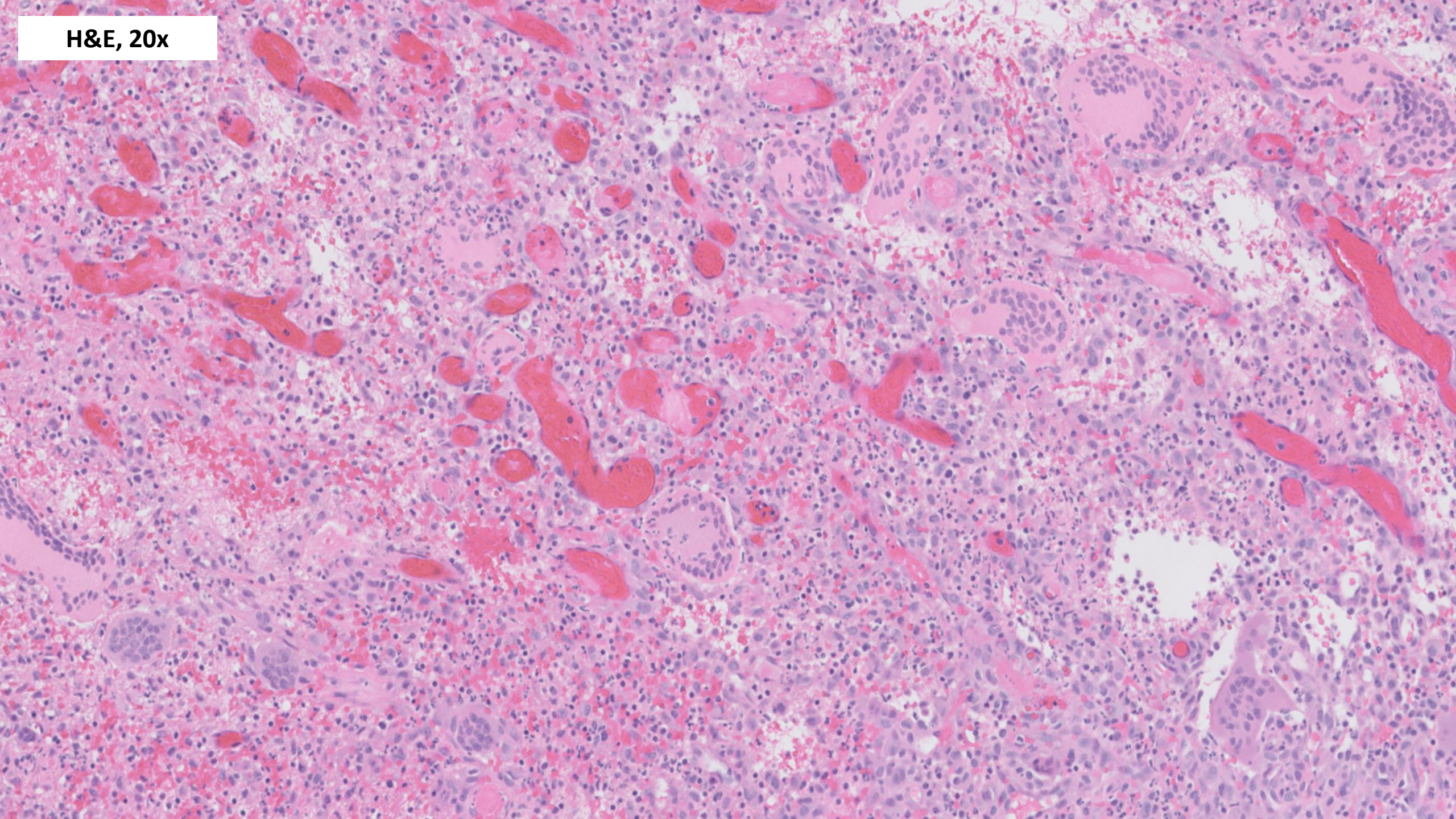
**Natalia Sanchez, Sarah Umetsu and Cornelia Ding; UCSF**

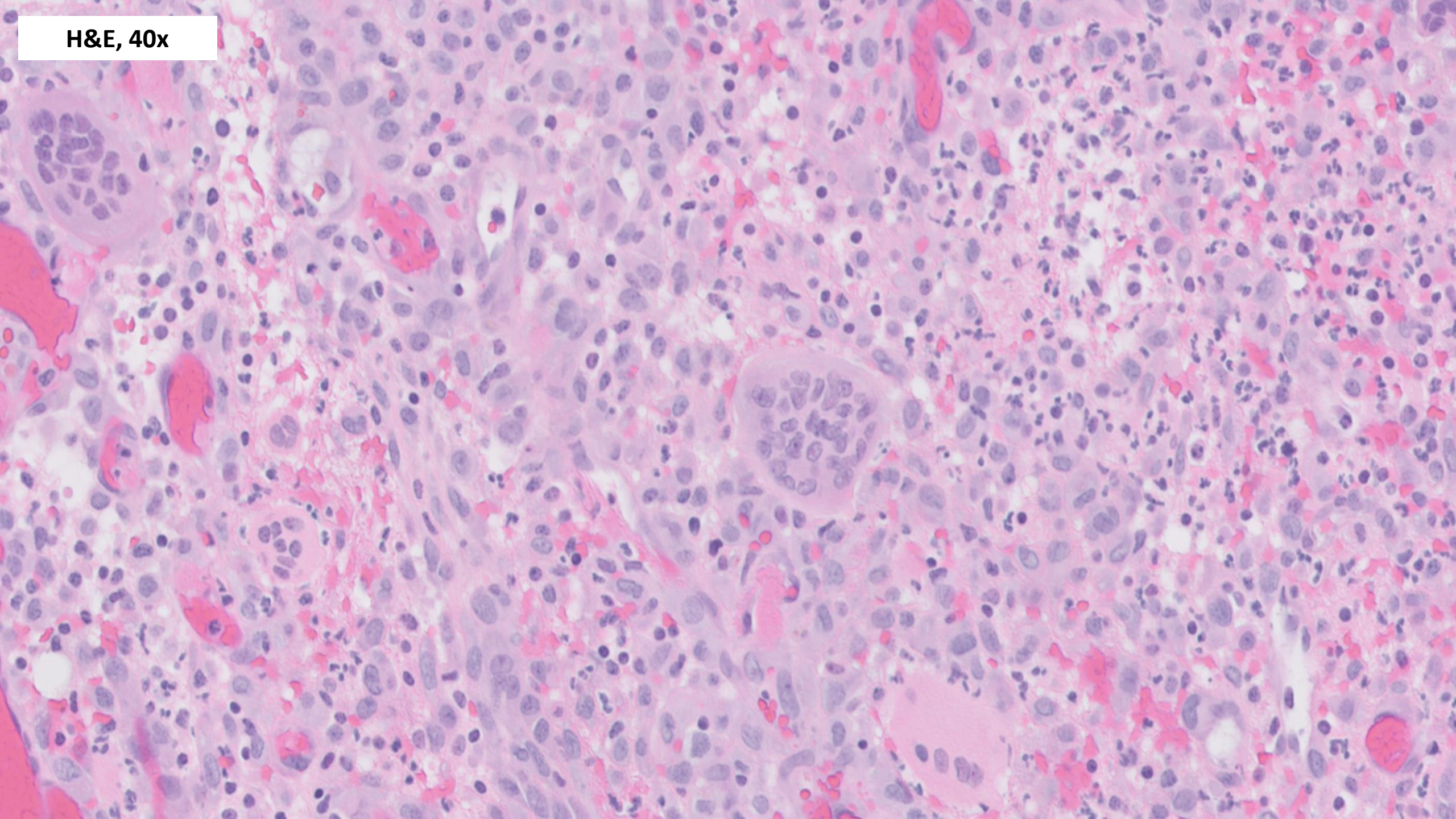
80-year-old male with history of metastatic urothelial carcinoma status post-radiation. Presenting with duodenal bulb ulcer on EGD which is biopsied.

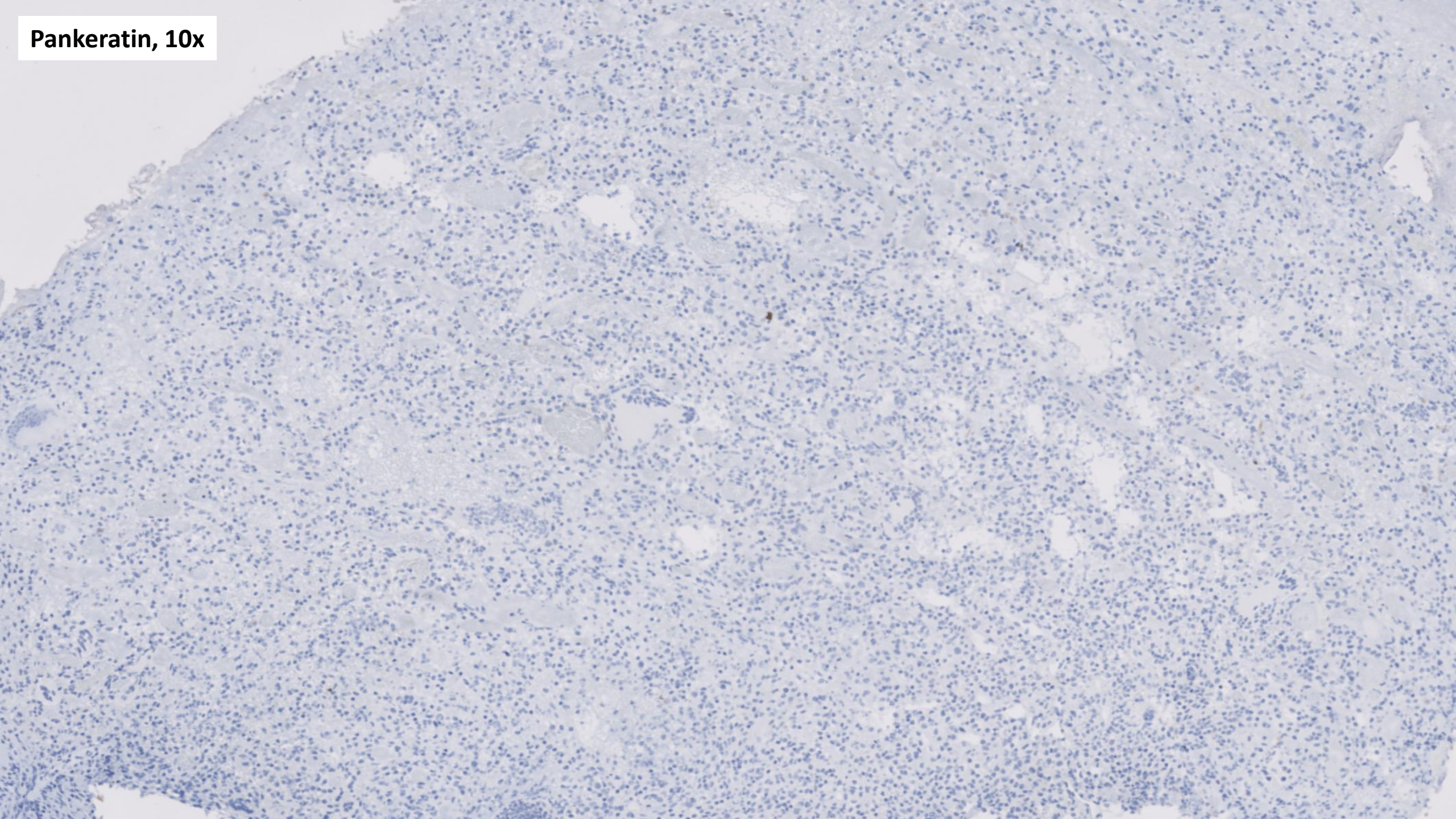
H&E, 2x

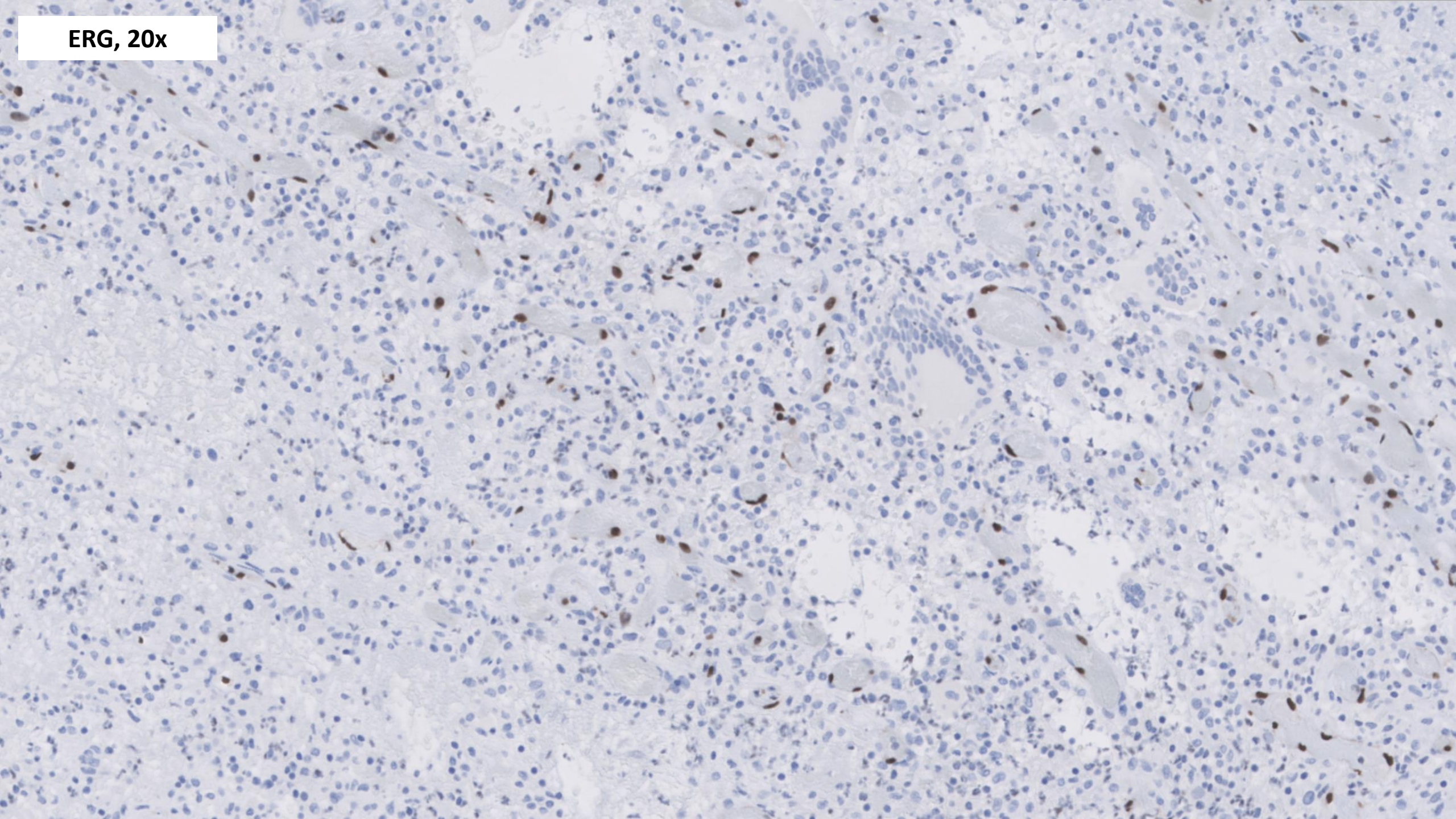


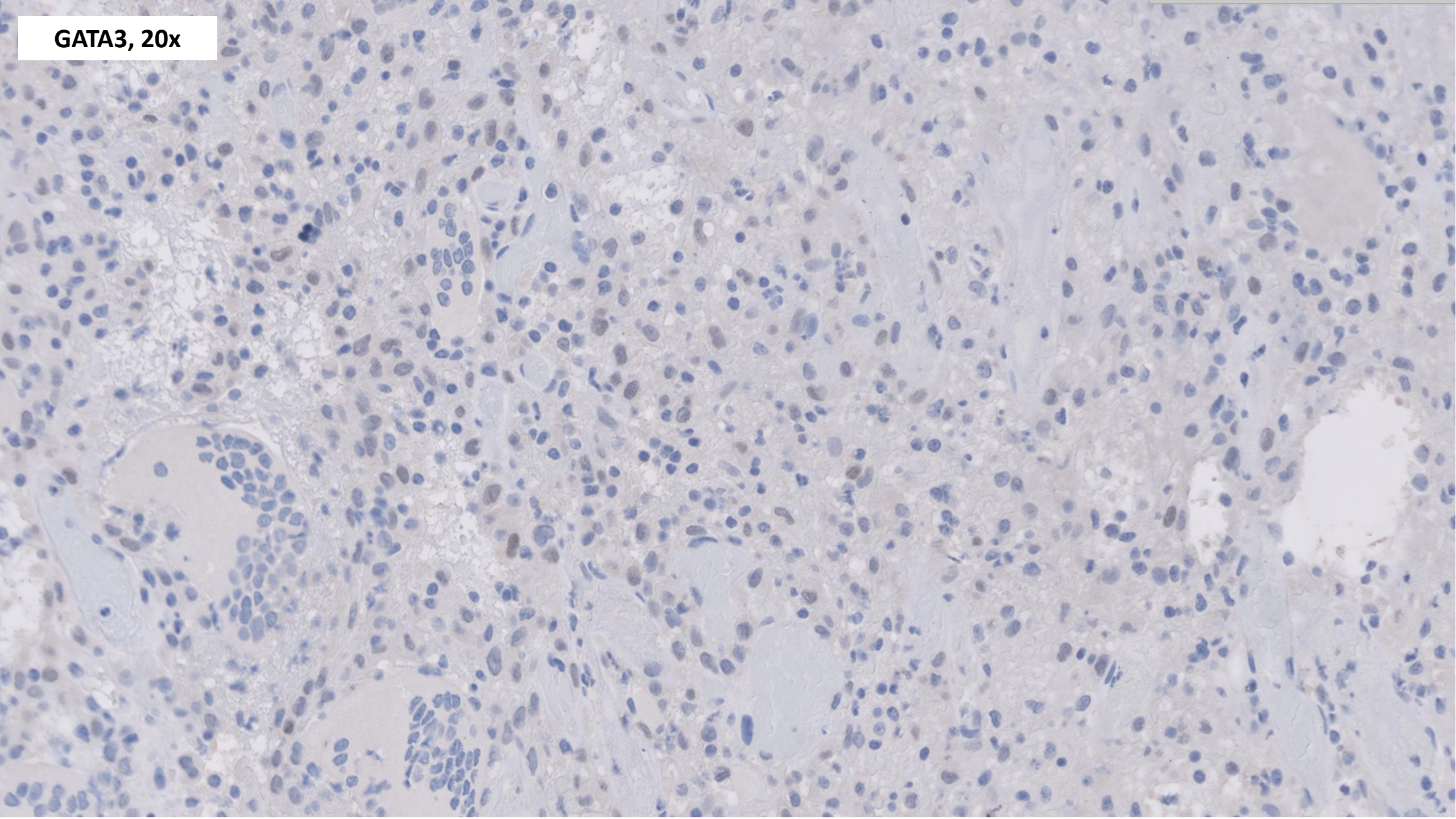

H&E, 10x


H&E, 20x


H&E, 40x

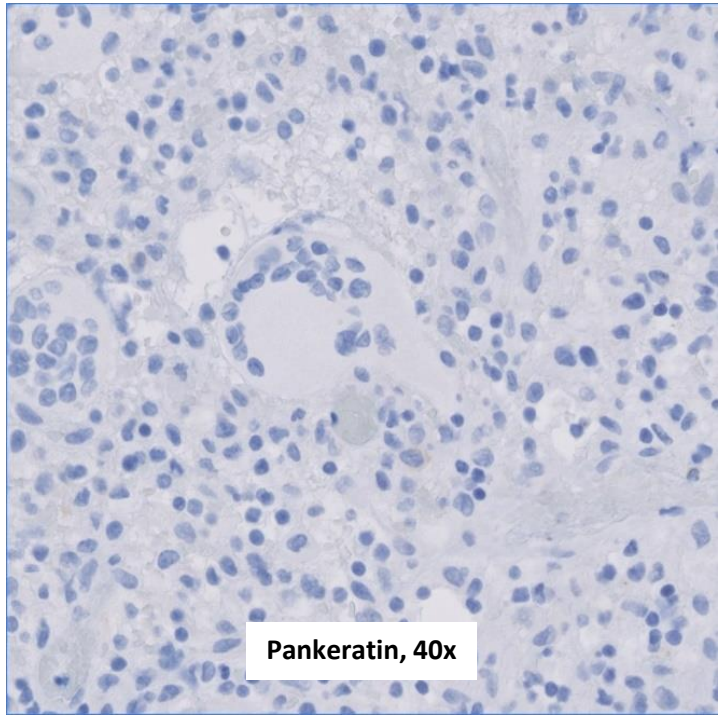

Pankeratin, 10x

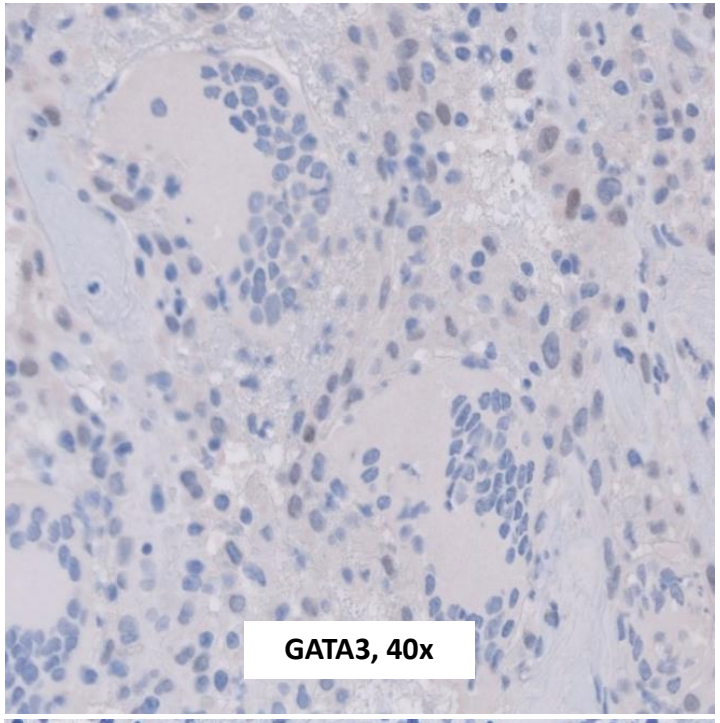

ERG, 20x

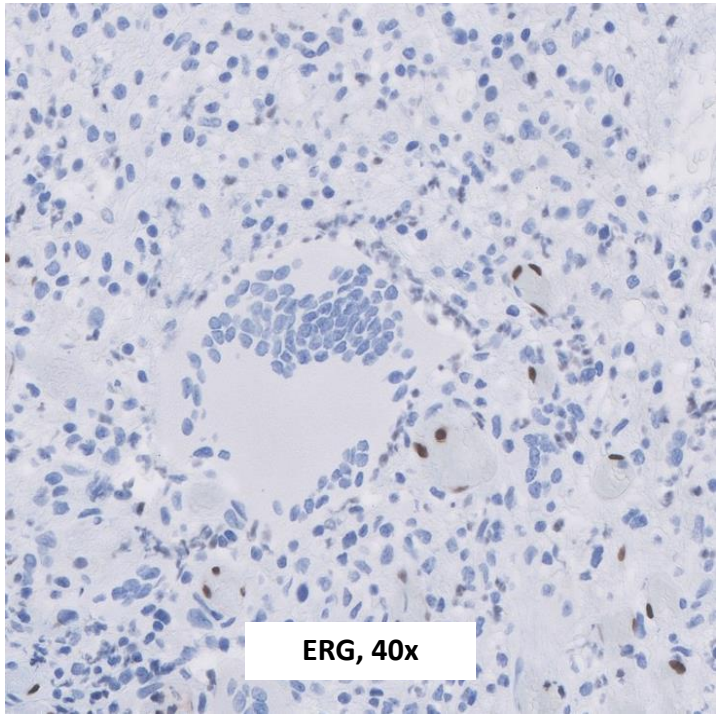

GATA3, 20x

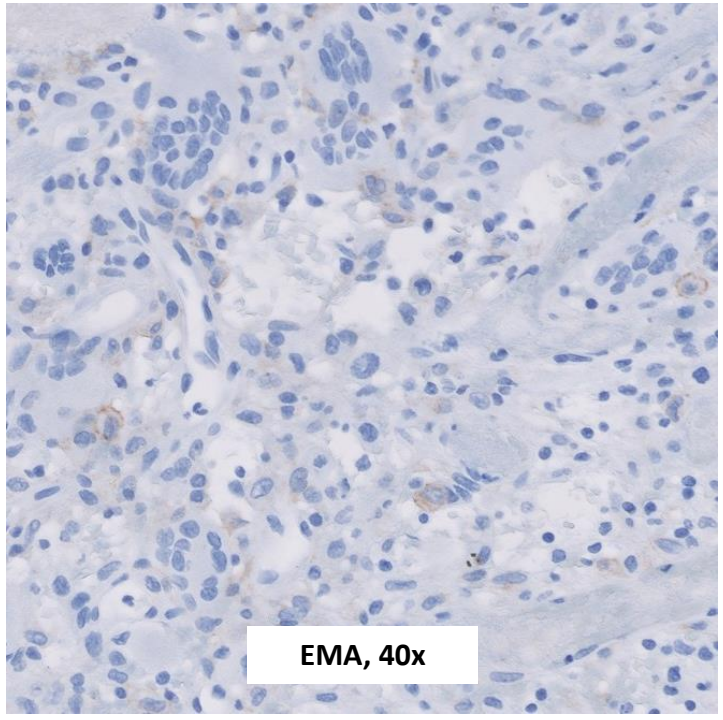
# DIAGNOSIS?

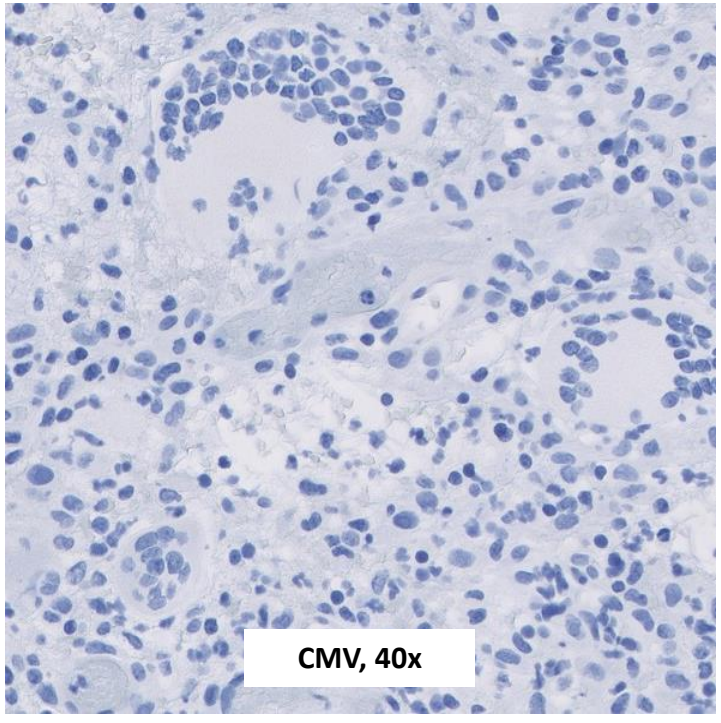
# IHC results

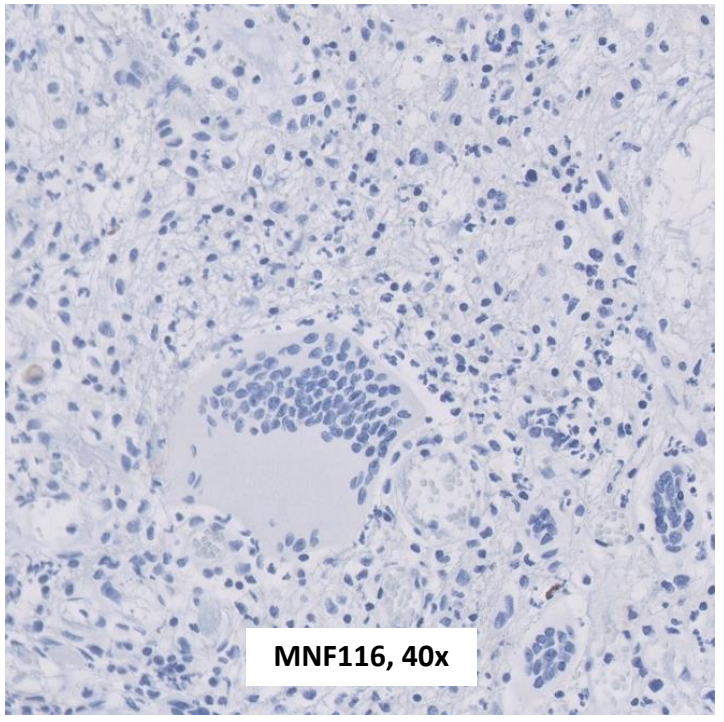


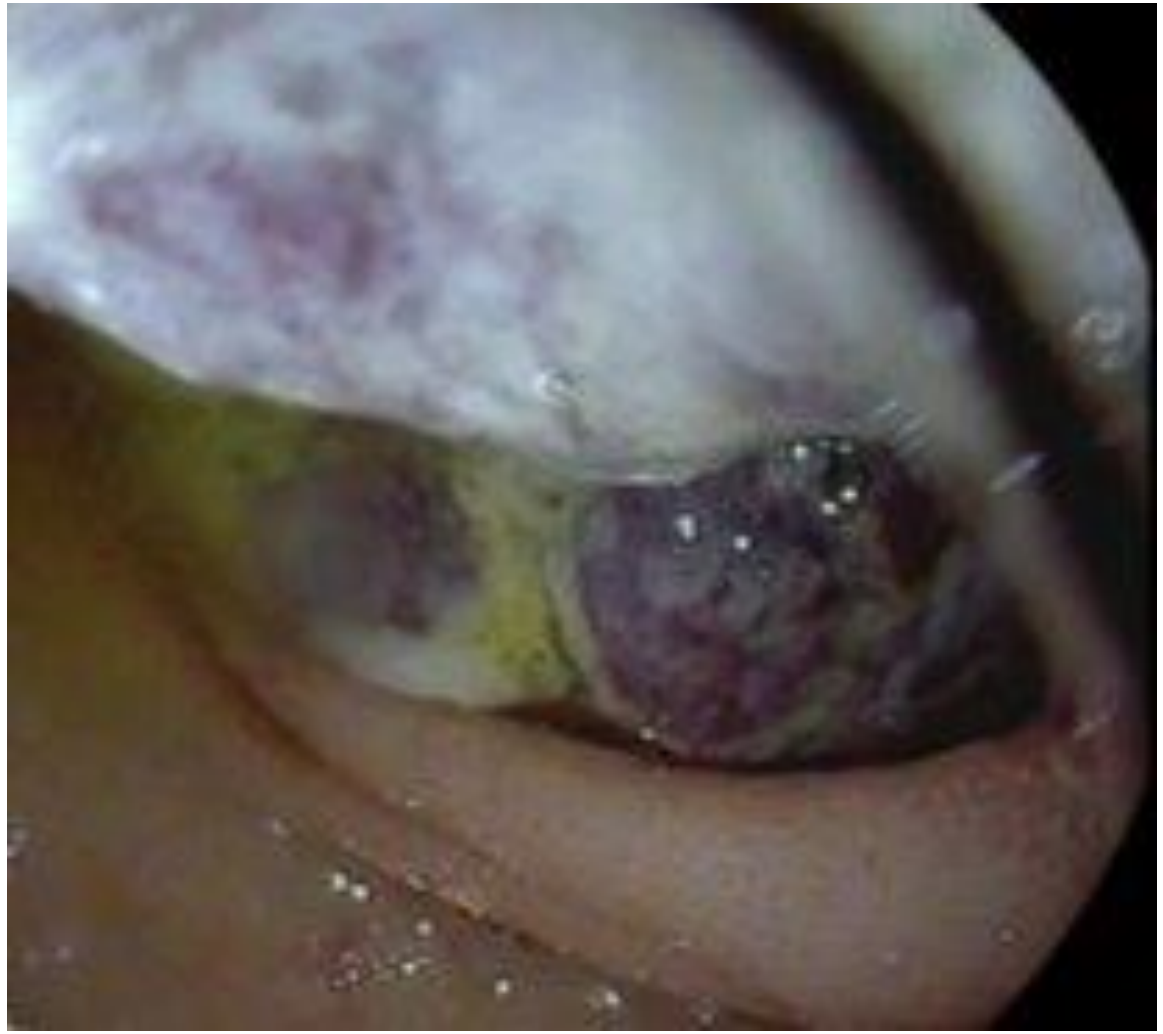



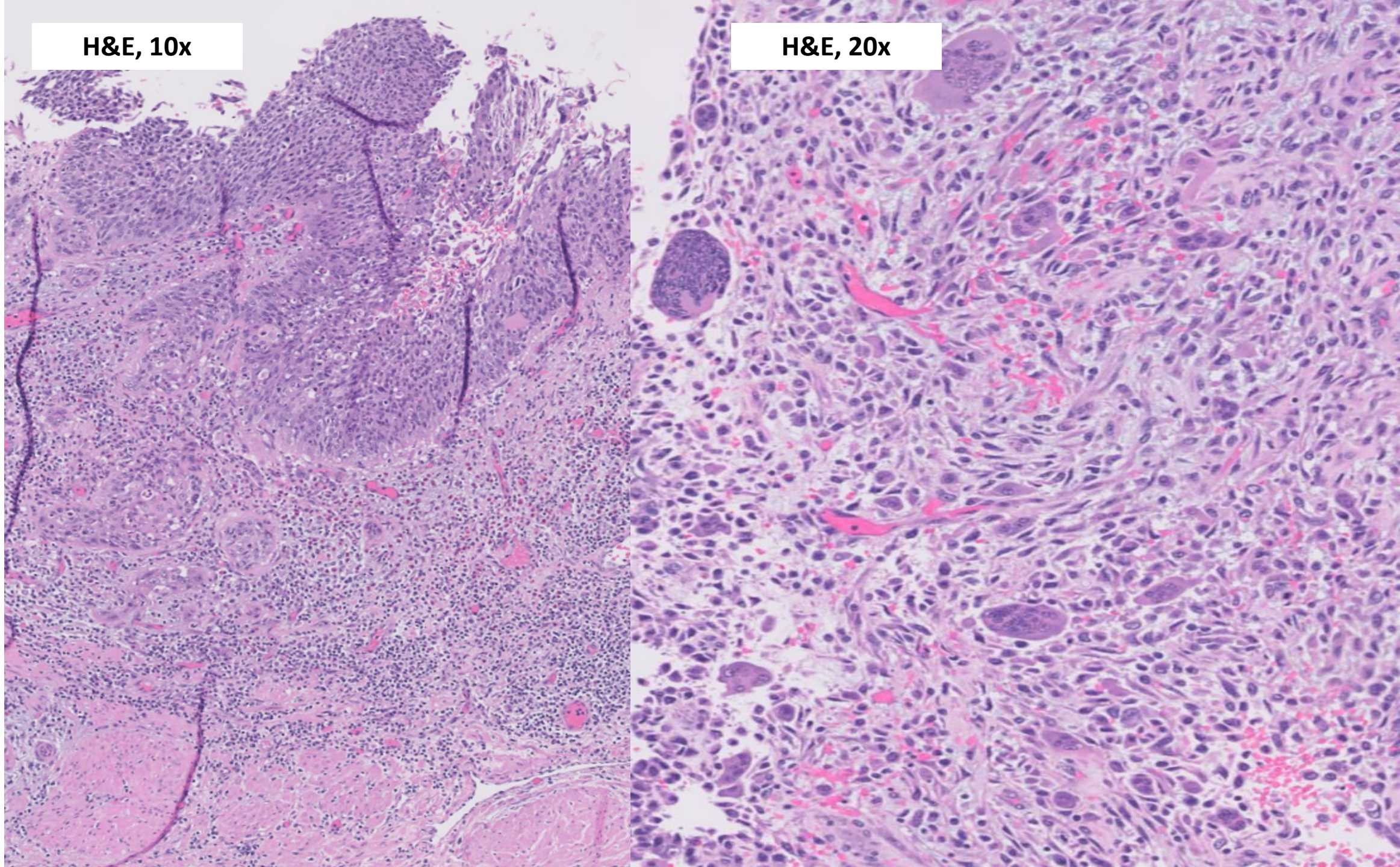
# EGD: Ulcerated ~3 cm mass with exudate.



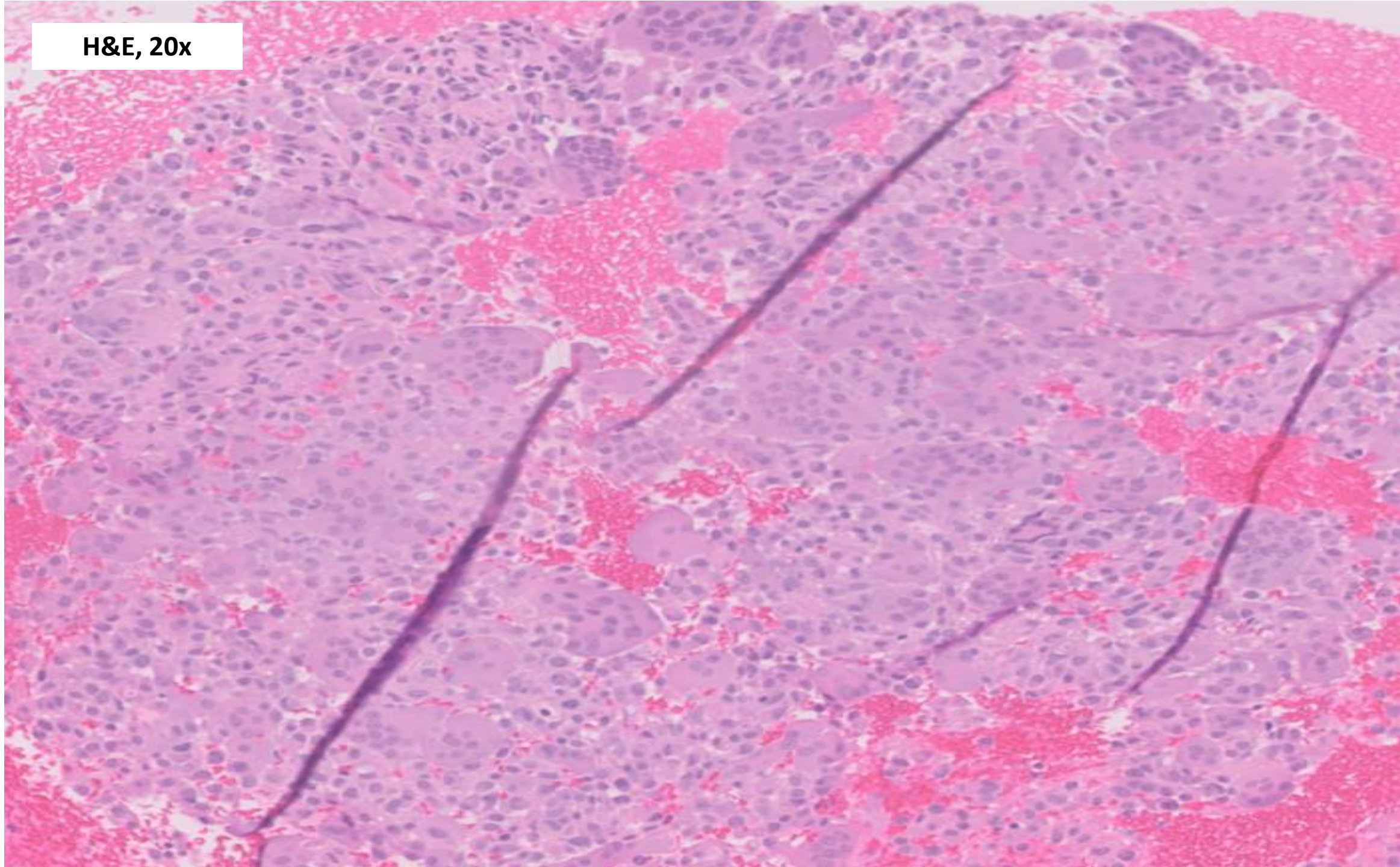
# Differential diagnosis

- Granulation tissue / ulcer
- Radiation change
- Metastatic urothelial carcinoma
  - Sarcomatoid urothelial carcinoma
  - Carcinomas with osteoclast-like cells

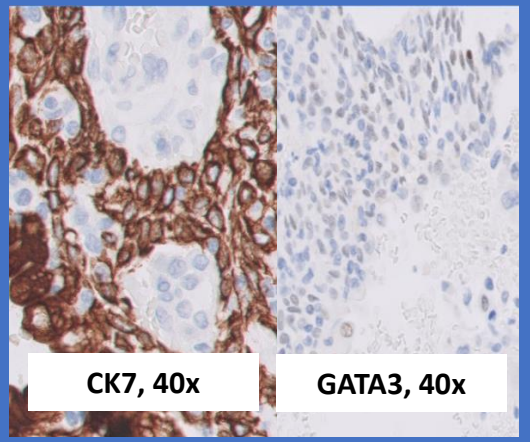
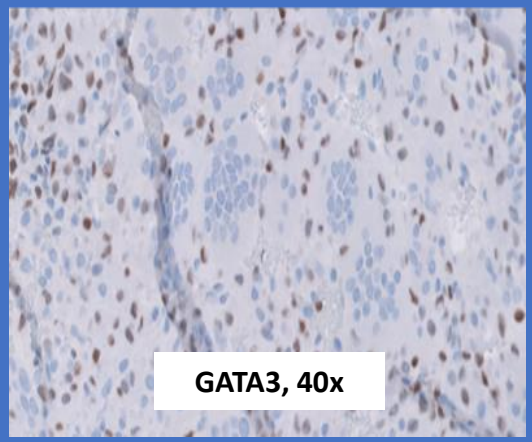
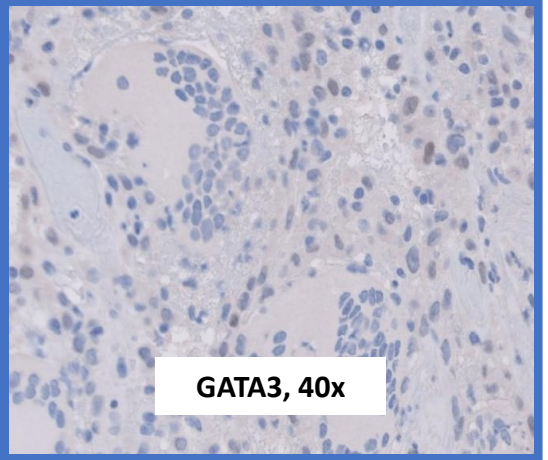
# Kidney tumor



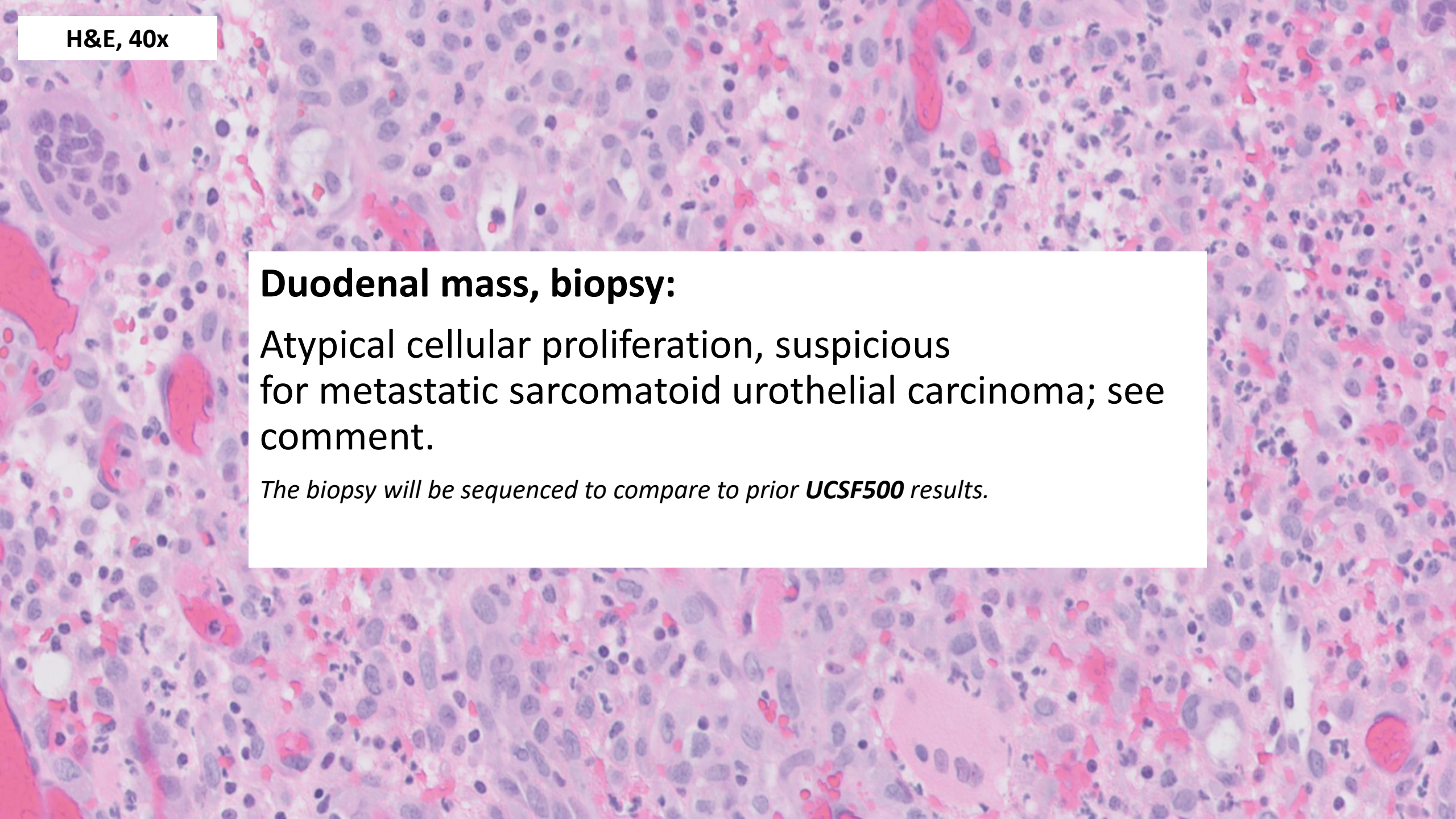
Paraaortic lymph node FNA



# IHC Results

| | Kidney | Lymph node | Duodenum |
|---|---|---|---|
| |  CK7, 40x GATA3, 40x |  GATA3, 40x |  GATA3, 40x |
| **Pankeratin** | N/A | N/A | Negative |
| **CK7** | Positive (UC, SV) | Negative | N/A |
| **CK20** | Negative | Negative | N/A |
| **GATA3** | Positive (UC, SV) | Positive (SV) | Positive (SV, weak) |

**UC = Conventional urothelial carcinoma, SV = Sarcomatoid variant urothelial carcinoma**

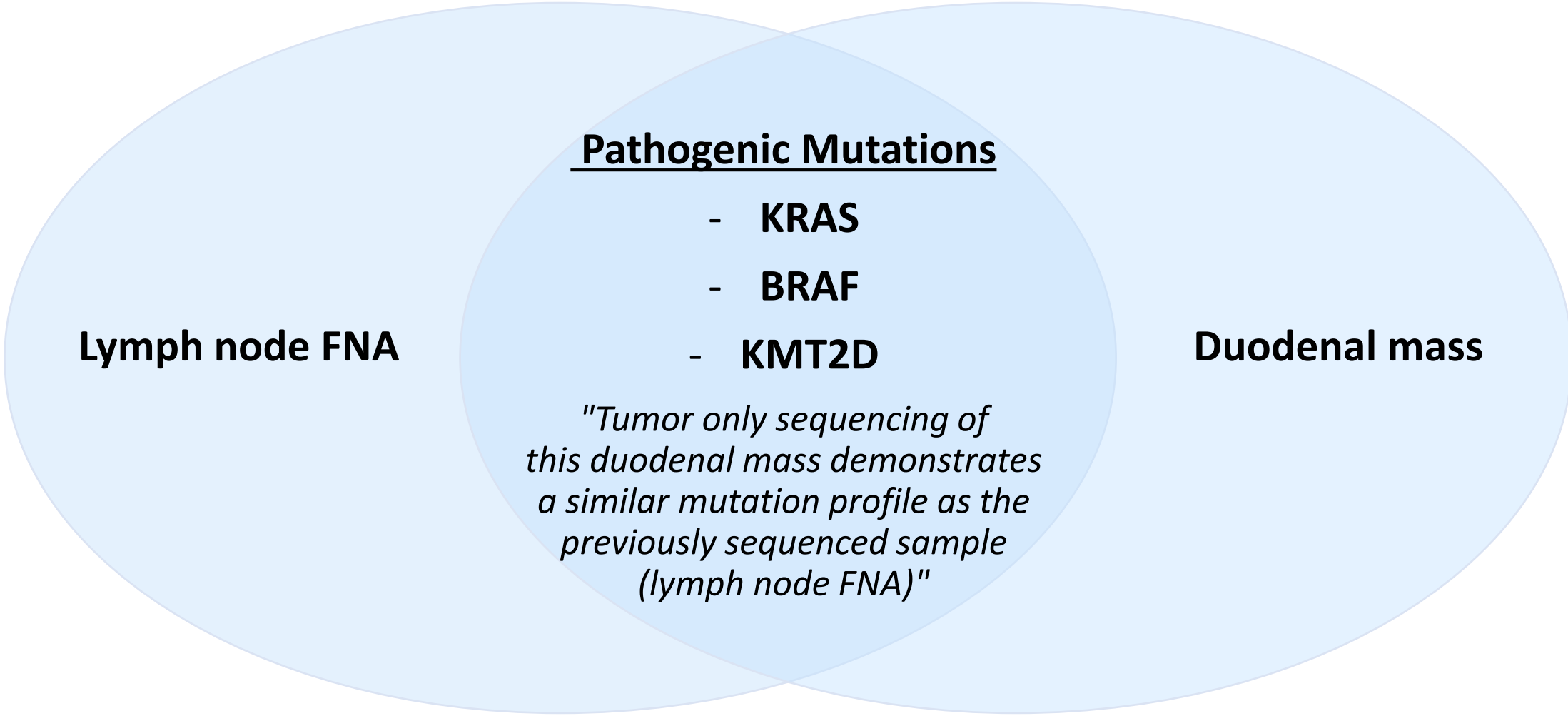



**Duodenal mass, biopsy:**

Atypical cellular proliferation, suspicious for metastatic sarcomatoid urothelial carcinoma; see comment.

*The biopsy will be sequenced to compare to prior **UCSF500** results.*

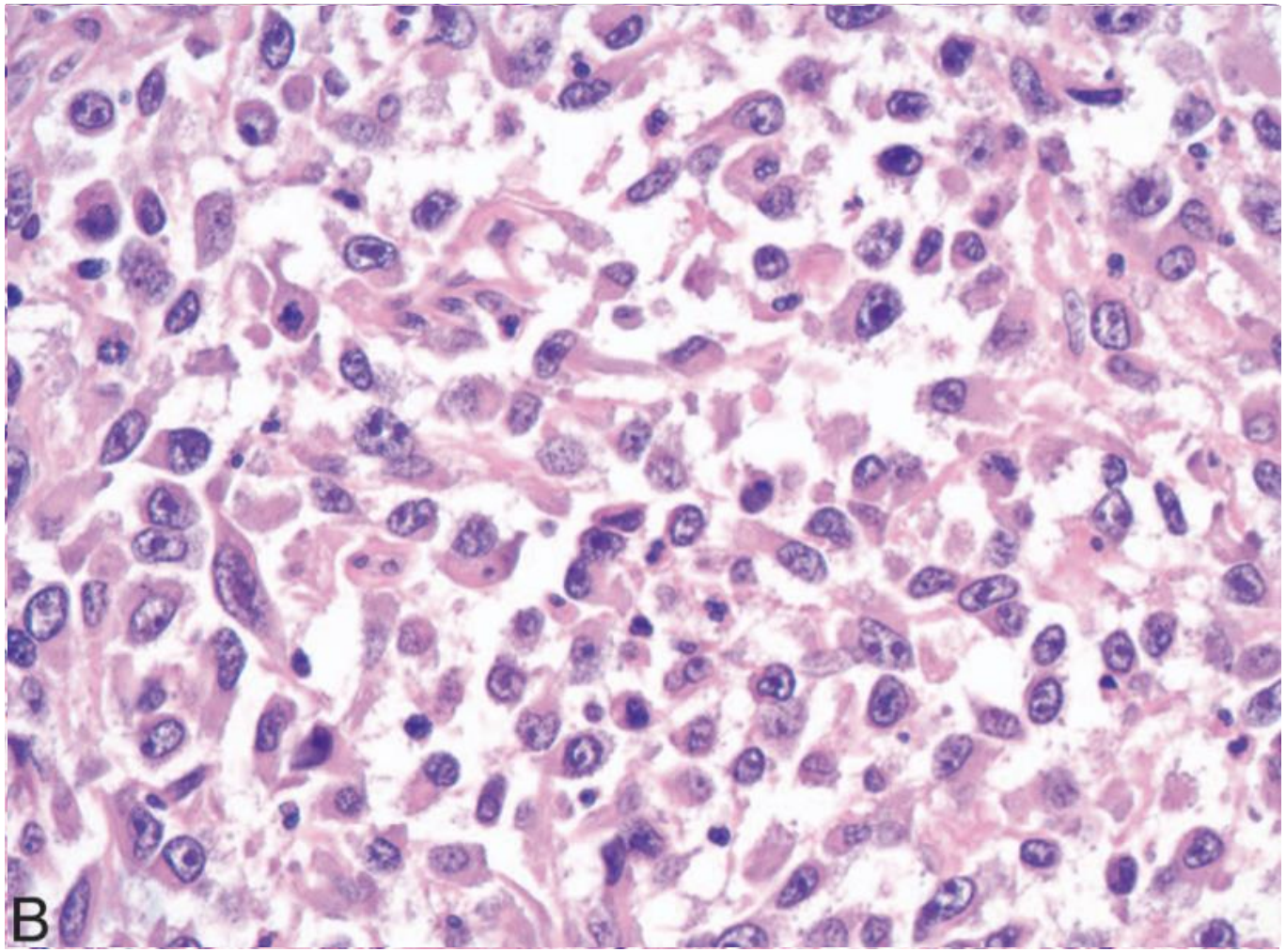
# UCSF500: Confirms identical tumors





1. Sjdahl G et al. A systematic study of gene mutations in urothelial carcinoma; inactivating mutations in TSC2 and PIK3R1. PLoS One. 2011;6(4):e18583. PMID: 21533174.
2. Buyucek S et al. Receptor Tyrosine Kinase Pathway and Infiltrating Urothelial Carcinoma. J Environ Pathol Toxicol Oncol. 2023;42(1):65-77. PMID: 36734953.

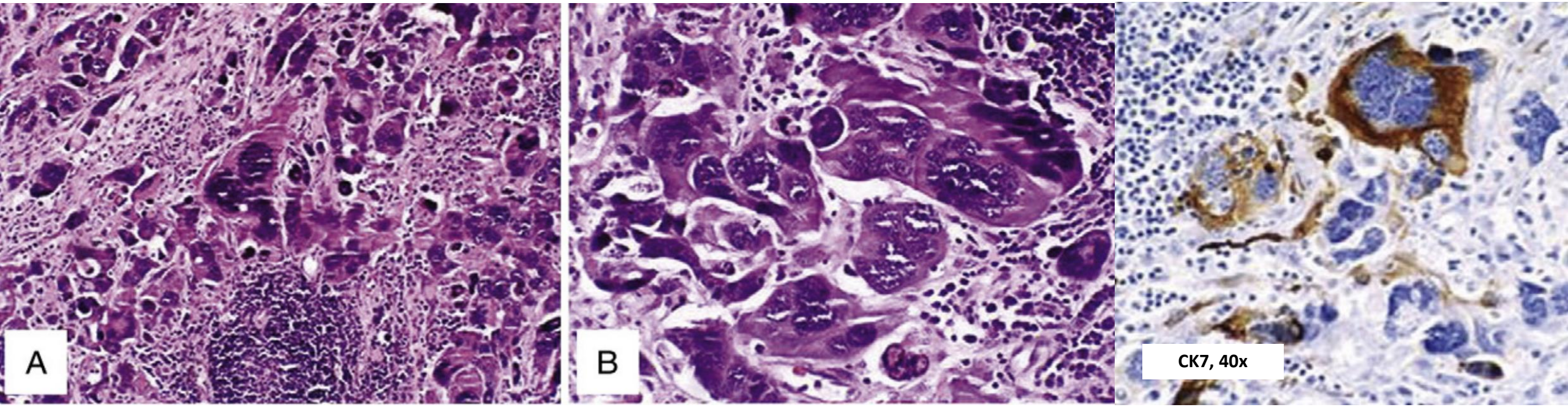
# Sarcomatoid Urothelial Carcinoma




- Rare
- Biphasic
  - Spindled to undifferentiated
  - ± Heterologous components
- Worse prognosis.
- IHC: variable p63, GATA3, HMWCKs.


1. Wang J, Wang FW, Lagrange CA, Hemstreet Iii GP, Kessinger A. Clinical features of sarcomatoid carcinoma (carcinosarcoma) of the urinary bladder: analysis of 221 cases. Sarcoma. 2010;2010:454792. PMID: 20706685.
2. Fatima N, Osunkoya AO. GATA3 expression in sarcomatoid urothelial carcinoma of the bladder. Hum Pathol. 2014 Aug;45(8):1625-9. doi: 10.1016/j.humpath.2014.03.015. Epub 2014 Apr 13. PMID: 24824028.
3. Sanfrancesco J, McKenney JK, Leivo MZ, Gupta S, Elson P, Hansel DE. Sarcomatoid Urothelial Carcinoma of the Bladder: Analysis of 28 Cases With Emphasis on Clinicopathologic Features and Markers of Epithelial-to-Mesenchymal Transition. Arch Pathol Lab Med. 2016 Jun;140(6):543-51. doi: 10.5858/arpa.2015-0085-OA. Epub 2016 Mar 31. PMID: 27031776.

# Giant Cell Urothelial Carcinoma




- Rare
- Bizarre pleomorphic giant tumor cells + UC.
- IHC: Positive epithelial and urothelial markers in bizarre tumor cells.
- Highly aggressive

Lopez-Beltran A, Blanca A, Montironi R, Cheng L, Regueiro JC. Pleomorphic giant cell carcinoma of the urinary bladder. Hum Pathol. 2009 Oct;40(10):1461-6. doi: 10.1016/j.humpath.2009.02.016. Epub 2009 May 20. PMID: 19467692.

# Osteoclast-rich undifferentiated carcinomas of the urinary tract

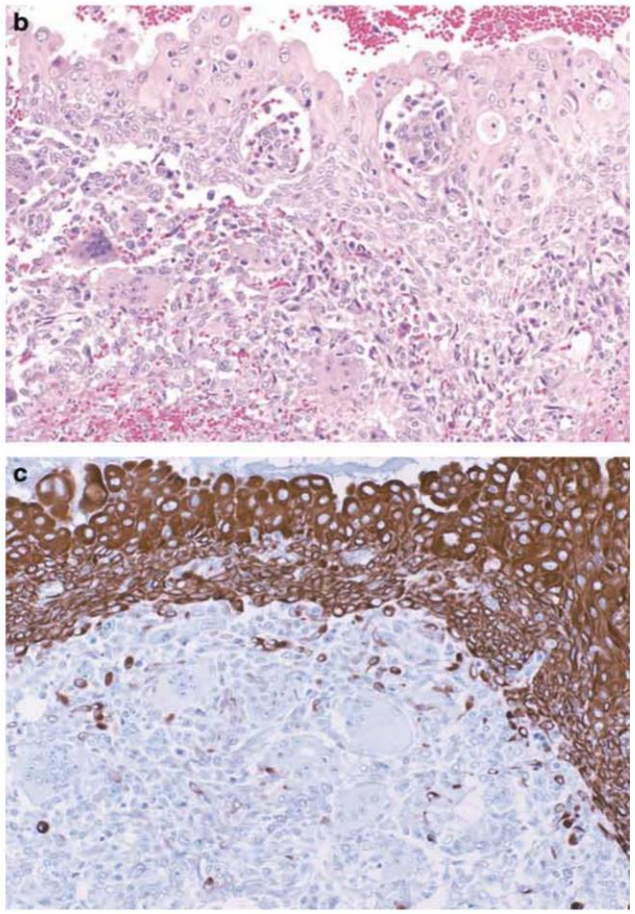



**Figure 6** (**a**) Osteoclast-like giant-cell tumor (bottom) accompanied by high-grade papillary urothelial carcinoma (top). (**b**) Carcinoma *in situ* overlying osteoclast-like giant-cell tumor. (**c**) Immunohistochemistry with cytokeratin 7 highlights keratin-positive mononuclear cells that appear to drop off from overlying CIS.

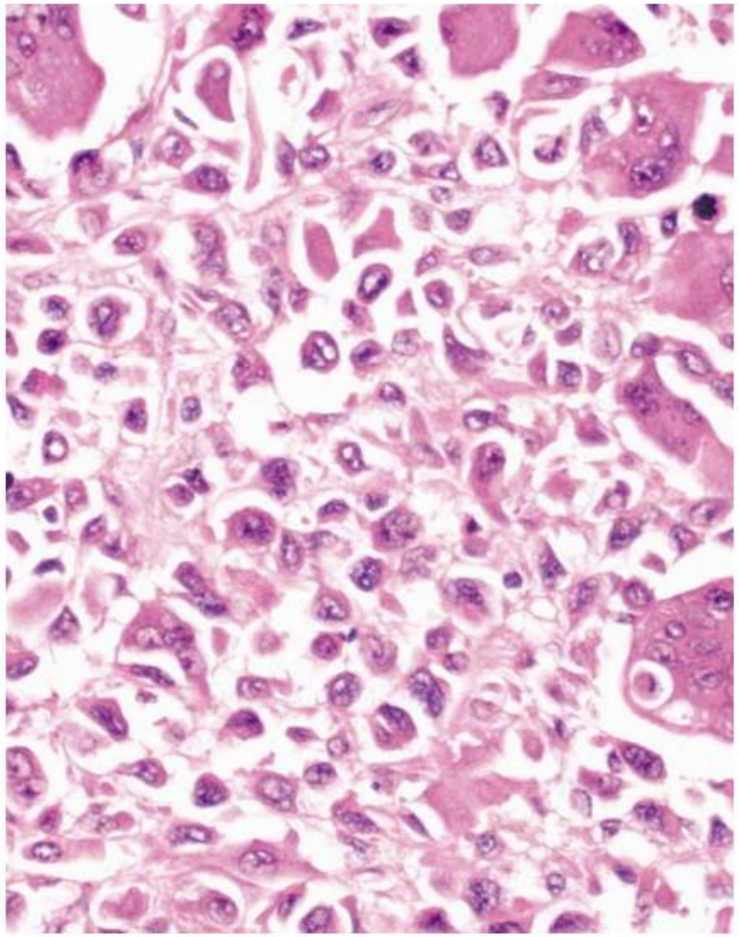


**Figure 3** Increased pleomorphism of mononuclear cells.

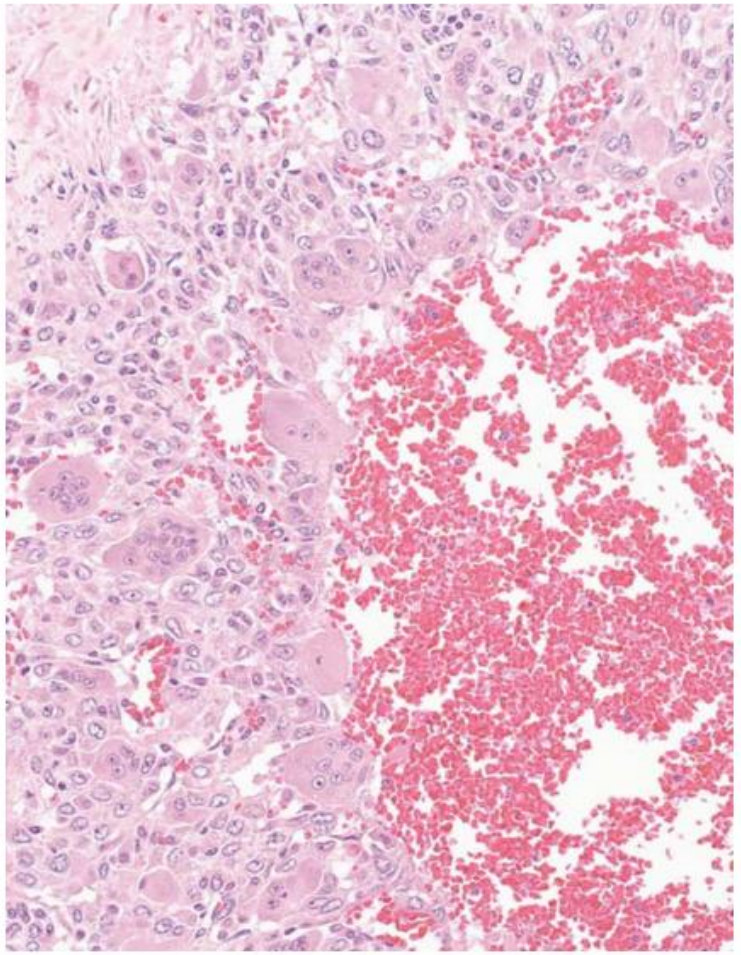


**Figure 4** Giant cells concentrate around erythrocyte extravasation and areas of hemorrhage.

Baydar, D., Amin, M. & Epstein, J. Osteoclast-rich undifferentiated carcinomas of the urinary tract. Mod Pathol 19, 161171 (2006).

# Take home points

- ✓ Sarcomatoid urothelial carcinoma is rare.
- ✓ Variable morphology.
- ✓ Worse prognosis (CaSS, T stage)
- ✓ Metastatic diagnosis difficult without conventional UC or UCIS.
- ✓ Inconsistent IHC results.
- ✓ Molecular pathology can be helpful.


1. Gu L, Ai Q, Cheng Q, Ma X, Wang B, Huang Q, Li X, Zhang P, Liu K, Zhao X, Li H, Zhang X. Sarcomatoid variant urothelial carcinoma of the bladder: a systematic review and meta-analysis of the clinicopathological features and survival outcomes. Cancer Cell Int. 2020 Nov 14;20(1):550. doi: 10.1186/s12935-020-01626-9. PMID: 33292281; PMCID: PMC7666462.
2. Fatima N, Osunkoya AO. GATA3 expression in sarcomatoid urothelial carcinoma of the bladder. Hum Pathol. 2014 Aug;45(8):1625-9. doi: 10.1016/j.humpath.2014.03.015. Epub 2014 Apr 13. PMID: 24824028.

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- Rosenkrantz AB, Melamed J, Stifelman M. Osteoclast-like giant cell tumor of the renal pelvis associated with urothelial carcinoma: computed tomography, gross, and histologic appearance. Urology. 2011;78(6):1310-1312.
- Wright JL, Black PC, Brown GA, Porter MP, Kamat AM, Dinney CP, Lin DW. Differences in survival among patients with sarcomatoid carcinoma, carcinosarcoma and urothelial carcinoma of the bladder. J Urol. 2007 Dec;178(6):2302-6; discussion 2307. doi: 10.1016/j.juro.2007.08.038. Epub 2007 Oct 15. PMID: 17936803.
- Baydar, D., Amin, M. & Epstein, J. Osteoclast-rich undifferentiated carcinomas of the urinary tract. Mod Pathol 19, 161171 (2006).
- Sjdahl G et al. A systematic study of gene mutations in urothelial carcinoma; inactivating mutations in TSC2 and PIK3R1. PLoS One. 2011;6(4):e18583. PMID: 21533174.
- Buyucek S et al. Receptor Tyrosine Kinase Pathway and Infiltrating Urothelial Carcinoma. J Environ Pathol Toxicol Oncol. 2023;42(1):65-77. PMID: 36734953.
- Wang J, Wang FW, Lagrange CA, Hemstreet Iii GP, Kessinger A. Clinical features of sarcomatoid carcinoma (carcinosarcoma) of the urinary bladder: analysis of 221 cases. Sarcoma. 2010;2010:454792. PMID: 20706685.
- Wright JL, Black PC, Brown GA, Porter MP, Kamat AM, Dinney CP, Lin DW. Differences in survival among patients with sarcomatoid carcinoma, carcinosarcoma and urothelial carcinoma of the bladder. J Urol. 2007 Dec;178(6):2302-6; discussion 2307. PMID: 17936803.
- Lopez-Beltran A, Blanca A, Montironi R, Cheng L, Regueiro JC. Pleomorphic giant cell carcinoma of the urinary bladder. Hum Pathol. 2009 Oct;40(10):1461-6. doi: 10.1016/j.humpath.2009.02.016. Epub 2009 May 20. PMID: 19467692.

# Questions?

Thank you Dr. Umetsu and Dr. Ding

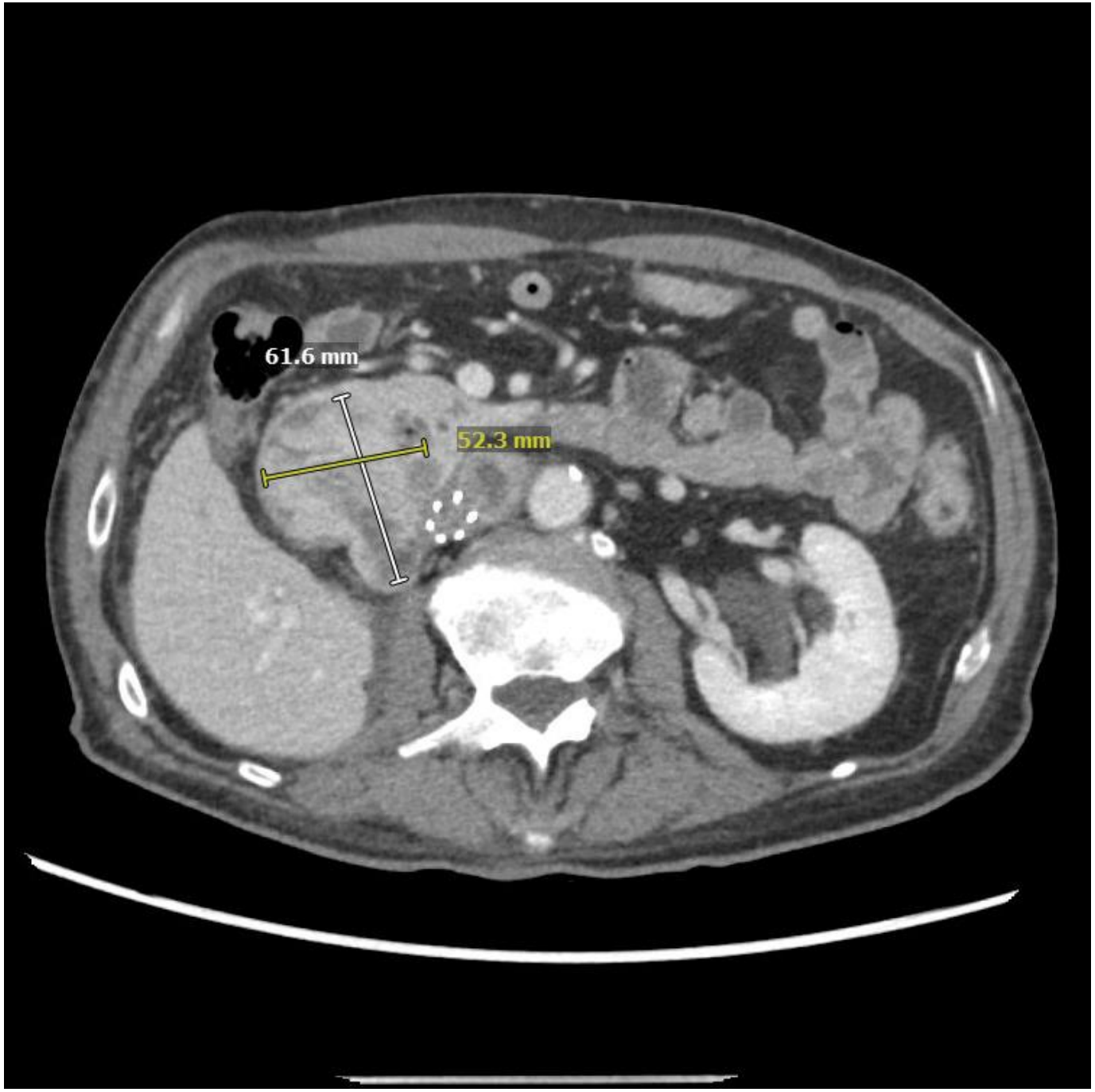
# Patient now

CT urogram:

- Slight increase in duodenal mass size (6.2 vs 5.9 cm).
- Stable aortocaval adenopathy (2.7 cm).

IVC filter placement.

Continues treatment with EV / Pembrolizumab.



# Osteoclast-rich undifferentiated carcinomas of the urinary tract

**Table 4** Immunohistochemical characteristics

| *Case* | *1* | | | *2* | | | *3* | | | *4* | | | *5* | | | *6*[a] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *UC* | *MO* | *GC* | *CIS* | *MO* | *GC* | *CIS* | *MO* | *GC* | *UC, CIS* | *MO* | *GC* | *UC, CIS* | *MO* | *GC* | MO | *GC* |
| CK AE1/3 | +++ | – | – | +++ | ++ | – | +++ | + | – | +++ | – | – | +++ | – | – | – | – |
| CAM5.2 | +++ | – | – | +++ | ++ | – | +++ | – | – | +++ | – | – | +++ | – | – | – | – |
| CK7 | +++ | – | – | +++ | ++ | – | +++ | – | – | +++ | – | – | +++ | – | – | – | – |
| CK20 | + | – | – | +++ | – | – | – | – | – | +++ | – | – | +++ | – | – | – | – |
| EMA | + | ++ | – | +++ | – | – | + | – | – | + | – | – | ++ | – | – | ++ | – |
| S-100 | – | +++ | – | – | +++ | – | – | ++ | – | – | – | – | – | – | – | + | – |
| Desmin | – | – | – | – | – | – | – | – | – | – | – | – | – | + | – | – | – |
| A-Actin | – | ++ | – | – | + | – | – | – | – | – | – | – | – | +++ | – | ++ | – |
| LCA | – | – | ++ | – | – | +++ | – | + | +++ | – | – | ++ | – | – | ++ | + | ++ |
| CD68 | | ++ | +++ | – | +++ | +++ | – | +++ | +++ | – | ++ | +++ | – | ++ | +++ | ++ | +++ |
| CD51 | – | – | +++ | – | – | +++ | – | – | +++ | – | – | +++ | – | – | +++ | – | +++ |
| CD54 | – | – | +++ | – | – | +++ | – | – | +++ | – | – | +++ | – | – | +++ | – | +++ |
| P53 | + | + | – | ++ | + | – | – | – | + | – | – | – | + | + | + | – | – |

UC, high-grade papillary carcinoma; CIS, carcinoma *in situ*; MN, Mononuclear cells; GC, osteoclast-like giant cells.
+, <25% of cells staining; ++, between 25 and 50% of cells staining; +++, >50% of cells staining.
[a]Accompanying urothelial neoplasm in this case was not available for evaluation.

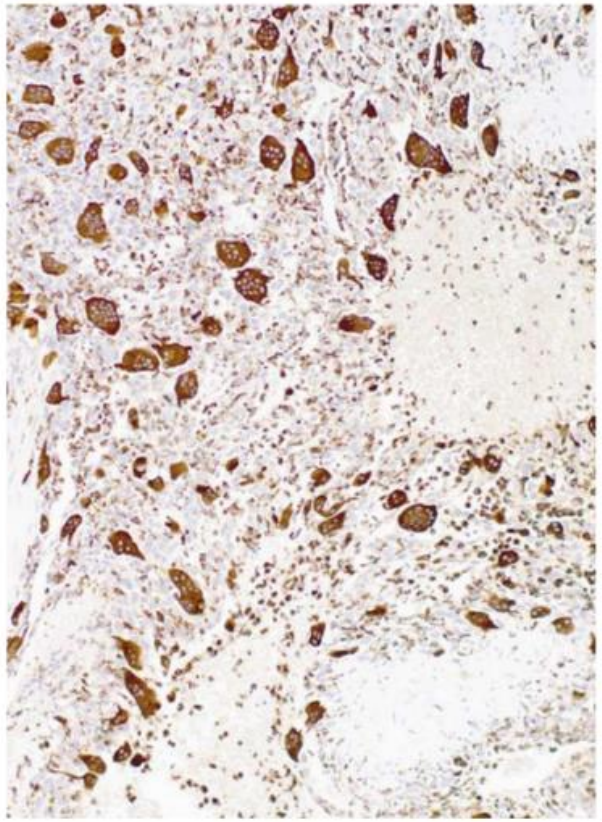


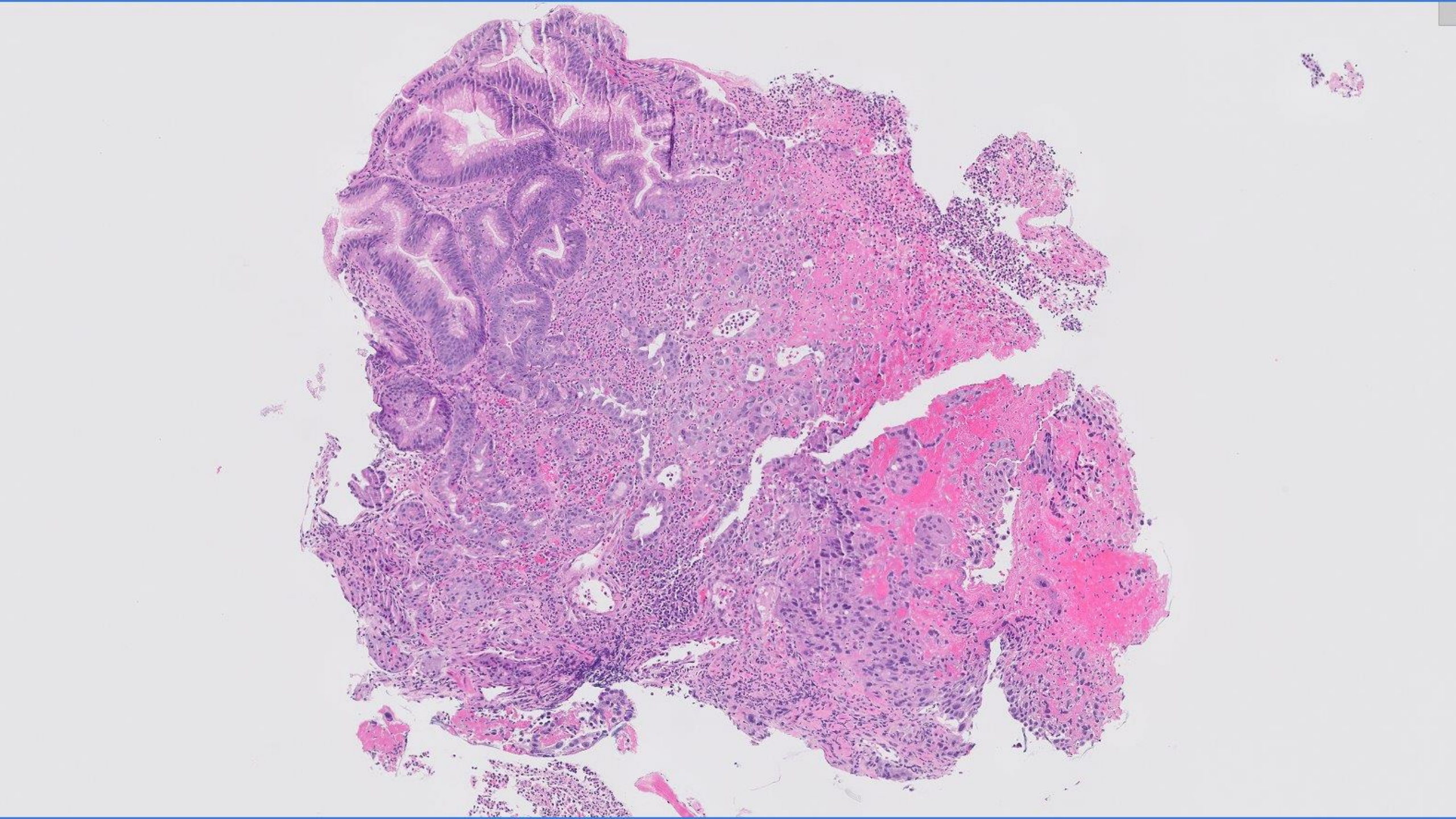
**Figure 10** Most of the mononuclear cells and all of the giant cells and are positive for CD68.

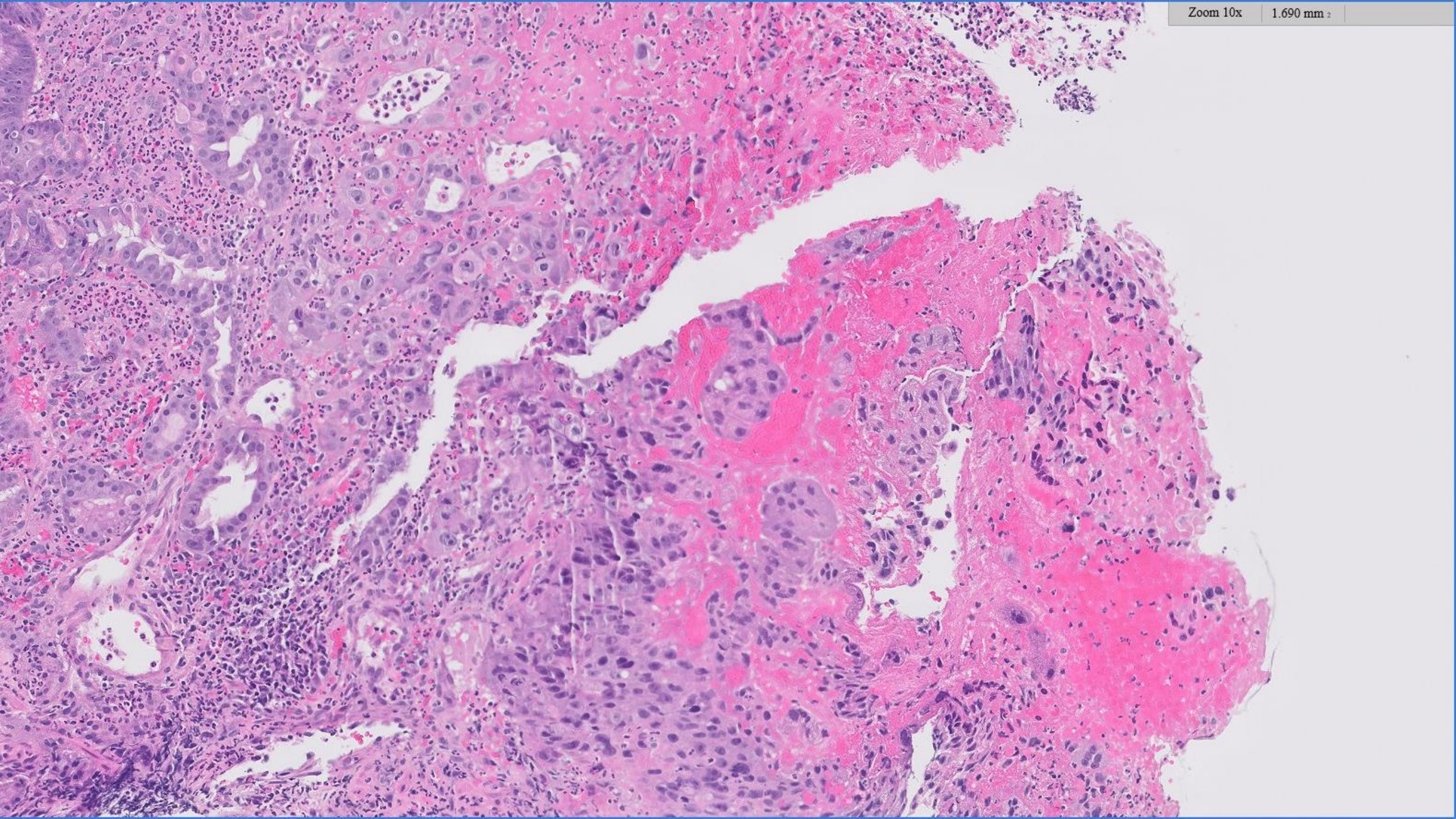
Baydar, D., Amin, M. & Epstein, J. Osteoclast-rich undifferentiated carcinomas of the urinary tract. Mod Pathol 19, 161171 (2006).

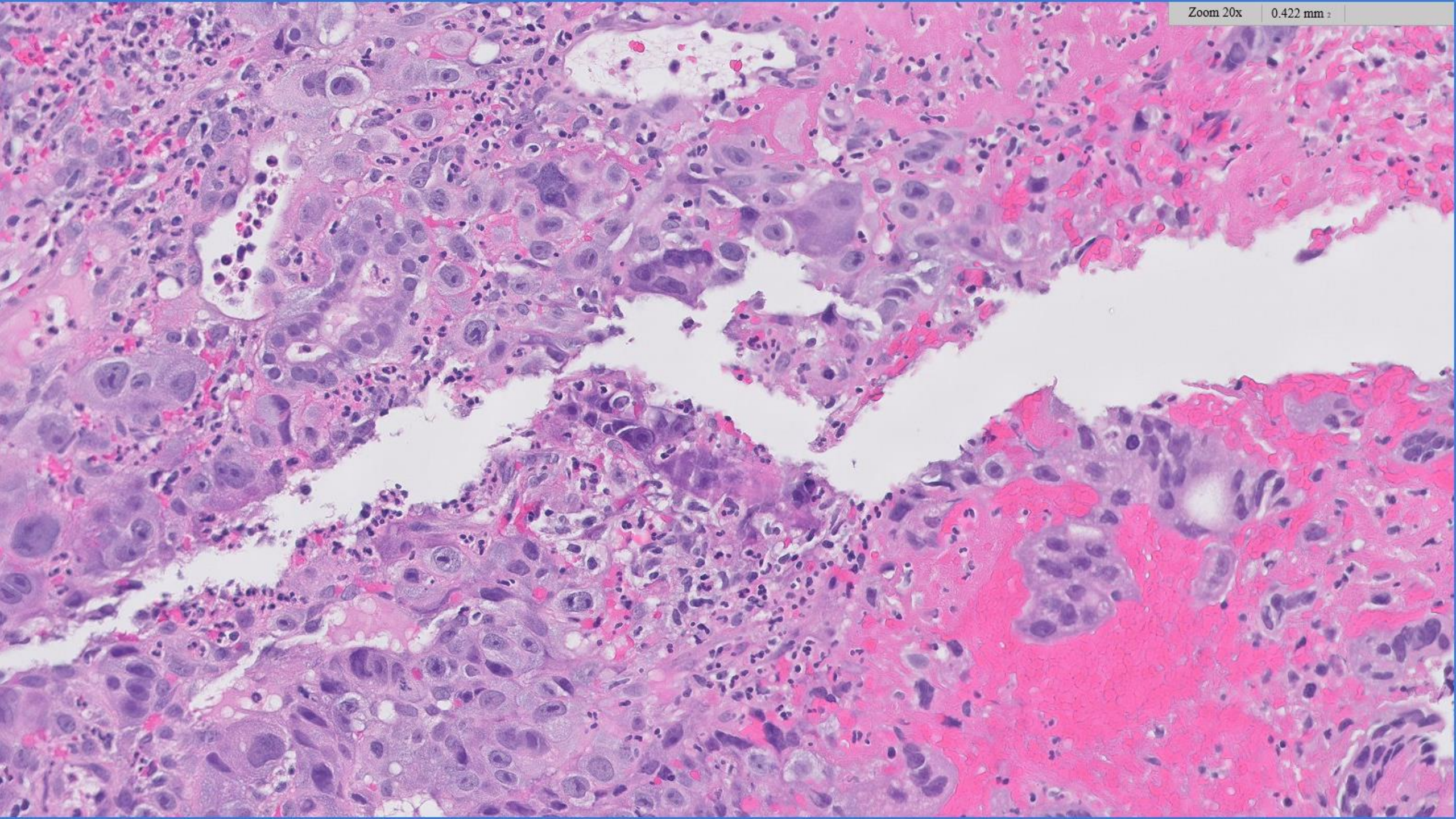
24-0106

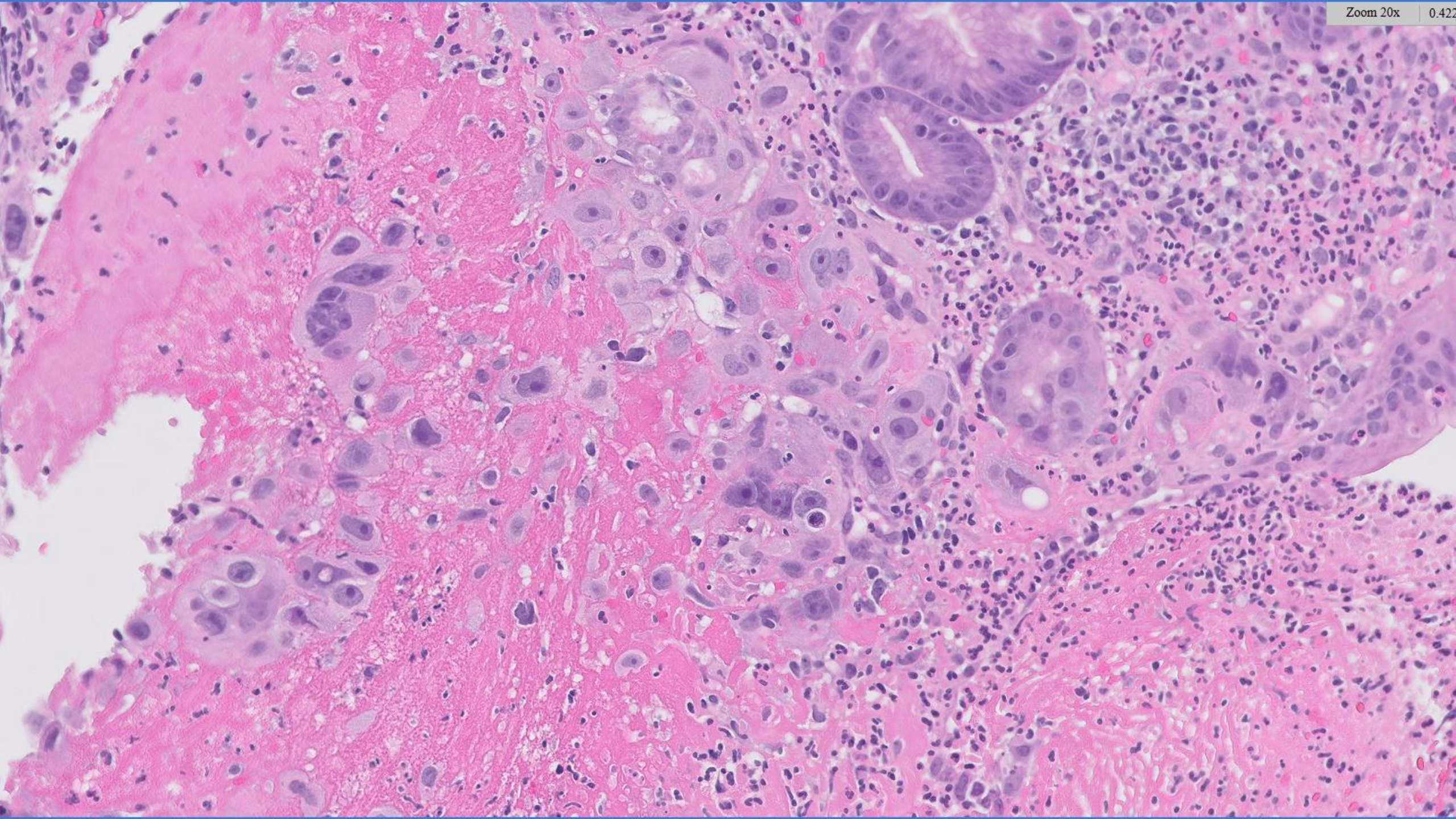
**Tyler Jankowski, Ankur Sangoi, Richard Hildebrandt; Stanford**

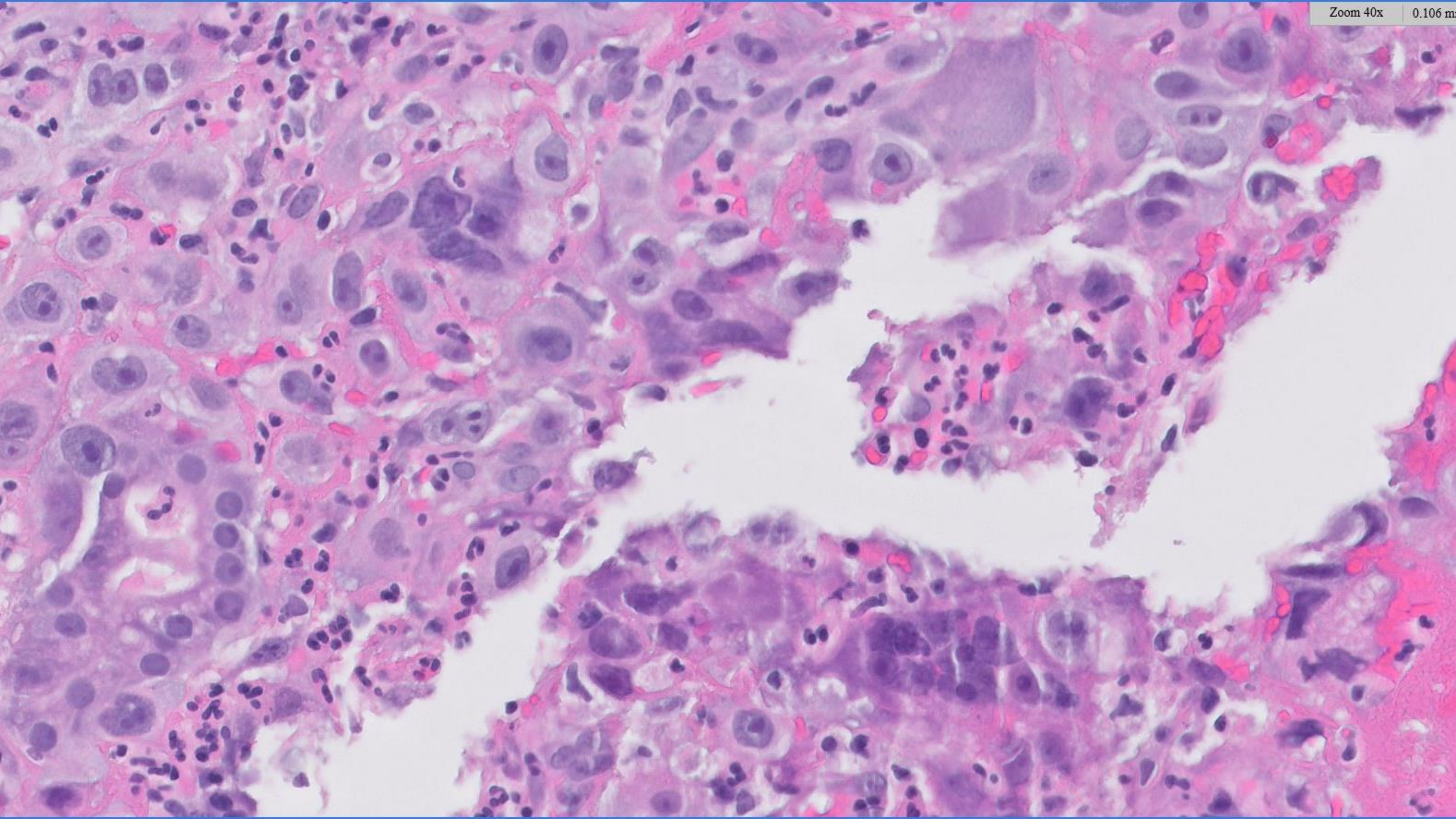
# 36-year-old man with melena and a gastric polyp




Zoom 10x
1.690 mm 2

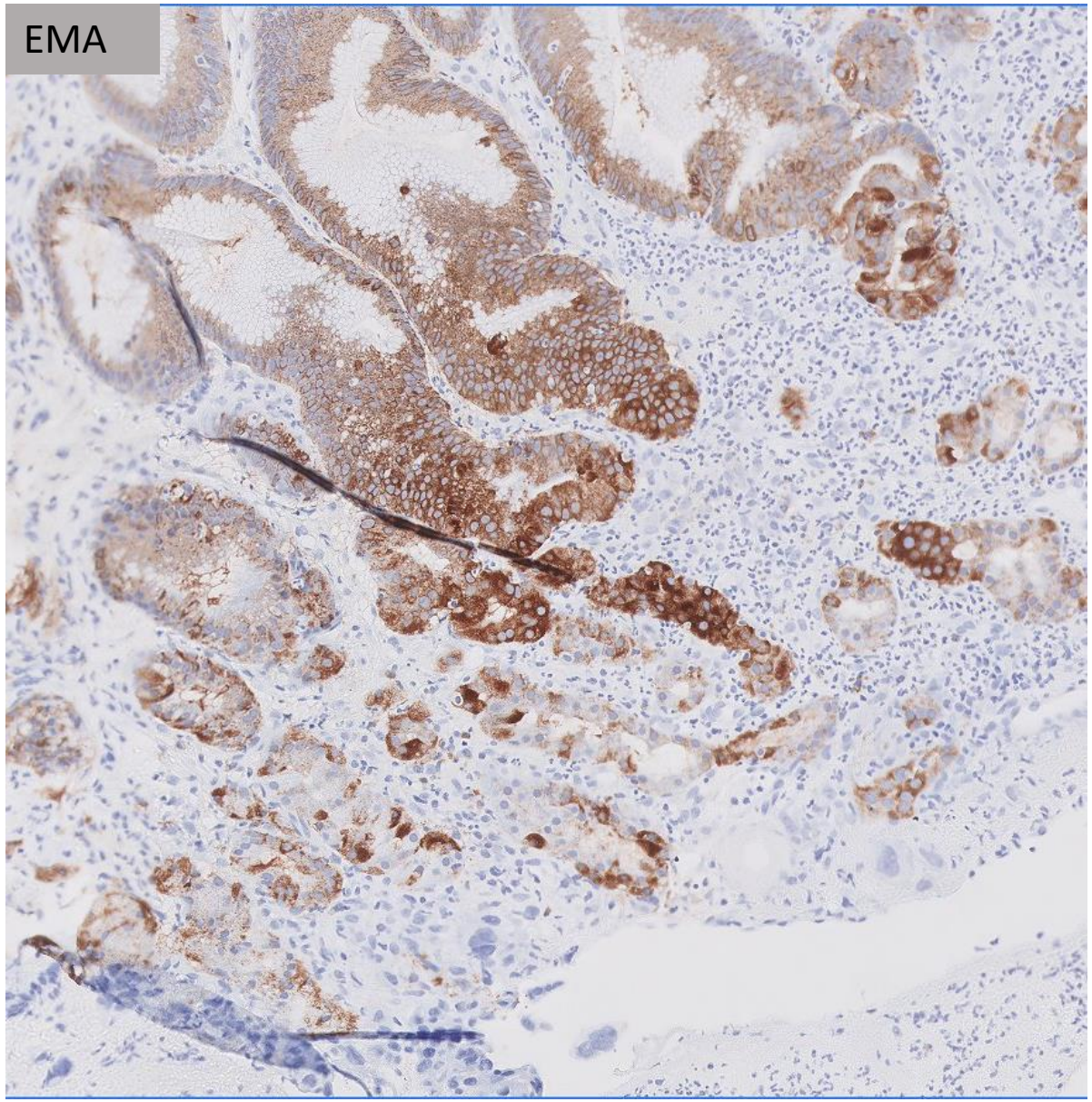

Zoom 20x
0.422 mm 2


Zoom 20x
0.422

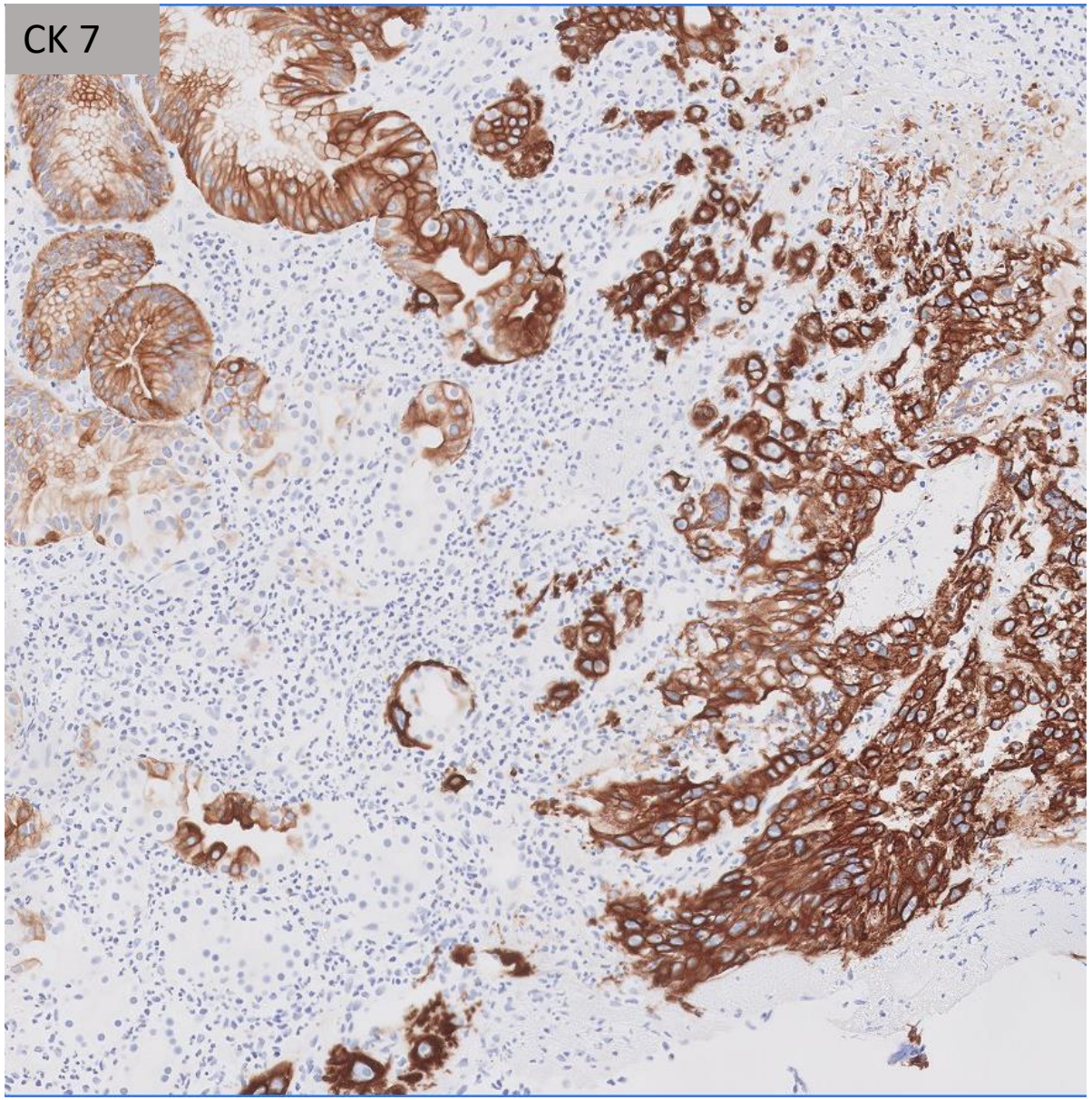

Zoom 40x
0.106 m

# DIAGNOSIS?

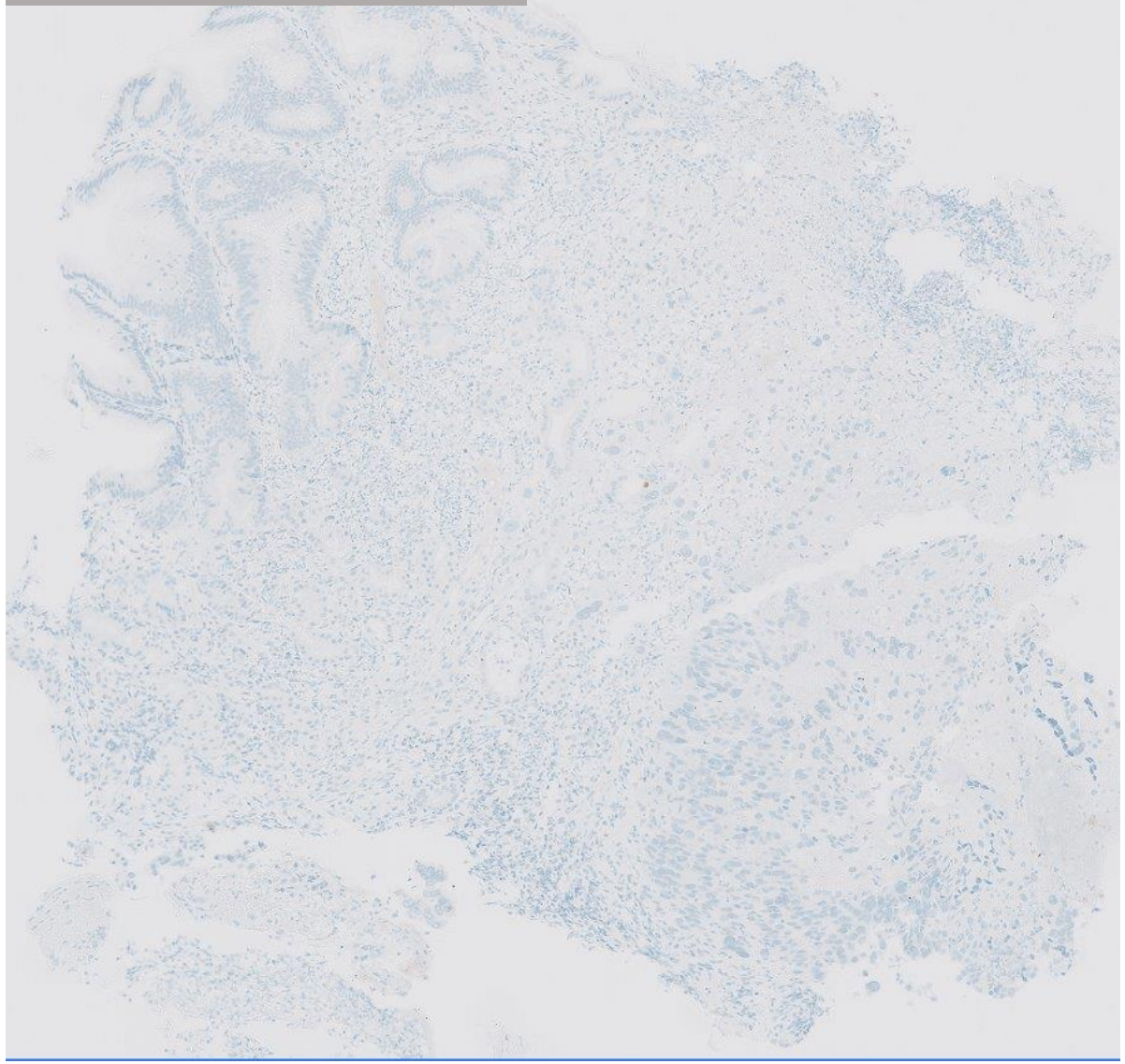
EMA



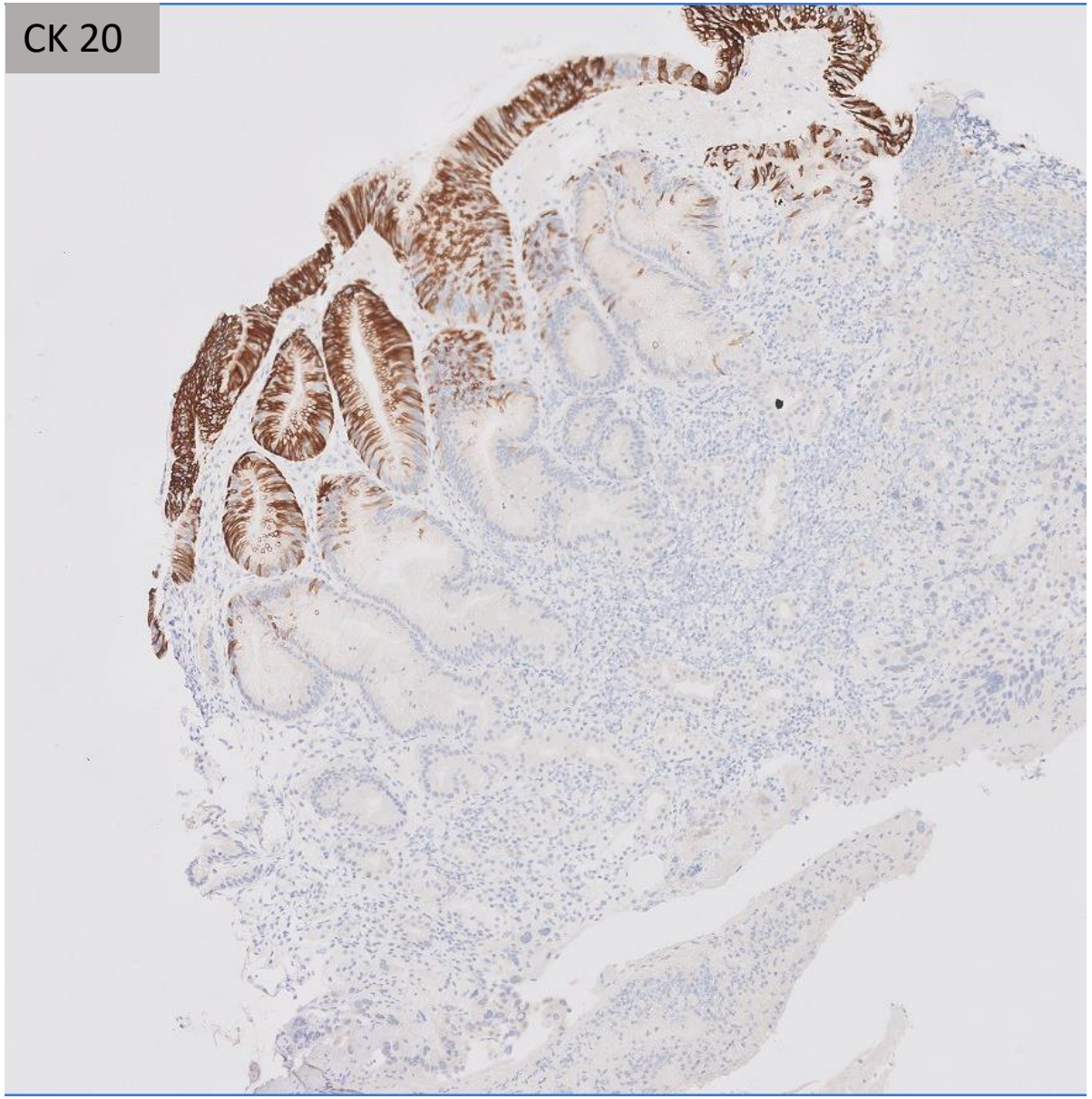
CK 7

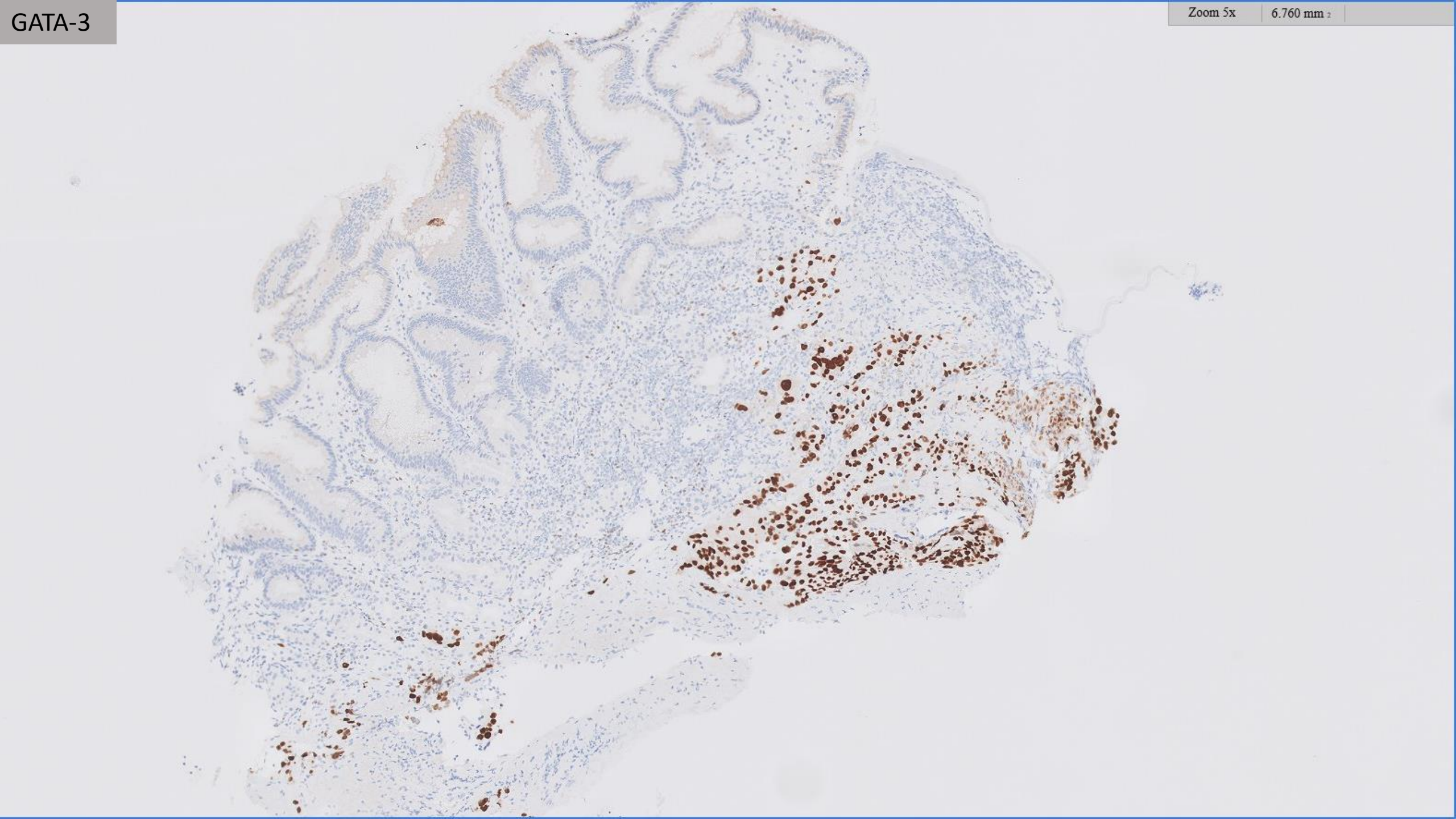


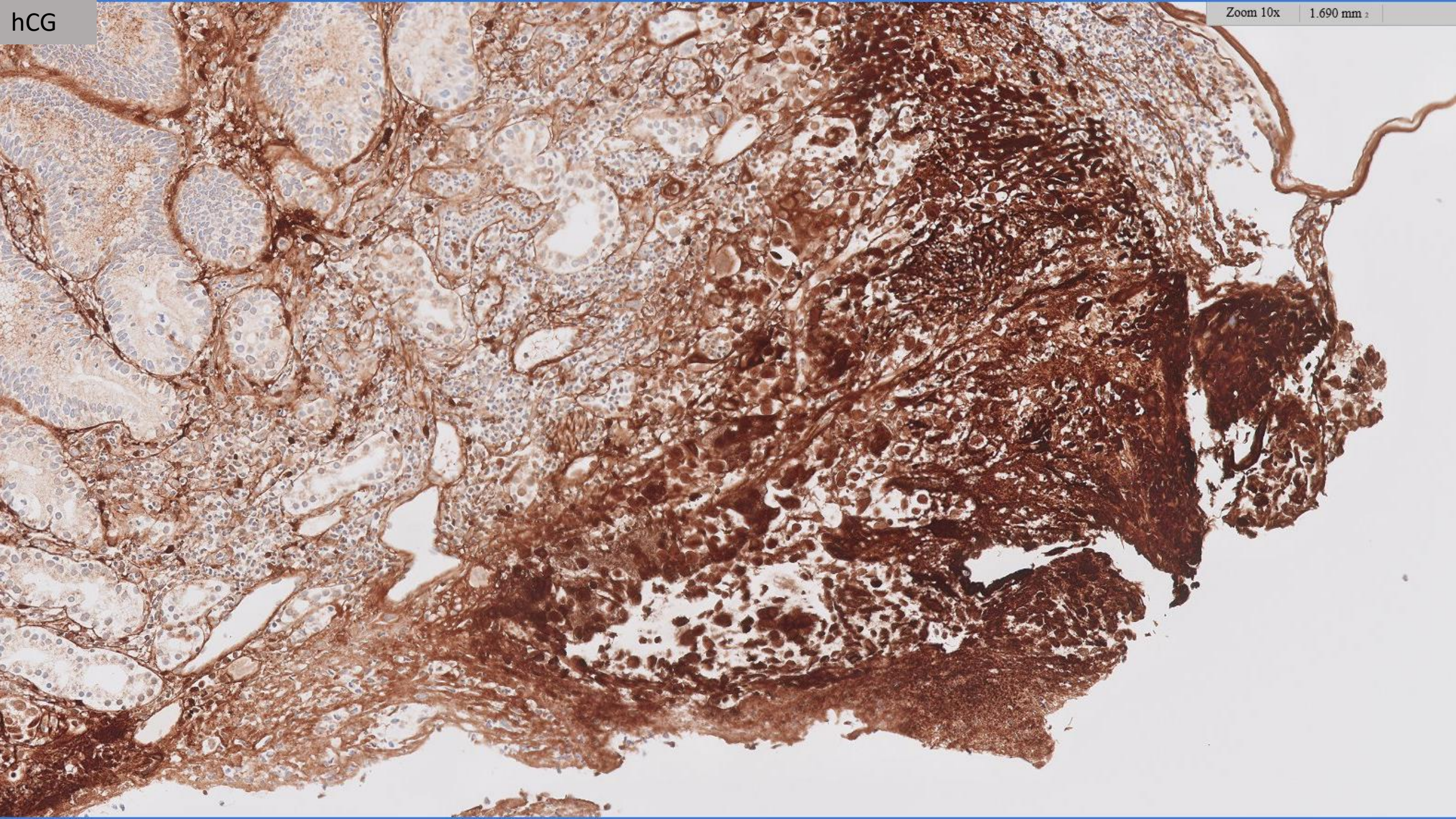
CK 5/6, TTF-1, PAX-8, S100



CK 20




GATA-3
Zoom 5x
6.760 mm 2


hCG
Zoom 10x
1.690 mm 2

# Final Diagnosis

- Choriocarcinoma (see comment)
  - IHC was also positive for SALL4, patchy inhibin, and focal HPL

- Few case reports with metastatic choriocarcinoma (and other entities presenting as primary gastric mucosal malignancies

**World Journal of Surgical Oncology**

BioMed Central

Research

Open Access

**Uncommon mucosal metastases to the stomach**

R Kanthan*[1], K Sharanowski[1], JL Senger[1], J Fesser[1], R Chibbar[1] and SC Kanthan[2]

Address: [1]Department of Pathology & Laboratory Medicine, College of Medicine, Saskatoon, Saskatchewan, Canada and [2]Department of General Surgery, College of Medicine, Saskatoon, Saskatchewan, Canada

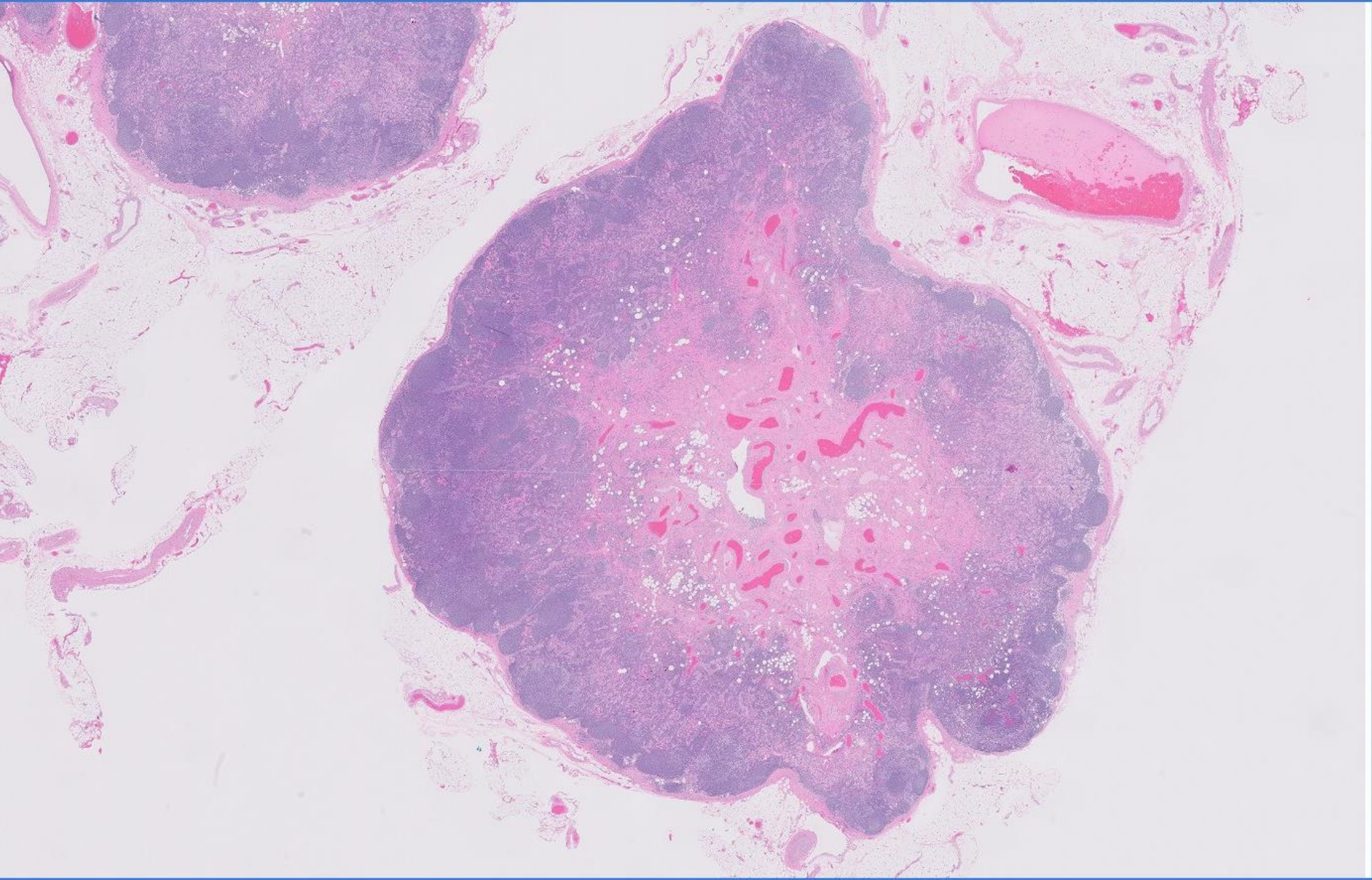
# Teaching Points

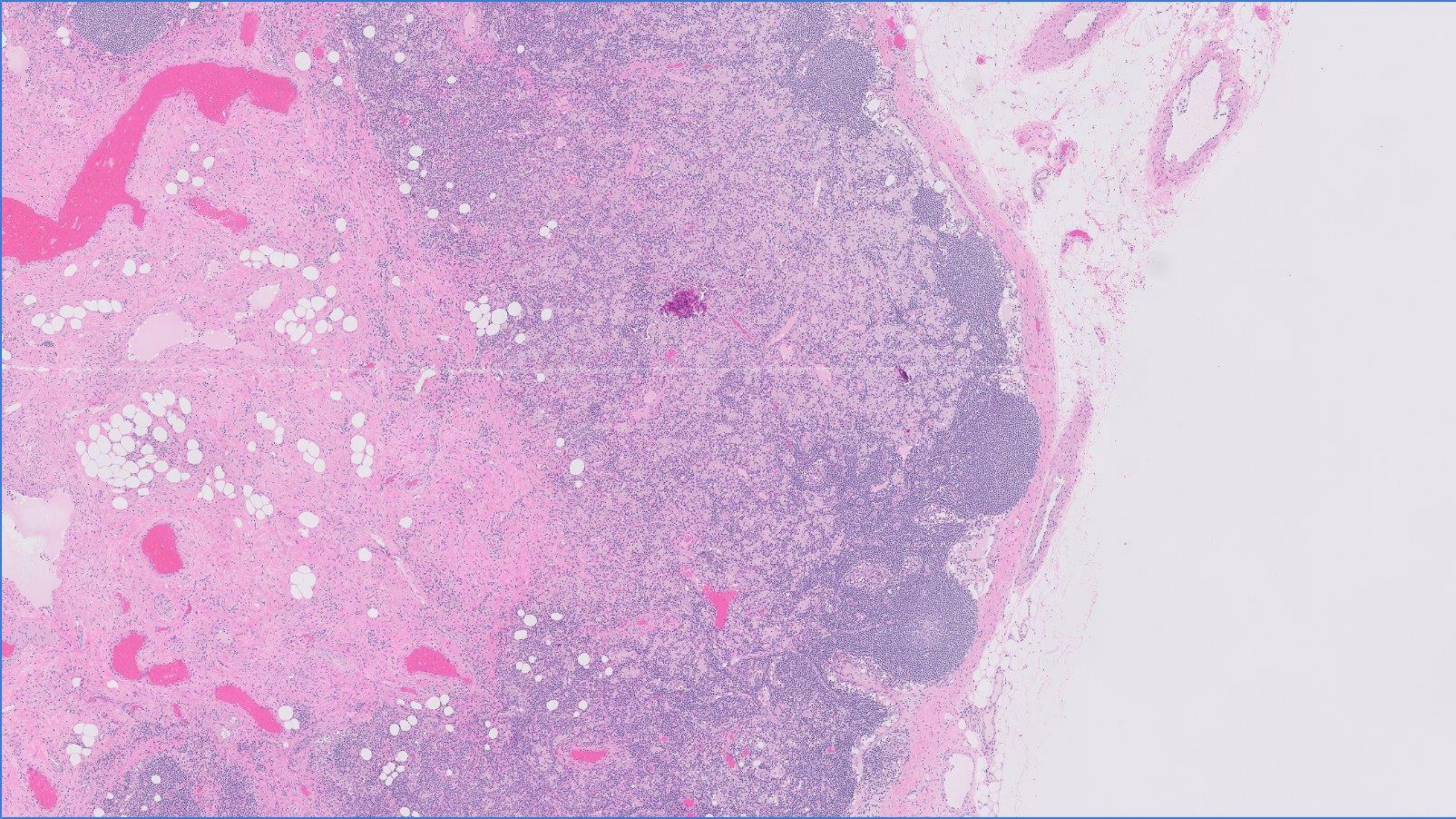
- Clinical presentation
  - Age, family history, other laboratory values (elevated LDH and hCG)
- Histology and Immunohistochemistry
  - CK7 is POSITIVE in choriocarcinoma- can’t always stop there!!
  - Poorly-differentiated adenocarcinoma is on the differential diagnosis among other high-grade malignancies
  - Histologic clues:
    - Biphasic tumor cells including multinucleated cells
    - Sheets of malignant cytotrophoblasts with “cap” of syncytiotrophoblasts
    - Central hemorrhage and necrosis (often if mass forming)
- Often patient’s present at advanced stage with poor prognosis

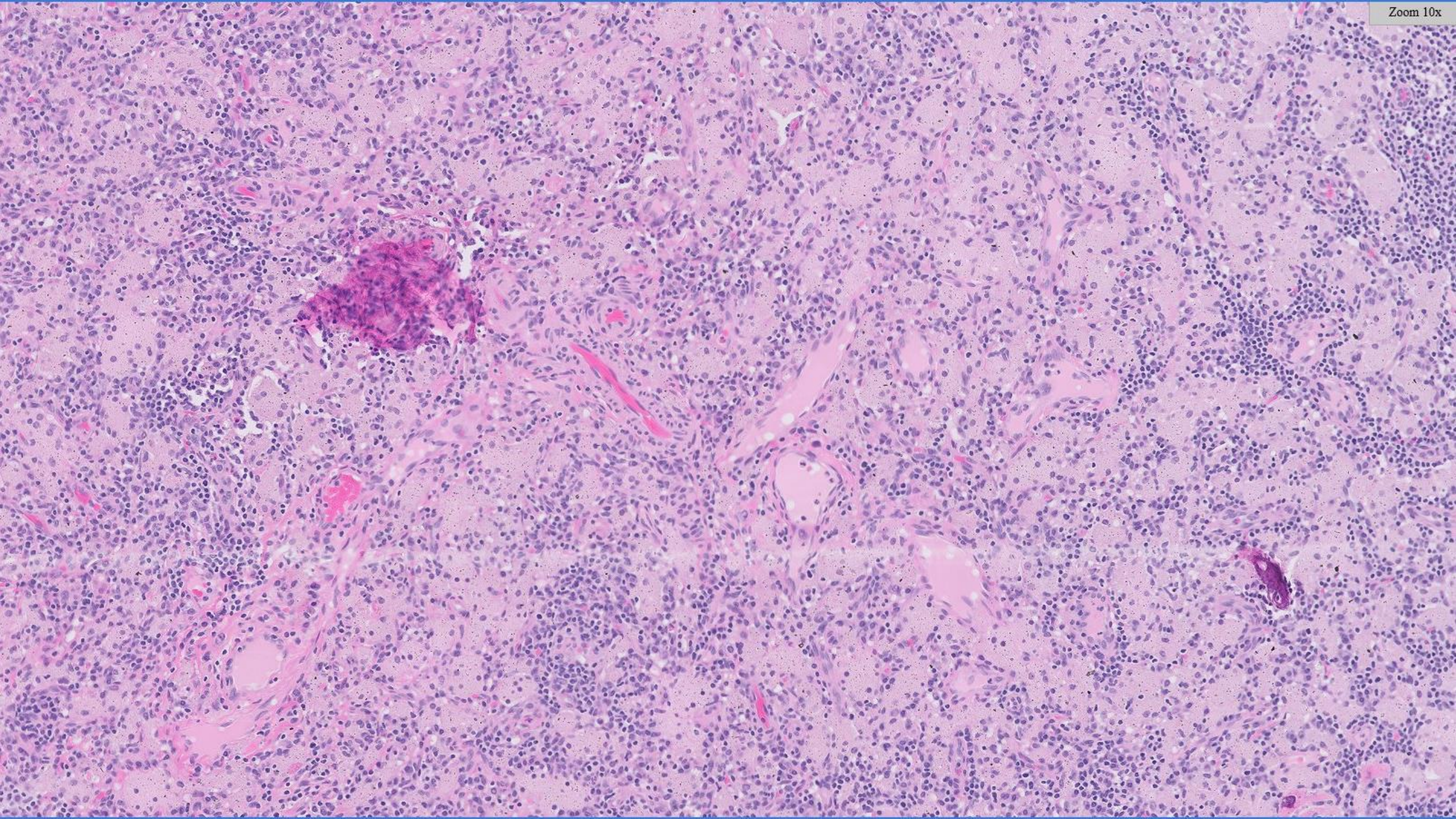
24-0107

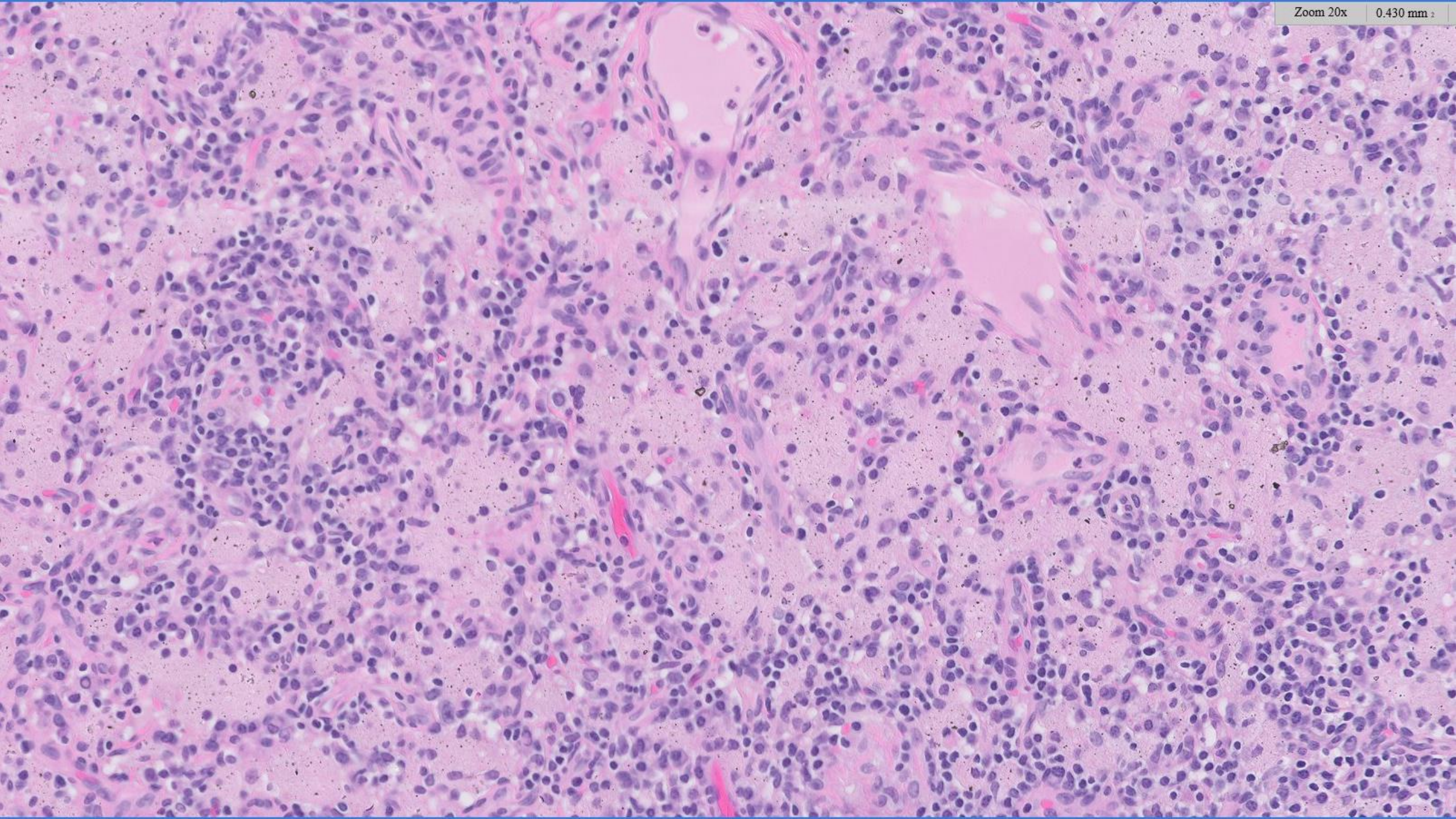
**Tyler Jankowski, Ankur Sangoi; Stanford**

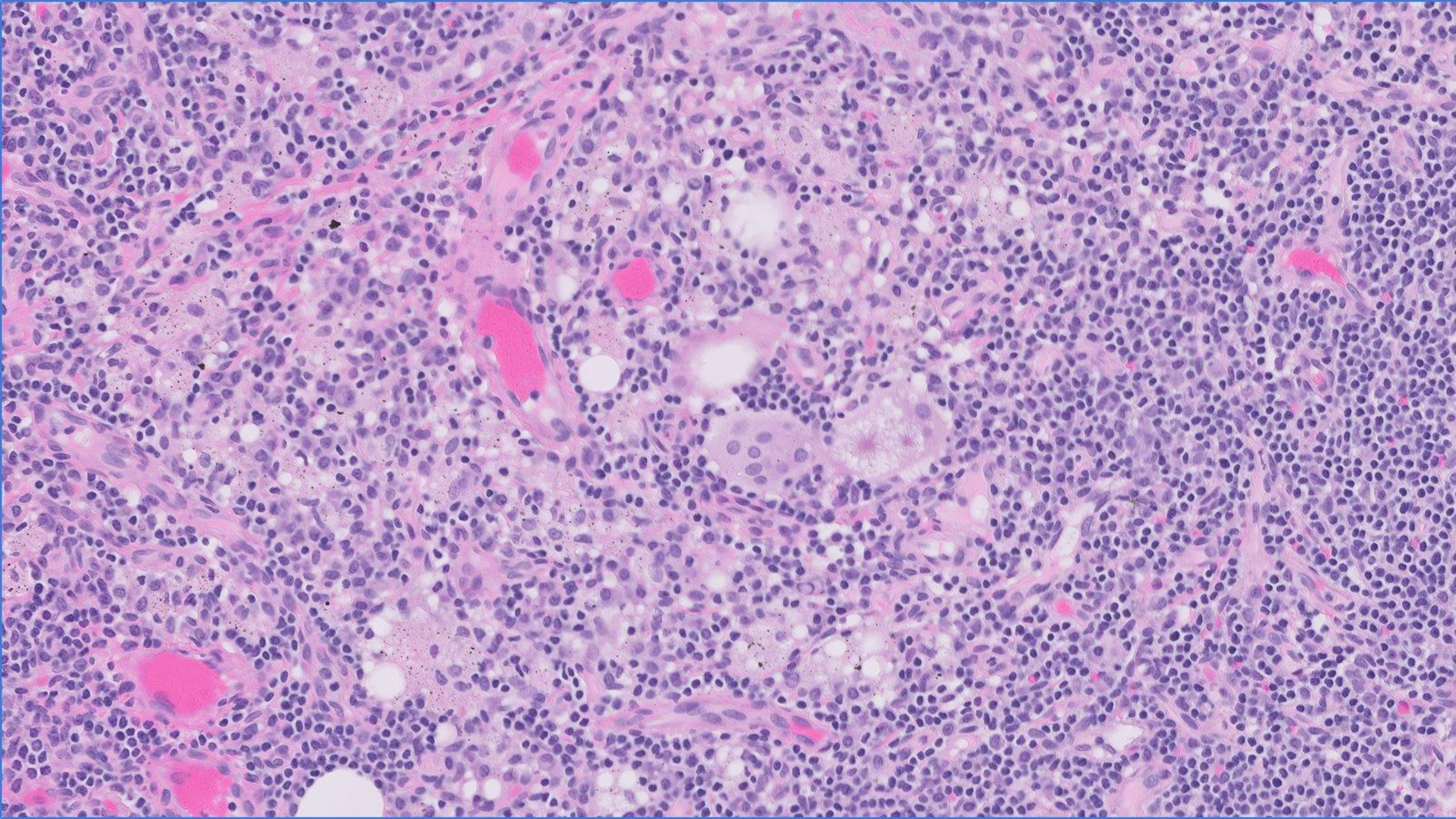
80-year-old man with hx of penile SCC and hip replacement. Now with bilateral inguinal lymphadenopathy

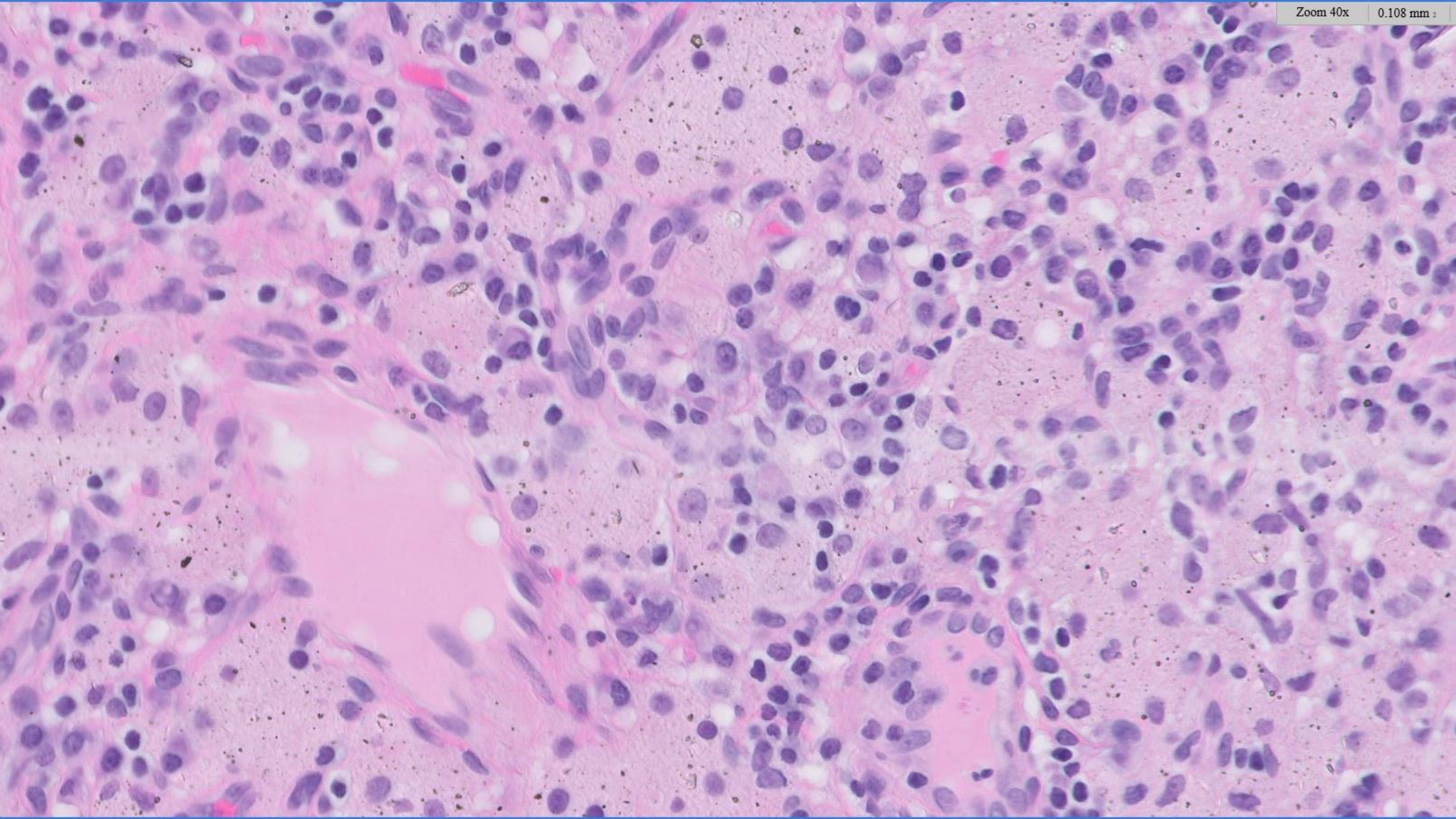




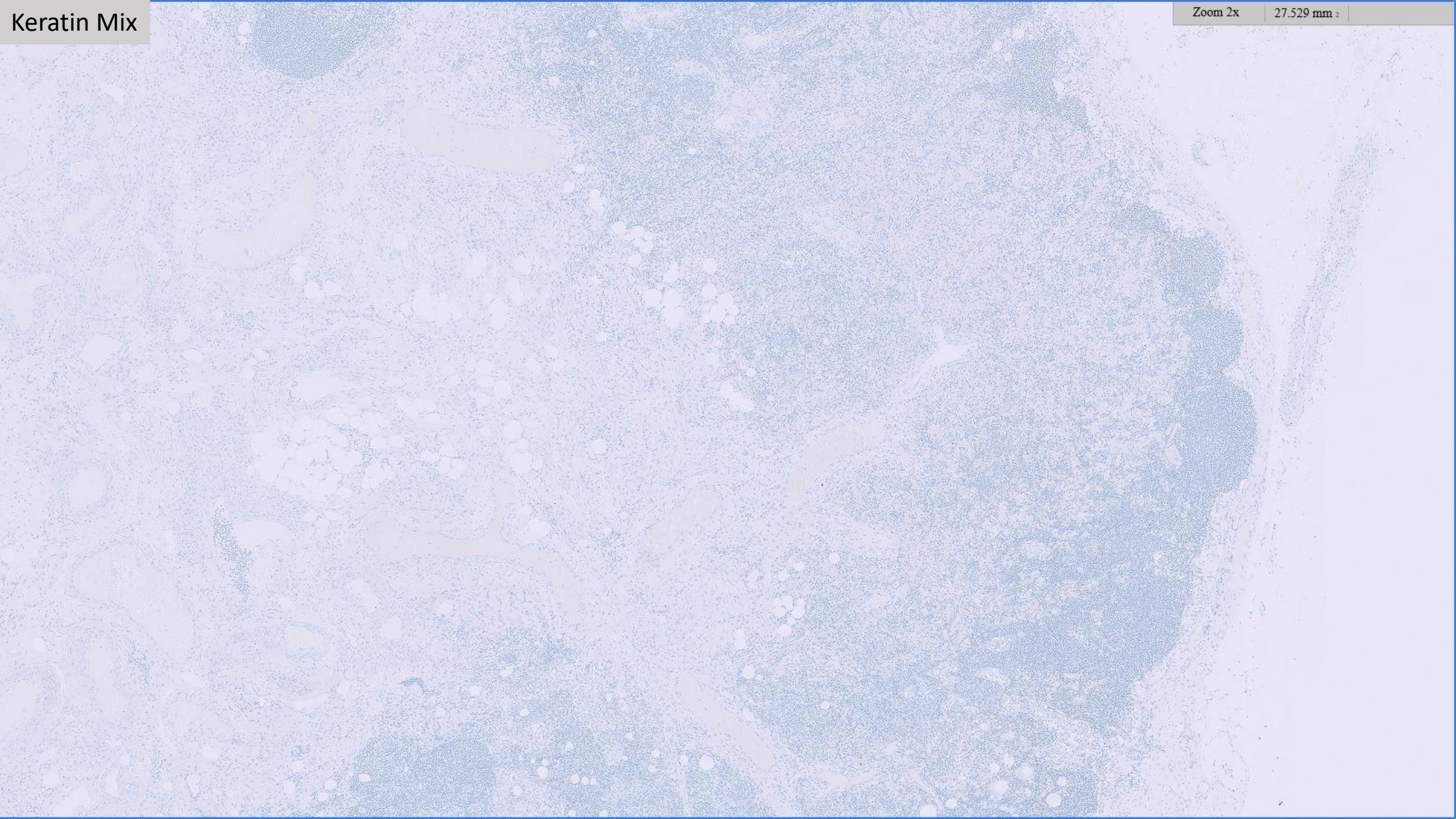

Zoom 10x


Zoom 20x
0.430 mm²

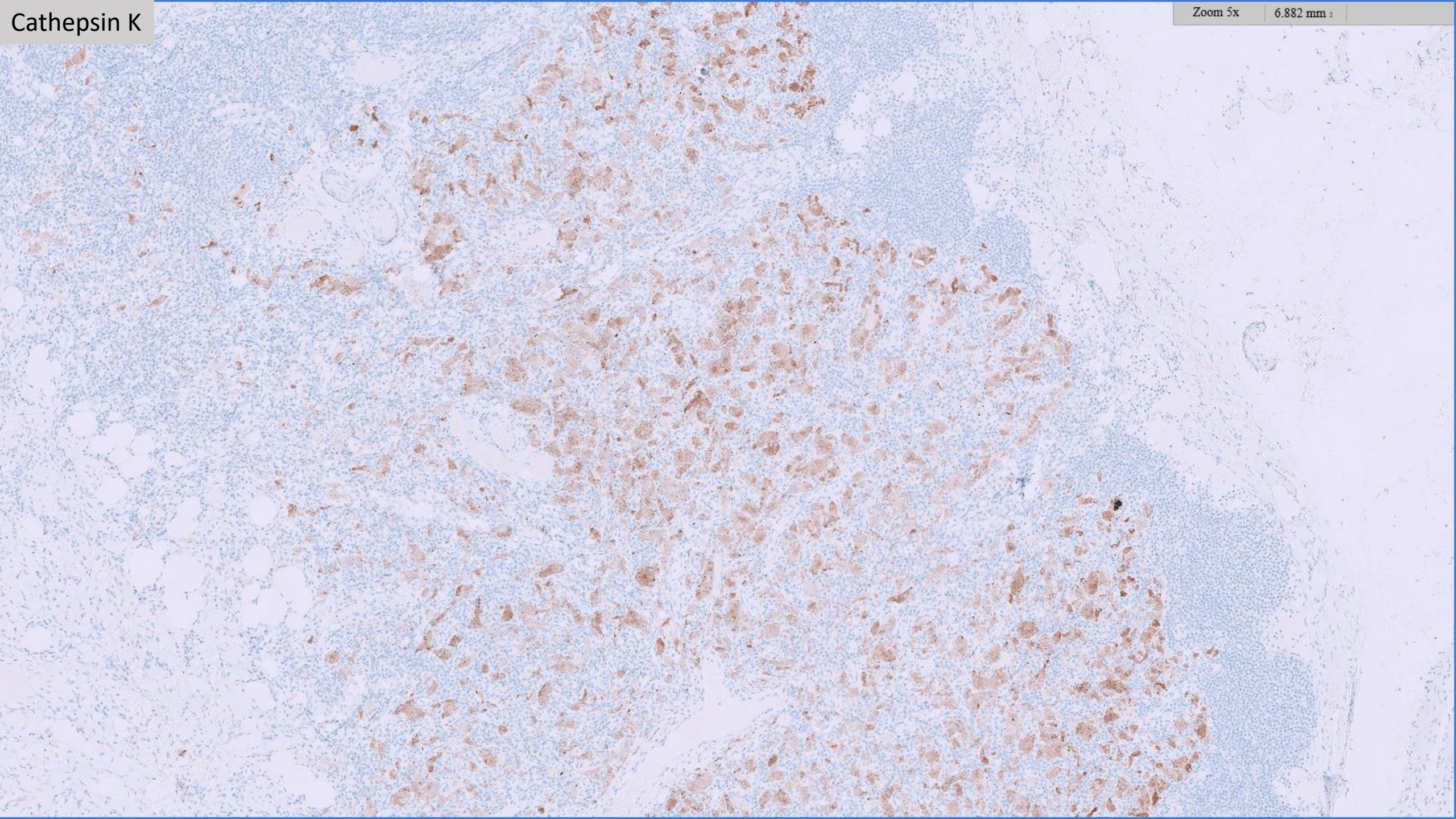


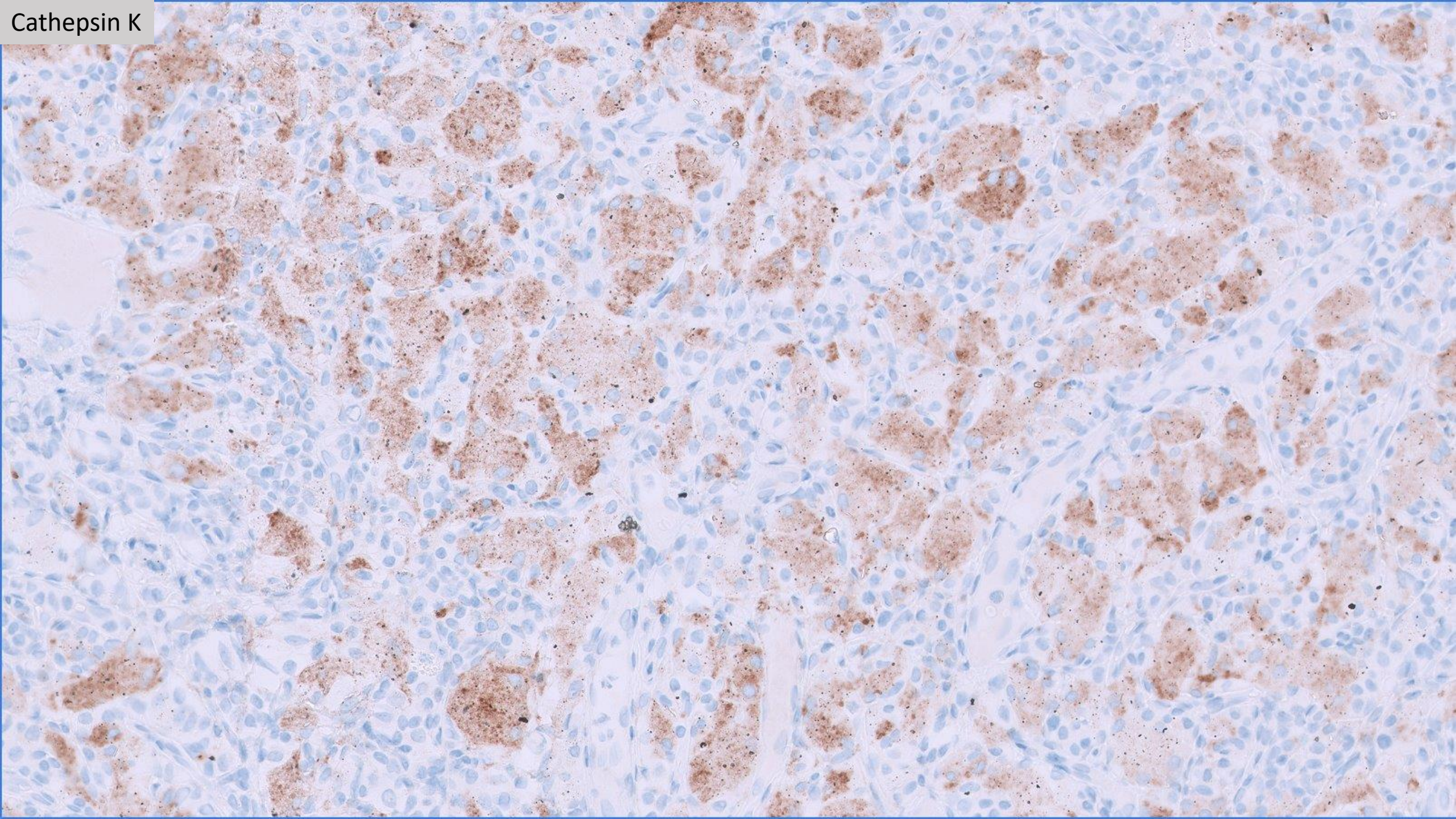

Zoom 40x
0.108 mm 2

# DIAGNOSIS?


Keratin Mix
Zoom 2x
27.529 mm 2

Cathepsin K




Cathepsin K

# Final Diagnosis

- Negative for carcinoma (see comment)

  Comment: Several of the bilateral lymph nodes show sinus expansion by histiocytes (showing overexpression for Cathepsin K, negative for keratin MIX) consistent with so-called "wear debris" histiocytosis, which is compatible with the patient's history of joint replacement

# Wear-debris histiocytes

- Cathepsin K is a cysteine protease key to bone remodeling
  - Upregulated in wear debris histiocytes associated with prosthetic joints
- Process is multifactorial but boils down to prosthetic joint polymers initiating local adverse tissue reaction and getting absorbed by macrophages
- Implants produce undergo microtrauma at weight bearing surfaces producing microscopic fragments of wear debris and resorption

ORIGINAL ARTICLE

# Expression of Cathepsin K by Wear Debris Histiocytes in Patients with Total Joint Prostheses

Anton Alexander Nolte Peterlin[1], MD; Charles M Lombard[2], MD

International Journal of Orthopaedics

Online Submissions: http: //www.ghrnet.org/index.php/ijo
doi: 10.17554/j.issn.2311-5106.2021.08.390

Int. J. of Orth. 2021 February 28; 8(1): 1425-1430
ISSN 2311-5106 (Print), ISSN 2313-1462 (Online)

- 12 wear-debris changes, 13 controls (lymph nodes/synovium/bone)
- Staining intensity, pattern and proportion scores were annotated with CatK IHC to calculate an H-score
  - Intensity, pattern, and score were all significantly higher in wear-debris changes opposed to controls
- All wear debris cases were strongly positive for CatK, while those from non-wear debris were negative or only weakly positive

- Conclusion: CathepsinK can be confidently used to delineate wear-debris  from non-wear debris histocytes in cases of histiocytosis in multiple tissue types.

**Table 1** Descriptive characteristics of wear debris and control histiocyte immunohistochemistry staining.

| Pathology | Site | Tissue Type | SP | SI | PS | H-score |
|---|---|---|---|---|---|---|
| Wear debris change | Pelvic | Lymph Node | He | 3 | 3 | 9 |
| Wear debris lymphadenopathy | Inguinal | Lymph Node | Ho | 3 | 3 | 9 |
| Wear debris associated osteolysis | Pelvic | Lymph Node | Ho | 3 | 3 | 9 |
| Wear debris associated changes | Pelvic | Lymph Node | Ho | 3 | 3 | 9 |
| Wear debris change | Pelvic | Lymph Node | Ho | 2 | 3 | 6 |
| Wear debris associated osteolysis | L. knee Osteolytic lesion | Bone | Ho | 3 | 3 | 9 |
| Wear debris changes | R. knee failed prosthesis | Bone | Ho | 3 | 3 | 9 |
| Wear debris changes | R. knee failed prosthesis | Bone | Ho | 3 | 3 | 9 |
| Wear debris associated changes | R. foot | Bone | Ho | 3 | 2 | 6 |
| Wear debris changes | L. knee failed prosthesis | Synovium | Ho | 3 | 3 | 9 |
| Wear debris changes | R. knee failed prosthesis | Synovium | Ho | 3 | 3 | 9 |
| Wear debris associated changes | L. knee failed prosthesis | Synovium | [No Title] | 2 | 3 | 6 |
| Controls | | | | | | |
| Kikuchi's lymphadenitis | Cervical | Lymph Node | He | 1 | 1 | 1 |
| Anthracotic change; benign | Mediastinal | Lymph Node | Ho | 0 | 0 | 0 |
| Benign sinus histiocytes | Peripancreatic | Lymph Node | Ho | 0 | 0 | 0 |
| Sinus histiocytosis | Pelvic | Lymph Node | Ho | 0 | 0 | 0 |
| Degenerative joint disease | L. femoral head | Bone | He | 1 | 2 | 2 |
| Osteomyelitis | R. great toe | Bone | He | 2 | 1 | 2 |
| Degenerative joint disease | L. knee | Bone | He | 2 | 1 | 2 |
| Osteomyelitis | L. 5th metatarsal head | Bone | Ho | 1 | 1 | 1 |
| Rheumatoid arthritis | R. knee | Bone | He | 1 | 1 | 1 |
| Degenerative joint disease | R. femoral head | Bone | Ho | 0 | 0 | 0 |
| Avascular necrosis | L. femoral head | Bone | Ho | 0 | 0 | 0 |
| Giant cell tumor of tendon sheath | R. 5th finger | Synovium | He | 1 | 1 | 1 |
| Rosai-Dorfman disease | Soft tissues of back | Soft Tissue | Ho | 0 | 0 | 0 |

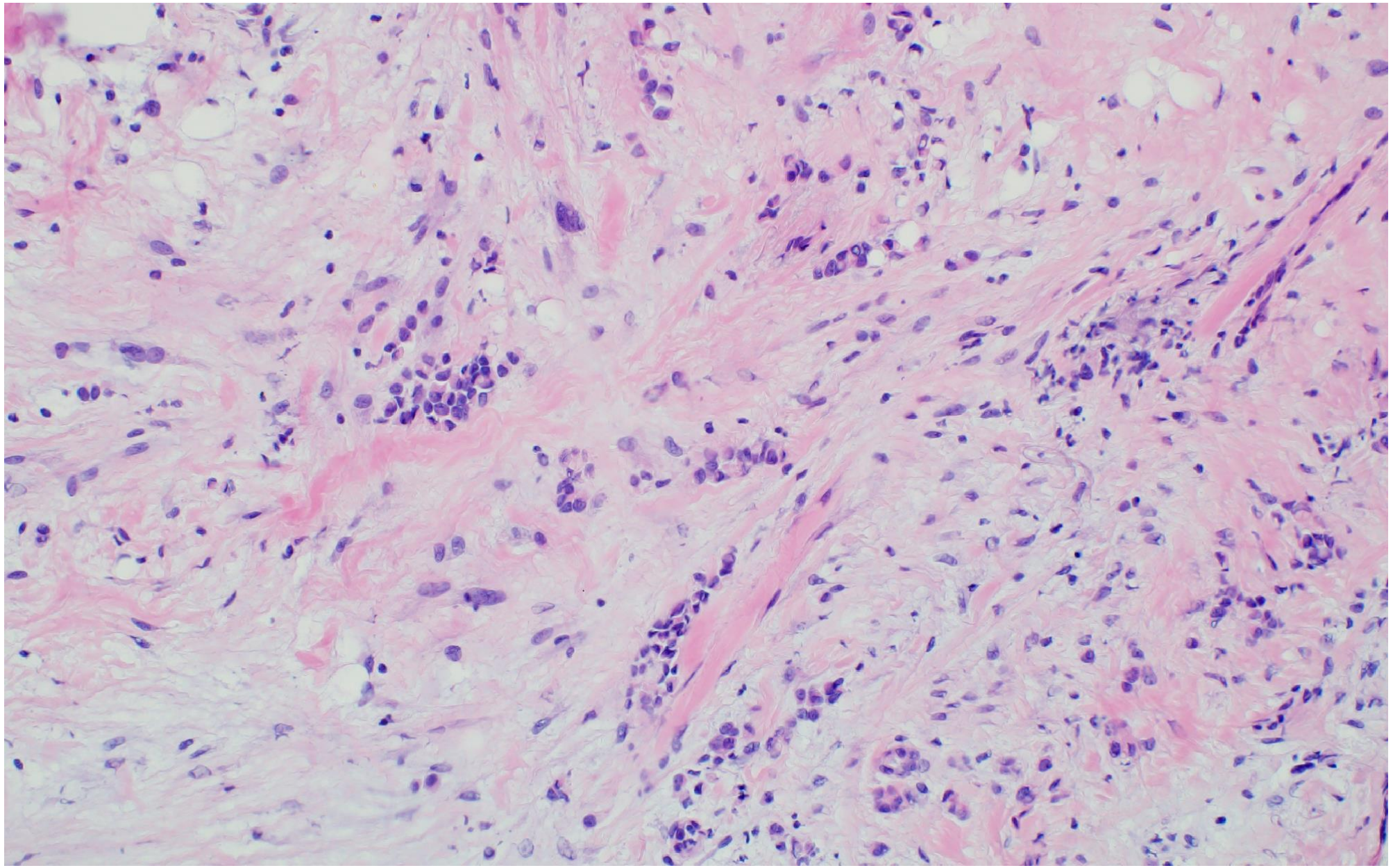
Abbreviations: Heterogenous (He); Homogenous; (Ho); Left (L); Right (R), Staining Pattern (SP); Staining Intensity (SI); Porportion Score (PS).

24-0108

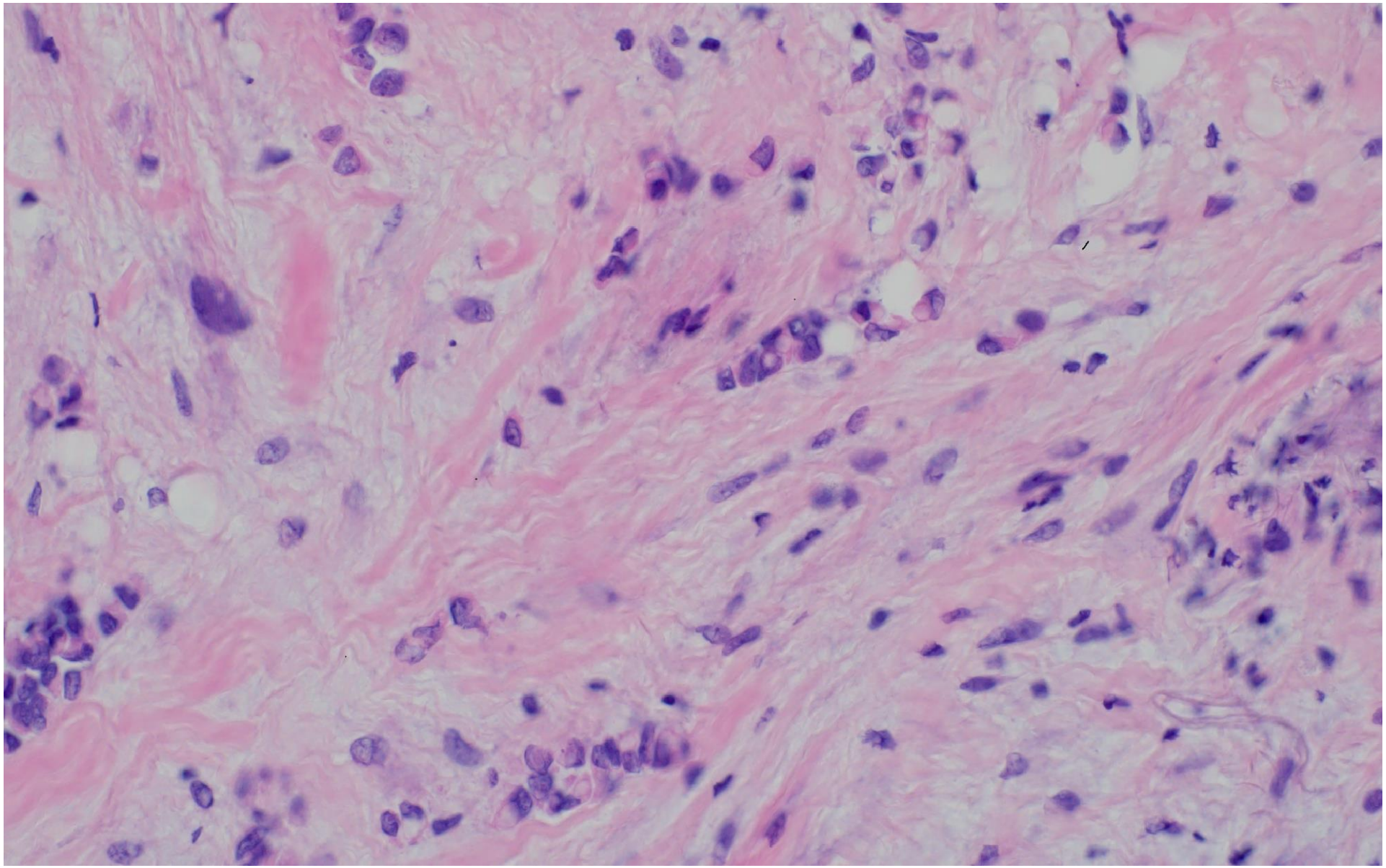
**Yang Hu, Xiaoming Zhang; Stanford**

# 68-year-old woman with 2.6 cm endometrial mass and frozen section of anterior abdominal wall lesion

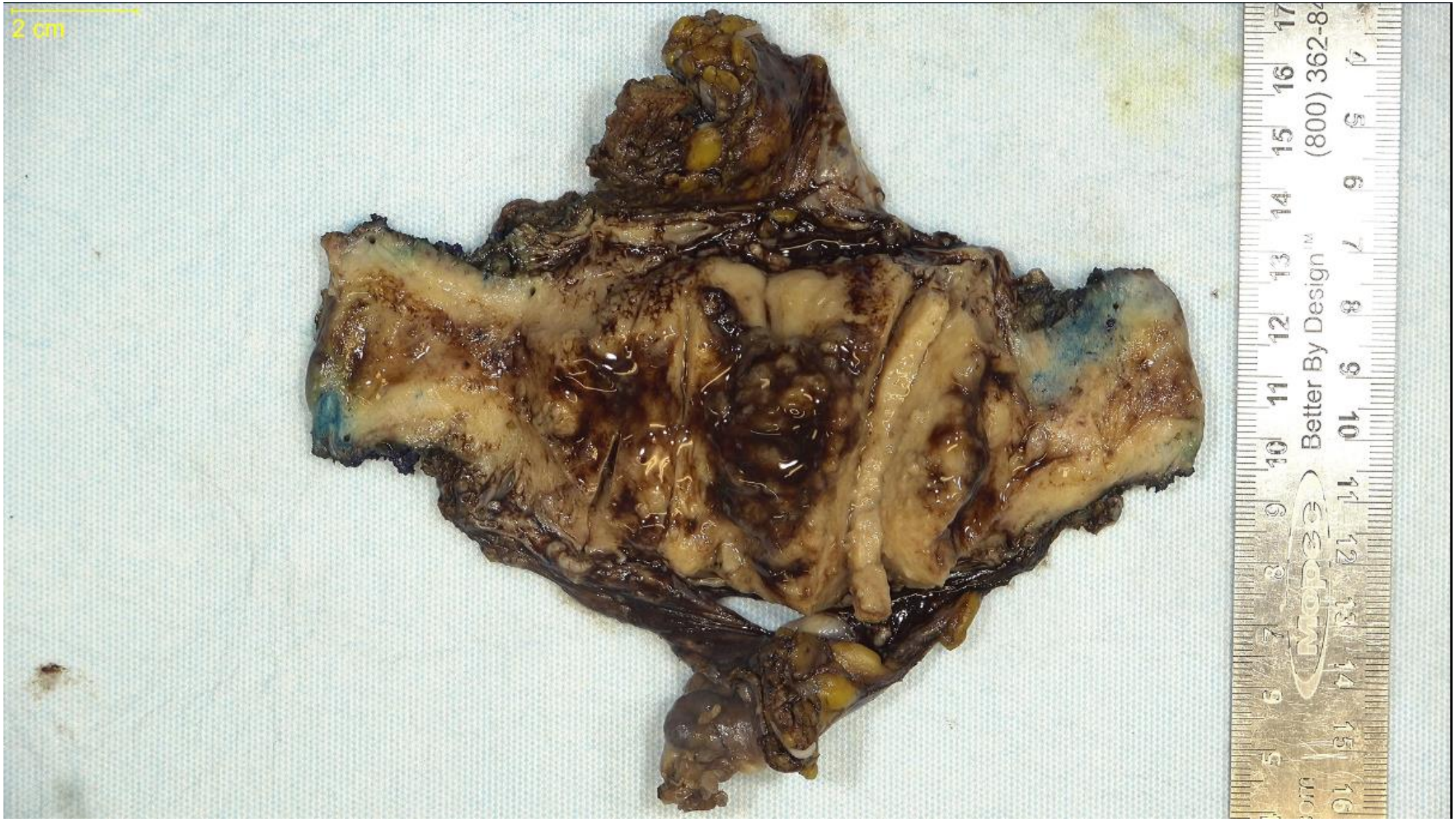
# Frozen section of abdominal wall lesion

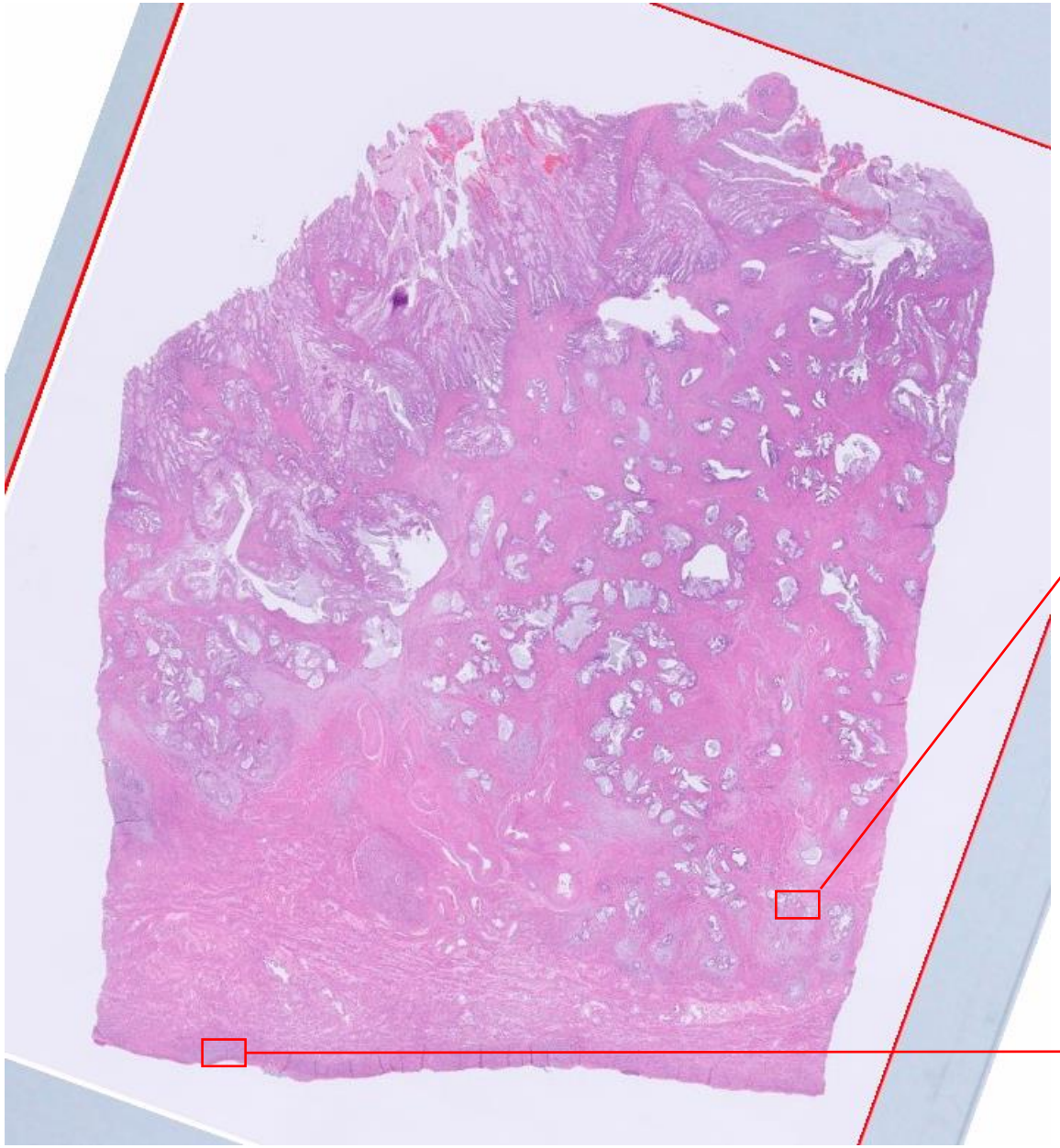


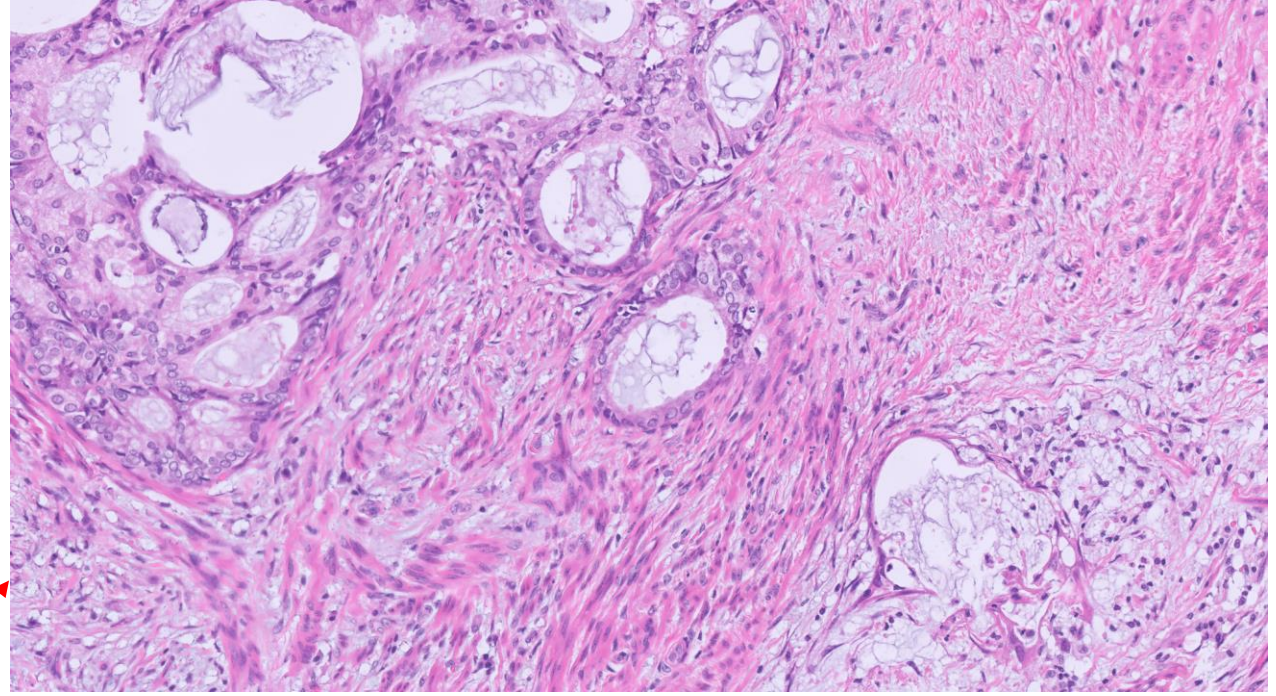
# Frozen section of abdominal wall lesion

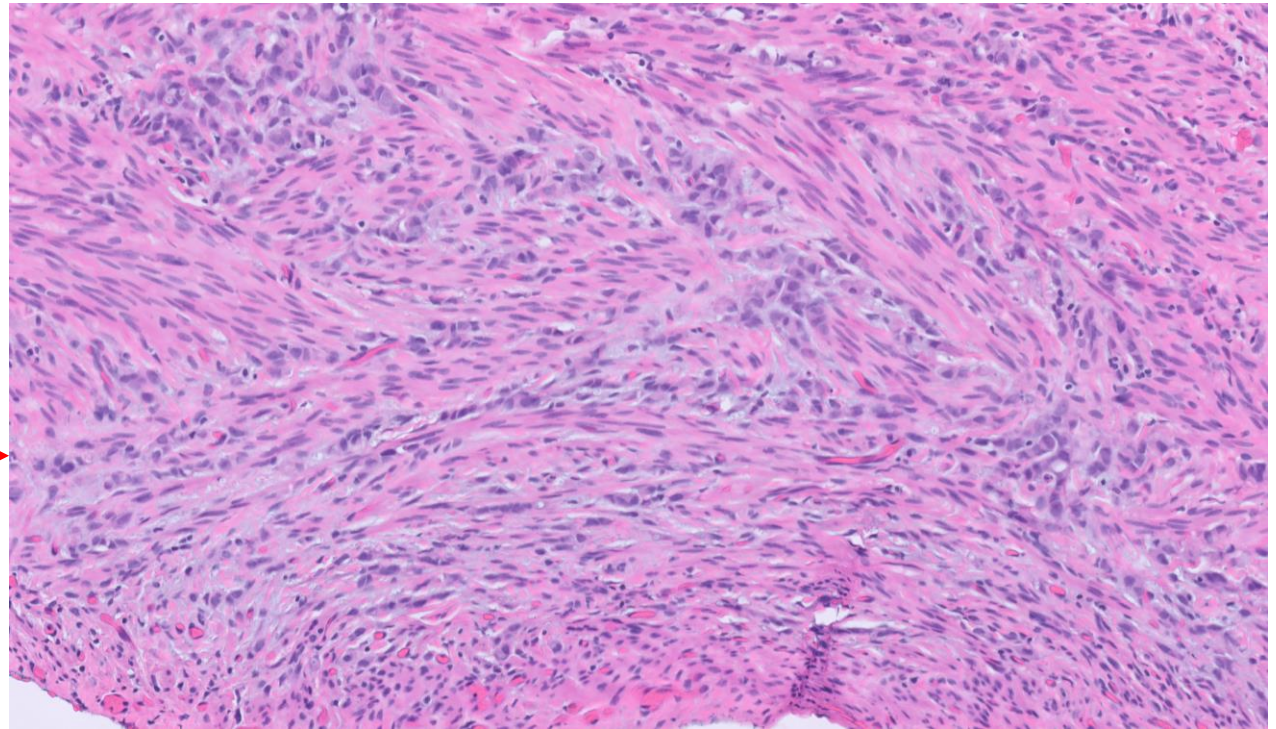


# Endometrial lesion

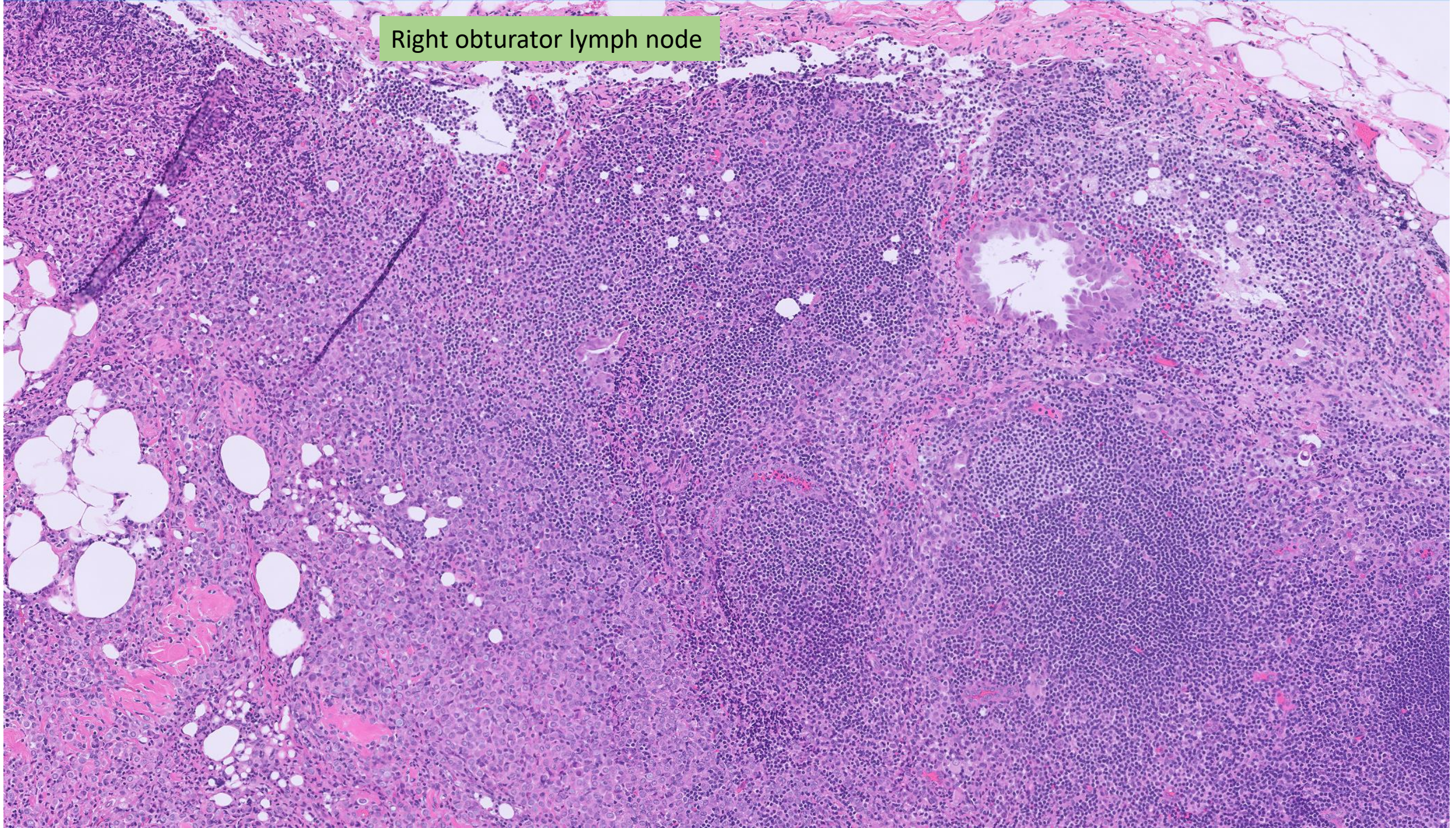




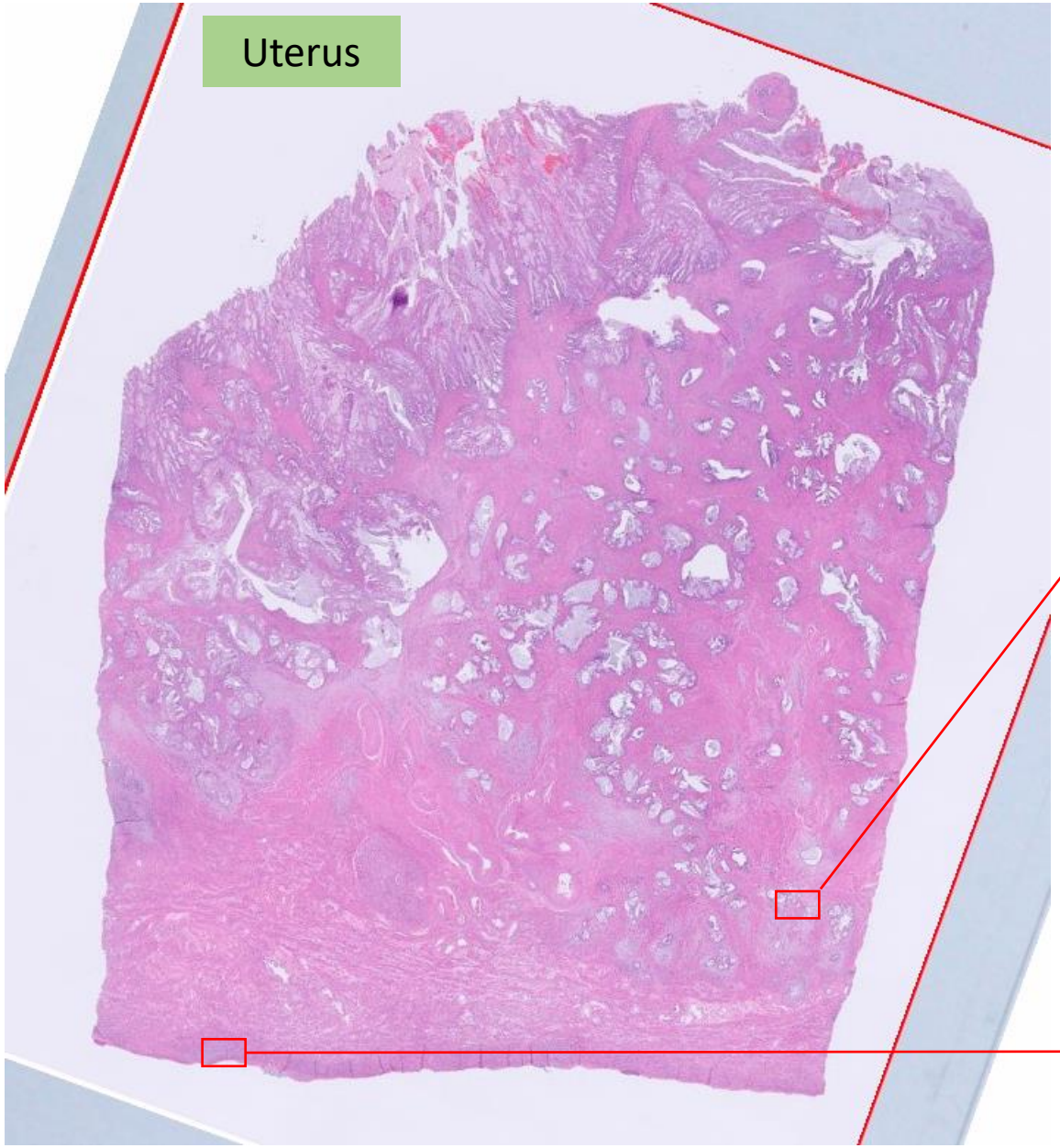




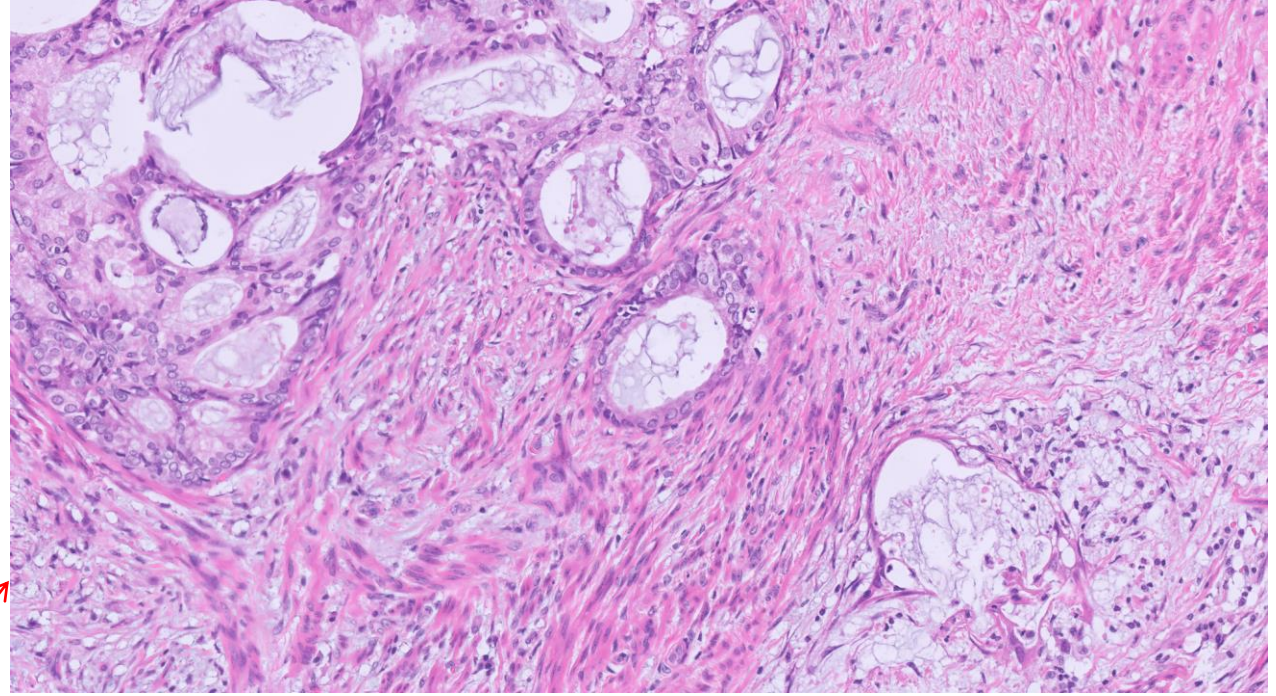
Uterus

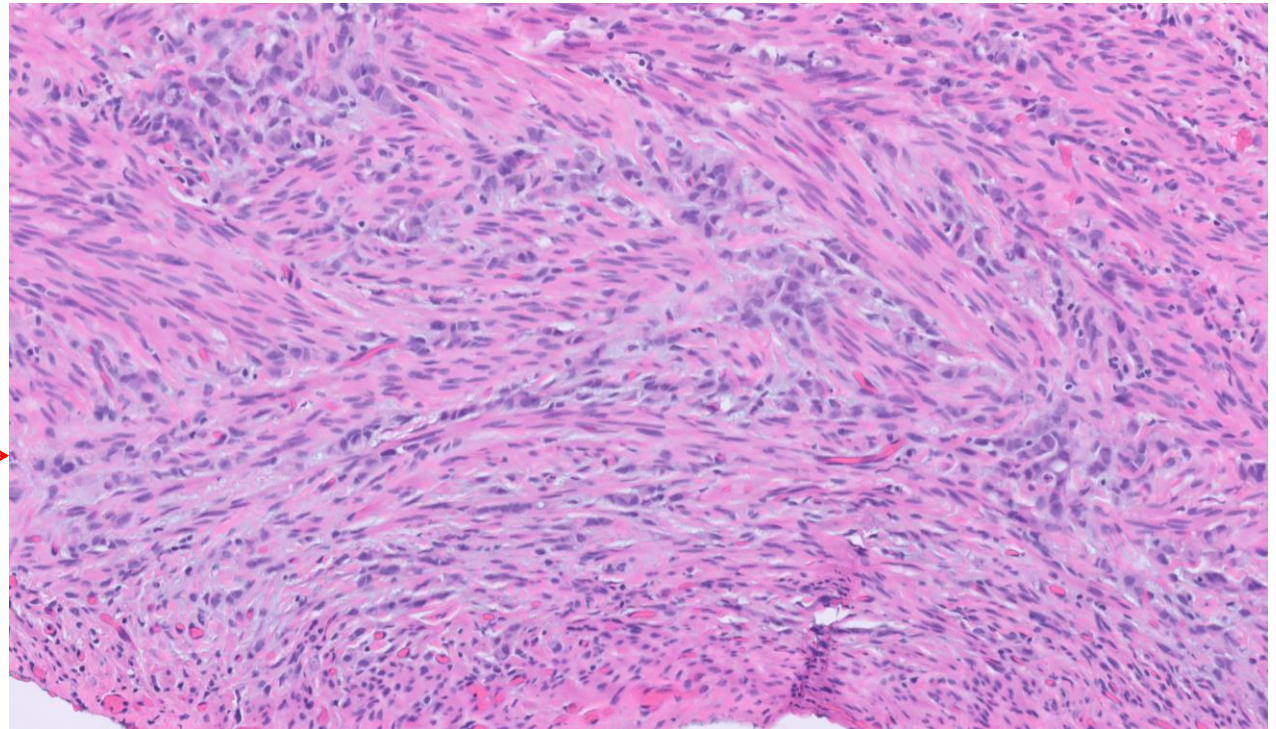

Right obturator lymph node

# DIAGNOSIS?

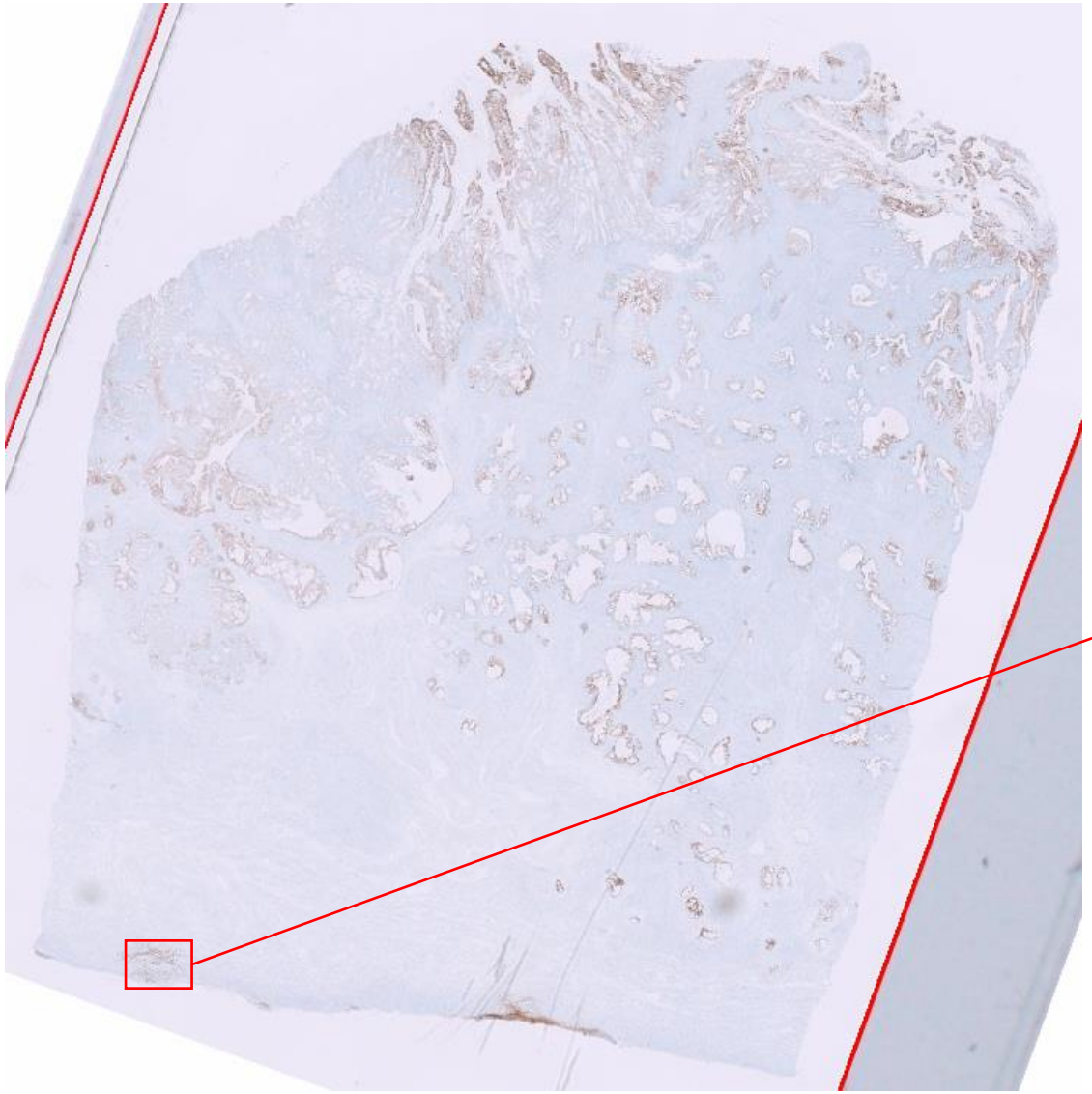


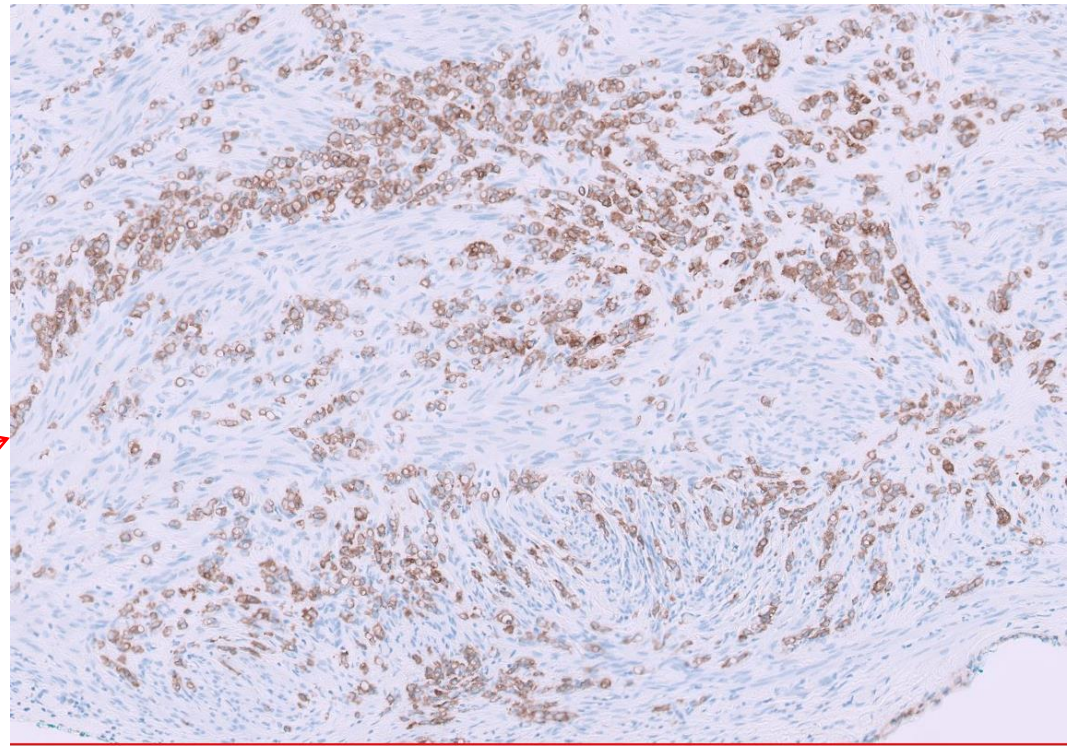

Uterus



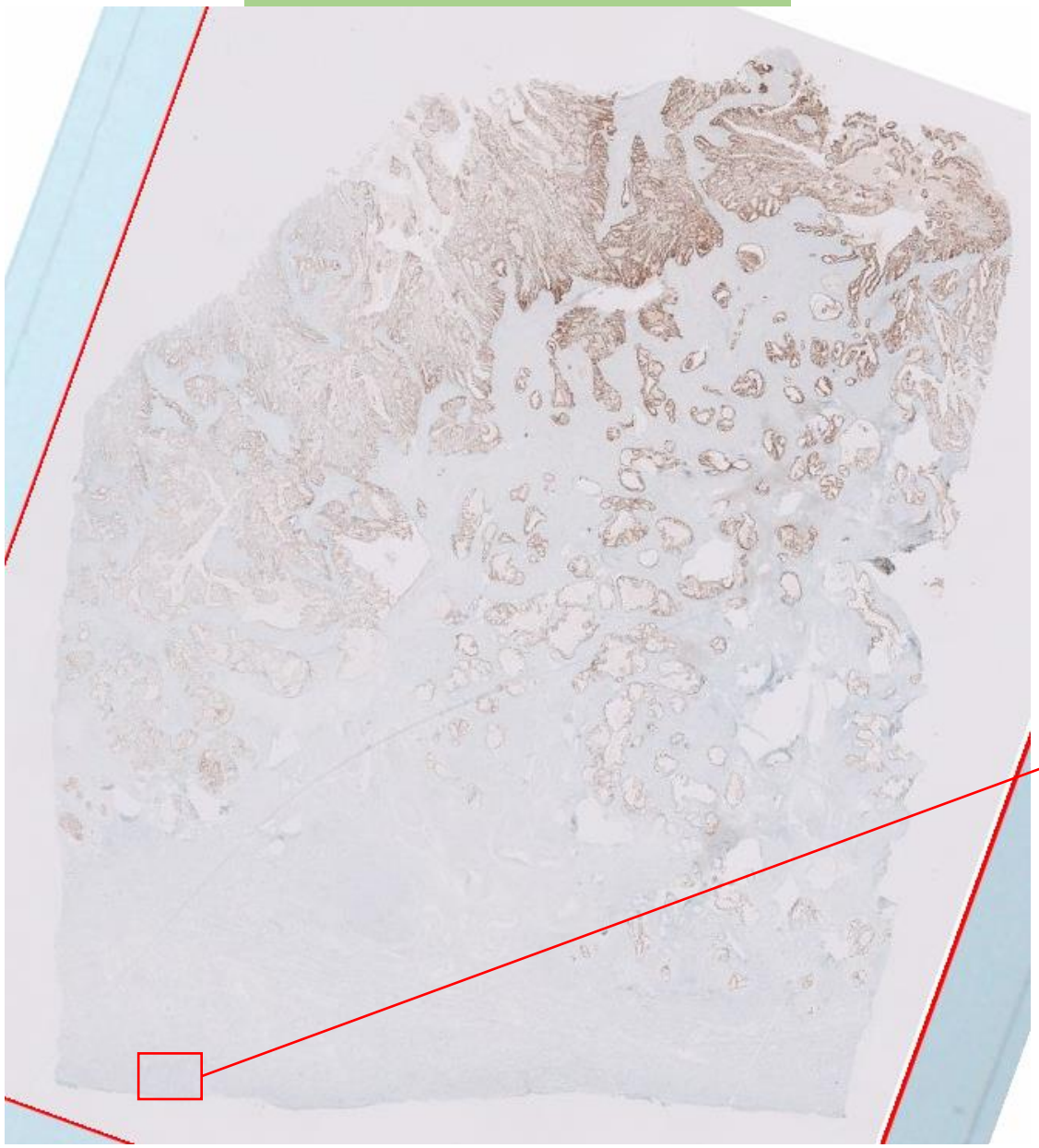


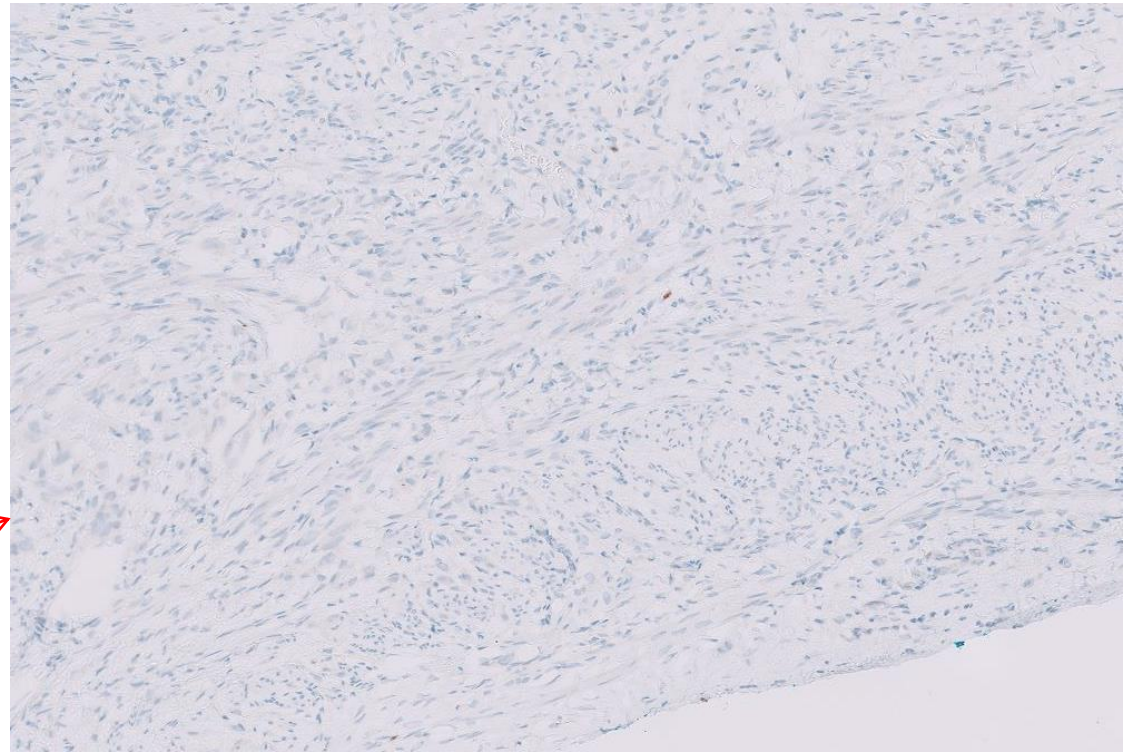
# Keratin Mix





# PAX8





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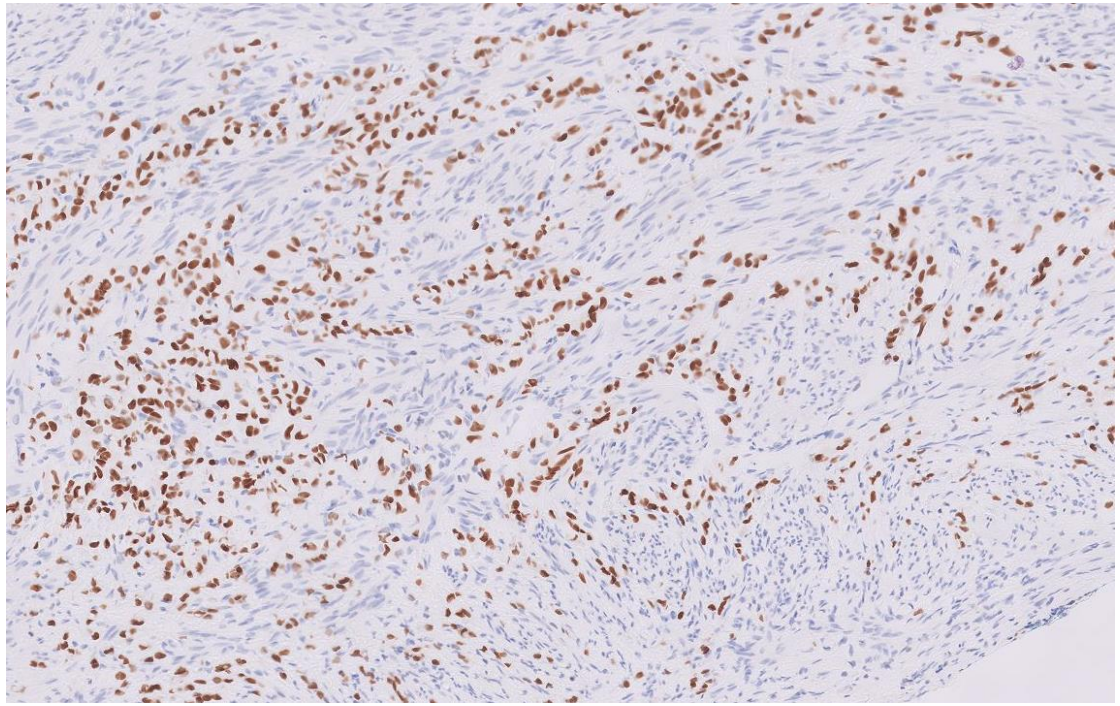
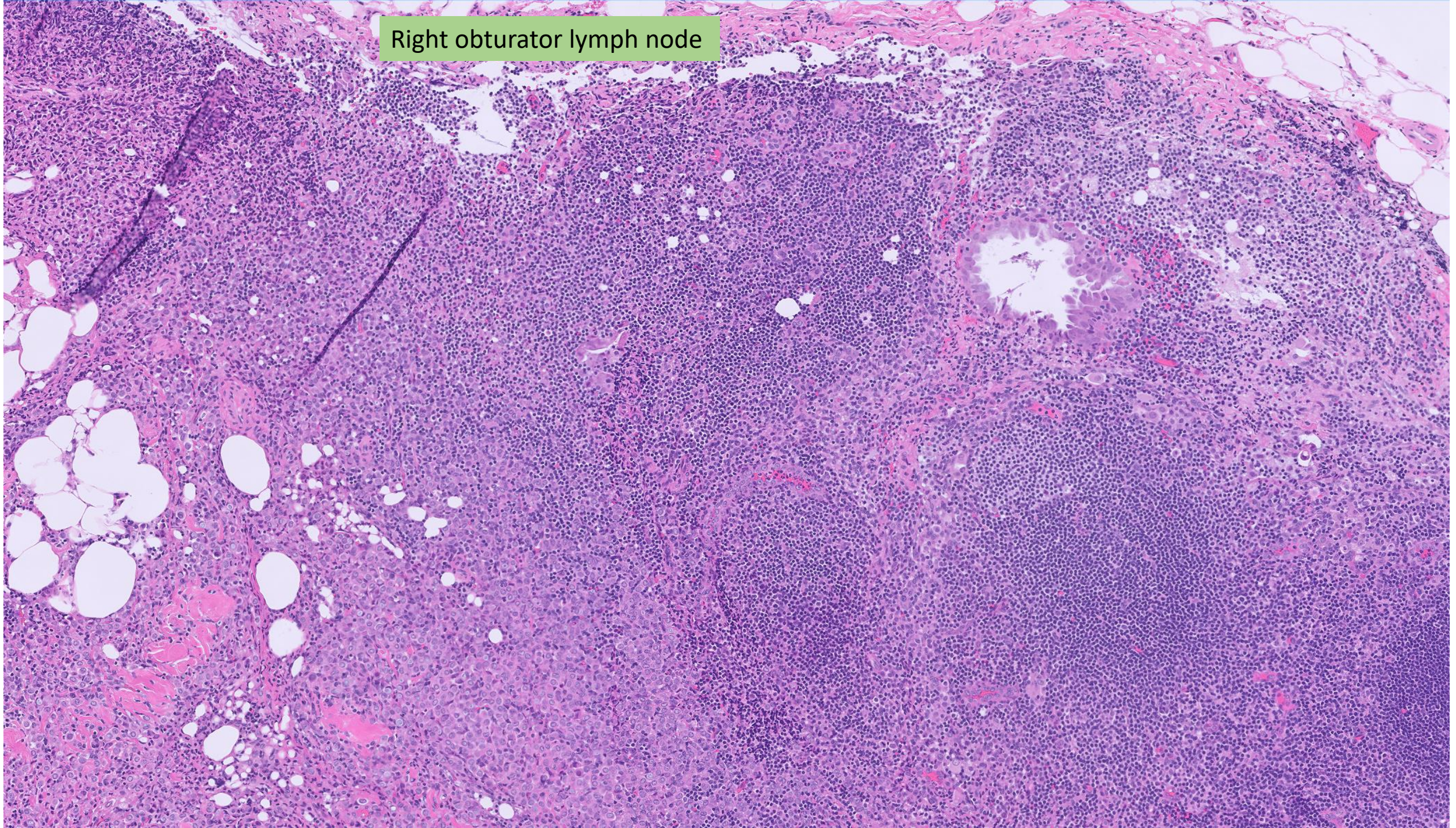
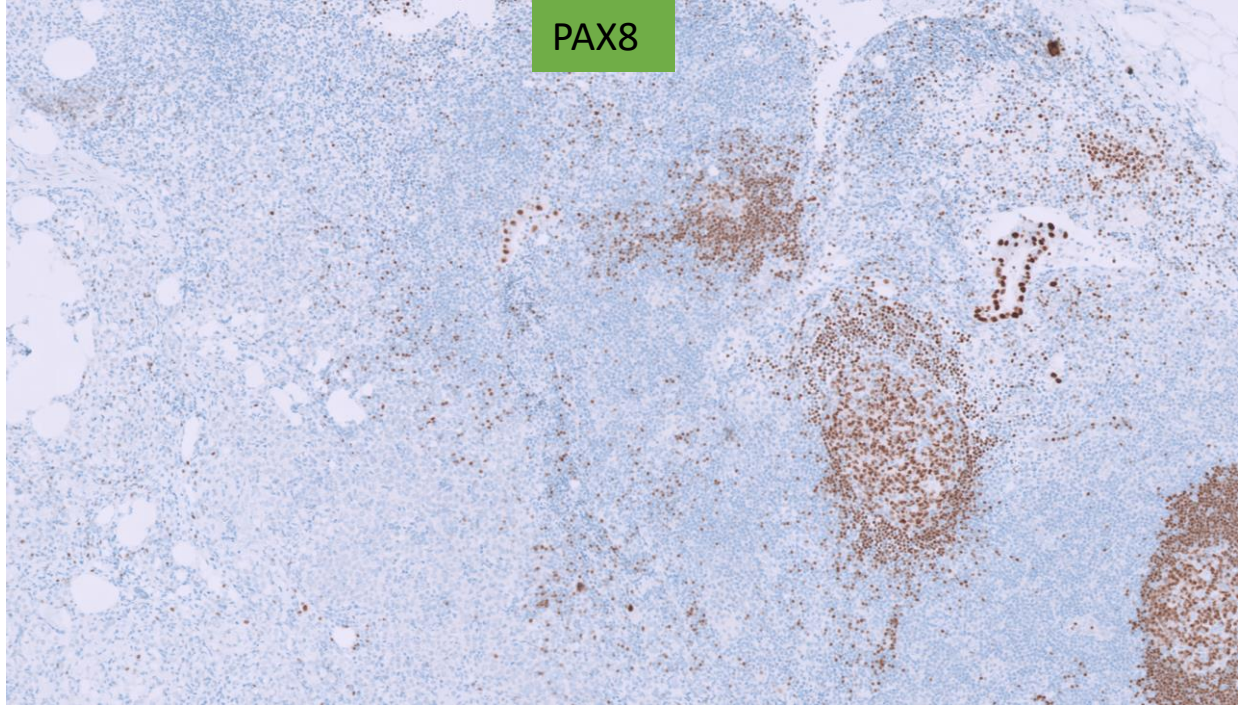
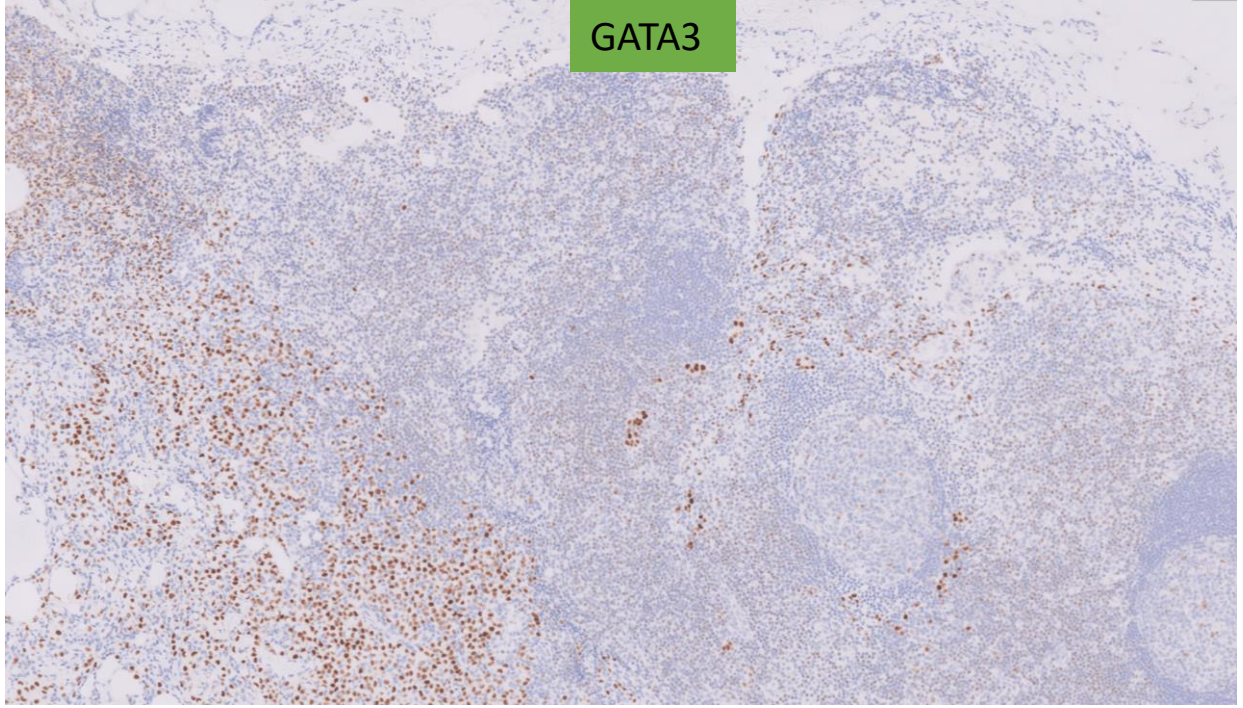
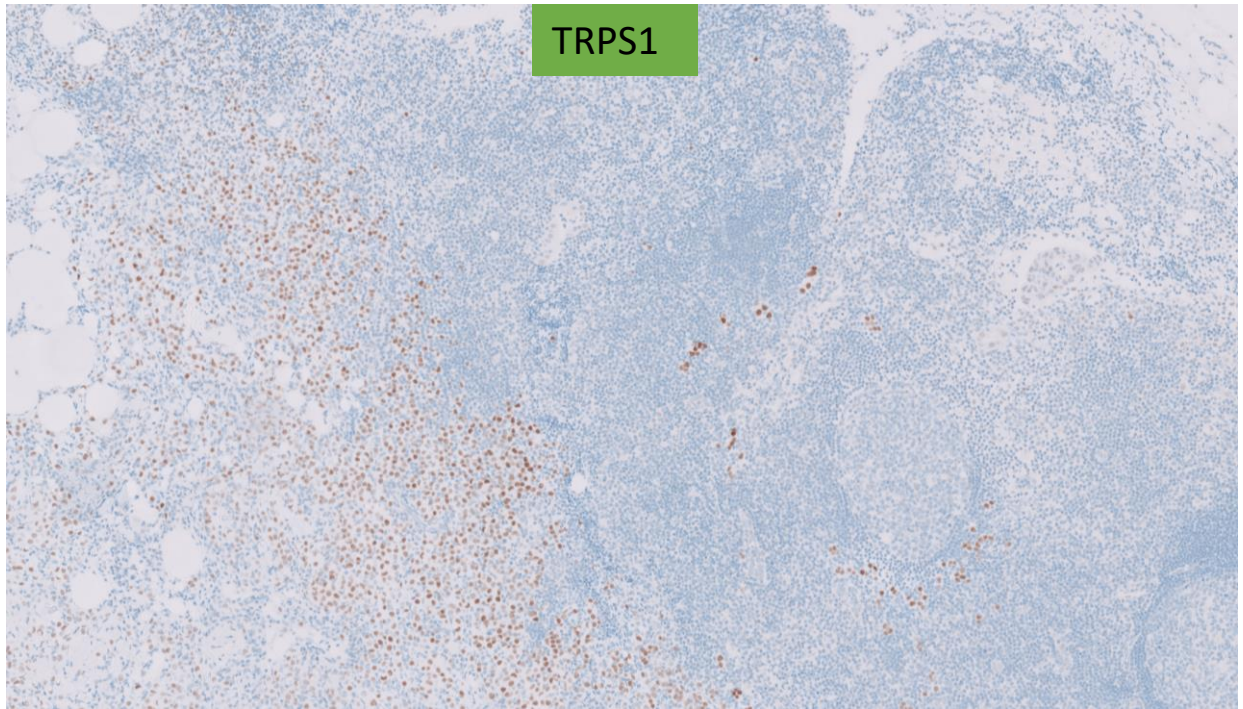
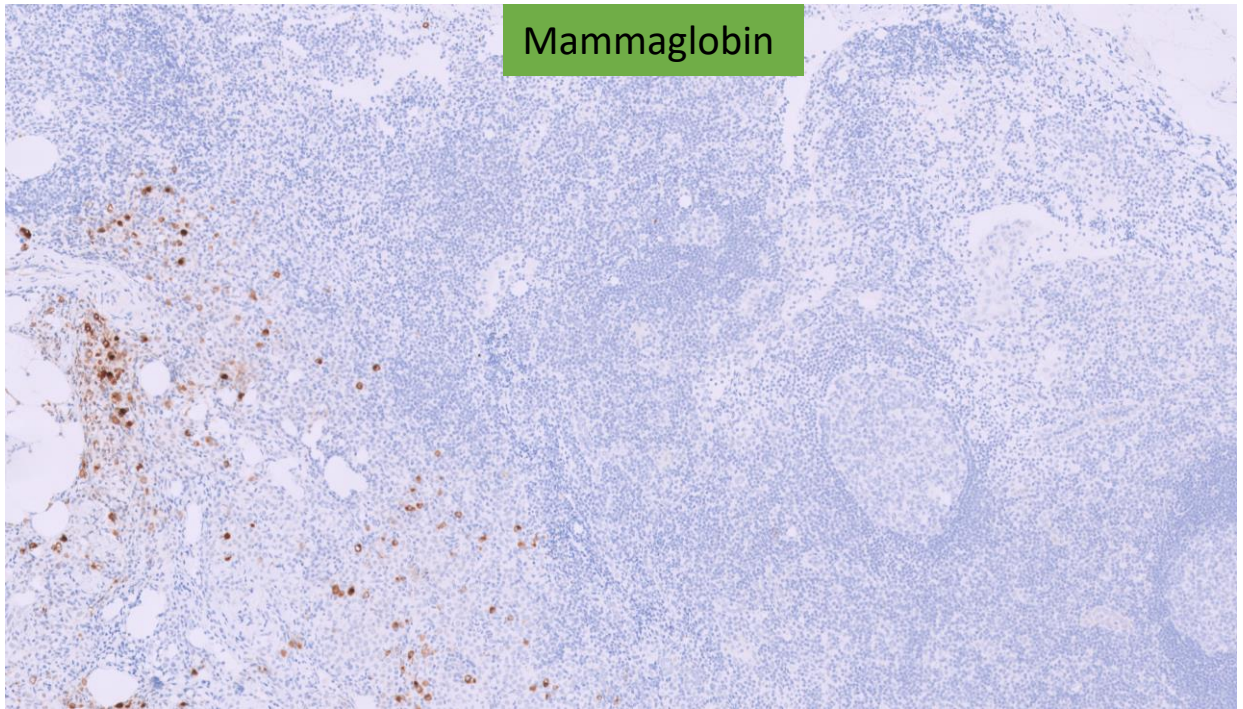



Right obturator lymph node

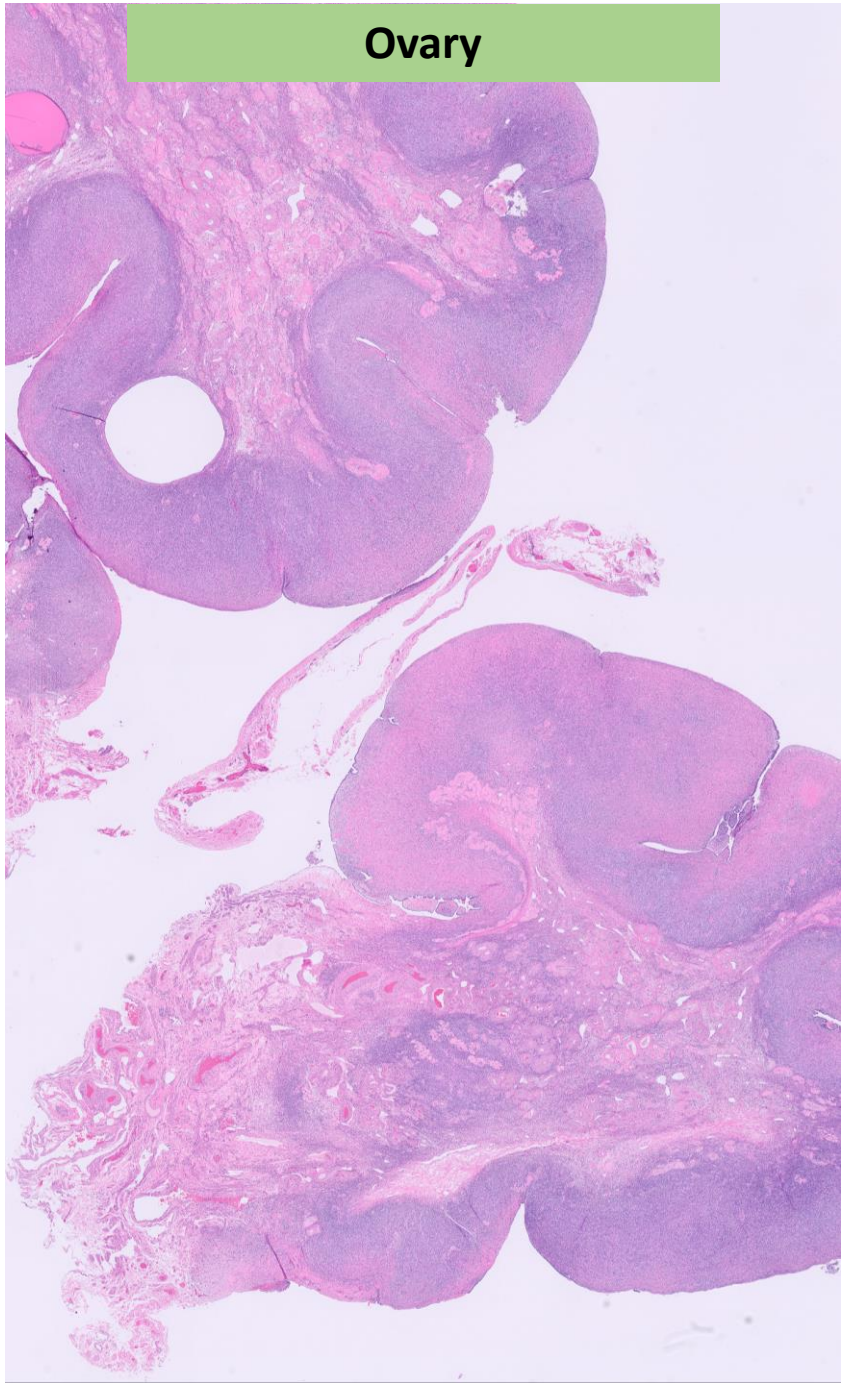

PAX8


GATA3

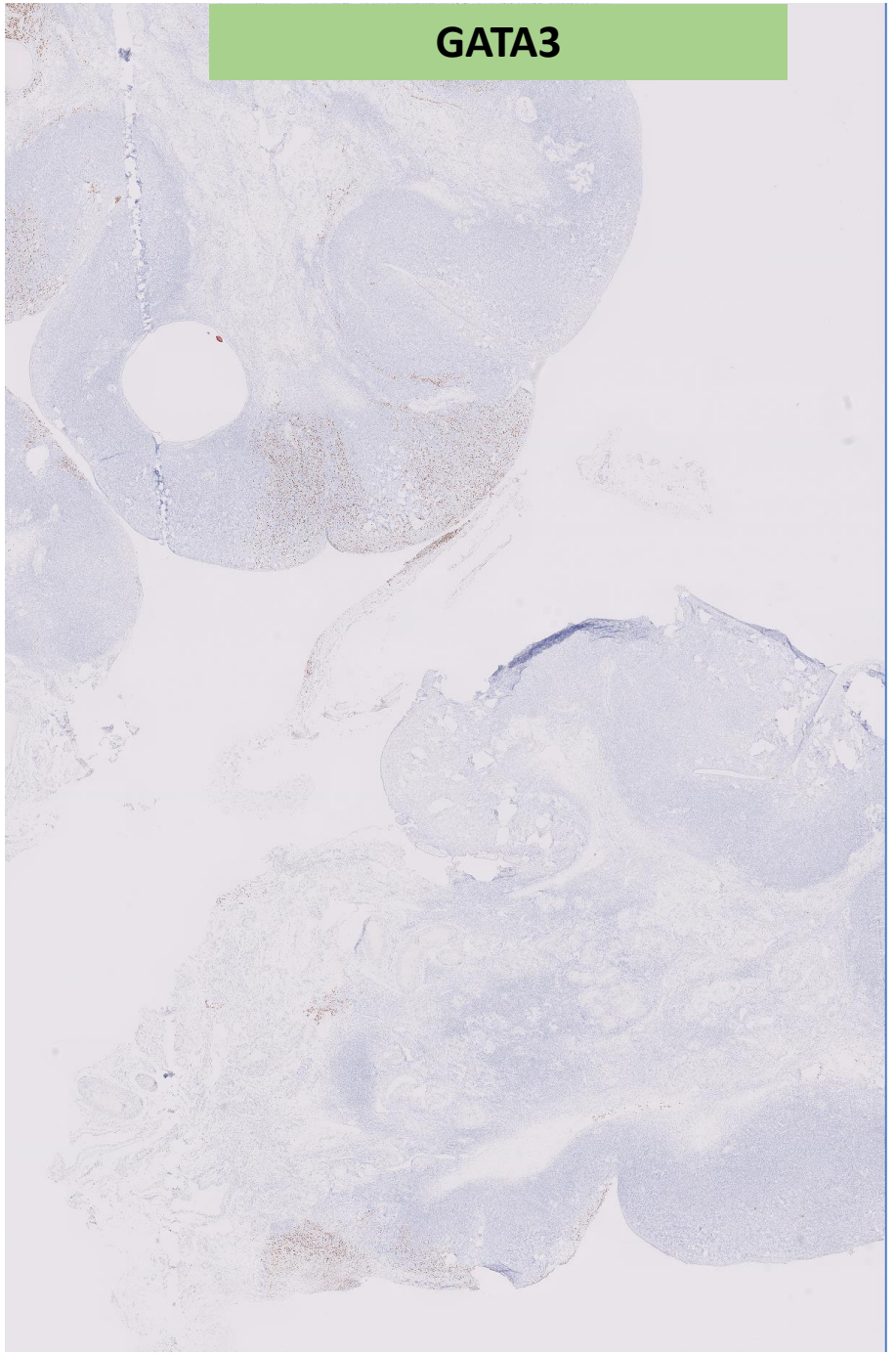

TRPS1

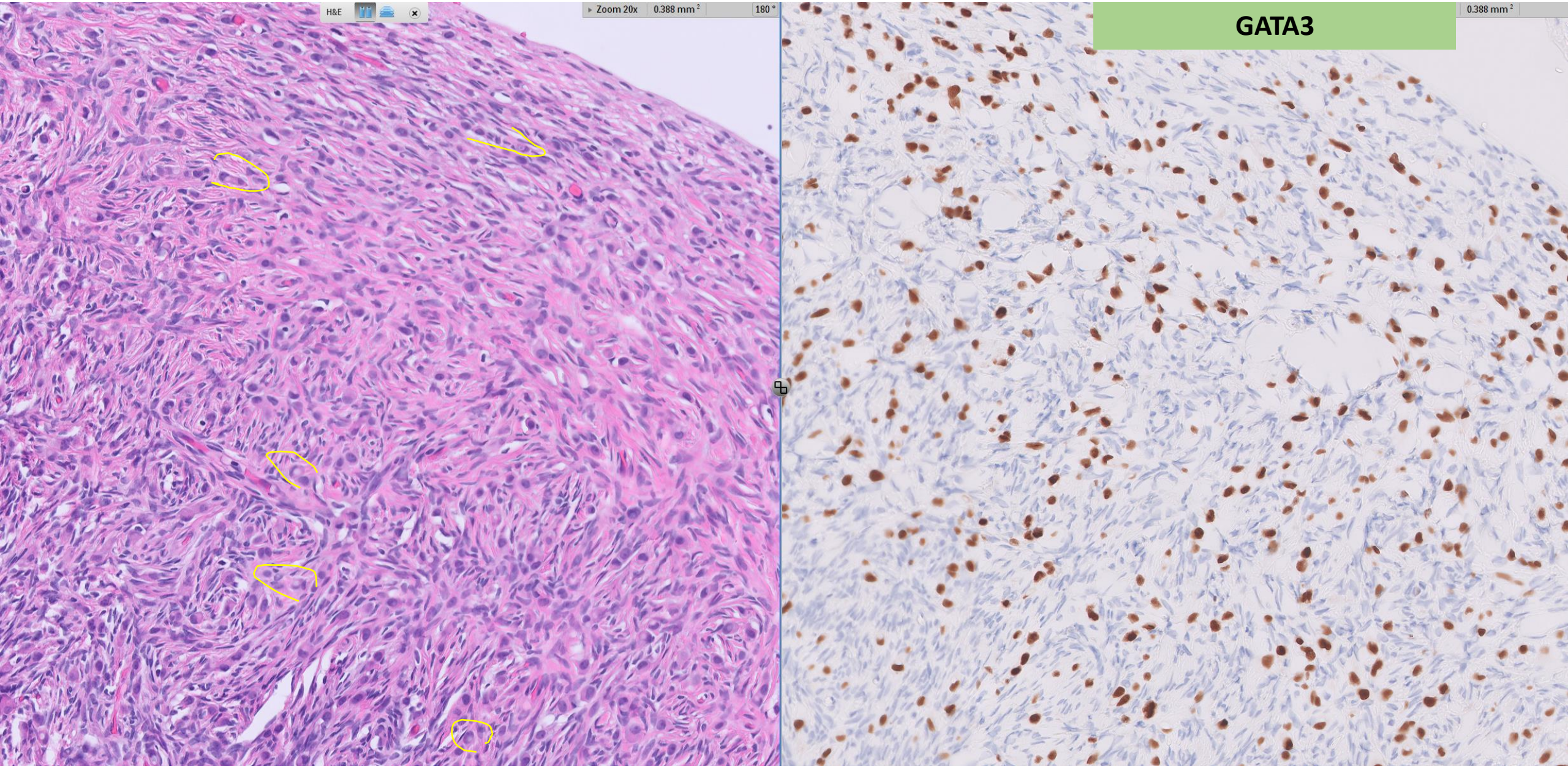

Mammaglobin

Ovary

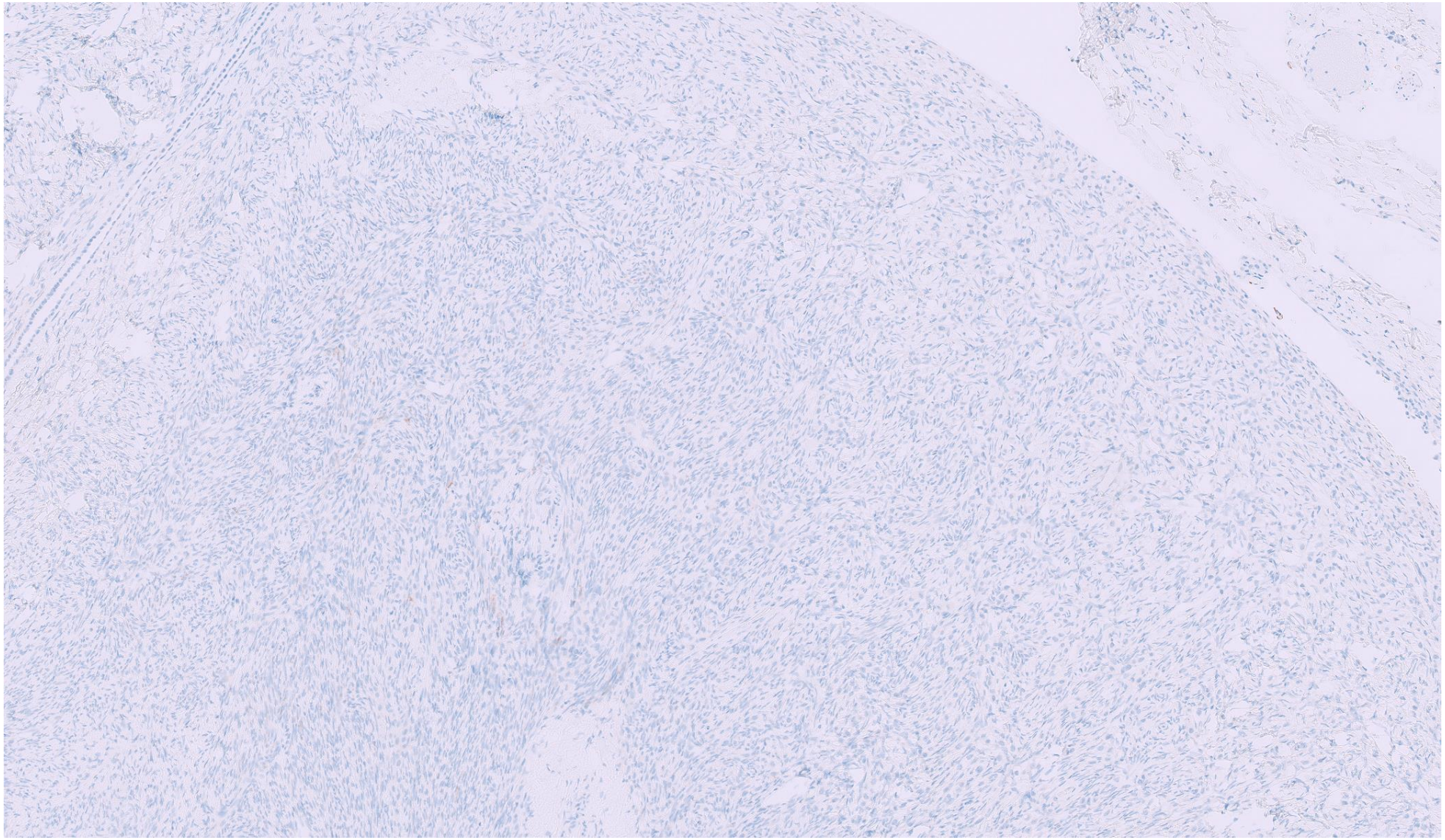


GATA3

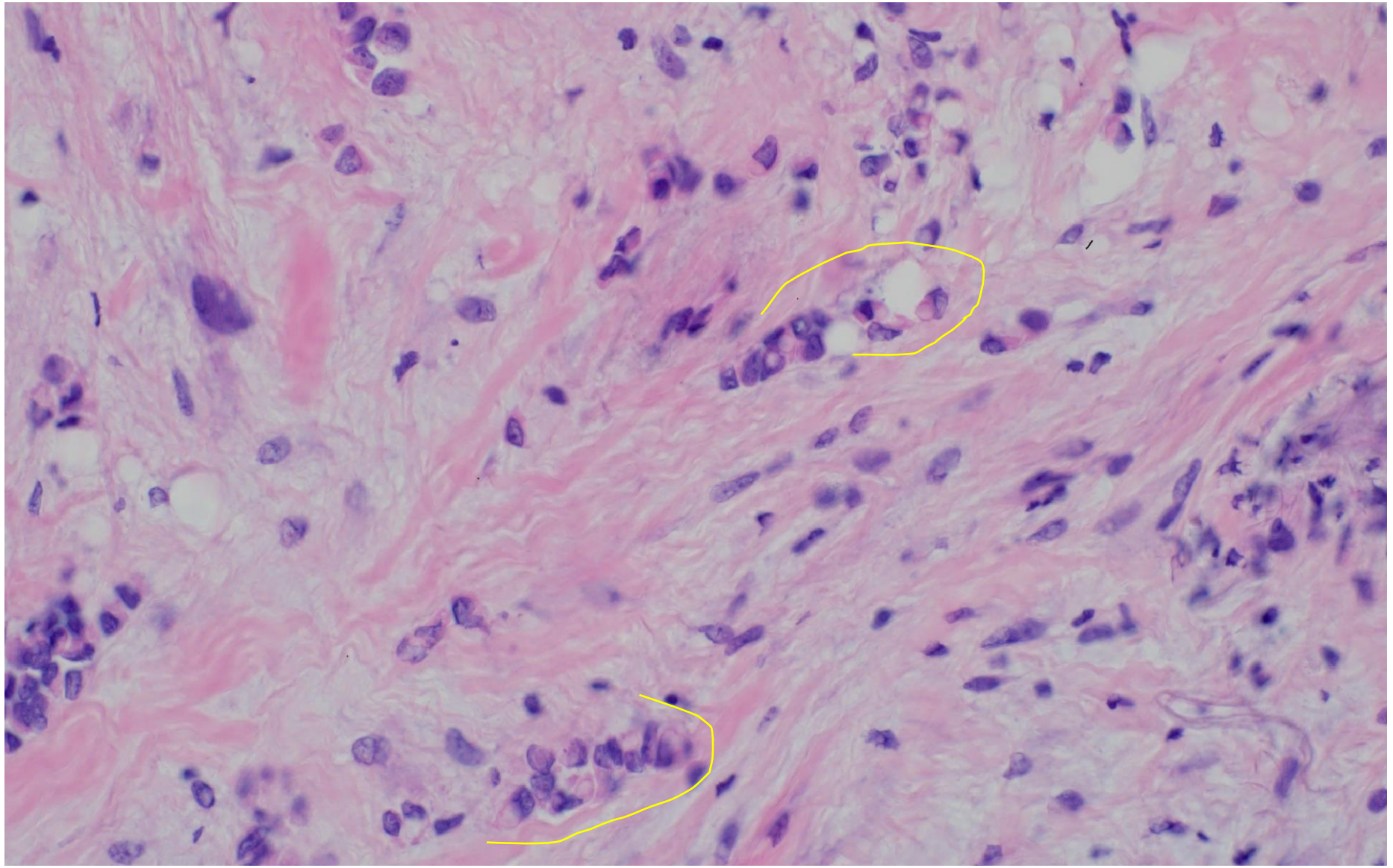



H&E
Zoom 20x
0.388 mm²
180 °
GATA3
0.388 mm²

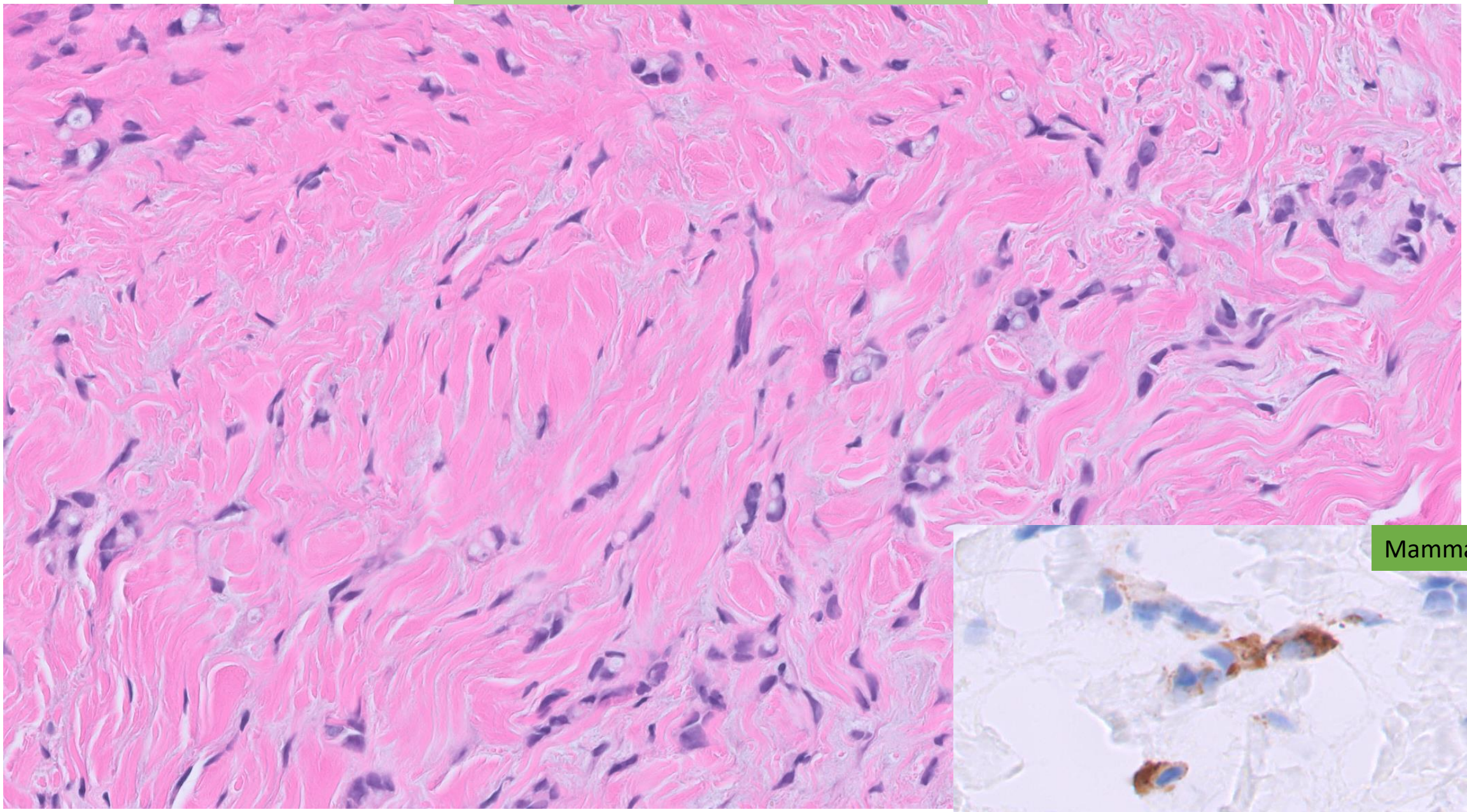
# E-caderin



# Frozen section of abdominal wall



Permanent section of abdominal wall





Mammaglobin

# We are not alone…

Yousef *et al. Journal of Medical Case Reports* 2010, **4**:175
http://www.jmedicalcasereports.com/content/4/1/175

JOURNAL OF MEDICAL CASE REPORTS

**CASE REPORT** **Open Access**

## Invasive lobular carcinoma of the breast presenting as retroperitoneal fibrosis: a case report

George M Yousef[*†1,2], Manal Y Gabril[†3], Sahar Al-Haddad[1,2], Anna Marie Mulligan[1,2] and R John Honey[4]

…tissue was submitted for frozen section consultation that was consistent with RPF. However, the permanent sections were diagnostic for lobular breast carcinoma….

Wong *et al. Insights into Imaging* (2021) 12:181
https://doi.org/10.1186/s13244-021-01120-4

Insights into Imaging

**EDUCATIONAL REVIEW** **Open Access**

Check for updates

## Infiltrative pattern of metastatic invasive lobular breast carcinoma in the abdomen: a pictorial review

Ying Mei Wong[1*], Pooja Jagmohan[1], Yong Geng Goh[1], Thomas Choudary Putti[2], Samuel Guan Wei Ow[3], Yee Liang Thian[1] and Premilla Pillay[1]

And many others….

INTERNATIONAL JOURNAL *of* BIOMEDICAL SCIENCE

CASE REPORT

## Unique Presentations of Invasive Lobular Breast Cancer: A Case Series

Muhammad Tariq Shakoor[1], Samia Ayub[2], Ramesh Mohindra[3], Zunaira Ayub[4], Abdul Ahad[5]

*[1]Department of Internal Medicine, Baystate Medical Center (Tufts University School of Medicine), Springfield, MA, USA; [2]Department of Pulmonary and Critical Care, University of Arkansas for Medical Sciences, Little Rock, AR, USA; [3]Department of Hematology/Oncology, St Mary Mercy Hospital, Livonia, MI, USA; [4]Medical Student, Fatima Jinnah Medical College, Lahore, Pakistan; [5]Medical Student, Nishter Medical College, Multan, Pakistan*

Slide from Dr. Megan Troxell

# Diagnosis and Take Home

- Dx: Endometrial adenoCA, FIGO1; outer half; 2/3 LN, no serosal CA
- ILC involving peritoneal surfaces, outer myometrium, B ovaries, 3/3 LN
  - Subsequent mammogram and breast biopsy shows ILC (ipsilateral to TNBC)
    - ??Present w/ G3 TNBC dx and AC-T chemo??
- FS: Correlate with known clinical and available pathology (WSI)
  - FS dx likely different if known ILC or diffuse gastric CA
    - Clues: strings of cells, eccentric cytoplasm or vacuoles
  - No impact on surgical procedure—its not endometrial CA
- Permanents:
  - Comprehensive history is can be important
  - Peritoneum (GI, Gyn) is a favorite site for ILC met
    - Look for single-filing, discohesive cells and presence of mucin
  - Look for abnormal architecture in GYN organs at higher power

Modified slide, original from Dr. Megan Troxell

# Krukenberg tumor

- Metastatic breast cancer accounts for up to 33.5% of metastases to the ovary
- The ovary is also the most common gynecologic site of metastatic breast cancer
- Lobular carcinomas show a greater propensity to metastasize to the gynecologic tract than ductal carcinomas although metastatic ductal carcinomas are encountered slightly more frequently (55% vs. 44%) due to their greater incidence

Chuang, Am Jour Surg Path, 2022
Franco-Marquez, Case Rep Pathol, 2019

# Questions?

Thank you to Dr. Xiaoming Zhang for sharing this case and to Dr. Megan Troxell and Dr. Zhang for sharing slides