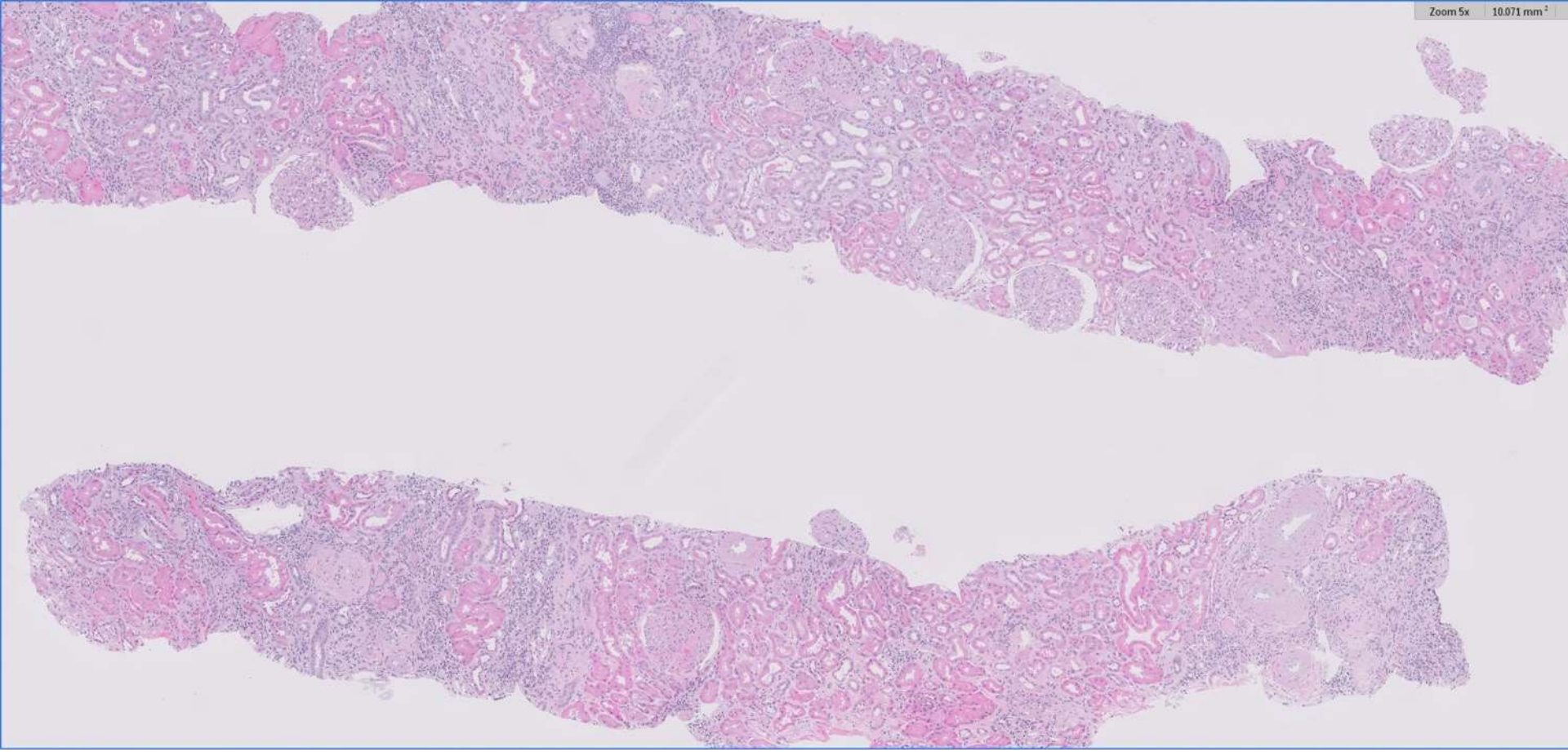
APRIL 2022 DIAGNOSIS LIST

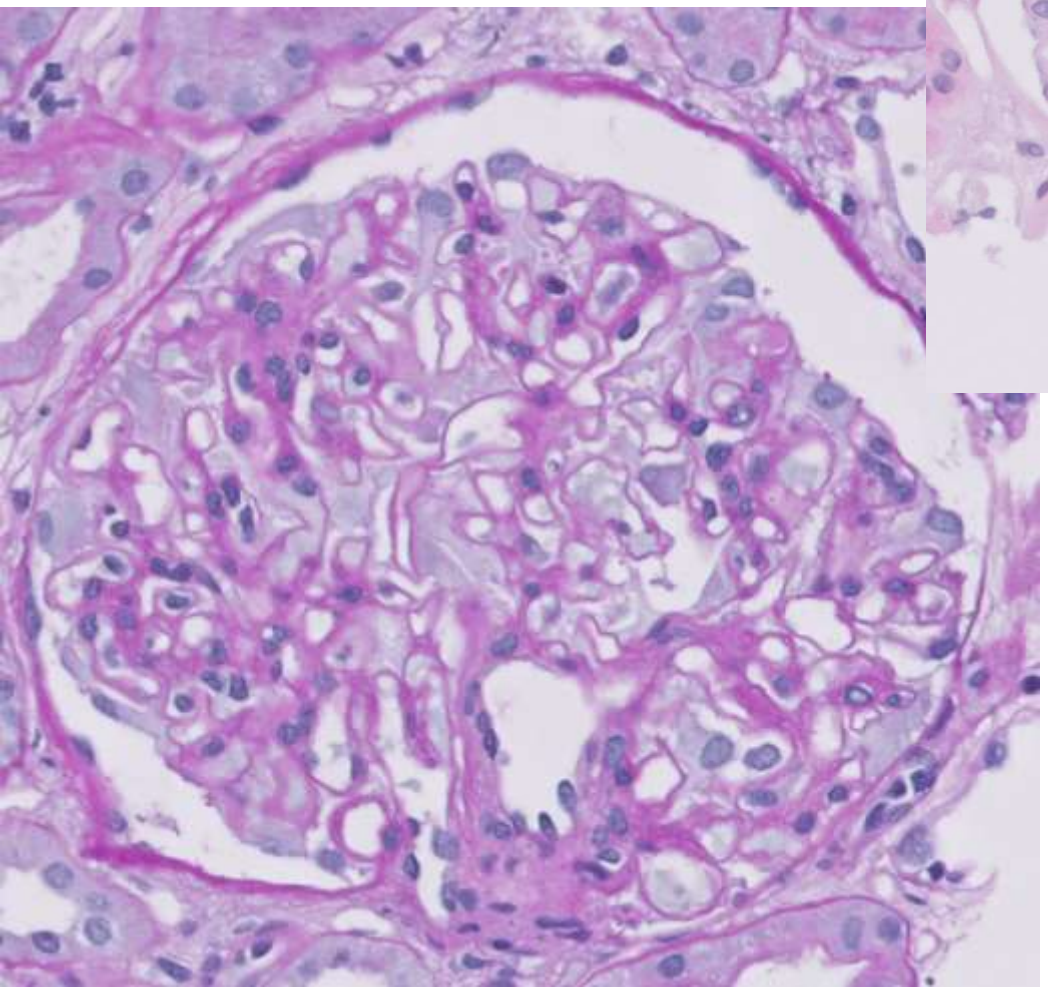
22-0401: membranous nephropathy, NELL1 (medical kidney; kidney)
22-0402: adenoid basal-like tumor (GYN path; cervix)
22-0403: placental mesenchymal dysplasia (GYN path; placenta)
22-0404: pyloric gland adenoma (GI path; gallbladder)
22-0405: glomus tumor (GI path; stomach)
22-0406: syphilis (GIpath IDpath; liver)
22-0407: null phenotype CIS (bladder; GU path)

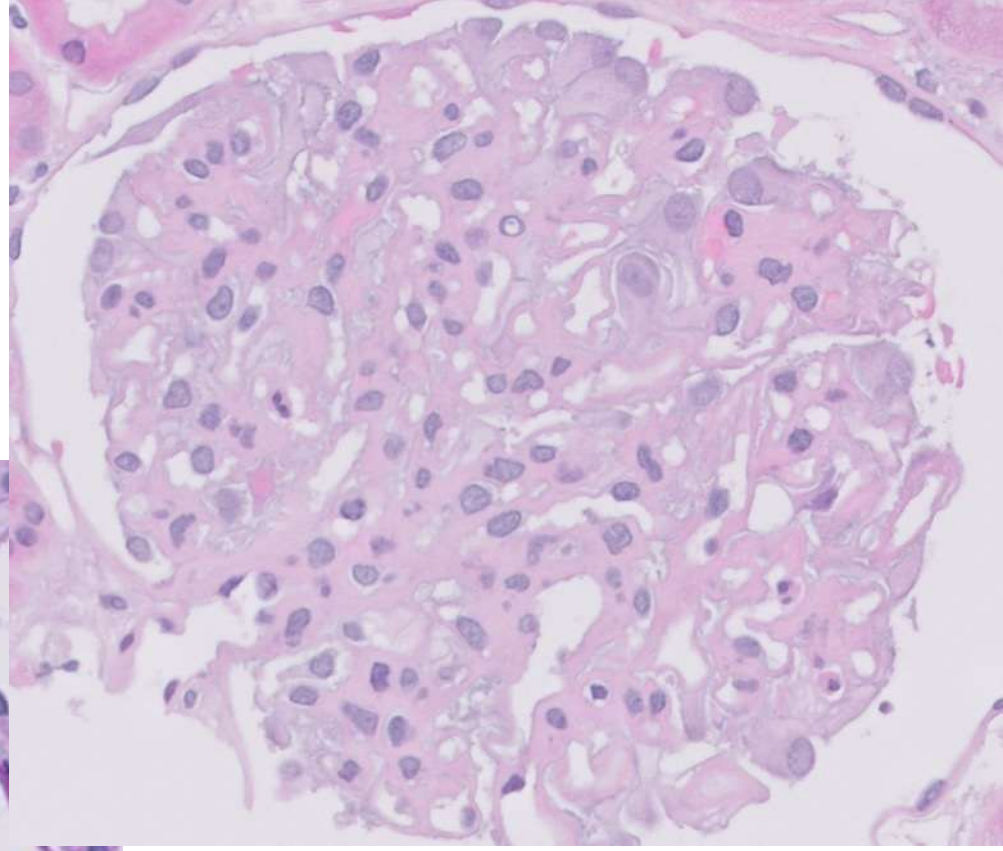
22-0401

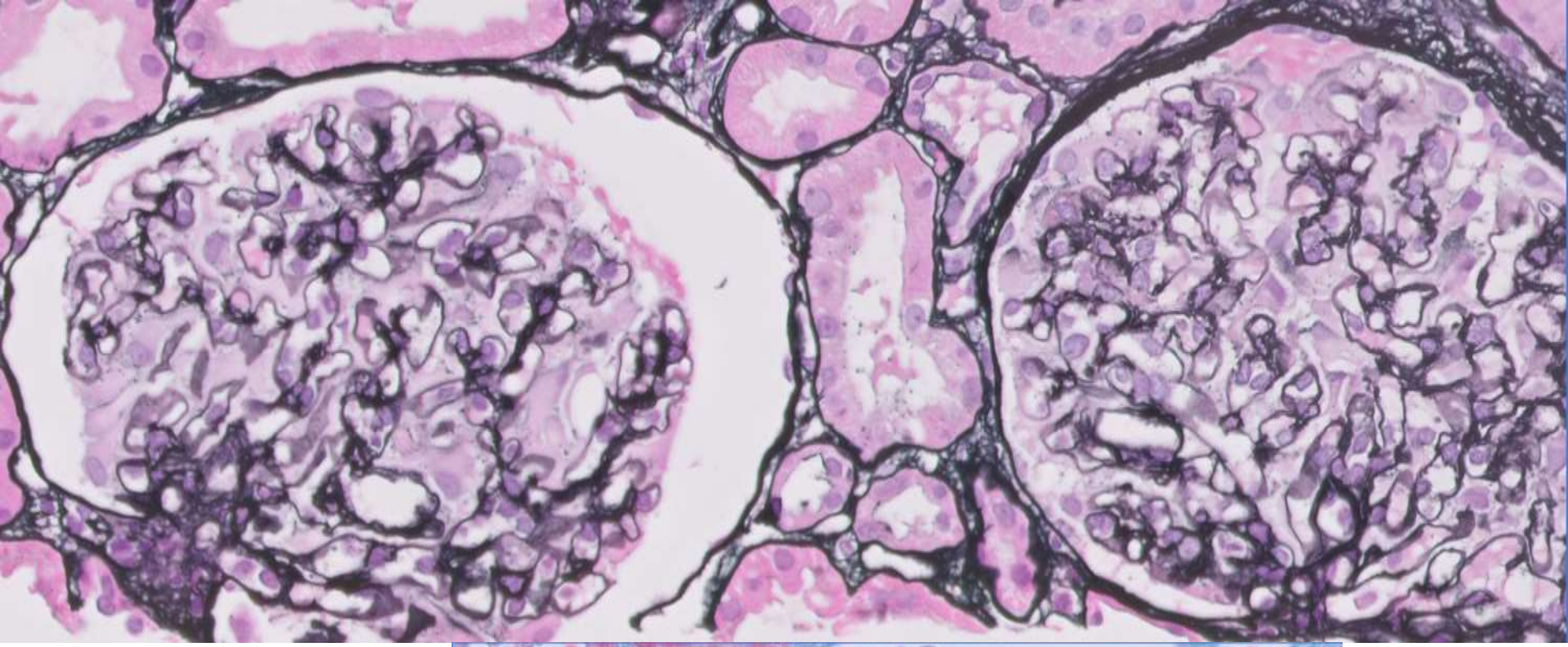
Megan Troxell/Ankur Sangoi; Stanford/El Camino Hospital

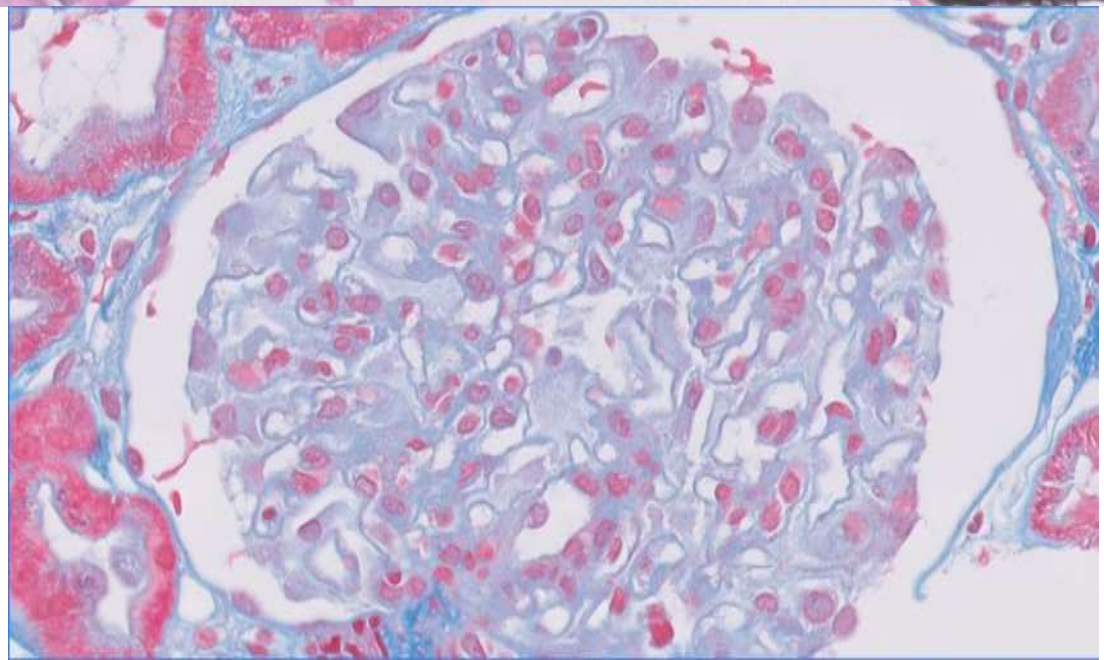
Elderly woman with nephrotic range proteinuria, COPD, smoking, squamous cell lung carcinoma, renal cell carcinoma, gout. ANA+.

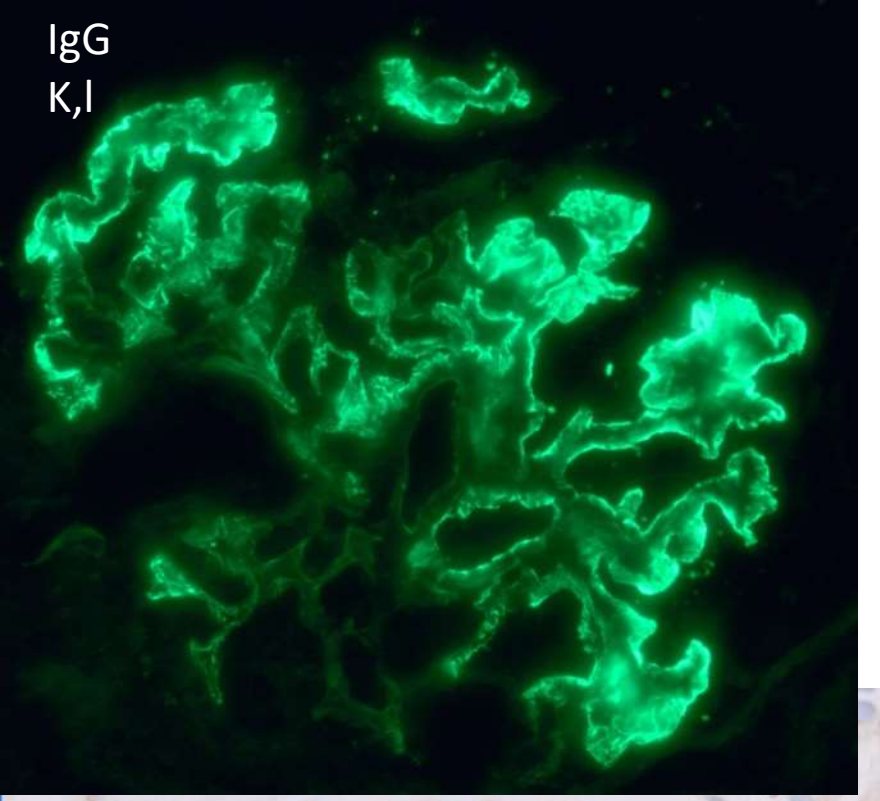

Zoom 5x
10.071 mm²

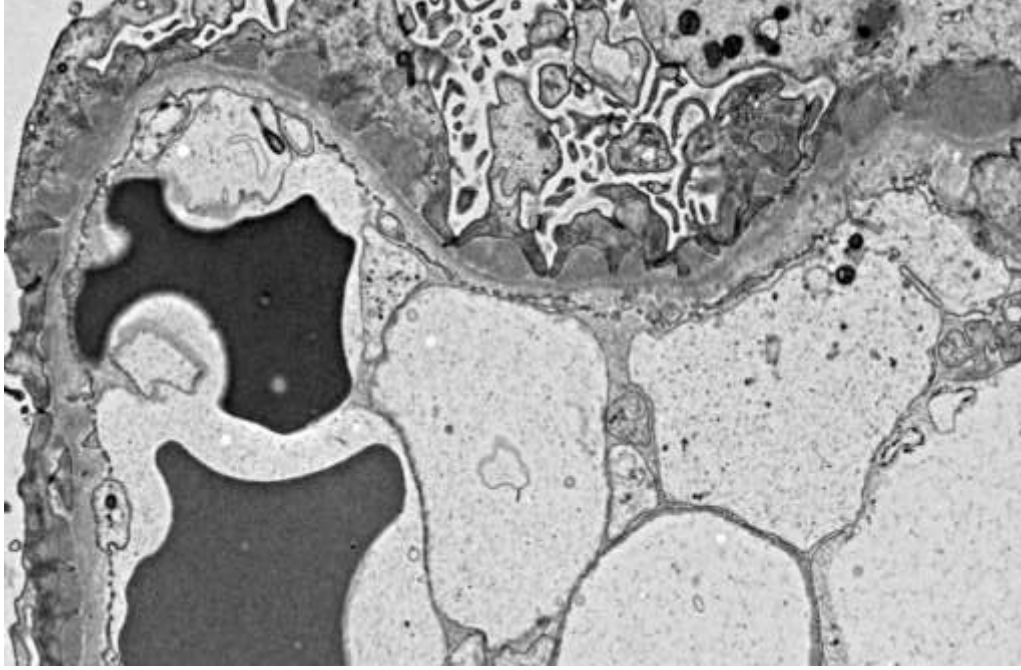


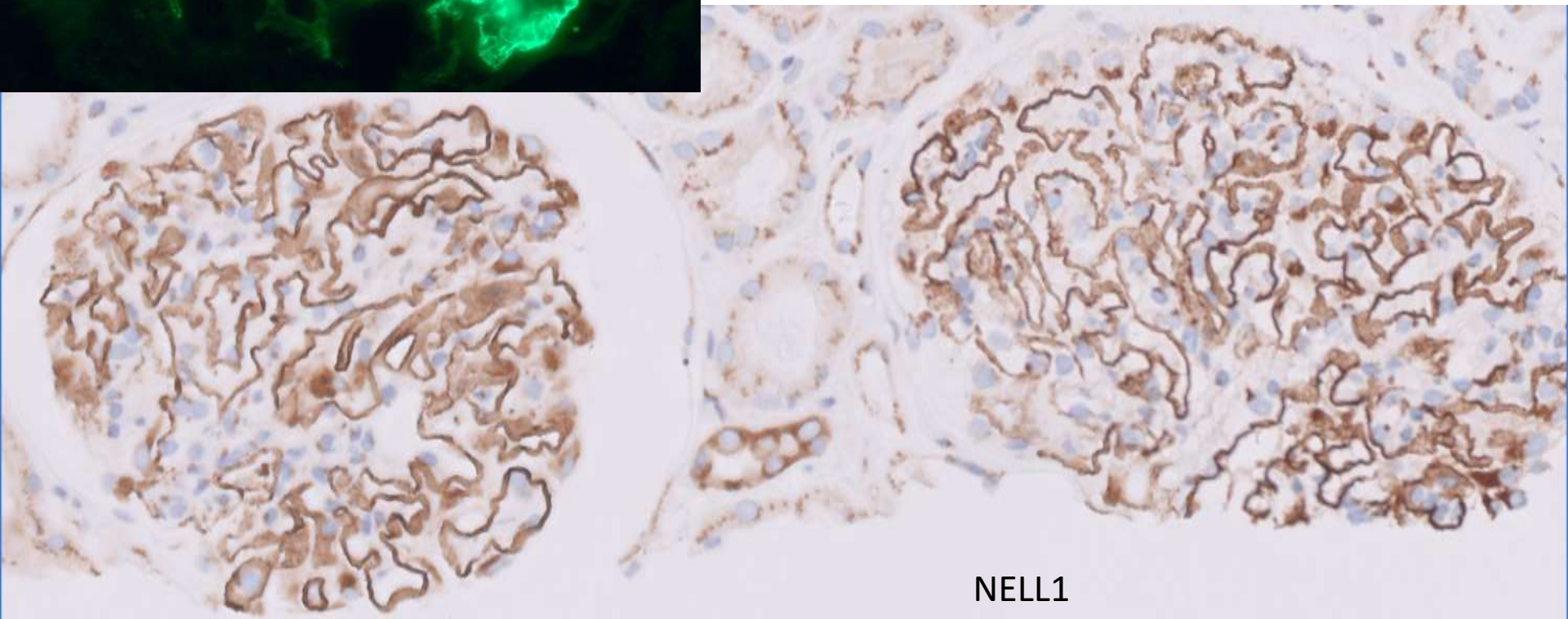


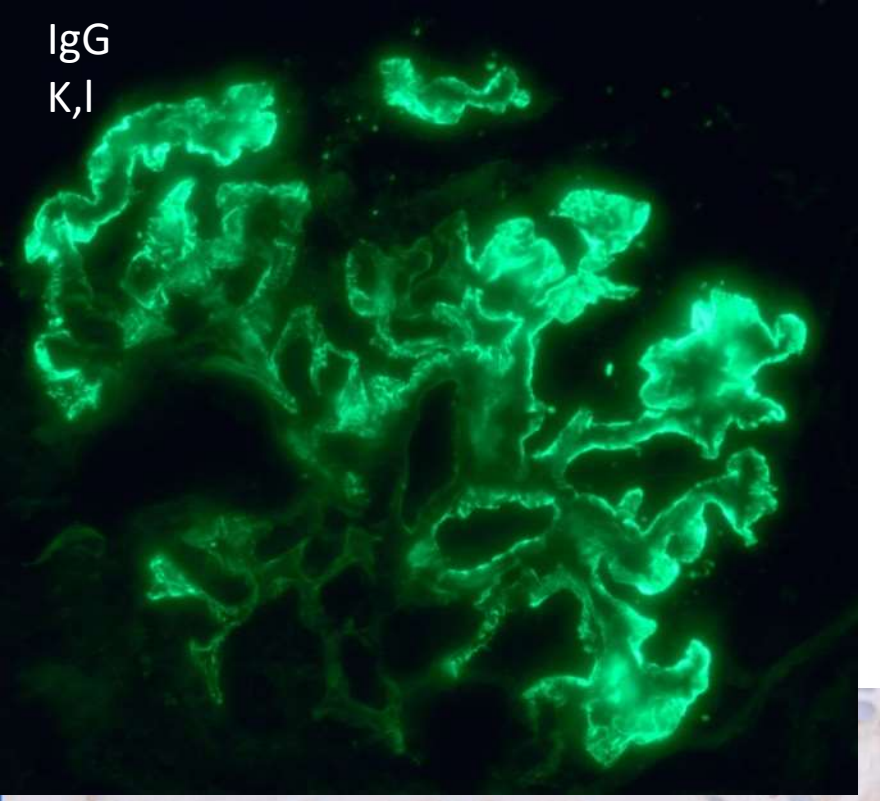


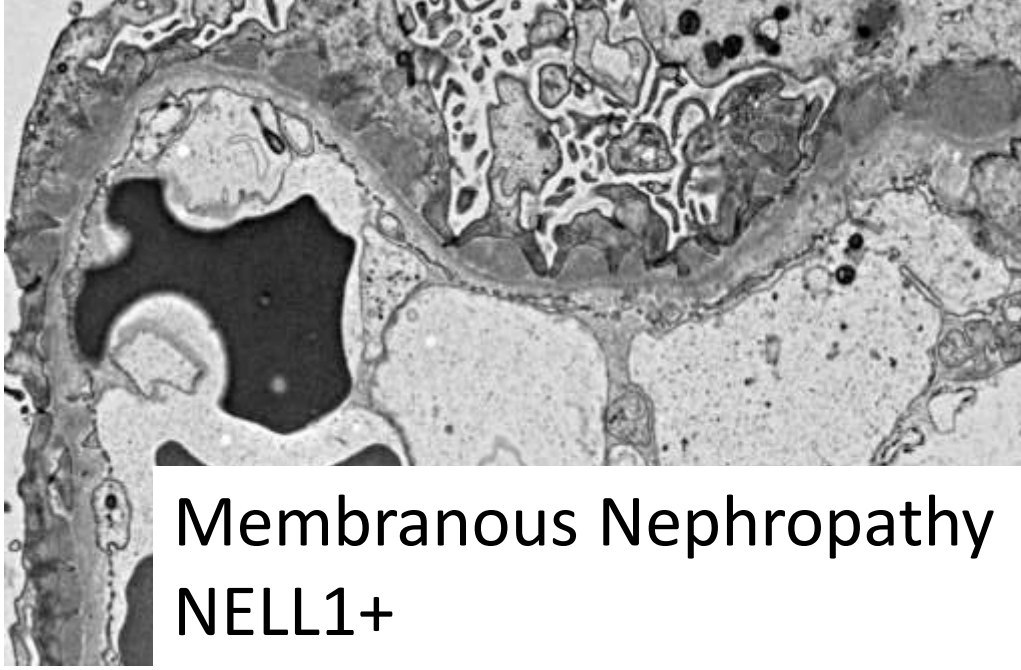



IgG
K,l

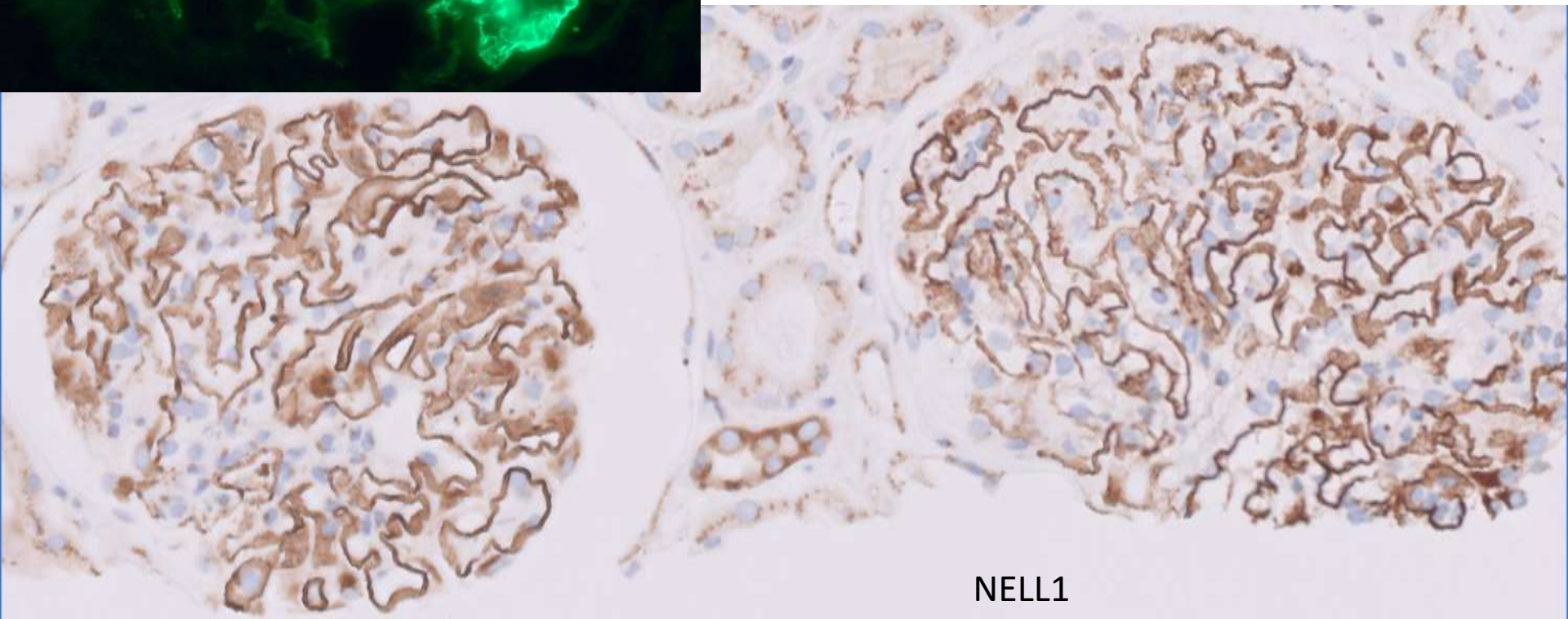



NELL1

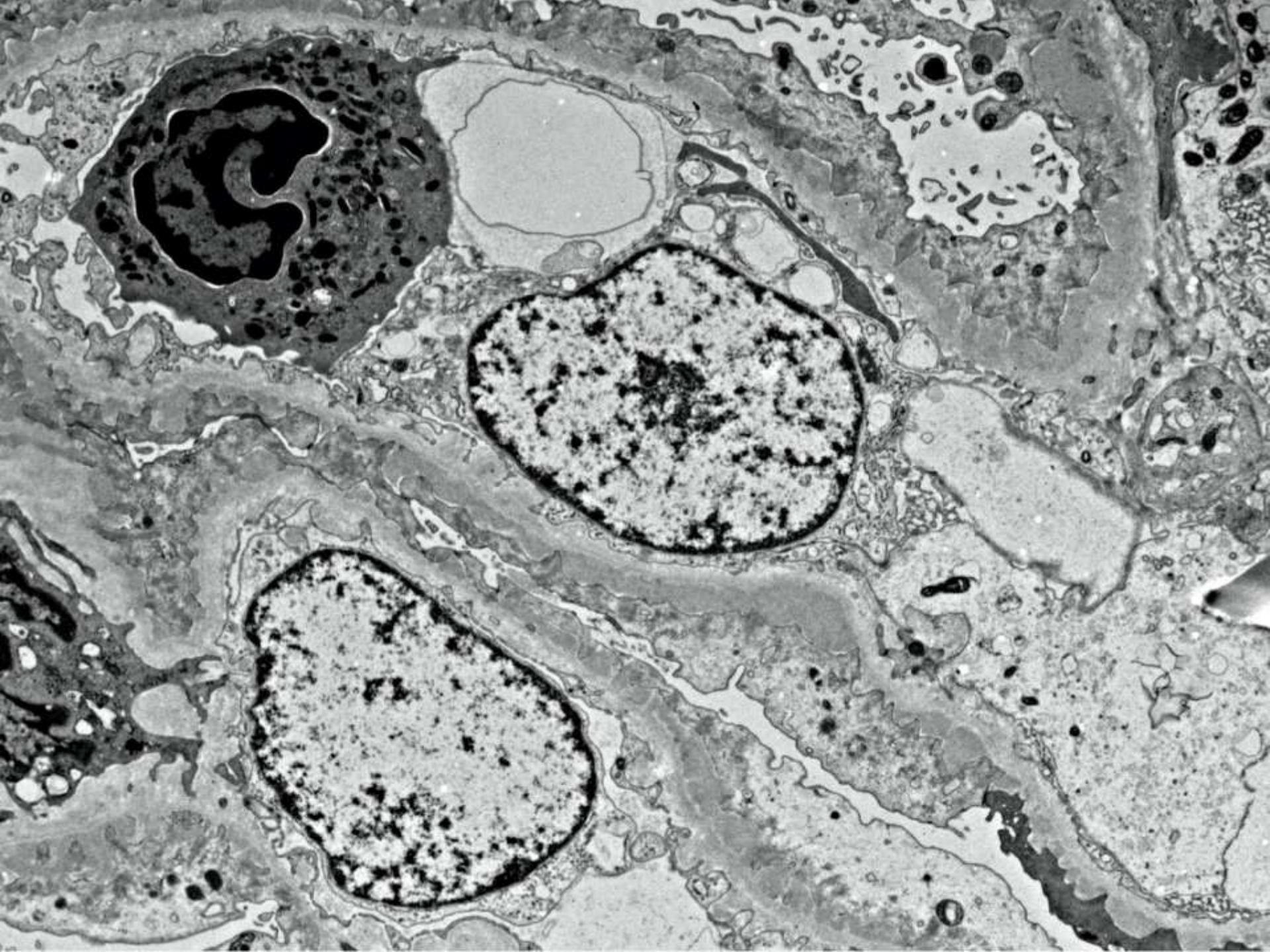




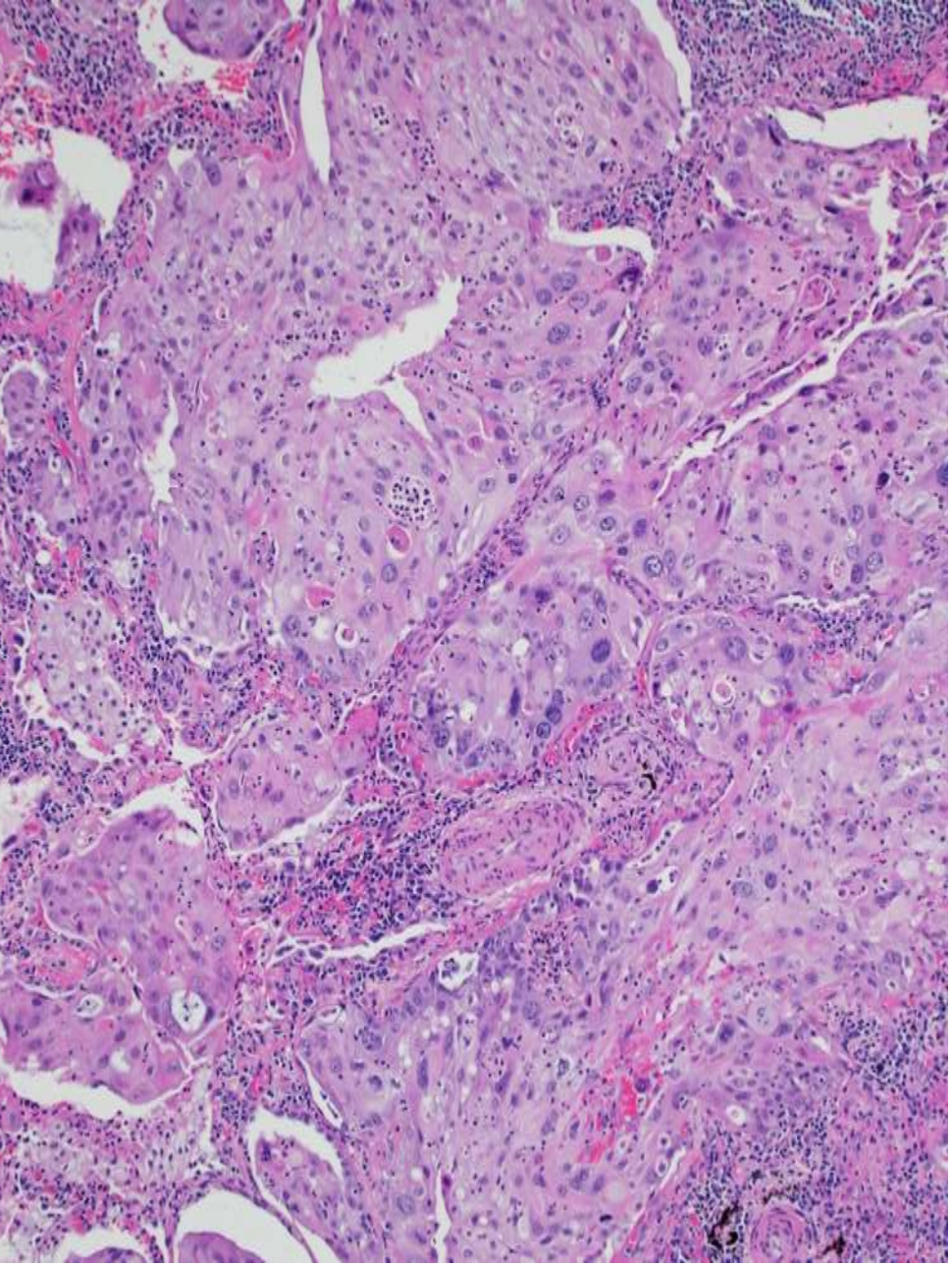
Membranous Nephropathy
NELL1+

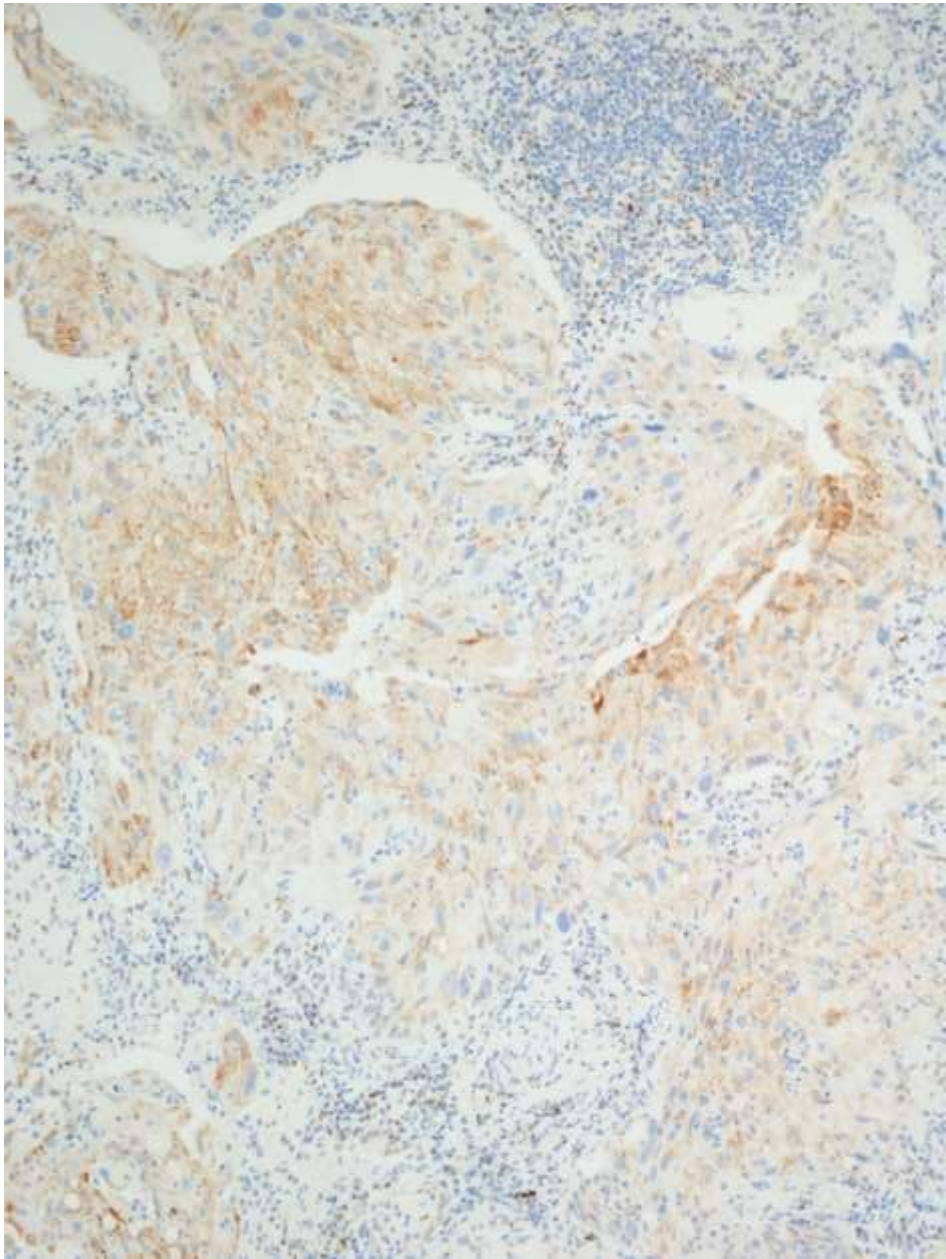


NELL1

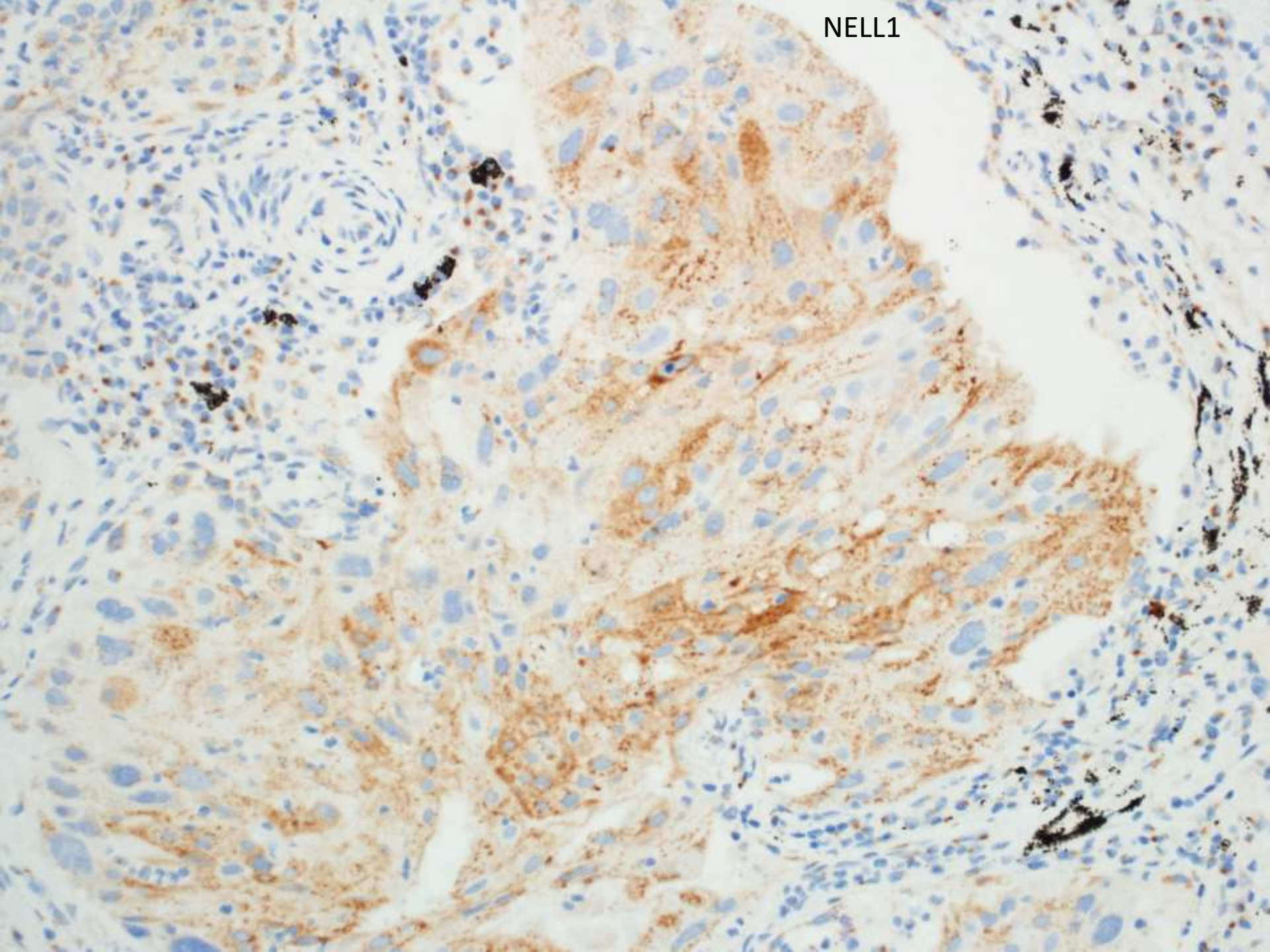


Lung SCC NELL1+





NELL1


NELL1

Membranous Nephropathy

Previously

- Primary
- Secondary
  - Lupus, RA, Sarcoid etc
  - Malignancy
  - NSAIDs, drug
  - Hepatitis
  - Syphilis, other infection
  - IgG4-RSD
  - BMT

- By antigen
  - **PLA2R (75% 'primary')**
  - THSD7A
  - **NELL1**
    - Cancer, BMT, ?NSAID
    - Lipoic acid supple (ALA)
  - EXT1/2 (lupus)
  - SEMA3B (pediatric)
  - NCAM
  - PCDH7
  - FAT1-BMT
  - CNTN1

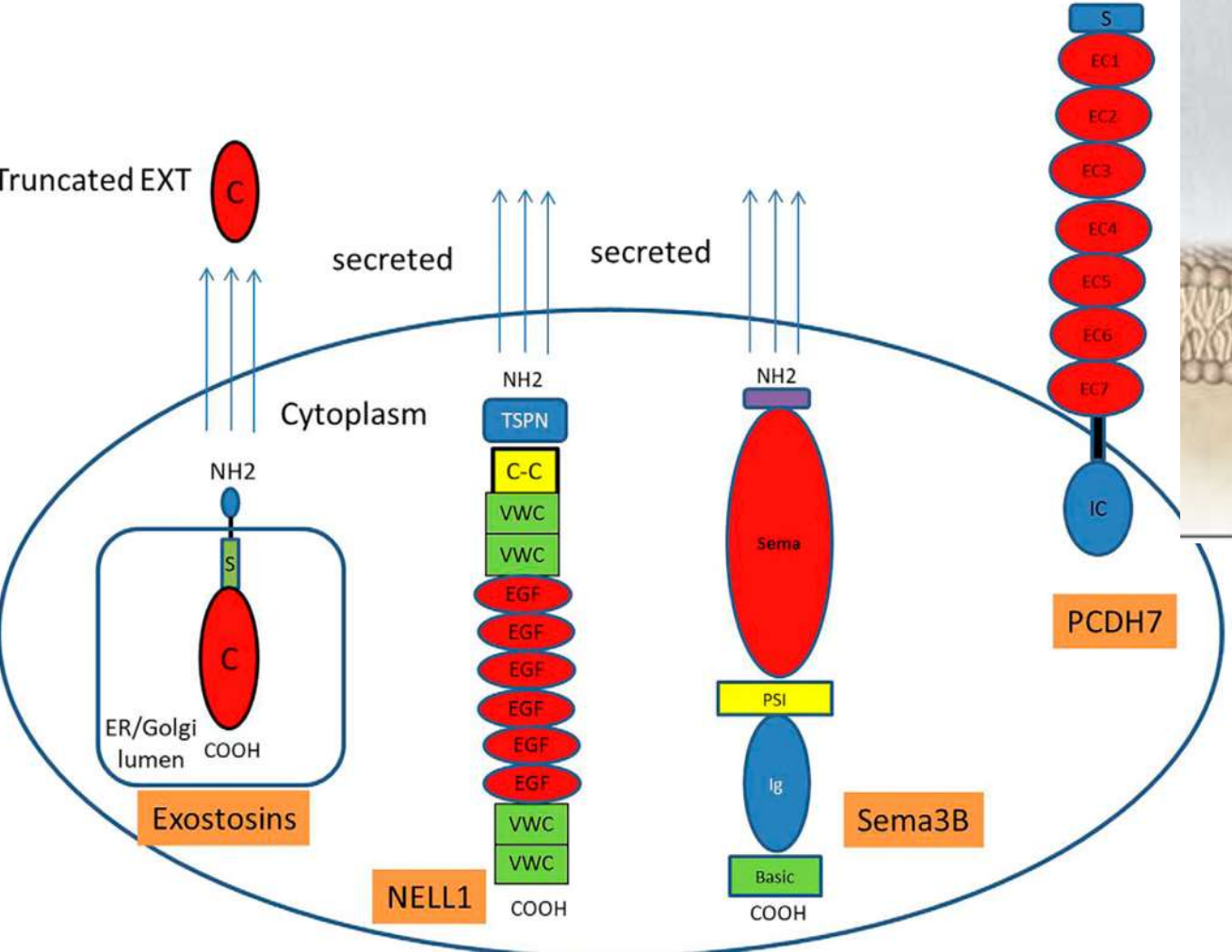
REVIEW www.jasn.org

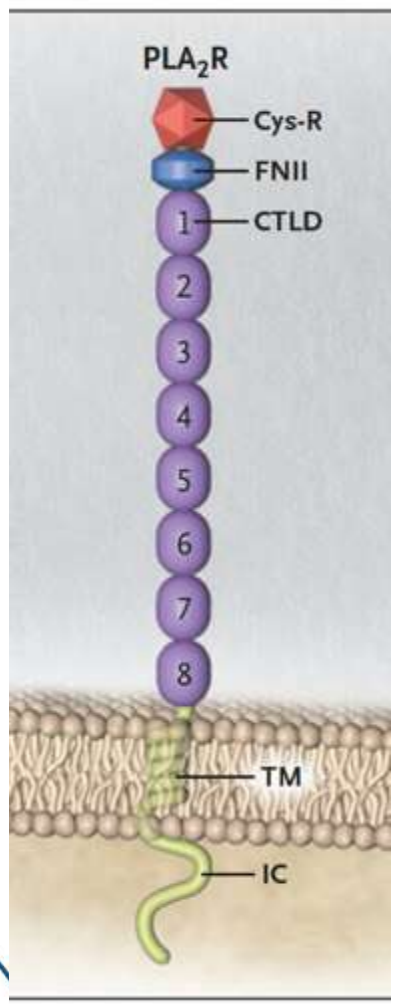
JASN 32: 268–278, 2021.

New 'Antigens' in Membranous Nephropathy

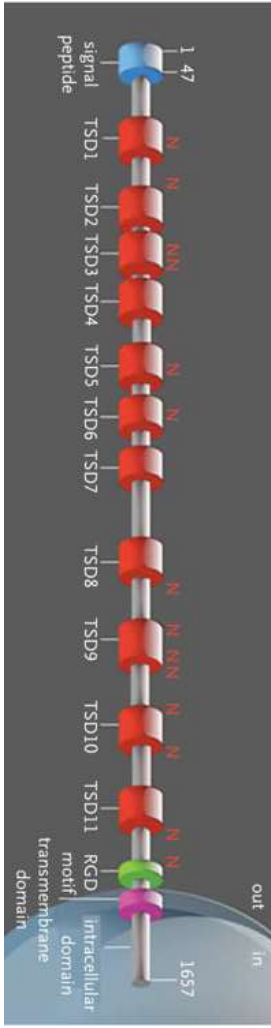
Sanjeev Sethi

Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, Minnesota





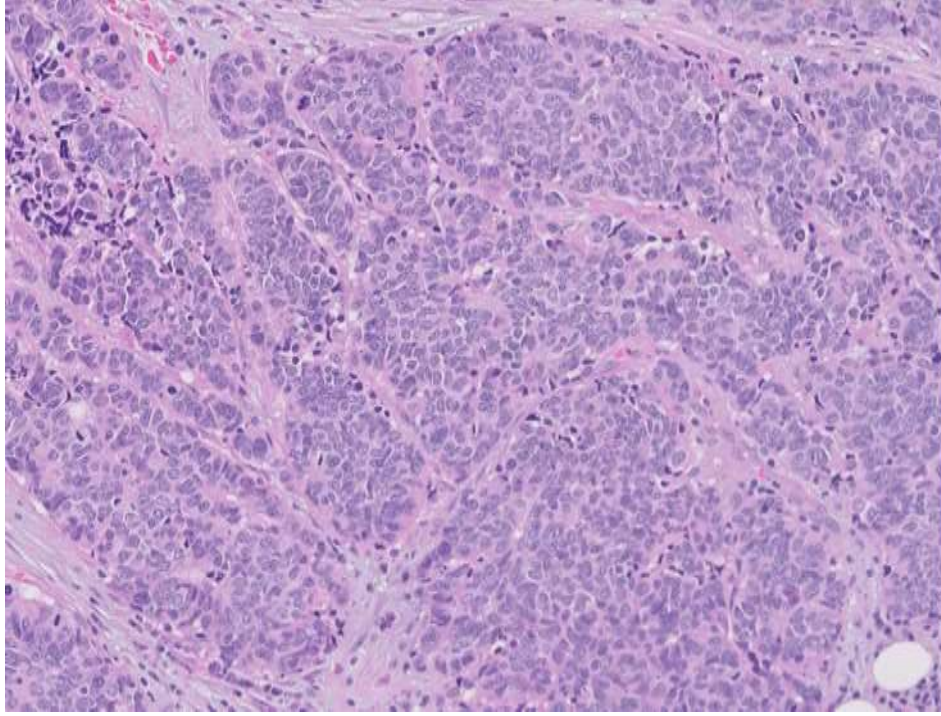
NEJM. 2009; 361:11-21

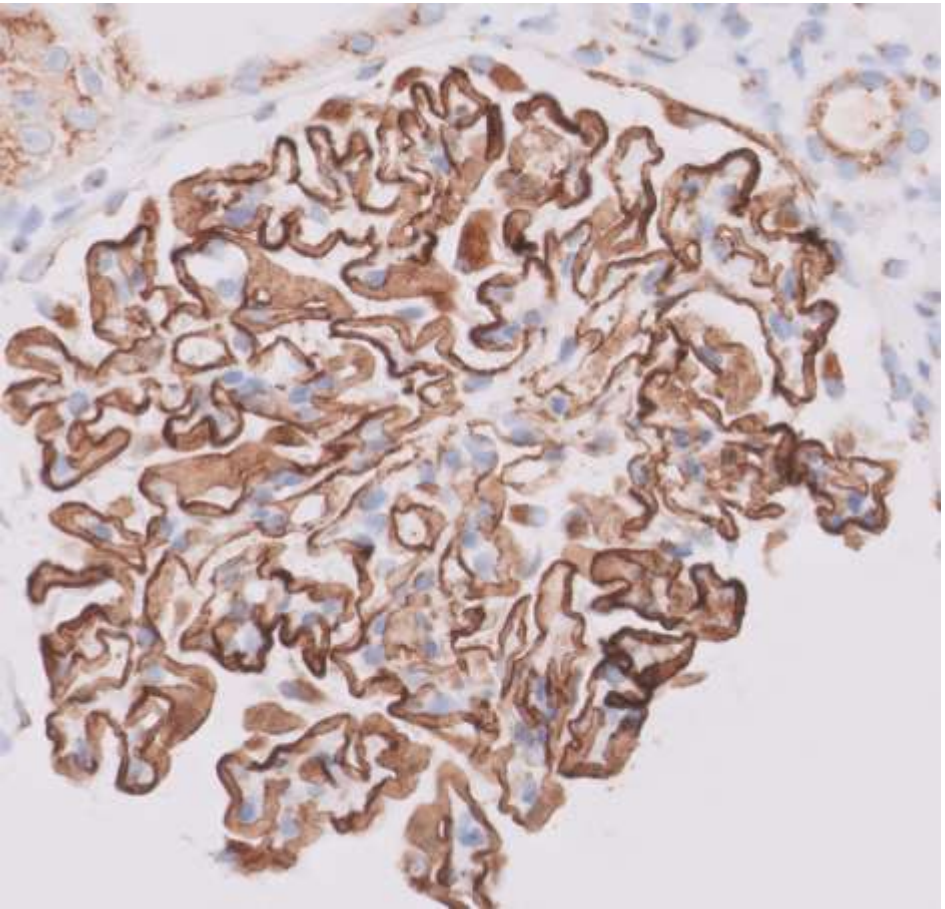


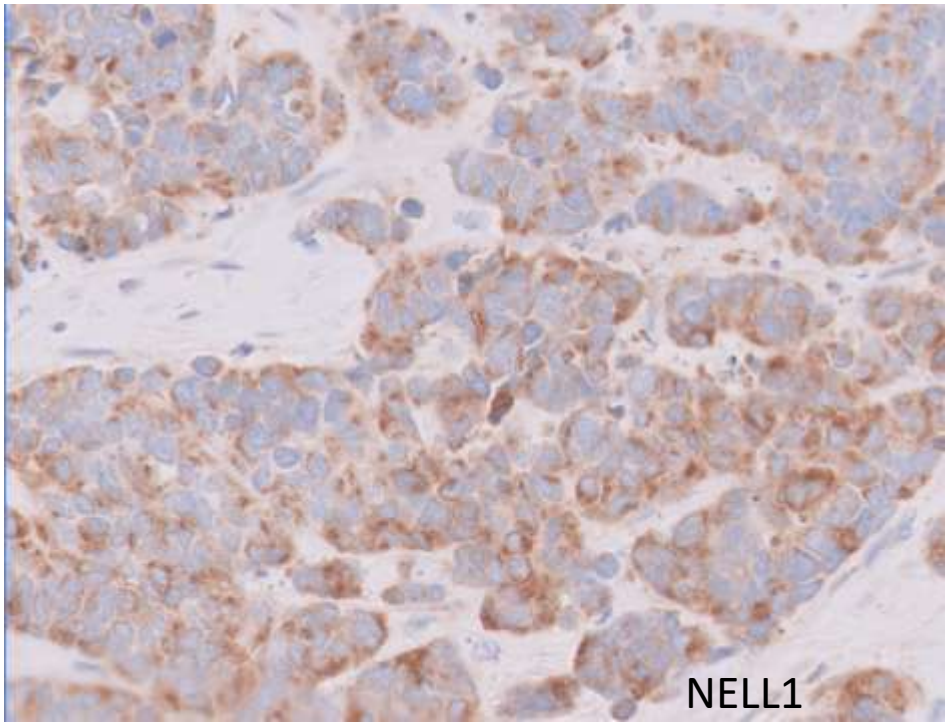
TSHD7a
NEJM. 2014; 371:2277-87.

Another MGN

- NELL1+ MGN
- NELL1+ Lung cancer
- NS after drug exposure



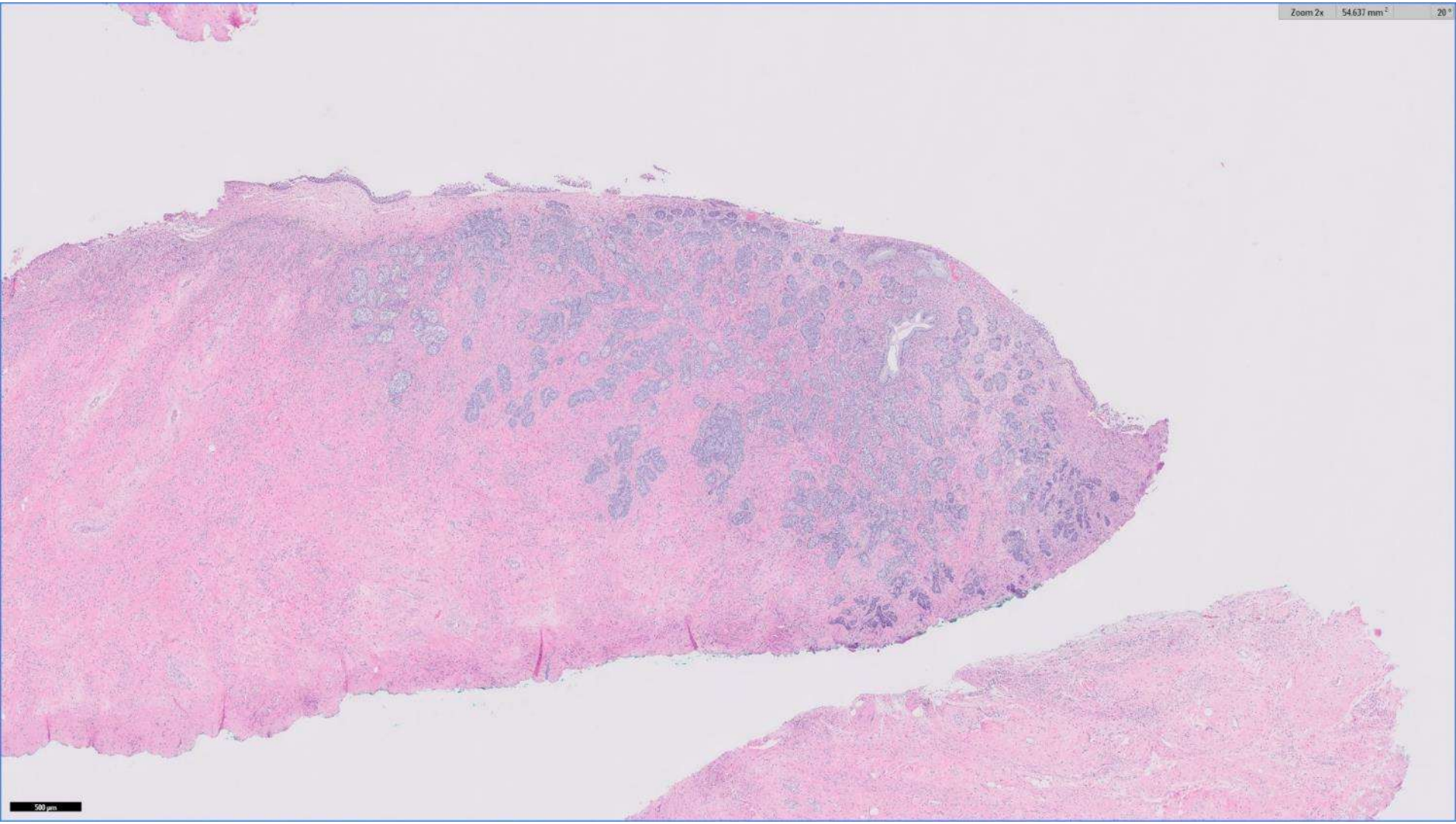


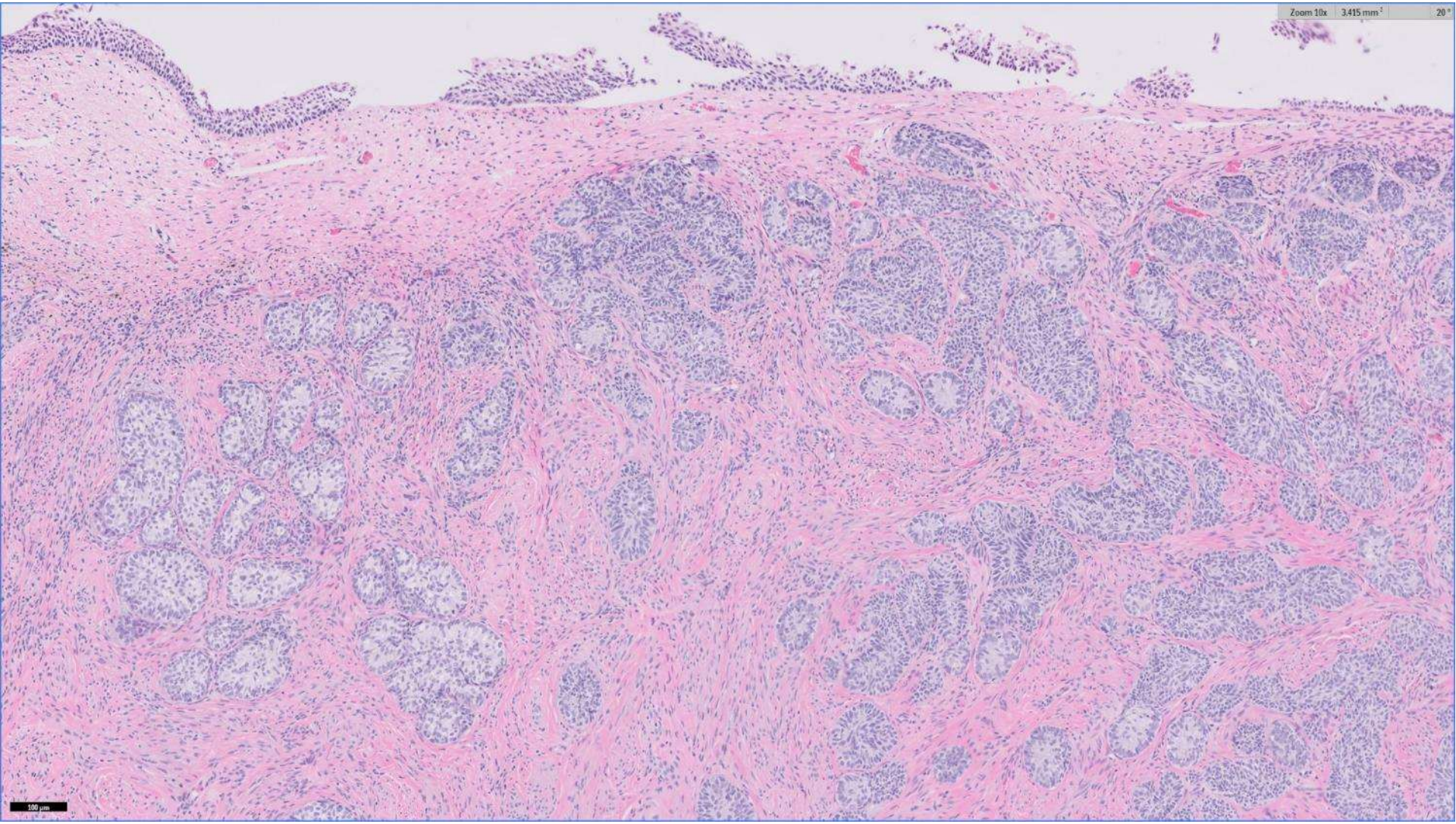


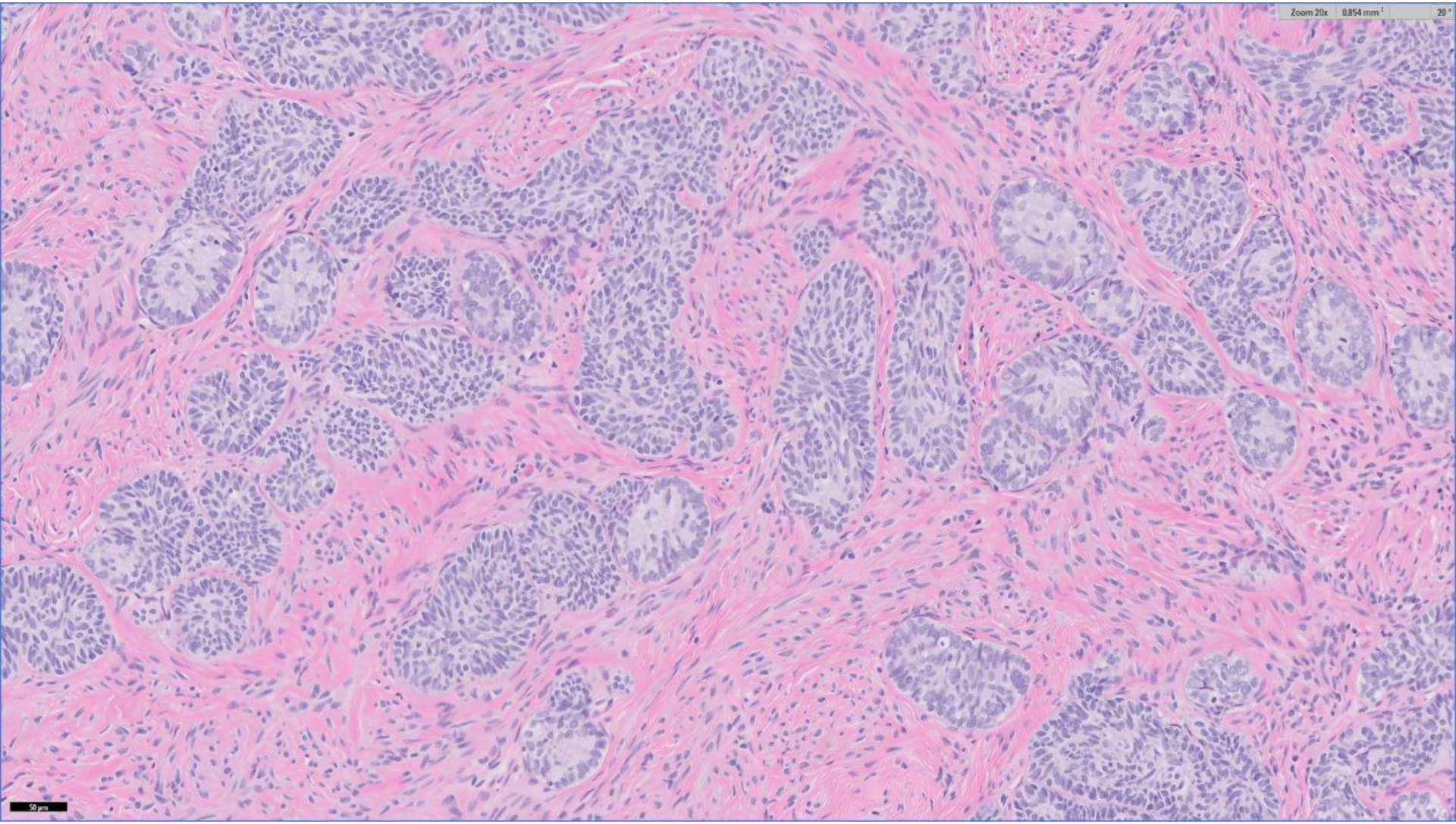
22-0402

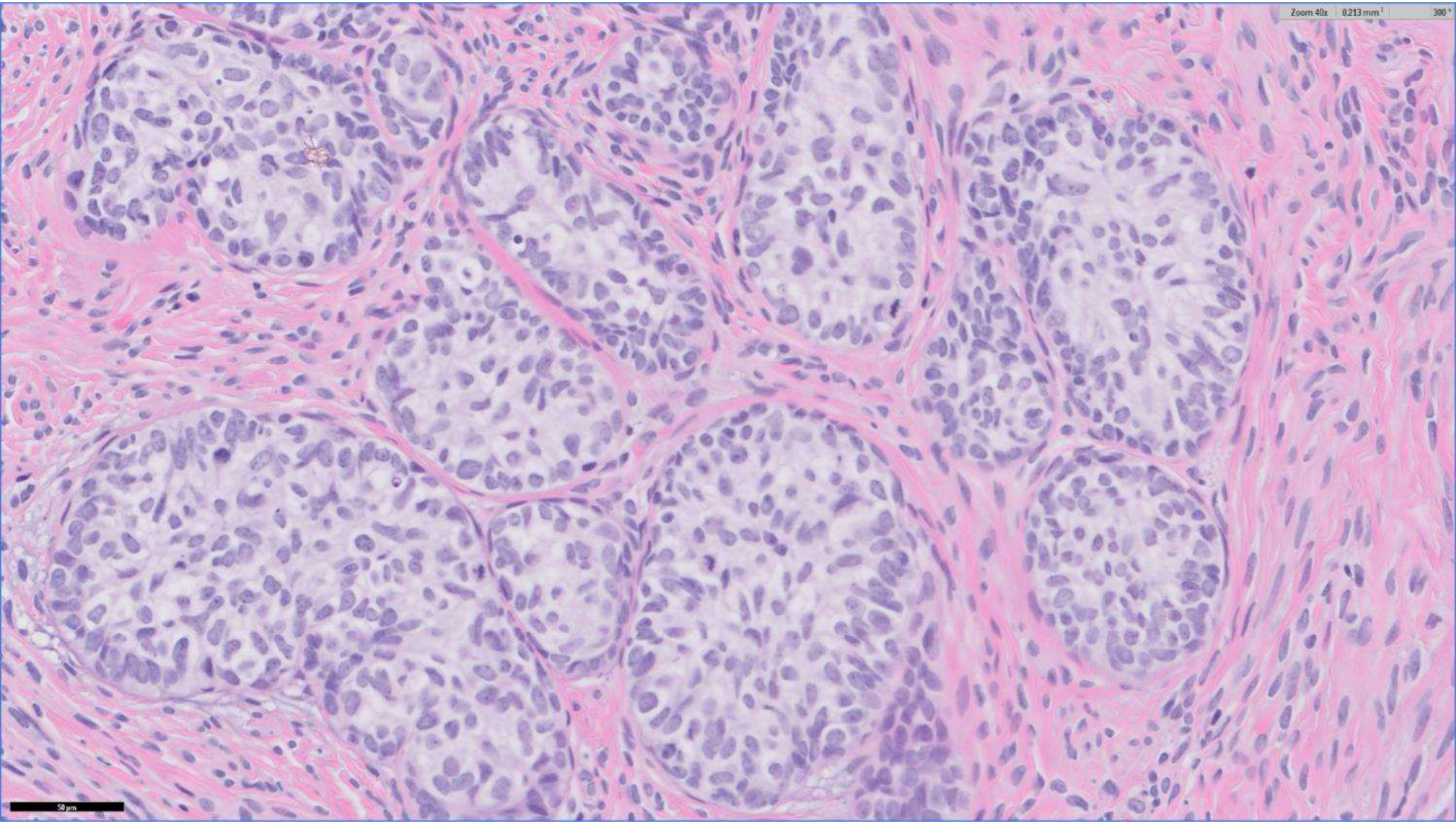
Amanda Borgen/Nicholas Ladwig; UCSF

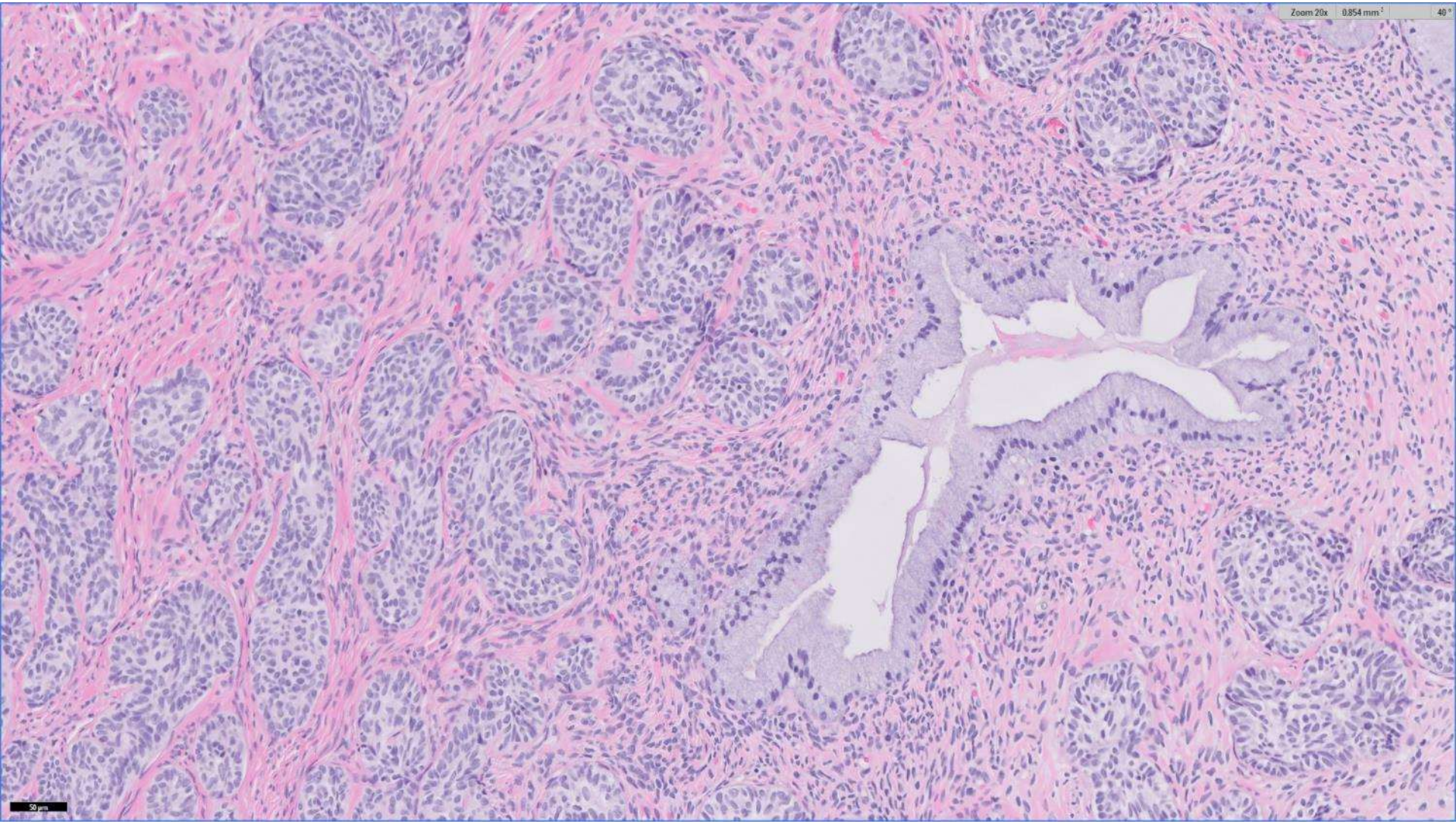
70ish F with persistent HPV+ ASCH cervical cytology and unsatisfactory colposcopy who underwent LEEP.

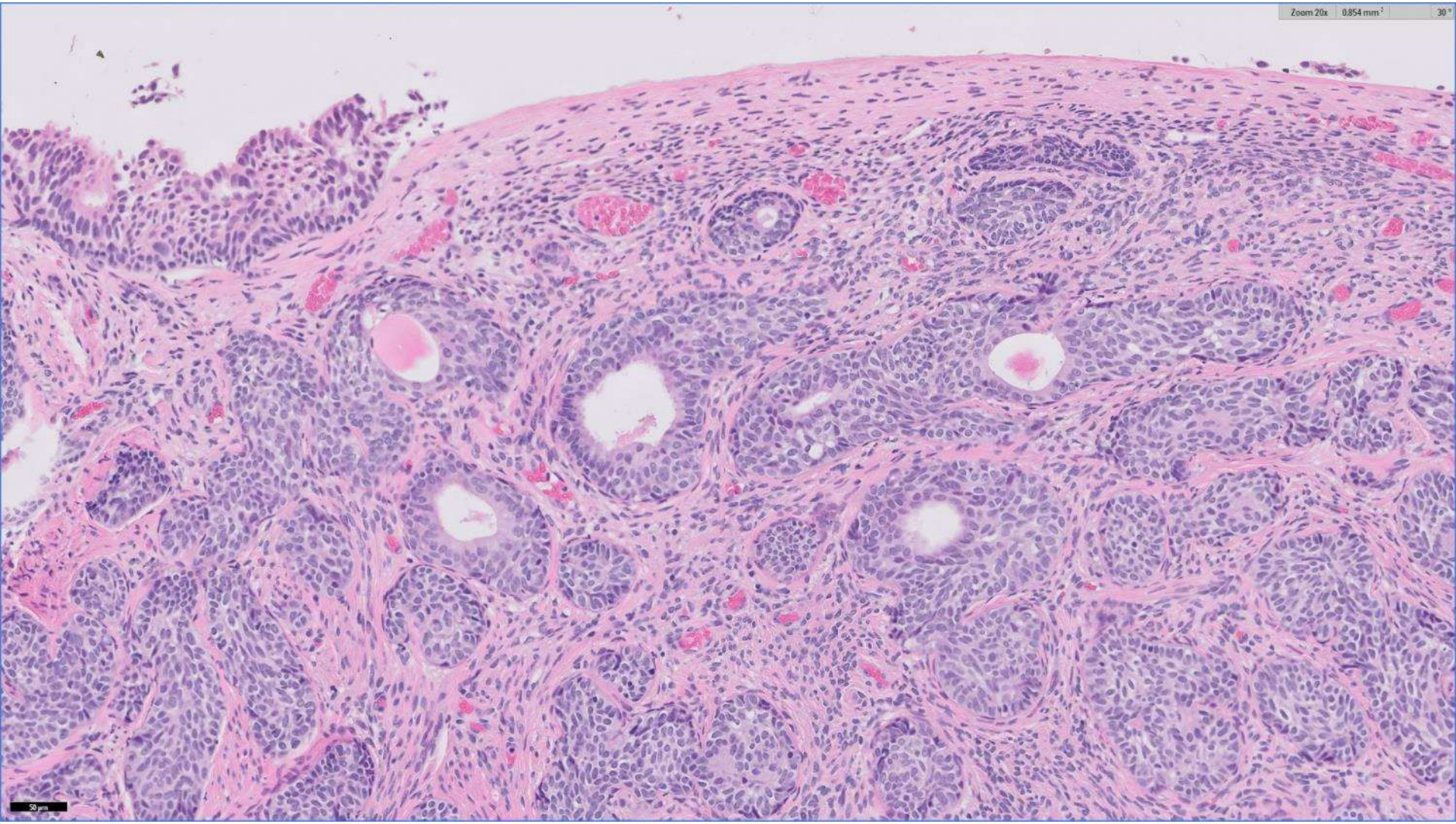

Zoom 2x
54.637 mm²
20 °
500 µm


Zoom 10x
3.415 mm⁻¹
20 °
100 µm


Zoom 20x
0,854 mm²
20 °
50 µm


Zoom 40x
0.213 mm²
300 °
50 µm


Zoom 20x
0.854 mm²
40 °
50 µm


Zoom 20x
0,854 mm²
30 °
50 µm

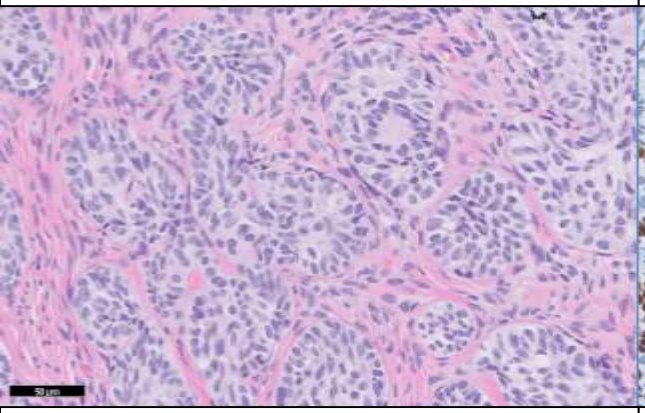
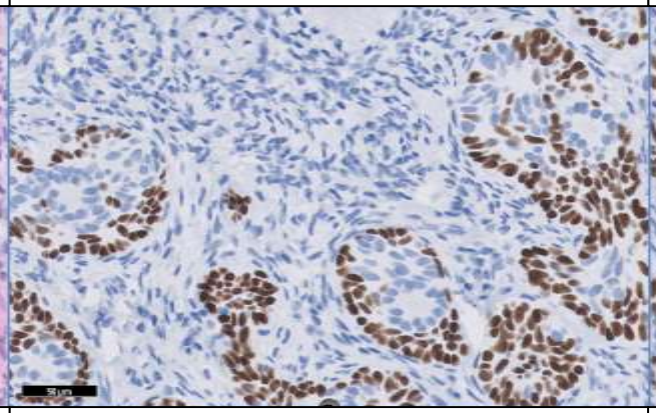
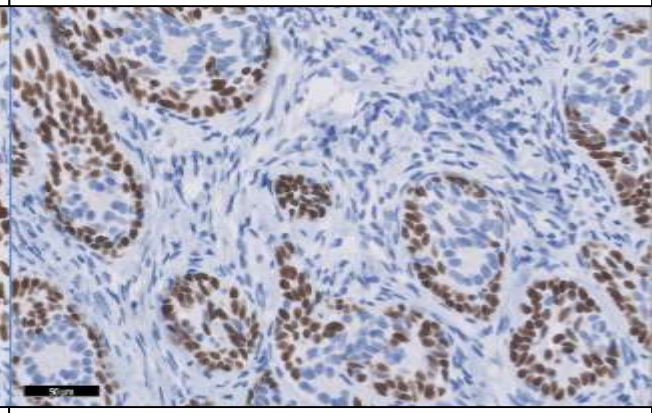
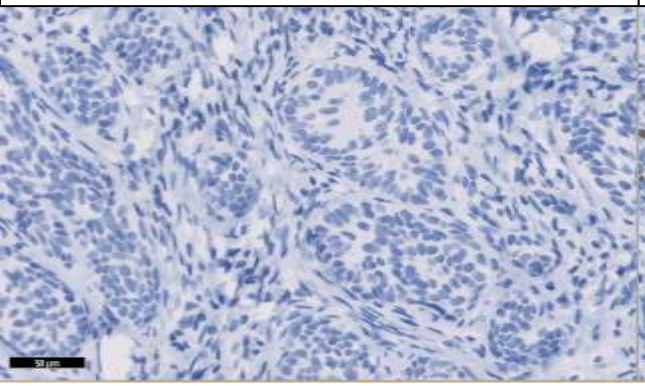
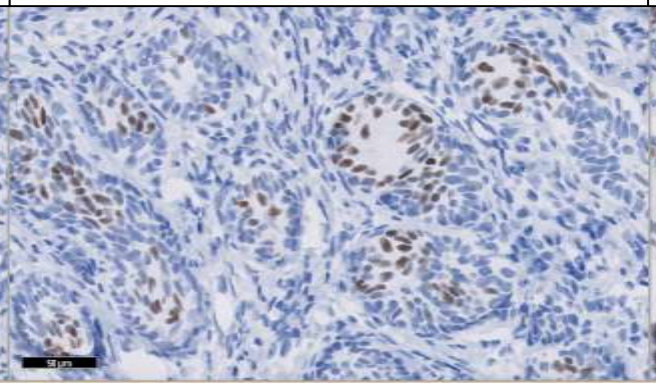
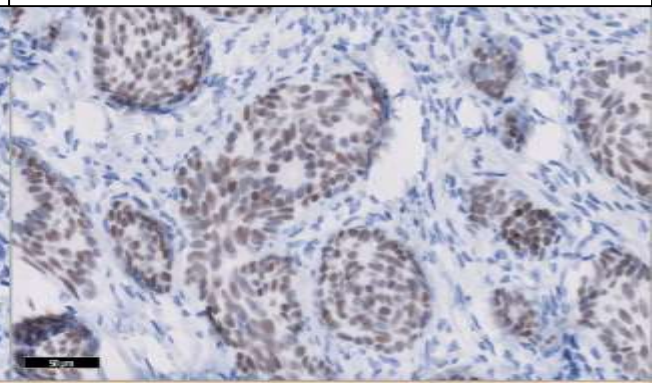
Adenoid Basal-like Tumor in Cervical LEEP

Southbay Case for 4/2022

Amanda Borgen & Nicholas Ladwig

Differential Diagnosis

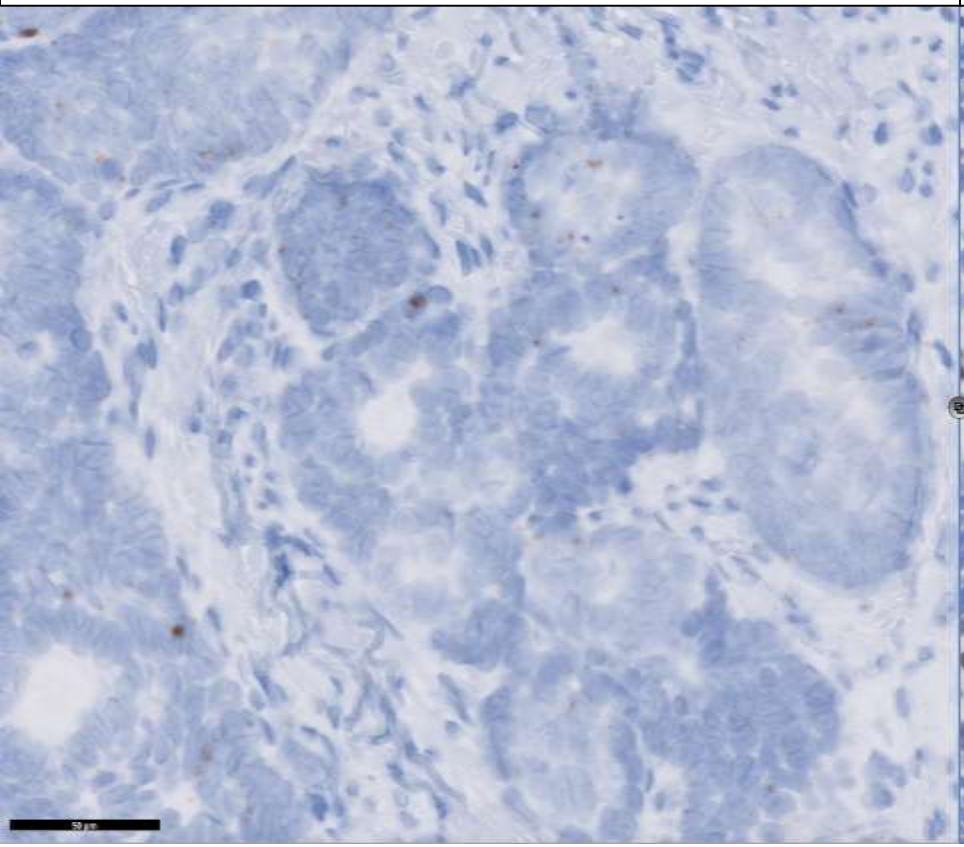
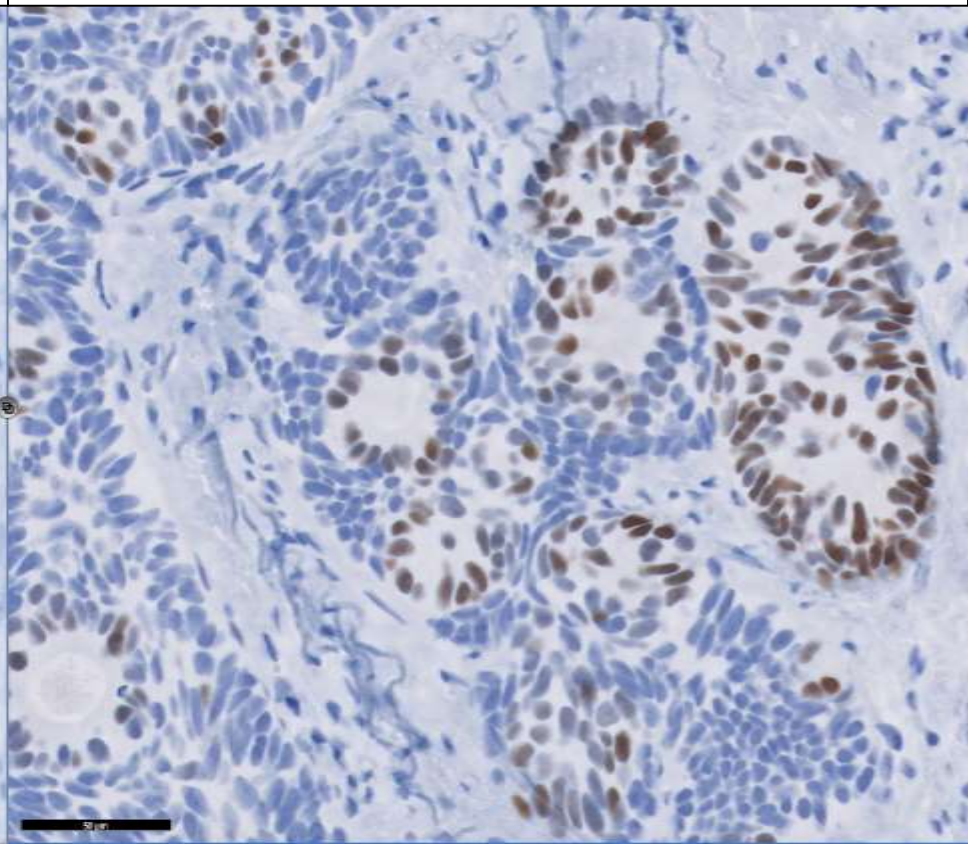
- HPV-associated cervical carcinoma
  - Mixed squamous cell carcinoma and adenocarcinoma (”adenosquamous”)
  - Adenocarcinoma with areas of stratified mucinous carcinoma (iSMILE)
  - Adenoid basal tumor
- HPV-independent cervical carcinoma
  - Mesonephric carcinoma (although these usually arise deep in the cervical wall where mesonephric remnants exist)
- Direct extension of endometrial carcinoma into cervix

H&E	p40	p63
		
PAX8 / CK7 / ER	NKX3.1	GATA3
		

Immunohistochemical Summary

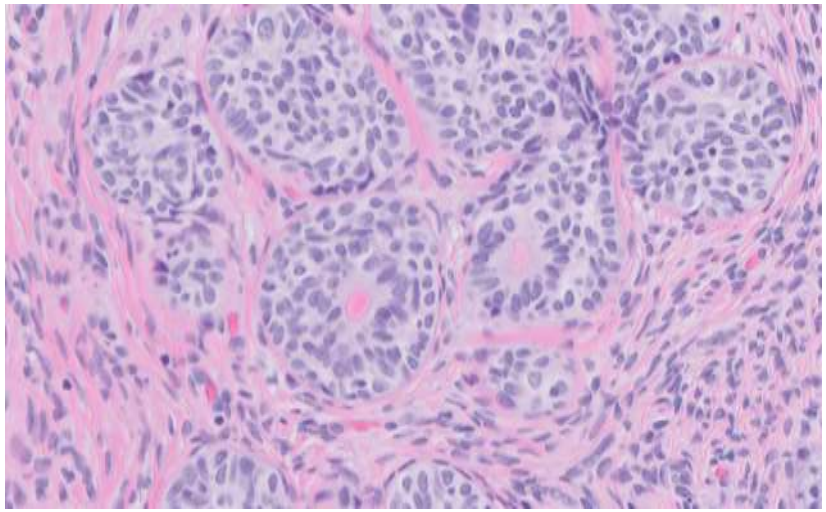
Antibody	Glandular/Luminal Cells	Basaloid/Peripheral Cells
HRHPV RNA ISH	Positive	Positive
NKX3.1	Positive	Negative
p63	Negative	Positive
p40	Negative	Positive
CK7	Negative	Negative
PAX8	Negative	Negative
ER	Negative	Negative
Mucicarmine	Negative	Negative
GATA3	Weak, variable	Weak, variable

NKX3.1 (+) and HRHPV (+) is an unusual combination

HRHPV RNA (ish)	NKX3.1
	

Adenoid Basal-Like Tumors of the Cervix

- Rare finding in cervix
- Usually incidental when pure; but often admixed with usual-type HPV-associated cervical carcinomas
- Resembles basal cell hyperplasia in the prostate
  - Biphasic, nested growth pattern
  - Peripheral cells = basaloid with palisading
  - Central cells = glandular



Suggested Terminology – 2014 WHO

When admixed with usual-type HPV-associated carcinoma

- "Invasive endocervical adenocarcinoma with adenoid basal like features"
- Clinical behavior will be driven by the usual-type carcinoma
- Adenoid basal-like areas will have no impact on behavior

If lesion excised and pure adenoid basal morphology without usual type carcinoma

If no infiltration and HRHPV-negative

- "Adenoid basal hyperplasia" is current recommendation
- Previously called adenoid basal epithelioma
- Incidental benign finding

If infiltrative and HRHPV-positive

- "Adenoid basal tumor" is current recommendation
- Previously called adenoid basal carcinoma
- In pure form, no cases have reportedly metastasized/recurred
- Likely benign

Key Points – Adenoid Basal Tumor

- Rare cervical tumors with a prostatic phenotype
- Biphasic tumors resembling basal cell hyperplasia of prostate
  - NKX3.1+ and HRHPV+ is an unusual IHC combination, unique to this entity
- Adenoid basal tumors are often admixed with traditional HPV-associated adenocarcinoma / squamous cell carcinoma with a minor adenoid basal component
- Pure adenoid basal tumor is very rare, but have benign behavior thus far
- Must recommend further excision if lesion extends to the margin to exclude a component of conventional HPV-associated carcinoma

References

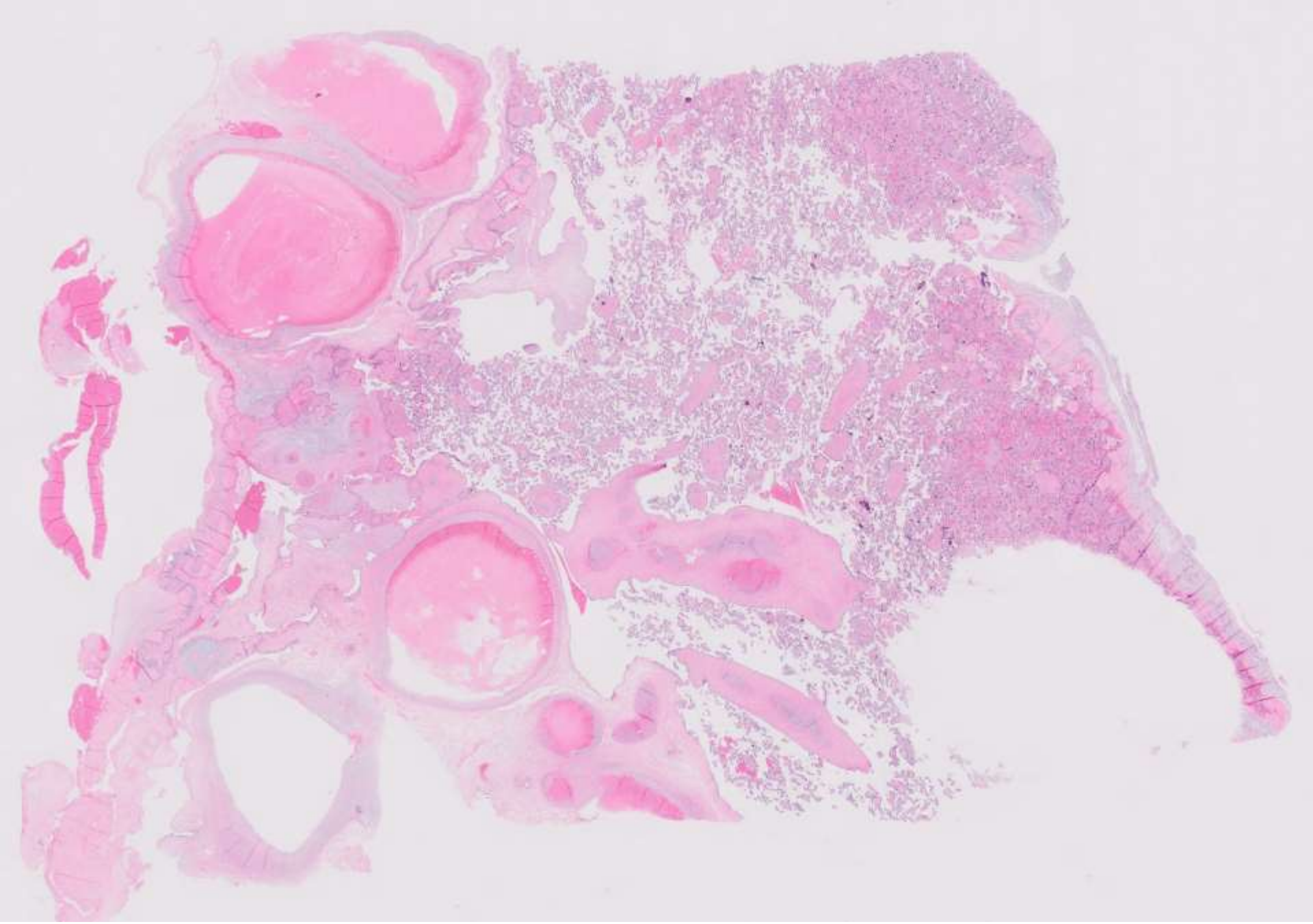
- Stewart CJR, Moses J. NKX3.1 expression in cervical 'adenoid basal cell carcinoma': another gynaecological lesion with prostatic differentiation? Pathology. 2021 Feb;53(2):193-198. Epub 2020 Oct 5. PMID: 33032811.

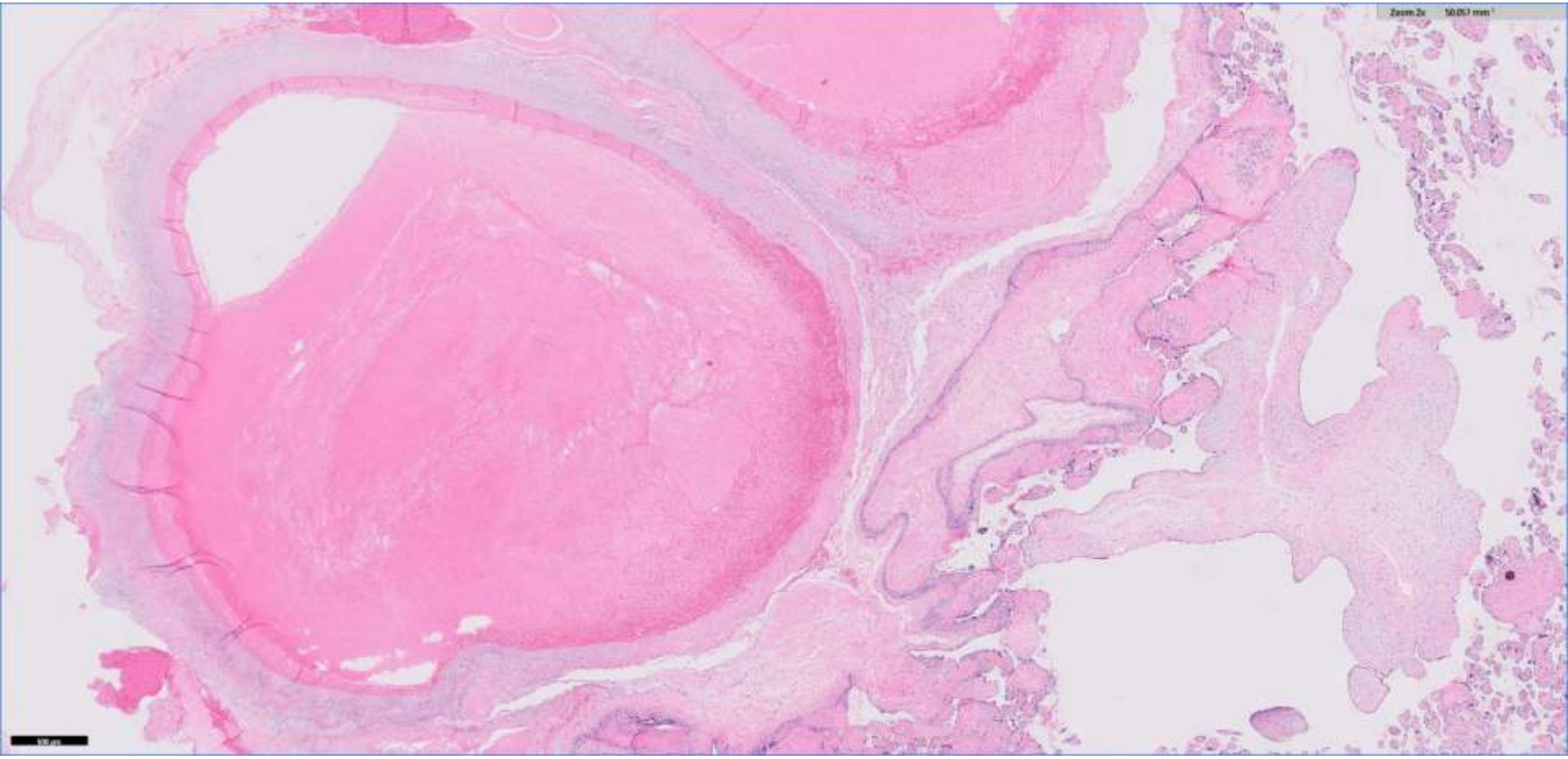
- Russell MJ, Fadare O. Adenoid basal lesions of the uterine cervix: evolving terminology and clinicopathological concepts. Diagn Pathol. 2006 Aug 15;1:18.. PMID: 16911774; PMCID: PMC1564042.

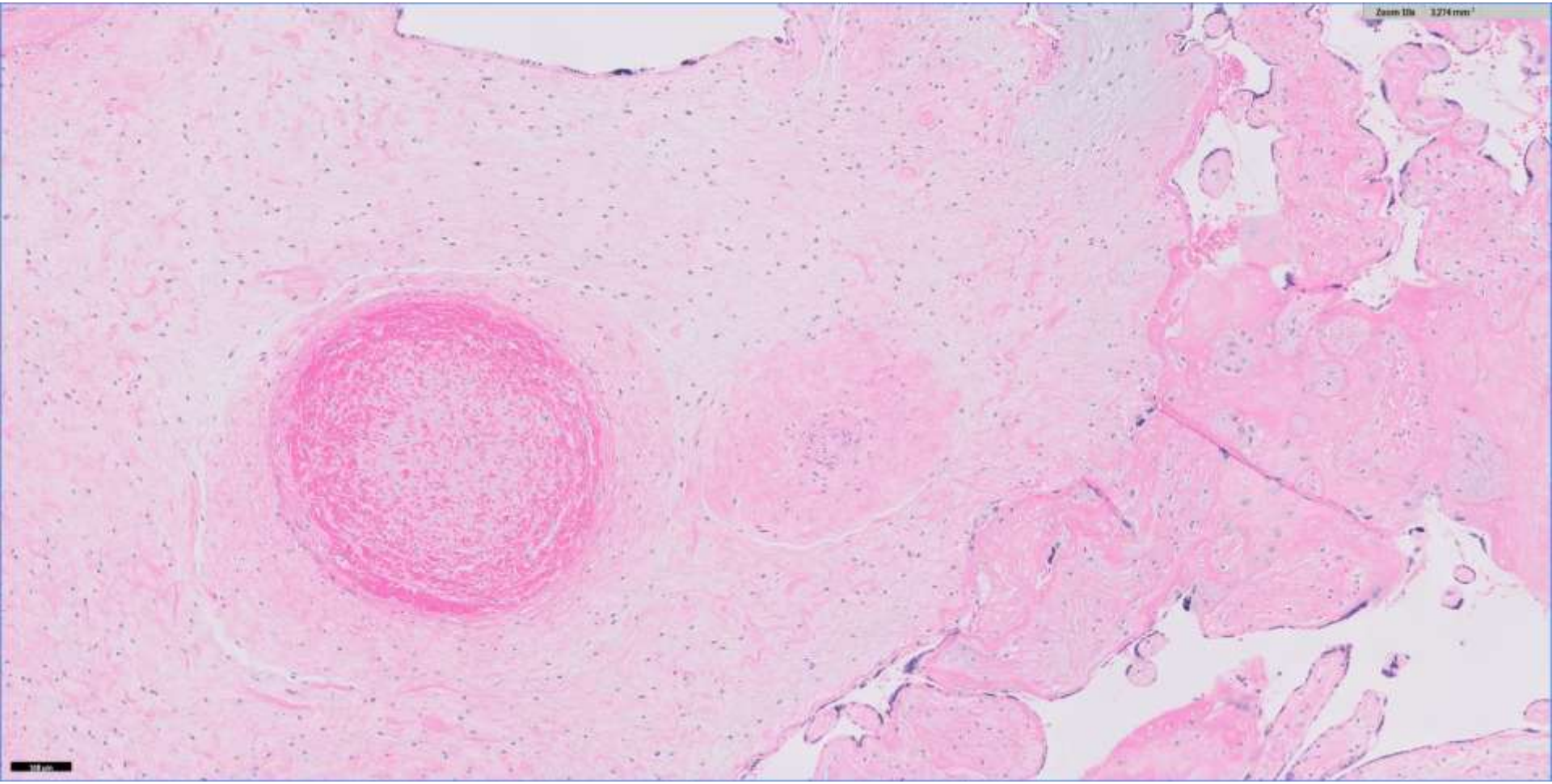
22-0403

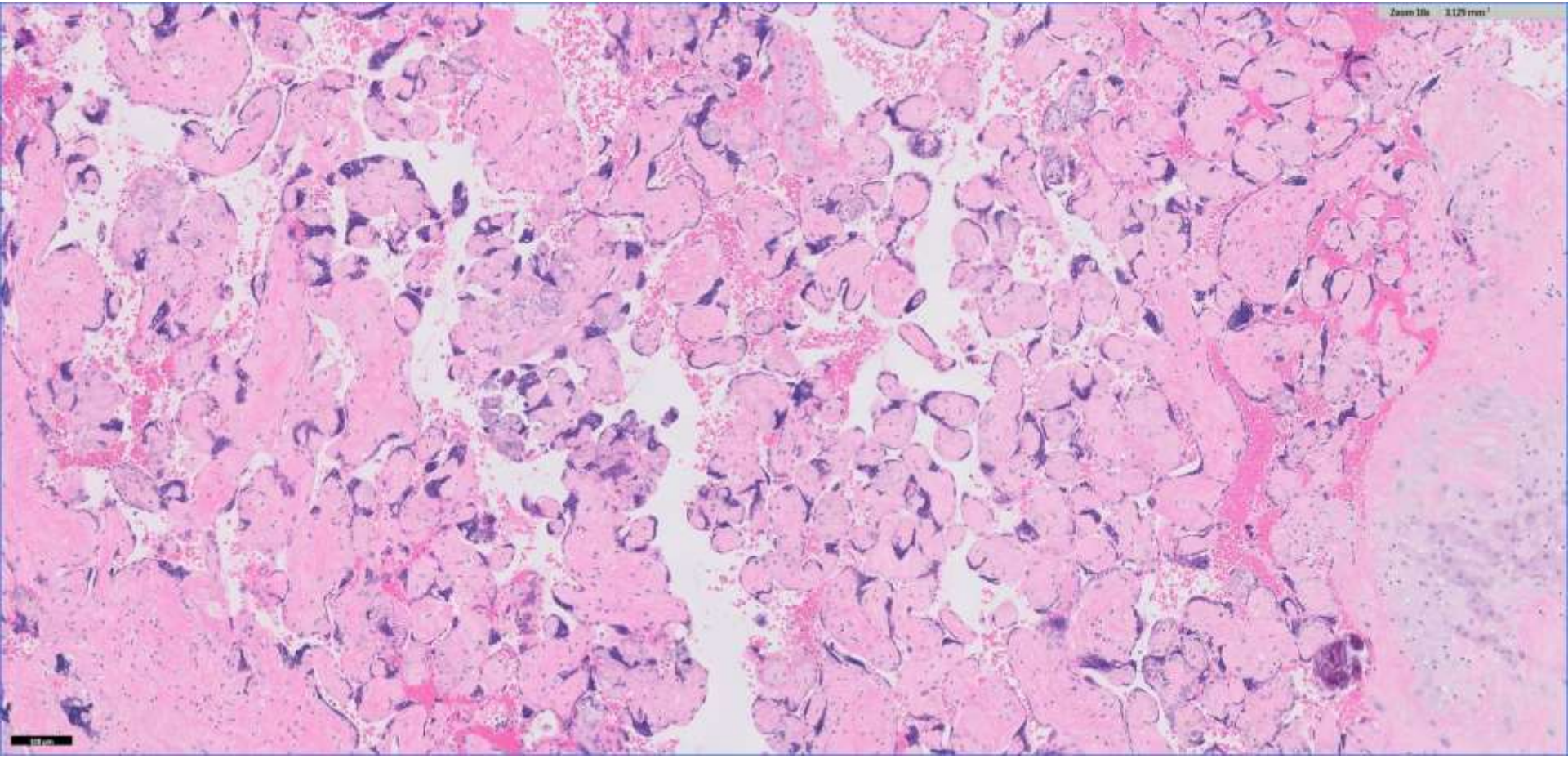
Kara Tanaka/Nicholas Ladwig; UCSF

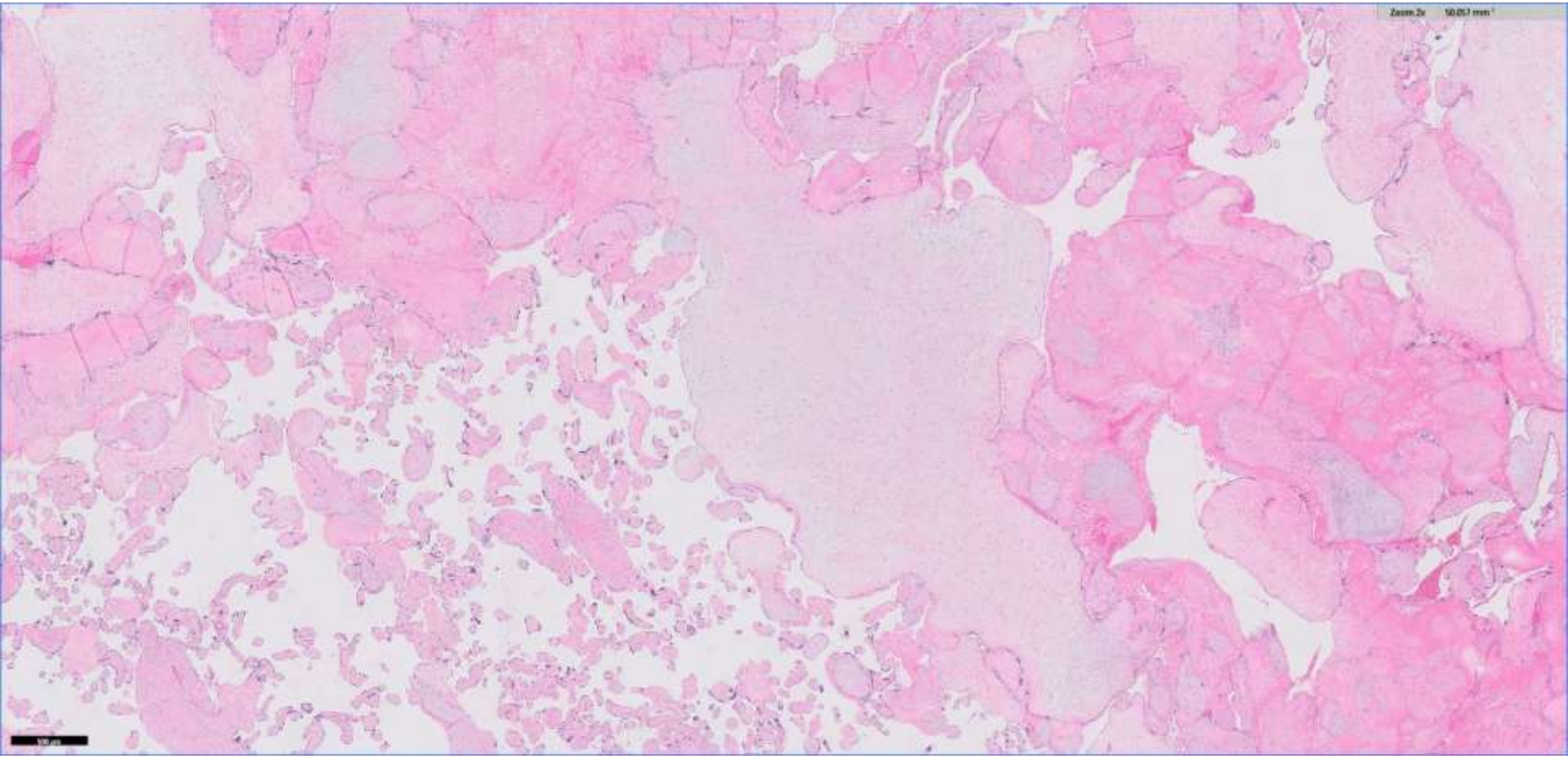
Reproductive age F with enlarged multicystic placenta.







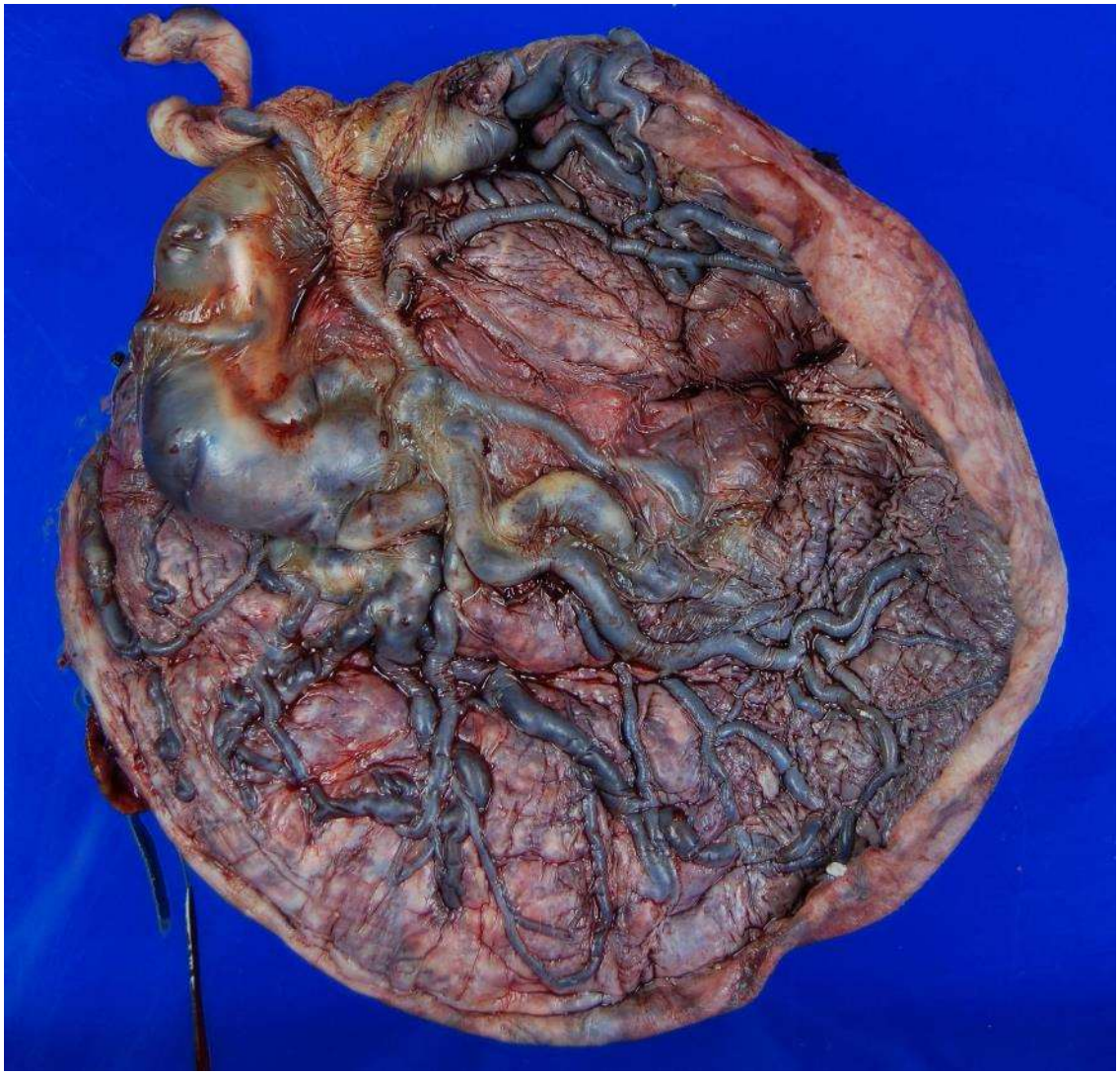


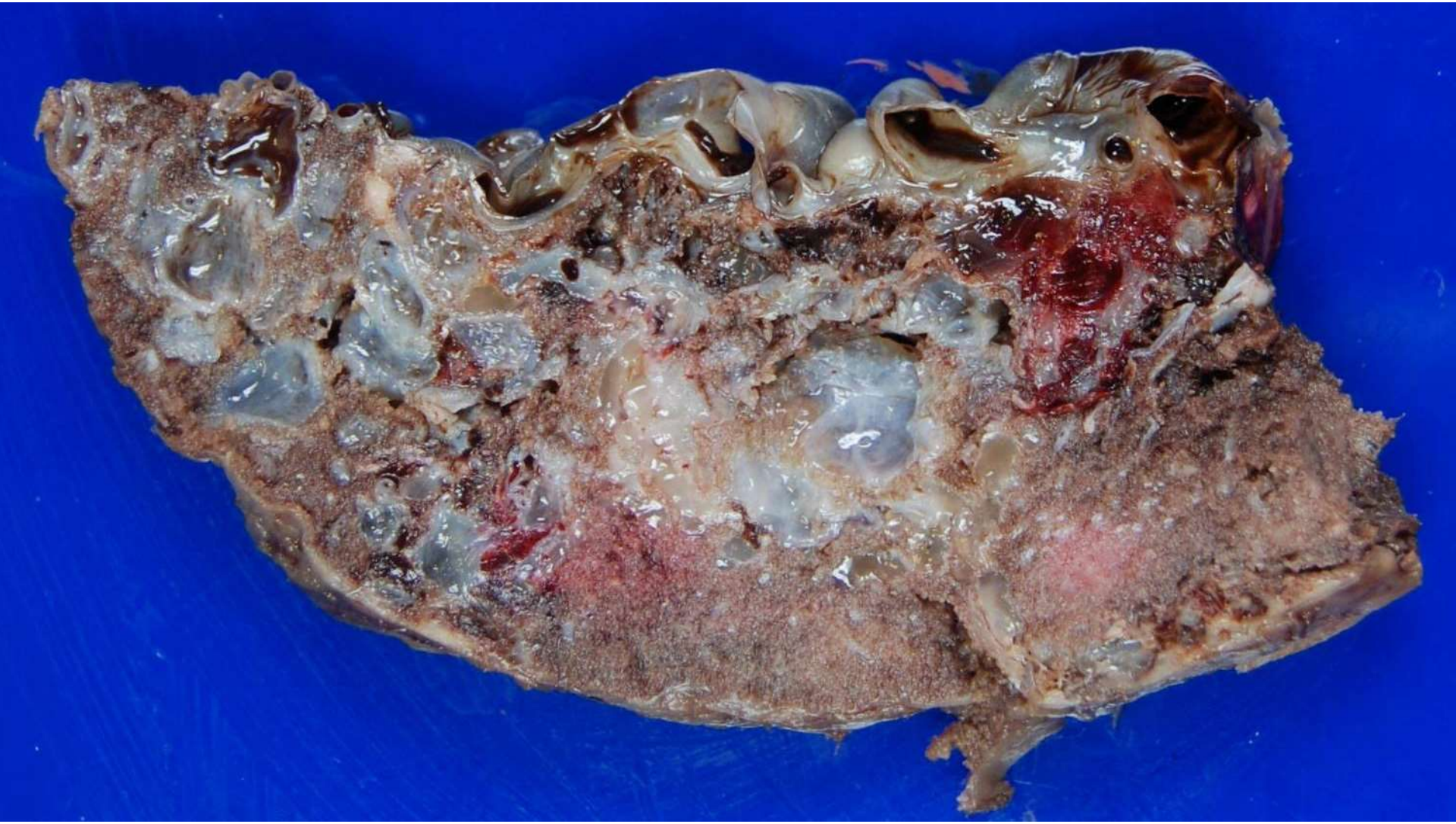


South Bay Pathology Society
April 2022

Kara Tanaka, MD, MFA
Nicholas Ladwig, MD

No financial disclosures.





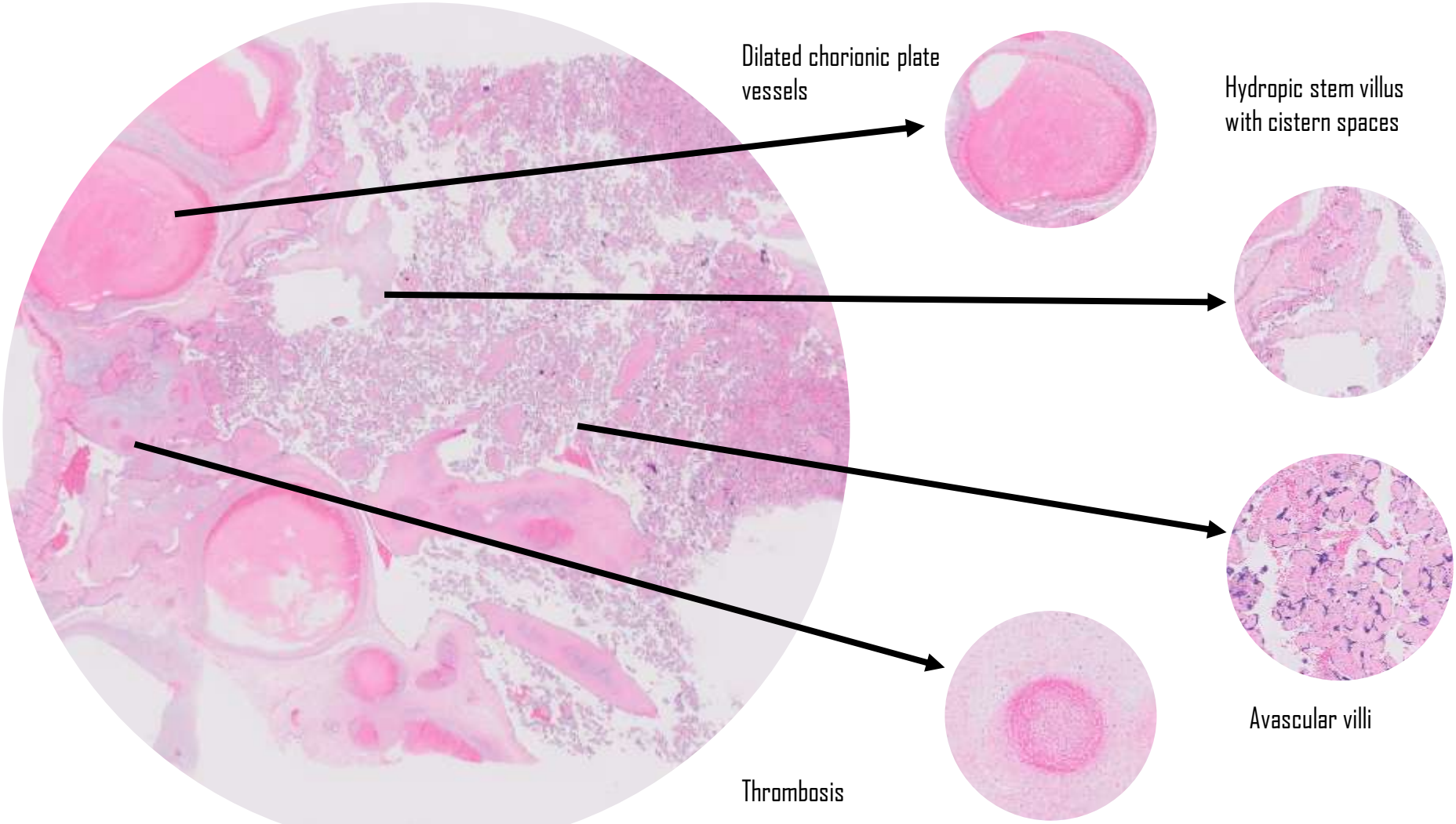
DIFFERENTIAL DIAGNOSIS

GESTATIONAL TROPHOBLASTIC DISEASE

- Partial hydatidiform mole (PHM)
- Complete hydatidiform mole (CHM) with coexistent fetus (e.g., twin gestation in which one twin is a complete mole)

OTHERS

- Nonspecific hydronic changes


Dilated chorionic plate vessels
Hydropic stem villus with cistern spaces
Avascular villi
Thrombosis

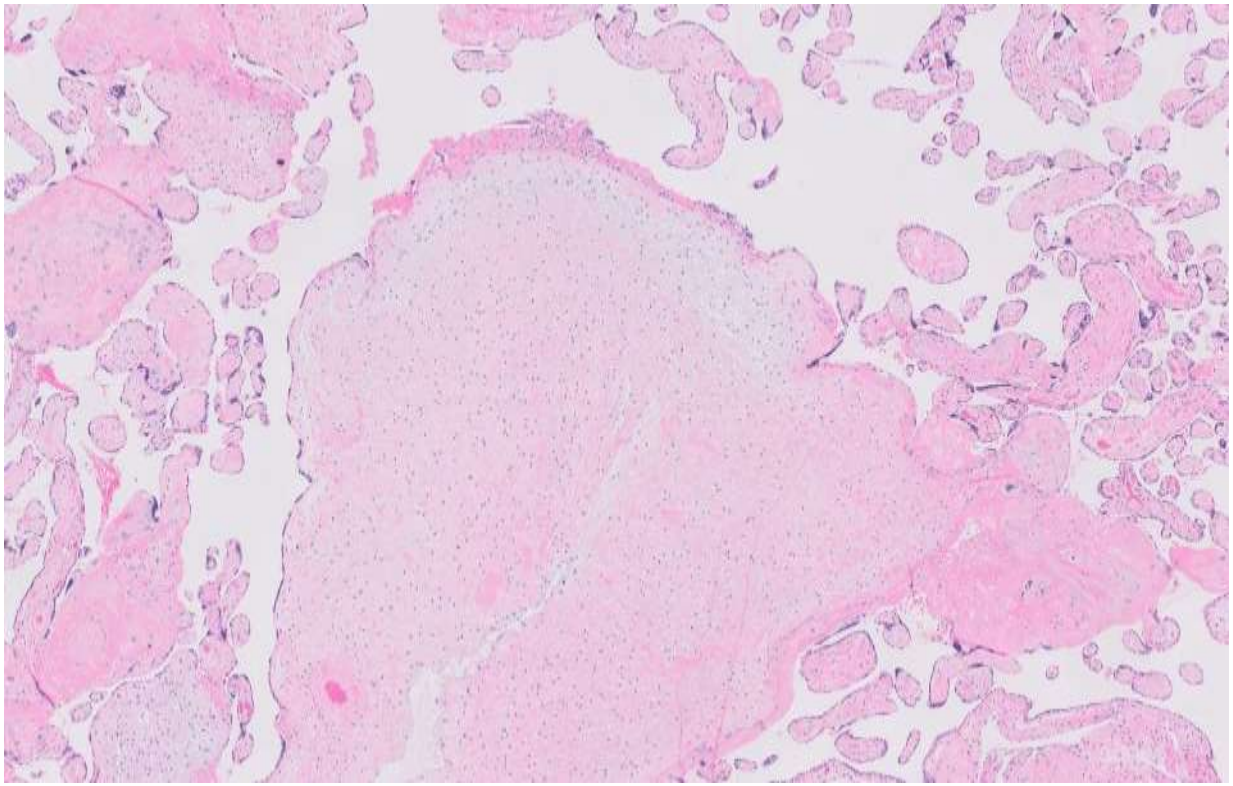
PROMINENT STEM VILLI

+ cistern-like spaces

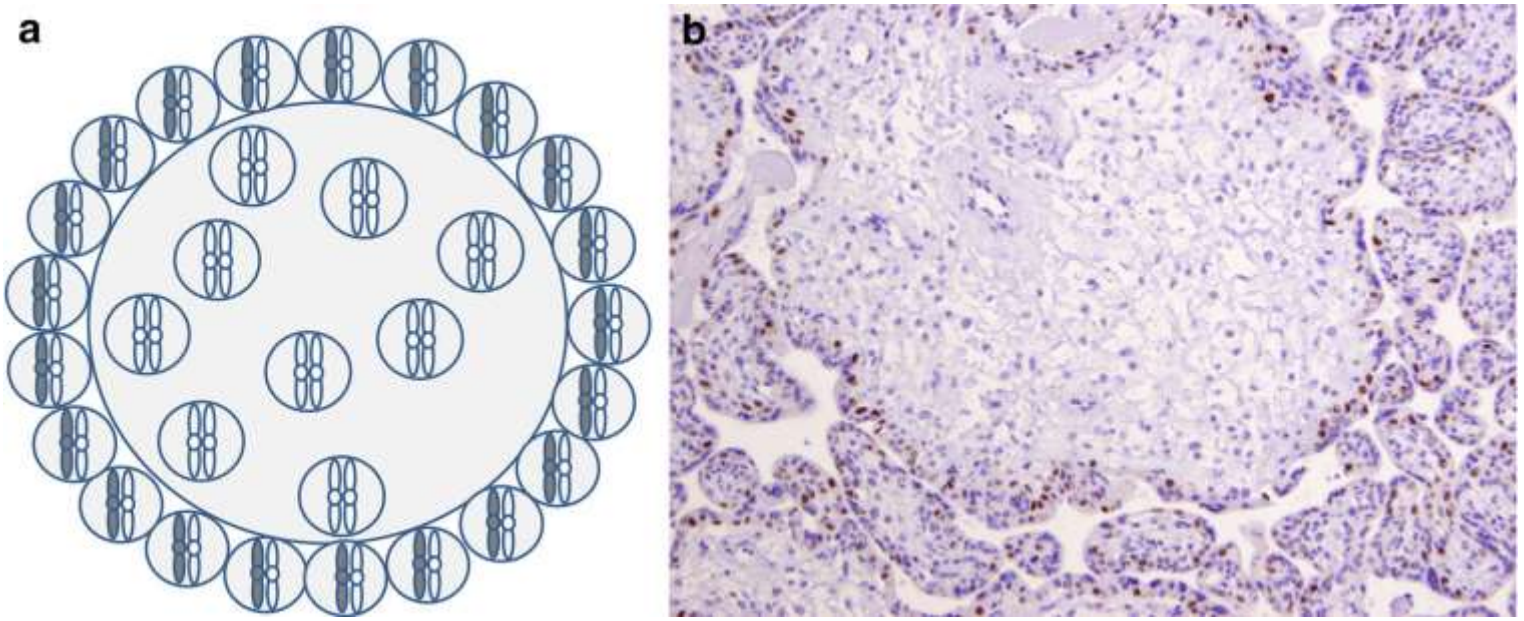
+ thick-walled/
  thrombosed
  vessels

+ expansion of villous
mesenchyme

absent trophoblastic
proliferation



PMD IS CAUSED BY ANDROGENETIC BIPARENTAL MOSAICISM



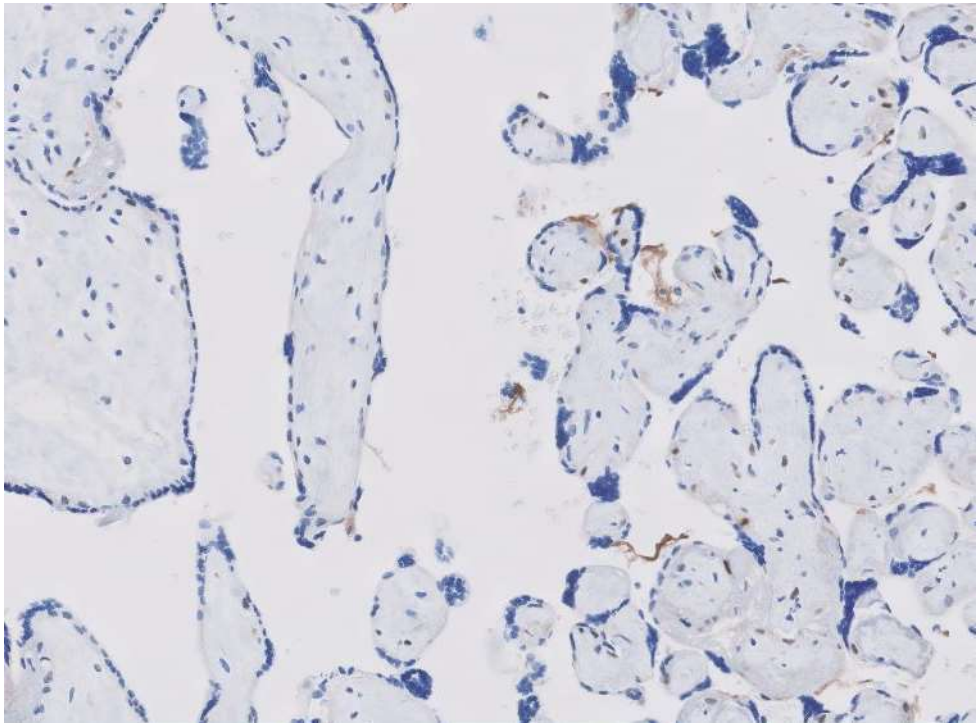
Ernst, 2015. https://doi.org/10.1007/s40556-015-0056-9

CHARACTERISTIC P57 STAINING

Cytotrophoblast cells:
- p57 positive

Stromal cells:
- p57 negative

Pattern is distinct from complete mole (both negative) or partial mole (both positive)



J. Fetal Med. (September 2015) 2:127–133
DOI 10.1007/s40556-015-0056-9

REVIEW ARTICLE

Placental Mesenchymal Dysplasia

Linda M. Ernst[1]

Received: 26 June 2015 / Accepted: 5 October 2015 / Published online: 24 October 2015

Abstract This is an updated review of the recently described entity, placental mesenchymal dysplasia, which has been shown to have recognizable antenatal characteristics, distinctive gross and microscopic pathologic findings, associated fetal and neonatal morbidity and mortality, and unique pathogenic mechanisms. Recent understanding of the frequently associated genotype, androgenetic biparental mosaicism, is reviewed and the spectrum of changes discussed.

hydrops of placental stem villi, diploid karyotype, and fetal omphalocele. The author suggested a possible association with Beckwith-Wiedemann syndrome. Several other reports of pseudo-partial mole [4, 5] described similar features. Initially, there was some debate about whether to call the lesion PMD or placental mesenchymal hyperplasia [4, 6–9], but to date PMD is the preferred terminology. More than 100 cases of PMD have been reported in the literature. However, discussion of this unique placental entity in contemporary surgical pathology textbooks is still inconsistent.

Ernst, L.M. Placental Mesenchymal Dysplasia. J. Fetal Med. 2, 127–133 (2015). https://doi.org/10.1007/s40556-015-0056-9

PMD VS. MOLAR GESTATION

	Placental Mesenchymal Dysplasia (PMD)	Complete/Partial Hydatidiform Mole (CHM, PHM)
Blood flow (Doppler)	Abundant "stained-glass" pattern	Absent; with "snowstorm" appearance
Cystic placental tissue (MRI)	Within the fetal sac	Outside the fetal sac
Prenatal workup	Elevated α-fetoprotein Normal (diploid) karyotype ABM: mix of androgenetic cell line + biparental cell line Viable fetus	Elevated β-hCG Diploid karyotype (CHM) Triploid karyotype (PHM) No viable fetus
Gross features	Placentomegaly with cystic dilation	"grapelike" placenta
Histologic features	No trophoblastic hyperplasia Hydropic stem villi Thick-walled/thrombotic vessels	Trophoblastic hyperplasia, inclusions Hydropic, scalloped, distal villi
p57 nuclear staining Villous stromal cells: Villous cytotrophoblast cells:	 Lost in some/all Retained	CHM PHM Lost Retained Lost Retained

PLACENTAL MESENCHYMAL DYSPLASIA

- Viable fetus; increased risk of maternal and fetal adverse outcomes
  - Fetal growth restriction
- Beckwith-Wiedemann syndrome (BWS)
- Paternal uniparental disomy: BWS locus – chromosome 11p15.5
- No persistent gestational trophoblastic disease

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22-0404

Kyra Berg/John Higgins; Stanford

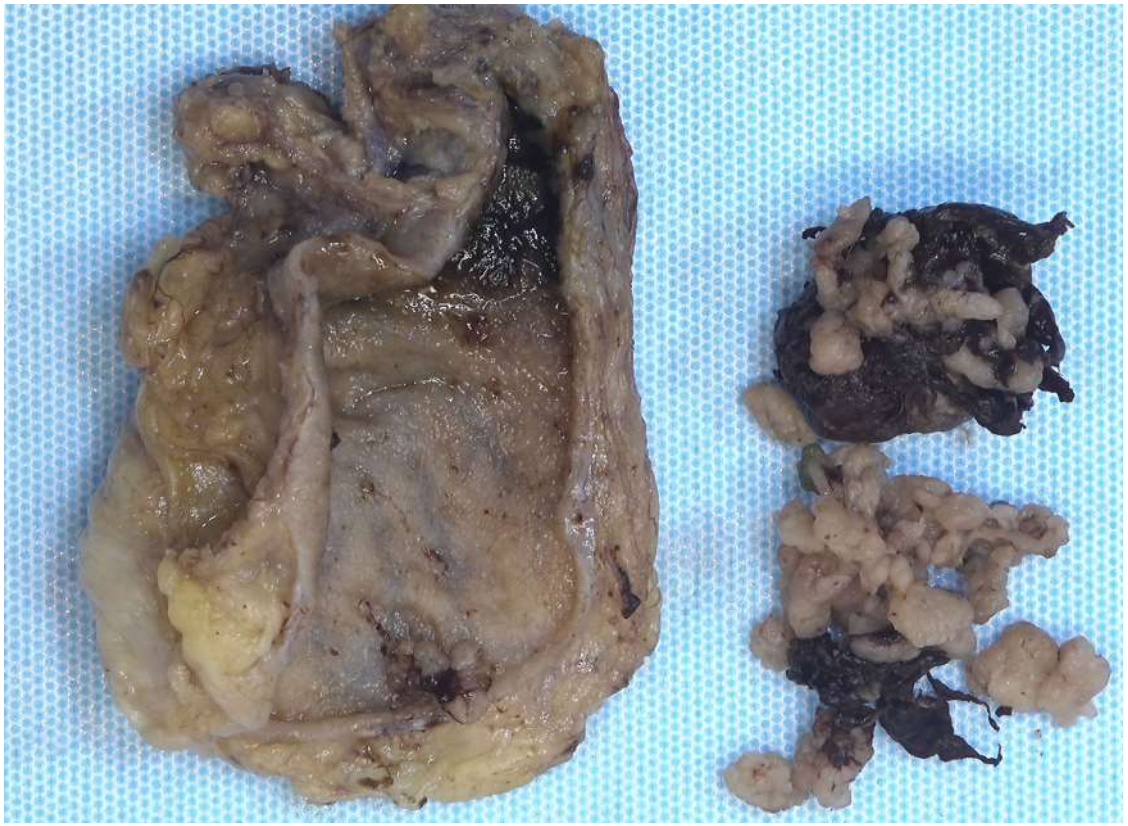
80ish F with gallbladder tumor on imaging.

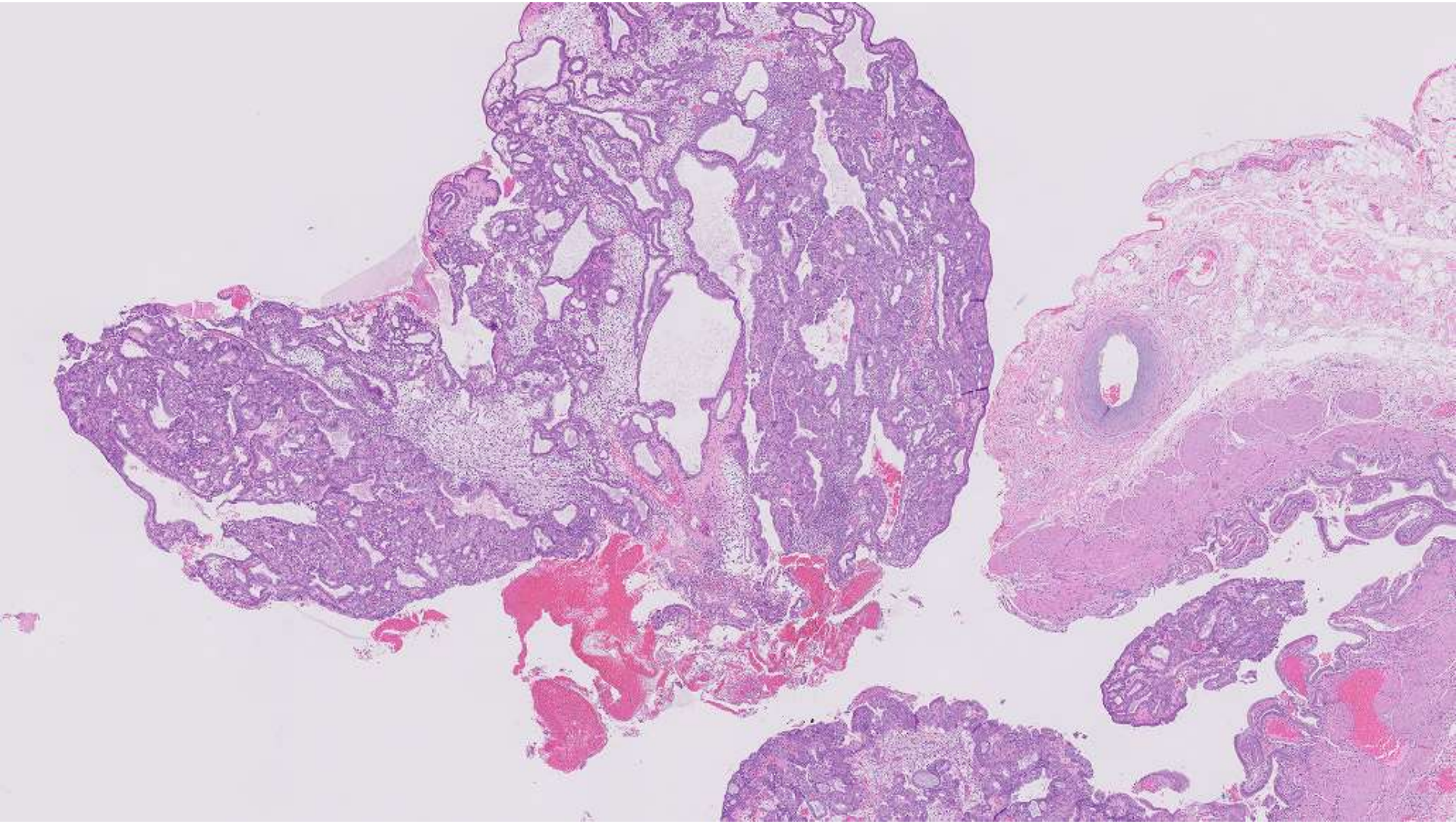
Case History

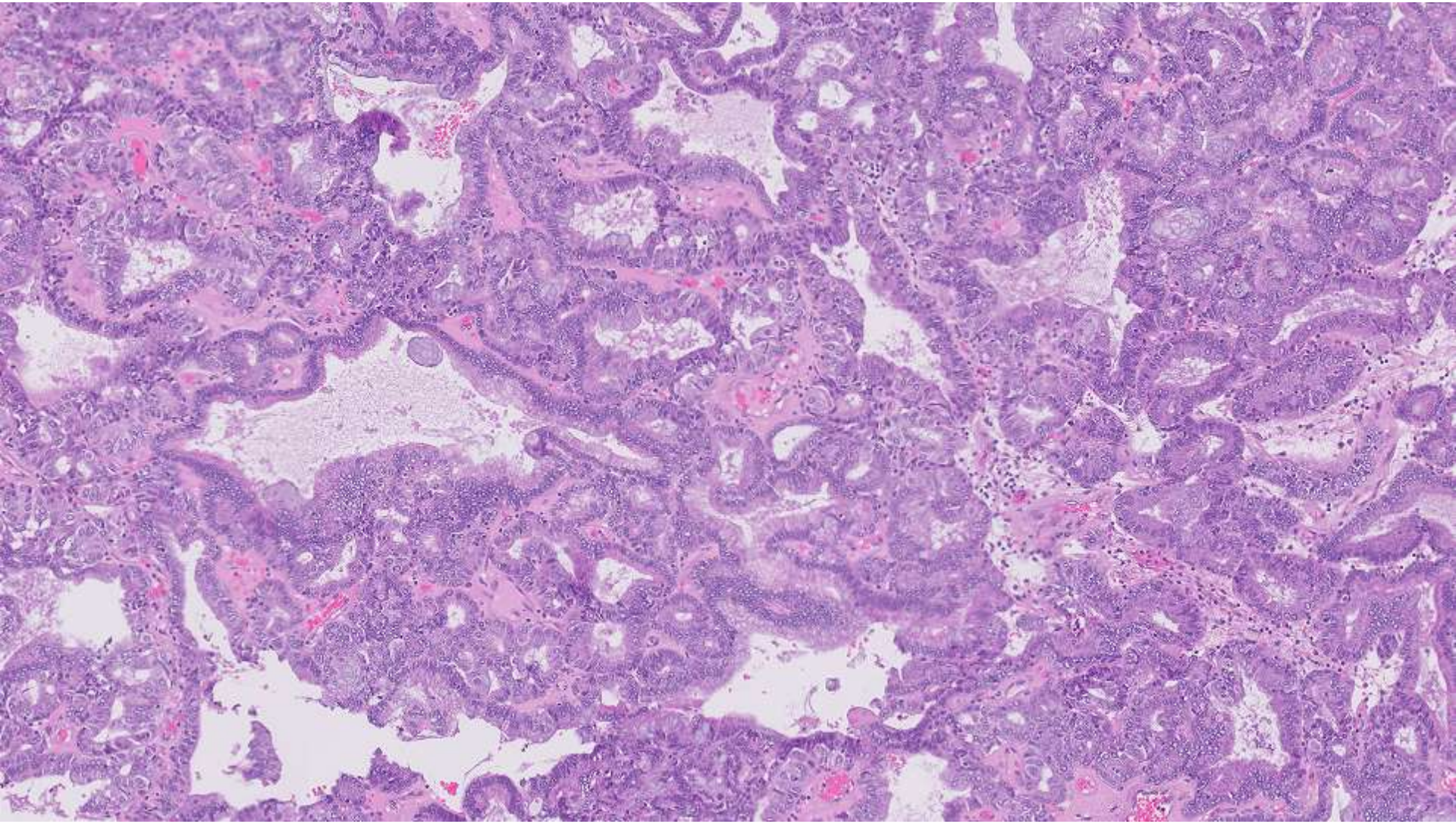
- 82-year-old female who presented with epigastric pain and was admitted
- Past medical history includes congestive heart failure
- Her in-patient work-up included a MRI that showed a gallbladder mass, 2.7 cm, enhancing that was concerning for malignancy
- Underwent a cholecystectomy with porta hepatic and celiac lymphadenectomy

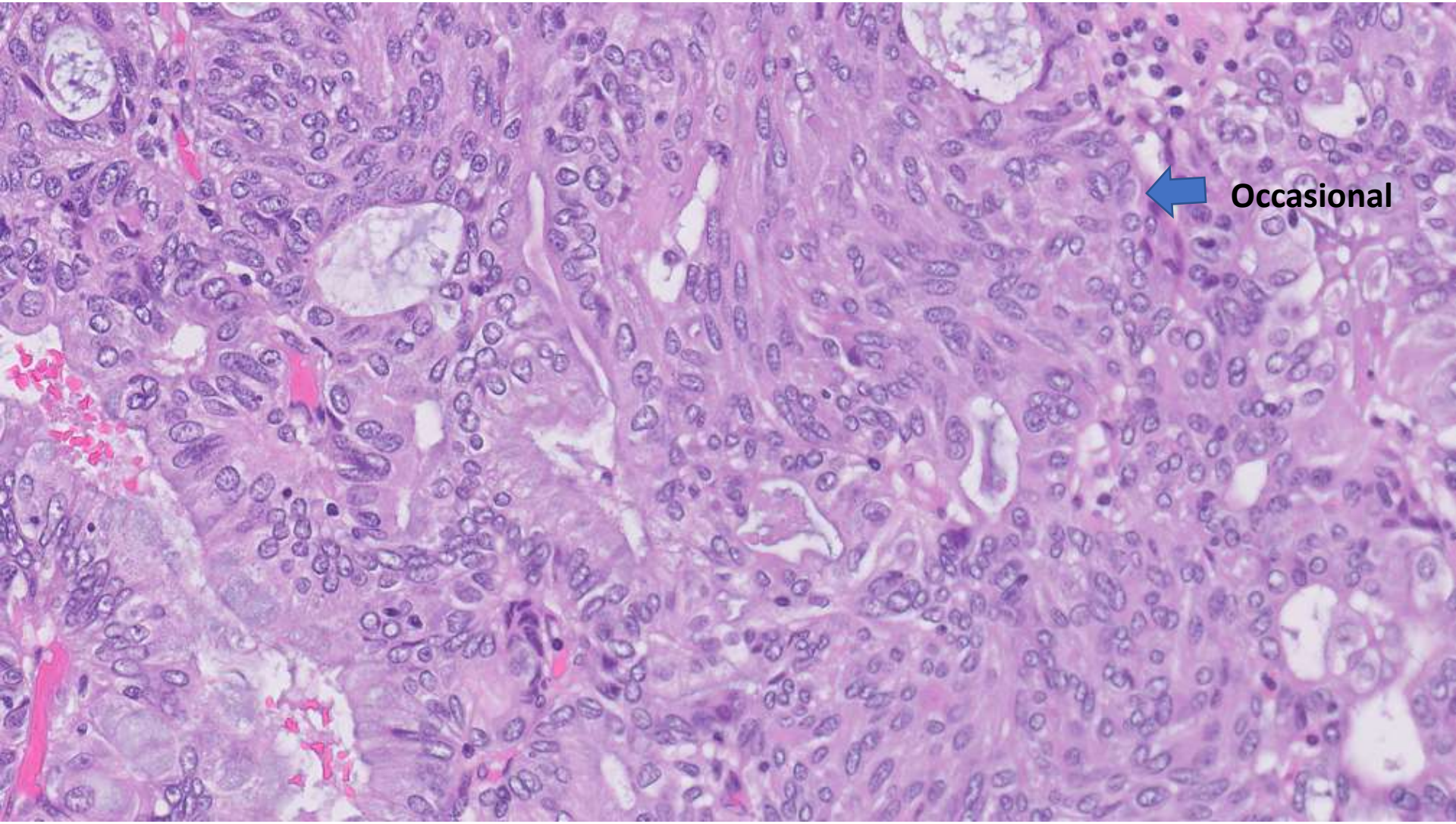
Gross

- Showed a gallbladder polyp at the fundus(0.9 x 0.7 x 0.2 cm) with a thin stalk
- Also detached polypoid fragments aggregating to 2.9 cm

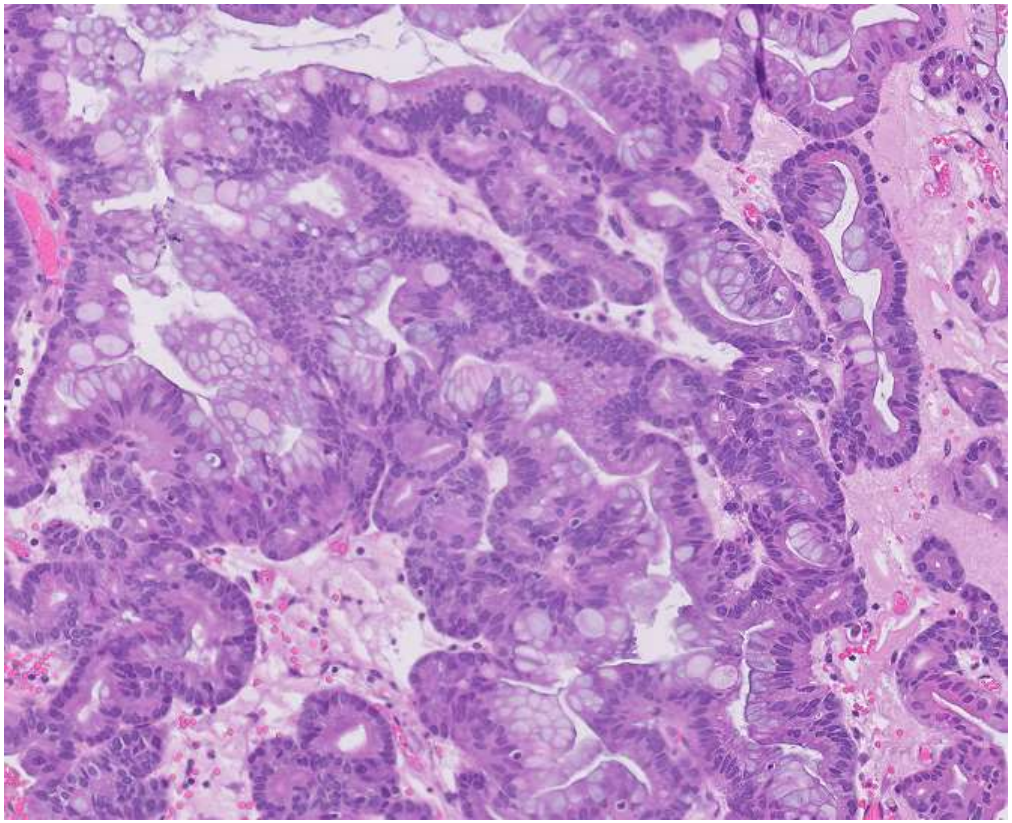







Occasional

Very Focal



Case History

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- Past medical history includes severe aortic stenosis with congestive heart failure
- Her in-patient work-up included a MRI that showed a gallbladder mass, 2.7 cm, enhancing that was concerning for malignancy
- Underwent a cholecystectomy with porta hepatic and celiac lymphadenectomy

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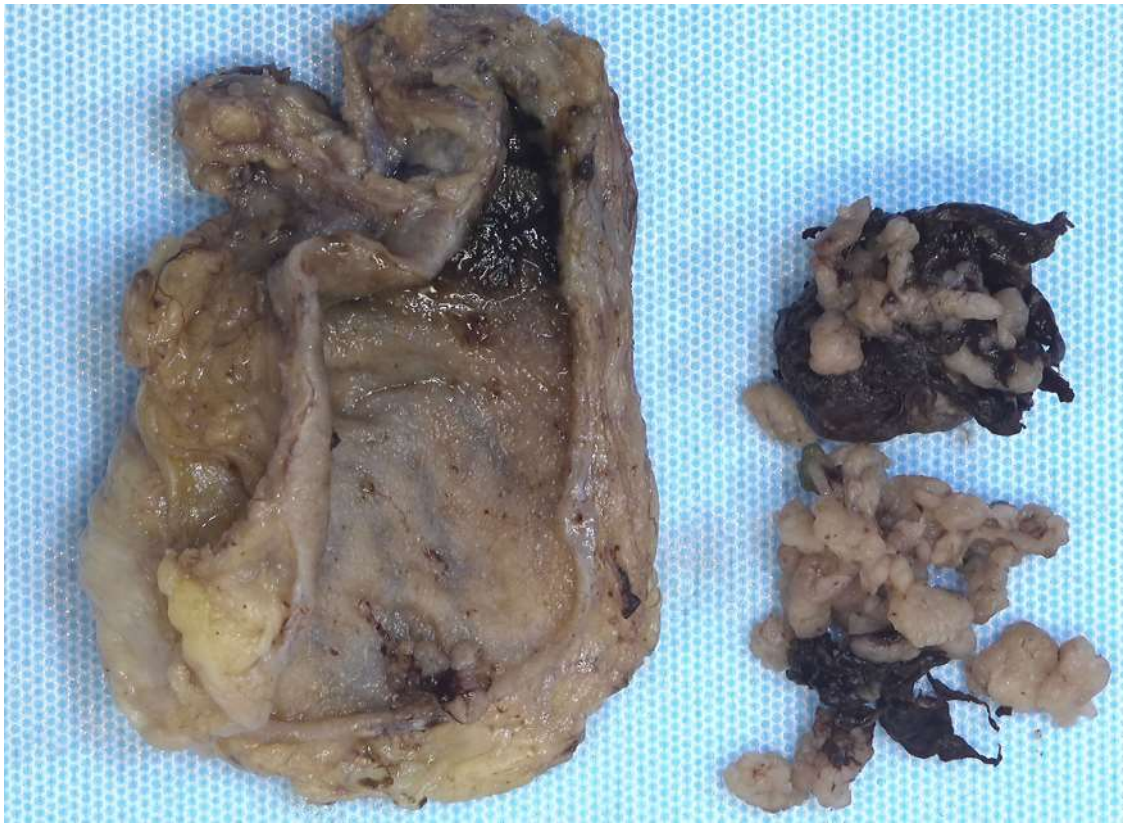

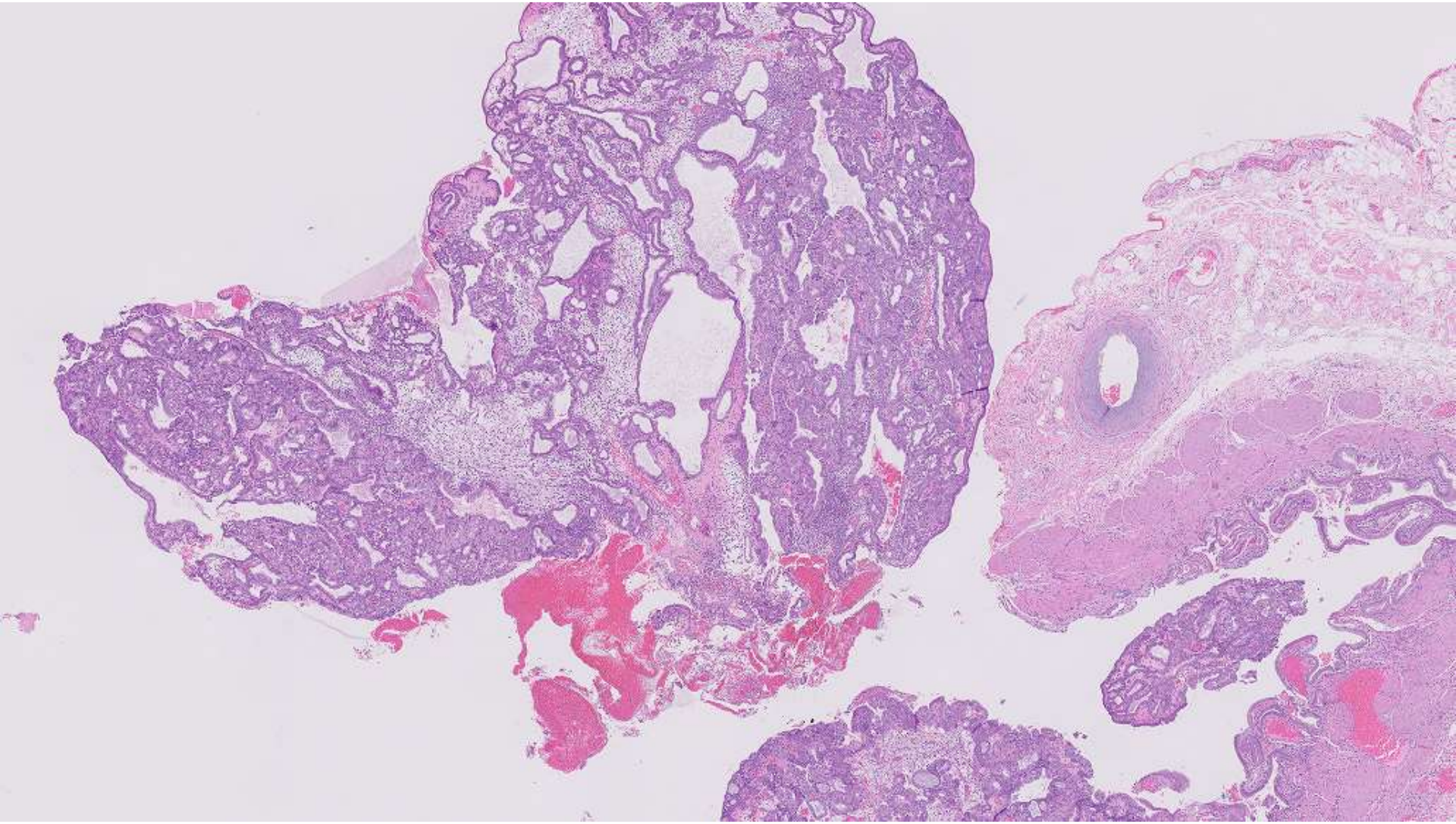

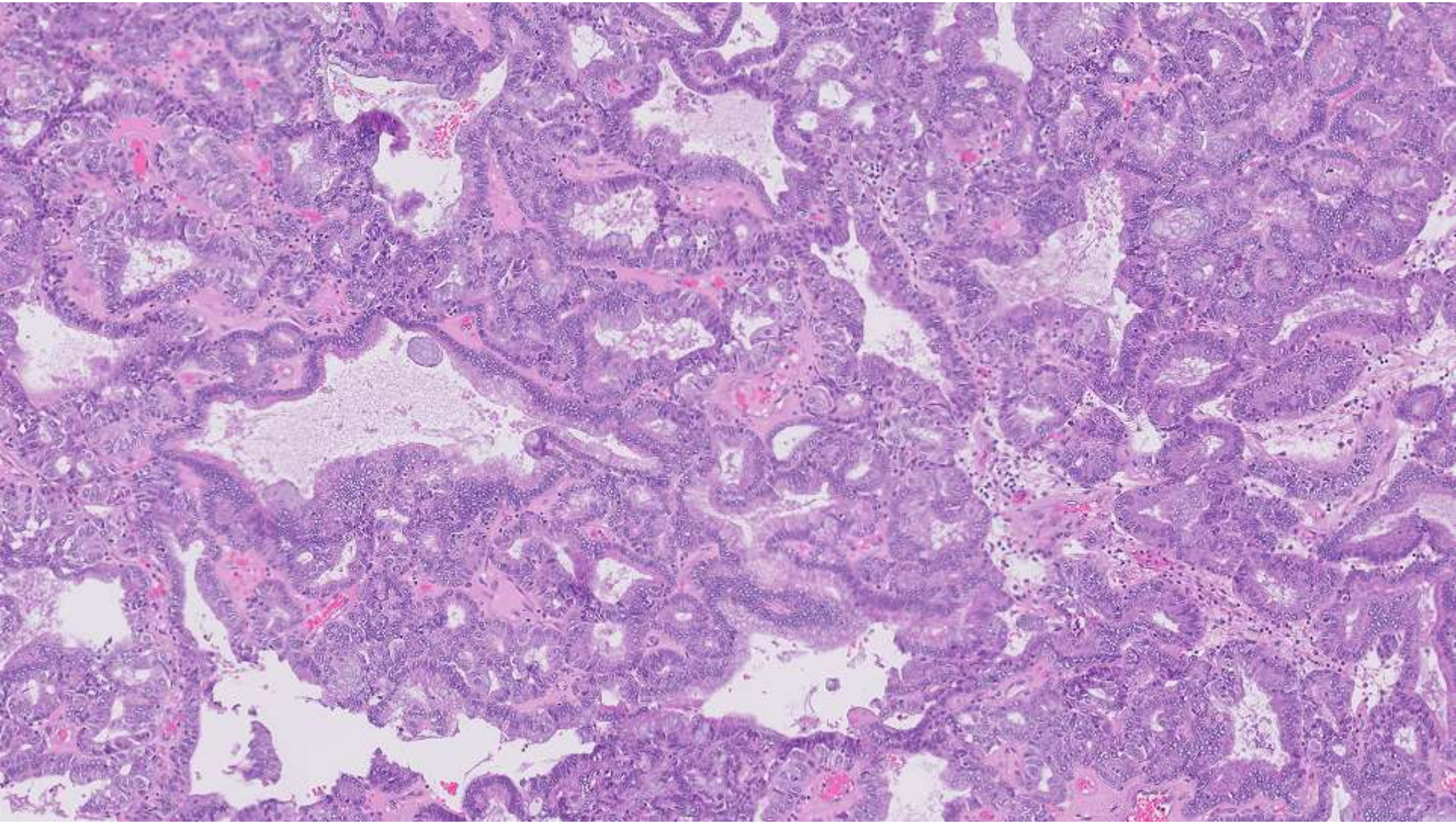

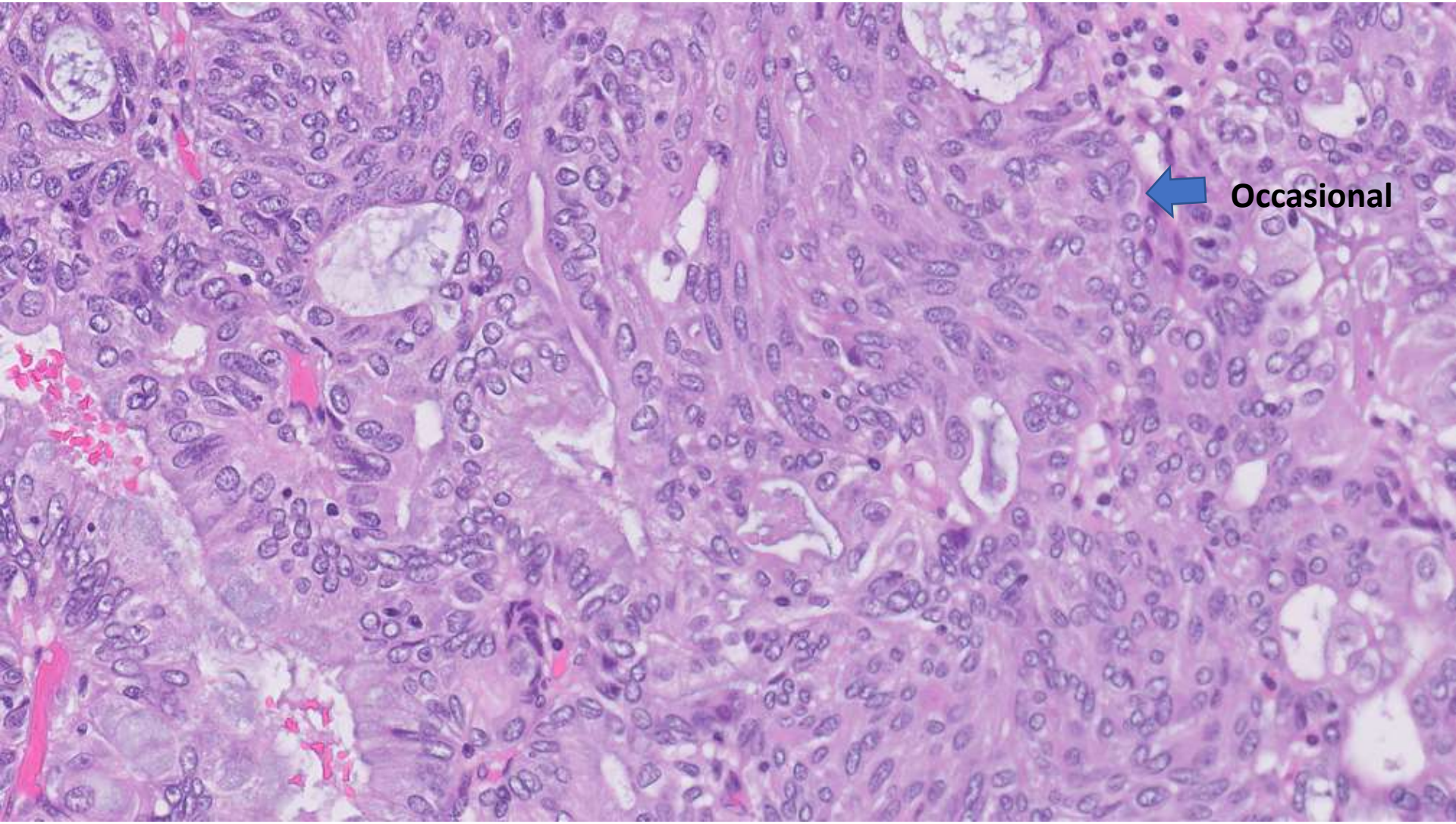
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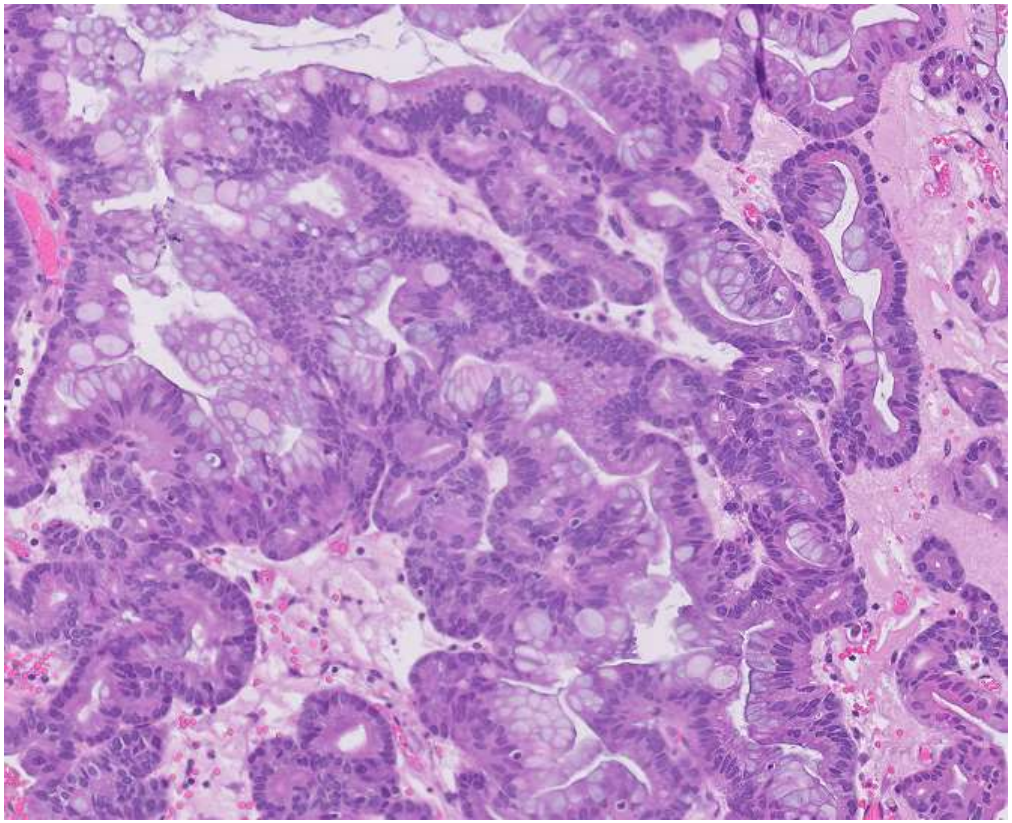
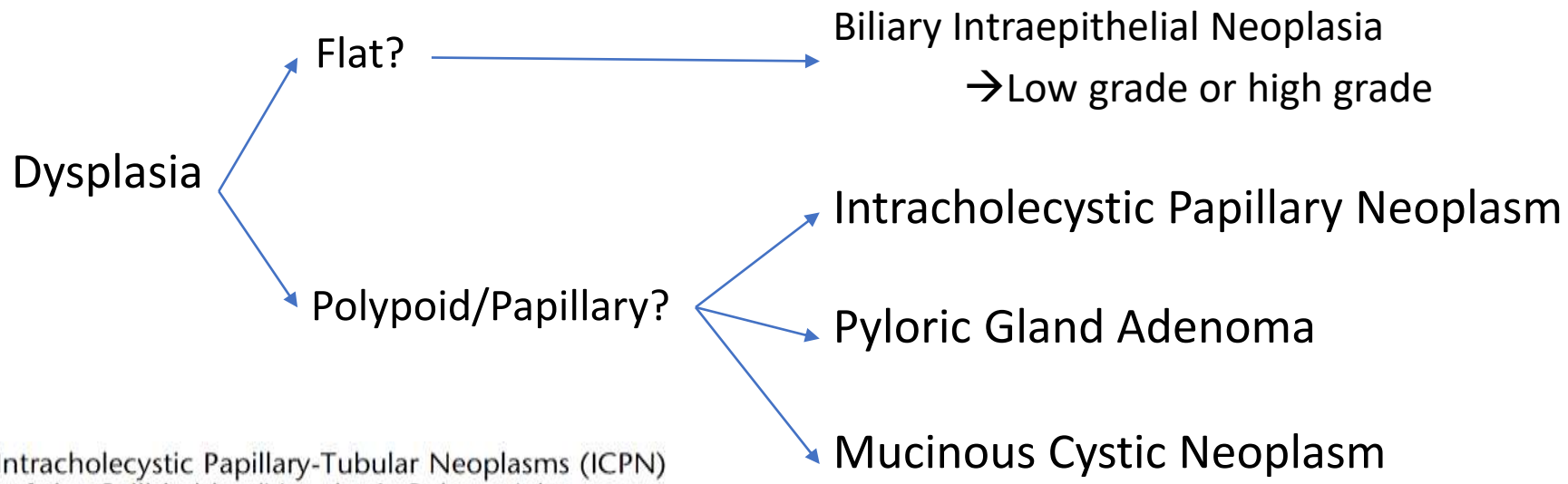


Classification in the Biliary Tract



Intracholecystic Papillary-Tubular Neoplasms (ICPN) of the Gallbladder (Neoplastic Polyps, Adenomas, and Papillary Neoplasms That Are ≥ 1.0 cm)

Clinicopathologic and Immunohistochemical Analysis of 123 Cases

Adsay et al. Am J Surg Pathol. 2012. 36(9): 1279-1301.

DDx

- Intracholecystic Papillary Neoplasm, gastric subtype
- Pyloric gland adenoma

Pyloric Gland Adenoma (PGA) of the Gallbladder

A Unique and Distinct Tumor from PGAs of the Stomach, Duodenum, and Pancreas

Cong He, MD, Yuki Fukumura, MD, PhD,* Akane Toriyama, MD, PhD,† Kanako Ogura, MD, PhD,‡ Noriko Sasahara, MT,* Keiko Mitani, MT,* and Takashi Yao, MD, PhD**

Am J Surg Pathol 2018;42:1237–1245)

Case series of 24 cases of gallbladder pyloric gland adenomas.

- Definition of PGA: polypoid tumor (any size) closely packed tubules with a monolayer of cuboidal to low columnar epithelial cells
- Found beta-catenin mutations in 21/21 that they were able to get DNA from
- Rate of HGD was 29.2% (7/24)
- Rate of carcinoma was 8.3% (2/24)
- Divided into mucin-rich versus mucin-poor on PAS
- Squamoid morules in 25% (all in mucin-poor)

Pathological features of pyloric gland adenoma of the gallbladder in comparison with gastric subtype of intracholecystic papillary neoplasm

Yasuni Nakanuma [a,b,*], Takashi Sugino [a], Katsuyuki Nomura [c], Takuro Terada [d], Yasunori Sato [e], Yoshifumi Ohnishi [f]

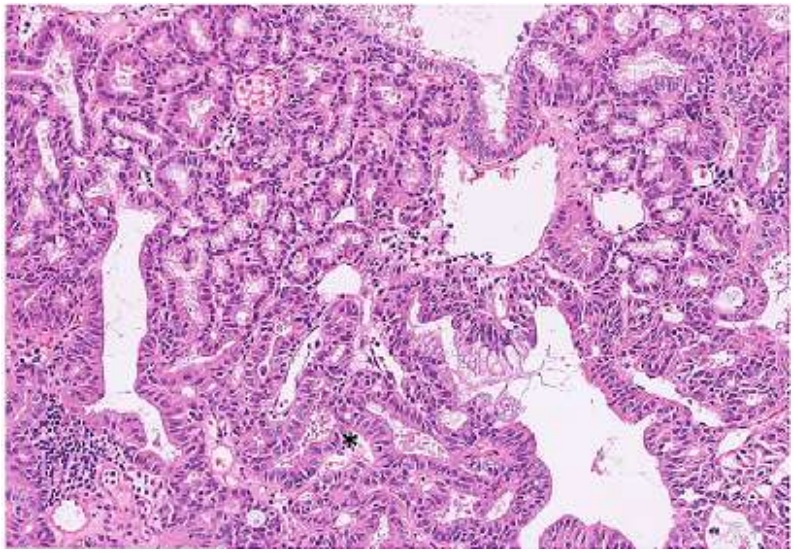
Definition of Pyloric Gland Adenoma:

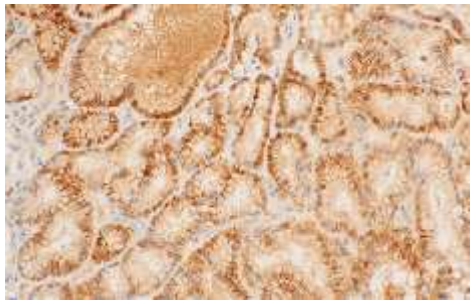
- Polypoid lesion, well-demarcated from surrounding mucosa
- Uniform back to back pyloric glands, tubular only → 7 cases
- Frequent luminal dilatation and cystic changes of glands
- Required >0.5 cm

Definition of Intracholecystic Papillary Neoplasm, Gastric subtype:

- Grossly visible and > 1 cm largest diameter
- Height >0.5 cm (otherwise considered BilIN) → 14 cases
- Regional differentiation towards gastric foveolar or pyloric glands
- Divided into foveolar predominant (>70%), pyloric predominant (>70%) and mixed foveolar/pyloric (each component more than 30%)

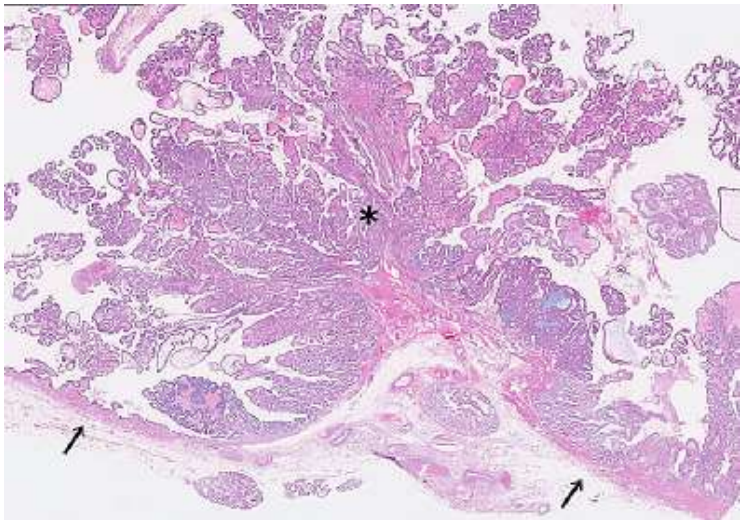
Pyloric Gland Adenoma





Beta-catenin

“Conglomerated” gICPN



Microscopic Findings

- Pyloric Gland Adenoma
  - Packed tubular components with cuboidal/low columnar cells with basal nuclei
  - Stroma was fine fibrovascular, edematous or inflammatory
  - Intratumoral cholesterosis in 2/7
  - Squamous morules in 2/7
- gICPN
  - Papillary and tubular components
  - Stroma was fine fibrovascular
  - 2 pyloric predominant, 6 foveolar predominant, and 2 mixed pyloric/foveolar
  - No pyloric predominant solitary→ were all classified as PGA

Dysplasia

Table 1
Incidence of histologic featues in PGA and gICPN of the gallbladder.

	PGA (n = 7)	gICPN		
		Total (n = 14)	Solitary (n = 5)	Conglomerated (n = 9)
Low-grade:high-grade dysplasia	2:5	0:14	0:5	0:9
Type 1:type 2	7:0	7:7	3:2	4:5
Focal stromal invasion	0	3	0	3
Squamoid morules	2	0	0	0
Intratumoral cholesterosis	2	0	0	0

PGA, pyloric gland adenoma; gICPN, intracholecystic papillary neoplasm of gastric subtype.

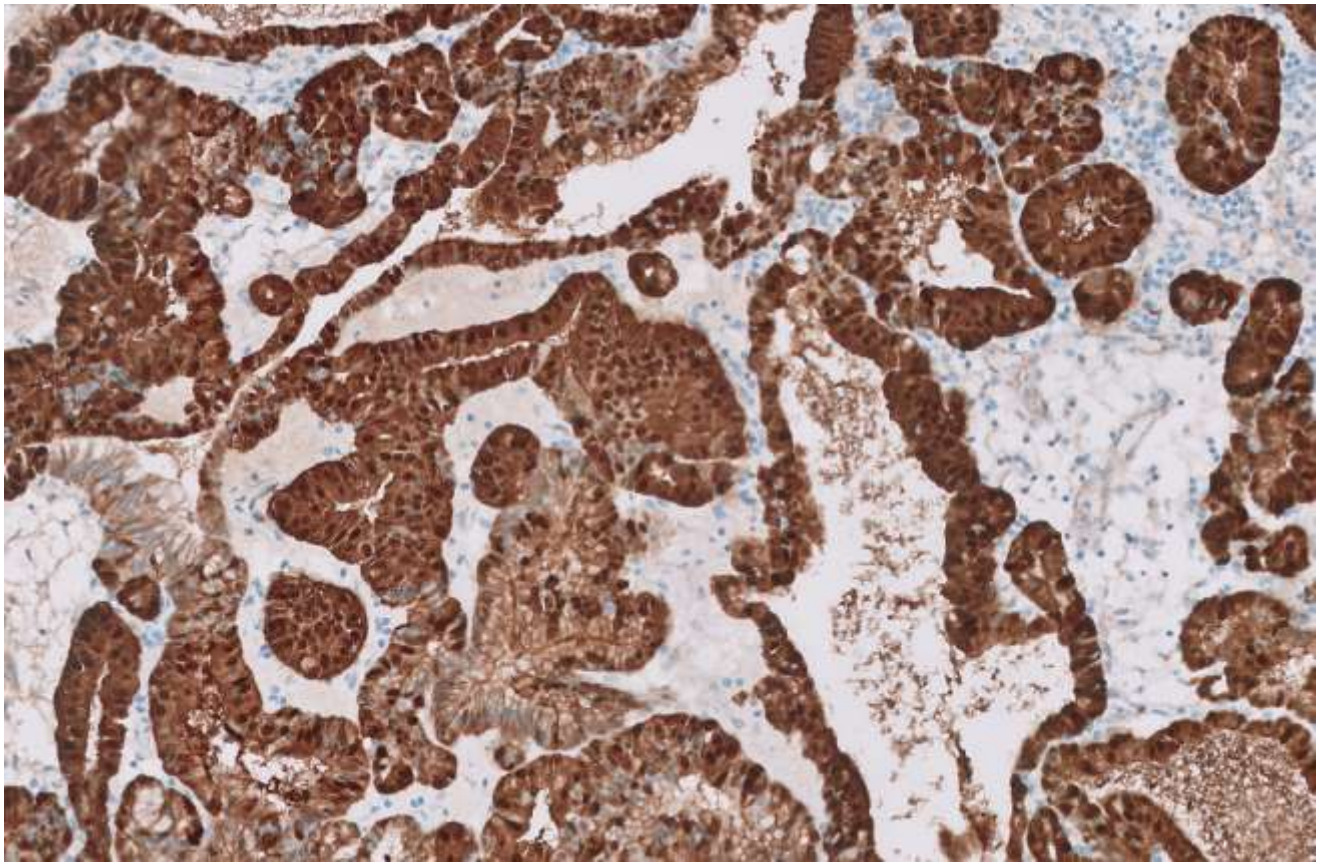
Immunohistochemistry

Table 2
Immunohistochemical findings in PGA and gICPN of the gallbladder.

	PGA (n = 7)	gICPN		
		Total (*n* = 8)	Solitary (*n* = 3)	Conglomerated (n = 5)
β-catenin (negative: positive)	1:6	8:0	3:0	5:0
P53 (-:+:++ ~+++)	6:1:0	5:2:1	3:0:0	2:2:1
dPAS (-:+:++ ~+++)	0:6:1	2:5:1	1:1:1	1:2:2
MUC1 (-:+:++ ~+++)	7:0:0	4: 3:1	2:1:0	2:2:1
MUC2 (-:+:++ ~+++)	6:1:0	5:1:2	2:1:0	3:0:2
MUC5AC (-:+:++ ~+++)	0:5:3	1:4:3	0:2:1	1:2:2
MUC6 (-:+:++ ~+++)	0:0:7	0:4:4	0:2:1	0:2:3
CK7 (-:+:++ ~+++)	0:0:7	1:0:7	0:0:3	1:0:4
CK20 (-:+:++ ~+++)	6:1:0	4:1:3	2:1:0	2:1:2
CDX2 (-:+:++ ~+++)	6:1:0	6:2:0	2:1:0	3:2:0

PGA, pyloric gland adenoma; gICPN, intracholecystic papillary neoplasm of gastric subtype;
-, negative; +, 1–10% positive neoplastic cells in whole tumor; ++-+++, 10–100% positive neoplastic cells in whole tumor.

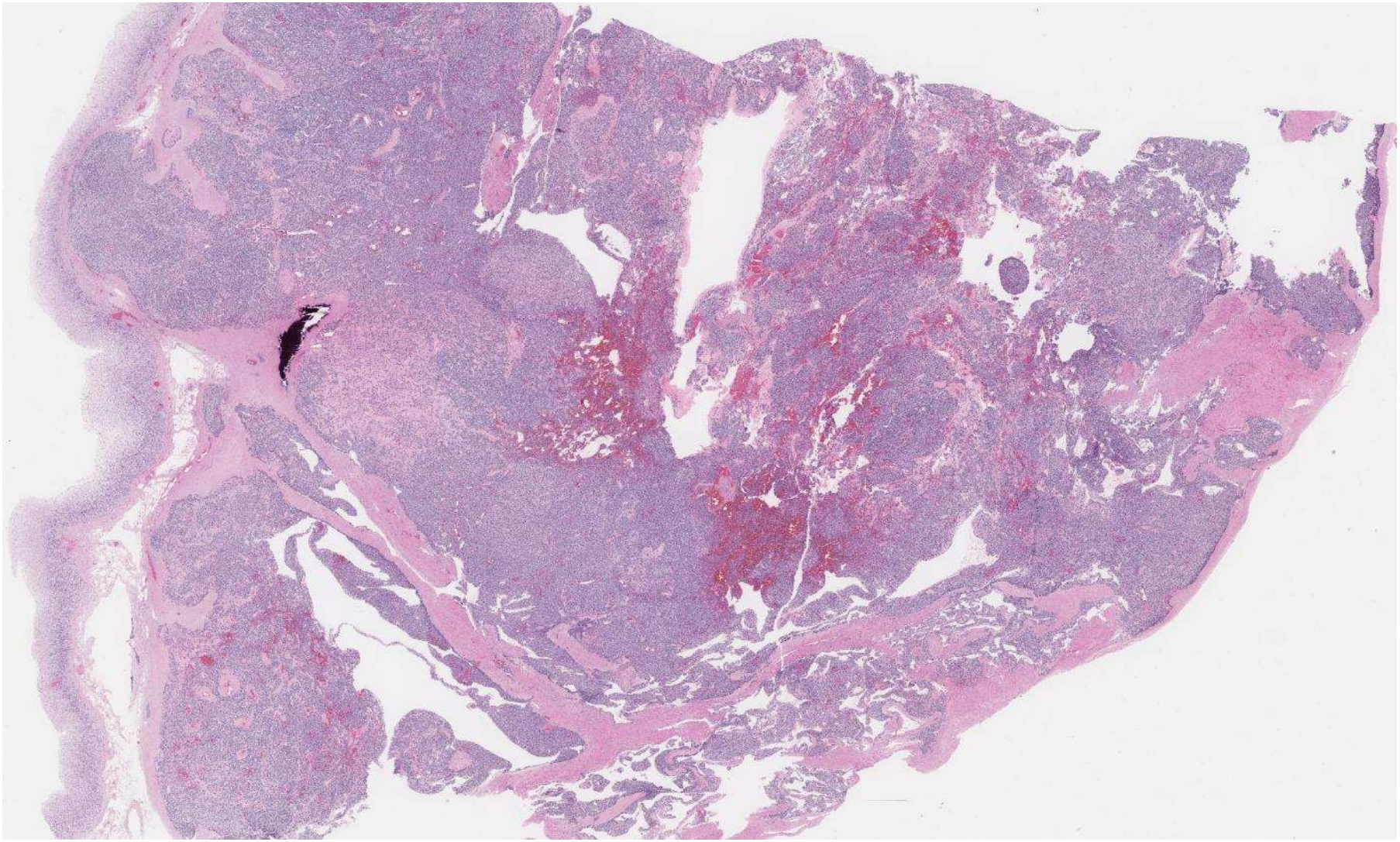
Beta Catenin

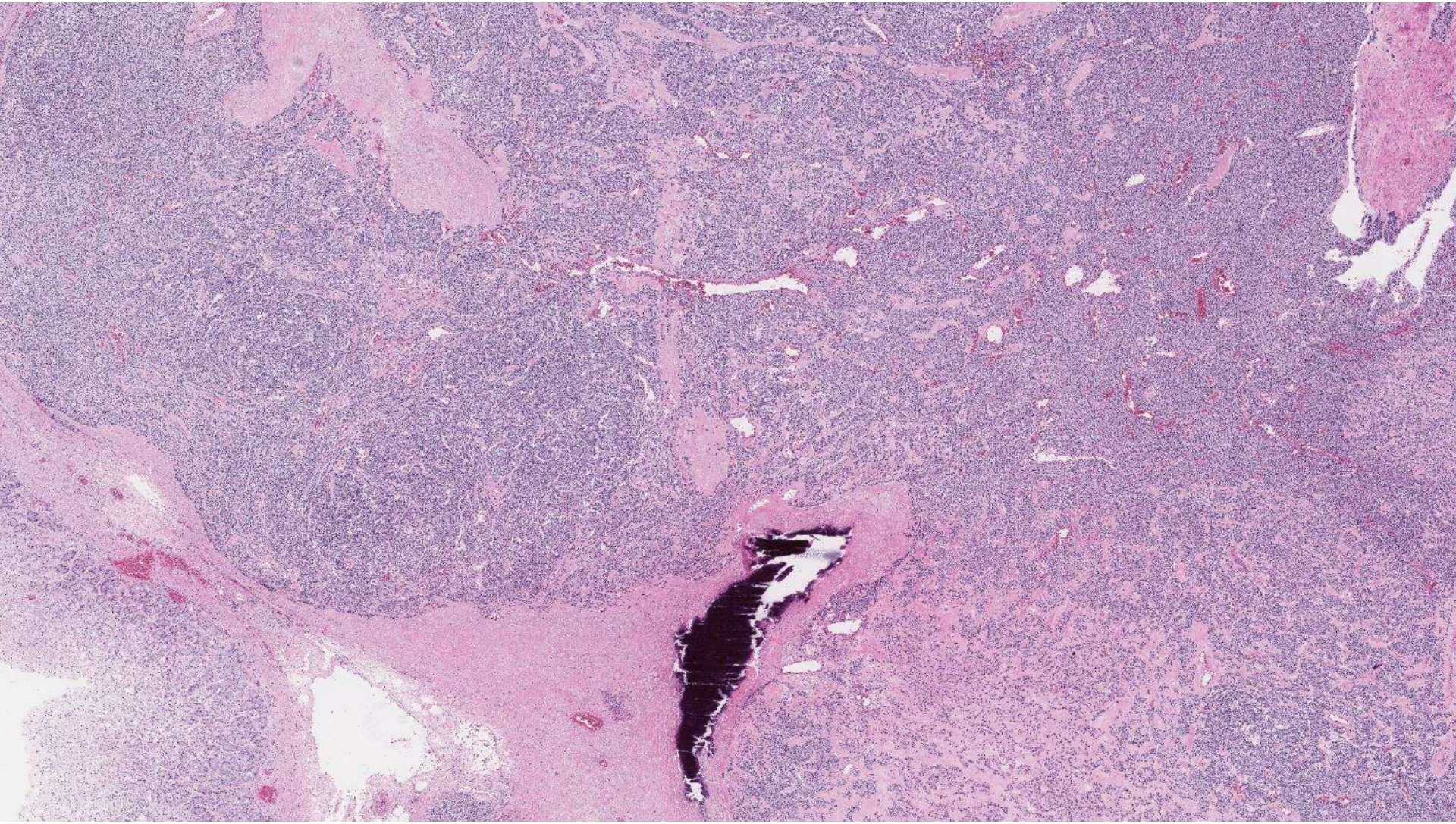


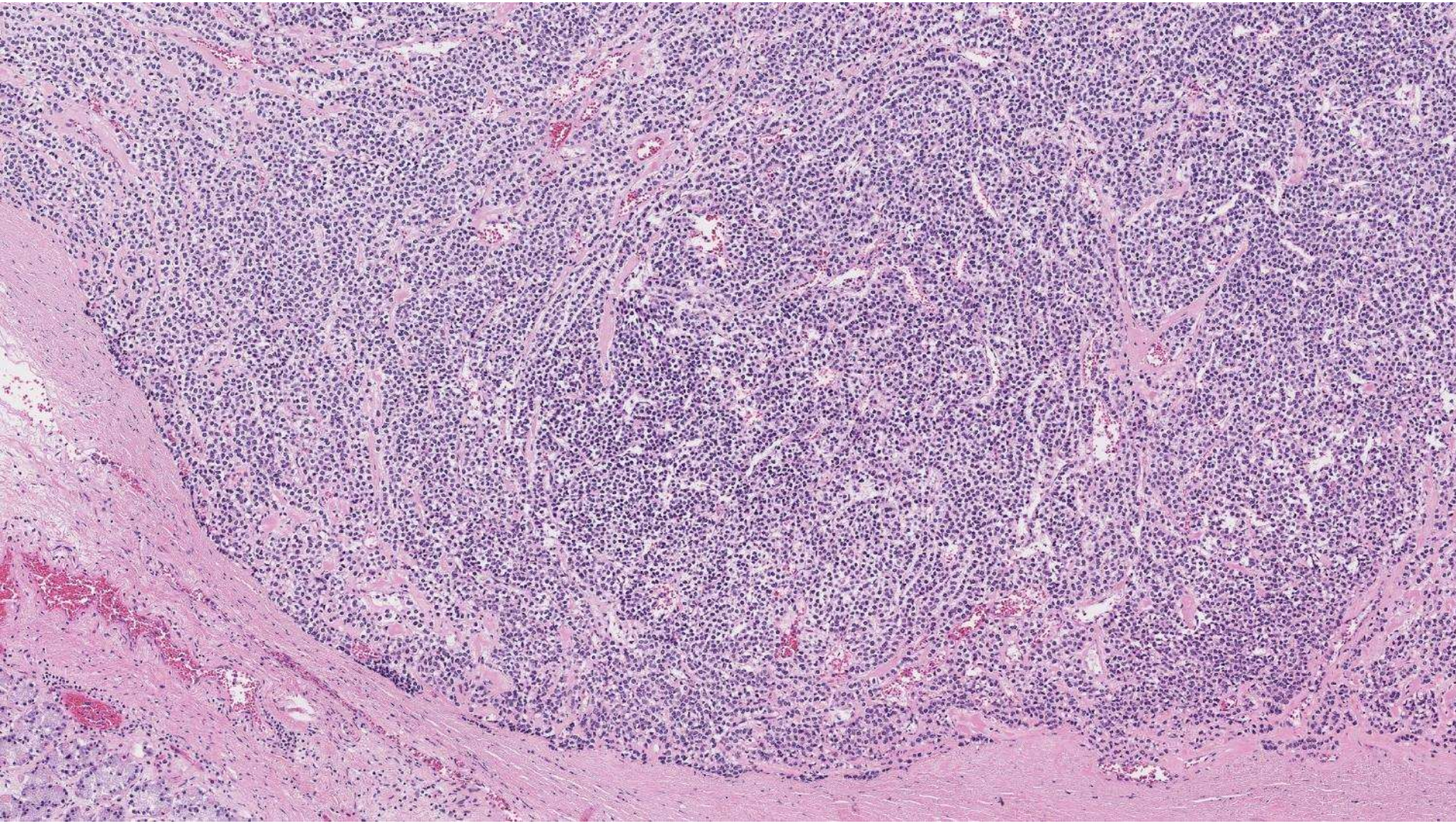
22-0405

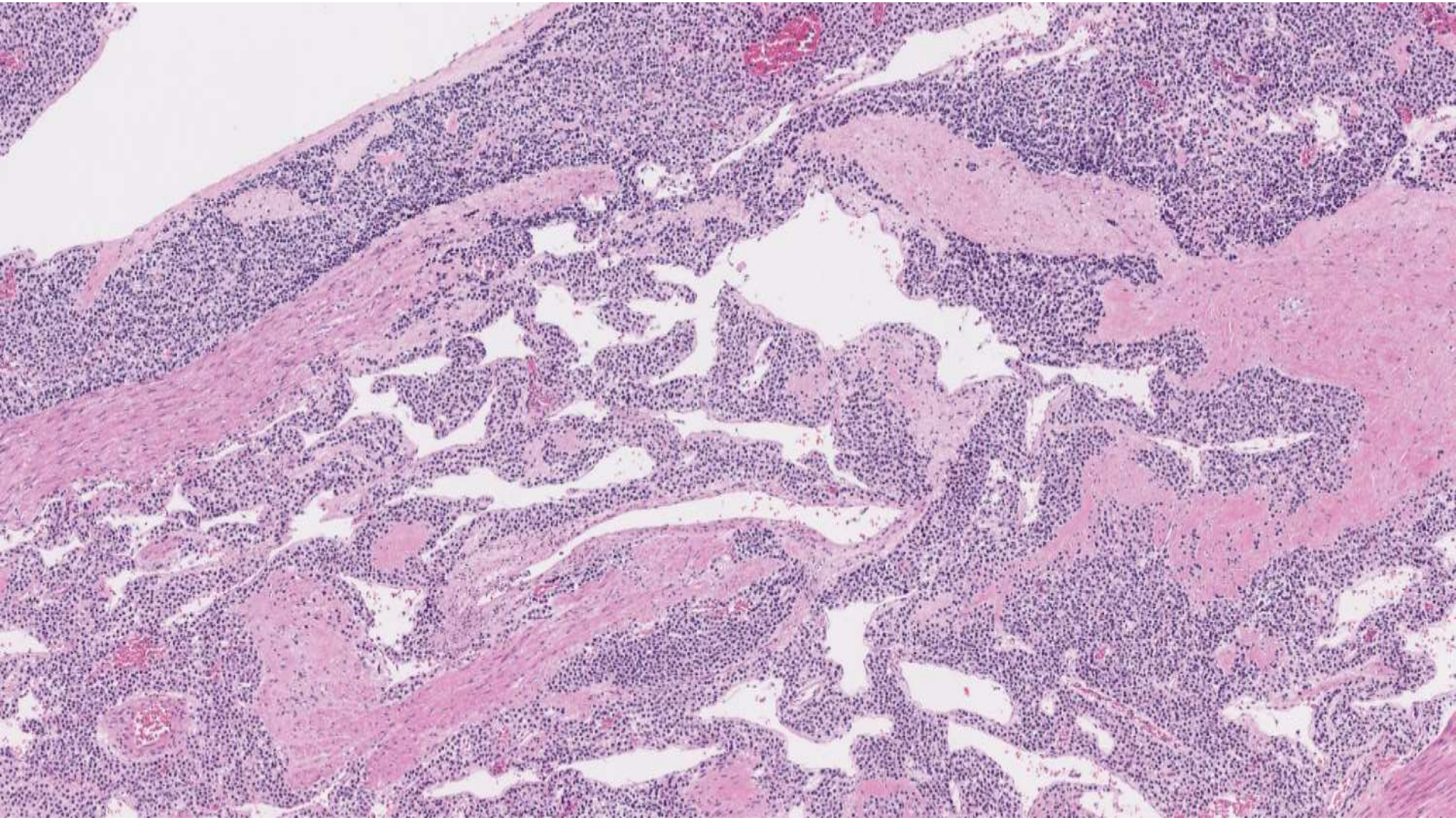
Andrew Xiao/Sarah Umetsu; UCSF

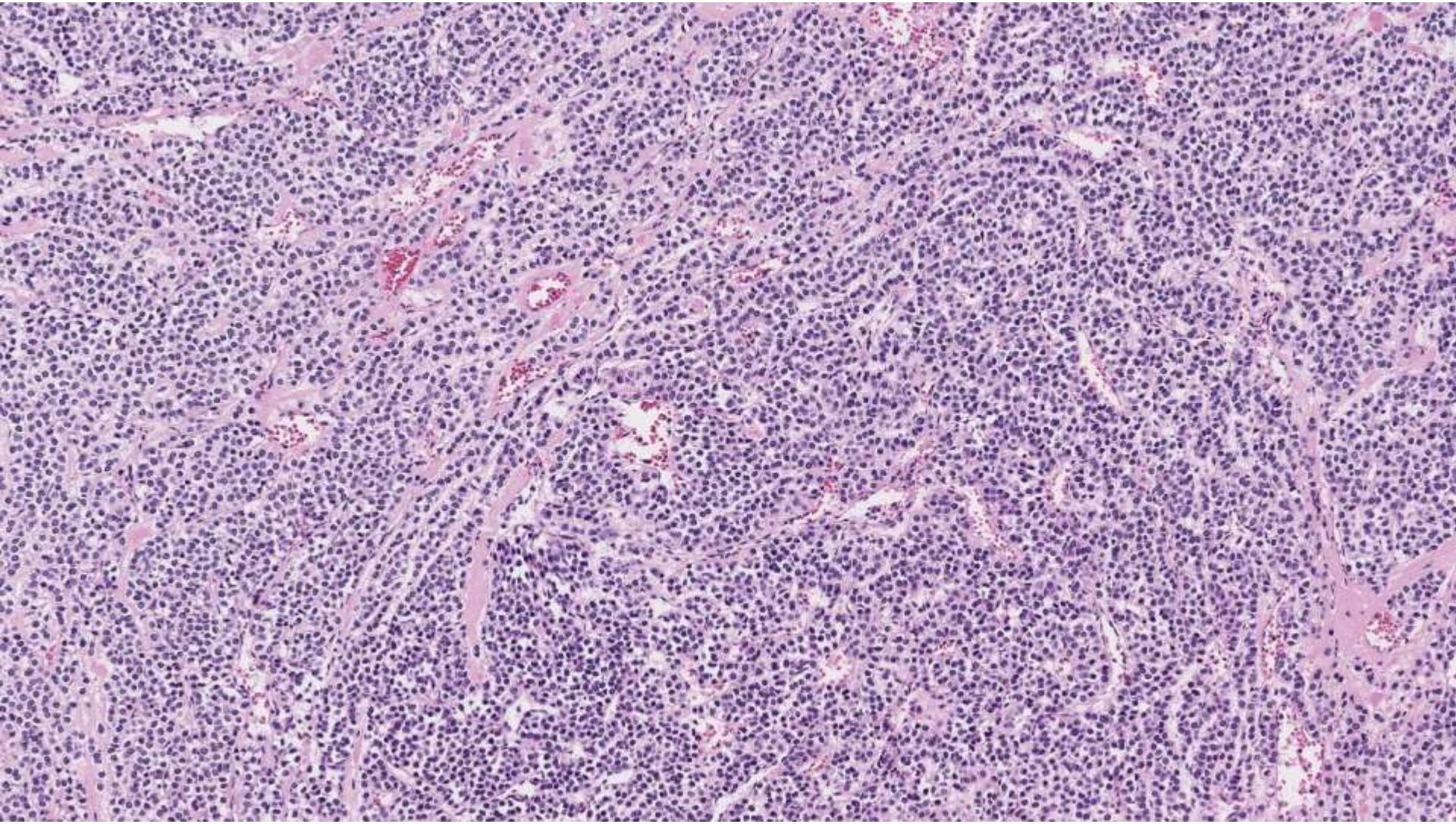
60ish M underwent radical prostatectomy for prostatic adenocarcinoma and expired from cardiac arrest during procedure. At autopsy, 2.5cm mass was identified in gastric body.

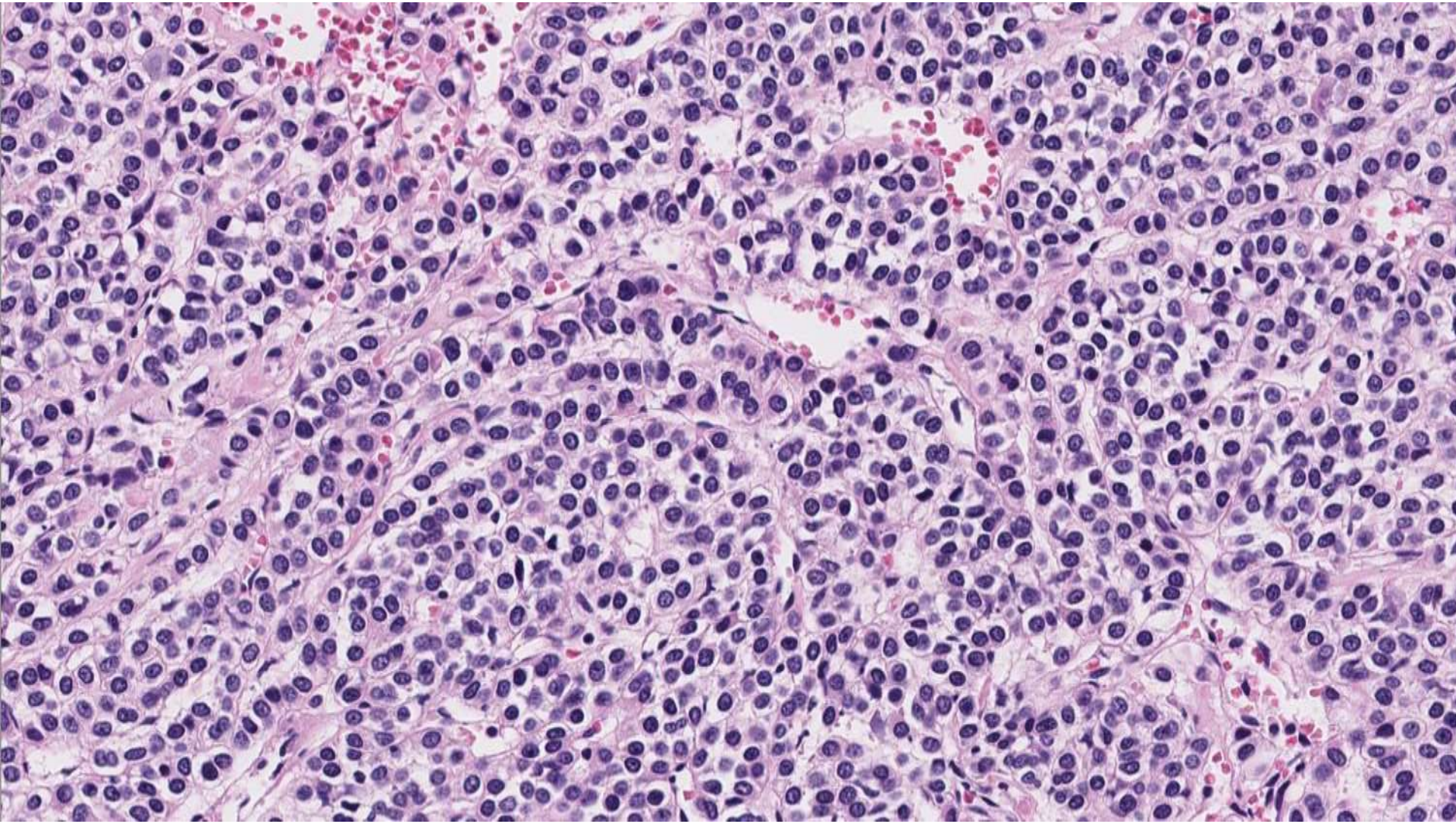






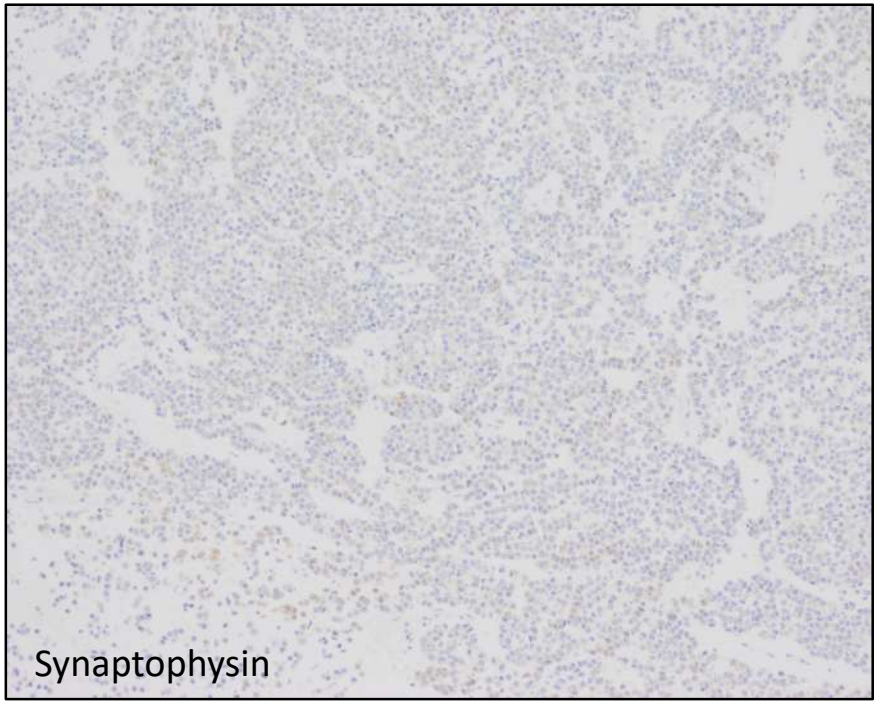


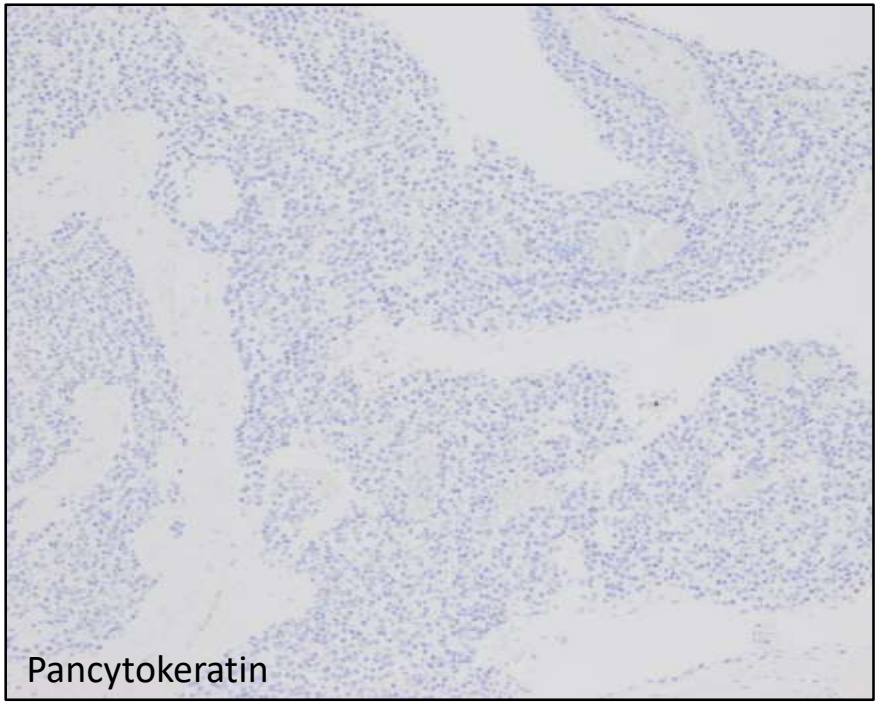


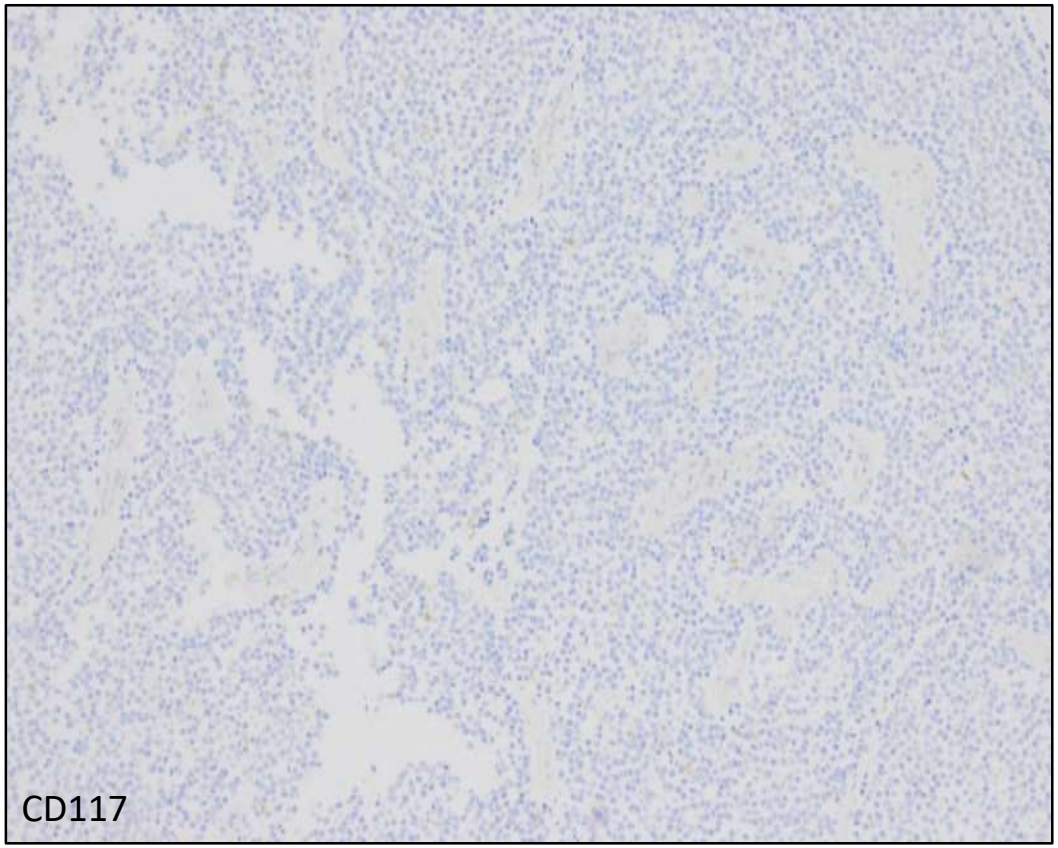


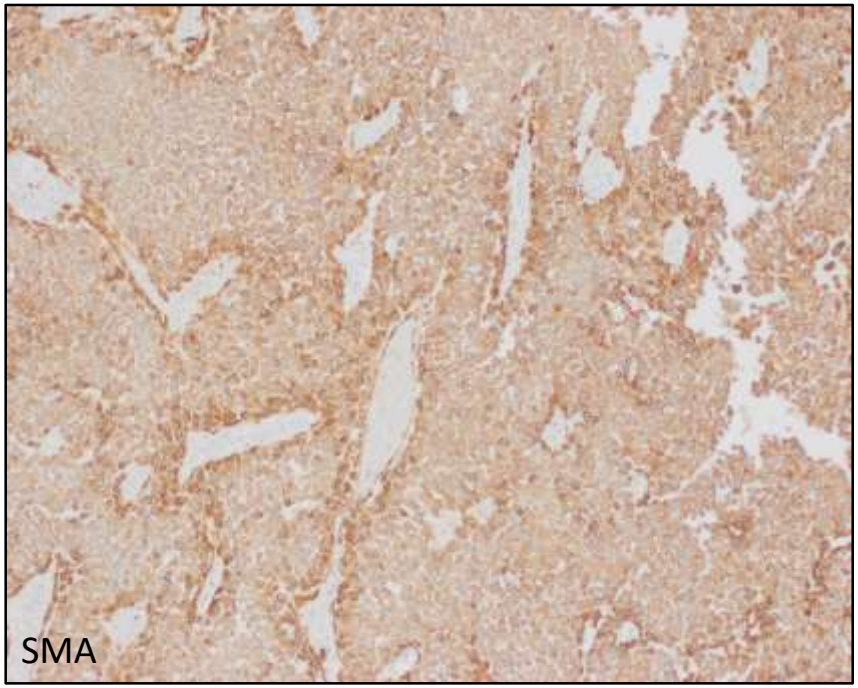
Differential Diagnosis

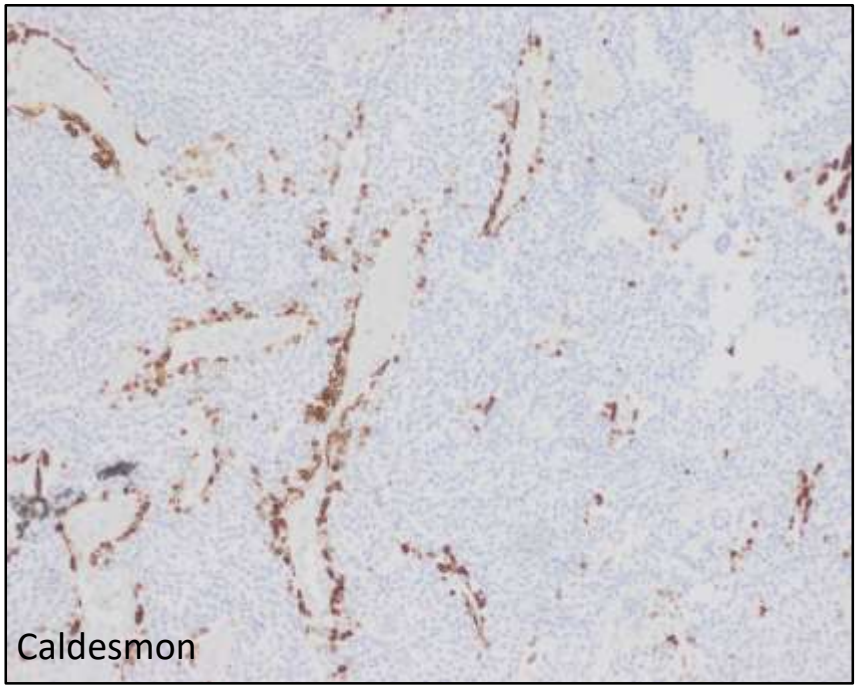
- Well-differentiated neuroendocrine tumor
- Epithelioid gastrointestinal stromal tumor
- Paraganglioma
- Glomus tumor
- Vascular neoplasm


Synaptophysin


Pancytokeratin

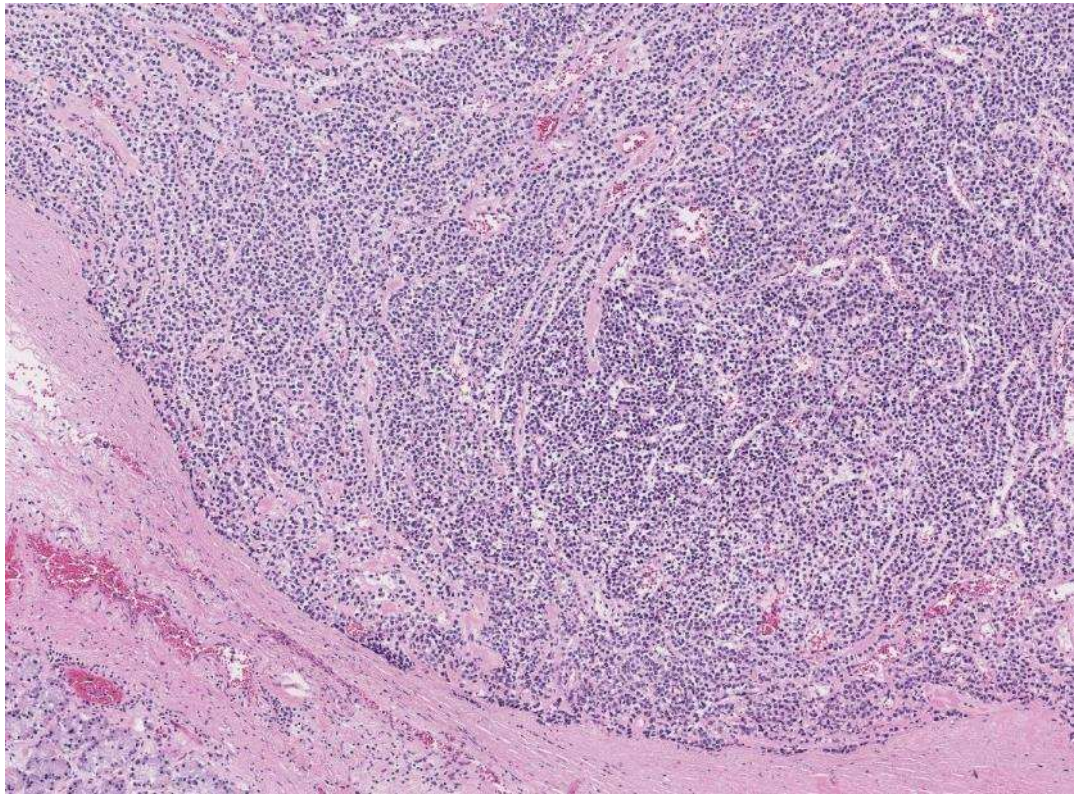

CD117


SMA


Caldesmon

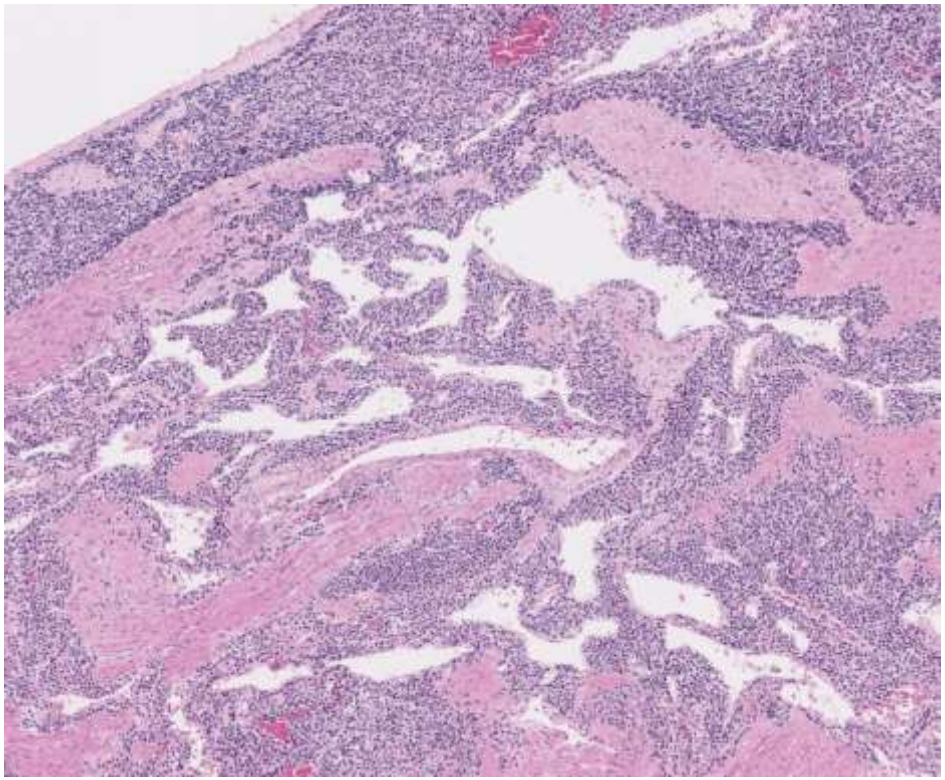
Glomus Tumor

Key Microscopic Features



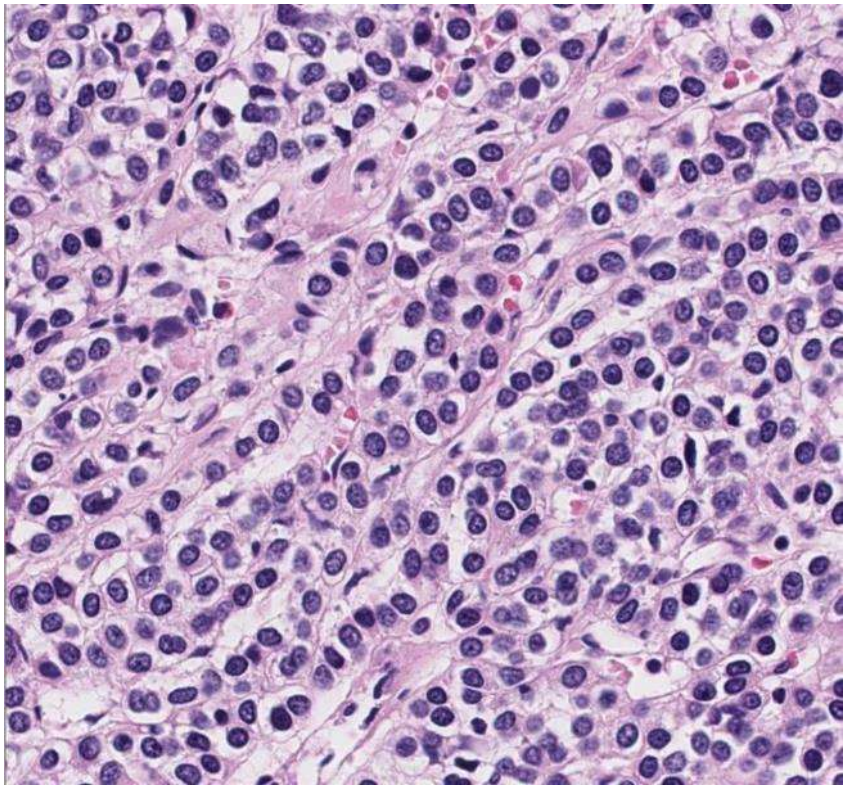
- Solid to nodular architecture
- Sharply demarcated

Key Microscopic Features



- Often organized around prominently dilated vascular spaces
- Hemorrhage is common

Key Microscopic Features



- Polygonal cells with centrally located **round** nuclei
- Pale eosinophilic to clear cytoplasm
- Delicate chromatin
- Inconspicuous nucleoli
- Low mitotic activity (most cases <1/50 HPF)

Glomus Tumor - Clinical Profile

- All locations
  - Slight female predilection (~63%)
  - Median age: 55
  - Location:
    - Often in the skin, distal extremities
    - Rare cases can arise in GI tract & retroperitoneum
- Gastric glomus tumor can present with GI bleeding or ulcer-like symptoms
- Largely benign behavior; malignant counterpart is exceedingly rare

References

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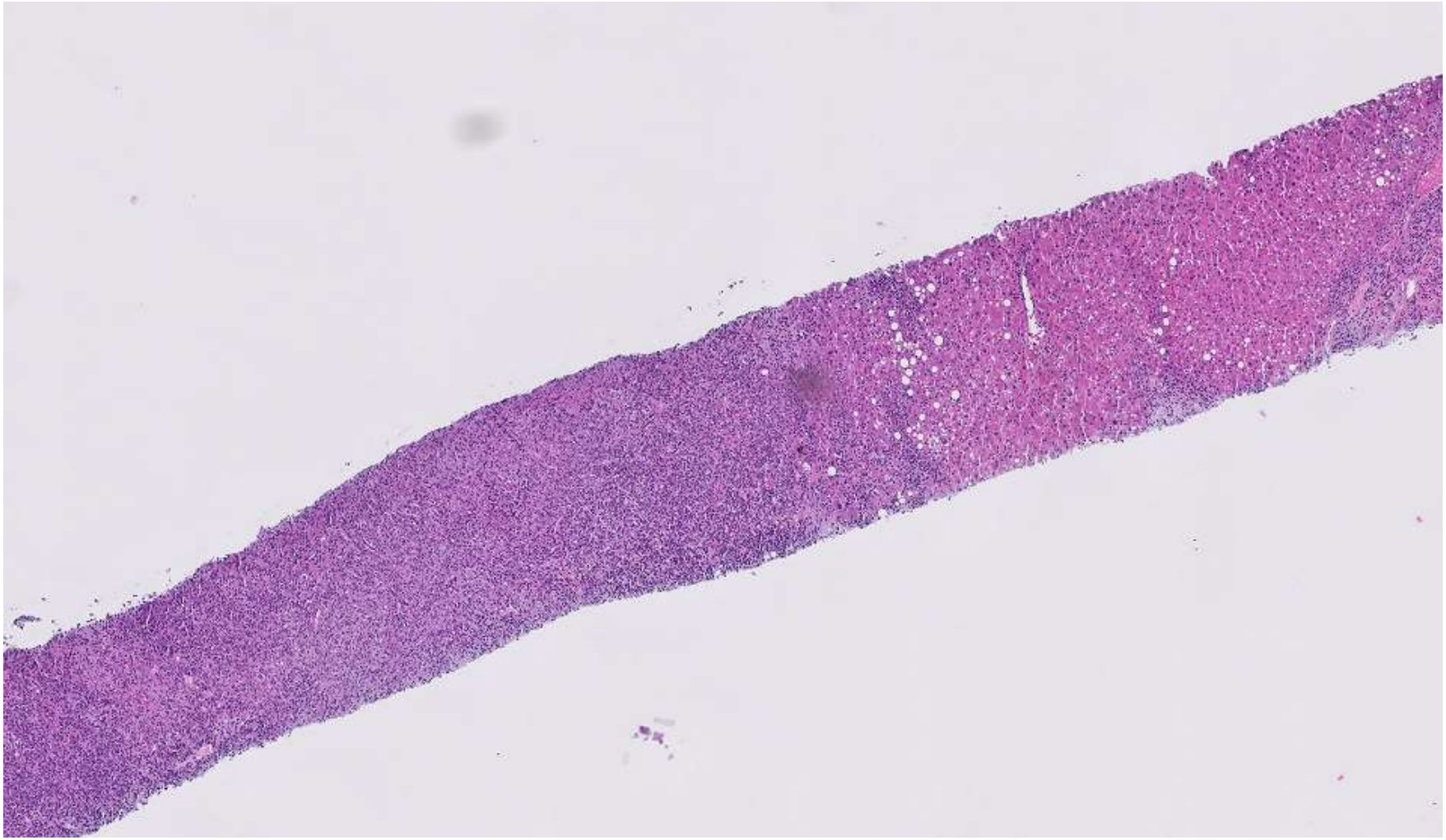
22-0706

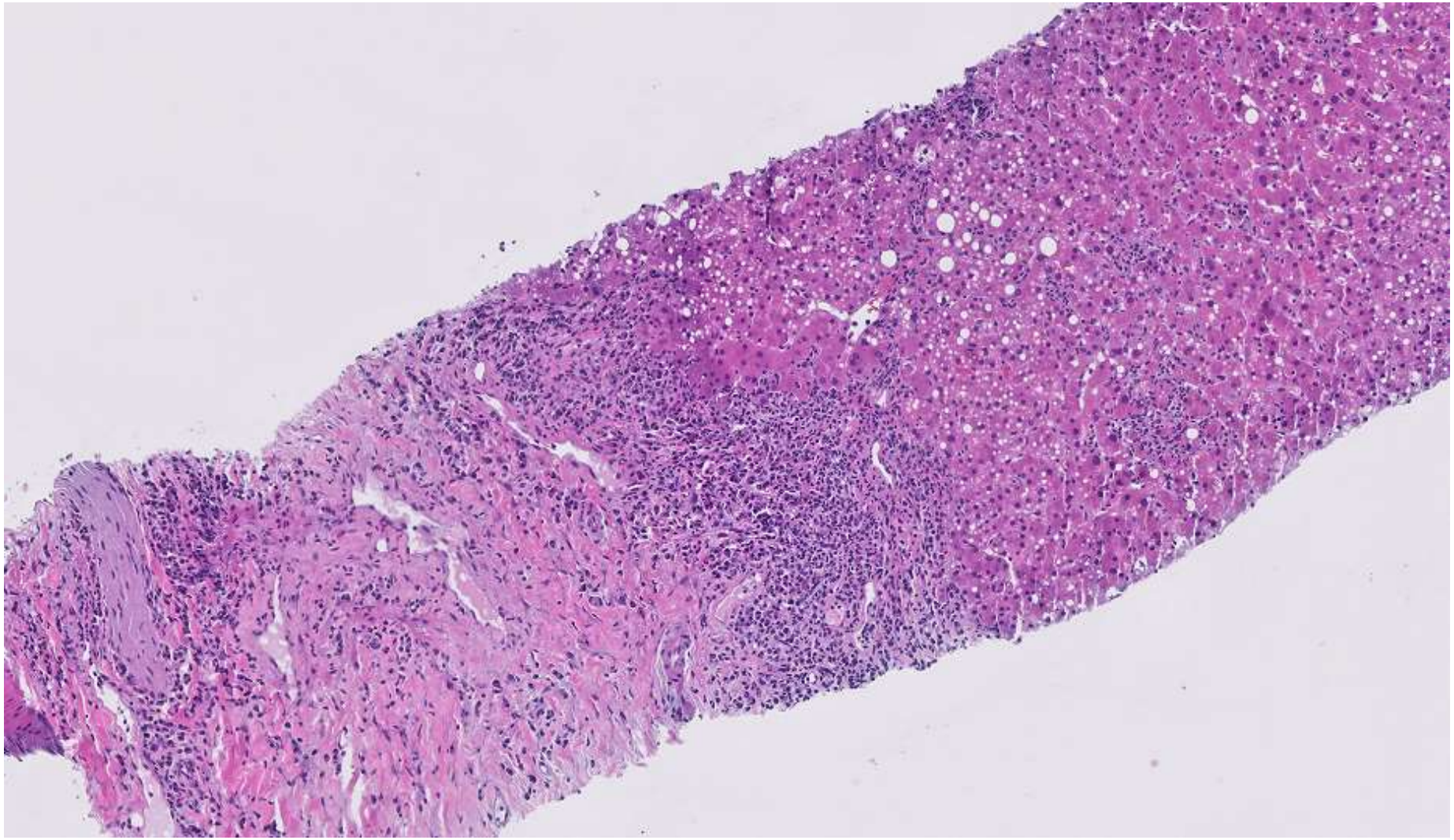
Nikka Khorsandi/Bob Ohgami; UCSF

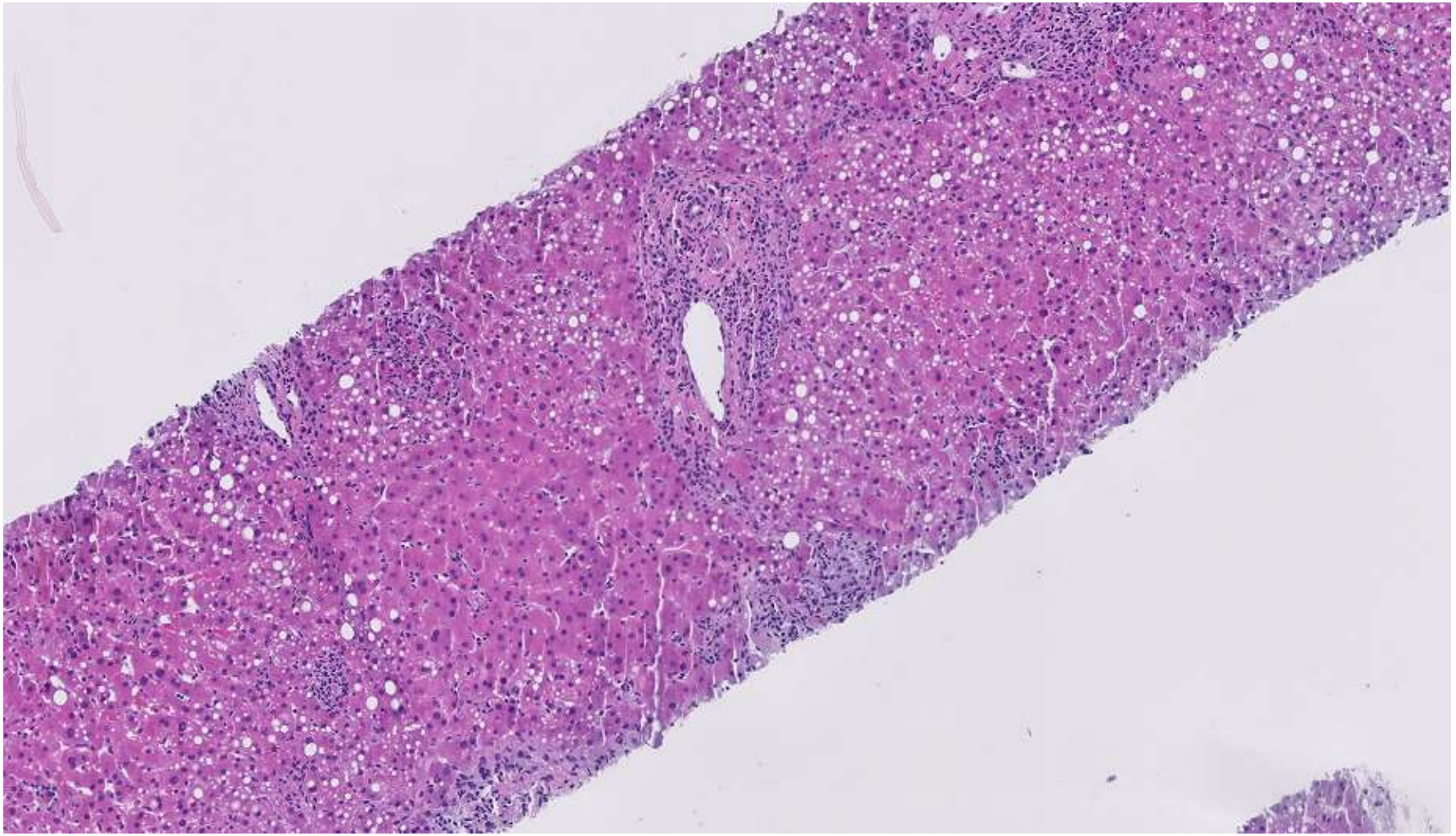
Middle-aged M with 1 year h/o night sweats, weight loss, lymphadenopathy, and bone/liver lesions. Liver bx.

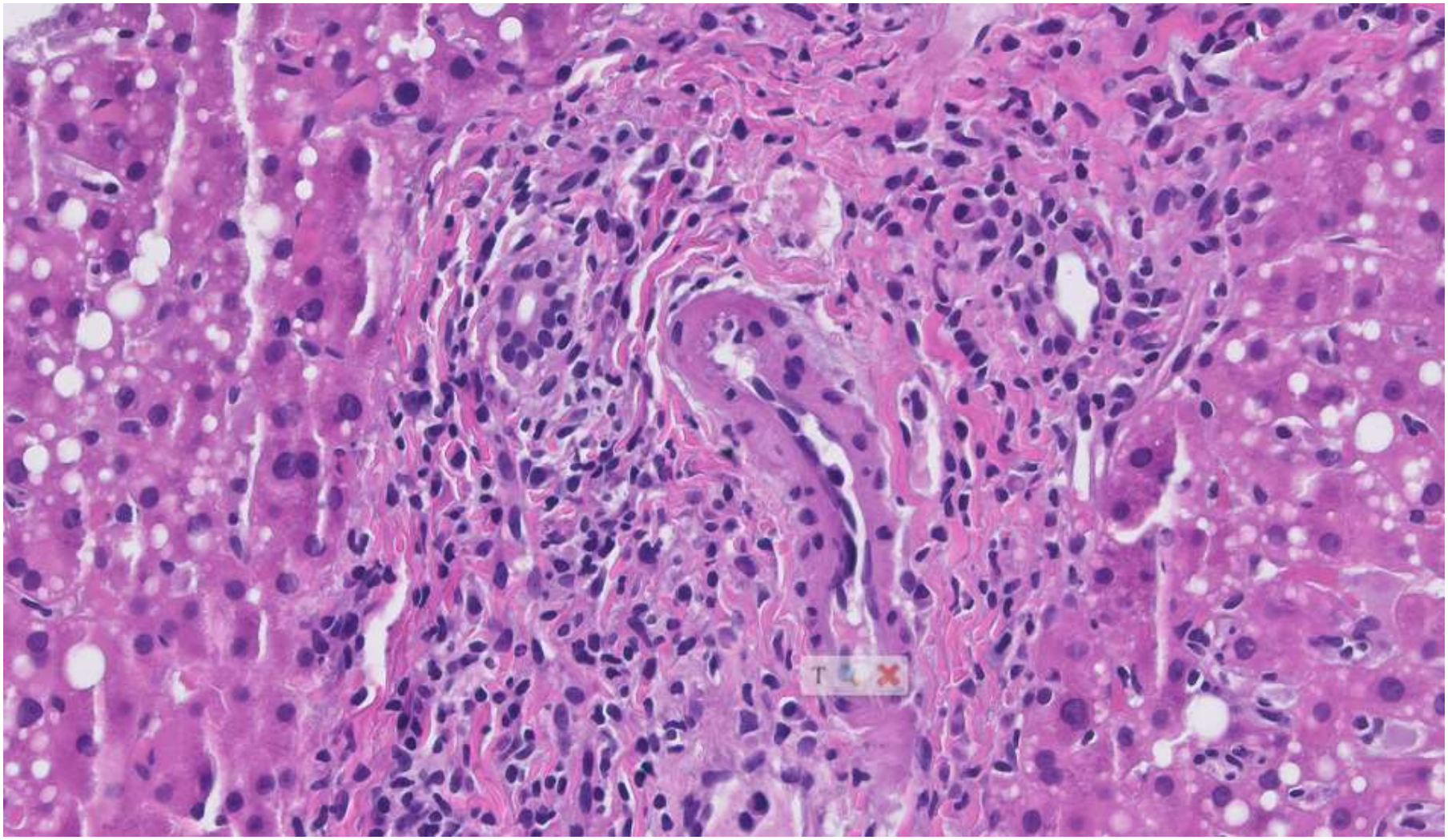
Clinical History

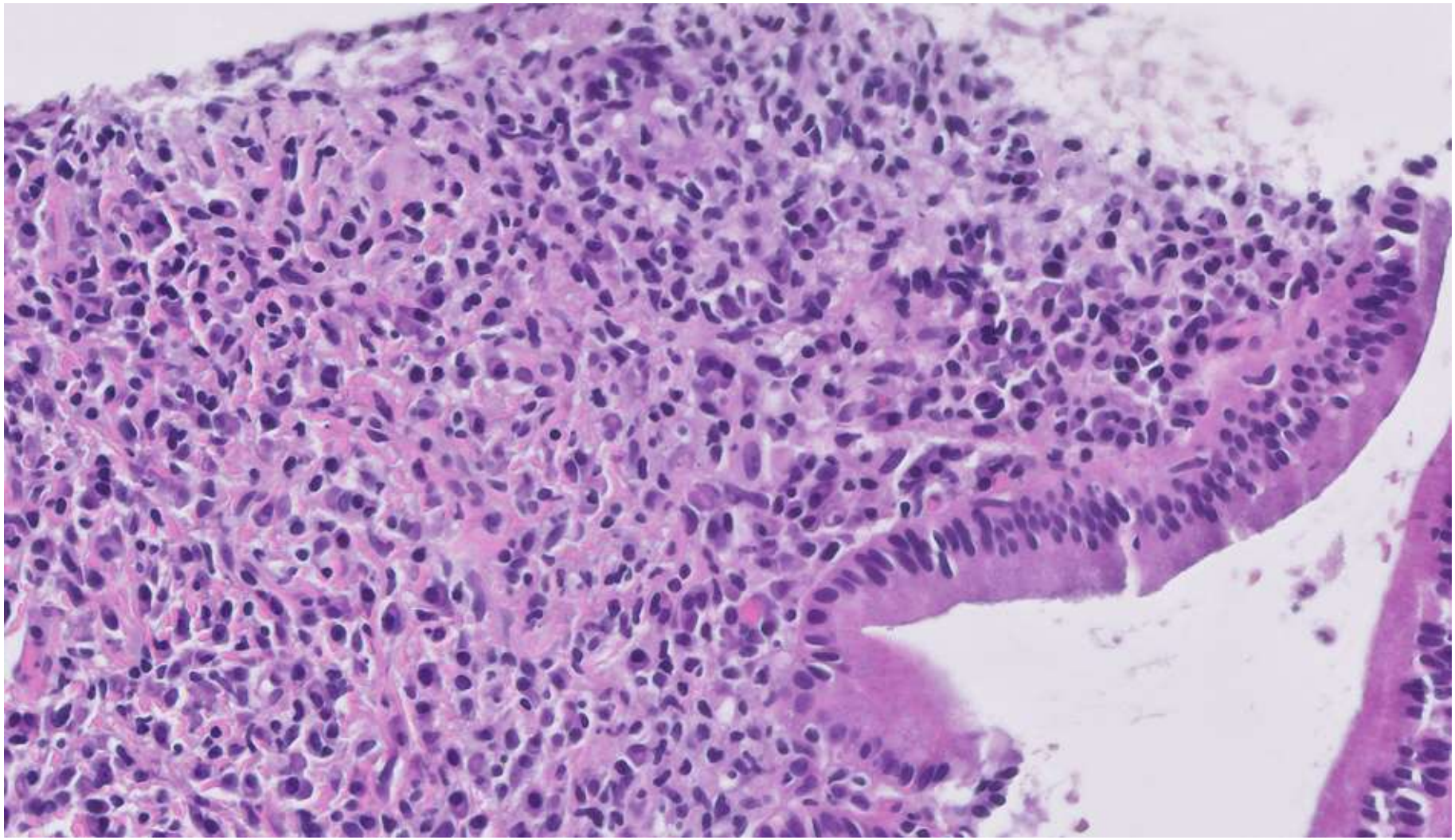
- 38 year old man
- 1 year of night sweats and weight loss, cervical lymphadenopathy (normal by ultrasound); stated weeks after a mild COVID infection.
- Small sclerotic bone lesions (sternum, ribs, spine)
- Multiple, small hypoechoic liver lesions (largest two were 1.1 cm, each)
- Lymph nodes, liver lesions, and bone lesions all PET avid.
- Labs:
- AlkP 130 (H), AST 77 (H), ALT 45 (H), Tbili 1 (N).
- Hepatitis panel consistent with previous vaccination.
- CRP 22 (H).
- Normal BMP
- CBC showed HGB 12.9 (L), PLT 442 (H).











IHC Stains

- CD30: Negative
- CD15: Negative
- PAX5: Highlights B cells
- CD45: Positive in lymphocytes, histiocytes, and plasma cells
- CD20: Highlights B cells
- CD3: Highlights T cells
- CD8: Highlights T cells
- CD4: Highlights histiocytes and T cells
- CD138: Highlights plasma cells
- CD56: Negative
- EBV: Negative
- Kappa: Lambda: ~2:1
- BCL6: Negative
- Gram stain: No organisms identified
- Fite stain: No organisms identified
- PAS-F: No organisms identified
- Cam5.2 and AE1/3: Negative
- CD1a: Negative
- PD1: Negative
- IgG4 and IgG: Rare positive subset among IgG positive cells.

Unknown Case Presentation

Nikka Khorsandi, MD, MPH, PGY-1, UCSF

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Ruth Zhang, MD, GI Pathology Fellow, UCSF

Elizabeth Williams, MD, Boise Pathology Group

Clinical History

- 38 year old man
- 1 year of night sweats and weight loss, cervical lymphadenopathy (normal by ultrasound); stated weeks after a mild COVID infection.
- Small sclerotic bone lesions (sternum, ribs, spine)
- Multiple, small hypoechoic liver lesions (largest two were 1.1 cm, each)
- Lymph nodes, liver lesions, and bone lesions all PET avid.
- Labs:
- AlkP 130 (H), AST 77 (H), ALT 45 (H), Tbili 1 (N).
- Hepatitis panel consistent with previous vaccination.
- CRP 22 (H).
- Normal BMP
- CBC showed HGB 12.9 (L), PLT 442 (H).

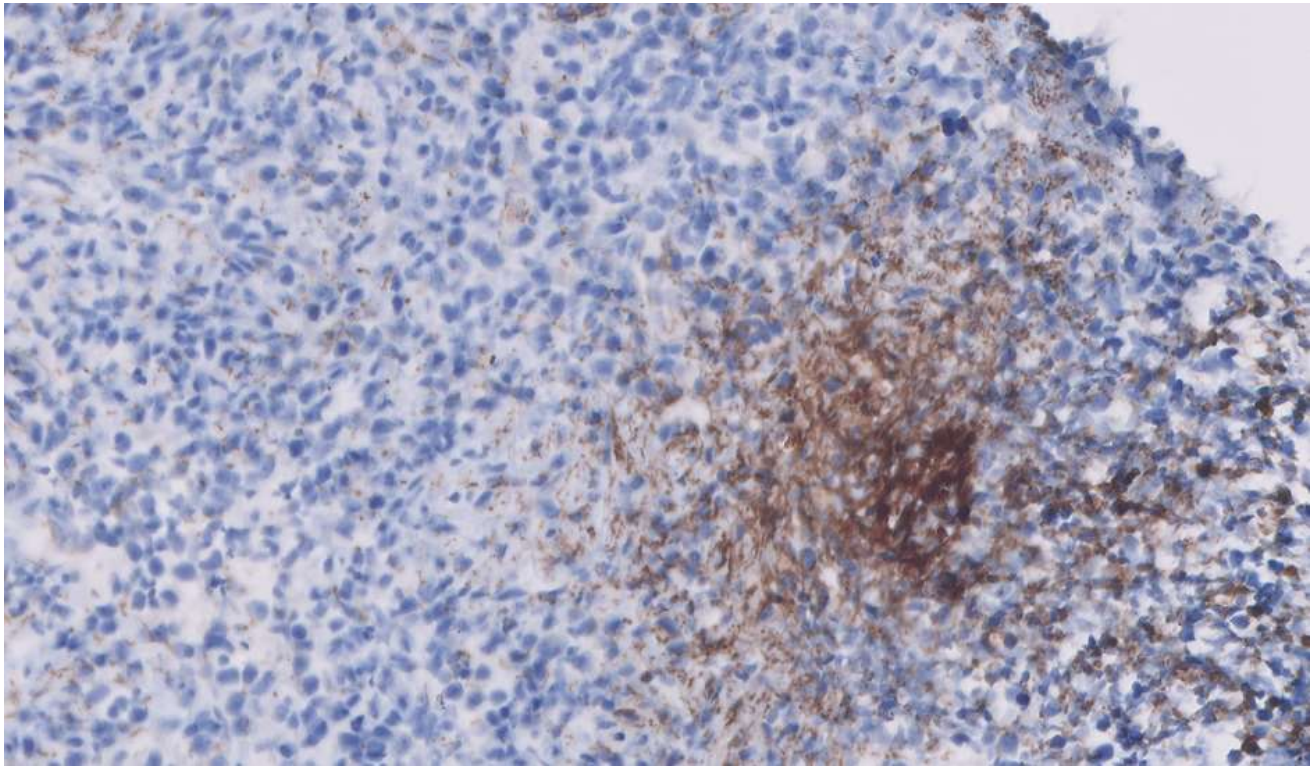
IHC Stains

- CD30: Negative
- CD15: Negative
- PAX5: Highlights B cells
- CD45: Positive in lymphocytes, histiocytes, and plasma cells
- CD20: Highlights B cells
- CD3: Highlights T cells
- CD8: Highlights T cells
- CD4: Highlights histiocytes and T cells
- CD138: Highlights plasma cells
- CD56: Negative
- EBV: Negative
- Kappa: Lambda: ~2:1
- BCL6: Negative
- Gram stain: No organisms identified
- Fite stain: No organisms identified
- PAS-F: No organisms identified
- Cam5.2 and AE1/3: Negative
- CD1a: Negative
- PD1: Negative
- IgG4 and IgG: Rare positive subset among IgG positive cells.

Differential Considerations?

- Hematologic malignancies (stains showed no abnormal lymphoproliferation)
- Autoimmune hepatitis (AST/ALT usually >> AlkP)
- Hodgkin Lymphoma (No RS cells, CD30 and CD15 negative)
- IgG4 Disease (IgG4 only highlighted rare positive cells)
- Infectious agents (Negative bug stains)
- Others?

Treponema Pallidum IHC



Additional History

- Patient had longstanding history of skin lesions previously biopsied as “atypical lymphoid infiltrate”.
- Also positive with T. pallidum IHC.

Histology of Hepatic Secondary Syphilis

- Rate of primary and secondary syphilis increasing 11.2%/yr (2018-19) in the US.
  - In 2019, California had 4th highest rate of primary and secondary syphilis.
- Primary: Painless chancre with lymphadenopathy
- Secondary: Disseminated disease can involve skin, liver, GI tract, synovium, periosteum, kidney, eyes, and meninges.
- Review of 14 liver biopsy cases of secondary syphilis that identified five patterns of histologic presentation:
  - Malvar G, Cardona D, Pezhouh MK, et al. Hepatic Secondary Syphilis Can Cause a Variety of Histologic Patterns and May Be Negative for Treponeme Immunohistochemistry. The American Journal of Surgical Pathology. 2021 Dec. DOI: 10.1097/pas.0000000000001848. PMID: 34864775.

Patterns of Secondary Syphilis (in 14 cases)

1. Biliary Pattern
   a. Ductular reaction, lymphocytic cholangitis, pericholangitis, portal edema, and cholestasis
2. Acute Hepatitis Pattern
   a. Lobular inflammation, patchy hepatocyte dropout, and necrosis.
3. Autoimmune Hepatitis Pattern
   a. Portal inflammation and interface hepatitis with plasma cells.
4. Necroinflammatory Mass Lesion Pattern
   a. Fibroblastic reactions with lymphoplasmacytic and neutrophilic inflammation around central necrotizing abscess.
5. No Particular Pattern
   a. Some combination of the patterns above.

Lessons Learned

- Secondary syphilis involving the liver can present with a variety of histologic manifestations living up to its title of “great imitator”
- Prognosis usually very good with treatment, so it is important to catch
- T. pallidum IHC is useful (however may be negative if patient has already started treatment)

References

- Centers for Disease Control and Prevention (2021). National Overview of STDs, 2019. Sexually Transmitted Disease Surveillance 2019; National Overview. https://www.cdc.gov/std/statistics/2019/overview.htm.
- Malvar G, Cardona D, Pezhouh MK, et al. Hepatic Secondary Syphilis Can Cause a Variety of Histologic Patterns and May Be Negative for Treponeme Immunohistochemistry. The American Journal of Surgical Pathology. 2021 Dec. DOI: 10.1097/pas.0000000000001848. PMID: 34864775.

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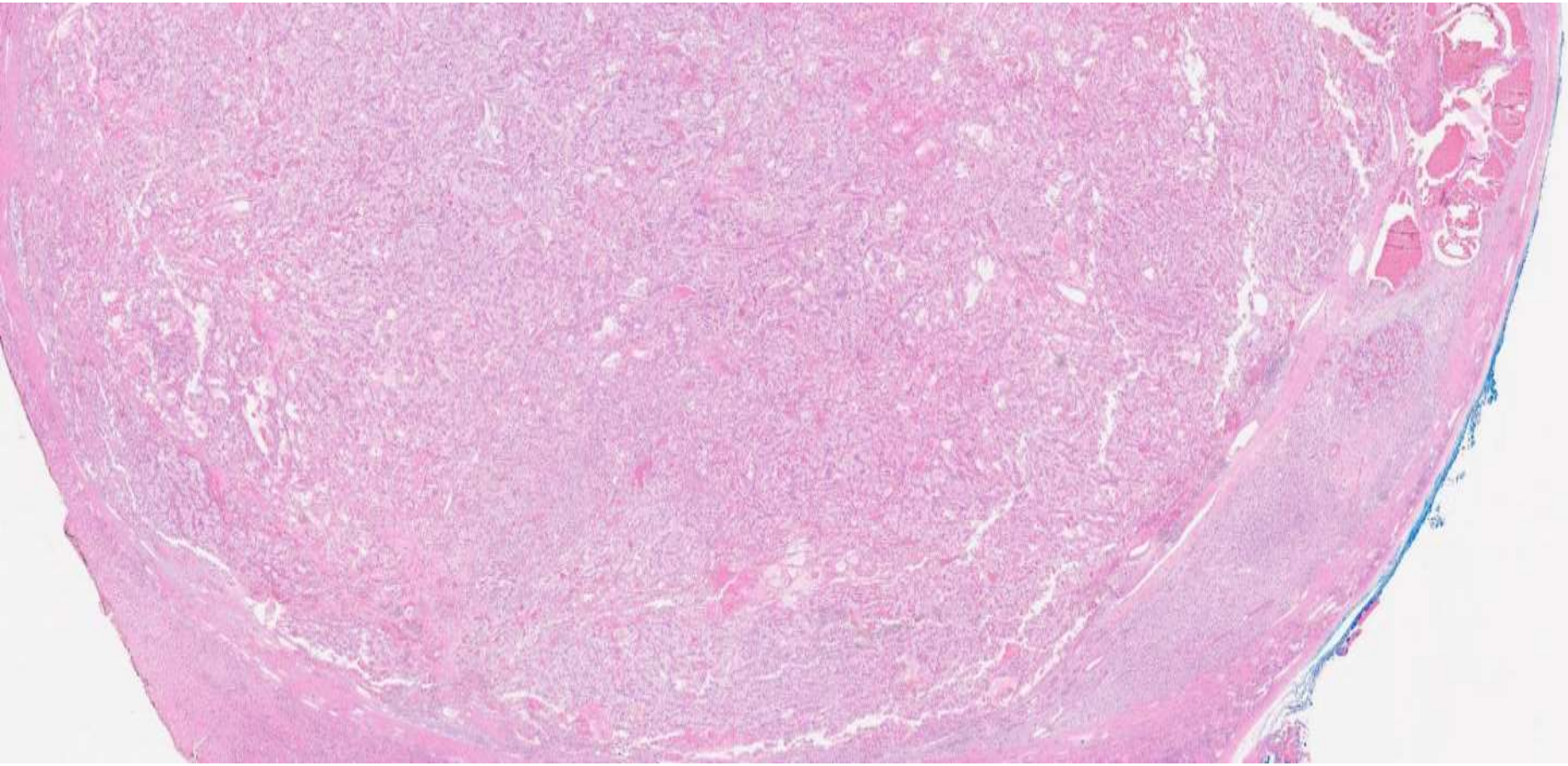
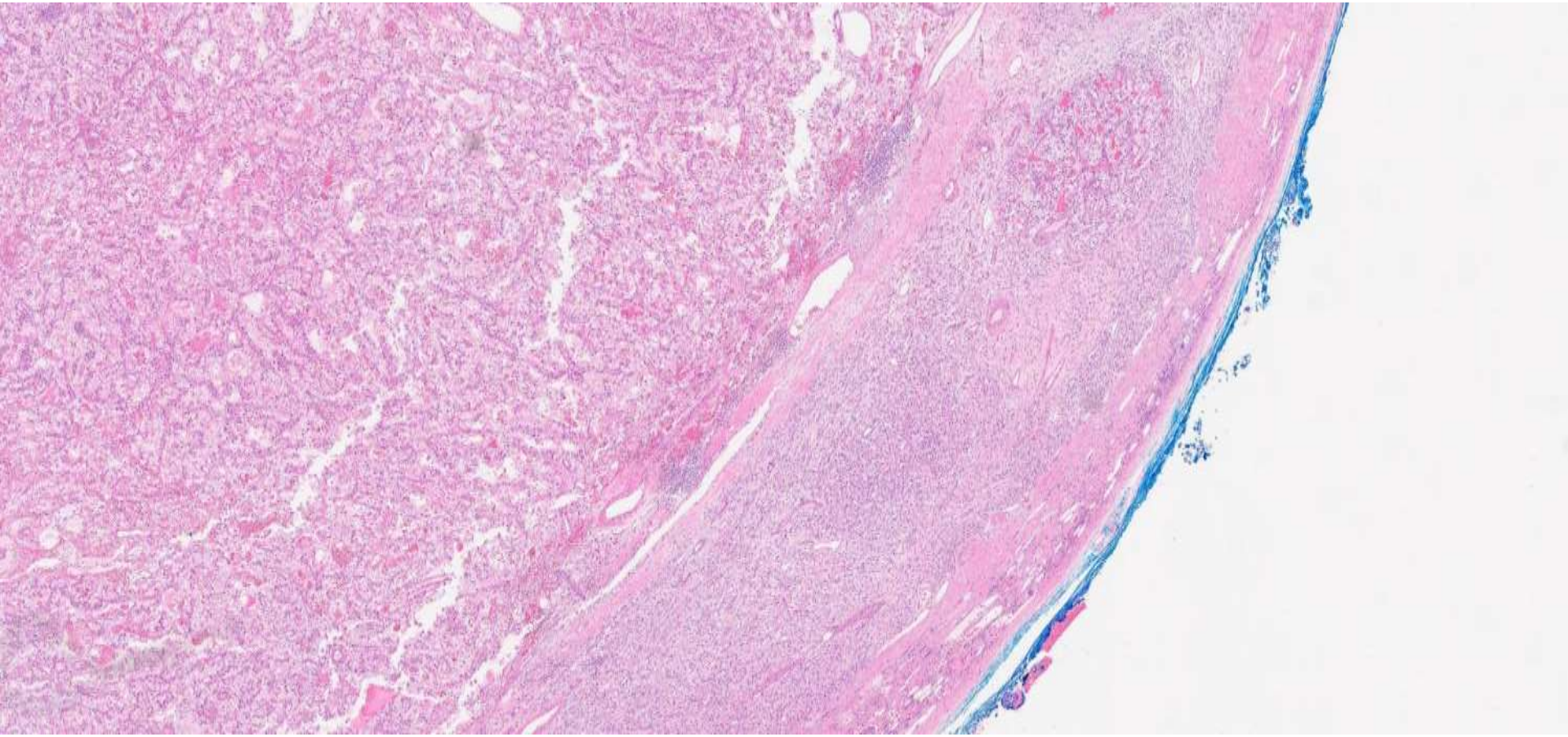
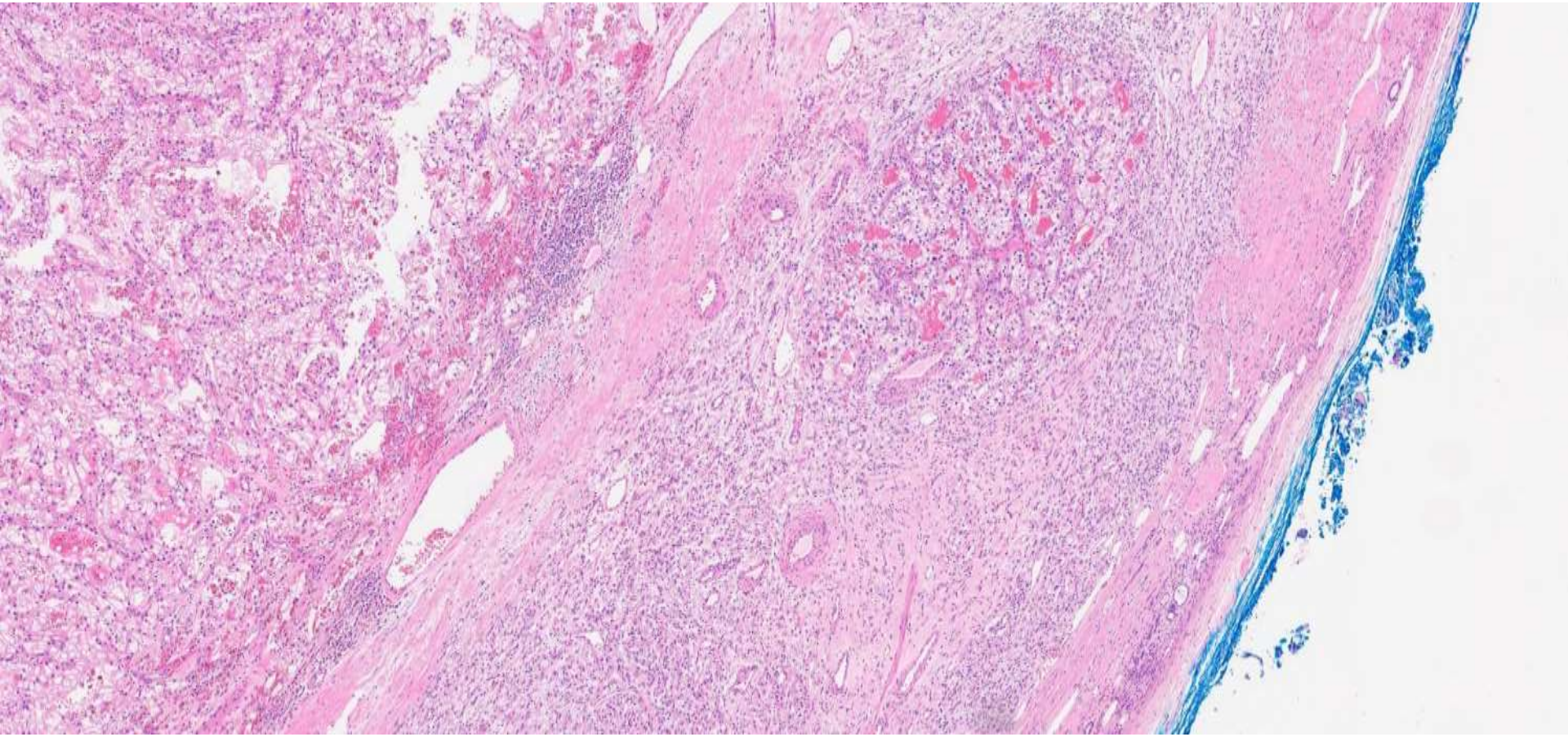
Direct links to scanned slides:
https://pathpresenter.net/#/public/display?token=e64f766c

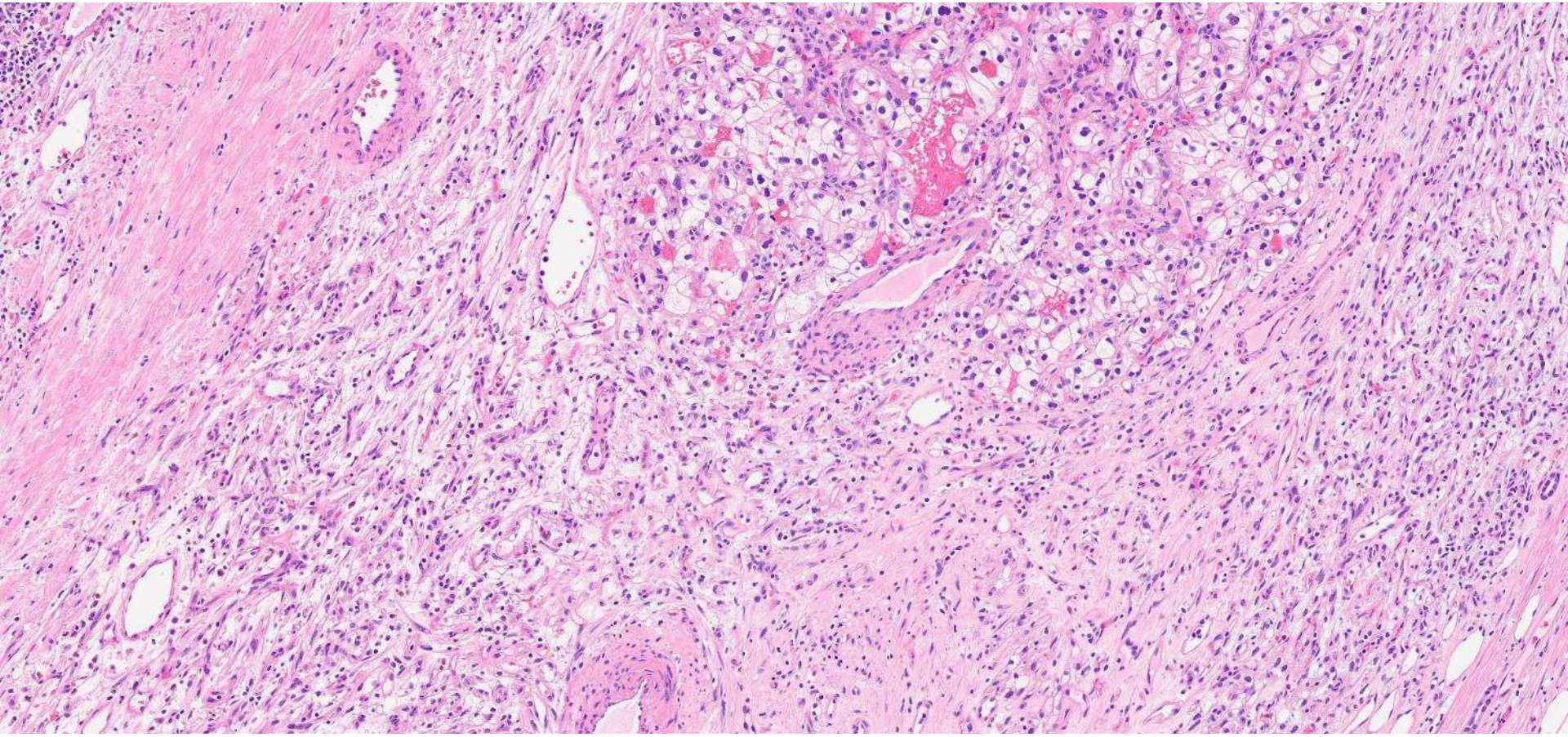
Ankur Sangoi; El Camino Hospital

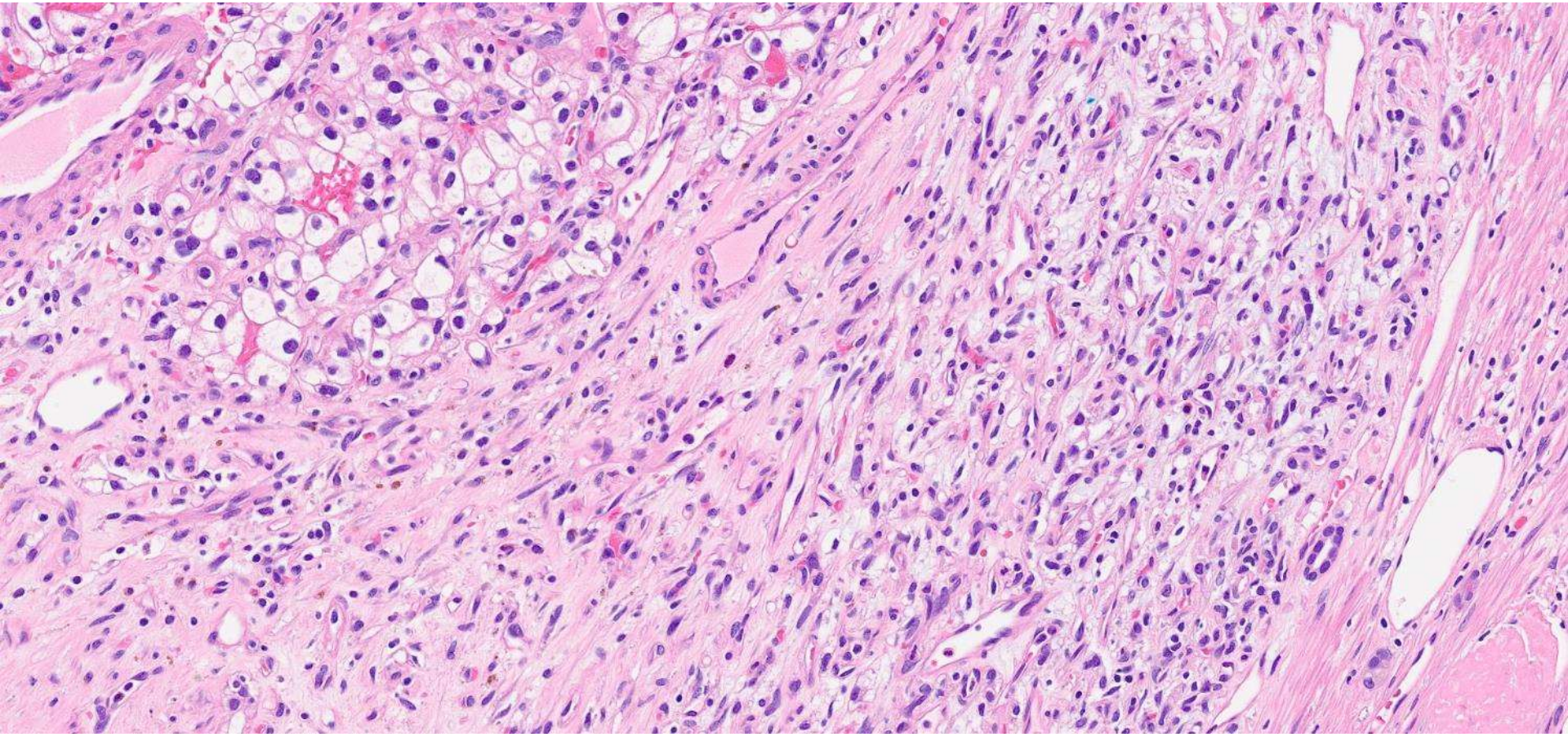
60ish M with renal mass, partial nephrectomy.

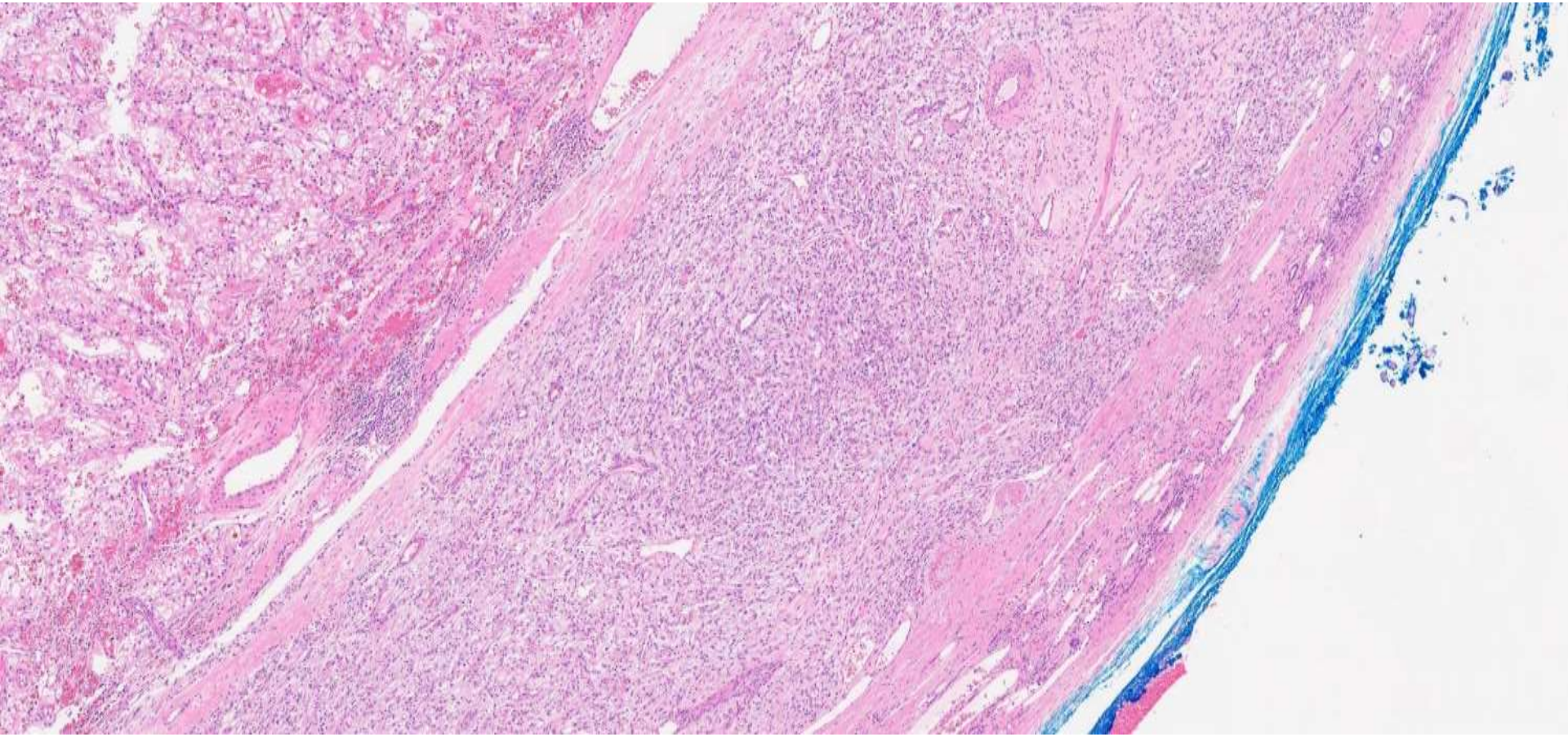


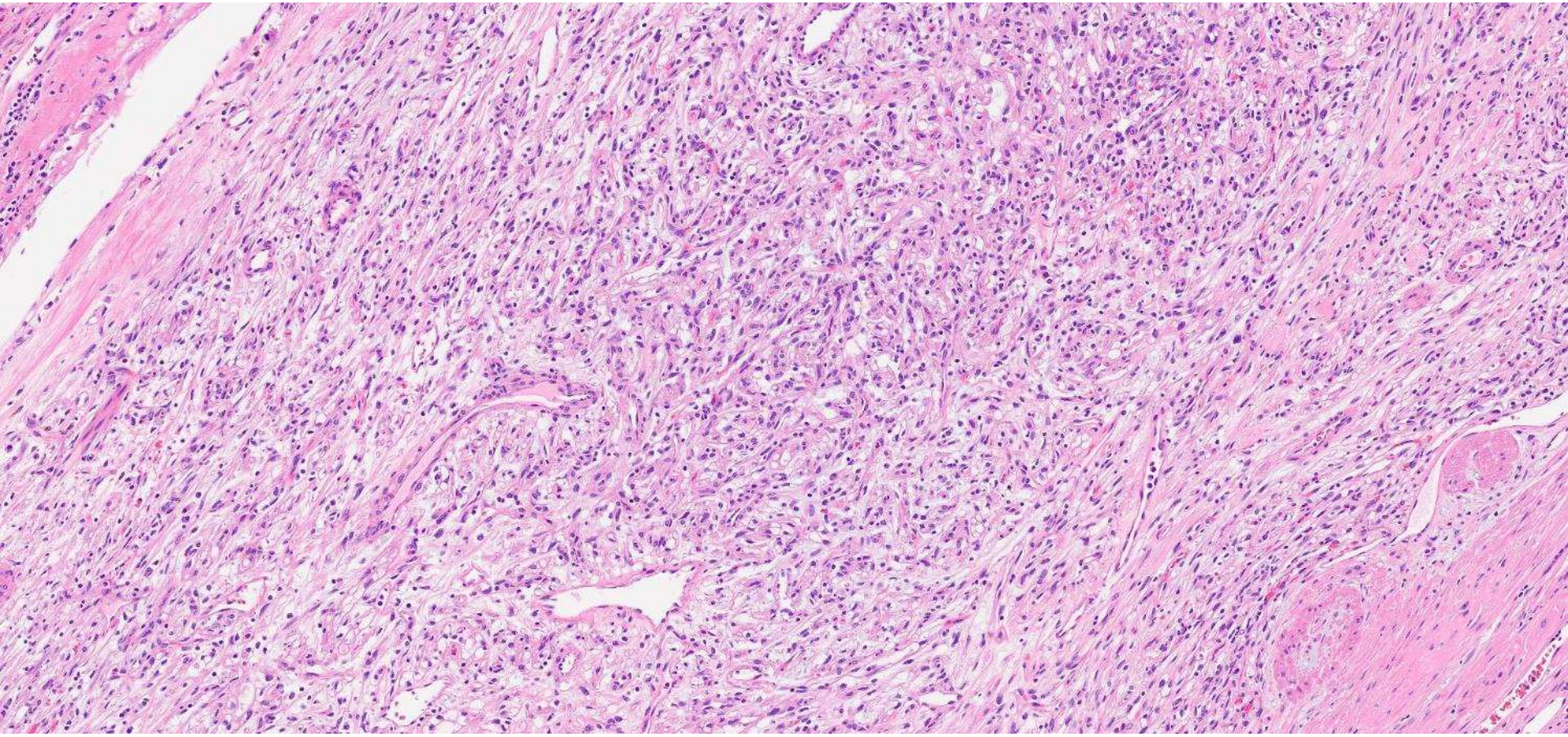


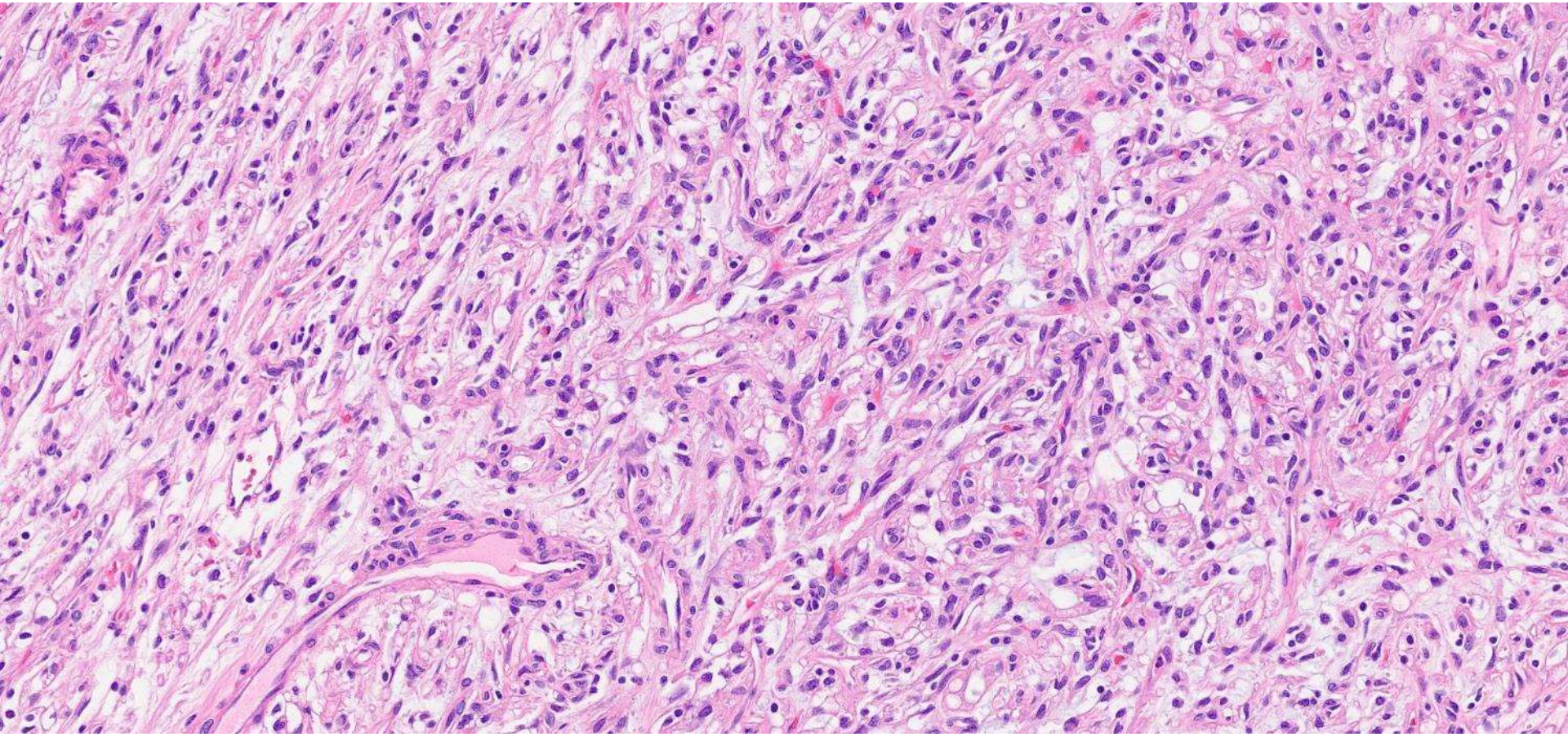












DDx

- **Clear cell RCC with spindle cell change**
- **Clear cell RCC with sarcomatoid differentiation**
- **Clear cell papillary RCC**
- **Mucinous tubular spindle cell carcinoma**
- **Epithelioid AML**
- **Collision clear cell RCC + another tumor/lesion**
  - Papillary adenoma/RCC
  - AML
  - Xanthogranulomatous pyelonephritis

Dx & IHC summary

- **Low grade clear cell RCC**
  - With admixed spindle cell foci
  - NOT sarcomatoid differentiation

- **CAIX + complete membranous**
- **CD10+**
- **CK7-**
- **AMACR-**

Histopathology 2018, 72, 804–813. DOI: 10.1111/his.13447

Low-grade spindle cell proliferation in clear cell renal cell carcinoma is unlikely to be an initial step in sarcomatoid differentiation

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Low-grade spindle cell proliferation in clear cell renal cell carcinoma is unlikely to be an initial step in sarcomatoid differentiation

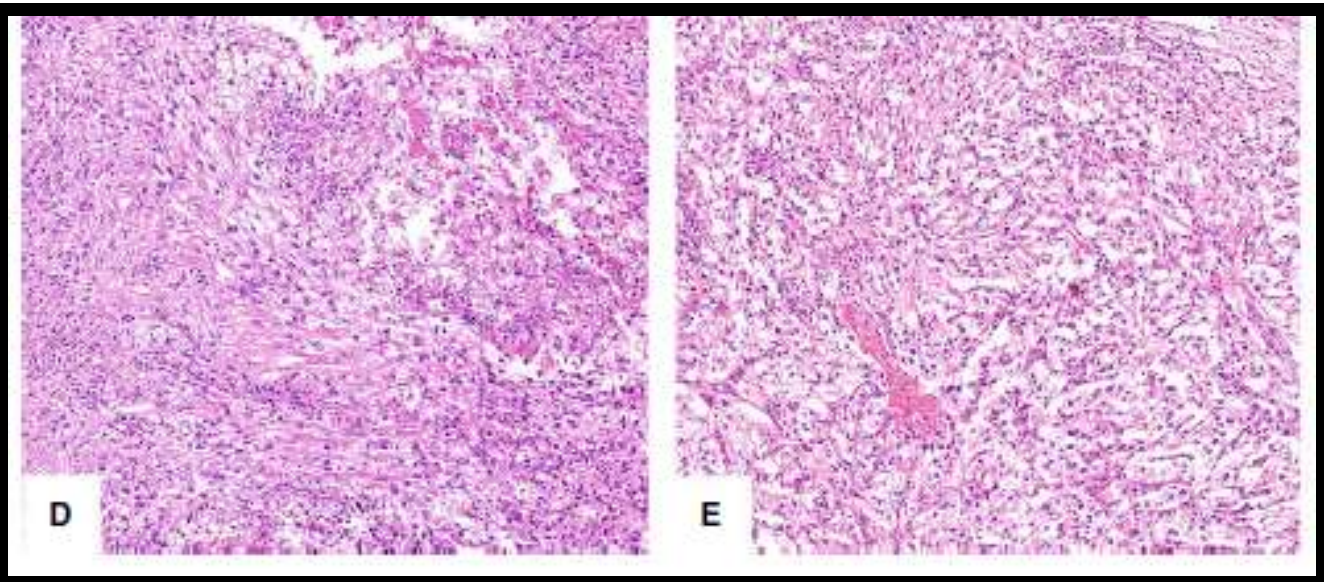


Table 1. Clinicopathological data of ccRCCs with LG-SCP cases

Case no.	Age (years)	Sex	Tm size (cm)	Stage	Status	F/U months
1	64	F	7	pT3a	AW	12
2	81	M	1.7	pT1	AW	144
3	75	F	8.5	pT3a	AW	4
4	67	NA	NA	NA	NA	NA
5	60	F	5	pT1b	AW	36
6	68	M	5.5	pT1b	NA	NA
7	75	M	8.5	NA	AW	36
8	64	M	4.8	pT1b	AW	3
9	61	F	8	pT3a	AW	48
10	77	M	12	PT3a	AW	108
11	62	F	10	pT3a	AW	12

ccRCC, Clear cell renal cell carcinoma; LG-SCP, Low-grade spindle cell proliferation; F, Female; M, Male; Tm, Tumour; AW, Alive without disease; NA, Not available; F/U, Follow up.

Table 2. Histopathological findings of ccRCCs with LG-SCP

Case no.	Pure CC	Eos-gra diff %	SCP %	Necrosis %	Regression %	SCP (ISUP)	CC (ISUP)	Tumour including blocks
1	+	–	10	10	30	2	3	9
2	+	–	80	–	5	2	2	1
3	+	–	60	10	10	2	3	9
4	+	–	20	5	–	2	3	1
5	+	–	15	10	5	2	2	6
6	+	–	80	20	5	2	2	4
7	+	–	25	20	<5	2	2	2
8	+	–	5	10	<5	2	3	11
9	–	5	20	10	–	2	2	3
10	–	80	20	30	–	2	3	2
11	–	50	20	10	–	2	3	9

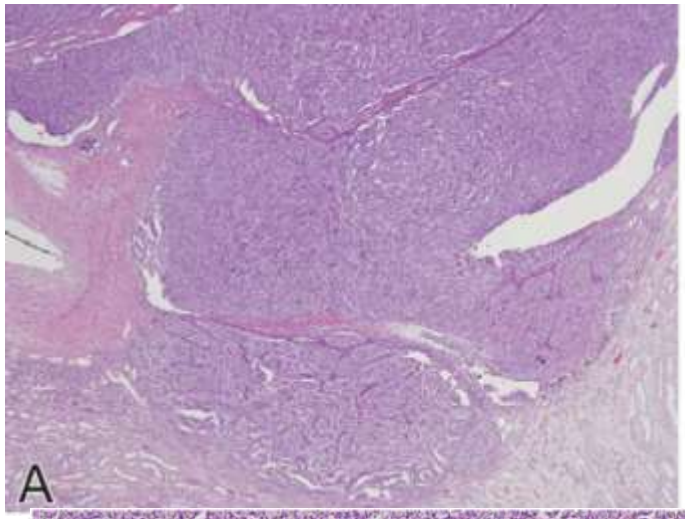
Papillary Renal Cell Carcinoma With Low-grade Spindle Cell Foci

A Mimic of Mucinous Tubular and Spindle Cell Carcinoma

Pedram Argani, MD,† George J. Netto, MD,* and Anil V. Parwani, MD, PhD‡*

Abstract: The solid variant of papillary renal cell carcinoma (PRCC) is distinguishable genetically from mucinous tubular and spindle cell carcinoma (MTSC) of the kidney by the presence of trisomy for chromosomes 7 and 17; however, at the morphologic and immunohistochemical levels, these neoplasms overlap significantly. The key morphologic feature distinguishing these two is thought to be the low grade of the spindle cell areas of MTSC; spindle cell areas in PRCC generally signify sarcomatoid change and are high grade. We report 5 cases of PRCC with low-grade spindle cell foci, closely mimicking MTSC. All patients were male, and ranged in age from 17 to 68 years. All tumors were predominantly solid, featuring compact areas of low-grade spindle cells lining thin, angulated tubules. Mucinous stroma was not appreciated in any case. All cases were diffusely immunoreactive for cytokeratin 7, and focally CD10 positive. All 5 cases showed trisomy of chromosome 7, and 3 of 5 showed trisomy of chromosome 17 by fluorescence in situ hybridization, supporting classification as PRCC. These cases further reported morphologic overlap between MTSC and PRCC. Before a diagnosis of metastatic MTSC or MTSC with unusual morphology is rendered, the possibility of PRCC with low-grade spindle cell foci should be considered. Fluorescence in situ hybridization analysis effectively separates these morphologically very similar yet genetically distinctive entities.

Key Words: renal cell carcinoma, fluorescence in situ hybridization, mucinous tubular and spindle cell carcinoma, papillary renal cell carcinoma



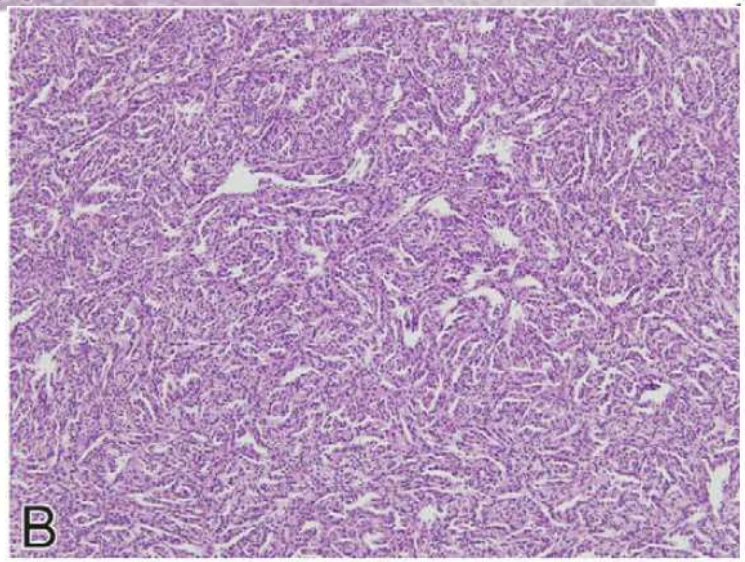


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TABLE 2. WHO/ISUP Grade for Clear Cell Renal Cell Carcinoma and Papillary Renal Cell Carcinoma

Grade	Description
1	Nucleoli are absent or inconspicuous and basophilic at ×400 magnification
2	Nucleoli are conspicuous and eosinophilic at ×400 magnification and visible but not prominent at ×100 magnification
3	Nucleoli are conspicuous and eosinophilic at ×100 magnification
4	There is extreme nuclear pleomorphism, multinucleate giant cells, and/or rhabdoid sarcomatoid differentiation

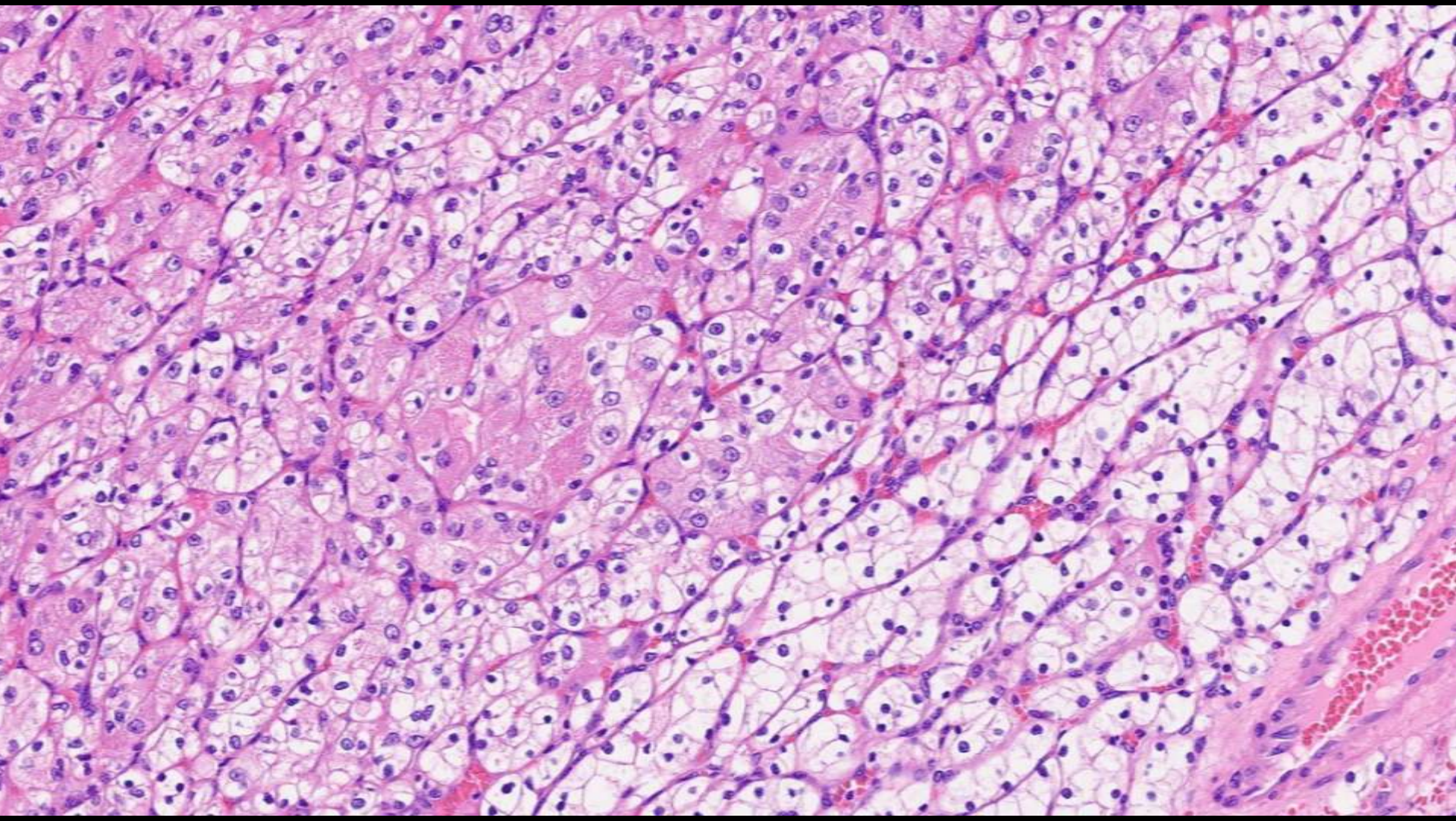
Updates in Grading of Renal Cell Carcinomas Beyond Clear Cell Renal Cell Carcinoma and Papillary Renal Cell Carcinoma

Gladell P. Paner, MD,† Vaibhav Chumbalkar, MD,**
Rodolfo Montironi, MD,‡ Holger Moch, MD,§ and Mahul B. Amin, MD‖¶

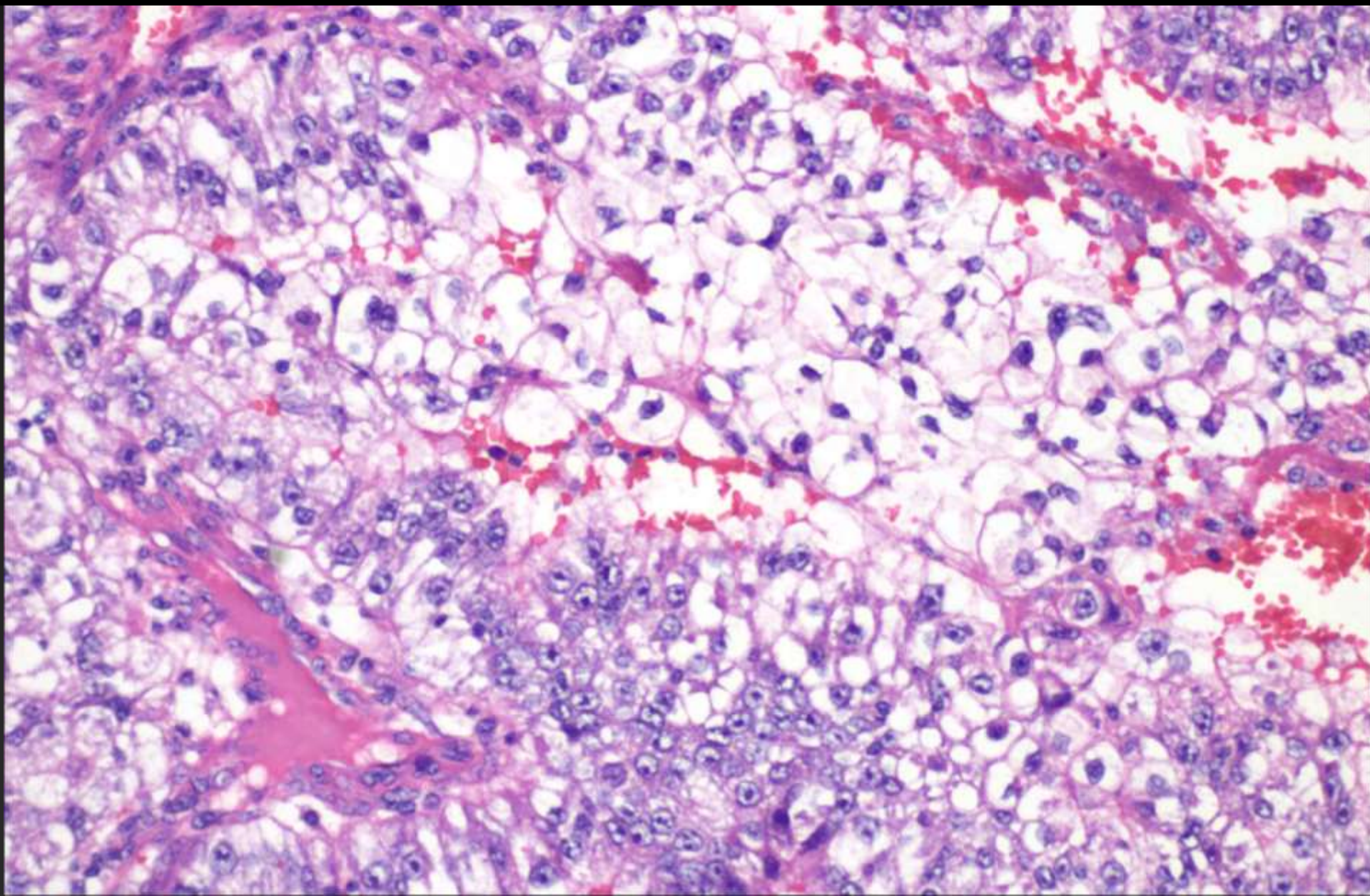
TABLE 3. Role of WHO/ISUP Grading in Renal Cell Tumor Types

1. RCC subtypes validated for WHO/ISUP grading	
Clear cell RCC	
Papillary RCC	
2. RCC subtypes where WHO/ISUP grading is not applicable	
ChRCC	WHO/ISUP grading is not applicable; alternative schemes have been proposed such as CTG and grading by necrosis and sarcomatoid change have shown prognostic value
TFE3 RCC	Studies show that WHO/ISUP grade may not be useful
3. RCC subtypes where WHO/ISUP grading is potentially useful	
TFEB RCC	WHO/ISUP grade may help separate aggressive TFEB amplified over TFEB translocation RCC
SDH-deficient RCC Mucinous tubular and spindle cell carcinoma TCEB1/ELOC1-mutated RCC	Low-grade and high-grade features using the Fuhrman or WHO/ISUP grading appear to be associated with outcome suggesting potential value
RCC, unclassified	Heterogenous group of tumors in whom providing information on nuclear grade, even descriptively as low-grade and high-grade would be helpful to communicate potential prognosis to the clinicians
FH-deficient RCC including HLRCC-RCC*	Most tumors have high-grade nuclei consistent with aggressive behavior, but rare low-grade tumors potentially indolent tumors have been reported
4. Inherently aggressive RCC subtypes irrespective of WHO/ISUP grading	
Collecting duct carcinoma Medullary carcinoma	Inherent high-grade nuclei and almost uniform aggressive clinical course in these tumor types obviates use of nuclear grading
5. Renal epithelial neoplasms where WHO/ISUP grading is potentially misleading	
Tubulocystic carcinoma Acquired cystic disease-associated RCC Eosinophilic solid and cystic RCC Eosinophilic vacuolated tumor	Nuclear grading may be problematic because of pure or predominantly "high-grade" appearing nuclei despite of the overall indolent behavior of tumor types
6. Renal epithelial neoplasms where low WHO/ISUP grade features are essential for accurate histologic classification	
Papillary adenoma Multilocular cystic renal neoplasm of low malignant potential Clear cell papillary RCC	
7. Renal epithelial neoplasms with no or limited data on grading or behavior	
ALK rearrangement–associated RCC Low-grade oncocytic tumor Thyroid-like follicular renal cell carcinoma	

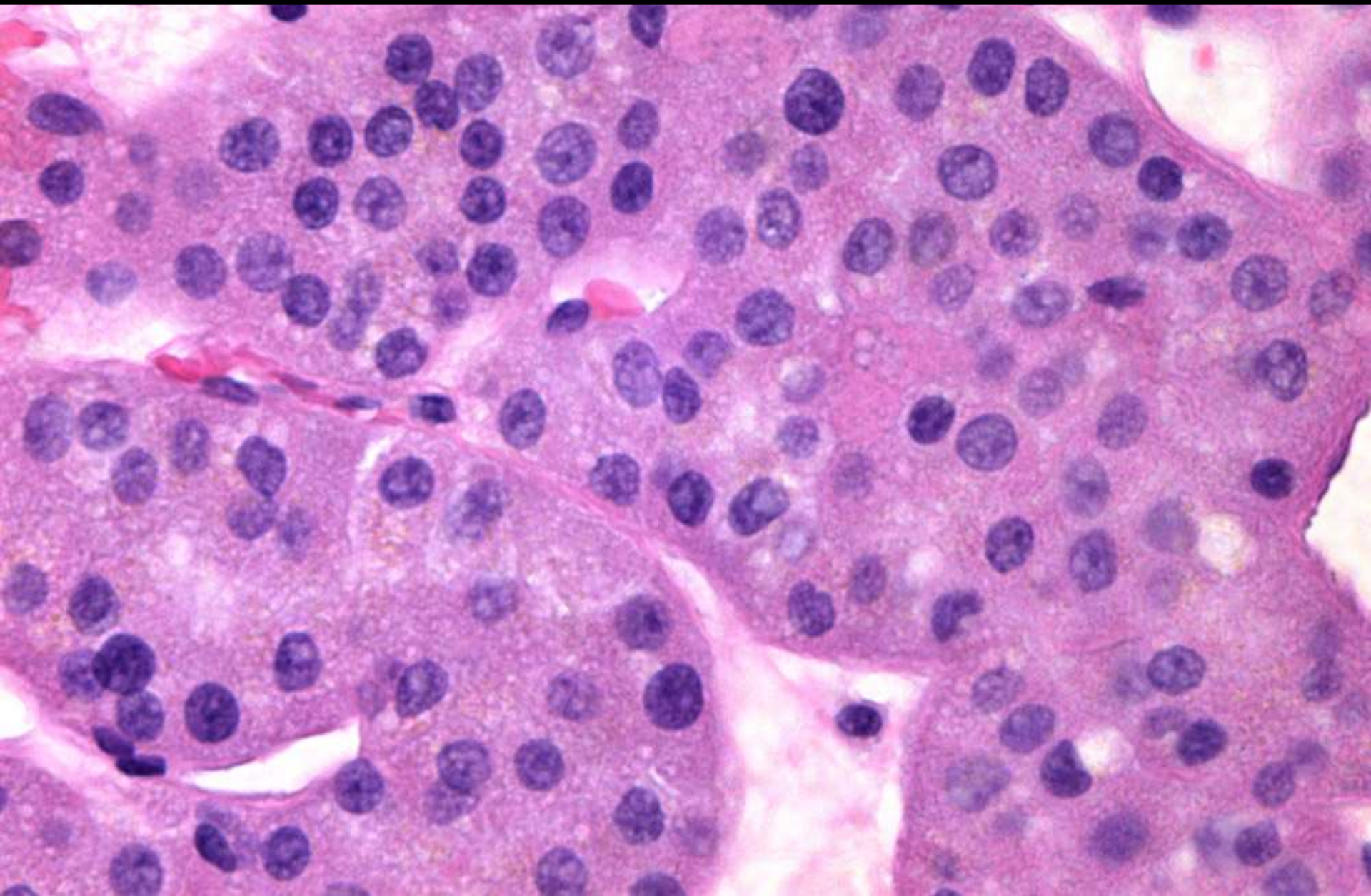
Nuclear/cytoplasmic synchrony: clear cell RCC



Nuclear/cytoplasmic dyssynchrony: NOT clear cell RCC (Xp11/TFE3 RCC)



Nuclear/cytoplasmic dyssynchrony: NOT clear cell RCC (oncocytoma)



Sarcomatoid differentiation

- NOT an RCC subtype
  - Most commonly seen in clear cell RCC followed by chromophobe RCC
    - Can occur in others!
- WHO/ISUP grade 4 by definition
- Malignant mesenchymal-like elements juxtaposed with neoplastic epithelial components
  - High grade features in at least 1 low power field
- Associated with poor prognosis
  - Even when focal