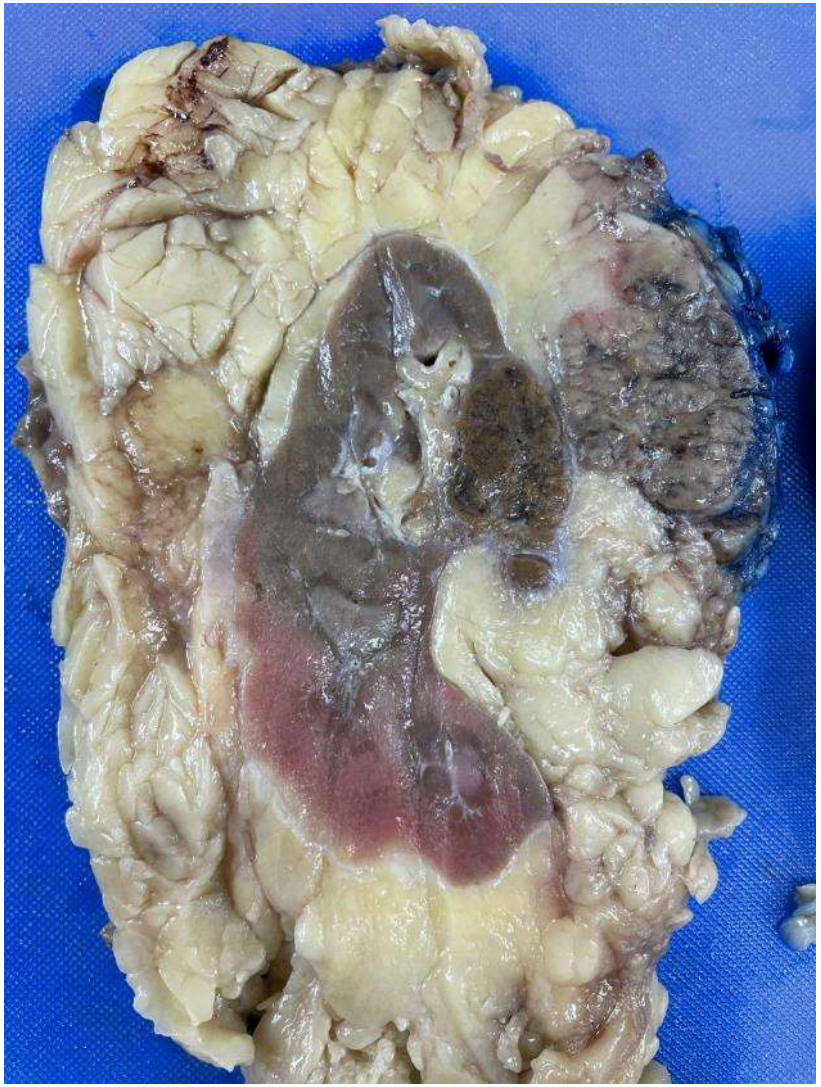
MARCH 2022 DIAGNOSIS LIST

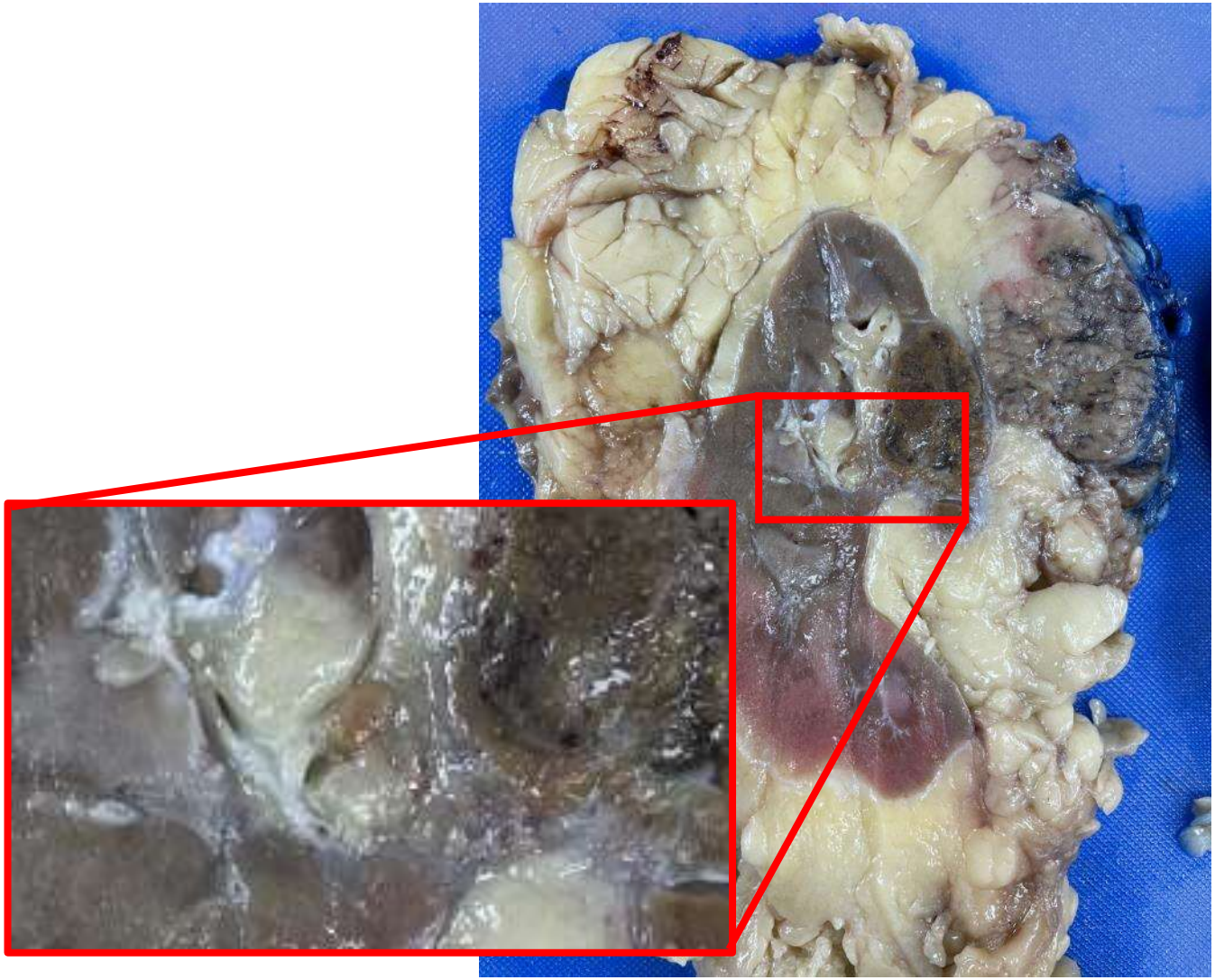
22-0301: oncocytoma with perinephric fat invasion and vascular invasion (kidney; GU path)
22-0302: adenocarcinoma arising from ovarian teratoma (ovary; GYN path)
22-0303: bladder melanosis (bladder; GU path)
22-0304: condyloma with pseudobowenoid change (vulva; GYN path)
22-0305: sclerosing polycystic adenosis (salivary gland; ENT path)
22-0306: chronic neutrophilic leukemia (bone marrow; hemepath)
22-0307: polyomaviral nephropathy (kidney; GU path)

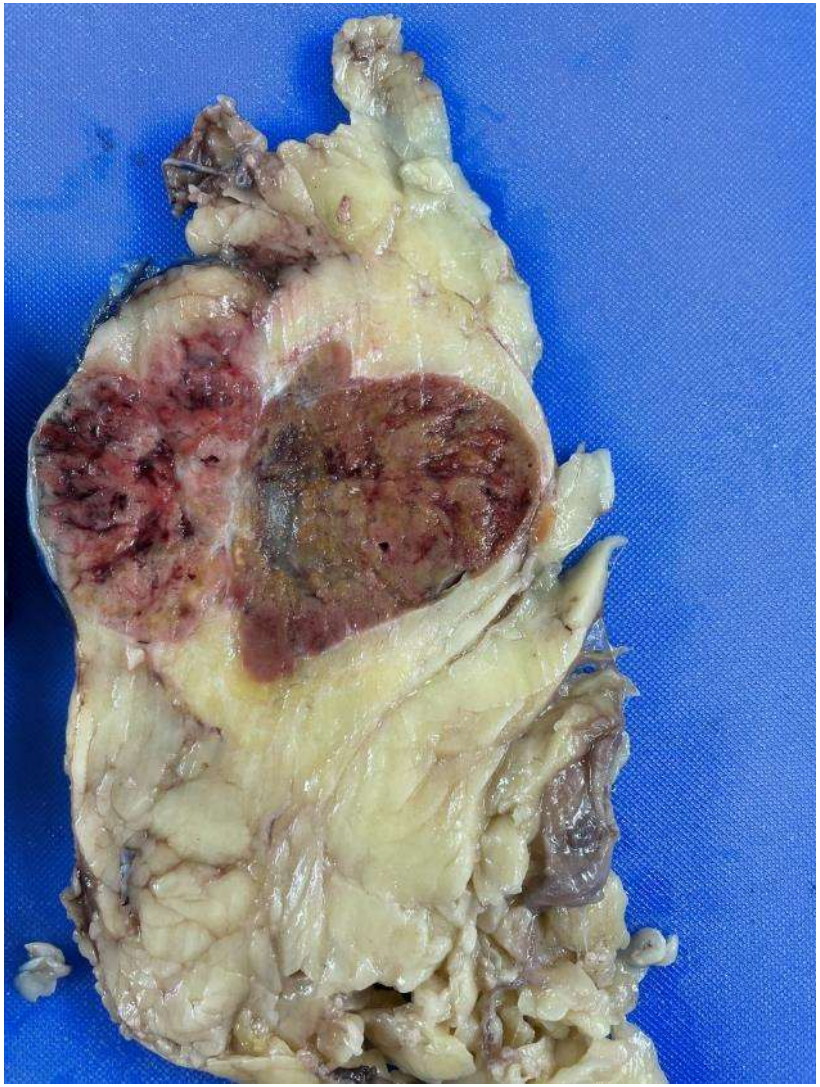
22-0301

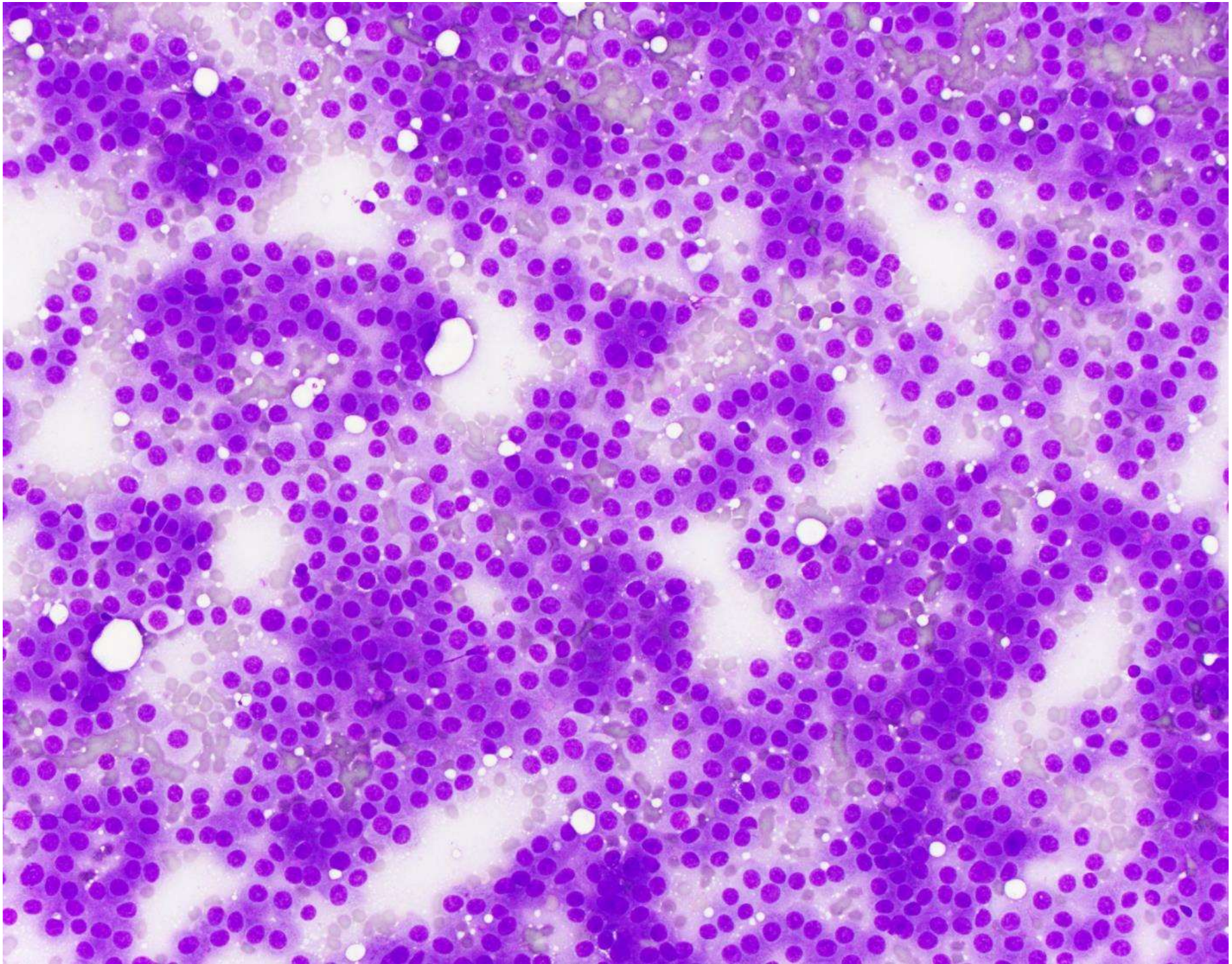
Ben Dulken/Hubert Lau; VA Palo Alto

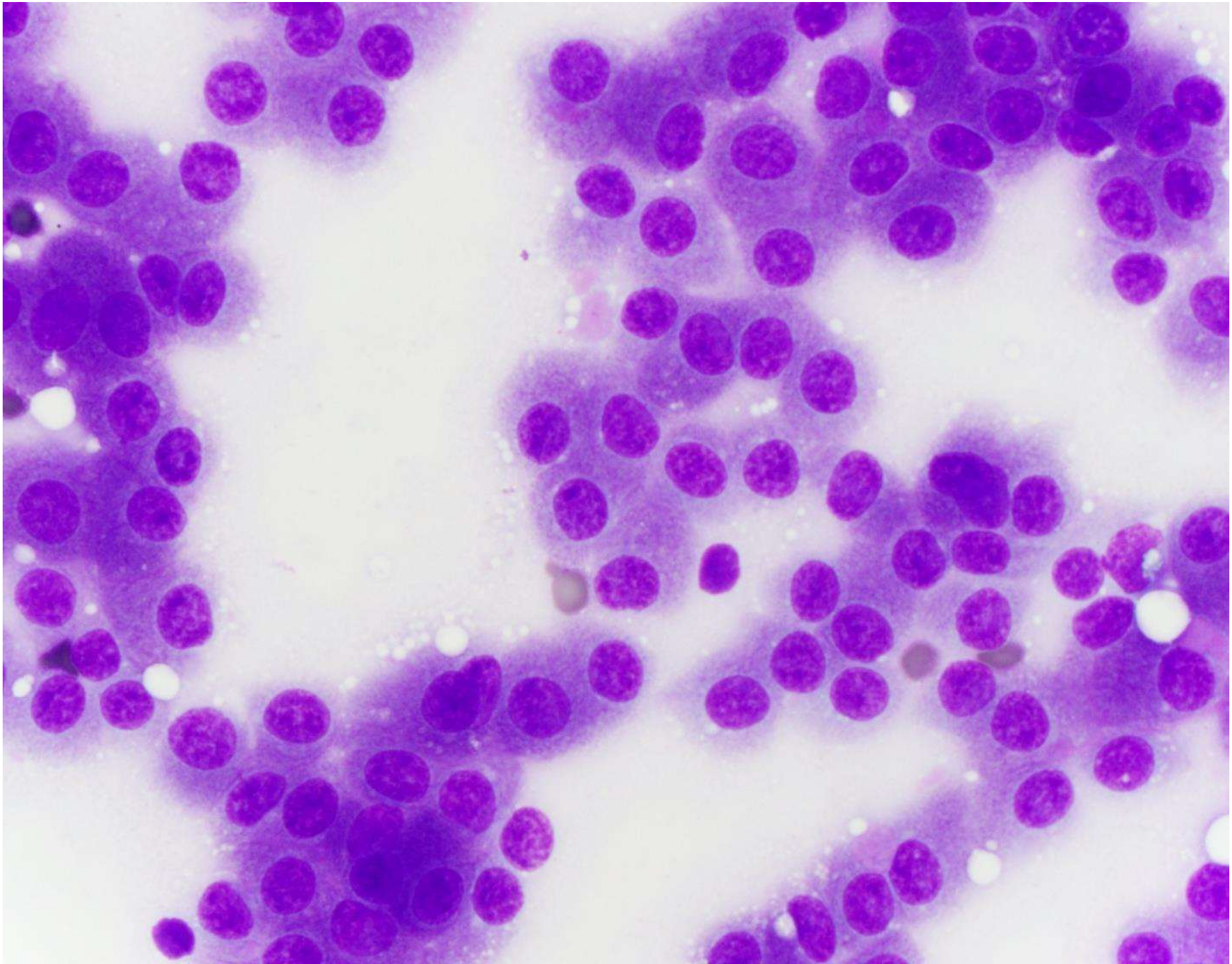
80ish M with incidentally discovered 10cm left renal mass.

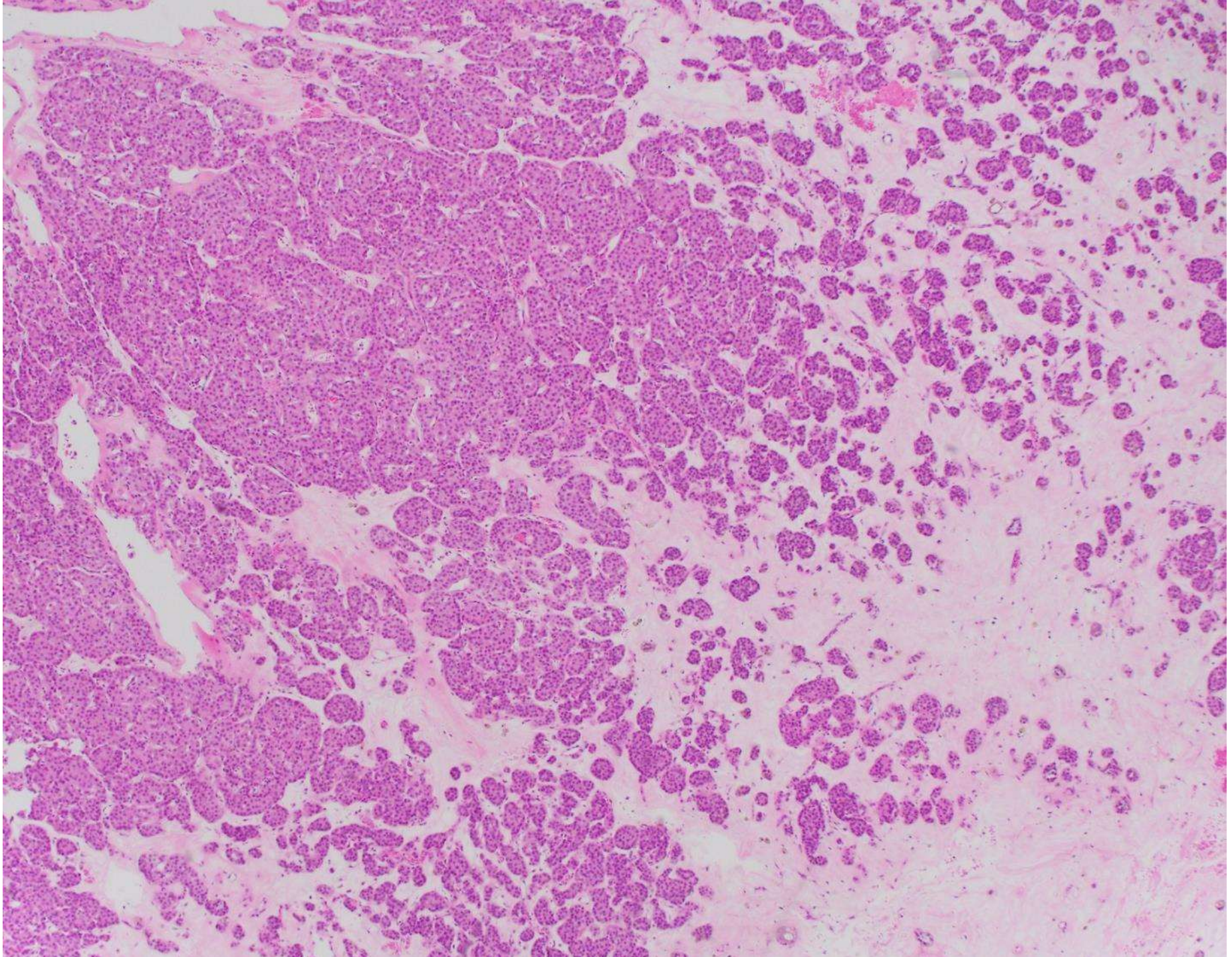


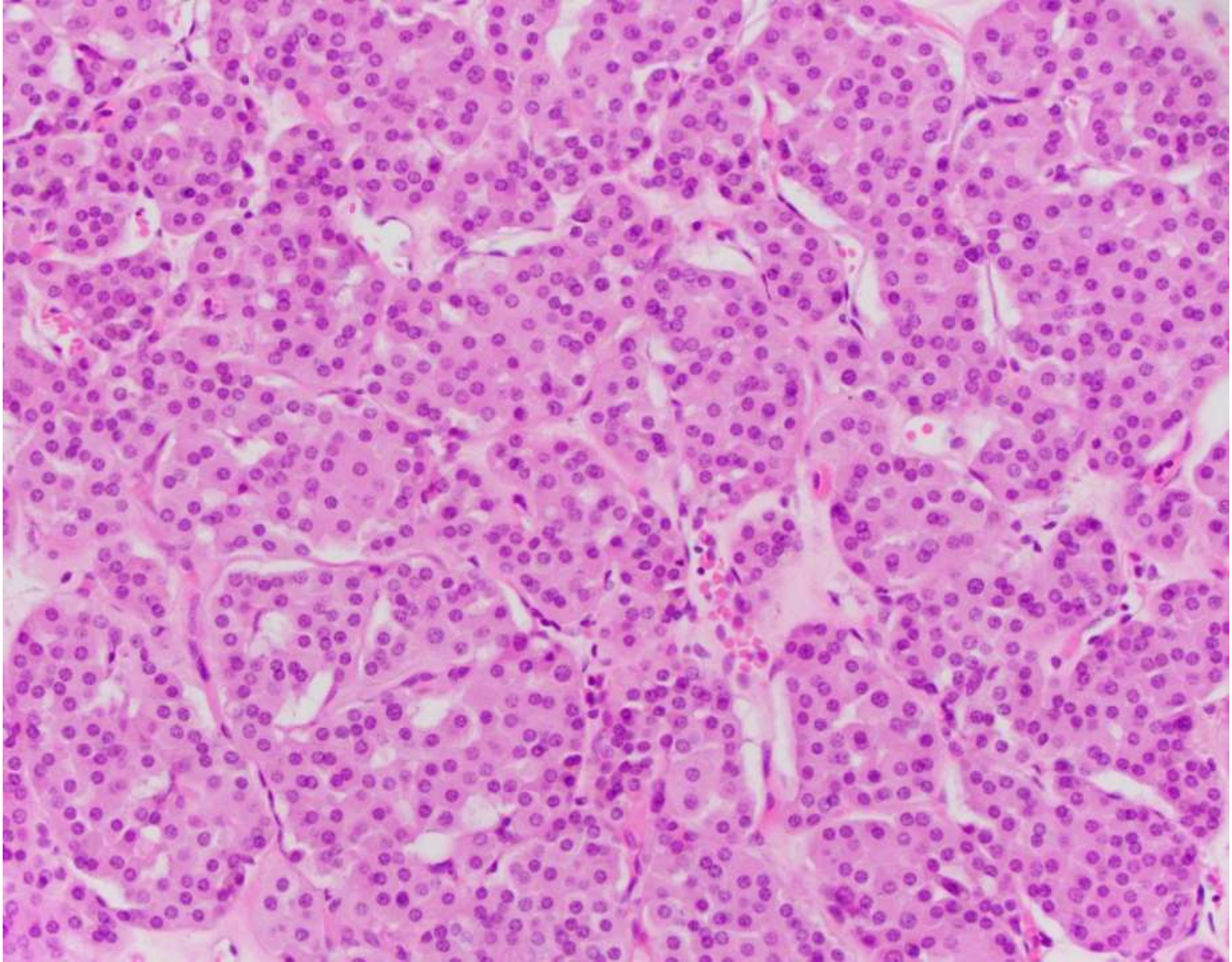


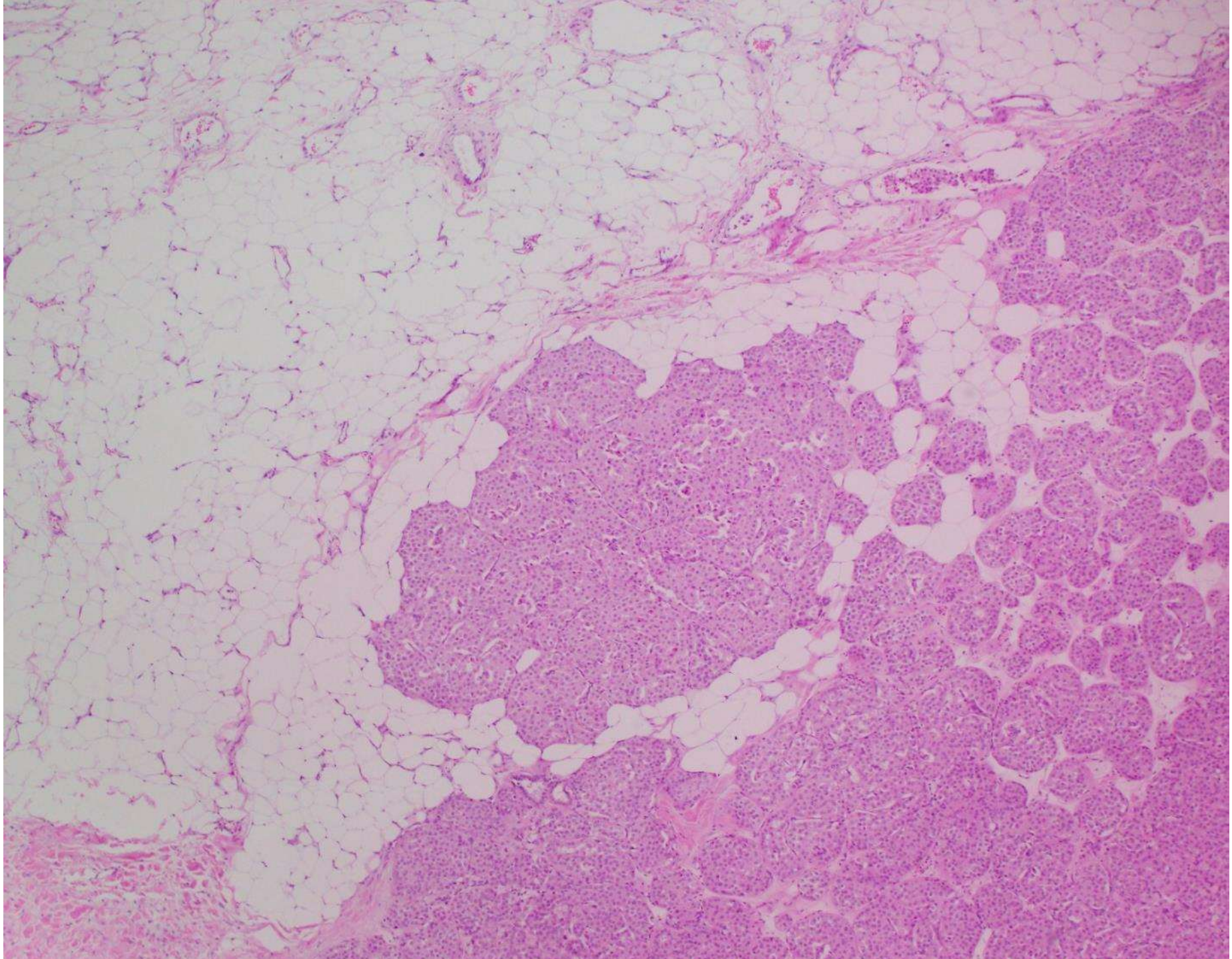


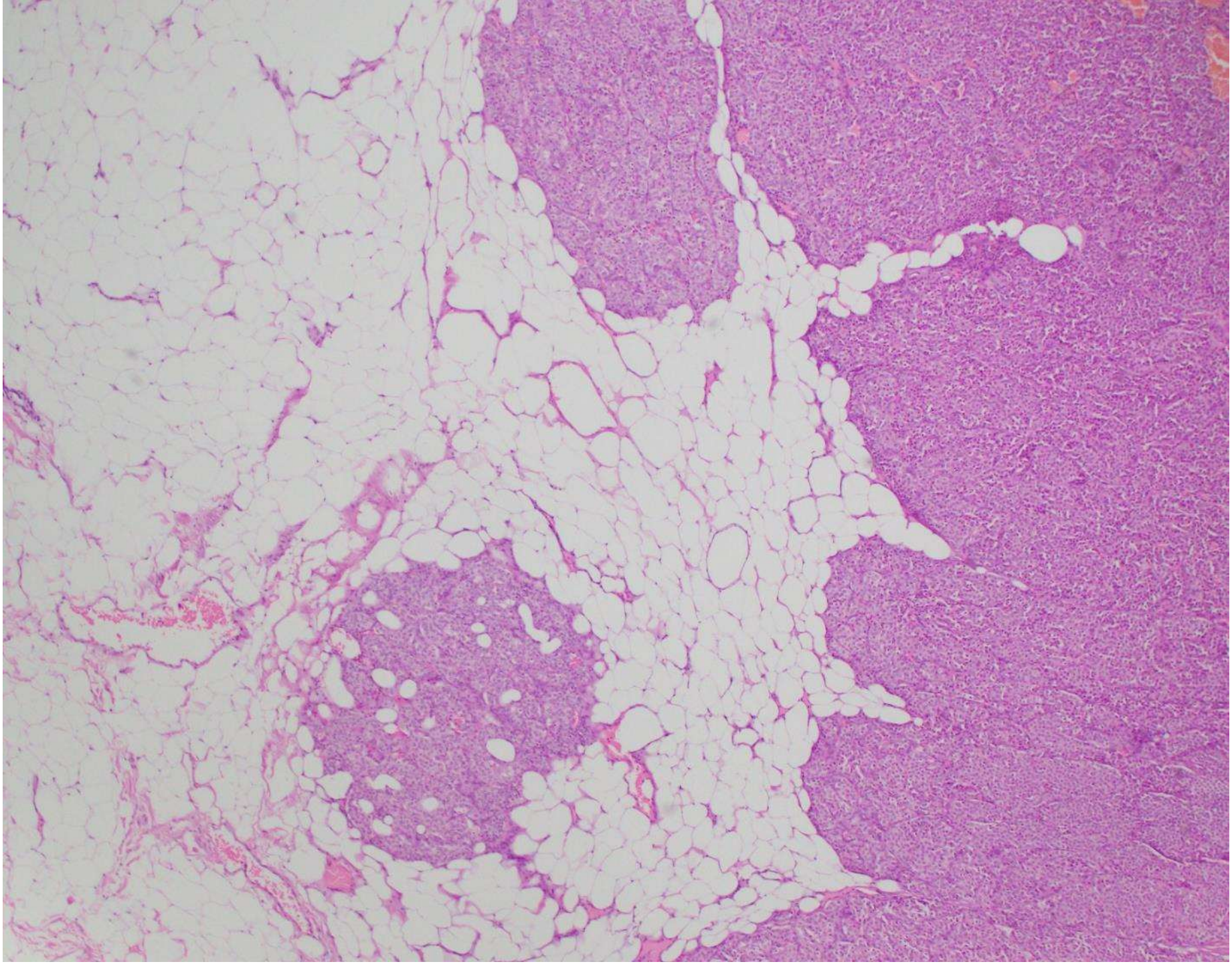


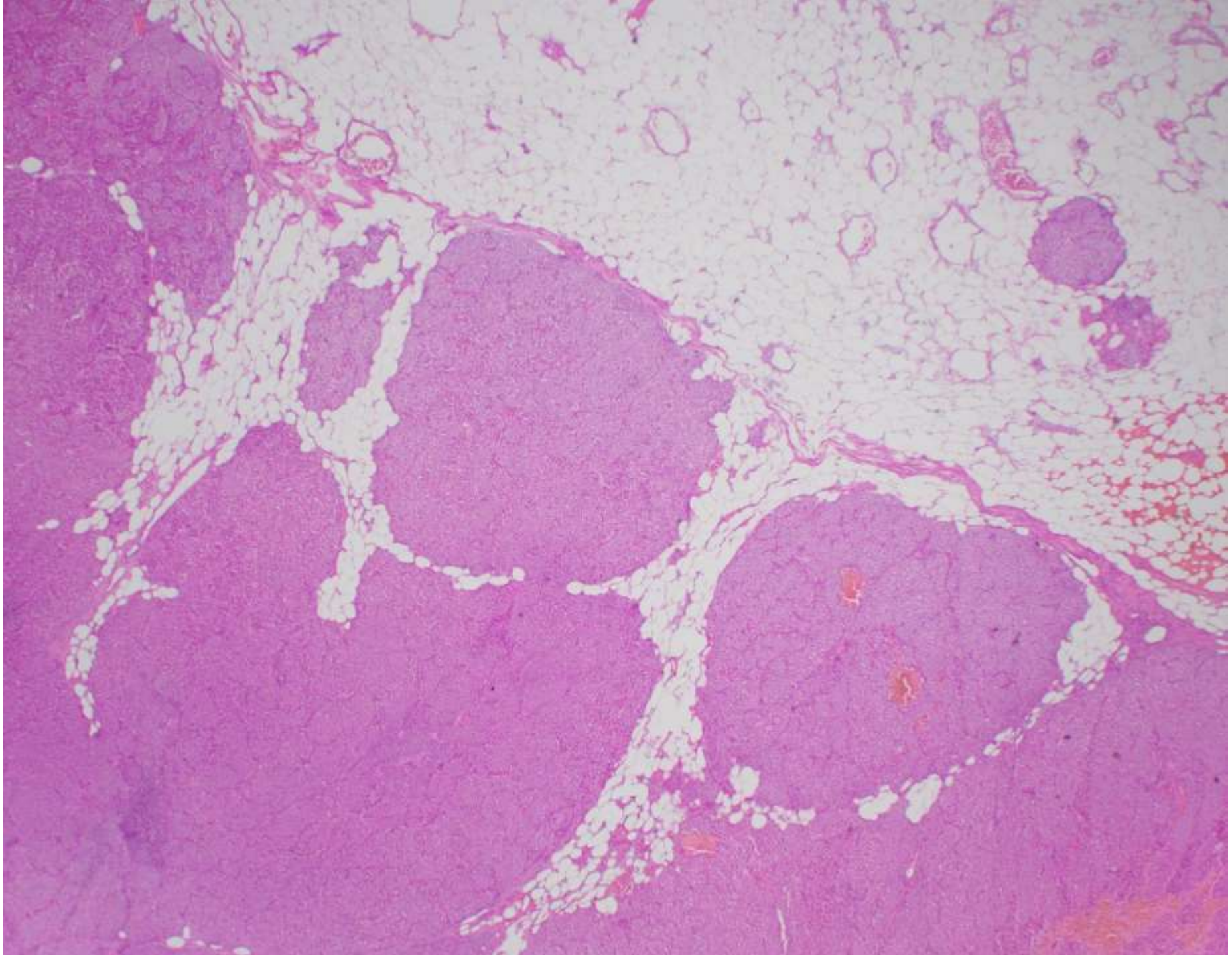


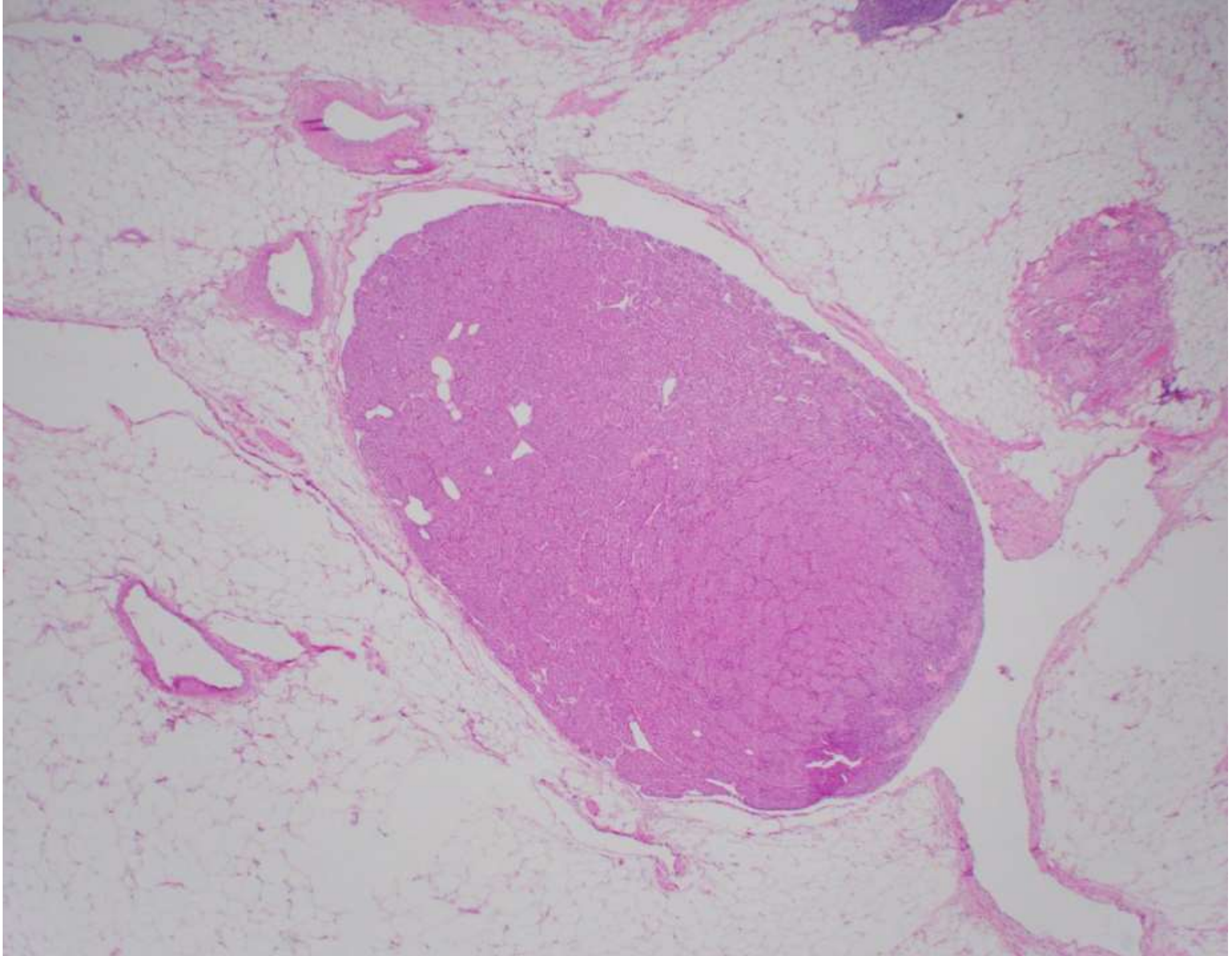




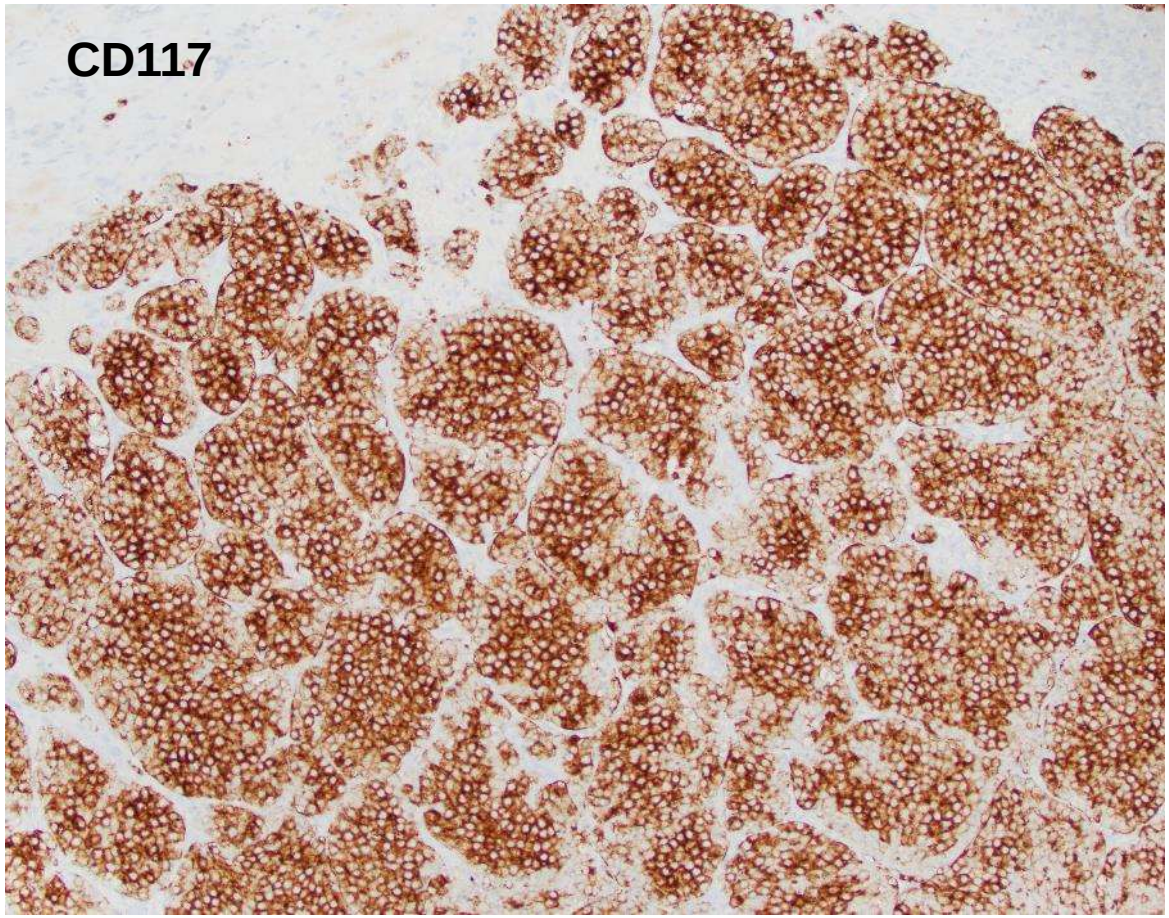








Immunohistochemistry



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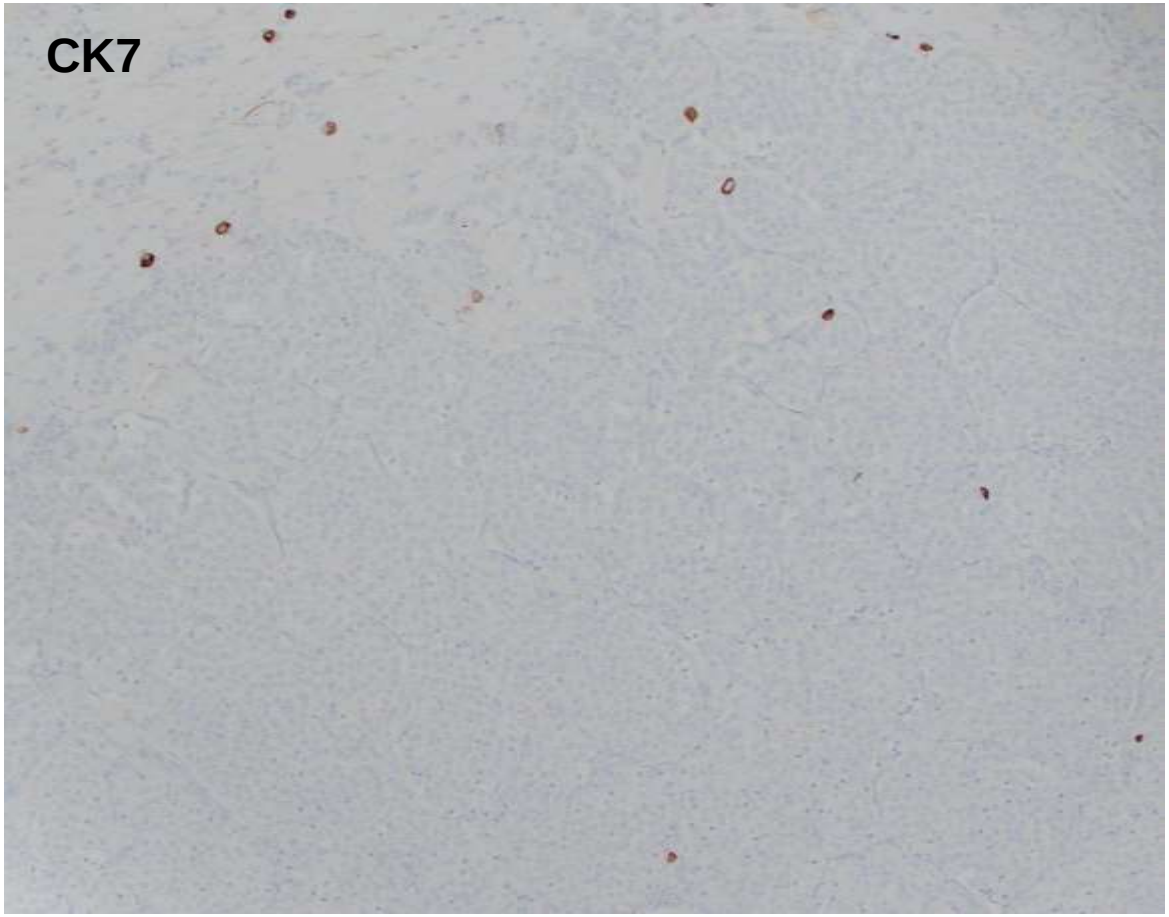


Renal Oncocytoma (with “adverse pathologic features”)

- Histologically identical to oncocytoma with the exception of features that would typically increase the tumor stage of an RCC:
  - Renal sinus fat involvement
  - Perinephric fat involvement
  - Small or large vessel involvement

- Other overtly malignant features are not acceptable:
  - Tumor cell necrosis
  - Increased mitotic activity (up to 1 per 10 HPF is acceptable) or atypical mitotic figures

Case series

	Number of cases	Any adverse feature	Vascular invasion	Perinephric fat invasion	Both adverse features	Follow up
Omiyale, et al. 2019	20	12.6%	6.3%	8.2%	1.9%	No recurrences (25.6 months)
Al-Obaidy, et al. 2021	50	5%	0.9%	4.4%	1.1%	No recurrences
Wobker, et al. 2016	22	Not reported	1.5%	0.5%	Not reported	No recurrences (29 months)
Hes, et al. 2008*	8	Not reported	2.2%	Not reported	Not reported	No recurrences (3.6 years)

- Hes, et al. also performed genetic analysis on their oncocytomas which exhibited adverse features and showed no major chromosomal rearrangements, no VHL mutations.
- No major difference in immunohistochemical staining profile to oncocytomas without adverse features.

Prognosis

- There is no evidence that renal oncocytoma with “adverse pathologic features” portends a significantly worse prognosis than oncocytomas that lack these features.

- If the histologic and immunohistochemical features support a diagnosis of oncocytoma, this diagnosis can be made even in the presence of these “pseudomalignant” features.

Key differential diagnosis

- Ruling out a malignant neoplasm is the most important aspect of the workup for an oncocytoma with “adverse” features.
- CD117 and CK7 immunohistochemistry is useful in supporting the diagnosis.

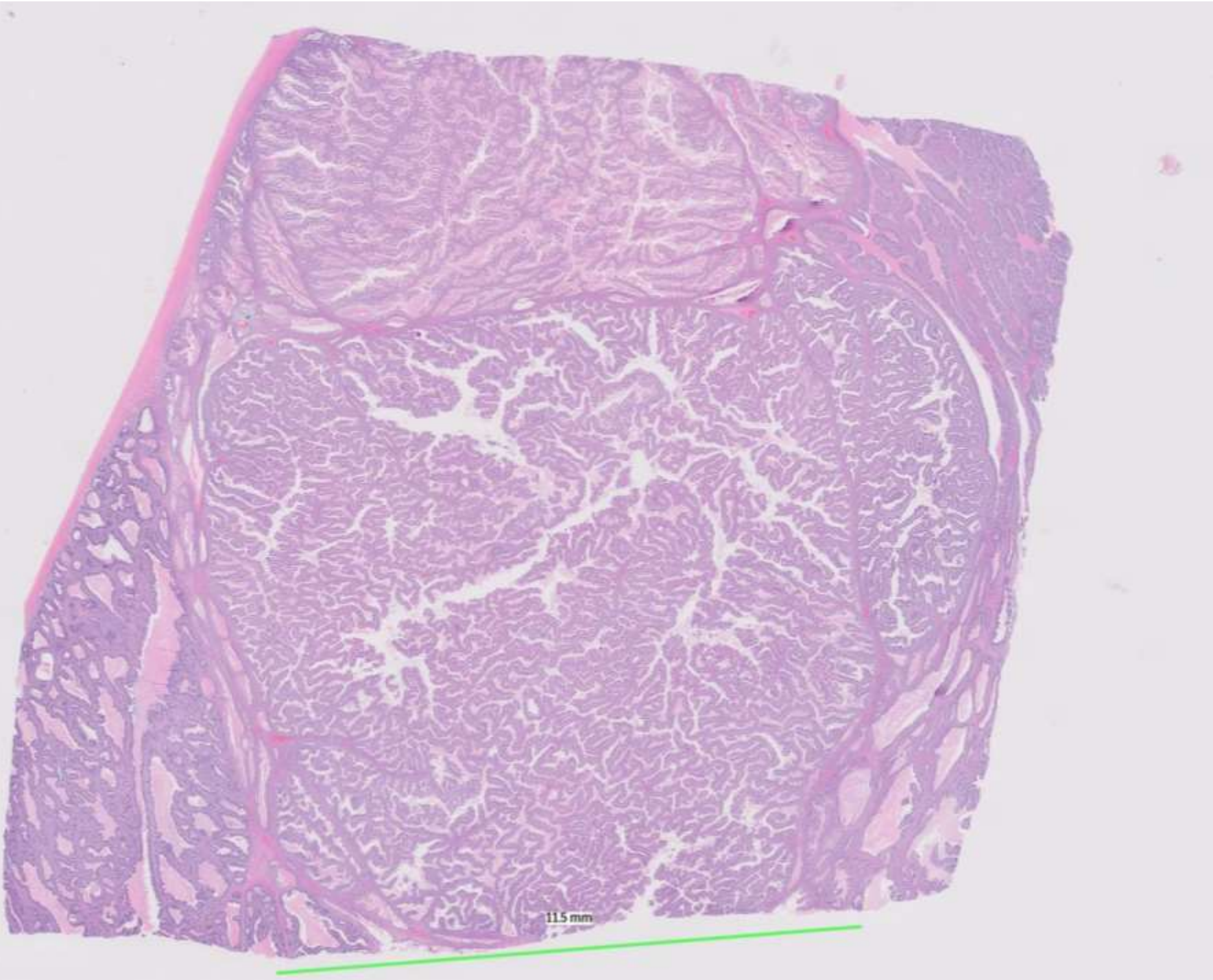
Key differential to consider includes other low nuclear grade eosinophilic tumors:

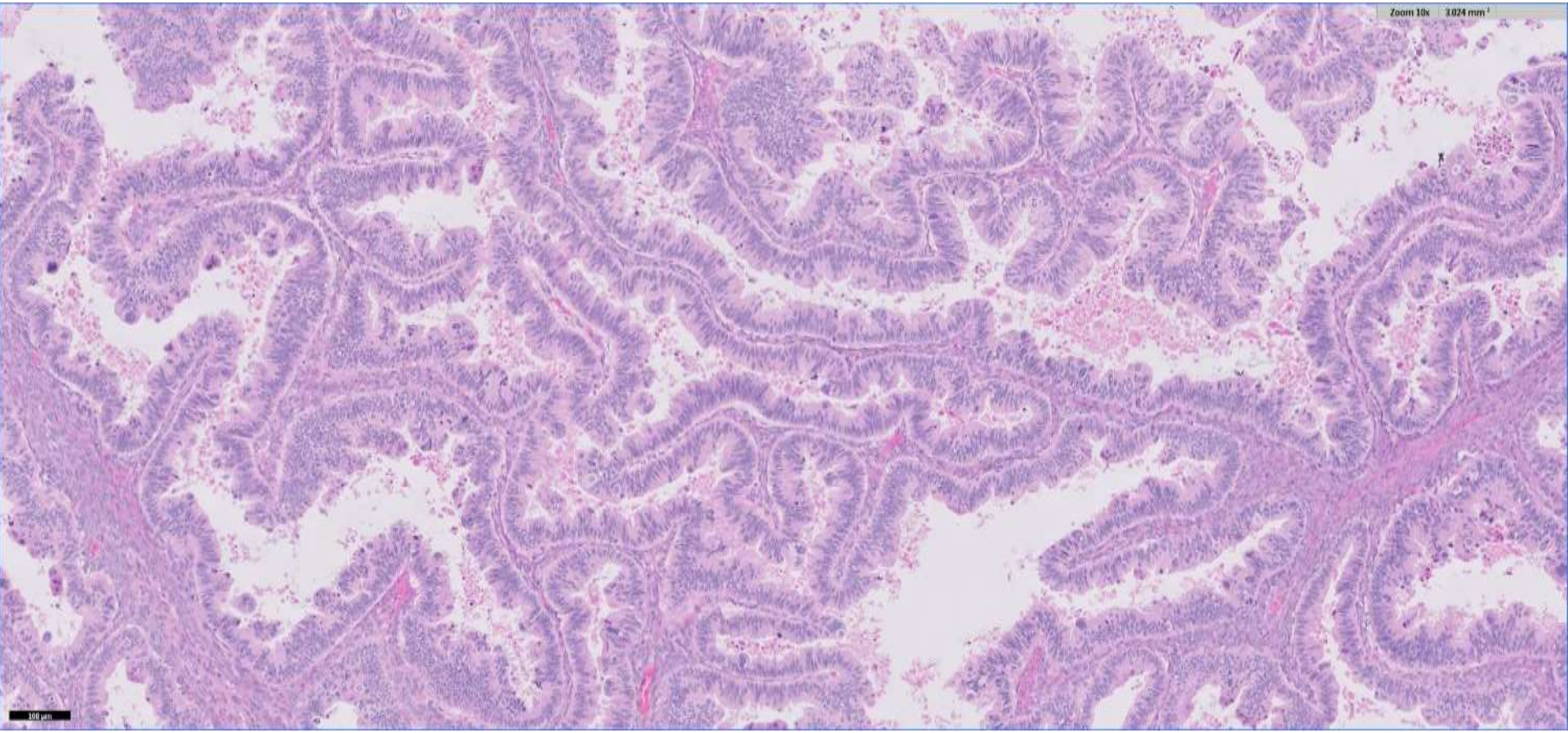
- Chromophobe RCC (eosinophilic variant)
  - Raisinoid nuclei, perinuclear clearing, prominent cell borders
  - Also CD117+, but should be diffusely positive for CK7 (oncocytoma is negative or has rare, scattered positive cells)
- Low-grade oncocytic tumor
  - Recently described entity that has substantial morphologic overlap with oncocytoma
  - Tends to have more cord-like growth and areas with tumor cell spindling
  - CD117- and CK7+ (opposite to oncocytoma)
- SDH deficient RCC
  - Distinctive flocculent cytoplasmic vacuoles
  - Loss of SDHB expression, CD117-
- Eosinophilic solid and cystic RCC
  - Cysts lined by hobnailing tumor cells, coarse basophilic intracytoplasmic inclusions
  - CK20+ and CD117-

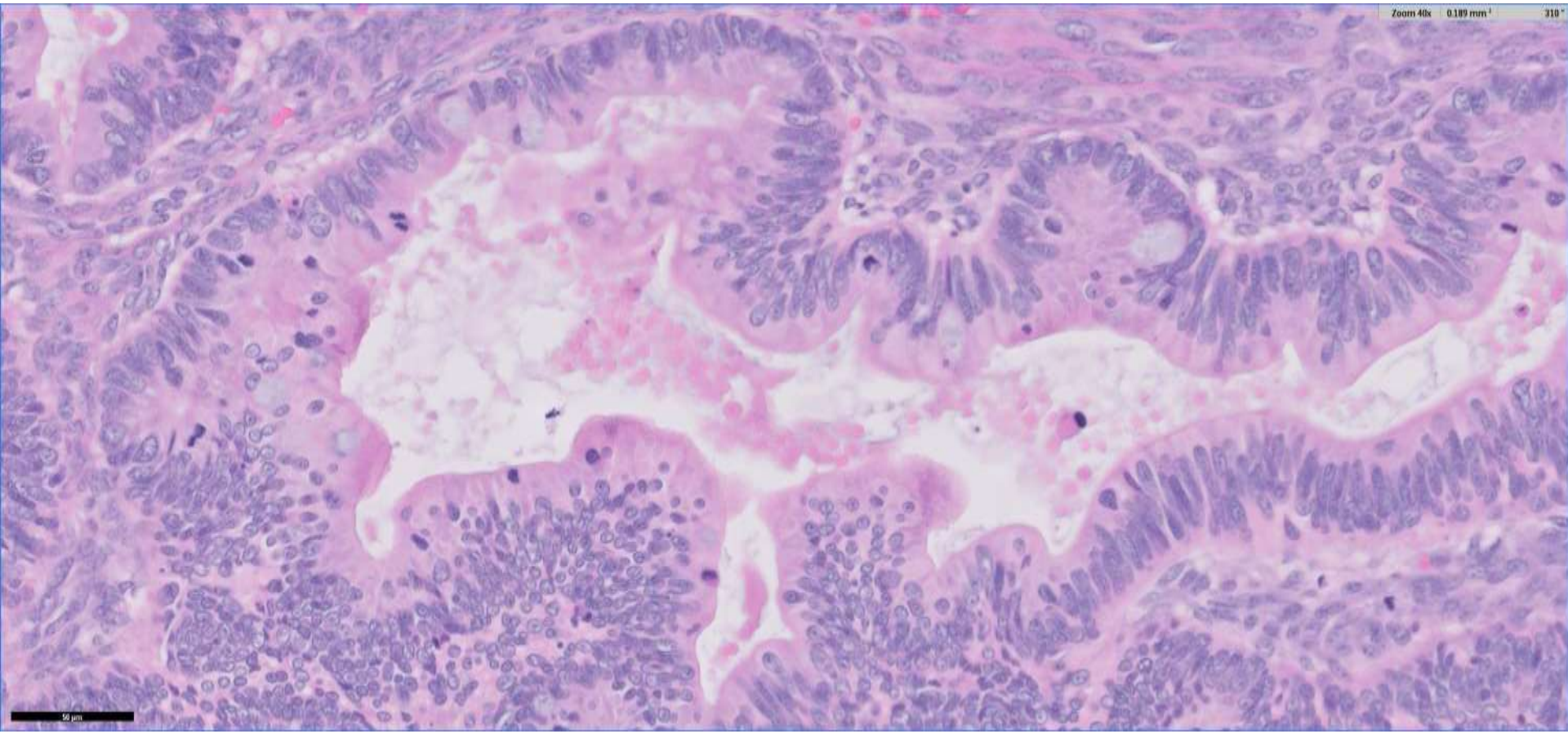
22-0302

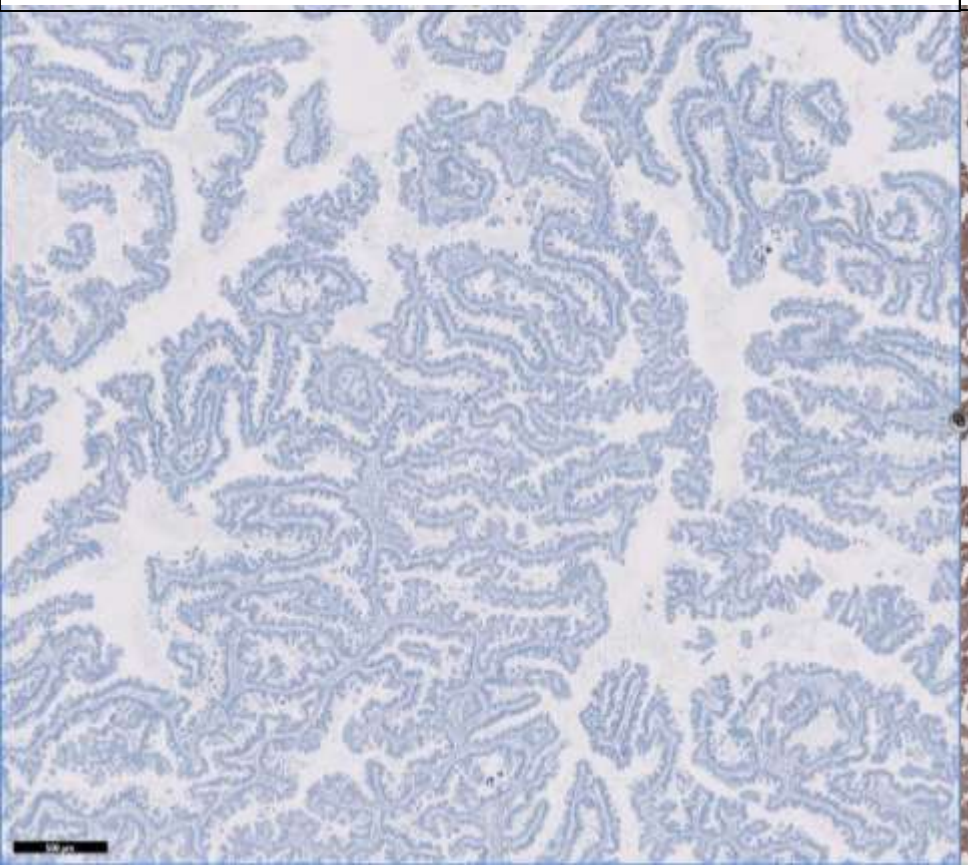
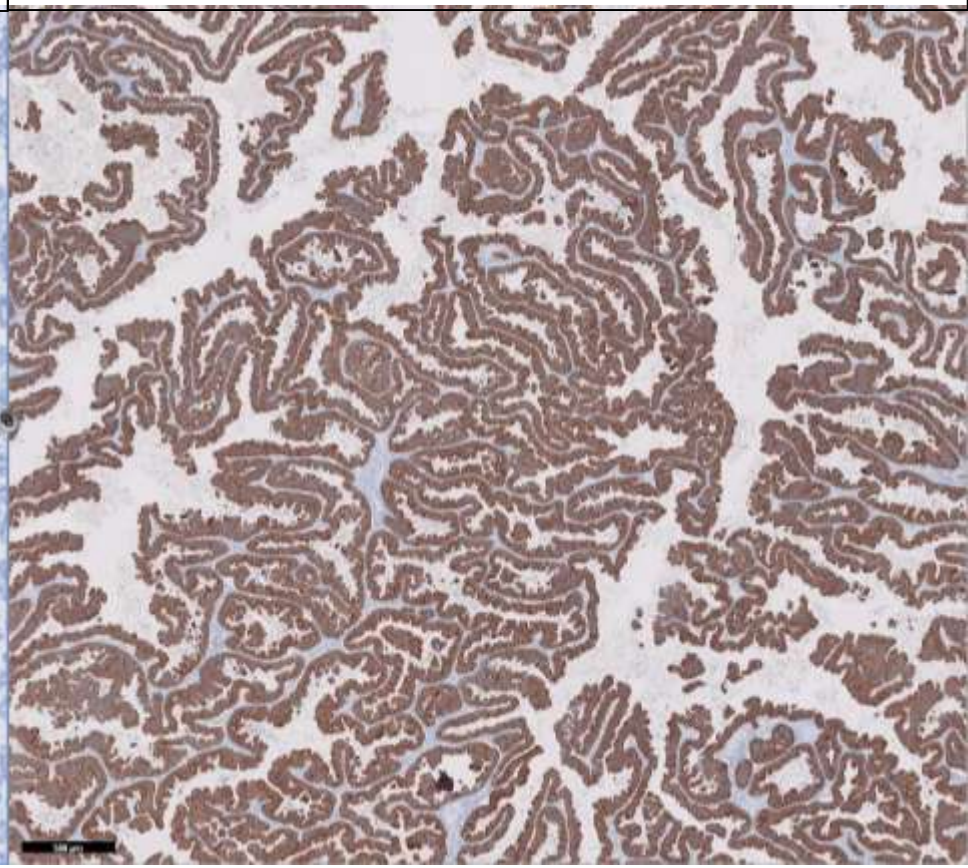
Sara Umetsu/Nick Ladwig; UCSF

Reproductive age F with solid and cystic adnexal mass.


11.5 mm


Zoom 10x
3.024 mm²
100 µm


Zoom 40x
0.189 mm ²
310 °
50 µm

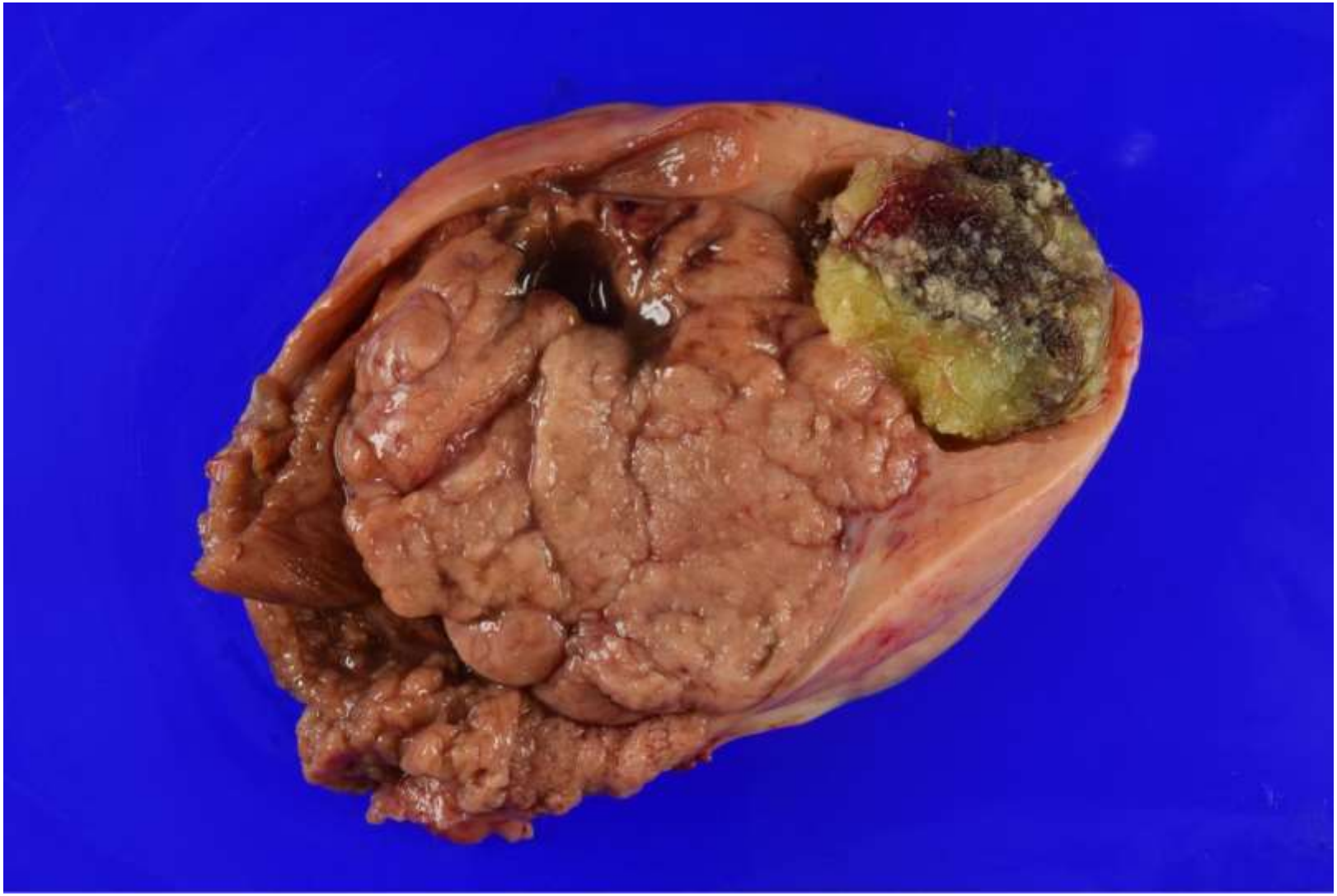
CK7	CK20
	

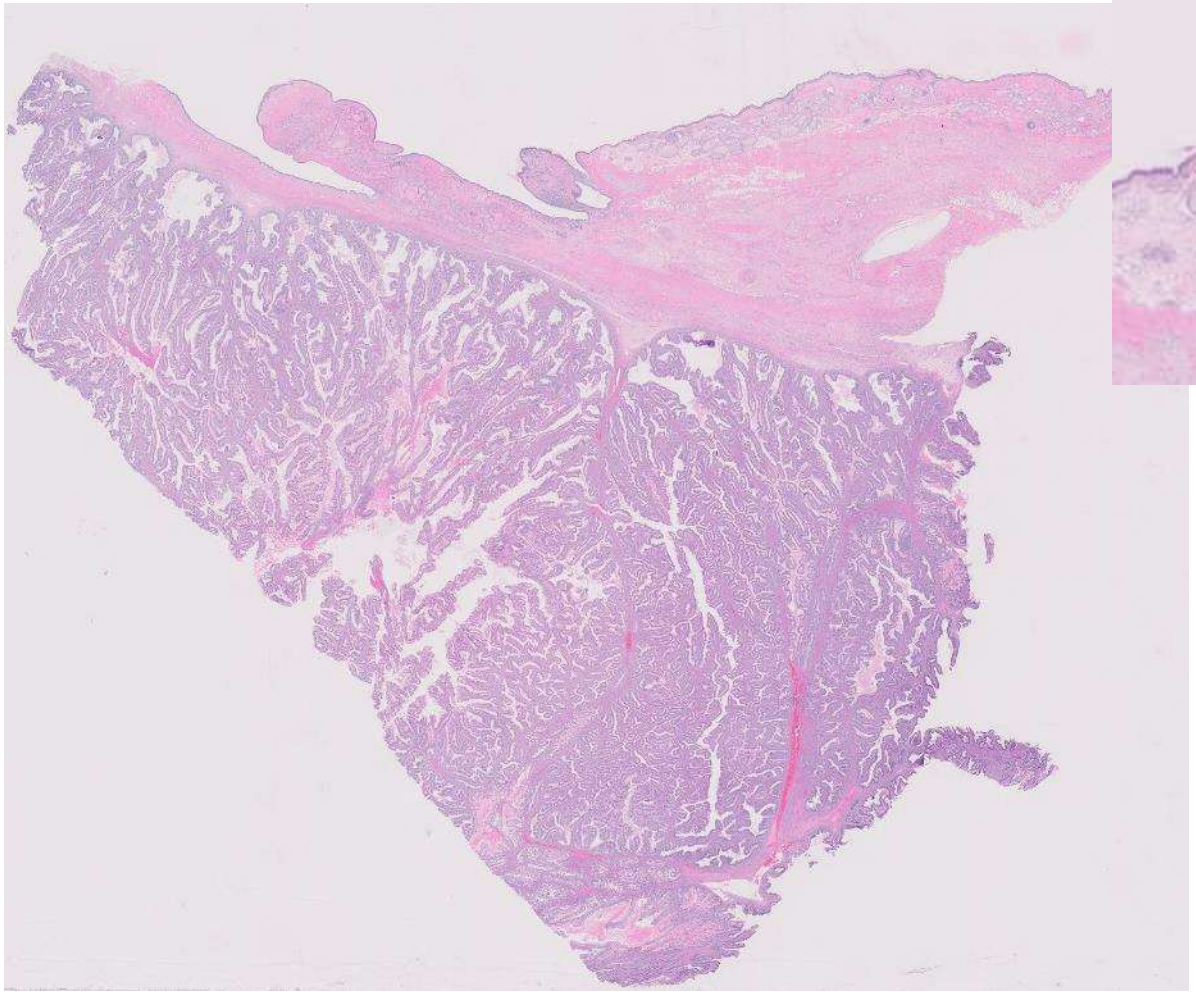
Mucinous carcinoma involving the ovary

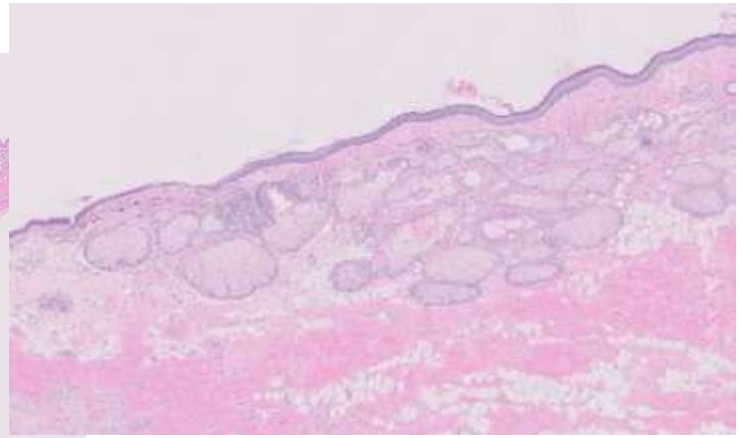
Primary Ovarian Neoplasm	Metastatic Adenocarcinoma
Clinicopathologic Features	
Unilateral	Bilateral
Confined to ovary	Involving ovarian surface
Size >10 cm	Size <10 cm
Single mass	Multinodular
Solid and cystic	Solid
No necrosis	Necrosis
Immunohistochemical	
PAX8 and ER negative	PAX8 and ER negative
CDX2 positive	CDX2 positive
CK7>>CK20	CK20>>CK7

Mucinous carcinoma involving the ovary

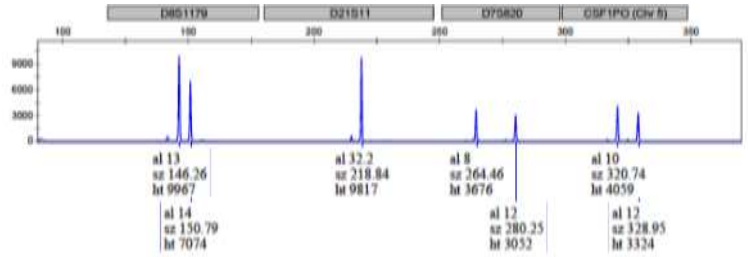
Primary Ovarian Neoplasm	Metastatic Adenocarcinoma
Histologic features favoring metastasis	**Histologic features favoring primary**
Lymphovascular invasion	Expansile pattern
Haphazard destructive growth	
Pseudomyxoma ovarii (LAMN)	



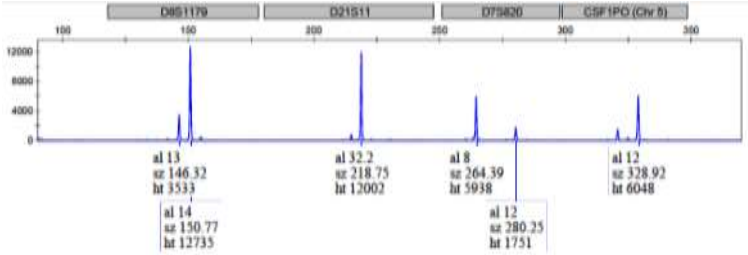




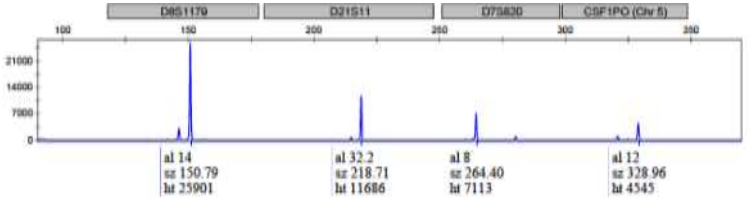
STR genotyping



Normal tissue



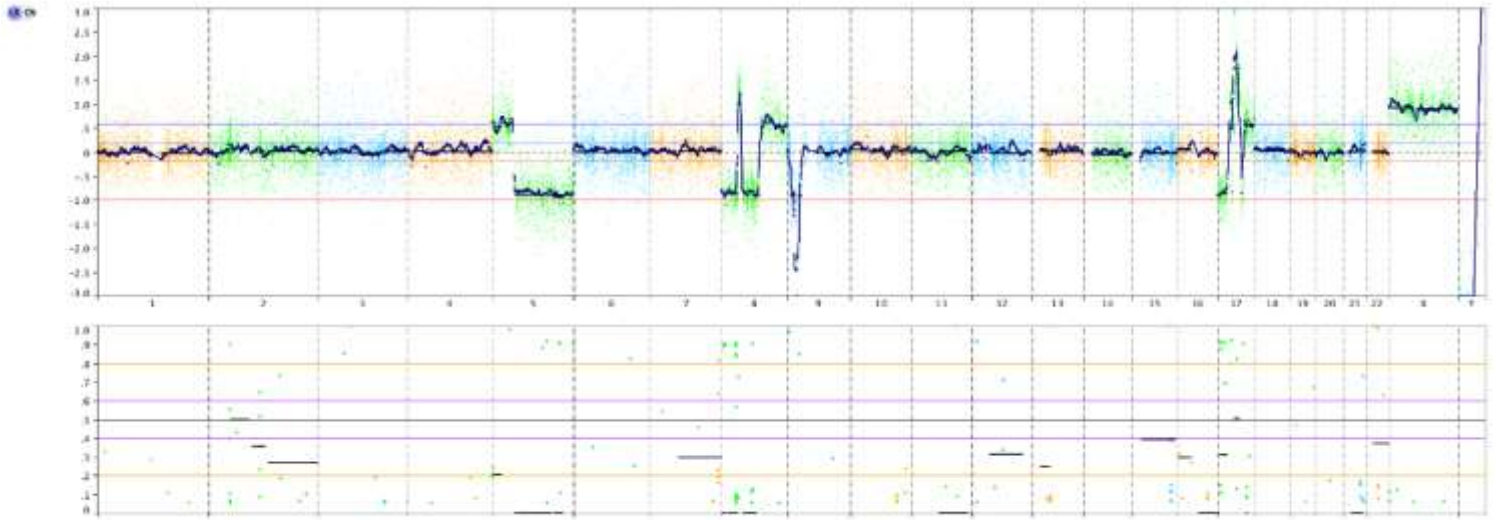
Teratoma



Adenocarcinoma

PATHOGENIC AND LIKELY PATHOGENIC ALTERATIONS

VARIANT	TRANSCRIPT ID	CLASSIFICATION	READS	MUTANT ALLELE FREQUENCY
CDKN2B,CDKN2A deep deletion	All	Pathogenic	N/A	N/A
ERBB2 amplification	All	Pathogenic	~17x	N/A
TP53 p.R175H	NM_000546.5	Pathogenic	610	88%
CEBPA p.E329fs	NM_004364.3	Likely Pathogenic	379	47%



ORIGINAL ARTICLE

Ovarian Mature Teratomas With Mucinous Epithelial Neoplasms: Morphologic Heterogeneity and Association With Pseudomyxoma Peritonei

Jesse K. McKenney, MD, Robert A. Soslow, MD,† and Teri A. Longacre, MD‡*

42 patients with ovarian teratomas and associated mucinous neoplasms

- 17 mucinous cystadenoma
- 16 intestinal-type mucinous epithelial neoplasm of LMP
- 5 mucinous carcinoma (3 with carcinomatosis)

Take home points

- Mucinous neoplasms arising in teratomas can perfectly mimic a metastasis to the ovary (both histologically and immunohistochemically)
- Thorough gross examination is helpful as teratomatous elements may be overgrown
- Ancillary molecular testing can be used to confirm teratoma origin
- Clinical behavior may be different than that of primary ovarian mucinous neoplasms without teratoma

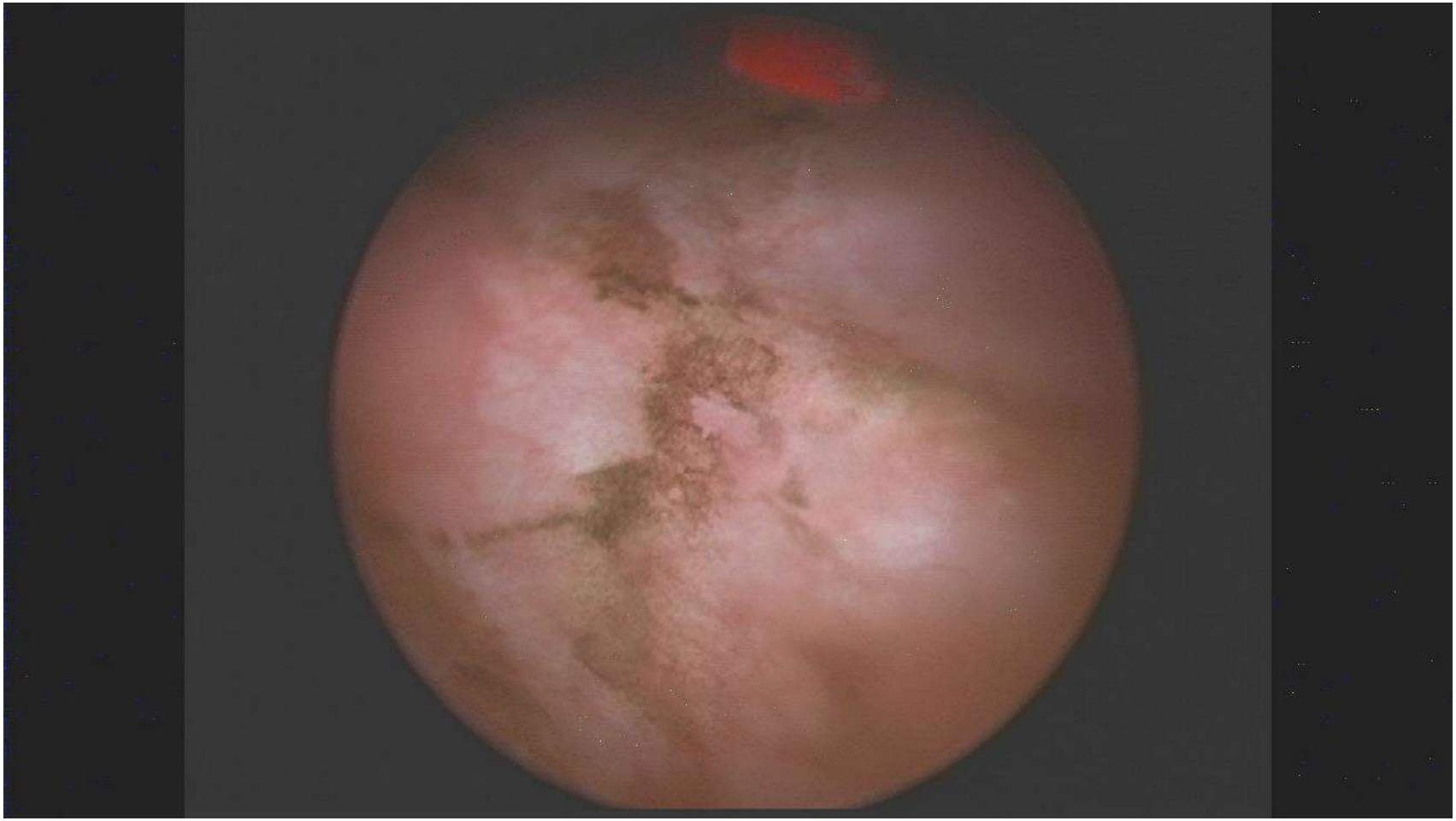
References

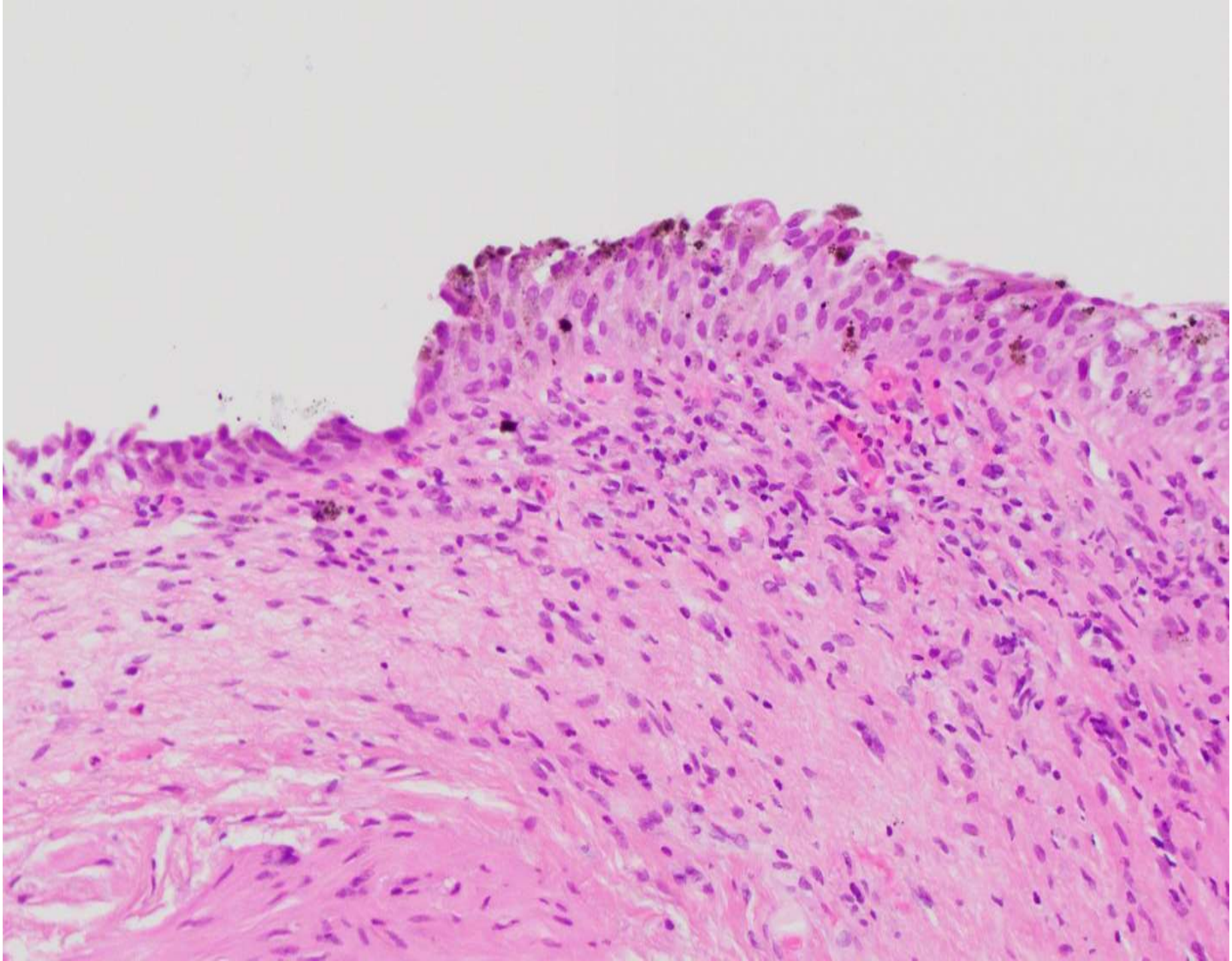
- McKenney JK, Soslow RA, Longacre TA. Ovarian mature teratomas with mucinous epithelial neoplasms: morphologic heterogeneity and association with pseudomyxoma peritonei. Am J Surg Pathol. 2008 May;32(5):645-55. doi: 10.1097/PAS.0b013e31815b486d. PMID: 18344868.

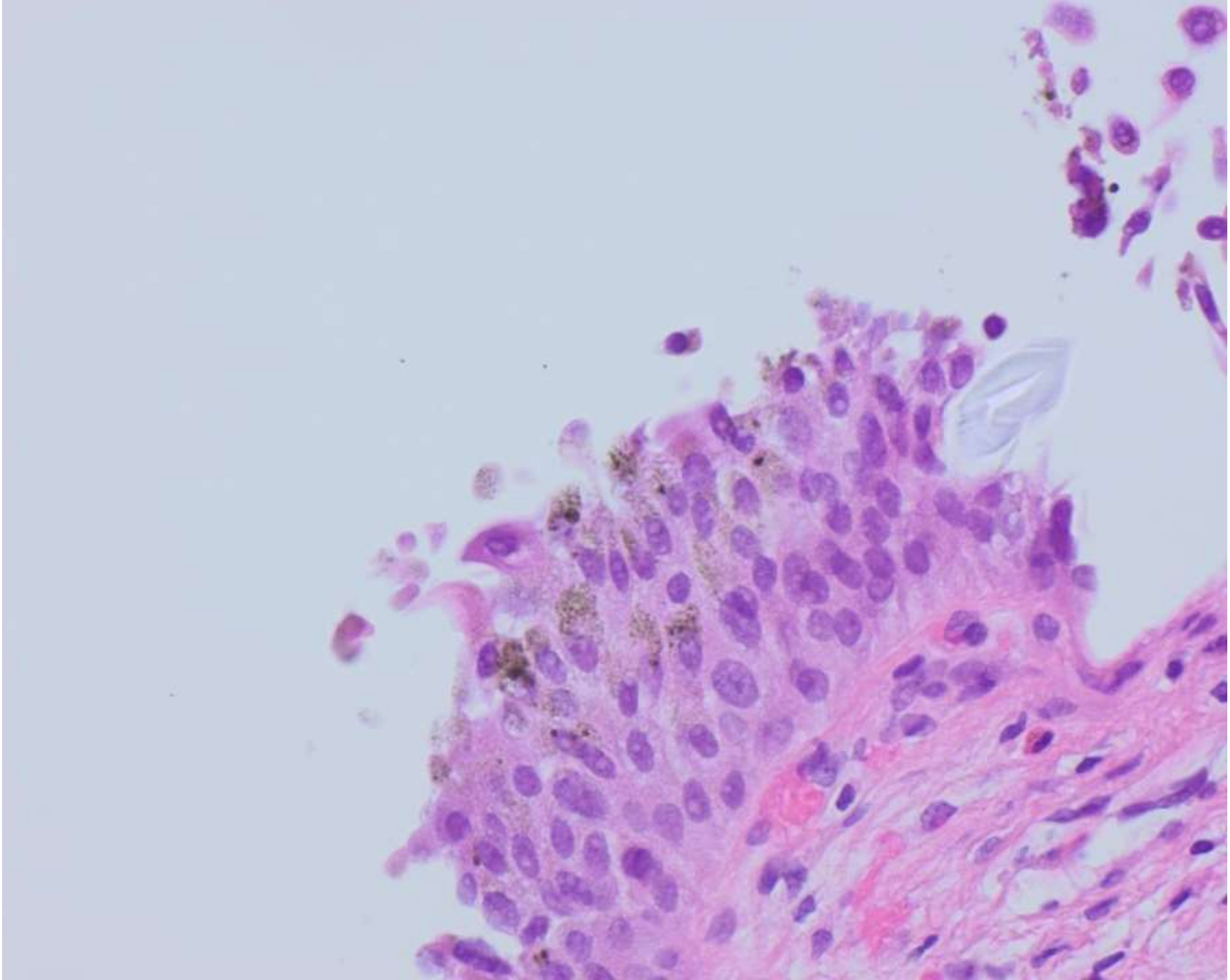
22-0203

Alexandra Chang-Graham/Hubert Lau/Christine Louie; VA Palo Alto/Stanford

Elderly M with h/o recurrent low grade pTa urothelial carcinoma, presenting with diffuse brown charcoal patches on recent surveillance cystoscopy.





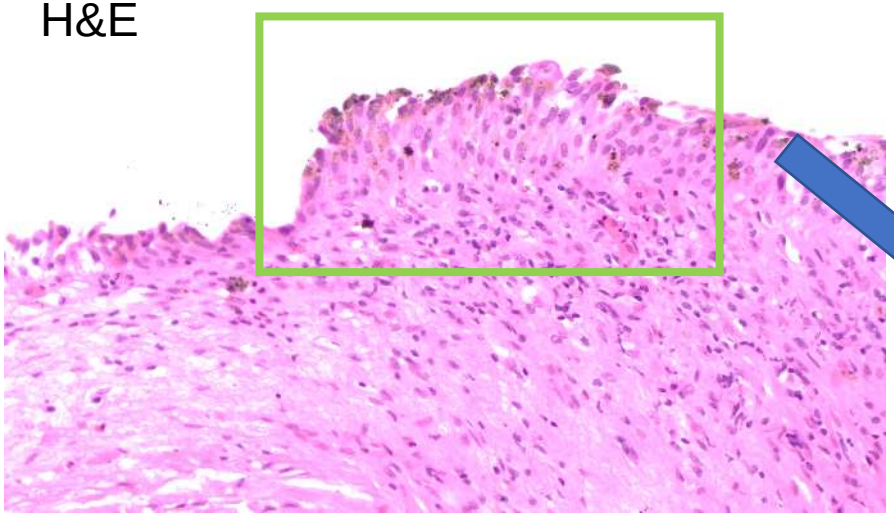


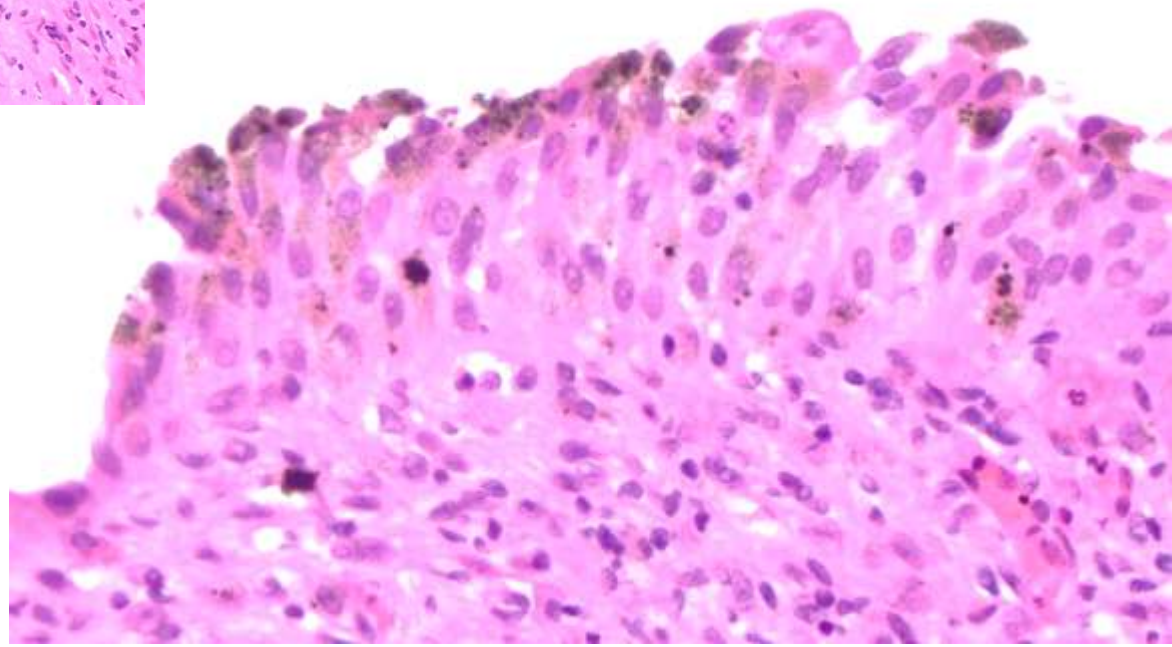
Clinical history:
Elderly male with history of recurrent LG Ta urothelial carcinoma, presenting with diffuse brown-charcoal patches on recent surveillance cystoscopy.

Alex Chang-Graham, Hubert Lau, Christine Louie

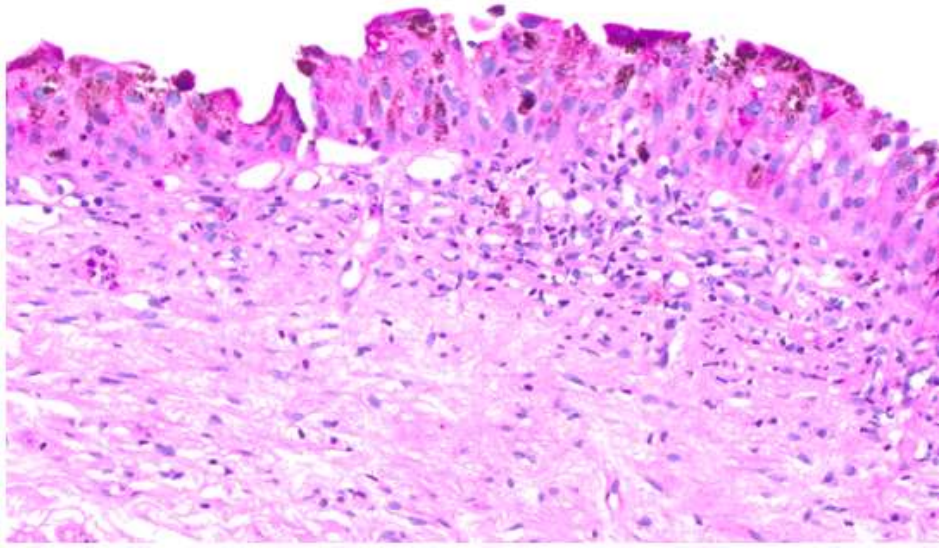
VA Palo Alto Healthcare System/Stanford University

H&E

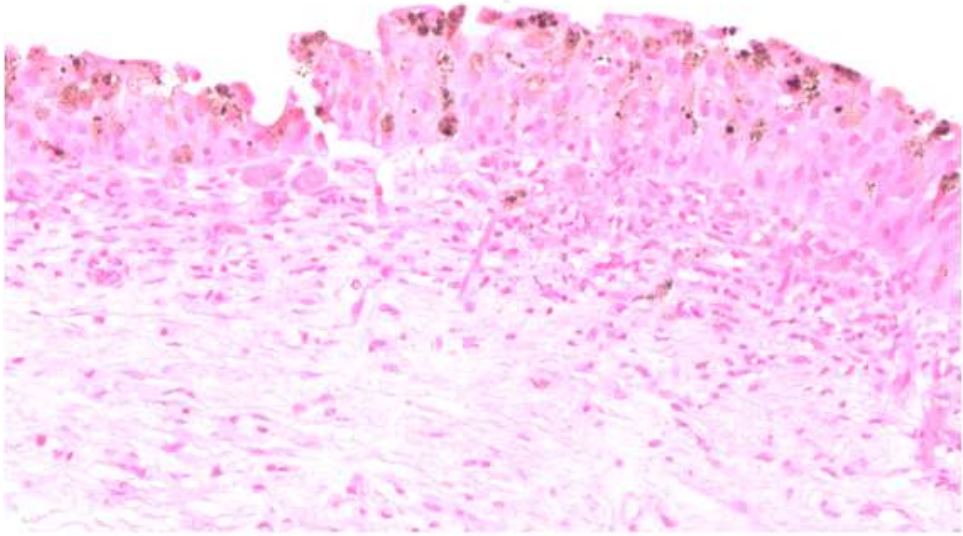




PAS

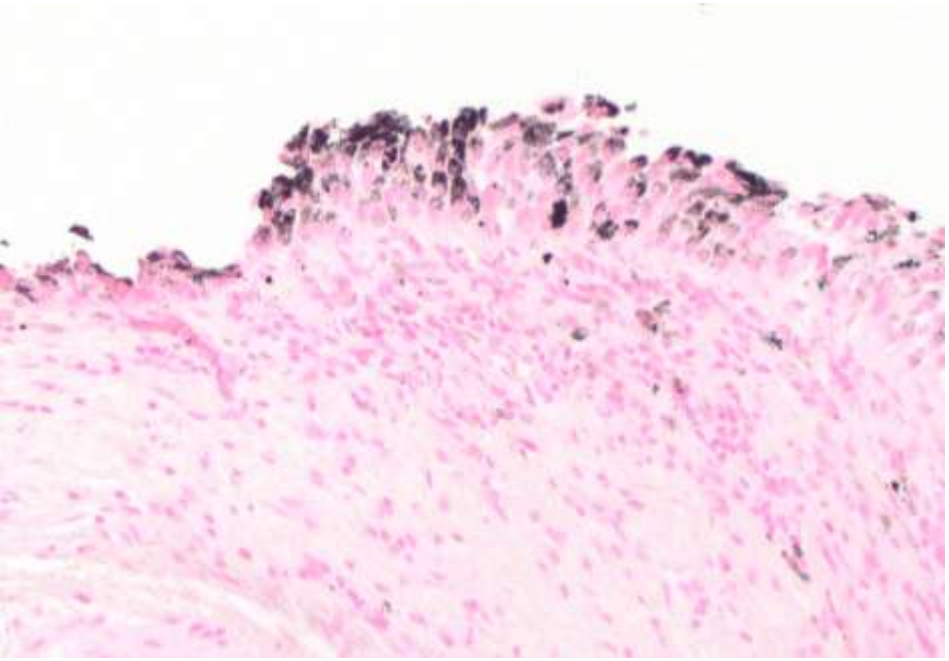


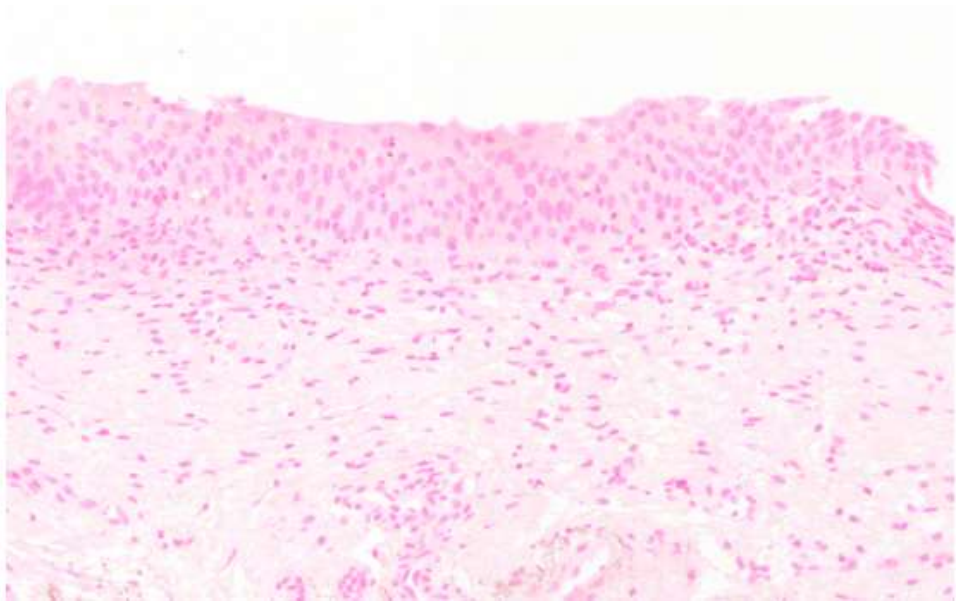
Iron



Fontana-Masson stain

+ oxidizing agent



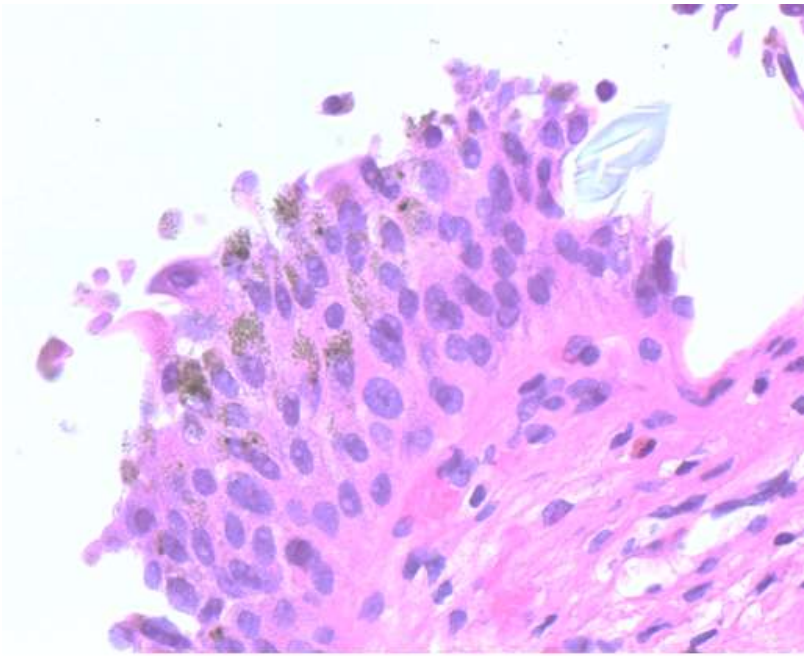


Differential diagnosis

	S100, MelanA, HMB45	PASd	Iron	Fontana-Masson
Primary or metastatic melanoma	**(+)**			
Lipofuscinosis		**(+)**		
Hemosiderosis			**(+)**	
Melanosis				**(+)**

Bladder melanosis: a rare histopathologic finding

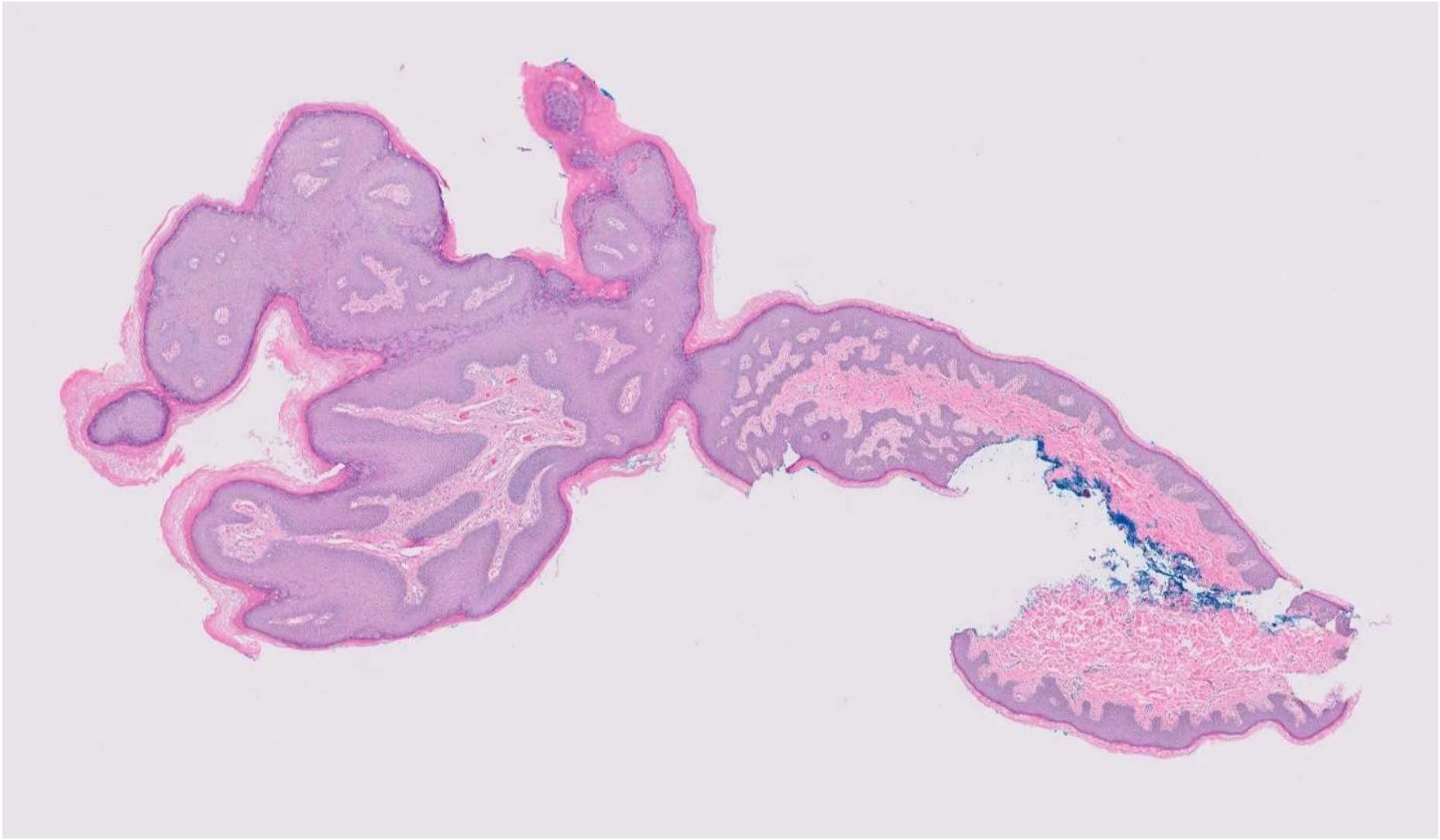
- Bladder melanosis = deposition of melanin in urothelium and/or in lamina propria macrophages
- Bladder mucosa appears dark brown/black
- Rare, ~25 cases reported in literature
- Considered a benign, incidental finding
- Fontana-Masson stain turns pigment black and oxidizing agent then bleaches it→ confirms pigment is melanin
- Source of the pigment granules unknown

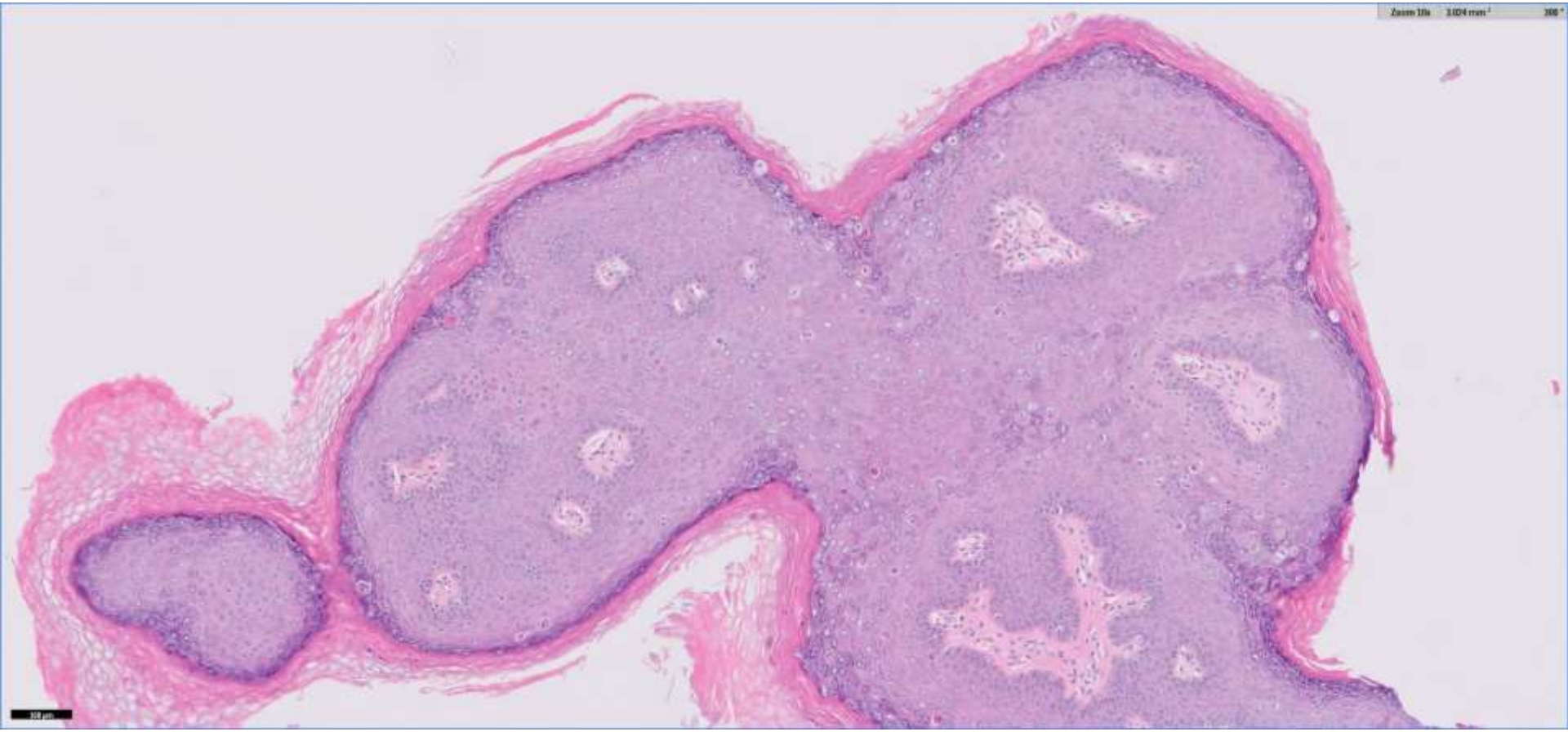


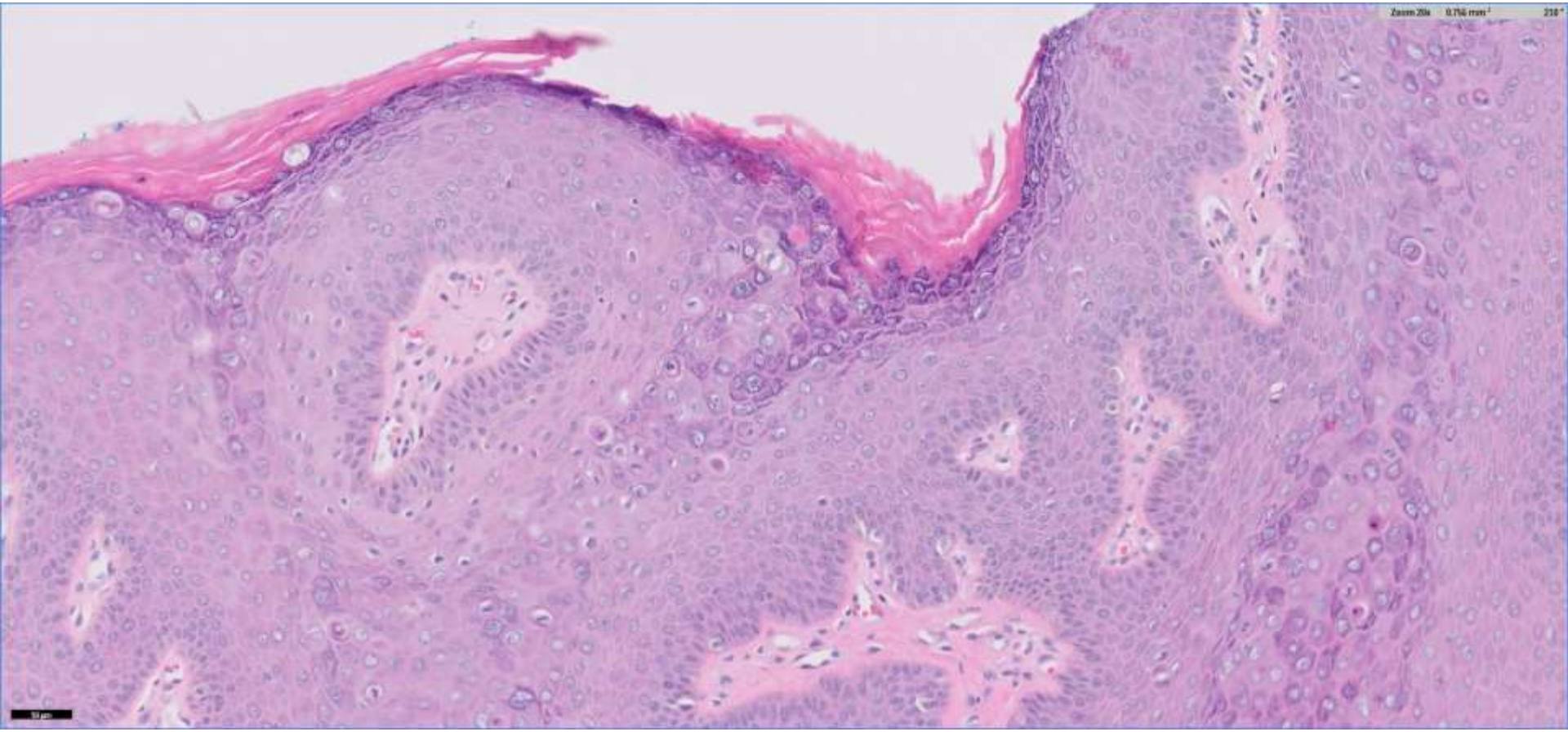
22-0304

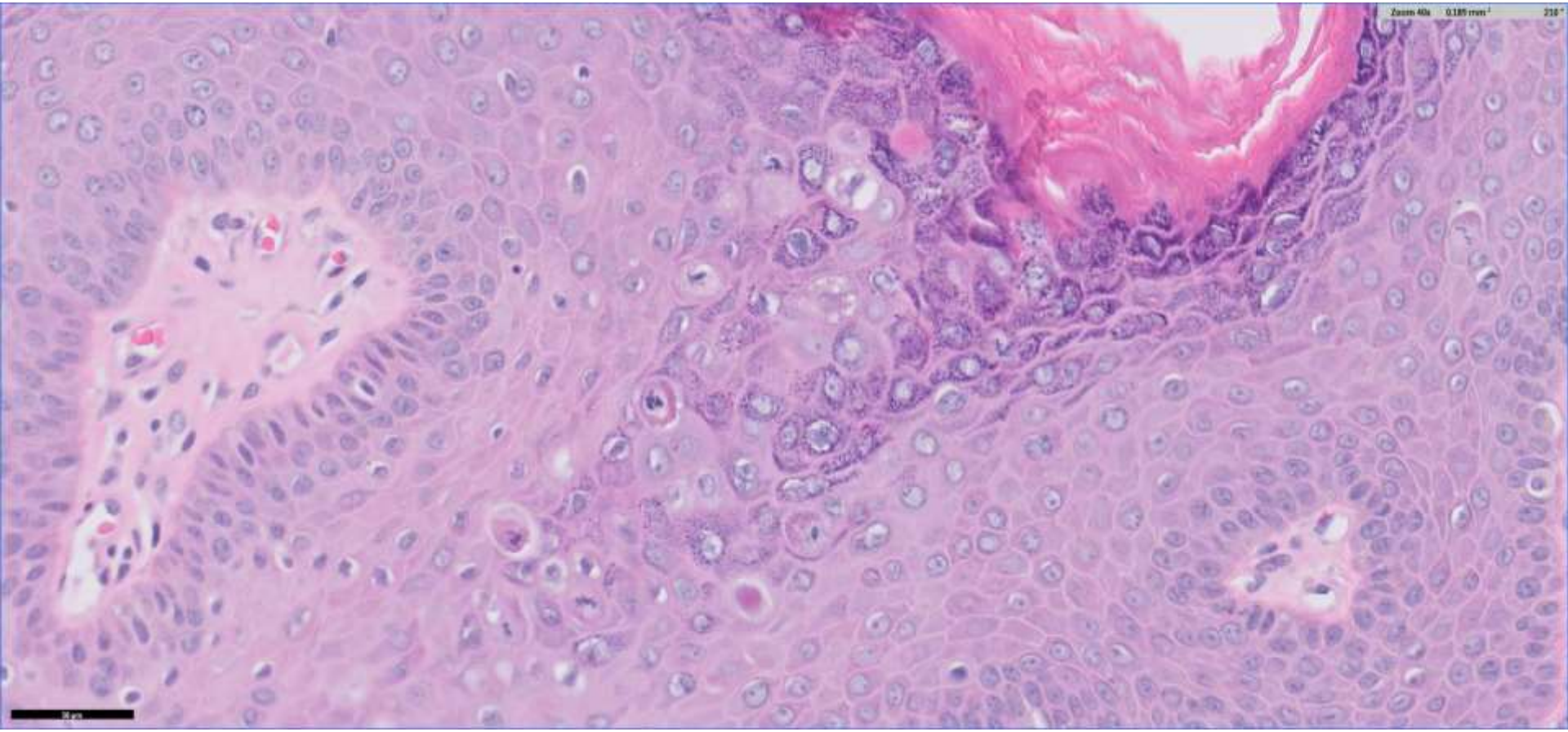
Nick Ladwig; UCSF

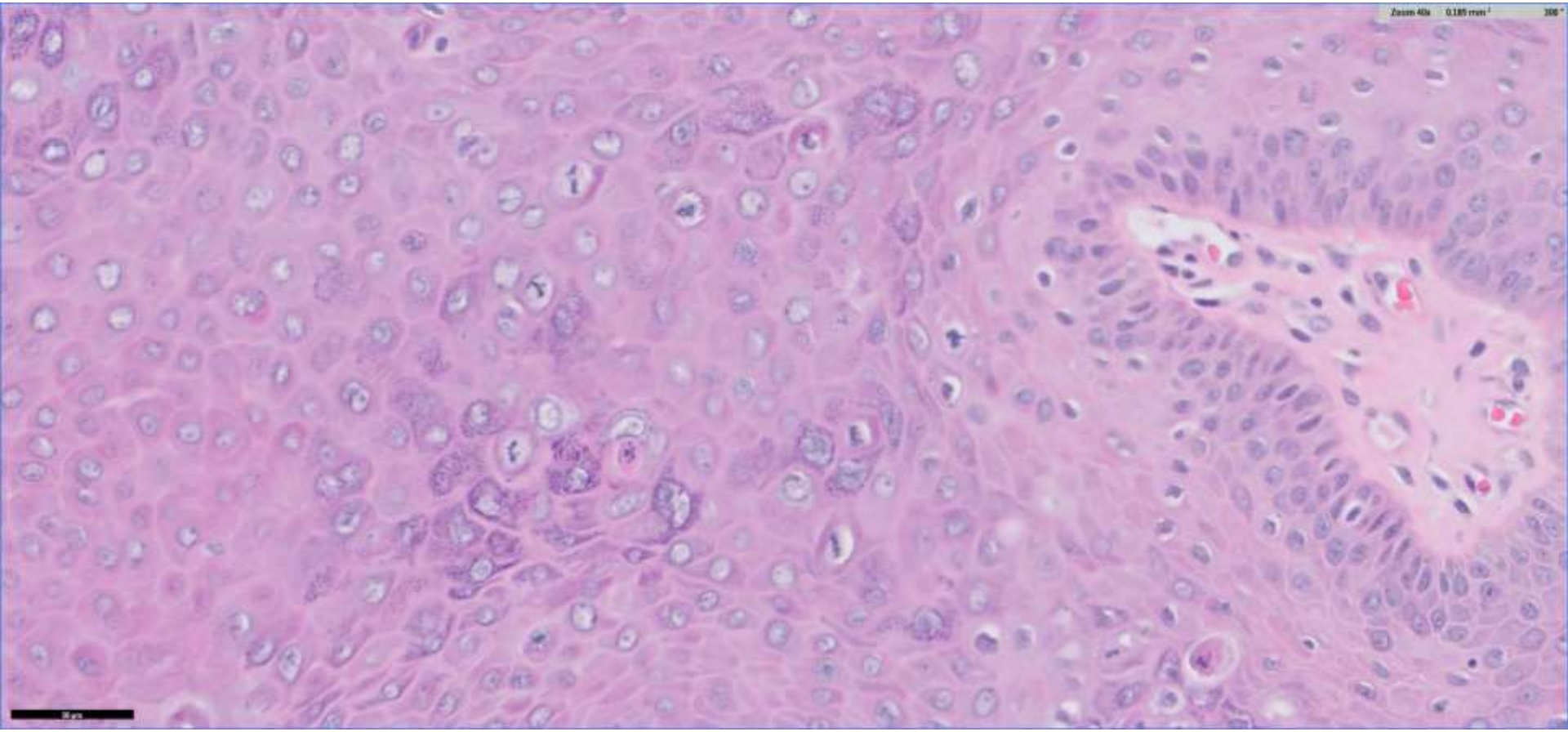
Reproductive age F with exophytic vulvar lesion.





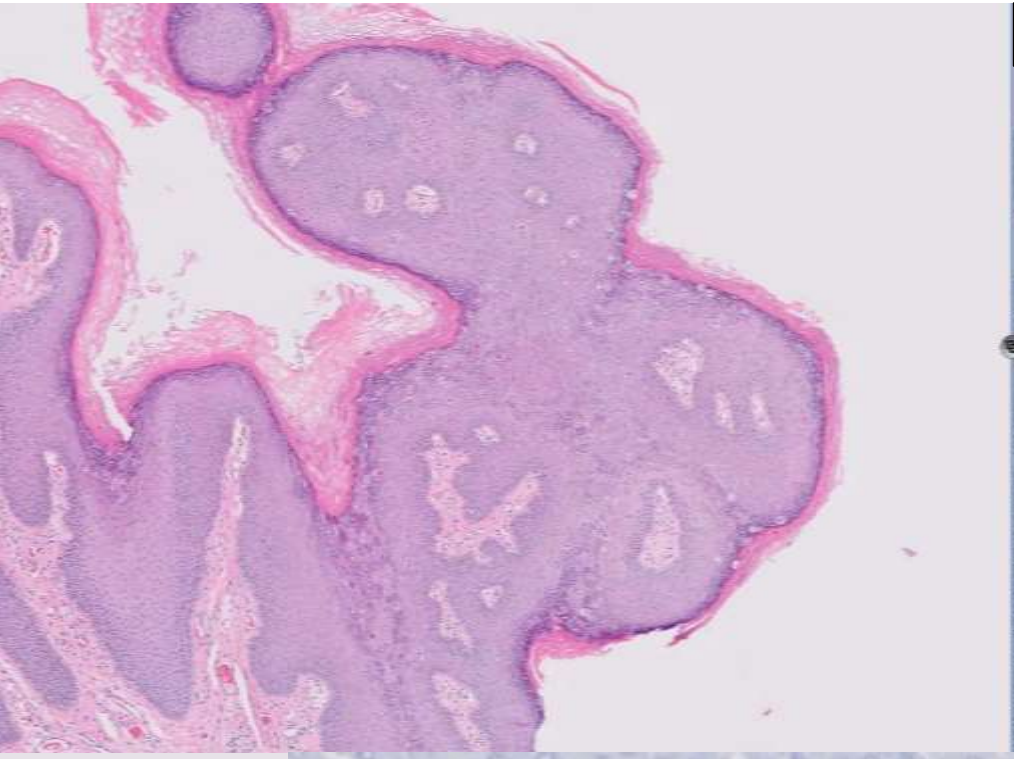


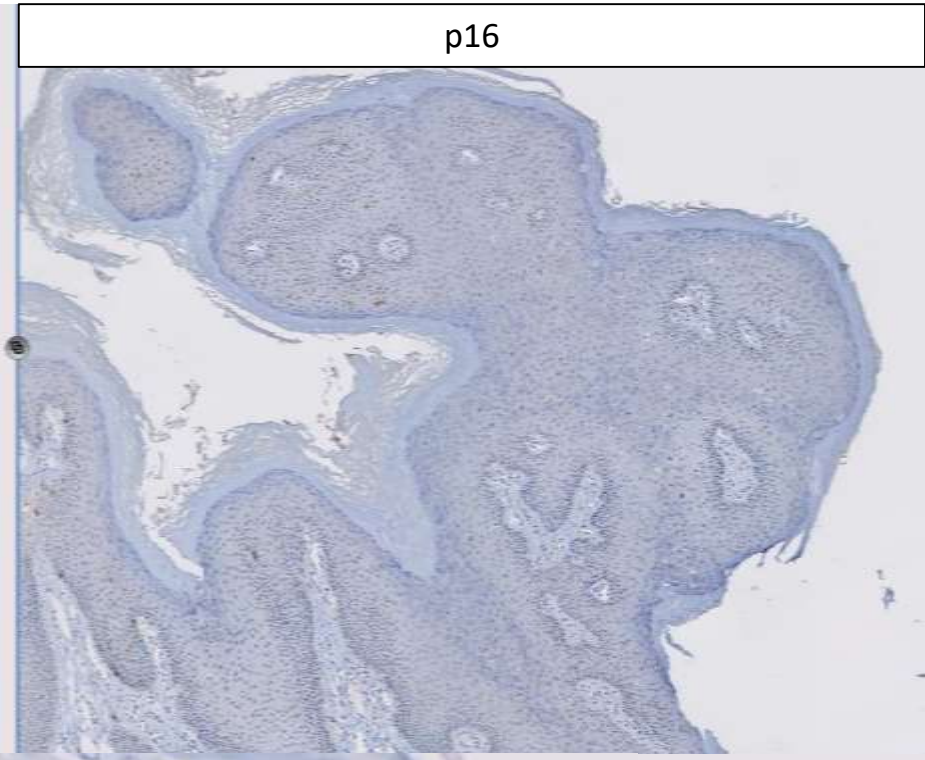




Differential Diagnosis

- Benign squamous proliferation
  - Squamous papilloma
  - Fibroepithelial polyp
- Condyloma (low-risk HPV-associated LSIL)
- High-grade squamous intraepithelial lesion (HSIL)
  - High-risk HPV-associated HSIL
  - HPV-independent (dVIN)
    - Differentiated vulvar intraepithelial neoplasia (dVIN) → p53-mediated
    - Non-HPV, non-p53-associated proliferations
      - Vulvar acanthosis with altered differentiation (VAAD)
      - Differentiated exophytic vulvar intraepithelial lesion (DEVIL)





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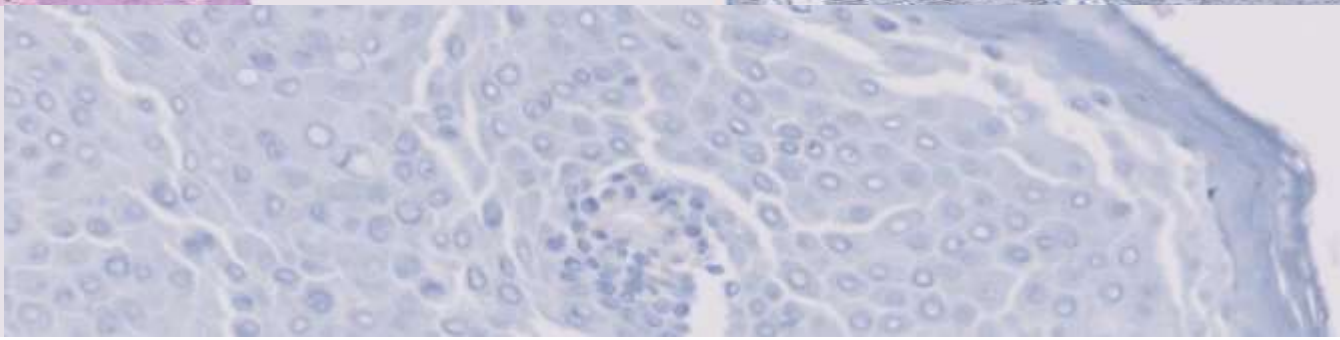
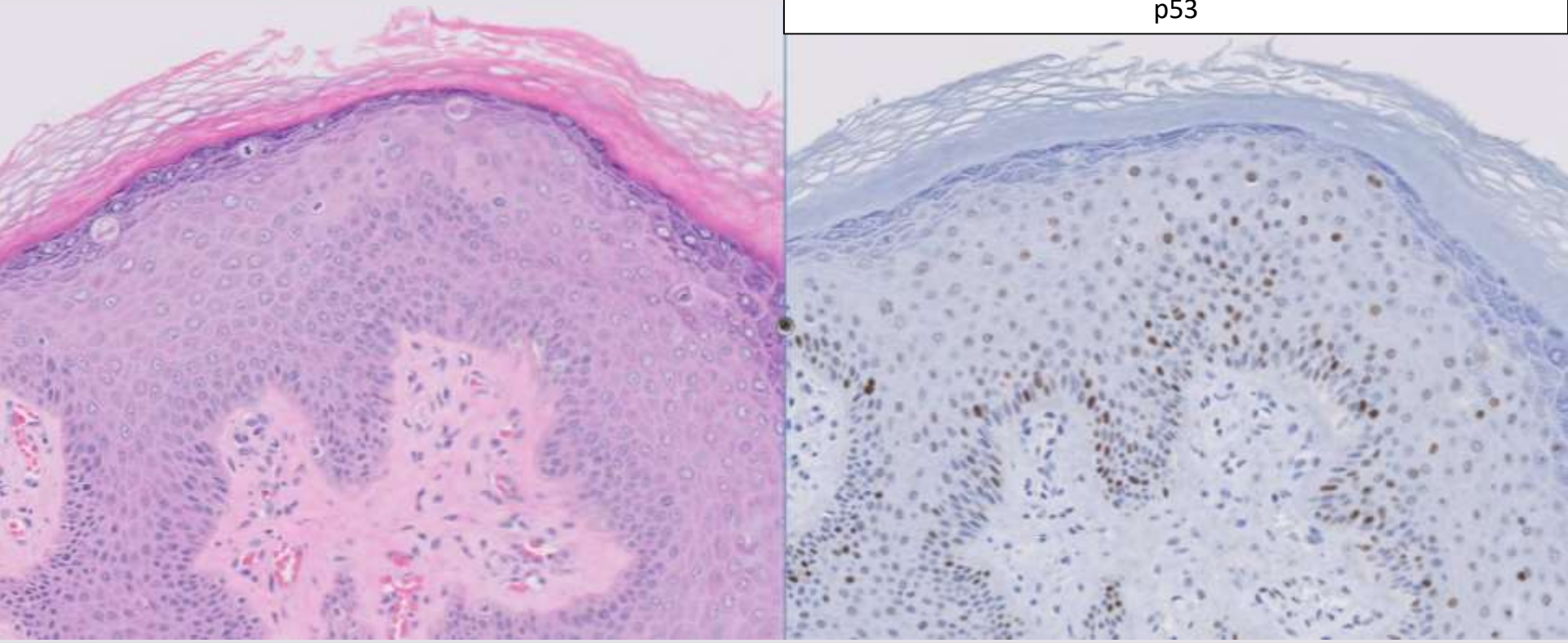


HRHPV RNA
(ish)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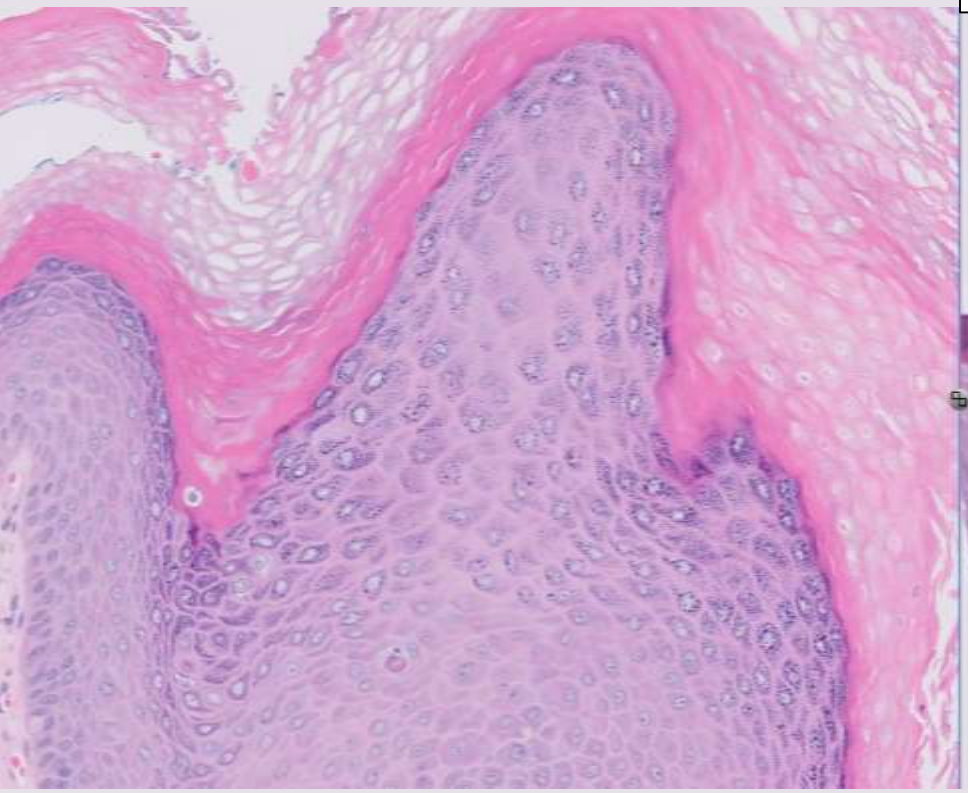
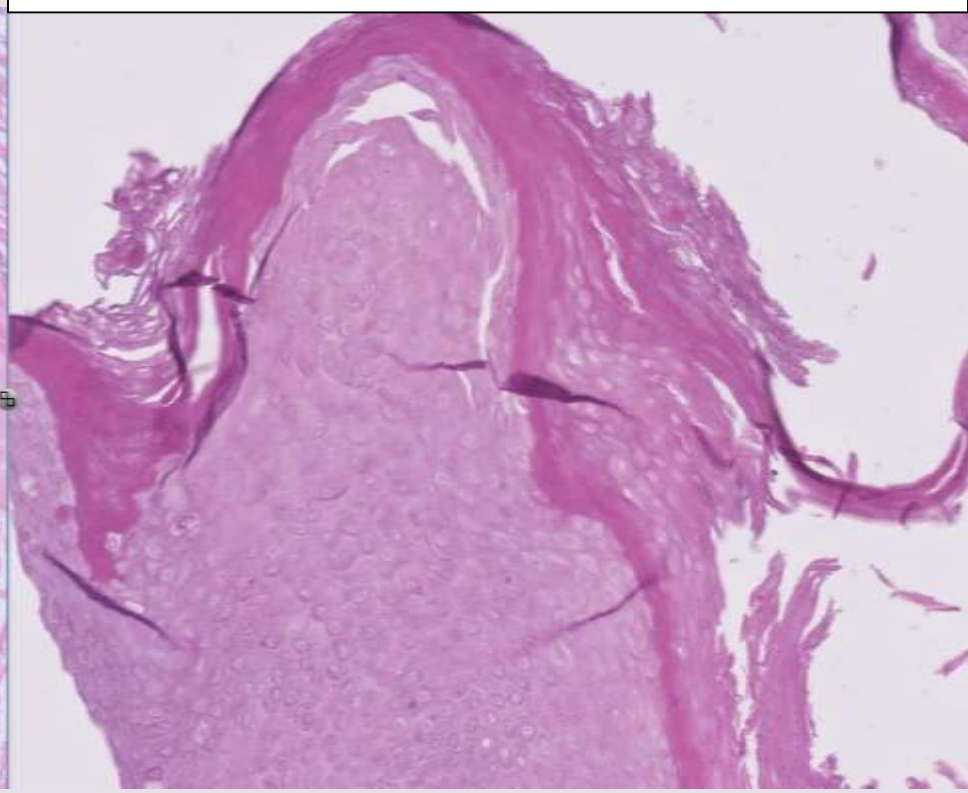
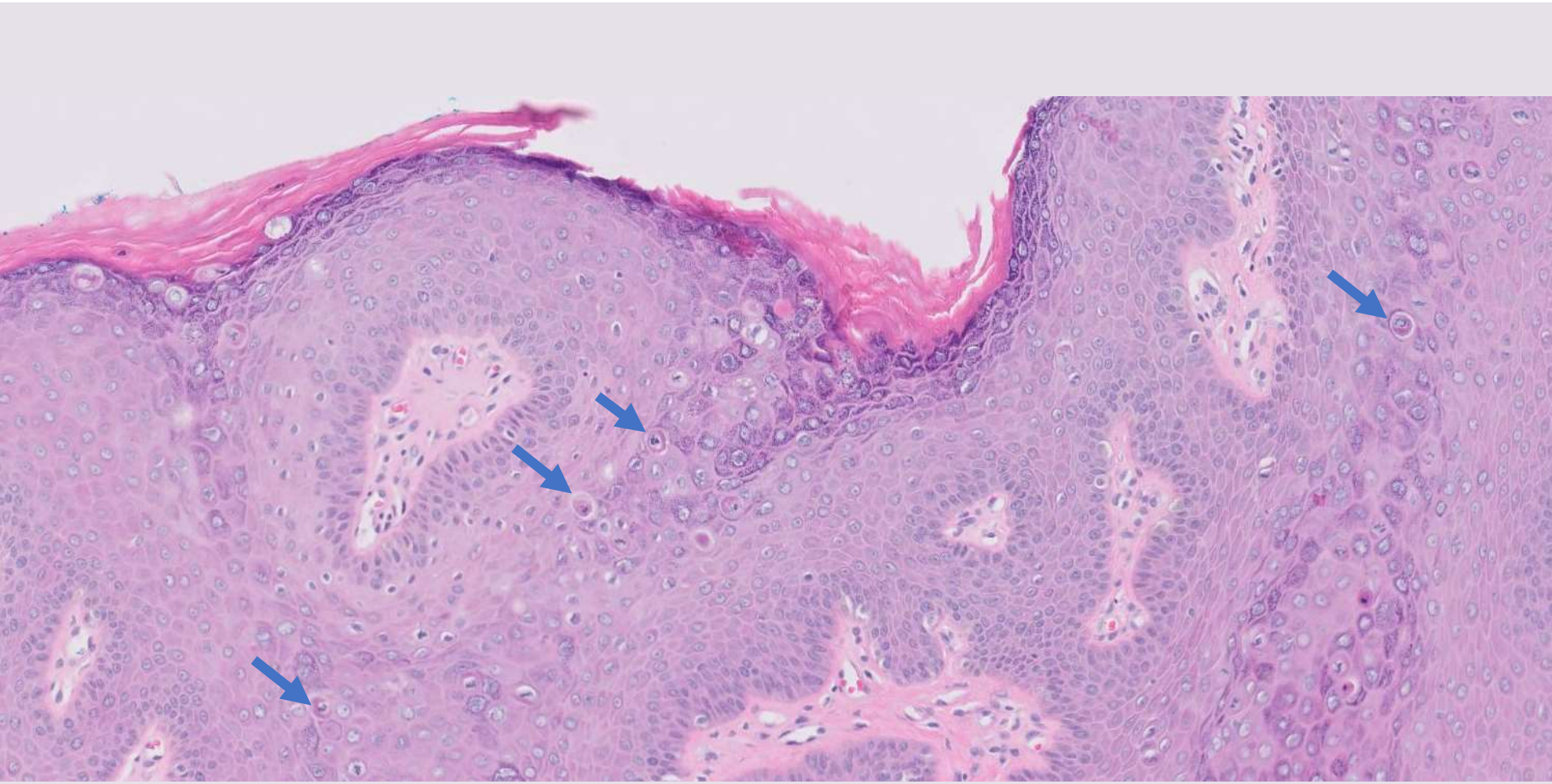
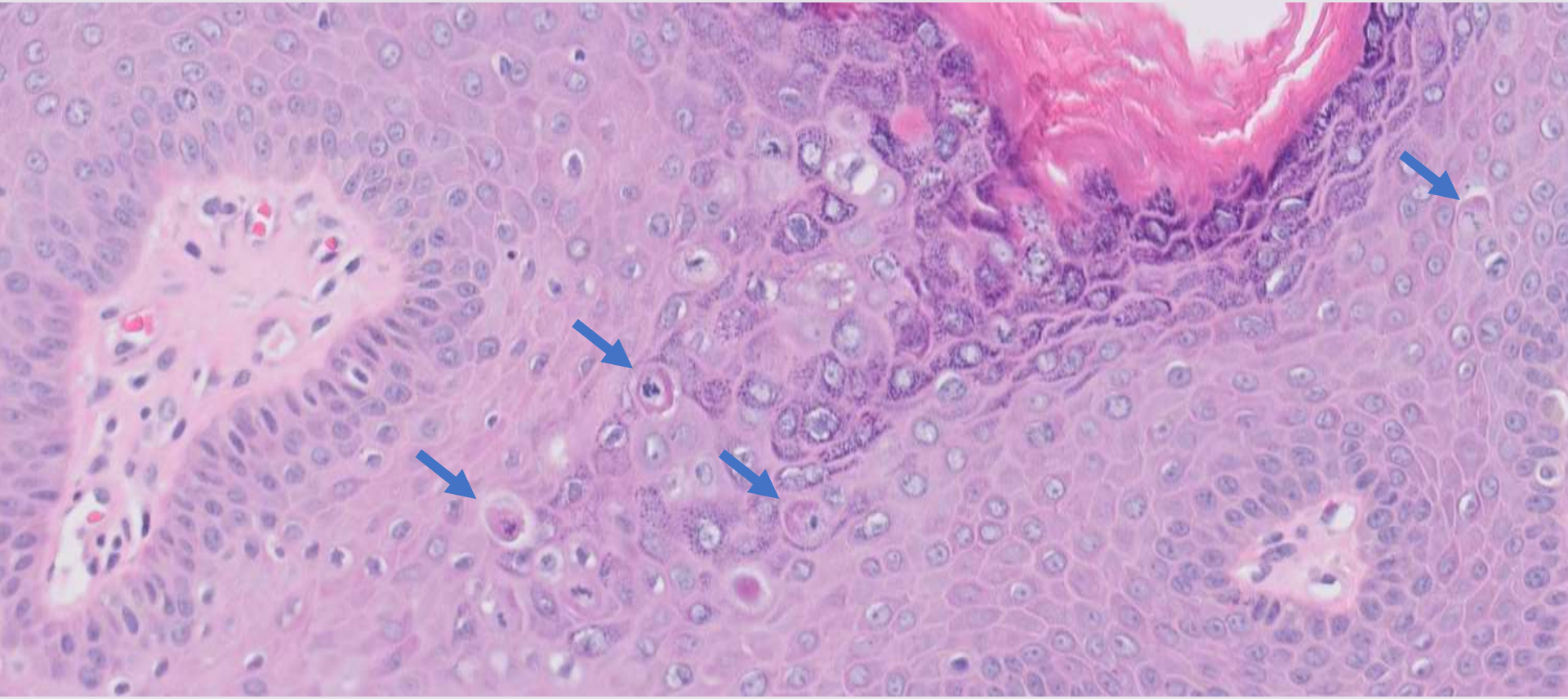


HPV 6/11 (ish)







Pseudobowenoid Vulvar Change: Untreated Condyloma Acuminatum

Marisa R. Nucci, M.D., David R. Genest, M.D., James E. Tate, M.S., Candace K. Sparks, M.T., Christopher P. Crum, M.D.

Division of Women's and Perinatal Pathology, Department of Pathology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts

TABLE 1. Morphologic Comparison of Vulvar Intraepithelial Neoplasia, Podophyllin-Treated Condyloma and Pseudobowenoid Change

Parameter	Vulvar intraepithelial neoplasia	Podophyllin-treated condyloma	Pseudobowenoid change
Karyorrhexis	All levels	Lower levels	Upper levels
Mitoses	Atypical; all levels	Arrested metaphases in lower epidermis (podophyllin cells)	Dispersed chromatin mimicking metaphase in upper one-third only (target cells)
Multinucleation	Frequent; lower layers	Rare-to-absent in lower layers	Rare-to-absent in lower layers
Dyskeratosis	Frequent, including abnormal mitoses	Infrequent	Characteristic
Nuclear atypia	Prominent; all layers	Mild; upper layers only	Mild; upper layers only
Cell crowding	Prominent	Minimal	Minimal

HPV/DNA Analysis

Three of the four specimens analyzed were negative for HPV DNA by polymerase chain reaction analysis, and one was positive for an unknown HPV type by restriction fragment length polymorphism analysis. One of four was positive for HPV DNA by *in situ* hybridization, with two of four scoring positive for HPV by both techniques.

CORRESPONDENCE RE: NUCCI MR, GENEST DR, TATE JE, SPARKS CK, CRUM CP: PSEUDOBOWENOID VULVAR CHANGE: UNTREATED CONDYLOMA ACUMINATUM. MOD PATHOL 9:375, 1996

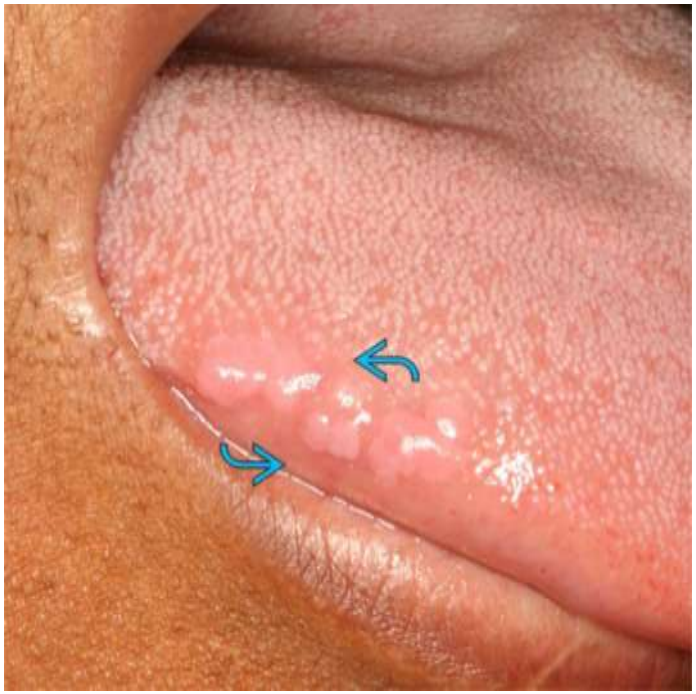
To the Editor: In their description of a "new" finding in the upper portion of condylomata, Dr. Nucci and her colleagues seem to have rediscovered a phenomenon reported in the oral pathology literature as mitusoid cells. They describe cells in the upper spinous layer of the epidermis with a "perichromatin halo delineated by a rim of dense cytoplasm, beyond which a second zone of uniform clearing was observed." The cells in question are illustrated in Figure 1B.

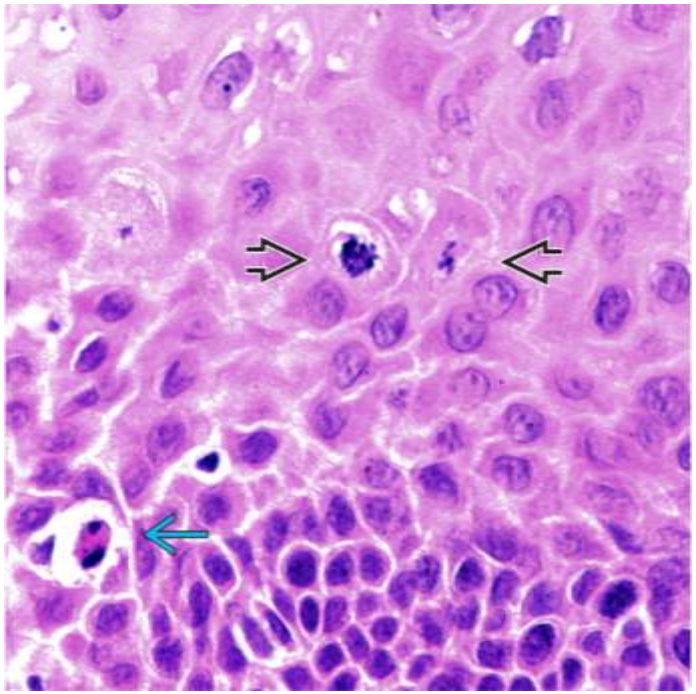
Mitusoid cells were (I believe) first noted in focal epithelial hyperplasia, or Heck's disease (1). At the time of their description, the role of human papillomavirus (HPV) in Heck's disease was yet to be discovered. Mitusoid cells are so named because human papillomavirus infection alters their nuclei so that the pattern of chromatin resembles that seen in a mitotic figure. An excellent illustration of mitusoid cells is found in a current oral pathology text (2).

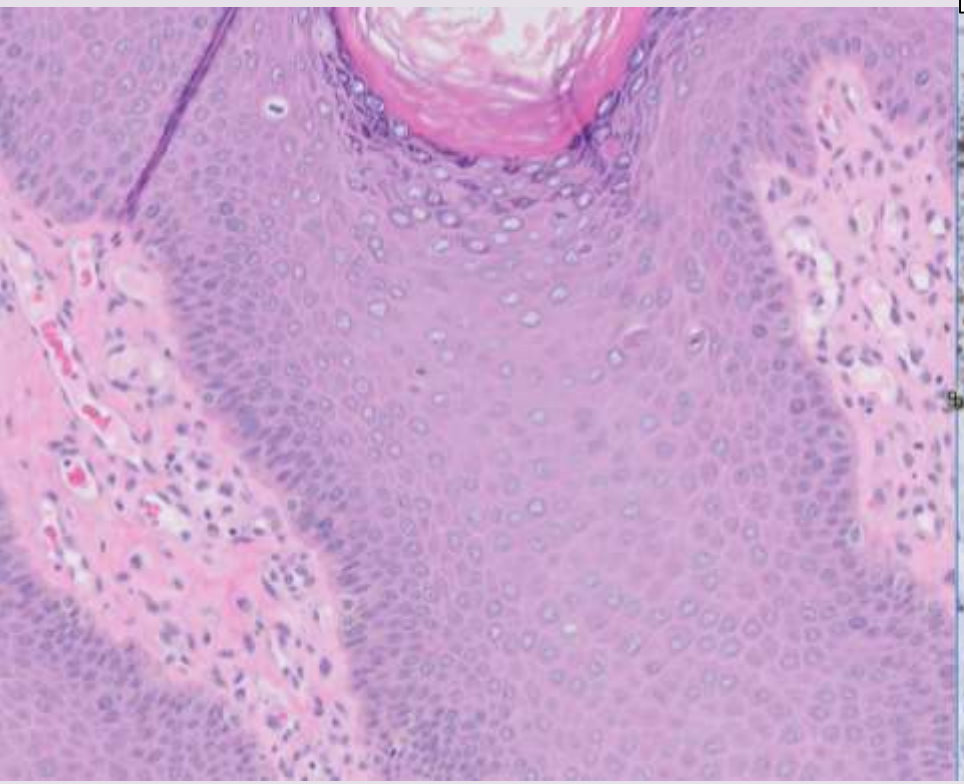
It would be interesting to study these bodies further, to determine which HPVs they are associated with. Heck's disease is usually caused by HPV 13, but HPV 32, which can infect genital skin, is sometimes isolated. It would also be interesting to determine whether the cells in question are in mitosis, or in apoptosis, or in the midst of both processes simultaneously, as can occur in Bowen's disease of the skin.

Philip E. LeBoit, M.D.
University of California, San Francisco
San Francisco, California

Focal Epithelial Hyperplasia of Oral Cavity (Heck's Disease)







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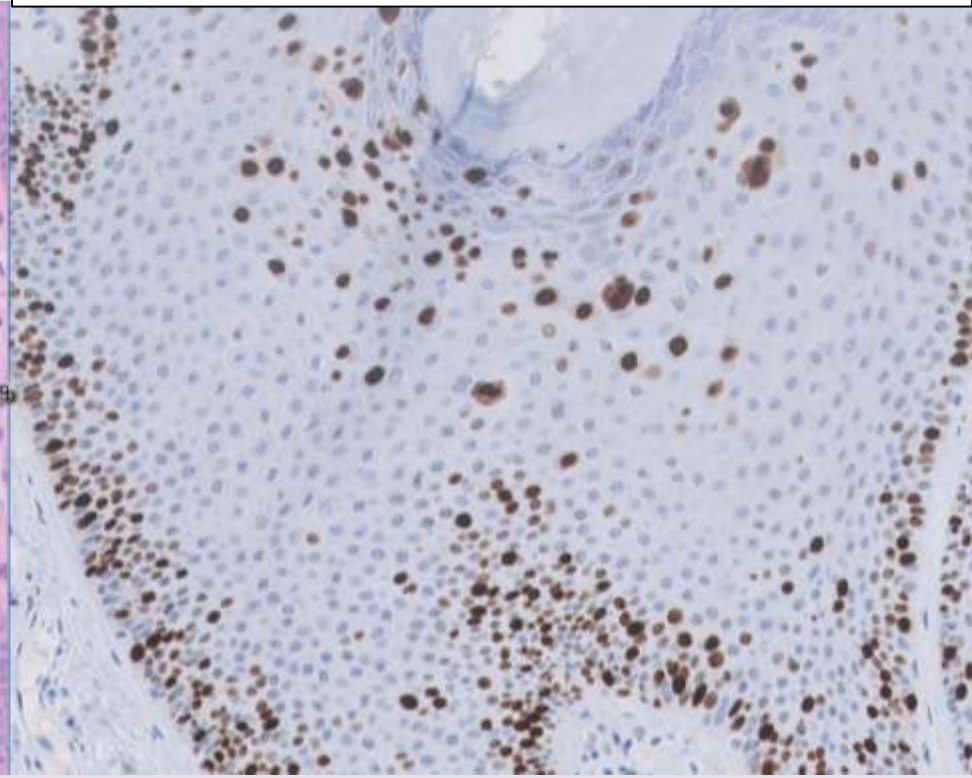
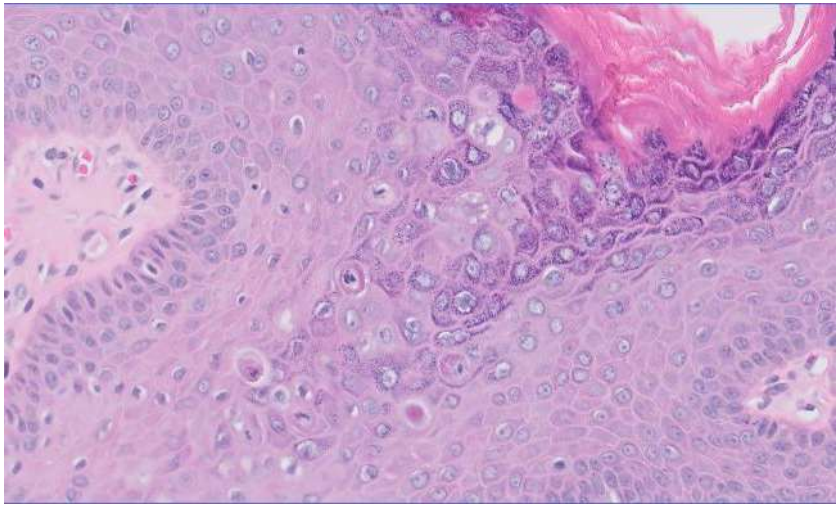


Summary:
Condyloma with pseudobowenoid change

- “Mitusoid bodies” can be seen in vulvar condyloma and may mimic HSIL
- Possibly due to unusual HPV type (HPV 13, 32)
- May be seen in the absence of topical therapy
- IHC (p16 / HRHPV [ish] / p53) can be used to exclude HSIL



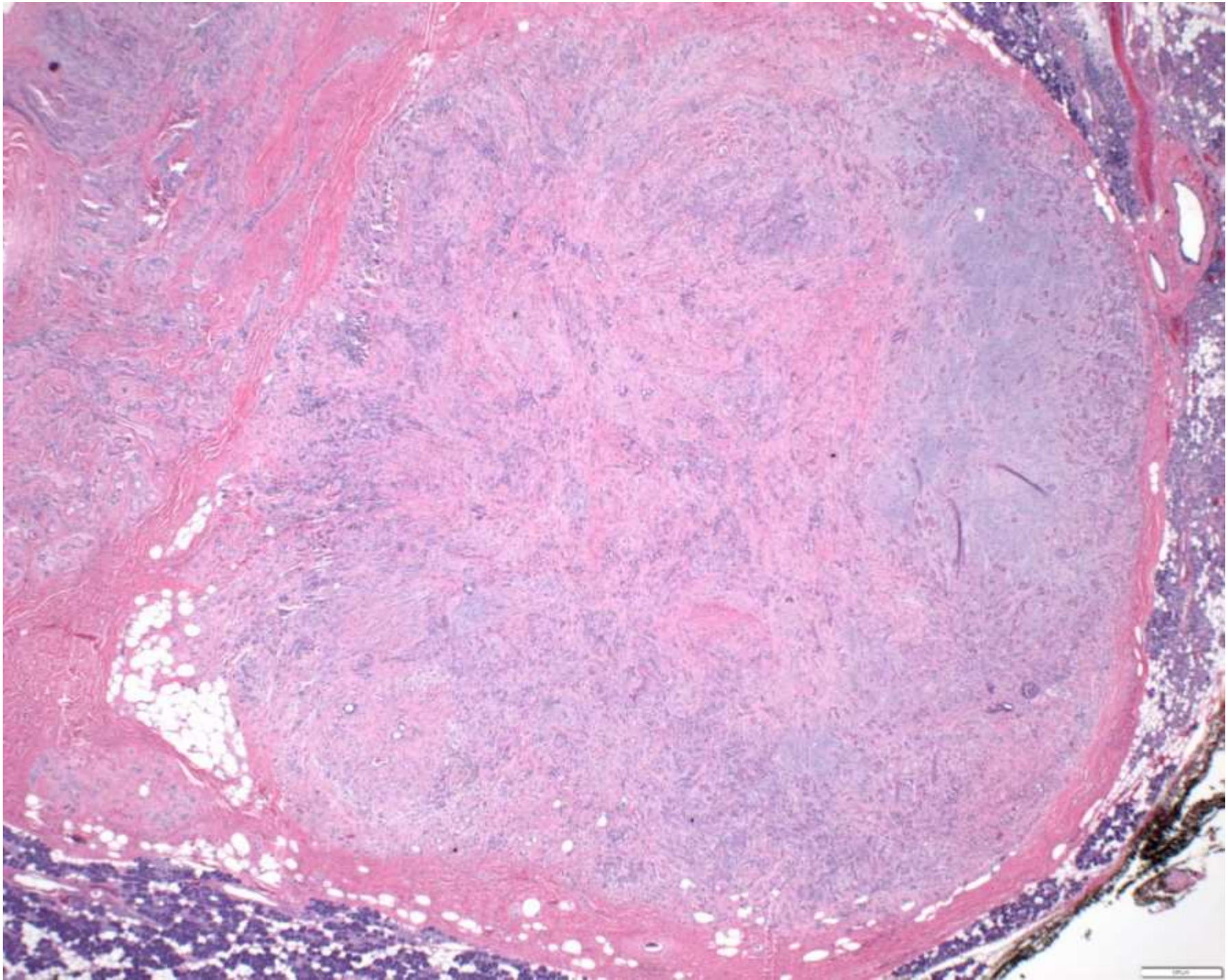
References

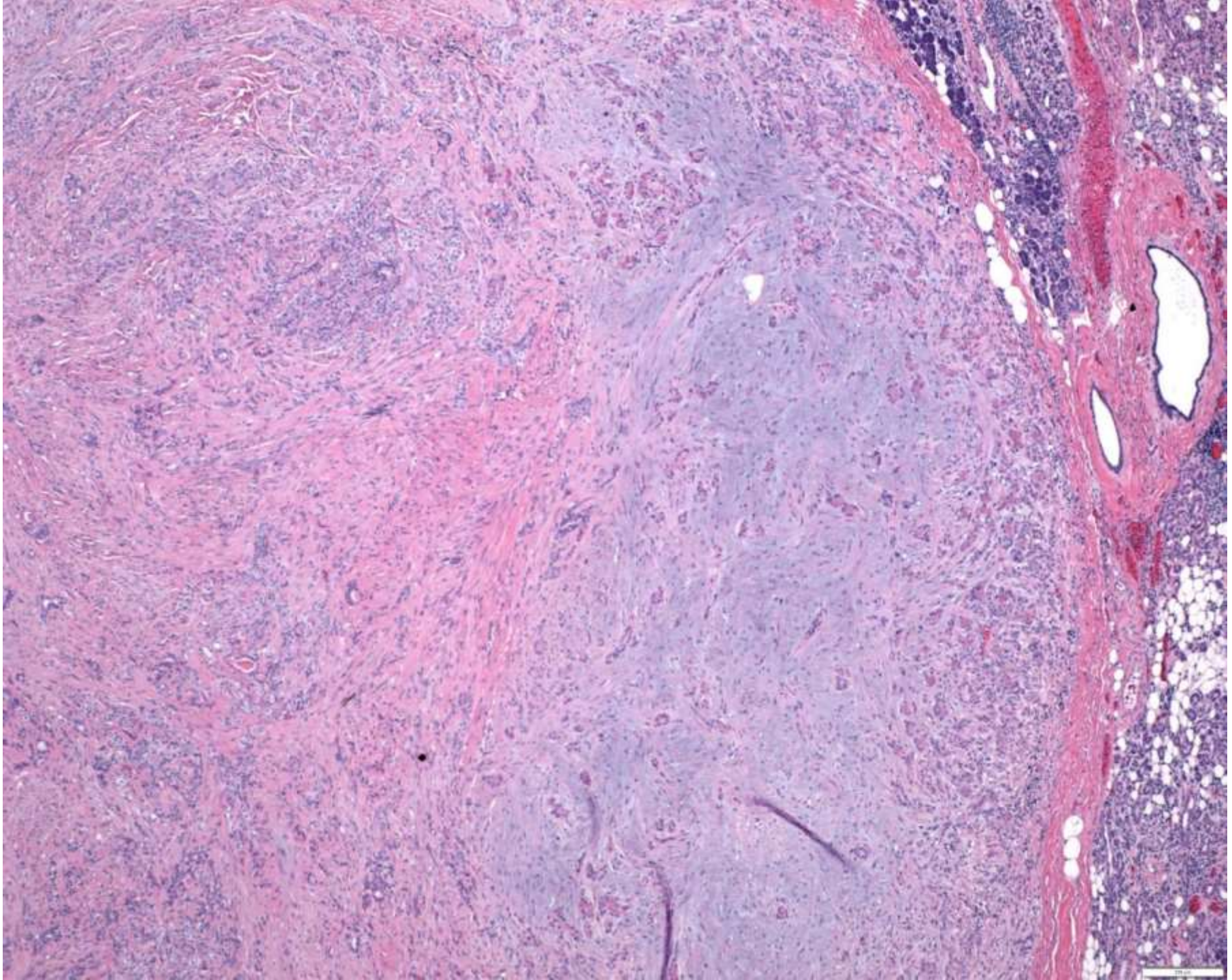
1. Nucci MR, Genest DR, Tate JE, et al. Pseudobowenoid change of the vulva: a histologic variant of untreated condylata acuminatum. *Mod Pathol.* 1996;9:375-379.
2. LeBoit PE. Correspondence re: Nucci MR, Genest DR, Tate JE, Sparks CK, Crum CP: pseudobowenoid vulvar change: untreated condyloma acuminatum. Mod Pathol 9:375, 1996. Mod Pathol. 1996 Aug;9(8):870-1. PMID: 8871933.
3. Thompson LDR, Müller S, Nelson BL. *Diagnostic pathology: head and neck*. Salt Lake City: Elsevier; 2022.

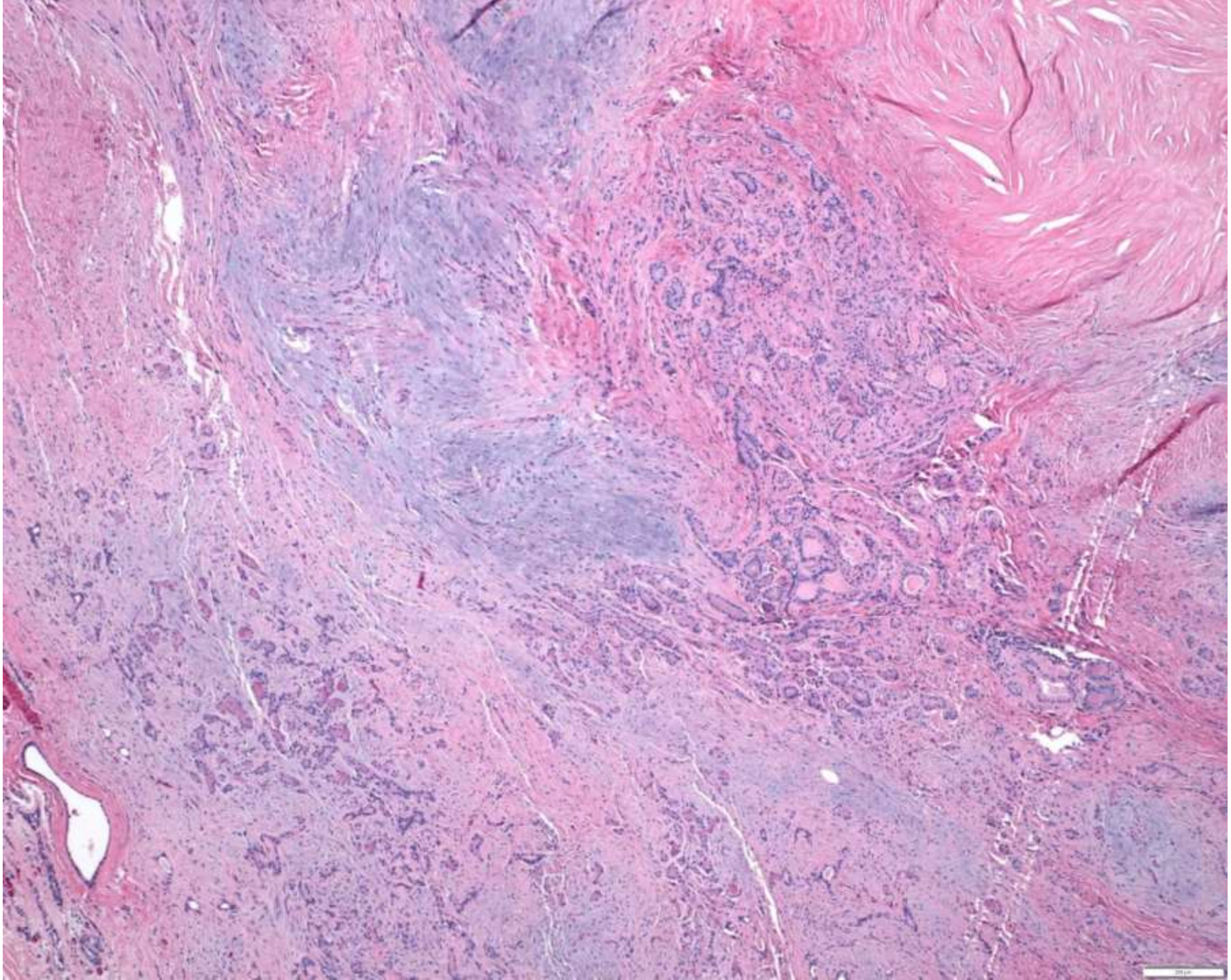
22-0305

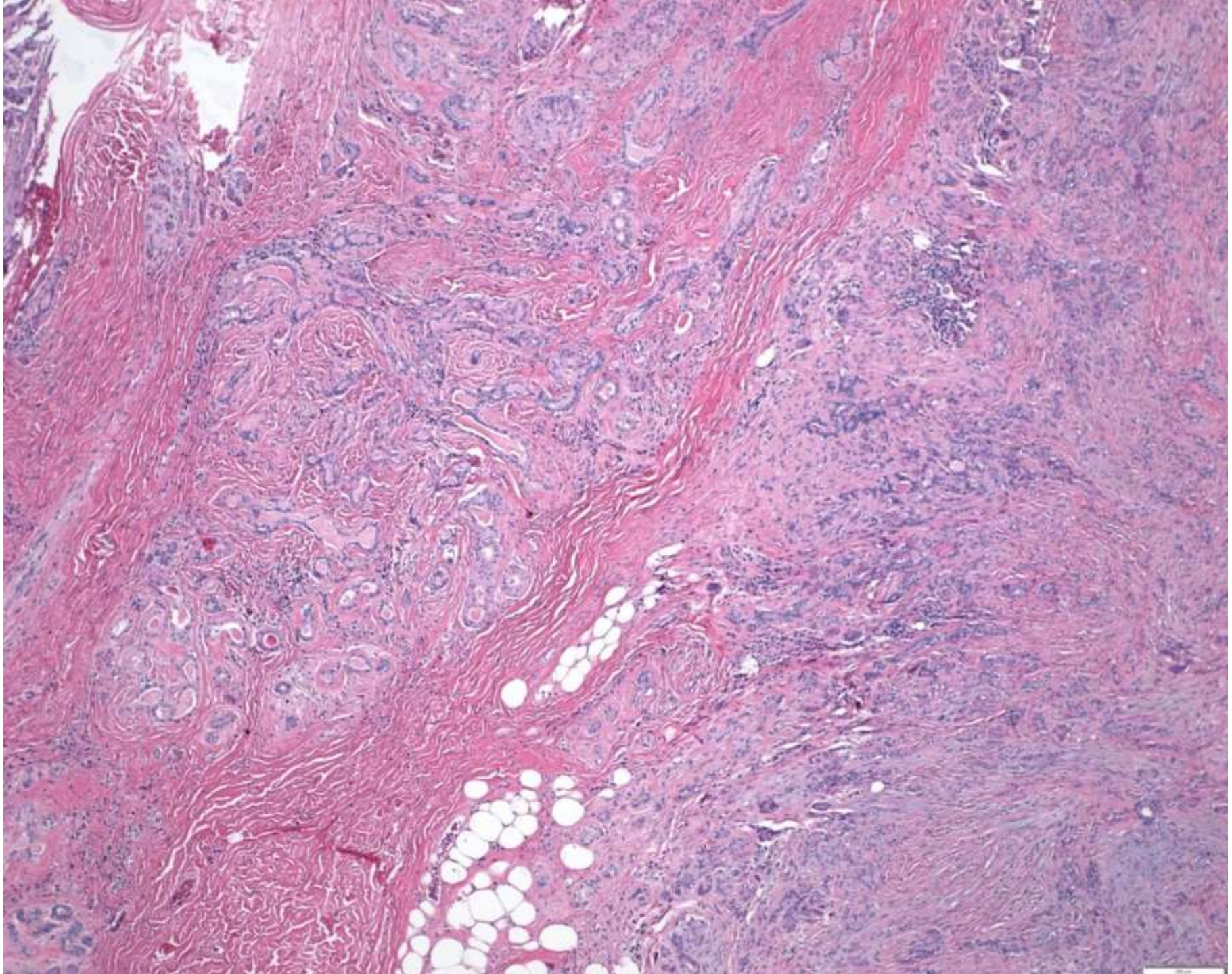
Andrew Xiao/Steve Long; UCSF

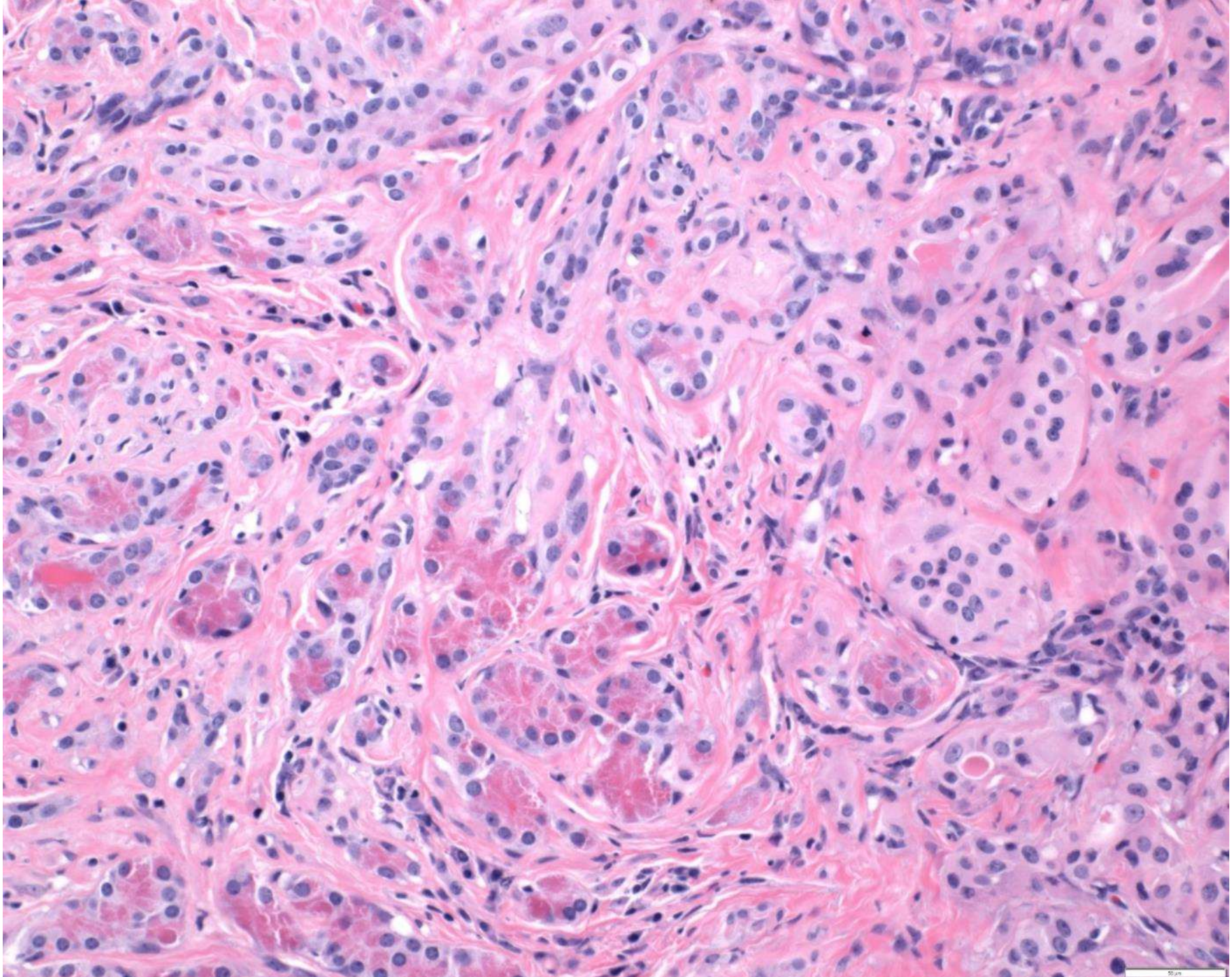
Middle aged F with incidentally found 11mm enhancing lesion on MR brain in the right parotid gland. US-guided FNA suggested a neoplasm without definite diagnosis of benign vs malignant tumor. Right parotidectomy yielded 2.8cm firm, tan white, oval-shaped mass.

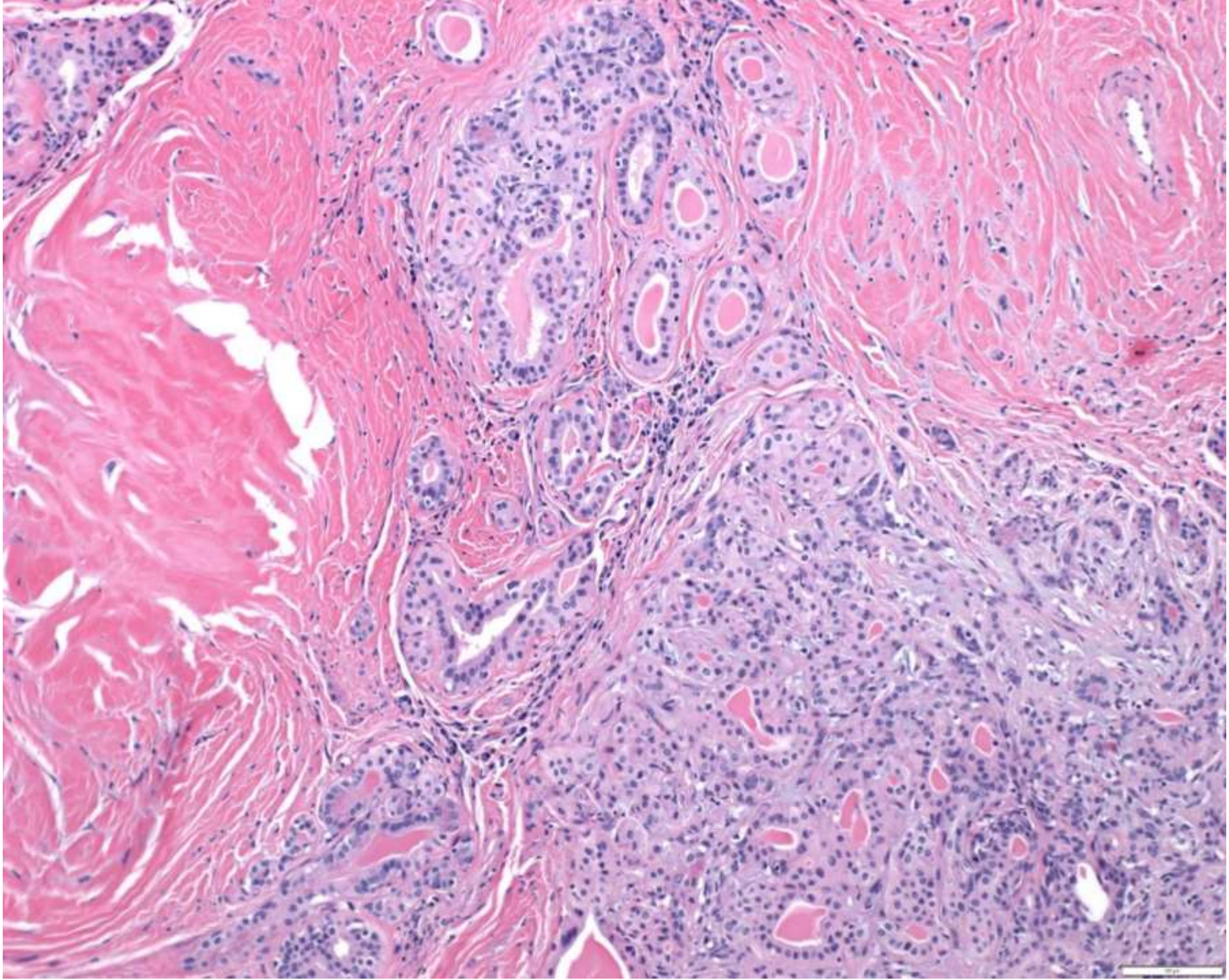


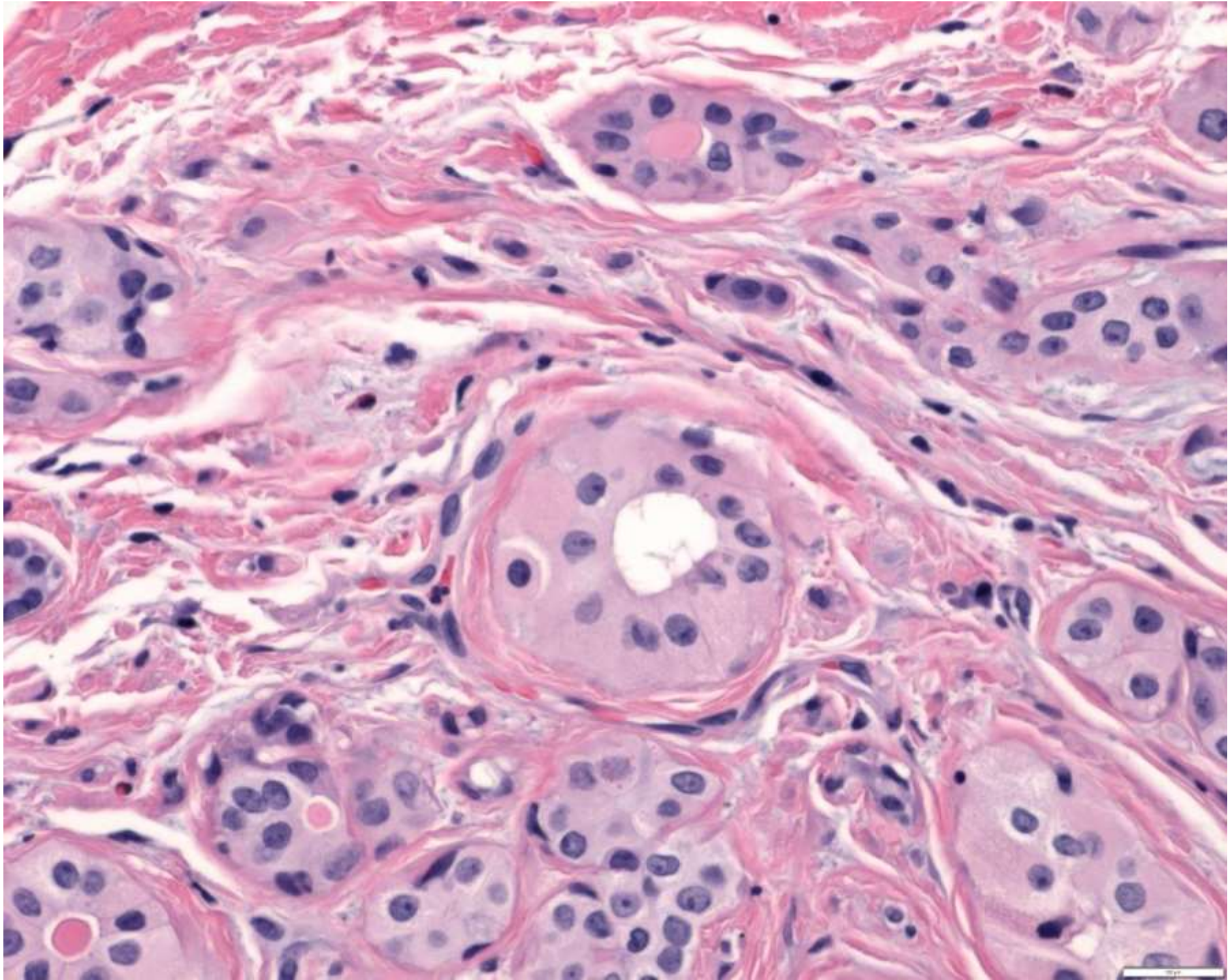


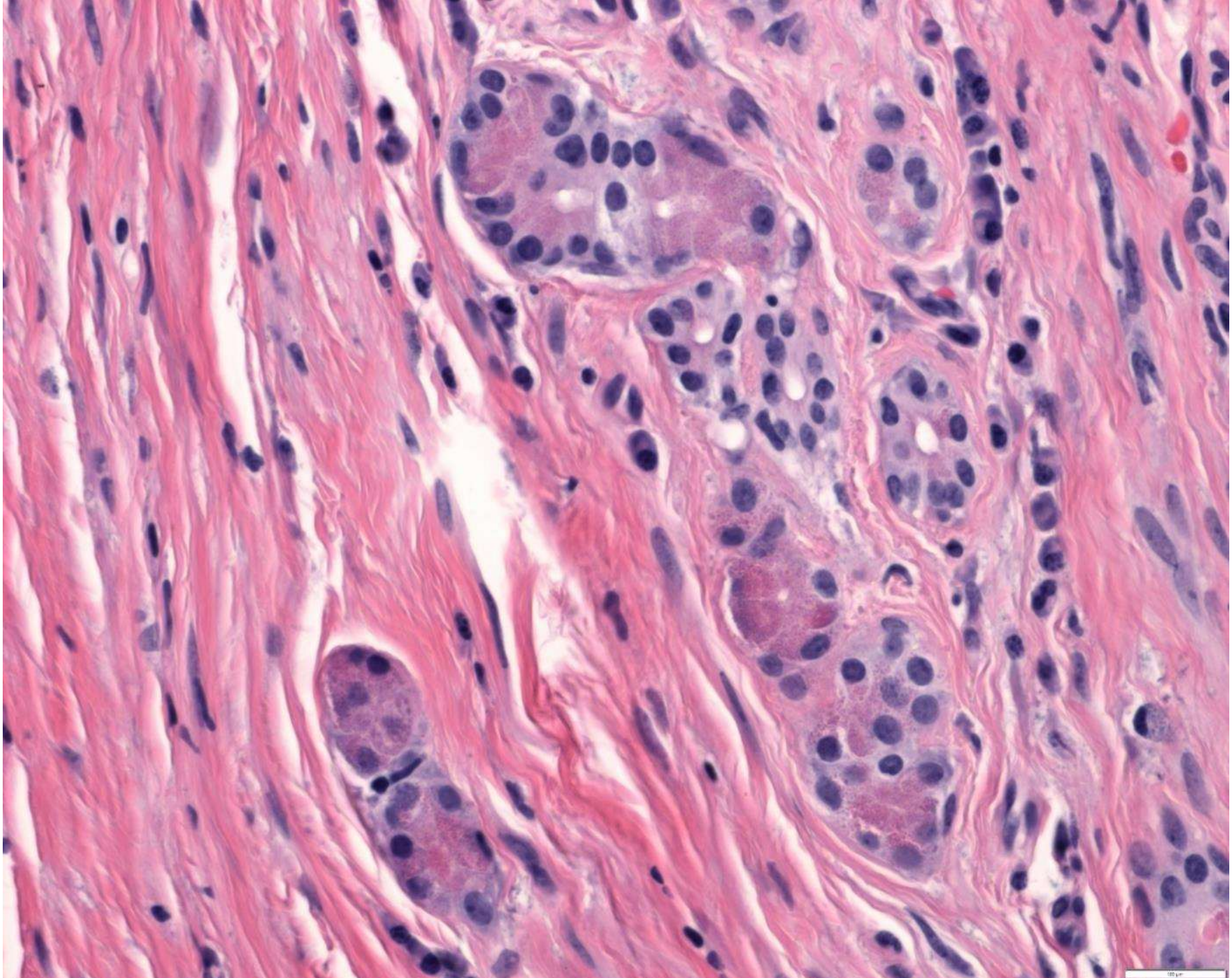












Sclerosing Polycystic Adenoma (SPA)

Clinical Profile

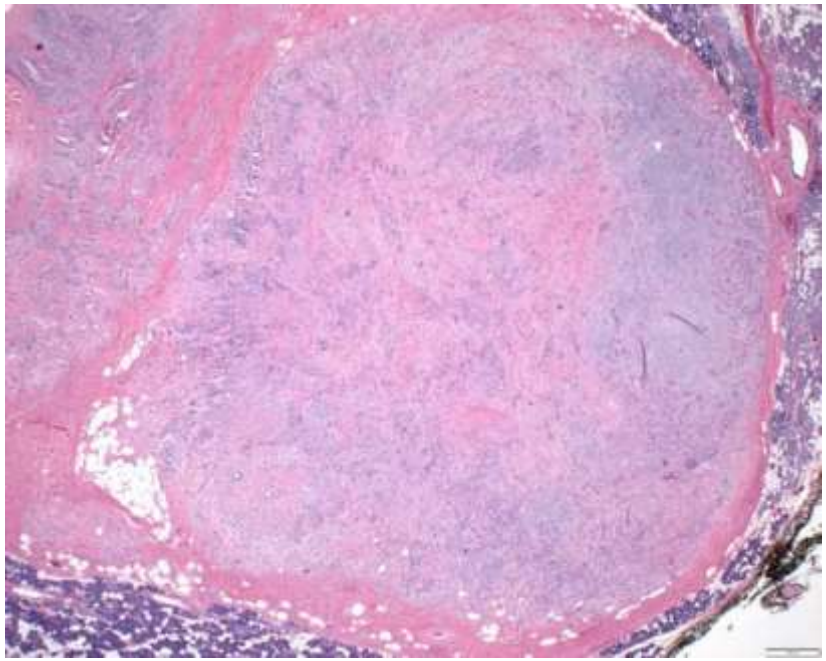
- Painless, slow-growing mass
- ~70% arise in the parotid gland
- Mean age: 40s
- Female:Male::1.3:1

Key Microscopic Features

- Well-circumscribed or encapsulated
- Proliferative ducts, myoepithelial cells, and acini
- **Acini: large, hypereosinophilic cytoplasmic granules**
- Other possibilities:
  - Varying hyalinized fibrosis
  - Apocrine metaplasia
  - Intraductal apocrine proliferation

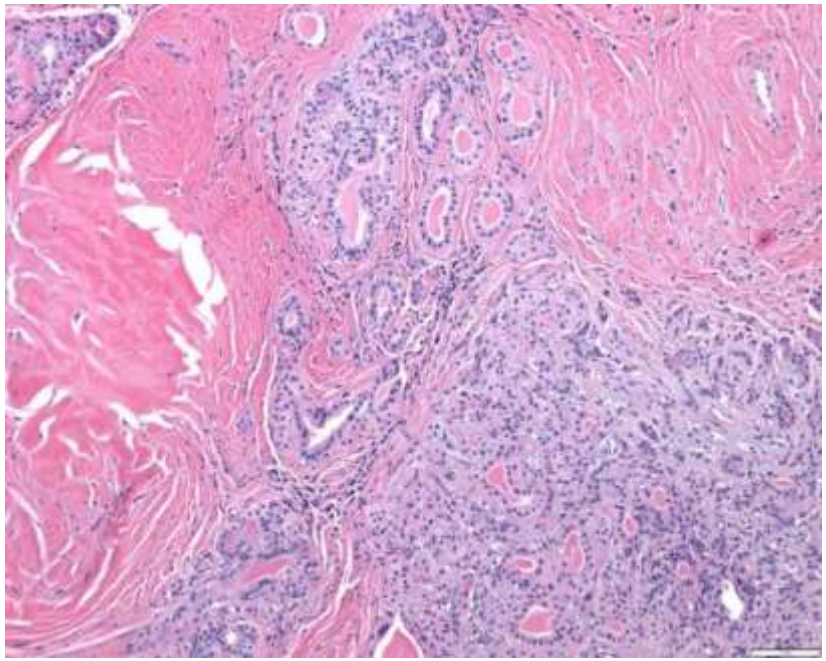
Review of H&E

- Well-circumscribed
- Sclerotic stromal-like elements



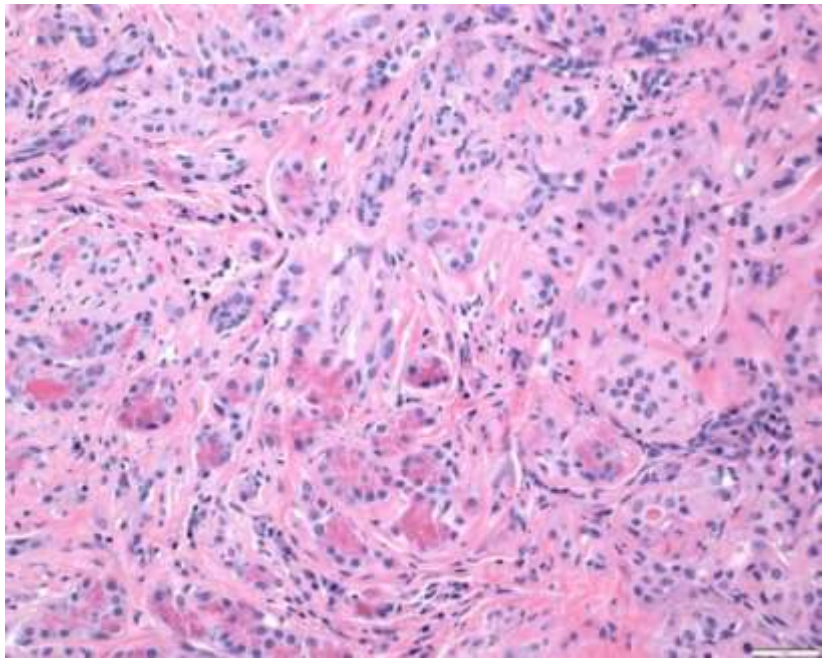
Review of H&E

- Proliferation of:
  - Ducts
  - Myoepithelial cells
  - Acini
- Cystic-like spaces



Review of H&E

- Mixture of:
  - Oncocytic epithelium
  - Acini with prominent eosinophilic granules
- Bland-looking epithelium



Immunohistochemistry

- Should be a H&E diagnosis, but if needed …
- SOX10: highlights small ductules, myoepithelial cells, and acini
- DOG1: negative or weak and focal in acini
- SMA, p40, calponin, S100: highlights intact myoepithelial cells
- AR, GCDFP-15: positive in apocrine ductal tumor cells

Differential Diagnosis

- Polycystic / dysgenetic disease
- Pleomorphic adenoma
- Intercalated duct lesion / adenoma
- Acinic cell carcinoma
- Salivary duct carcinoma
- Apocrine variant of intraductal carcinoma
- Mucoepidermoid carcinoma

References

- Bishop JA, Gagan J, Baumhoer D, et al. Sclerosing polycystic “adenosis” of salivary glands: A neoplasm characterized by PI3K pathway alterations more correctly named sclerosing polycystic adenoma. *Head and Neck Pathology*. 2019;14(3):630-636. doi:10.1007/s12105-019-01088-0
- Bishop JA, et al. Sclerosing Polycystic Adenoma. Head and Neck Pathol (2020) 14:630-636.

22-0306

Liz Treynor; Washington Hospital

80ish F with numerous non-infectious pruritic skin lesions and progressive neutropenia over 6 months. Bone marrow biopsy performed.

80 y/o F with numerous non-infectious puritic skin lesions and progressive neutrophilia over 6 months.

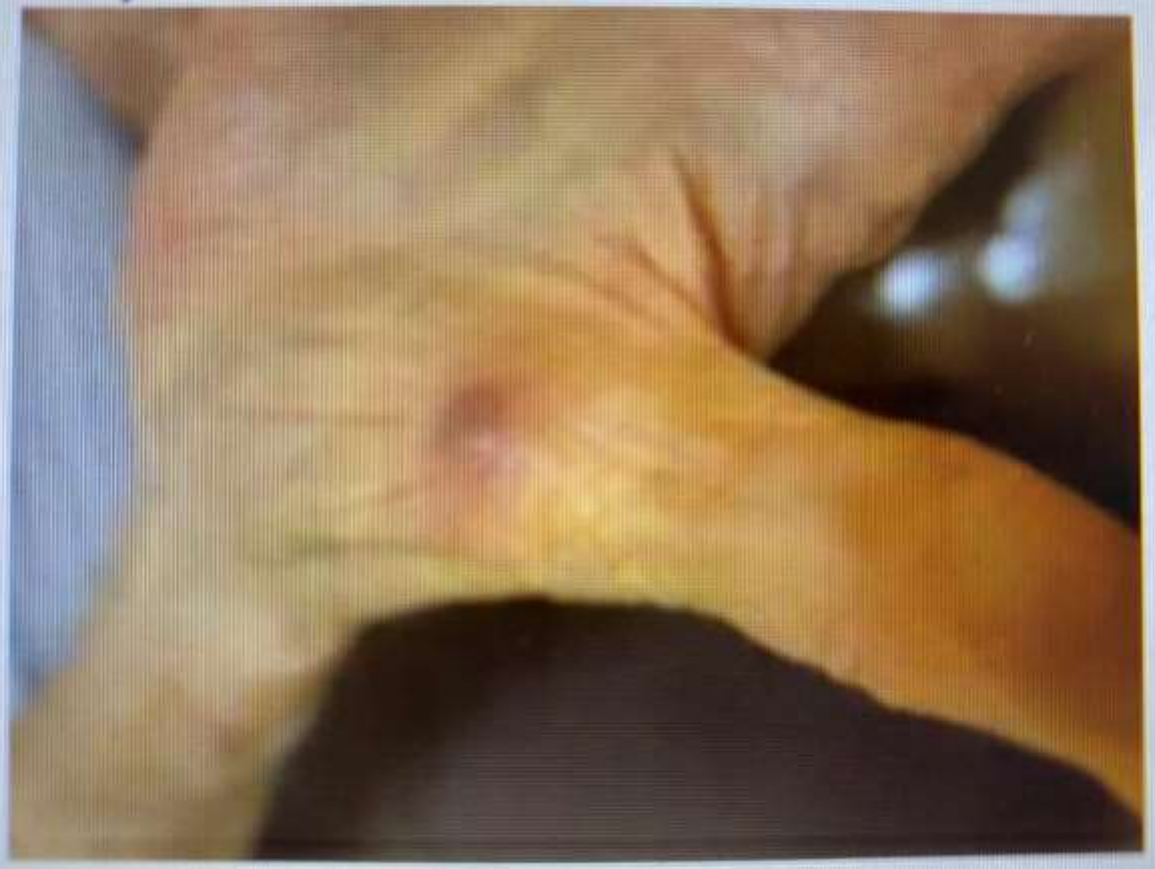
Lab data: WBC 43k/uL, Hgb 11.4g/dL, HCT 36%, MCV 101, PLT 346 k/uL; Abs Neuts 36.7 k/uL, Abs Monos 1.36 k/uL, Abs Lymphs 1.86 k/uL, Abs Eos 1.0 k/uL

BMBx Differential:
17% PMNs, 19% bands, 10% metas, 28%myelocytes, 3% monos, 3% eos, 7% lymphs

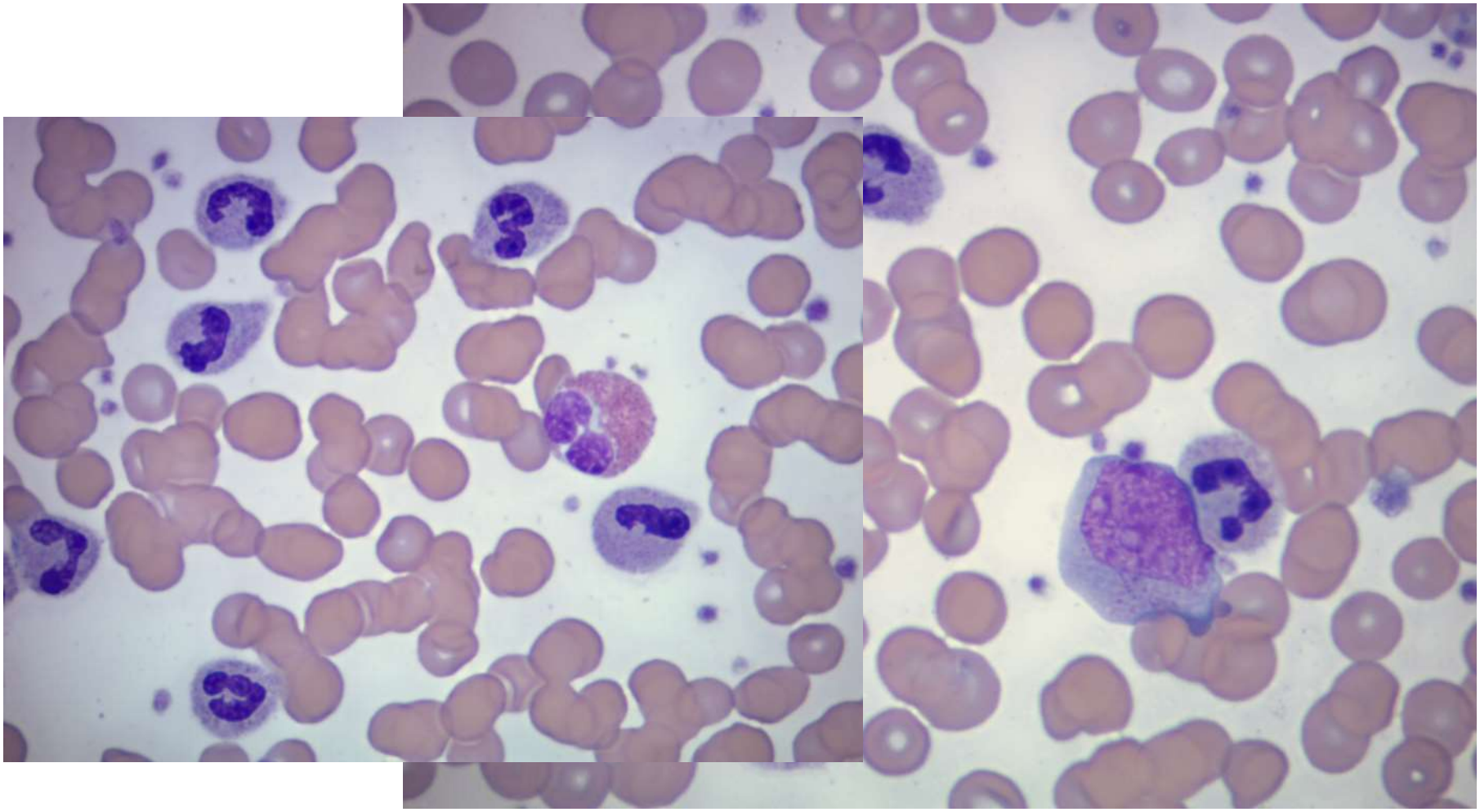
BCR-ABL1 FISH negative and 46,XX karyotype (but only 1 metaphase).

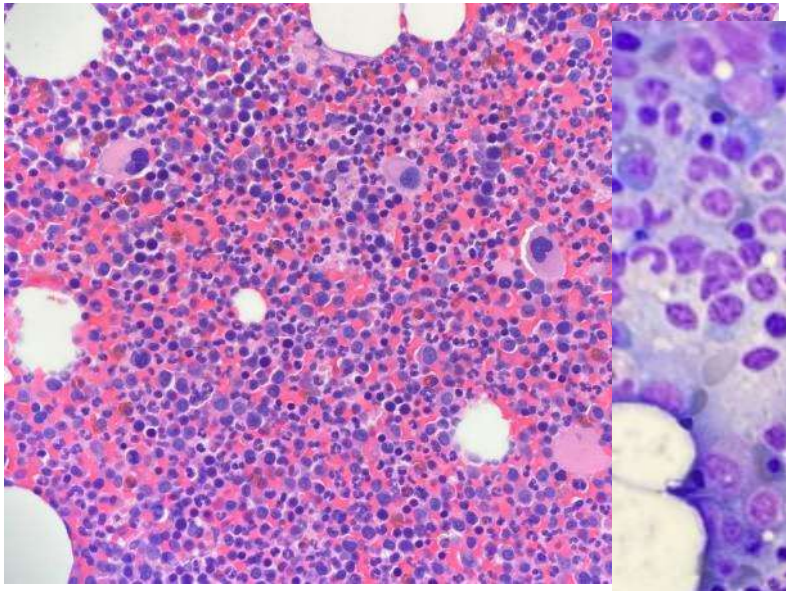
Flow: 1% CD34 –positive blasts

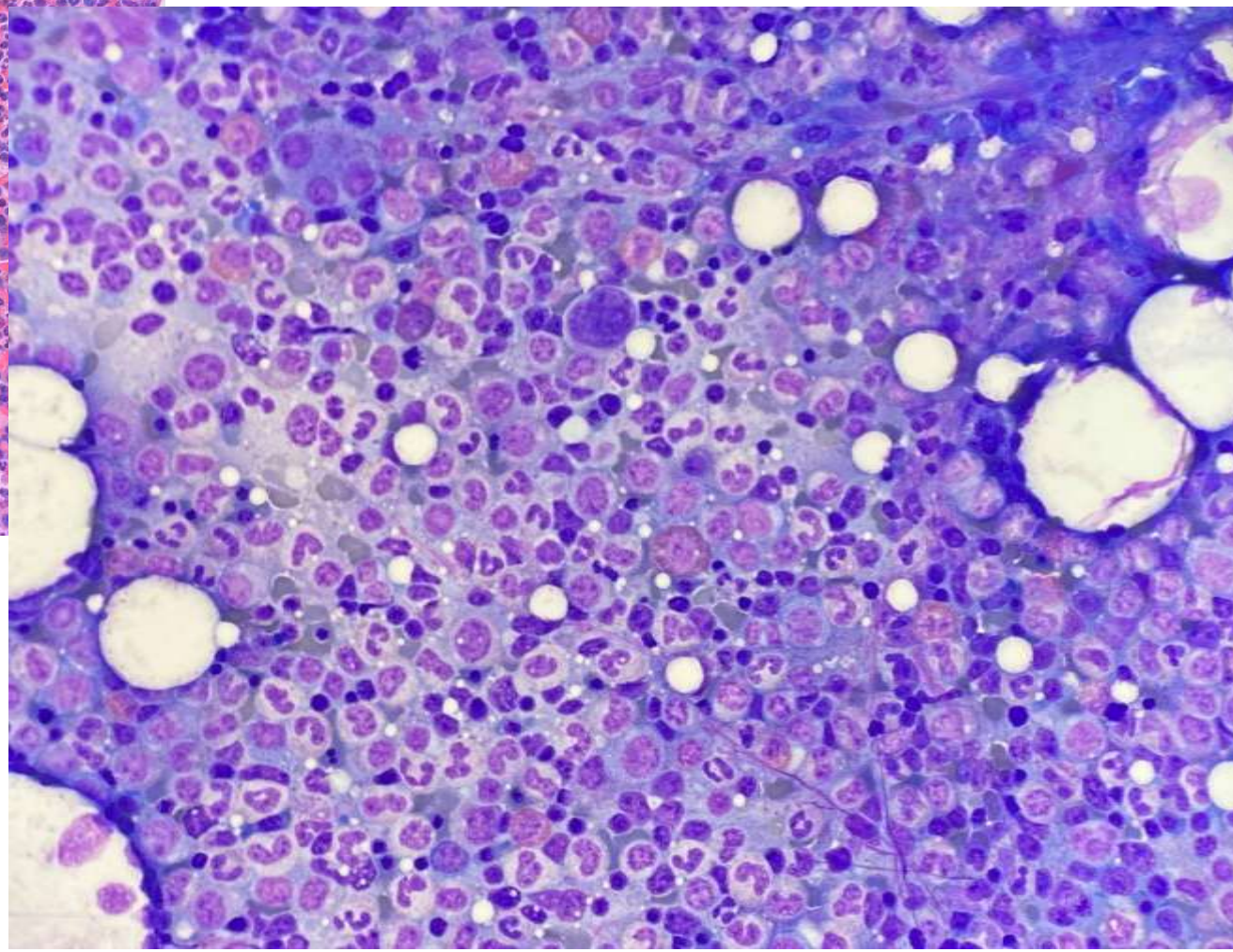
Early lesion on the hand.

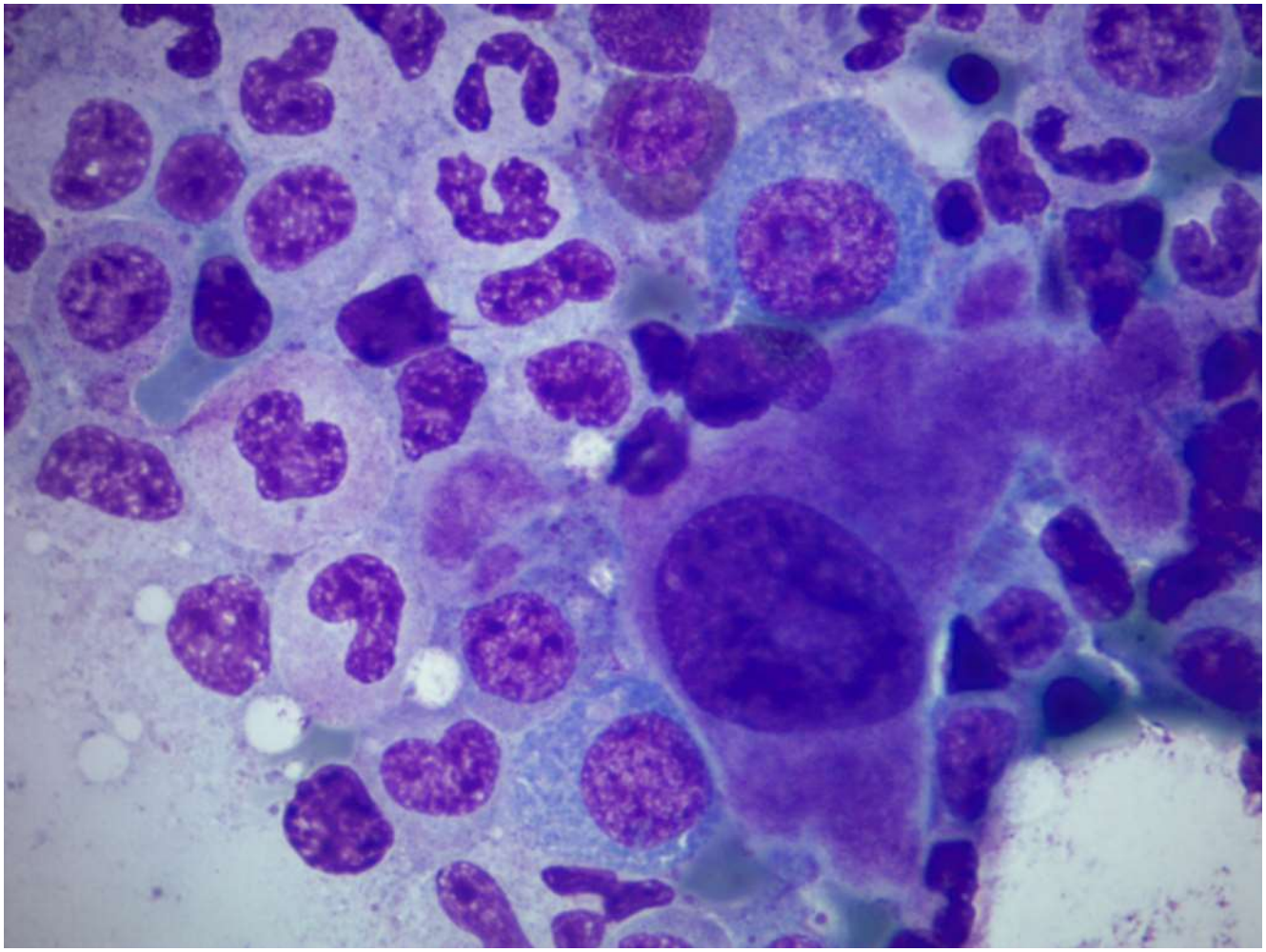


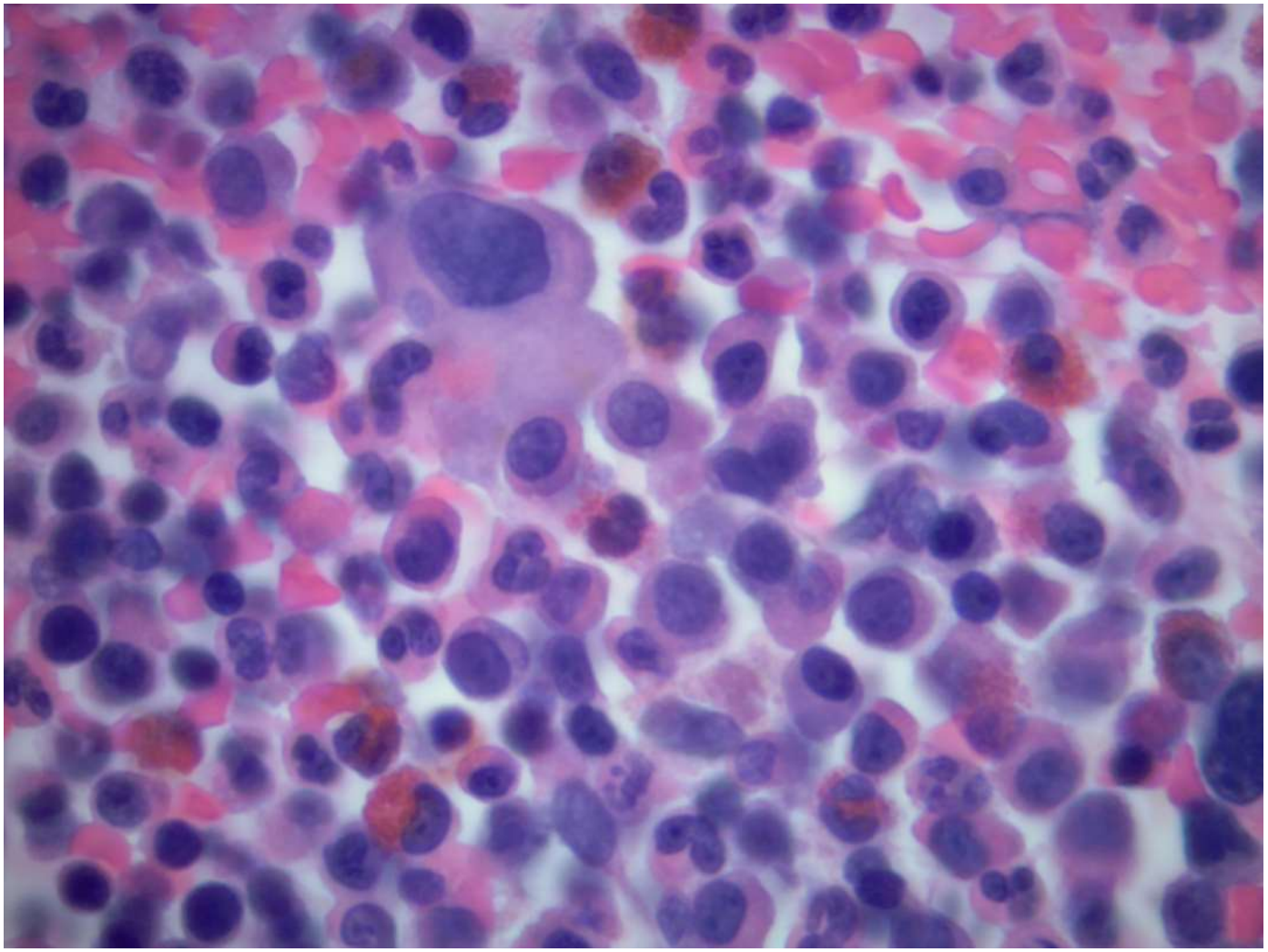
Late lesion, excoriated











Quiz: What molecular abnormality is most likely with these findings?

- SRSF2
- CSF3R T618I
- CSF3R P733T
- SETBP1
- SF3B1

Quiz: What molecular abnormality is most likely with these findings?

- SRSF2
- CSF3R T618I
- CSF3R P733T
- SETBP1
- SF3B1
- BCR-ABL1 p230

Differential Considerations

- CML (no BCR-ABL1 by FISH/cytogenetics; pending molecular)
- aCML (no significant dysplasia)
- CMML (<10% monocytes, no significant dysplasia)
- CNL

NGS:

- CSF3R T618I
- SETBP1
- SRSF1
- SF3B1

Chronic Neutrophilic Leukemia: Blood

- WBC >25k/uL
- Monos <1 k/uL
- No blasts and <10% myeloid precursors in periphery
- No dysgranulopoiesis

Chronic Neutrophilic Leukemia: Marrow

- < 5% blasts
- Normal maturation

Chronic Neutrophilic Leukemia: Cytogenetics

- No BCR-ABL1
- No PCM1-JAK2
- No PDGFRA/B or FGFR1 rearrangement

Chronic Neutrophilic Leukemia: Molecular

- **CSF3R T618I (or other activating CSF3R mutation) is seen in 80% of CNL & our patient may respond to JAK inhibitors**

- SETBP1 is seen in a third of CNL cases, worse survival
  (also poor prognosis in CMML, MDS)

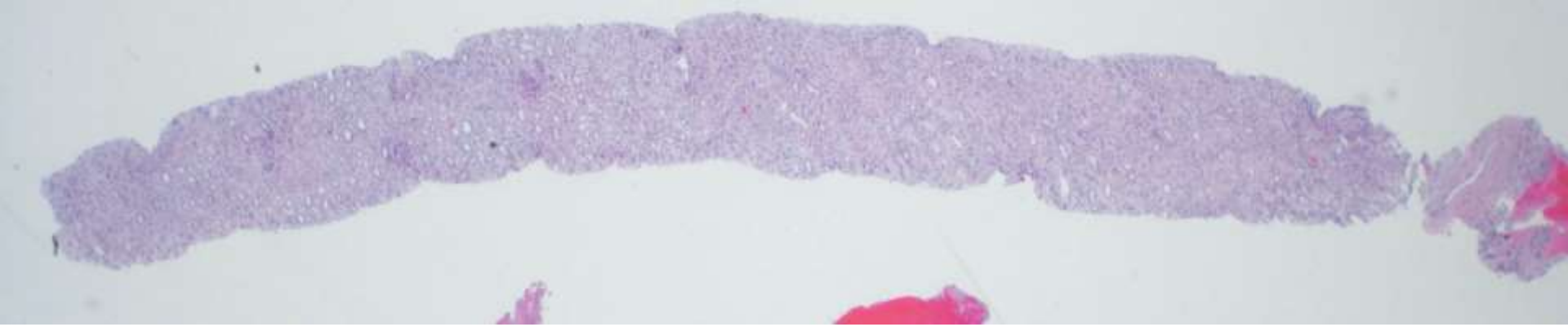
- SRSF1 poor prognosis in CMML, MDS, AML, PV, PMF

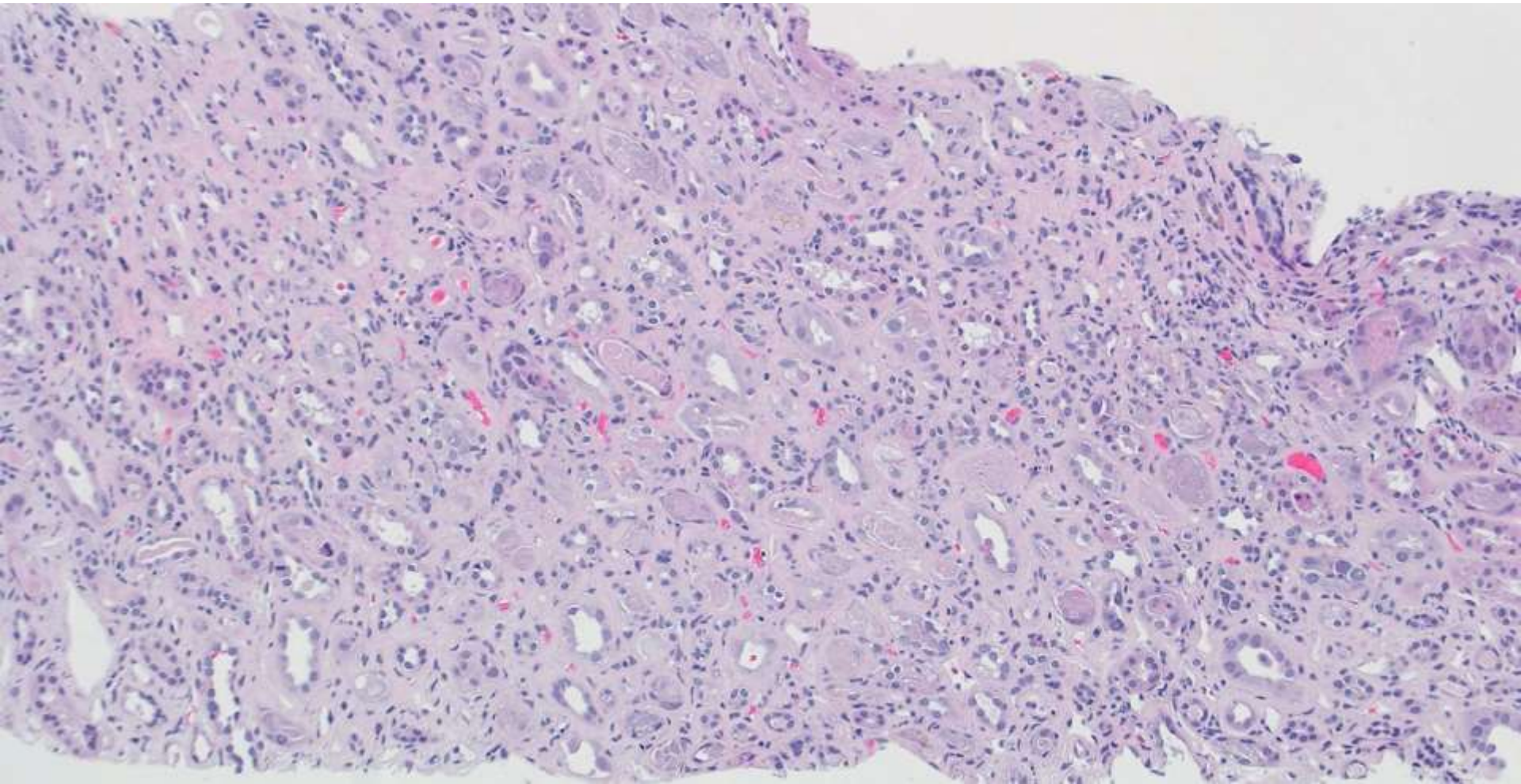
- SF3B1 association with ring sideroblasts

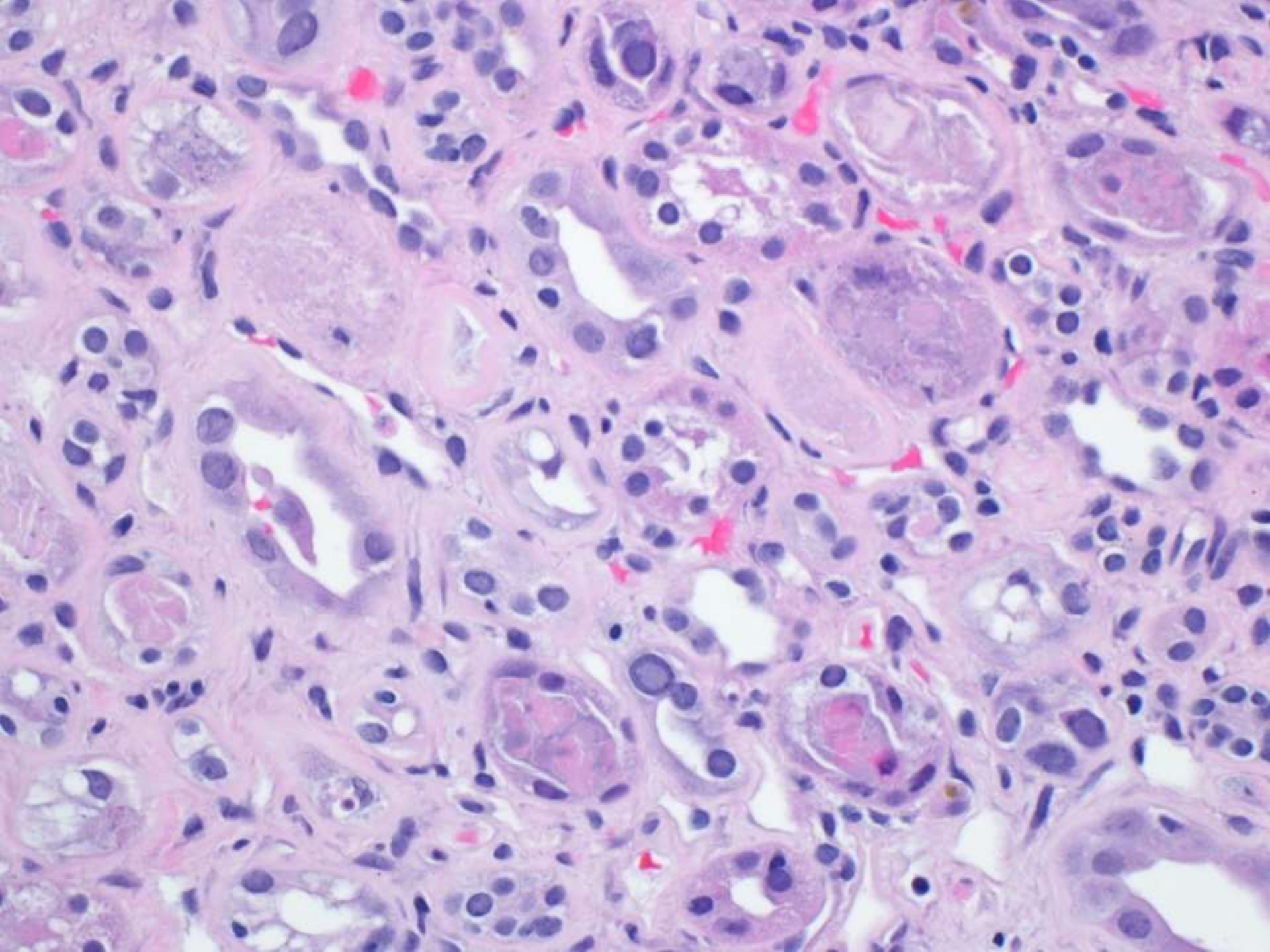
22-0307

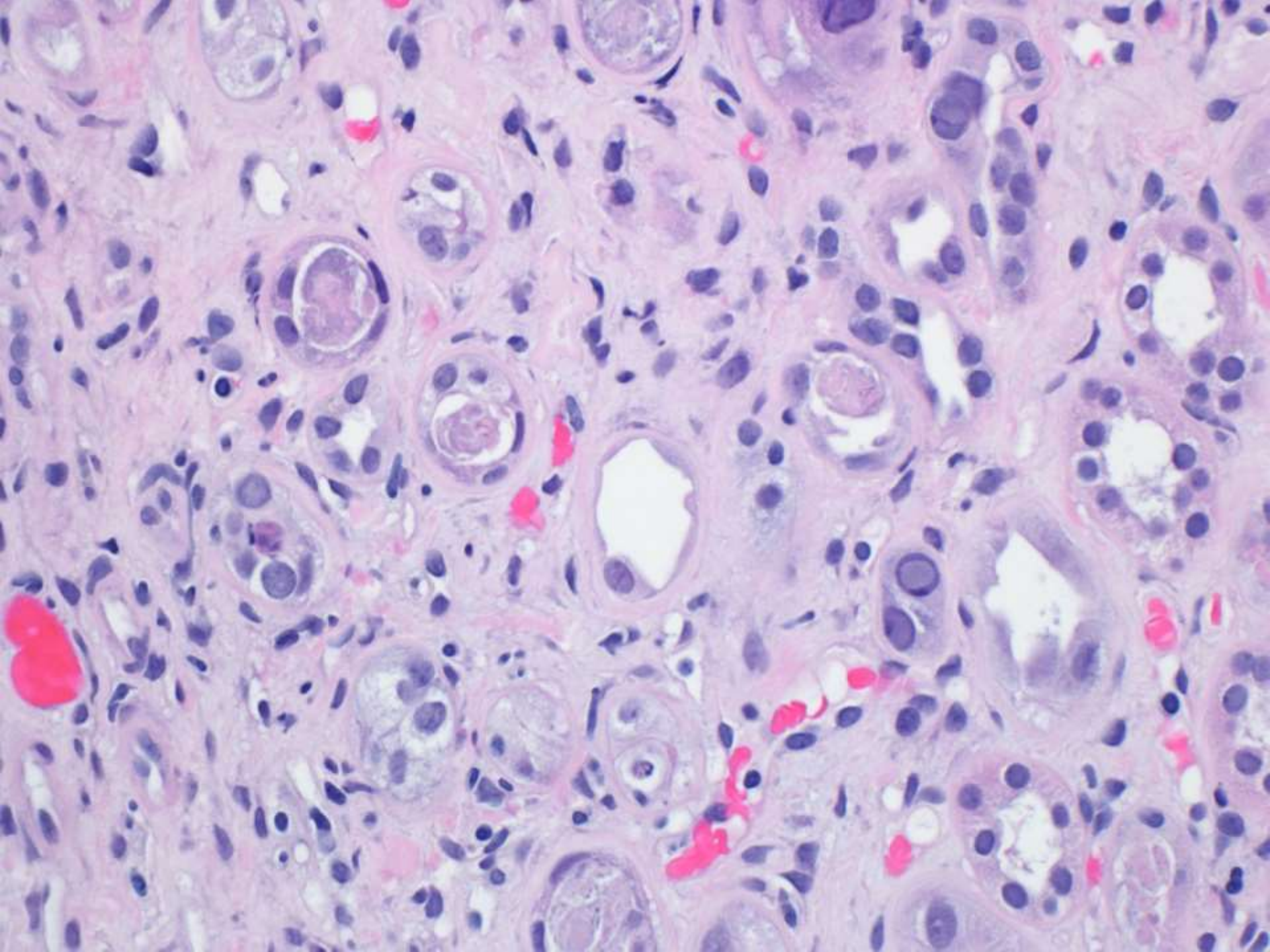
Megan Troxell; Stanford

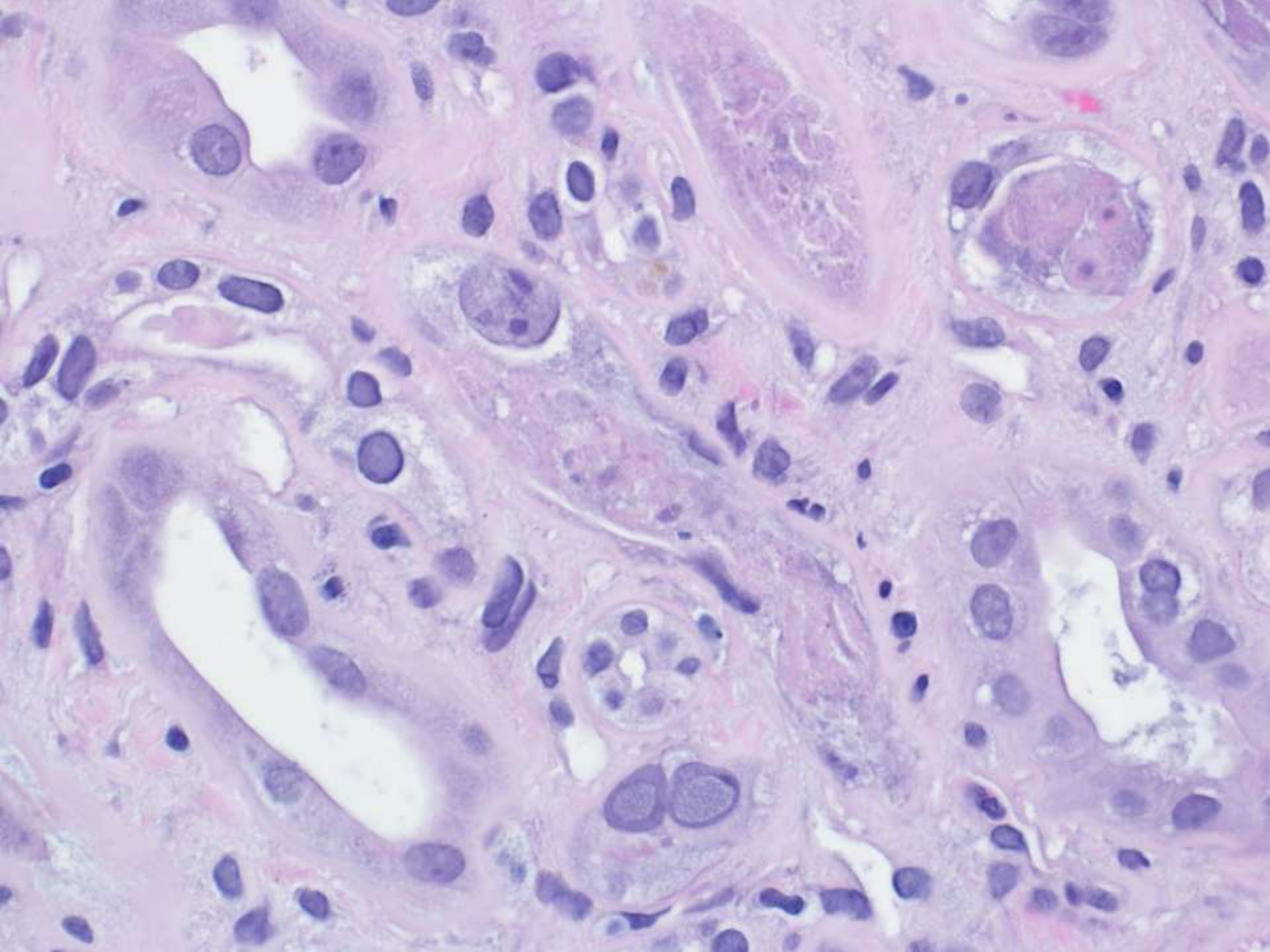
Middle-aged M with HIV, treated for DLBCL 6 months ago. Progressively increasing creatinine (1 to 3.6 mg/dL over 6 months). No hematuria or proteinuria. Native kidney bx performed.











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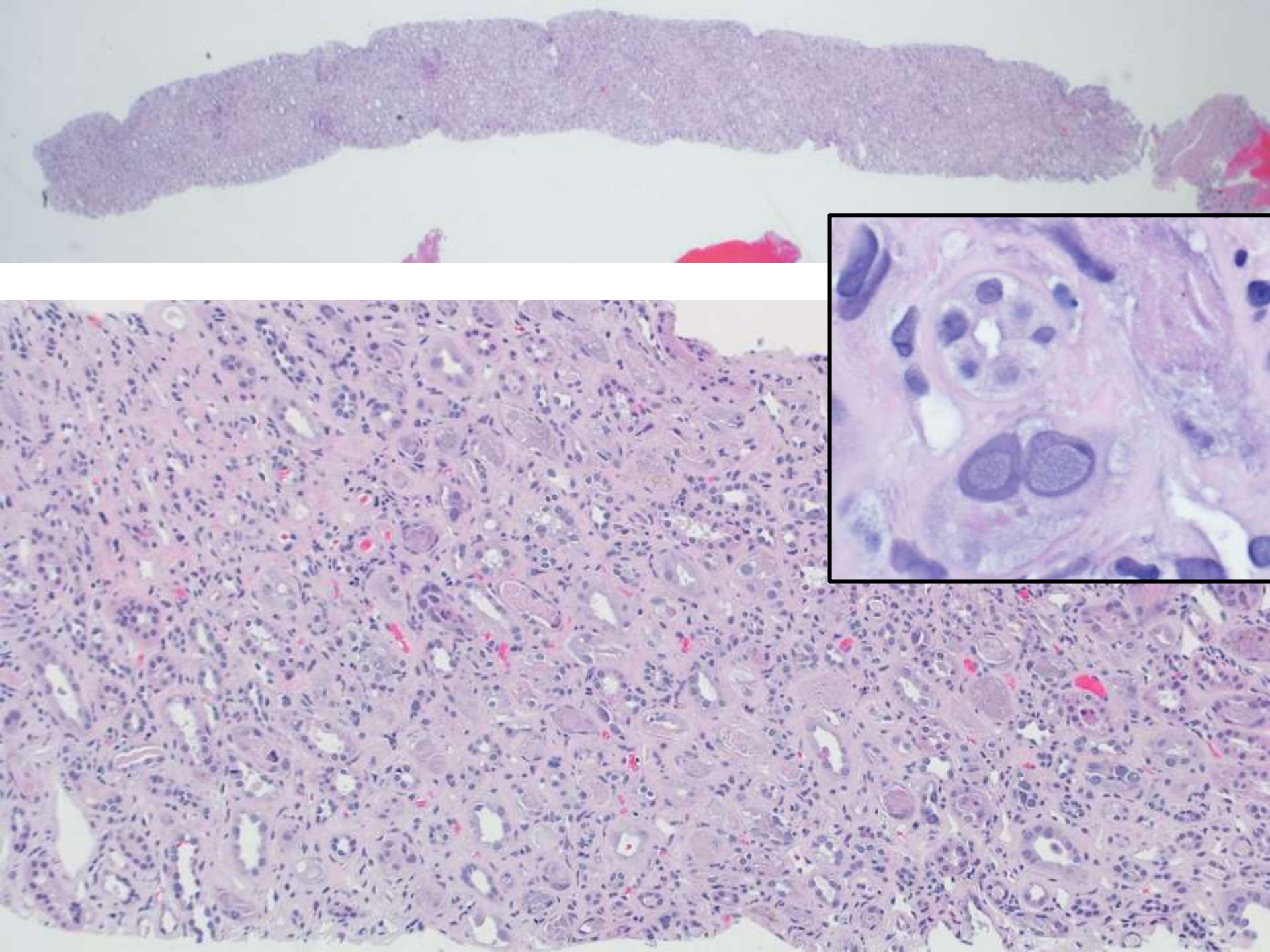
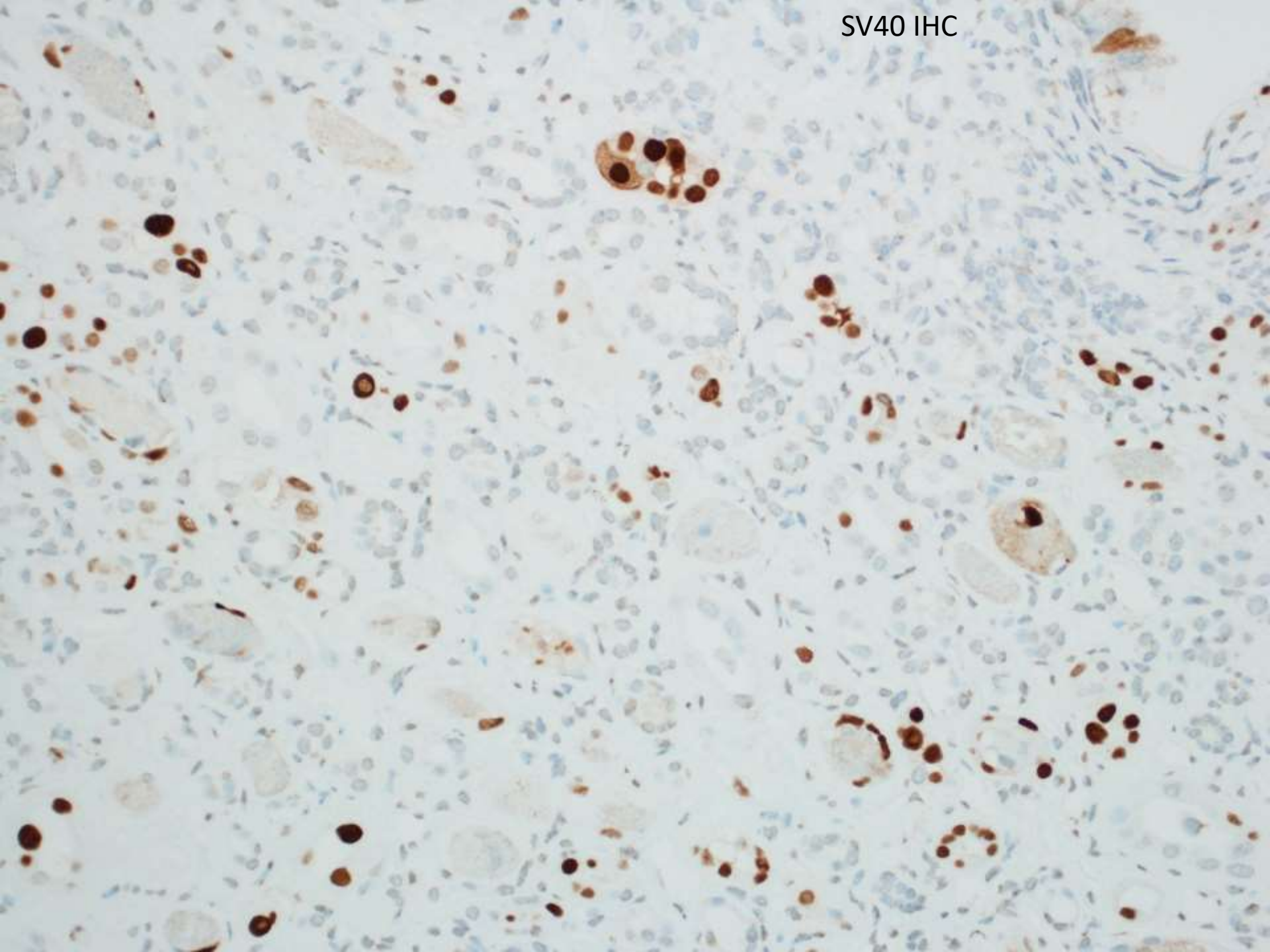
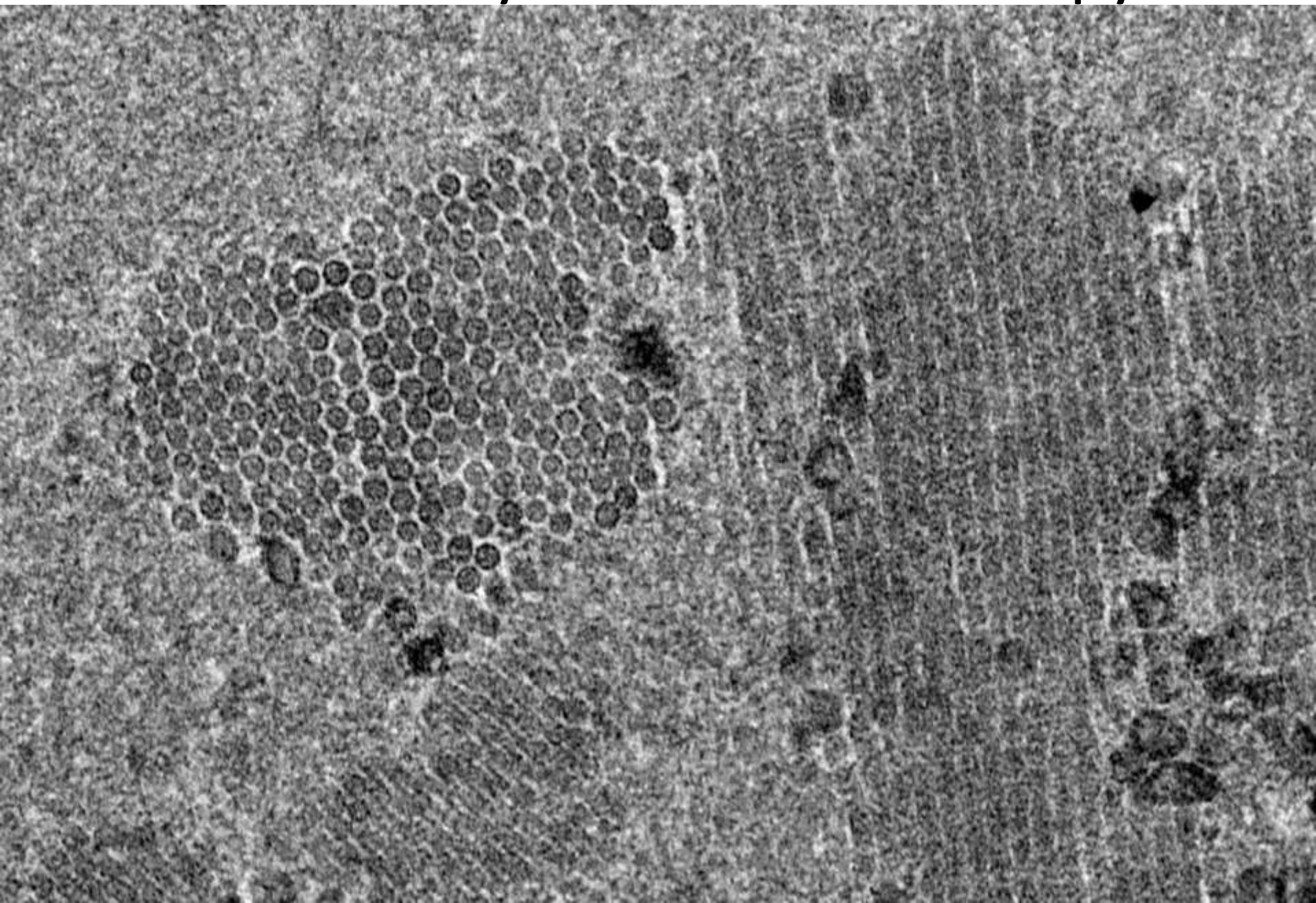



SV40 IHC

Virions by electron microscopy



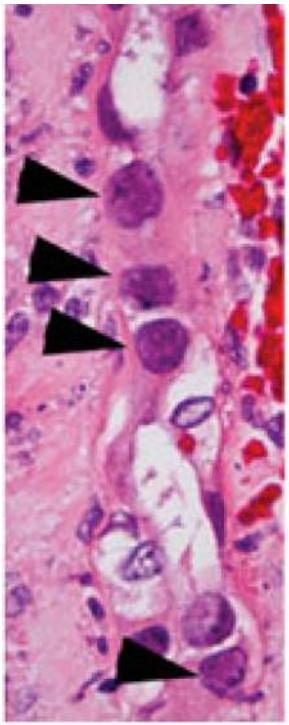
Polyomavirus

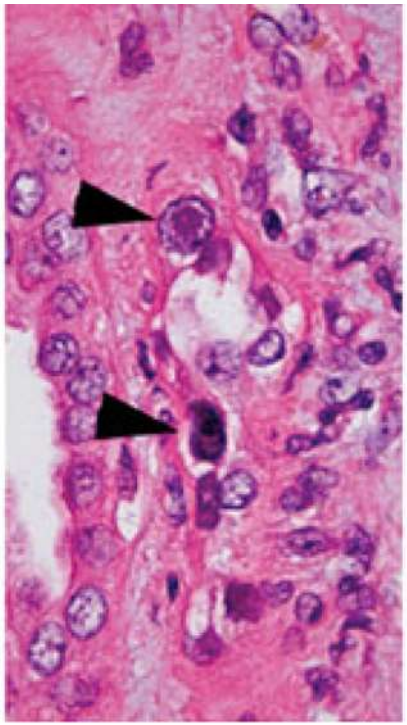
- Establishes latency in GU tract
- Reactivation with immunosuppression
  - Renal transplant: BK polyomavirus nephritis
  - Bone marrow transplant: JC hemorrhagic cystitis
- Can occur in native kidneys too, and rarely in surgical specimens

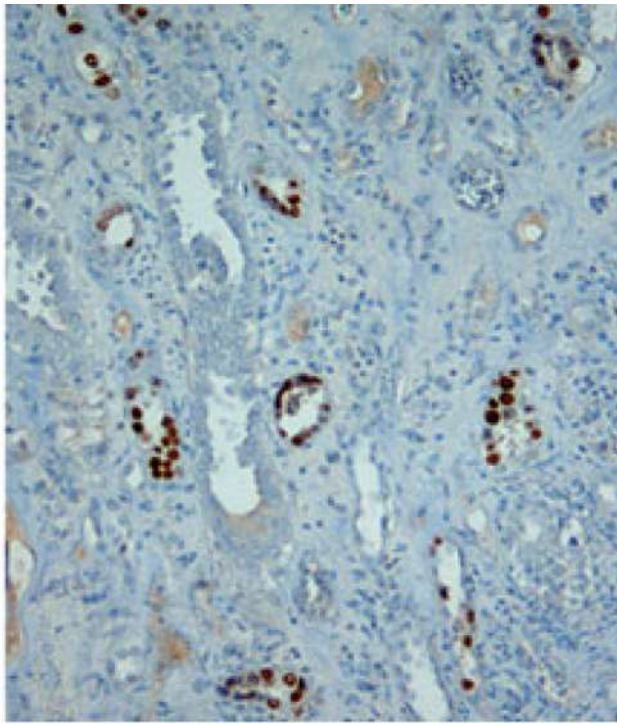
- Below:

Renal medulla

Nephrectomy







Go. Int Urol Nephrol. 2012 Oct;44(5):1585-8

CIS vs BK at frozen? No thanks!