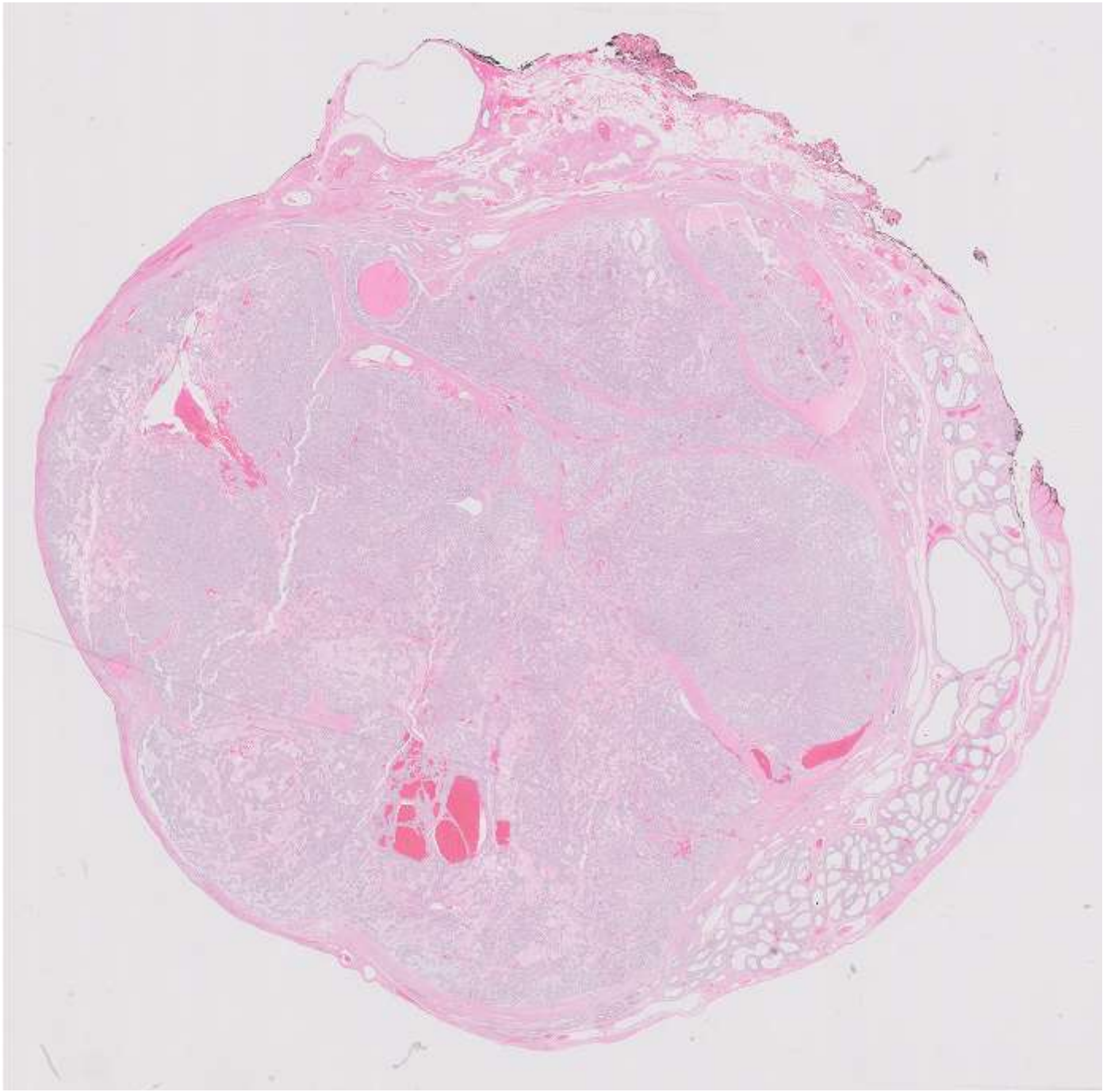
OCT 2021 DIAGNOSIS LIST

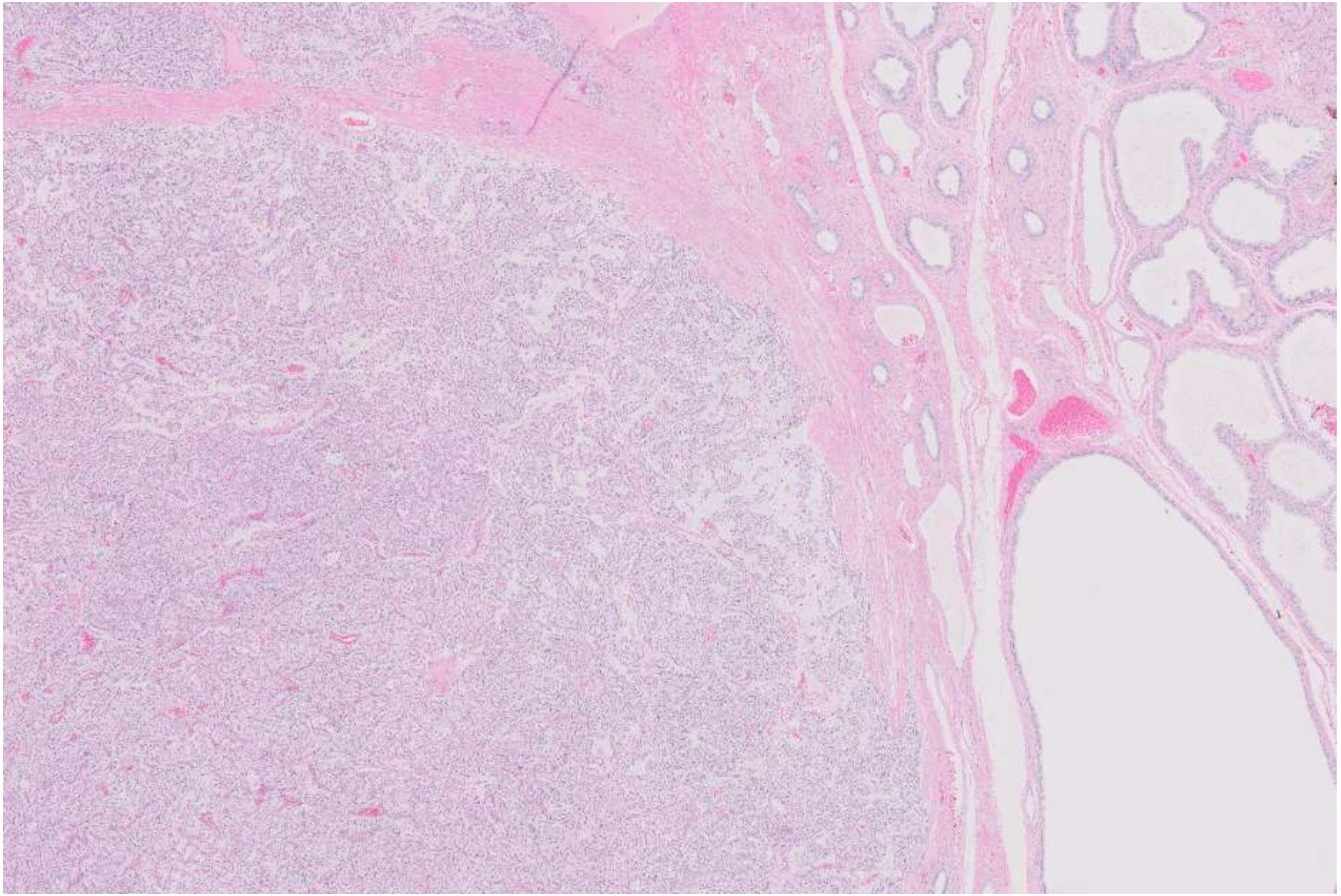
21-1001: clear cell papillary cystadenoma (testis; GU path)
21-1002: corded and hyalinized pattern endometrial carcinoma (uterus; GYN path)
21-1003: large cell neuroendocrine carcinoma (bladder; GU path)
21-1004: intravascular B-cell lymphoma (lung; lung path)
21-1005: mixed nested and microcystic variants urothelial carcinoma (bladder; GU path)
21-1006: fibromyxoid variant nephrogenic adenoma (prostate; GU path)
21-1007: angiomyolipoma with epithelial cyst (kidney; GU pathology)

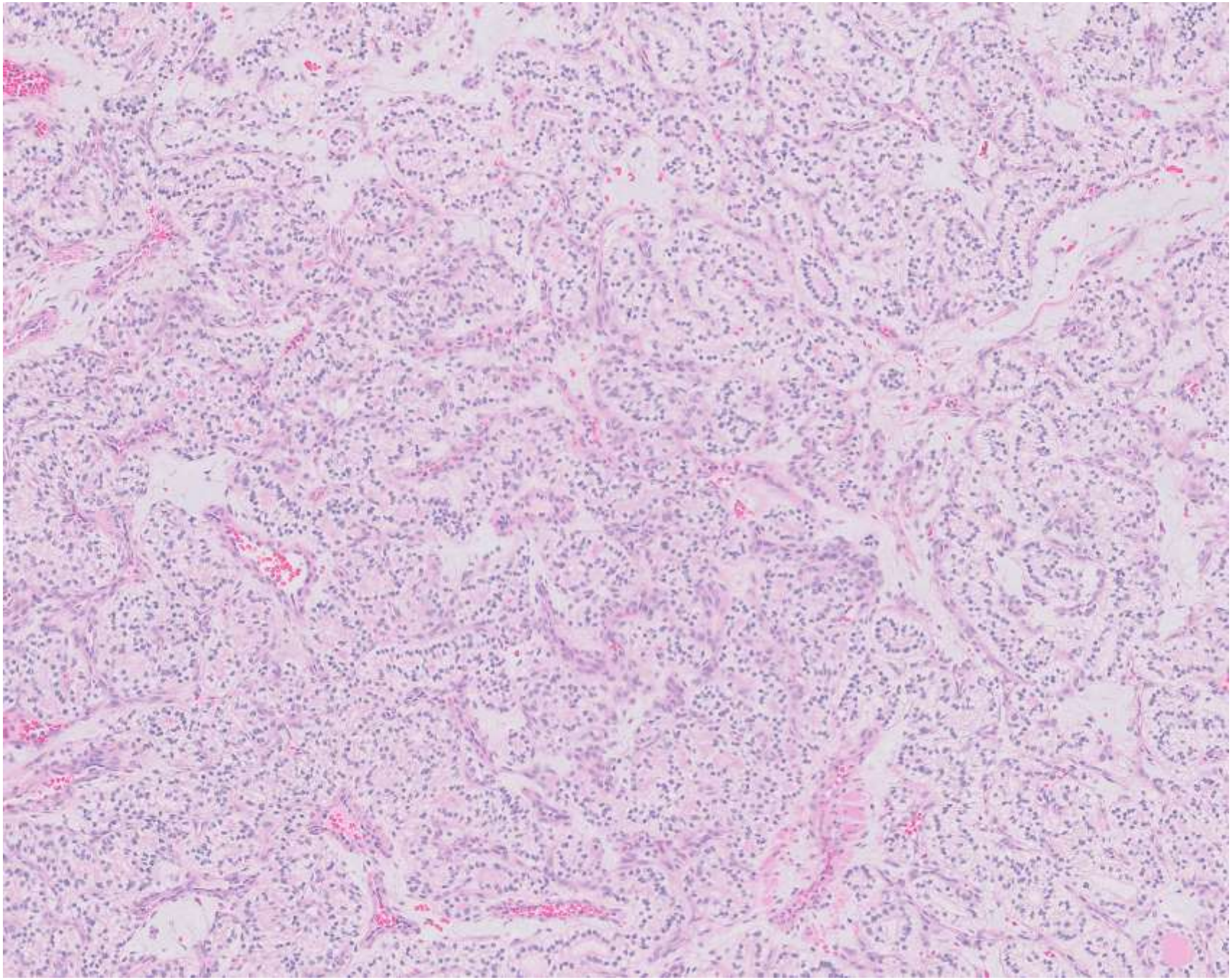
21-1001

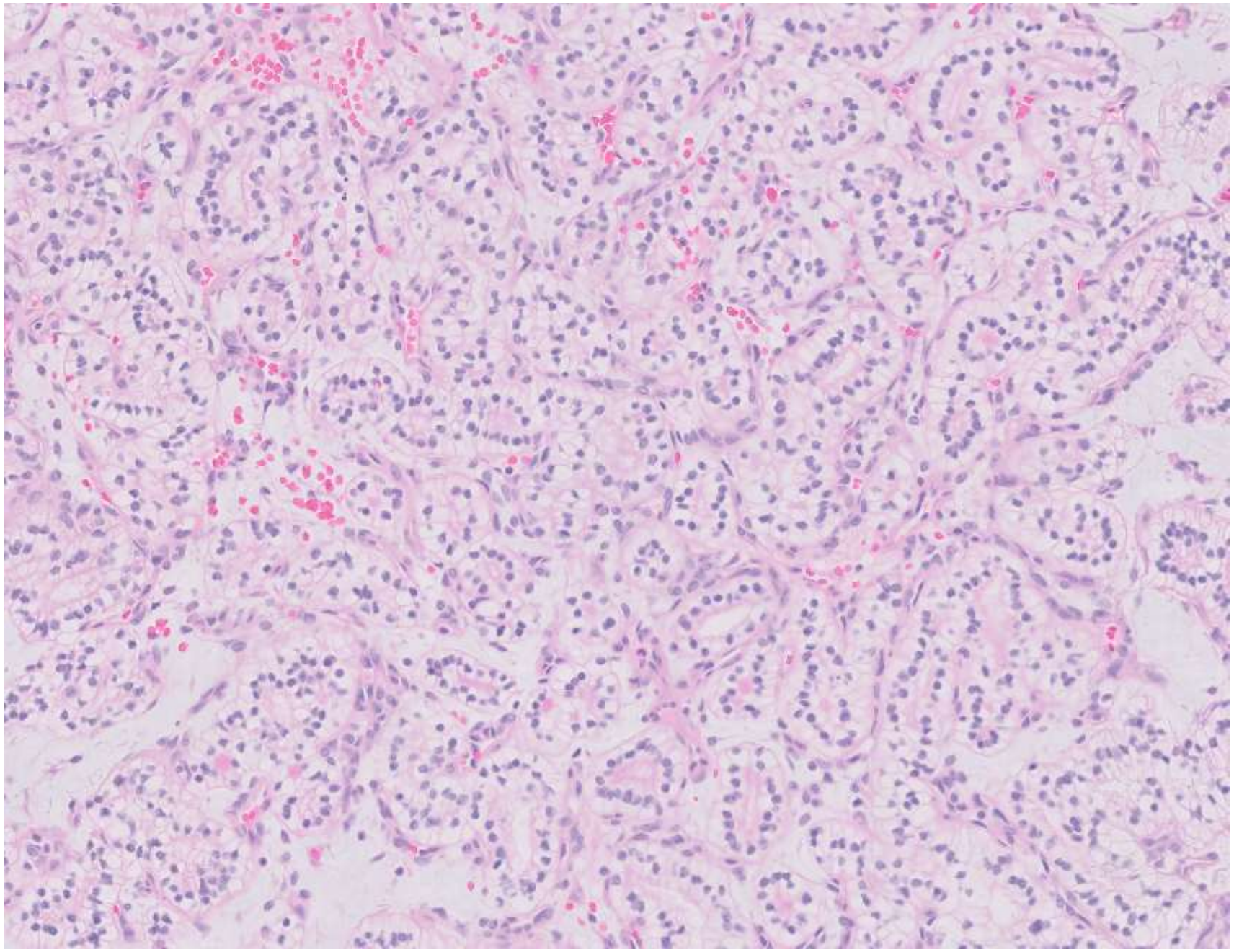
Emily Chan; USCF

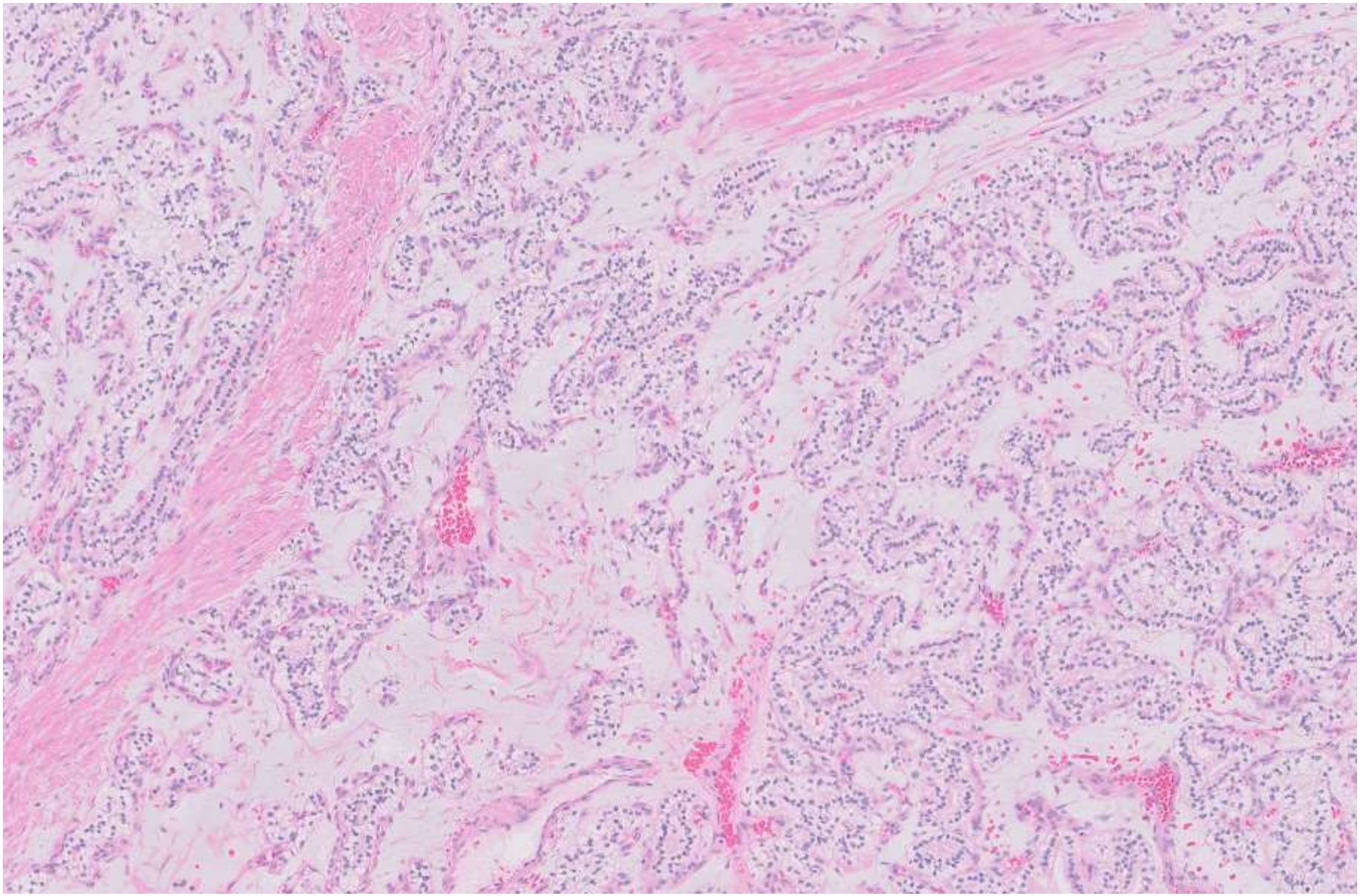
75-year-old man with 2.5 cm right epididymal mass

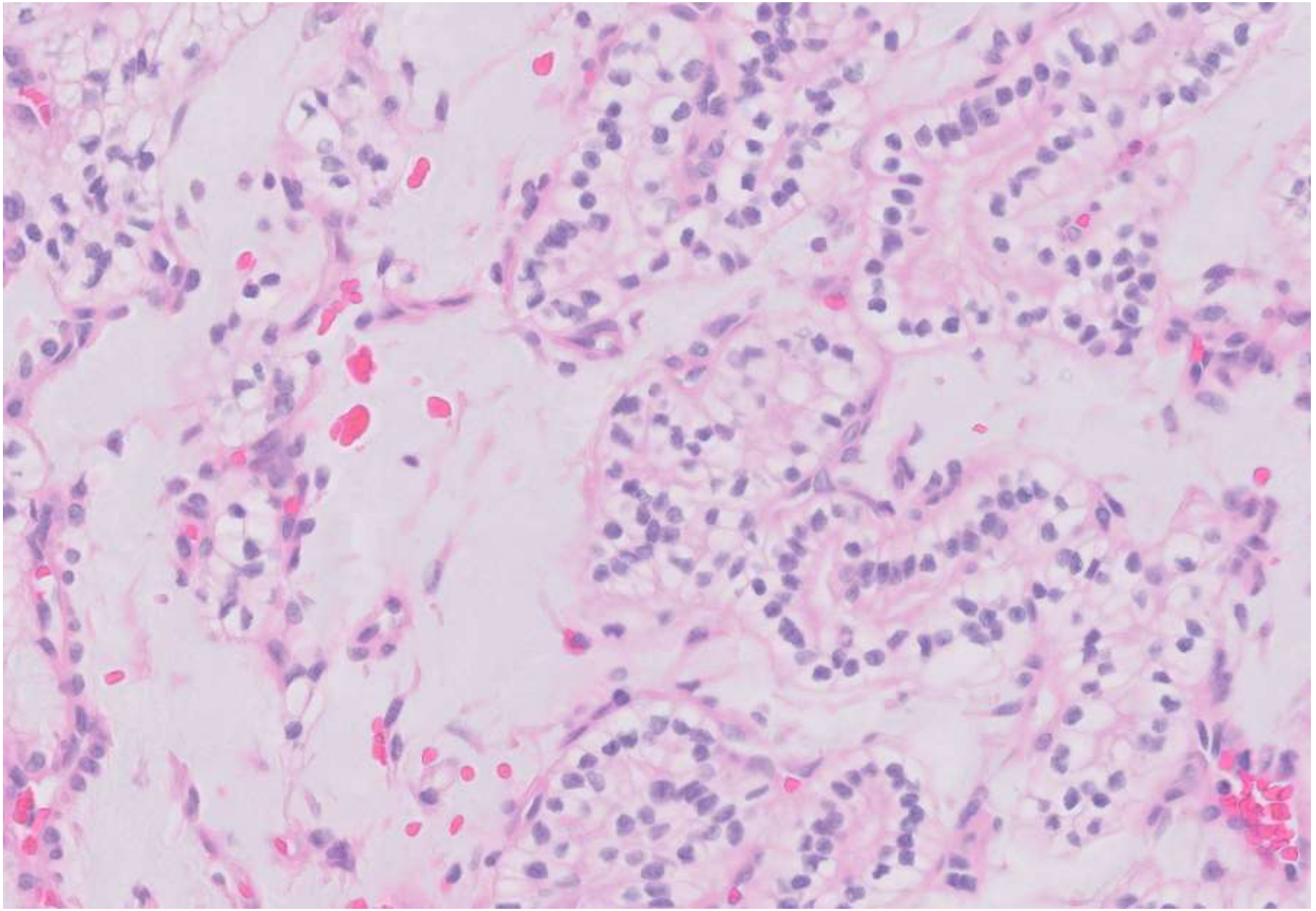






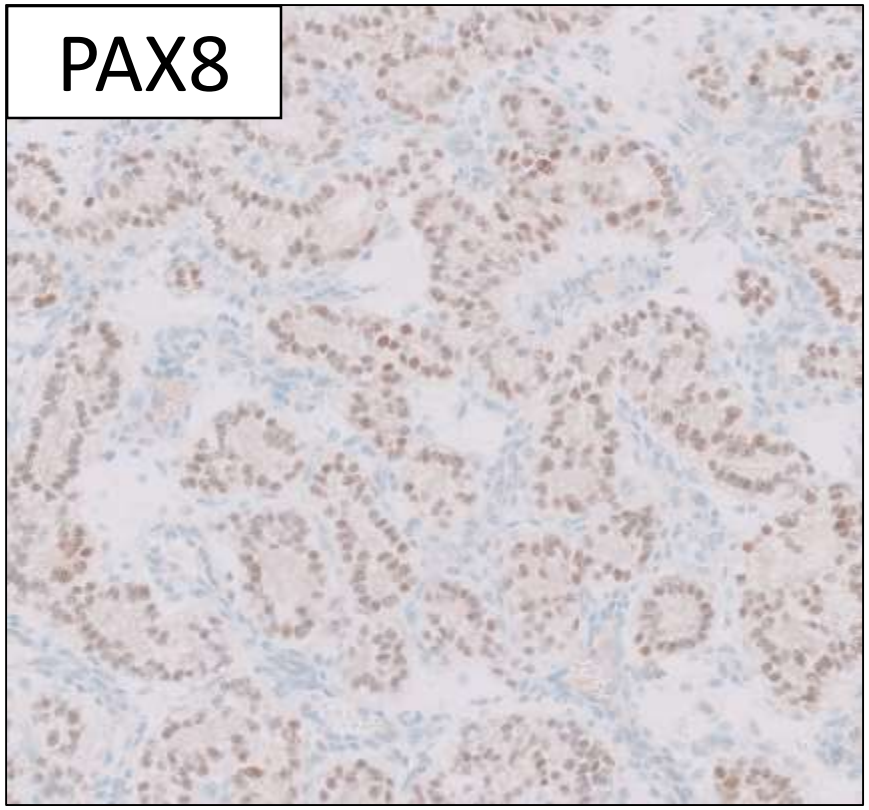


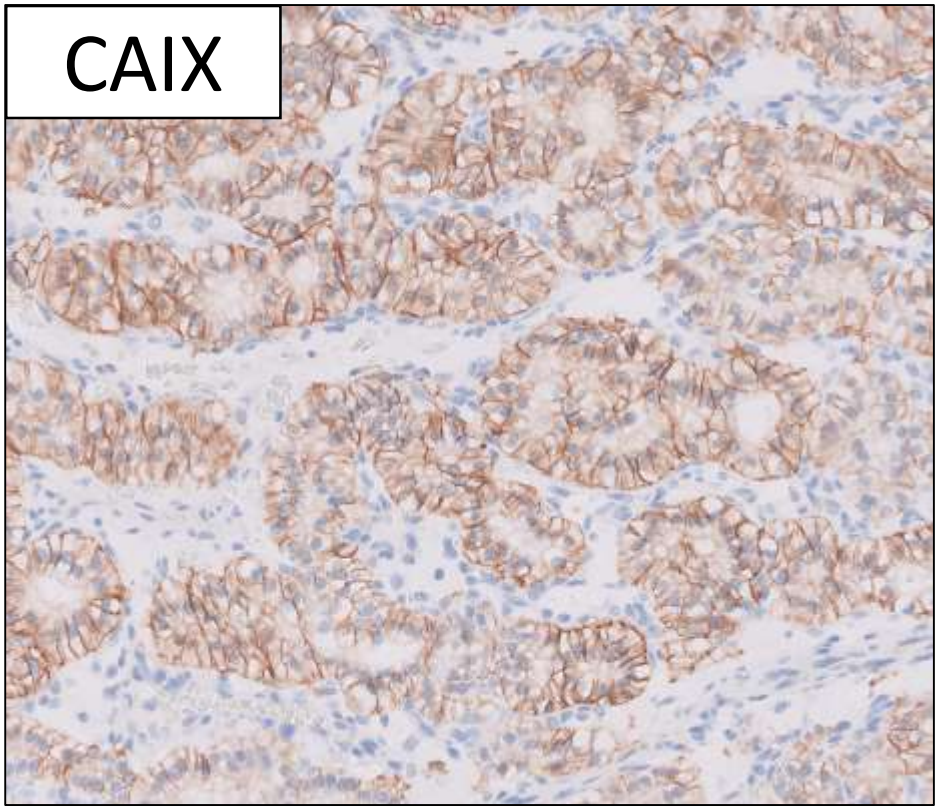


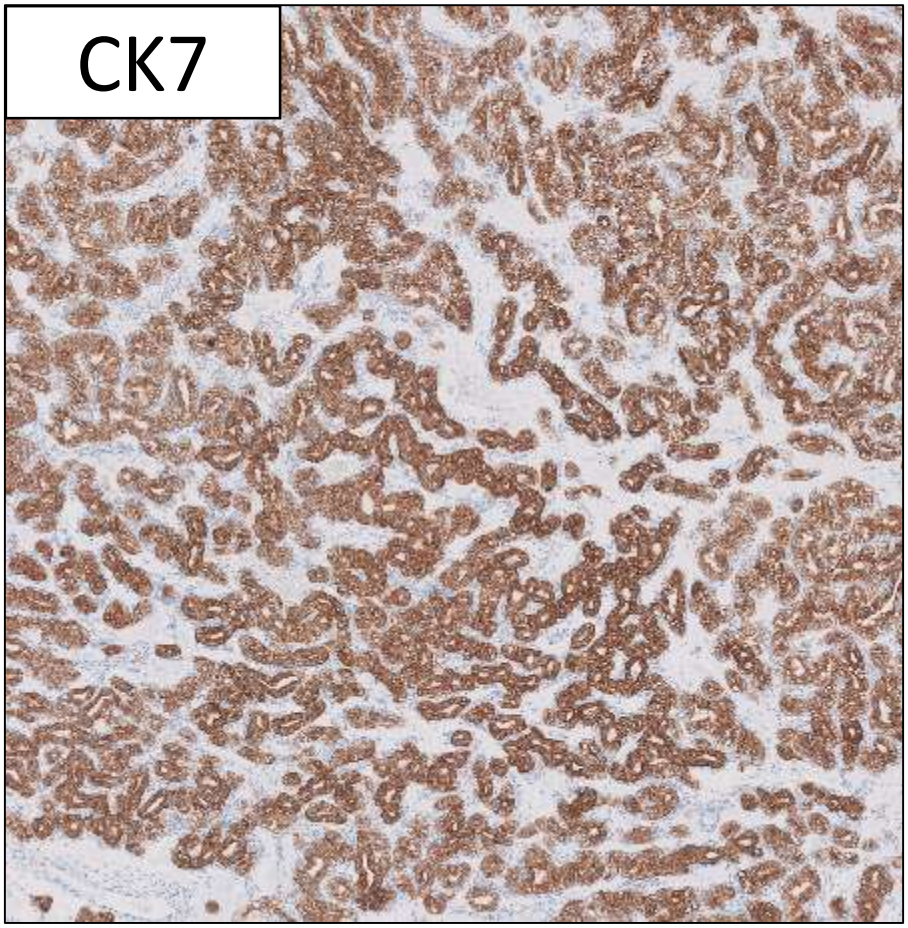


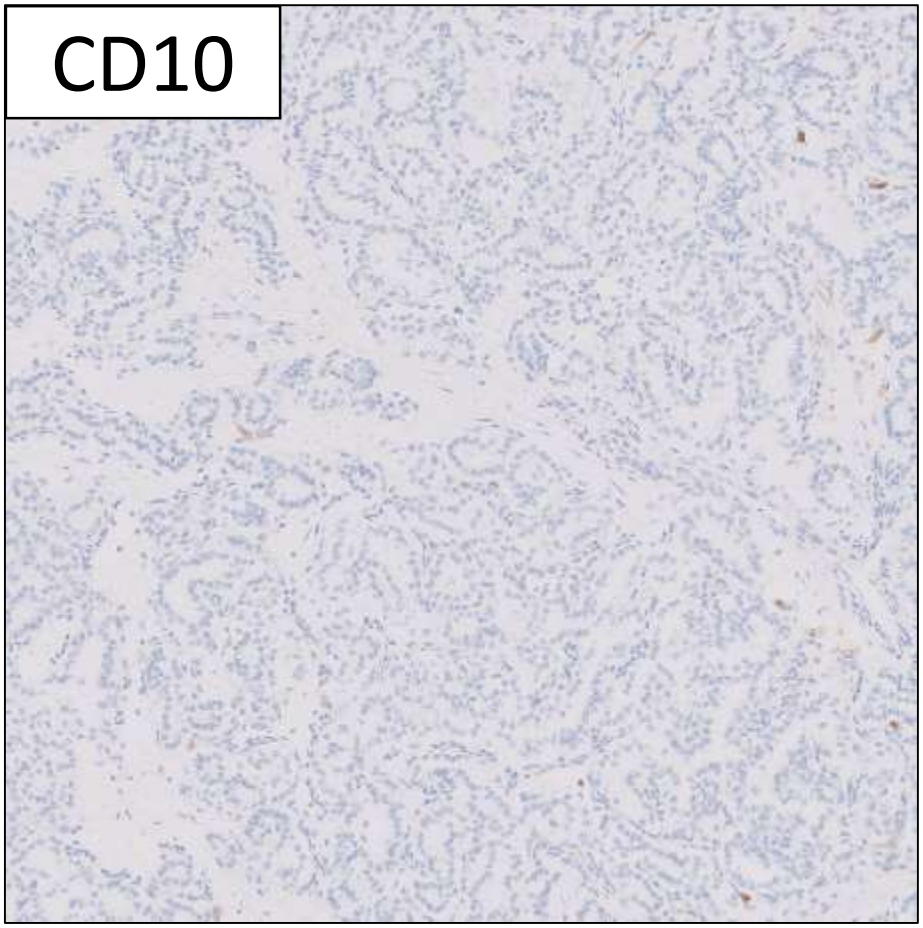
Differential diagnosis

- Metastatic clear cell renal cell carcinoma
- Metastatic clear cell papillary renal cell carcinoma
- Clear cell papillary cystadenoma of the epididymis


PAX8


CAIX


CK7


CD10

Diagnosis: Clear cell papillary cystadenoma of epididymis

- Rare benign tumor of the epididymis
- Sporadic or associated with von Hippel-Lindau (VHL) disease (especially if bilateral)
- Age range at presentation: 16-81 years
- Morphologically can have areas resembling low-grade clear cell RCC
- Also some immunohistochemical overlap of common markers used to diagnose metastatic ccRCC (PAX8, CAIX)

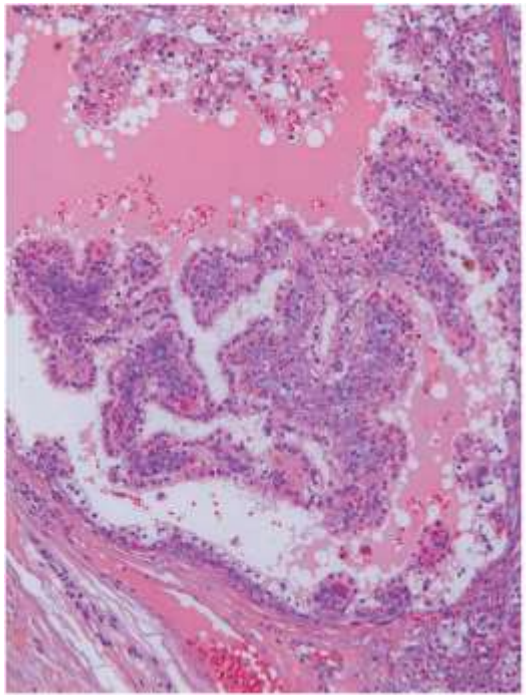
Clear Cell Papillary Cystadenoma of the Epididymis and Mesosalpinx

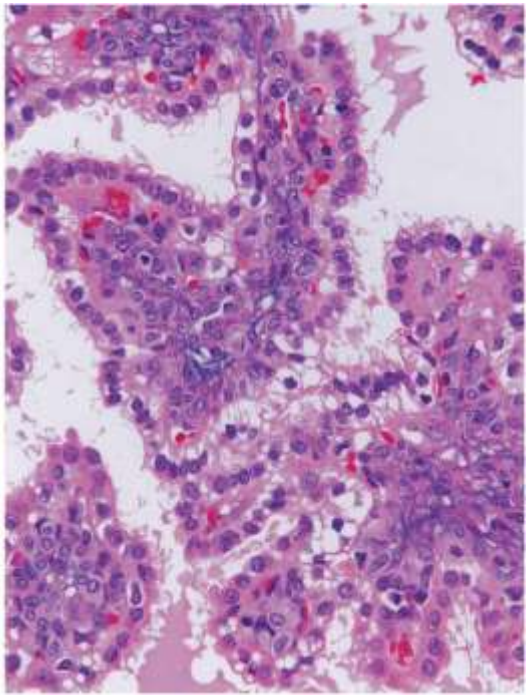
Immunohistochemical Differentiation From Metastatic Clear Cell Renal Cell Carcinoma

Hakan Aydin, MD, Robert H. Young, MD,† Brigitte M. Ronnett, MD,* and Jonathan I. Epstein, MD**

AJSP 2005; 29:520-523

- 5 cases: 3 from epididymis, 2 from mesosalpinx
- Two in setting of VHL (one case was first presentation)
- Recommended IHC panel to distinguish from metastatic ccRCC: CK7+,RCC-,CD10-





Clear Cell Papillary Cystadenoma of the Epididymis and Mesosalpinx

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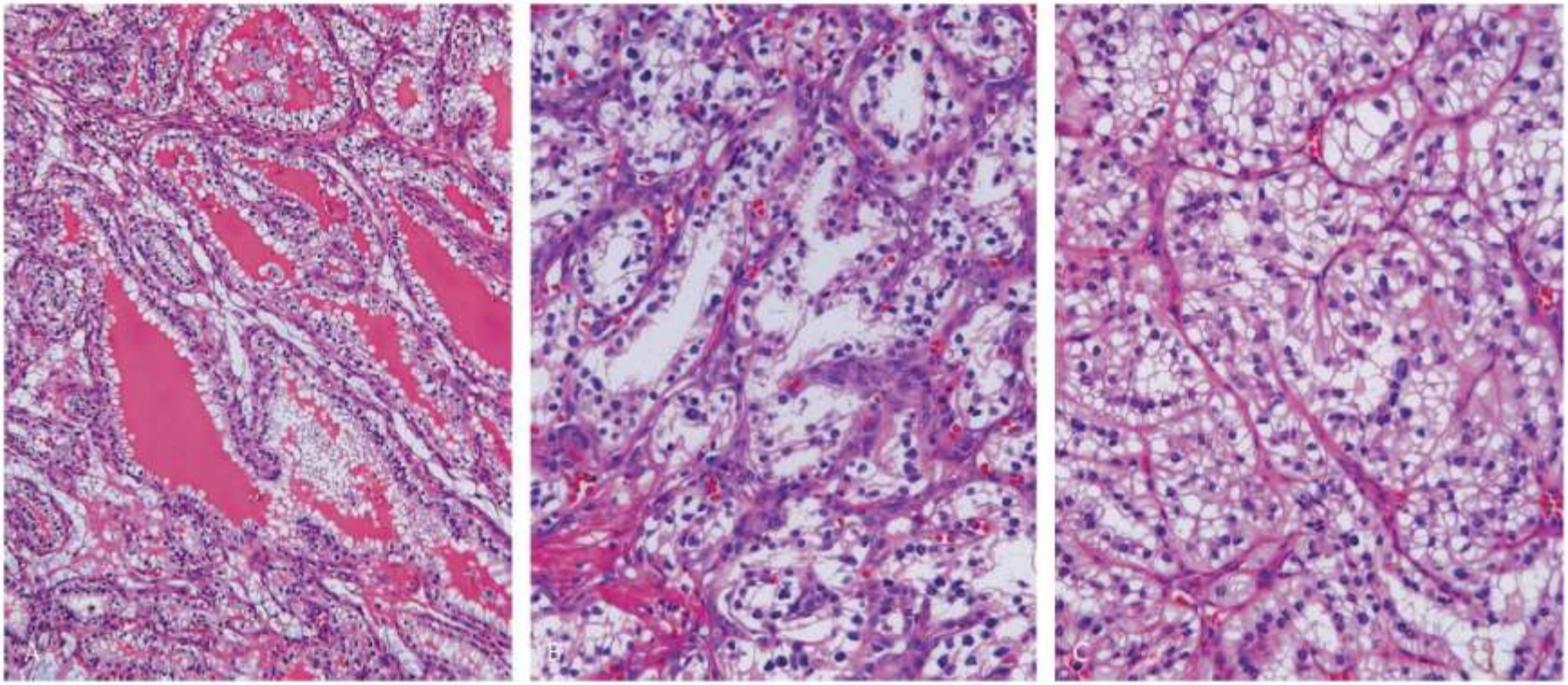


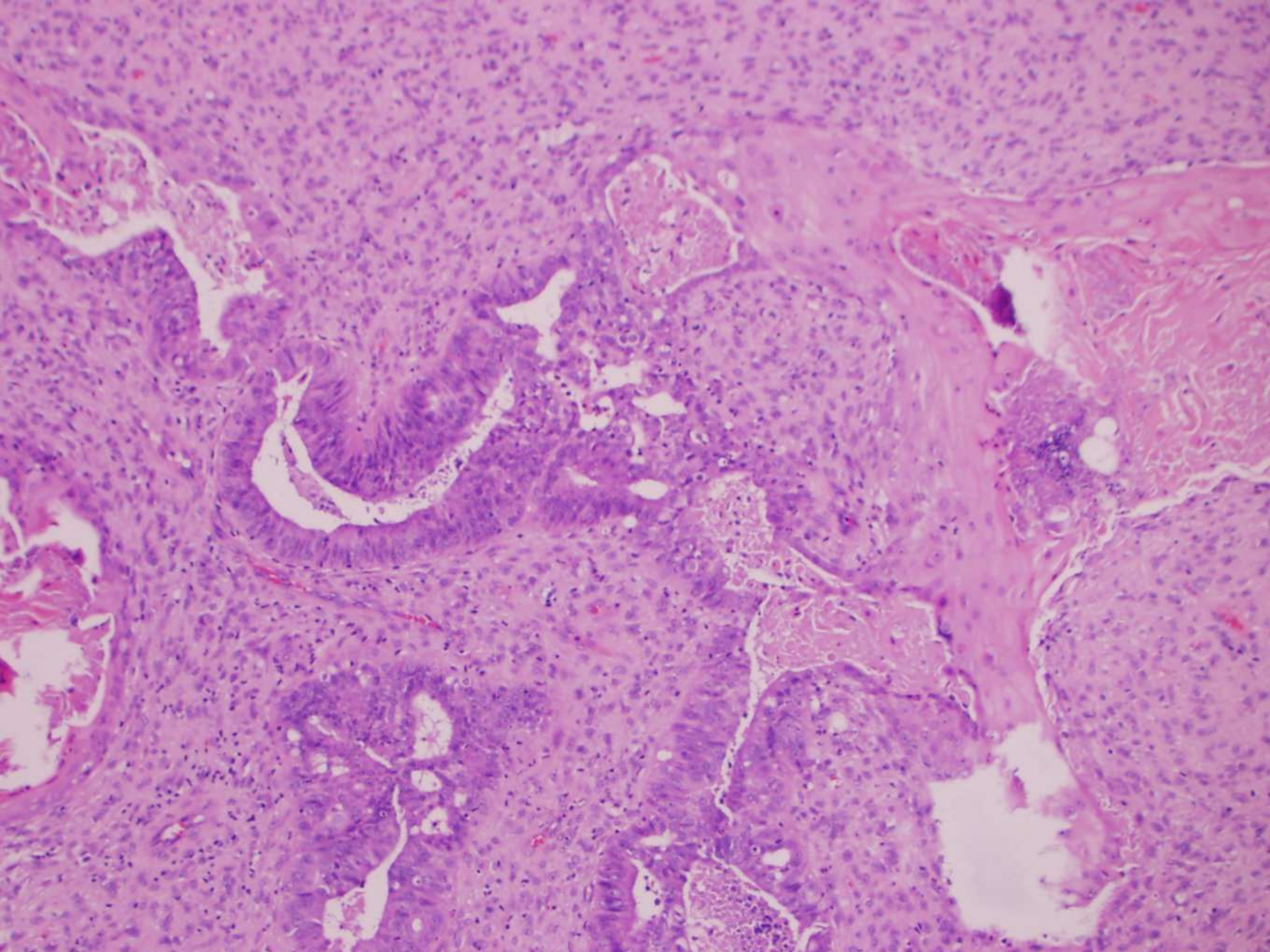
Clear cell papillary cystadenoma of the epididymis: Take home points

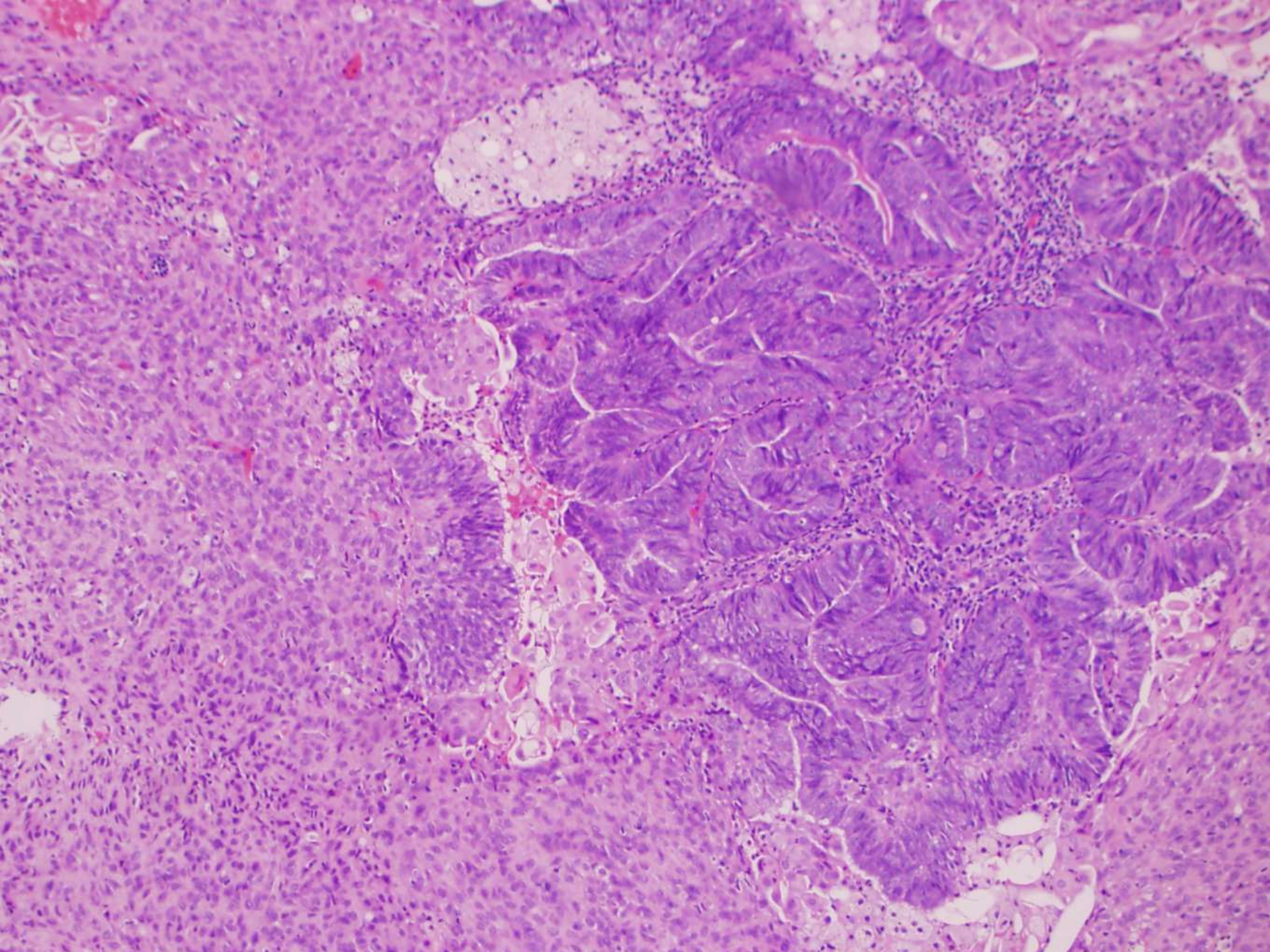
- Don’t mistake for metastatic clear cell renal cell carcinoma
  - Useful IHC: CK7, RCC, CD10
  - IHC that can get you into trouble: PAX8, CAIX
- Raise the possibility of VHL disease

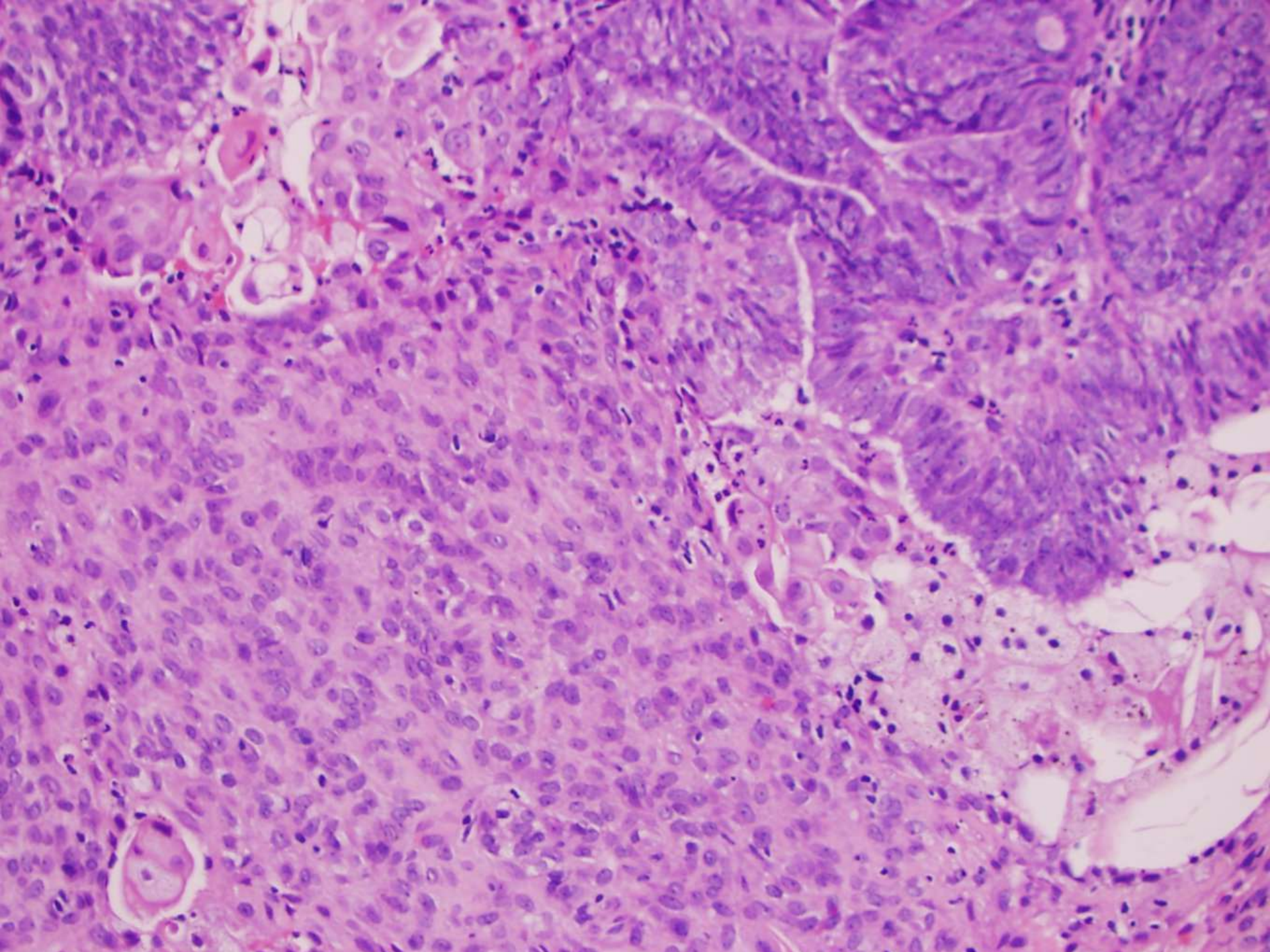
21-1002

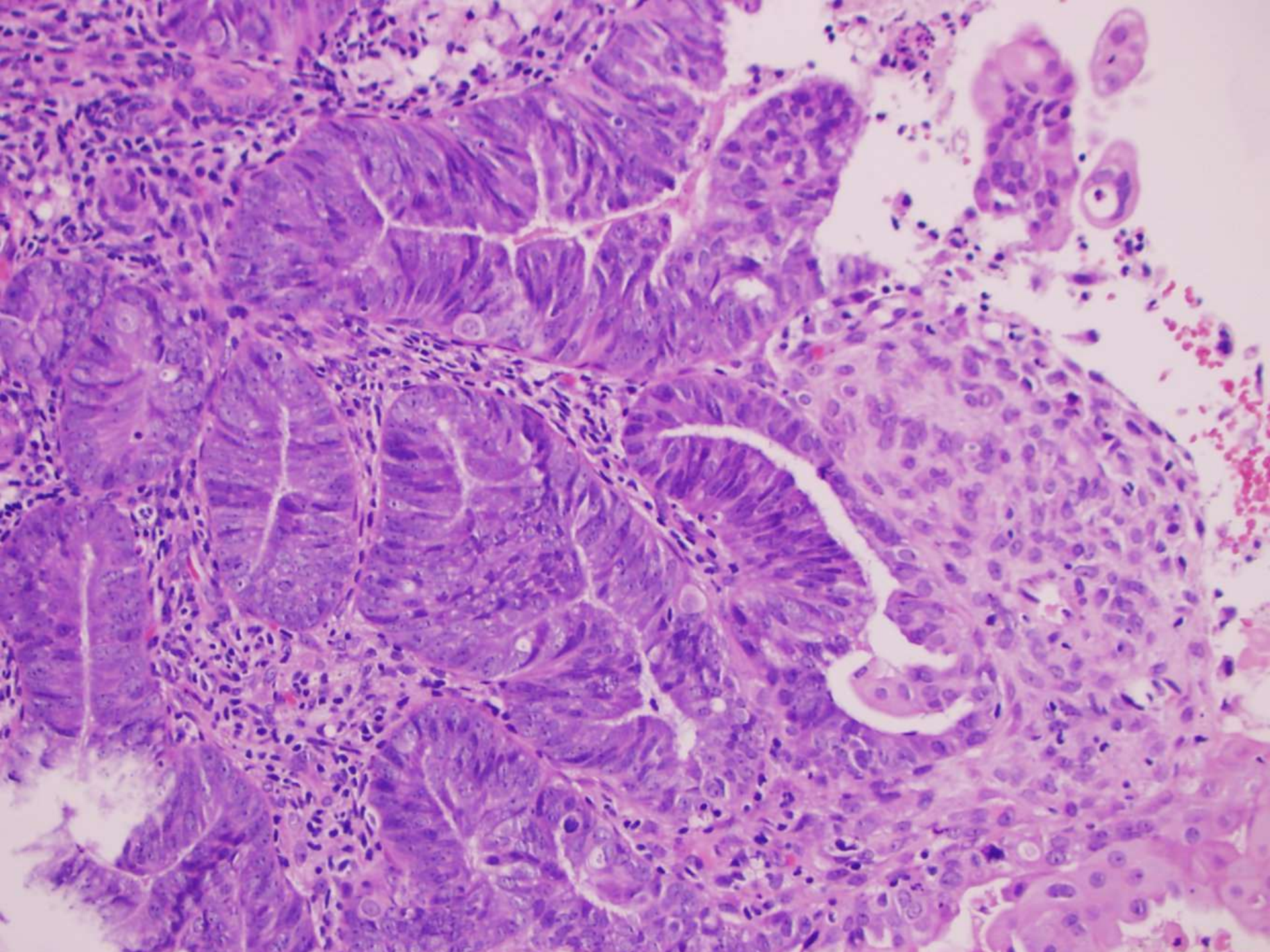
Greg Rumore; Kaiser Diablo

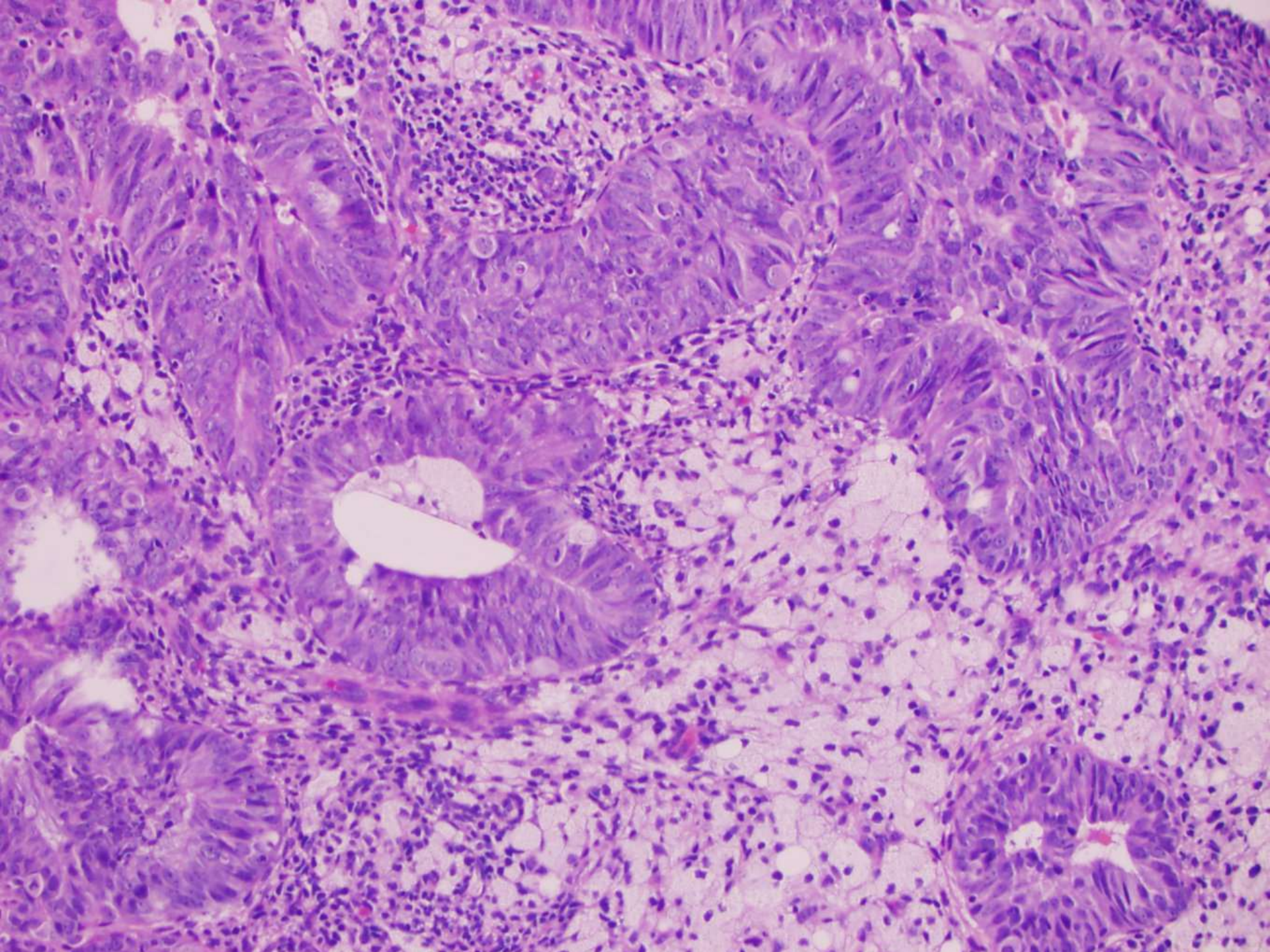
35-year-old F with abnormal uterine bleeding.

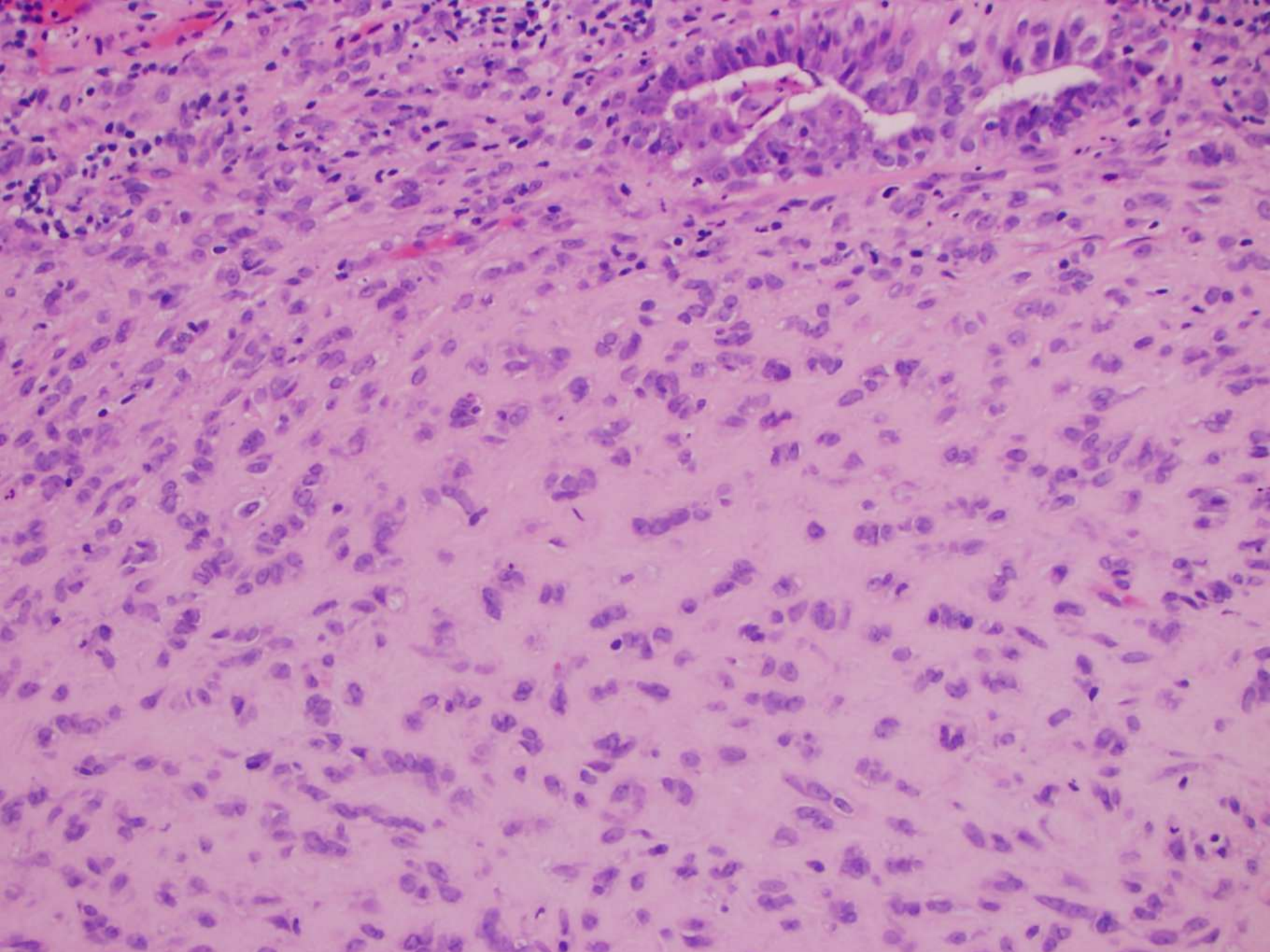


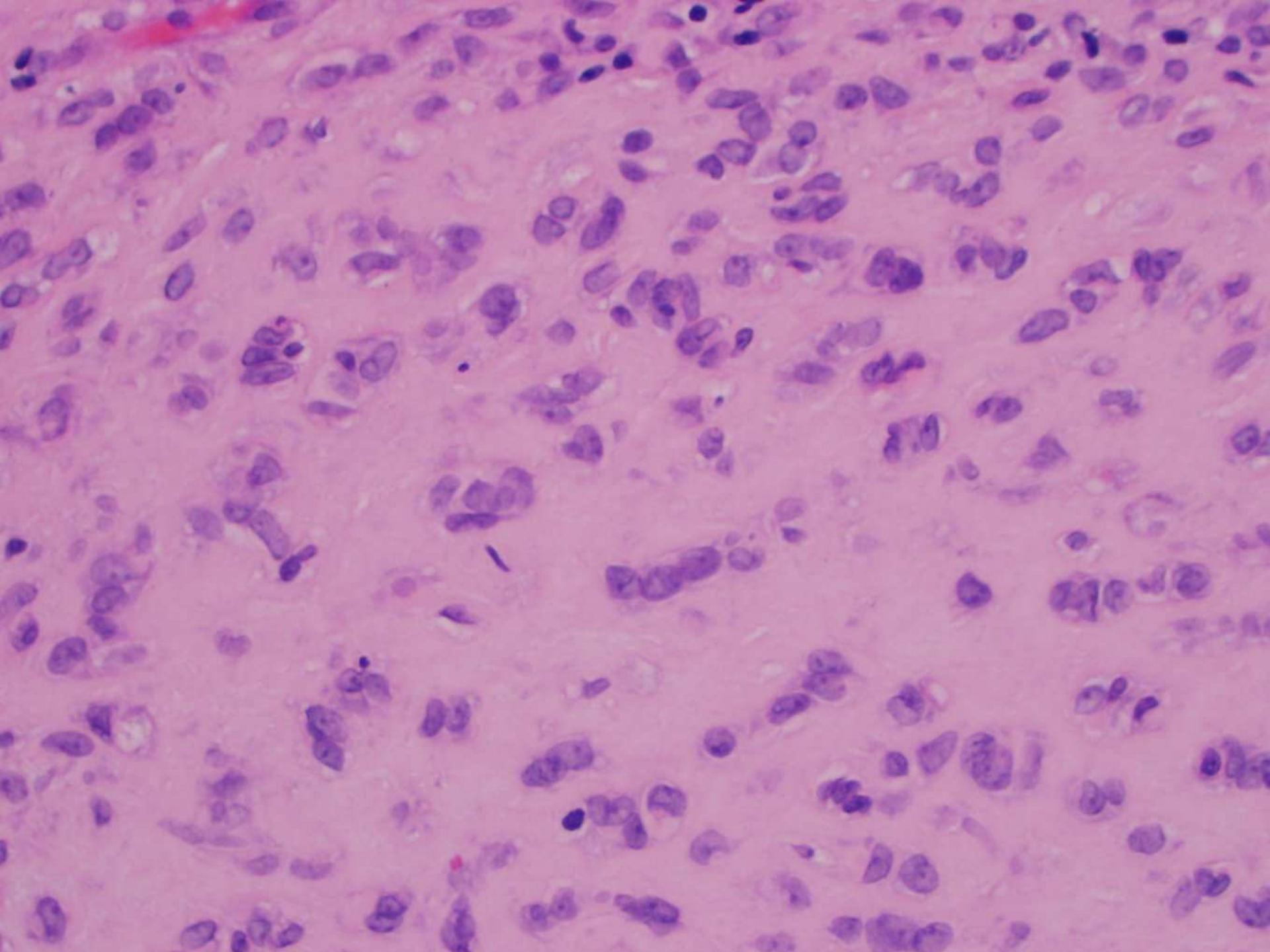


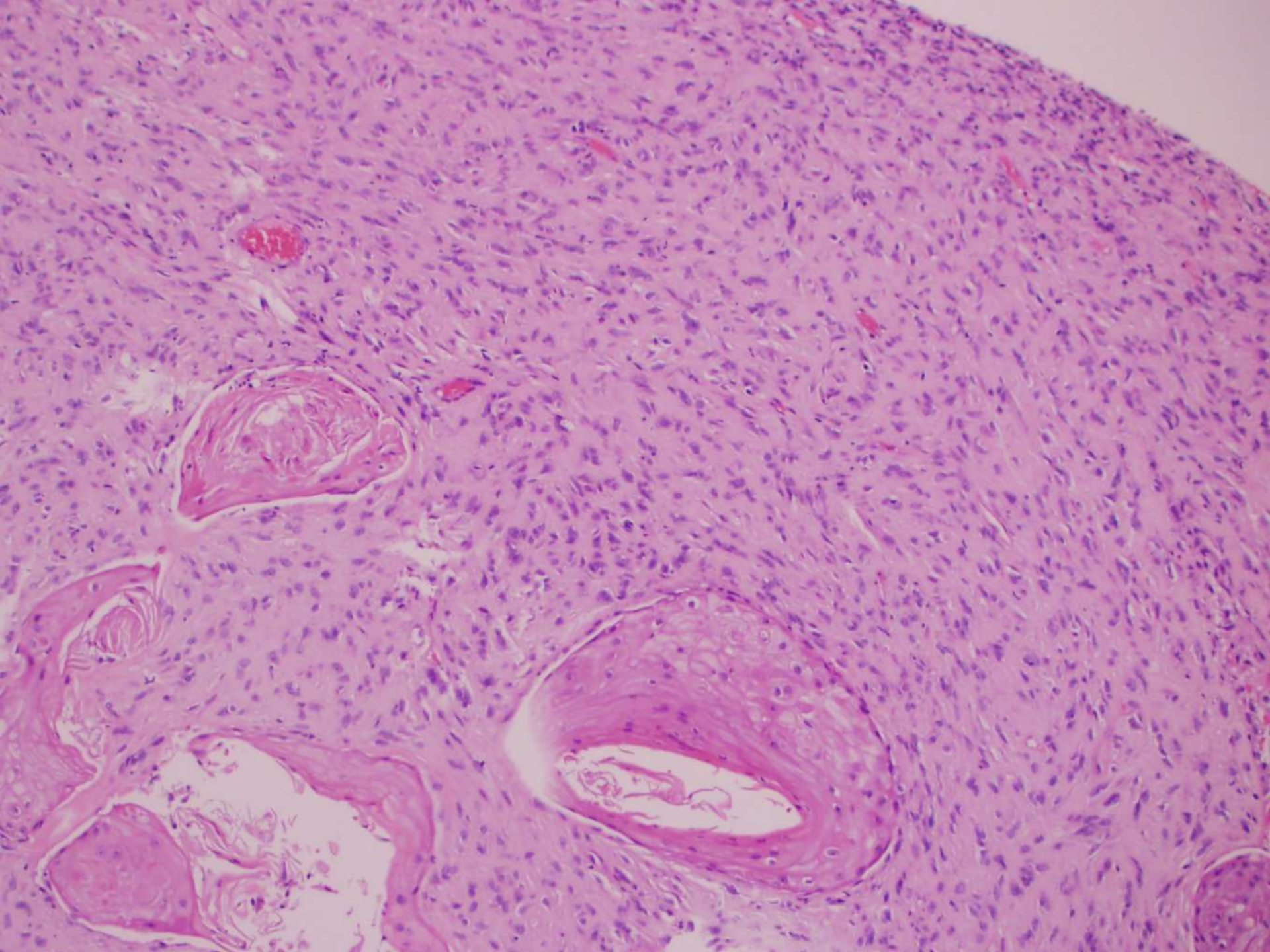


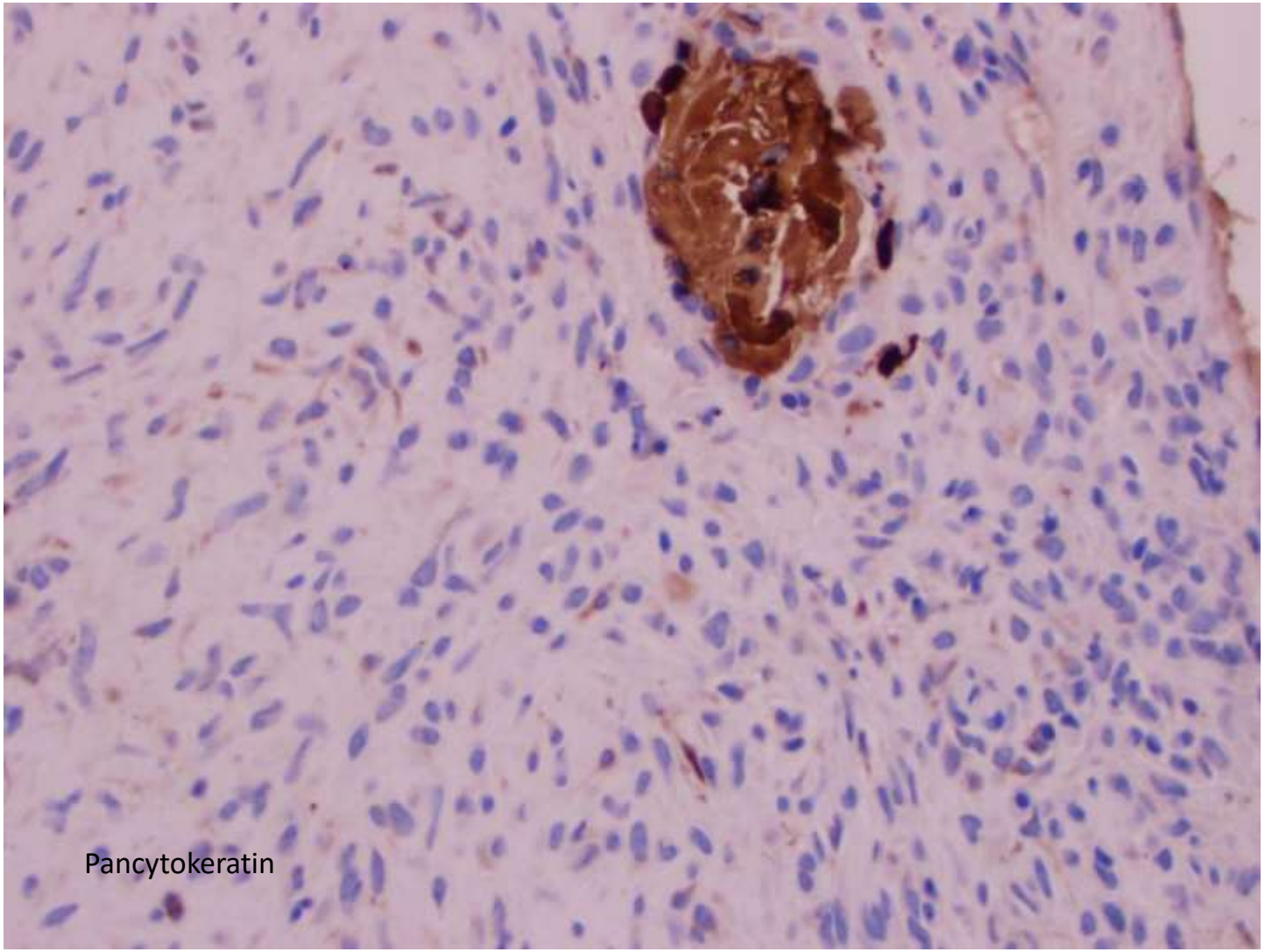


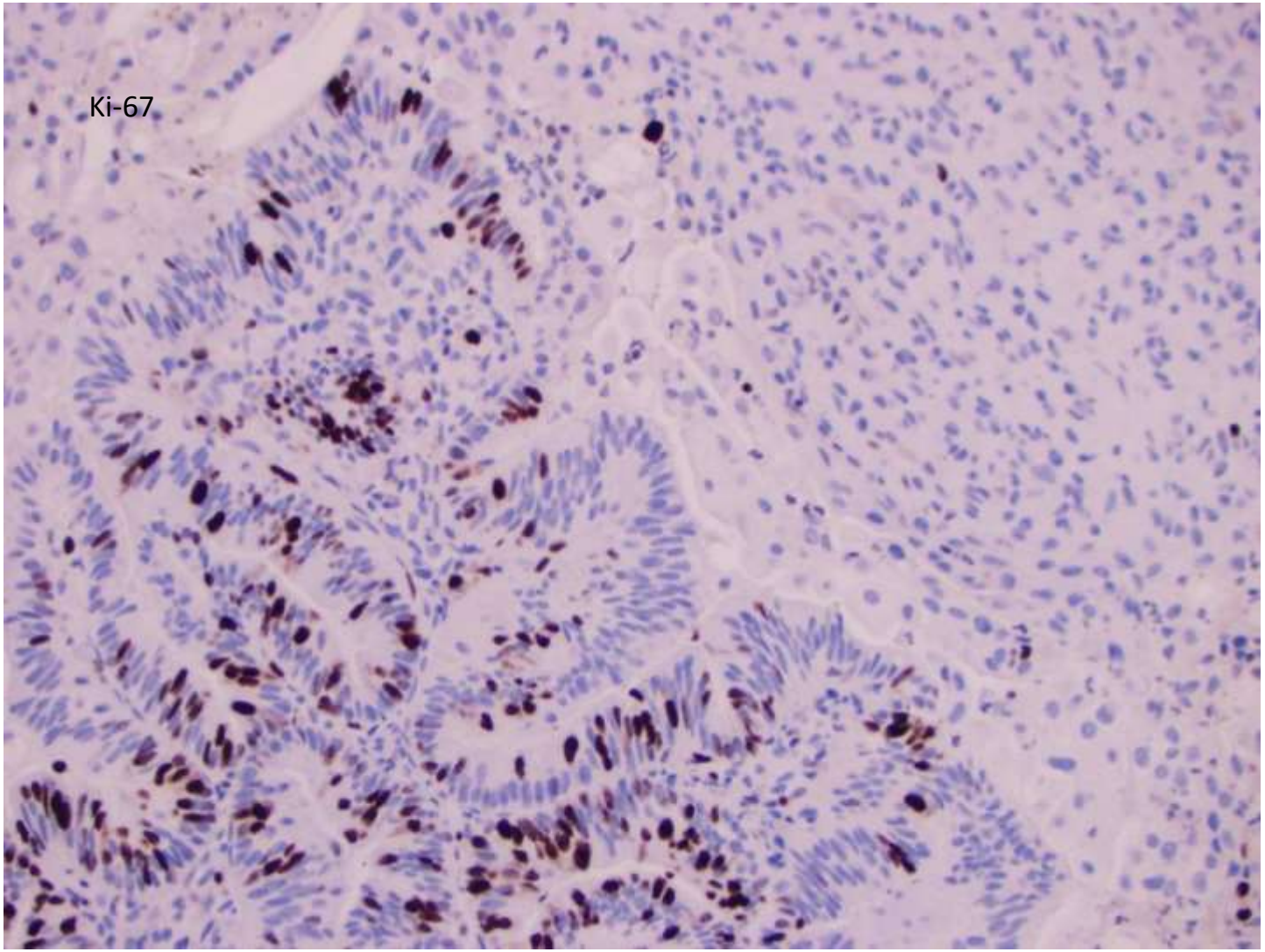









Pancytokeratin


Ki-67

Endometrioid Carcinoma, Corded and Hyalinized Pattern

- Unusual variant of endometrial CA
- Epithelioid and spindled to fusiform cells in hyalinized stroma
- Younger patients (mean age=52, vs. 60 for EMCA)
- Endometrioid component tends to be low grade (Gr. 1-2)
- 70% have squamous differentiation
- May have osteoid
- Grade on basis of glandular (endometrioid) component only
- Usually low stage, good prognosis

Differential Diagnosis- MMMT

- Older age group
- Both epithelial and mesenchymal components are high grade
- Useful stains=p53, epithelial markers (EMA, broad spectrum cytokeratins)

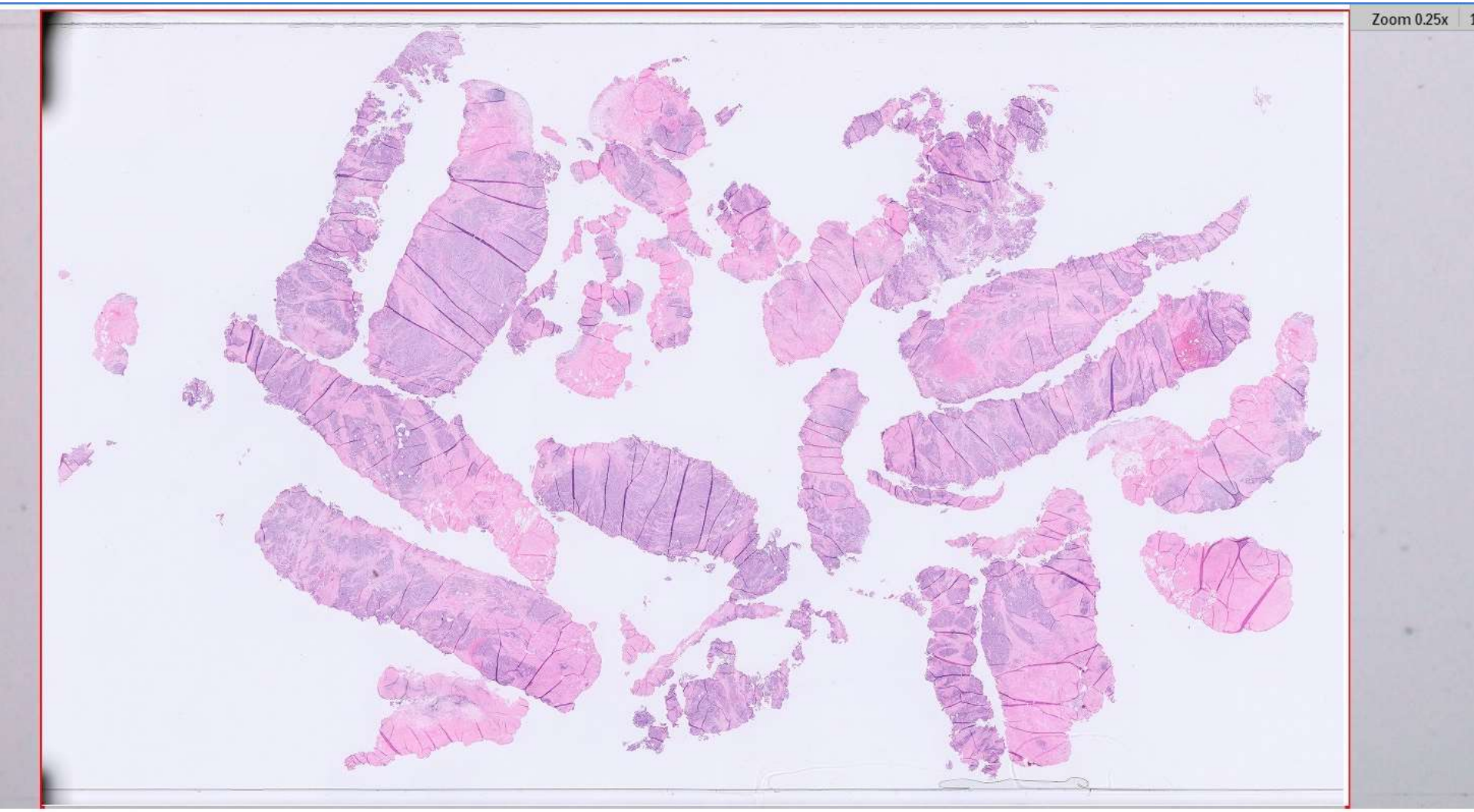
References

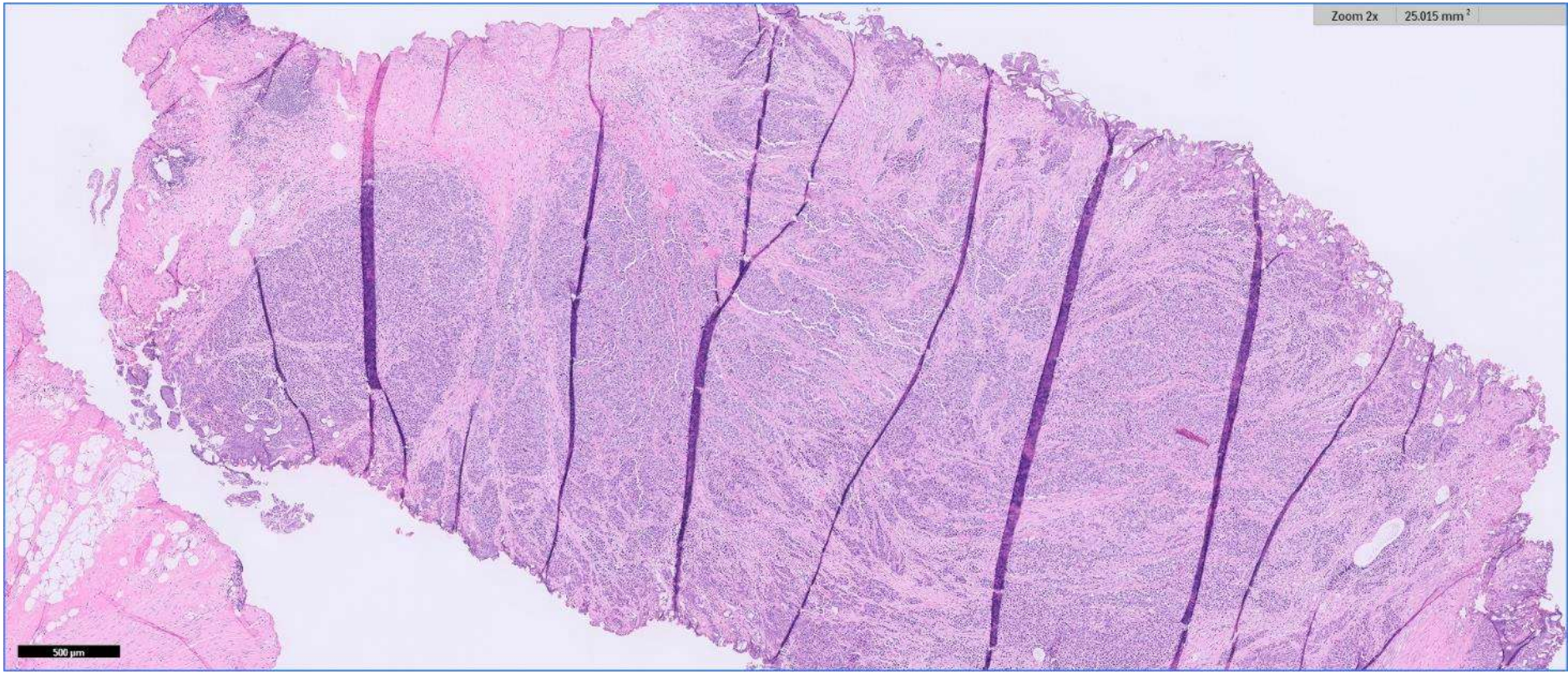
- Murray, S., Clement, P., Young, R., Endometrioid Carcinomas of the Uterine Corpus with Sex Cord-like Formations, Hyalinization, and Other Unusual Morphologic Features, AJSP Vol. 29, No.2, Feb 2005
- Rabban, J.T., et al, Issues in the Differential Diagnosis of Uterine Low-grade Endometrioid Carcinoma, Including Mixed Endometrial Carcinomas: Recommendations from the International Society of Gynecological Pathologists, Int J Gynecol Pathol, 2019 Jan; 38 (Iss 1 Suppl 1); S25-S39

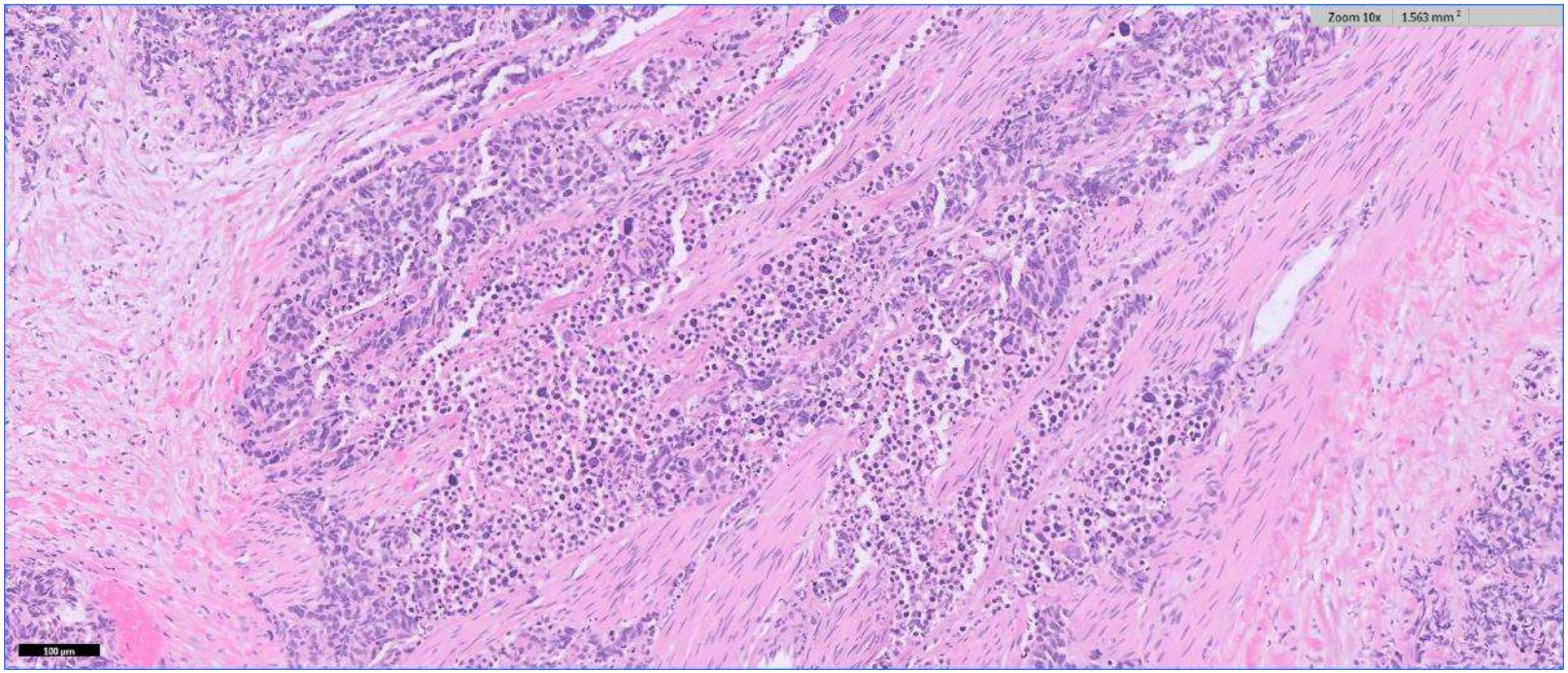
21-1003

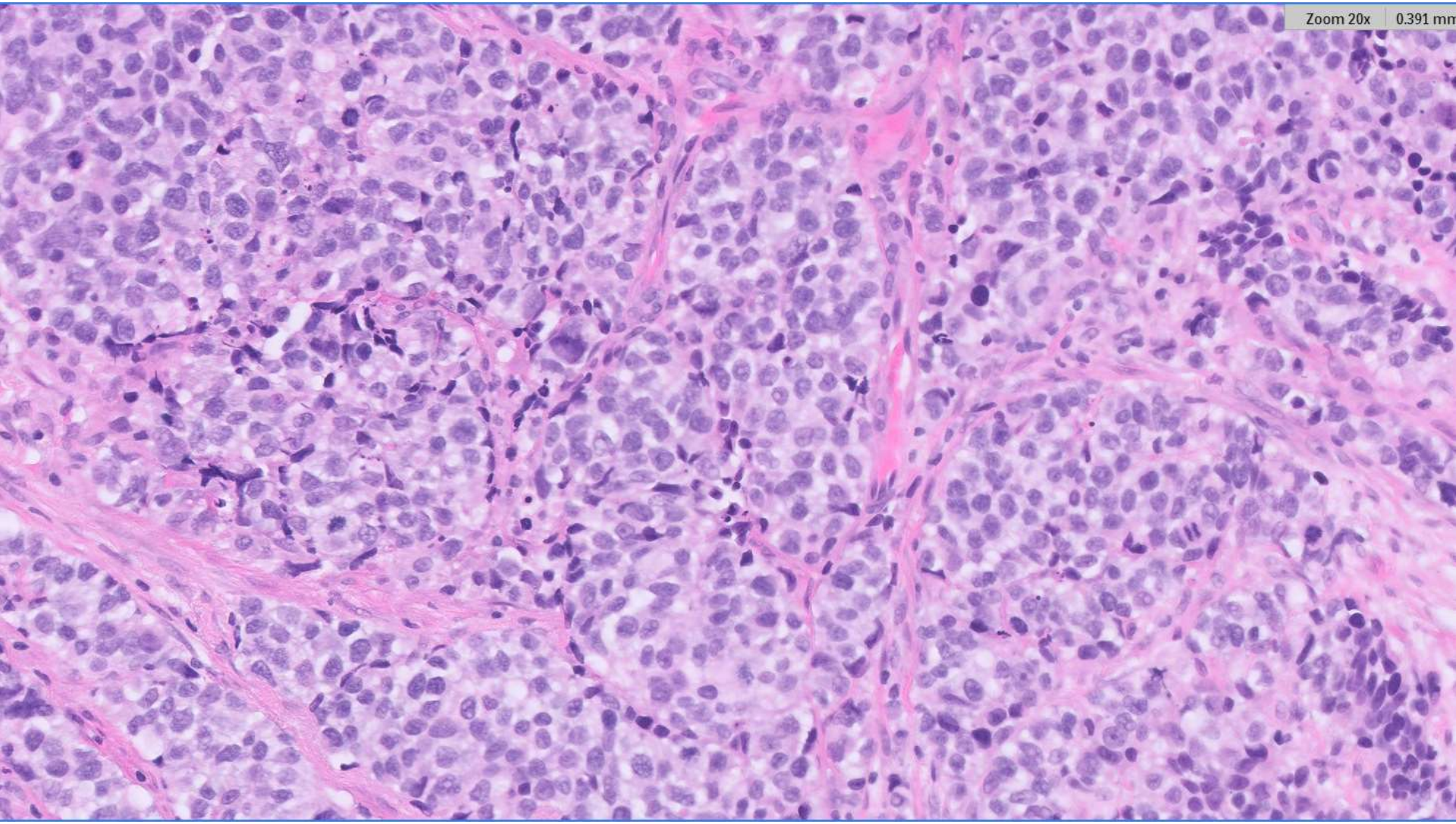
Osama Khan/Sunny Kao; Stanford

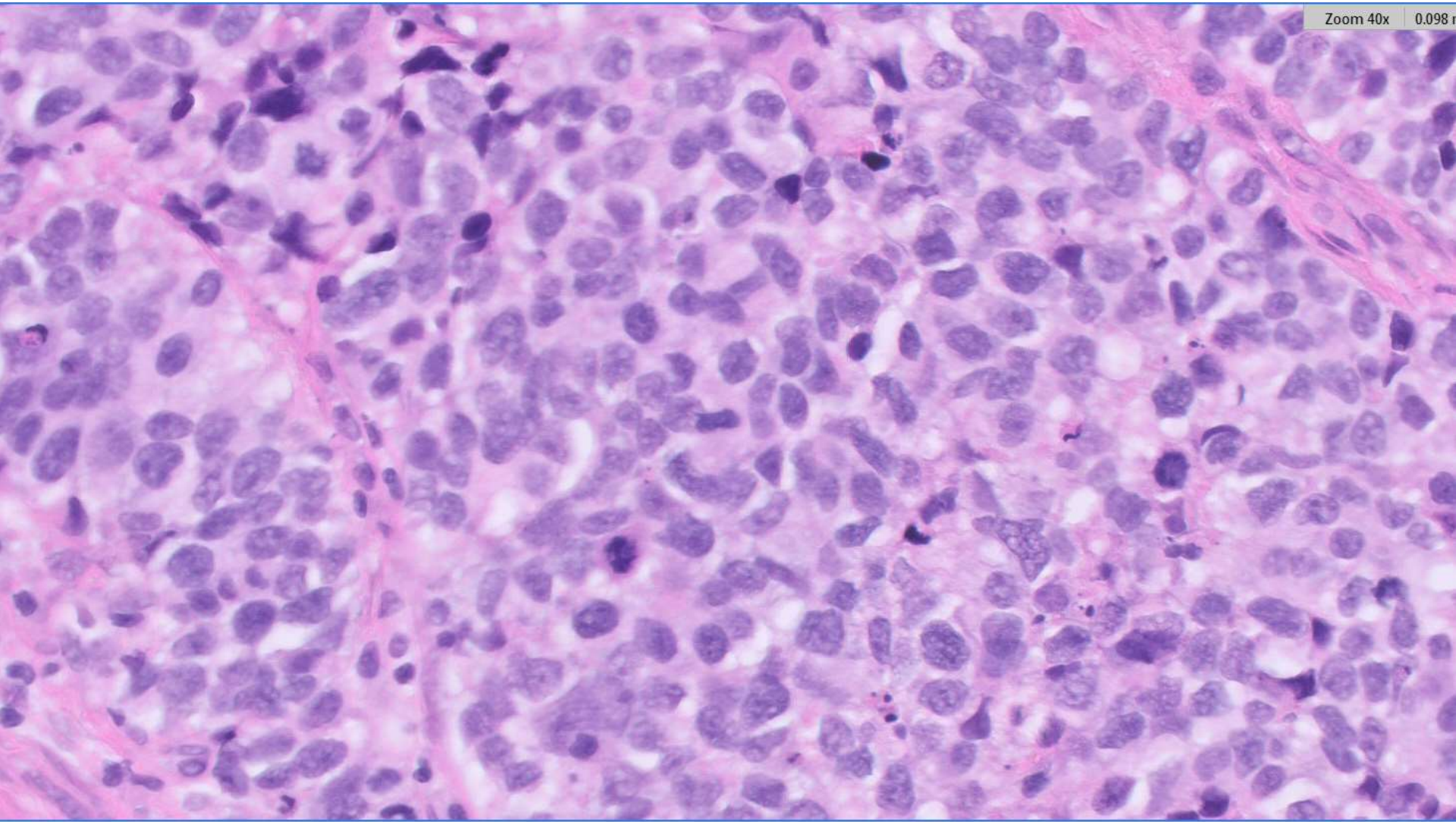
82-year-old M with developed hematuria 1 year ago. Surveillance cystoscopy showed 6cm anterior wall suspicious lesion.


Zoom 0.25x


Zoom 2x
25.015 mm²
500 µm


Zoom 10x
1.563 mm²
100 µm


Zoom 20x
0.391 mm


Zoom 40x
0.098

Differential Diagnosis

- Poorly differentiated/undifferentiated carcinoma of renal or urothelial origin
- Lymphoma
- Metastatic Carcinoma
- Melanoma
- Neuroendocrine carcinoma of bladder

Immunohistochemistry results

Positive

- **Synaptophysin**, CKMIX, 34BE12

Negative

- **INSM1**, GATA-3, p63, NKX3.1, and Chromogranin

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Expression of novel neuroendocrine marker insulinoma-associated protein 1 (INSM1) in genitourinary high-grade neuroendocrine carcinomas: An immunohistochemical study with specificity analysis and comparison to chromogranin, synaptophysin, and CD56

Jie-Fu Chen[a], Chen Yang[b], Yue Sun[c], Dengfeng Cao[a,*]

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[b] Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, USA
[c] Department of Pathology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA

INSM1 and its utility in GU HGNECs

- Insulinoma-associated protein 1 (INSM1) has been recently identified as a novel marker for neuroendocrine differentiation.
- Chen et al compared INISMI staining in GU HGNECs in comparision to synaptophysin, chromogranin and CD56 in 39 GU-HGNECs
- In 33 SmCCs/components, INSM1 showed similar sensitivity (93.9 %) to synaptophysin (93.9 %), chromogranin (87.8 %) and CD56 (87.8 %)
- In 8 LCNECs/components, INSM1 is similar to chromogranin, synaptophysin or CD56 in sensitivity (62.5 %, 75 %, 62.5 %, respectively)
- INSM1 is more sensitive for genitourinary SmCCs than LCNECs.

Diagnosis:
Large Cell Neuroendocrine Carcinoma

- Large cell polygonal morphology, trabecular or sheet-like pattern, with more abundant cytoplasm, low NC ratio (in comparison to SmCC) and prominent nucleoli
- Increased mitotic activity (>10 per 10hpf) and necrosis
- Due to negative immunomarkers could not definitively prove urothelial origin

Large Cell Neuroendocrine Carcinoma (Bladder)

- One of the rarest types of bladder cancer (<1%) with only a few case reports/series in the literature
- High grade carcinoma exhibiting NE features on H&E similar to pulmonary LGNEC and immunohistochemical evidence of neuroendocrine differentiation
- Some cases associated with conventional urothelial carcinoma
- Extremely aggressive subtype with an aggressive clinical course often presenting with metastases

ORIGINAL ARTICLE

OPEN

Urinary Large Cell Neuroendocrine Carcinoma

A Clinicopathologic Analysis of 22 Cases

Gang Wang, MD, PhD,† Ren Yuan, MD, PhD,†‡ Chen Zhou, MD, PhD,*†*
Charles Guo, MD, PhD,§ Carlos Villamil, MD,† Malcolm Hayes, MD,*†*
Bernhard J. Eigl, MD,†‖ and Peter Black, MD†¶

Treatment of GU NECs vs conventional UC

- **GU NECs** - initial systemic neoadjuvant chemotherapy (platinum-based), followed by re-evaluation and consideration for definitive local therapy with either cystectomy or radiation therapy
- **Conventional UC** – depends on stage; BCG therapy (T1) vs radical cystectomy (T2).
  - Locally advanced usually treated with chemotherapy, immunotherapy or radiation

Key Learning Points

- DDx for neuroendocrine carcinomas of the bladder
- INSM1 staining utility in GU-HGNECs
- Histologic features of LCNEC vs SCC of Bladder
- Importance of recognition of a HGNEC for treatment implications

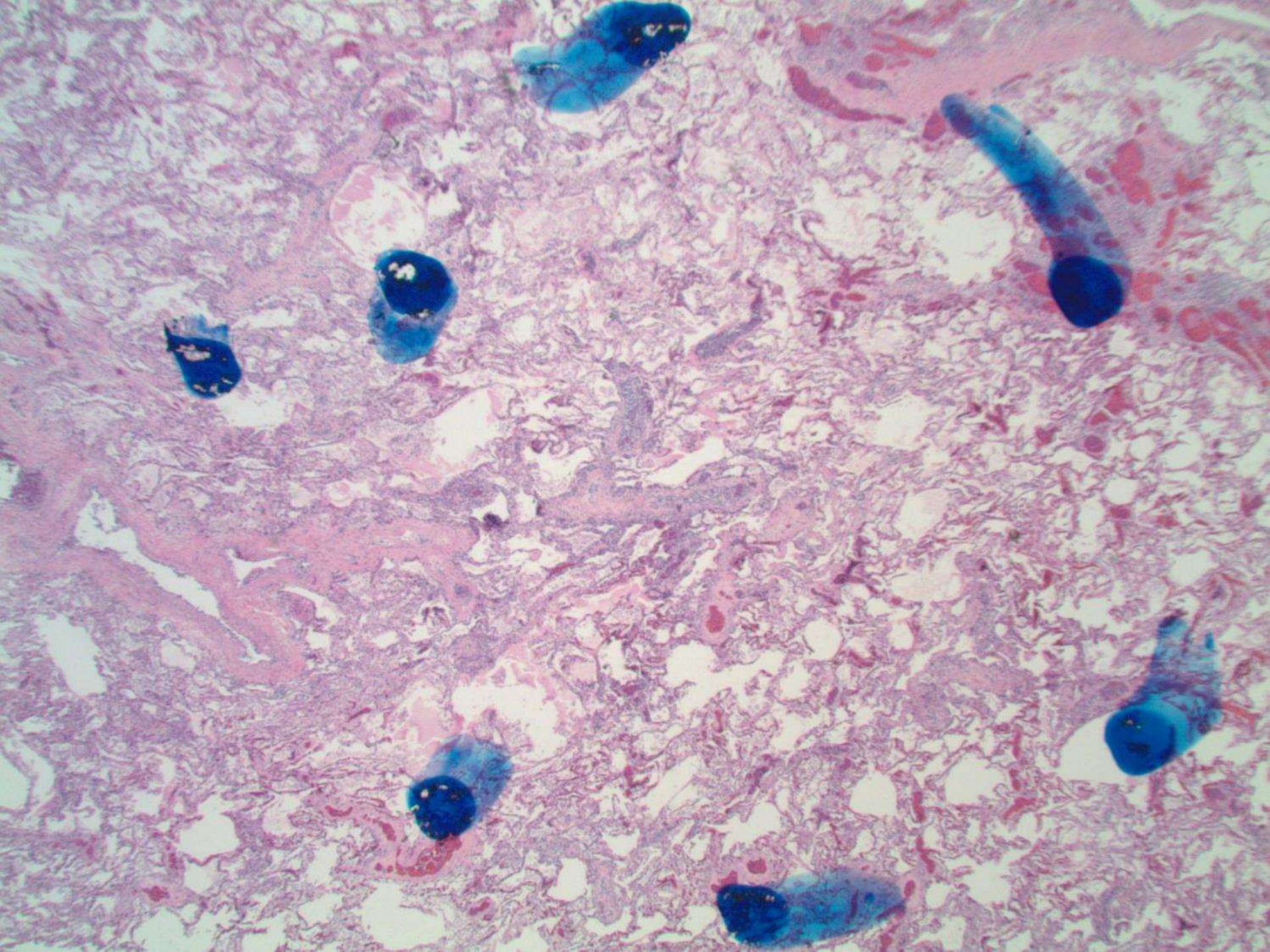
References

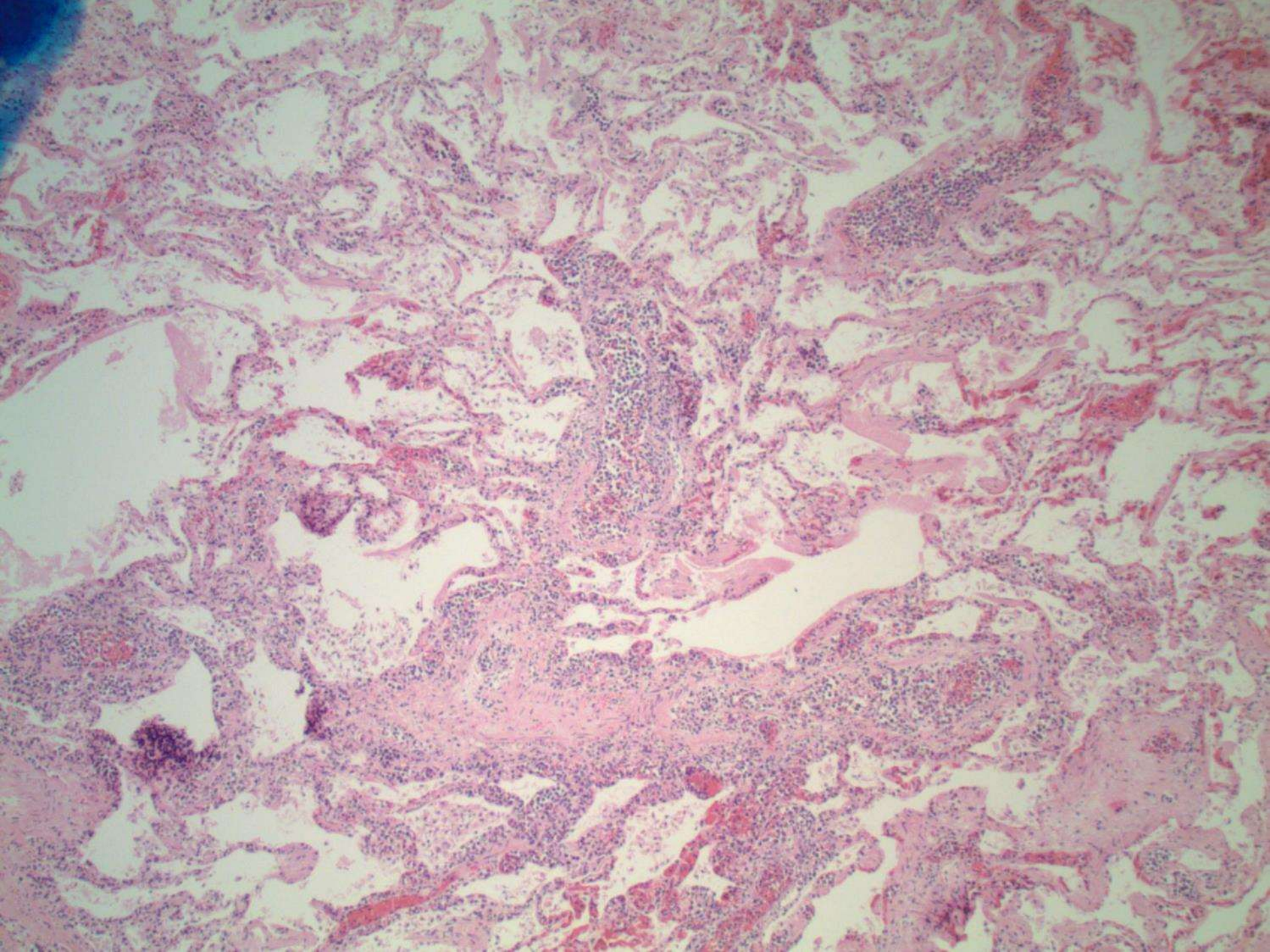
- Gupta S et al. High grade neuroendocrine carcinoma of the urinary bladder treated by radical cystectomy: a series of small cell, mixed neuroendocrine and large cell neuroendocrine carcinoma. Pathology. 2015 Oct;47(6):533-42
- Wang G et. al. Urinary Large Cell Neuroendocrine Carcinoma: A Clinicopathologic Analysis of 22 Cases. Am J Surg Pathol. 2021 Oct 1;45(10):1399-1408
- Chen JF et al. Expression of novel neuroendocrine marker insulinoma-associated protein 1 (INSM1) in genitourinary high-grade neuroendocrine carcinomas: An immunohistochemical study with specificity analysis and comparison to chromogranin, synaptophysin, and CD56. Pathol Res Pract. 2020 Jun;216(6):152993
- Coelho HM, Pereira BA, Caetano PA. Large cell neuroendocrine carcinoma of the urinary bladder: case report and review. Curr Urol. 2013 Feb;7(3):155-9. doi: 10.1159/000356270. Epub 2014 Feb 10. PMID: 24917779; PMCID: PMC4024968.

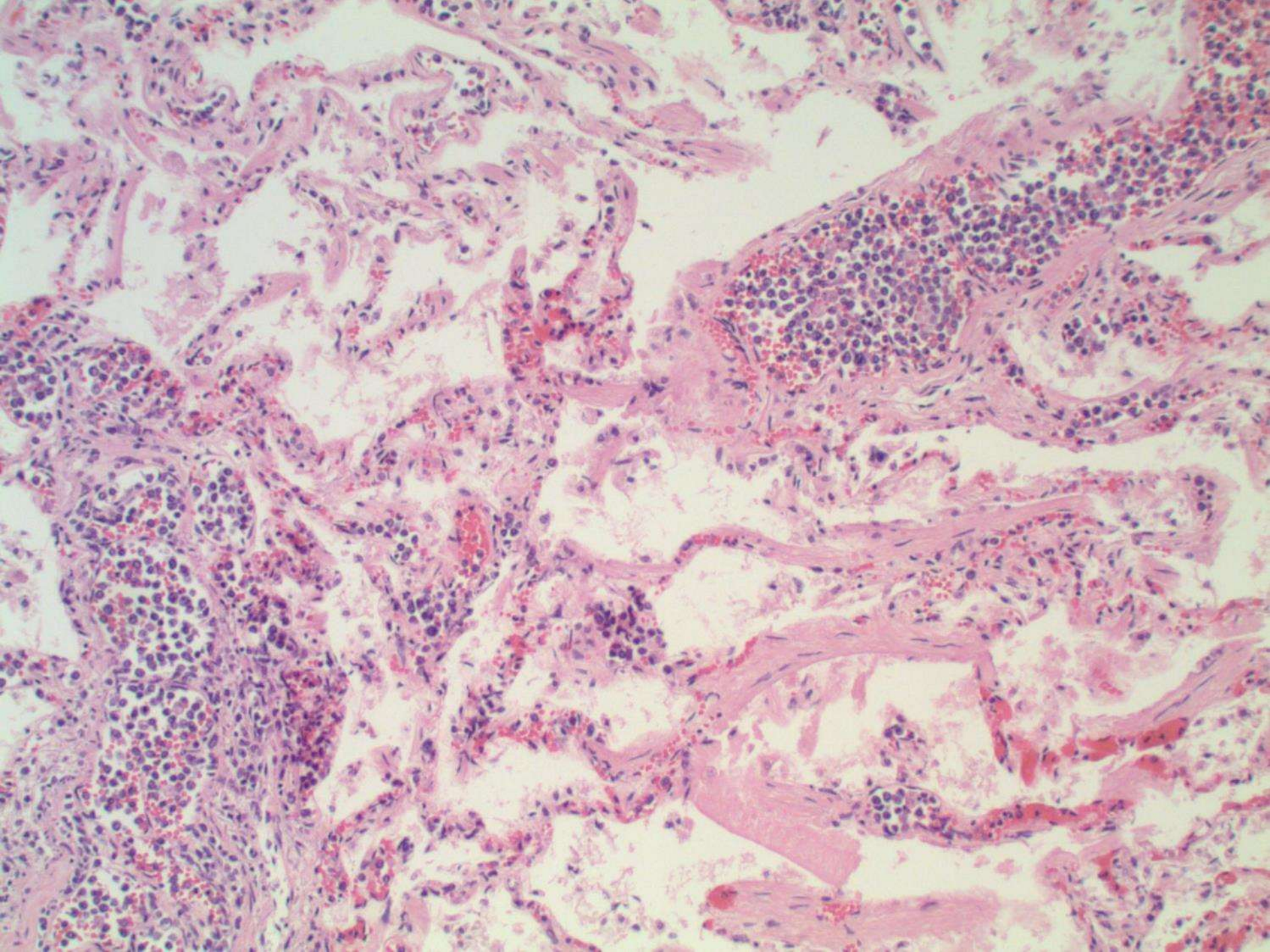
21-1004

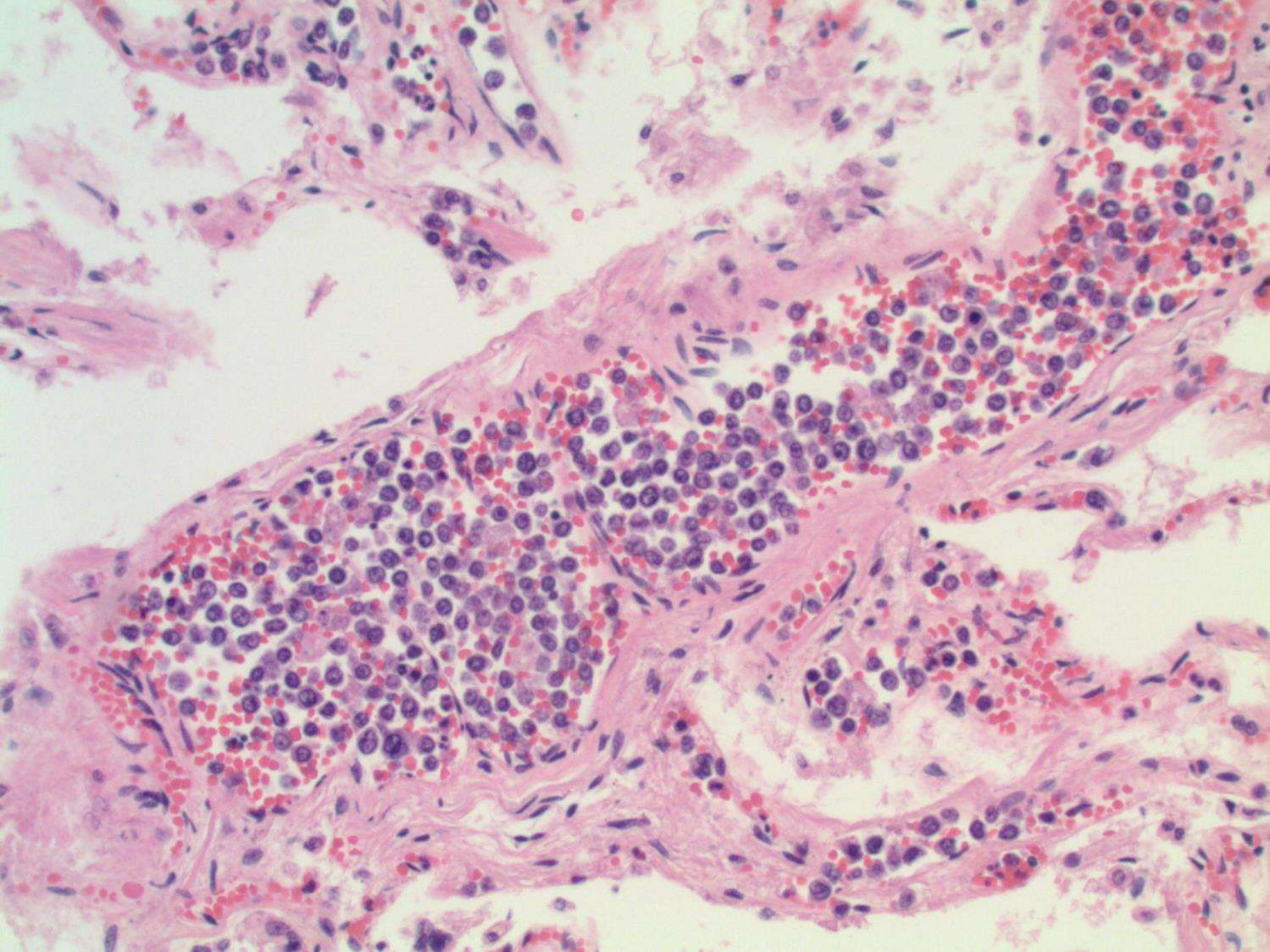
Keith Duncan; Mills-Peninsula

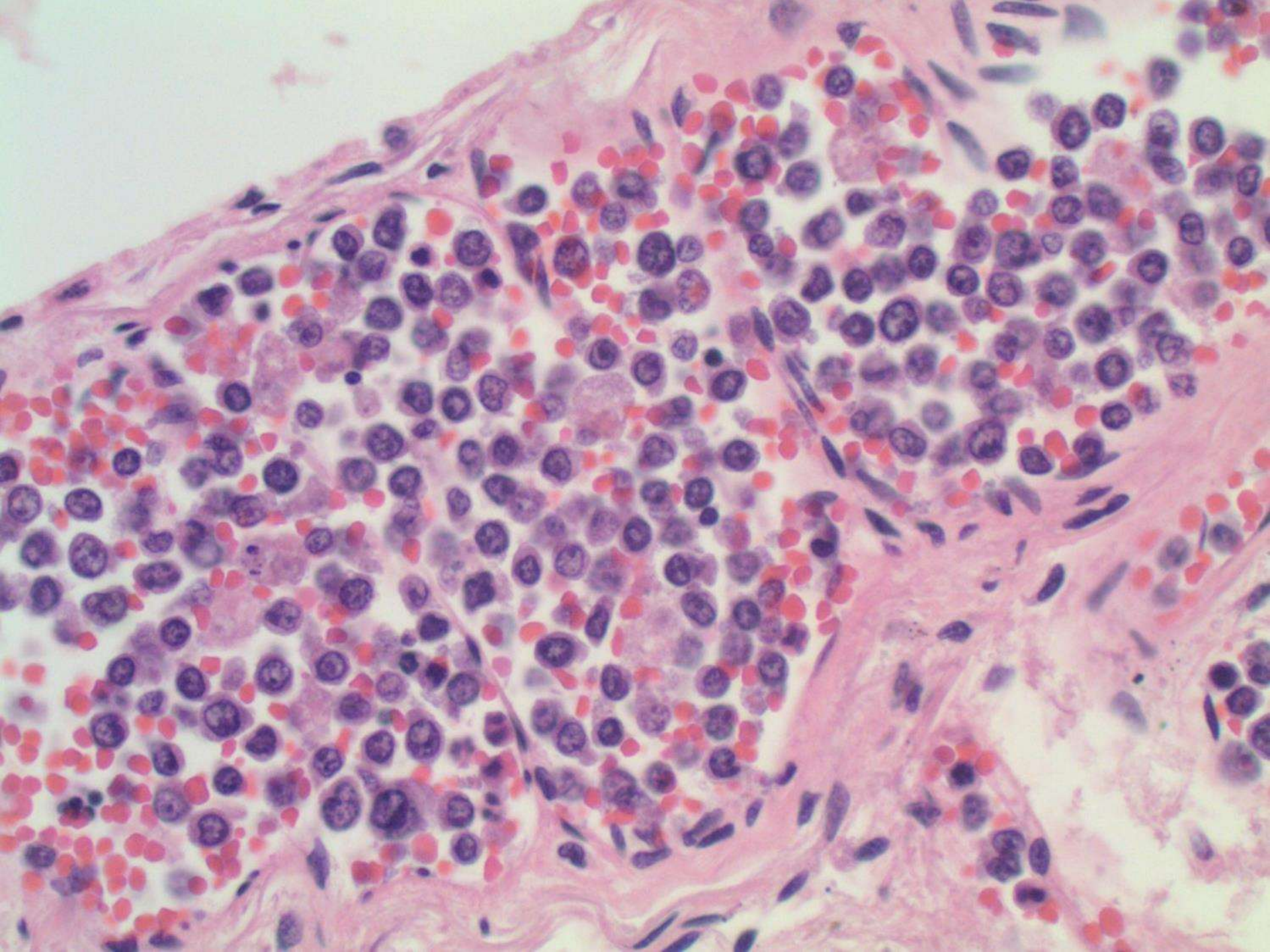
69-year-old F presenting with SOB, fatigue, and chills for 1 month. Shock and sepsis occurred with multi-organ failure. At autopsy, lungs were congested (700g, 780g), with section shown.

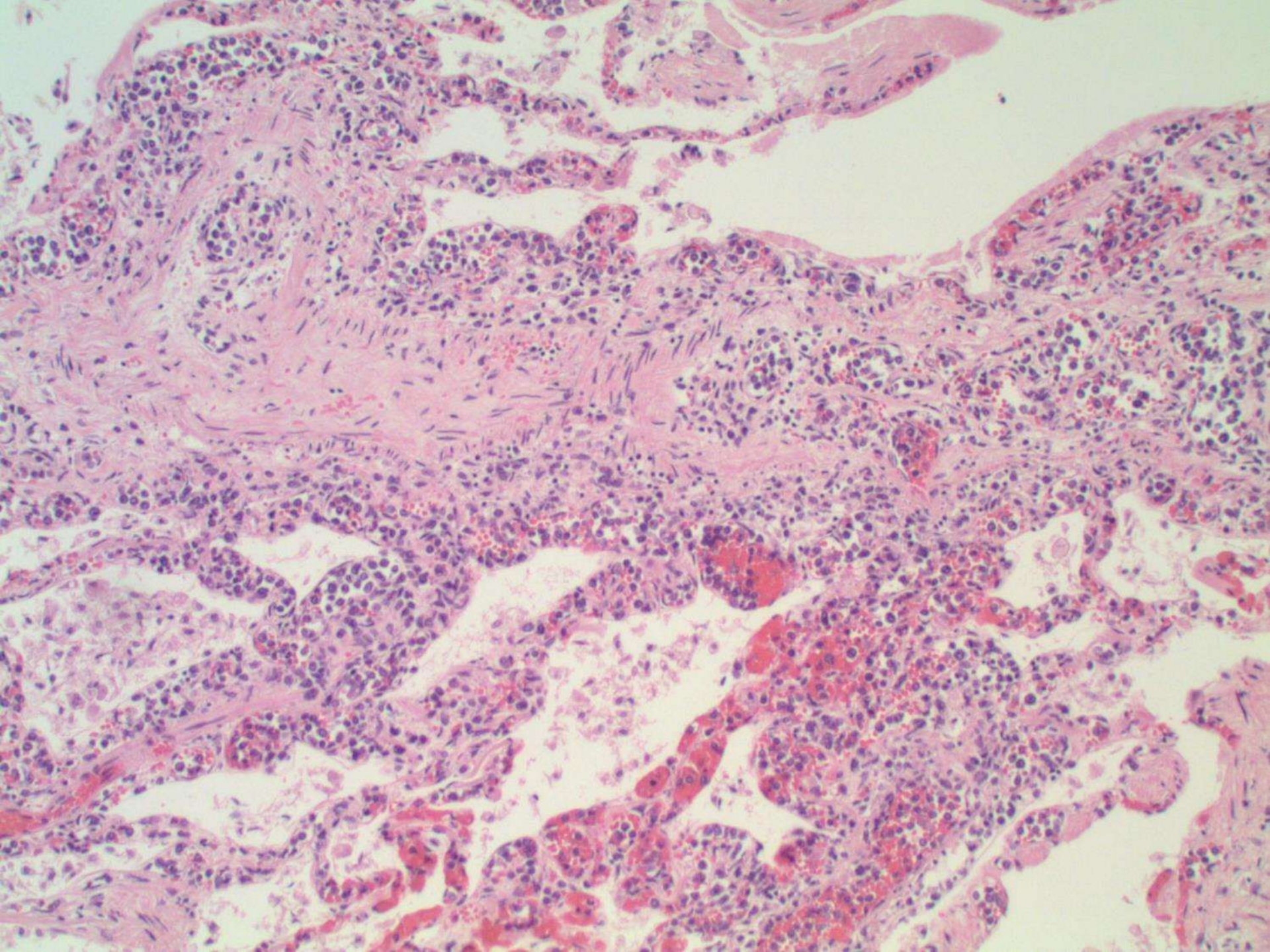


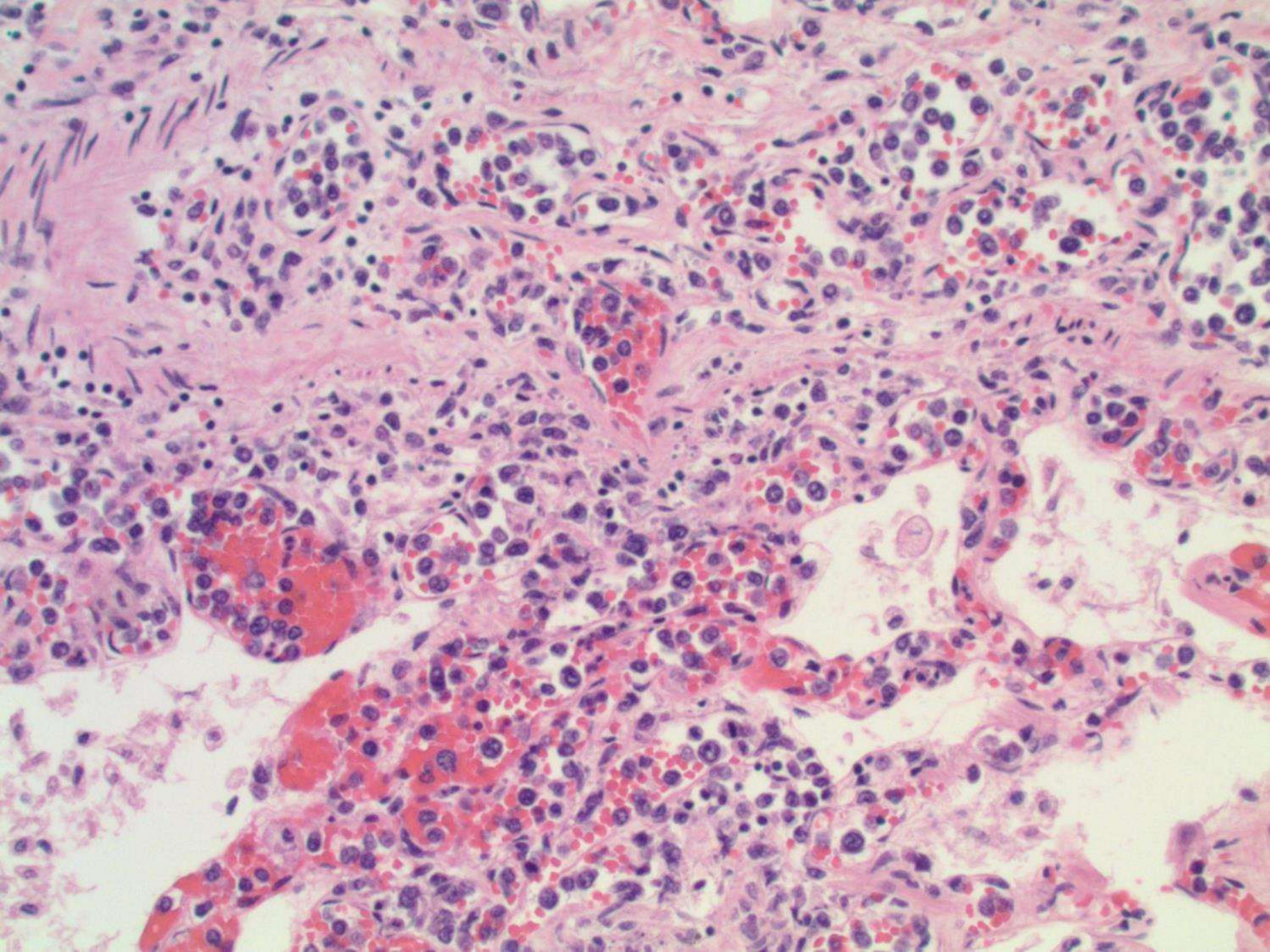


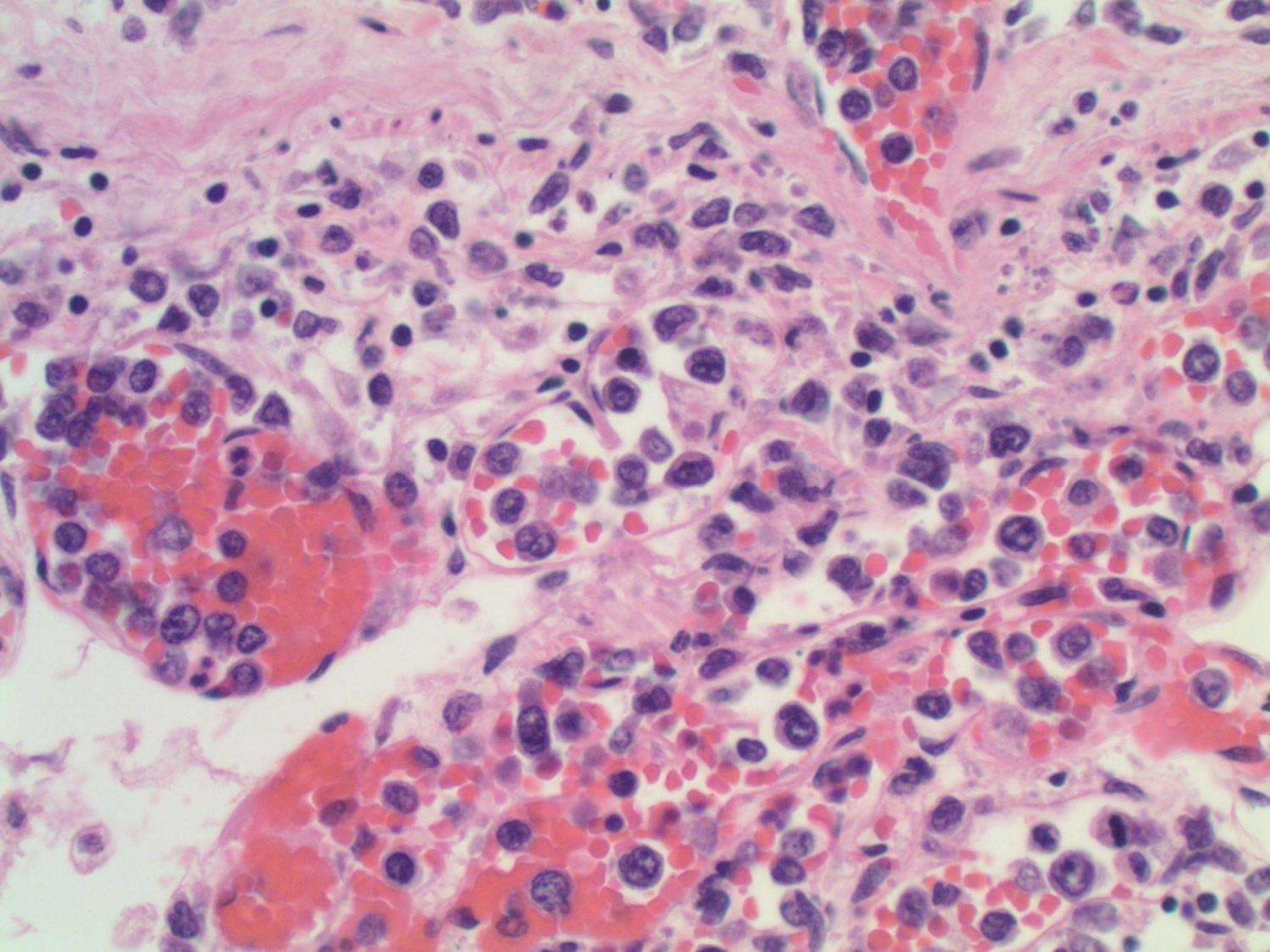


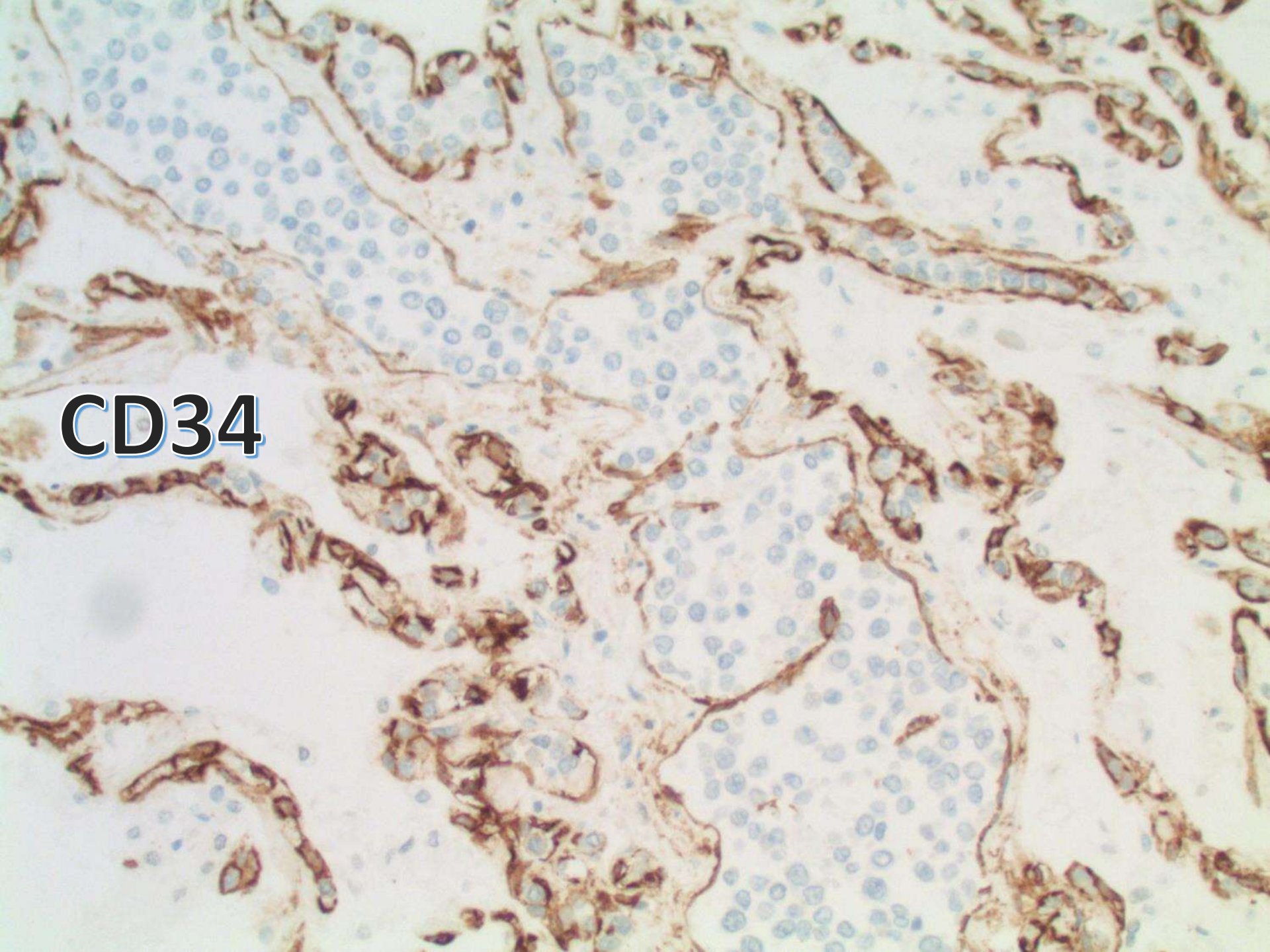


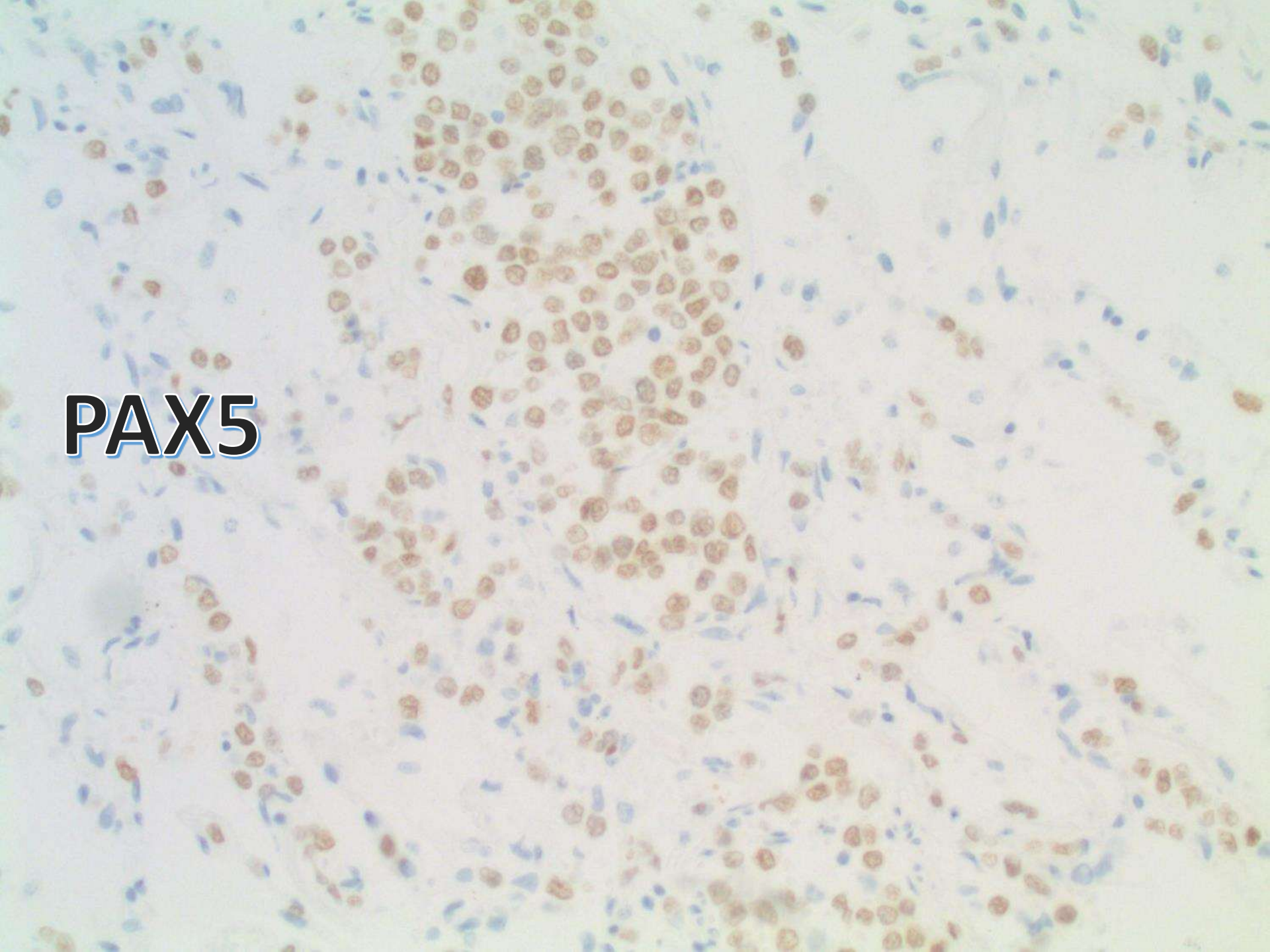









CD34


PAX5

Intravascular large B cell lymphoma

- Rare
- Median age 71 years, often fatal
- Complex non-specific signs and symptoms, including FUO, skin rash, mental status changes, rapidly progressive dementia
- Frequent delay in diagnosis =poor prognosis
- Symptoms are related to the main organ involved
- Often diagnosed at autopsy with involvement of multiple organs
- Cases limited to the skin, following extensive staging workup, are called cutaneous variants and show a better prognosis

Intravascular large B cell lymphoma

Microscopic description
•Large centroblast-like lymphoid cells with prominent nucleoli within small vessel lumina (often capillaries) except in lymph nodes
•Frequent mitotic figures; often fibrin thrombi

Positive stains
•Similar to diffuse large B cell lymphoma (positive for **CD19**, **CD20**, **CD22**, **CD79a**) Usually **BCL2** positive
•**CD10** (13% cases) and **CD5** (38% cases)
•CD10 negative cases are **IRF4 / MUM1** positive

Negative stains
•**CD29** and **CD54** (adhesion molecules, causing the intravascular growth pattern, **Hum Pathol 2000;31:220**)
•**EBV**

Intravascular large B-cell lymphoma: a chameleon with multiple faces and many masks.
Ponzoni M, Campo E, Nakamura S. Blood. 2018 Oct 11;132(15):1561-1567.

Diagnosis of **intravascular large B cell lymphoma**: novel insights into clinicopathological features from 42 patients at a single institution over 20 years.
Matsue K, Abe Y, Narita K, Kobayashi H, Kitadate A, Takeuchi M, Miura D, Takeuchi K.
Br J Haematol. 2019 Nov;187(3):328-336.

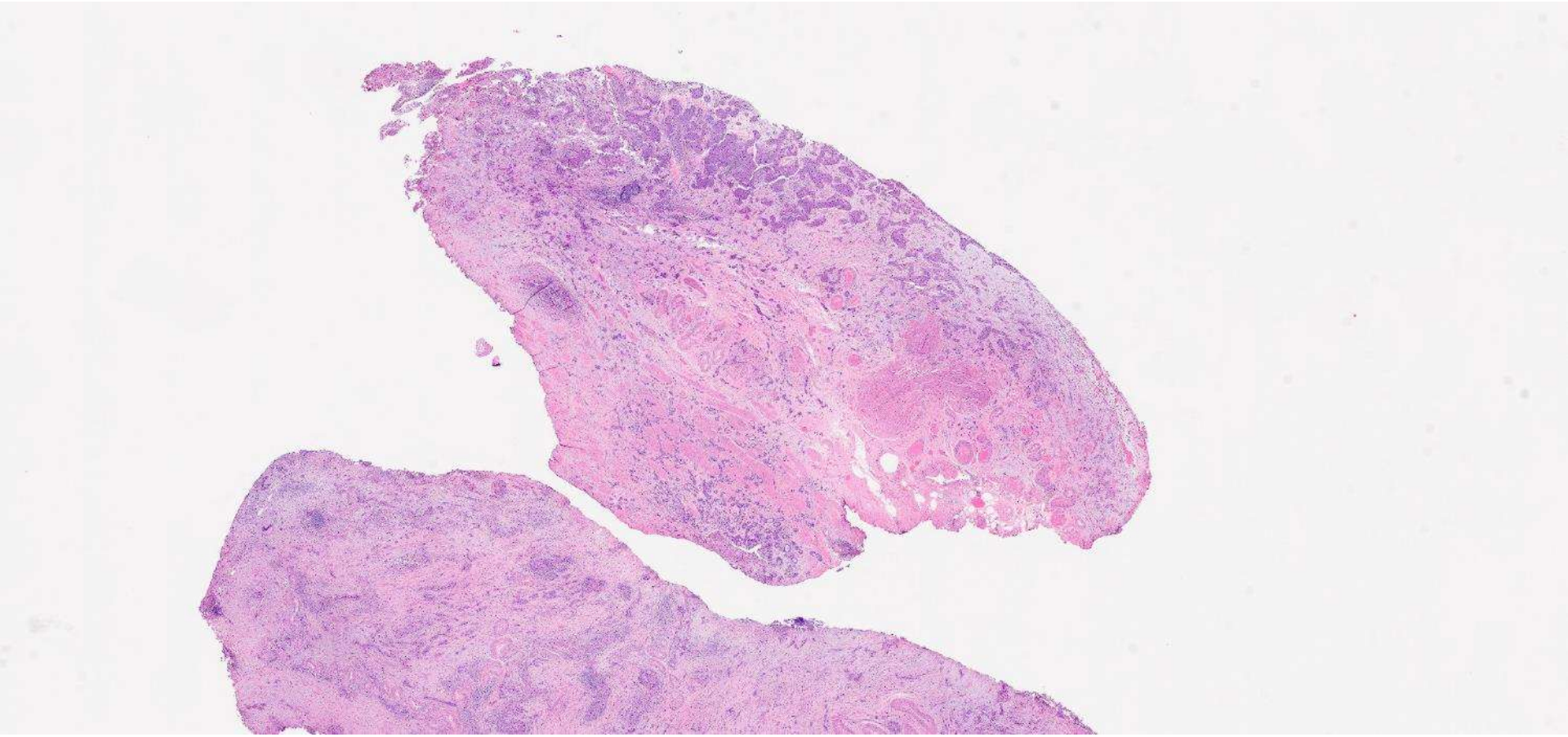
The majority of patients were diagnosed via random skin biopsy (70%) followed by bone marrow biopsy alone (20%).

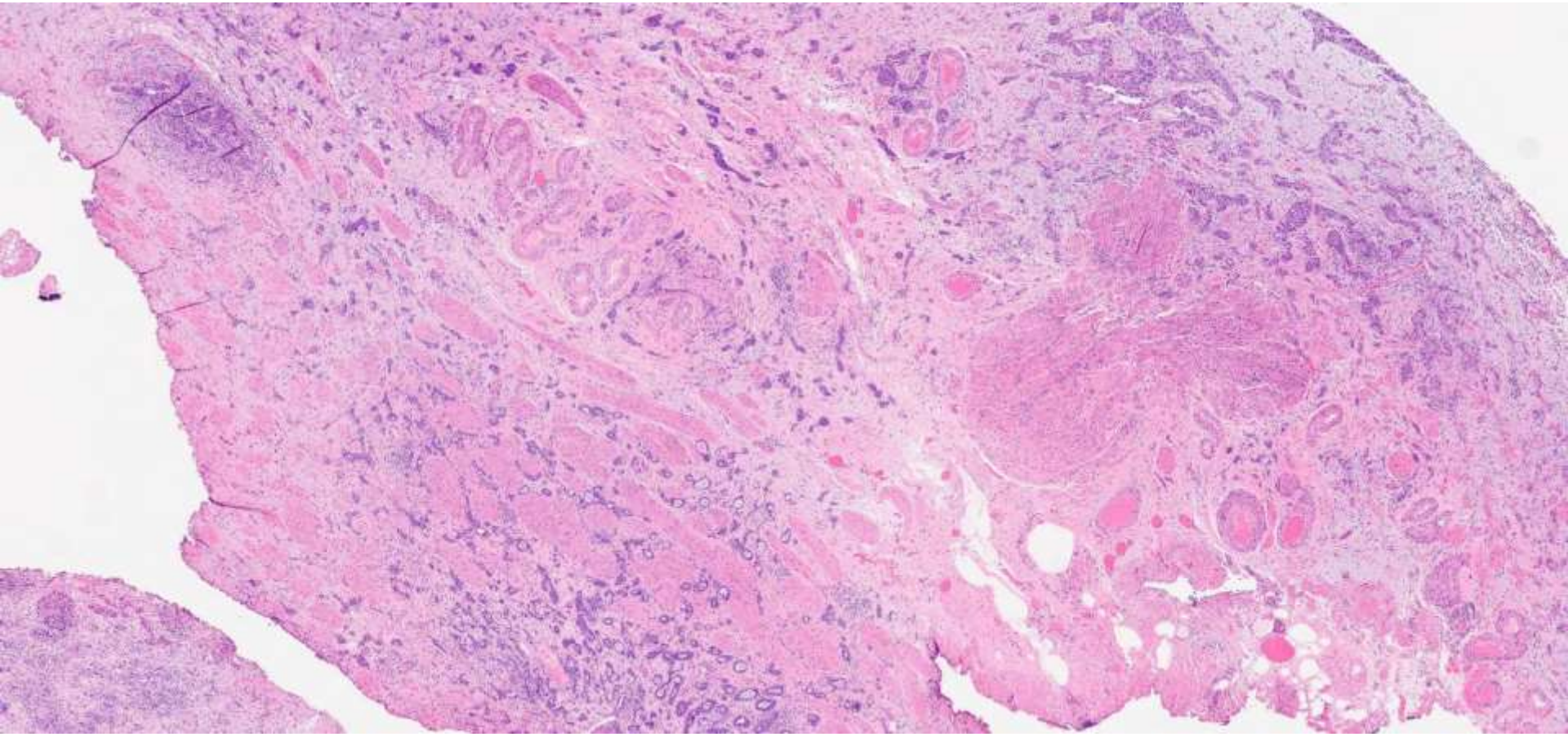
PET SCAN: high incidence of bone marrow (75%), spleen (60%) & adrenal gland (25%) involvement.
60% IVLBCL patients in whom in vivo diagnosis was possible survived > 5 years with combo chemotx.

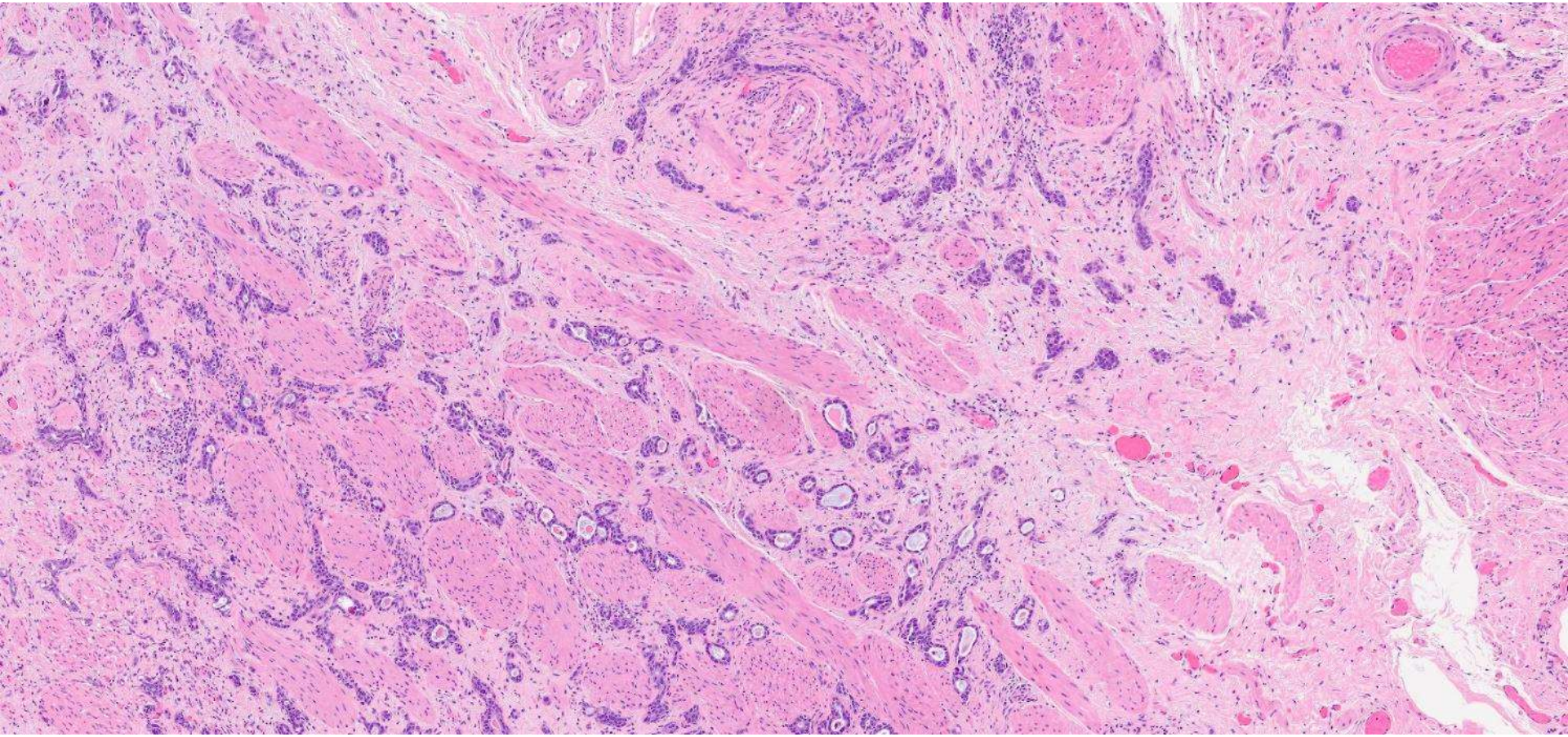
21-1005

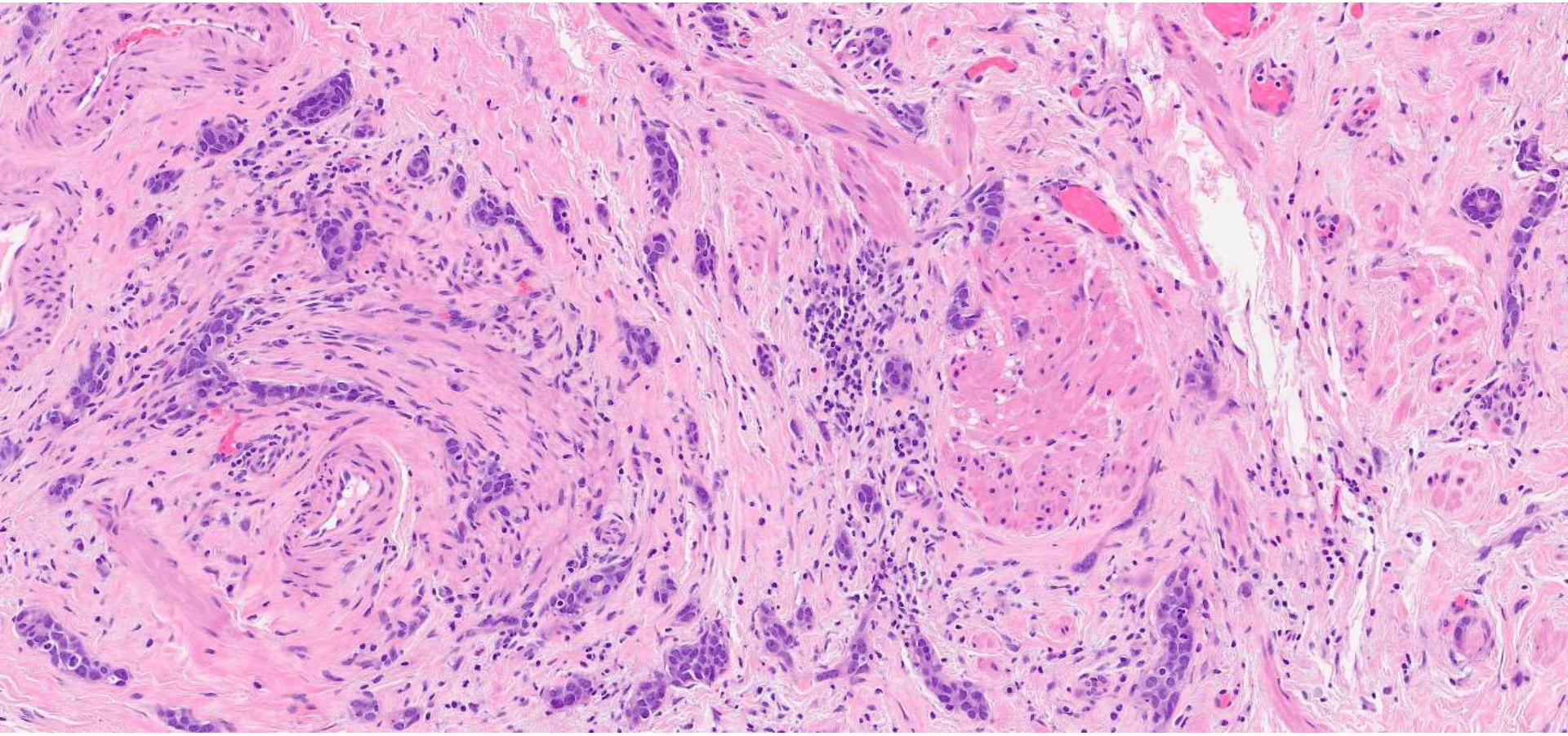
Ankur Sangoi; El Camino Hospital

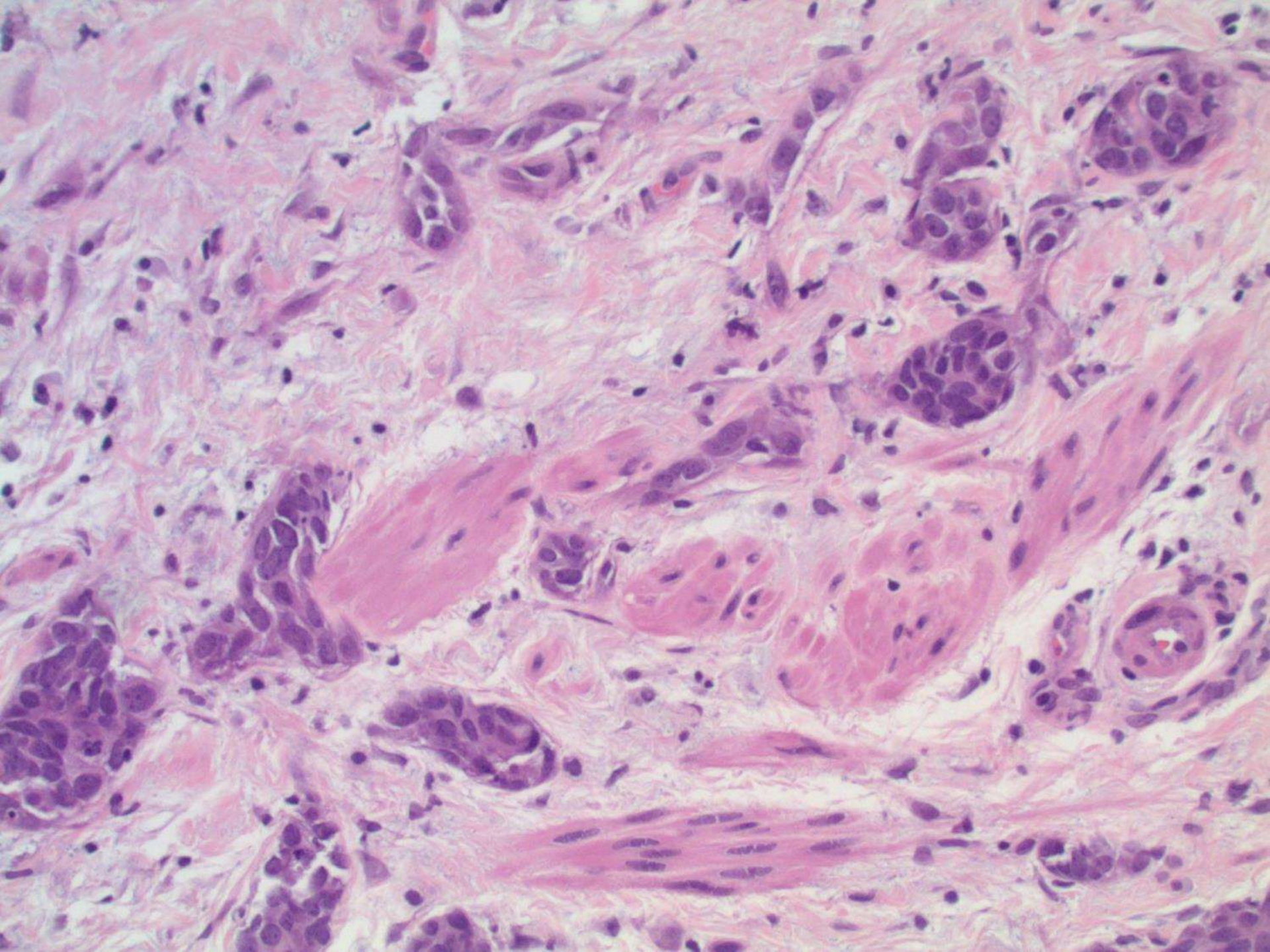
84-year-old F with bladder tumor, TURBT performed.

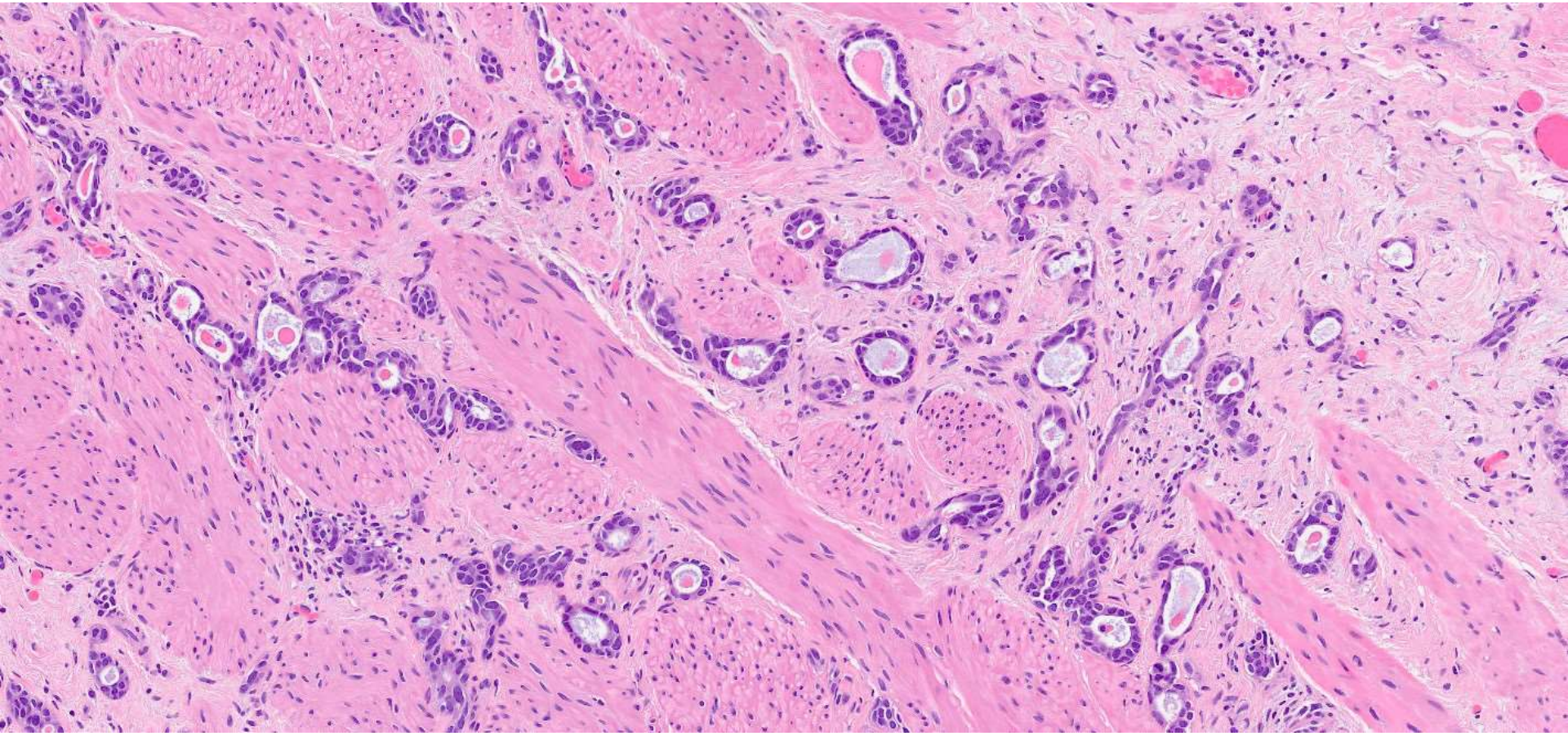


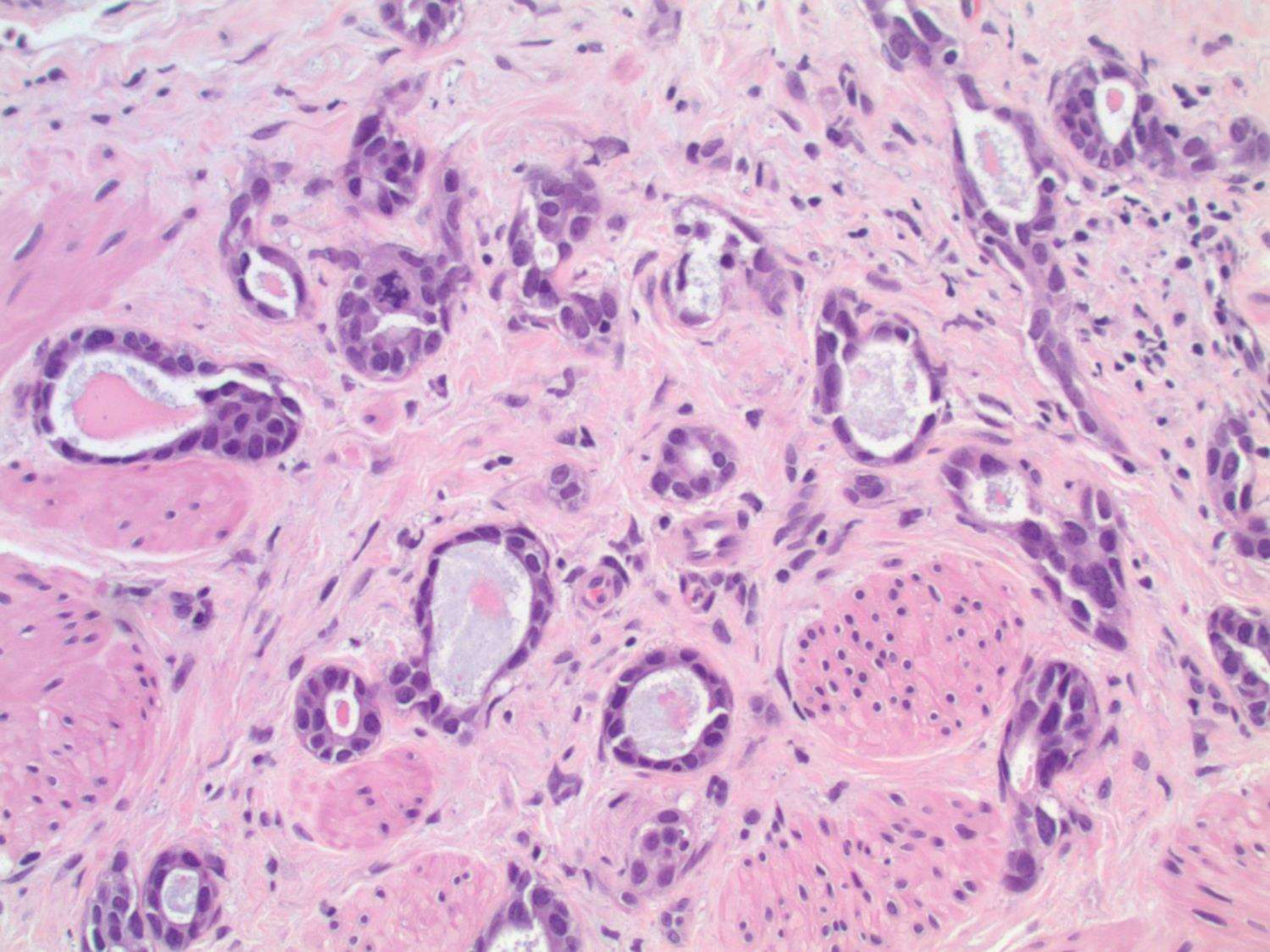










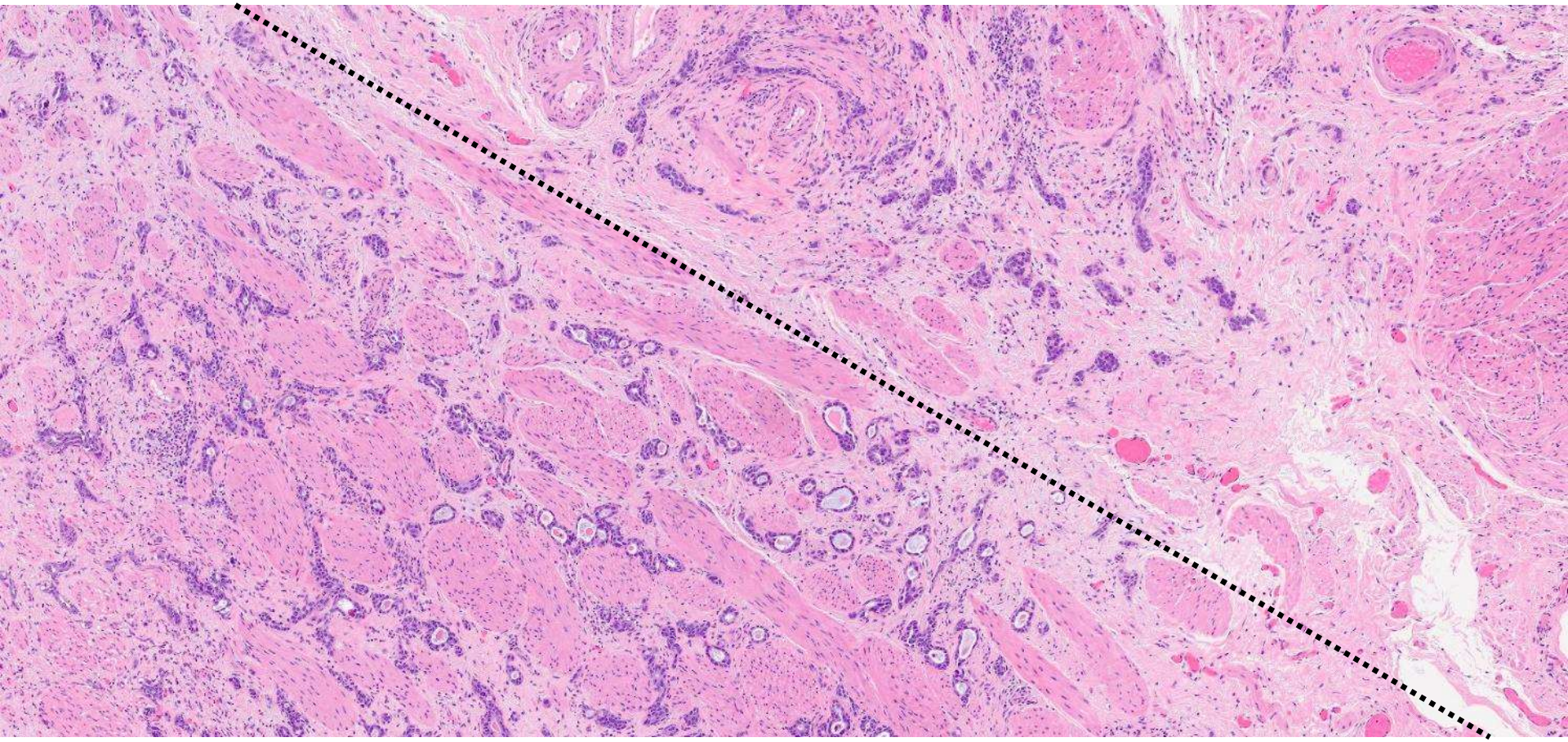


DDx

- Nested +microcystic variants urothelial carcinoma
- Prostatic adenocarcinoma
- Cystitis cystica glandularis
- Nephrogenic adenoma

Dx: nested+microcystic variants invasive urothelial carcinoma

- **Both can show deceptively bland cytology, yet be deeply invasive**
  - More atypia at deeper aspect
  - Variant in size/shape of epithelial formations, haphazard growth
- **Patterns may occur together**
- **Show typical IHC of urothelial ca**



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Original contribution

PAX8 positivity in nested variant of urothelial carcinoma: a potential diagnostic pitfall☆

Teklu Legesse MD[a], Andres Matoso MD[a], Jonathan I. Epstein MD[a,b,*]

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Received 12 August 2019; revised 25 September 2019; accepted 28 September 2019

Keywords:
PAX8;
Nested variant of urothelial carcinoma;
Nephrogenic adenoma;
Bladder;
Immunohistochemistry

Summary Nested variant of urothelial carcinoma is a rare variant of urothelial carcinoma morphologically characterized by infiltrative nests of cytologically bland urothelial cells. It is widely recognized that nested variant of urothelial carcinoma can closely mimic von Brunn nests. However, nested variant of urothelial carcinoma with tubule formation can also resemble nephrogenic adenoma, where immunohistochemical positivity for PAX8 has been used to establish the diagnosis of nephrogenic adenoma. Following anecdotal examples of PAX8 positive nested variant of urothelial carcinoma, we formally evaluated 23 cases of nested variant of urothelial carcinoma from 2011 to 2018. Cases were collected from our institution and evaluated for their architectural pattern and PAX8 expression. Except for 1 case from the renal pelvis, cases were located in the bladder. The majority (14/23 [61%]) showed solid nests with at least focal tubular differentiation. PAX8 immunoreactivity was strong (3+) in 7 (30%), moderate (2+) in 6 (26%), and negative in 10 (44%) cases. Four (57%) of the cases with strong expression and 3 (50%) of those with moderate staining showed diffuse immunoreactivity. Moderate-strong immunoreactivity was seen in 4/6 (66.7%) cases with solid nests, 8/14 (57.1%) with solid nests and tubules, and 1/3 (33.3%) with large nests. In conclusion, PAX8 can be positive in a significant proportion of nested variant of urothelial carcinoma cases, and recognition of this finding is important to avoid misdiagnosis of nested variant of urothelial carcinoma as nephrogenic adenoma based on PAX8 expression, particularly in cases with tubular differentiation and limited sampling.

Distinguishing Nested Variants of Urothelial Carcinoma From Benign Mimickers by *TERT* Promoter Mutation

Minghao Zhong, MD, PhD, Wei Tian, MD,† Jian Zhuge, PhD,* Xiaoyong Zheng, MD, PhD,* Tiangui Huang, MD, PhD,* Dongming Cai, MD, PhD,‡ David Zhang, MD, PhD,§ Ximing J. Yang, MD, PhD,‖ Pedram Argani, MD,† John T. Fallon, MD, PhD,* and Jonathan I. Epstein, MD†*

Abstract: Nested variant of urothelial carcinoma (NVUC) is an uncommon variant with minimally atypical cytology, which may overlap with benign urothelial lesions such as von Brunn nests, cystitis cystica, cystitis glandularis, and nephrogenic adenoma. Because of the tumor's deceptively bland appearance, these cancers can potentially be misdiagnosed as benign lesions, leading in some cases to a significant delay in correct diagnosis and appropriate treatment. Prior studies suggest that Ki67 and p53 are useful markers in distinguishing NVUC from benign lesions. However, the overlap in the rates of immunoreactivity has prevented pathologists from using these markers as reliable adjunct markers in differentiating NVUC from mimickers. In addition, large nested variant urothelial carcinoma (LNVUC), a relatively new entity, shares features of both the NVUC and papillary urothelial carcinomas with an inverted growth pattern. They also mimic benign lesions, such as proliferation of von Brunn nests and inverted urothelial papilloma. With the recent demonstration of a strong association of *TERT* promoter mutations and urothelial carcinoma, we hypothesized that *TERT* promoter mutations would be a useful marker to distinguish NVUC and LNVUC from other benign urothelial lesions. We have therefore sequenced the *TERT* promoter region of 20 cases of NVUC, 10 cases of LNVUC, 5 cases of von Brunn nests, 3 cases of cystitis cystica, 3 cases of cystitis glandularis, and 3 cases of nephrogenic adenoma. We found that 17 of 20 cases of NVUC and 8 of 10 cases of LNVUC had *TERT* promoter mutation: C228T; no mutation was found in any of the benign mimickers (0/14). This result strongly suggests that *TERT* promoter mutation is a useful adjunct biomarker to distinguish NVUC and LNVUC from benign mimickers.

Key Words: nested variants of urothelial carcinoma, *TERT* promoter mutation, benign mimickers

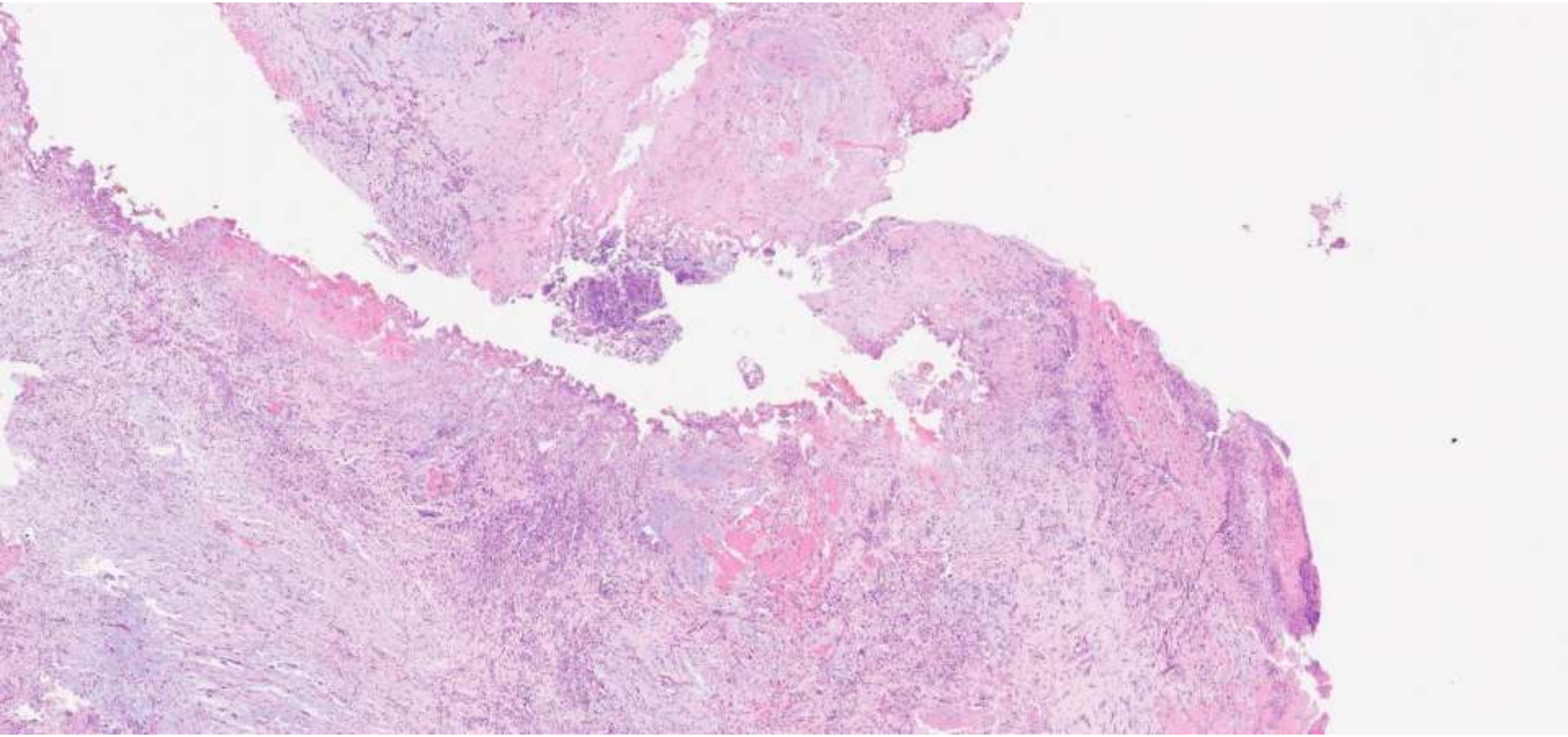
(*Am J Surg Pathol* 2015;39:127–131)

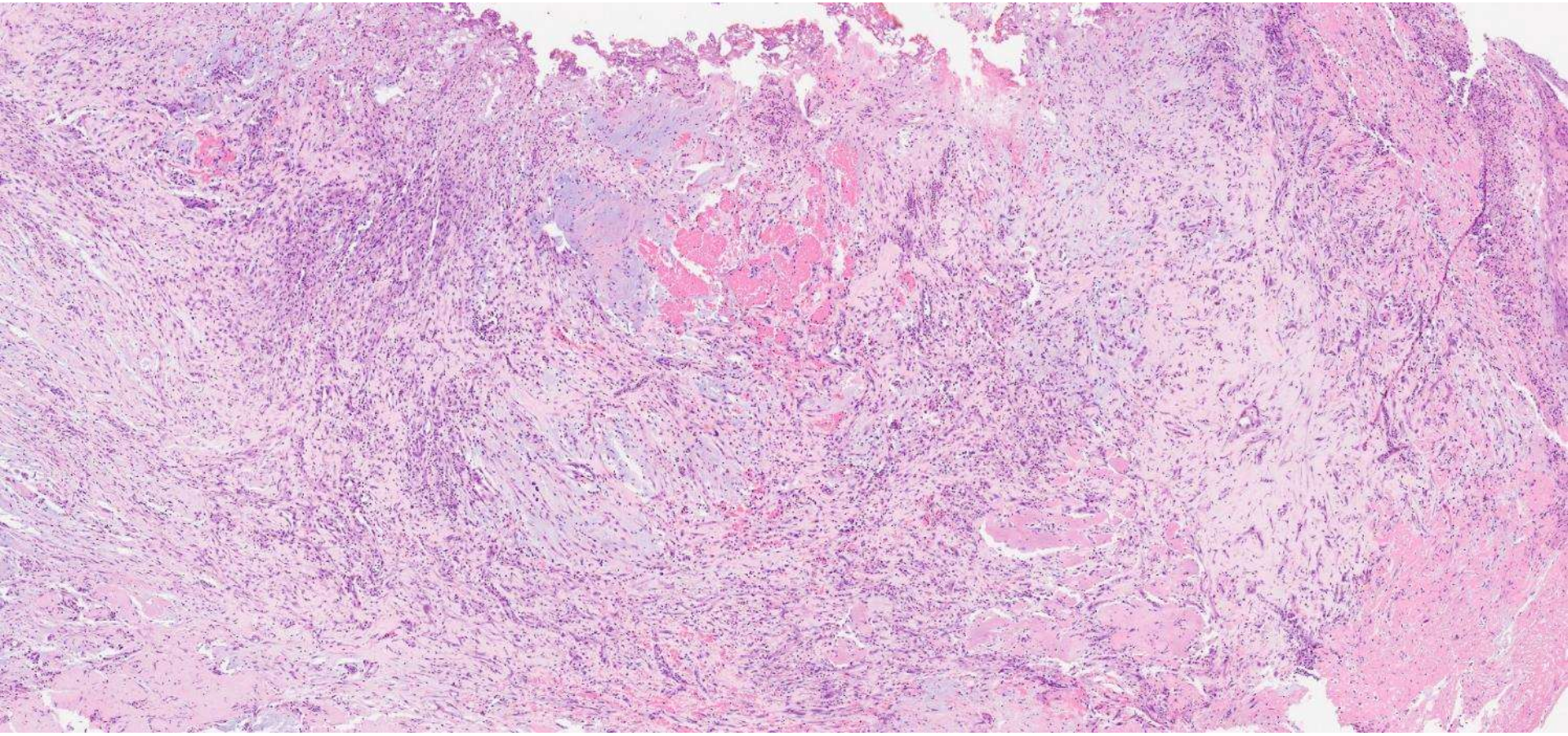
Most invasive urothelial carcinomas (UCs) are high grade with prominent cytologic atypia. Nested variant of urothelial carcinoma (NVUC) is an uncommon morphologic variant that is characterized by an unusual, bland morphology but a clinical behavior similar to that of high-grade conventional UCs.[1] NVUC was interpreted as a benign bladder tumor related to von Brunn nests when it was first reported in 1979.[2] Later, 1 study reported 3 cases of this entity in 1989 and described them as the carcinomas of the urinary bladder with deceptively benign-appearing foci.[3] Murphy and Deana[1] in 1992 coined the term *nested variant of transitional cell carcinoma*, as it resembled proliferation of von Brunn nests. Because of its bland cytology, NVUC may be misinterpreted as benign. A few studies have tried to use immunohistochemical (IHC) markers to distinguish

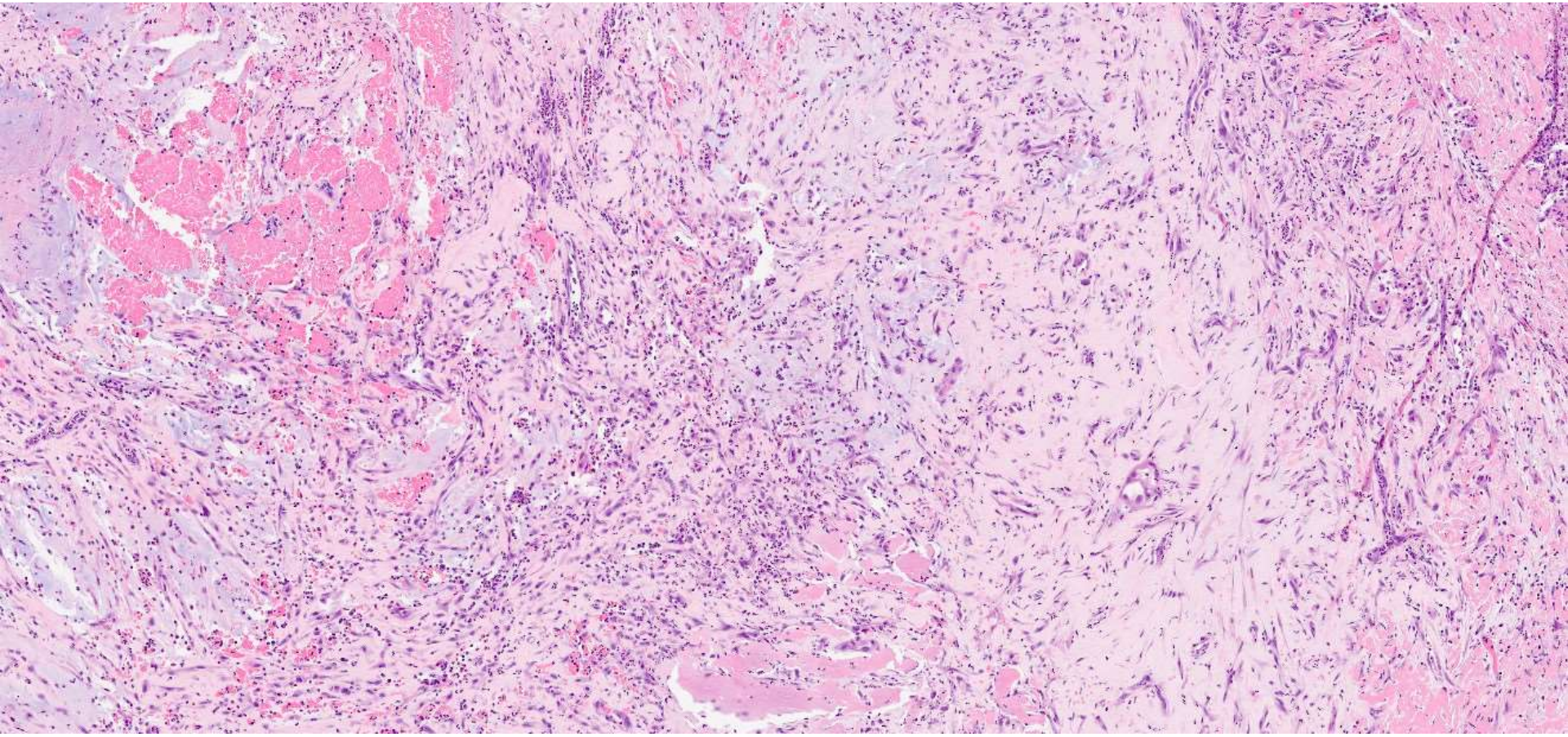
21-1006

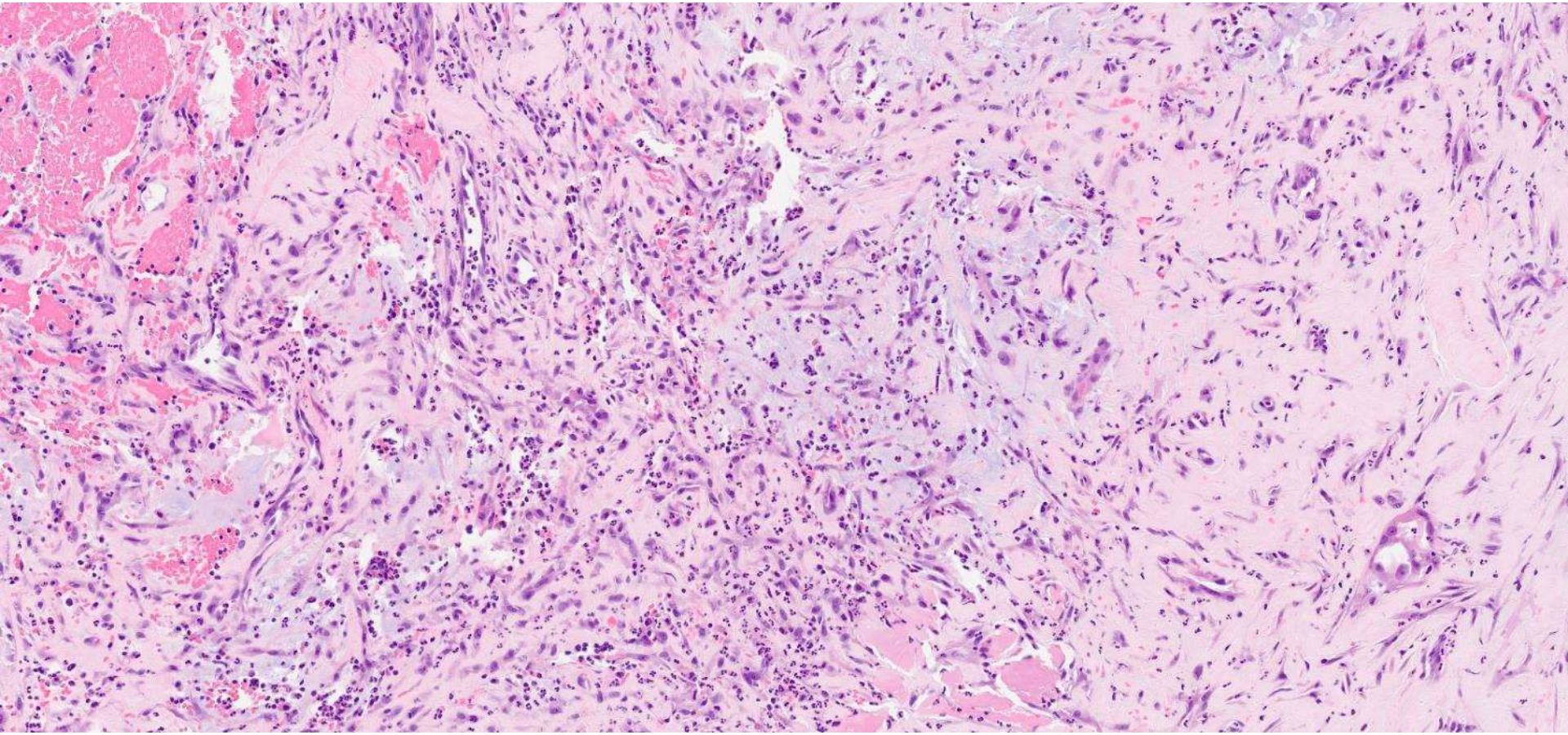
Ankur Sangoi; El Camino Hospital

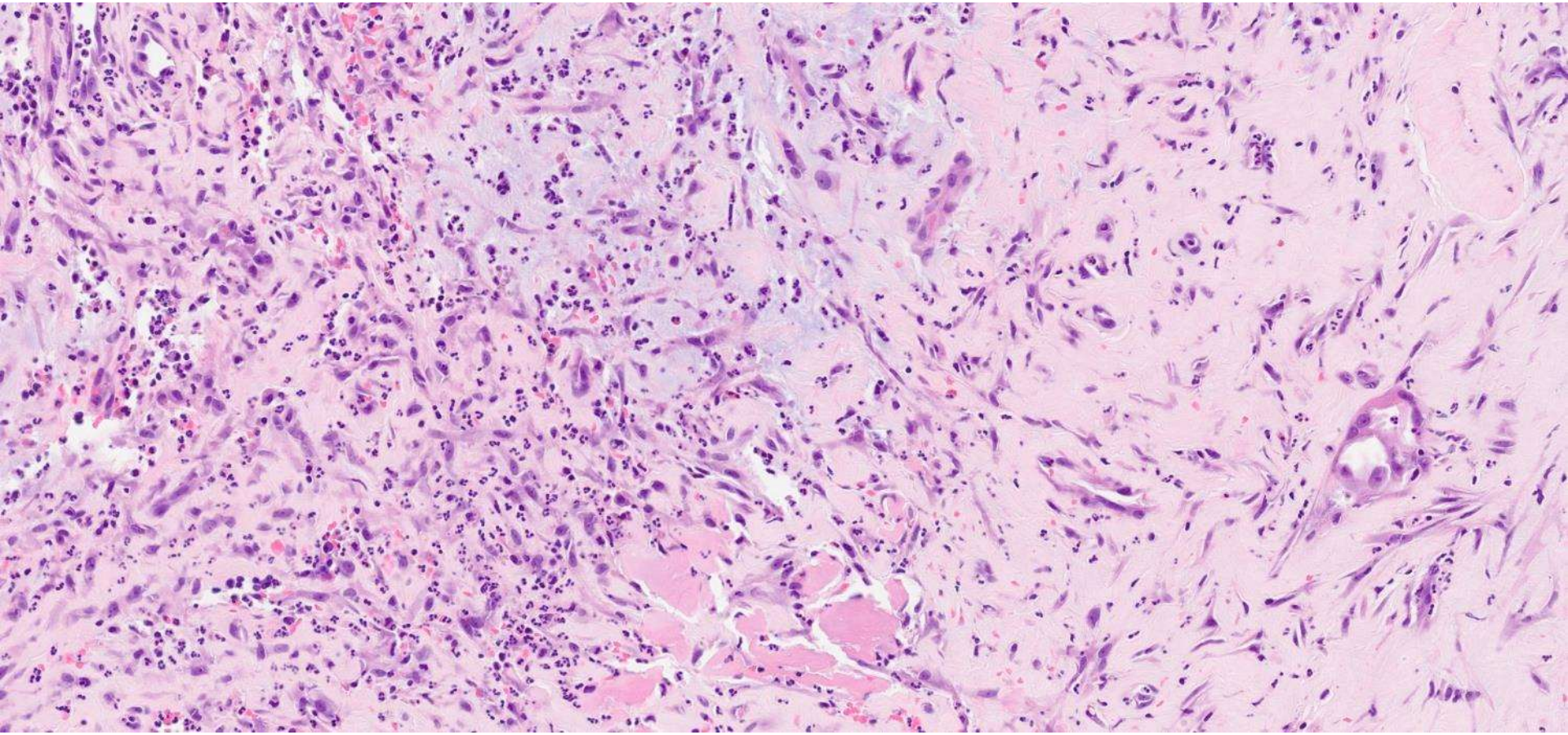
67-year-old M with h/o prostate cancer s/p XRT. TURP performed.

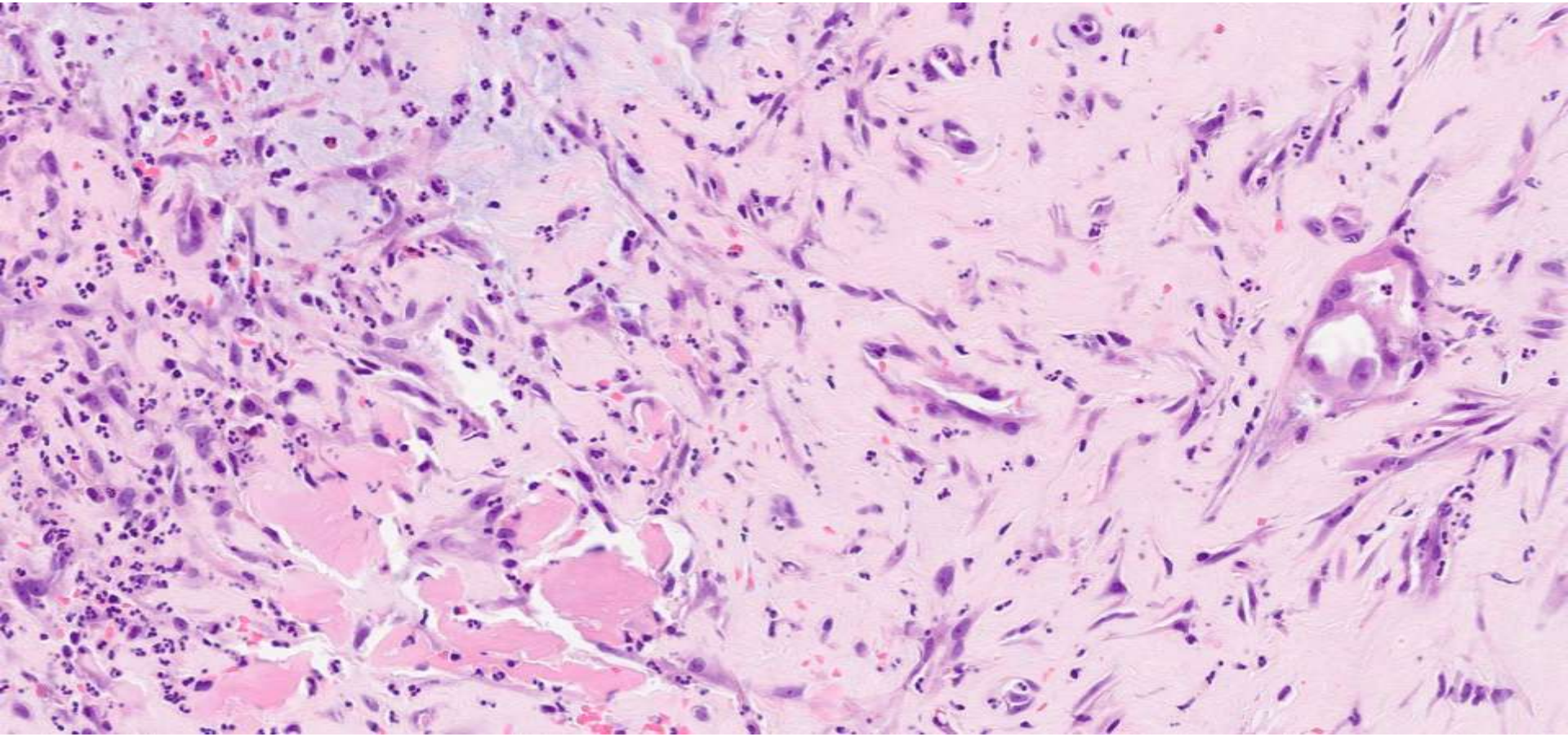


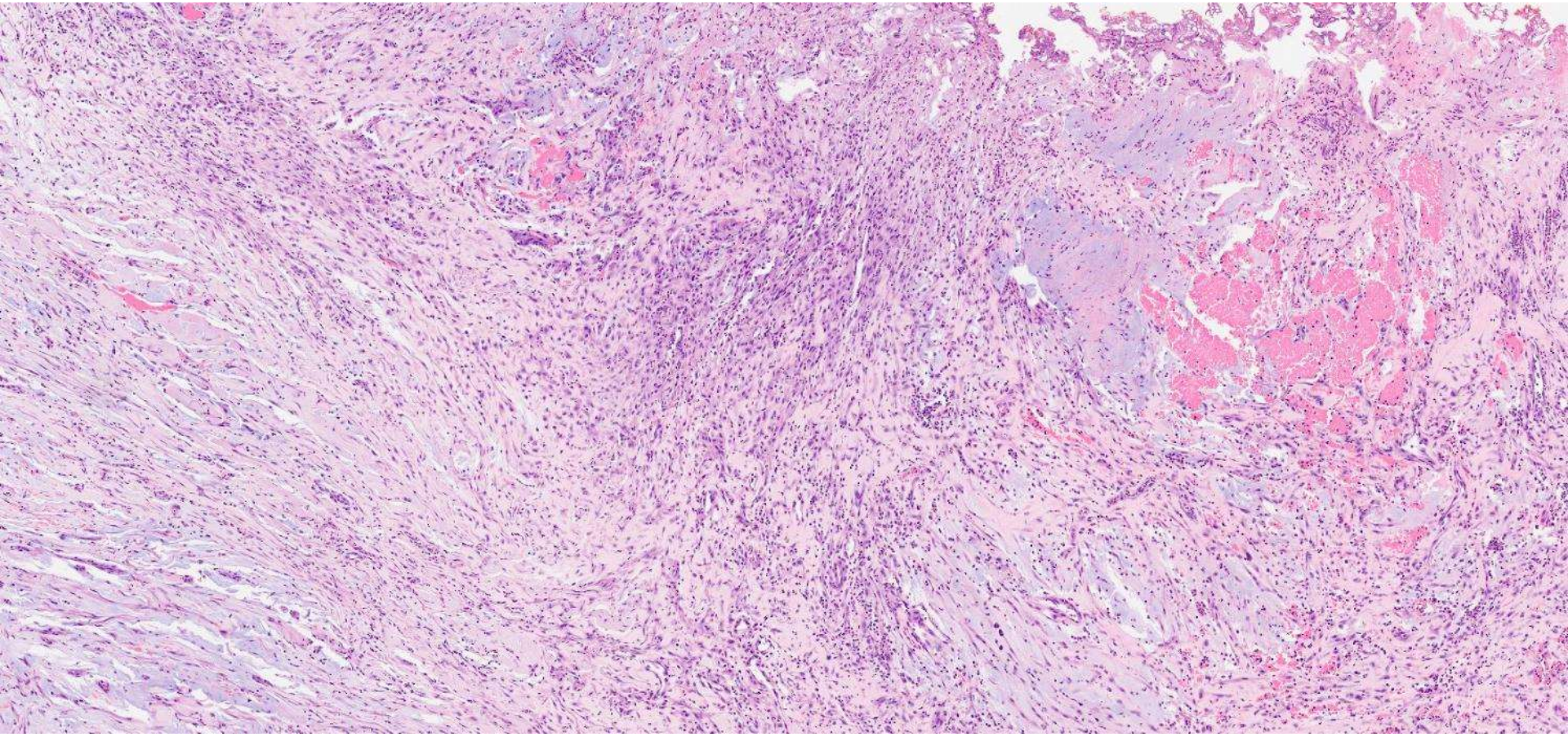


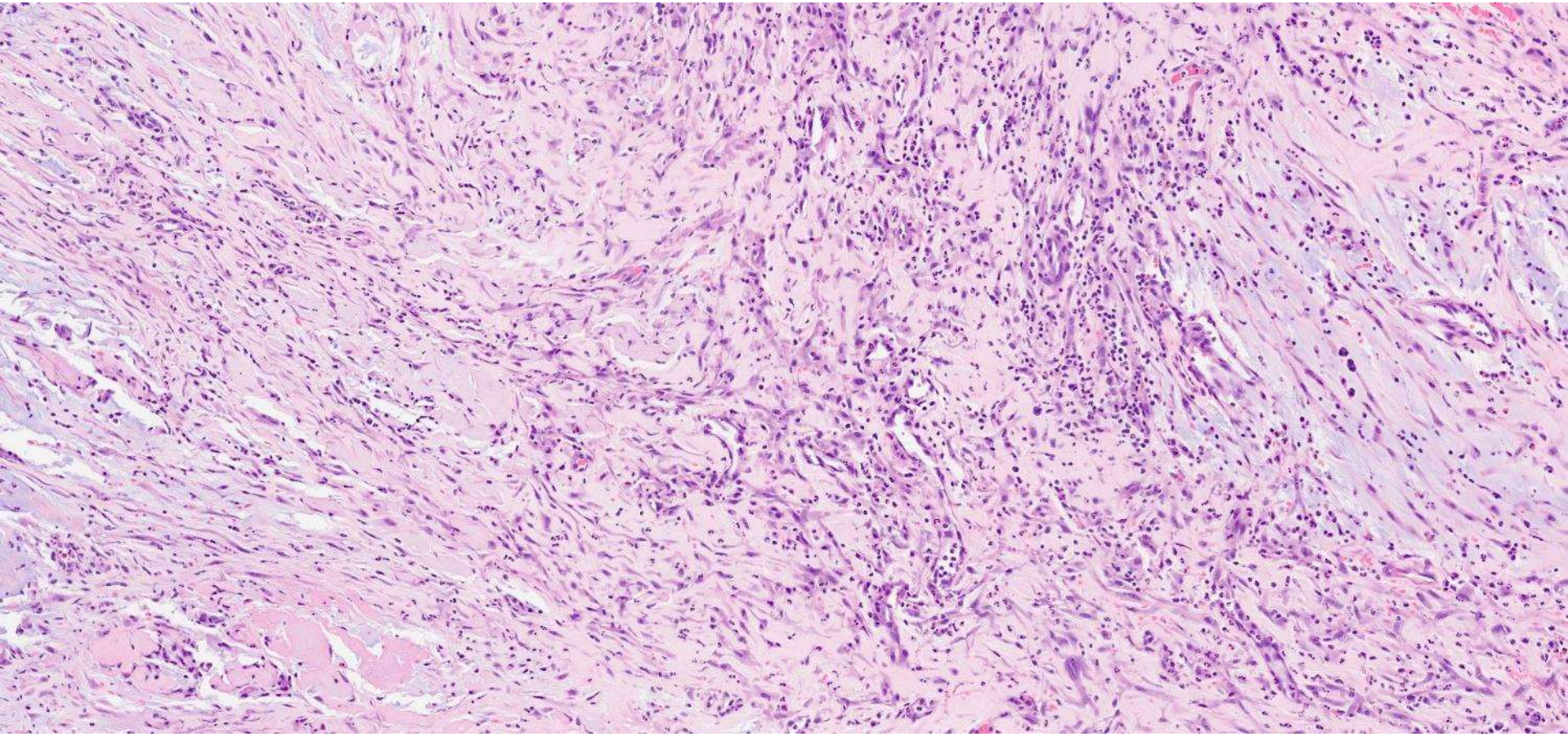


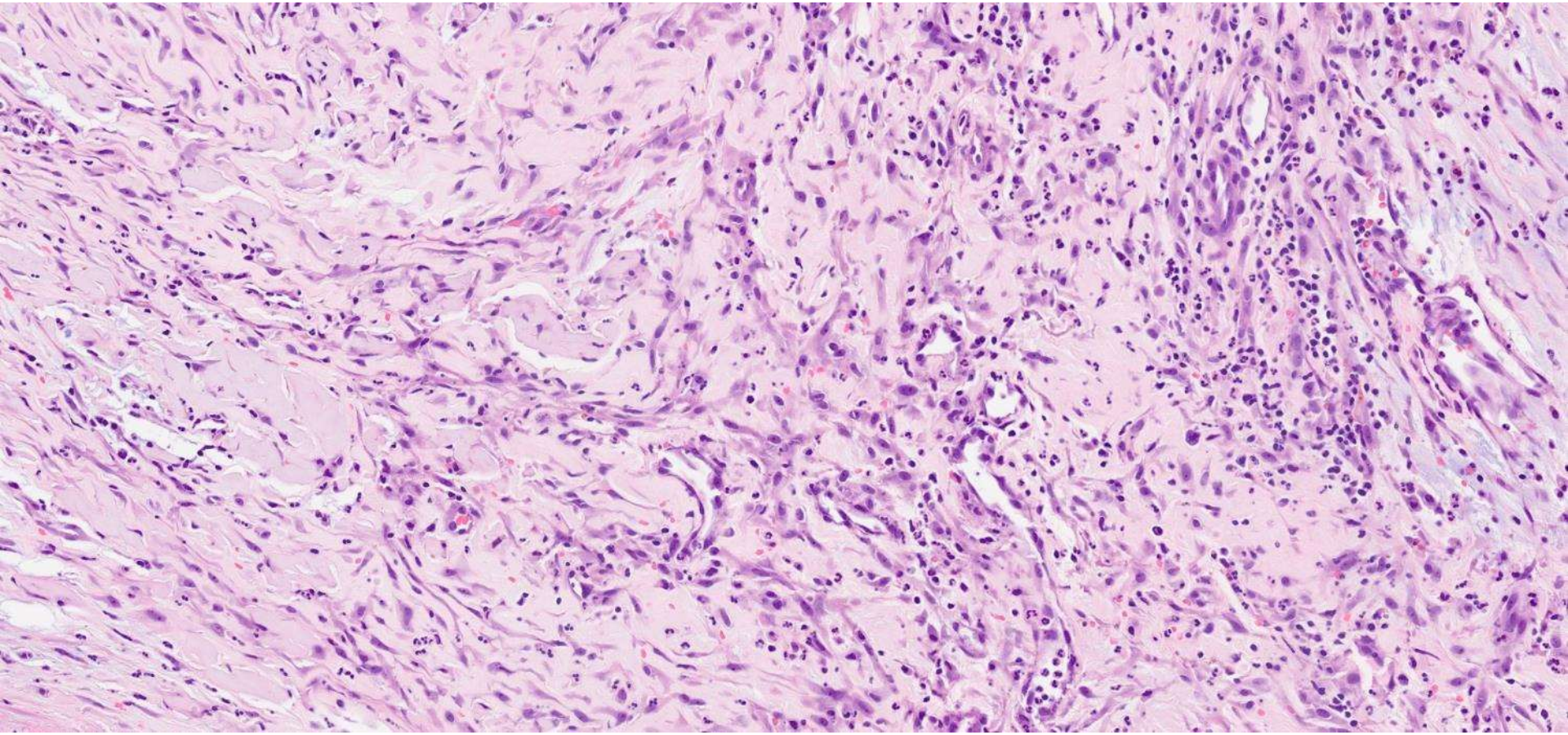


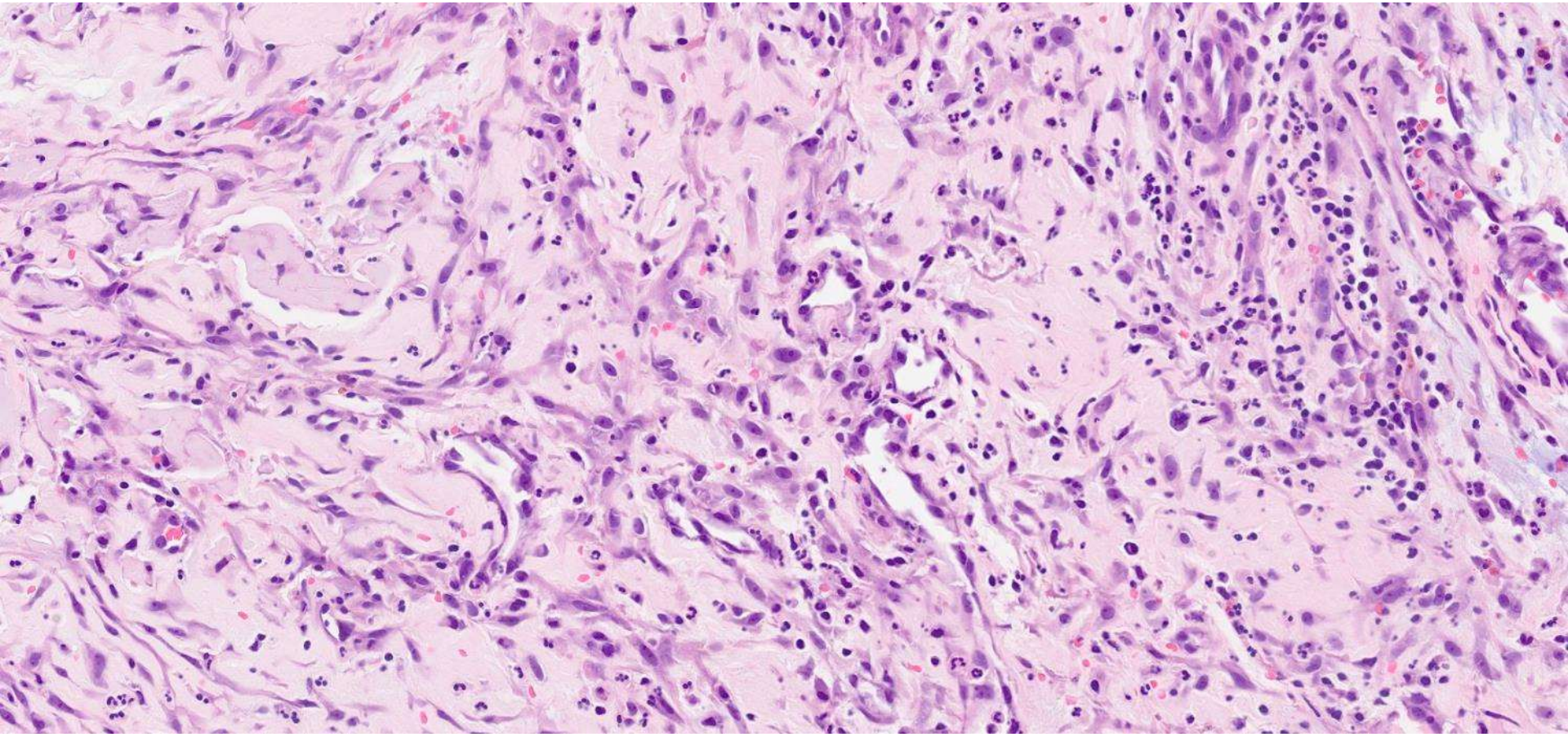


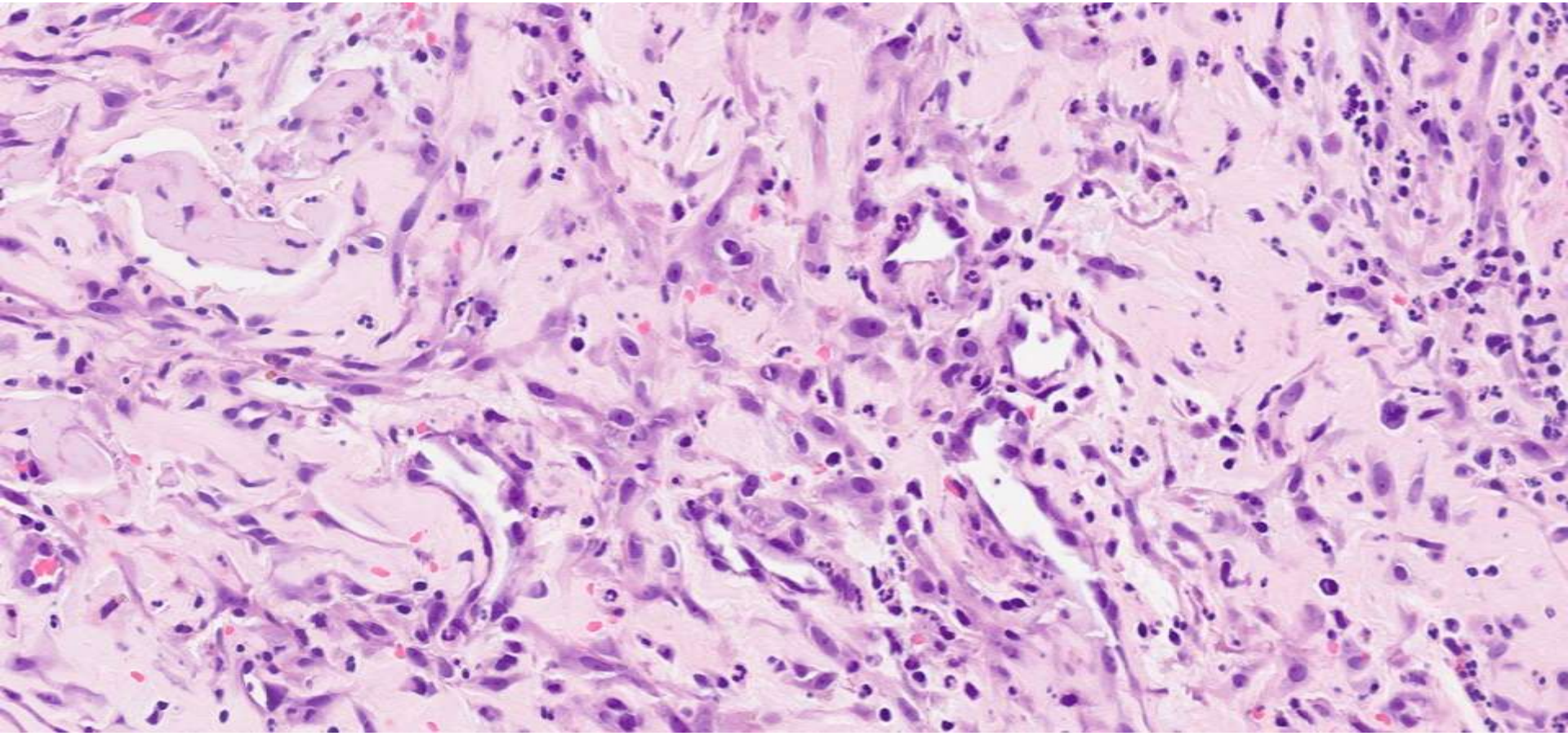


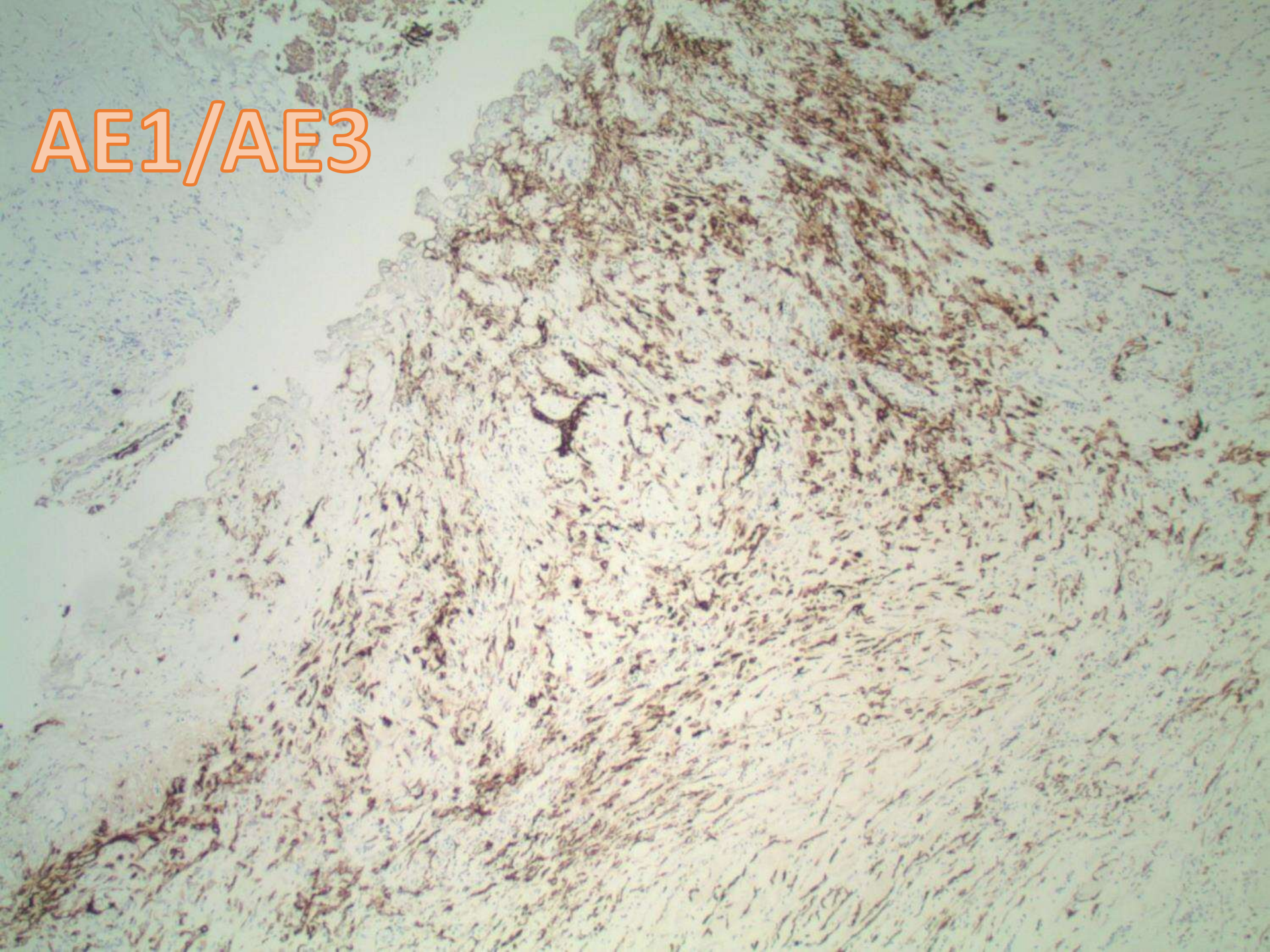


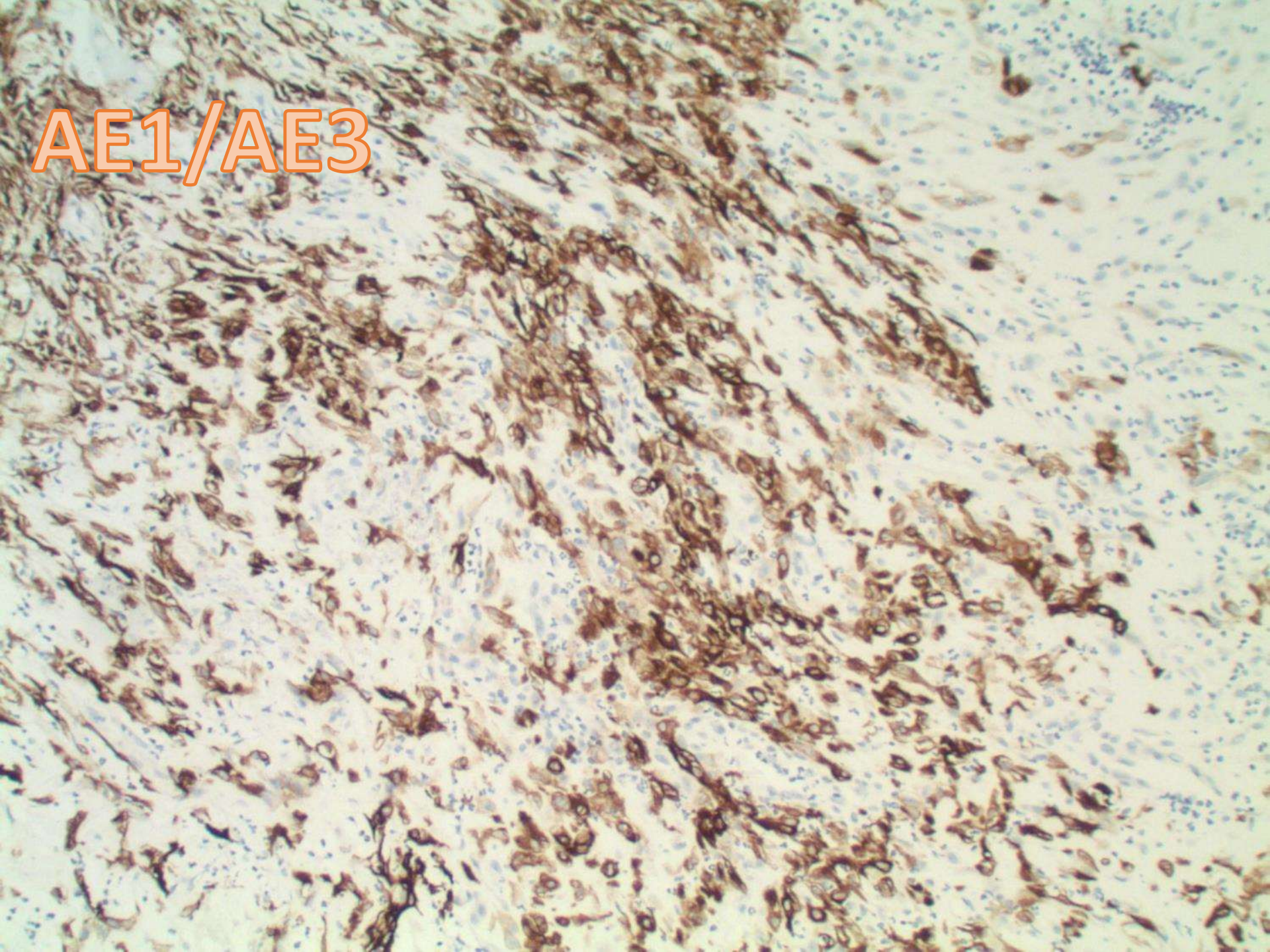






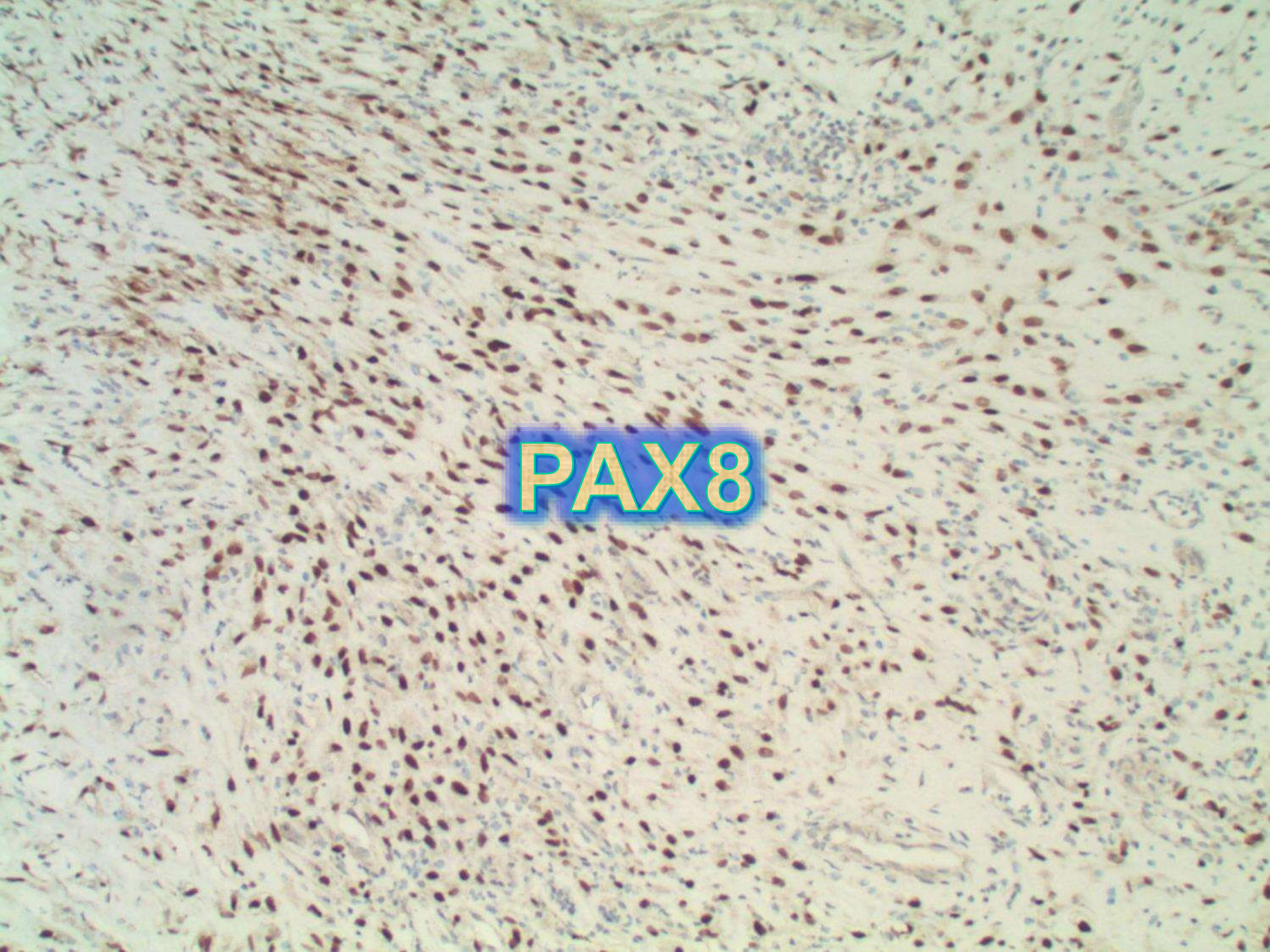


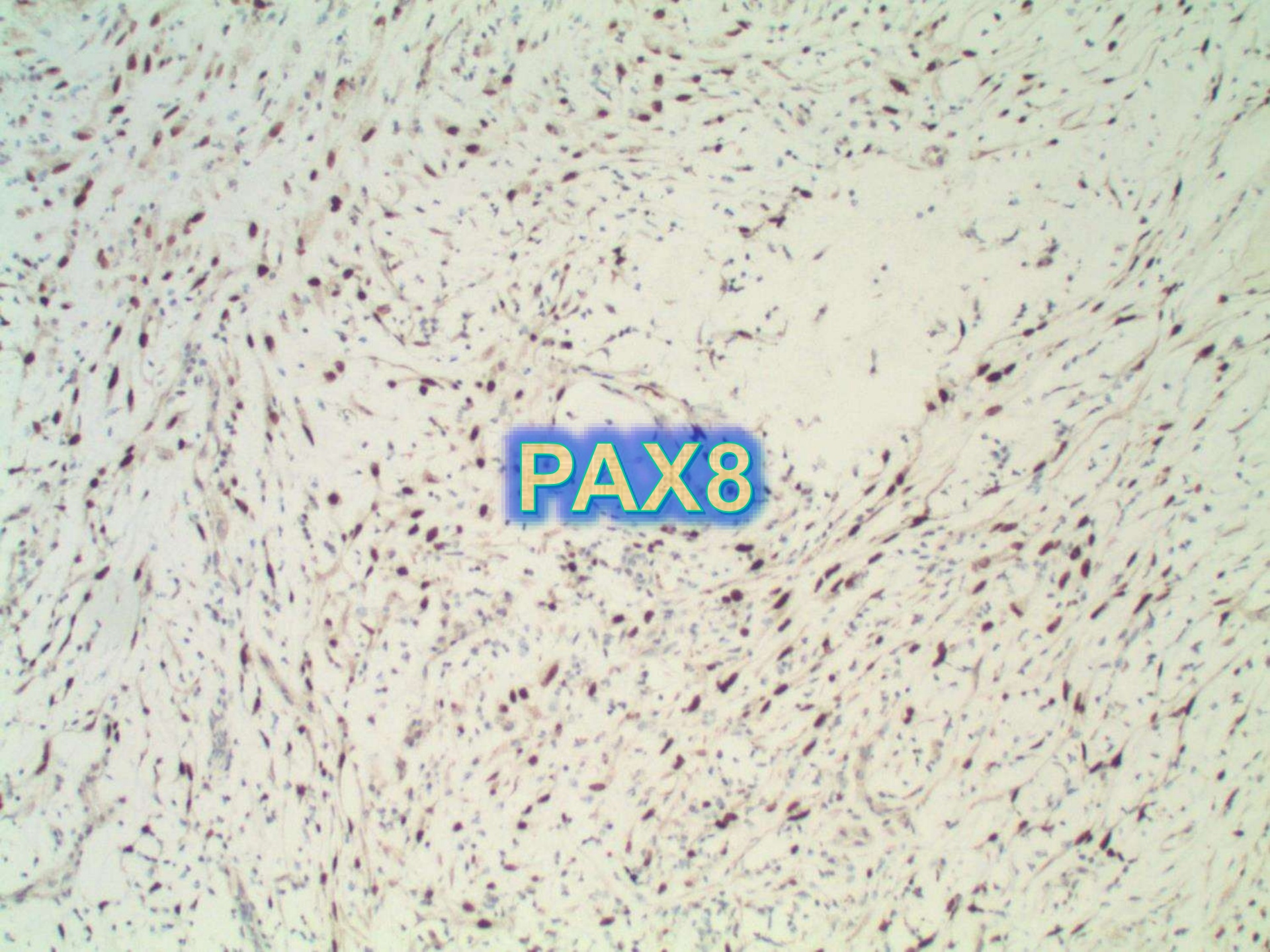

AE1/AE3


AE1/AE3

DDx

- Treated prostatic adenocarcinoma
- Sarcomatoid urothelial carcinoma
- Inflammatory myofibroblastic tumor
- Nephrogenic adenoma


PAX8


PAX8

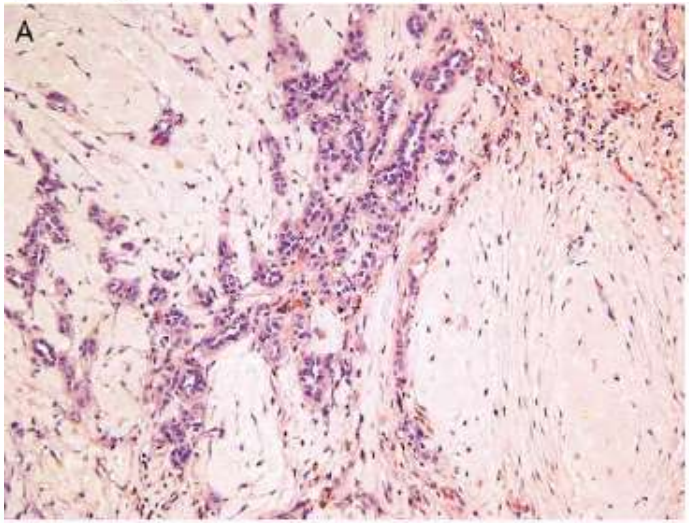
Fibromyxoid Nephrogenic Adenoma: A Newly Recognized Variant Mimicking Mucinous Adenocarcinoma

Donna Elizabeth Hansel, MD, PhD, Tibor Nadasdy, MD,† and Jonathan I. Epstein, MD‡§‖*

Abstract: Nephrogenic adenomas demonstrate a variety of morphologic patterns that may occasionally be confused with malignant processes, including urothelial and prostatic carcinoma. In this series, we describe 8 cases of nephrogenic adenoma that contain an admixture of the classic tubular form of nephrogenic adenoma and an unusual spindled and fibromyxoid form of nephrogenic adenoma that closely mimics infiltrating carcinoma. In all cases, the classic tubular form of nephrogenic adenoma composed only a small proportion of the lesion, whereas the remainder consisted of compressed spindled cells within a fibromyxoid background, with only rare tubular and cordlike structures. On close examination, minimal nuclear atypia was identified in 2 cases, which included small, pinpoint nucleoli, and nuclear pseudoinclusions. All 8 patients were elderly men who had a prior or concurrent history of acinar prostate cancer (n = 4), combined acinar prostate and urothelial carcinoma (n = 1), urothelial-type adenocarcinoma of the prostate (n = 1), bladder urothelial carcinoma (n = 1), or no prior reported prostatic or urothelial abnormalities (n = 1). Five patients received prior treatment with radiotherapy, 1 patient received intravesical mitomycin-C, and 1 also received bacillus Calmette-Guerin. The epithelial component of the lesions was positive in all cases for pancytokeratin (AE1/3) and racemase and demonstrated a variable cuff of type IV collagen surrounding the tubules. PAX-2 was positive with variable extent of labeling. Immunostains for prostate-specific antigen were negative. Histochemical stains identified some of the background matrix as mucin, with intense staining for periodic acid-Schiff and focal staining for mucicarmine. Stains for reticulin and amyloid (Congo red stain) and immunohistochemistry for Tamm-Horsfall protein were negative. This case series is the first report of a fibromyxoid subtype of nephrogenic adenoma. Awareness of this entity and the use of ancillary techniques can aid in the diagnosis of this unusual form of nephrogenic adenoma.

Key Words: bladder, mucin, urothelial carcinoma, prostate carcinoma, spindle cell

(*Am J Surg Pathol* 2007;31:1231–1237)



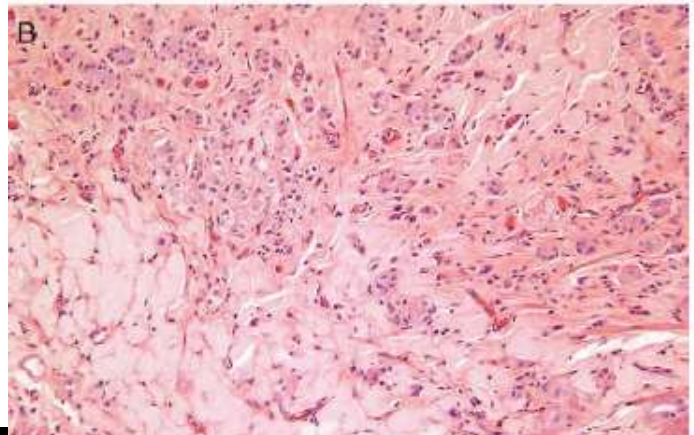
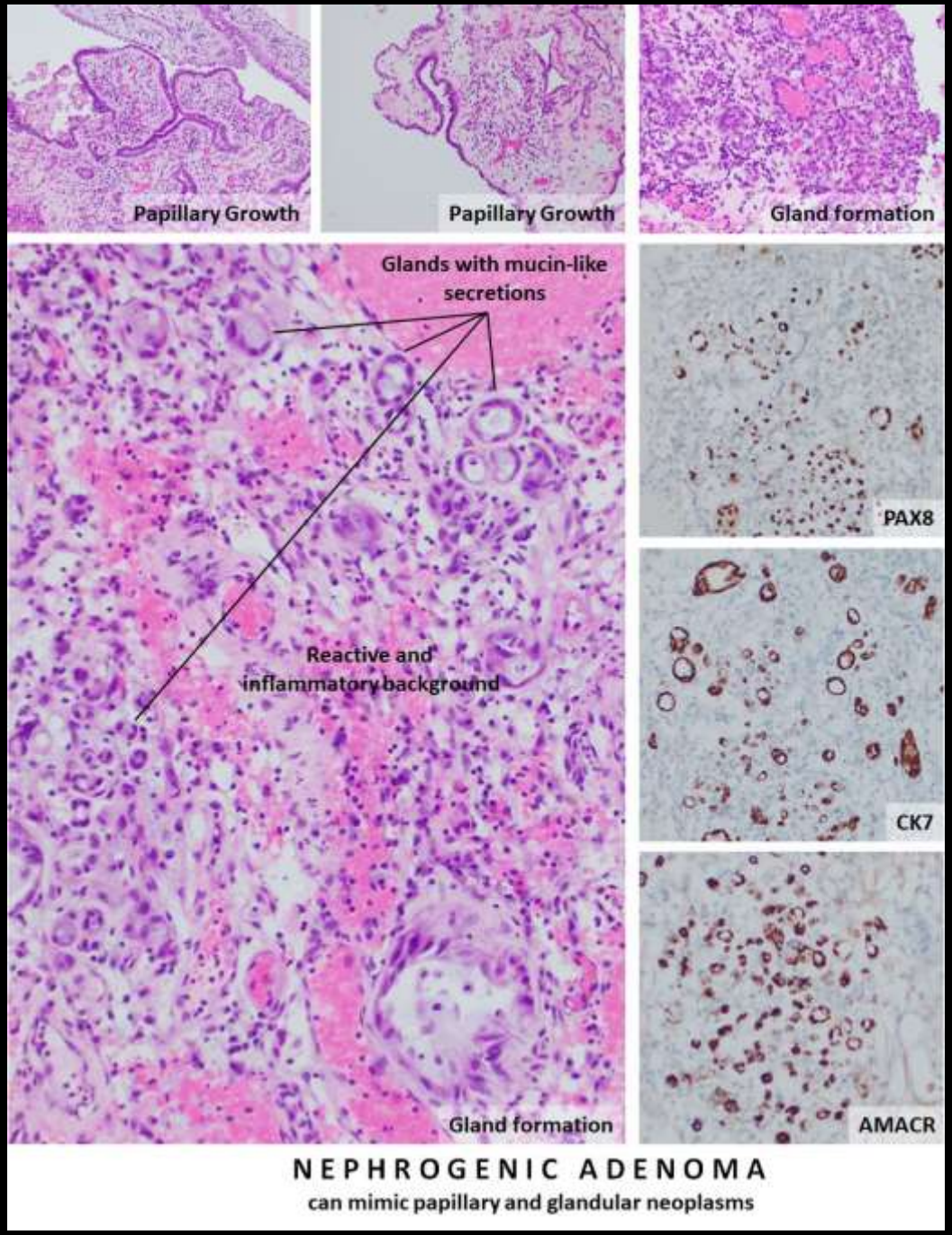


TABLE 1. Patient Demographics and Prior Genitourinary Tract History

Patient	Age	Sex	Specimen	Prior History
1	76	M	TURP	XRT for prostate cancer; CIS with BCG therapy
2	70	M	Bladder base biopsy	Urothelial carcinoma and CIS treated with intravesical mitomycin-C
3	72	M	Bladder neck biopsy	Prostate cancer treated with radioactive seed implants
4	62	M	Urethral biopsy	No prior prostate or bladder abnormalities
5	77	M	Urethral biopsy	Prostate cancer treated with brachytherapy, XRT, Lupron treatment
6	79	M	Radical nephrectomy, ureterectomy	Prostate cancer treated with XRT
7	65	M	TURP	Prostate cancer treated with brachytherapy
8	76	M	Cystoprostatectomy	Concurrent urothelial-type prostatic adenocarcinoma

CIS indicates carcinoma in situ; TURP, transurethral resection of the prostate; XRT, external beam radiation.



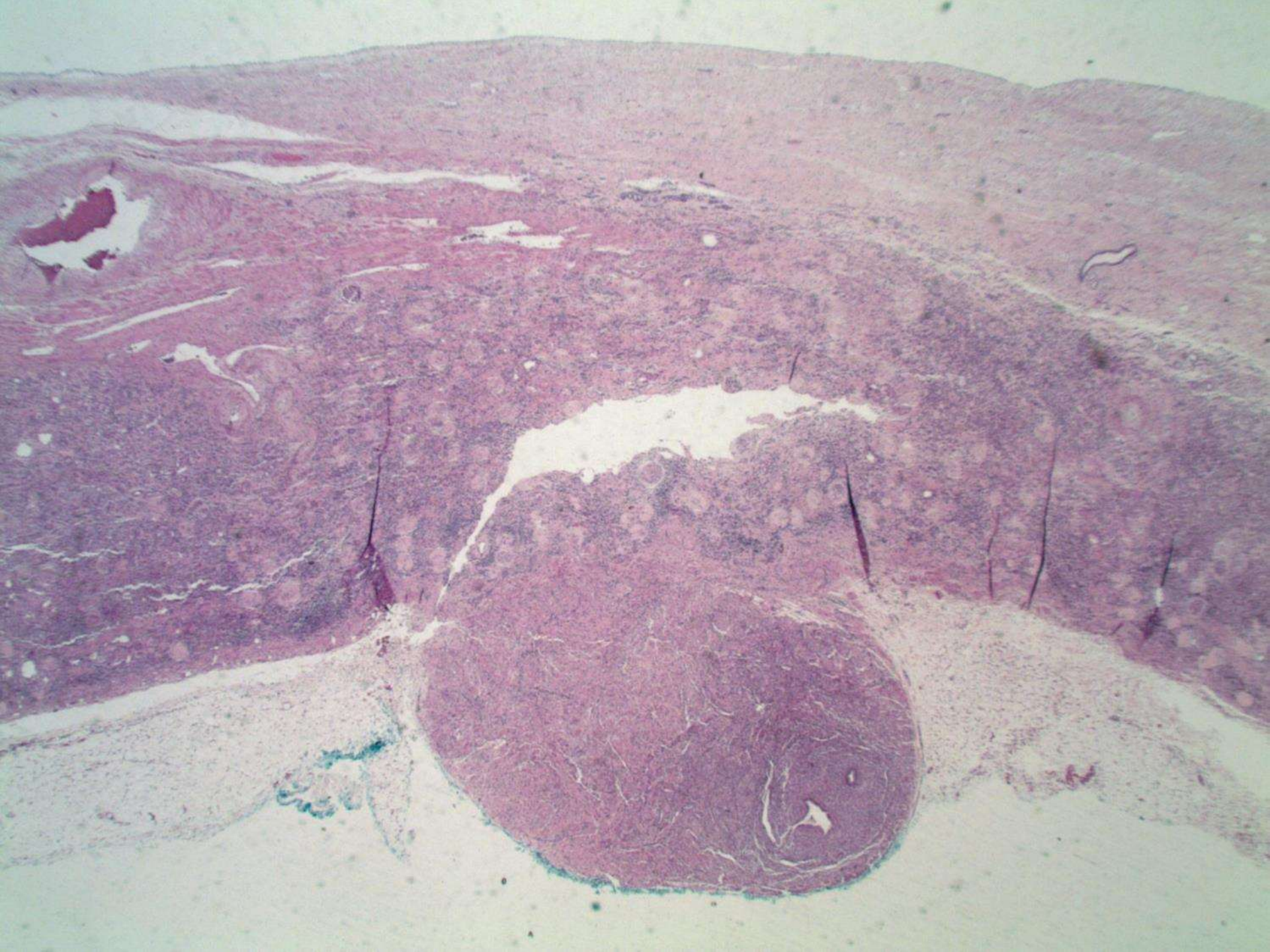
NEPHROGENIC ADENOMA

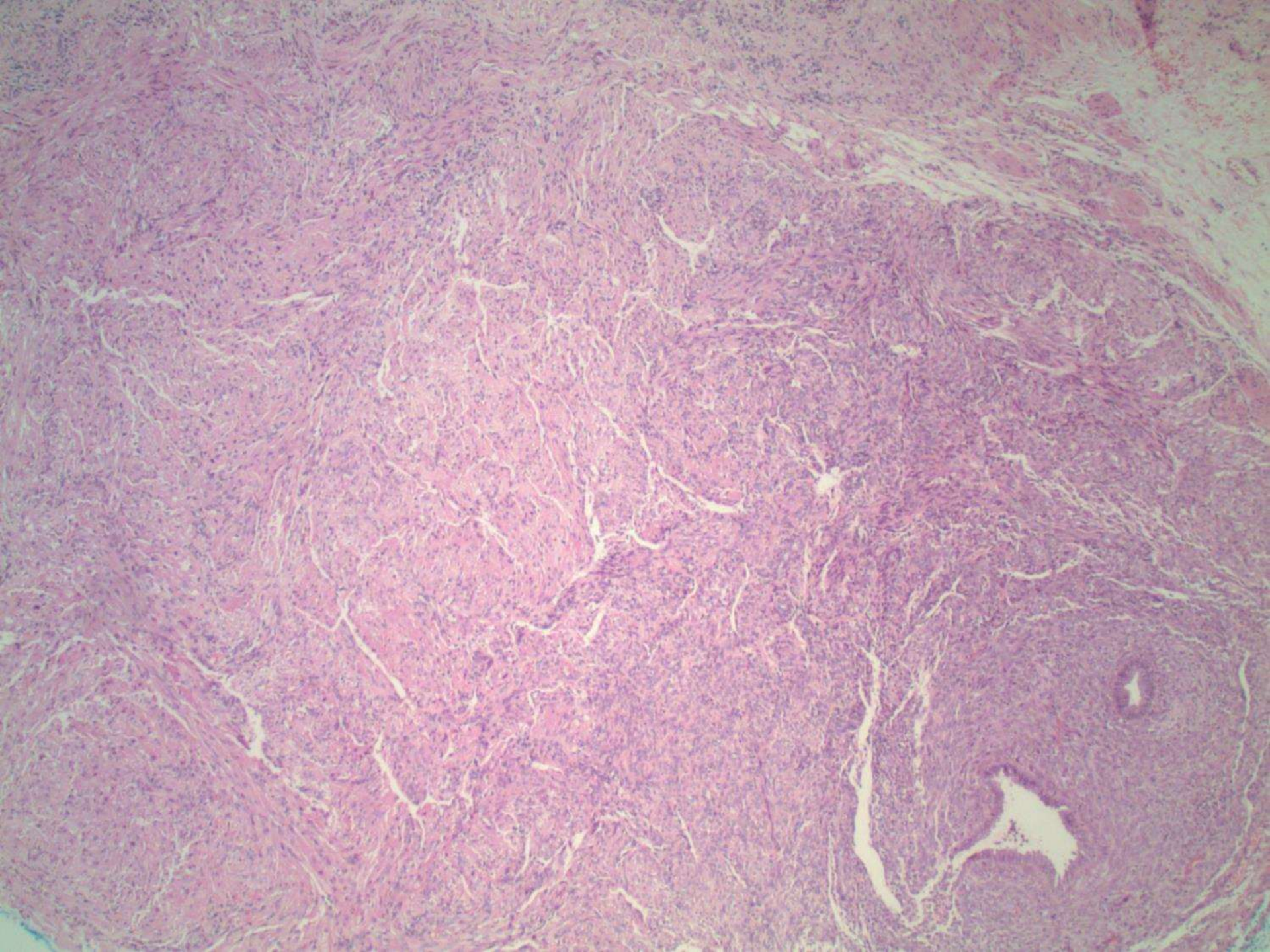
can mimic papillary and glandular neoplasms

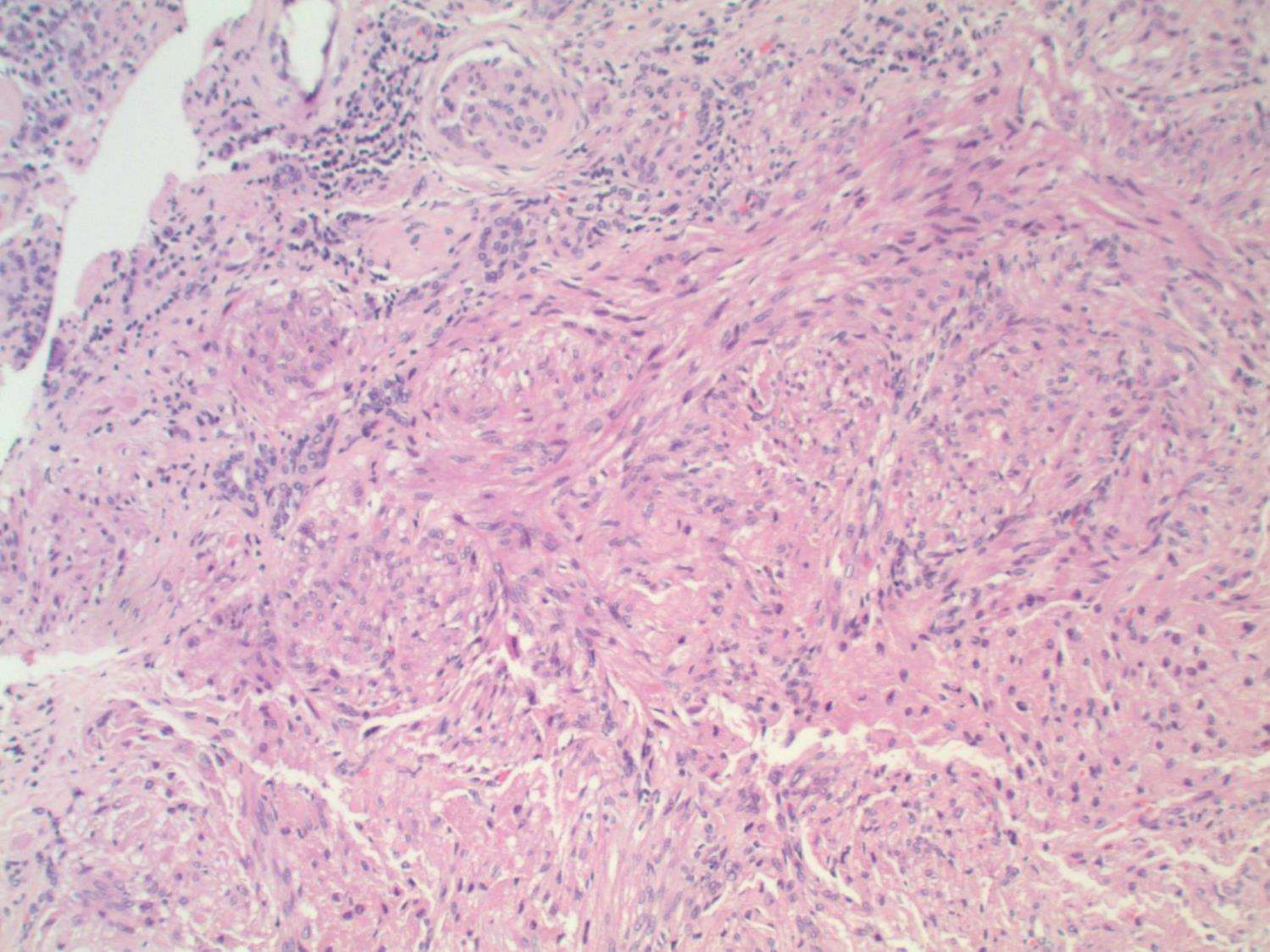
Fibromyxoid variant nephrogenic adenoma

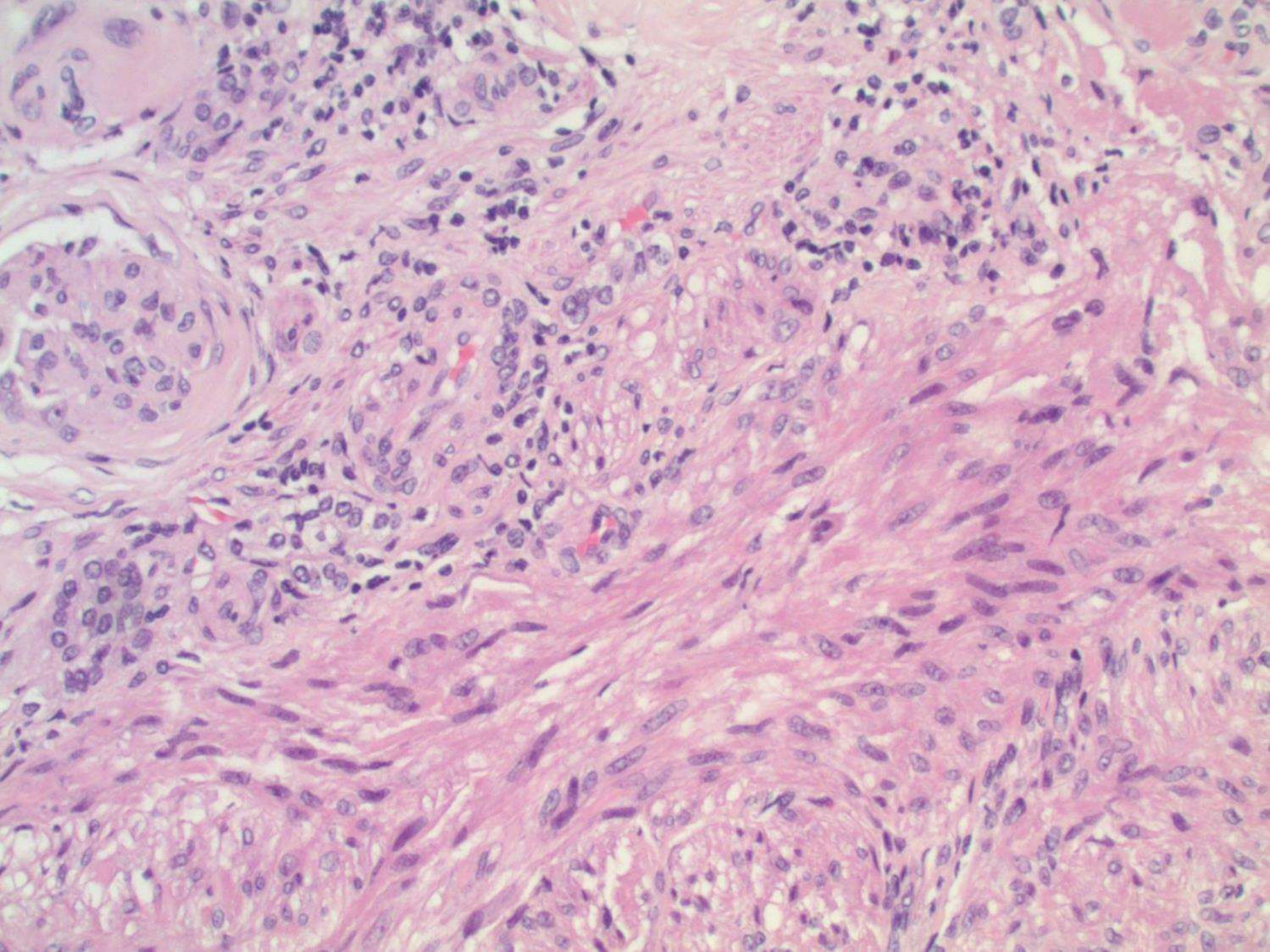
- **Helpful to find classic tubular pattern NA**
  - Minimal atypia or mitosis
  - Often have amyloid-like background stroma

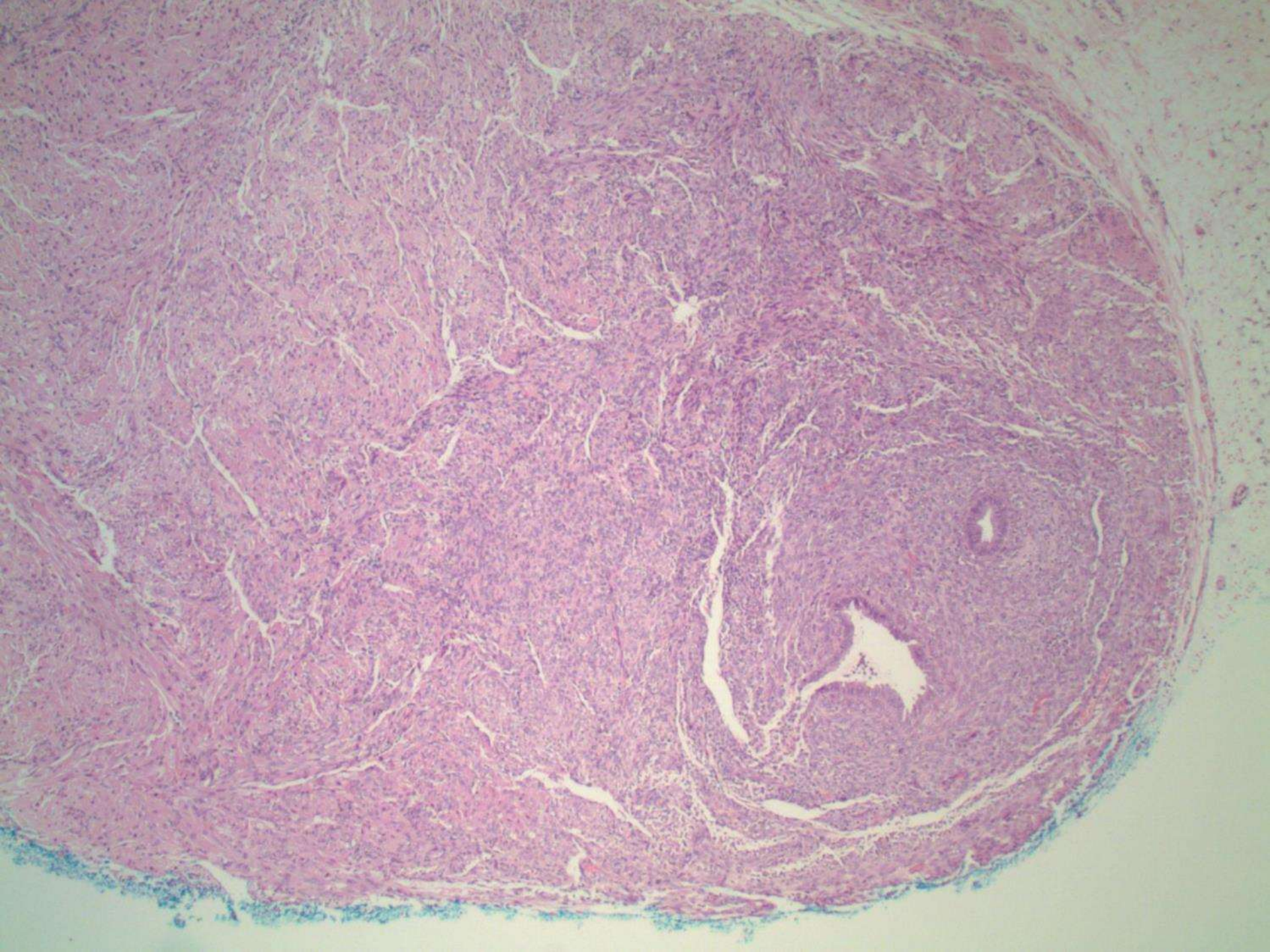
- **PAX8+ AMACR+**
  - Caution on GATA3, PSAP/PSA
    - Nephrogenic adenoma can be + !!!

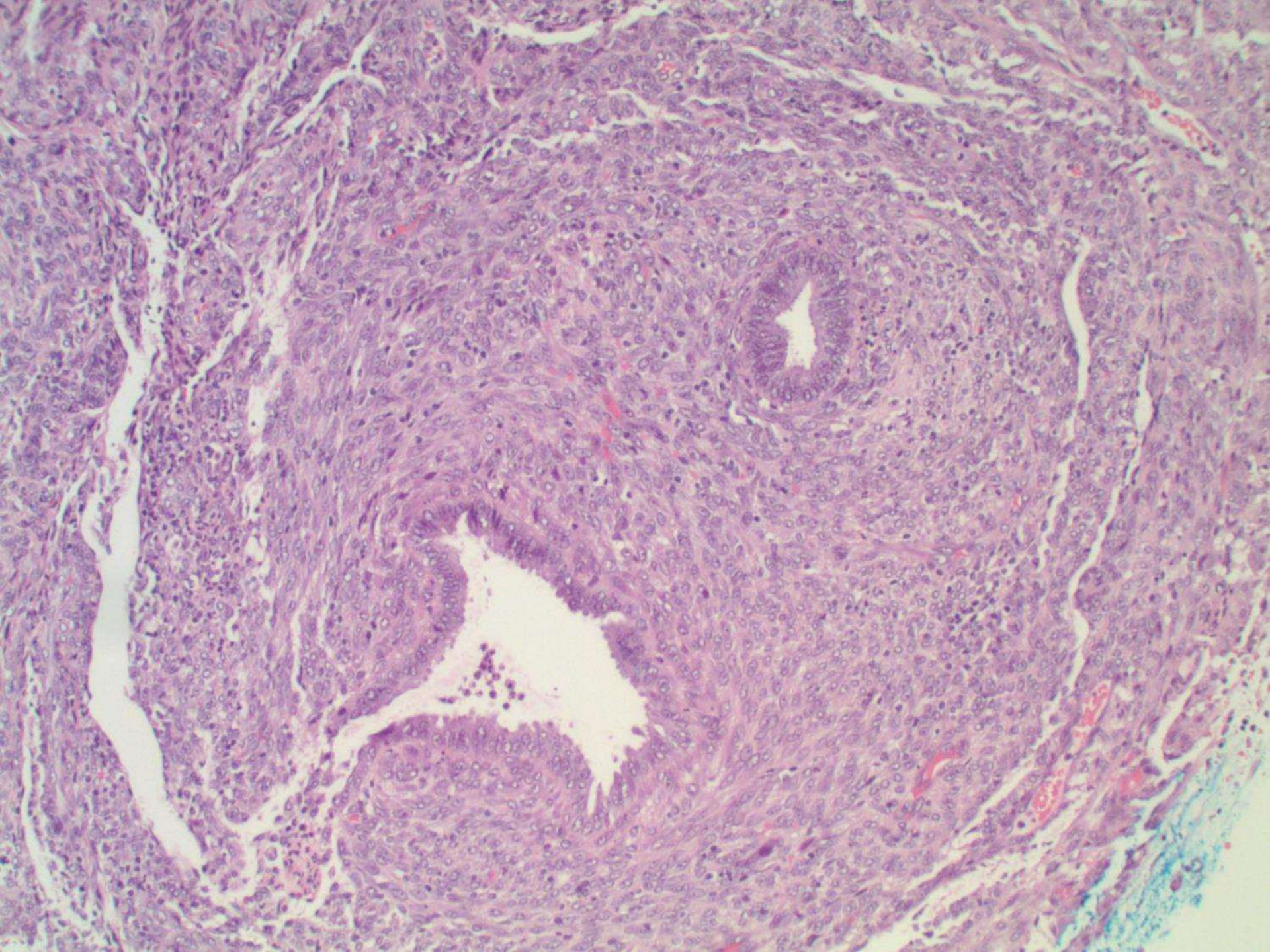


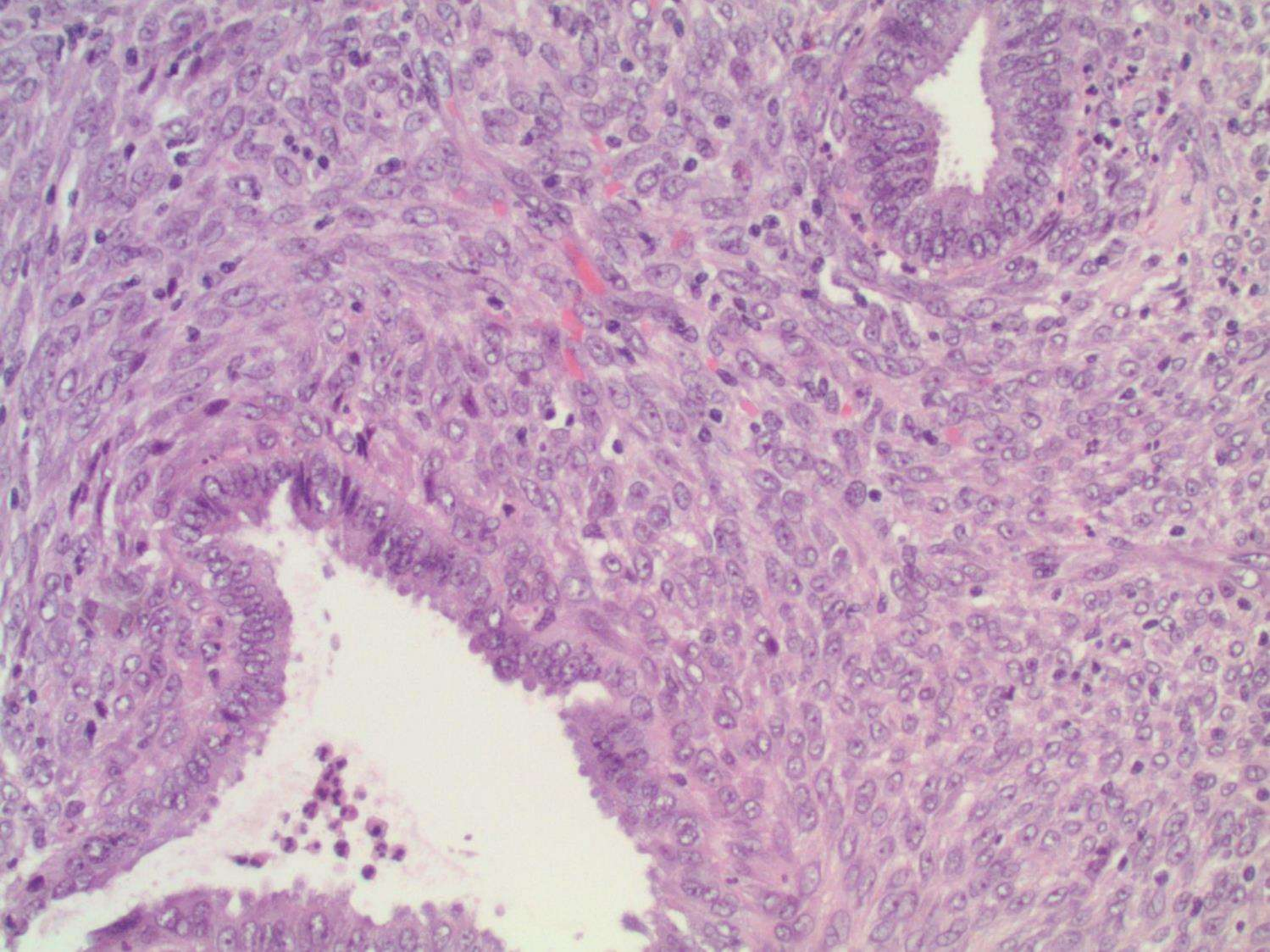


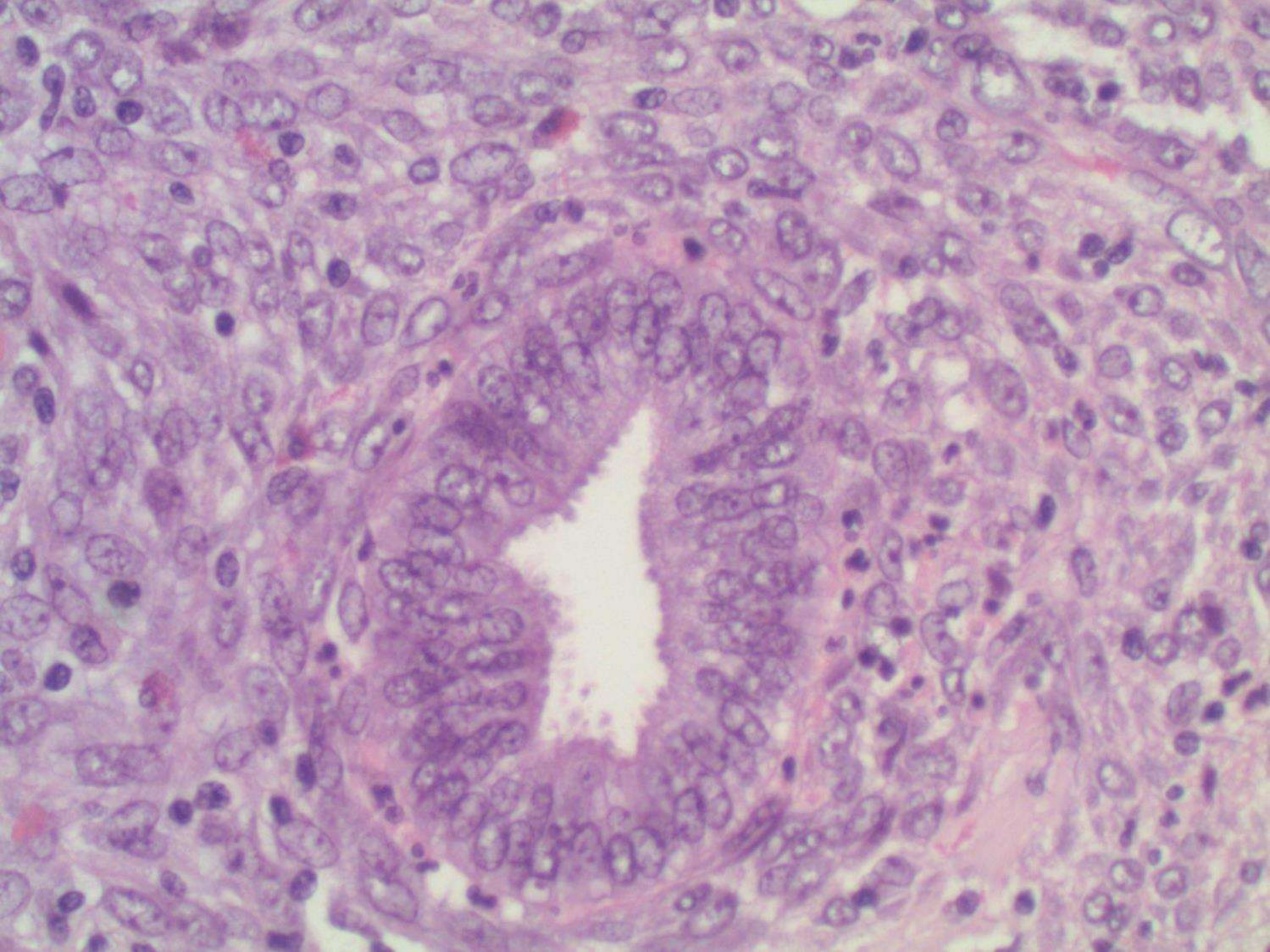






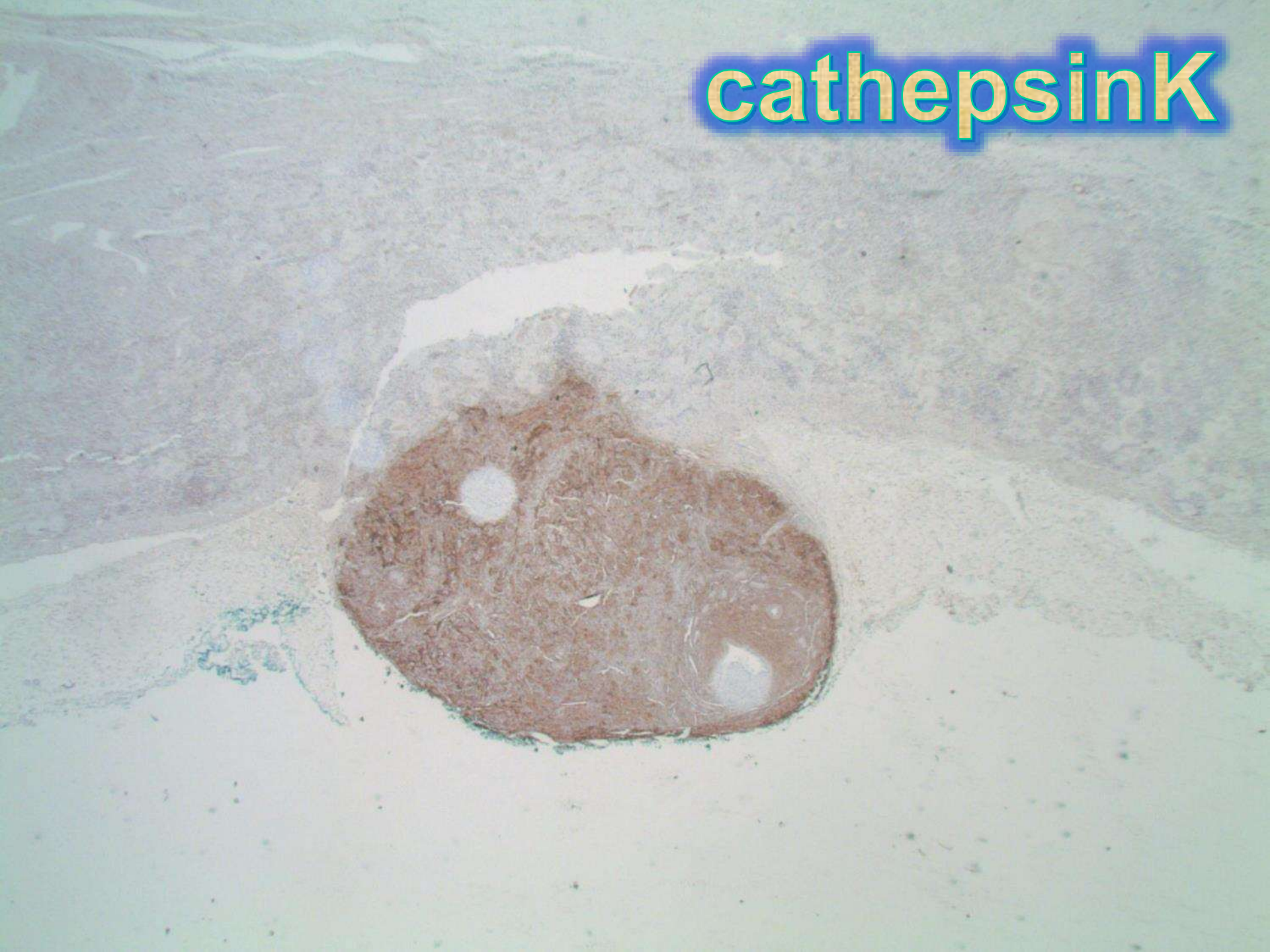


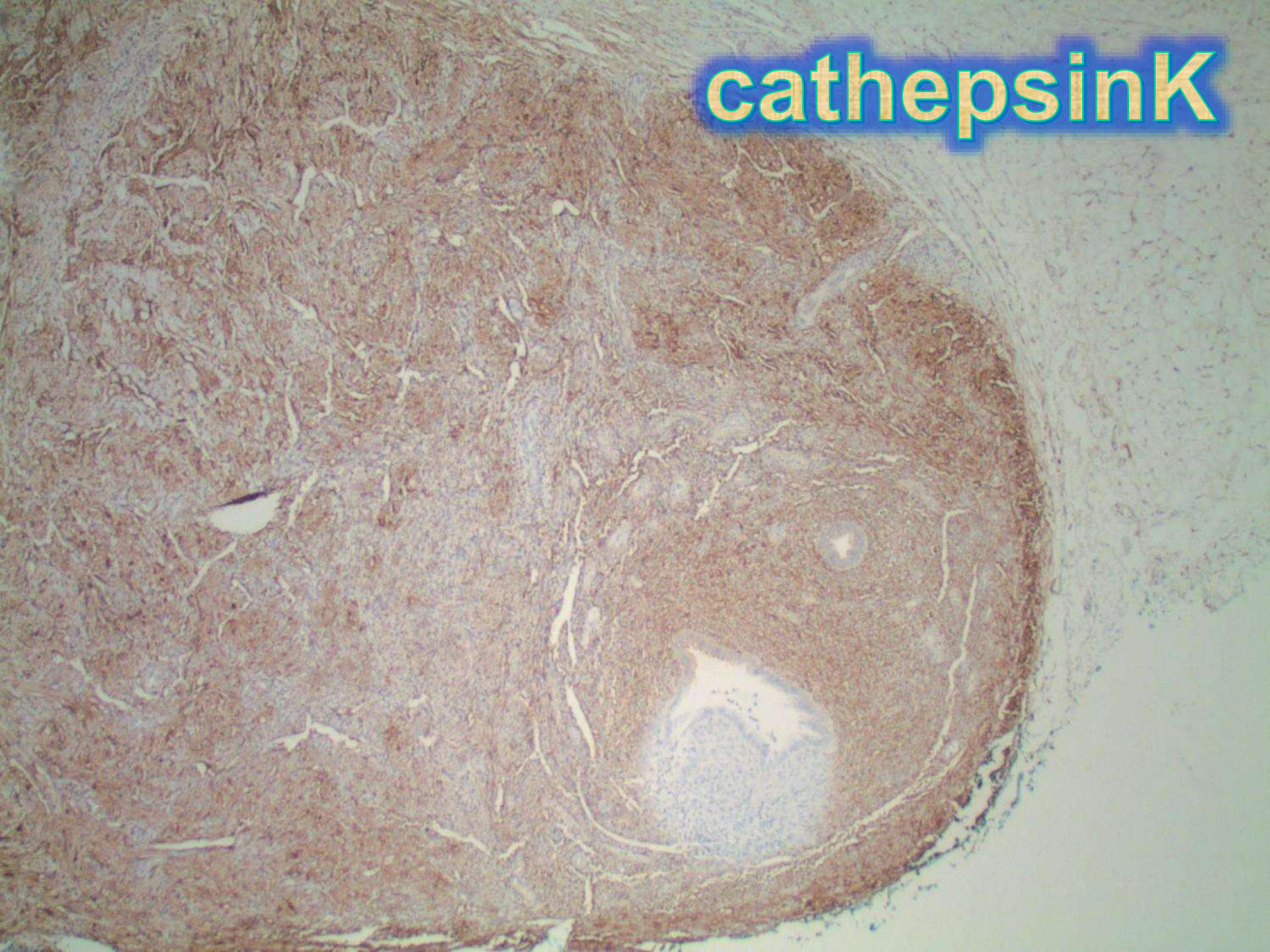


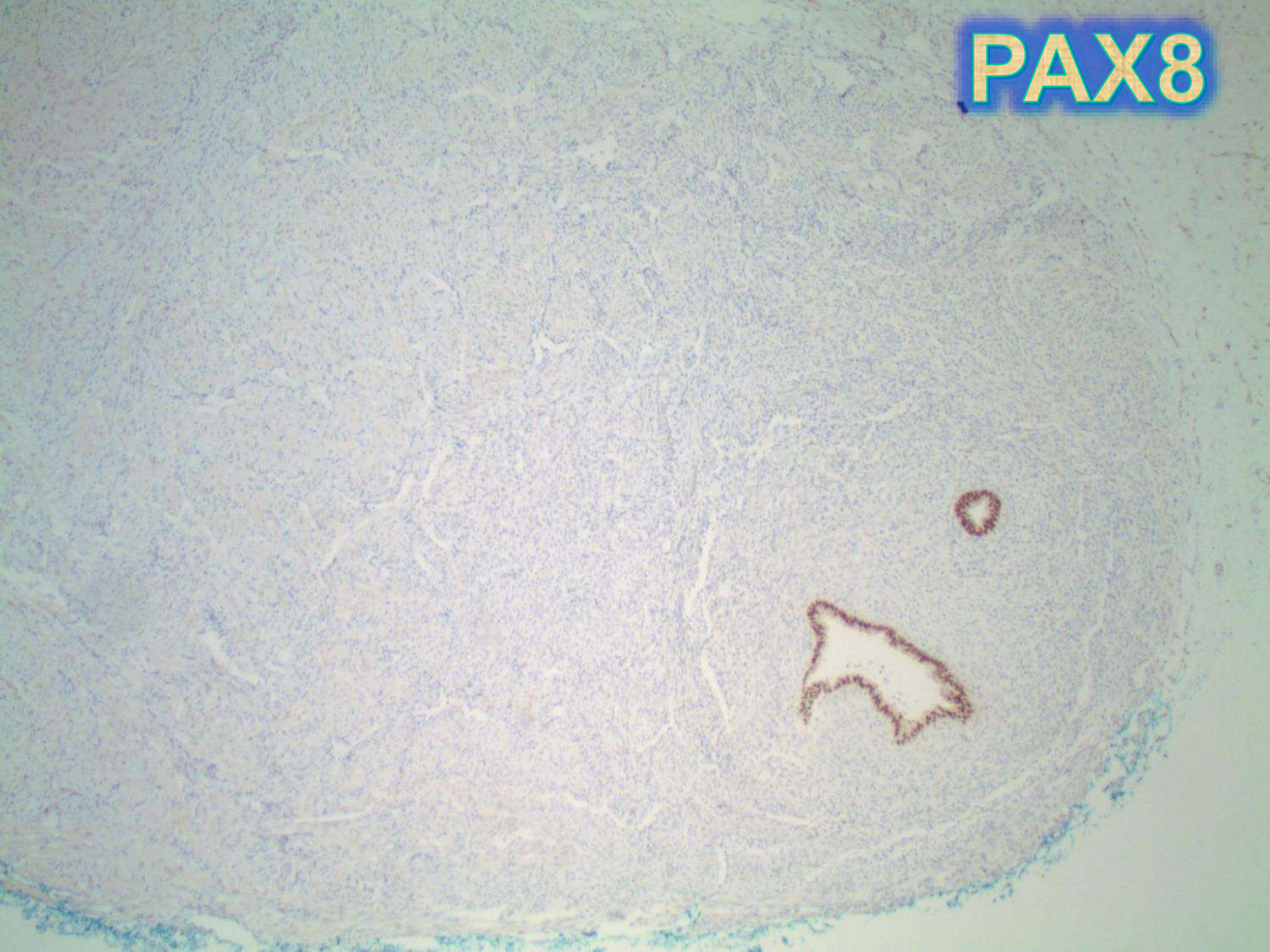


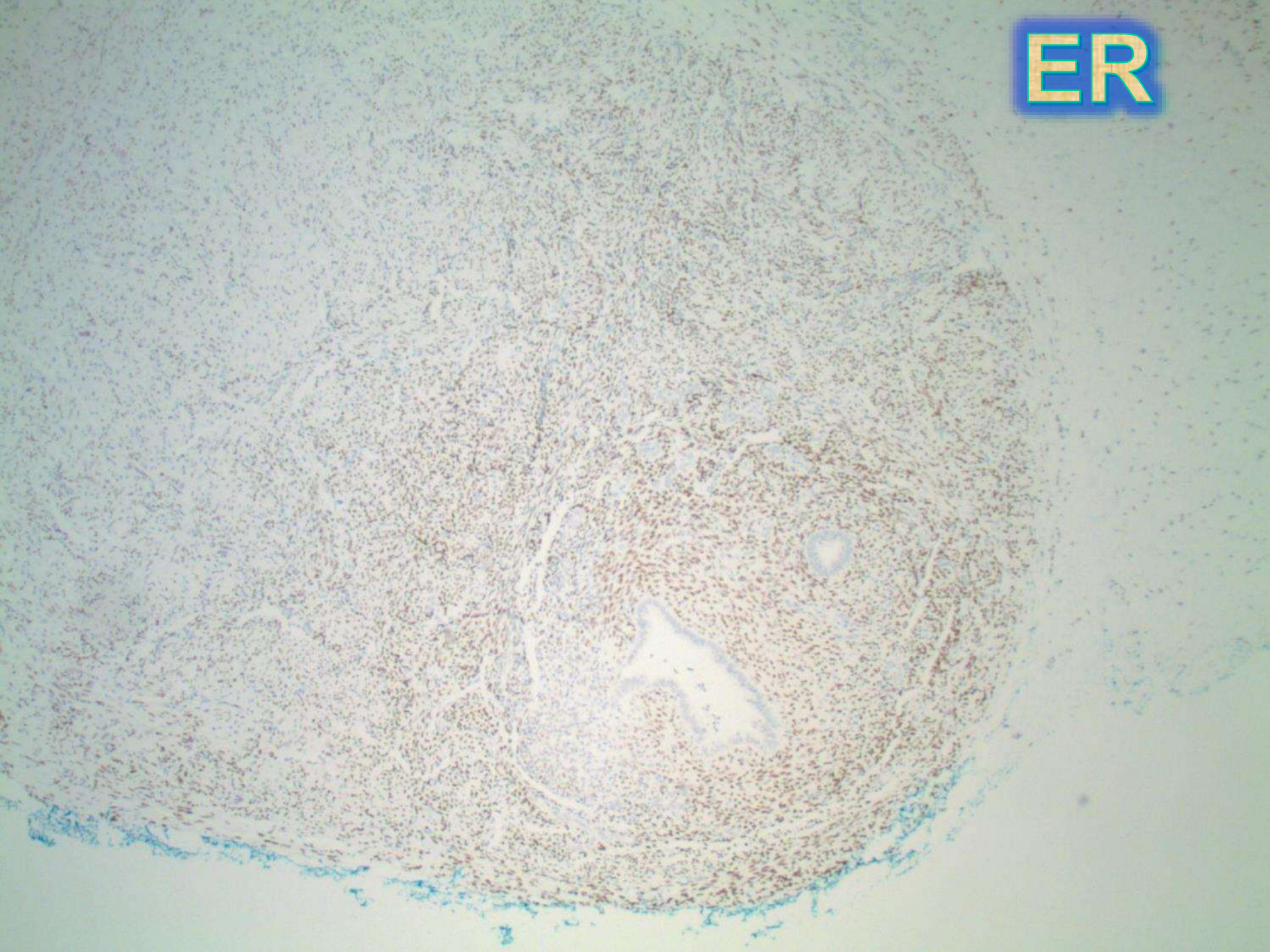
DDx

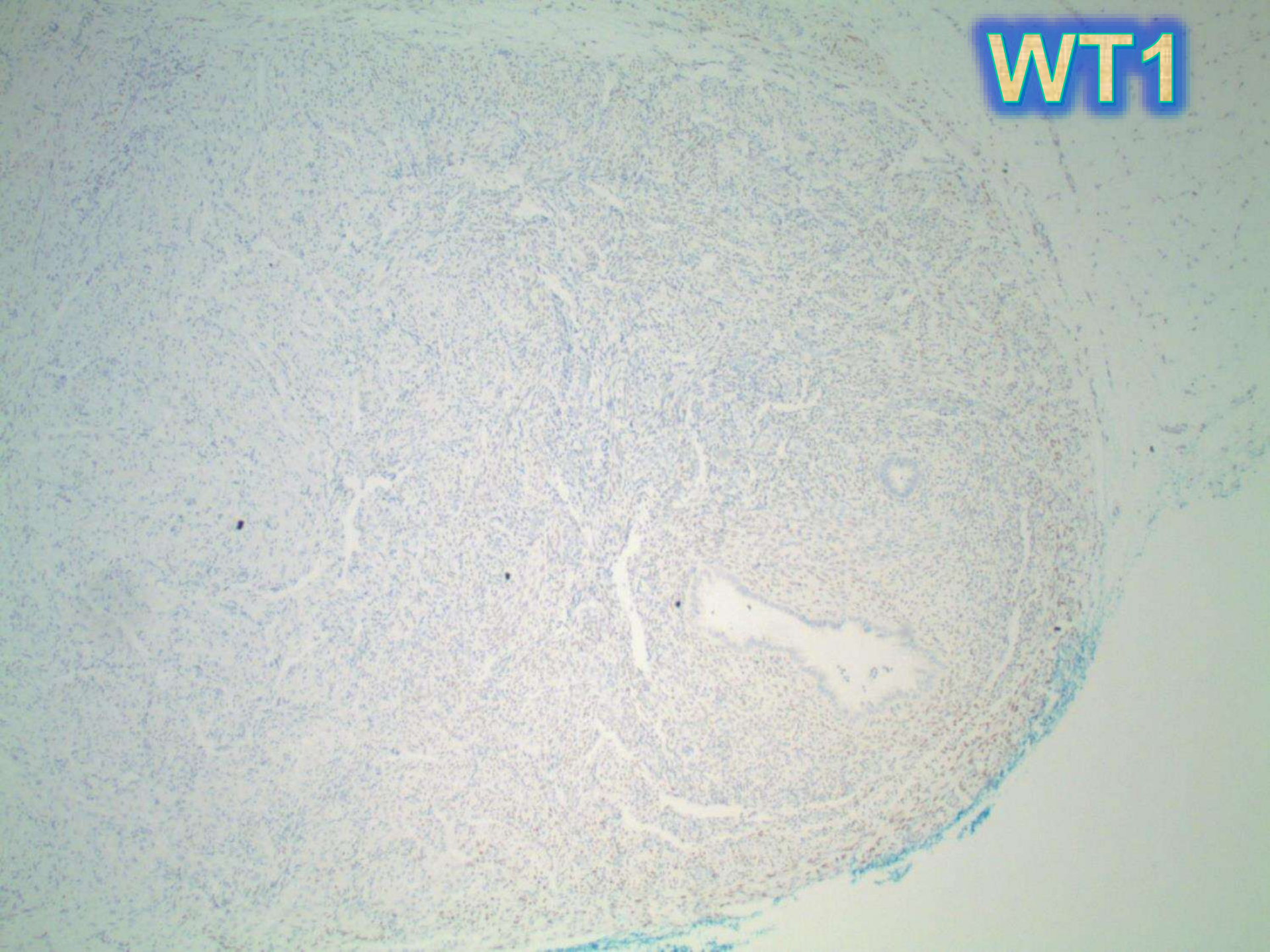
- Angiomyolipoma with epithelial cysts (AMLEC)
- Endometriosis
- Metastatic carcinosarcoma
- Capsular leiomyoma
- Cystic nephroma/mixed epithelial stromal tumor


cathepsinK


cathepsinK


PAX8


ER


WT1

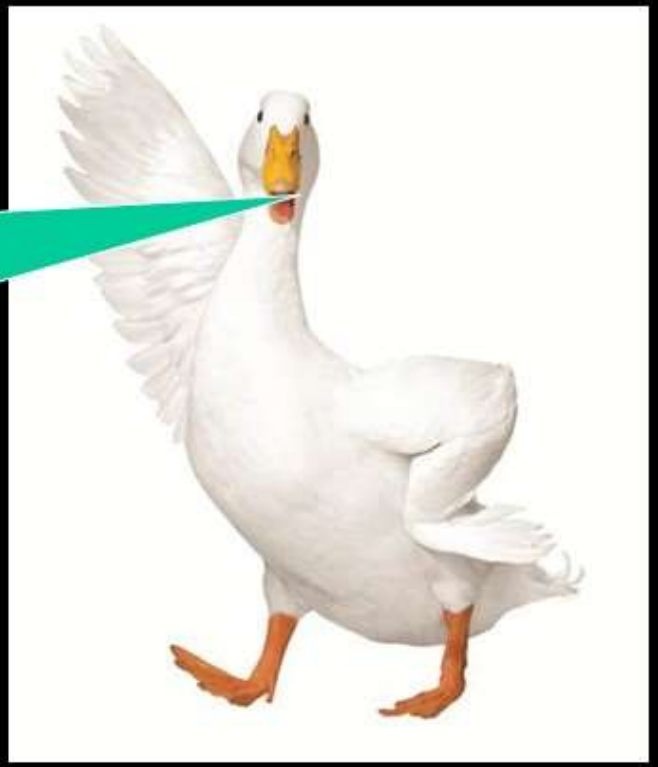
Angiomyolipoma With Epithelial Cysts (AMLEC)

A Distinct Cystic Variant of Angiomyolipoma

Samson W. Fine, MD, Victor E. Reuter, MD,§ Jonathan I. Epstein, MD,*† ‡ and Pedram Argani, MD*‡*

Am J Surg Pathol • Volume 30, Number 5, May 2006

AMLEC!



staining for a panel of antibodies (Table 1) was performed in each case. This study was approved by the Institutional Review Board of the Johns Hopkins Hospital allowing for data collection regarding patient demographics, clinical presentation, and outcomes from the patients' urologist/personal physician.

CASE REPORTS

Case No. 1

A 42-year-old man with no previous urologic history presented with microscopic hematuria and groin pain. A CT scan revealed a complex right mid-renal mass with calcifications, suspicious for renal cell carcinoma. The patient underwent radical nephrectomy, which revealed a central 2.8-cm cystic mass that was smooth-lined and confined by the renal capsule. The patient is alive with no evidence of disease 8 years following surgery.

Case No. 2

A 76-year-old man with mild dysuria, but no known history or stigmata of tuberous sclerosis, underwent CT scan that revealed bilateral cystic renal masses. The patient underwent right partial nephrectomy to remove the smaller of the two lesions, which grossly was a 4.5-cm firm, nodular tumor bearing a smooth-walled, 2.4-cm cyst. The patient is alive, with a stable, nongrowing cystic mass in the left kidney, 5 years following surgery.

Case No. 3

A 55-year-old woman with no history of gynecologic surgery or hormonal therapy underwent CT scan as part of a routine workup following a motor vehicle accident. Imaging revealed a solid mass in the upper pole of the left kidney and a partially cystic mass in the midportion of the same kidney (the latter corresponding to AMLEC) that appeared to extend into perinephric fat. She underwent radical nephrectomy which revealed two 2.5-cm lesions, an upper pole, solid, tan mass and a mid-pole, partially cystic mass growing through the capsule into perinephric fat, but not beyond Gerota's fascia. A 1-cm thin-walled simple cyst was also found in the lower pole. The patient is alive with no evidence of disease, one year postoperatively.

Case No. 4

A 37-year-old woman with a known history of tuberous sclerosis complex presented with chronic renal insufficiency secondary to multiple renal masses. On CT scan, multiple lesions were noted in the left kidney, including a septated cystic structure in the lower pole and a smaller single cyst in the upper pole with an adjacent 1.0-cm soft tissue nodule suspicious for renal cell carcinoma. The right kidney disclosed a single cyst in the mid-lower pole. At the time of left radical nephrectomy, 1.8- and 1.0-cm solid nodules were noted in the upper pole, whereas multiple firm areas were present in the mid-lower pole. Additionally, the lower pole displayed a 1.3-cm cystic lesion (corresponding to AMLEC). The patient is stable, with the previously detected cyst in the right kidney, 6 months post-operatively.

RESULTS

Histopathologic and Immunohistochemical Findings

Microscopically, all four lesions demonstrated three components. The first was cystic or multicystic spaces lined by epithelium, which ranged from flat to cuboidal to columnar. Whereas the cuboidal to columnar cells had unremarkable clear cytoplasm, the flat cells had abundant eosinophilic cytoplasm with nuclei that often protruded into the lumen, yielding a hobnailed appearance (Fig. 1A). The second component was a "cambium-like" condensation of small stromal cells with indistinct cytoplasm immediately subjacent to the cyst epithelium. This stroma was associated with prominent capillary vasculature, yielding a strong resemblance to endometrial stroma, and demonstrated prominent lymphoplasmacytic inflammation in all cases (Fig. 1B). The third component was a thick exterior wall of plump smooth muscle cells with focally clear cytoplasm arranged in poorly formed fascicles, often appearing to emanate from irregular and tortuous blood vessels (Fig. 1C). This third component was typical of stromal-predominant AML. In all cases, noncystic glands consistent with native renal tubules were observed within this exterior muscular wall (Fig. 2).

Cystic angiomyolipoma of the kidney: a clinicopathologic description of 11 cases

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This report deals with 11 examples of renal angiomyolipomas (AML) which appear to include an epithelial element as a part of the neoplasm in the form of gross or microscopic cysts—usually both. There were seven females and four males between the ages of 20 and 70 years with mean age of 45 years. Three of these were known to be symptomatic: intermittent flank pain and gross hematuria for 2 months; recurrent hematuria both before and after flank trauma and a third patient with acute abdomen due to a ruptured tumor blood vessel. Cysts were described in three of the six cases where radiographic data were available. Seven tumors were in the right kidney and four in the left. In gross descriptions, cysts were mentioned in seven and they ranged from 6.0 to 2.0 cm with a median and mean maximal diameter of 5.0 and 4.0 cm, respectively. Microscopically, virtually all of the tumors included multiple smaller cysts and these were lined by flat, cuboidal or columnar epithelium and occasionally hobnail epithelium. There was usually a subepithelial collar of poorly differentiated cells, but the solid element of all tumors was myomatous angiomyolipoma; only one case had any adipose tissue. A dominant histological feature was the prominent lymphatic channels—identical to those of lymphangiomyomas and myomatous or triphasic AMLs. They are much more conspicuous in these cystic cases. Immunohistochemically, all tumors tested were reactive with actin, desmin and HMB-45, with the latter being more intensely positive in the subepithelial collars. Estrogen and progesterone receptors were usually positive, also. The behavior of these lesions appears to be no different from that of other AMLs.
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Table 3 Clinicopathologic features of the study group

	Age (years)	*Sex*	*Side*	*Clinical presentation*	*Imaging*	*Treatment*	*Gross pathology*
Case 1	61	F	L	Incidental finding	Retrograde pyelogram: large cyst distorting pelvocalyceal system. Brown's fluid aspirated	Nephrectomy	6.0 cm upper pole cyst with focal nodular luminal contour
Case 2	45	F	R	Intermittent flank pain and and gross hematuria for 2 months	Excretory urogram: Right lower pole mass	Nephrectomy	Circumscribed 3.5 cm yellow-gray tumor
Case 3	21	F	R	NA	NA	Nephrectomy	5.0 cm cyst in upper pole. Lower pole: tan, hemorrhagic $7 \times 4 \times 3\,cm^3$ mass
Case 4	37	F	R	Incidental finding in diabetic nephropathy	Vascular lower pole tumor by angiography	Partial nephrectomy	A 'partially cystic' gray-white tumor $5 \times 4 \times 3\,cm^3$
Case 5	39	F	L	Retroperitoneal hemorrhage with acute abdomen from ruptured vessel in hilus	NA	Nephrectomy	Tumor obscured by extensive hemorrhage at renal hilus
Case 6	20	M	L	Recurrent hematuria several months before and after flank trauma	Mass in the lower pole	Partial nephrectomy	A 5.0 cm cyst filled with blood clot
Case 7	70	M	R	NA	NA	Partial nephrectomy	A 2.0 cm cyst with folding of luminal contour. $4 \times 3\,cm^2$ nodule in wall of cyst
Case 8	27	F	R	NA	CT scan: 2.5 cm, largely exophytic cyst with some peripheral enhancement	Nephrectomy	A $3 \times 2.7 \times 2\,cm^3$ cystic mass protrudes from renal surface. Cut surface: multicystic
Case 9	61	F	R	Incidental finding on metastatic survey for lung cancer	Ultrasound: complex exophytic cyst laterally, with septations. $3.8 \times 3 \times 2.6\,cm^3$ solid mass in lower pole	Nephrectomy	Hemorrhagic capsular cyst $5 \times 4 \times 2.5\,cm^3$ laterally. Lower pole: $3.5 \times 3.1 \times 2.5\,cm^3$ mass
Case 10	50	M	R	NA	NA	Partial nephrectomy	White-tan nodule. Size not given
Case 11	67	M	L	NA	NA	Excision	Exophytic mass $3 \times 2.7 \times 1.8\,cm^3$ with a 2.7 cm cyst with clear fluid