OCT 2019 DIAGNOSIS LIST

19-1001: Whipple's disease; lymph node/hematopathology and infectious disease pathology
19-1002: prostatic-type polyp (bladder/GU pathology)
19-1003: endometrial polyp with infarction changes AND isolated vasculitis of GYN tract (uterus/GYN pathology)
19-1004: glomangiopericytoma (nasal cavity/head and neck pathology)
19-1005: myeloid sarcoma (eye/hematopathology)
19-1006: IgG4-related sclerosing lymphadenopathy (lymph node/hematopathology)
19-1007: TFEB amplified renal cell carcinoma (kidney/GU pathology)
19-1008: TFEB MiT family translocation renal cell carcinoma (kidney/GU pathology)
19-1009: atypical epidermoid metaplasia (esophagus/GI pathology)
19-1010: myopathic process, favor post-ischemic changes (muscle/neuropathology)

Disclosures
Oct 7, 2019

The following planners and presenters had disclosures:

Ankur Sangoi, MD	Google	Consultant
Keith Duncan, MD	ABBvie	Consultant

South Bay Pathology Society has determined that these relationships are not relevant to the clinical cases being presented.

The following planners and faculty had no financial relationships with commercial interests to disclose:

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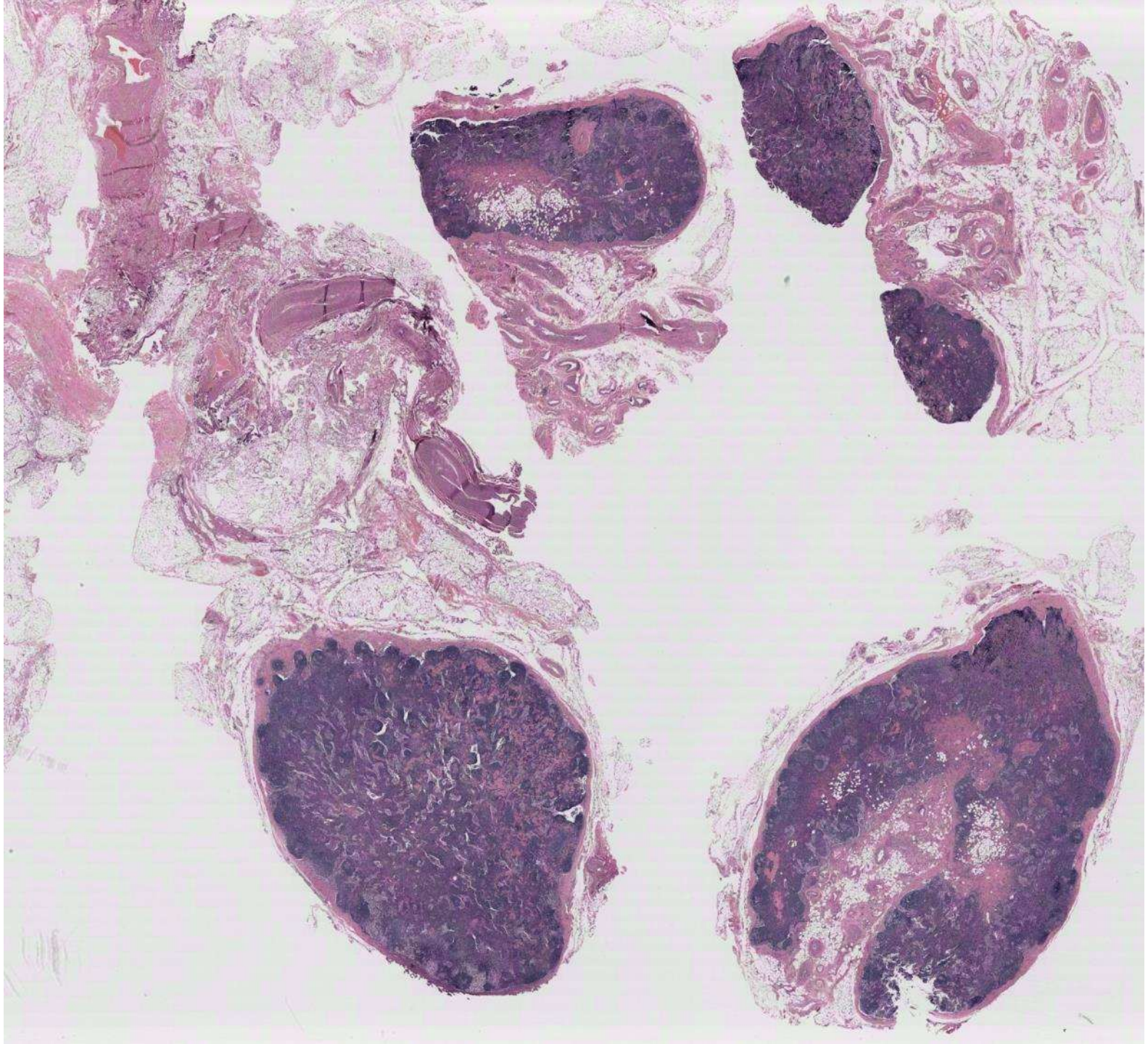
Kristin Jensen, MD

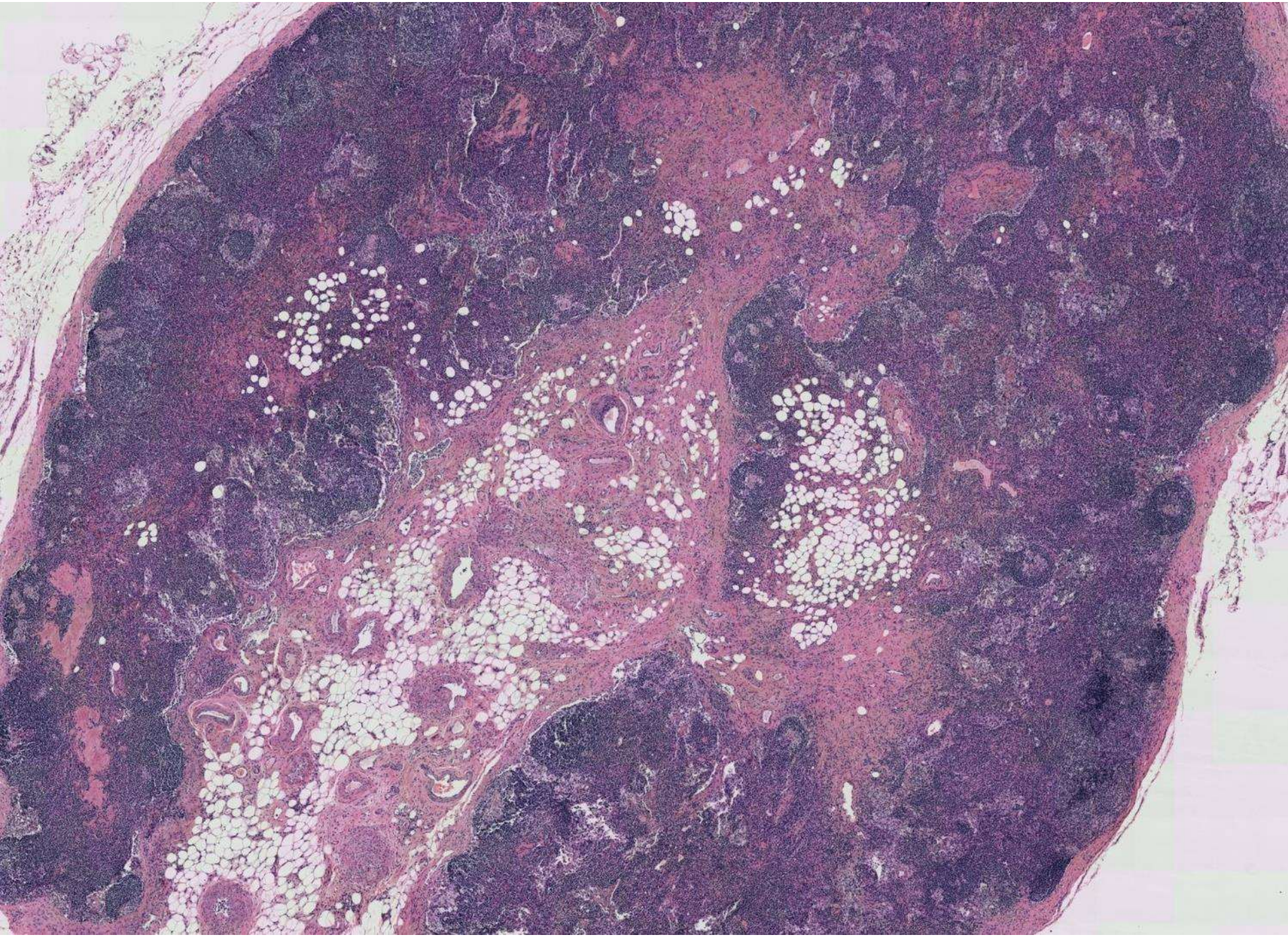
Megan Troxell, MD

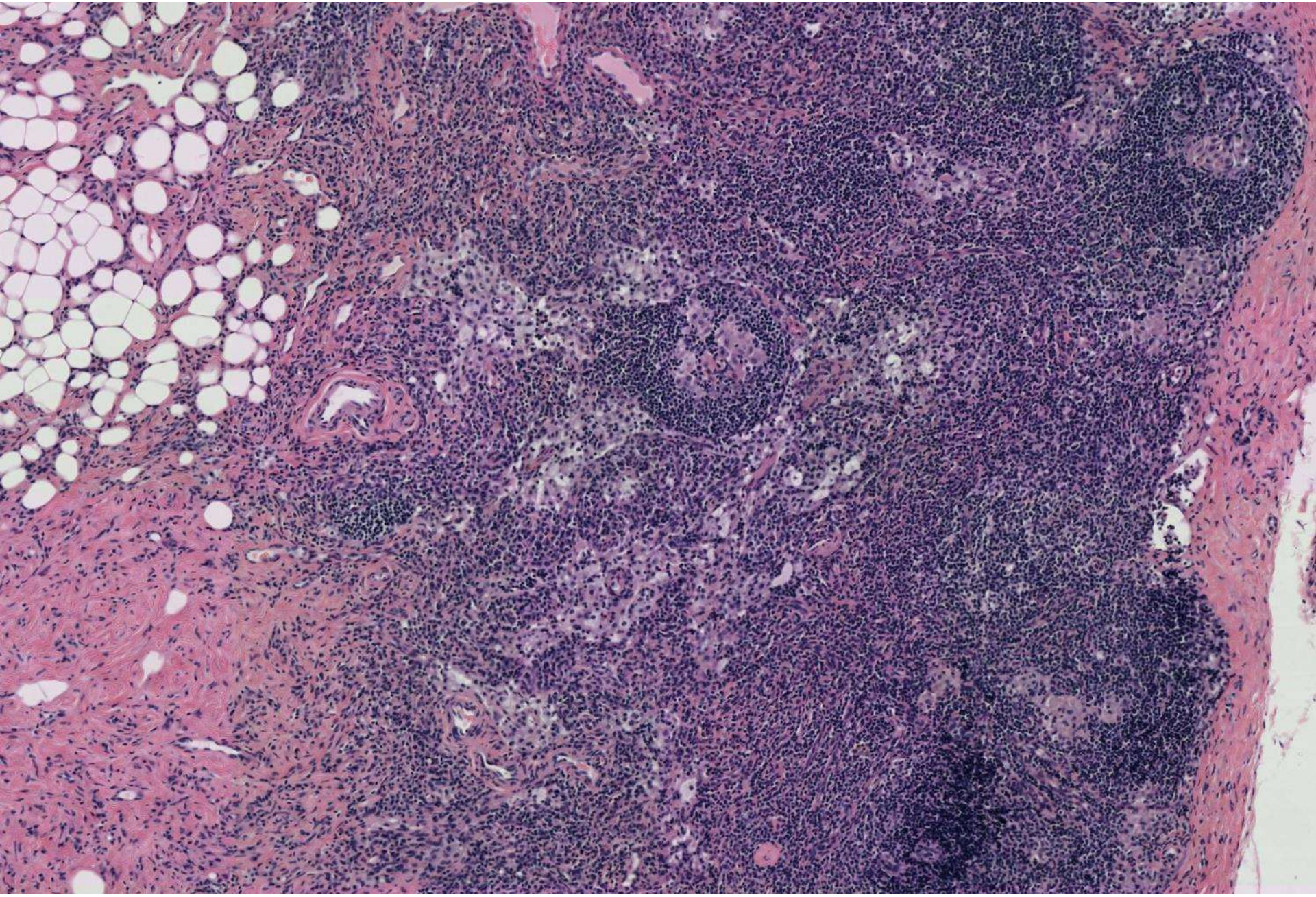
19-1001
scanned slide available!

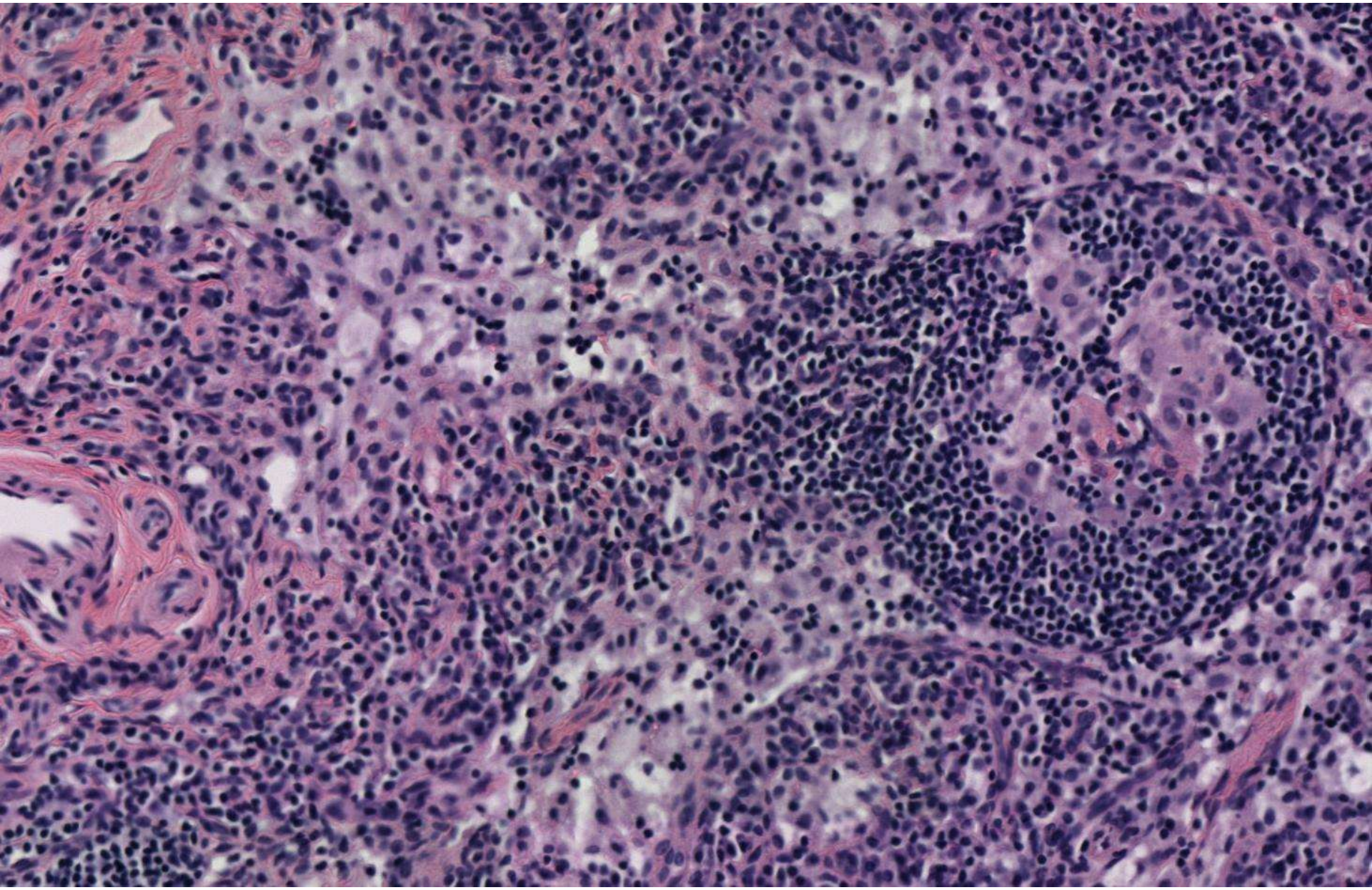
Keith Duncan; Mills-Peninsula

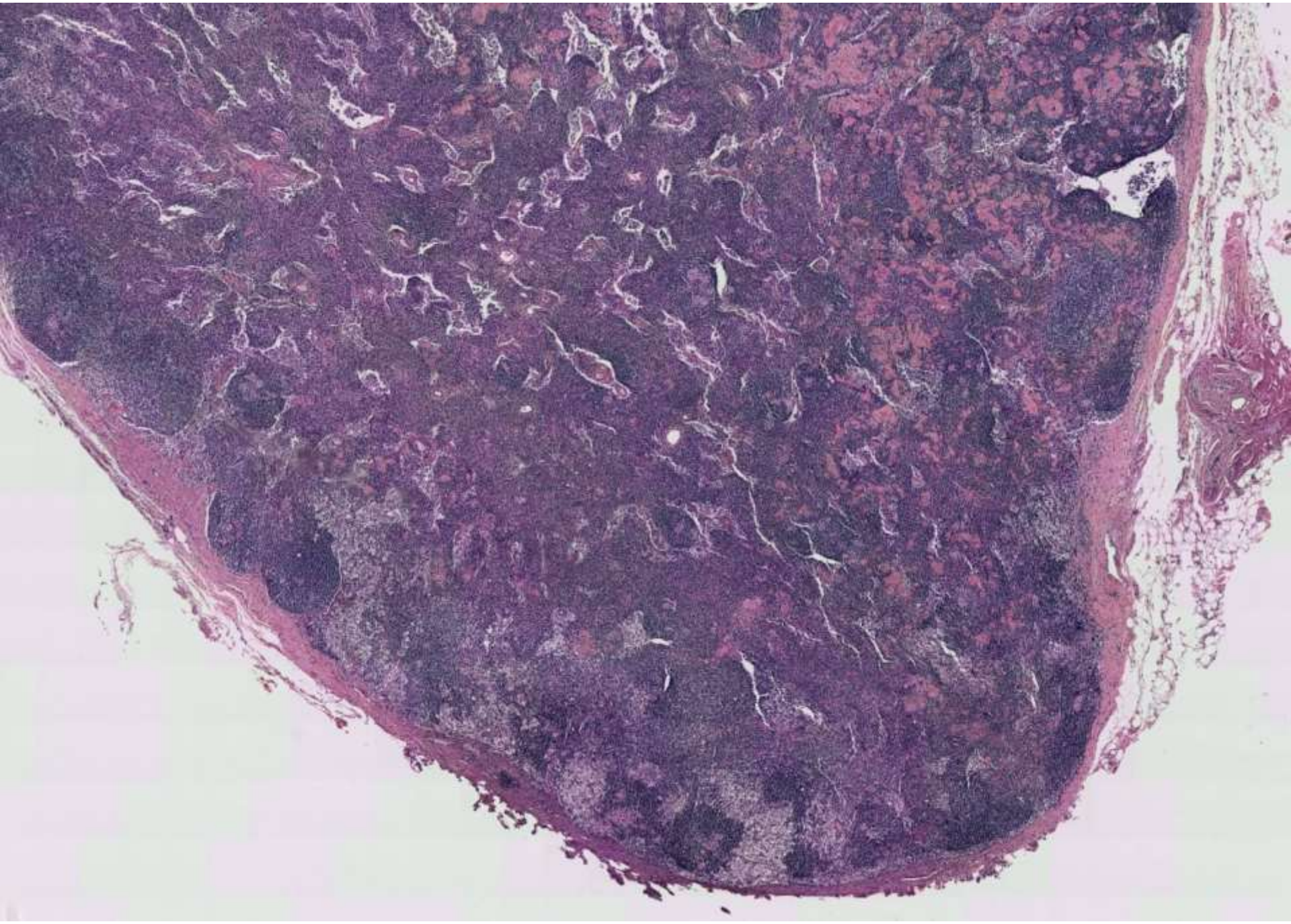
75-year-old male with weight loss and significant lymphadenopathy.

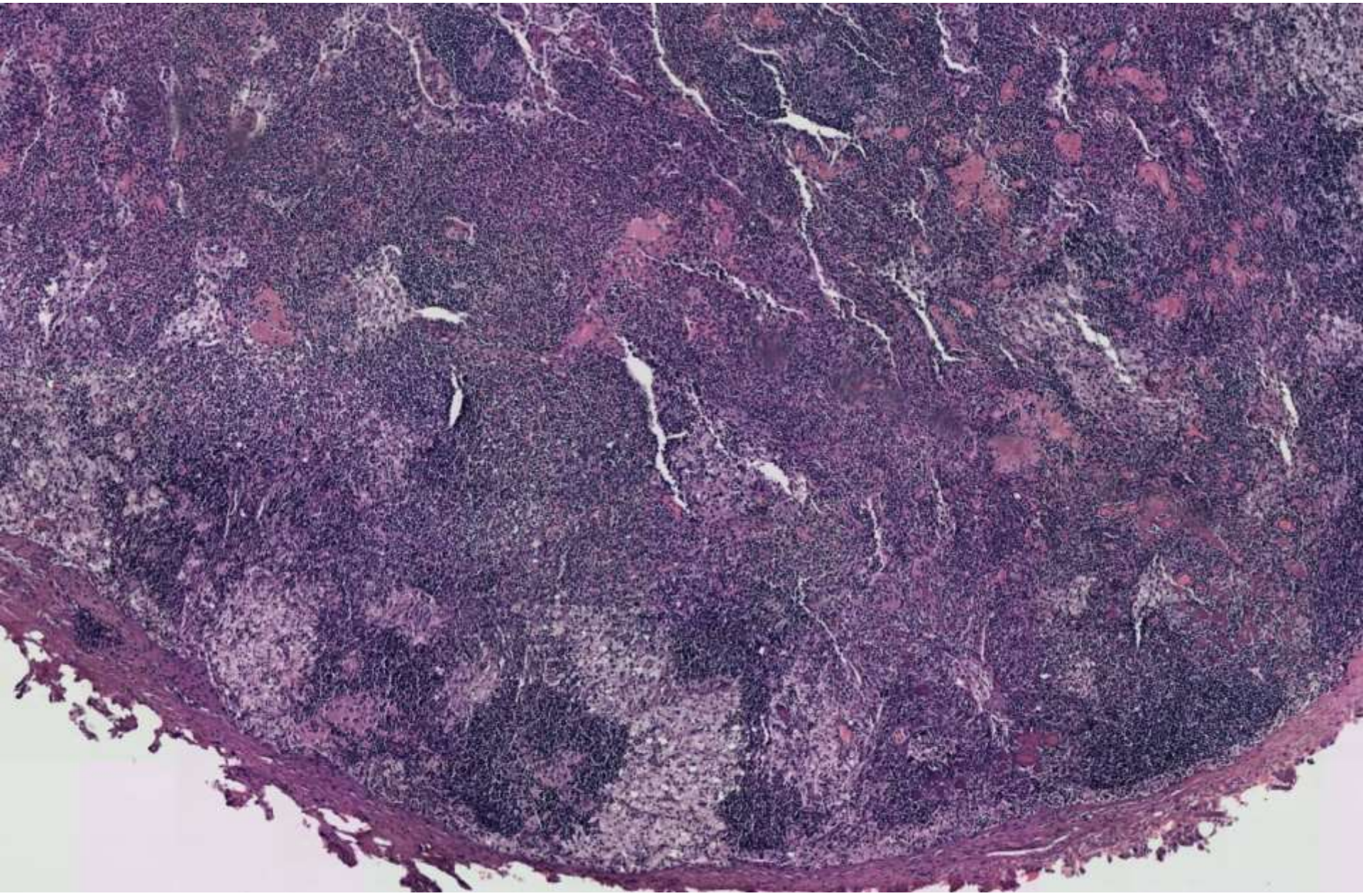


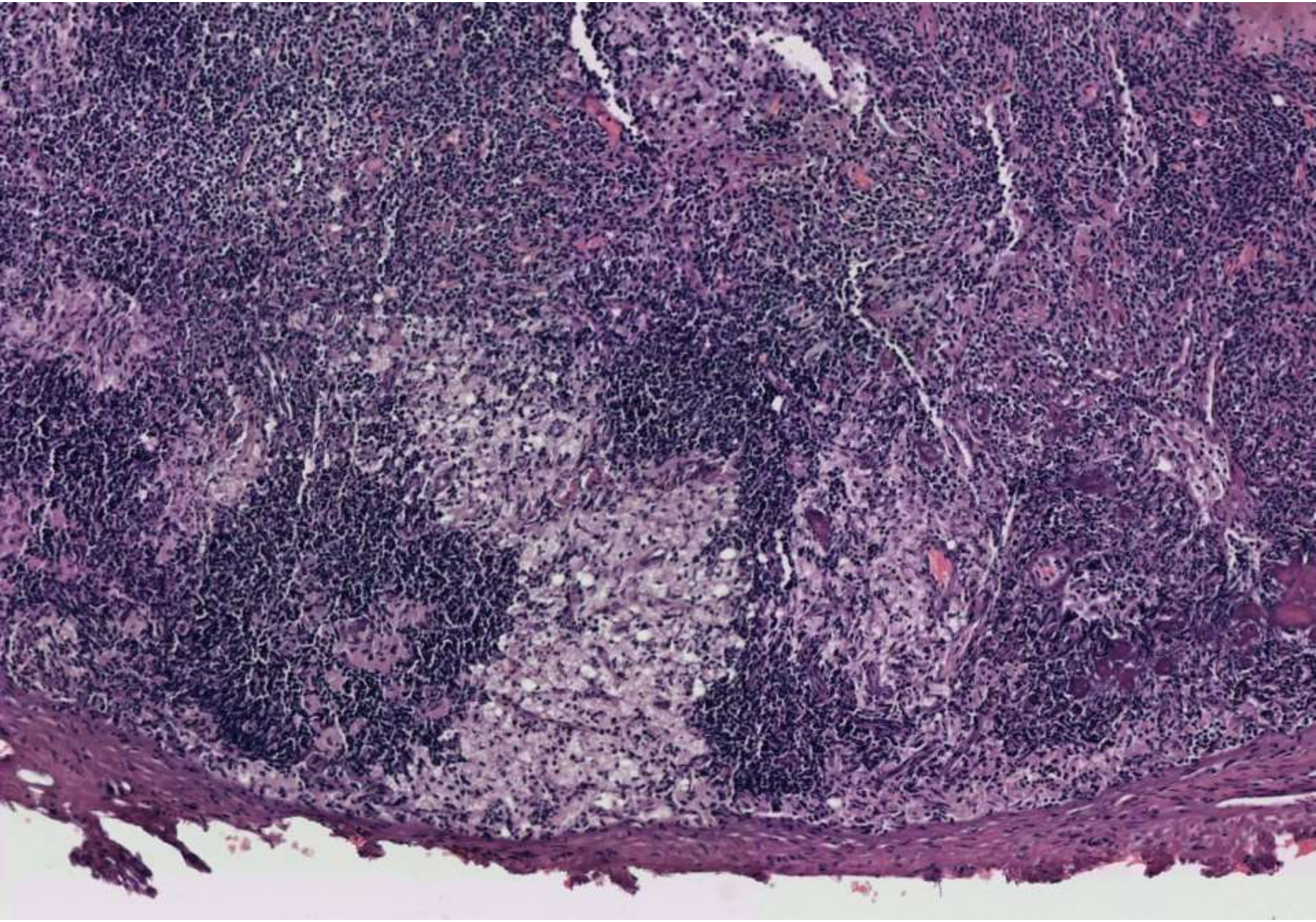


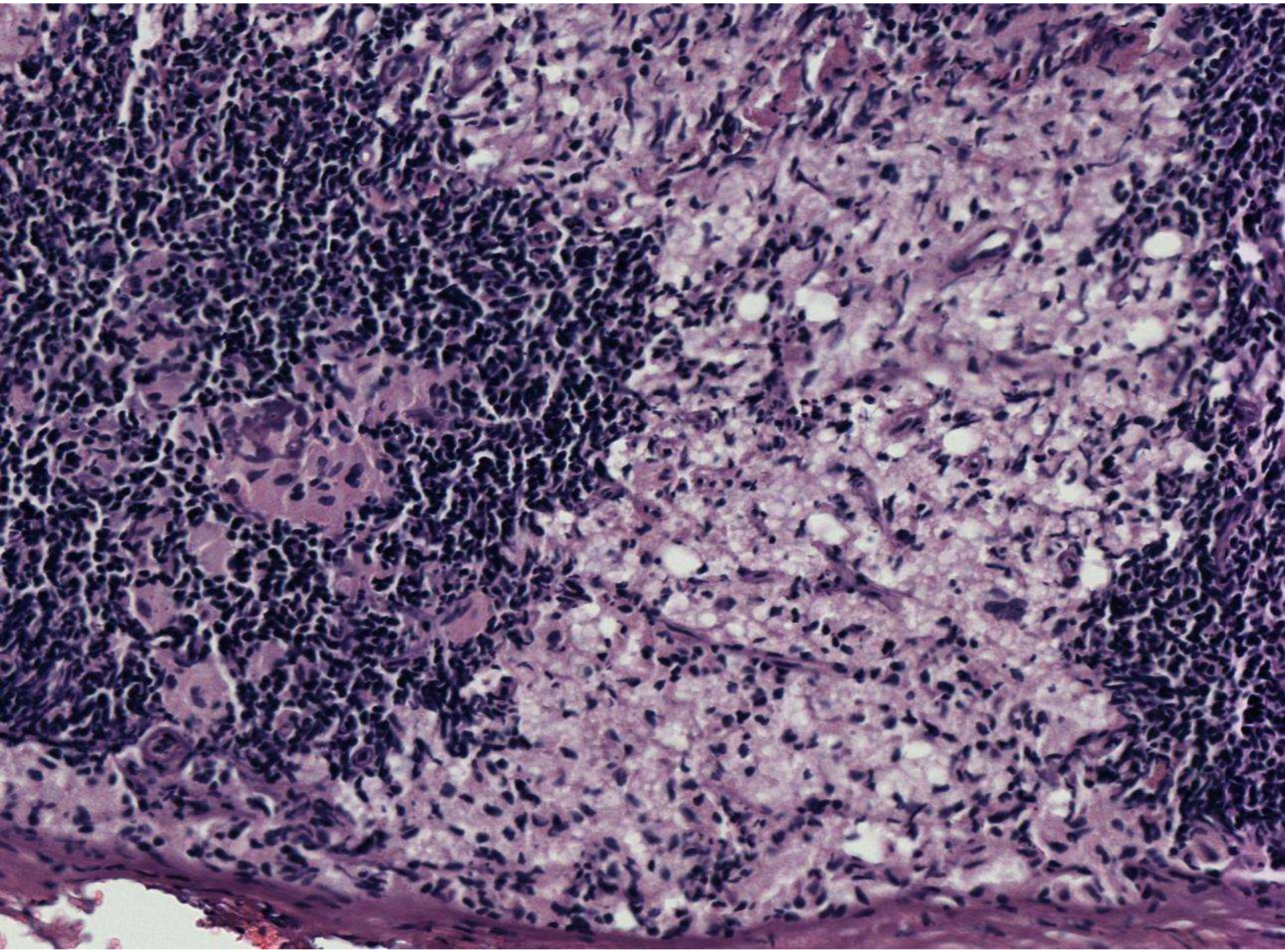


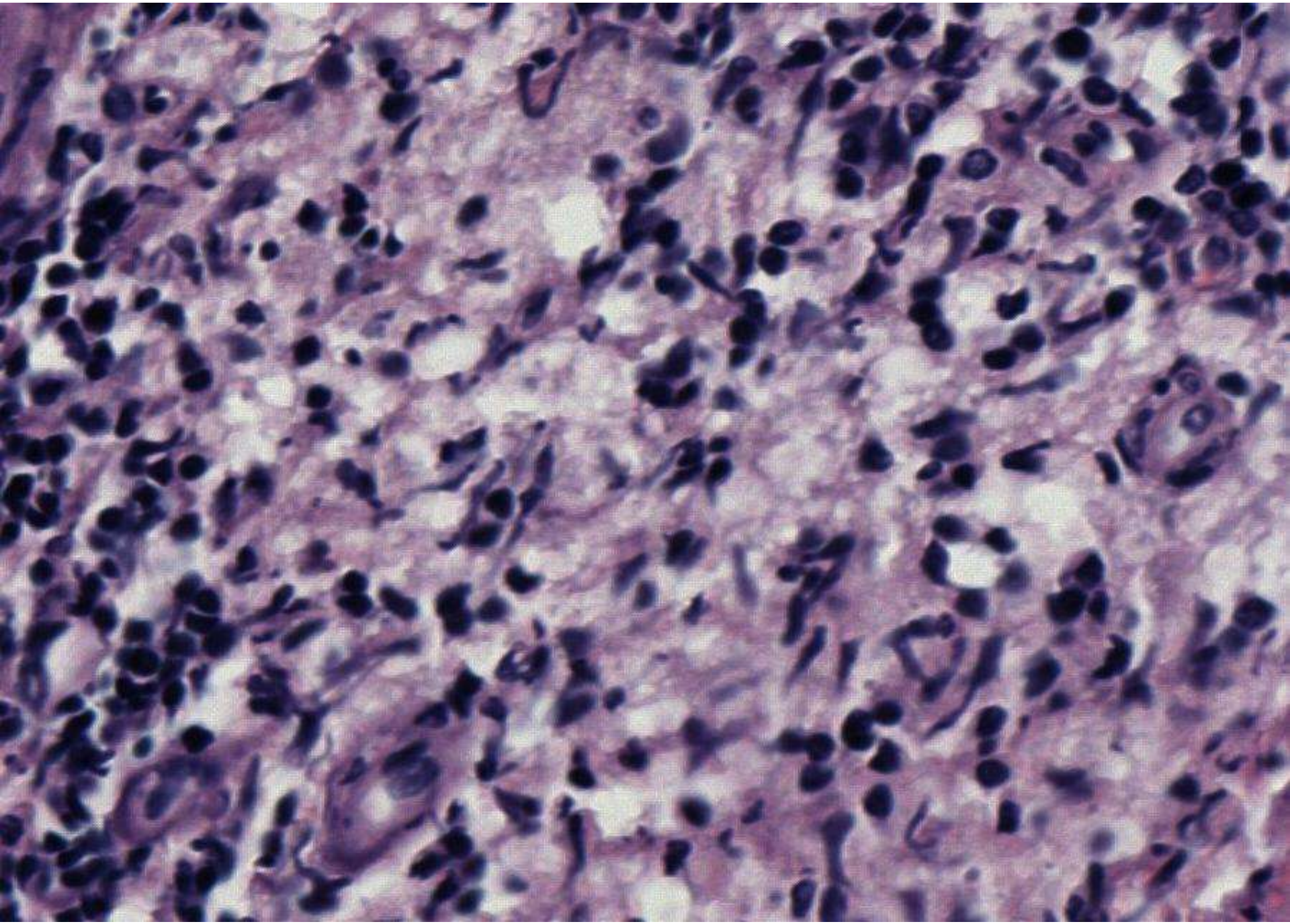


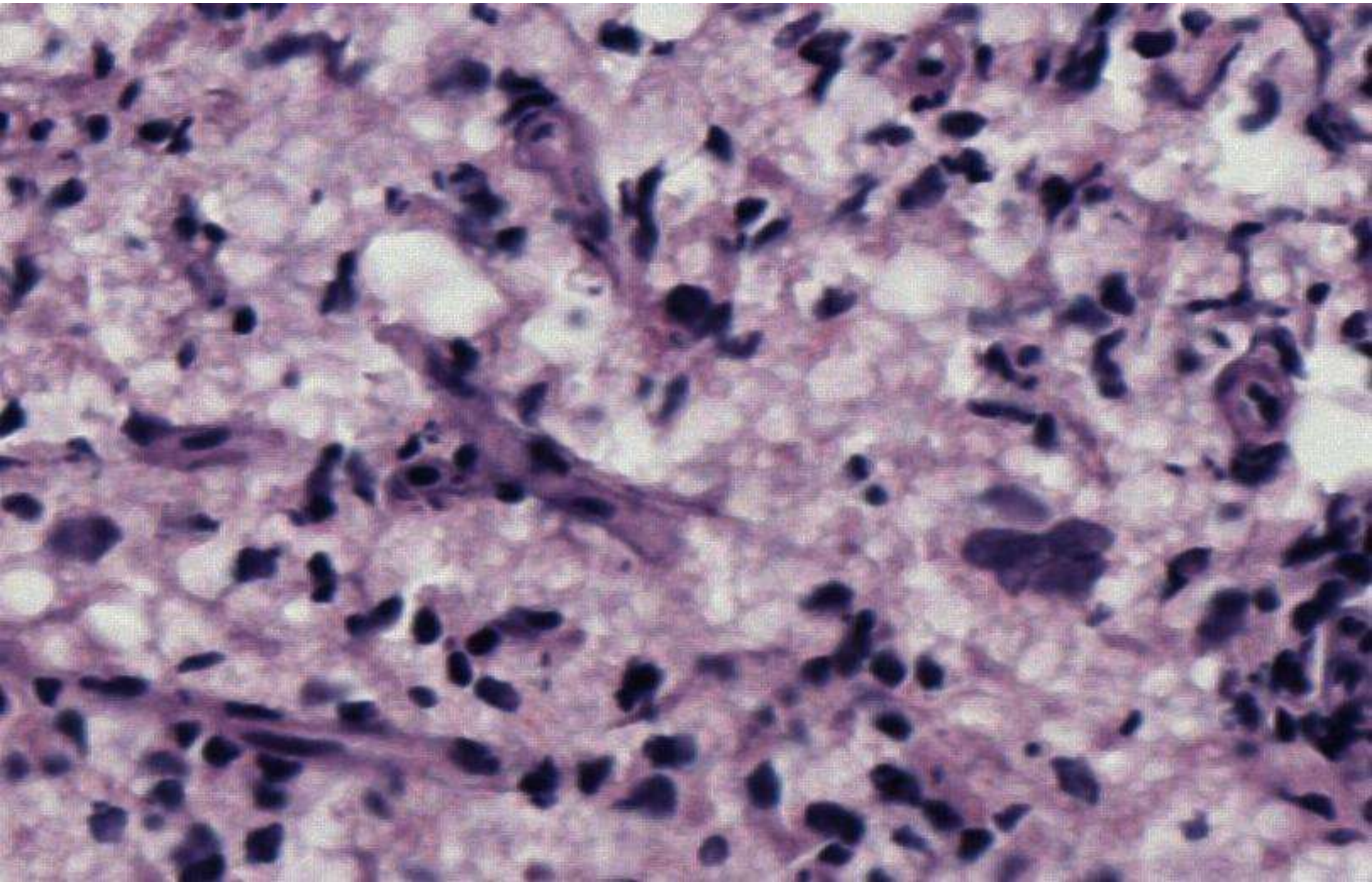


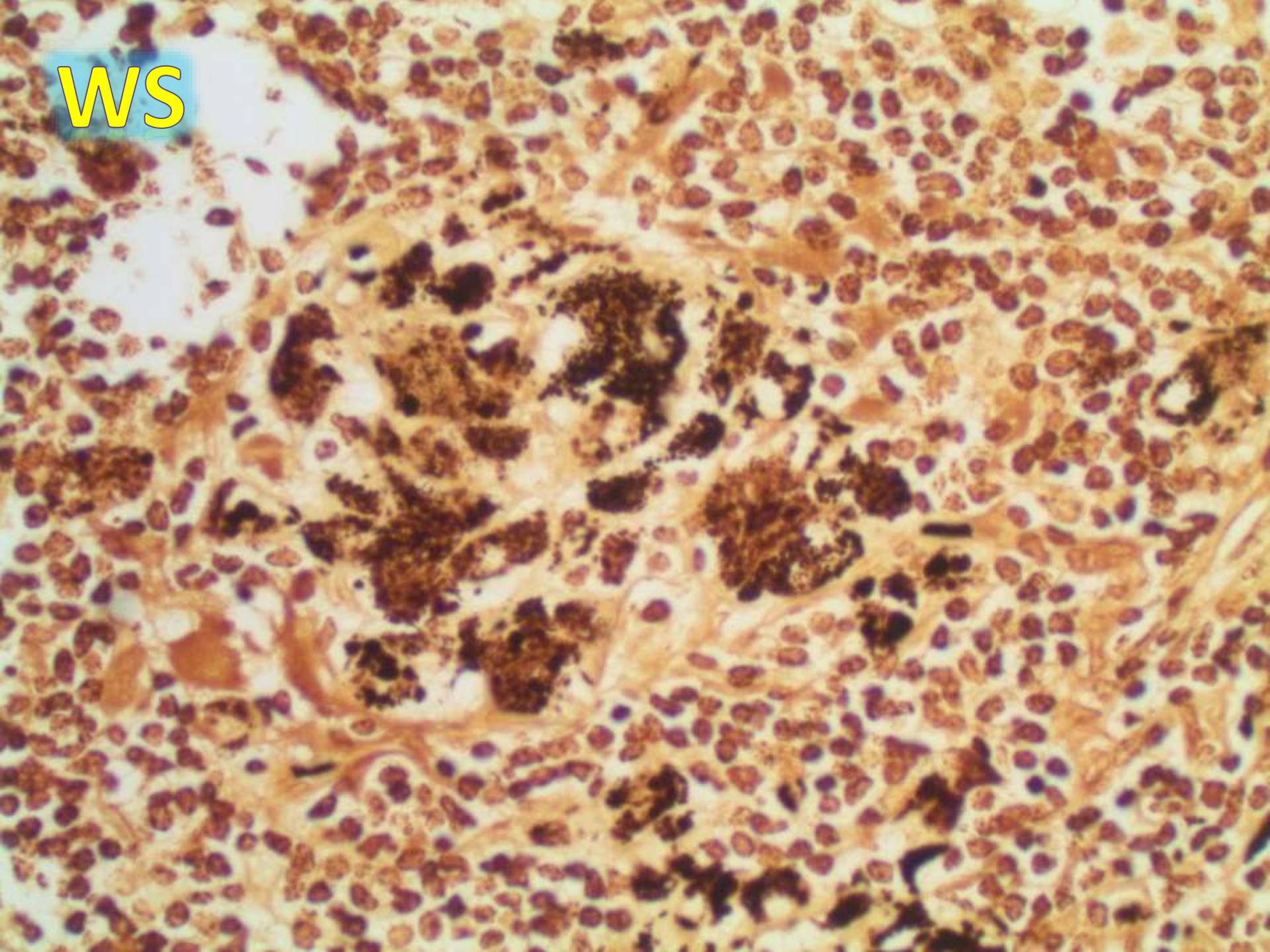








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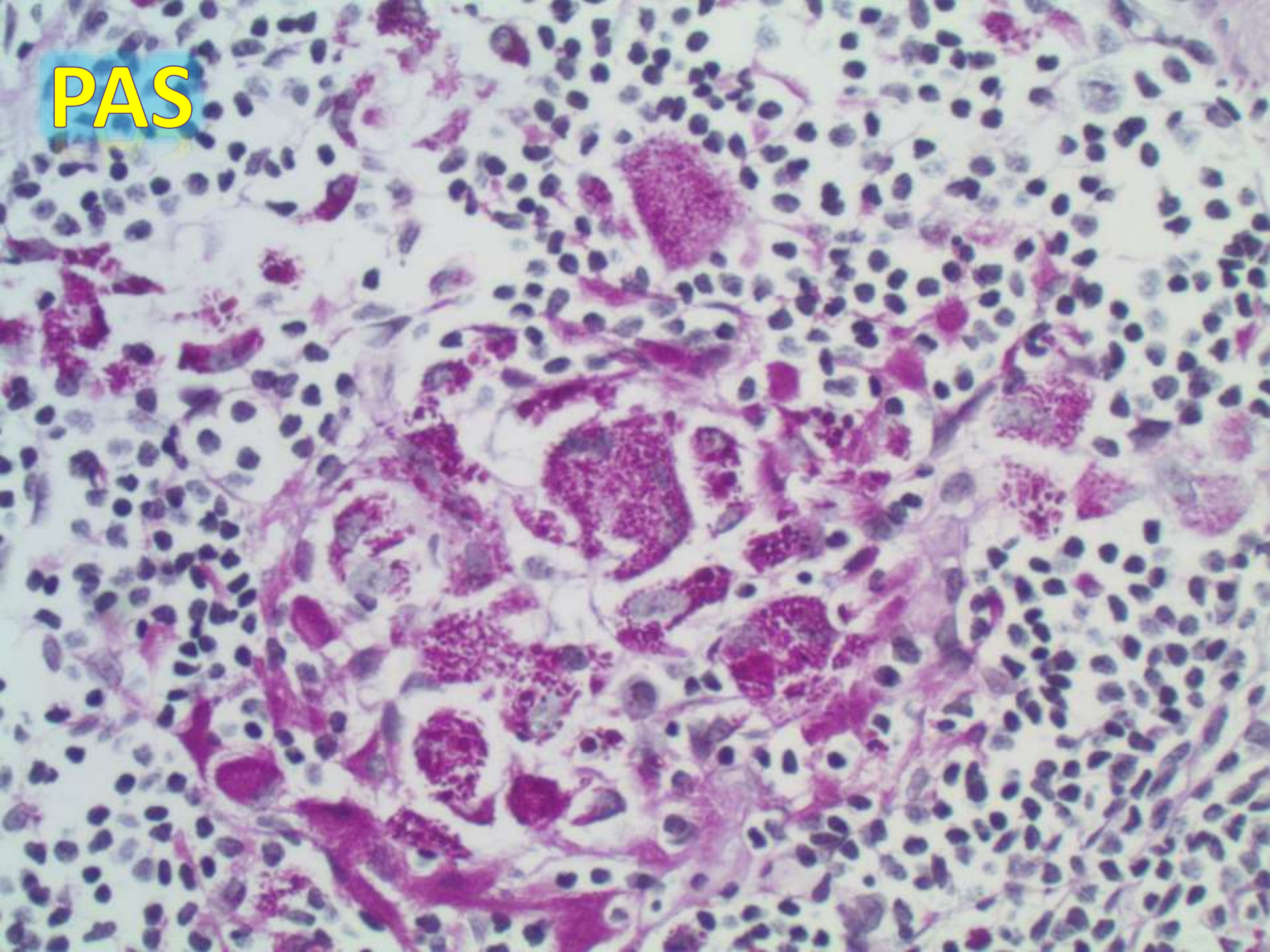
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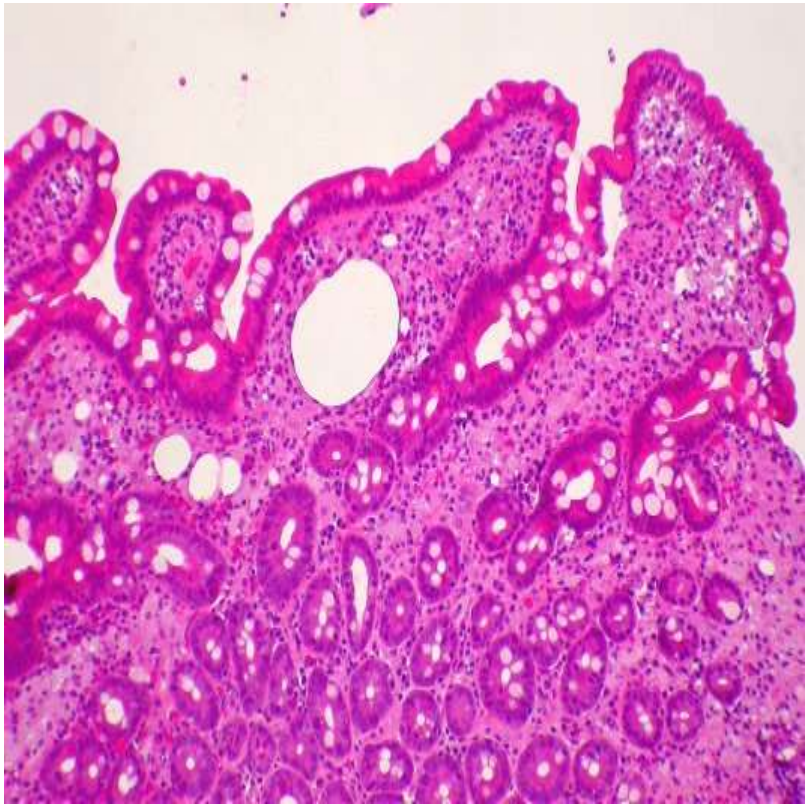
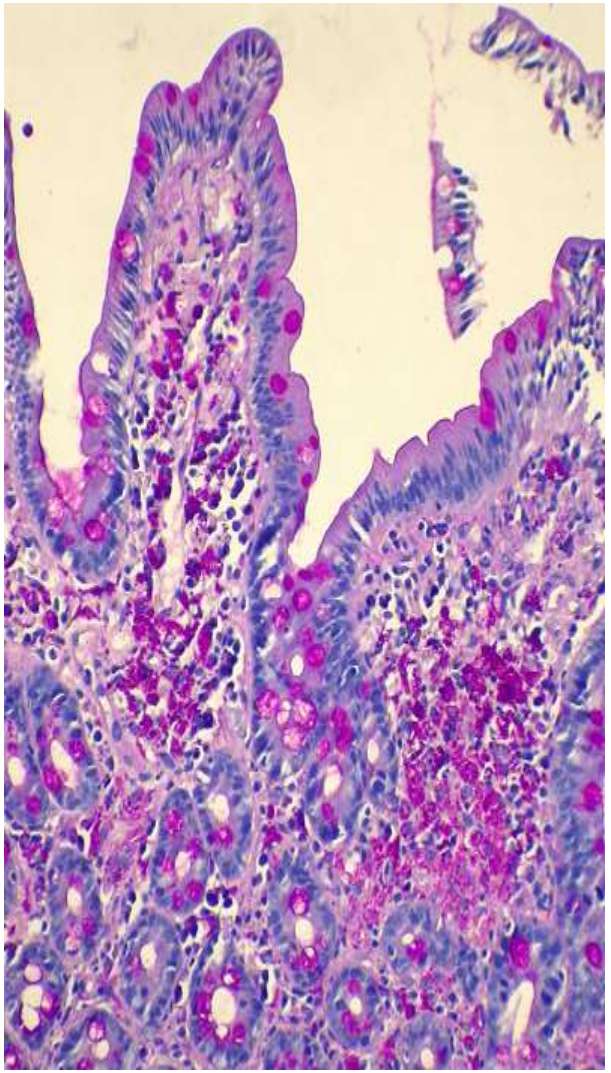
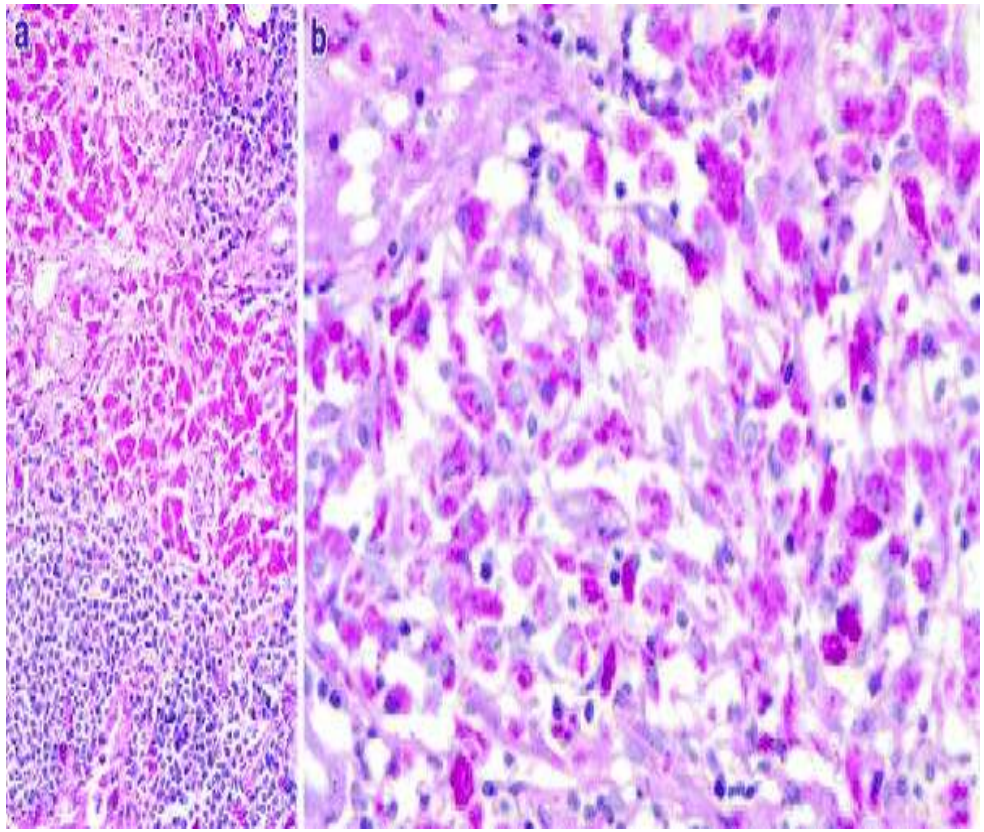





a
b

WHIPPLE DISEASE

- Rare; Infection by *Tropheryma whipplei*, present in soil and sewage
- Affects farmers and outdoor workers
- Symptoms include diarrhea, malabsorption, weight loss, fever, arthralgias; also occasional CNS and cardiac involvement
- May cause marked enlargement of mesenteric and periaortic LNs; enlargement of peripheral LNs may occur early
- Dx requires massive involvement of node plus intense PAS+ staining (small aggregates of PAS+ macrophages are nonspecific) or PCR

WHIPPLE DISEASE

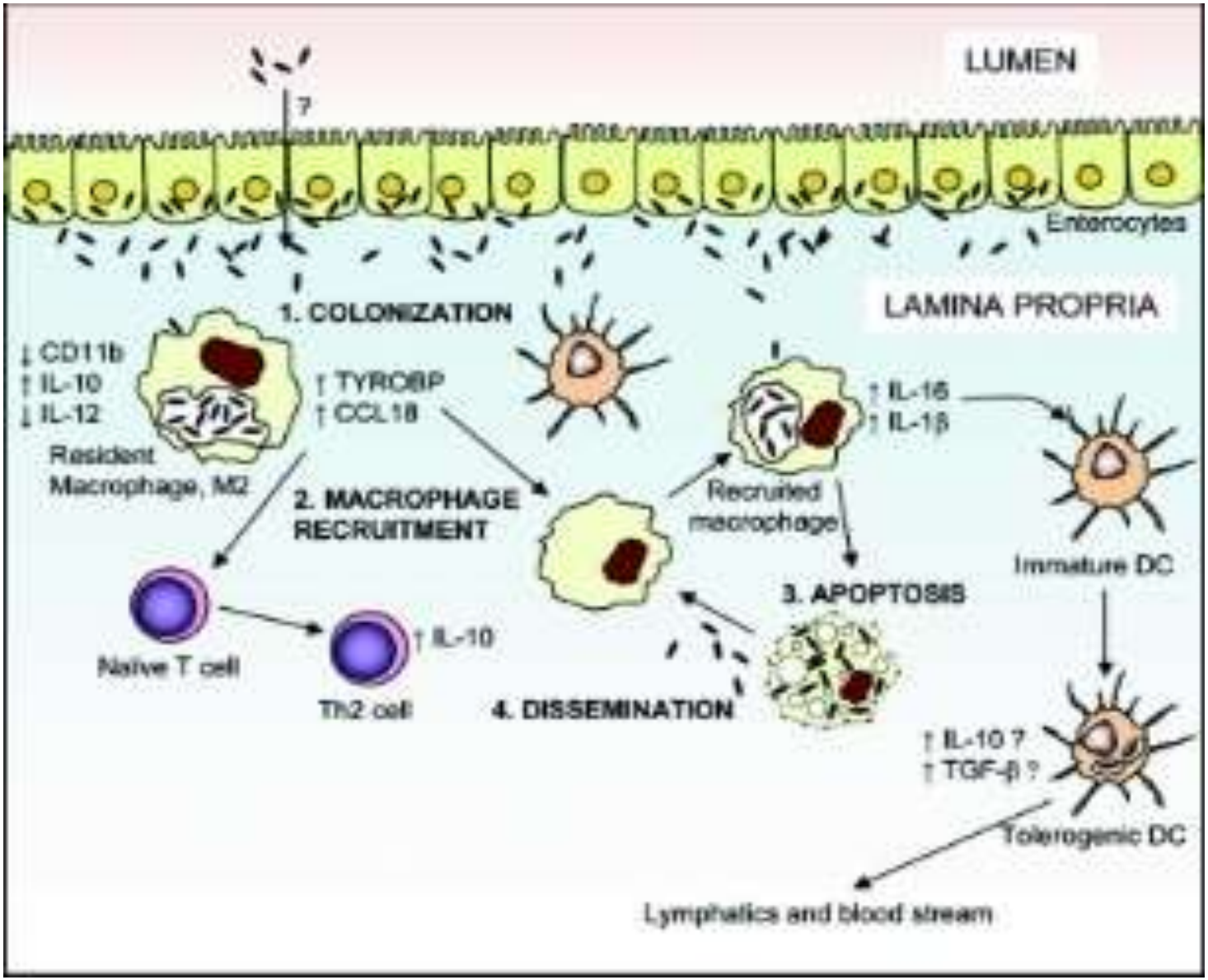
Microscopic description
Nodal architecture obscured by ill defined lipogranulomas
Involvement of sinuses by macrophages with foamy cytoplasm

Positive stains
•PAS+ diastase resistant bacilli within histiocytes
•Immunostains for bacteria (Am J Clin Pathol 2002;118:742)
•PCR

Differential diagnosis of lipogranulomas

Secondary to inflammatory and neoplastic conditions or primary lesion of LN
Commonly due to mineral oil ingestion or total parenteral nutrition
Fabry disease

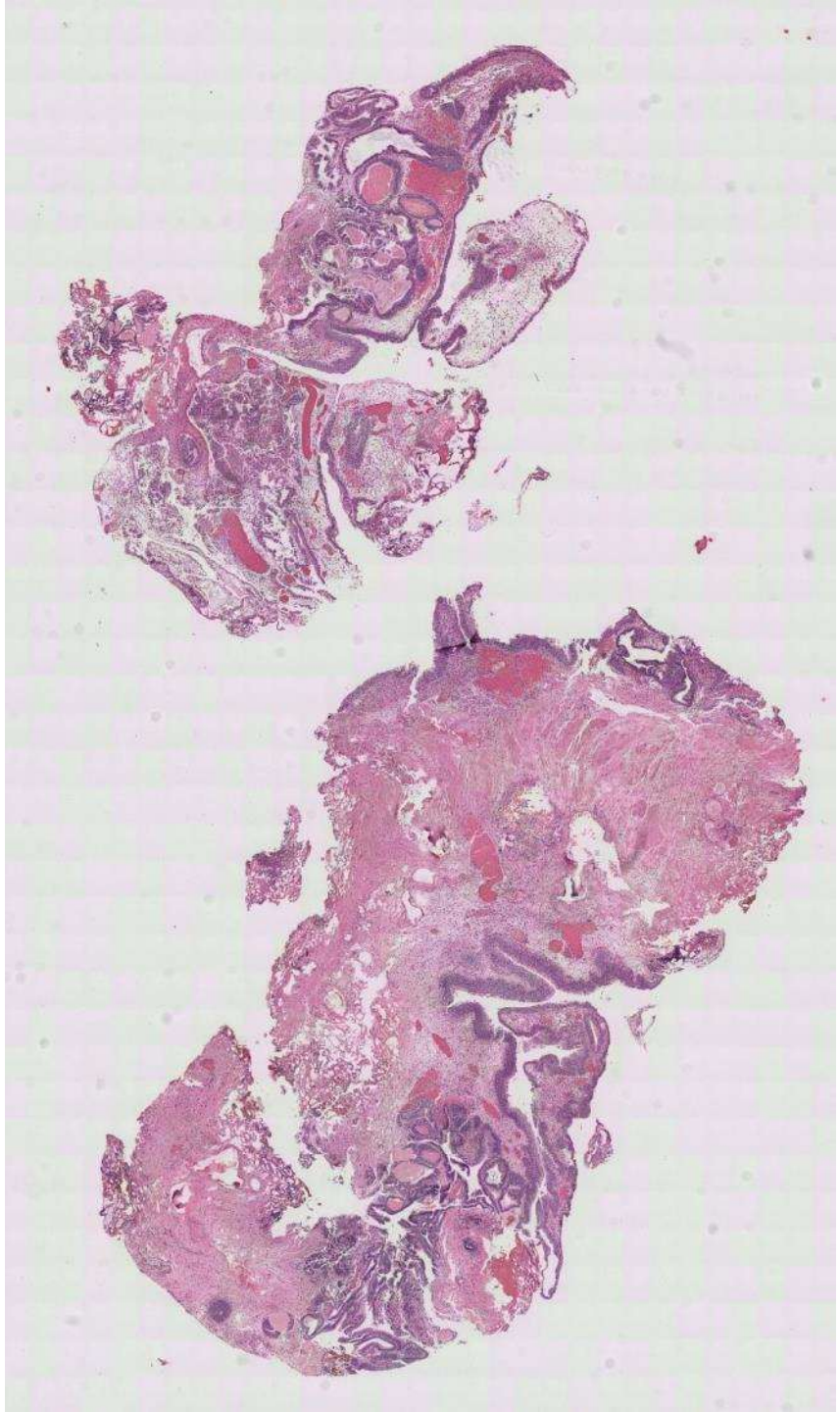
Whipple's disease: surprised by the surprise
Jean-Christophe Lagier, Florence Fenollar, Didier Raoult
LANCET VOL. 384, ISS. 9949, P1184-85, SEPT. 27, 2014

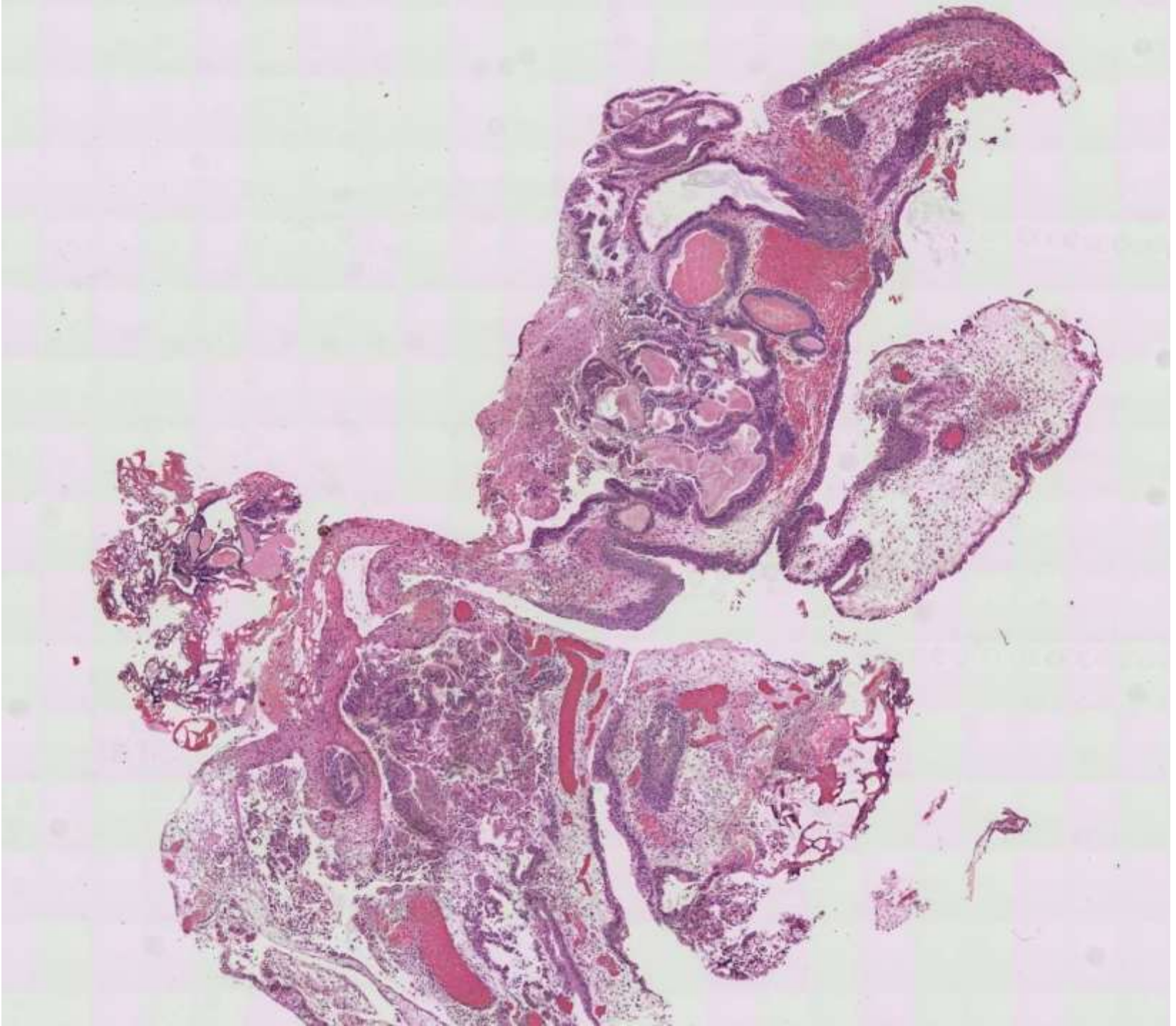

LUMEN
?
Enterocytes
LAMINA PROPRIA
1. COLONIZATION
↓ CD11b
↑ IL-10
↓ IL-12
Resident
Macrophage, M2
↑ TYROBP
↑ CCL18
2. MACROPHAGE
RECRUITMENT
Recruited
macrophage
↑ IL-1α
↑ IL-1β
Immature DC
3. APOPTOSIS
Naive T cell
↑ IL-10
Th2 cell
4. DISSEMINATION
↑ IL-10 ?
↑ TGF-β ?
Tolerogenic DC
Lymphatics and blood stream

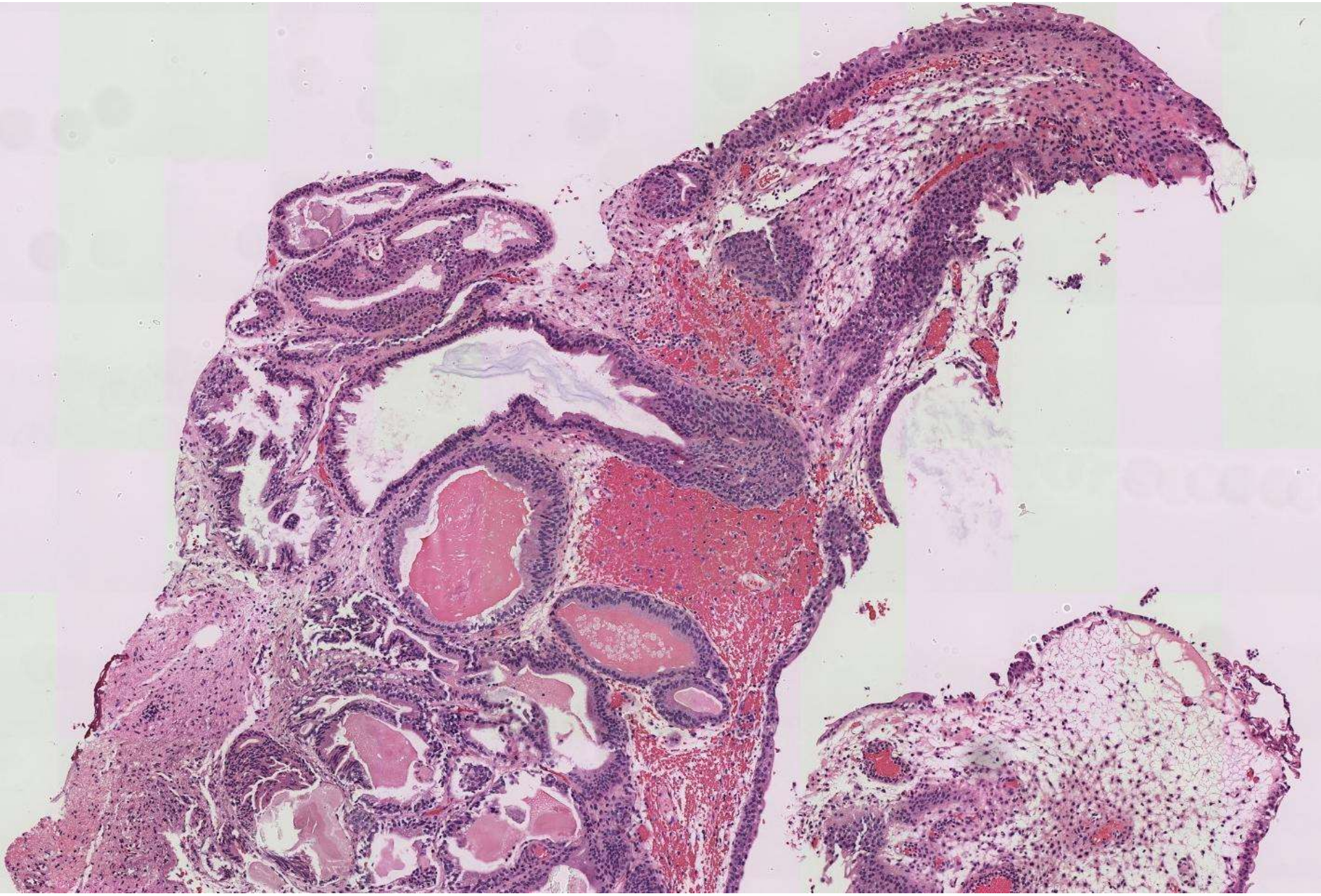
19-1002
scanned slide available!

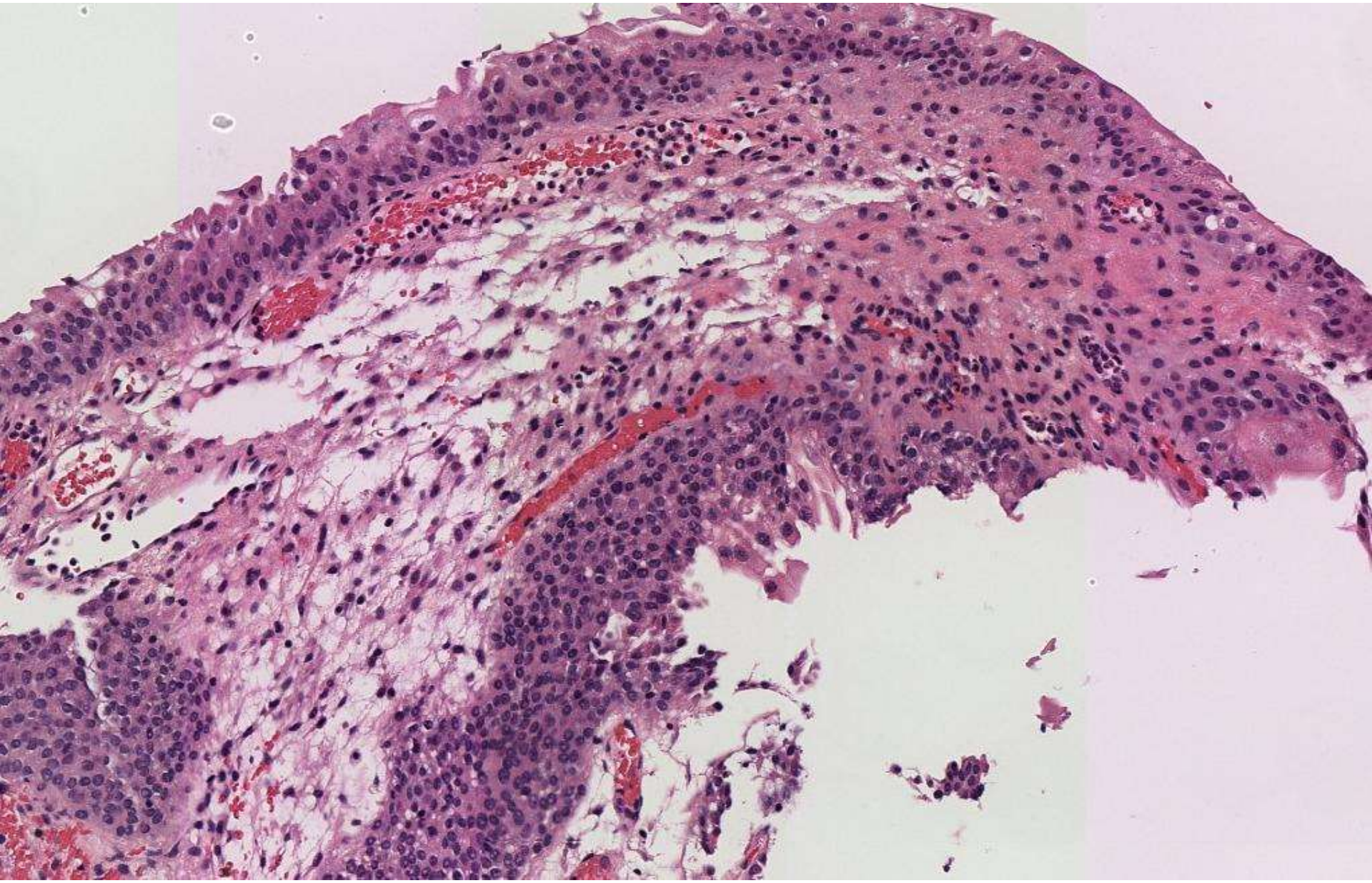
Ankur Sangoi; El Camino Hospital

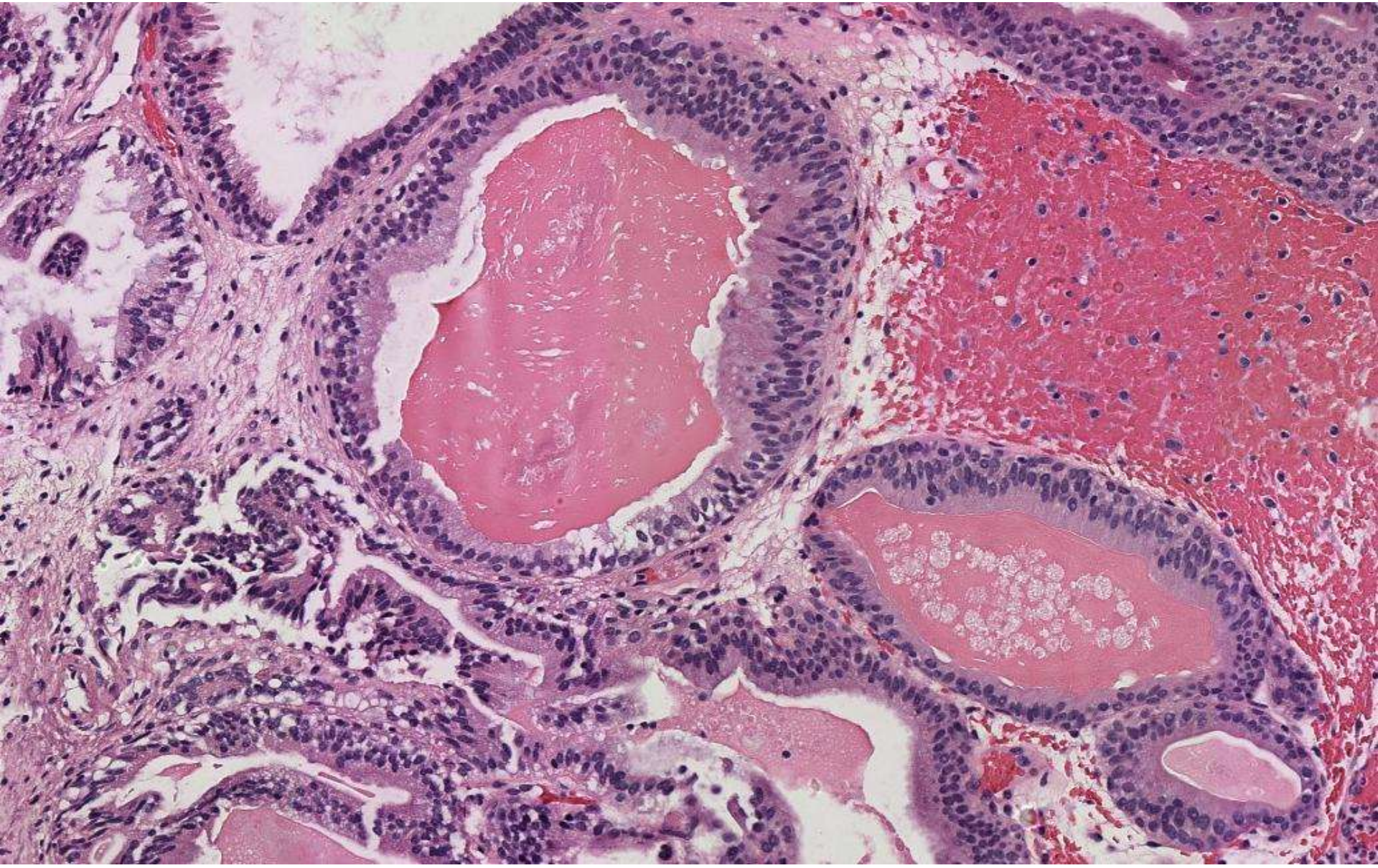
76-year-old male with hematuria. On cystoscopy, found to have bladder lesion.

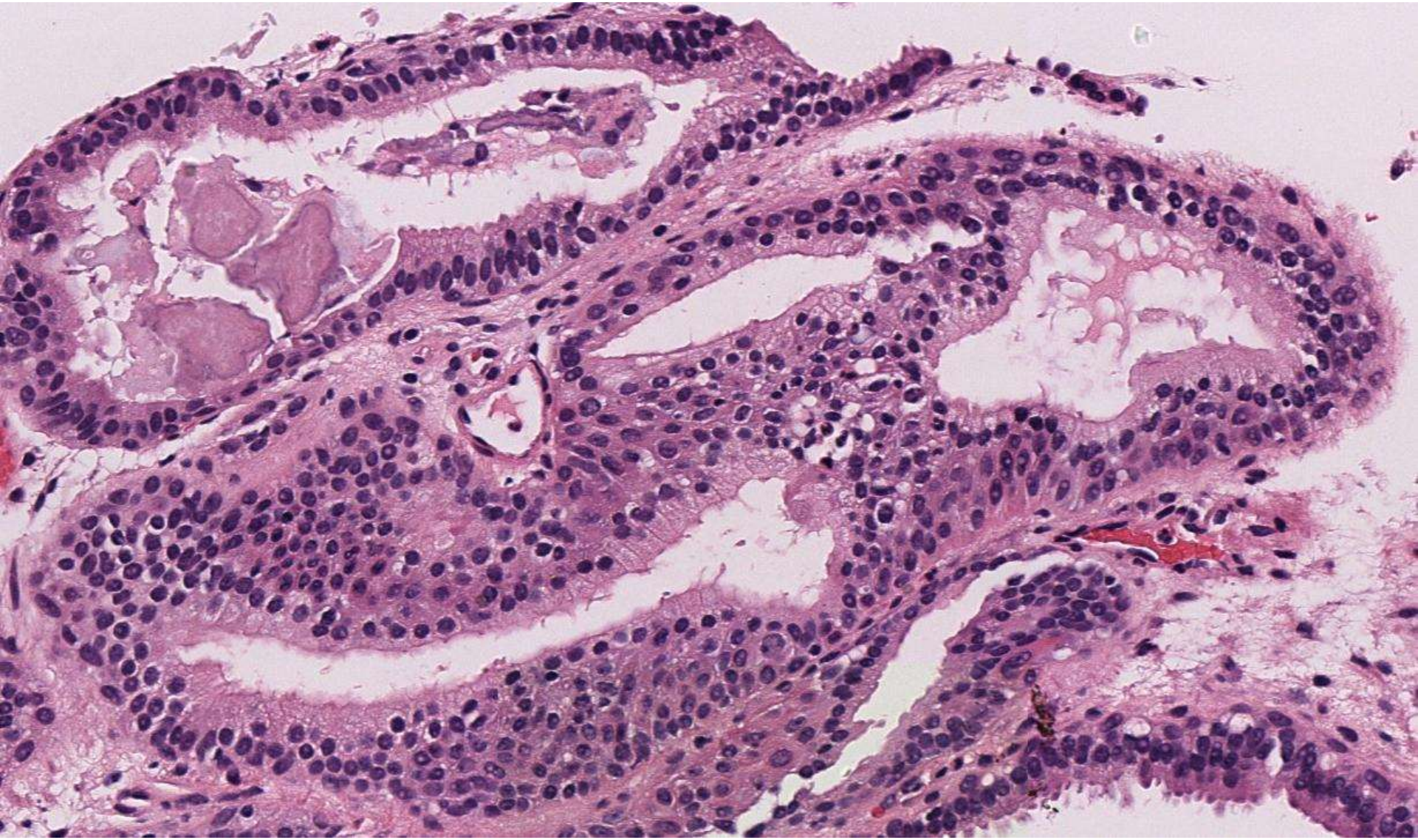


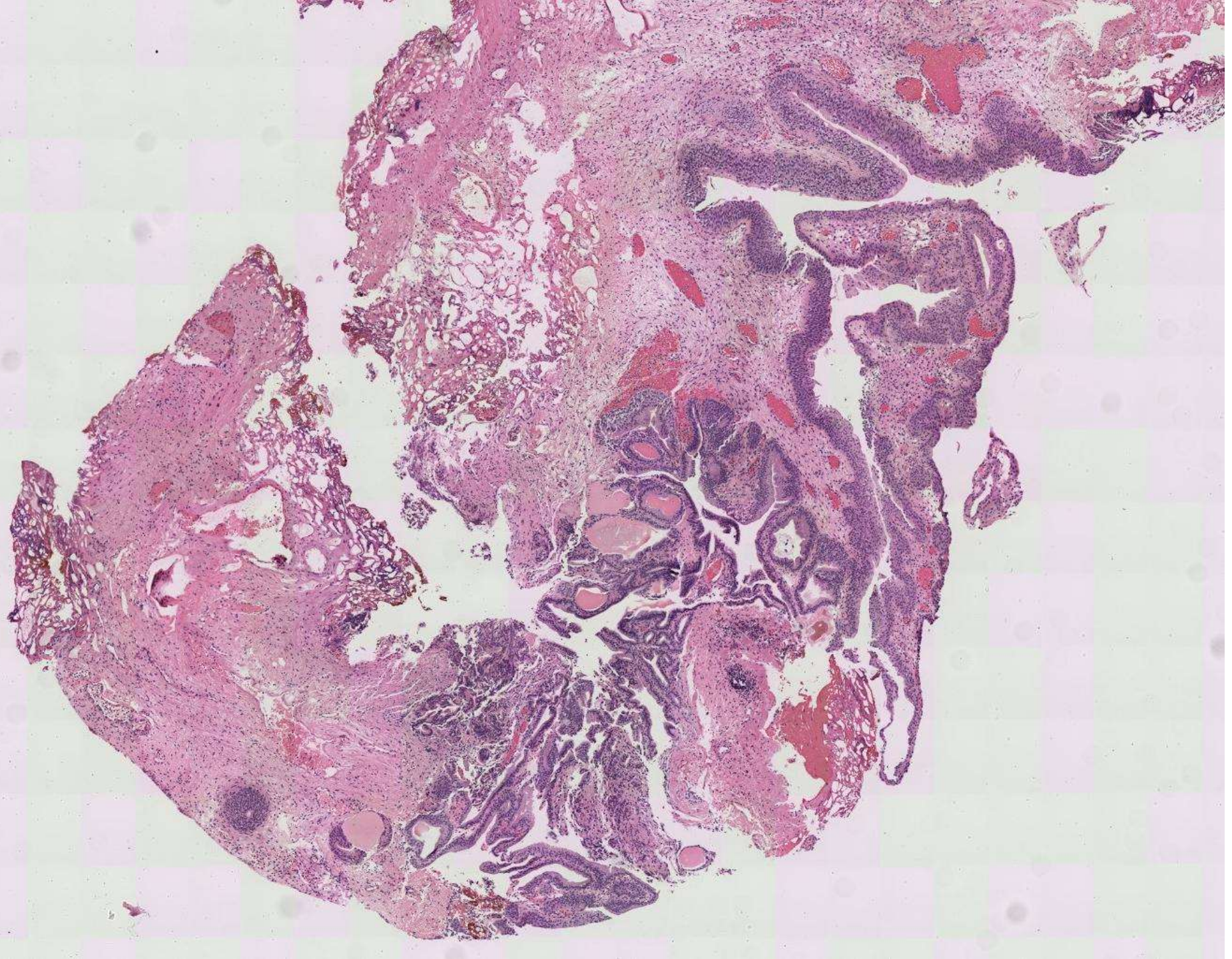


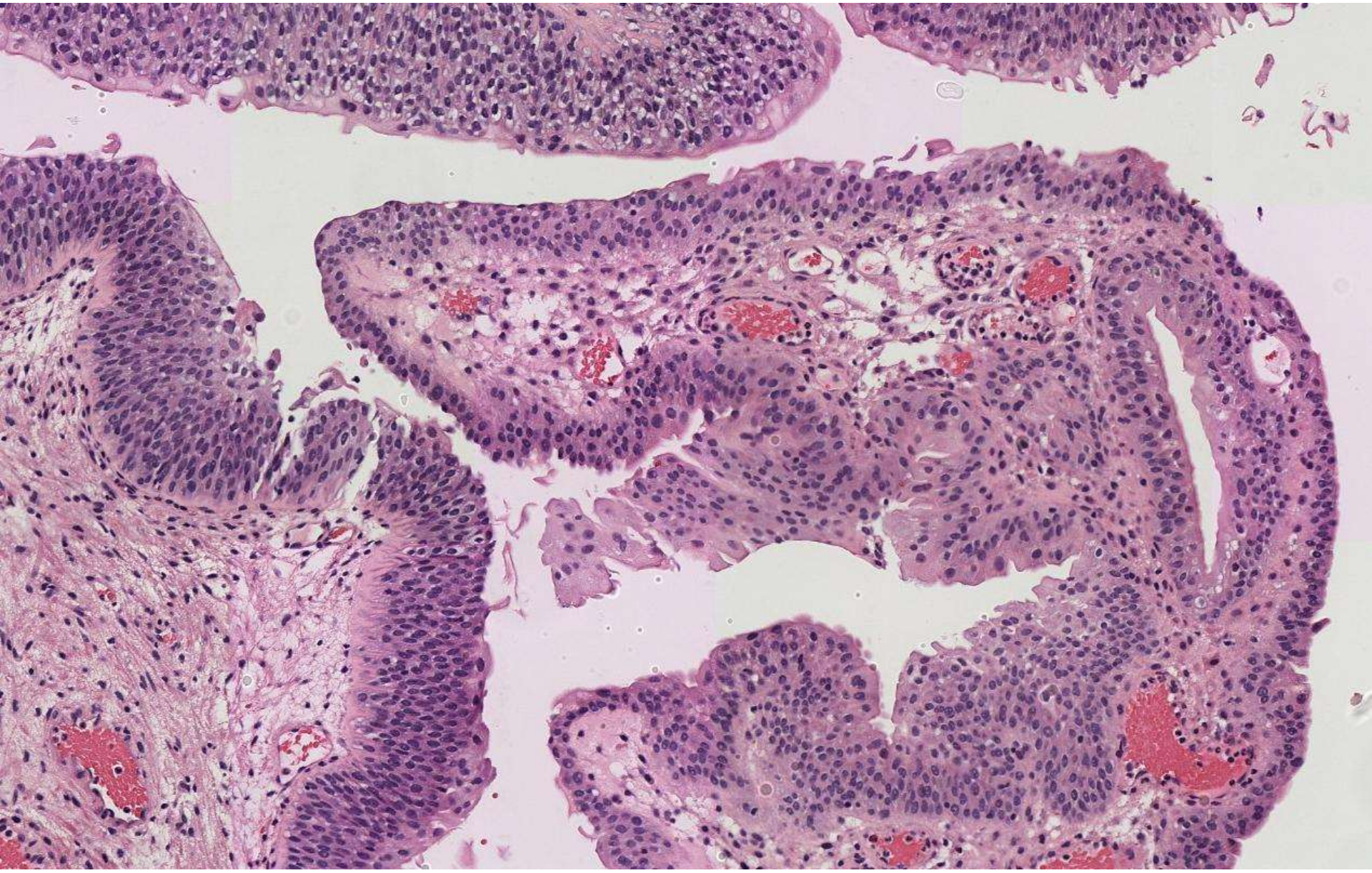


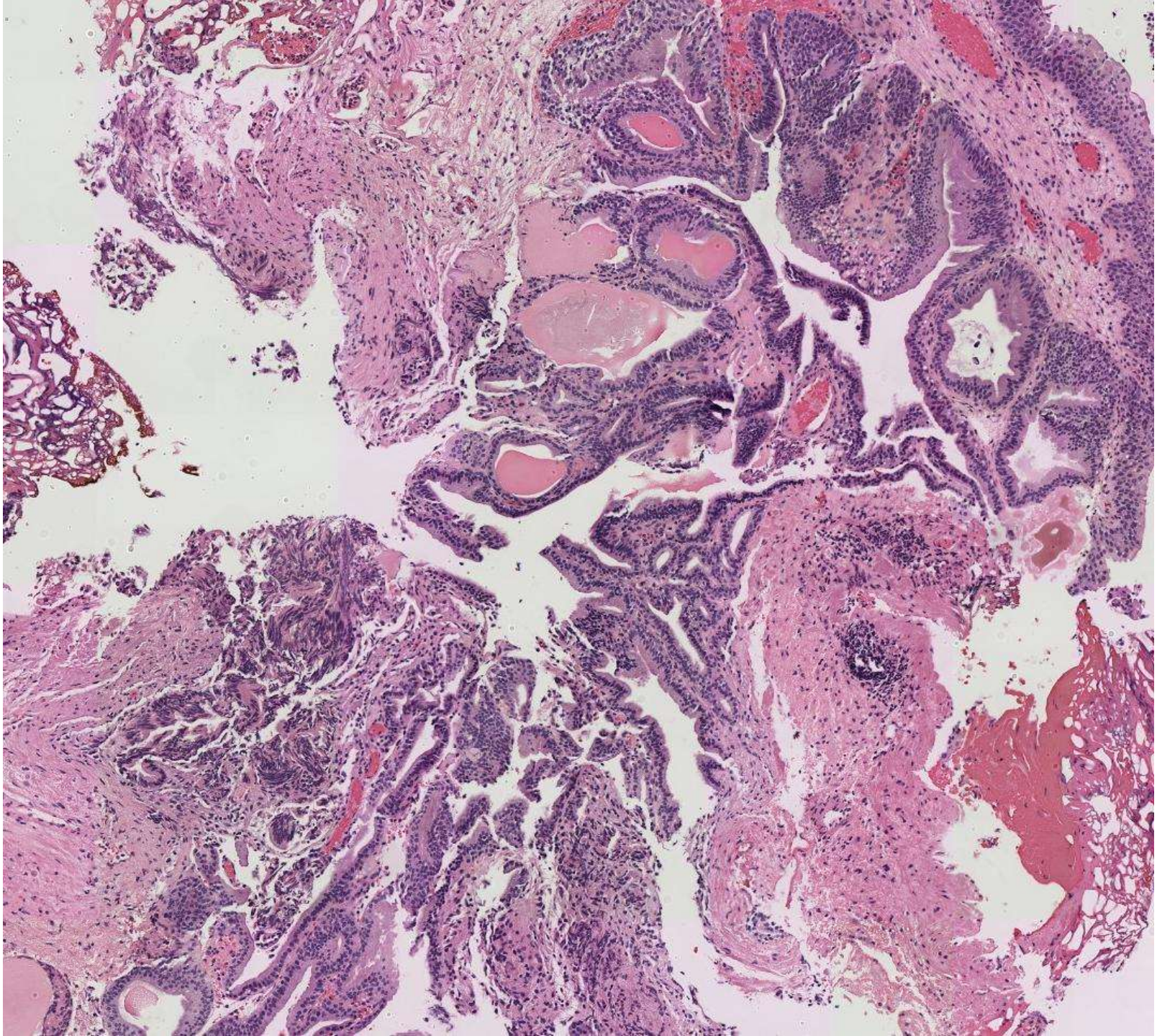


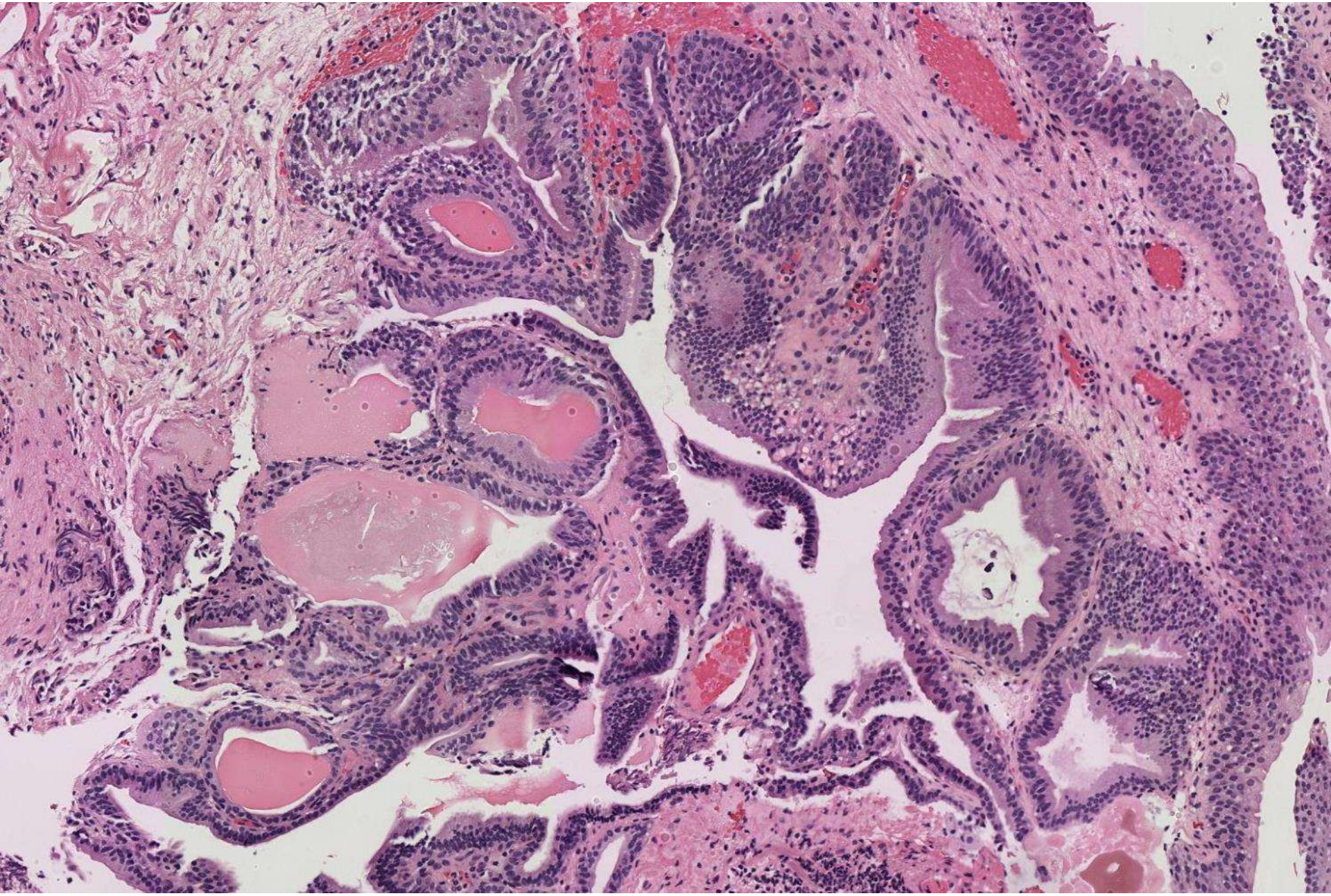


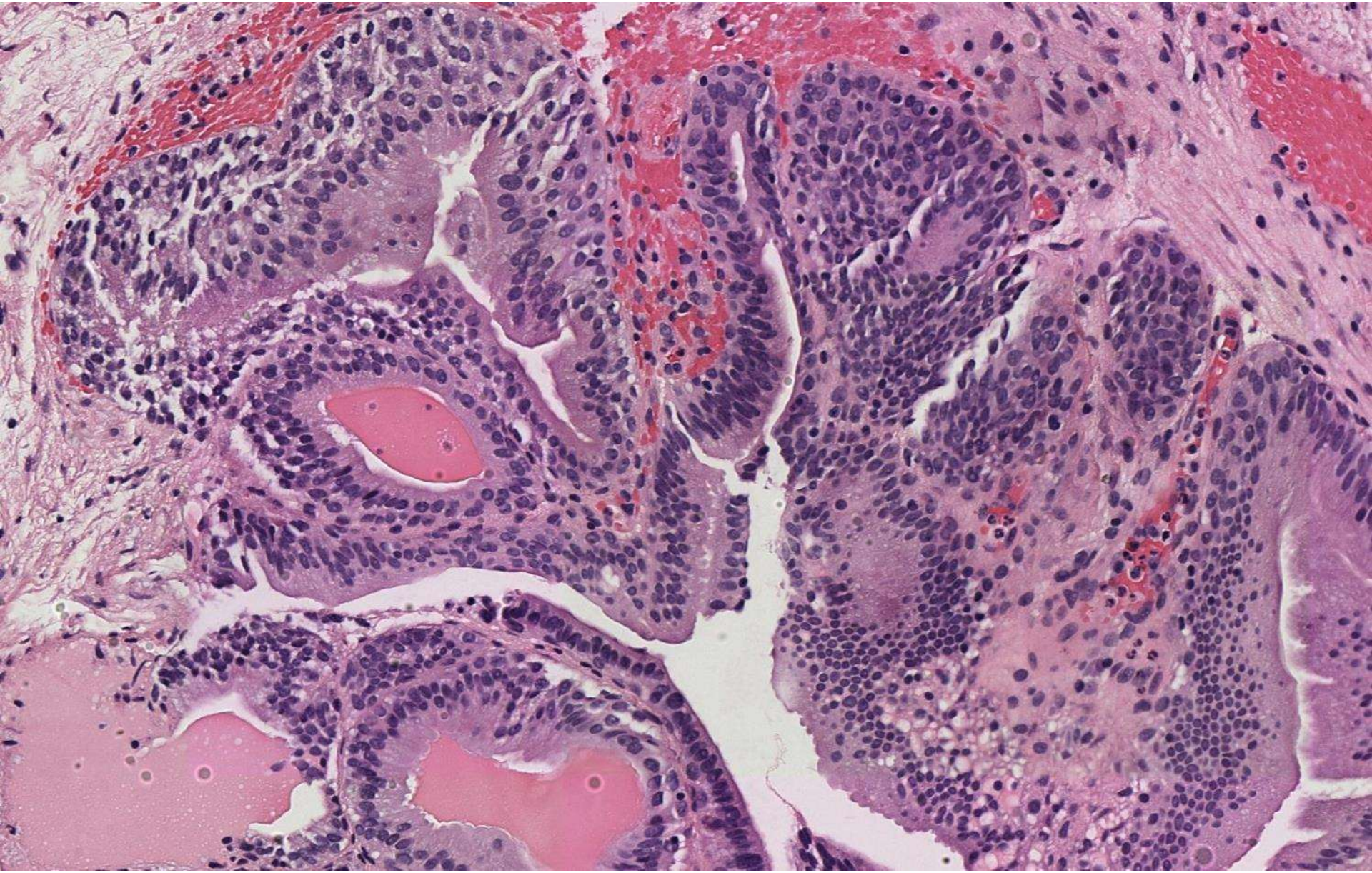


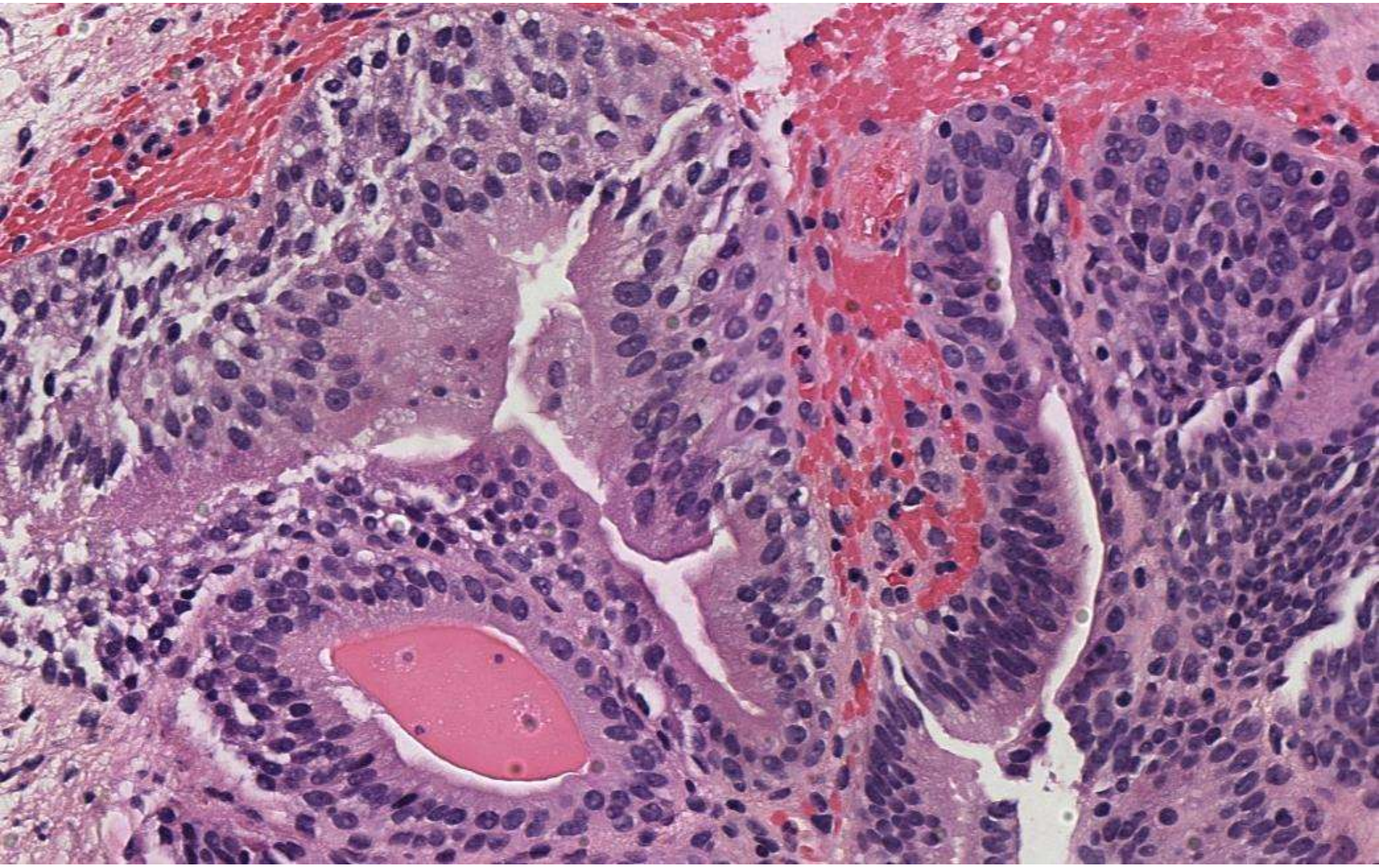






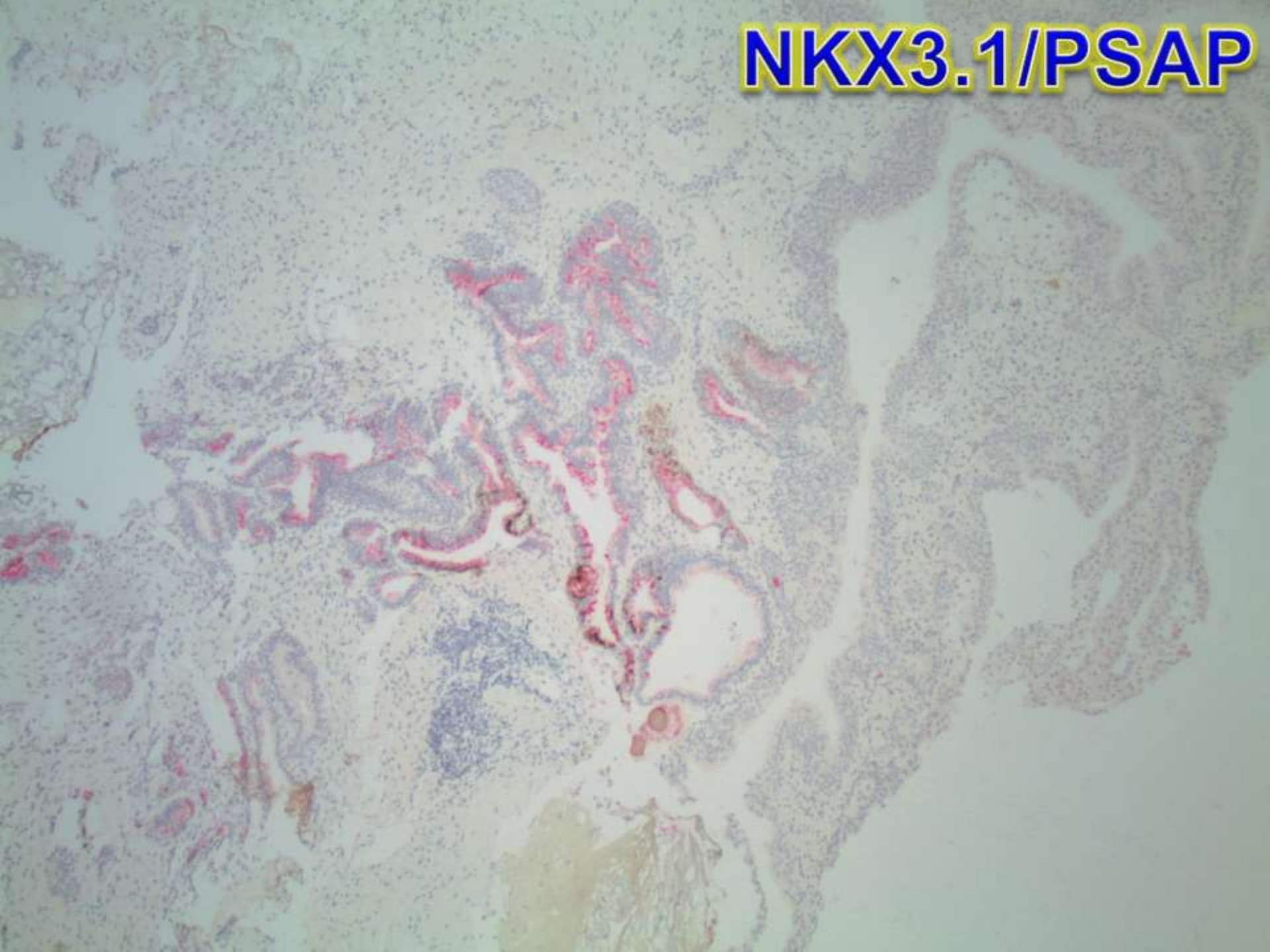


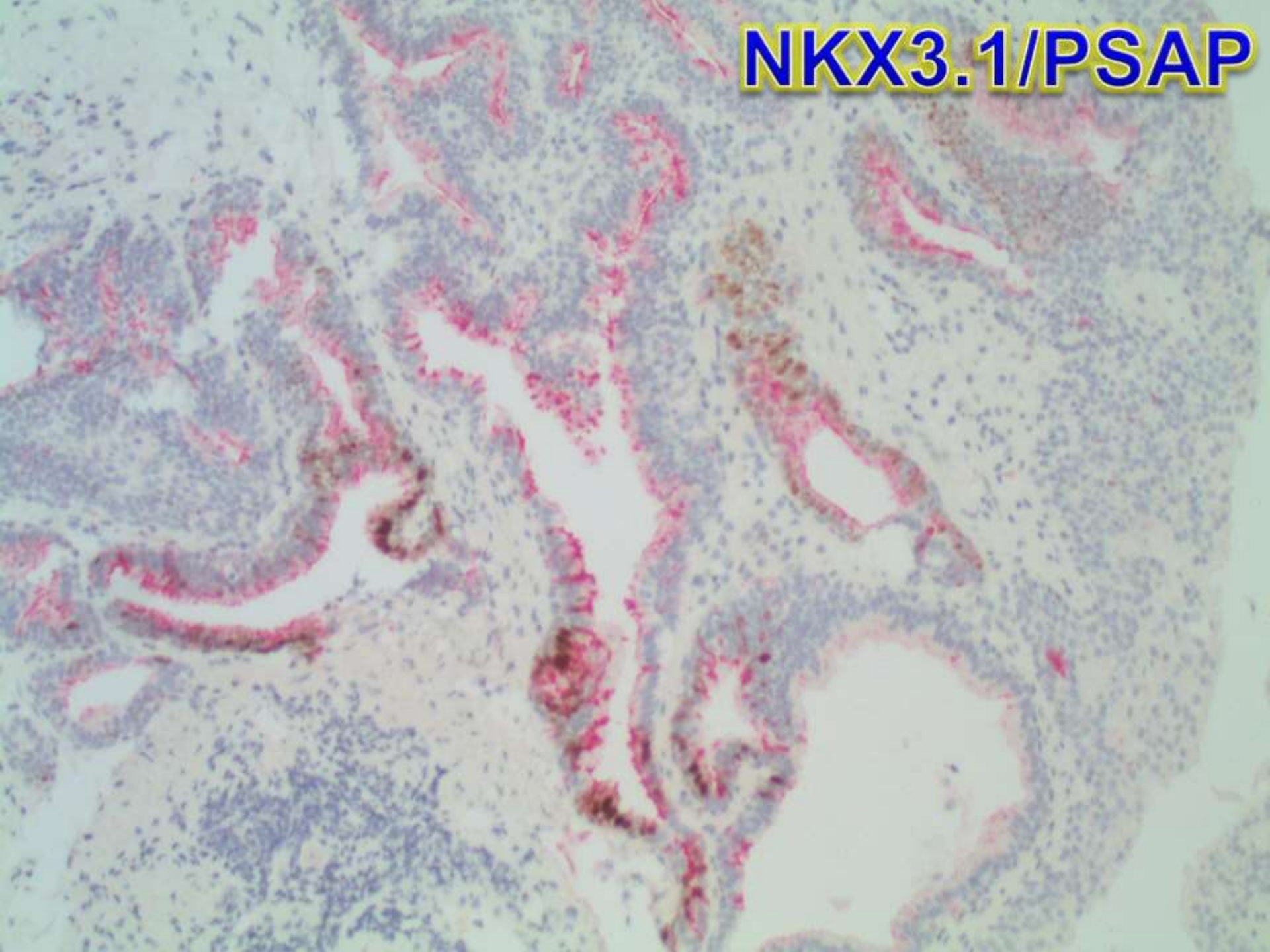




DDx

- Prostatic-type polyp (“ectopic prostate tissue”)
- Prostatic ductal adenocarcinoma
- Papillary urothelial neoplasm
- Nephrogenic adenoma
- Papillary/polypoid cystitis
- Cystitis cystica glandularis


NKX3.1/PSAP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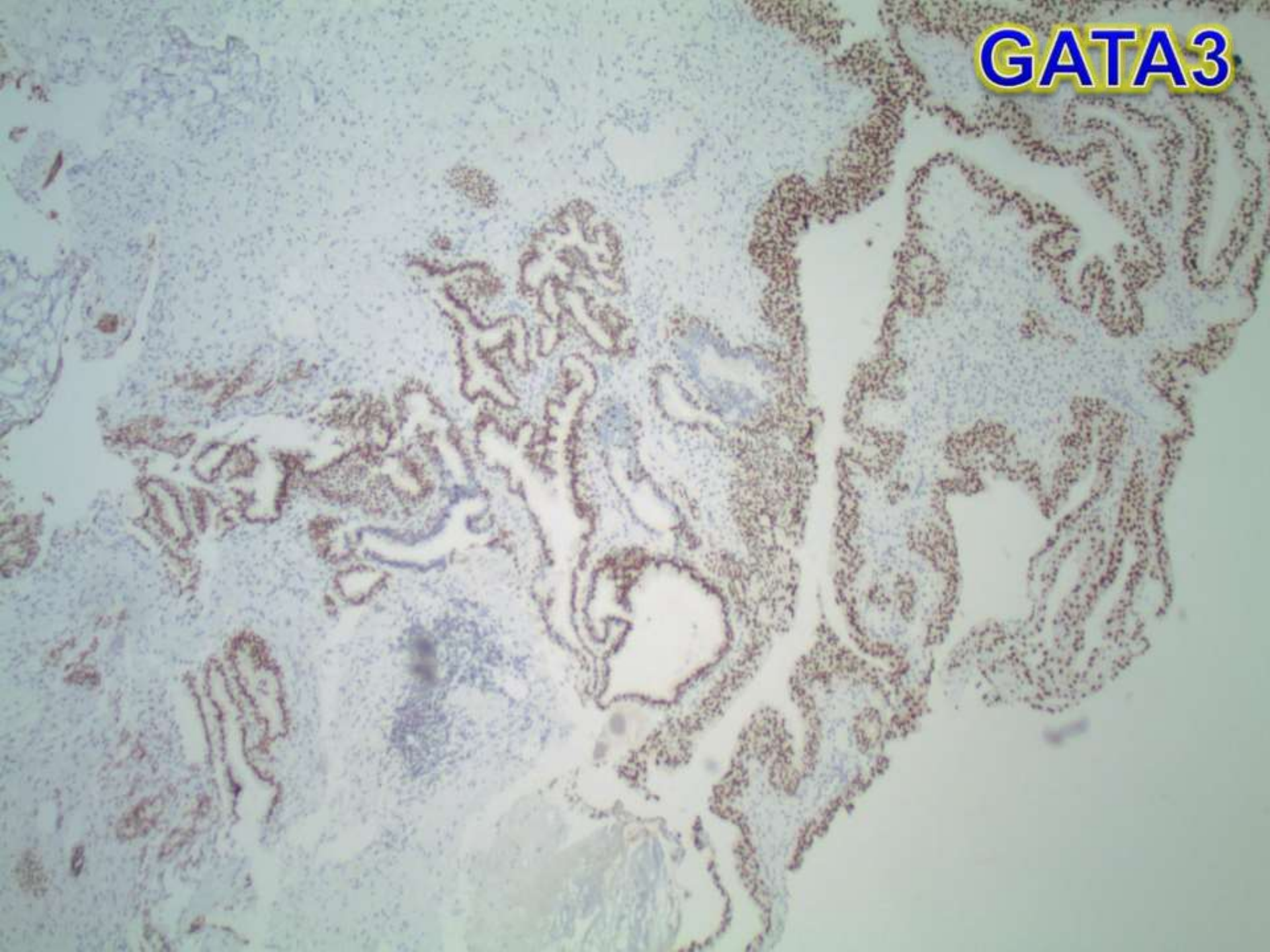
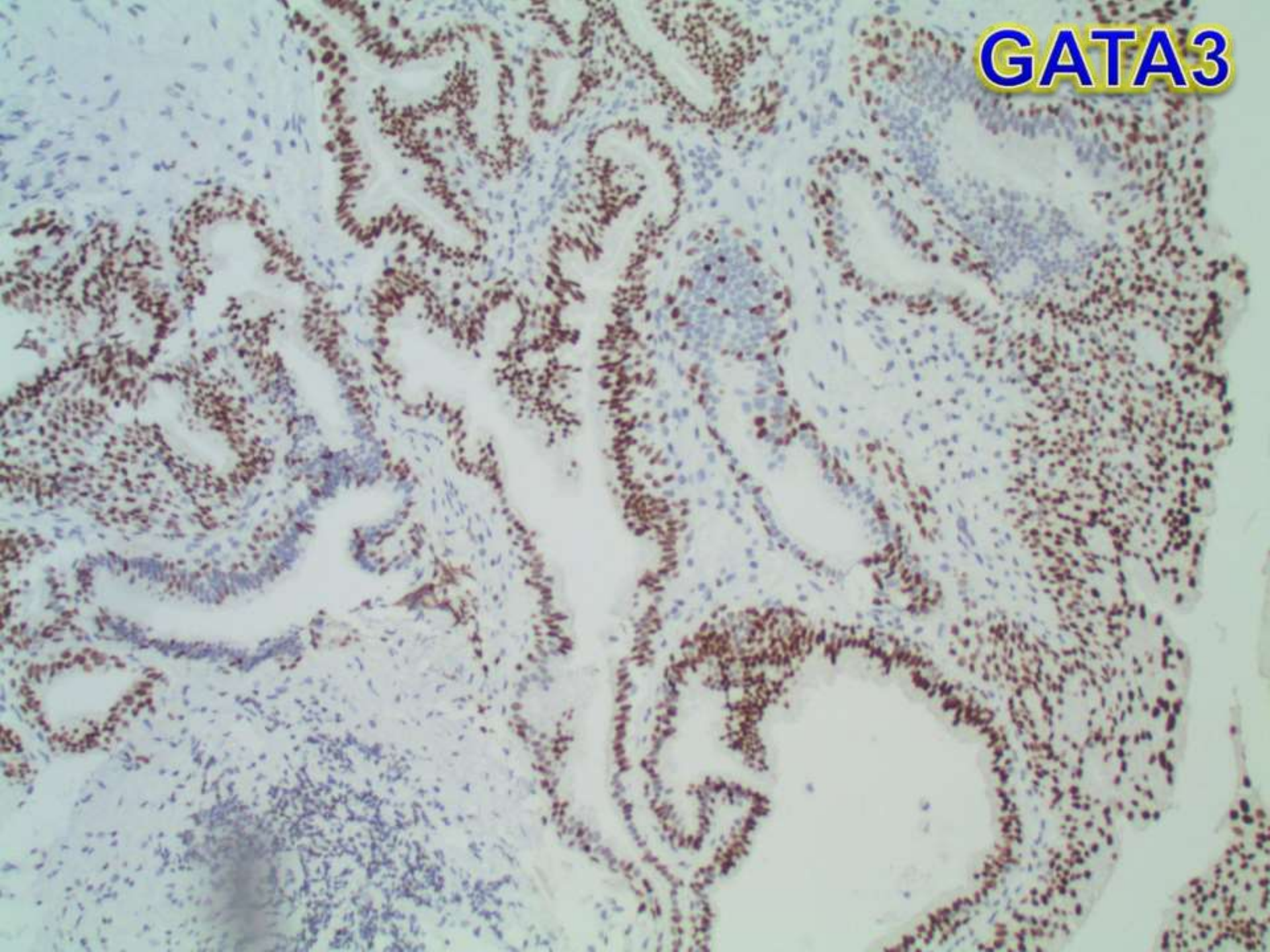

GATA3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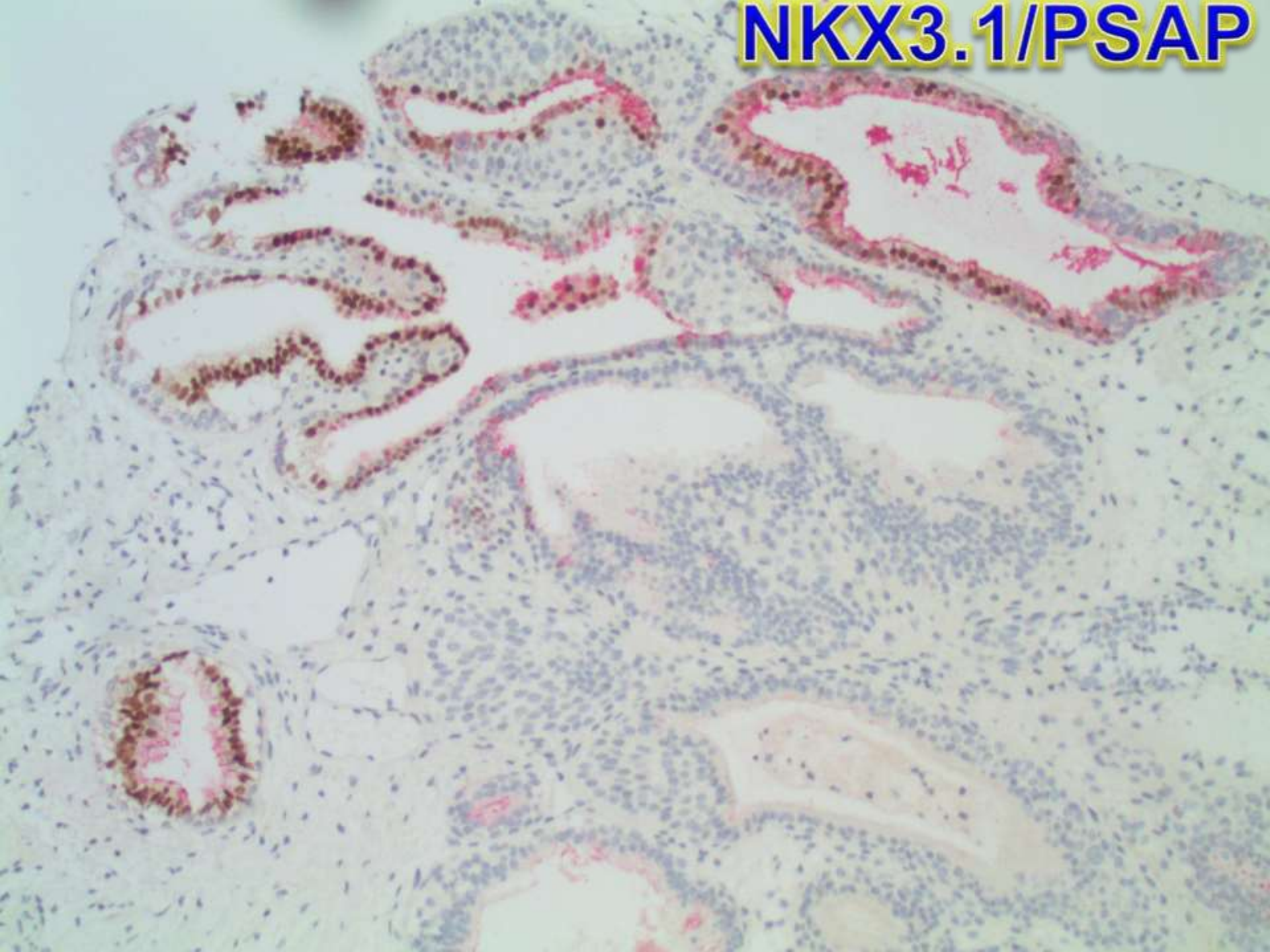
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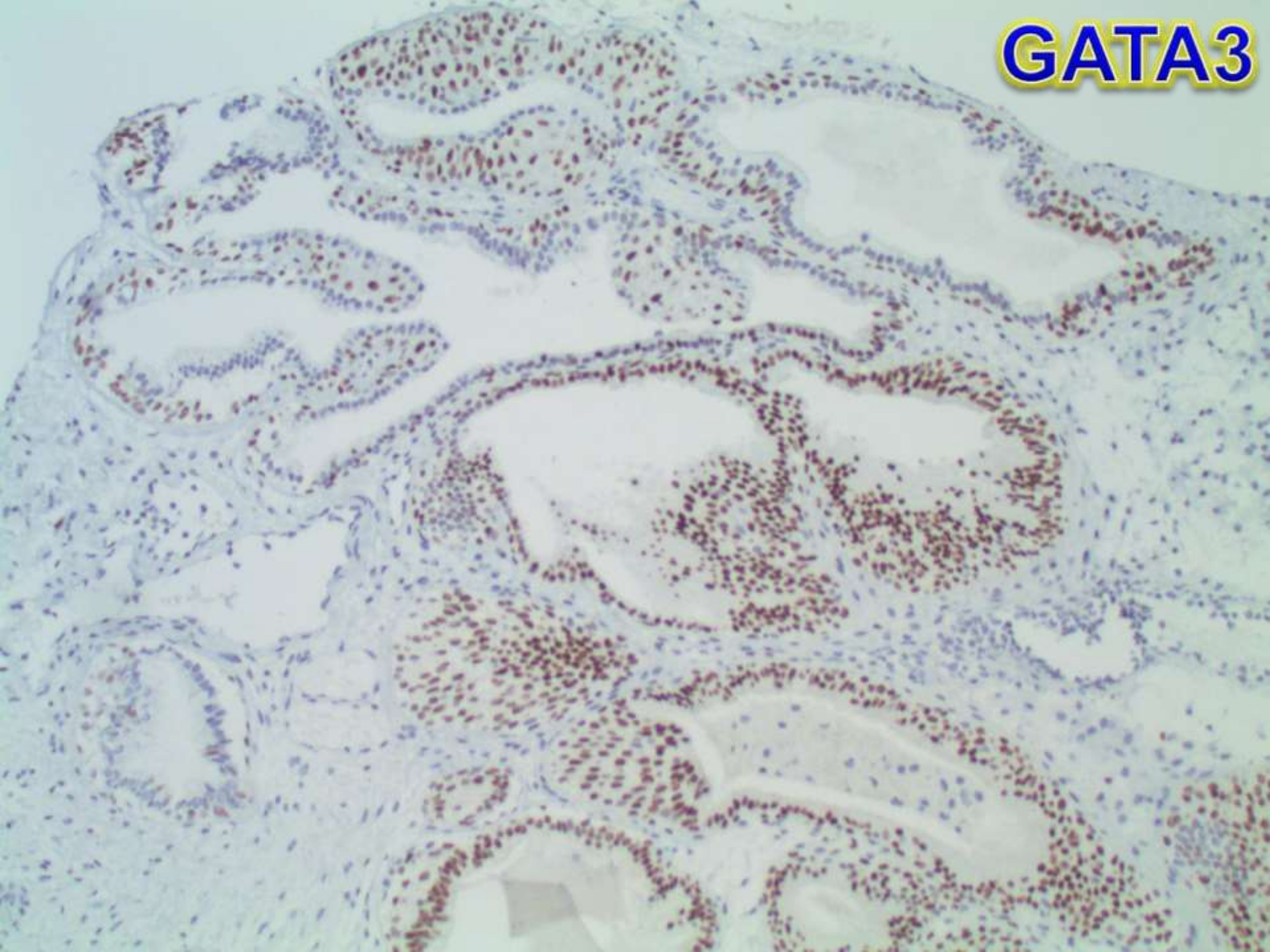

GATA3

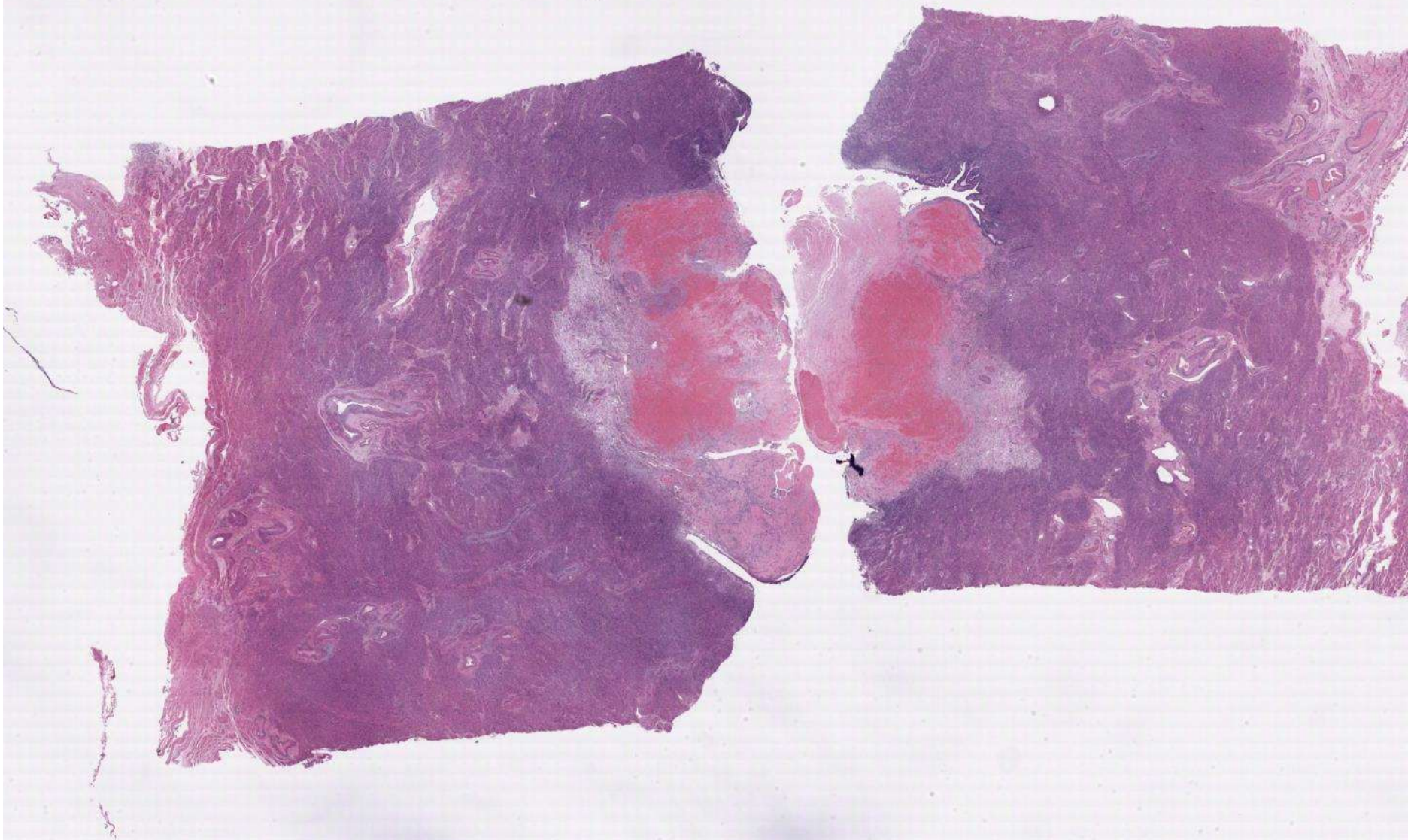
DIAGNOSIS: Prostate-type polyp

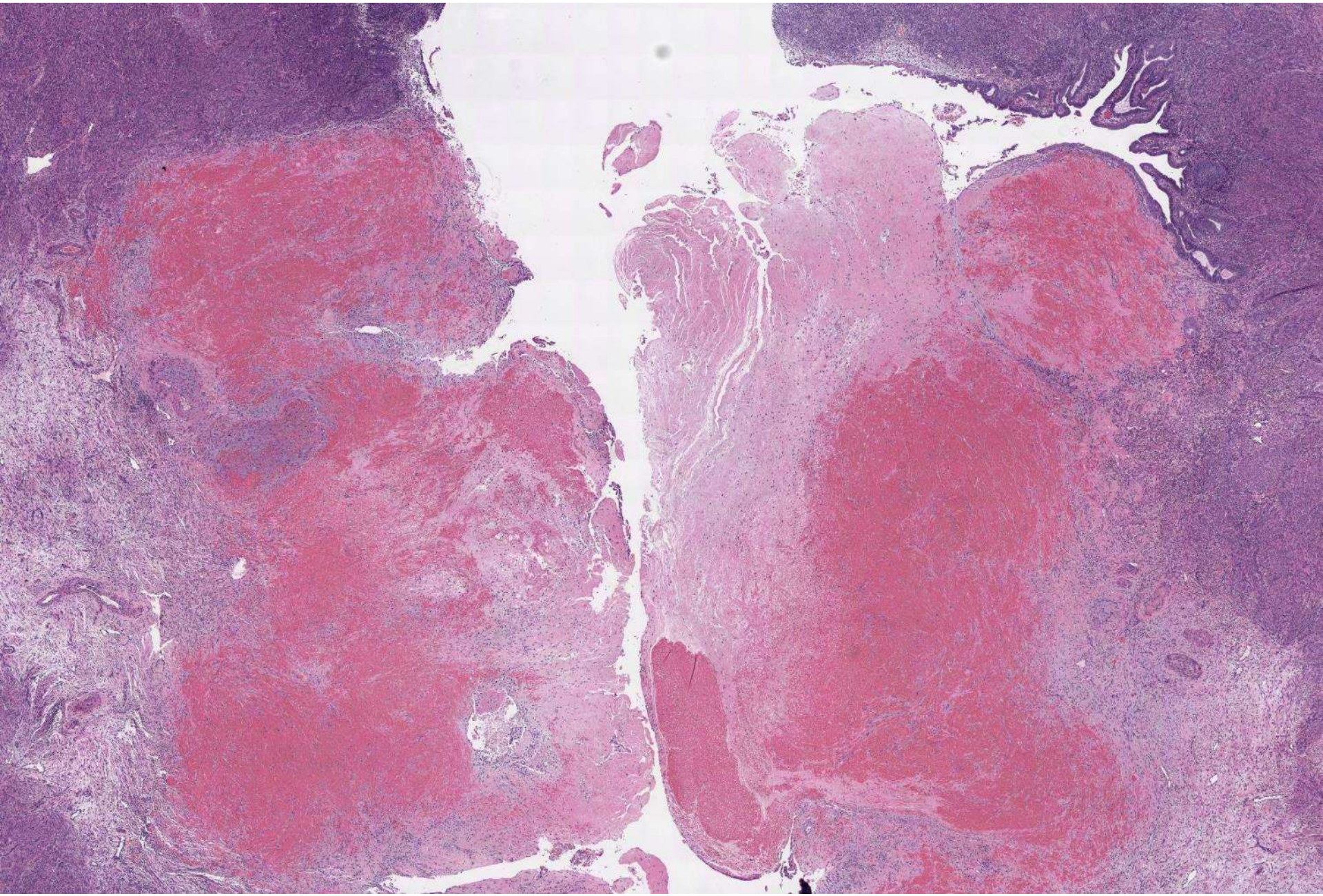
- **ETIOLOGY**
  - Ectopic prostatic tissue? Metaplastic? Developmental anomaly? Prolapse change?
- **AGE RANGE: wide**
- **SITES: prostatic urethra, bladder trigone**
- **PRESENTATION: hematuria, hematospermia**
- **CYSTOSCOPY: polypoid, frondlike mass**
- **Treatment/prognosis: excision; benign!**

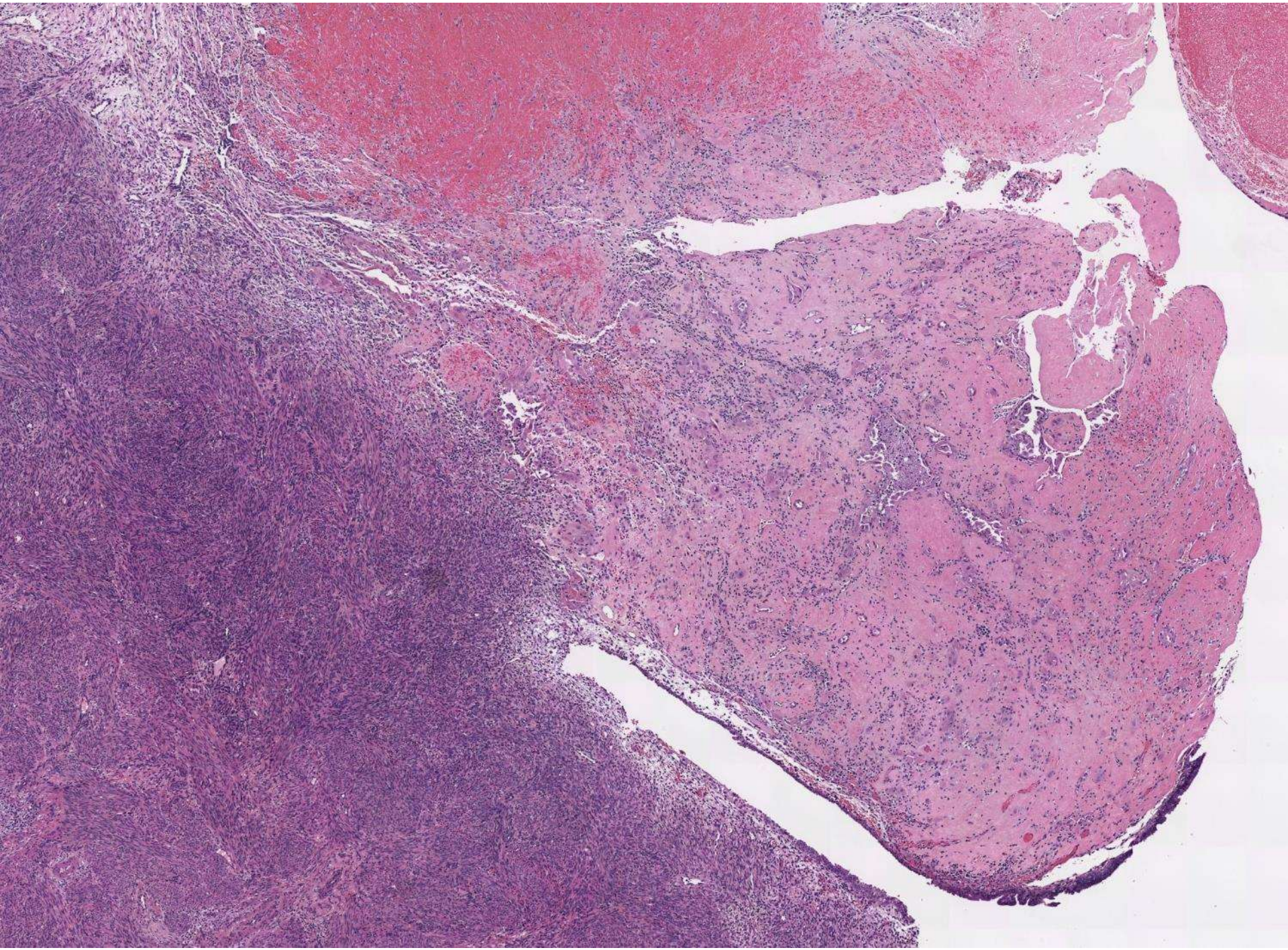
19-1003
scanned slide available!

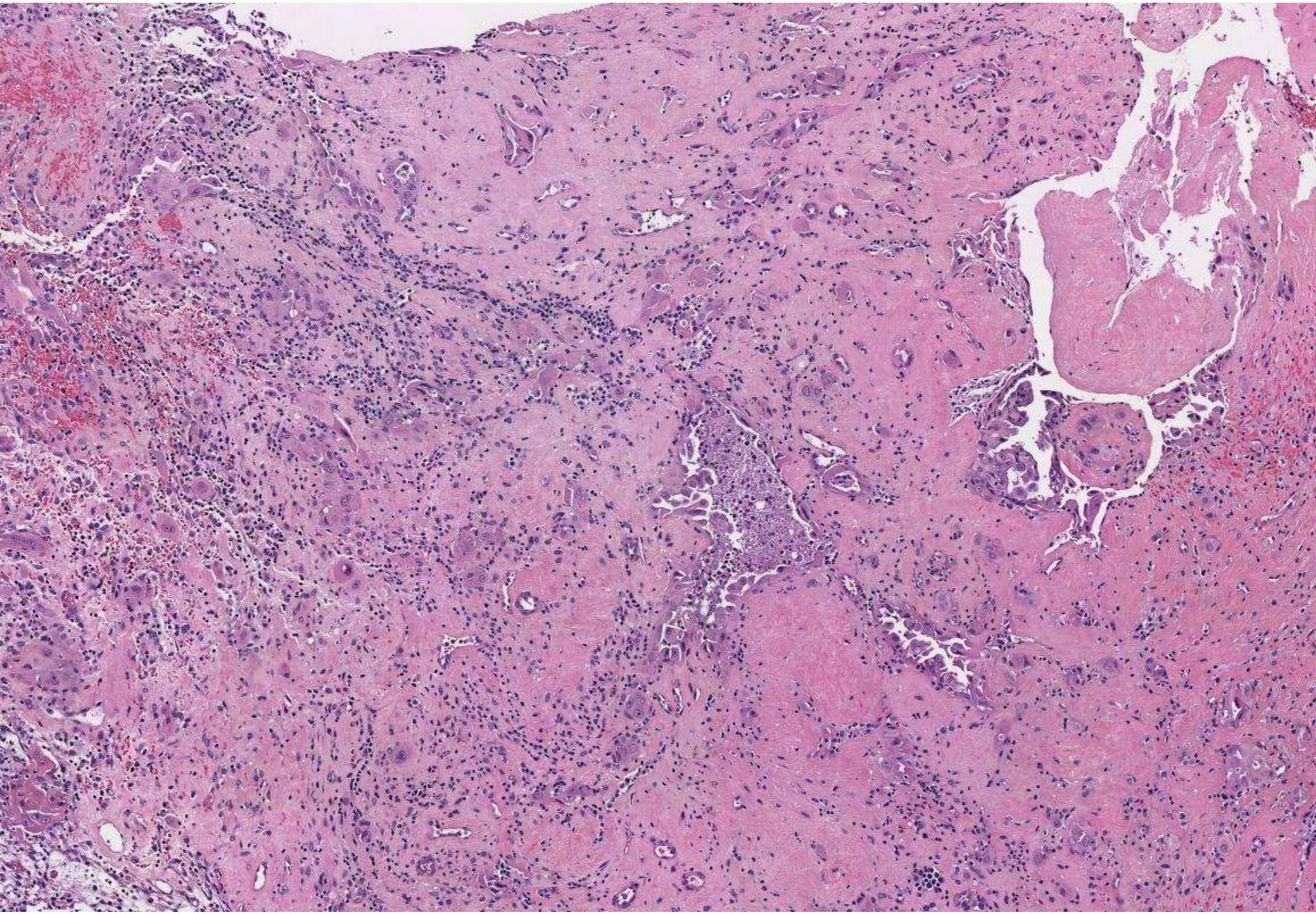
Ankur Sangoi; El Camino Hospital

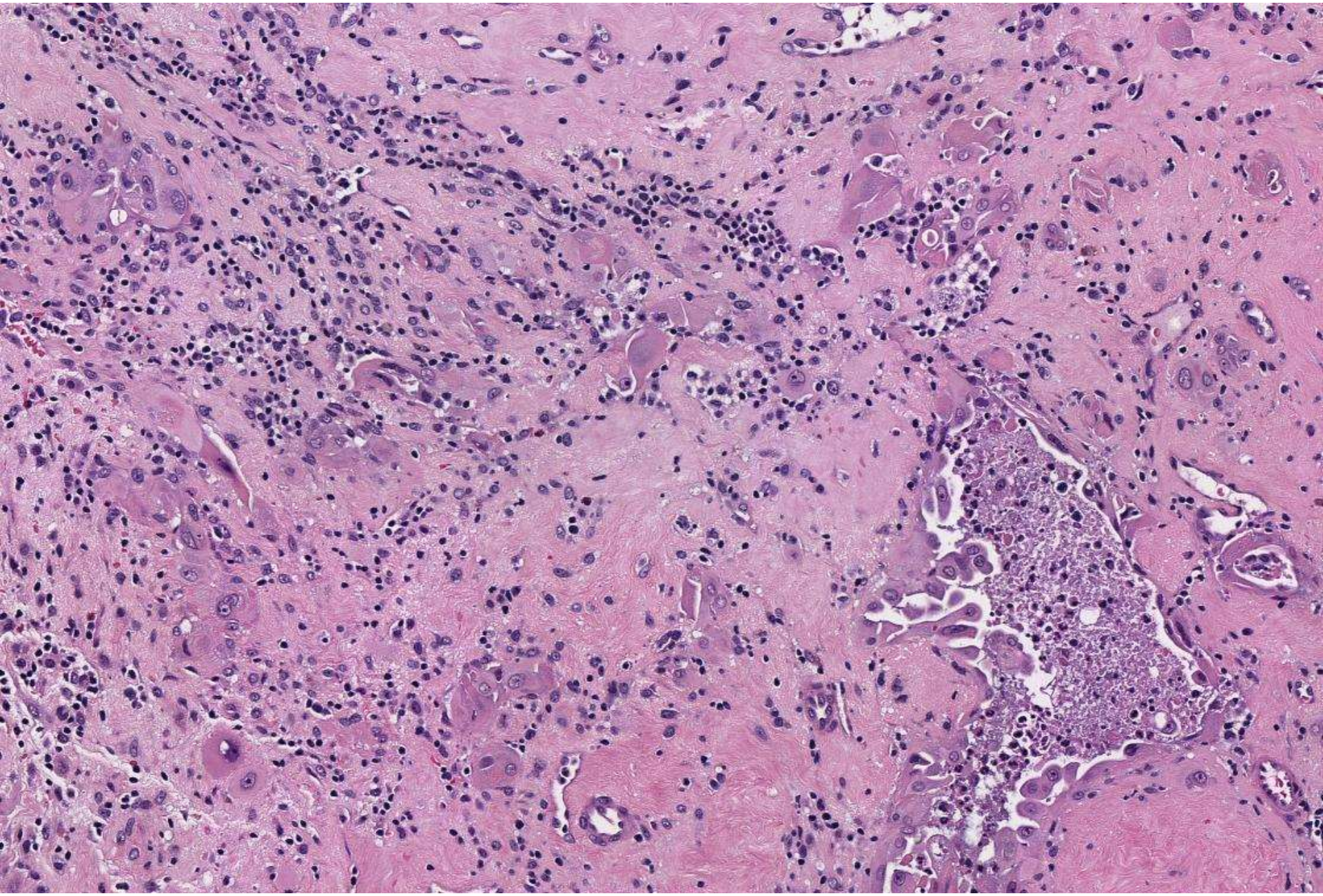
80-year-old female with vaginal bleeding. TAH/BSO performed.

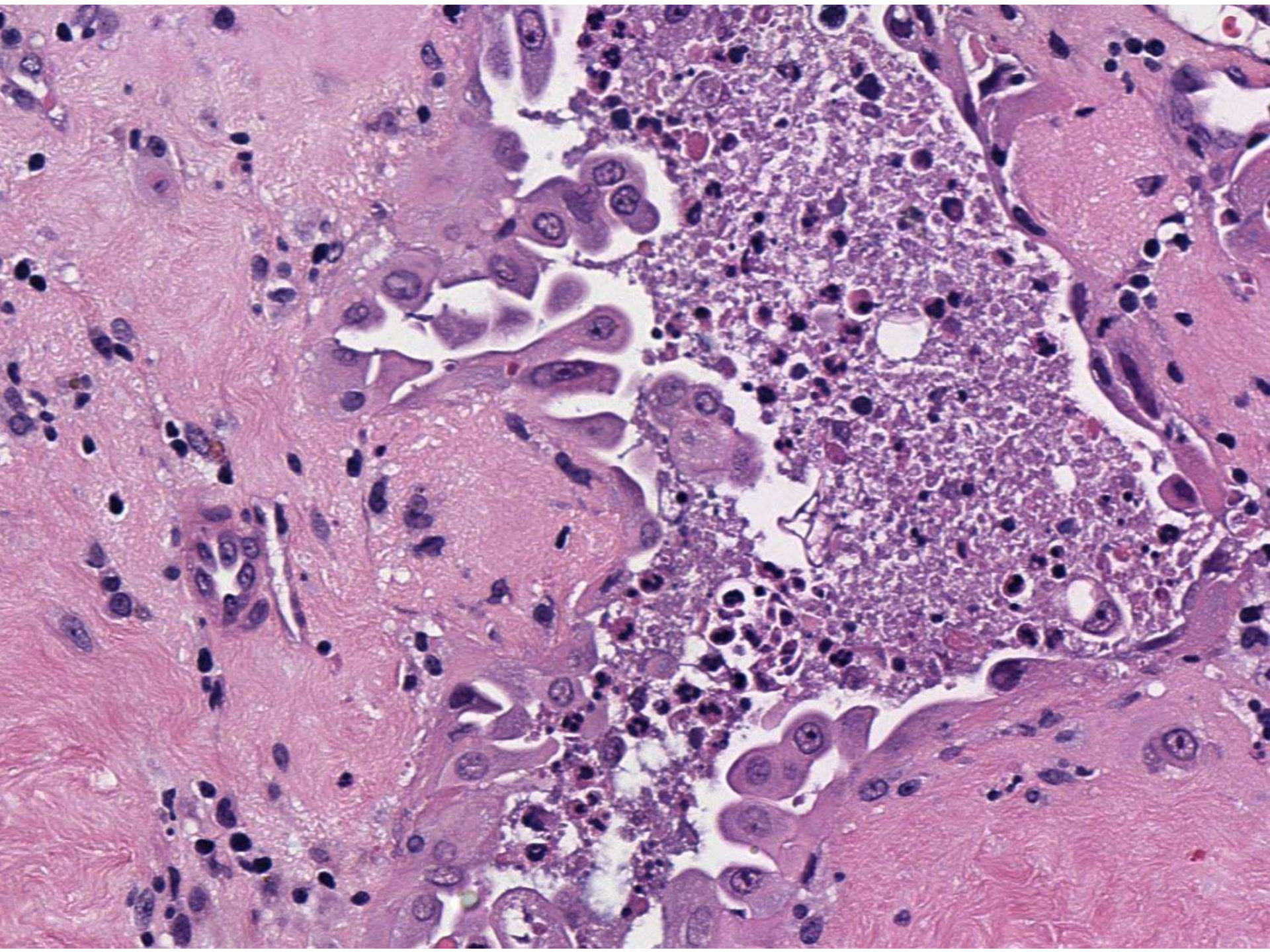


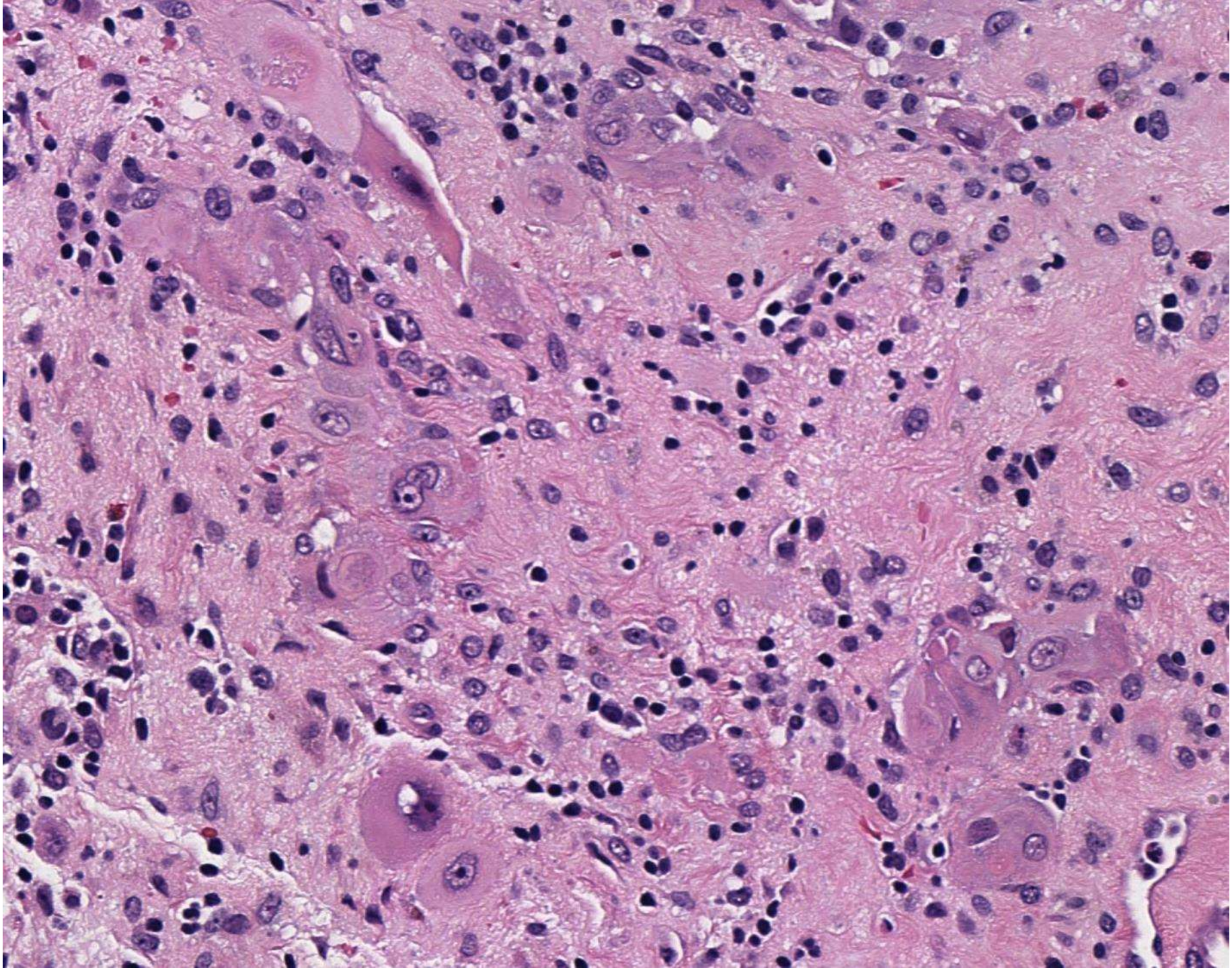


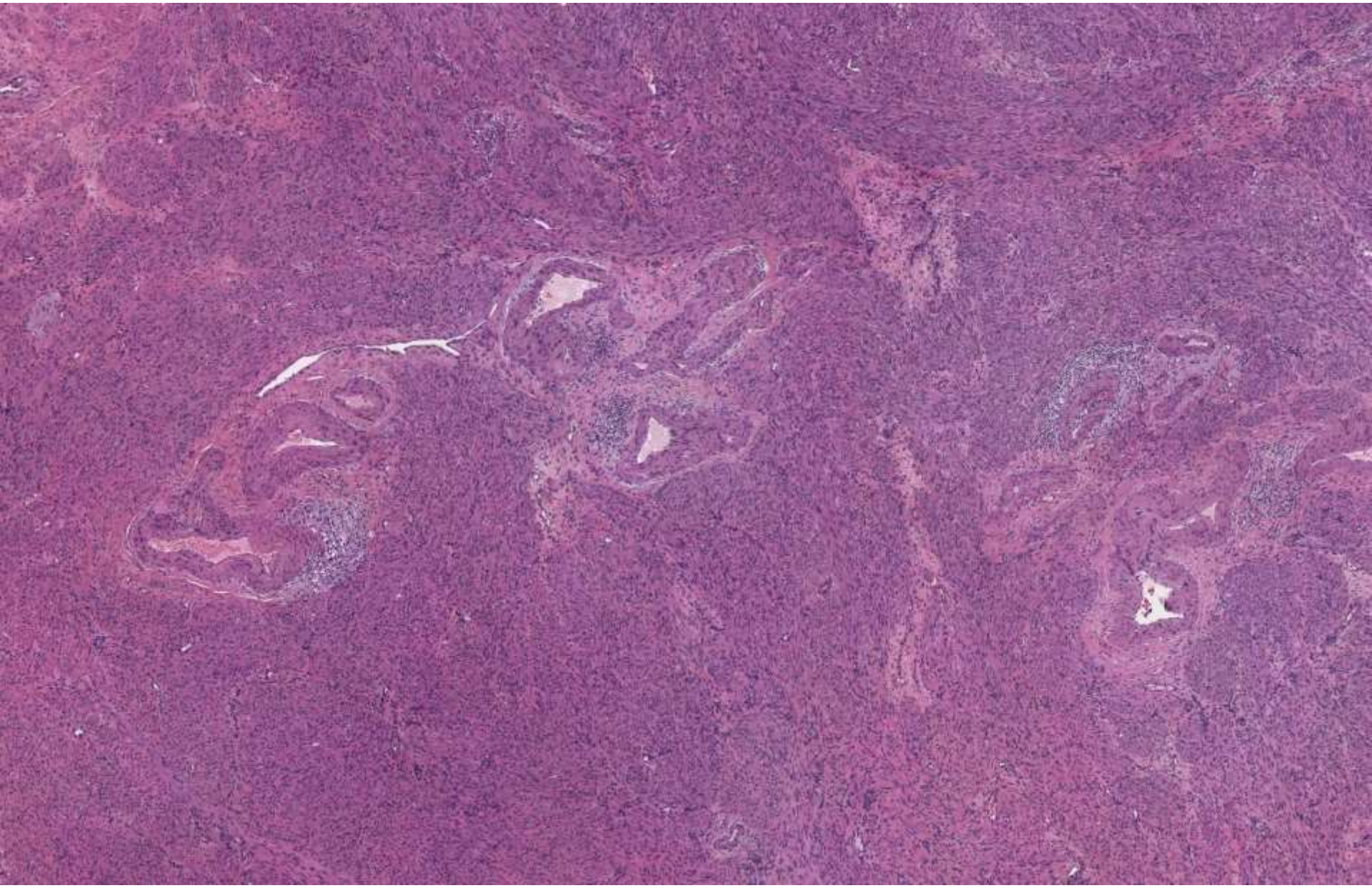


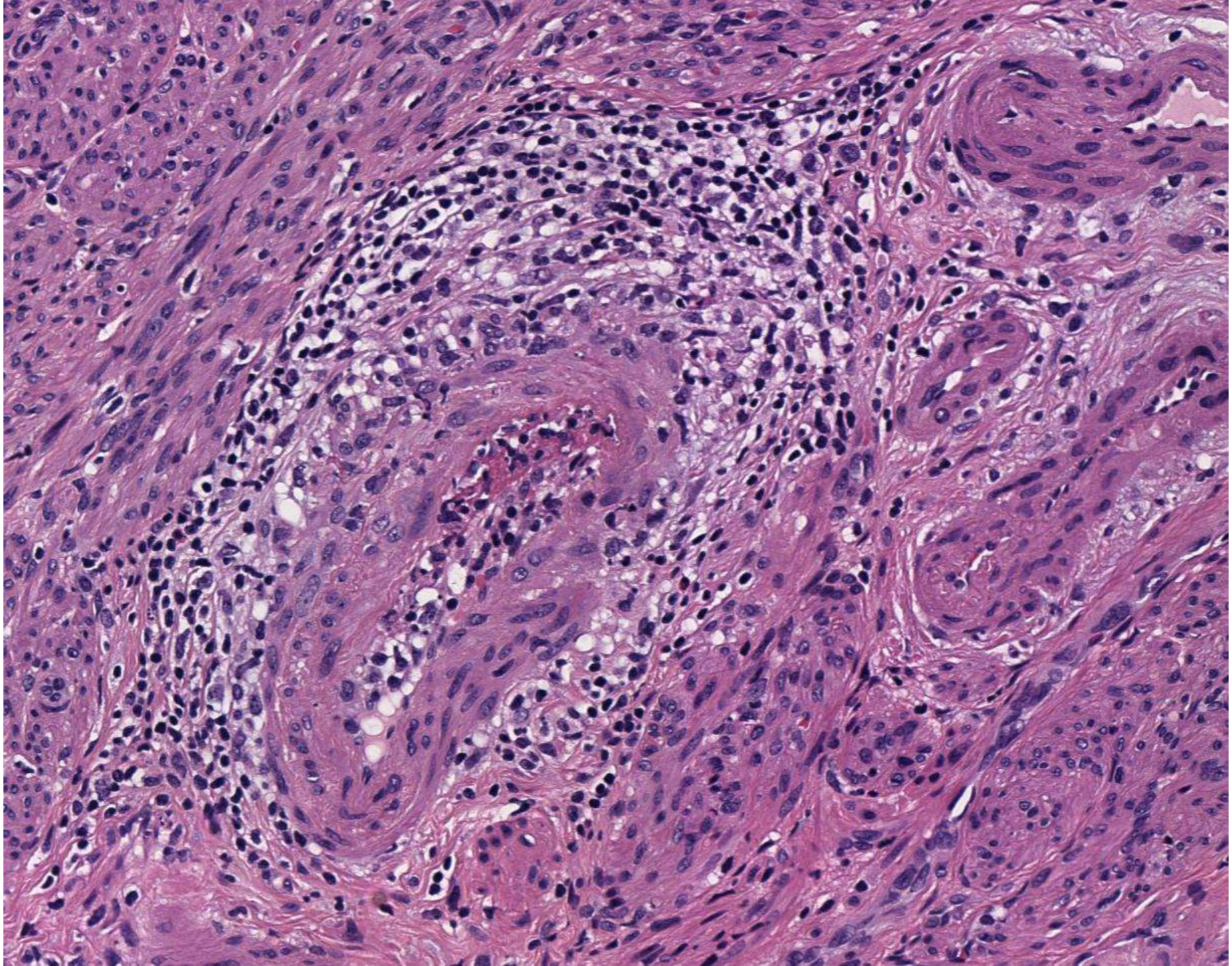


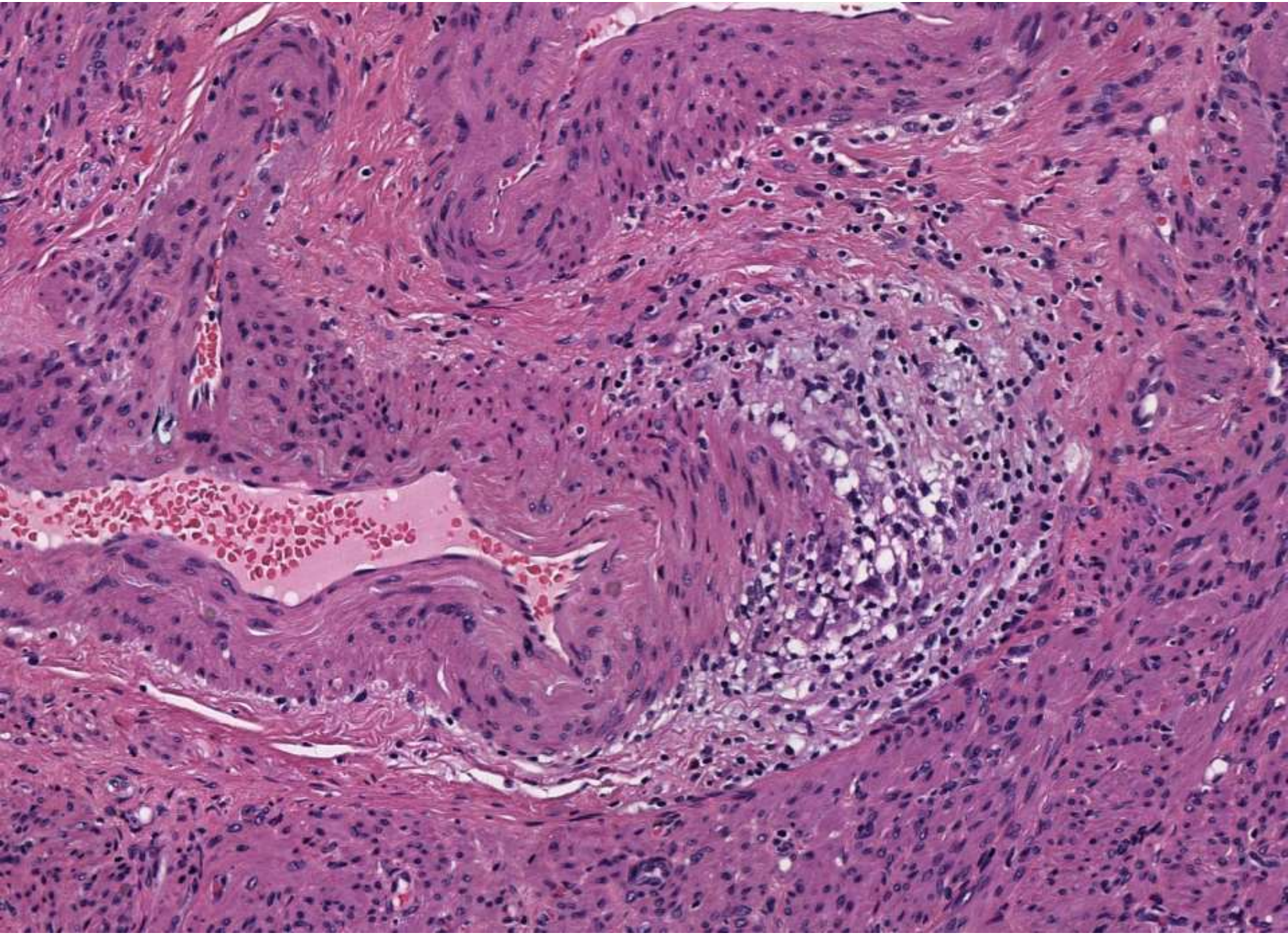


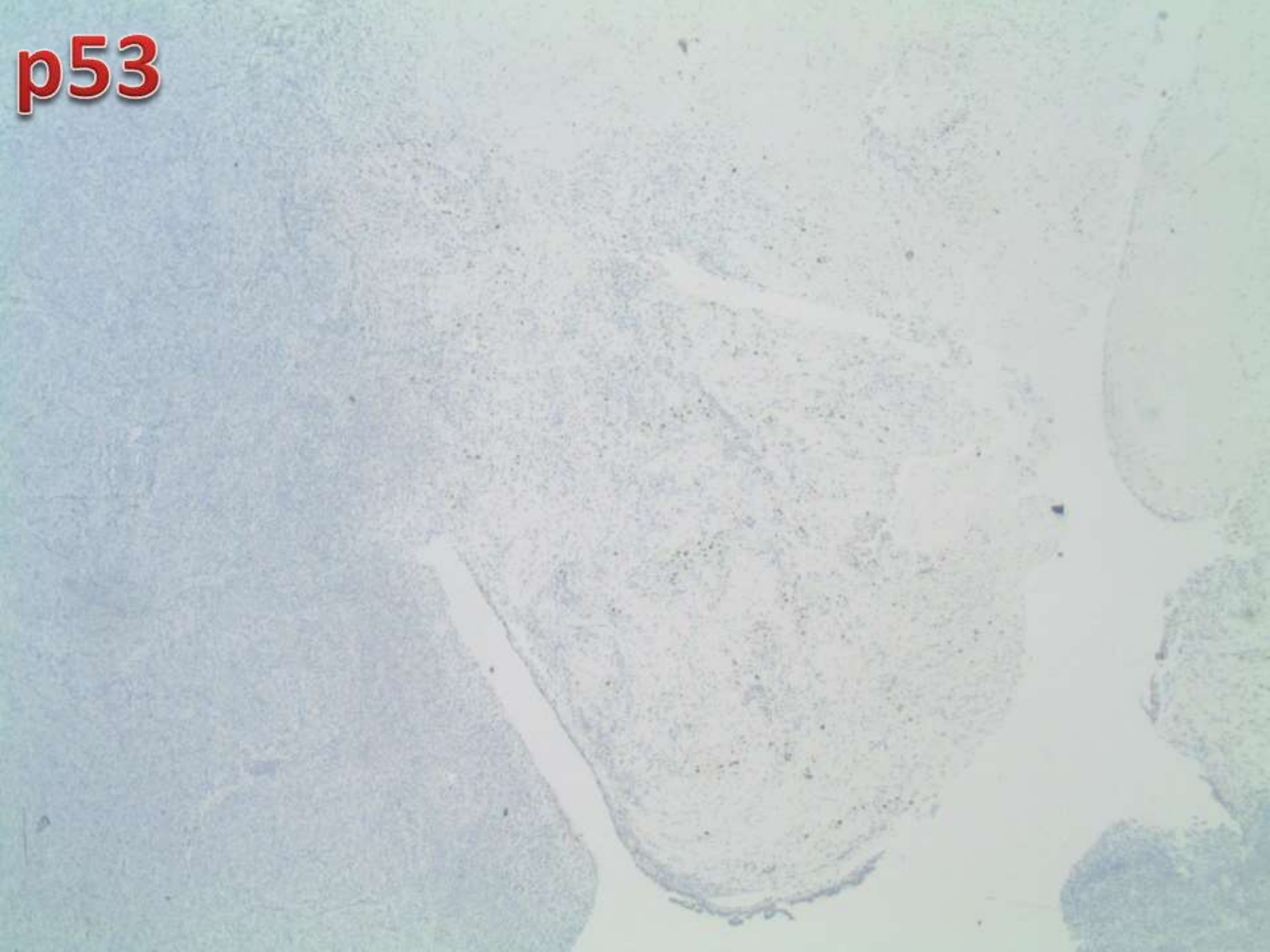








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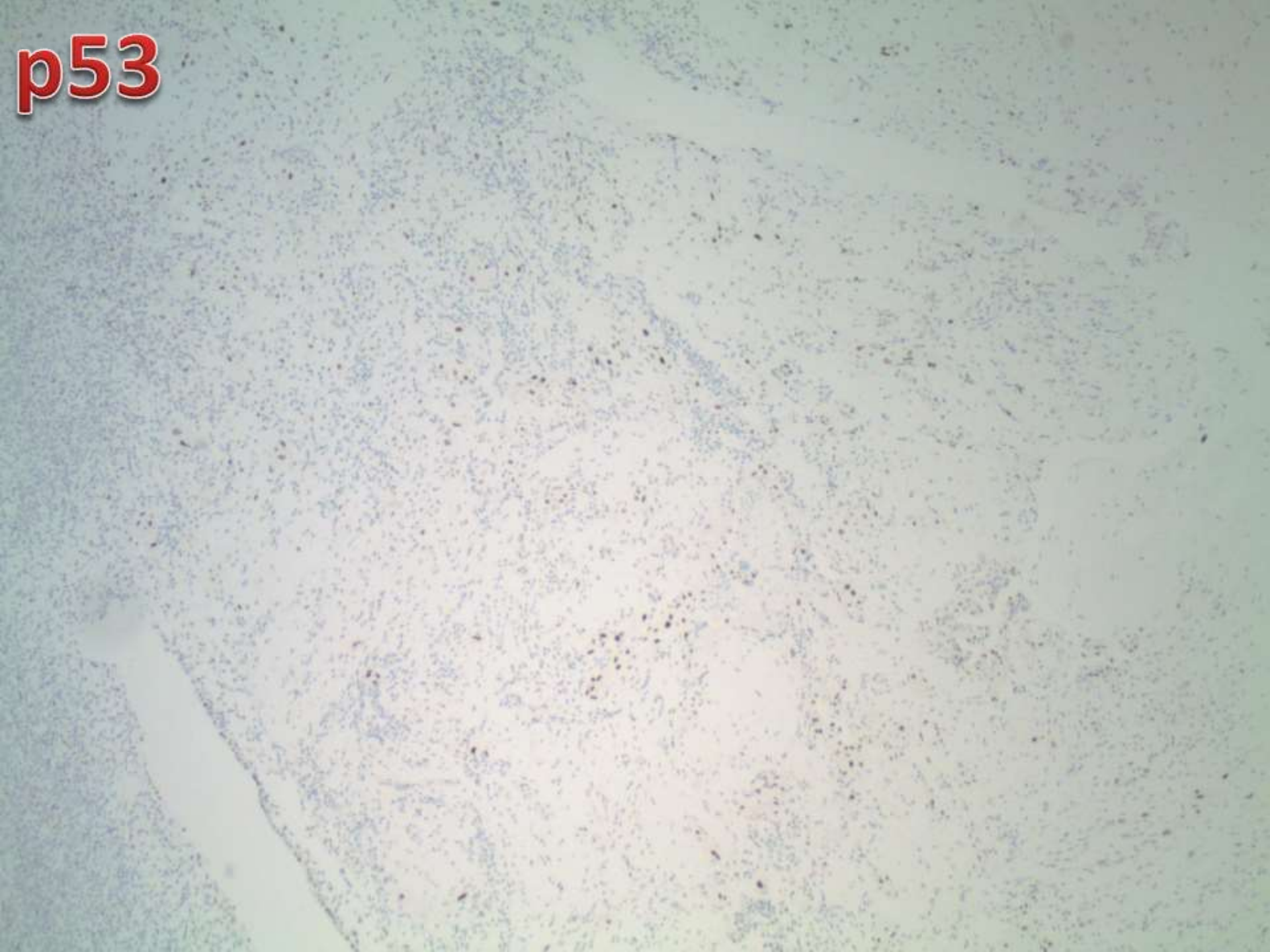
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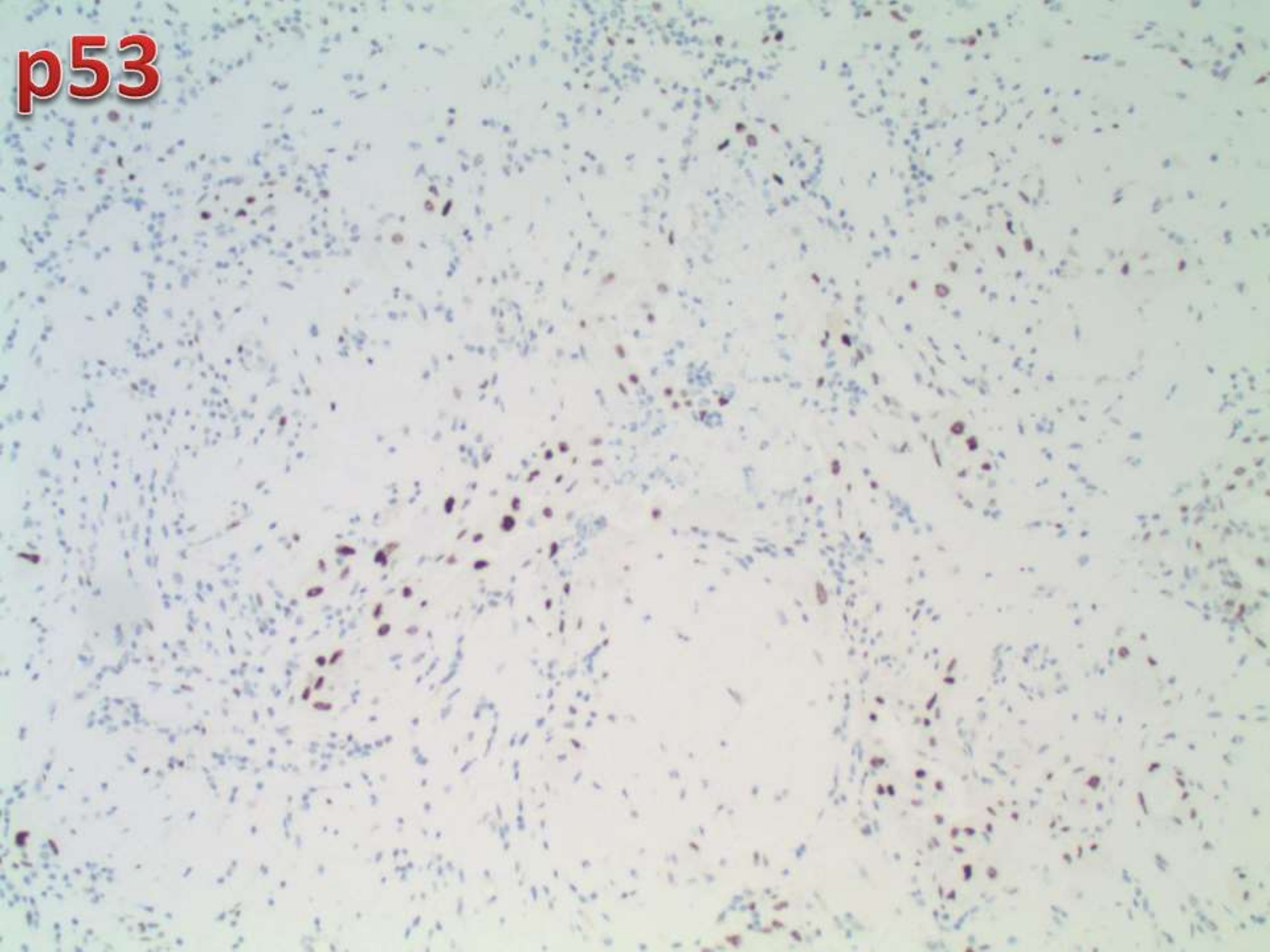
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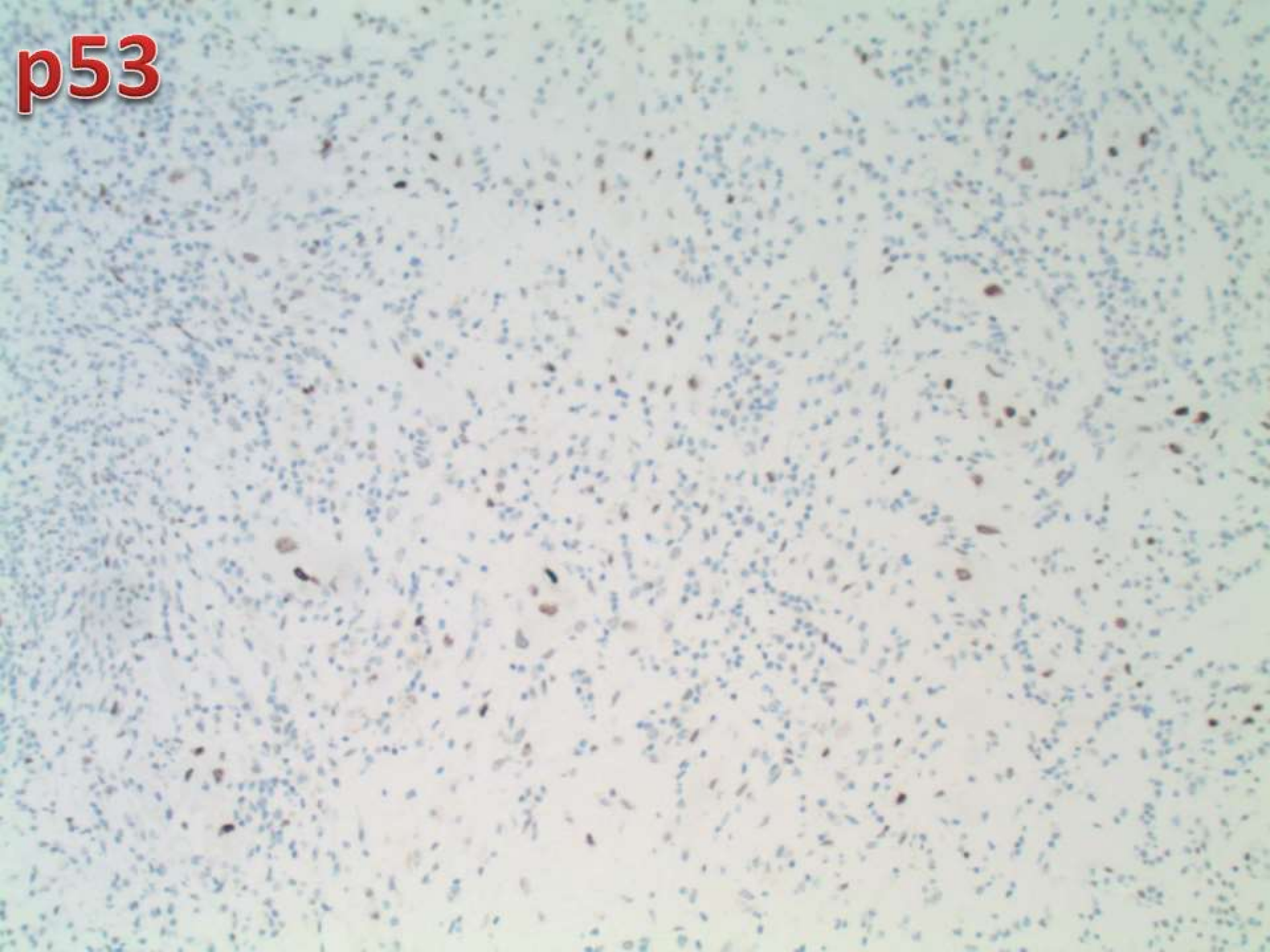
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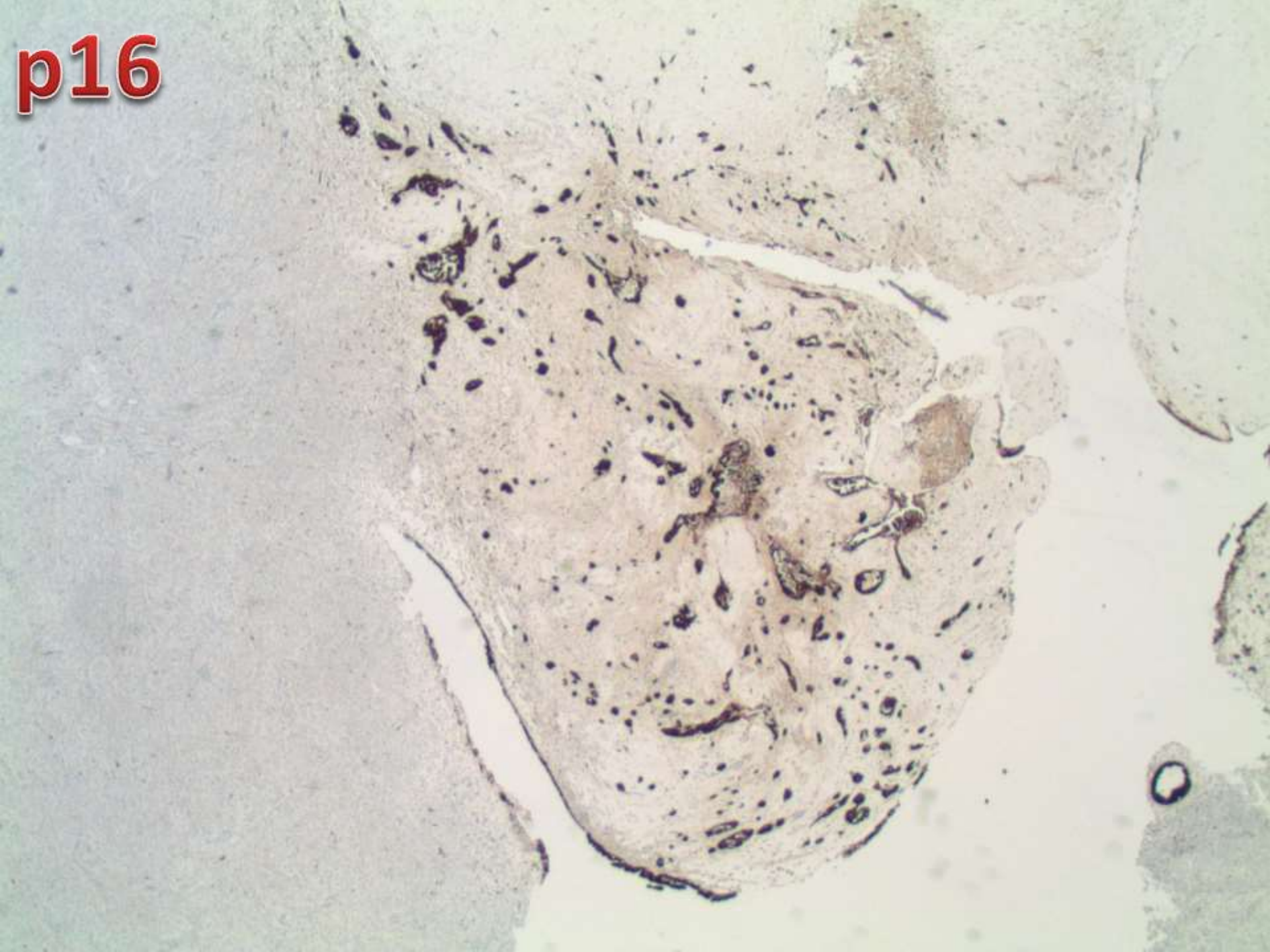
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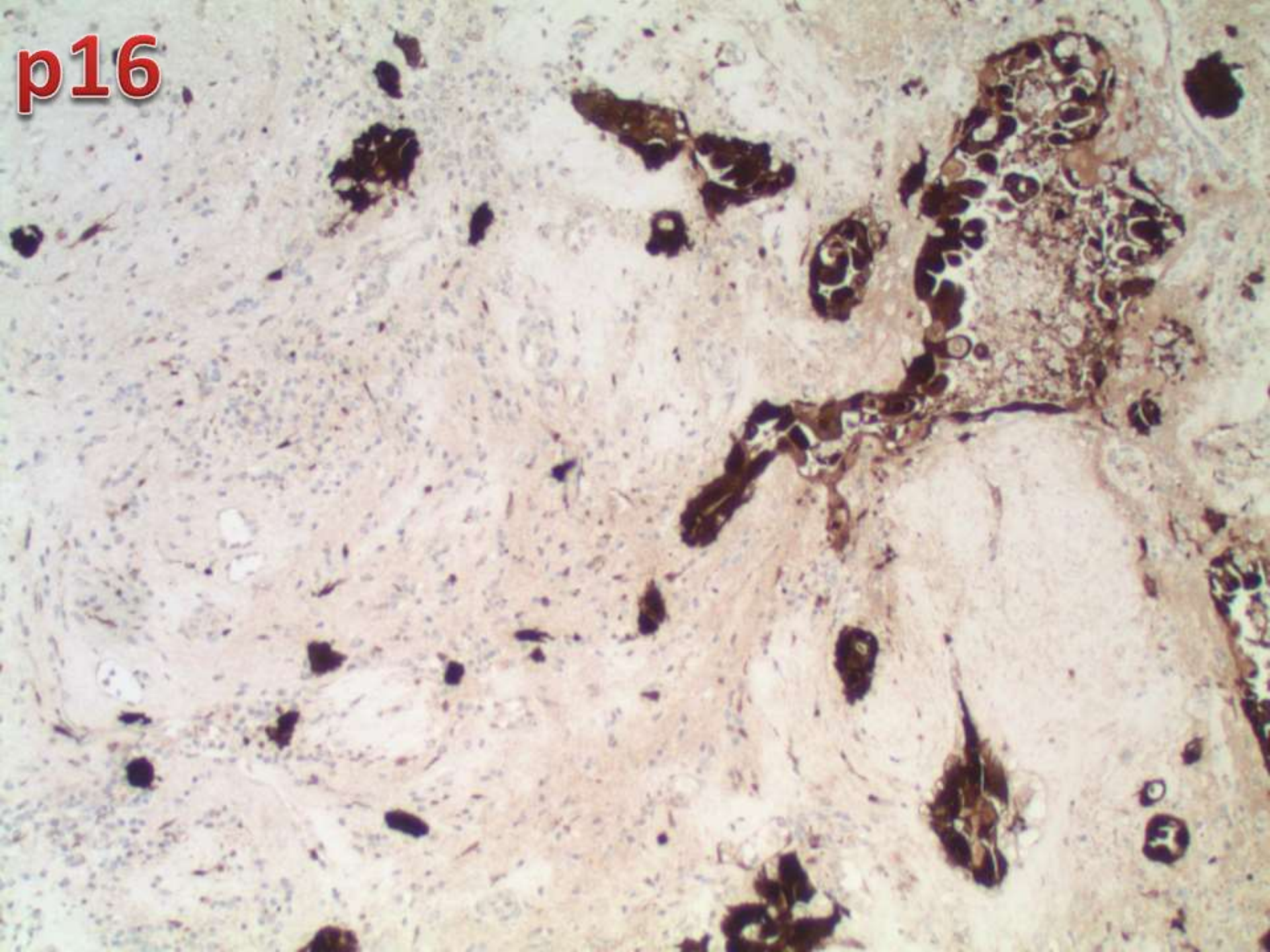
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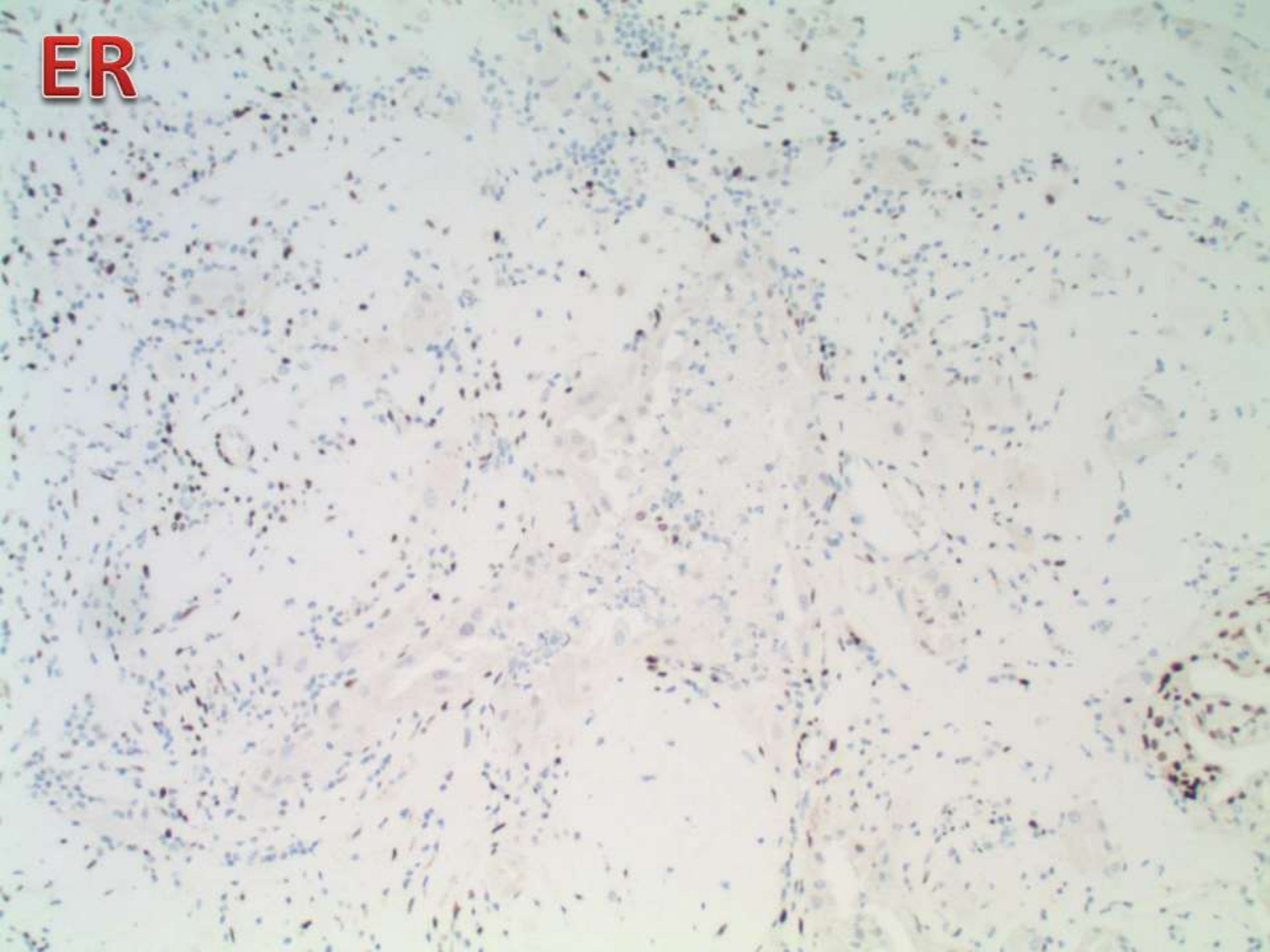
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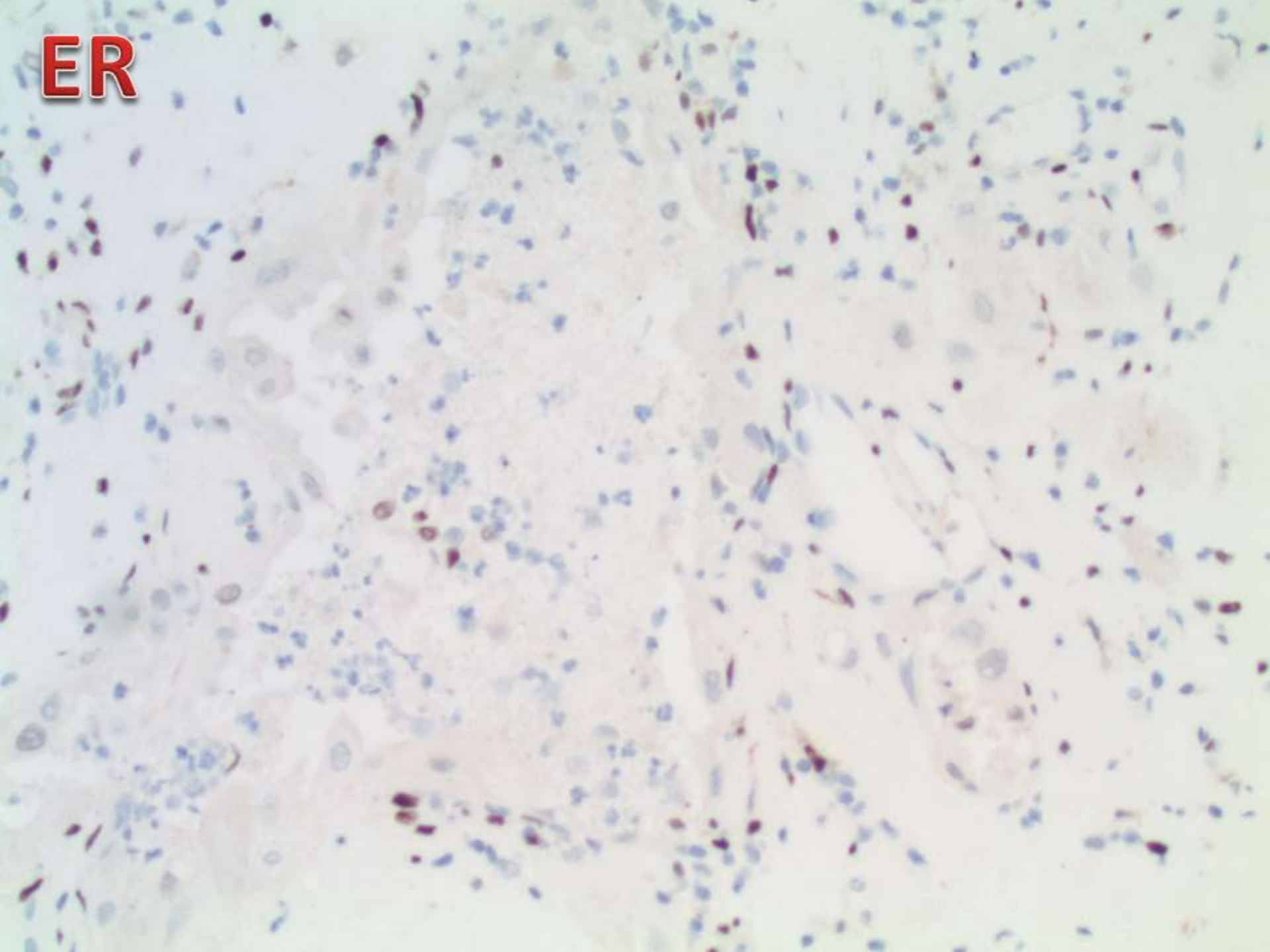
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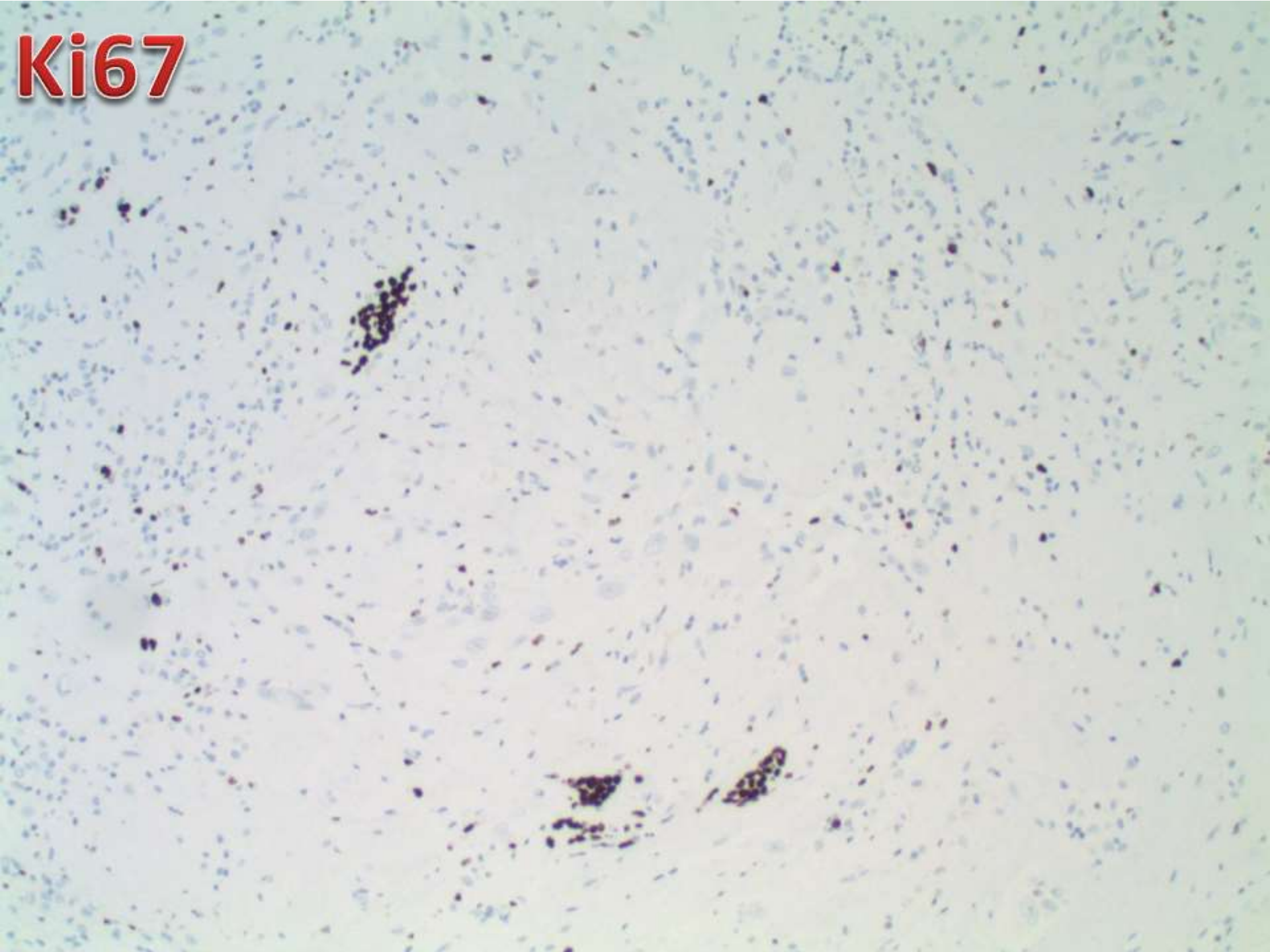

Ki67

DDx

- BENIGN
- MALIGNANT

DDx

- **BENIGN**
  - Endometrial polyp
    - With infarction change
    - Papillary syncytial metaplasia
- **MALIGNANT**
  - Serous carcinoma
  - Clear cell carcinoma

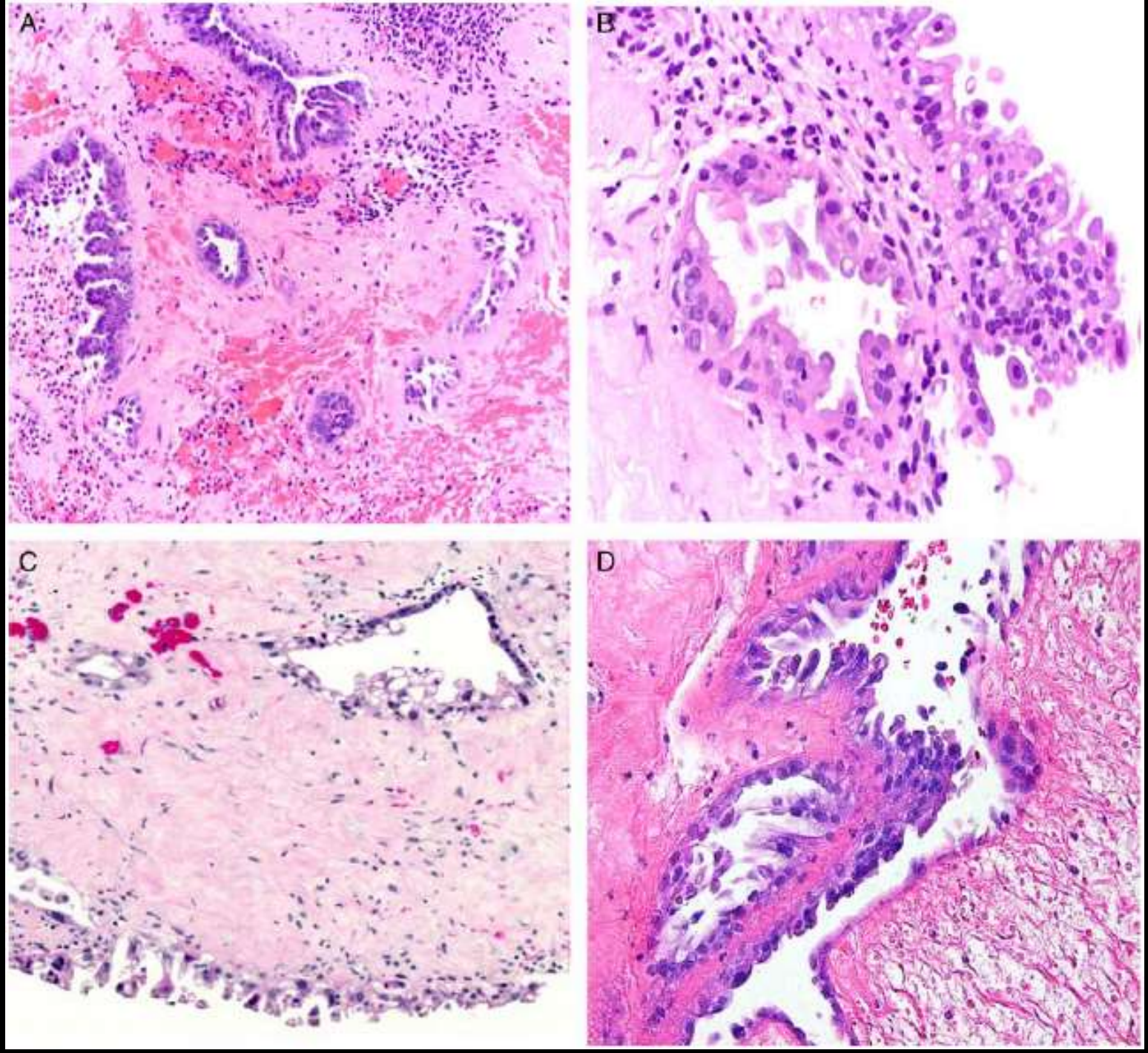
International Journal of Gynecological Pathology
38:32–43, Lippincott Williams & Wilkins, Baltimore

Original Article

The Spectrum of Morphologic Alterations Associated With Infarction in Endometrial Polyps: A Report of 41 Cases

Oluwole Fadare, M.D., Idris L. Renshaw, M.D., Ph.D., and Vinita Parkash, M.D.

Summary: The authors describe the clinicopathologic features of a group of endometrial polyps that exhibited large areas of infarction, to highlight the spectrum of morphologic alterations that may occur in this setting, including moderate cytologic atypia in a subset. Forty-one infarcted endometrial polyps, classified as such based on the presence therein of confluent zones of stromal necrosis and/or sharply demarcated zones of paucicellular to acellular stromal hyalinization, were assembled from multiple institutions. All were diagnosed in biopsies, polypectomies, or curettages. The morphologic profile of the epithelium associated with the infarcted zones was compared with those of a control group of 40 consecutive noninfarcted polyps. The patients with infarcted polyps ranged in age from 23 to 94 yr and were significantly older than the control group patients (mean ages, 60.8 vs. 49 yr respectively; $P=0.02$). The most common architectural alteration in infarcted polyps was a distinctive cellular tufting or pseudopapillary change, possibly representing an exuberant iteration of papillary syncytial change, which was seen in 39% of cases. Among the features that were significantly more prevalent in infarcted polyps than the control group were grade 2 pleomorphism (i.e., a 2–3-fold variation in nuclear size and/or shape) (37% vs. 2.5%, respectively; $P=0.00029$), cellular syncytia (44% vs. 15%; $P=0.069$), vesicular chromatin greater than background glands (56% vs. 7.5%; $P<0.0001$), hobnail cells (27% vs. 0%; $P=0.0004$), clear cells (12% vs. 0%; $P=0.055$), and eosinophilic cells (56% vs. 15%; $P=0.000115$). The 2 groups were not significantly different regarding mitotic index and a variety of other morphologic variables. Irrespective of morphology, epithelia within the infarcted zones at least focally showed a core immunophenotype (p53-wild type, p16-diffusely positive; low proliferative index) that was essentially identical to the phenotype displayed by foci of papillary syncytial metaplasia unassociated with polyps in a 10-case comparison group. None of the 34 patients with follow-up information has subsequently been diagnosed with a uterine neoplasm. In summary, infarcted endometrial polyps frequently display a spectrum of cytoarchitecturally atypical epithelial changes. These pseudoneoplastic alterations are most likely degenerative and/or metaplastic in nature. **Key Words:** Endometrial polyp—Infarct—Endometrial intraepithelial carcinoma.


A
B
C
D

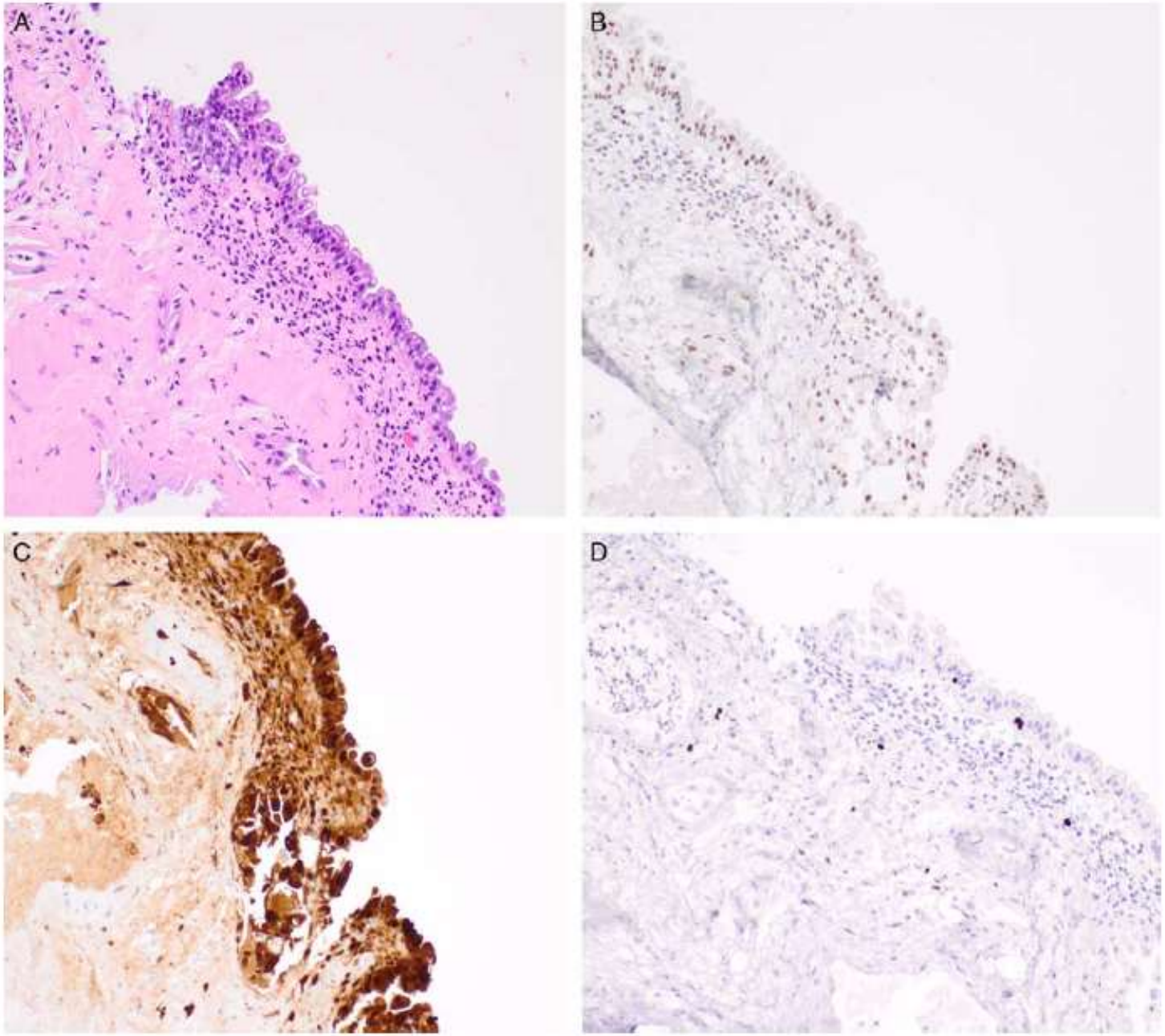
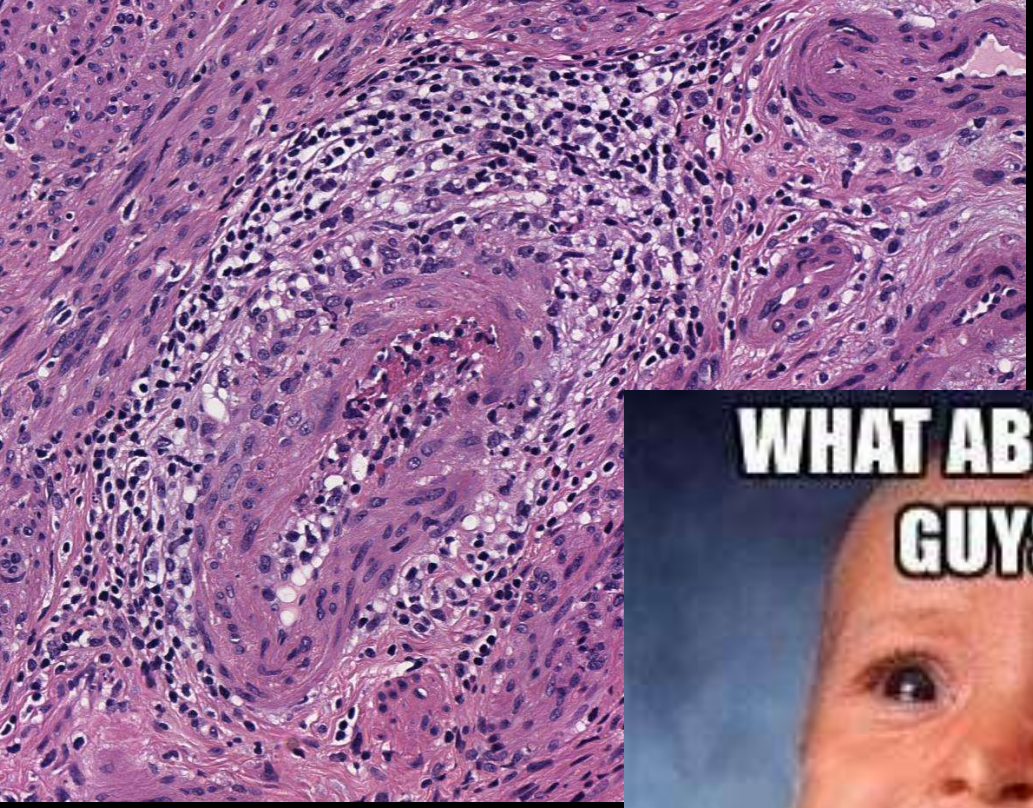


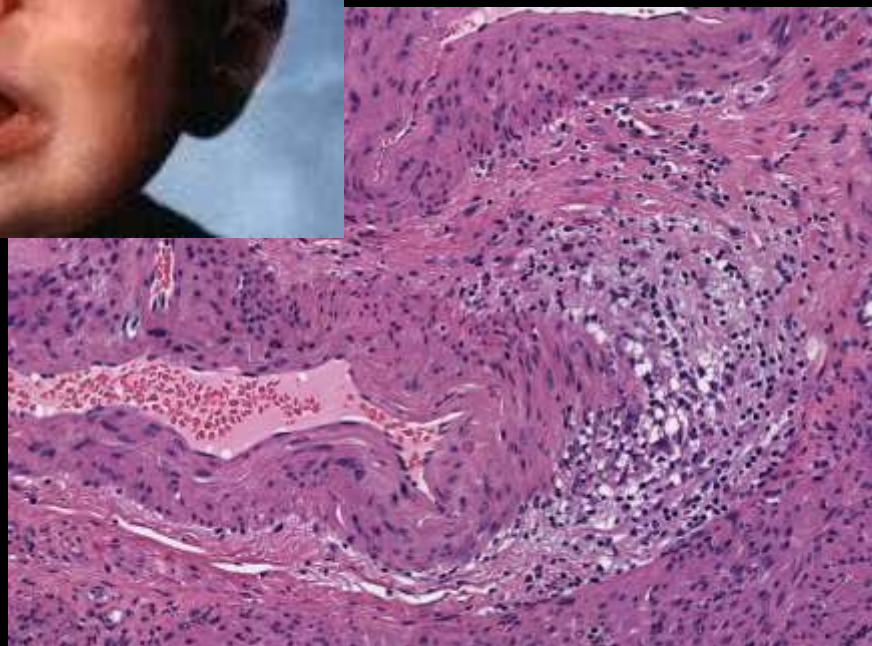
FIG. 5. A case of an infarcted endometrial polyp, showing pseudopapillary change (A), and a wild type immunophenotype for p53 (B), diffuse expression of p16 (C), and a low proliferative index (D).

Endometrial polyp with infarction changes

- **IHC:**
  - Increased p53 staining but still “wild type”
  - p16 can be diffuse/strong
  - Low Ki67
    - Low mitotic activity
- **MORPHOLOGY:**
  - Lack diffuse severe pleomorphism
  - Recognize background infarction changes




WHAT ABOUT ME
GUYS?



Significance of isolated vasculitis in the gynecological tract: what clinicians do with the pathologic diagnosis of vasculitis?☆

Andres A. Roma, MD [a,*], Catalina Amador-Ortiz, MD [b], Helen Liapis, MD [c]

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[c] Division of Anatomic and Molecular Pathology, Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO

ARTICLE INFO

Keywords:
Vasculitides
Vasculitis
Systemic vasculitis
Isolated vasculitis
Gynecological vasculitis

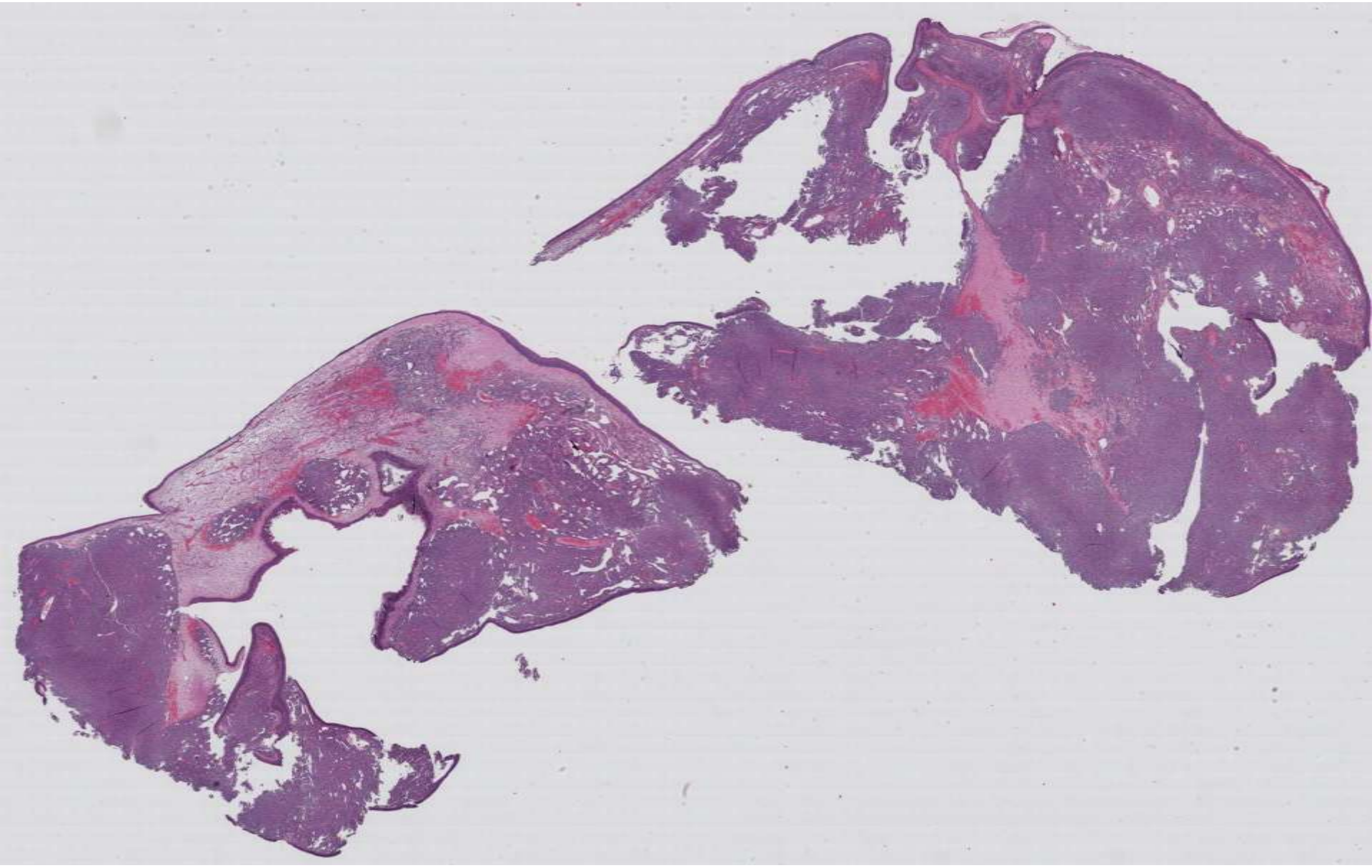
ABSTRACT

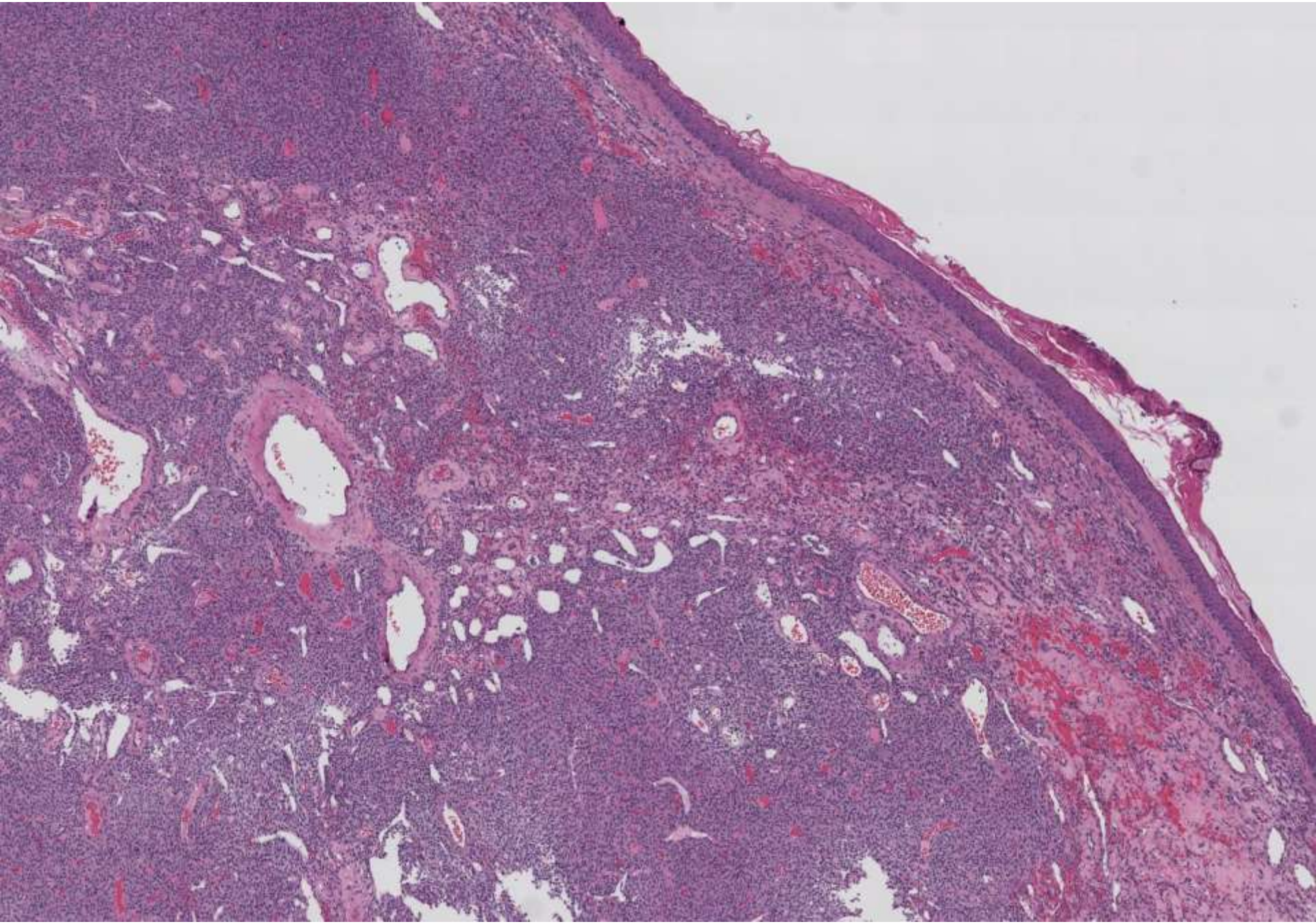
Vasculitides includes a heterogeneous group of disorders with the common histologic findings of vascular wall inflammation. Systemic or localized disease (eg, renal vasculitis) has serious consequences. The incidence of isolated gynecologic vasculitis diagnosed on pathology specimens and its significance is little known. We performed a 20 year retrospective review including 53 cases with vasculitis diagnosis affecting the female genital tract identified in pathology reports. None had prior symptoms or were diagnosed with generalized vasculitis, while one patient had prior diagnosis of fibromyalgia. Most patients presented with abnormal bleeding and were treated for conditions unrelated to vasculitis. The different types of vasculitis were: predominantly lymphocytic (nonspecific) 30 cases, necrotizing 17 cases and granulomatous 6 cases. Only 2 patients had additional serologic tests. None of the patients with isolated gynecologic vasculitis received corticosteroids or additional treatment related to the vasculitis. None of the patients developed systemic vasculitis at follow-up (2 months-19.5 years; mean, 5.5 years). Isolated gynecologic vasculitis diagnosed on pathology slides is rarely associated with systemic vasculitis. Potential isolated gynecologic vasculitis causes include: previous surgical interventions and vascular inflammation secondary to local neoplasm. In almost all cases, clinicians did not perform a thorough laboratory analysis to exclude systemic vasculitis and therapy was not required in any case, suggesting minimal clinical significance.

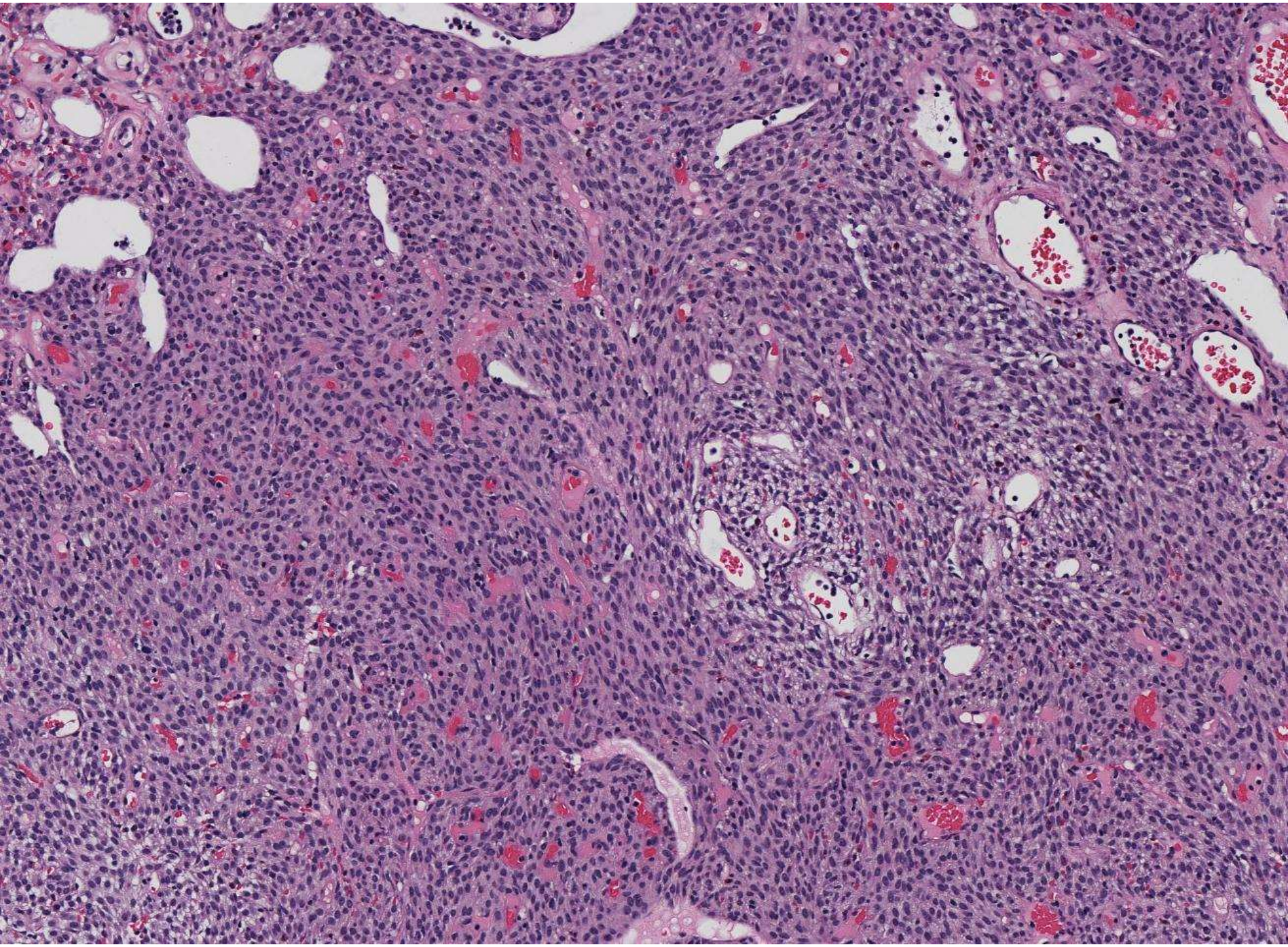
19-1004
scanned slide available!

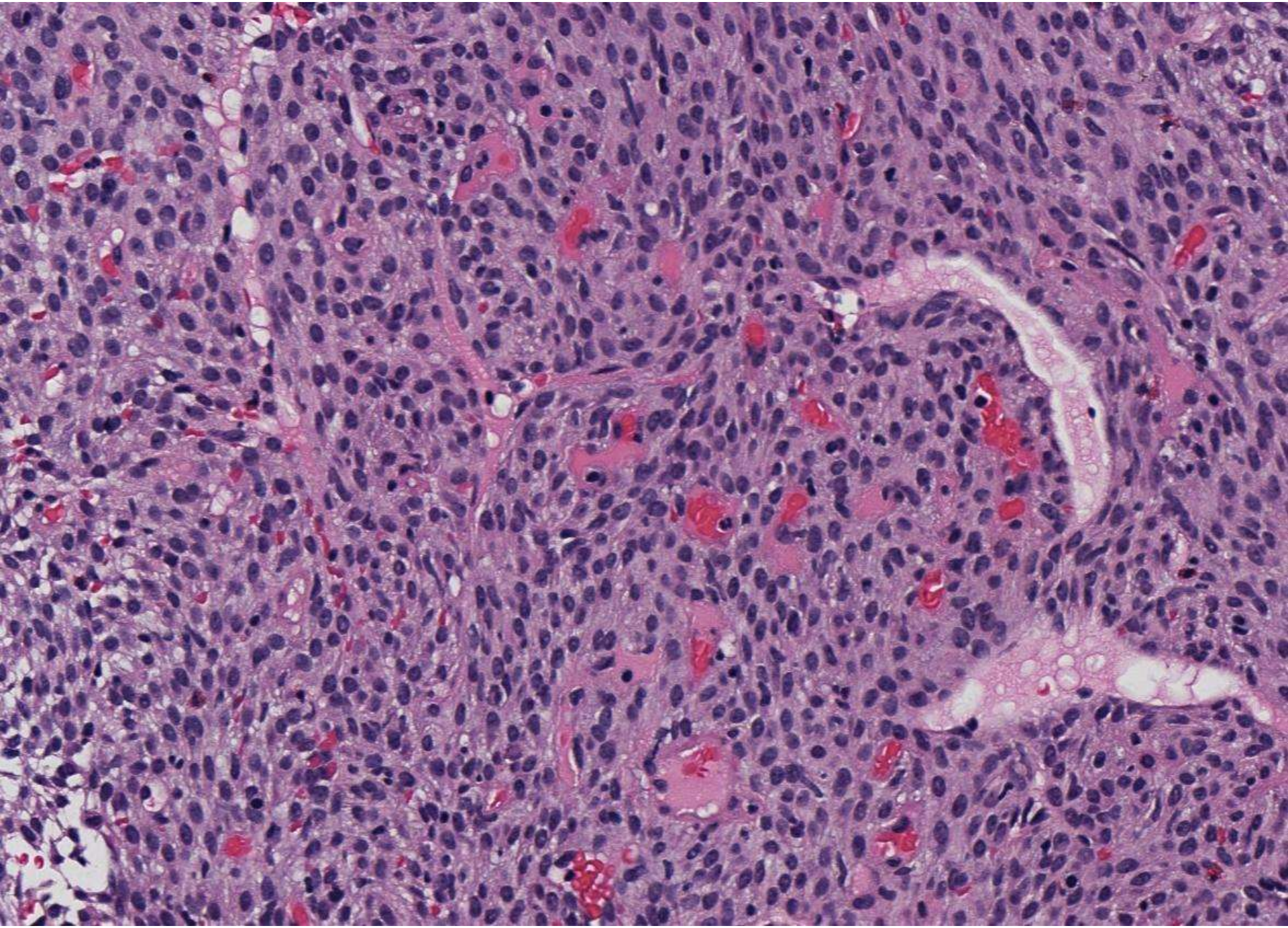
Ankur Sangoi; El Camino Hospital

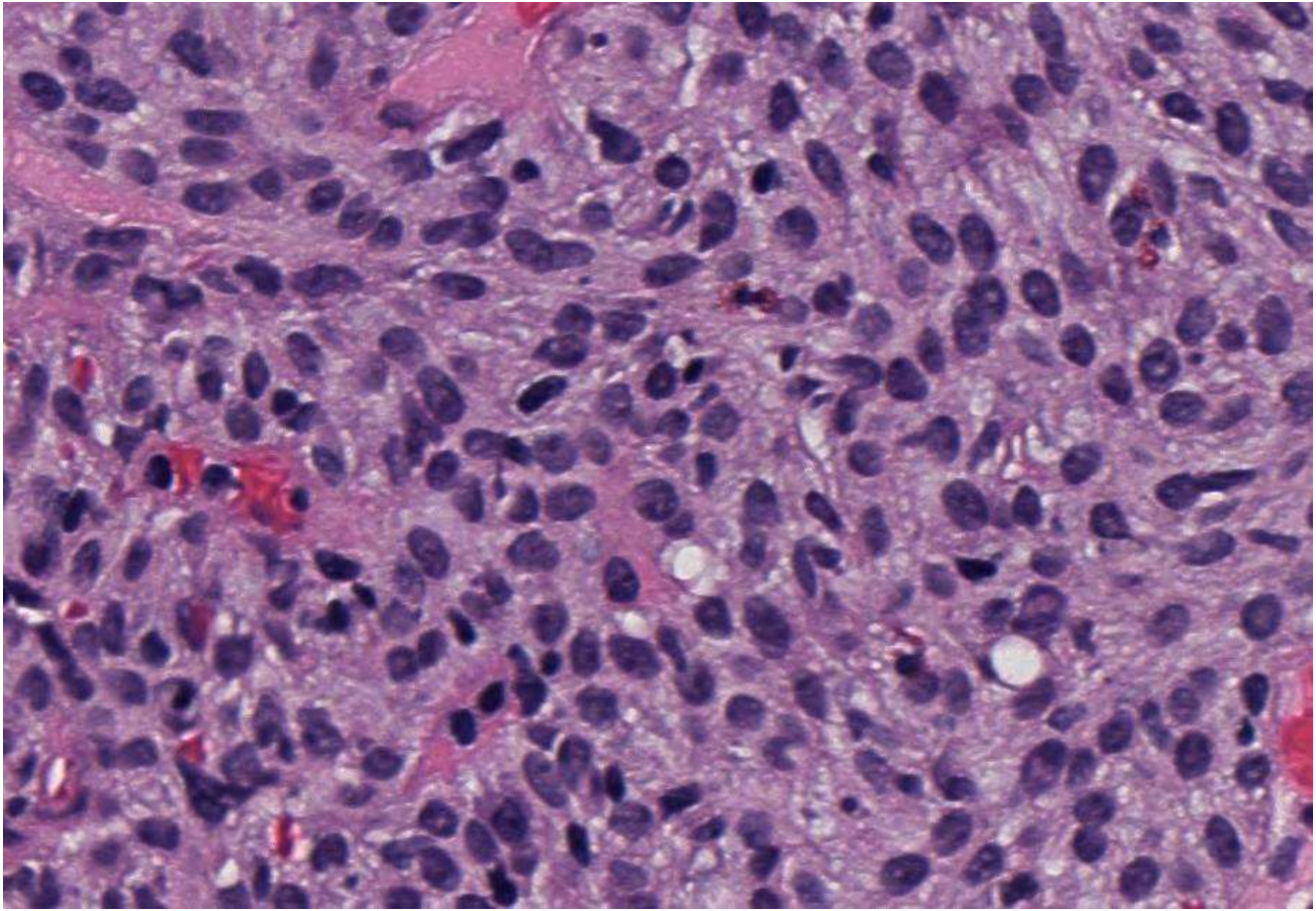
45-year-old female with left nasal cavity polyp.

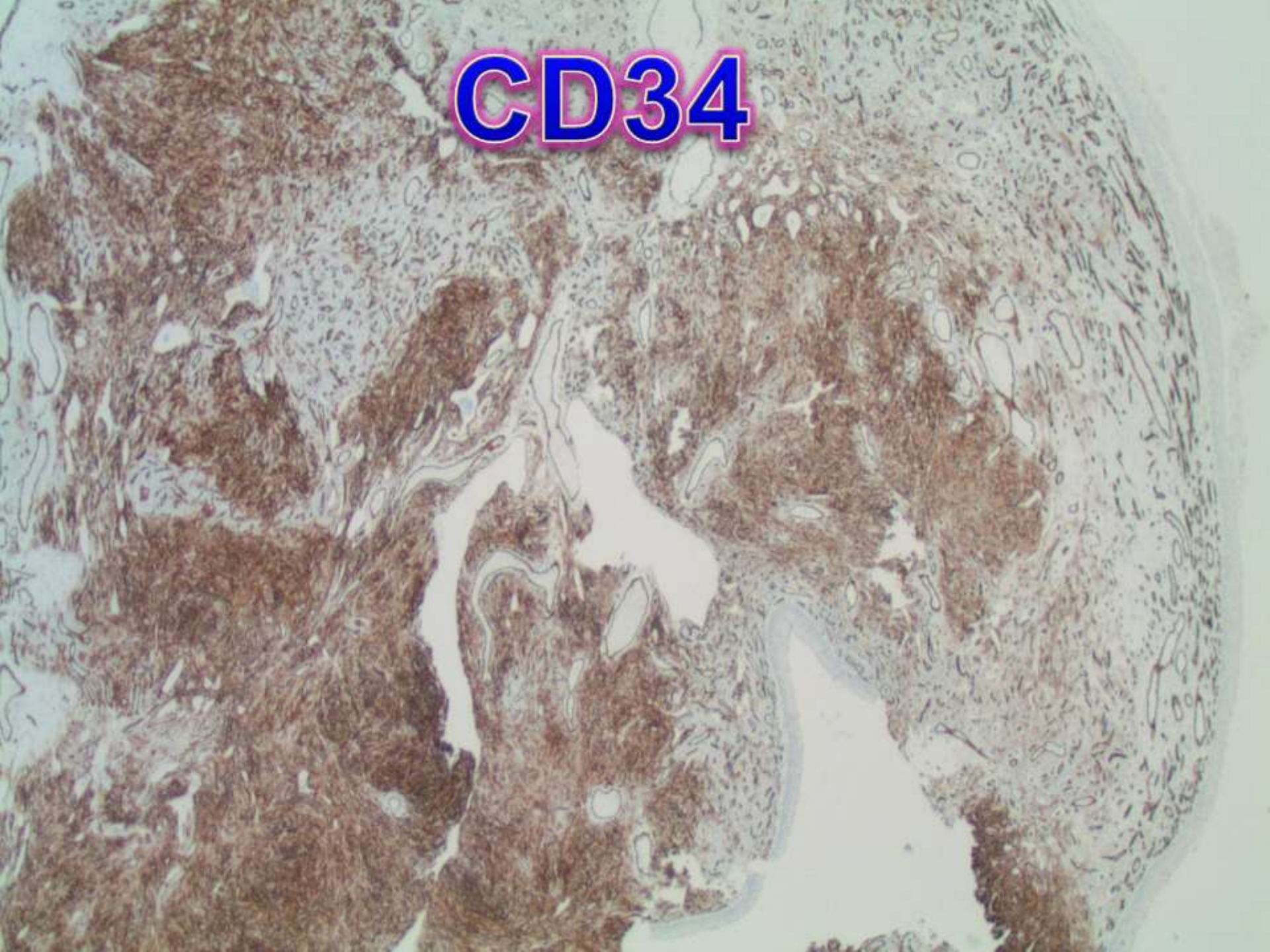


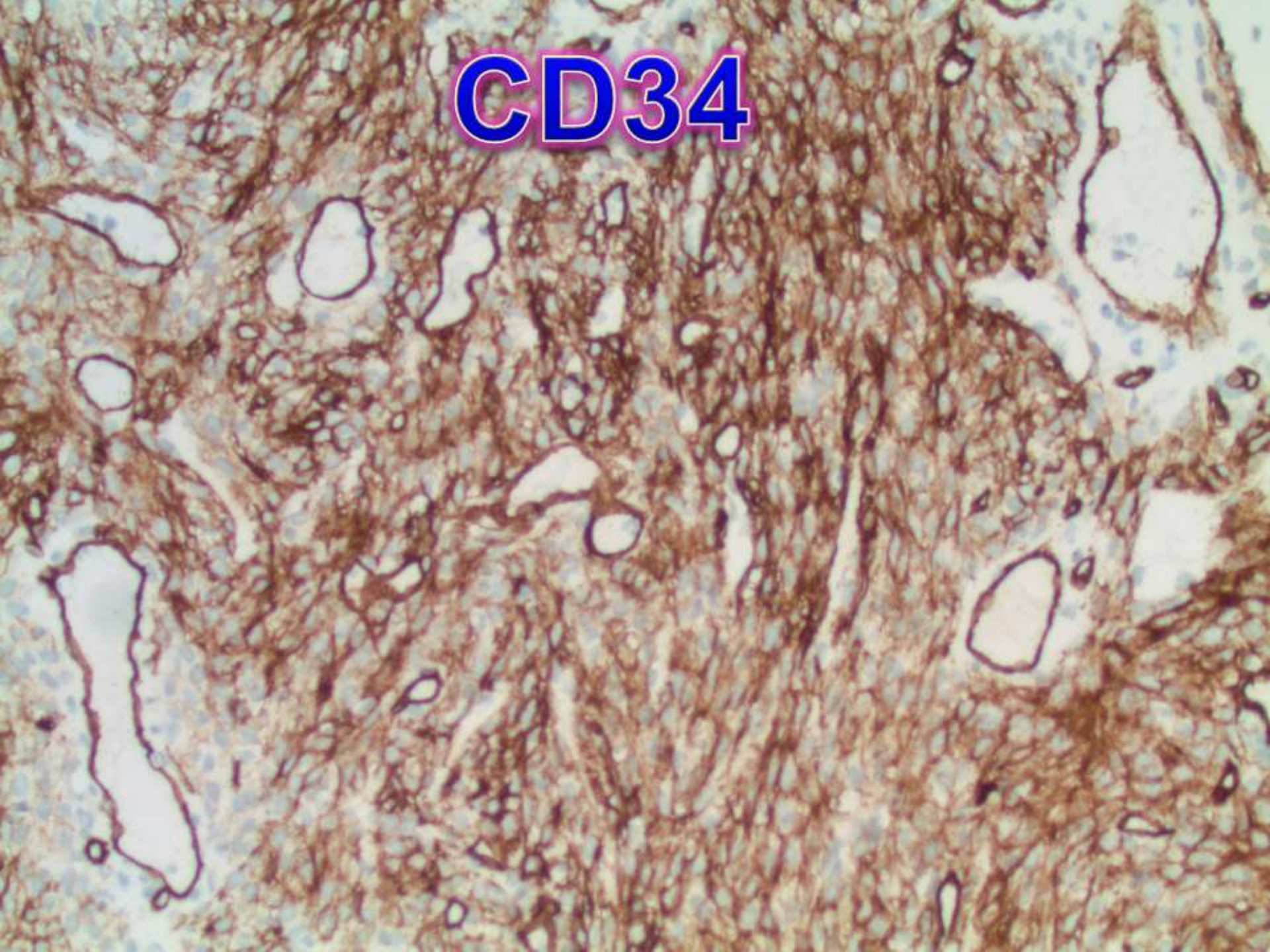









CD34


CD34

IHC SUMMARY

- **POSITIVE: CD34, SMA, nuclear beta-catenin**

- **NEGATIVE: STAT6, S100, EMA**

DDx

- **BENIGN/BORDERLINE**
  - Glomangiopericytoma
  - Solitary fibrous tumor
  - Myopericytoma
  - Lobular capillary hemangioma
  - Nasopharyngeal angiofibroma
  - Benign peripheral nerve sheath tumor
  - meningioma

DDx

- **MALIGNANT**
  - Monophasic synovial sarcoma
  - Biphenotypic sinonasal sarcoma
  - Malignant peripheral nerve sheath tumor

Head and Neck Pathology
https://doi.org/10.1007/s12105-019-01063-9

ORIGINAL PAPER

Variability of CD34 Expression in Sinonasal Glomangiopericytoma: A Potential Diagnostic Pitfall

Ankur R. Sangoi[1] · Justin A. Bishop[2]

Received: 1 July 2019 / Accepted: 3 August 2019

Abstract

Sinonasal glomangiopericytoma (GPC) is an uncommon primary sinonasal neoplasm showing a perivascular myoid differentiation. Originally perceived as an intranasal counterpart to soft tissue hemangiopericytomas, initial immunohistochemical reports showed mostly negative to focal weak reactivity for CD34 as useful in separating GPC (almost always benign) from morphologic mimics, mainly solitary fibrous tumor (potentially aggressive). In anecdotally encountering cases of GPC with CD34 reactivity beyond the expected weak/negative immunoprofile, we sought to formally evaluate CD34 staining in 10 cases of GPC from two different vendors in conjunction with a meta-analysis of other GPC series reporting CD34 staining. Ten cases of GPC were retrieved from the authors' pathology archives (left nasal cavity = 7, right nasal cavity = 3; 5 men, 5 women; average age 59.0 years with range of 43–77 years). Follow-up showed no evidence of disease after complete resection from all 10 cases (average follow-up length of 53.3 months, range 6–106 months). All 10 GPC cases (100%) showed positivity using CD34 from Leica (QBend10 clone), with most showing moderate to diffuse staining intensity and moderate extent, while only 2 of 10 cases (20%) showed positivity using CD34 from Ventana (QBend10 clone), with both positive cases showing weak staining intensity and focal extent. Literature review of other studies (reporting ≥ 5 GPC cases) found a wide spectrum of CD34 positivity ranging from 0 to 100%; including our GPC cases, CD34 showed a cumulative positivity of 28%. Although negative CD34 reactivity has been historically regarded as prototypic for GPC, in this study we have exposed laboratory variability in CD34 expression and have shown that reliance on expected negative reactivity in GPC can be a clinically relevant diagnostic pitfall. Our findings suggest a panel approach in selecting diagnostic immunostains rather than relying on CD34 alone in the assessment of spindle cell neoplasms in the sinonasal tract with admixed prominent staghorn-like vasculature.

Table 2 Review of CD34 immunohistochemical results for glomangiopericytoma

Study	Positive cases	Staining pattern	Antibody vendor/clone/dilution
Thompson et al. [3]	5/60 (8%)	Focal, weak	BioGenex Labs/unspecified clone/1:40
Tse et al. [4]	0/6 (0%)	None	Becton–Dickinson/My10/unspecified dilution
Kuo et al. [5]	0/5 (0%)	None	Dako/unspecified clone/1:50
Agaimy et al. [6]	4/6 (67%)	Focal, weak	Immunotech/QBend10/1:200
Lasota et al. [7]	13/13 (100%)	Variable	Dako/QBend10/1:150
Current	5/5 (100%)	Mostly moderate, diffuse	Leica/QBend10/ready-to-use
Current	1/5 (20%)	Focal, weak	Ventana/QBend10/ready-to-use
Total	28/100 (28%)		

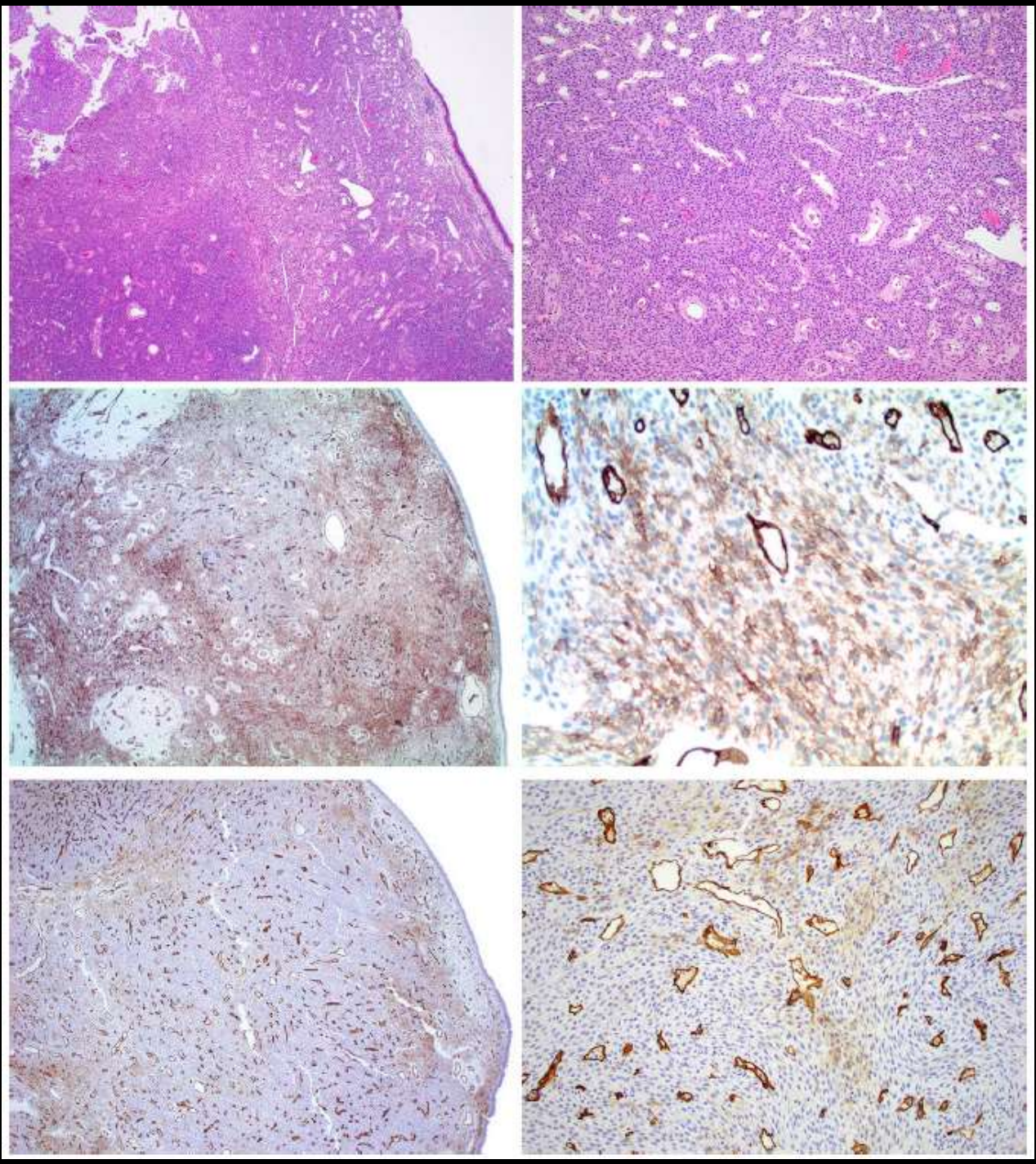


Table 3 Key differential diagnosis for glomangiopericytoma and suggested immunohistochemical panel

Benign/borderline tumors	Suggested immunoprofile
Glomangiopericytoma	SMA+, STAT6-, TLE1-, CD31-, CD117-, SOX10-, S100-, EMA-
Solitary fibrous tumor	STAT6+, TLE1-
Myopericytoma	Nuclear beta catenin-, STAT6-, TLE1-
Lobular capillary hemangioma	CD31+, SMA-, STAT6-, TLE1-
Nasopharyngeal angiofibroma	CD117+, AR+, SMA-, STAT6-, TLE1-
Benign peripheral nerve sheath tumor	SOX10+, S100+, STAT6-, TLE1-
Meningioma	EMA+, PR+, STAT6-, TLE1-
Malignant tumors	**Suggested immunoprofile**
Monophasic synovial sarcoma	TLE1+, STAT6-, SOX10-, S100-
Biphenotypic sinonasal sarcoma	PAX3+, S100+, SMA+, SOX10-, STAT6-, TLE1-
Malignant peripheral nerve sheath tumor	SOX10+, S100+, STAT6-, TLE1-, INI1- (epithelioid type), h3k27me3-
Melanoma	SOX10+, S100+, STAT6-, TLE1-

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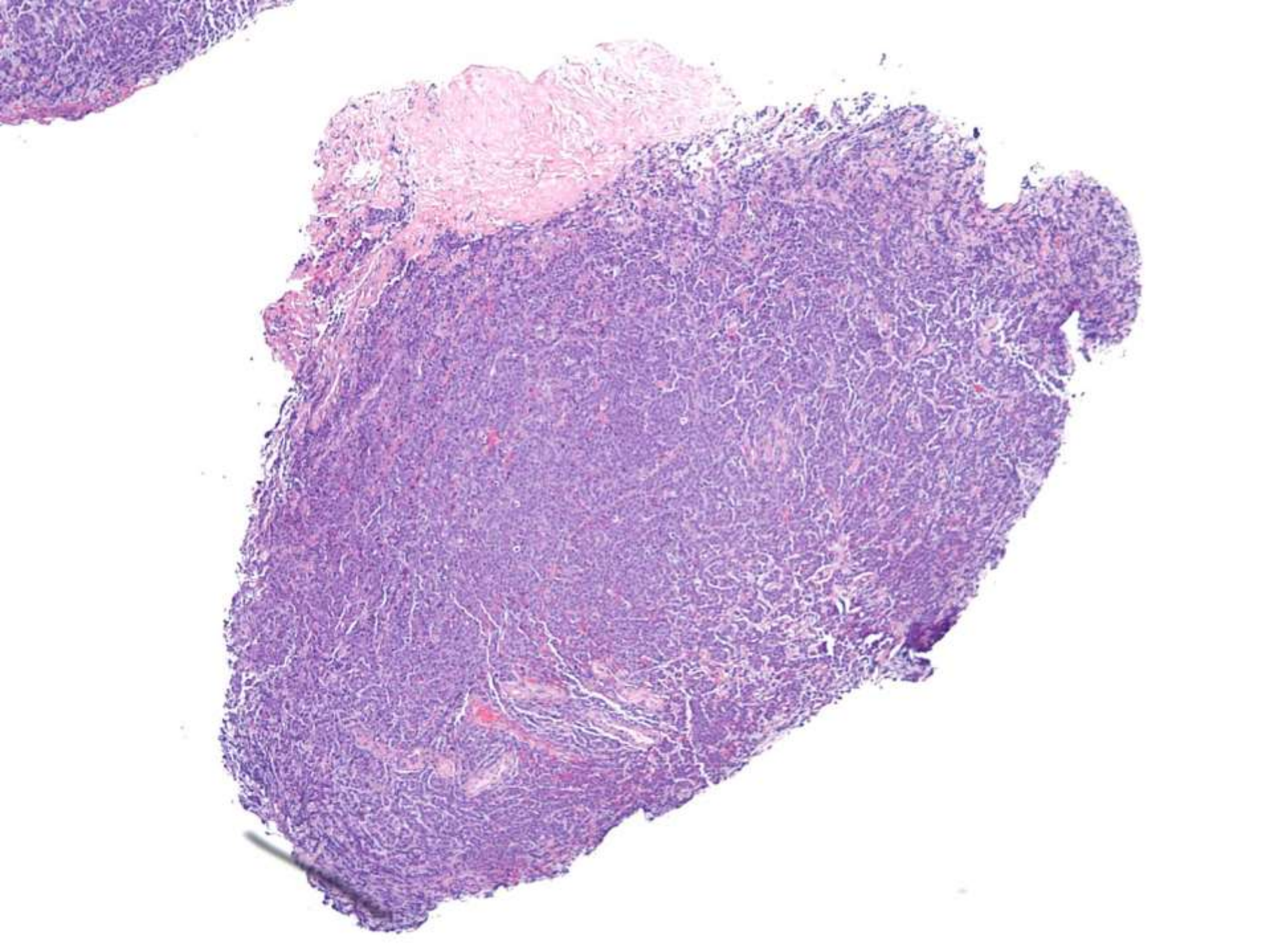
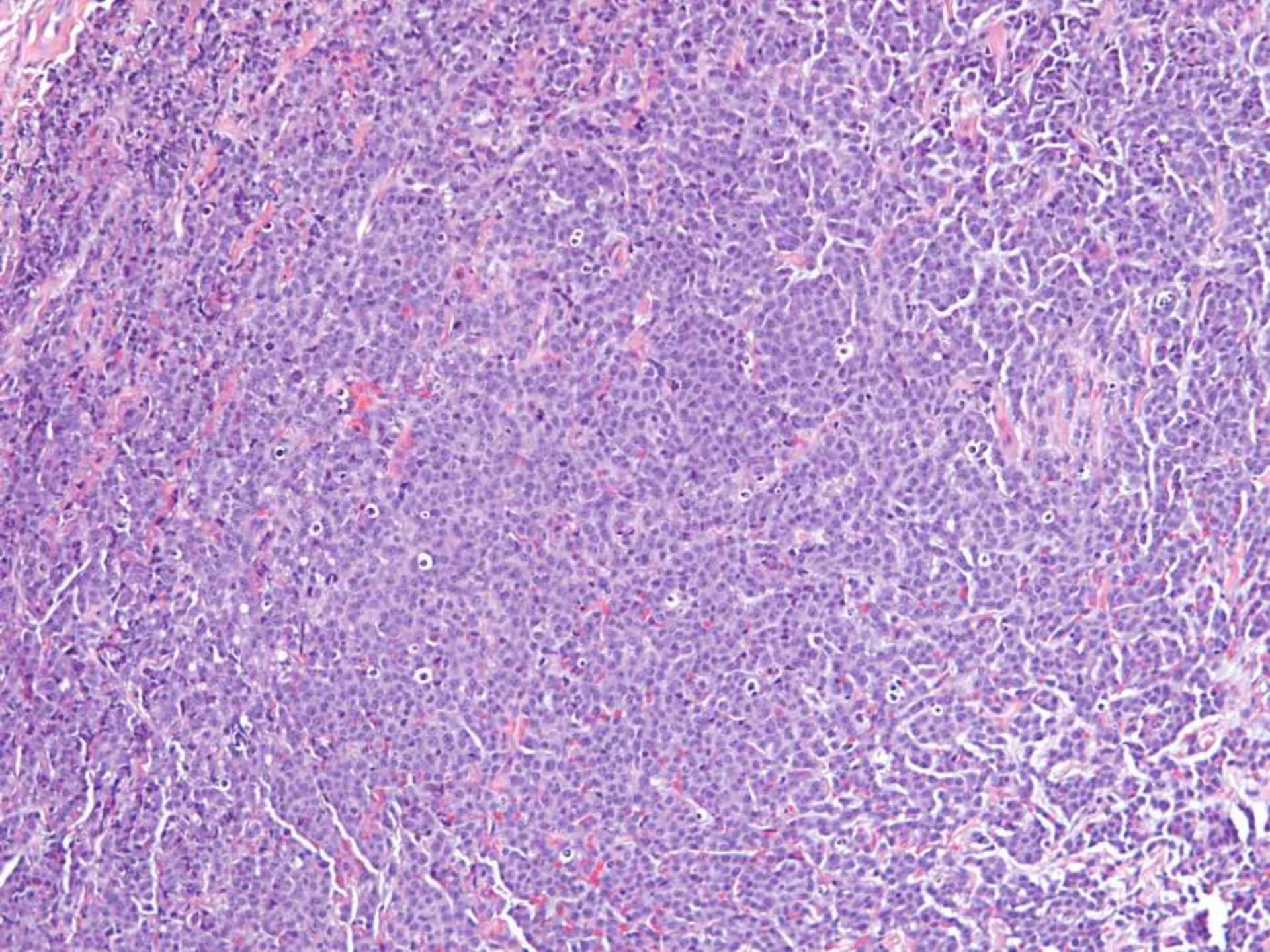
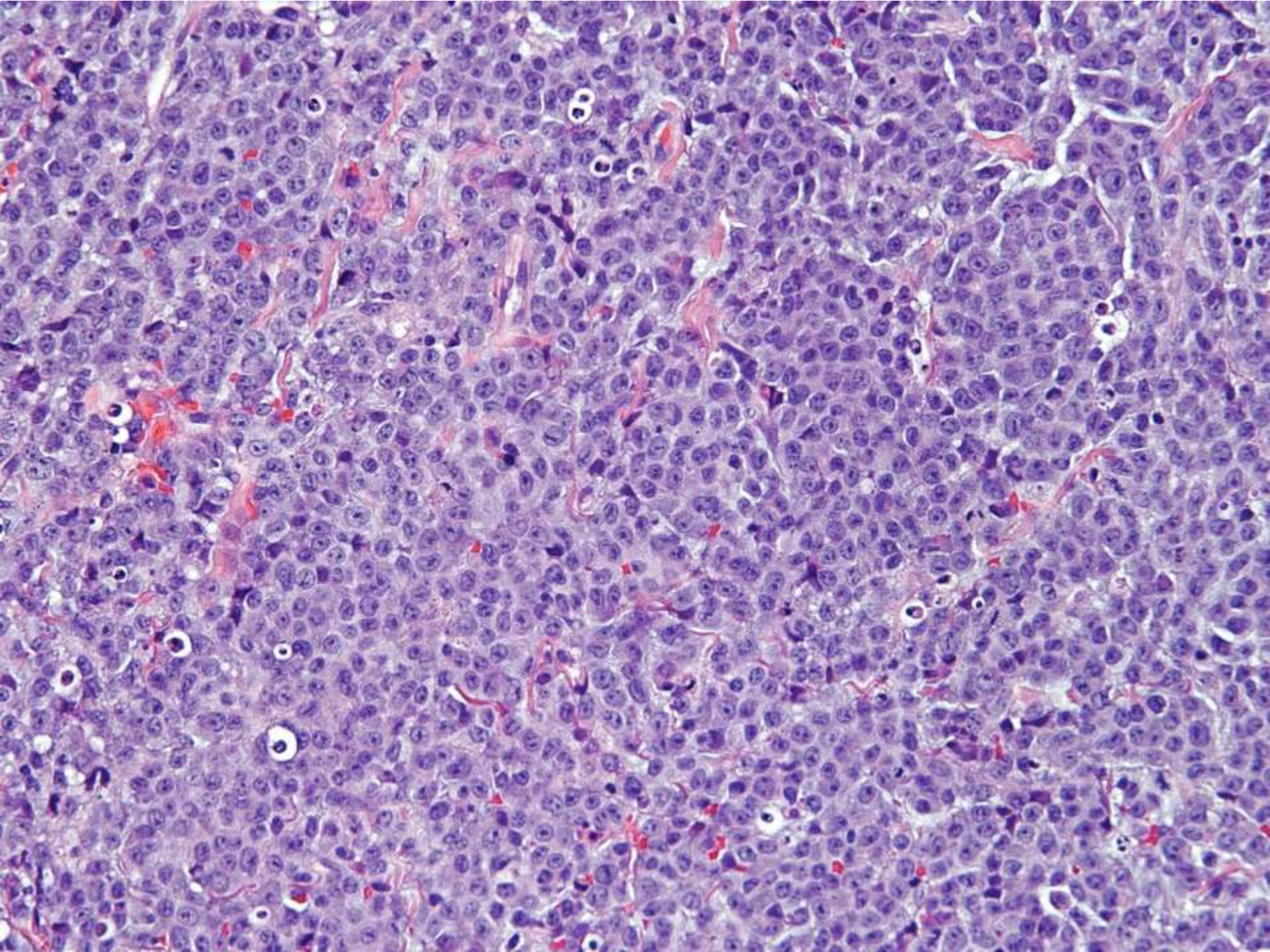
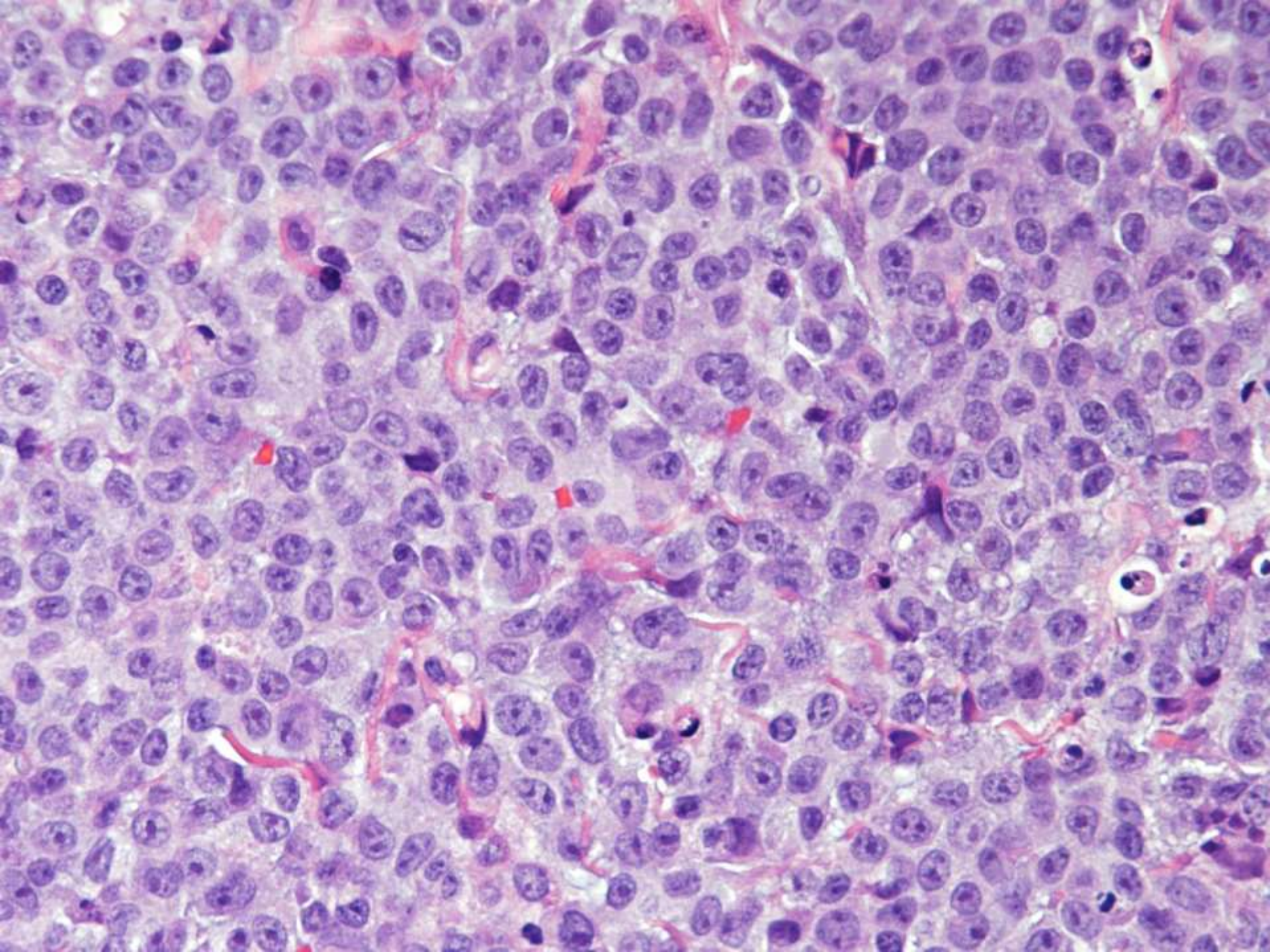
Sebastian Fernandez-Pol; Stanford

55-year-old with new salmon patch lesion on bilateral conjunctiva.



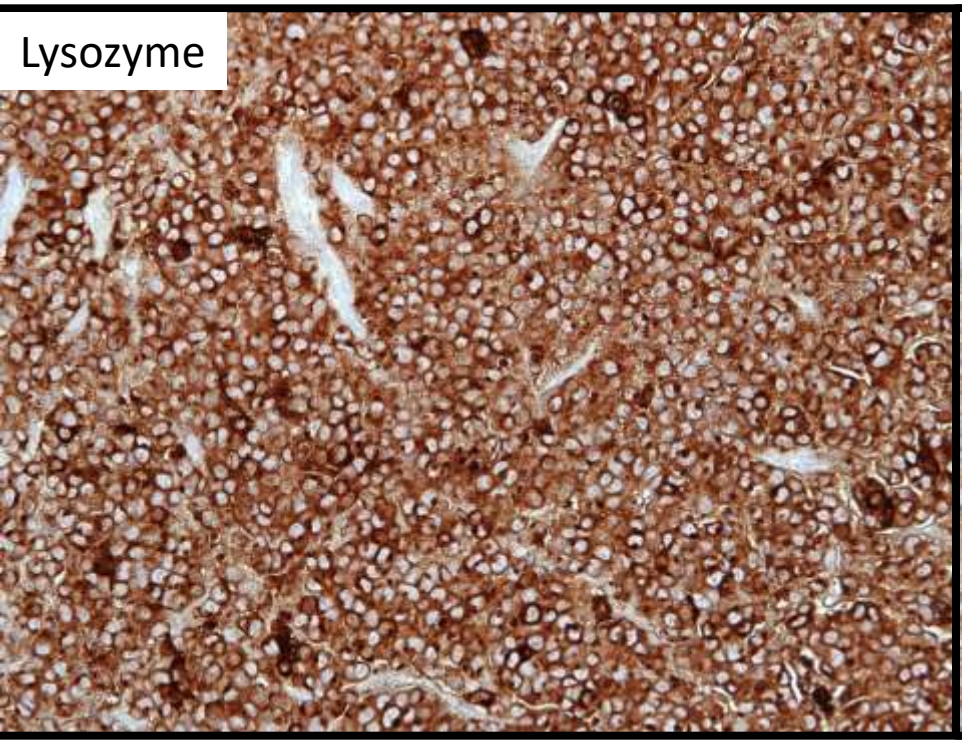


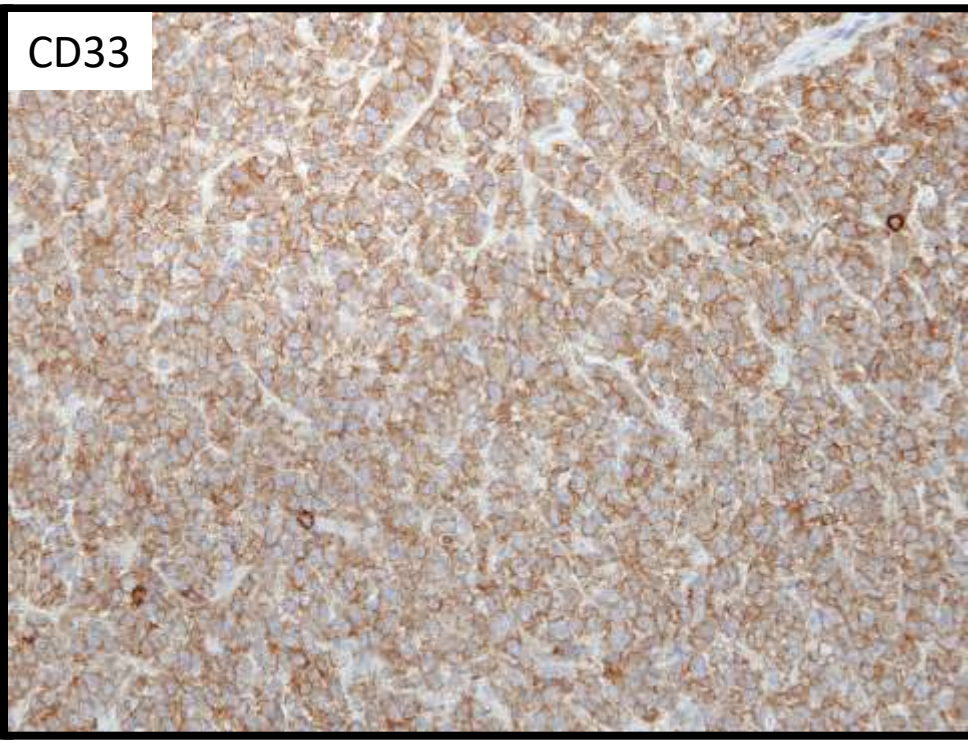




Negative stains

- Ckmix, CD34, CD14, CD117, TdT, MCT, CD19, CD22, CD79a, CD3, and CD138





Positive: CD33, lysozyme, CD45RB (moderate), CD43, and MPO (very dim)
Negative: Ckmix, CD34, CD14, CD117, TdT, MCT, CD19, CD22, CD79a, CD3, and CD138

Diagnosis

- Myeloid sarcoma
  - Extramedullary tumor mass consisting of myeloid blasts, with or without maturation
  - Tumor mass effaces tissue architecture

- Myeloid sarcoma = Acute myeloid leukemia

- Patient had history of chronic myelomonocytic leukemia - **AML with myelodysplasia related changes**

Follow up

- Chronic myelomonocytic leukemia with normal karyotype and with *ASXL1*, *CBL*, *SRSF2*, and *TET2*
- Azacitidine and decitabine
- 3 years after CMML diagnosis, transformed to AML with extramedullary disease
- Liposomal daunorubicin/cytarabine (Vyxeos)
- Developed invasive Rhizopus fungal pneumonia, neutropenic fever (resolved)
- End of treatment bone marrow with ~31% blasts and skin biopsy showed leukemia
- Deceased

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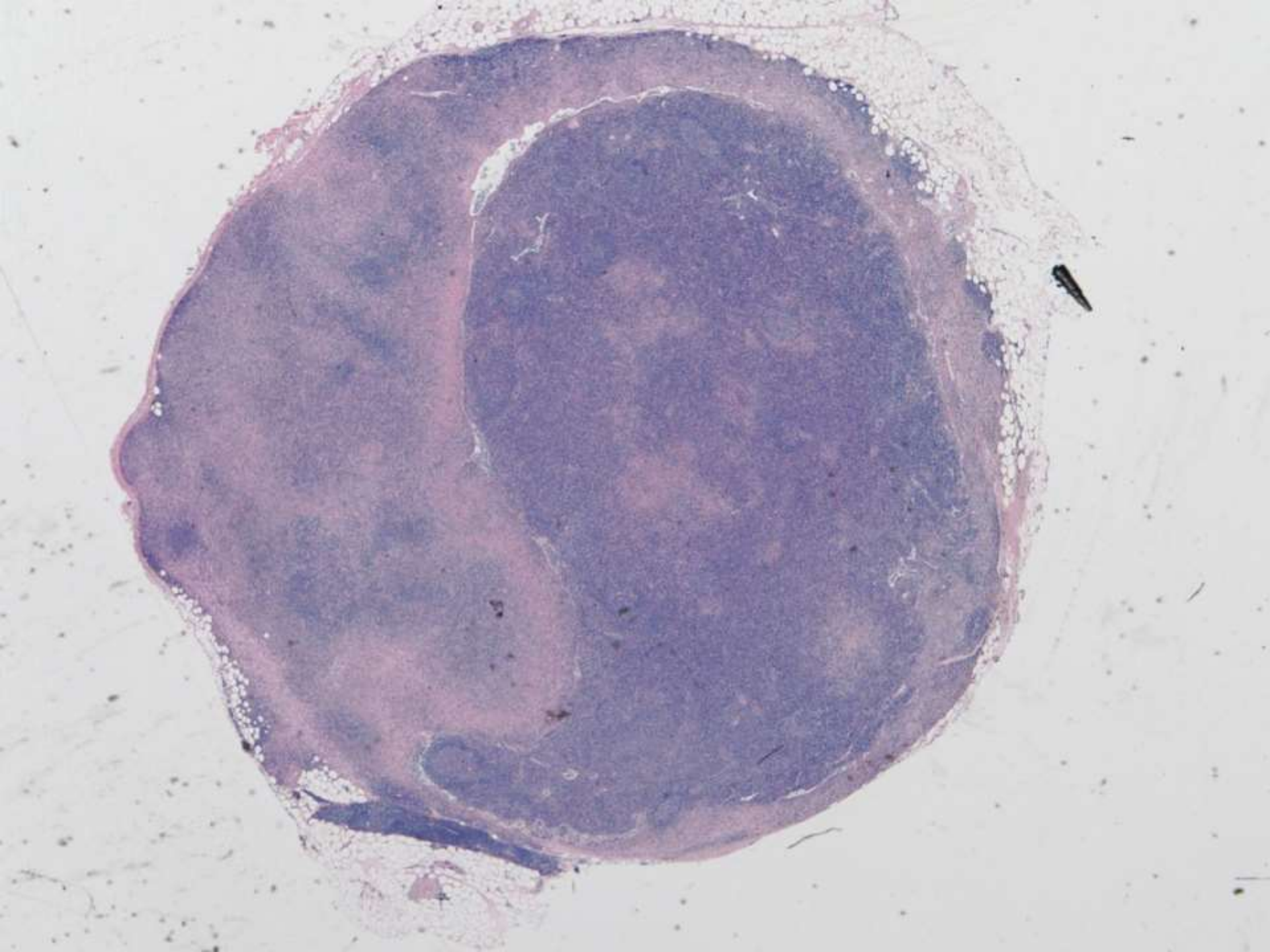
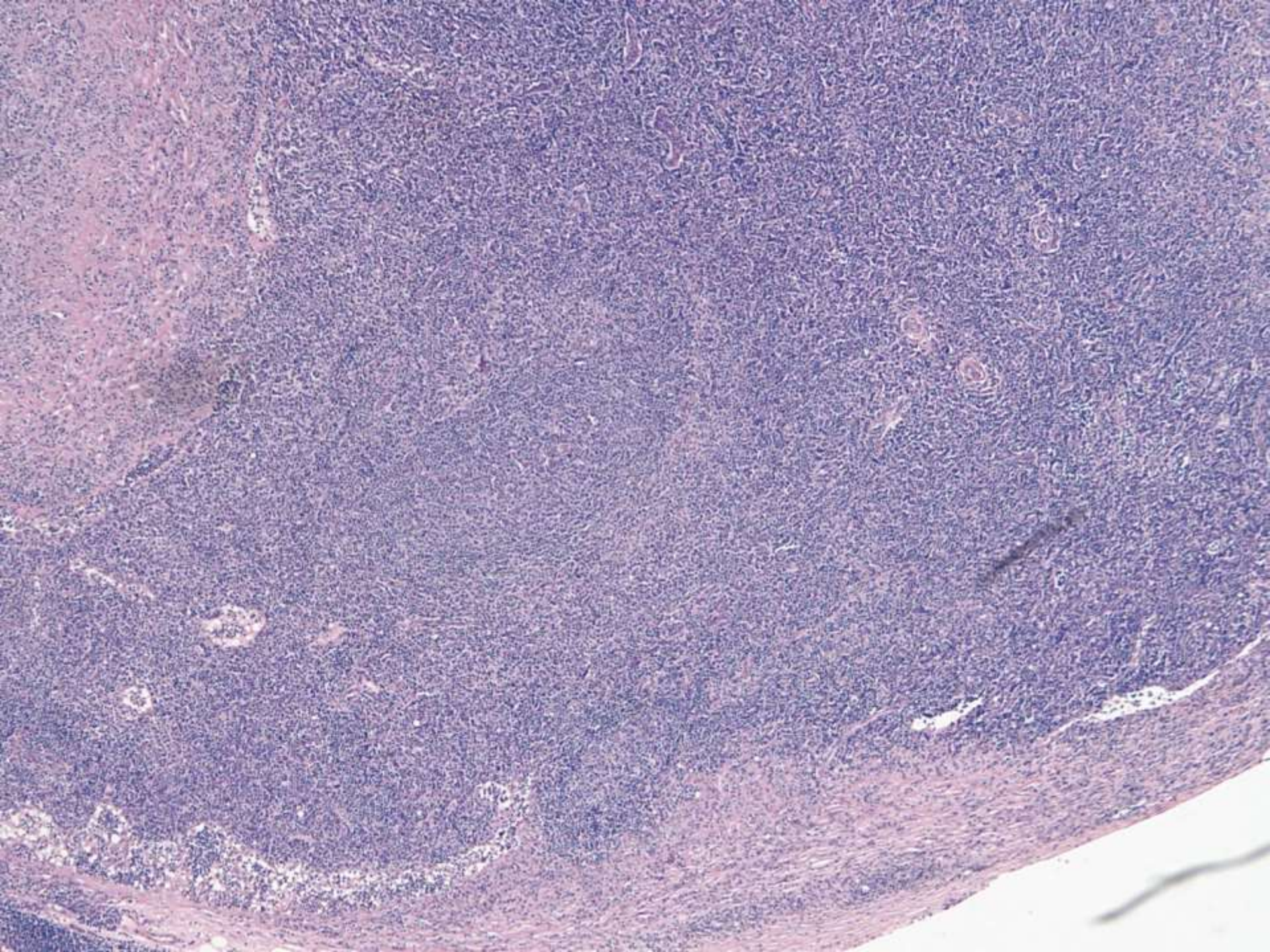
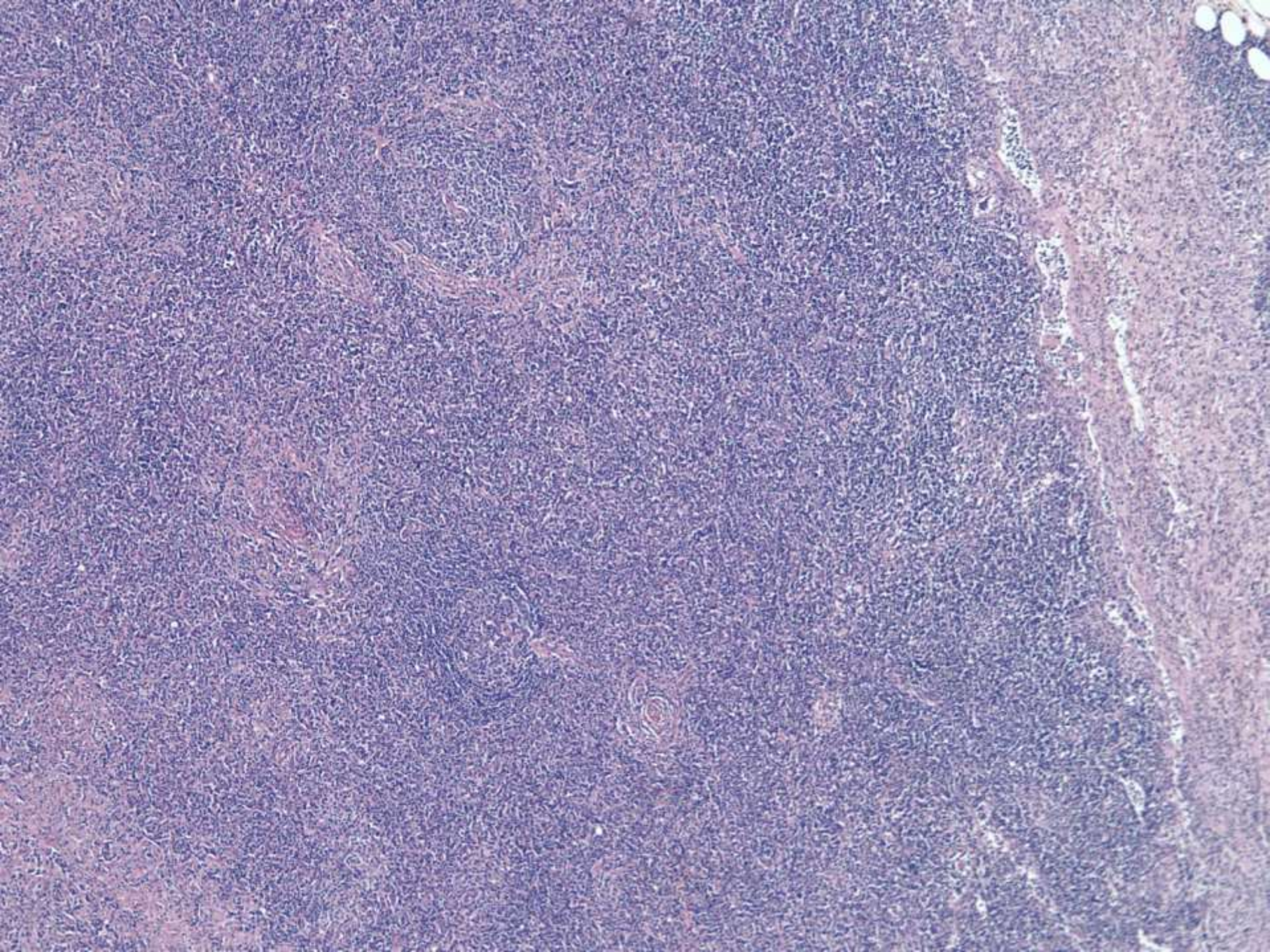
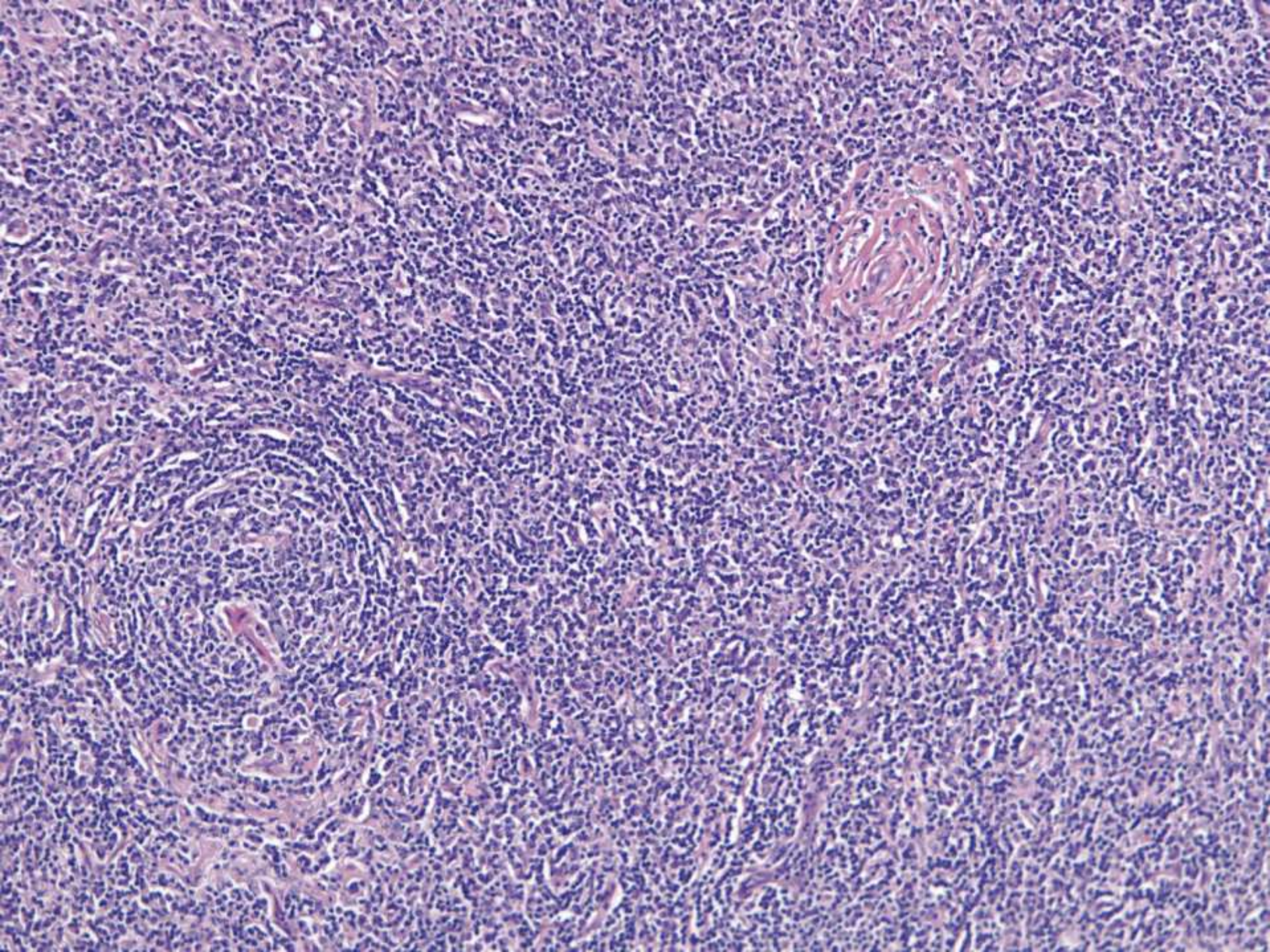
Sebastian Fernandez-Pol; Stanford

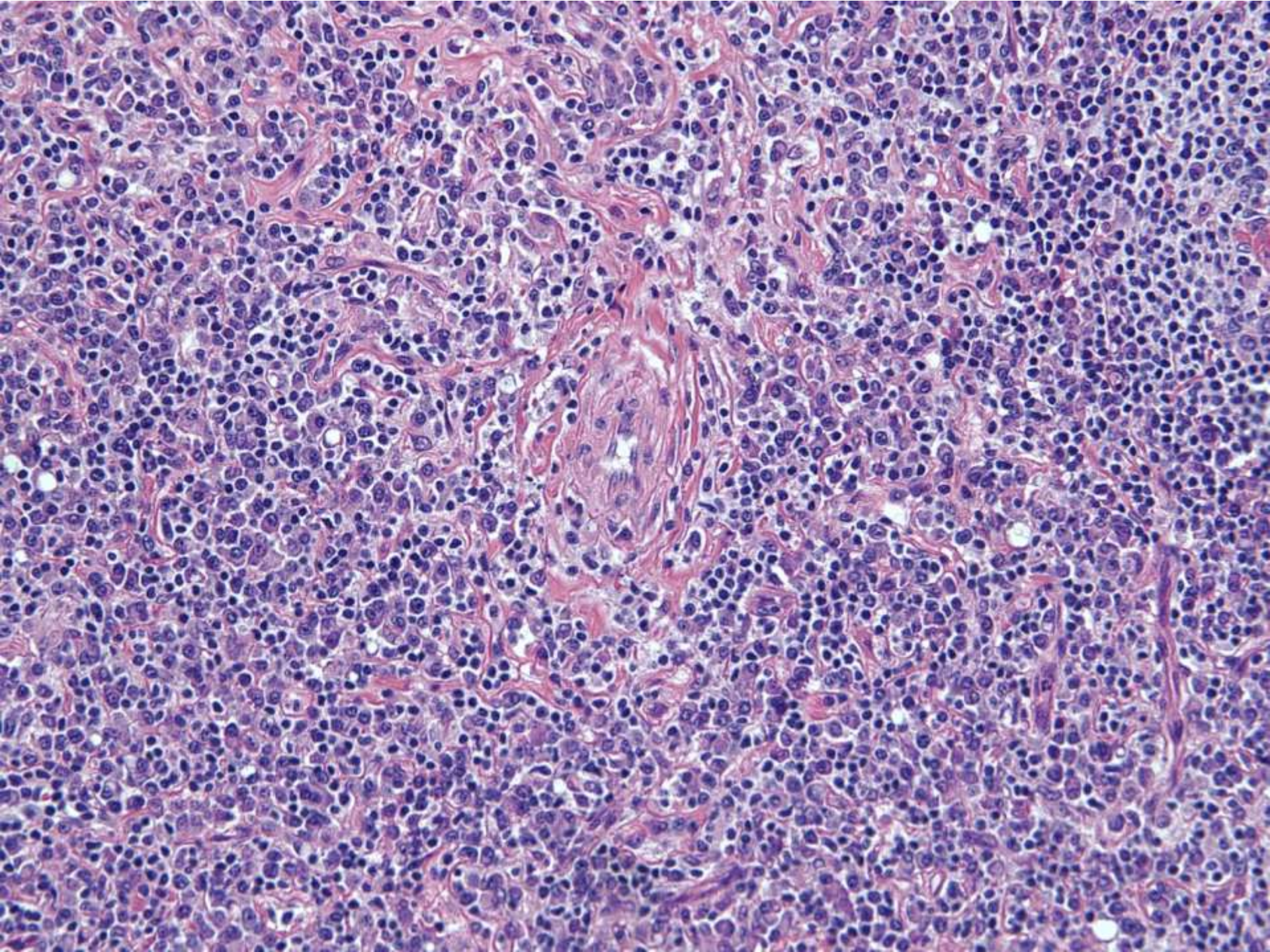
59-year-old male with right posterior neck mass.

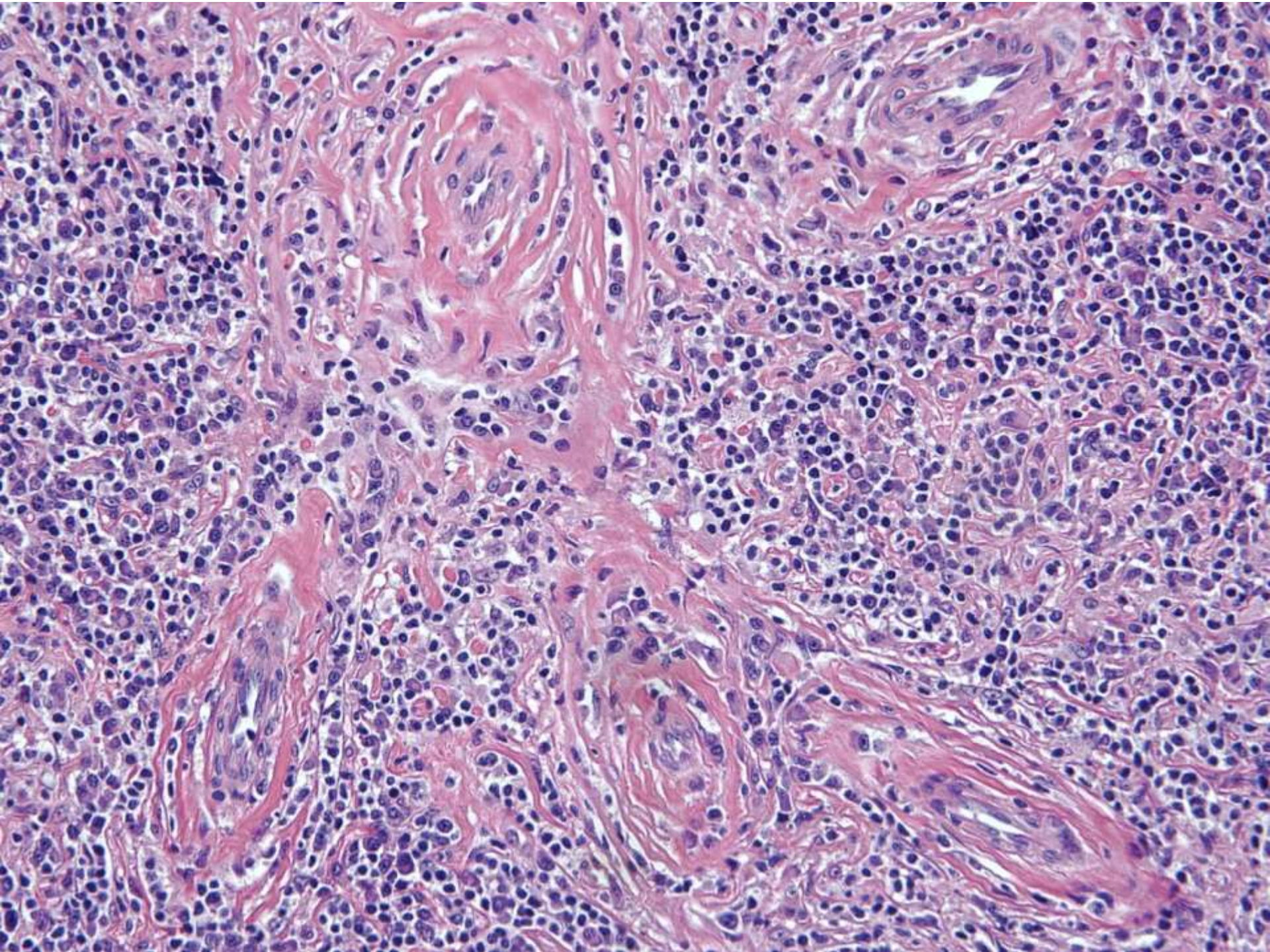


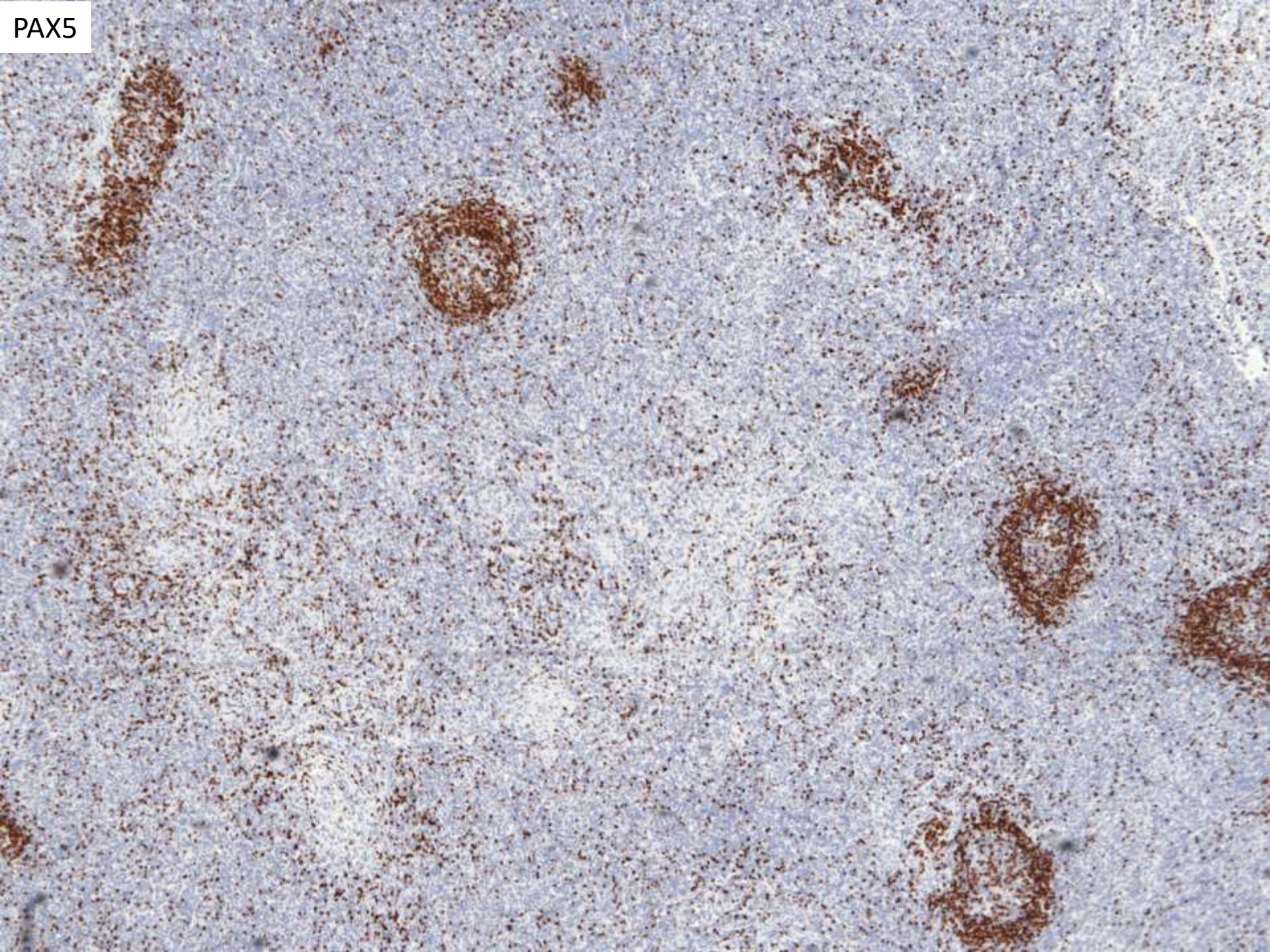


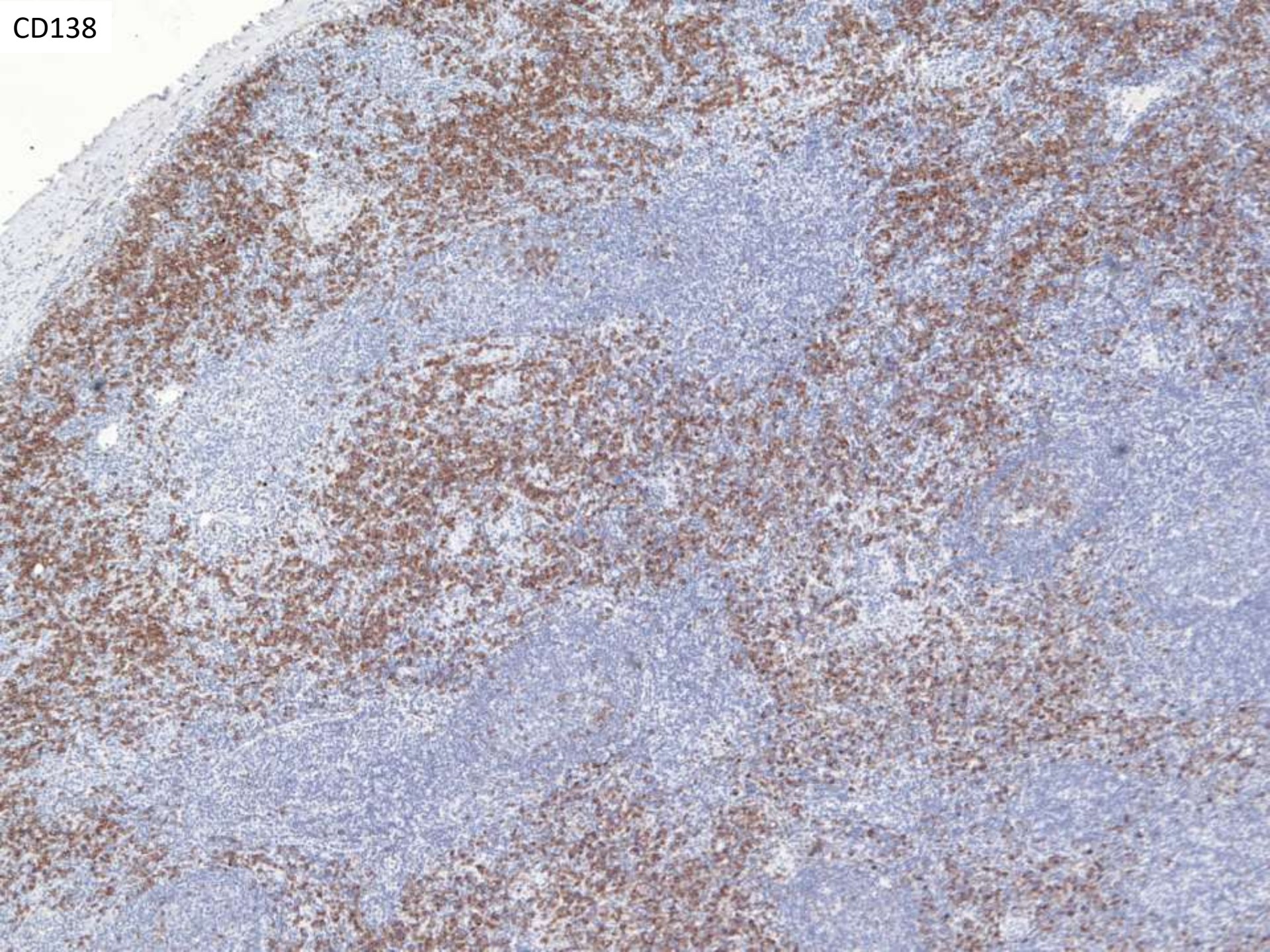


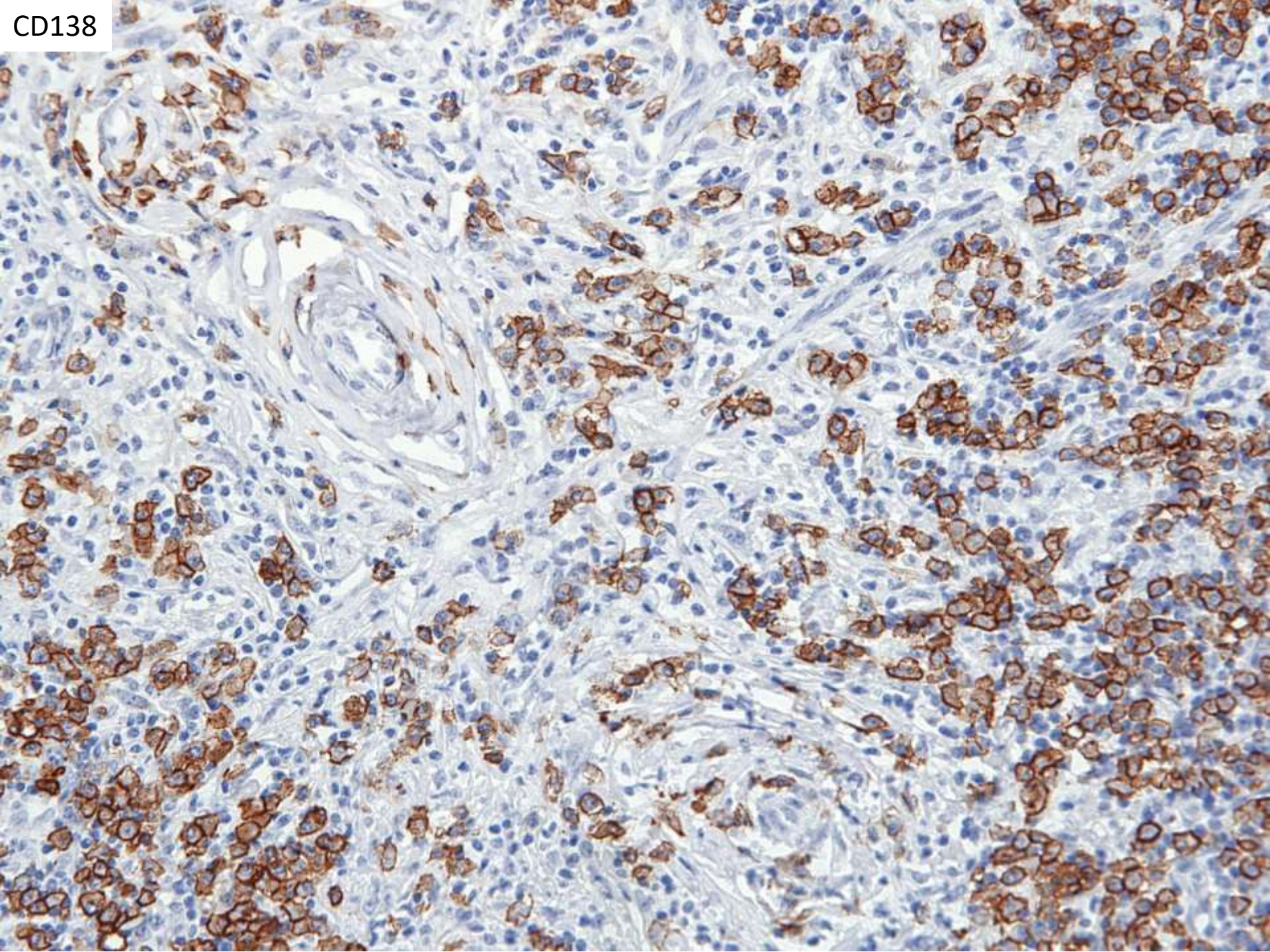




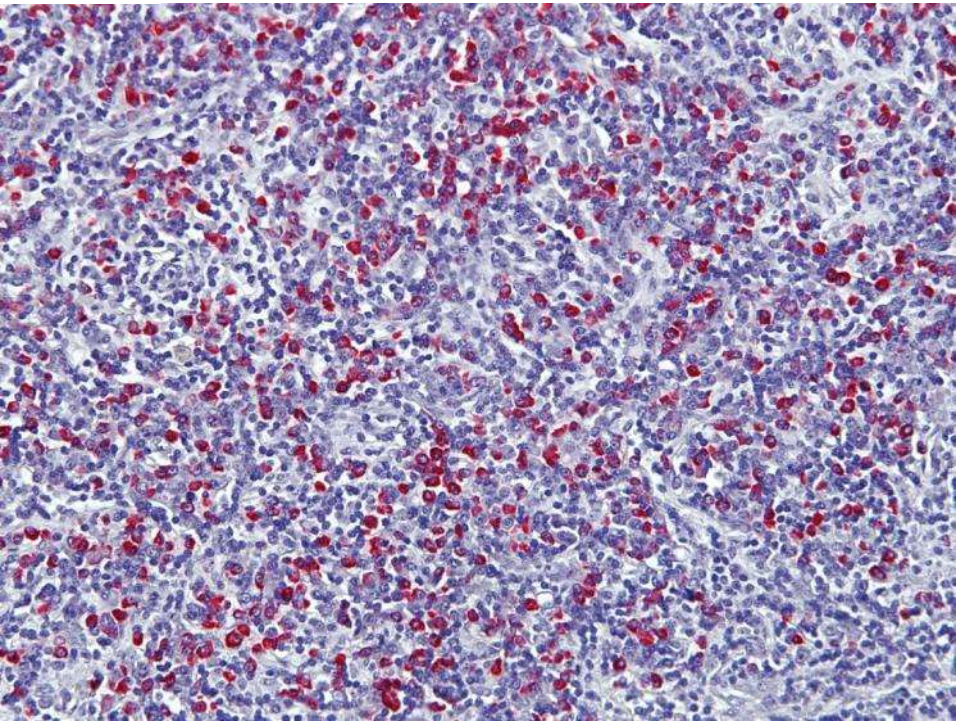



PAX5

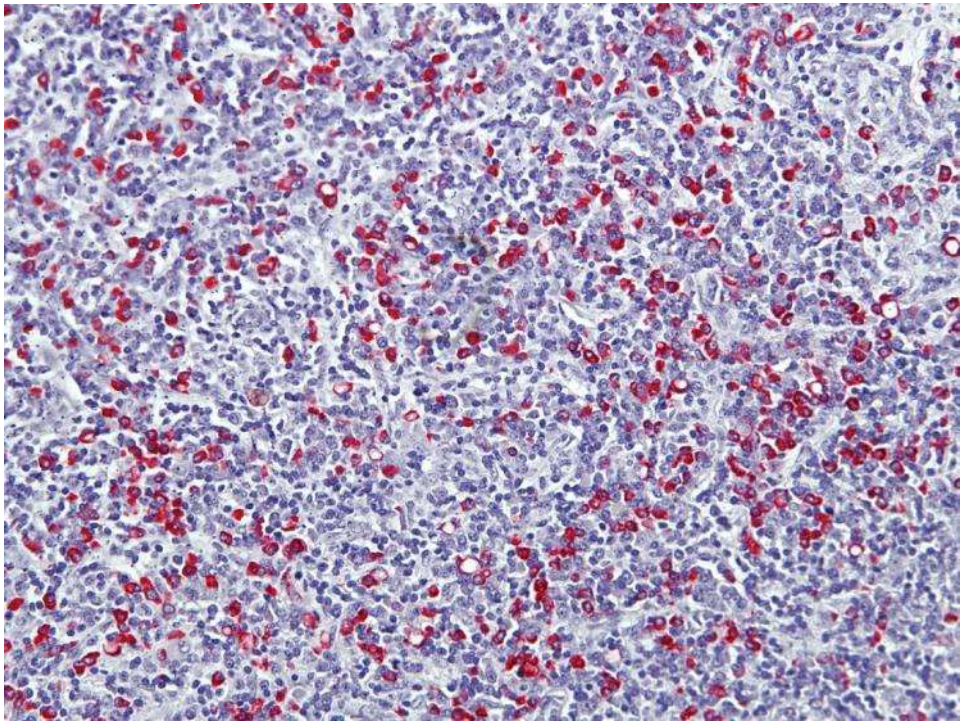

CD138


CD138

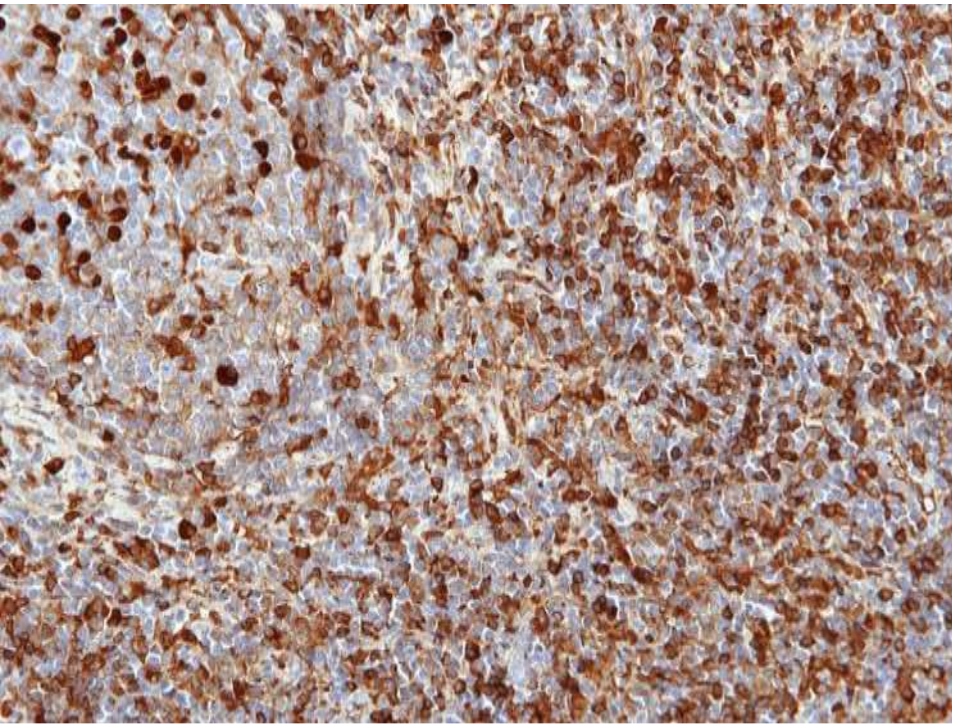
Kappa



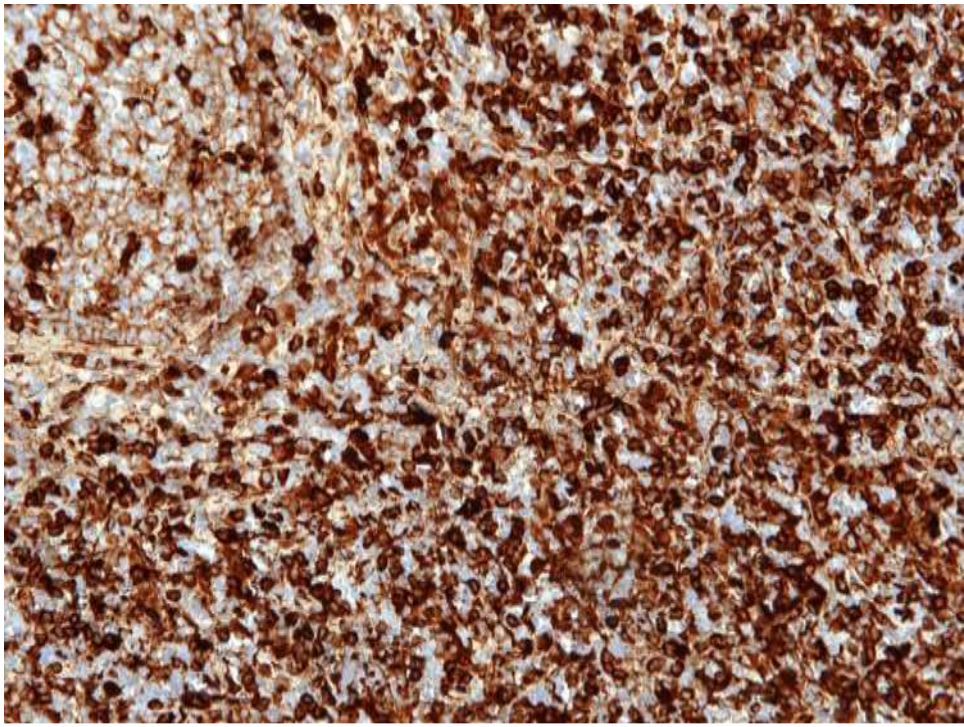
Lambda



IgG



IgG4



Diagnosis

- Reactive follicular hyperplasia with extensive plasmacytosis, compatible with IgG4-related sclerosing lymphadenopathy

Differential diagnosis for IgG4-related lympadenopathy

- Multicentric Castleman disease
- True inflammatory pseudotumor
- Luetic lymphadenitis (syphilis)
- Rosai-Dorfman disease
- Inflammatory myofibroblastic tumor

Wick MR, O'Malley DP. Lymphadenopathy associated with IgG4-related disease: diagnosis & differential diagnosis. Semin Diagn Pathol.

IgG4-related disease

- Characterized by tumefactive sclerosing inflammatory lesions predominantly affecting extranodal sites
  - Pancreas
  - Salivary gland
  - Lacrimal gland

Cheuk W, Chan JK. Lymphadenopathy of IgG4-related disease: an underdiagnosed and overdiagnosed entity. Semin Diagn Pathol. 2012 Nov;29(4):226-34.

Histology of IgG4-related disease in extranodal sites

Two or more characteristic features:

1) Dense lymphoplasmacytic infiltrate

2) Fibrosis that is typically storiform in pattern

3) Obliterative phlebitis

4) Increased number of IgG4+ plasma cells/HPF

5) IgG4+/IgG+ plasma cell ratio of >40%

Bledsoe JR, Della-Torre E, Rovati L, Deshpande V. IgG4-related disease: review of the histopathologic features, differential diagnosis, and therapeutic approach. APMIS. 2018;126:459-476.

Lymph node involvement by IgG4-related disease

- Lymphadenopathy can appear before, concurrent with, or after the diagnosis of IgG4-related disease (IgG4-RD)
- Constitutional symptoms are absent
- Up to 80% of patients with IgG4-related disease are found to have systemic lymphadenopathy on imaging

Cheuk W, Chan JK. Lymphadenopathy of IgG4-related disease: an underdiagnosed and overdiagnosed entity. Semin Diagn Pathol. 2012 Nov;29(4):226-34.

IgG4+ plasma cells in lymph nodes

- **IgG4-related lymphadenopathy**
  - Defined by lymphadenopathy developing in patients with IgG4-related sclerosing disease

- Increase of IgG4 cells and IgG4/IgG ratio in lymph node:
  - Some cases of rheumatoid arthritis
  - Rosai–Dorfman disease
  - Multicentric Castleman disease

Lymph node IgG4-related LAD Diagnostic "criteria"

- More than 100 IgG4+ plasma cells per hpf
  - Raised from 50 with increased specificity on minimal loss of sensitivity
- IgG4/IgG ratio higher than 40%
  - "Practically universal agreement for this threshold"
- IgG4 cells normally account for approximately 5% of all IgG cells

Cheuk W, Chan JK. Lymphadenopathy of IgG4-related disease: an underdiagnosed and overdiagnosed entity. Semin Diagn Pathol. 2012 Nov;29(4):226-34.

IgG4-related disease: Lymph node morphology

- Castleman disease-like (type I)
- Follicular hyperplasia (type II)
- Interfollicular expansion (type III)
- Progressive transformation of germinal centers (type IV)
- Inflammatory pseudotumor-like (type V)
- Infectious mononucleosis

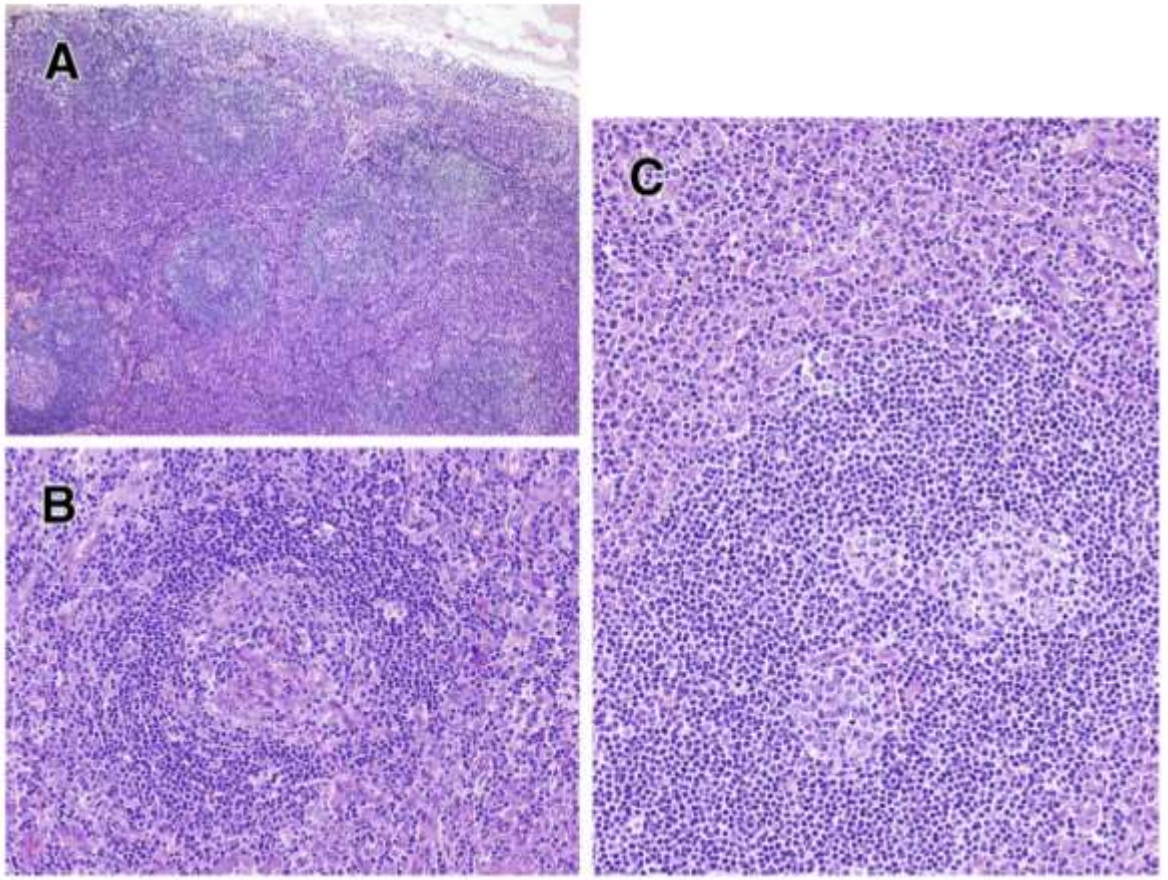
Cheuk W, Chan JK. Lymphadenopathy of IgG4-related disease: an underdiagnosed and overdiagnosed entity. Semin Diagn Pathol. 2012 Nov;29(4):226-34.

Lymph node involvement by IgG4-related disease

Multicentric Castleman disease-like (type I pattern)

Differential diagnosis:

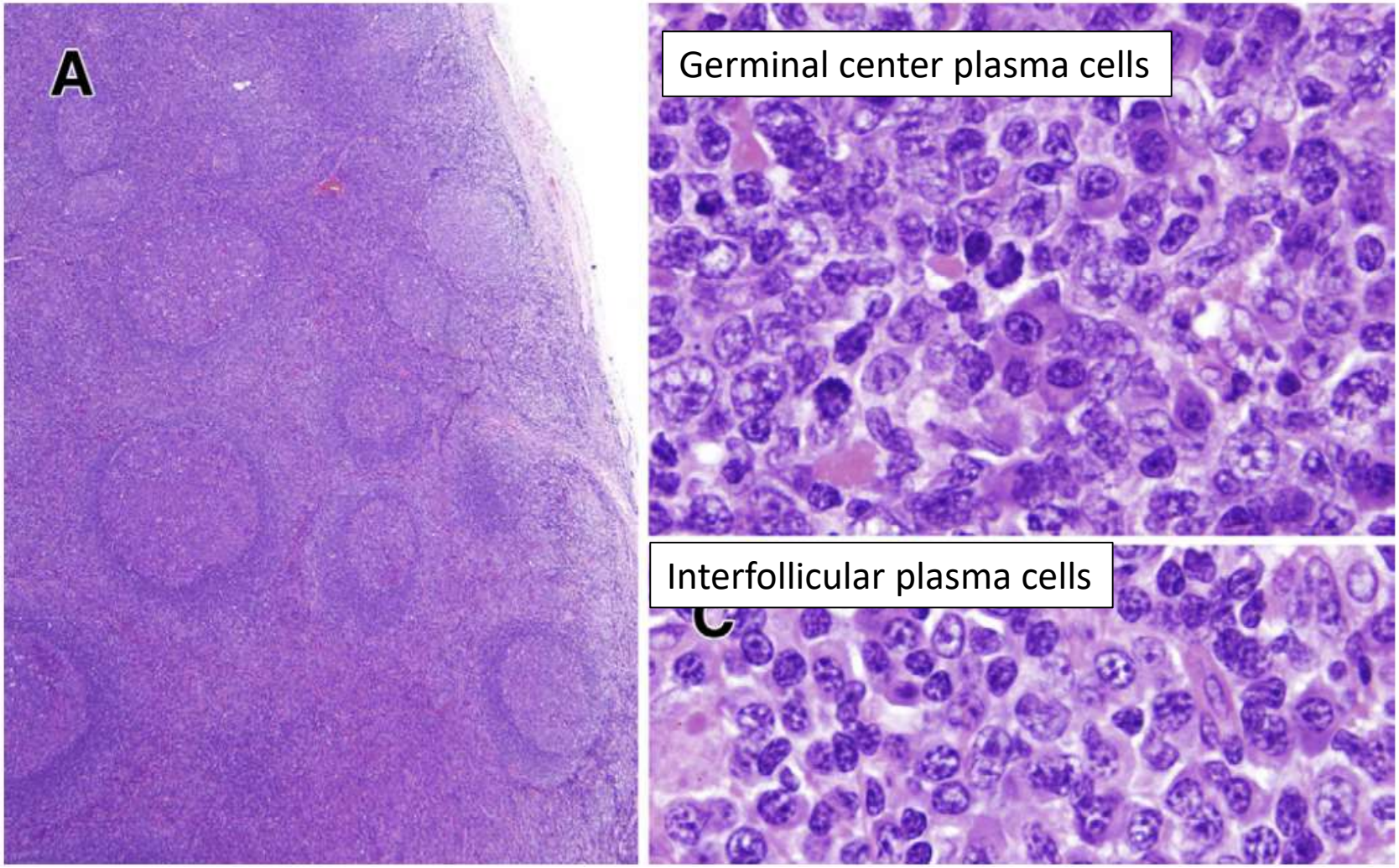
- Autoimmune disease–associated lymphadenopathy
- Rheumatoid arthritis
- Systemic lupus erythematosus



Cheuk W, Chan JK. Lymphadenopathy of IgG4-related disease: an underdiagnosed and overdiagnosed entity. Semin Diagn Pathol. 2012 Nov;29(4):226-34.

Lymph node involvement by IgG4-related disease

Follicular hyperplasia (type II pattern)

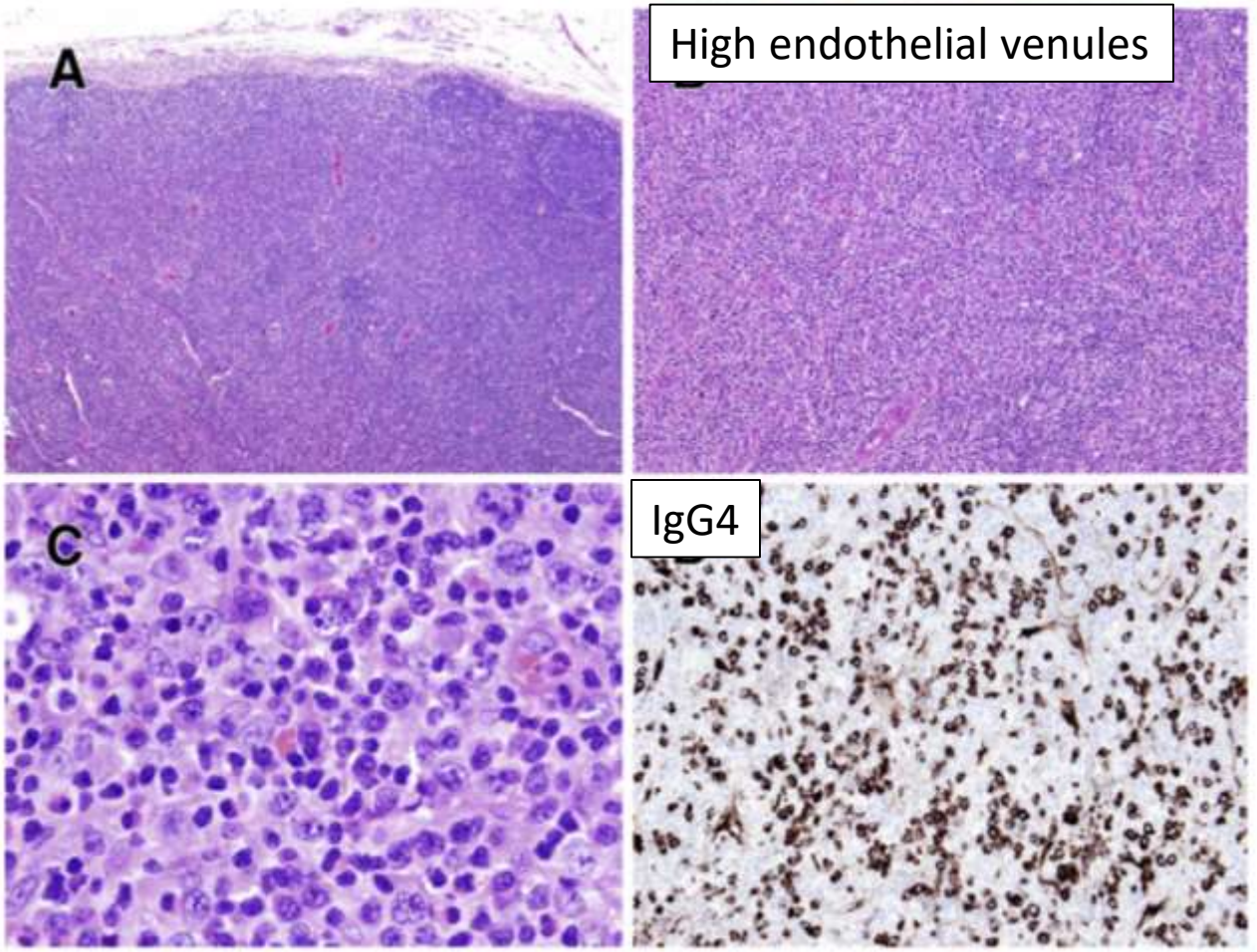


Cheuk W, Chan JK. Lymphadenopathy of IgG4-related disease: an underdiagnosed and overdiagnosed entity. Semin Diagn Pathol. 2012 Nov;29(4):226-34.

Lymph node involvement by IgG4-related disease

Interfollicular expansion (type III pattern)

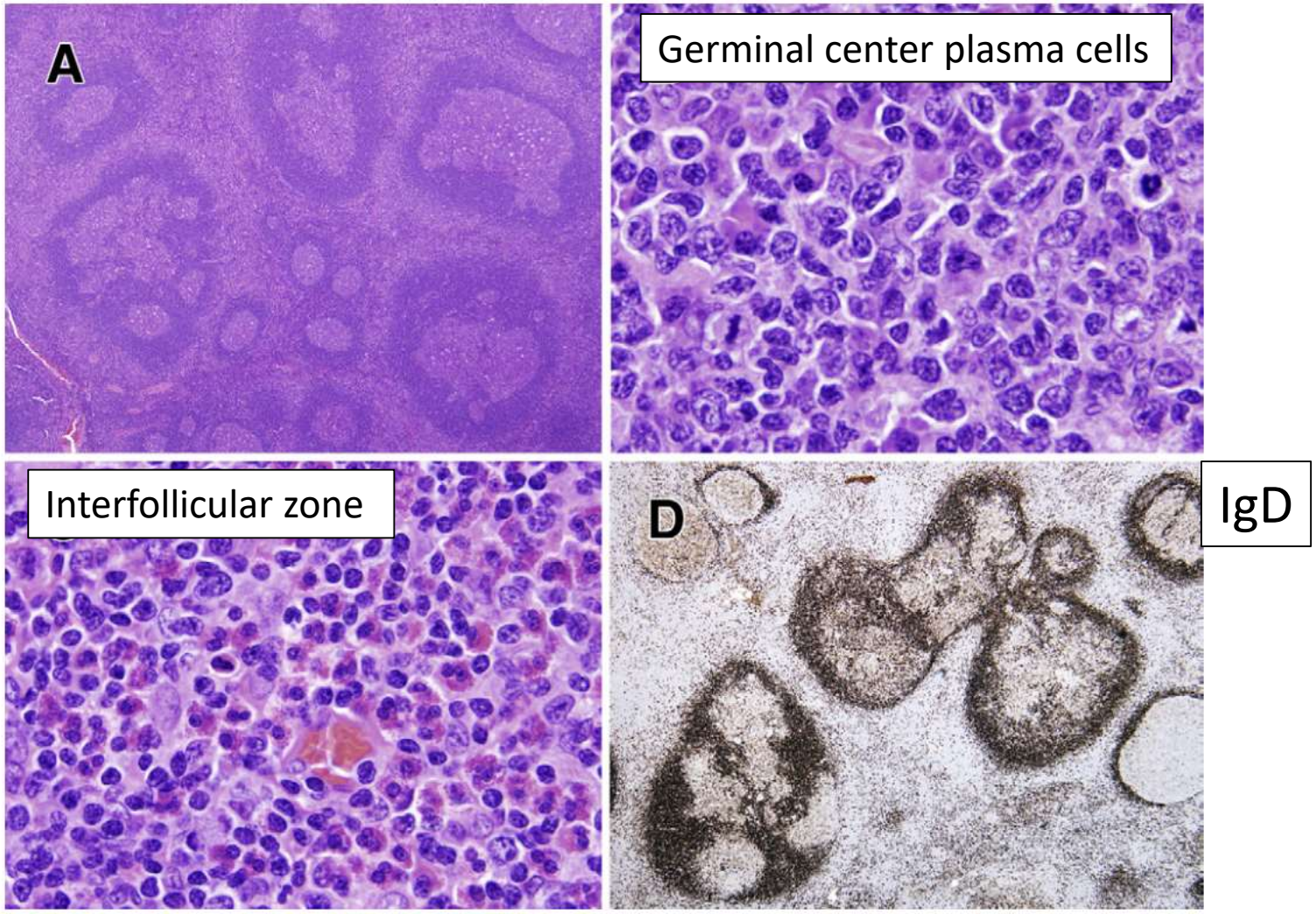
Differential diagnosis: Angioimmunoblastic T-cell lymphoma



Cheuk W, Chan JK. Lymphadenopathy of IgG4-related disease: an underdiagnosed and overdiagnosed entity. Semin Diagn Pathol. 2012 Nov;29(4):226-34.

Lymph node involvement by IgG4-related disease

Progressive transformation of germinal centers (type IV pattern)

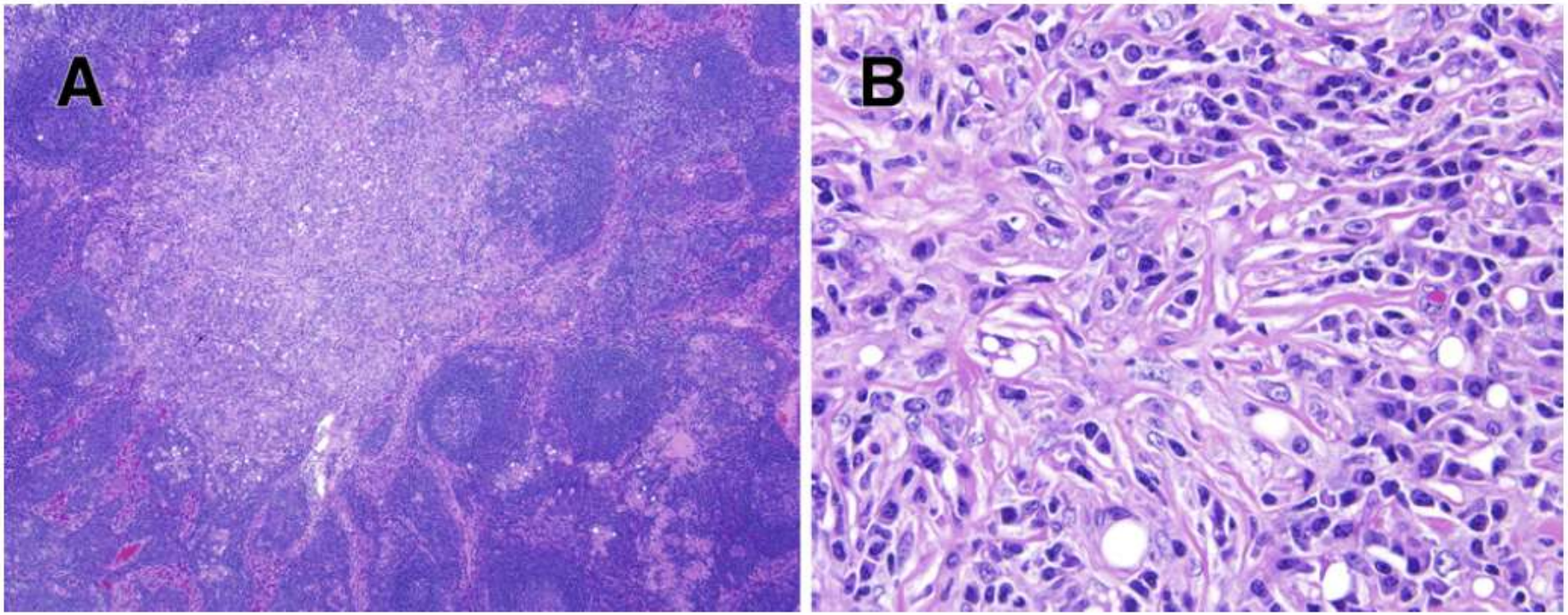


Cheuk W, Chan JK. Lymphadenopathy of IgG4-related disease: an underdiagnosed and overdiagnosed entity. Semin Diagn Pathol. 2012 Nov;29(4):226-34.

Lymph node involvement by IgG4-related disease

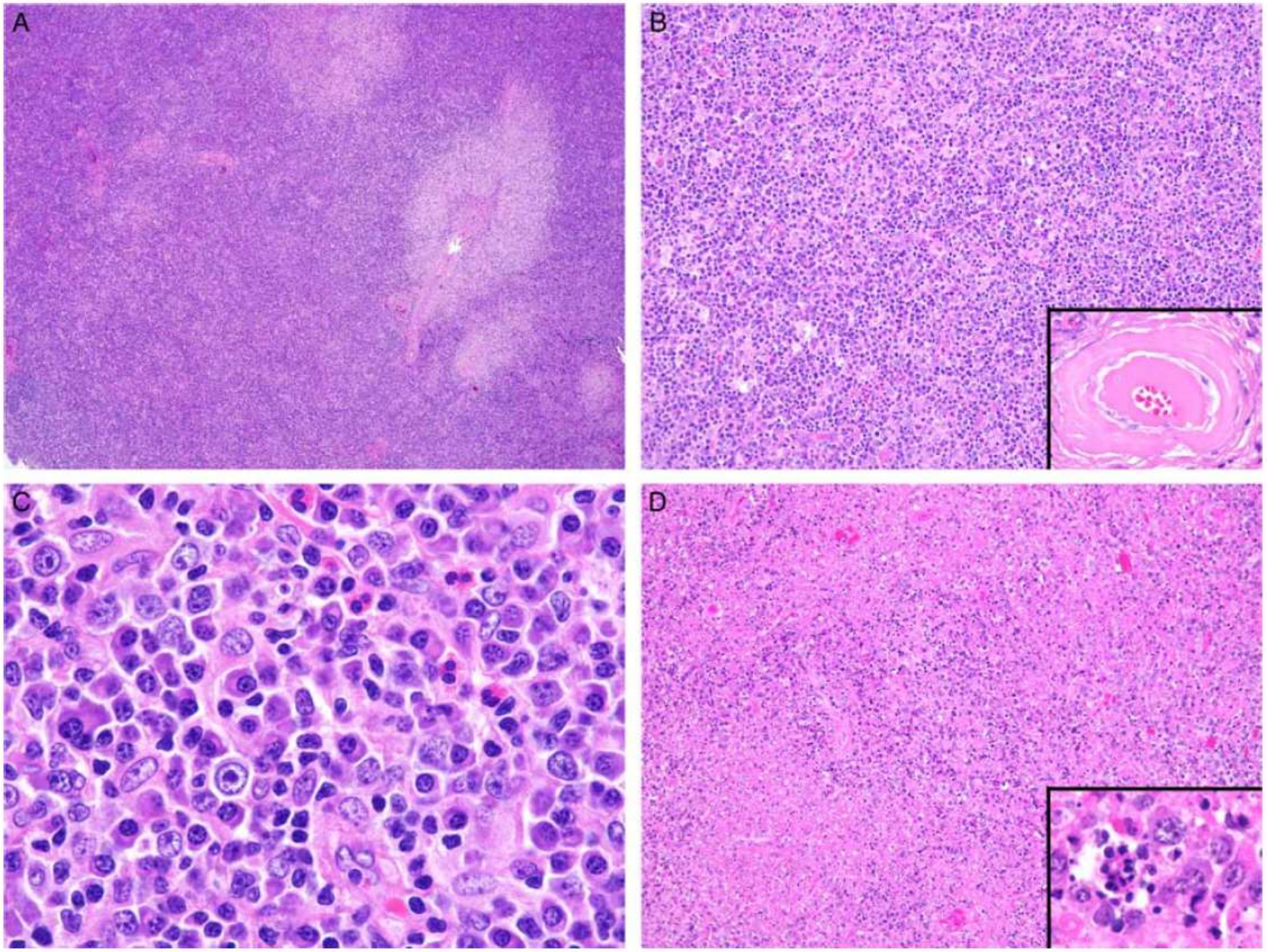
Inflammatory pseudotumor-like (type V pattern)

Differential diagnosis: inflammatory pseudotumor and inflammatory myofibroblastic tumor

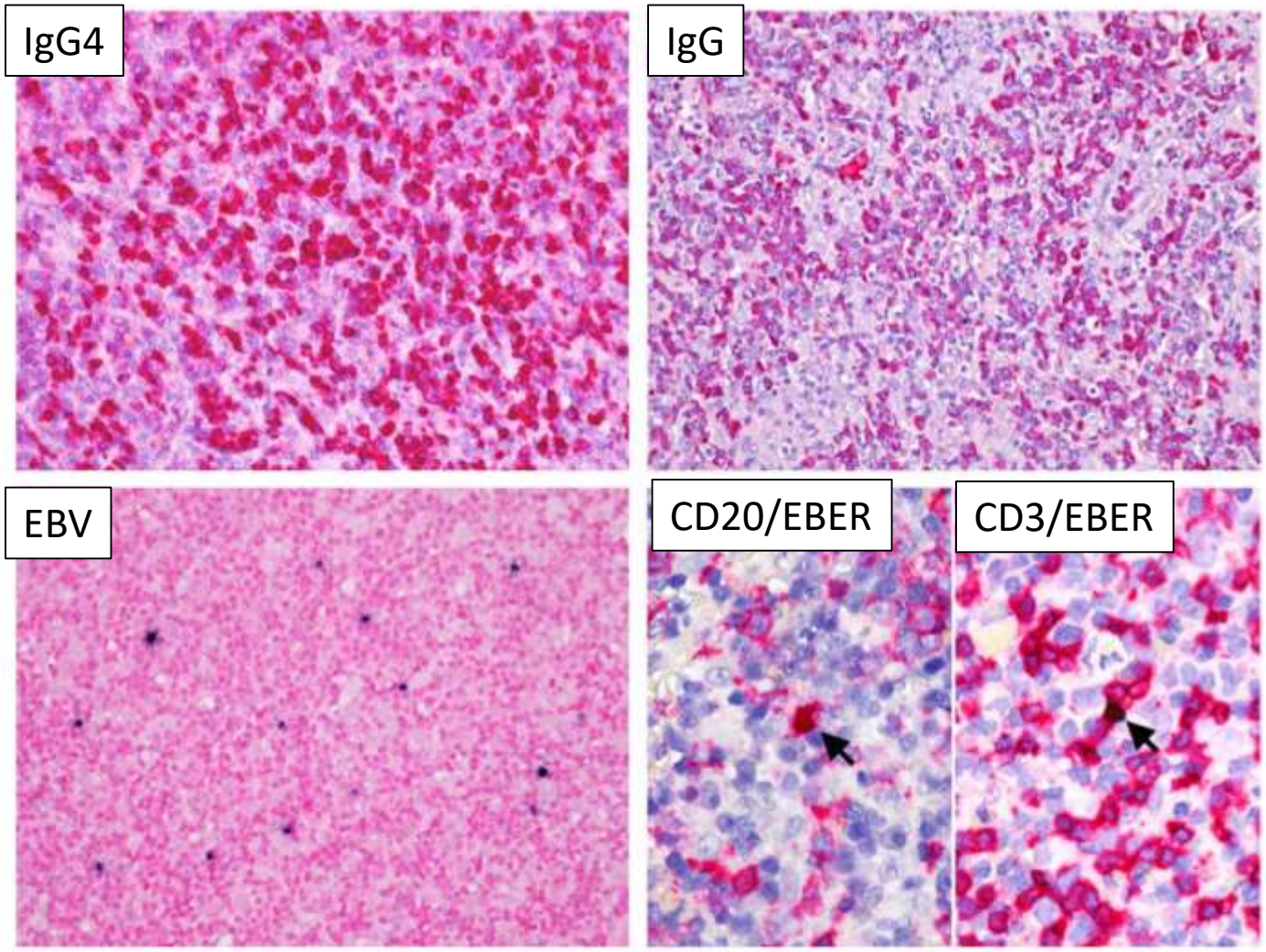


Cheuk W, Chan JK. Lymphadenopathy of IgG4-related disease: an underdiagnosed and overdiagnosed entity. Semin Diagn Pathol. 2012 Nov;29(4):226-34.

Infectious mononucleosis-like pattern of IgG4-related lymphadenopathy



Infectious mononucleosis-like pattern of IgG4-related lymphadenopathy



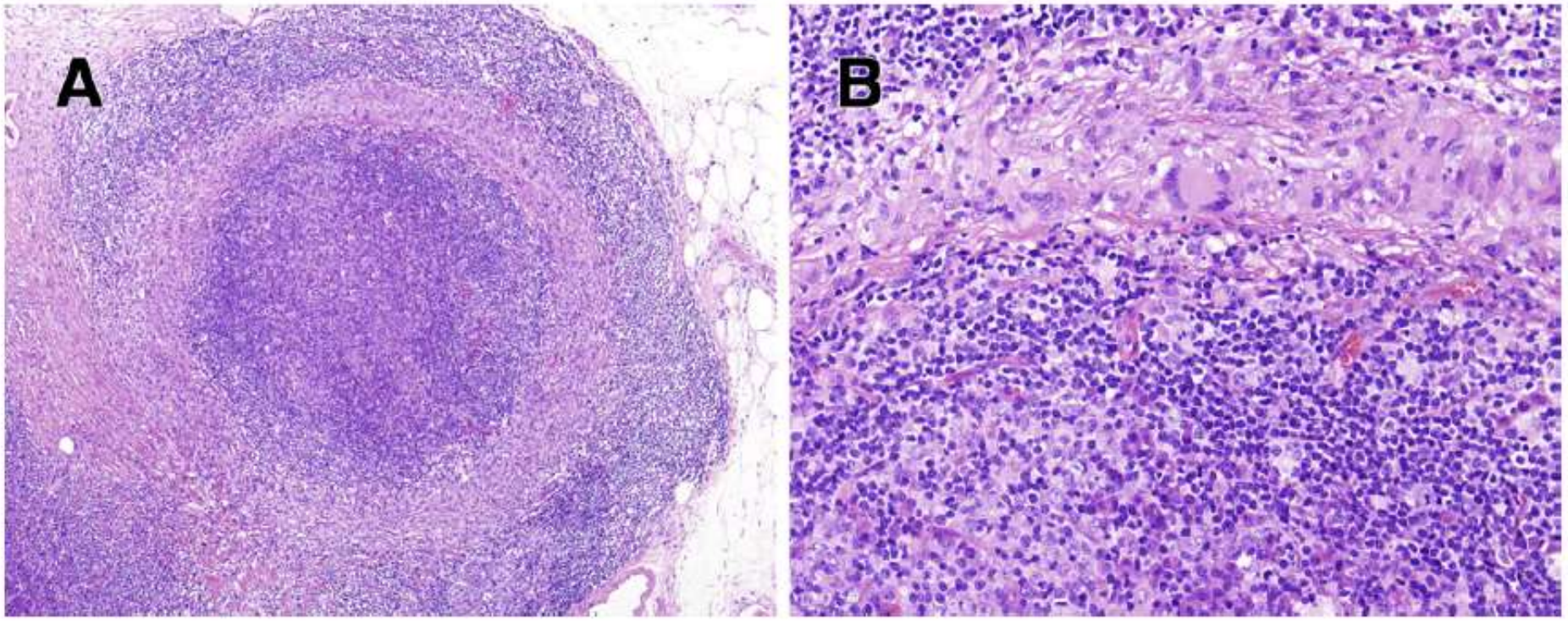
Serologic studies were negative for EBV VCA-IgM, and positive for EBV-VCA-IgG, EBV EA-IgG, and EBV NA-IgG, 4 days after the second lymph node biopsy was performed.

Serologic findings indicated EBV reactivation rather than acute EBV infection.

Lymph node involvement by IgG4-related disease

Perifollicular granuloma

Not specific!



Cheuk W, Chan JK. Lymphadenopathy of IgG4-related disease: an underdiagnosed and overdiagnosed entity. Semin Diagn Pathol. 2012 Nov;29(4):226-34.

EBV in IgG4-related lymphadenopathy

- Low numbers, usually interfollicular
- **Nodal IgG4:** Increased numbers of EBV-positive cells have been found in 58% cases of IgG4-related lymphadenopathy
- **Extranodal IgG4:** Increased EBV+ cells found in 21% in extranodal lesions of IgG4-related disease

In the absence of known IgG4-related disease:

Descriptive diagnosis is recommended:

- “Reactive lymphoid hyperplasia with increased IgG4+ cells”

- Recommend follow-up
  - IgG4-related disease will likely only ensue in a minority of such patients

Take home points

- IgG4-related disease is associated with a variety of histologic patterns
- Be descriptive when signing out a lymph node with increased IgG4+ plasma cells
  - "Reactive lymphoid hyperplasia with increased IgG4+ cells"
  - Recommend serum IgG/IgG4 and appropriate evaluation for extranodal sites of involvement
- Consider IgG4-related disease in cases of progressive transformation of germinal centers
- IgG4-related disease has been associated with few scattered EBV+ cells

References

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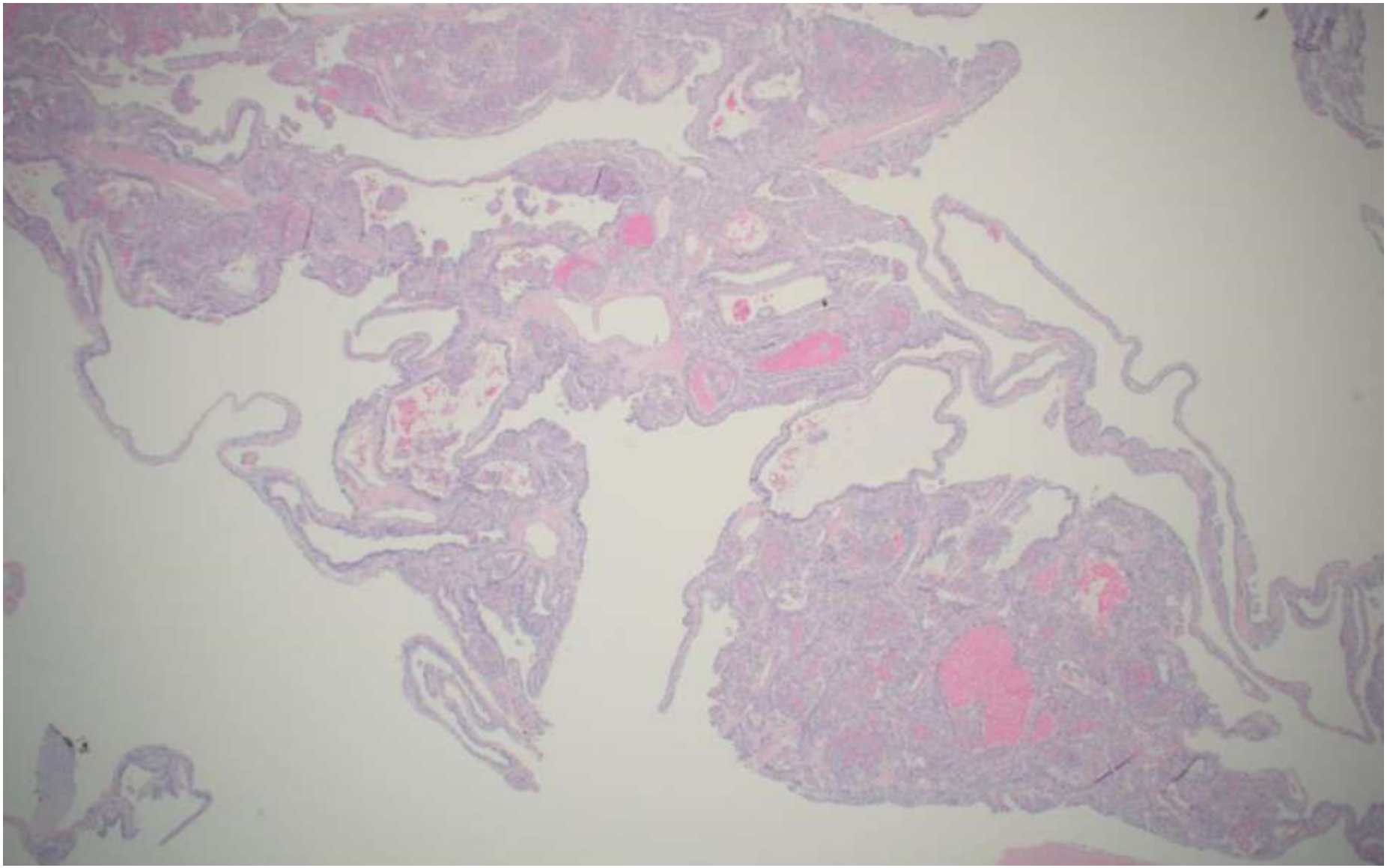
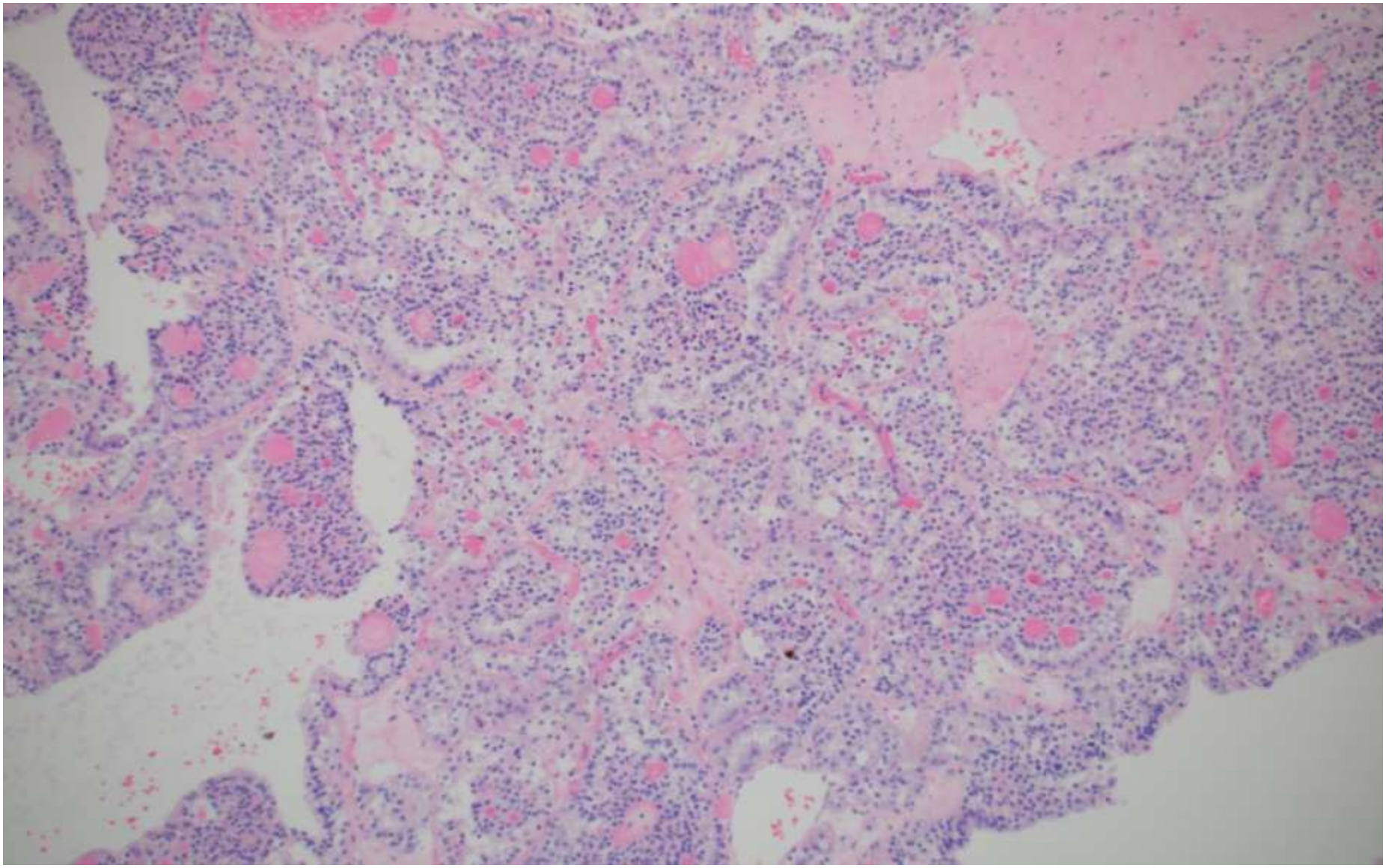
- Grimm KE, Barry TS, Chizhevsky V, Hii A, Weiss LM, Siddiqi IN, Brynes RK, O'Malley DP. Histopathological findings in 29 lymph node biopsies with increased IgG4 plasma cells. Mod Pathol. 2012;25:480–491.
- Chen YR, Chen YJ, Wang MC, Medeiros LJ, Chang KC. A Newly Recognized Histologic Pattern of IgG4-related Lymphadenopathy: Expanding the Morphologic Spectrum. Am J Surg Pathol. 2018 Jul;42(7):977-982.

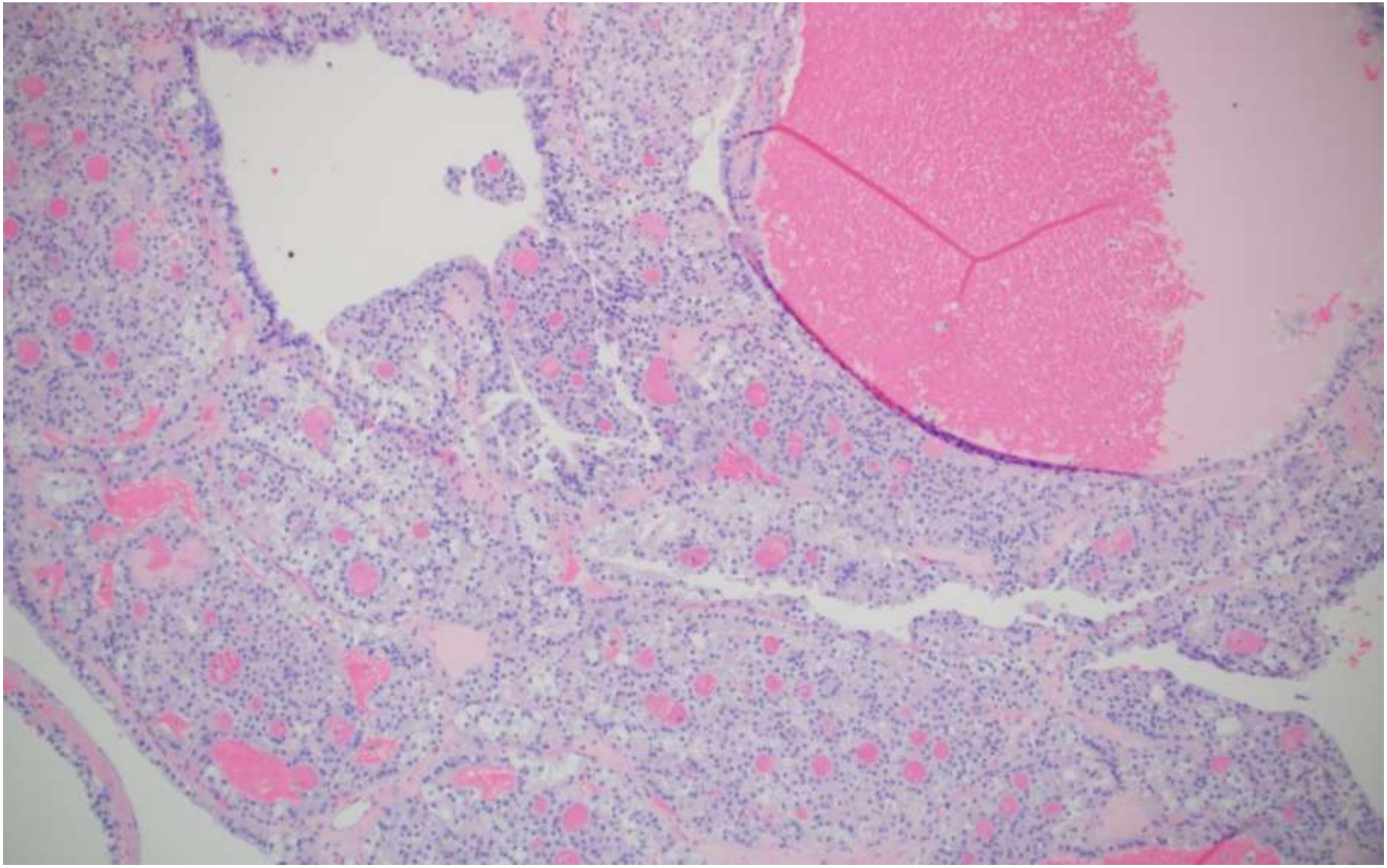
19-1007

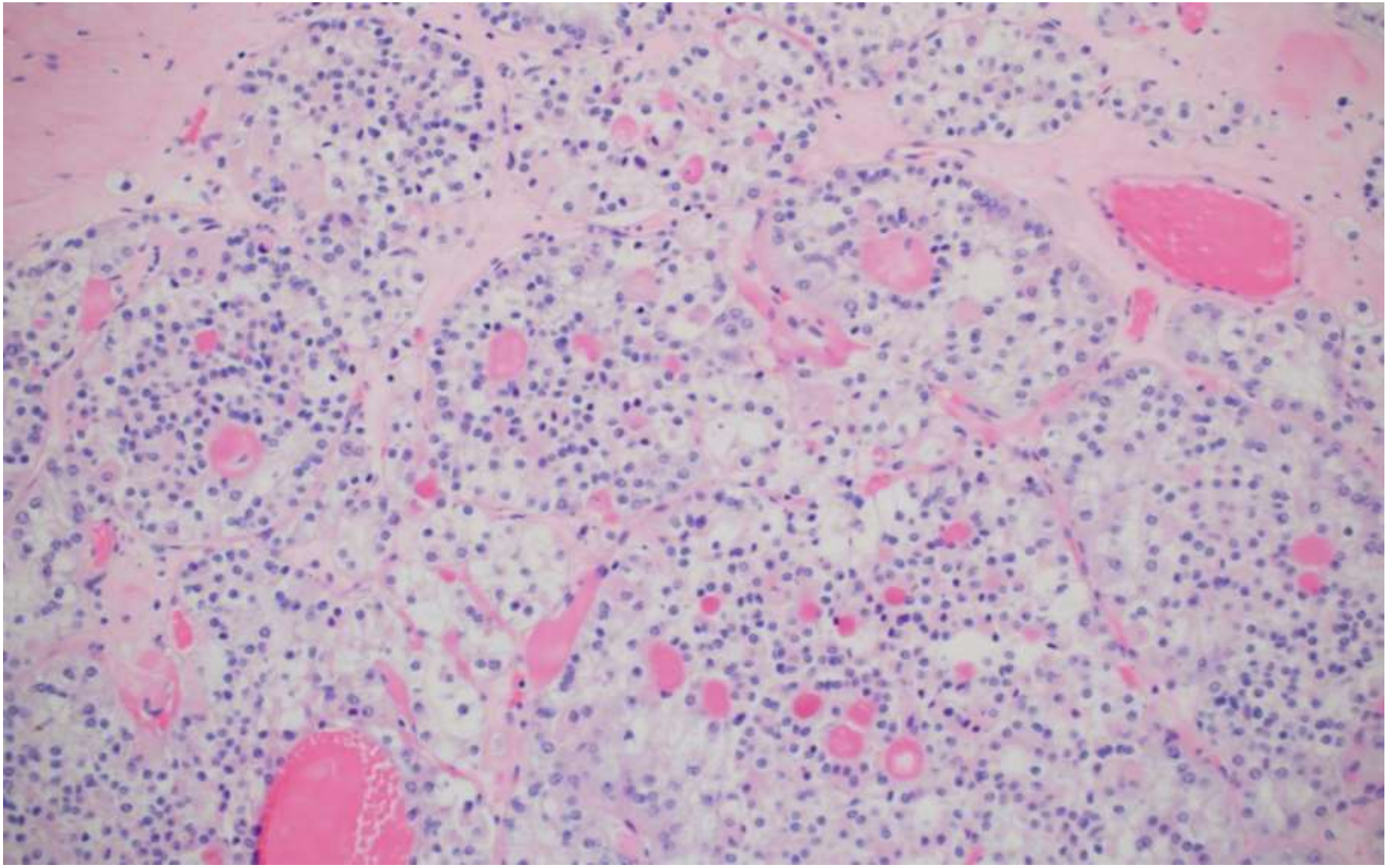
Rachael Fels-Elliott/Emily Chan; UCSF

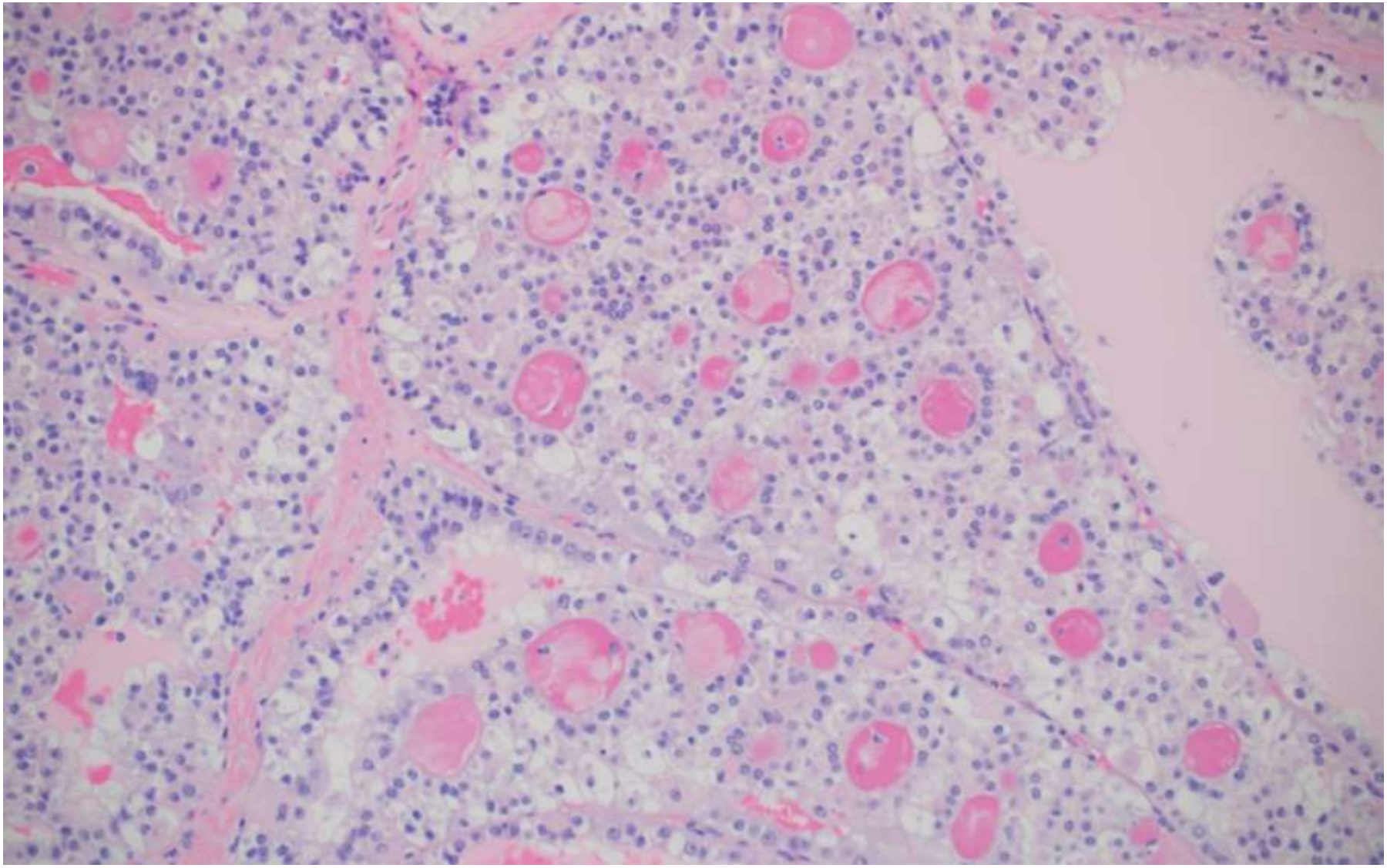
69-year-old male with 7.4cm left kidney mass.

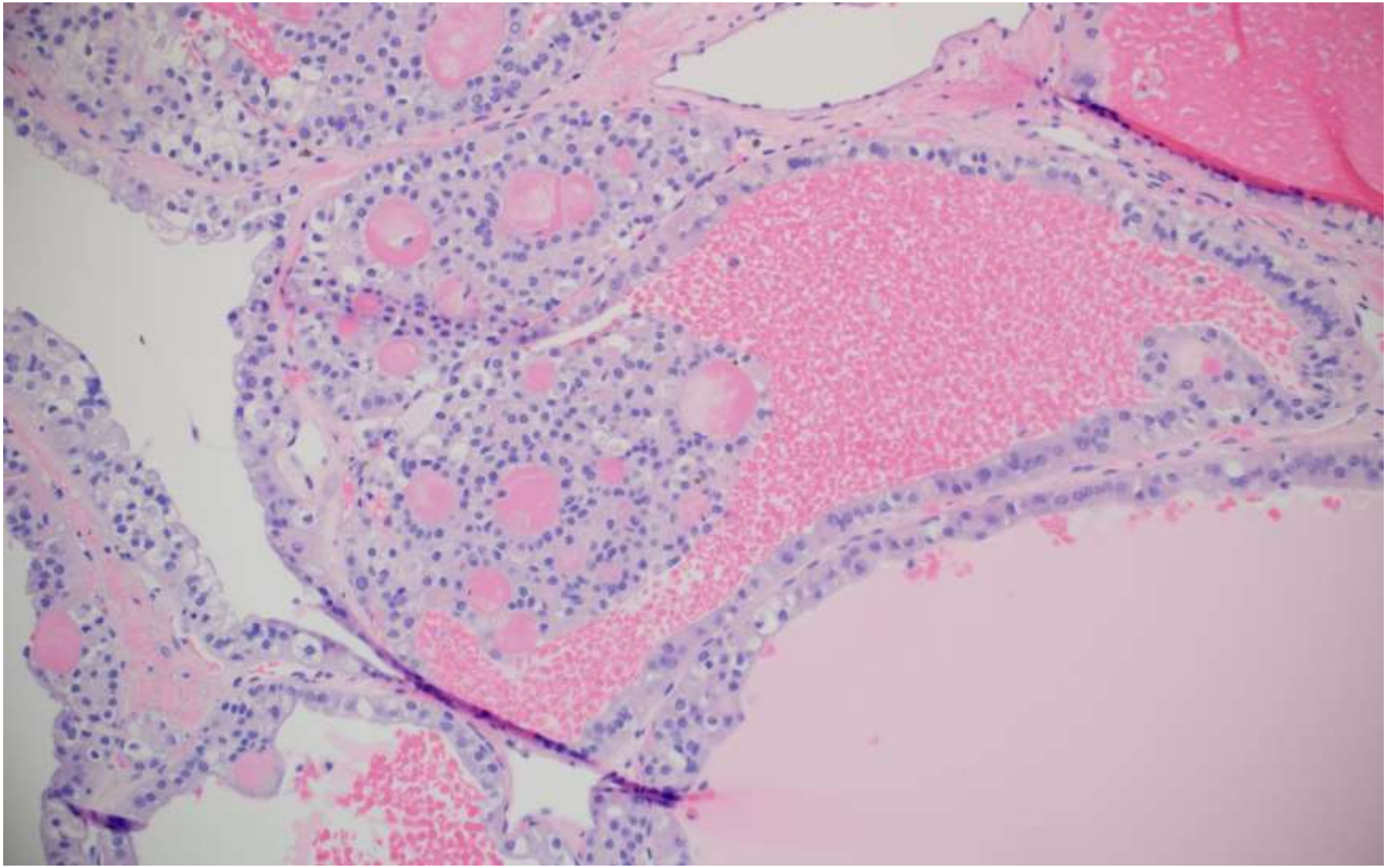


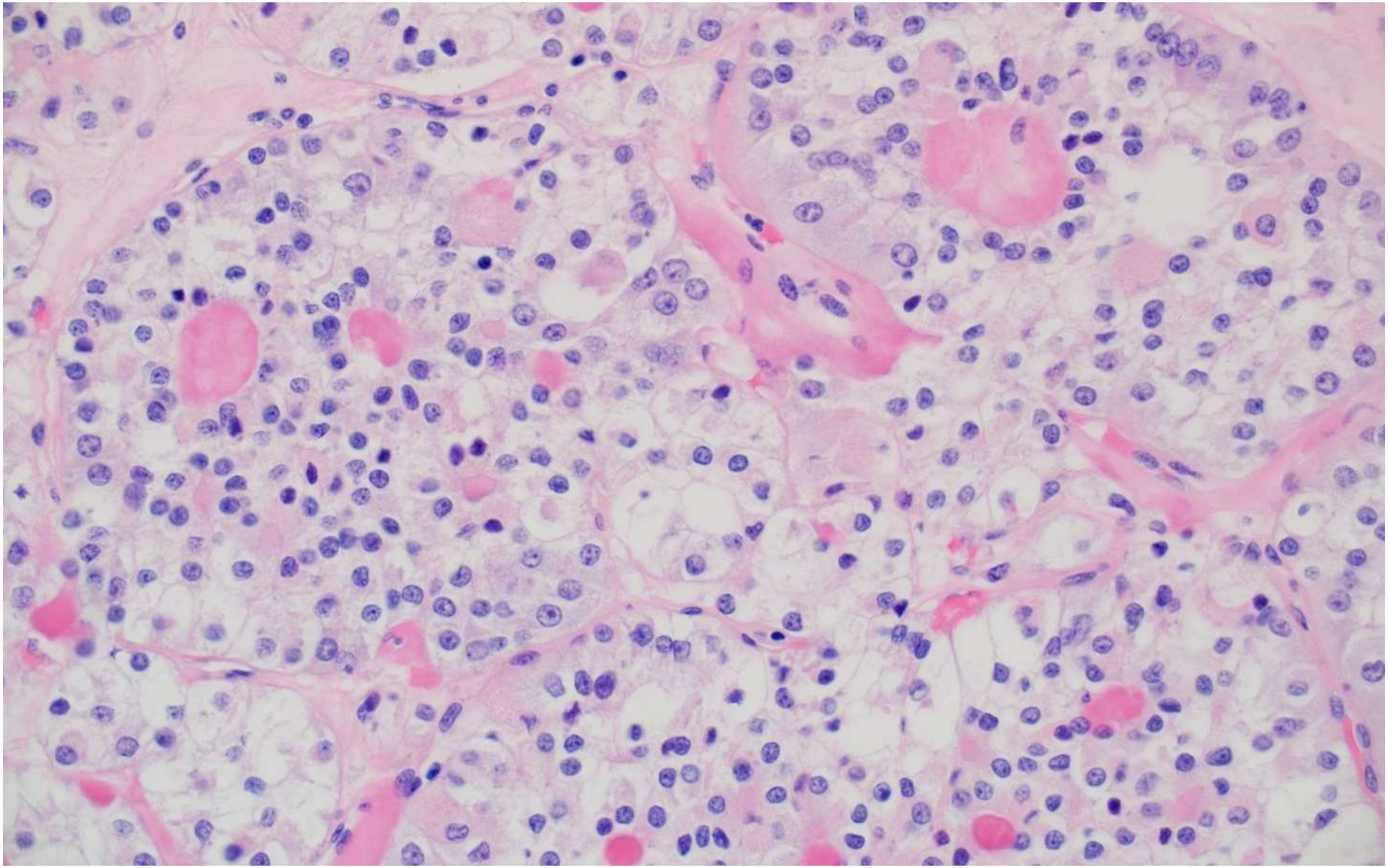


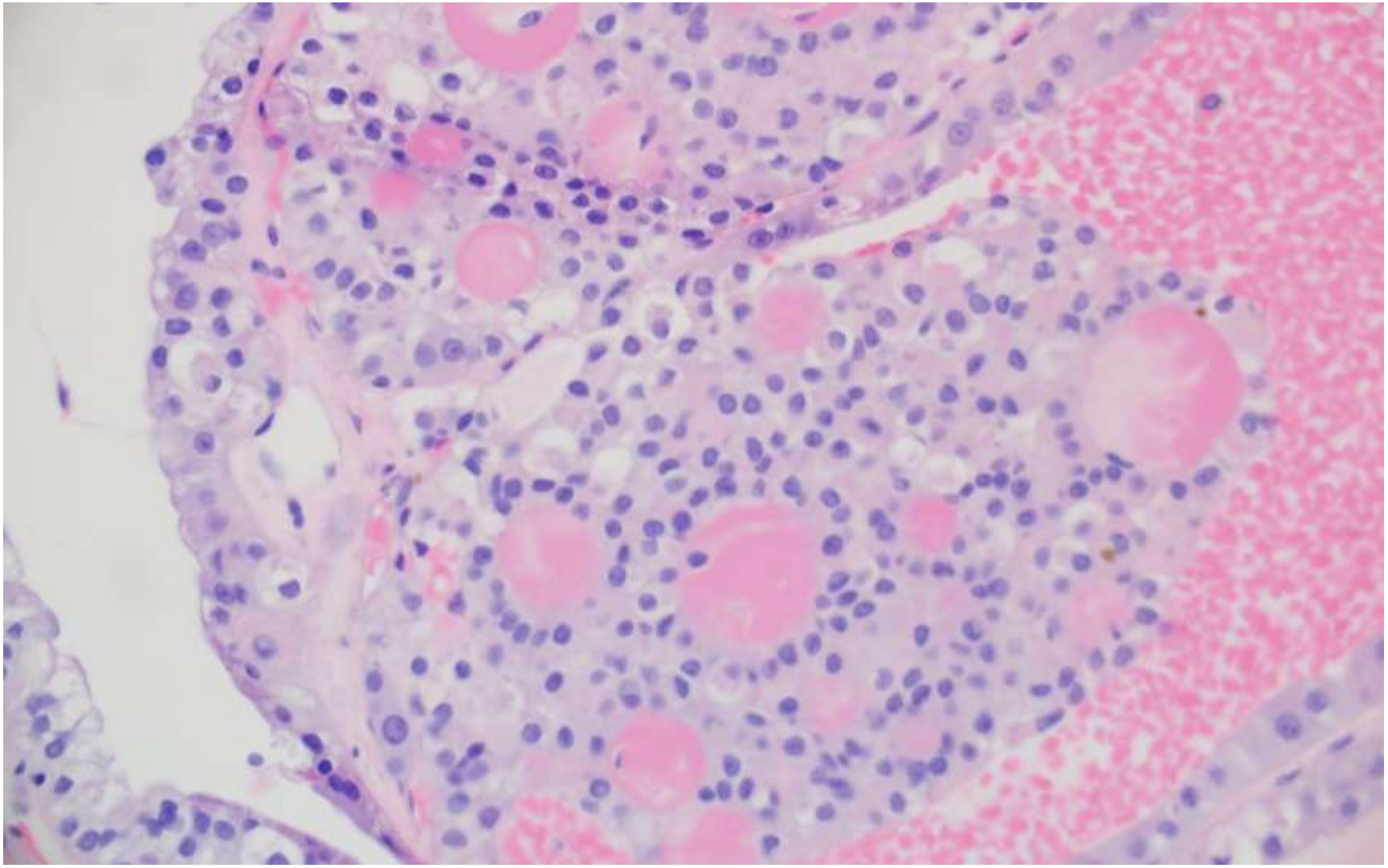






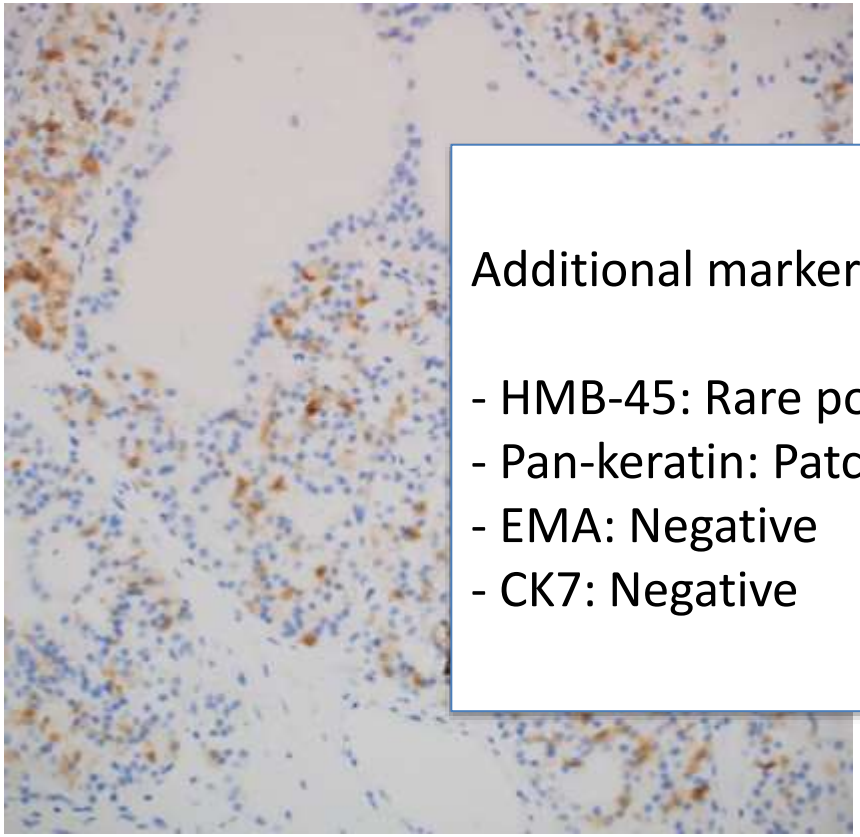




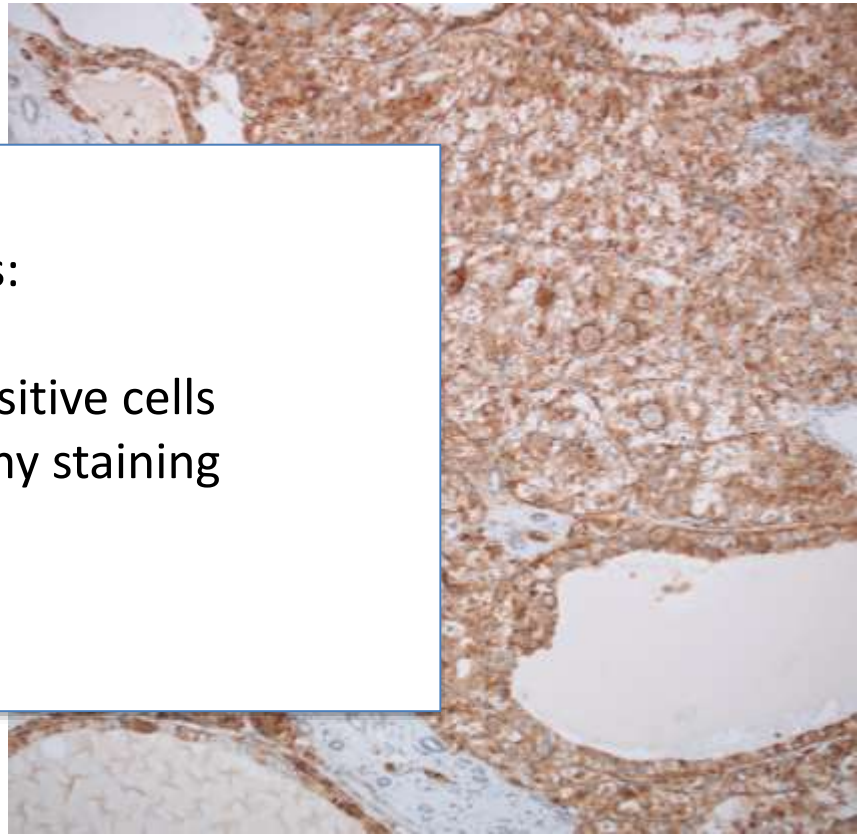


Case: IHC

Melan A



Cathepsin K



Additional markers:

- HMB-45: Rare positive cells
- Pan-keratin: Patchy staining
- EMA: Negative
- CK7: Negative

Case: Final diagnosis

- “Renal cell carcinoma, most consistent with TFEB MiT family translocation associated”

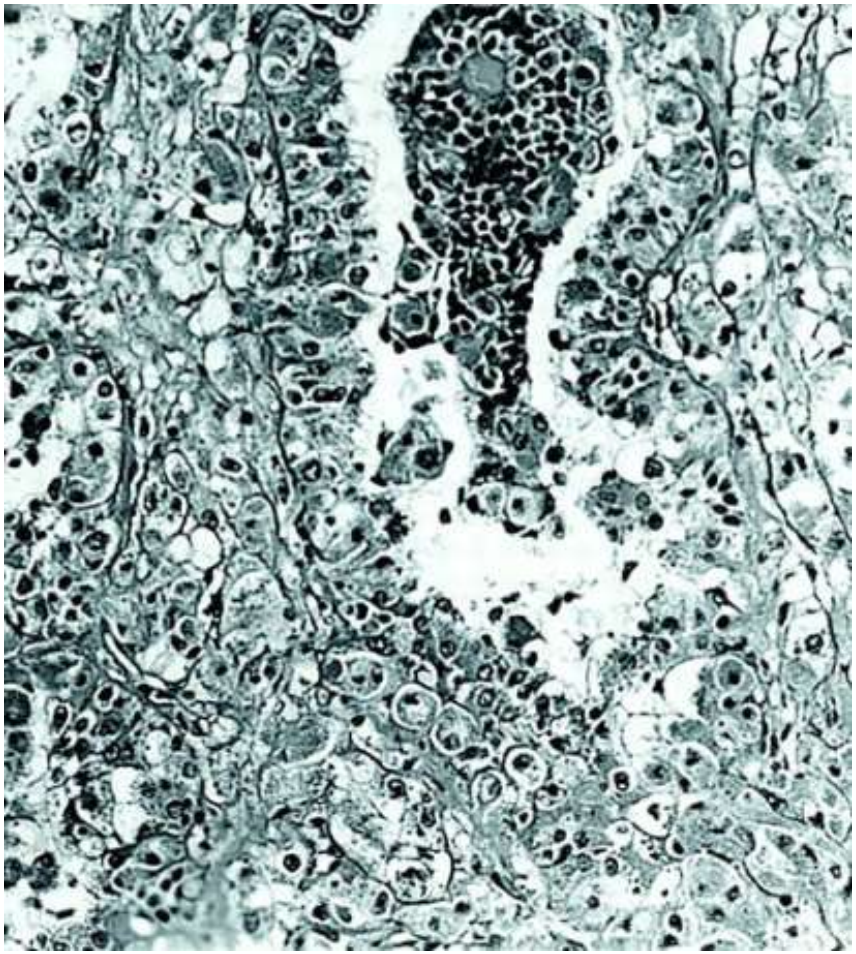
- Comment: If clinically indicated, molecular testing to probe for the t(6;11) translocation involving the TFEB gene could be performed to further support this diagnosis.

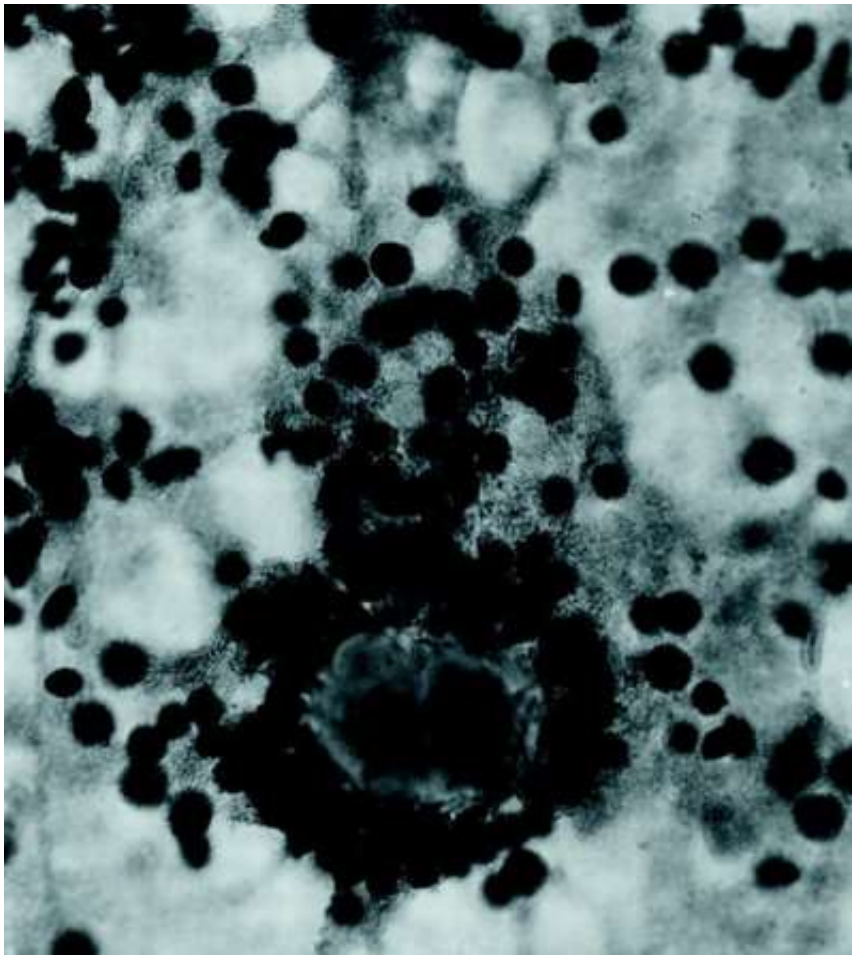
TFEB t(6;11) RCC

- MiT (micropthalmia) subfamily of transcription factors includes TFE3, **TFEB**, TFEC, and MITF
- Rare tumor (~50 cases reported)
- Majority in children and adolescents, **but wide age range**
- Median age 31 y (range 3 to 68 y)
- Generally more indolent, but may show aggressive clinical behavior

Argani P. Semin Diagn Pathol 2015

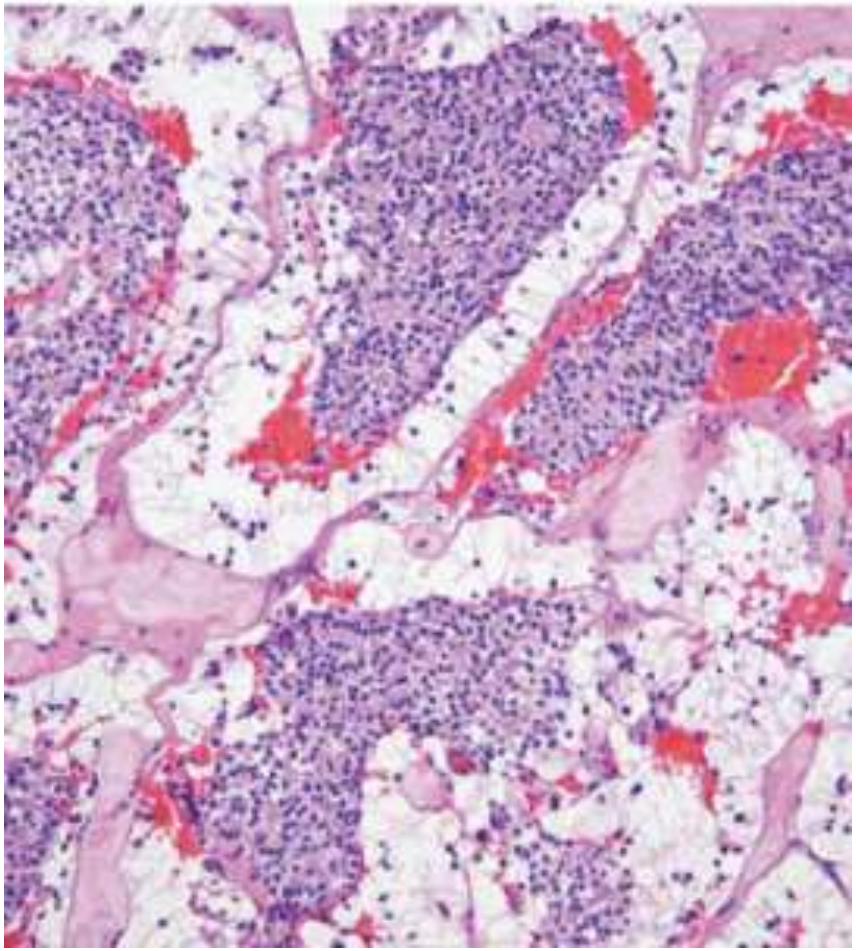
TFEB t(6;11): *Biphasic morphology*

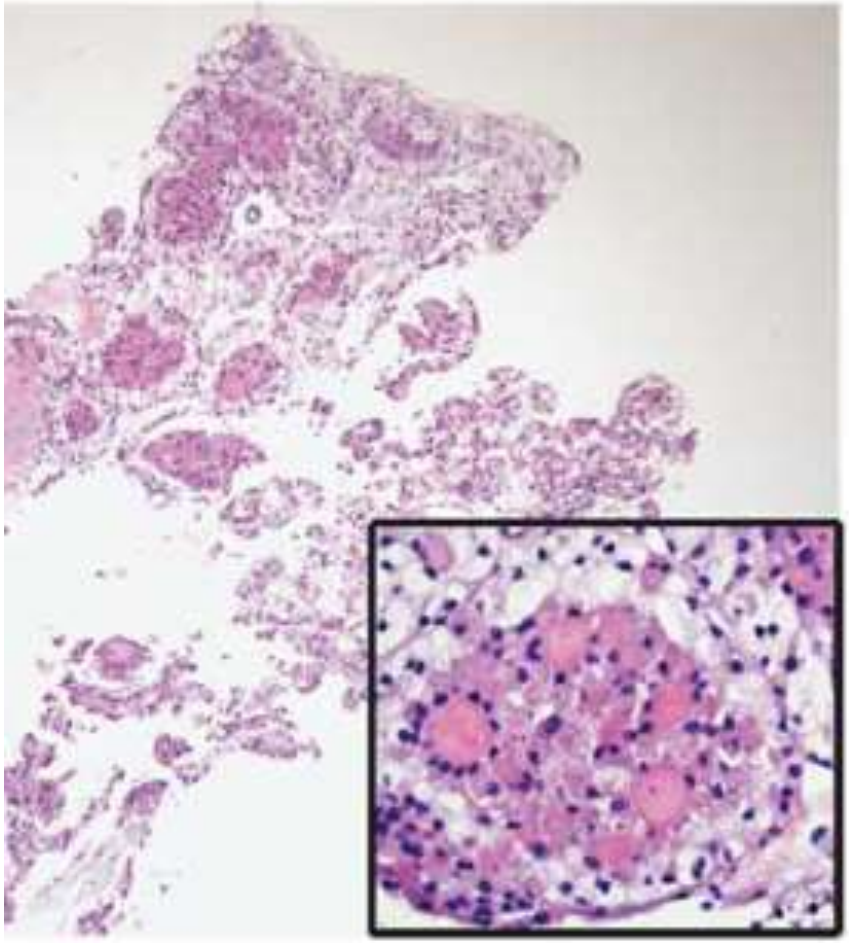




Argani et al. Am J Pathol. 2001

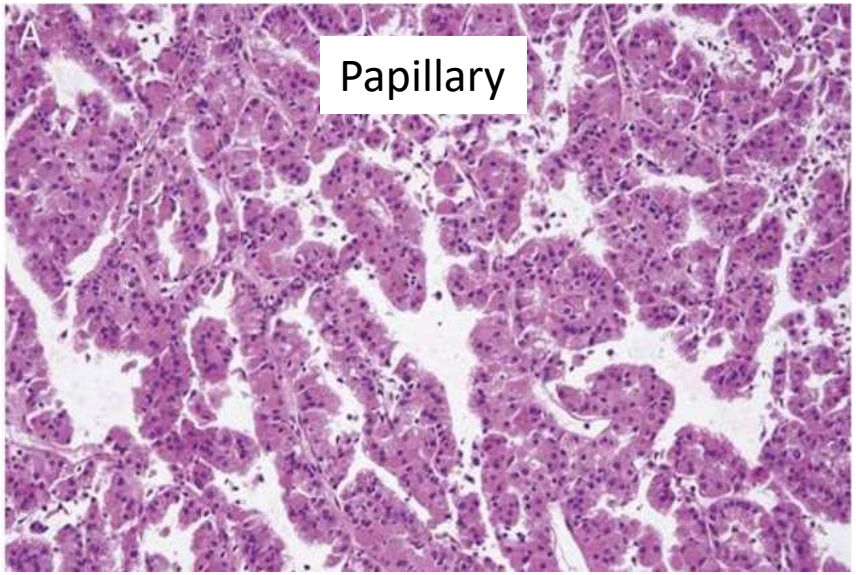
TFEB t(6;11): *Biphasic morphology*

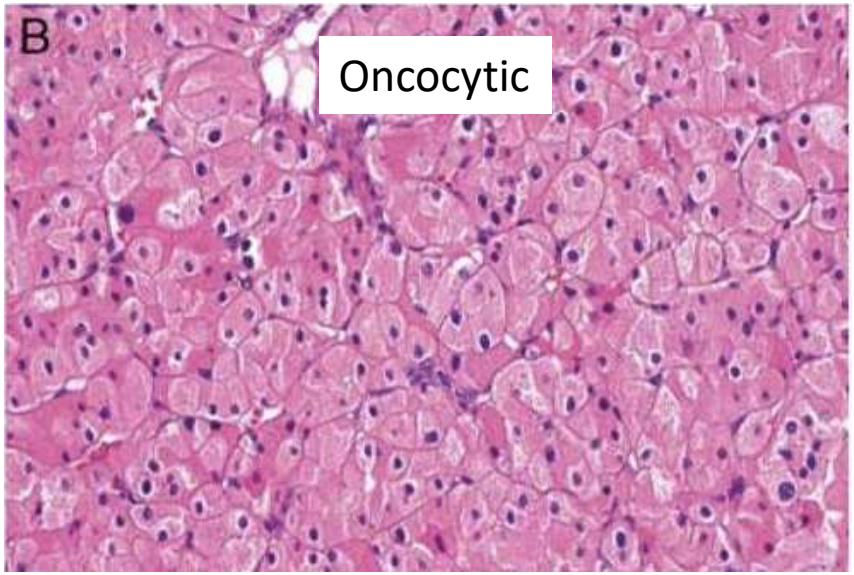


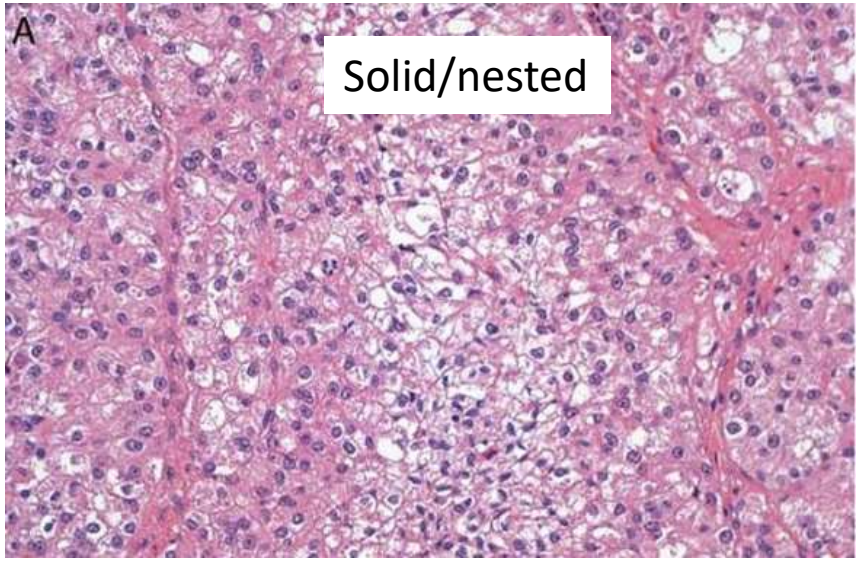


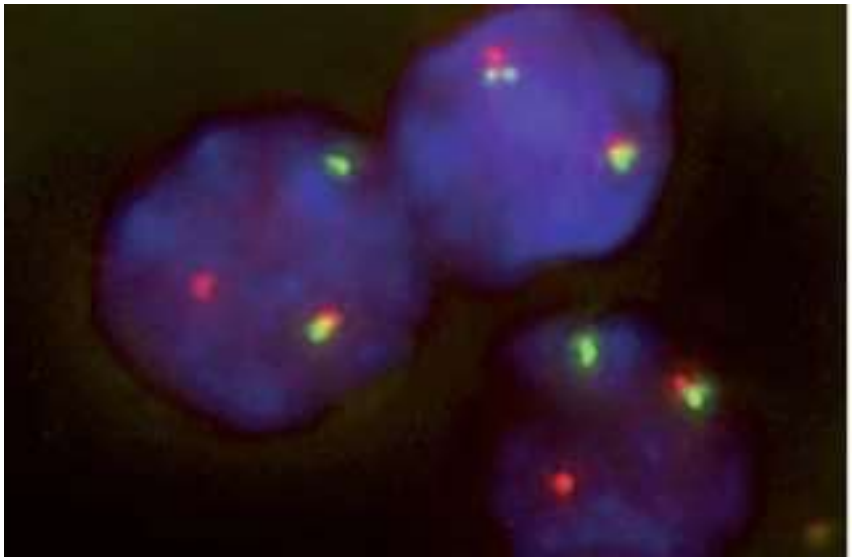
Skala et al. Modern Pathology. 2018

TFEB t(6;11): *Morphologic variability*



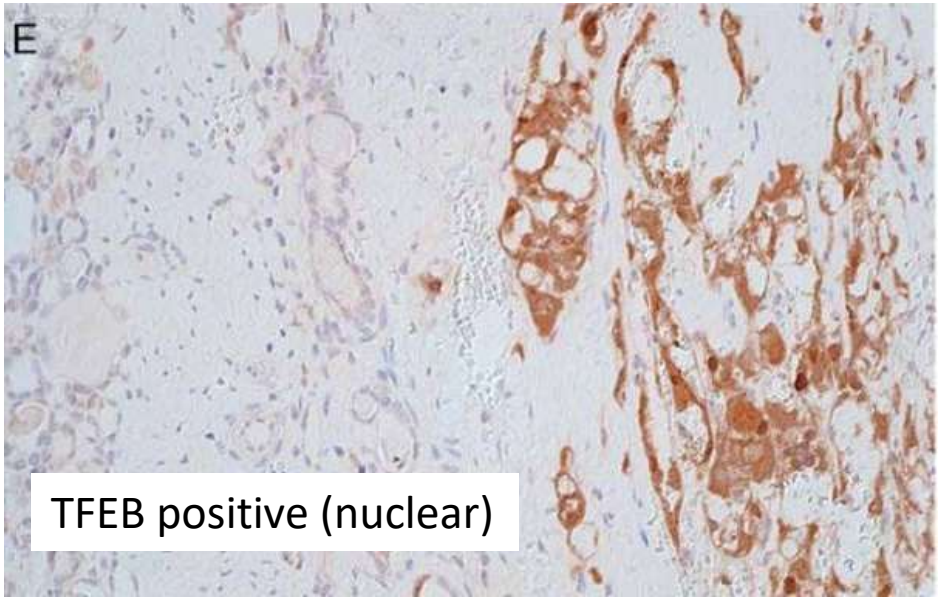


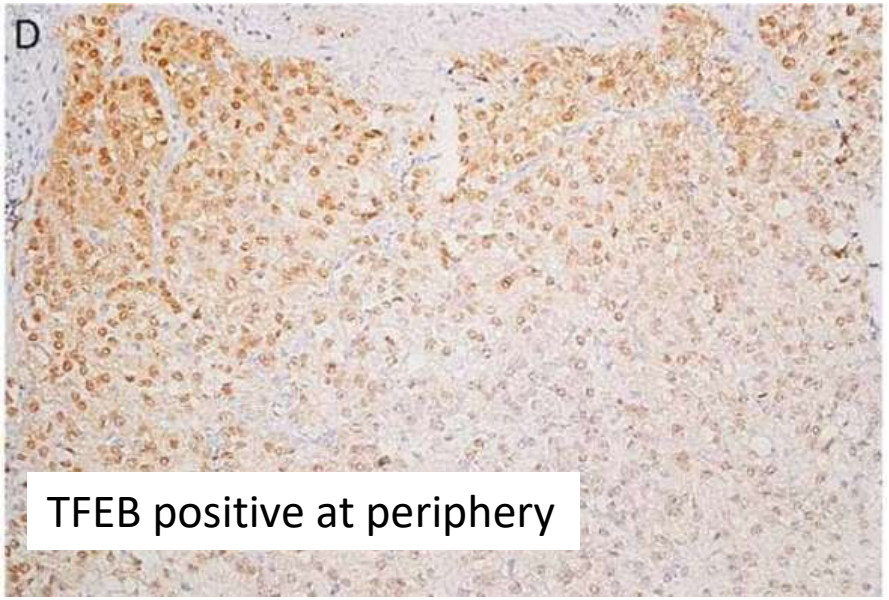


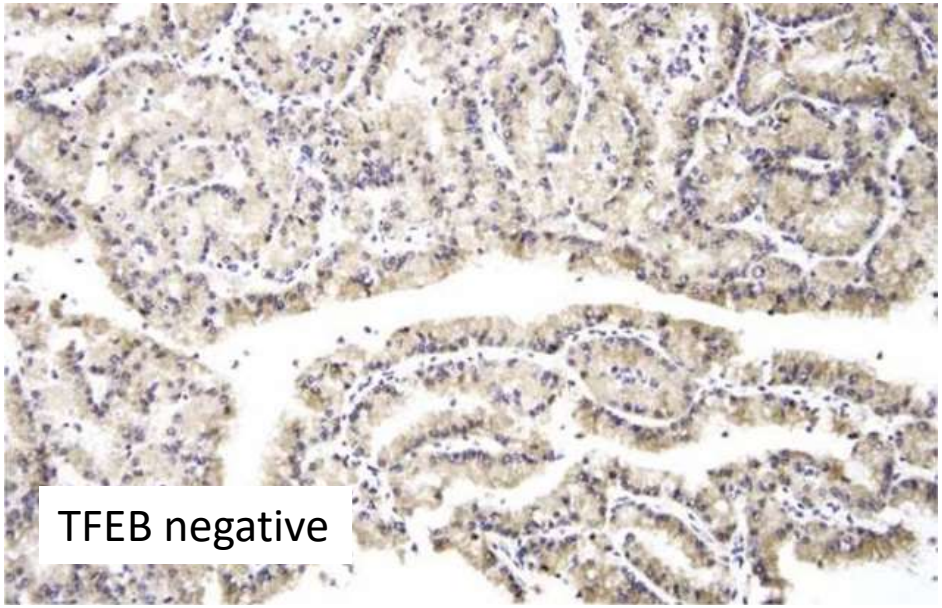


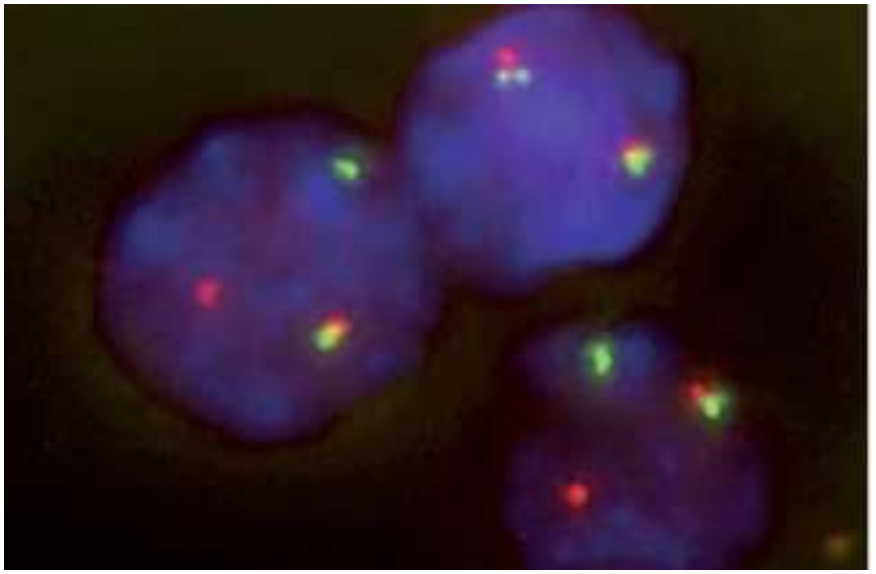
Argani et al. Am J Surg Pathol. 2012

TFEB t(6;11): *Immunohistochemistry*



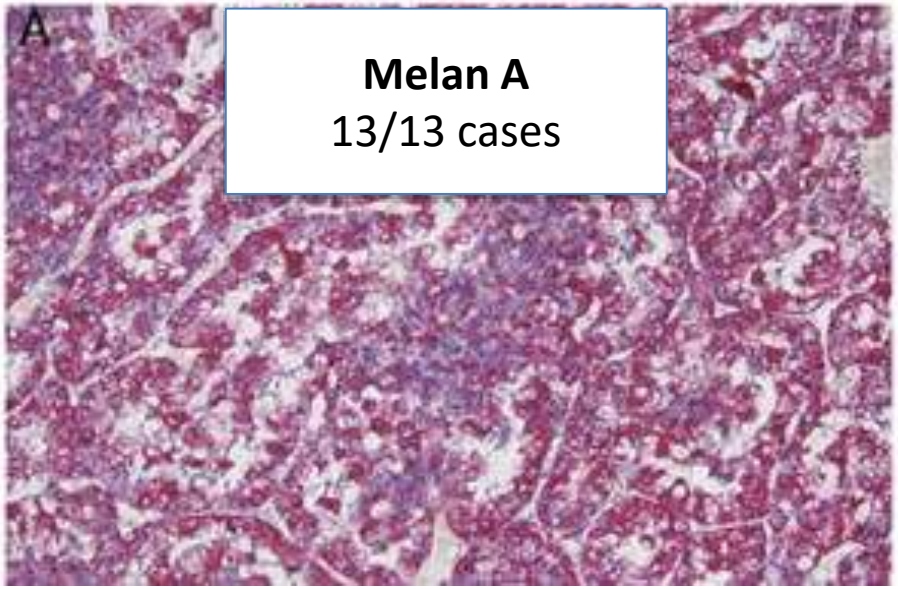


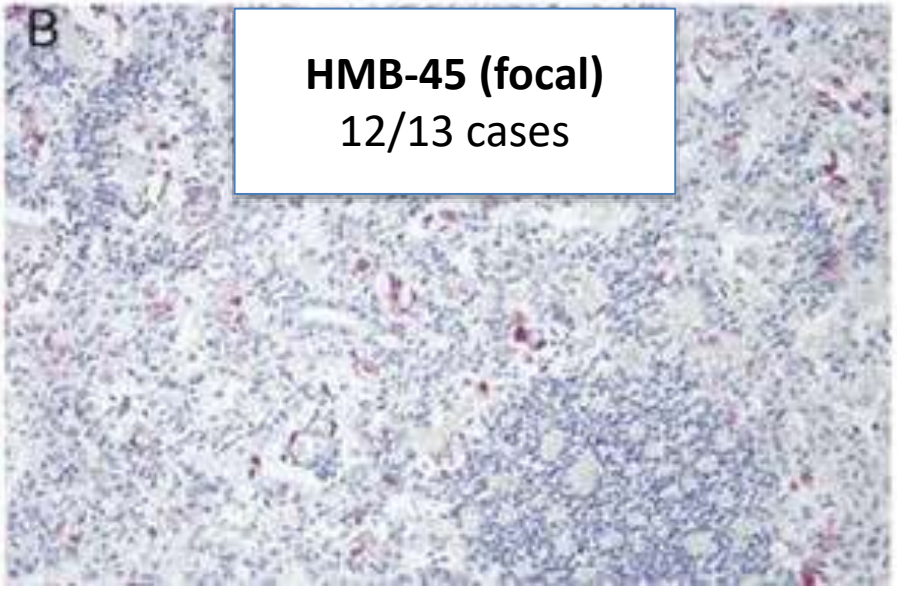


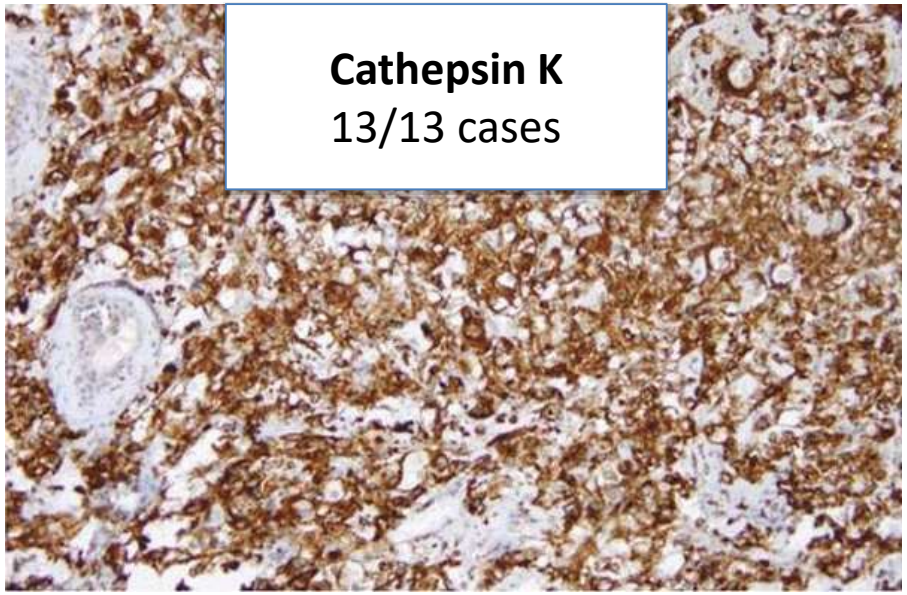


Argani et al. Am J Surg Pathol. 2012

TFEB t(6;11): *Immunohistochemistry*





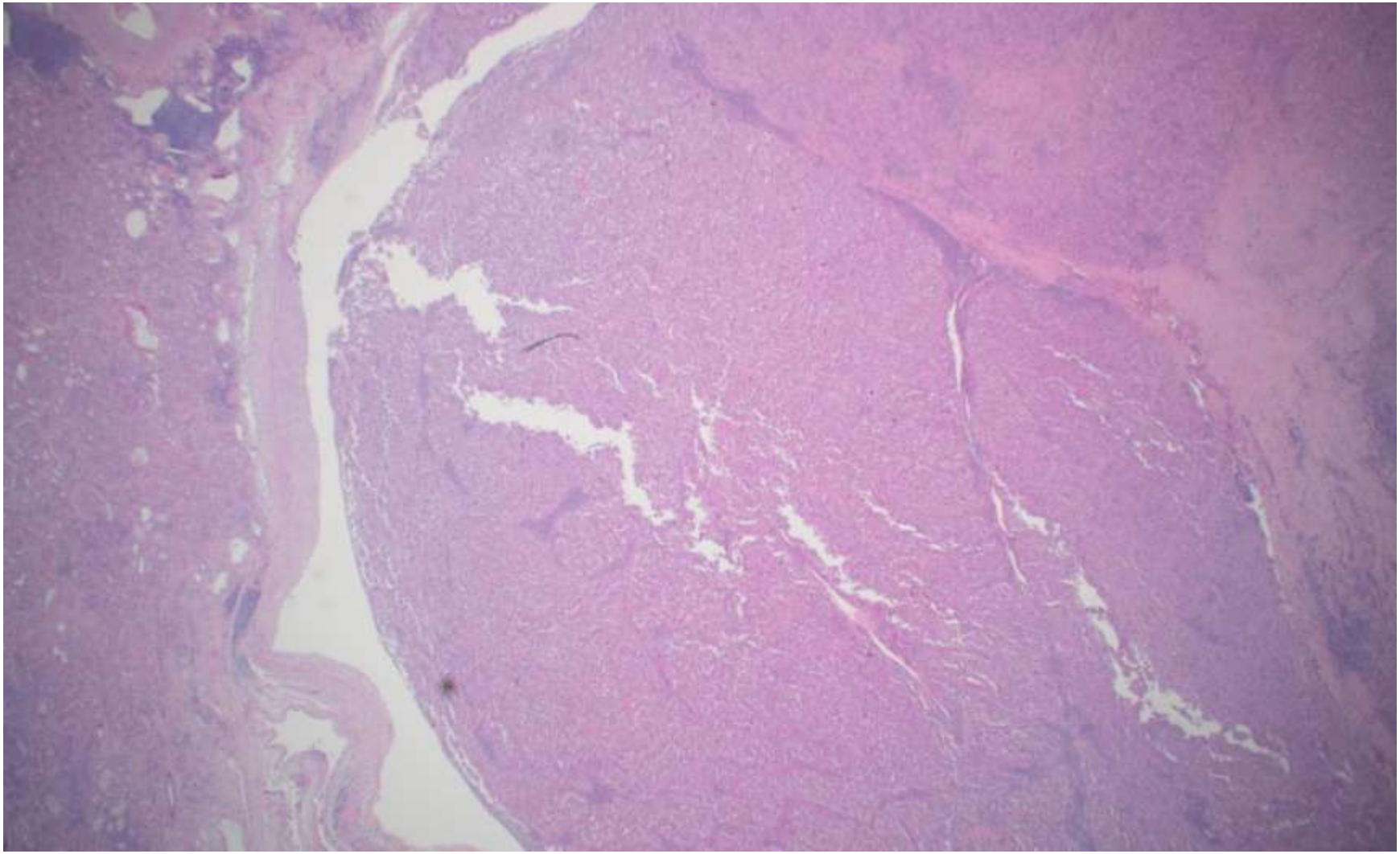


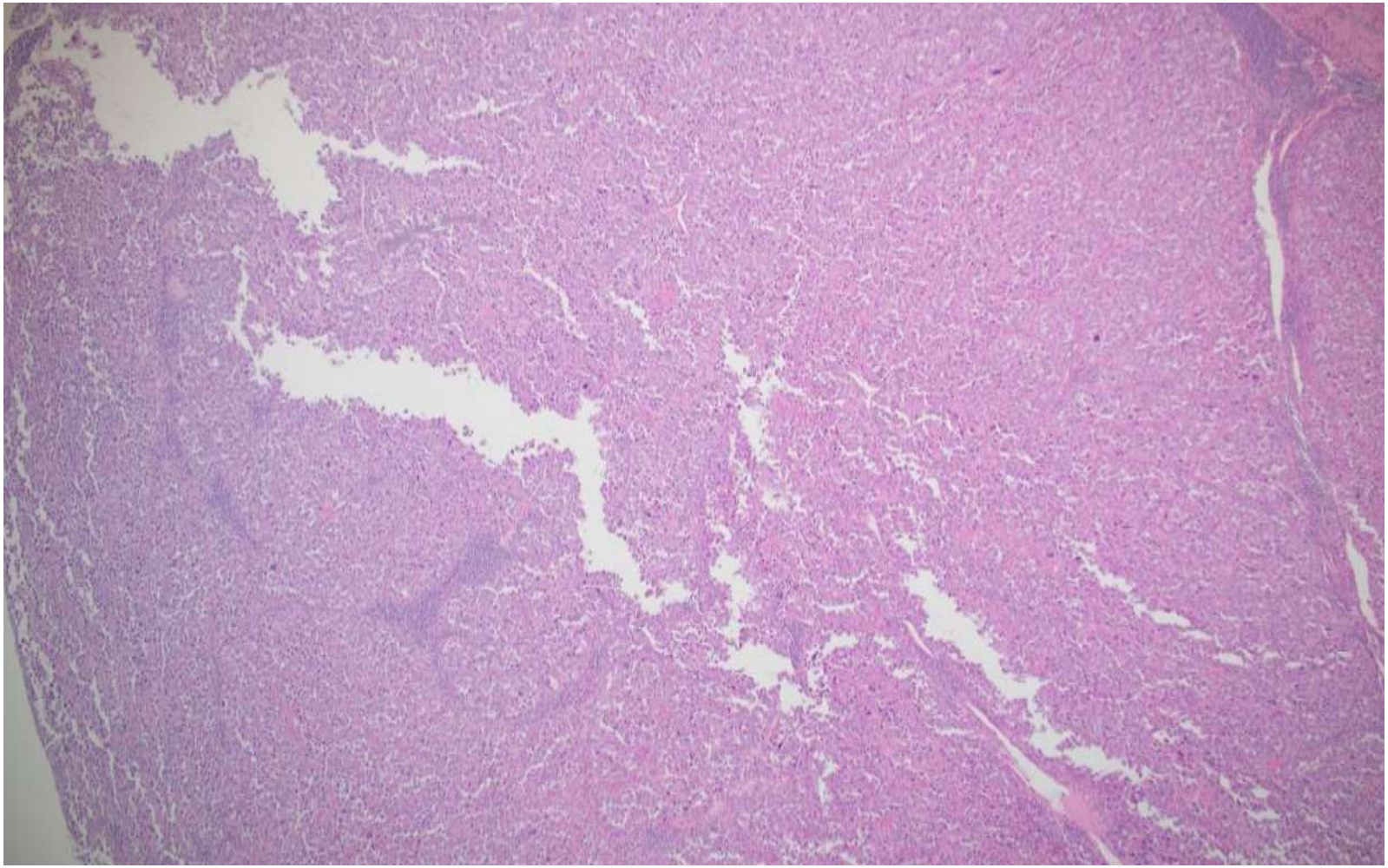
Argani et al. Am J Surg Pathol. 2014
Argani et al. Am J Surg Pathol. 2012

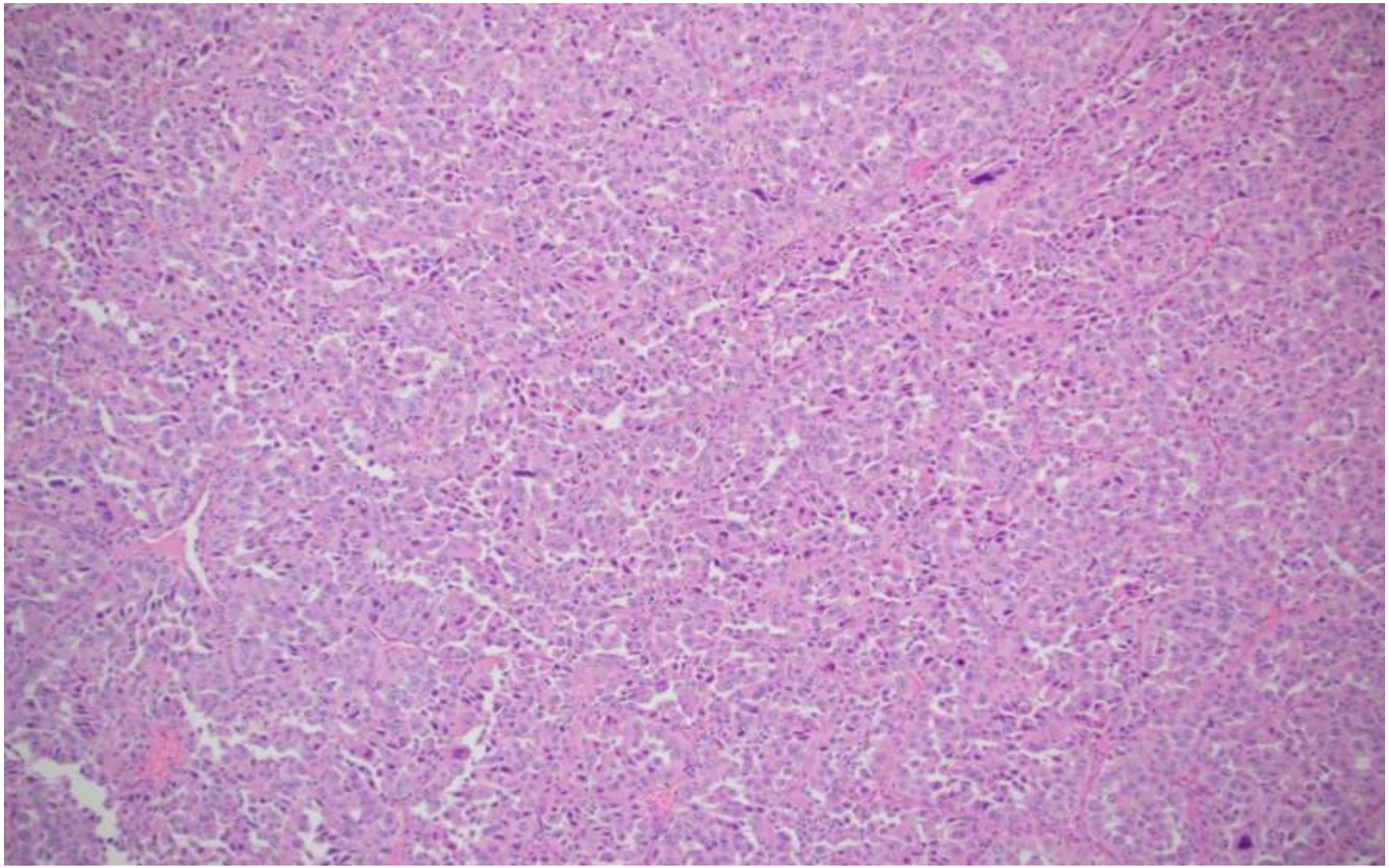
19-1008

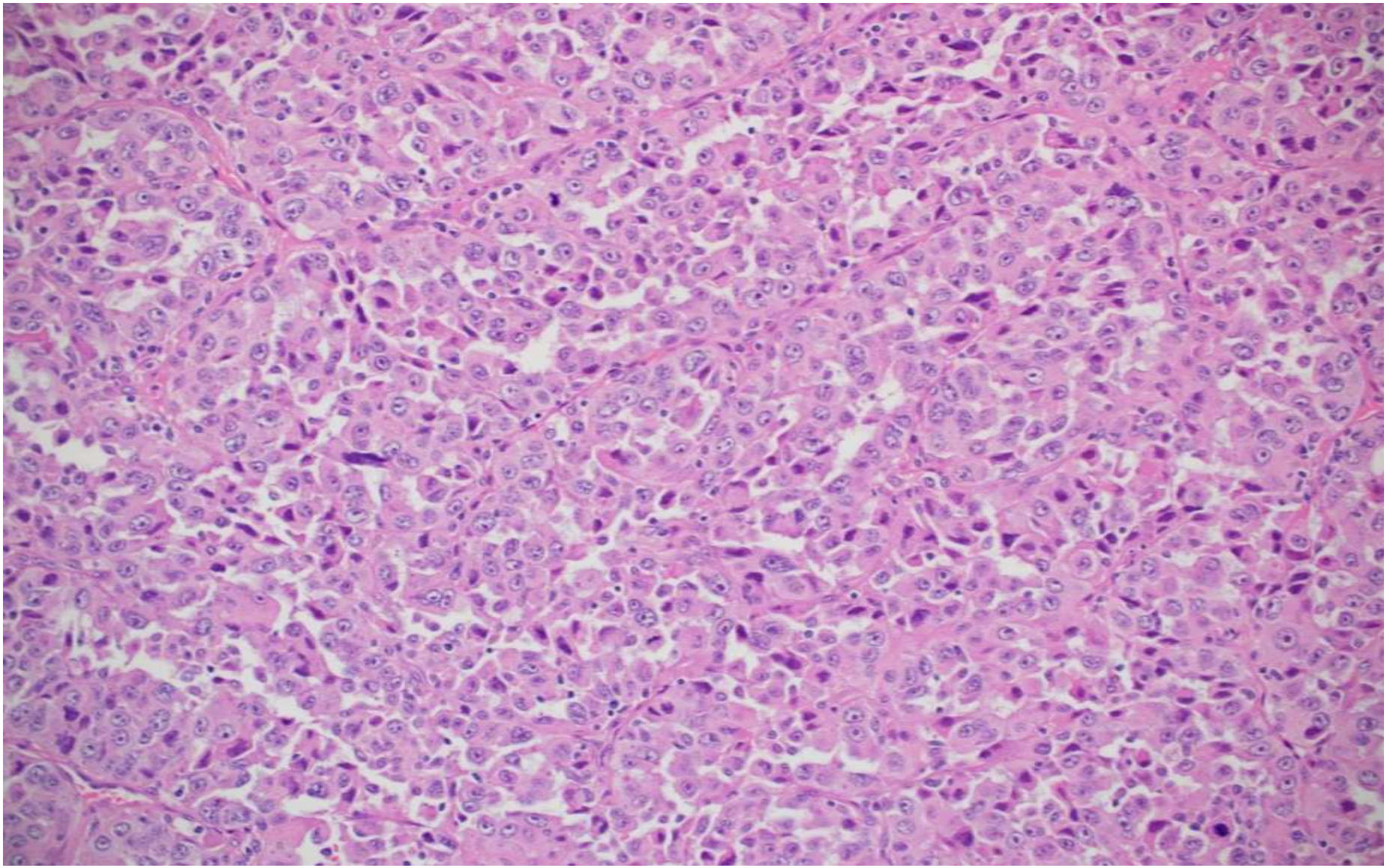
Emily Chan; UCSF

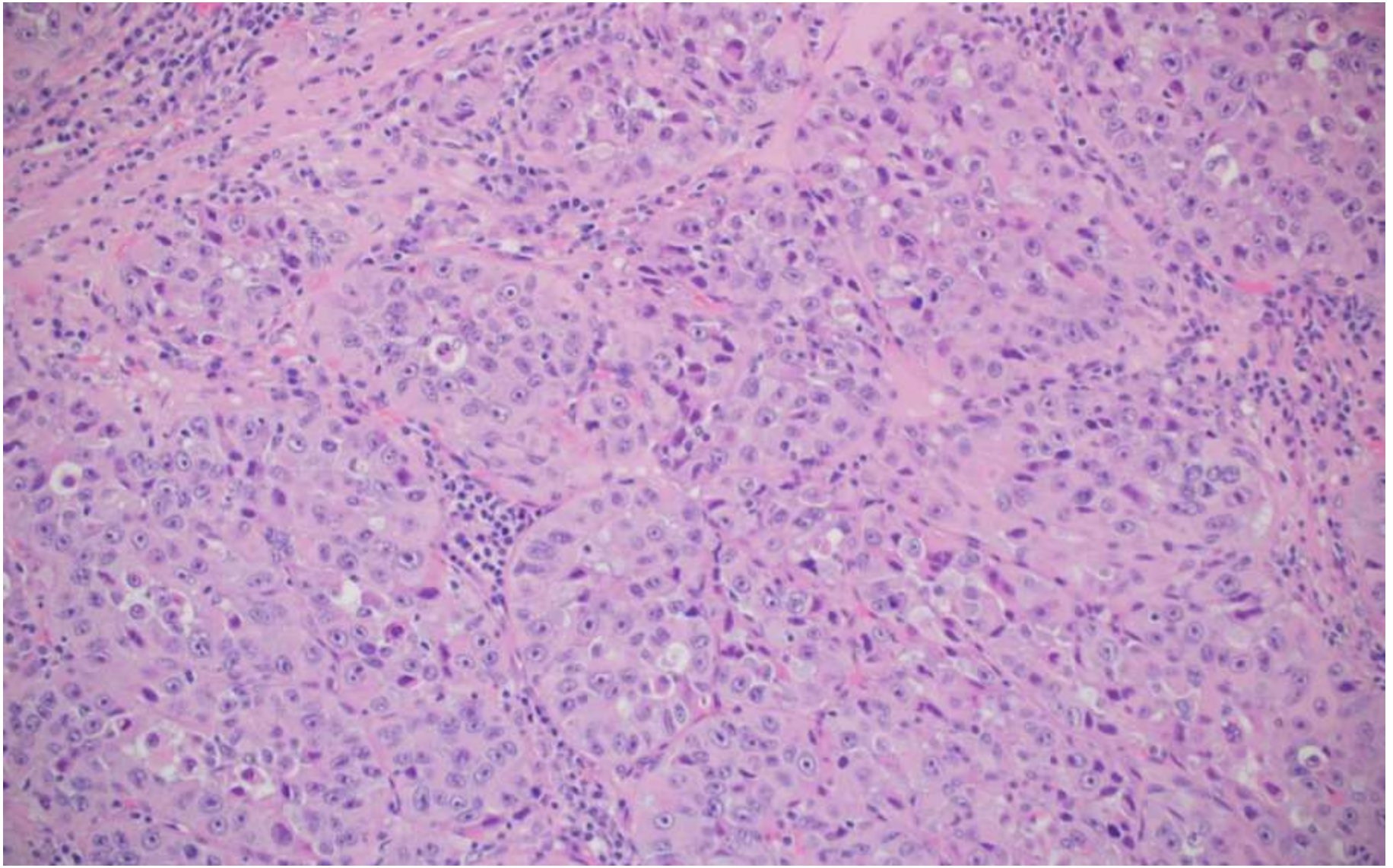
25-year-old female with 16cm left renal mass.

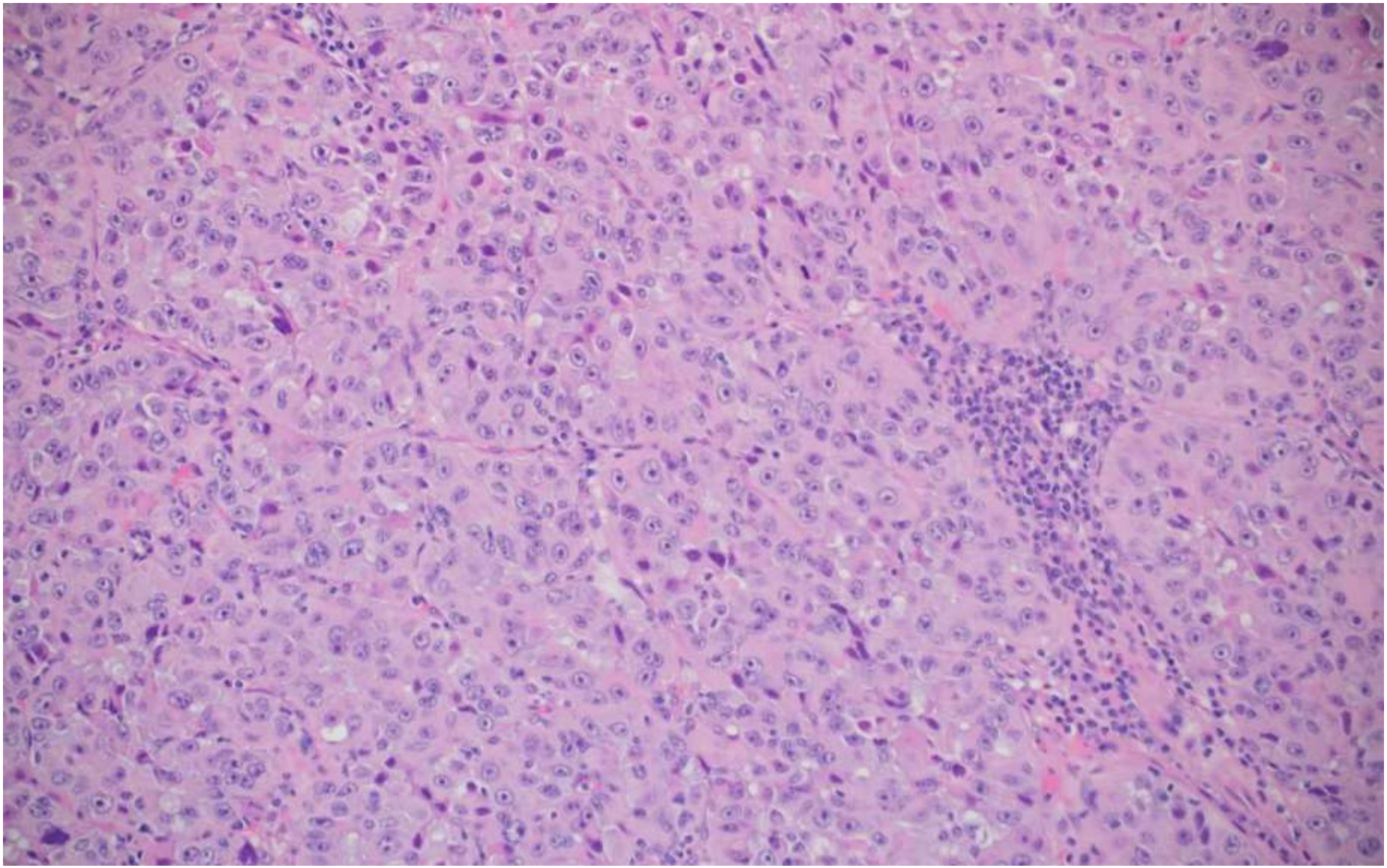


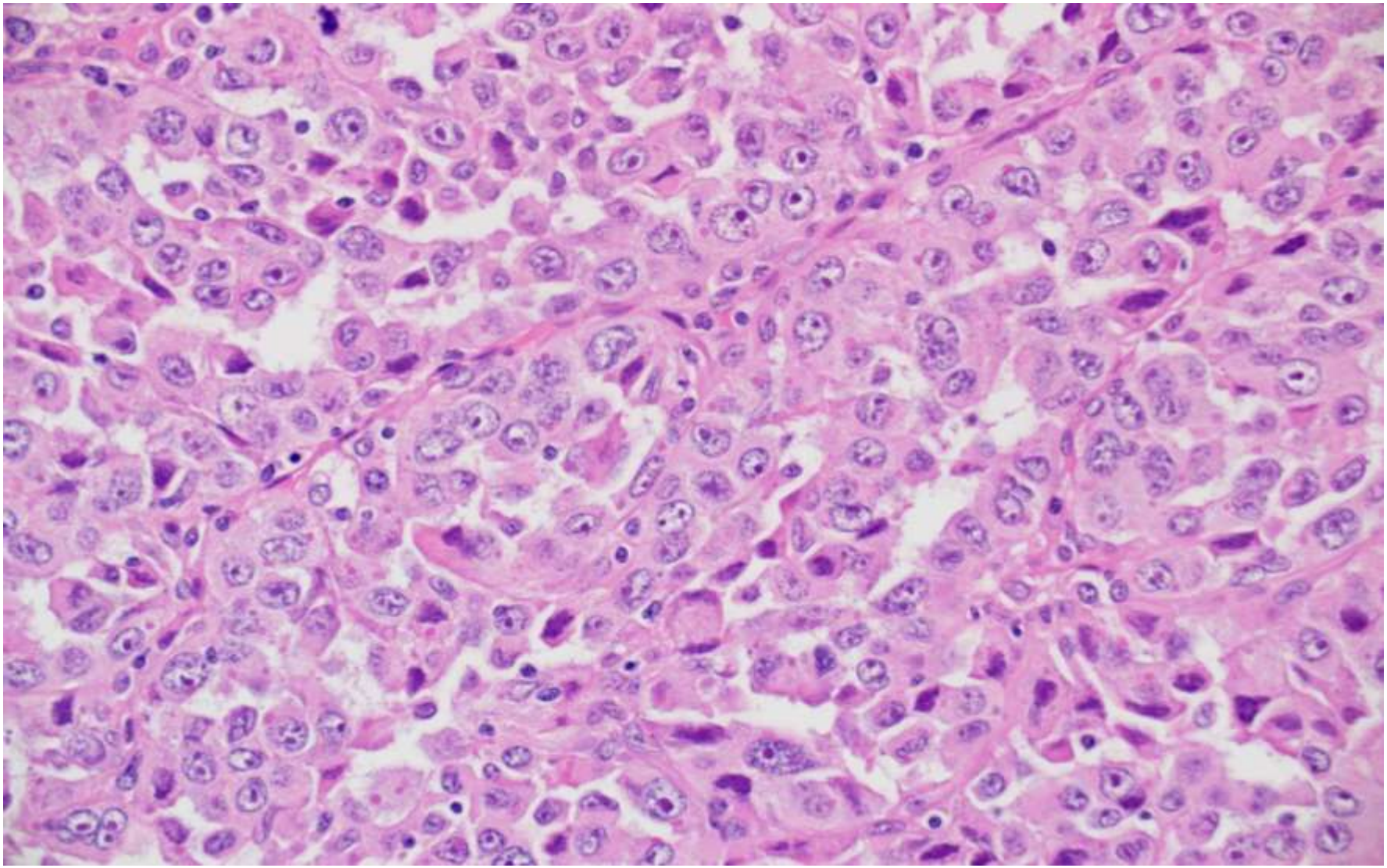










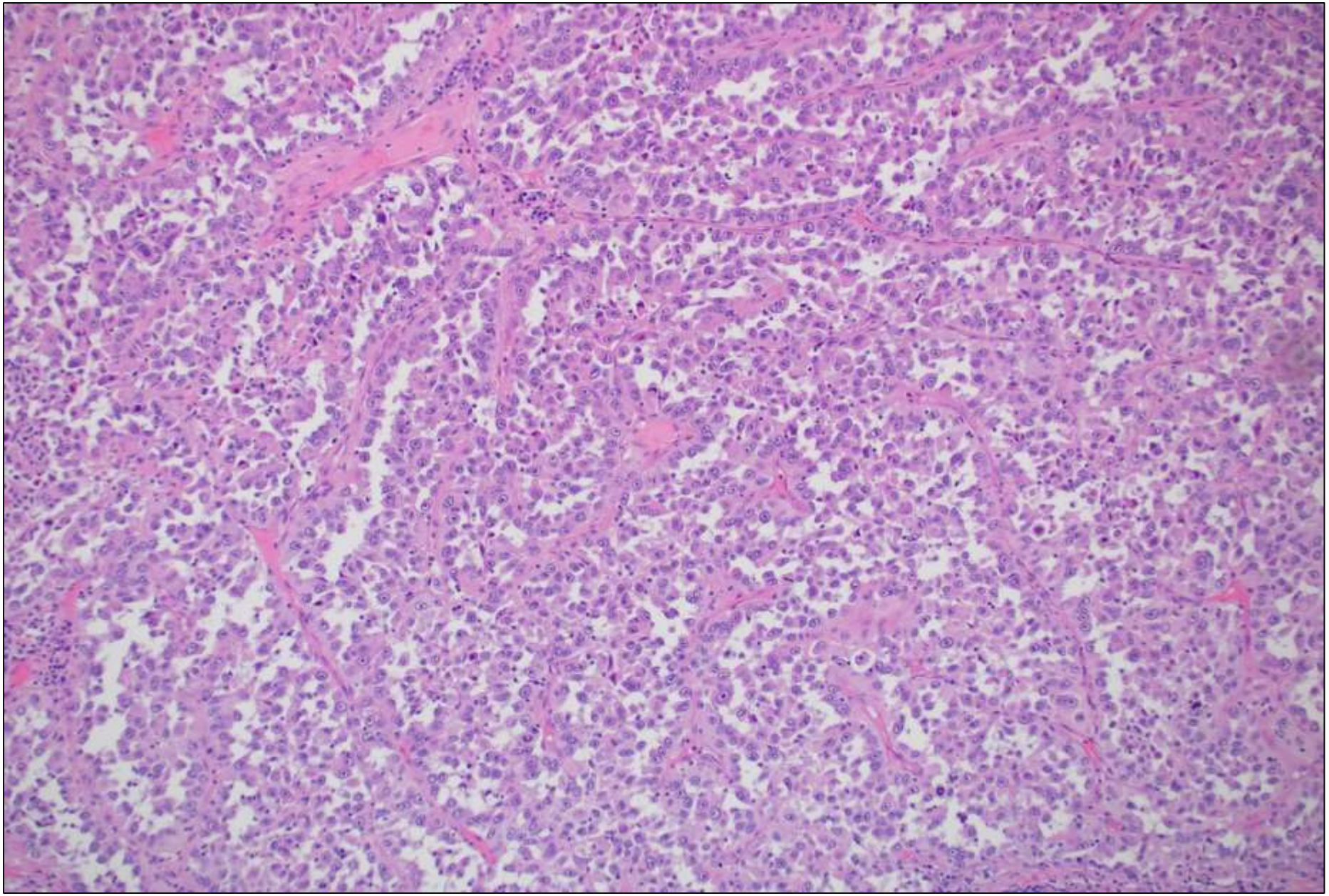


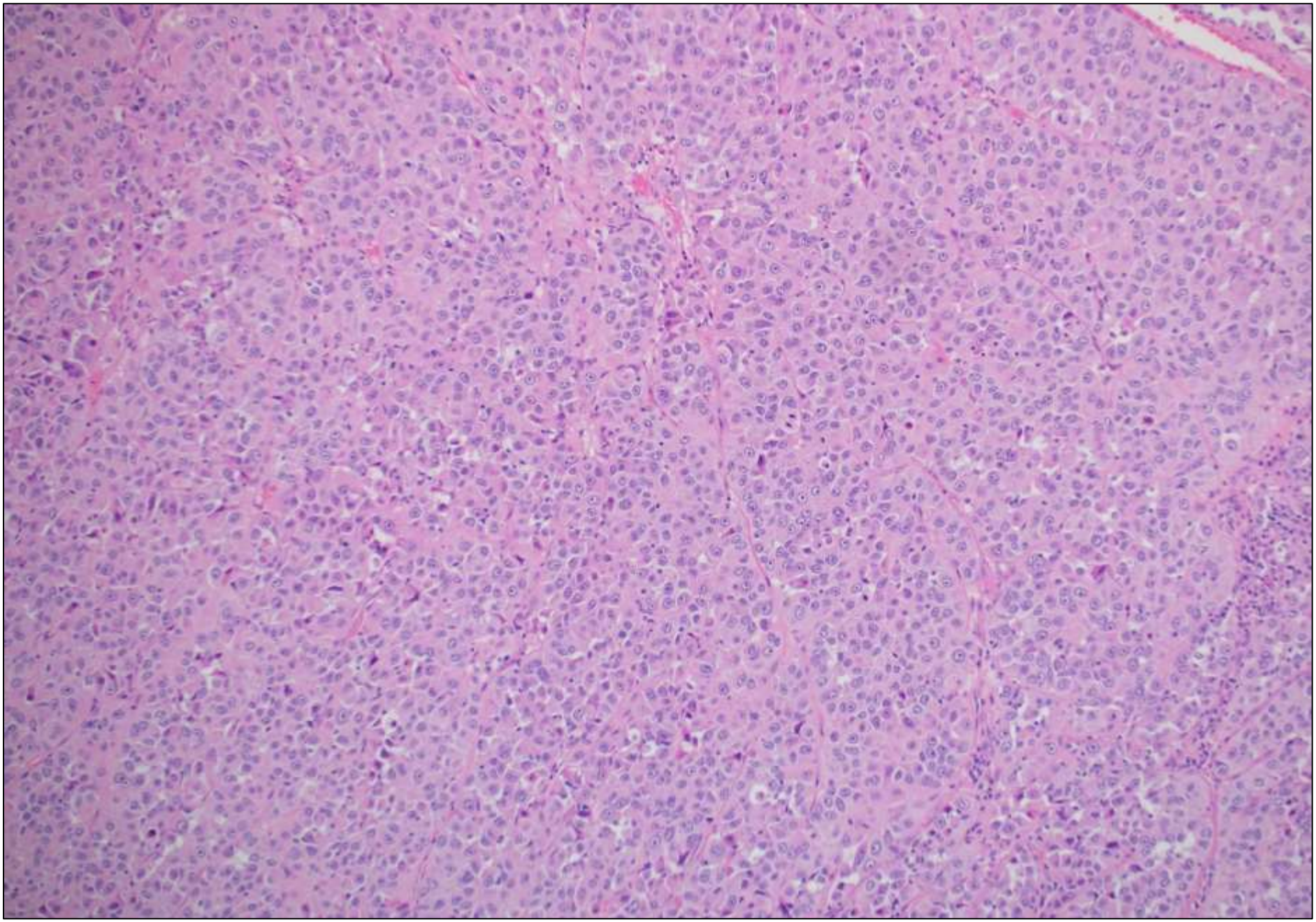
69 year-old man with 7.4 cm left kidney mass

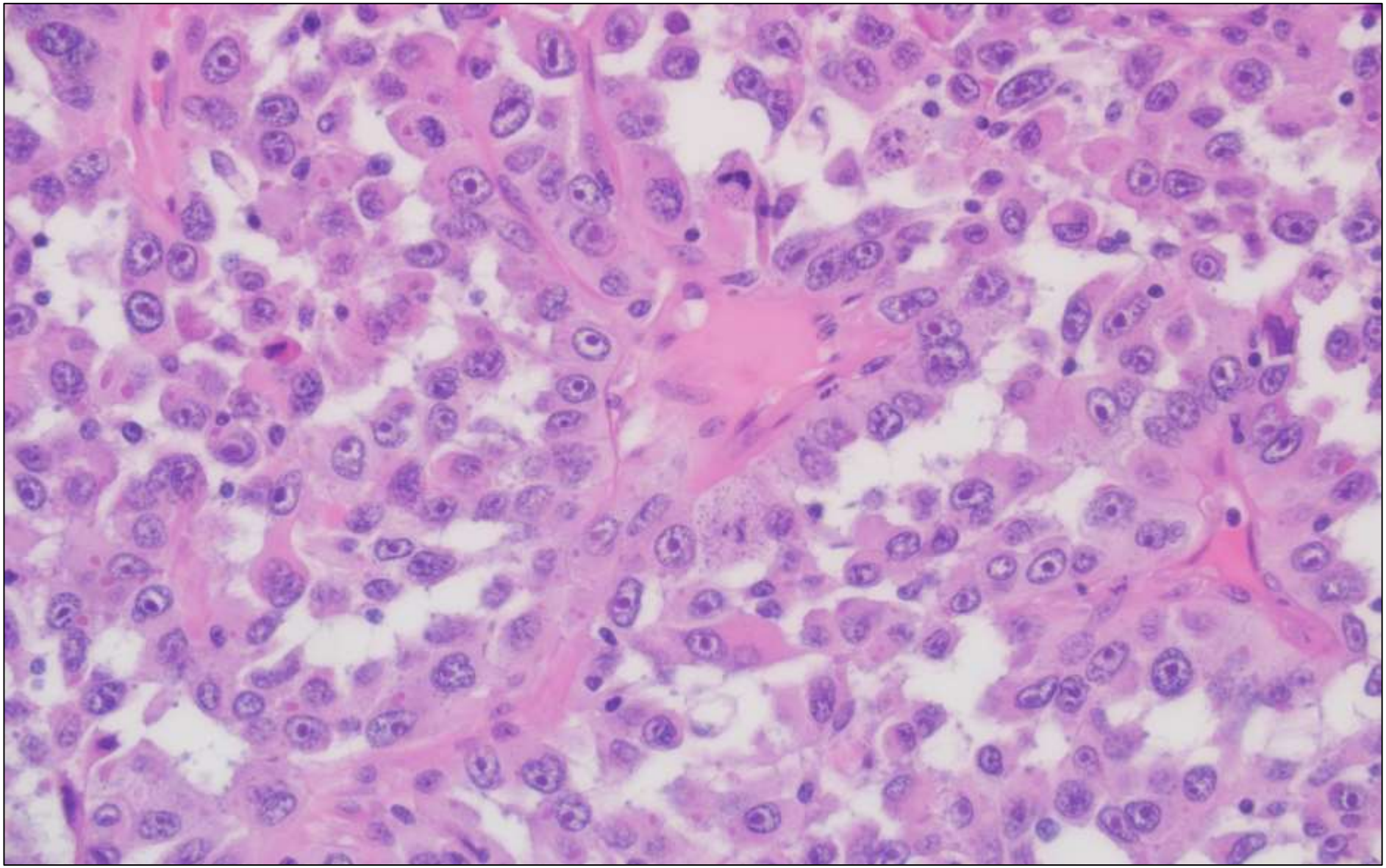
Emily Chan
UCSF

Southbay October 2019

(with permission from JP Grenert, Zuckerberg San Francisco General Hospital)





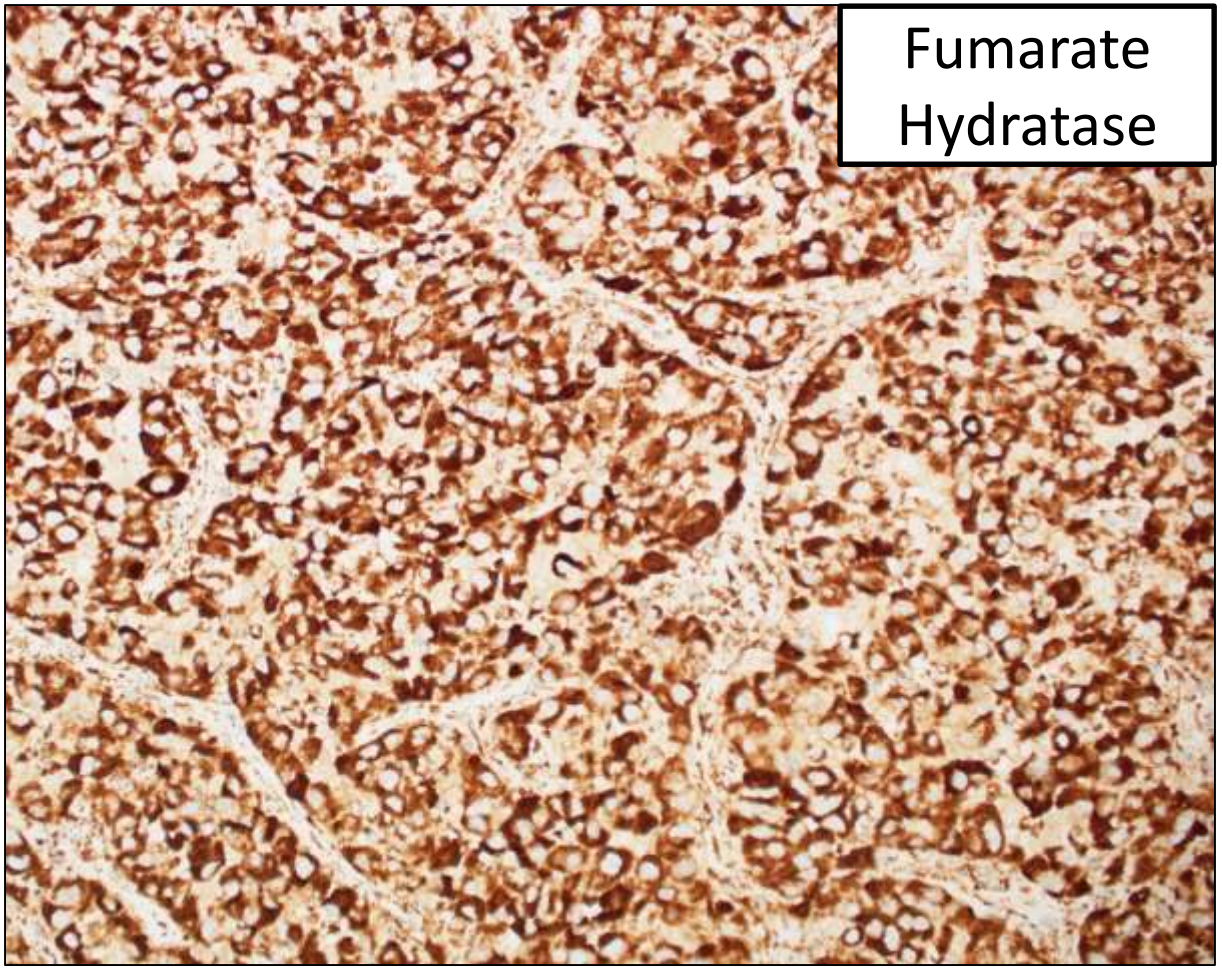


Differential diagnosis

- Fumarate hydratase (FH) deficient RCC
- Papillary RCC (conventional high-grade)
- RCC unclassified, with oncocytic and papillary features
- Urothelial carcinoma
- Renal medullary carcinoma

IHC

- Positive stains
  - PAX8
  - Pankeratin
- Negative stains:
  - CK7
  - CAIX
  - GATA3, P63
  - INI1 (retained)

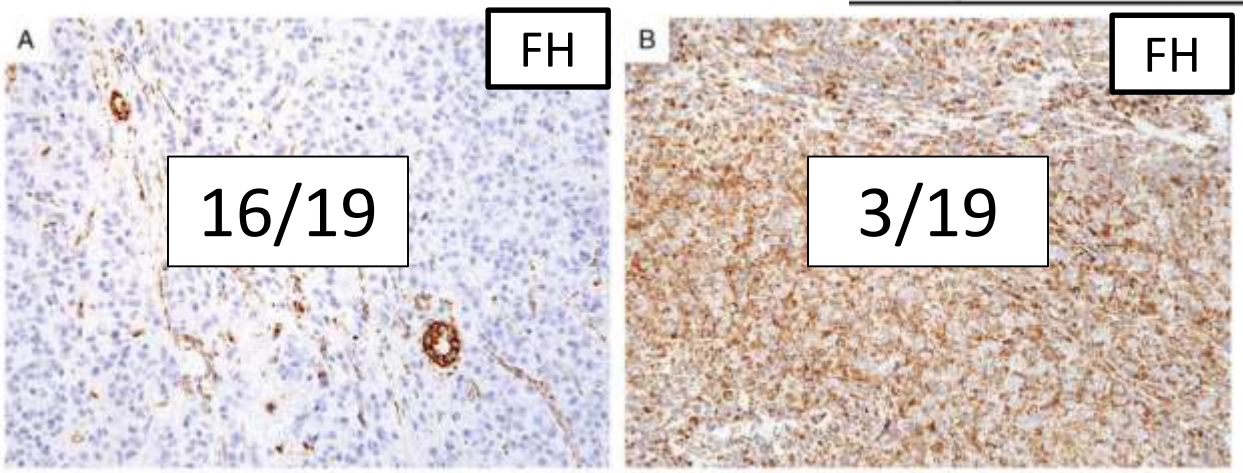


Fumarate hydratase (FH) IHC can be retained in setting of confirmed FH mutation

A Clinicopathologic and Molecular Analysis of Fumarate Hydratase-Deficient Renal Cell Carcinoma in 32 Patients

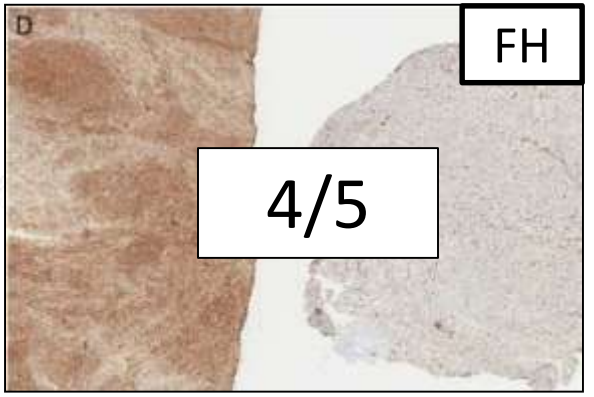
Hubert D. Lau, MD, Emily Chan, MD, PhD,† Alice C. Fan, MD,‡ Christian A. Kunder, MD, PhD,§ Sean R. Williamson, MD,‖ Ming Zhou, MD, PhD,¶ Muhammad T. Idrees, MD,# Fiona M. Maclean, MBBS,**†† Anthony J. Gill, MD,‡‡§§‖‖ and Chia-Sui Kao, MD§*

Am J Surg Pathol • Volume 00, Number 00, ■■ 2019



Detailed Morphologic and Immunohistochemical Characterization of Myomectomy and Hysterectomy Specimens From Women With Hereditary Leiomyomatosis and Renal Cell Carcinoma Syndrome (HLRCC)

Emily Chan, MD, PhD, Joseph T. Rabban, MD, MPH,* Julie Mak, MS,† Charles Zaloudek, MD,* and Karuna Garg, MD**



AJSP Sept 2019

Diagnosis???

Renal cell carcinoma, unclassified.

Recommend further molecular testing as retained FH IHC lends no support for but does not exclude an FH-deficient RCC

UCSF500 Next Generation Sequencing Assay

- No alterations in fumarate hydratase

PATHOGENIC AND LIKELY PATHOGENIC ALTERATIONS
VARIANT
ARID1B p.P1513fs
CCND3 co-amplification with TFEB
CDK4 amplification
PPM1D amplification as part of 17q23-q24 interstitial amplification
VEGFA amplification

TFEB-amplified Renal Cell Carcinomas

An Aggressive Molecular Subset Demonstrating Variable Melanocytic Marker Expression and Morphologic Heterogeneity

Pedram Argani, MD,† Victor E. Reuter, MD,‡ Lei Zhang, MD,‡ Yun-Shao Sung, MS,‡ Yi Ning, PhD,* Jonathan I. Epstein, MD,*† George J. Netto, MD,*† and Cristina R. Antonescu, MD‡*

AJSP 2016; 40: 1484-1495

Detection of 6 *TFEB*-amplified renal cell carcinomas and 25 renal cell carcinomas with MITF translocations: systematic morphologic analysis of 85 cases evaluated by clinical *TFE3* and *TFEB* FISH assays

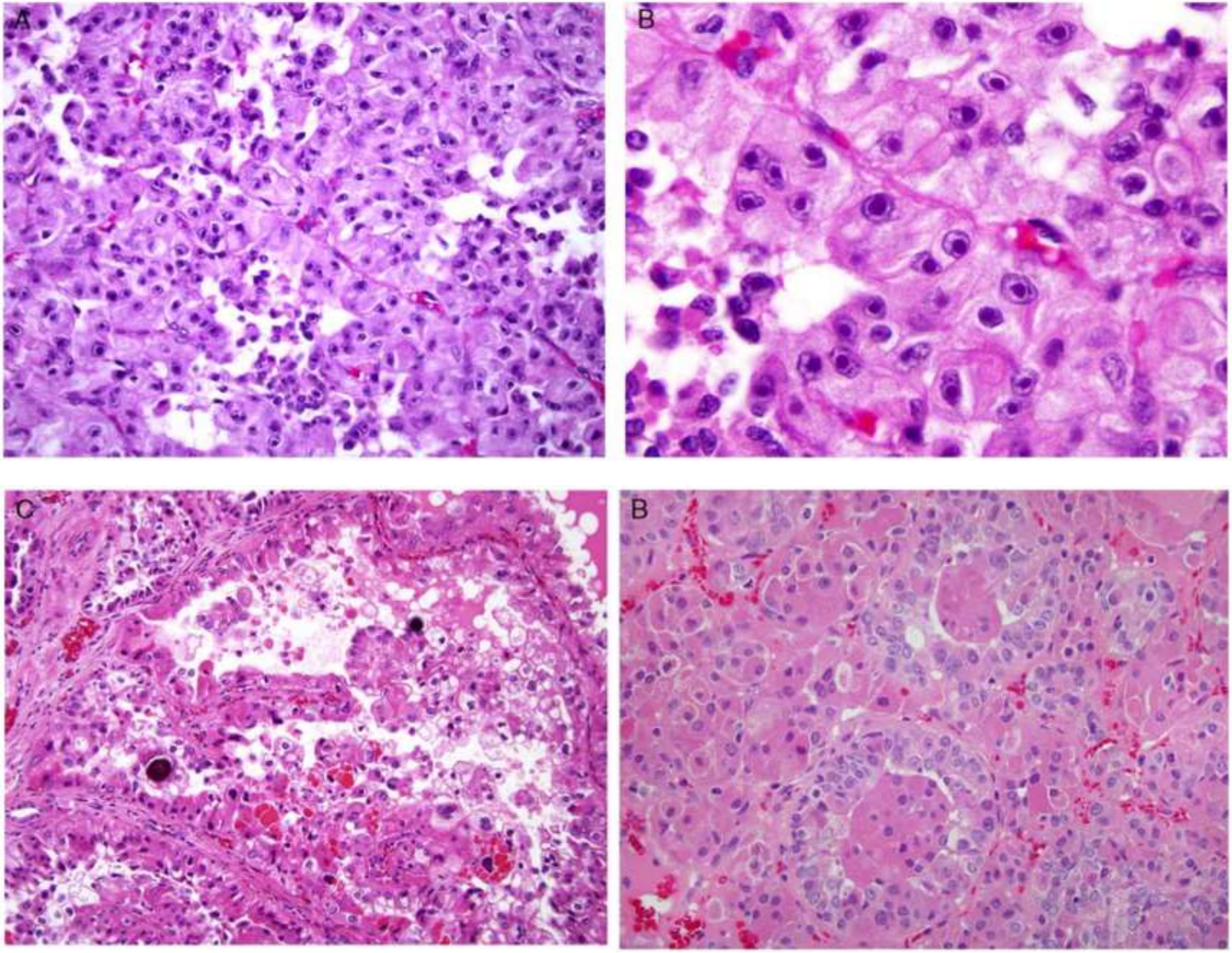
Stephanie L Skala[1], Hong Xiao[1,2], Aaron M Udager[1], Saravana M Dhanasekaran[3], Sudhanshu Shukla[3], Yang Zhang[2], Carrie Landau[2], Lina Shao[1,2], Diane Roulston[1,2], Lisha Wang[3], Javed Siddiqui[3], Xuhong Cao[3], Cristina Magi-Galluzzi[4], Miao Zhang[5], Adeboye O Osunkoya[6], Steven C Smith[7], Jesse K McKenney[4], Bryan L Betz[1], Jeffrey L Myers[1], Arul M Chinnaiyan[1,3,8,9], Scott A Tomlins[1,3,8] and Rohit Mehra[1,3,8]

Modern Path 2016; 31: 179-197

TFEB-amplified RCC

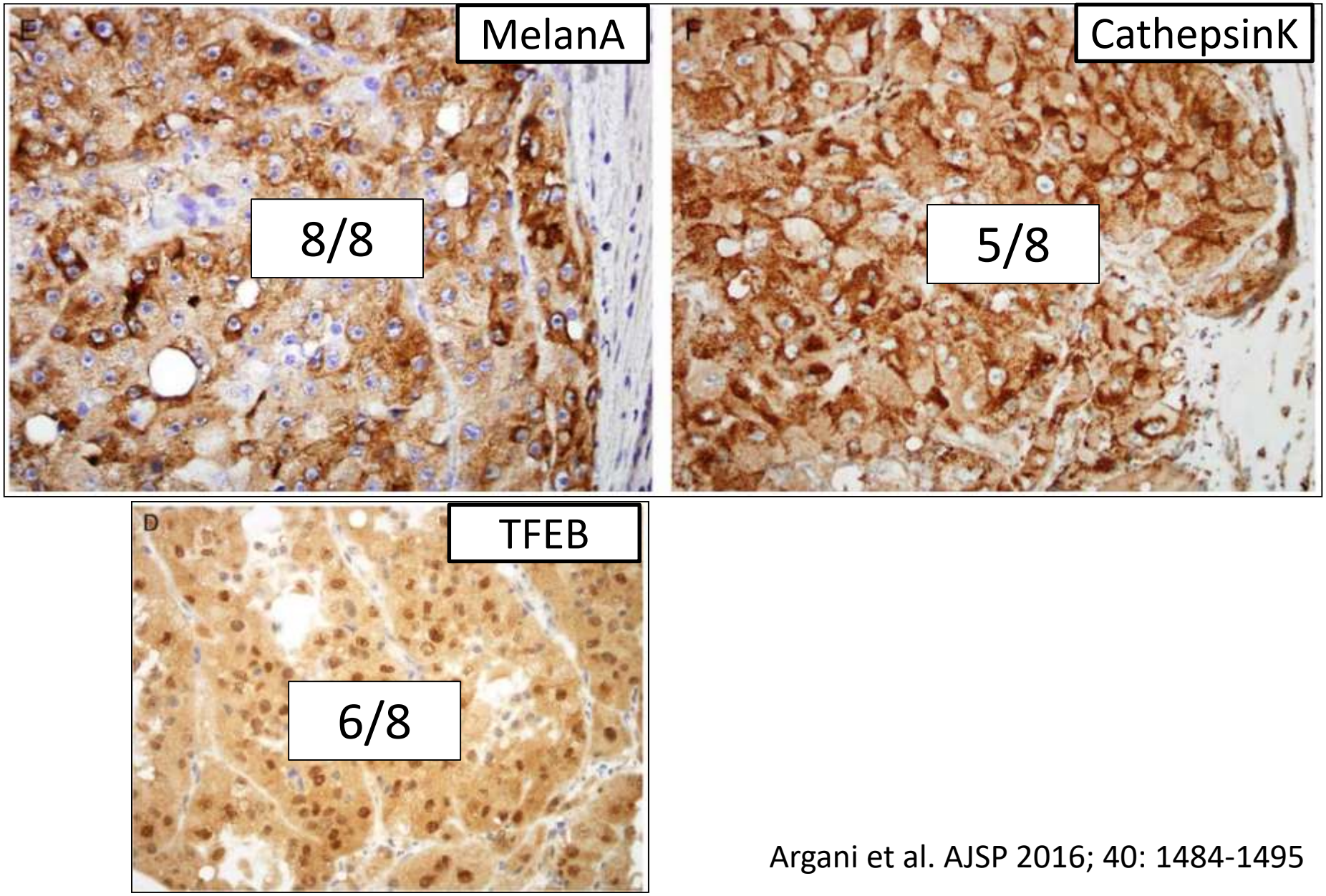
- Oncocytic with papillary and nested architecture
- High WHO nucleolar grade
- Older age group compared to TFEB translocation (range: 23-77, median 64, mean 62.5)
- More aggressive clinical behavior

Argani et al. AJSP 2016; 40: 1484-1495



Argani et al. AJSP 2016; 40: 1484-1495

TFEB-amplified IHC



Argani et al. AJSP 2016; 40: 1484-1495

Summary

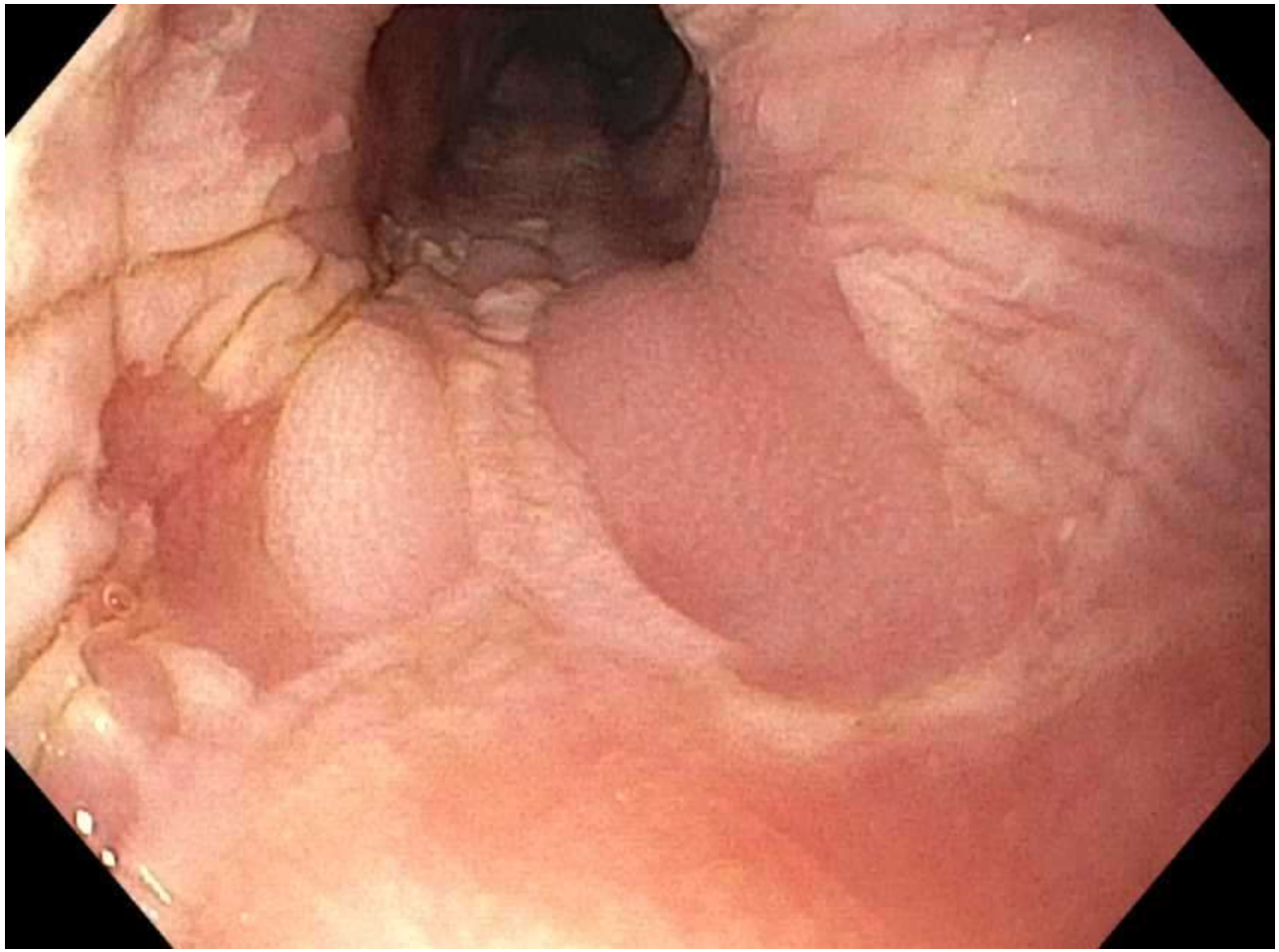
- Think about TFEB-amplified (or translocation) associated RCC when presented with an oncocytic tumor with papillary/solid/pseudopapillary architecture
- TFEB amplified RCC can mimic FH-deficient RCC
- Suggest molecular testing if morphology and supporting IHC is suggestive

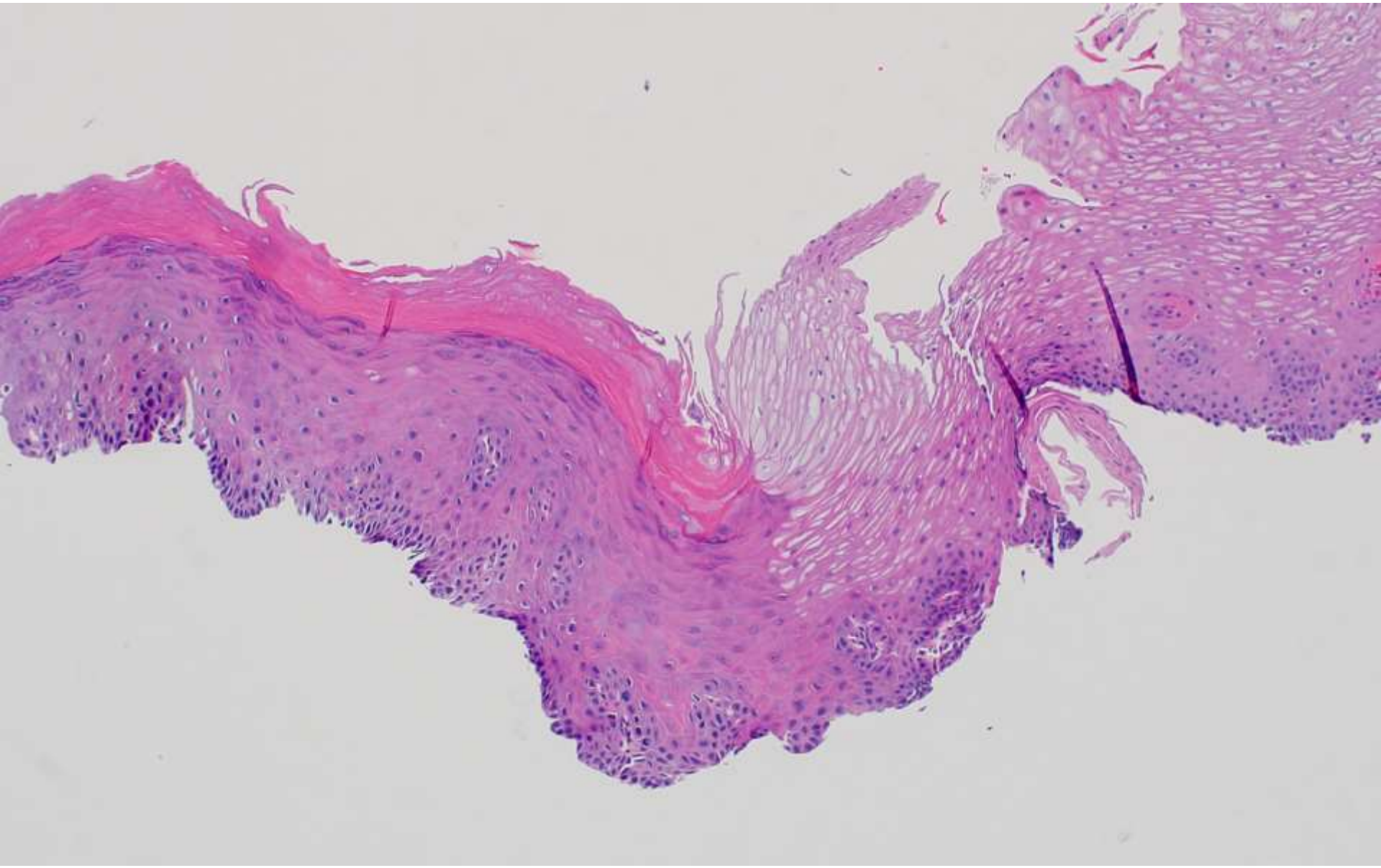
19-1009

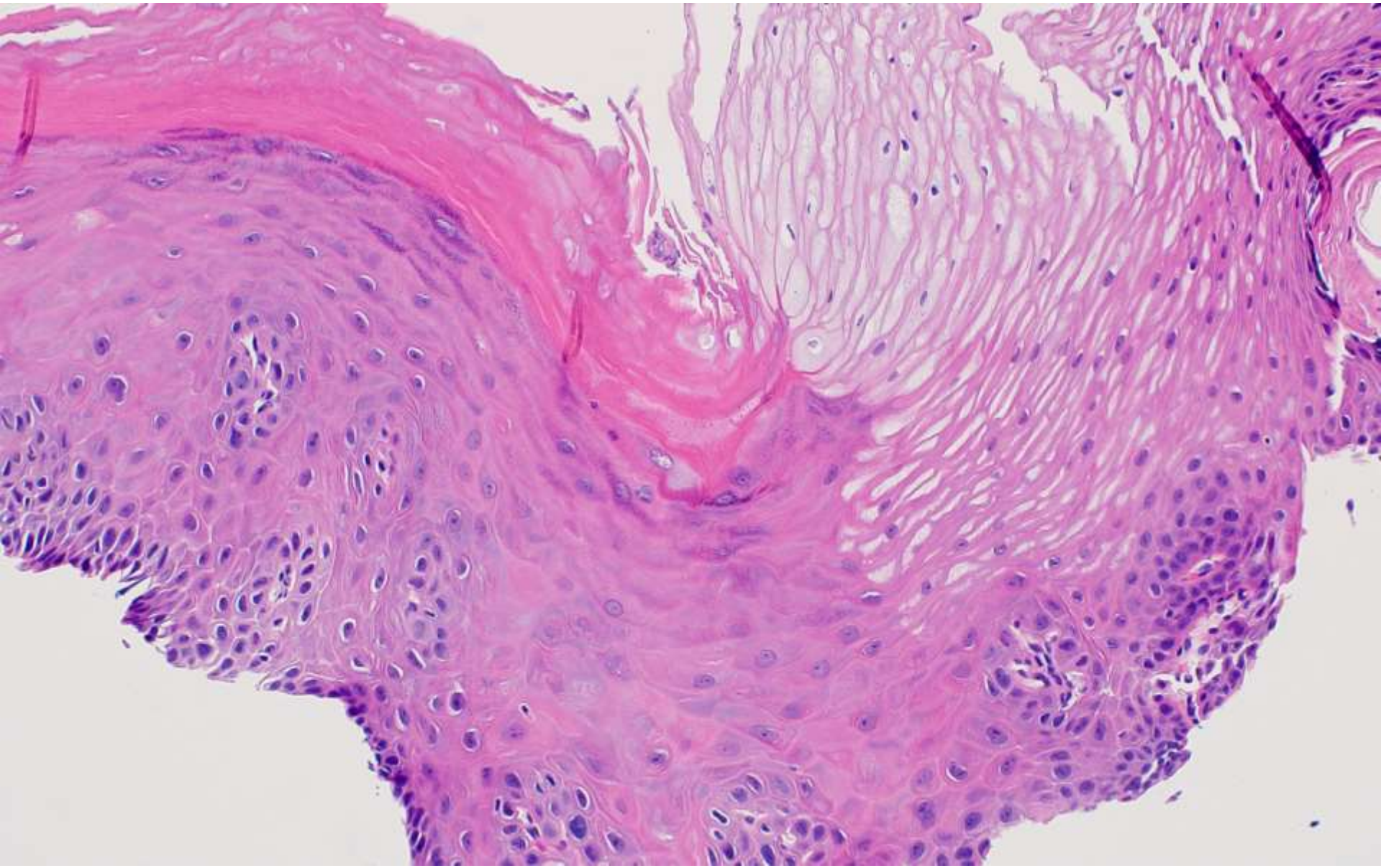
Jeff Cloutier/Brock Martin; Stanford

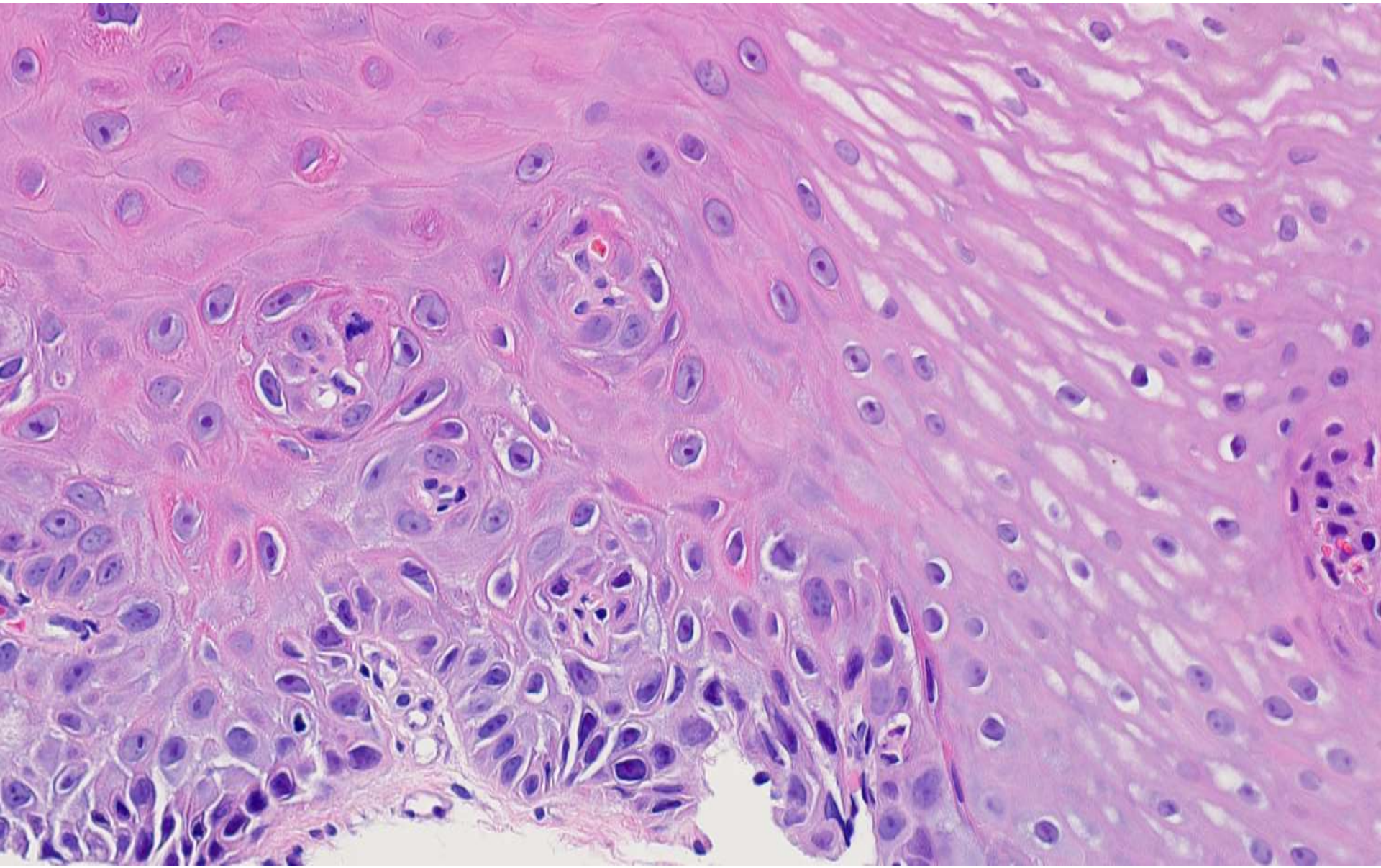
74-year-old male with h/o esophageal and duodenal ulcers, now presenting with nausea. Esophageal biopsy performed.

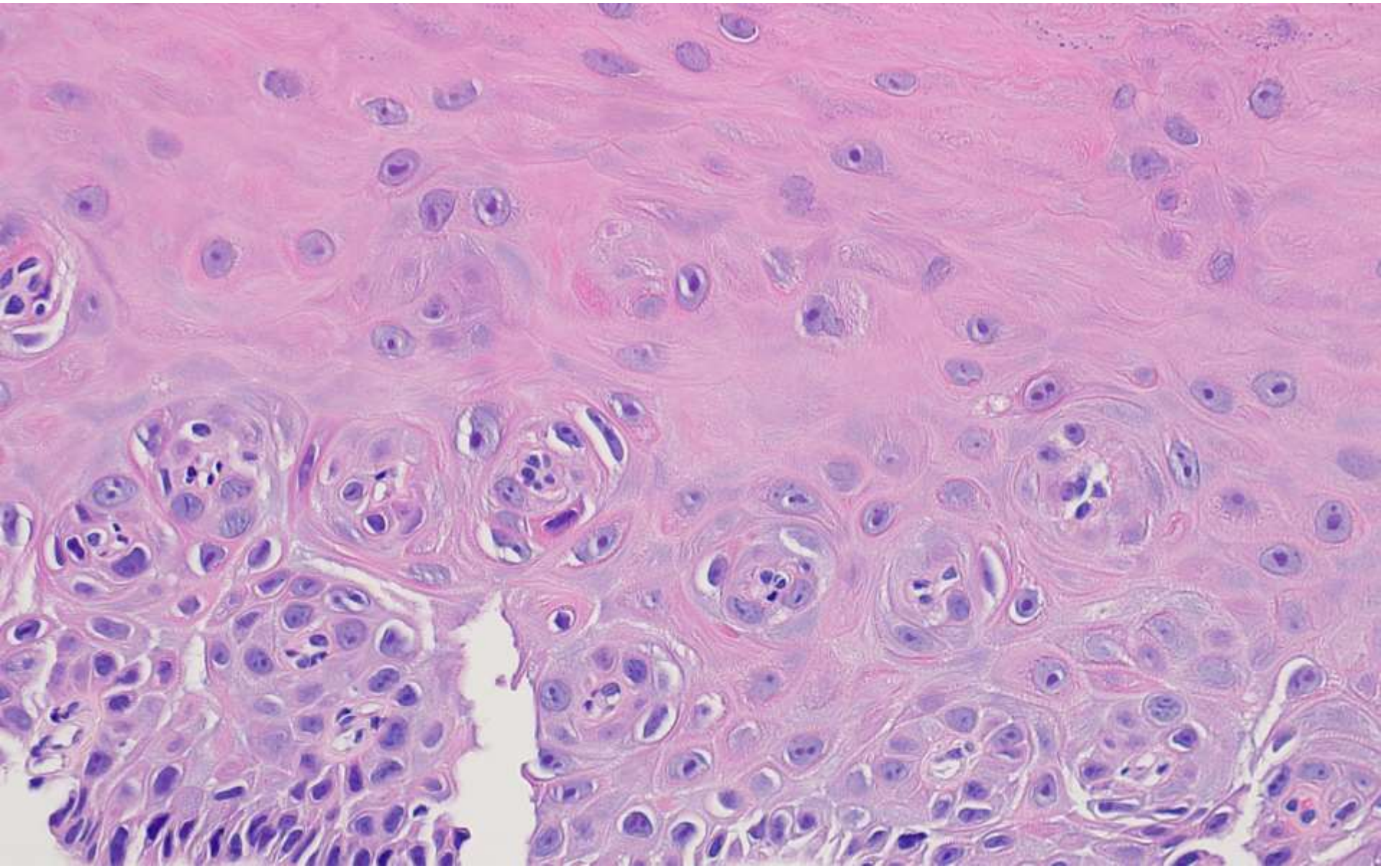
Mucosal sclerosis and thickening in mid-esophagus











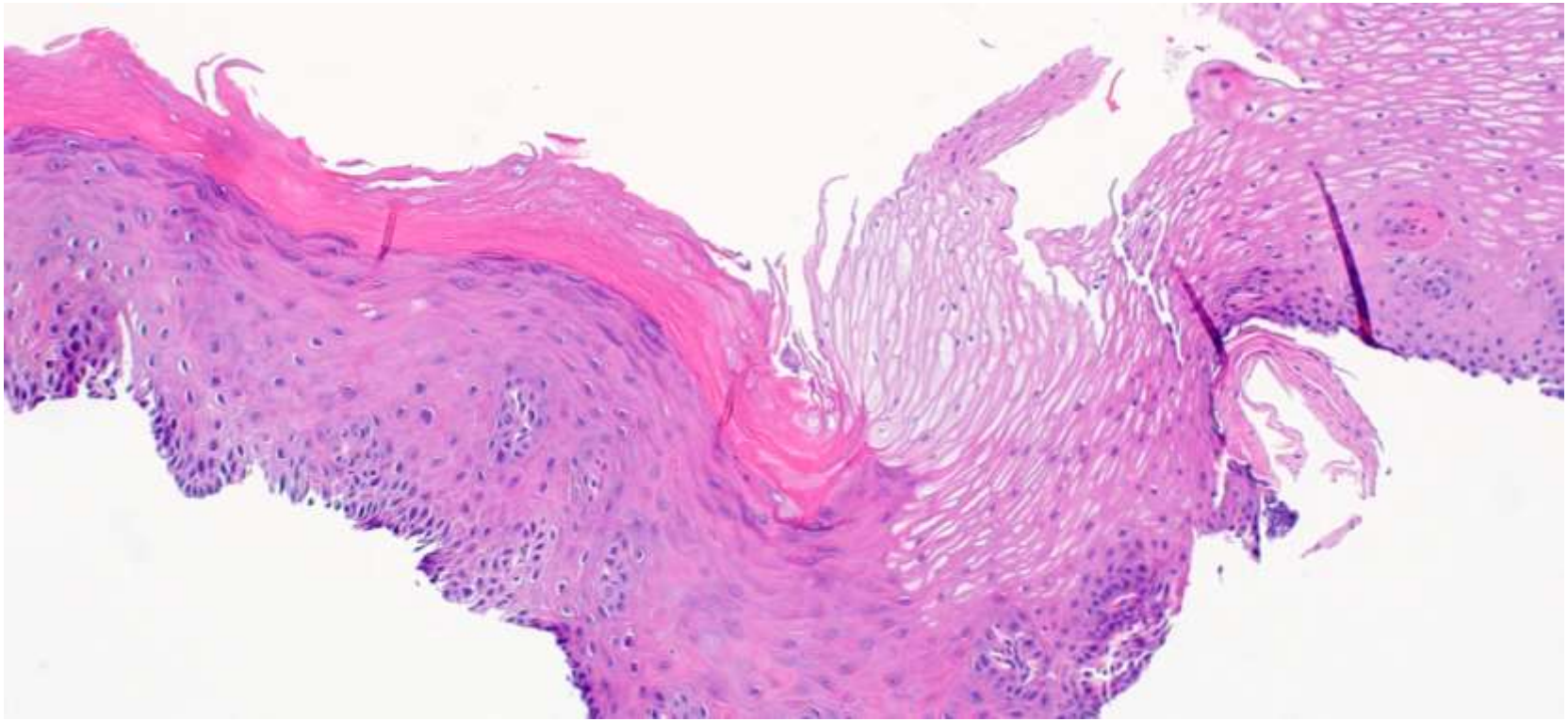
74-year-old man with history of esophageal and duodenal ulcers, now presenting with nausea

Esophagogastroduodenoscopy

Atypical Esophageal Epidermoid Metaplasia

Esophageal epidermoid metaplasia

Prominent granular layer with overlying compact hyperorthokeratosis, resembling epidermis of skin

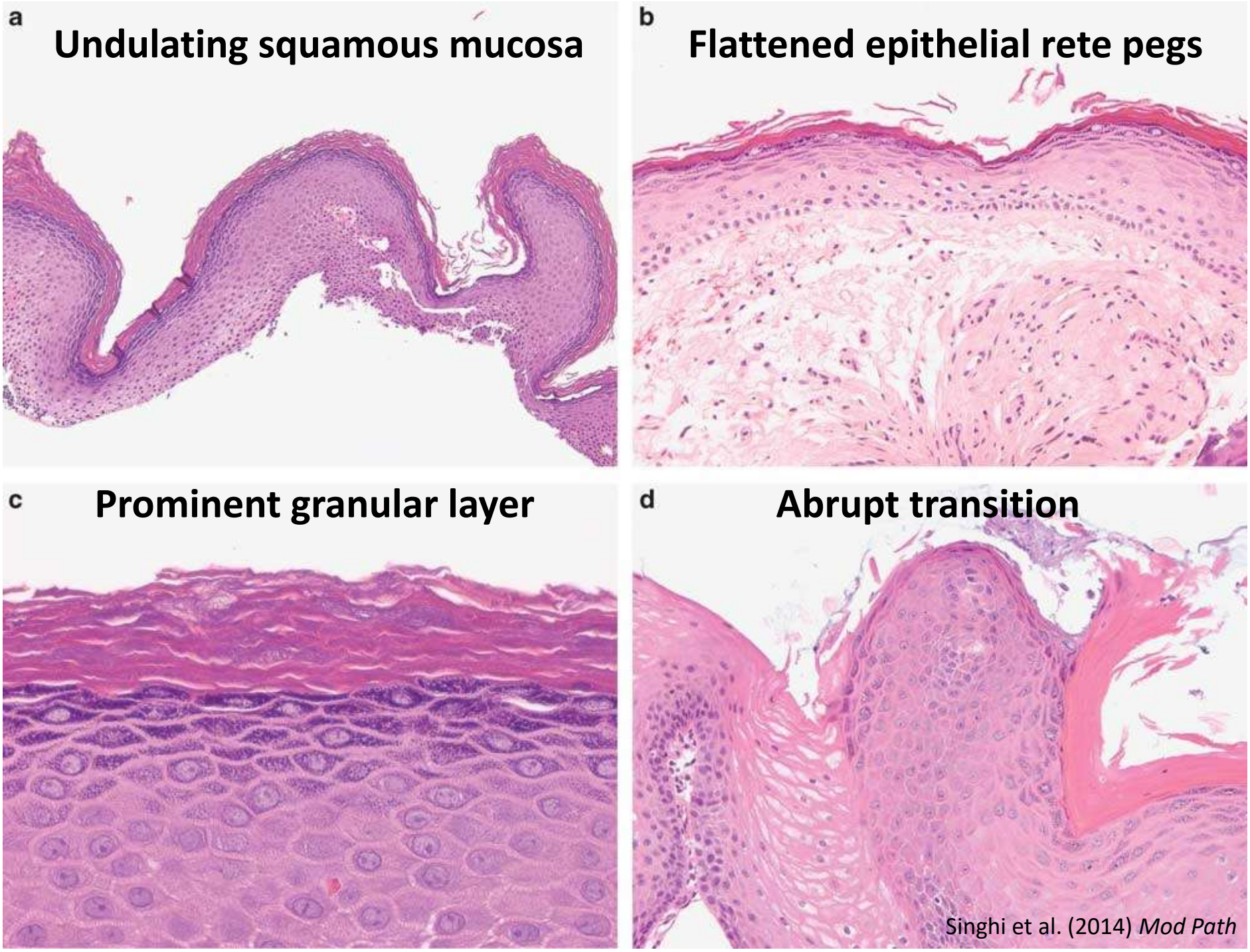


MODERN PATHOLOGY (2014) 27, 38–43

Esophageal leukoplakia or epidermoid metaplasia: a clinicopathological study of 18 patients

Aatur D Singhi[1], Christina A Arnold[2], Clinton D Crowder[3], Dora M Lam-Himlin[4], Lysandra Voltaggio[5] and Elizabeth A Montgomery[6]

[1]Department of Pathology, UPMC Presbyterian Hospital, Pittsburgh, PA, USA; [2]Department of Pathology, Ohio State University, Columbus, OH, USA; [3]Department of Pathology, Mercy Medical Center, Des Moines, IA, USA; [4]Department of Pathology, Mayo Clinic, Scottsdale, AZ, USA; [5]Department of Pathology, George Washington Hospital, Washington, DC, USA and [6]Department of Pathology, Johns Hopkins Hospital, Baltimore, MD, USA


a
Undulating squamous mucosa
b
Flattened epithelial rete pegs
c
Prominent granular layer
d
Abrupt transition
Singhi et al. (2014) *Mod Path*

Esophageal epidermoid metaplasia: a preneoplastic lesion?

Singhi *et al.* (2014) *Modern Pathology*:

- 3/18 patients with EEM had high-grade squamous dysplasia (n=2) and squamous cell carcinoma (n=1) in nearby biopsies

Contreau *et al.* (2016) *Histopathology*:

- 2/58 patients with squamous neoplasia had concurrent EEM (compared to 2/1048 in control group)

Ezoe *et al.* (2011) *Hepatogastroenterology*:

- 4/4 patients with EEM had synchronous or metachronous SCC of the esophagus and oropharynx

MODERN PATHOLOGY (2017) 30, 1613–1621

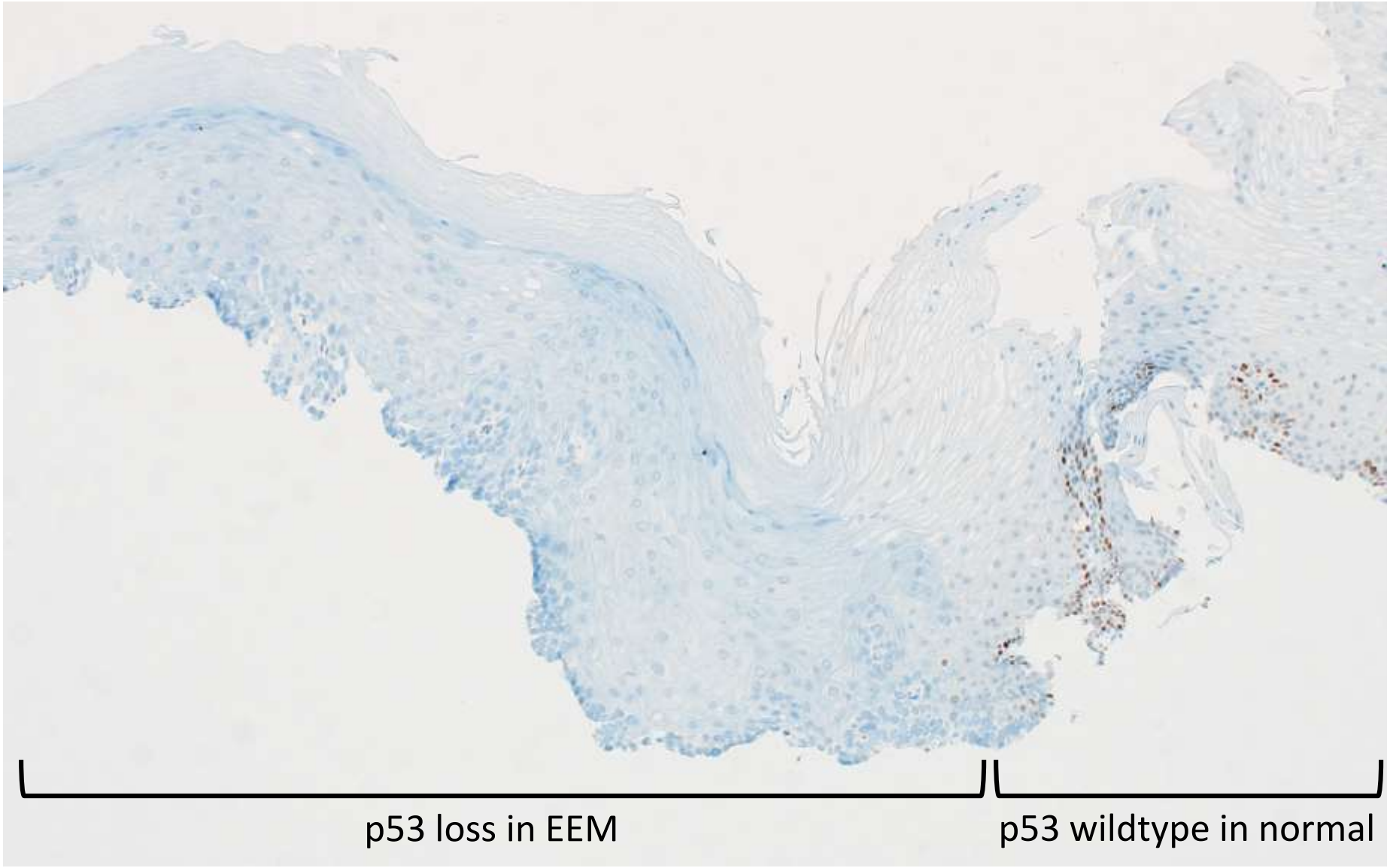
Targeted next-generation sequencing supports epidermoid metaplasia of the esophagus as a precursor to esophageal squamous neoplasia

Aatur D Singhi[1], Christina A Arnold[2], Dora M Lam-Himlin[3], Marina N Nikiforova[1], Lysandra Voltaggio[4], Marcia I Canto[4], Kevin M McGrath[1] and Elizabeth A Montgomery[4]

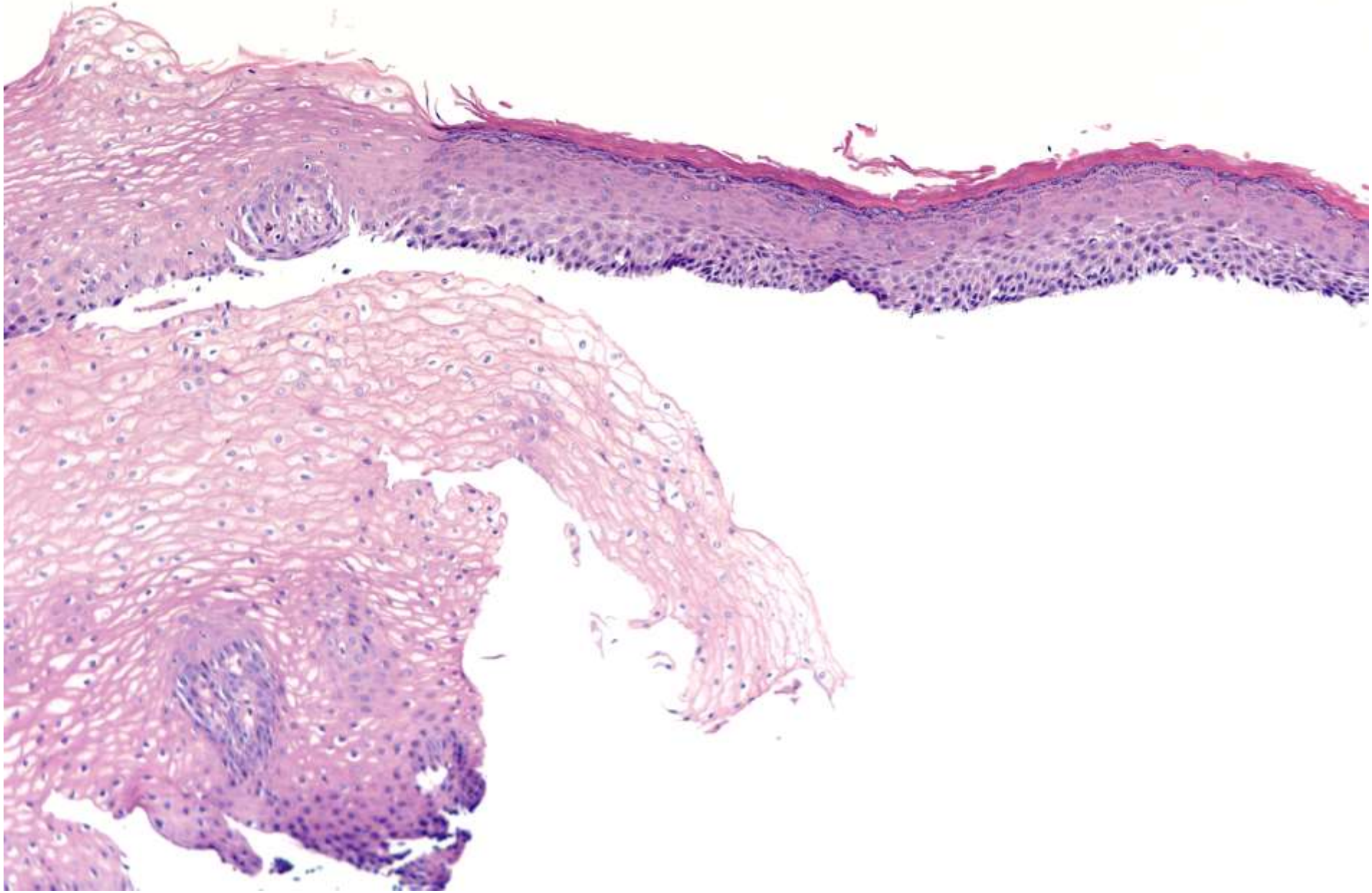
Frequent *TP53* mutations in both EEM and associated dysplasia and SCC

Patient	*Uninvolved esophageal mucosa*	*Esophageal epidermoid metaplasia*	*High-grade squamous dysplasia/squamous cell carcinoma*
1	No mutations found	*TP53* c.844C>T; p.R282W (4%) *PIK3CA* c.2176G>A; p.E726K (3%) *MYCN* c.793G>A; p.D265N (3%)	*TP53* c.844C>T; p.R282W (33%) *PIK3CA* c.2176G>A; p.E726K (36%) *MYCN* c.793G>A; p.D265N (21%) *CDKN2A* Homozygous Deletion
2	No mutations found	*TP53* c.734G>A; p.G245D (4%) *TP53* c.638G>A; p.R213Q (3%)	*TP53* c.734G>A; p.G245D (39%) *CDKN2A* Homozygous Deletion
3	No mutations found	*TP53* c.380C>A; p.H193R (3%) *TP53* c.559G>A; p.R248Q (3%)	*TP53* c.380C>A; p.H193R (10%) *TP53* c.559G>A; p.R248Q (8%) *CDKN2A* splice c.151-1G>A (8%)
4	No mutations found	*TP53* c.637C>T; p.R213* (4%)	*TP53* c.637C>T; p.R213* (14%)
5	No mutations found	*TP53* c.380C>A; p.S127Y (3%)	*TP53* c.380C>A; p.S127Y (10%) *TP53* c.559G>A; p.G187S (3%)
6	No mutations found	*TP53* c.638G>A; p.R213Q (6%)	Not applicable
7	No mutations found	*TP53* c.524G>A; p.R175H (3%)	Not applicable
8	No mutations found	*TP53* c.328C>T; p.R110C (3%) *TP53* c.797G>A; p.G266E (3%)	Not applicable
9	No mutations found	*TP53* c.641A>G; p.H214R (6%)	Not applicable
10	No mutations found	*TP53* c.328C>T; p.R110C (3%)	Not applicable
11	No mutations found	*EGFR* c.865G>A; p.A289T (46%)	Not applicable
12	No mutations found	*EGFR* c.865G>A; p.A289T (48%) *HRAS* c.34G>A; p.G12S (33%) *PIK3CA* c.1633G>A; p.E545K (8%) *TERT* −124C>T (48%)	Not applicable
13	No mutations found	No mutations found	Not applicable
14	No mutations found	No mutations found	Not applicable
15	No mutations found	No mutations found	Not applicable
16	No mutations found	No mutations found	Not applicable
17	No mutations found	No mutations found	Not applicable
18	No mutations found	No mutations found	Not applicable

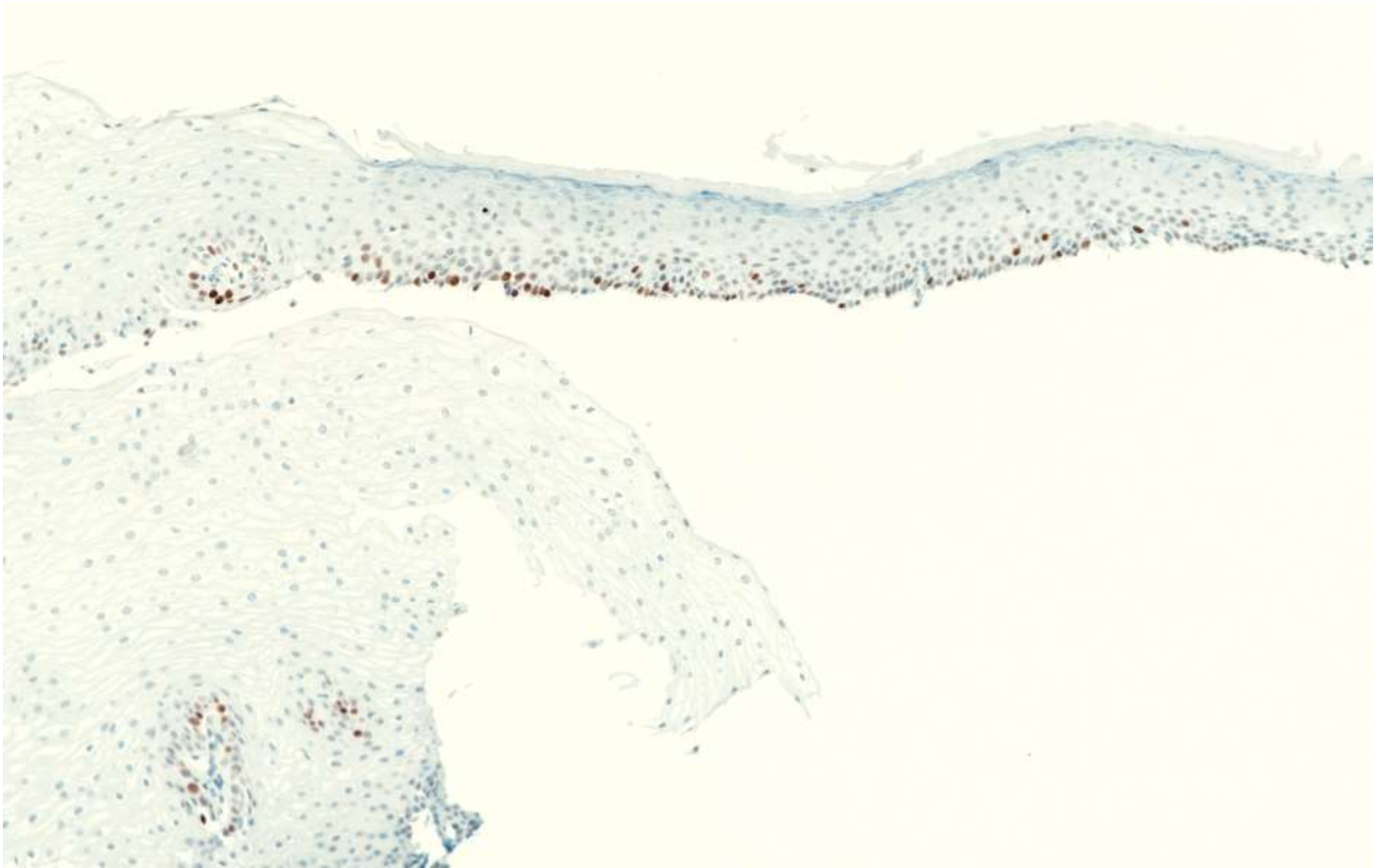
p53



Another case of EEM (without atypia)



Wildtype p53



Esophageal epidermoid metaplasia

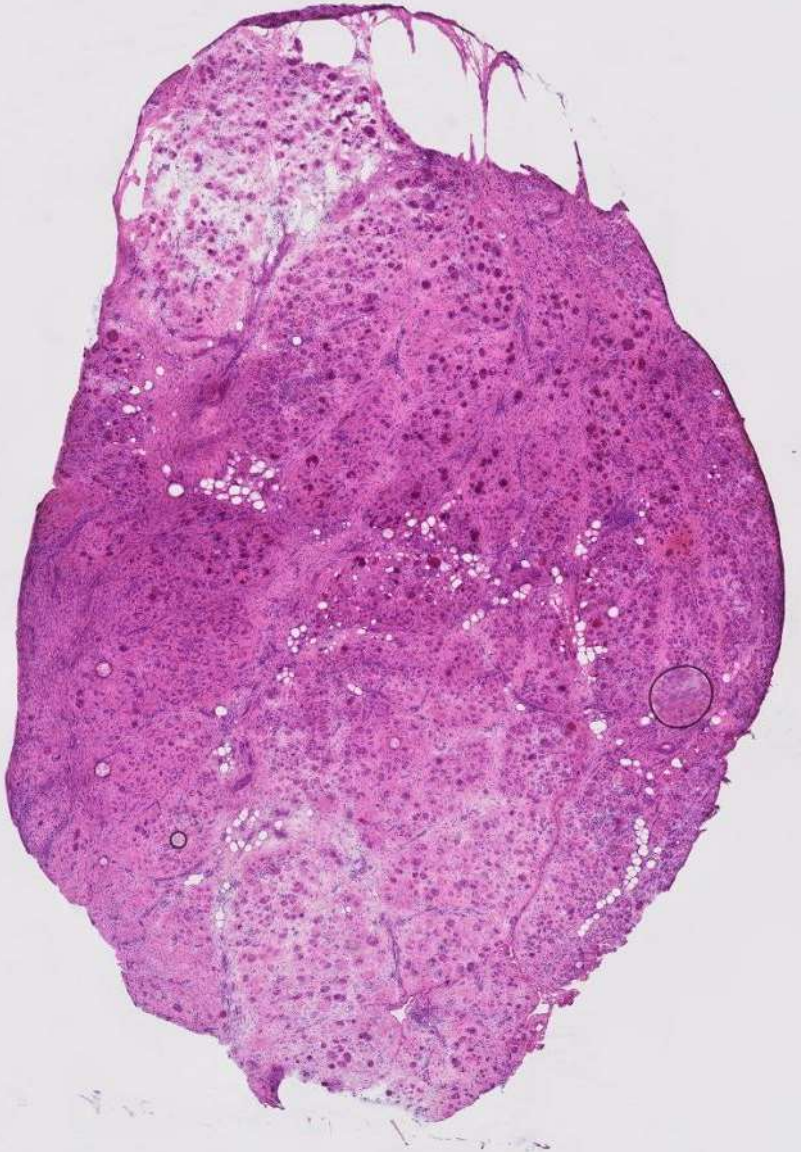
Take-home points:

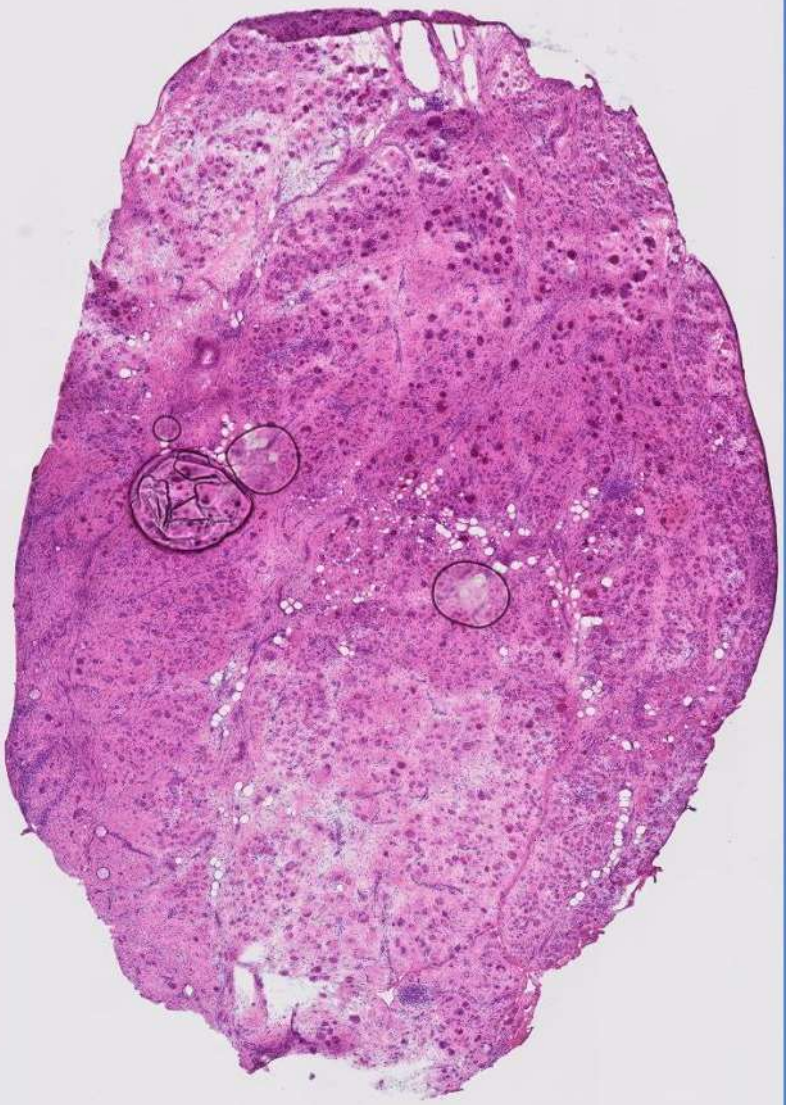
- Even without atypia, this lesion shows increased risk for squamous neoplasia
- *TP53* mutations may be an early biomarker for high-grade dysplasia or carcinoma in epidermoid metaplasia
- Needs increased surveillance/close follow up, ?additional sampling

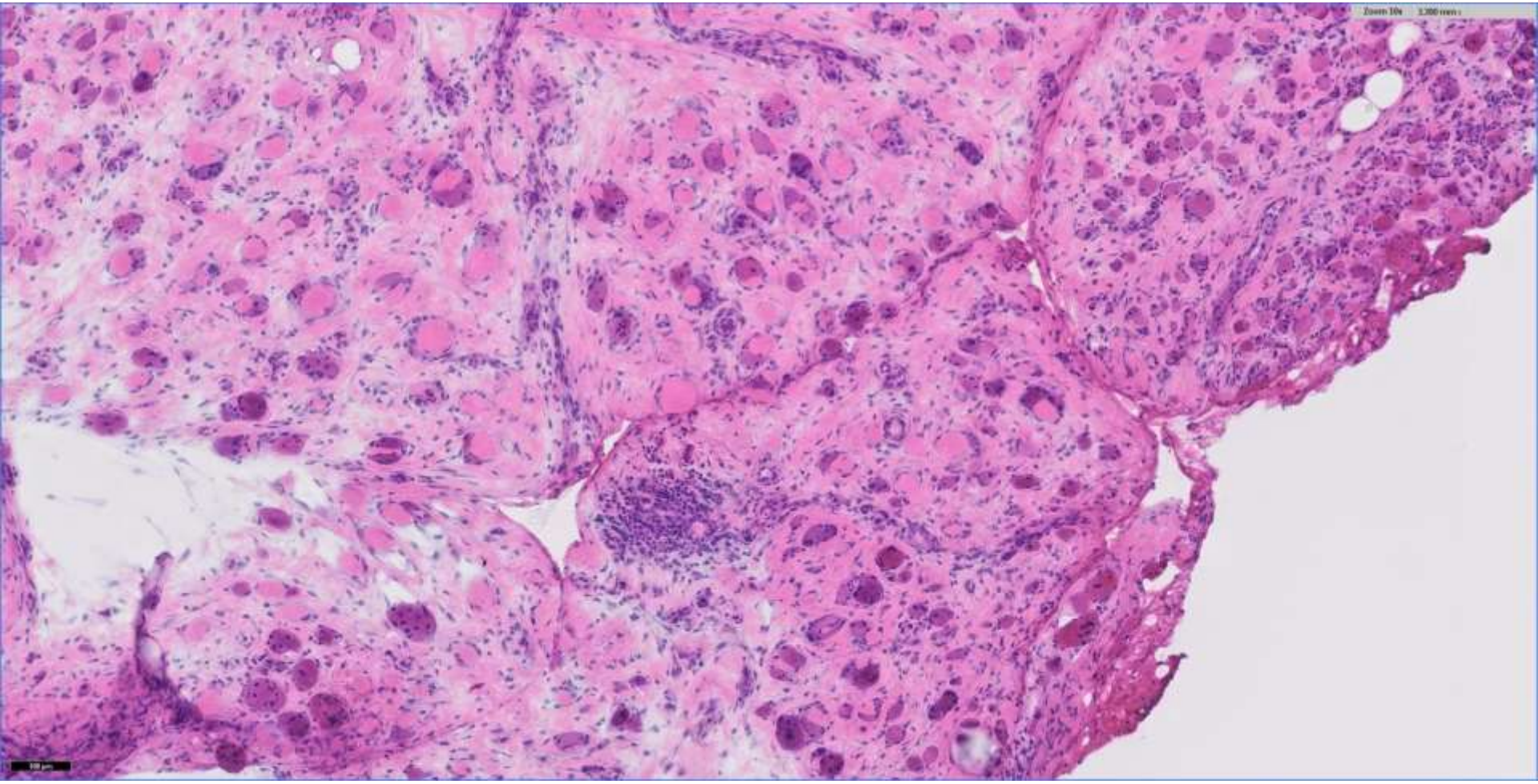
19-1010

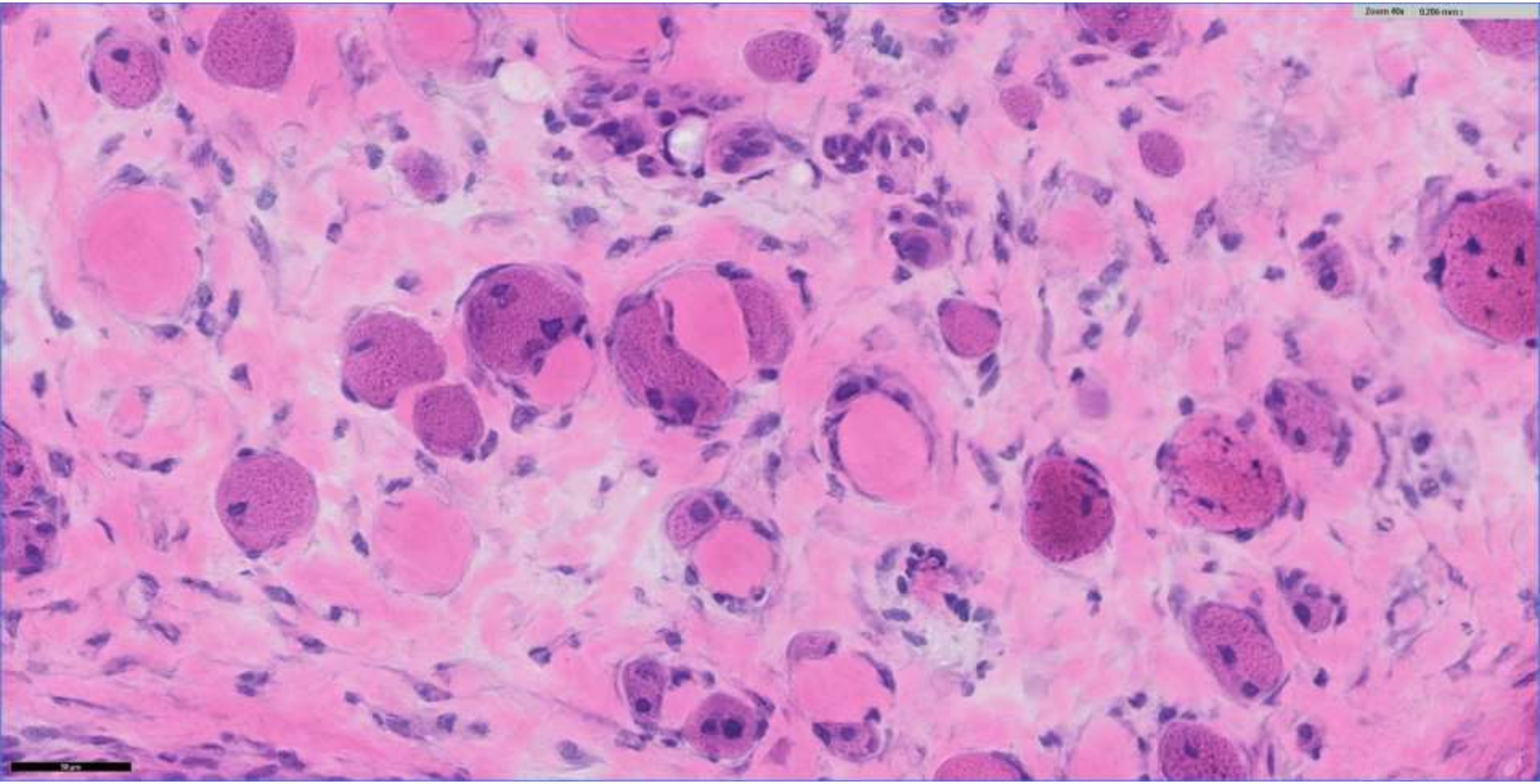
Hannes Vogel; Stanford

44-year-old female with poorly-controlled diabetes, hypothyroidism, and end-stage renal disease who presents with severe right thigh pain.





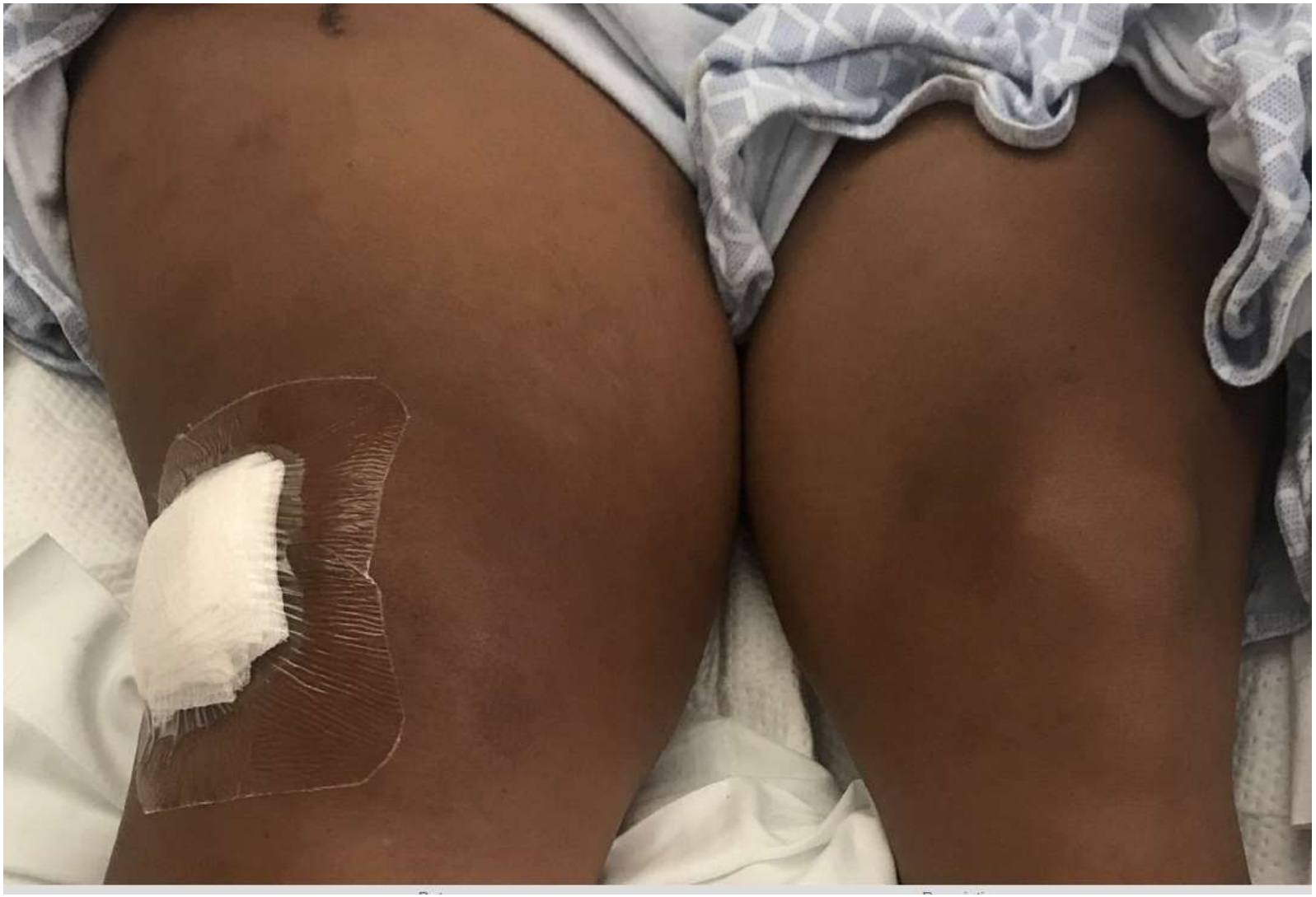




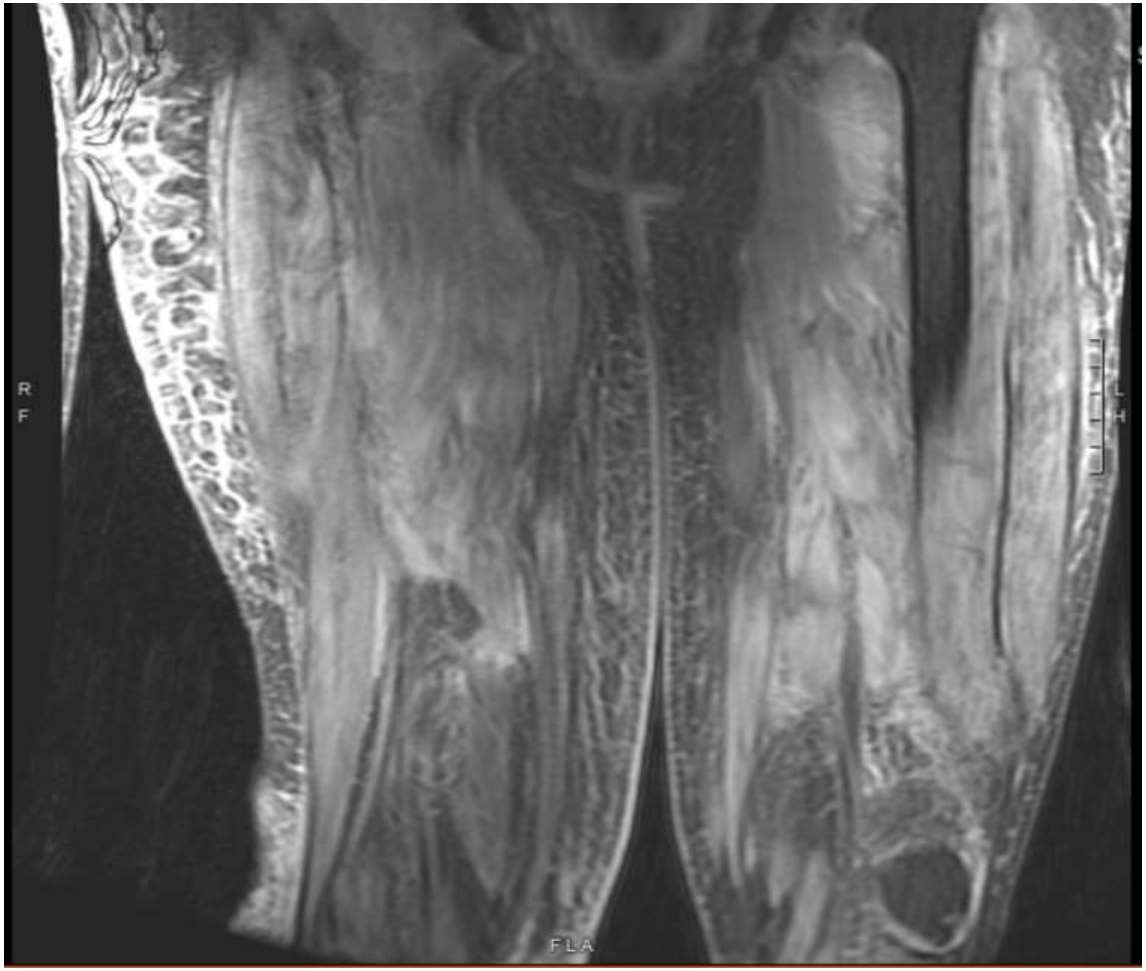
Clinical summary: 44 Y female with history of a history of hypothyroidsm, Type II DM and ESRD on dialysis who presents with right thigh muscle pain and swelling, rash, hand swelling, fevers, and lymphadenopathy.

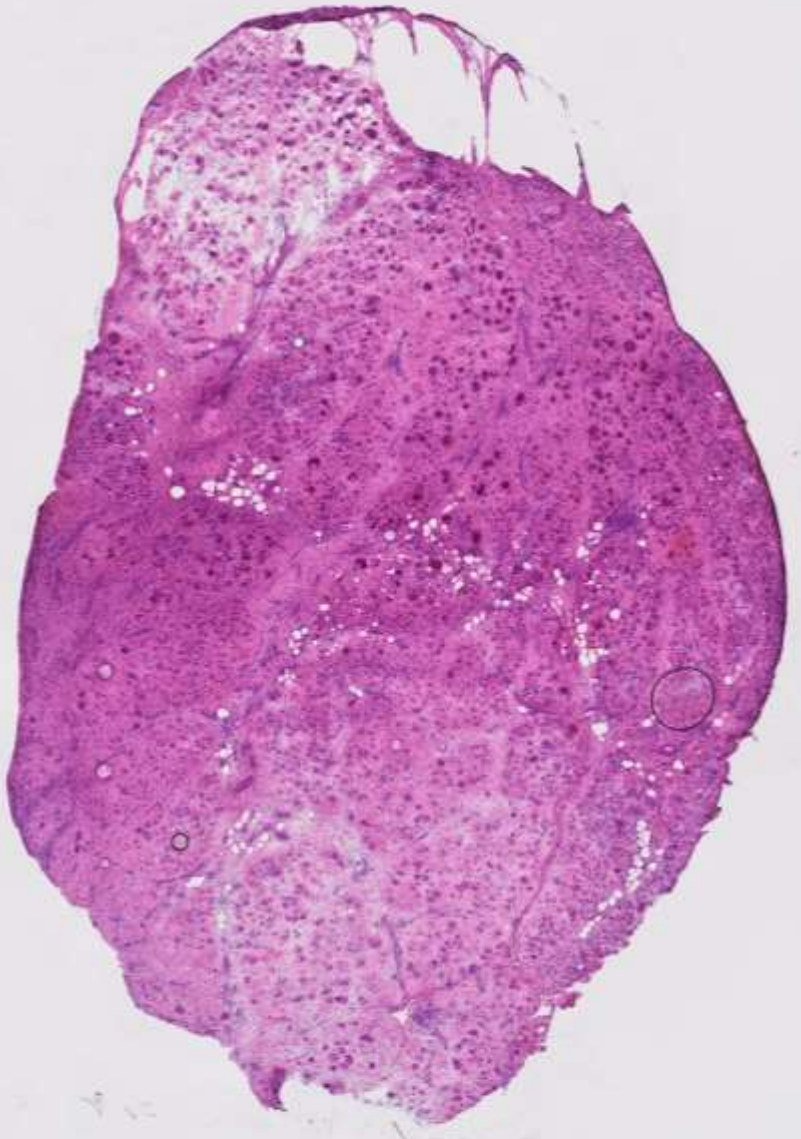
Had recent episode of left thigh pain and swelling which resolved on antibiotics.

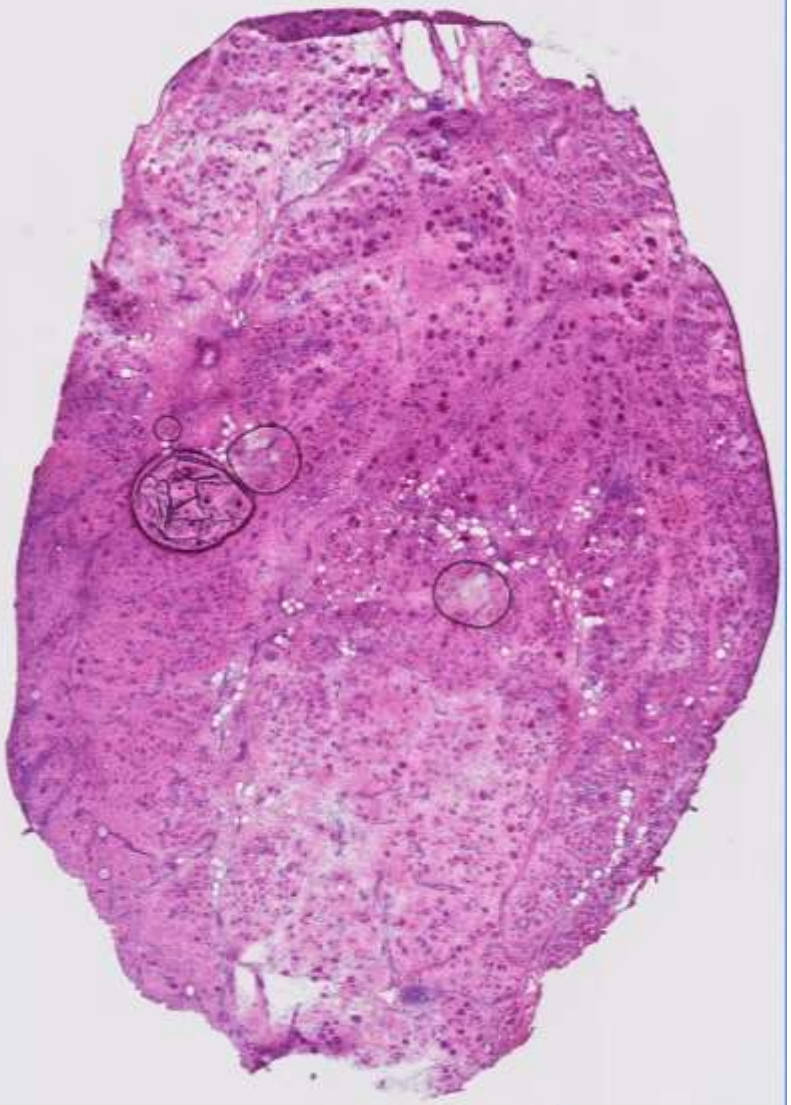
Right thigh muscle biopsy

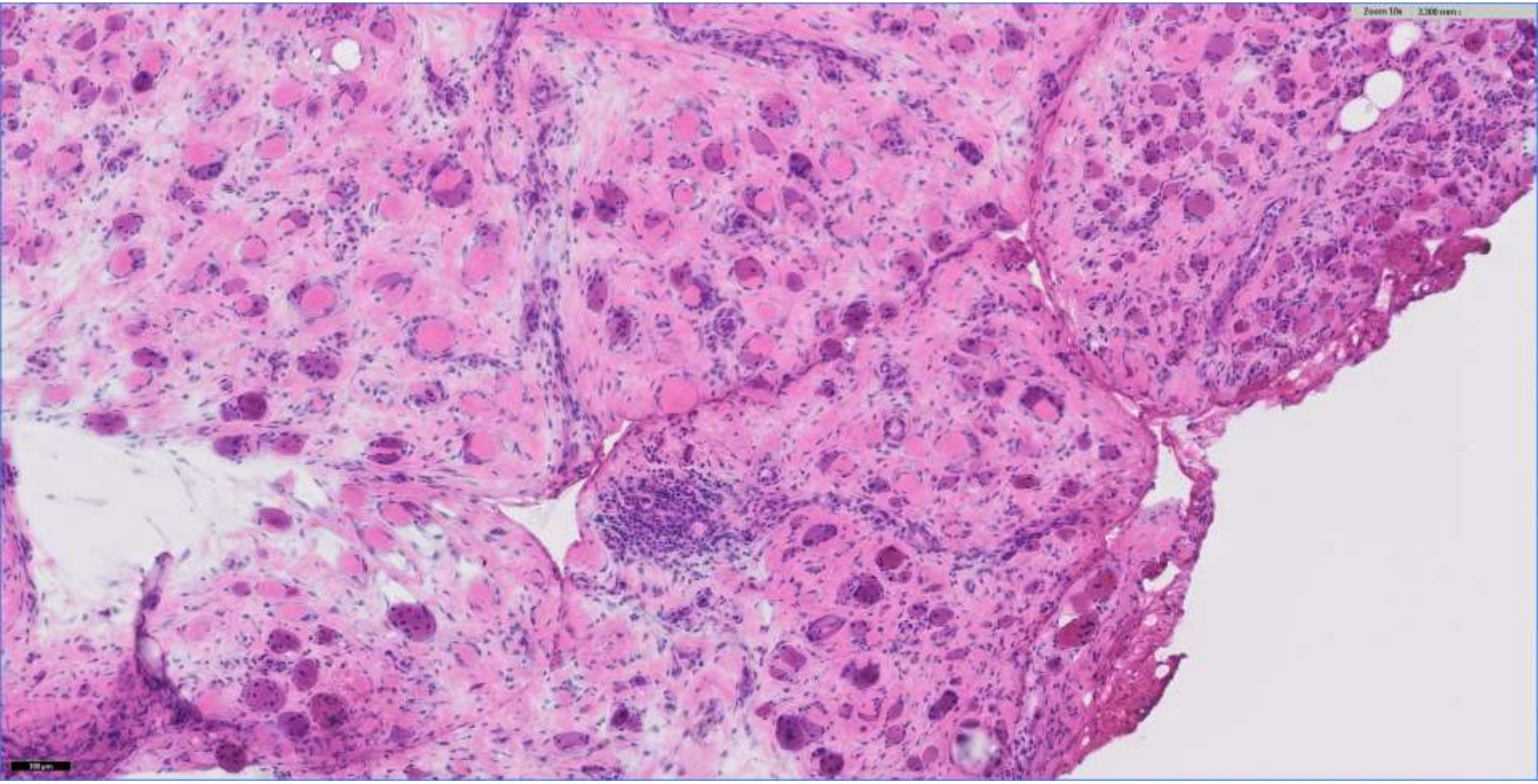


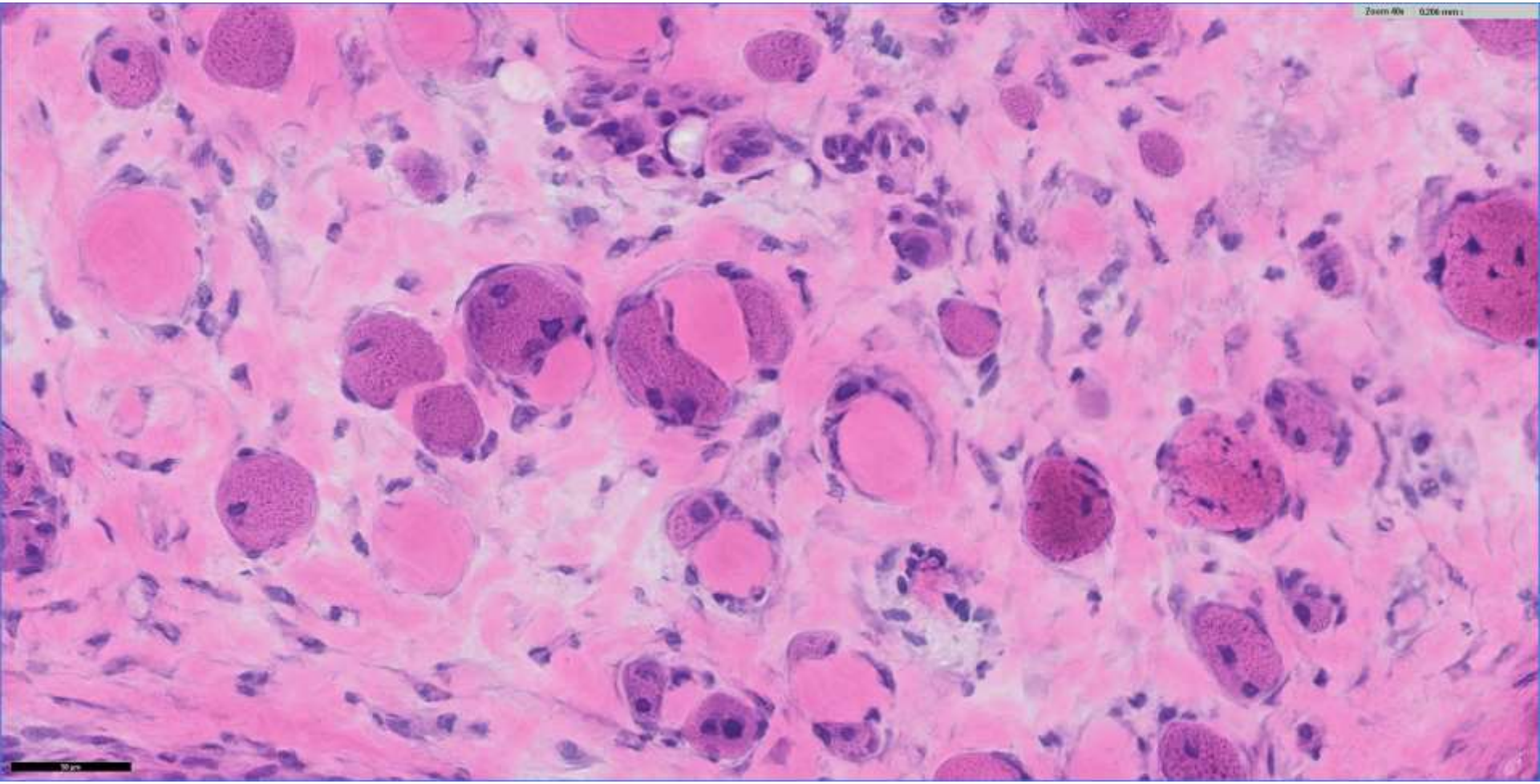
MRI thighs







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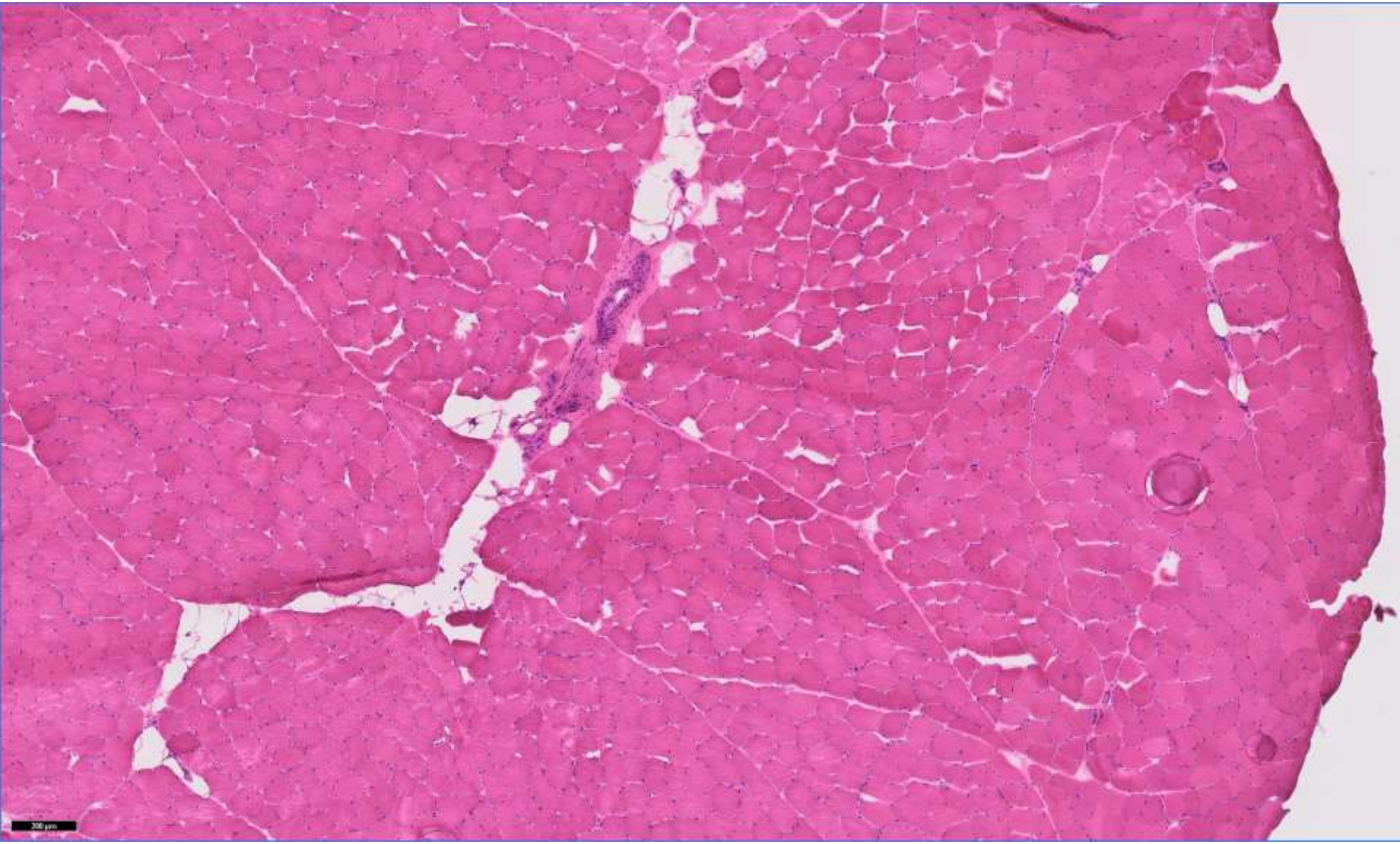
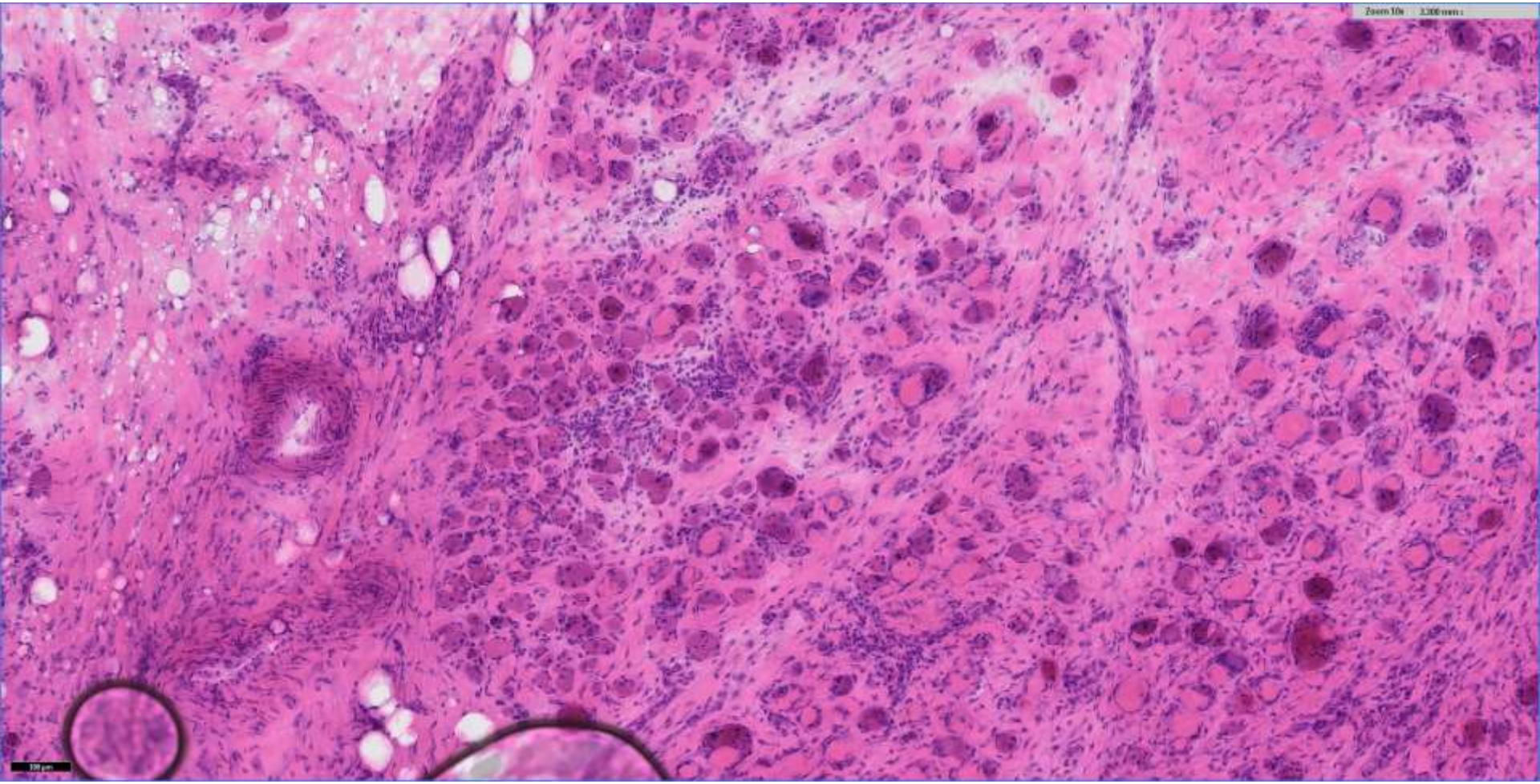
0,206 mm
50 µm

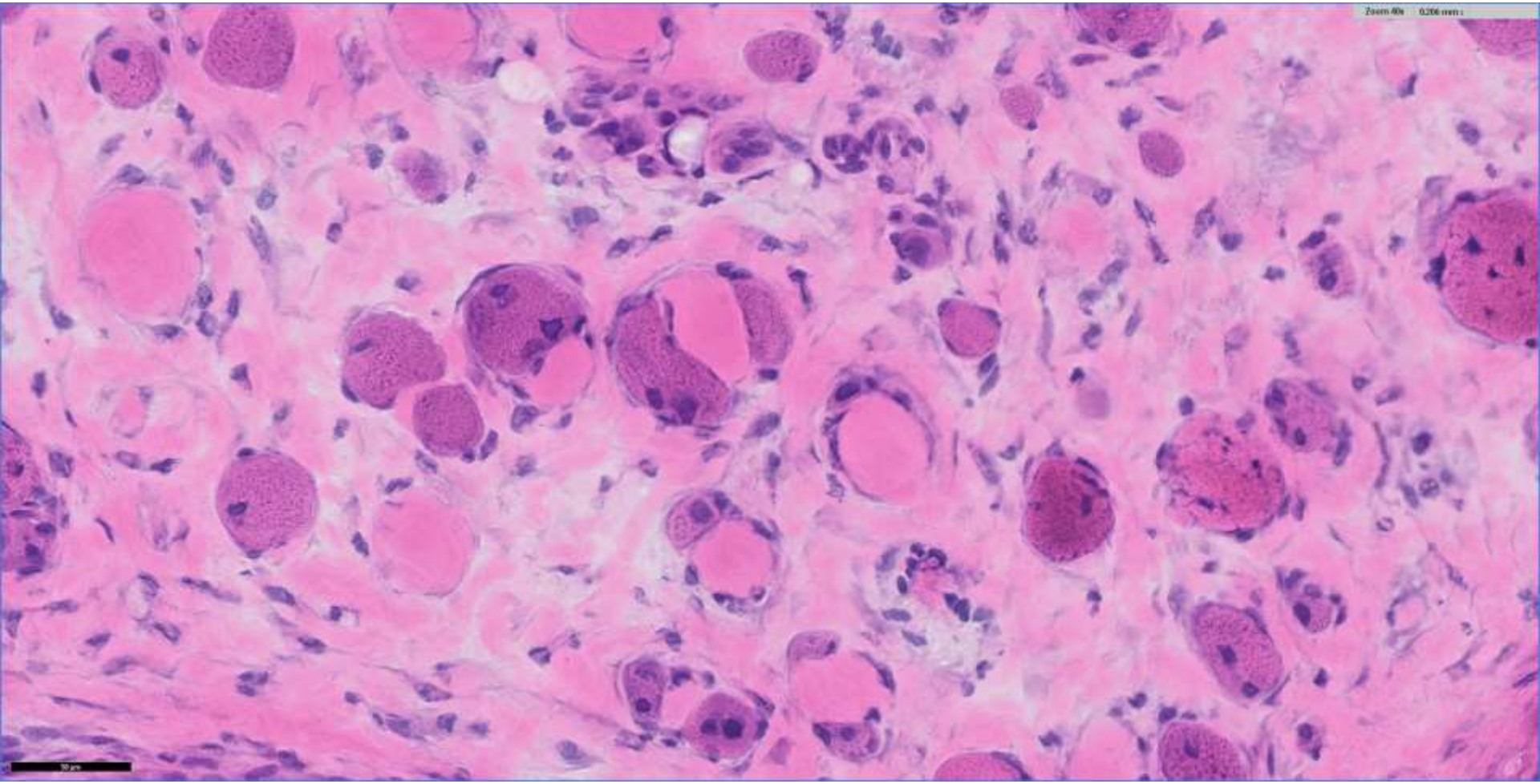
Normal Muscle for Reference



Myofiber necrosis in muscle pathology

- Roughly parallels serum CK elevation
- Nonspecific: Denervated muscle undergoing excessive work vs. primary myopathy
- "Monophasic": think recent episode of rhabdomyolysis
- Scattered, in different stages, without inflammation: think toxic, some autoimmune necrotizing myopathies
- Scattered, in different stages, with inflammation: think inflammatory myopathies (dermatomyositis, "polymyositis")
- With dystrophic features (increased connective tissue, fatty infiltration, marked variation in fiber sizes): think muscular dystrophies

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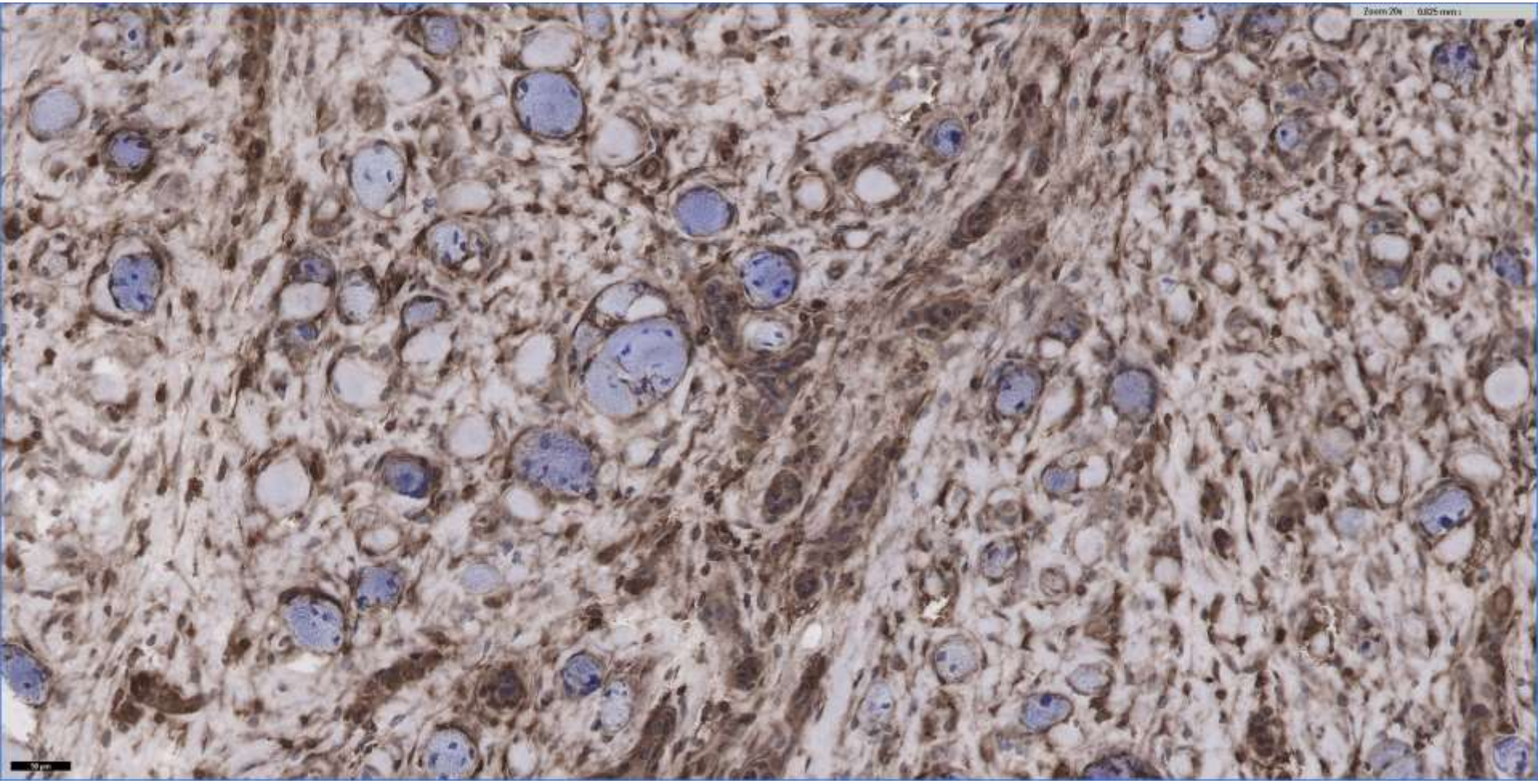
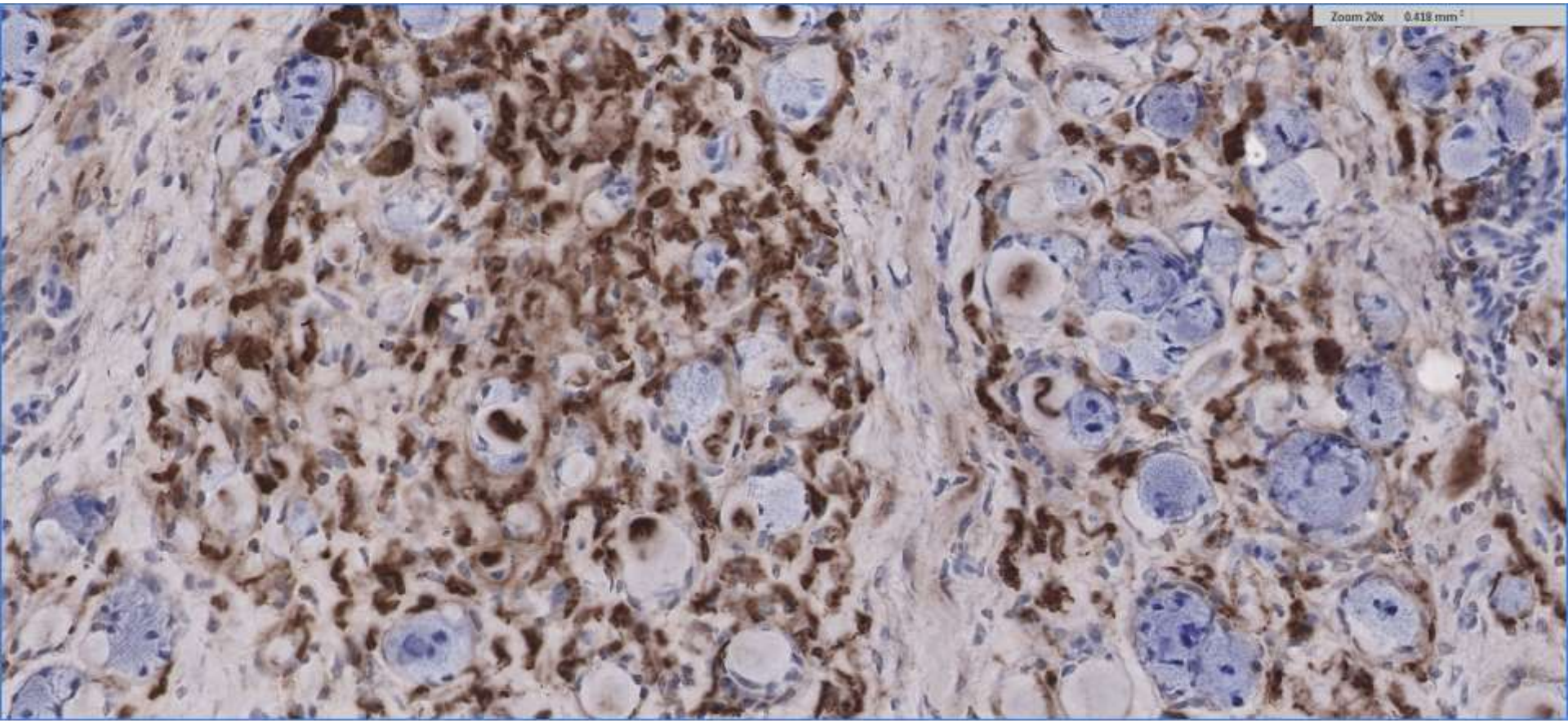
50 µm

MHC-I



MAC (membrane attack complex C5b-9)



DIAGNOSIS:

-MYOPATHIC PROCESS, FAVOR POST ISCHEMIC CHANGES

References:

1: Ganokroj P, Boonchaya-Anant P. Diabetic muscle infarction: rare complication with a distinct clinical manifestation. BMJ Case Rep. 2019 23;12

2: Trujillo-Santos AJ. Diabetic muscle infarction: an underdiagnosed complication of long-standing diabetes. Diabetes Care. 2003; 26:211-5.

Diabetic Muscle Infarction

An underdiagnosed complication of long-standing diabetes

A. J. Trujillo-Santos, MD

OBJECTIVE — To systematically review all the reported cases of diabetic muscle infarction (DMI) and its pathogenesis, clinical features, prognostic implications, and management.

RESEARCH DESIGN AND METHODS — We searched databases (MEDLINE and EMBASE) from their inception to August 2001 and reviewed bibliographies in reports retrieved. Data were extracted in a standardized form.

RESULTS — A total of 47 references were retrieved; 115 patients and 166 episodes were included. DMI was more frequent in women (61.5%, mean age at presentation 42.6 years). Of the cases, 59% had type 1 diabetes; the mean duration of disease was 14.3 years, and multiple diabetic end-organ complications were noted. DMI affects the lower limbs with abrupt onset of pain and local swelling. Diagnosis is made by biopsy, but the characteristic features in magnetic resonance imaging are very typical. Treatment includes bed rest and administration of analgesics, but recurrence is common.

CONCLUSIONS — DMI is a very uncommon complication of long-standing diabetes; presentation is well characterized and management is simple.

Diabetes Care 26:211–215, 2003

Diabetic Muscle Infarction

Two Cases: One With Recurrent and Bilateral Lesions and One With Usual Unilateral Involvement

Jorge A. Arroyave, MD, Dahyana Cadavid Aljure, MD,* Carlos A. Cañas, MD,† Juan D. Vélez, MD,‡ and Fabio Bonilla Abadía, MD†*

Abstract: Diabetic muscle infarction is a rare complication of diabetes. We describe 2 cases of diabetic muscle infarction, each one of them with a particular form of clinical presentation: recurrence, bilateral engagement, and unilateral compromise. Both cases had history of poorly controlled diabetes mellitus and diabetic nephropathy. The diagnosis was based on clinical, imaging, and anatomopathological features. The treatment was with a close control of diabetes mellitus, analgesics, short-term immobilization, and physical therapy.

Key Words: diabetes complication, diabetic muscle infarction, ischemic myonecrosis, aseptic myonecrosis

(*J Clin Rheumatol* 2013;19: 126–128)

"In a systematic review, the diagnosis of diabetic muscle infarct was confirmed by biopsy in 57% of patients, but because of the potential complications of excisional and incisional biopsy, it should be reserved for cases in which the clinical presentation is atypical, the diagnosis is not clear, or when appropriate treatment fails."

CASE REPORT

Diabetic muscle infarction: rare complication with a distinct clinical manifestation

Poranee Ganokroj,[1,2] Patchaya Boonchaya-anant[2,3]

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[2]Division of Endocrinology and Metabolism, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand
[3]Excellence Center for Diabetes, Hormones and Metabolism, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand

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Accepted 9 April 2019

SUMMARY

Diabetic muscle infarction is an unusual condition with distinctive clinical characteristics seen in patients with prolonged and uncontrolled diabetes. Clinical findings and imaging study are unique and challenging. Patients usually present with acute unilateral severe muscular pain and swelling, particularly in the lower extremities. The presentation is difficult to distinguish from other common conditions such as deep venous thrombosis and infectious myositis. However, early recognition of the clinical presentation and appropriate imaging selection can lead to the diagnosis and avoid unnecessary muscle biopsy. Here, we report a case of diabetic muscle infarction in a patient with poorly controlled type 1 diabetes who had a good clinical response after an early detection and appropriate treatment.

BMJ Case Rep. 2019