# JAN 2020 DIAGNOSIS LIST

20-0101: clear cell sarcoma-like tumor of GI tract (small bowel/GI and soft tissue pathology)
20-0102: polyphenotypic round and spindle cell sarcoma with EWSR1-PATZ1 fusion (soft tissue/soft tissue pathology)
20-0103: lipogranuloma (c/w history of petroleum jelly injection) (penis/GU pathology)
20-0104: endometrioid adenocarcinoma (c/w arising from endometriosis) (bladder/GU pathology)
20-0105: placental site nodule (uterus/GYN pathology)
20-0106: sessile serrated polyp with dysplasia (large bowel/GI pathology)
20-0107: Glioblastoma H3 G34 mutation, WHO grade IV (brain/neuropathology)
20-0108: atypical renal cyst (kidney/GU pathology)
20-0109: low grade oncocytic papillary renal cell carcinoma (papillary renal neoplasm with reverse polarity/type IV papillary renal cell carcinoma) (kidney/GU pathology)
20-0110: low grade oncocytic tumor (kidney/GU pathology)

# Disclosures
# January 6, 2020

Dr. Ankur Sangoi has disclosed a financial relationship with Google (consultant). Dr. Keith Duncan has disclosed a financial relationship with Abbvie (consultant/contractor). South Bay Pathology Society has determined that these relationships are not relevant to the planning of the activity (Dr. Sangoi) or the clinical cases being presented.

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

**Presenters:**

Jeff Cloutier, MD, PhD
Greg Charville, MD, PhD
Romain Cayrol, MD
Hannes Vogel, MD
Emily Chan, MD
Marietya Lauw, MD
Constance Chen, MD
Jordan Taylor, MD
Charles Zaloudek, MD
Natalie Patel, MD

**Activity Planners/Moderator:**

Kristin Jensen, MD
Megan Troxell, MD, PhD

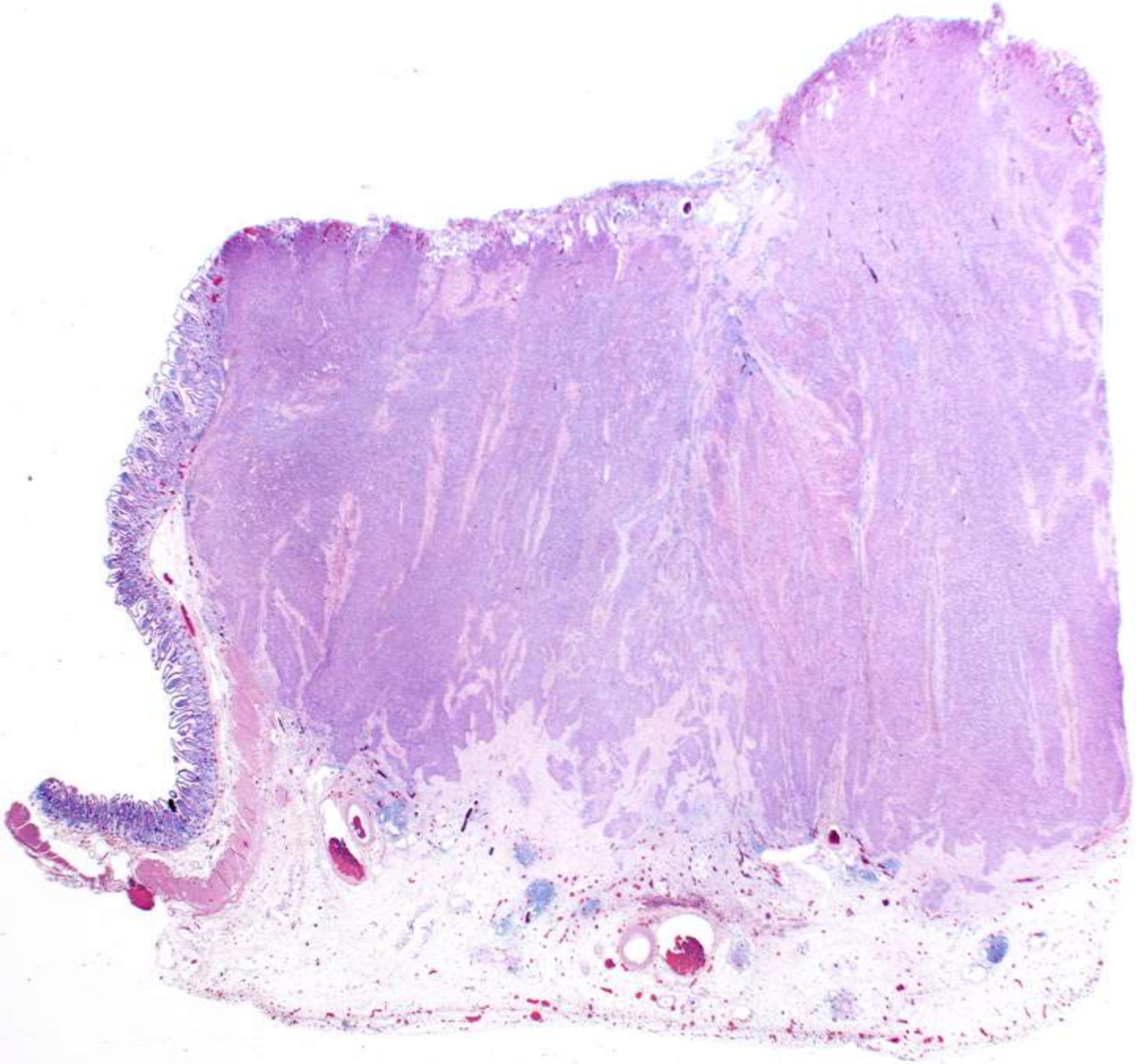
# 20-0101

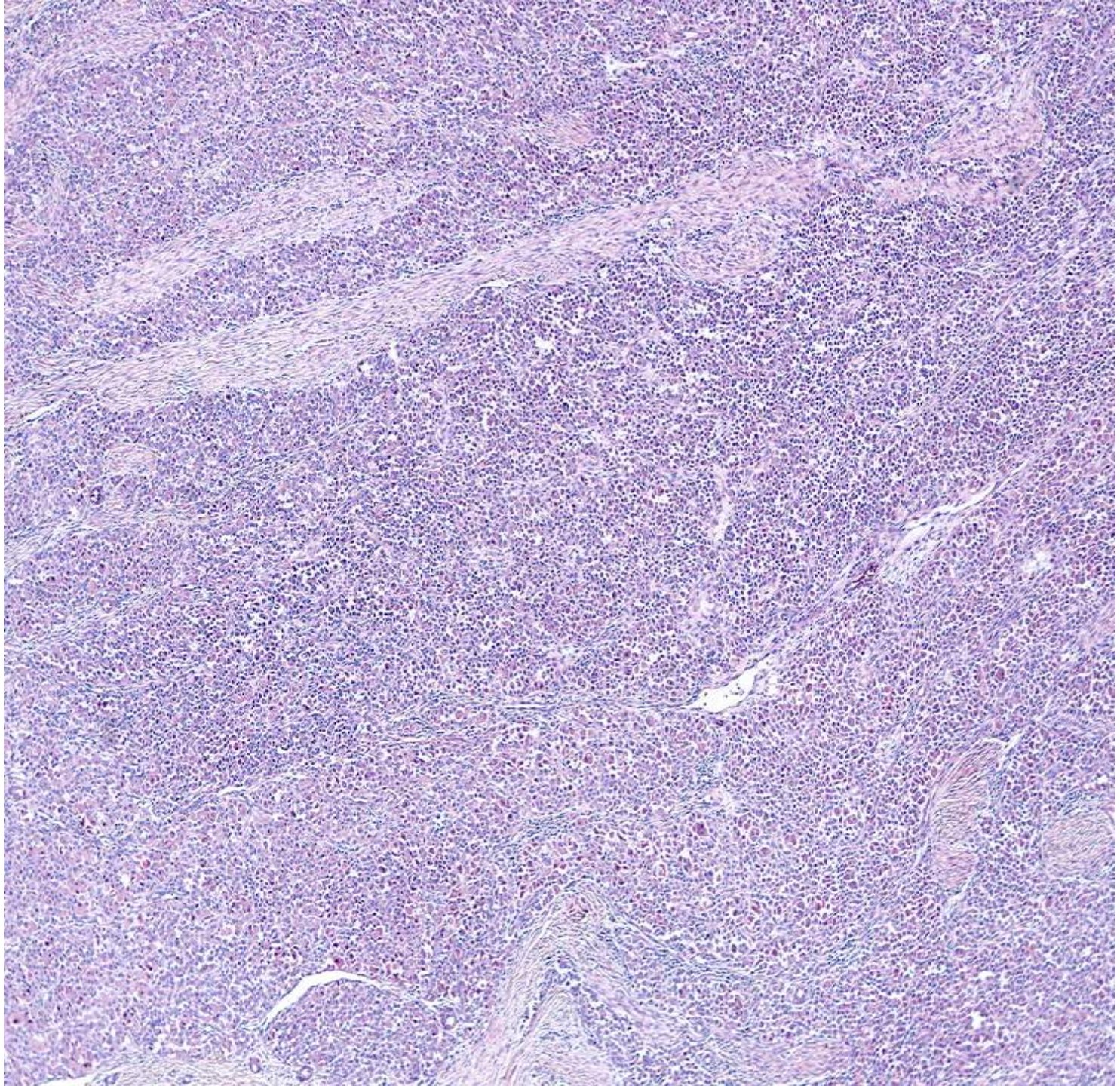
**Jeff Cloutier/Greg Charville; Stanford**

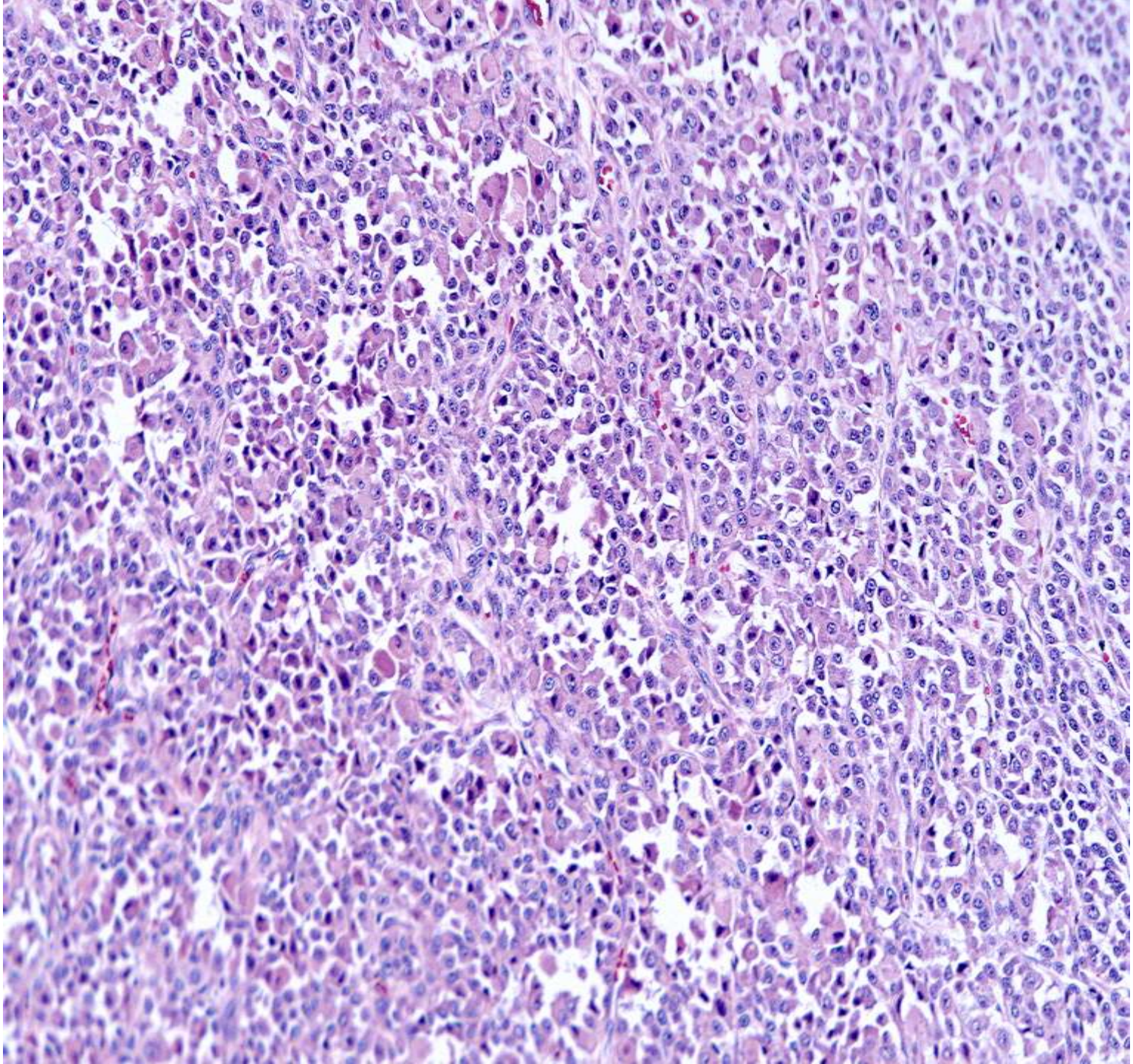
63-year-old F with h/o breast carcinoma and melanoma, presenting with 3.2cm small bowel mass.

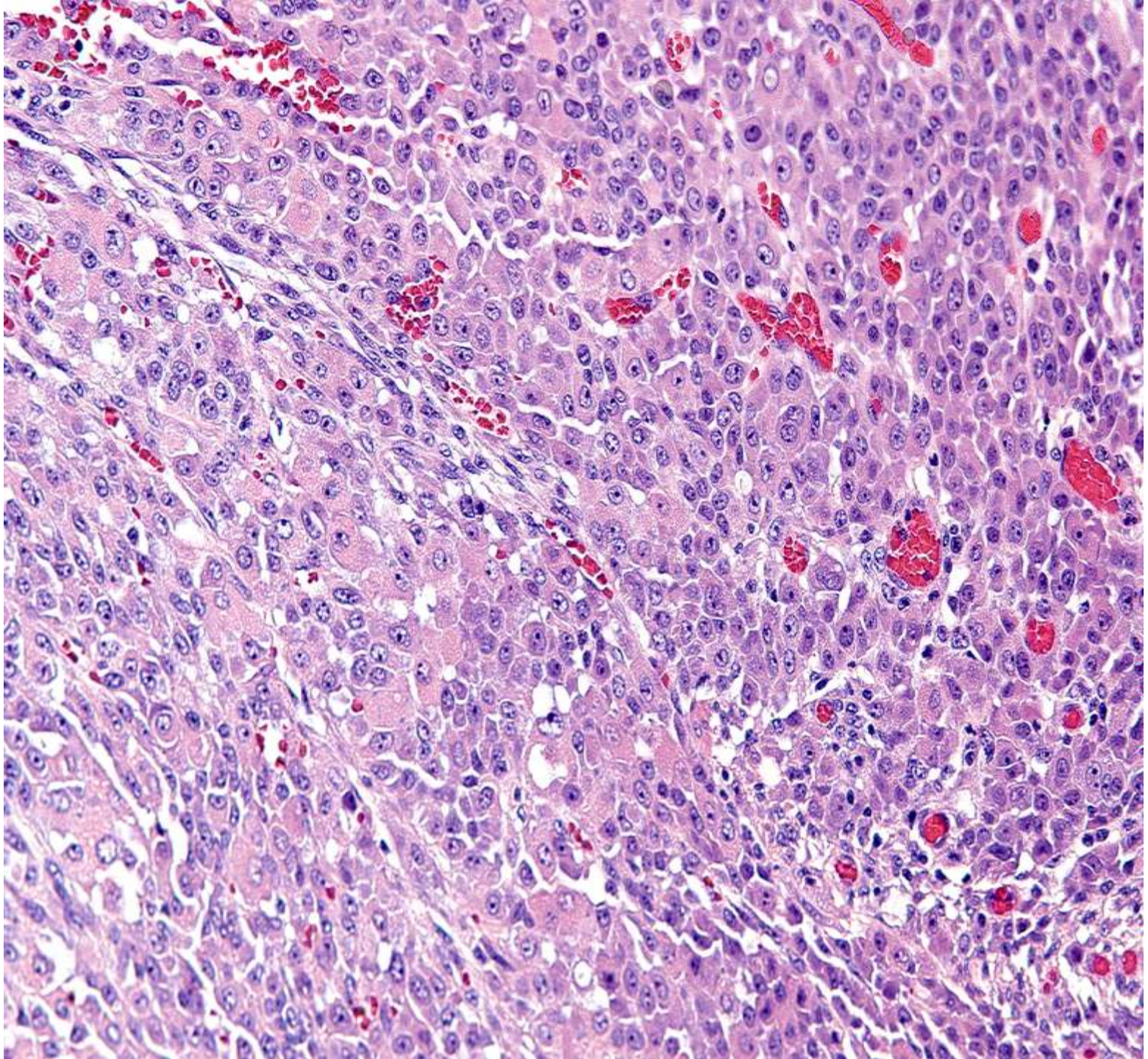
# 63yo F with history of breast carcinoma and melanoma, presenting with 3.2 cm small bowel mass (ileum).

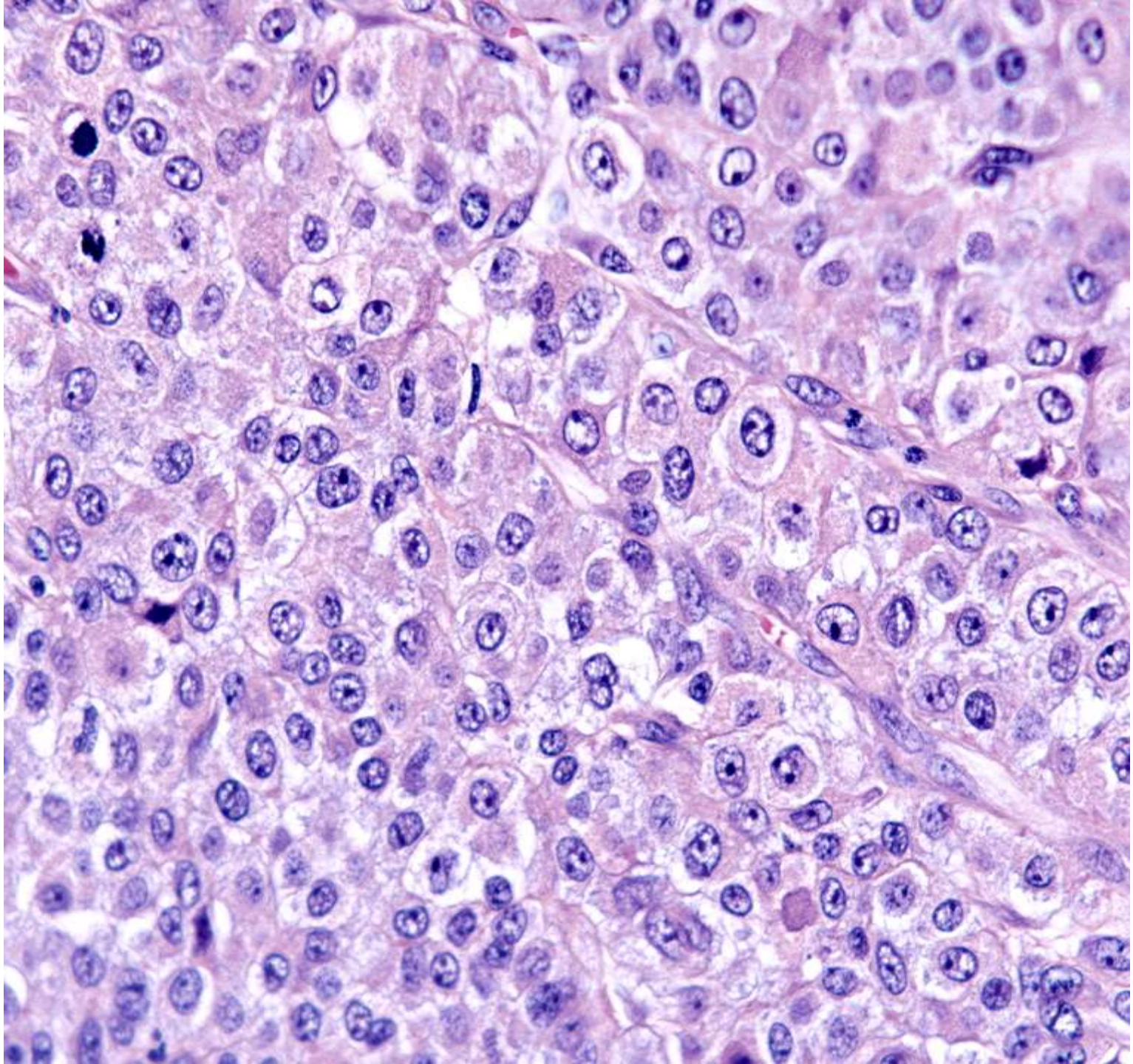
***Jeff Cloutier and Greg Charville***
***Stanford***



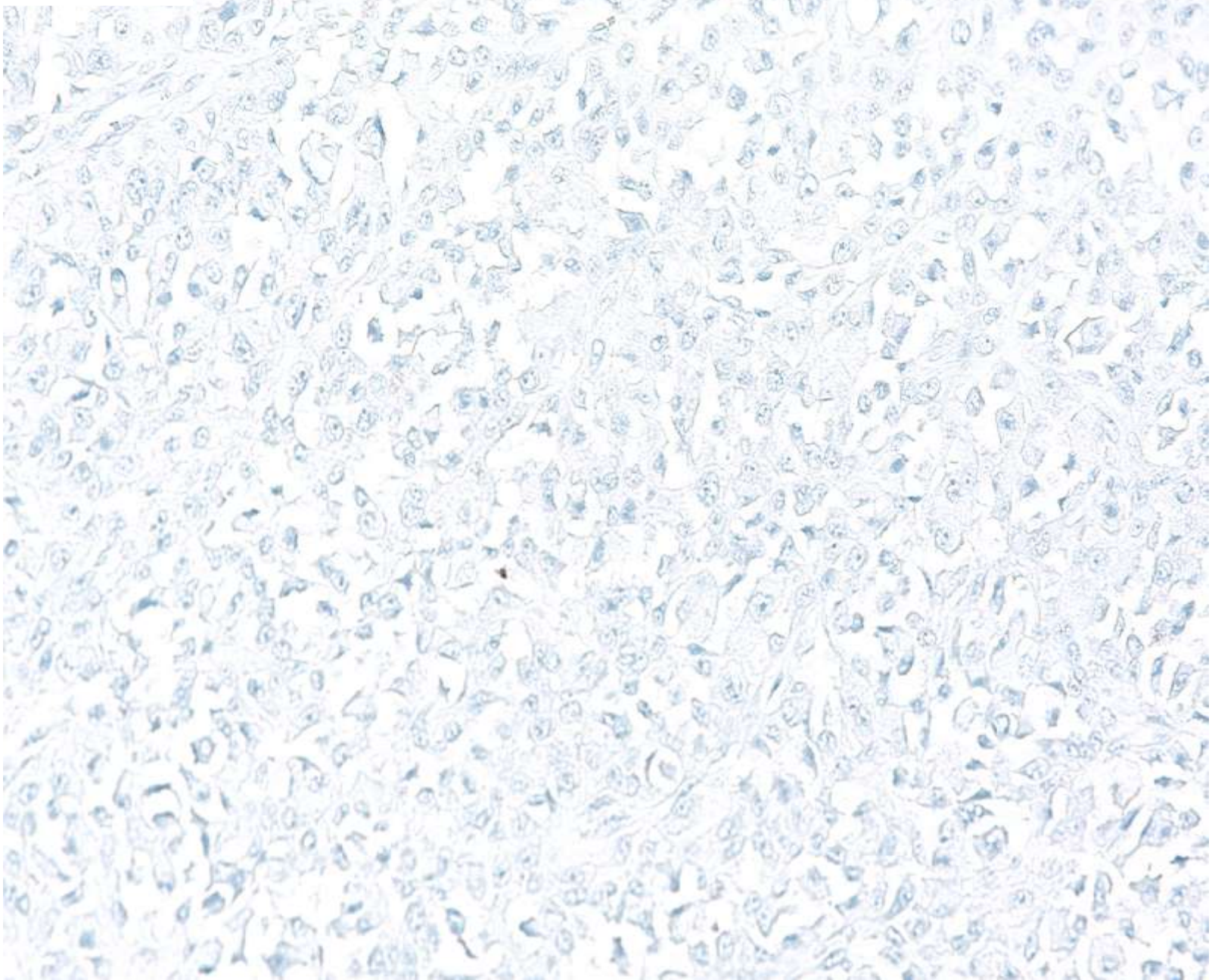




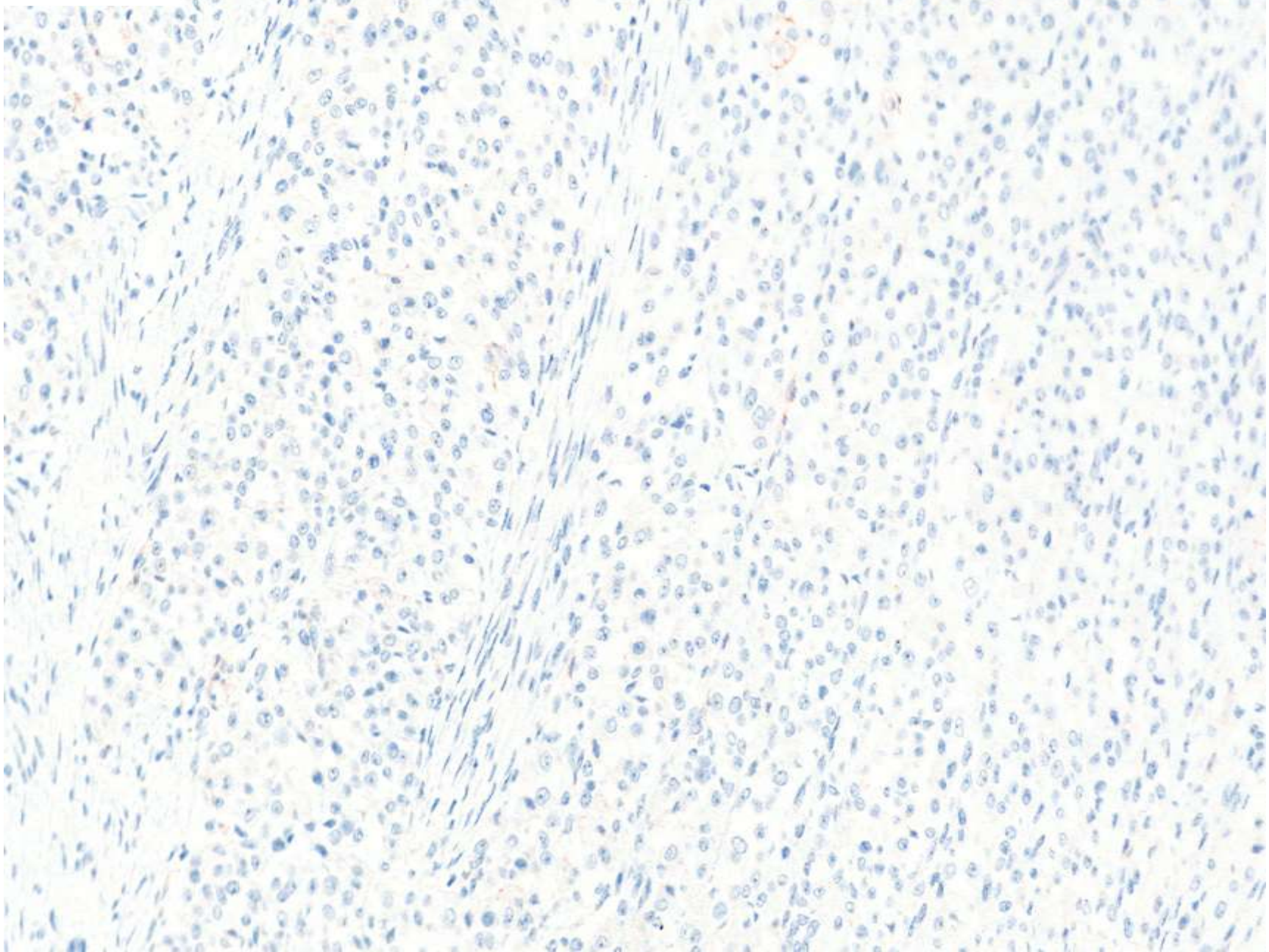




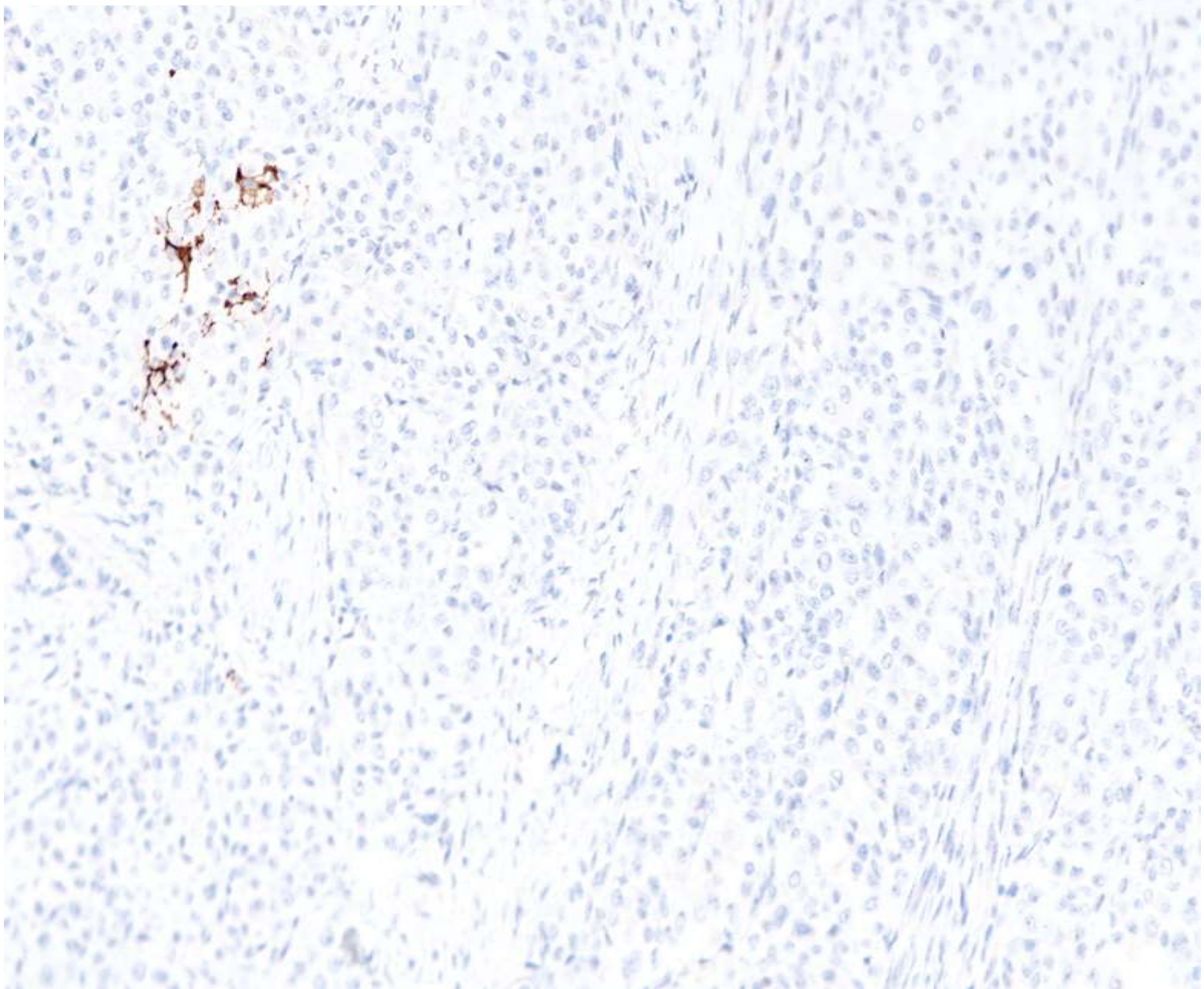
# CKMIX



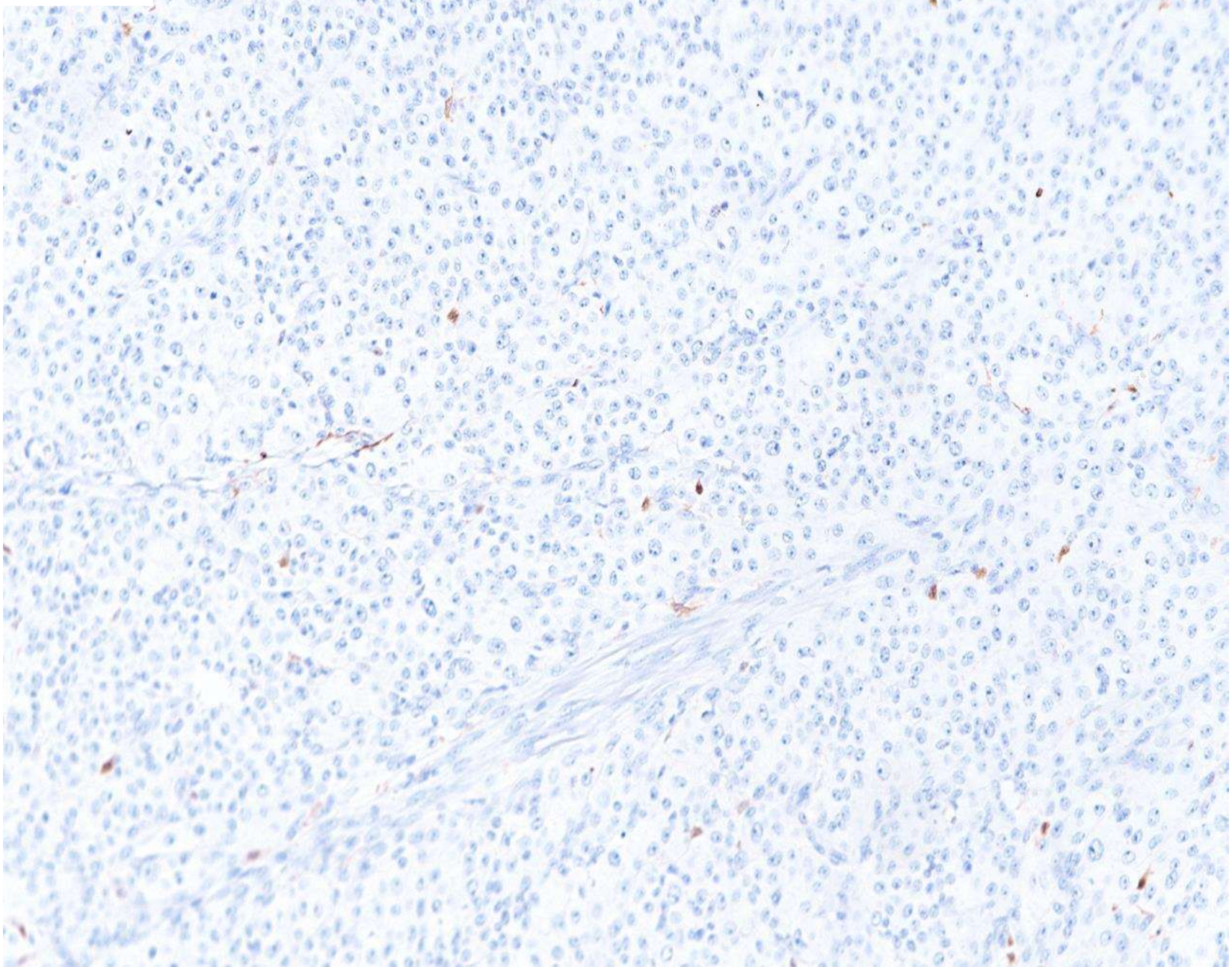
# DOG1



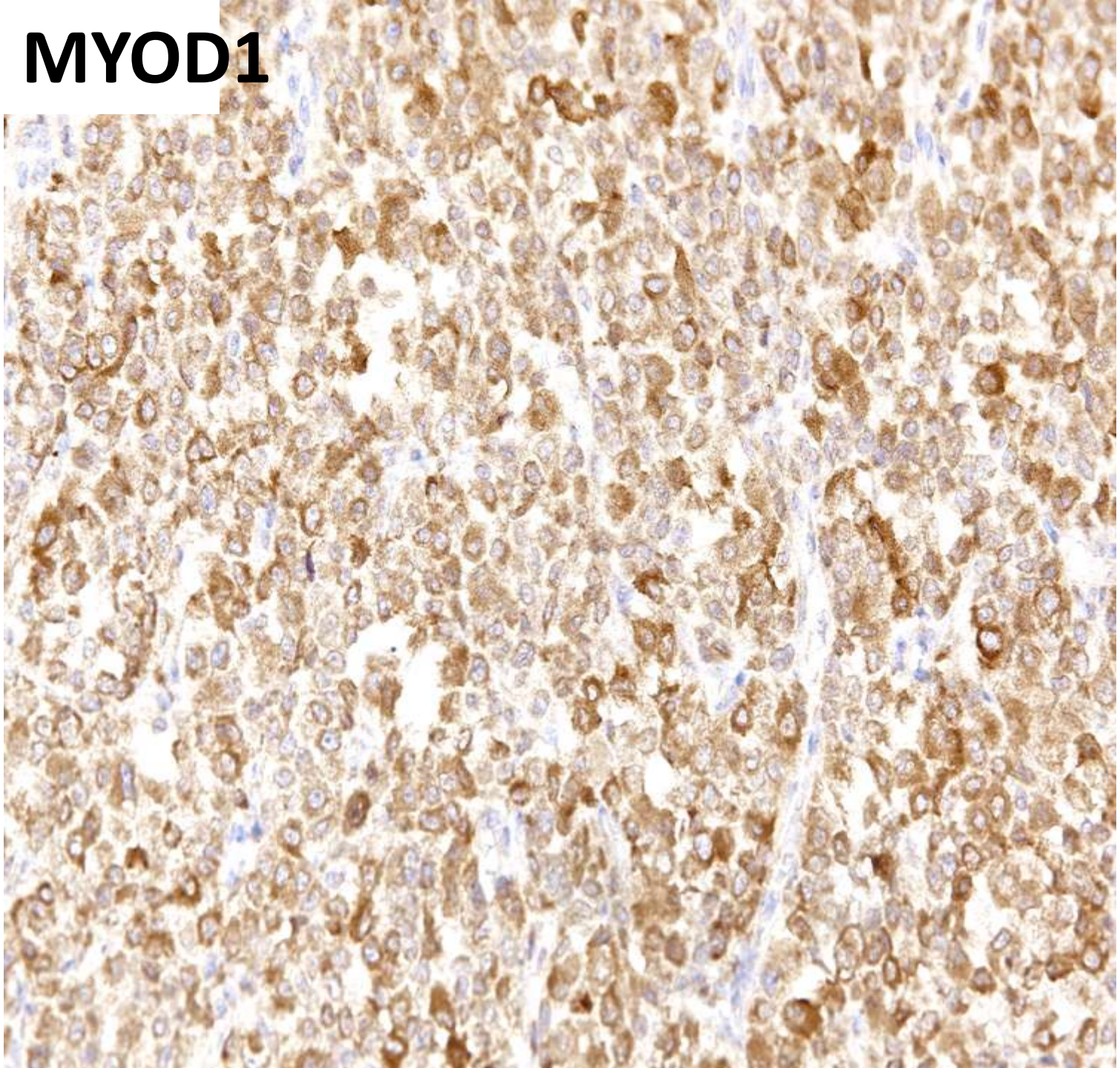
# SYNAPTOPHYSIN



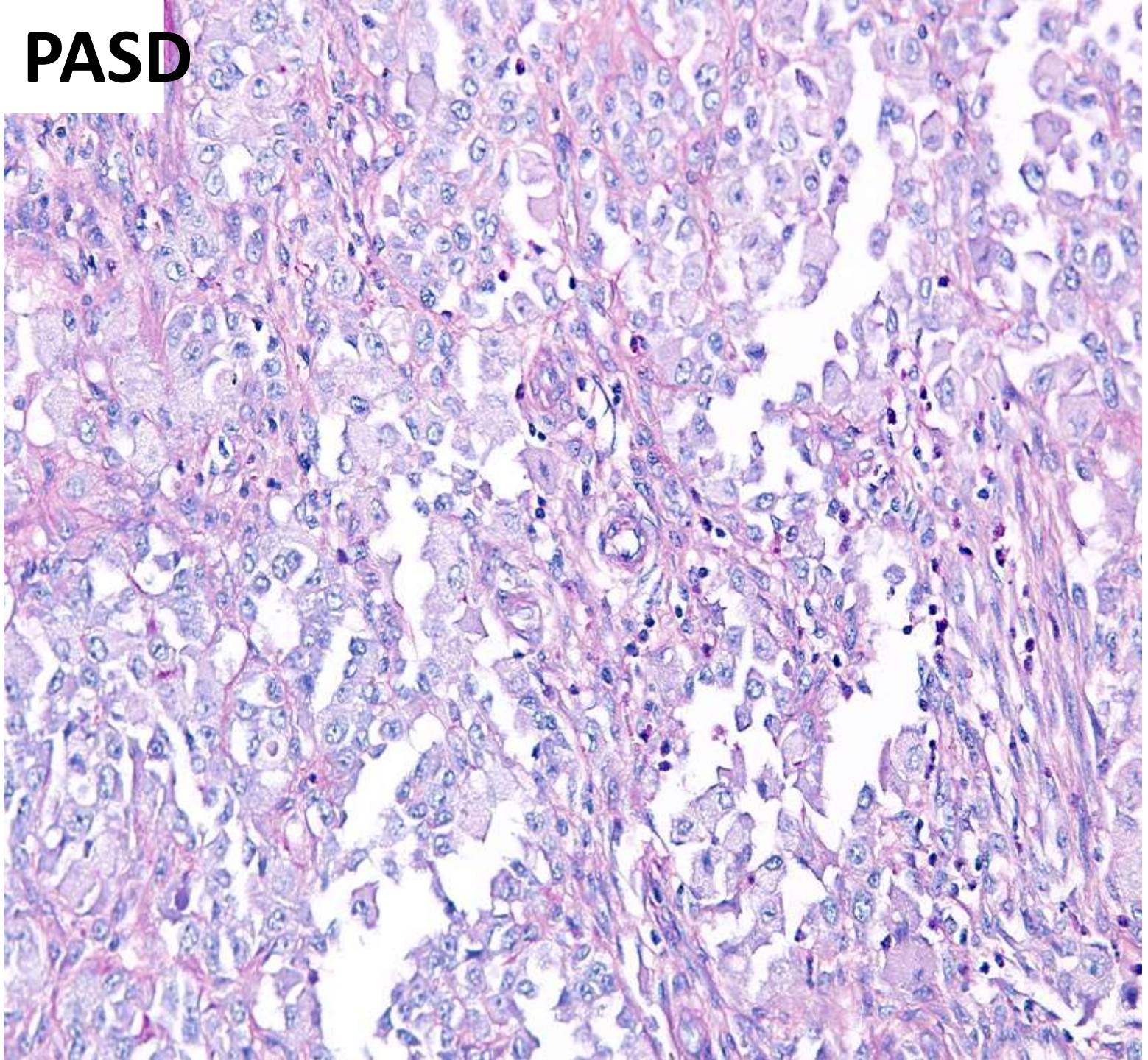
# S100



# MYOD1



# PASD



# Additional negative stains

HMB45

Desmin

CD30

CD45

# Additional diagnostic workup

- Negative immunohistochemical stains:
  - CK5/6, CK7, CK20, CAM5.2, EMA, CDX2, GATA3
  - Melan A
  - Myogenin
  - CD117
  - INSM1, chromogranin
  - CD163, CD68
  - INI1 (intact expression)

# Additional diagnostic workup

- TFE3 immunohistochemistry and FISH
  - *Negative*
  - Rules out alveolar soft part sarcoma

# Fusion-STAMP (Stanford Actionable Mutation Panel for Fusions)

- Targeted next generation sequencing panel to detect potentially actionable gene fusion events in cancer
- Captures mRNA transcript regions of interest of 43 genes
- Result:
  - Positive for ***EWSR1-ATF1*** **fusion**

# Tumors with *EWSR1-ATF1* fusion

- Conventional clear cell sarcoma of tendon sheath
- Clear cell sarcoma-like tumor of GI tract
- Angiomatoid fibrous histiocytoma
- Hyalinizing clear cell carcinoma of salivary gland

# Clear Cell Sarcoma-Like Tumor of GI Tract

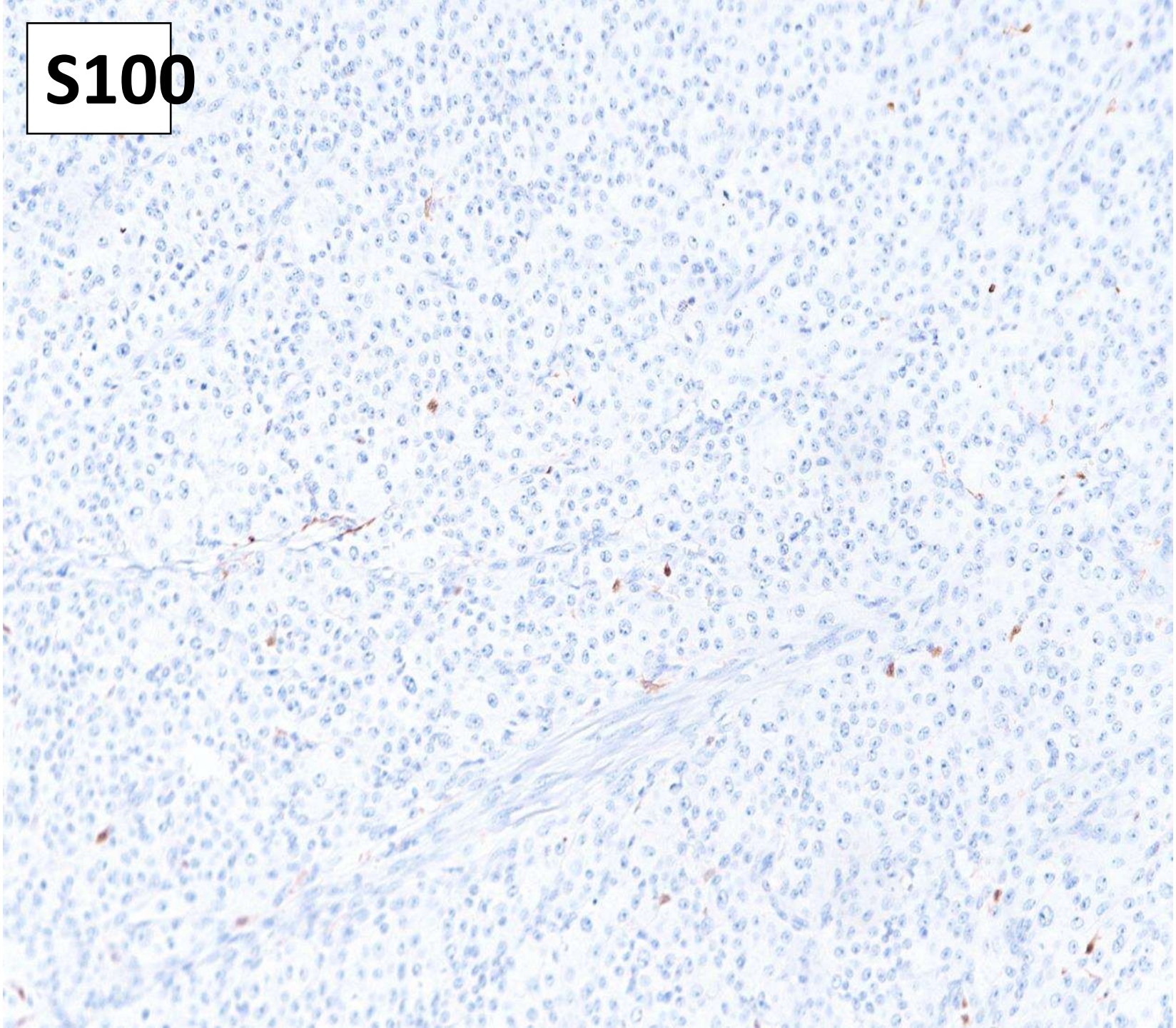
- High-grade sarcoma primary to the GI tract
- Uncommon tumor (<100 reported cases)
- Younger to middle-aged patients (range: 13-85 years)
- Ileum (70%) > stomach > colon > esophagus
- Poor prognosis (median survival – 10 months)

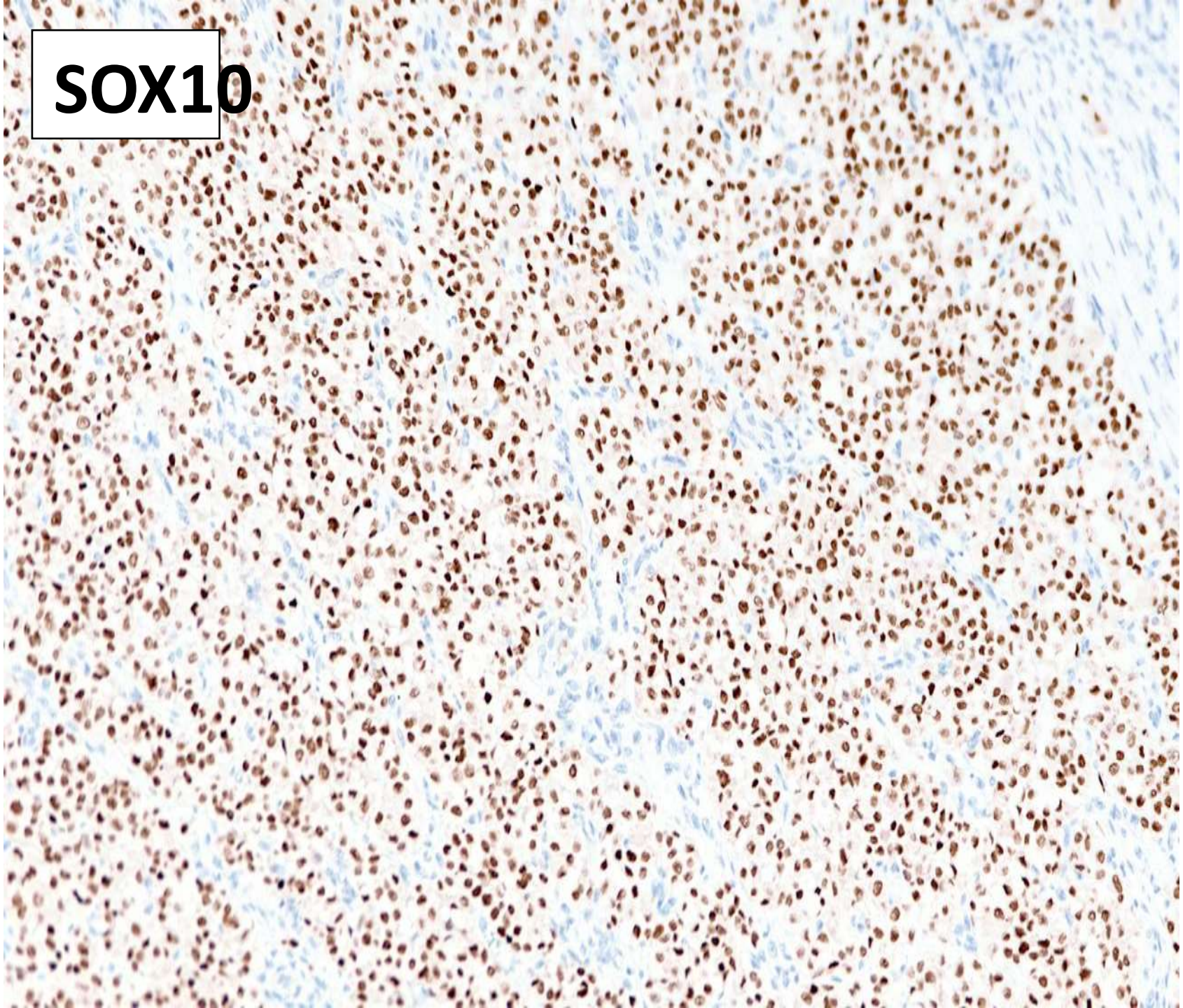
# Clear Cell Sarcoma-Like Tumor of GI Tract - Pathology

- Centered in muscularis propria
- Relatively uniform epithelioid cells
- Vesicular chromatin, +/- nucleoli, pale eosinophilic cytoplasm
- Nested, solid, pseudopapillary and pseudoalveolar patterns
- 50% - osteoclast-like giant cells
- Mitotic activity present

# Clear Cell Sarcoma-Like Tumor of GI Tract - Immunohistochemistry

- Positive
  - S100 and SOX10
  - +/- synaptophysin, NSE
- Negative:
  - Melanoma and PEComa markers (HMB45, Melan A, MITF)
  - GIST markers (CD117, DOG1)
  - Epithelial markers (keratins)


S100


SOX10

# Clear Cell Sarcoma-Like Tumor of GI Tract – Molecular Pathology

- Harbor gene fusion involving *EWSR1*
  - *EWSR1-ATF1* (most common)
  - *EWSR1-CREB1*

# "Clear Cell Sarcoma" Tumors – Terminology

- Clear cell sarcoma of tendons and aponeuroses (melanoma of soft parts)
  - Subcutis or deeper soft tissue, extremities
  - Express S100, SOX10 *and melanoma markers* (MelanA, HMB45, MITF)
- Clear cell sarcoma-like tumor of GI tract
  - GI tract
  - Express S100 and SOX10
  - *Negative for melanoma markers*

# “Clear Cell Sarcoma” Tumors – Terminology

- Malignant Gastrointestinal Neuroectodermal Tumor (GNET)
  - Proposed renaming of CCSLTGT (Stockman *et al*. 2012 *AJSP*)
  - Analysis of 16 cases:
    - Positive immunohistochemical stains:
      - S100 and SOX10 (100%)
      - CD56 (70%), synapto (56%), NB84 (50%), NSE (45%)
    - Ultrastructural analysis:
      - Features of primitive neuroectodermal cells

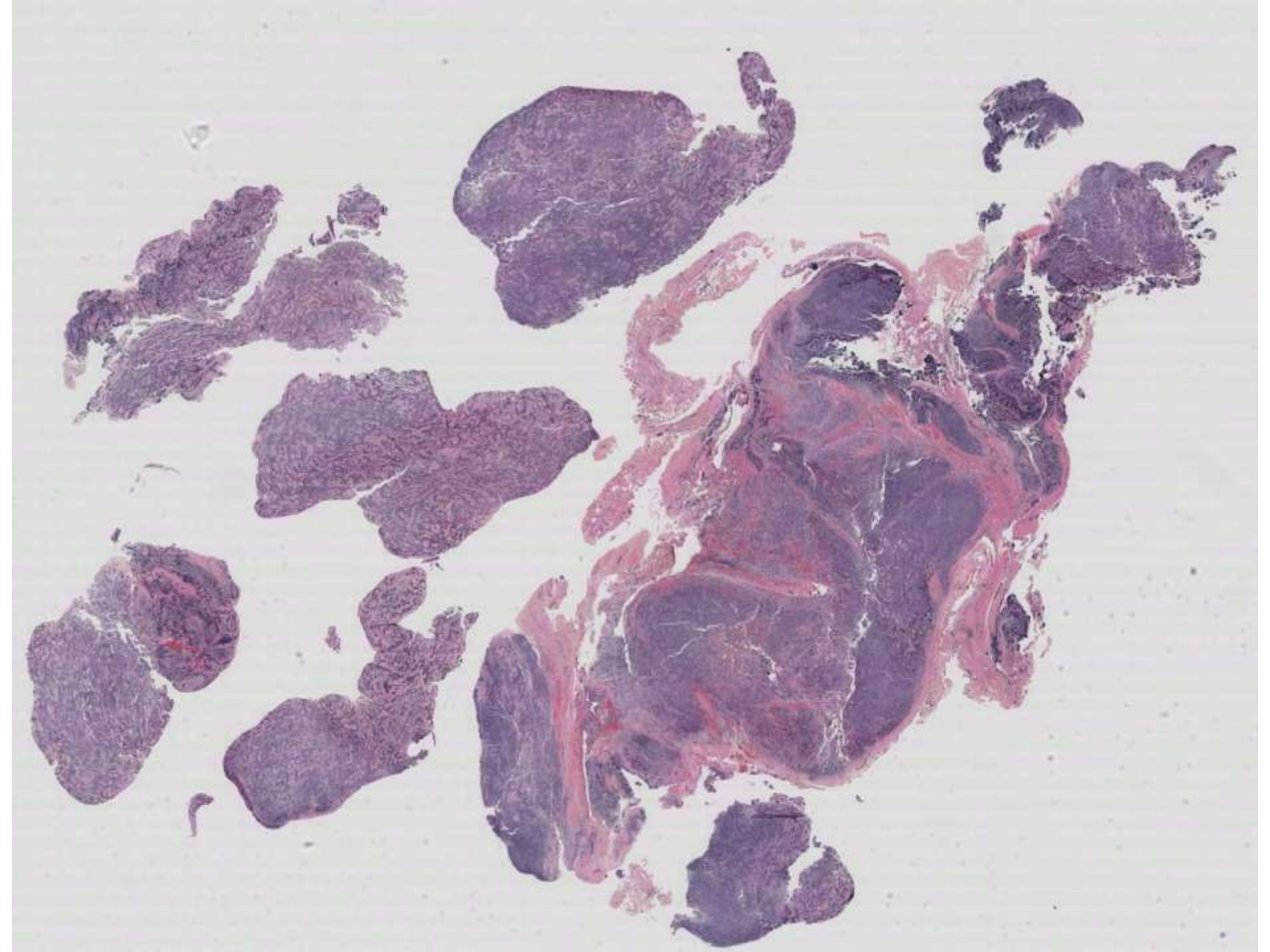
# Clear Cell Sarcoma-Like Tumor of GI Tract – Summary

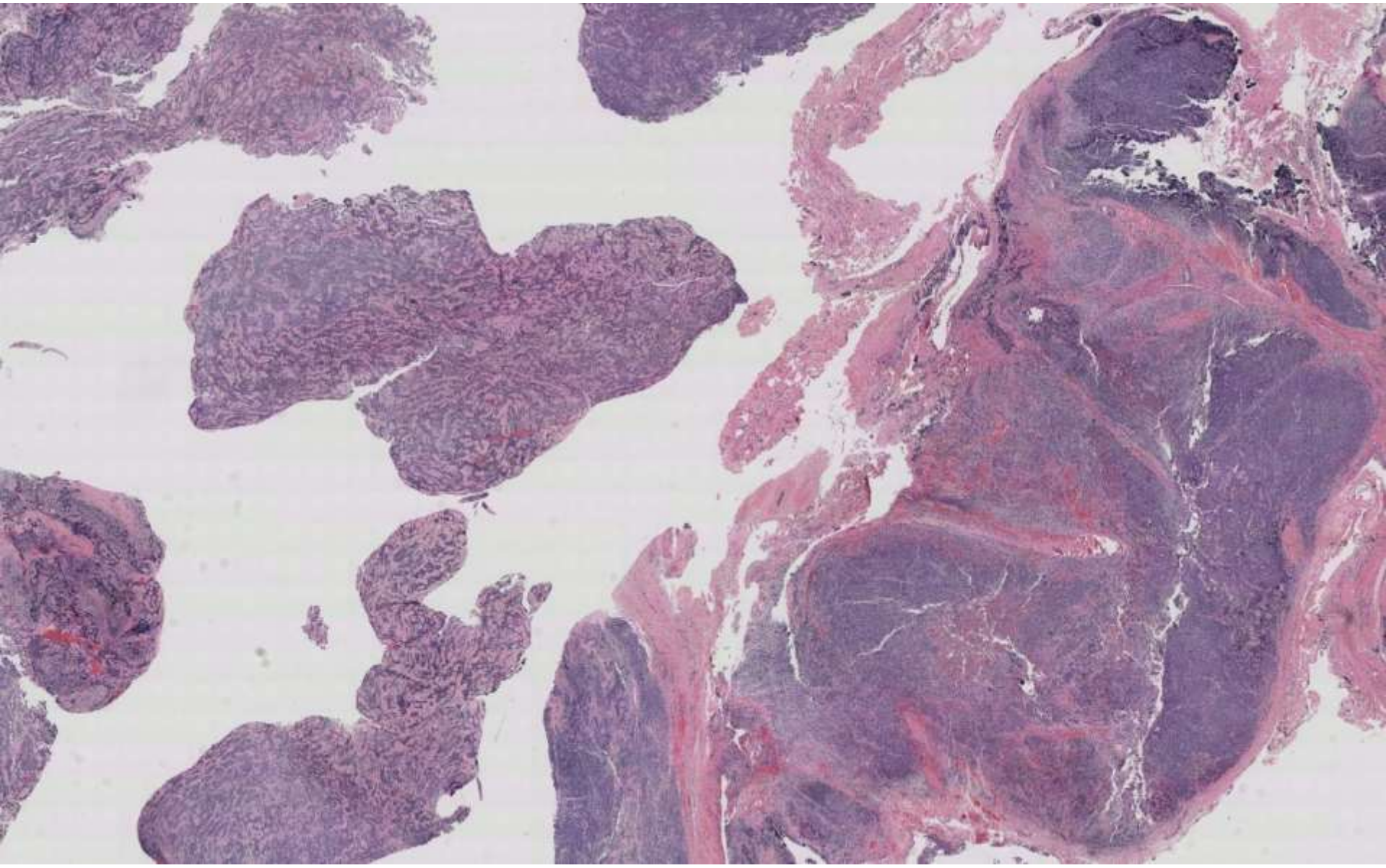
- Rare aggressive sarcoma of the GI tract with neuroectodermal differentiation
- Positive for SOX10 and S100
- Lacks expression of melanoma markers
- *EWSR1* fusions
- Evolving terminology

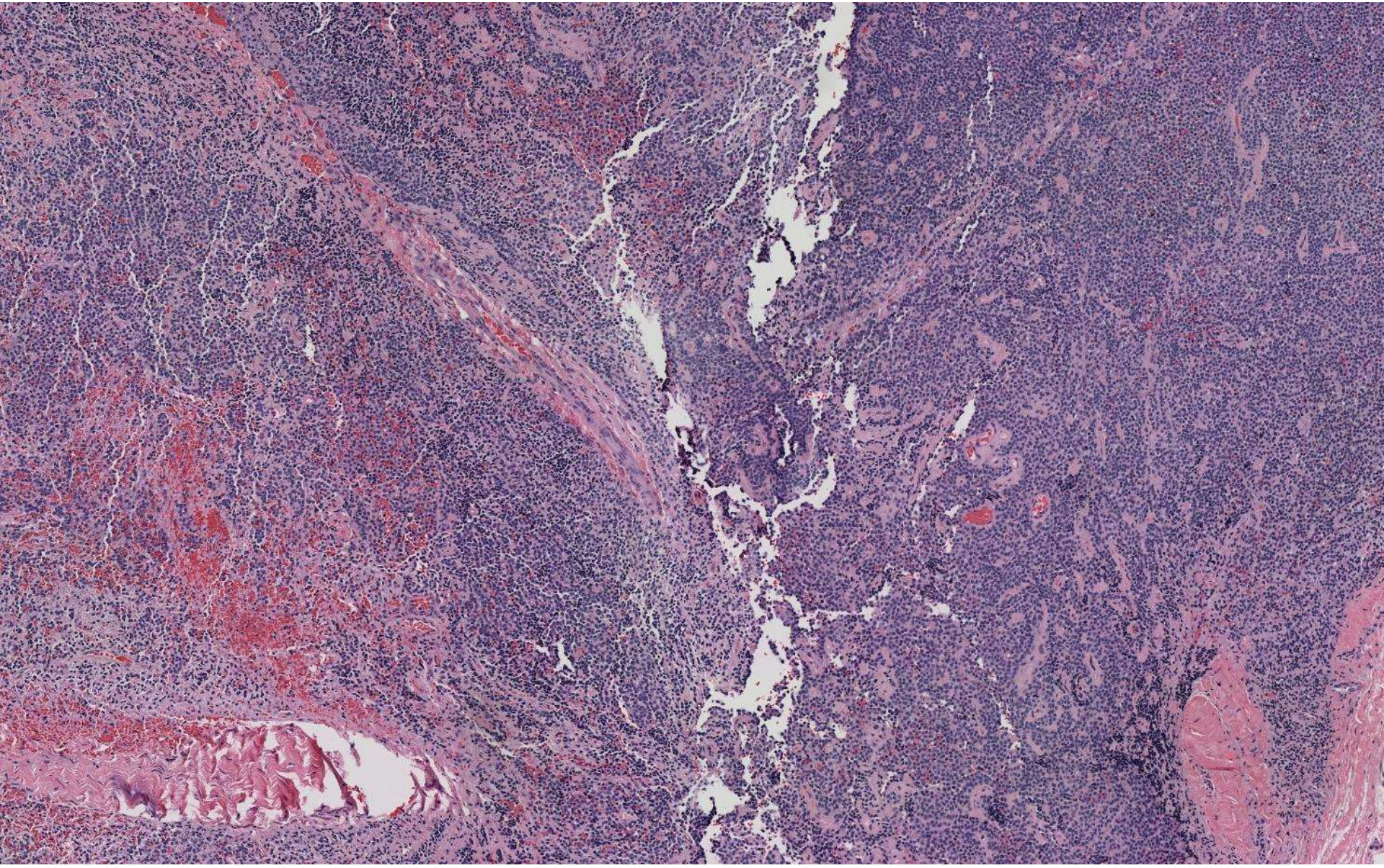
# 20-0102
# scanned slide available!

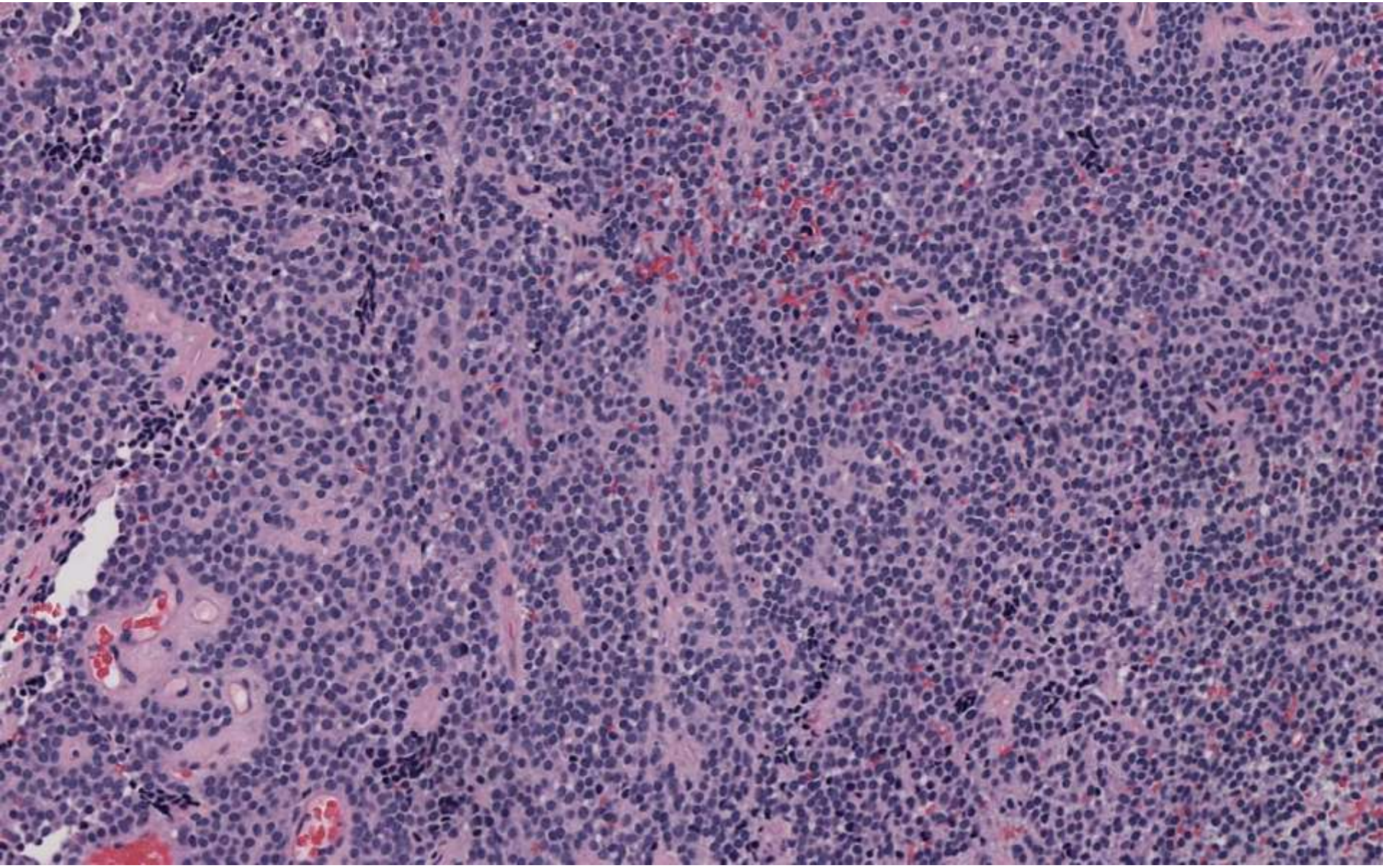
**Keith Duncan; Mills-Peninsula**

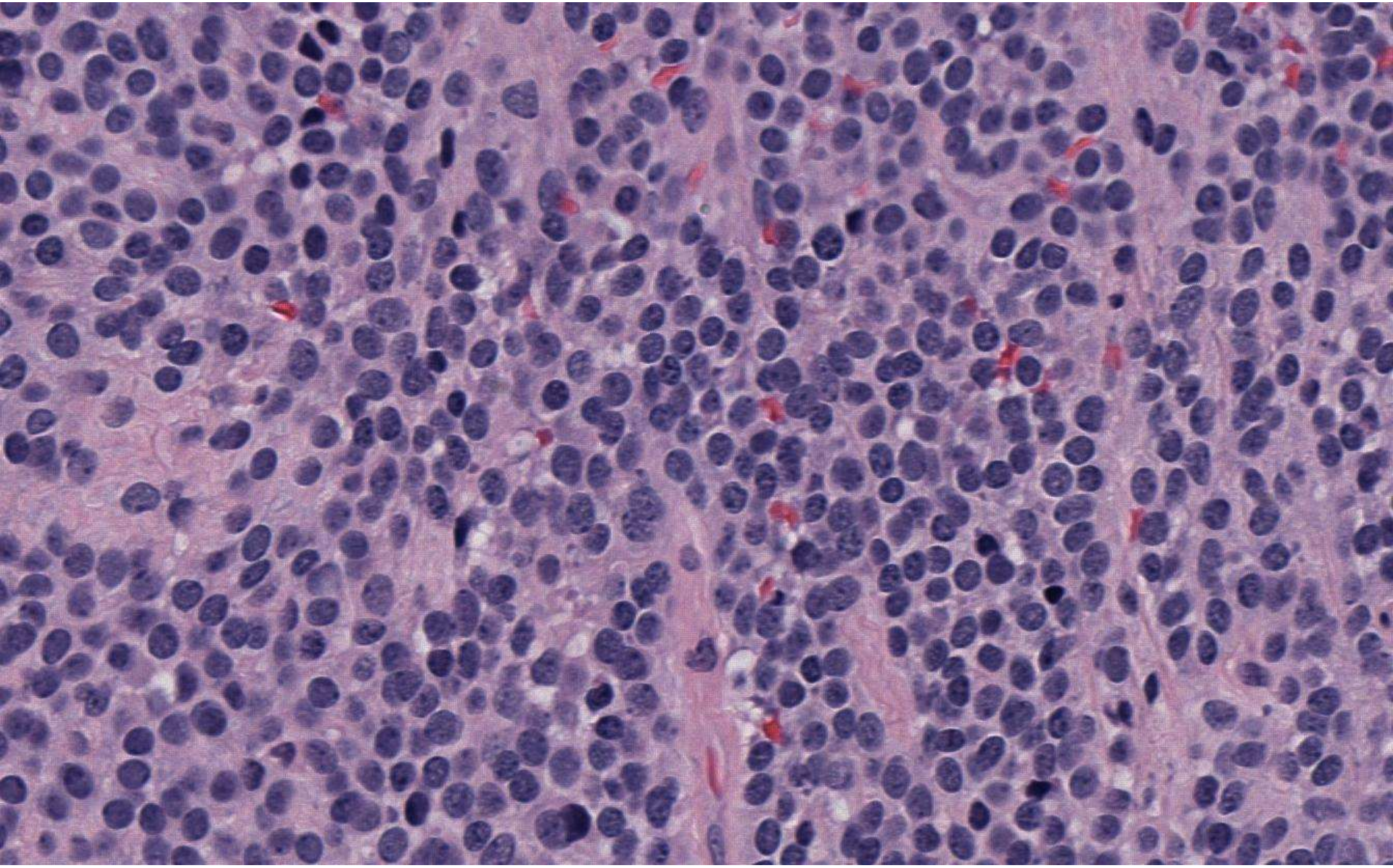
52-year-old F with 2.6cm Y-shaped bilobed mass near right middle scalene muscle originating near C3-C4 facet.

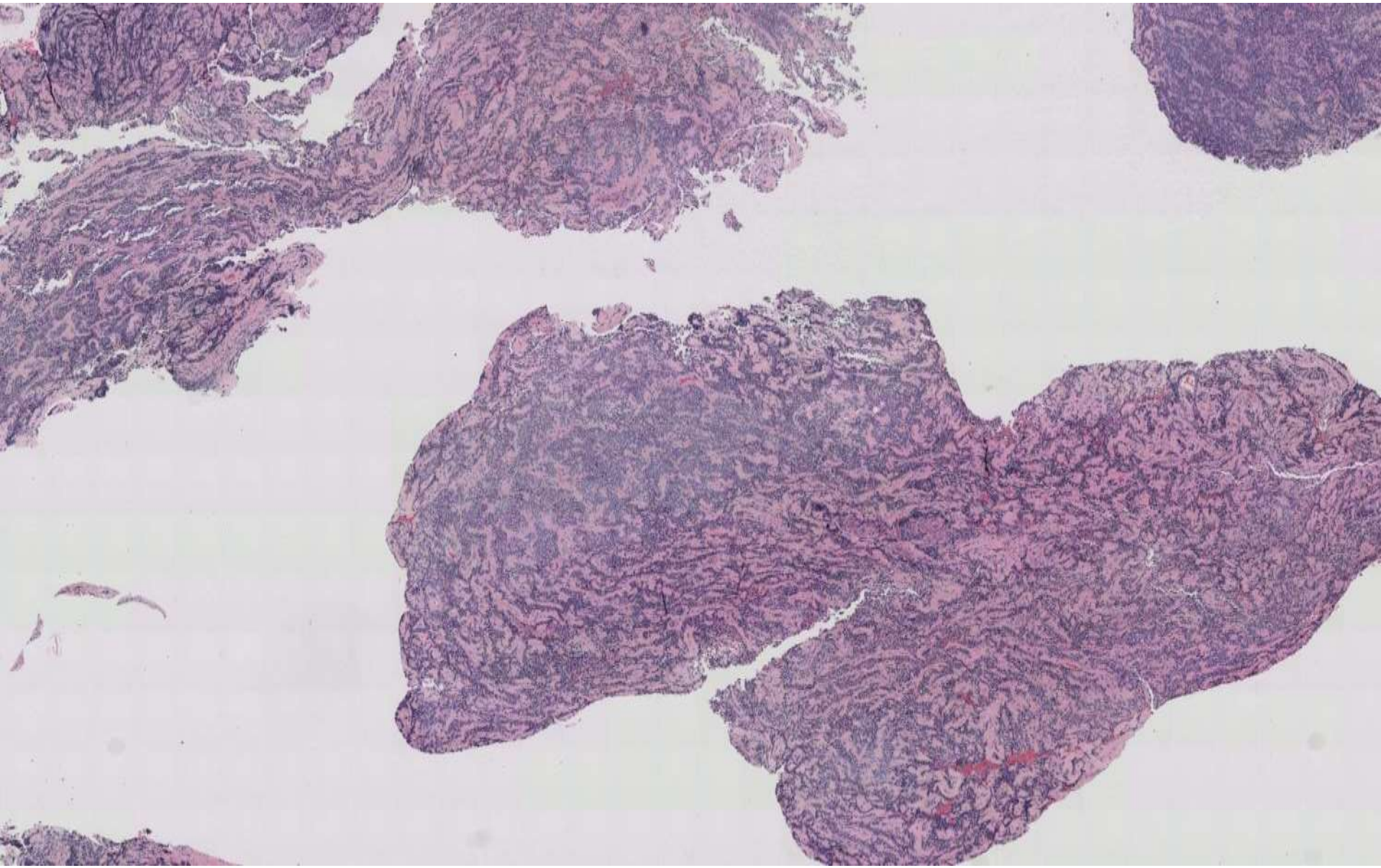


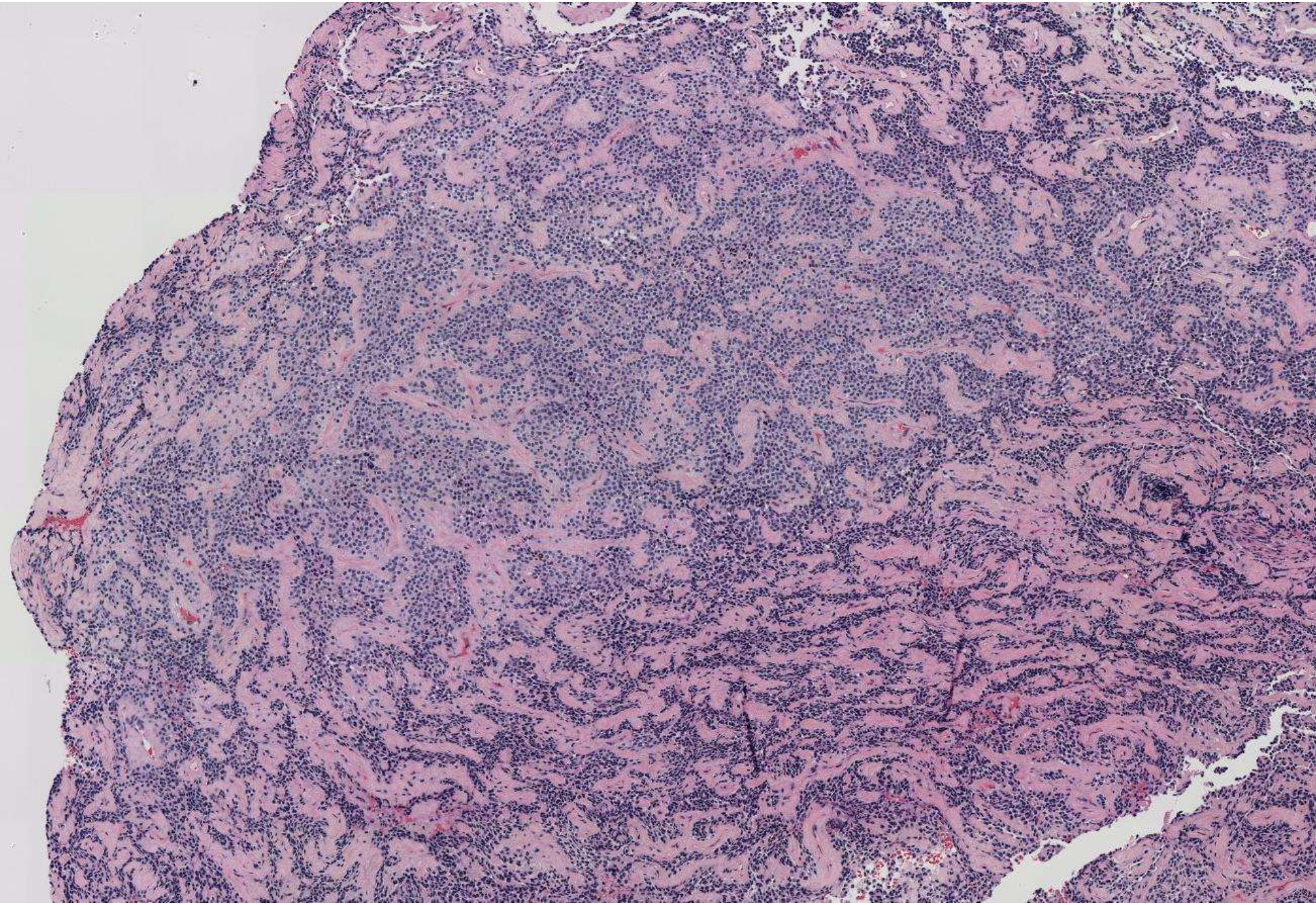


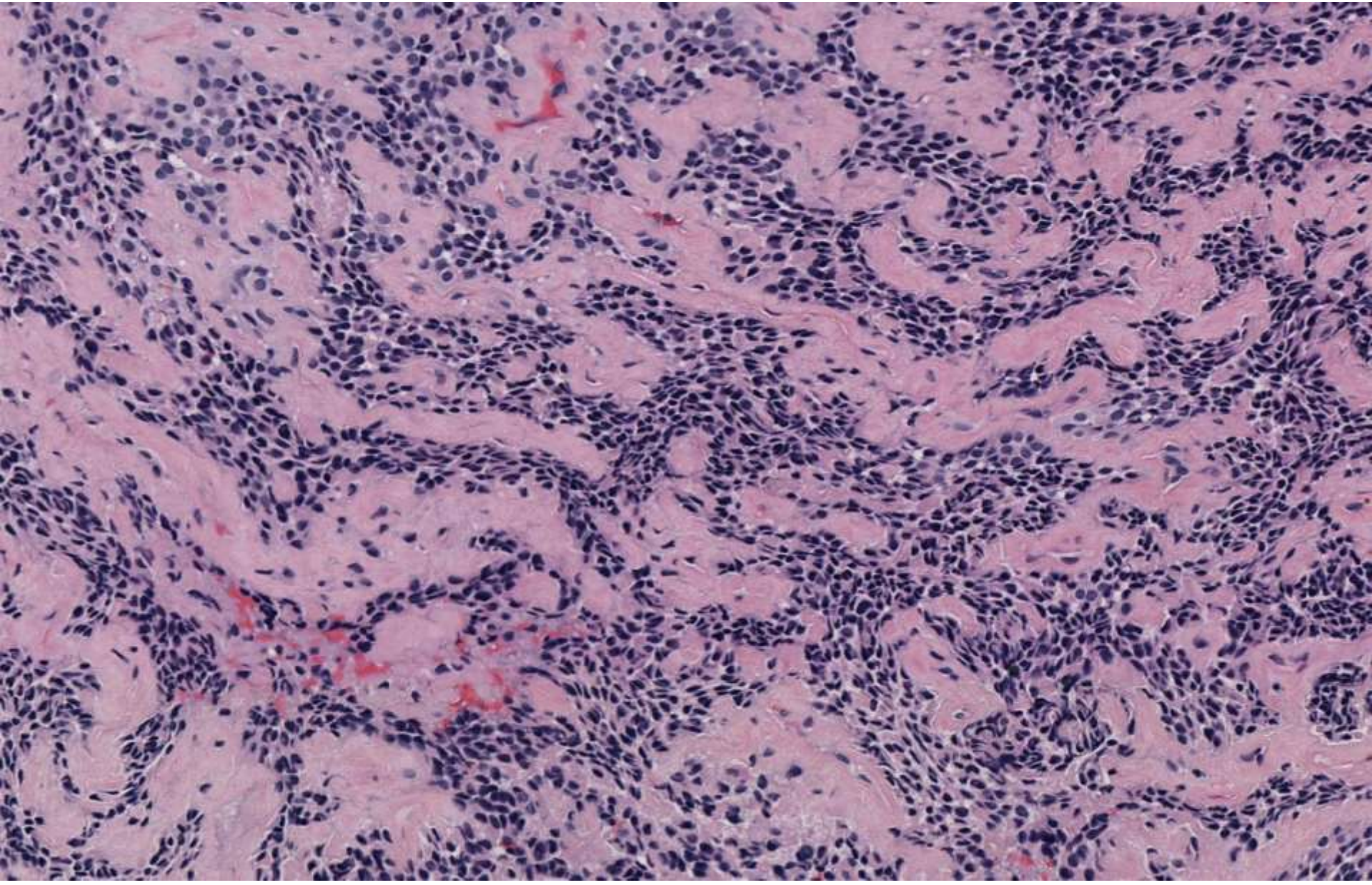


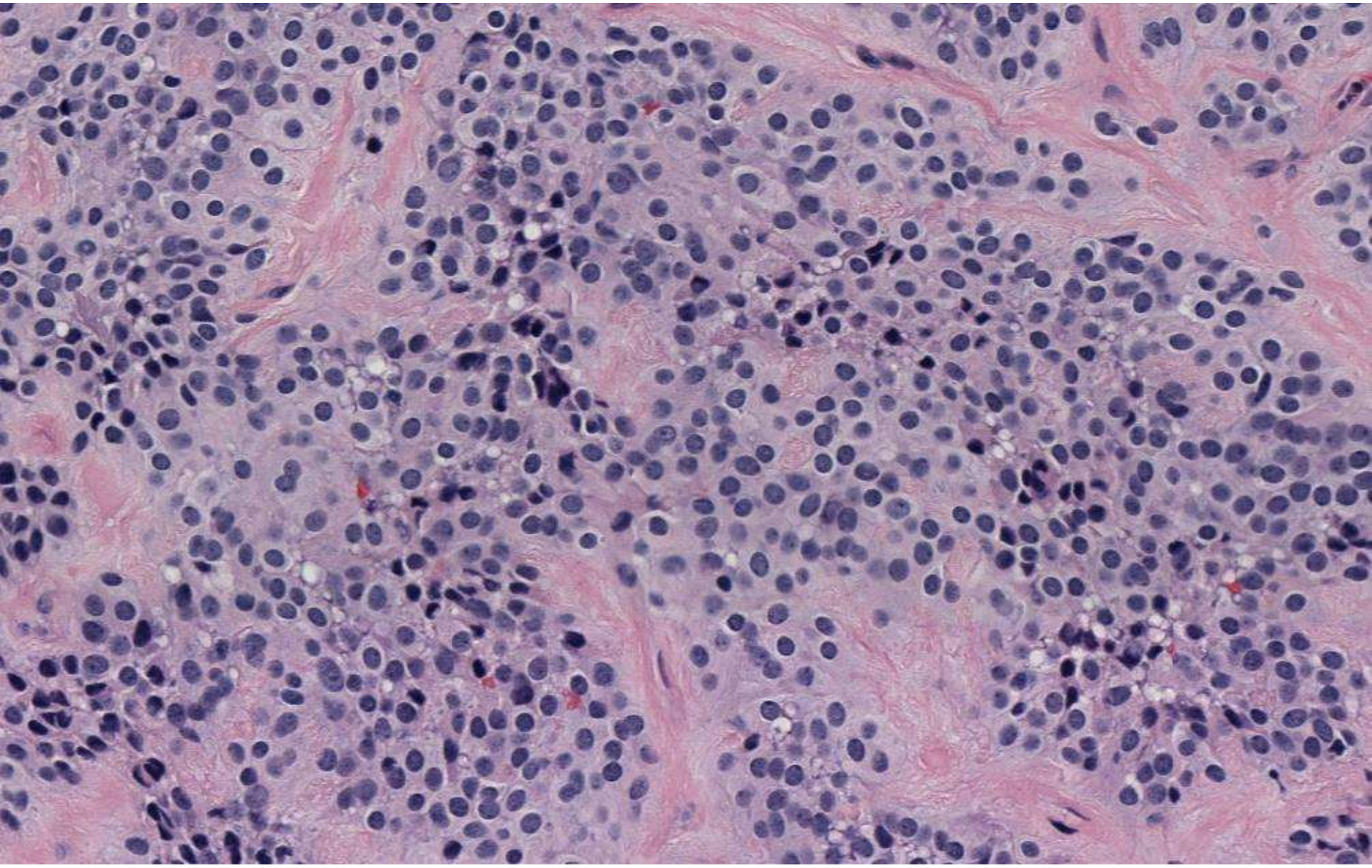


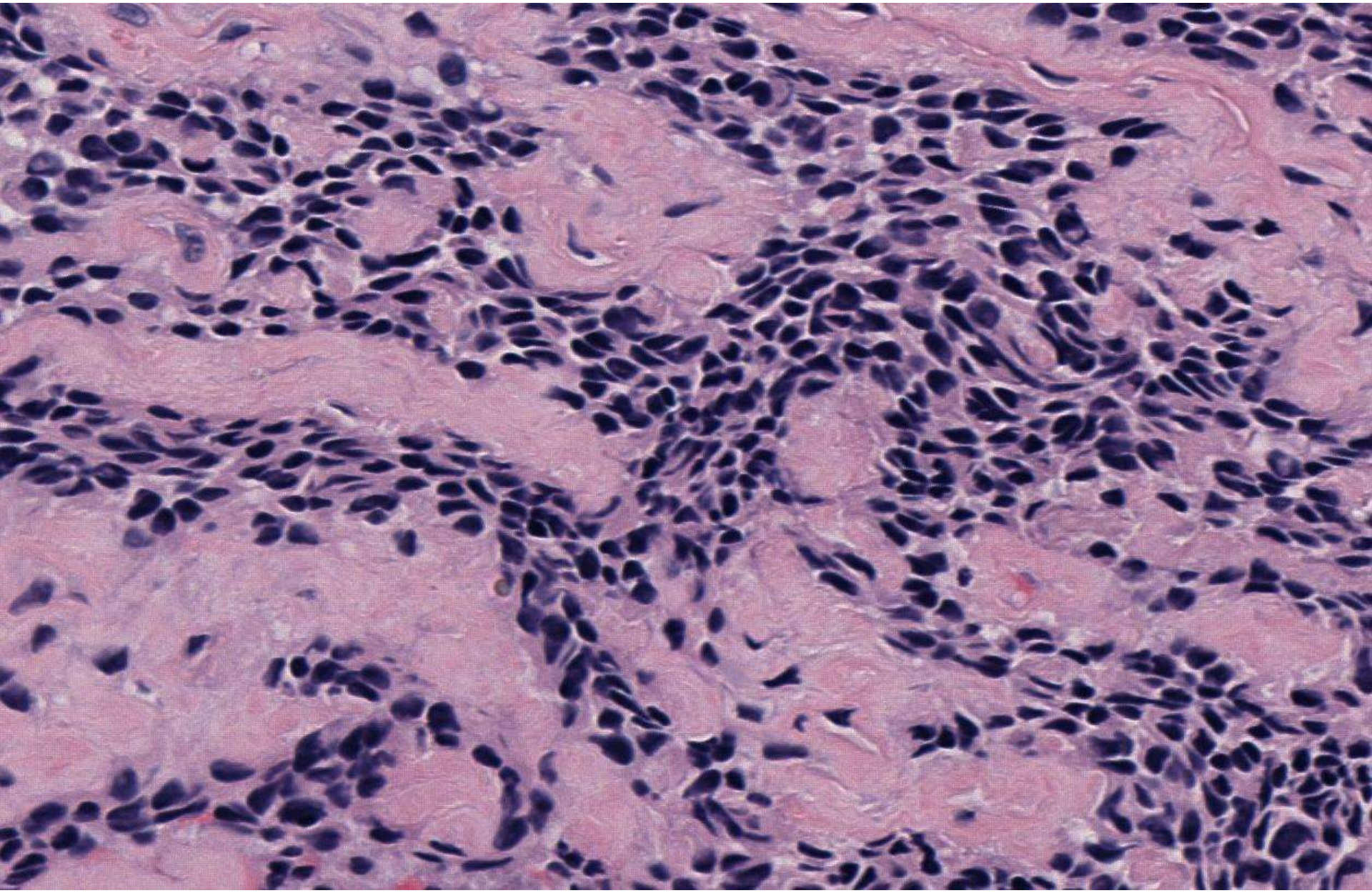












# Spindle and Round Cell Sarcoma With EWSR1-PATZ1 Gene Fusion: A Sarcoma With Polyphenotypic Differentiation

**Sheets and nests of round to spindle cells, fine chromatin, tiny conspicuous nucleoli, moderate cytoplasm, and thick bands of intratumoral fibrosis.**

**HISTO: MULTILOBULAR NEOPLASM COMPROSED OF SMALL ROUND CELLS WITH HIGH N/C RATIO & LIMITED AMOUNTS OF PALELY EOSINOPHILIC CYTOPLASM. NO SIGNIFICANT PLEOMORPHISM & MINIMAL MITOTIC ACTIVITY.**

# Spindle and Round Cell Sarcoma With EWSR1-PATZ1 Gene Fusion: A Sarcoma With Polyphenotypic Differentiation

- EWSR1-PATZ1 fusion positive spindle and round cell sarcomas show abundant intratumoral fibrosis and polyphenotypic differentiation, thus mimicking a range of tumors including desmoplastic small round cell tumor.

- Precise classification of this spindle and round cell sarcoma and its relationship to the Ewing sarcoma family of tumors remains to be determined.

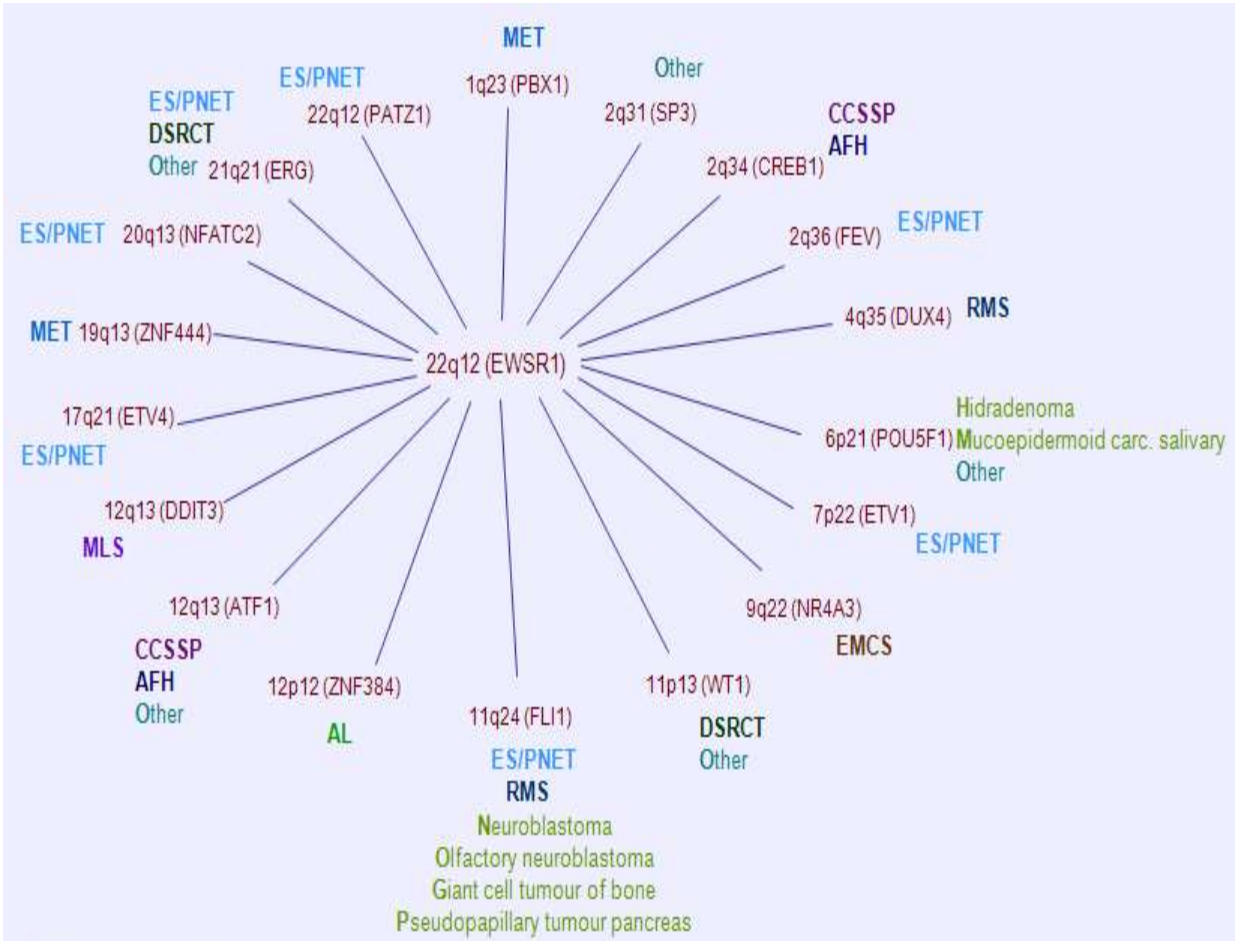
Am J Surg Pathol. 2019 Feb;43(2):220-228

# Spindle and Round Cell Sarcoma With EWSR1-PATZ1 Gene Fusion: A Sarcoma With Polyphenotypic Differentiation.

Chougule A[1], Taylor MS[1], Nardi V[1], Chebib I[1], Cote GM[2], Choy E[2], Nielsen GP[1], Deshpande V[1].

Department of Pathology.

Center for Sarcoma and Connective Tissue Oncology, MGH, Boston, MA.




AFH: Angiomatoid fibrous histiocytoma
AL: Acute leukemia
CCSSP: Clear cell sarcoma of soft parts
DSRCT: Desmoplastic small round cell tumour
EMCS: Extraskeletal myxoid chondrosarcoma
ES/PNET: Ewing sarcoma/Peripheral neurectodermal tumour
MET: Myoepithelial tumour
MLS: Myxoid liposarcoma
RMS: Rhabdomyosarcoma

Other: small round cell, undifferentiated, polyphenotypic tumours

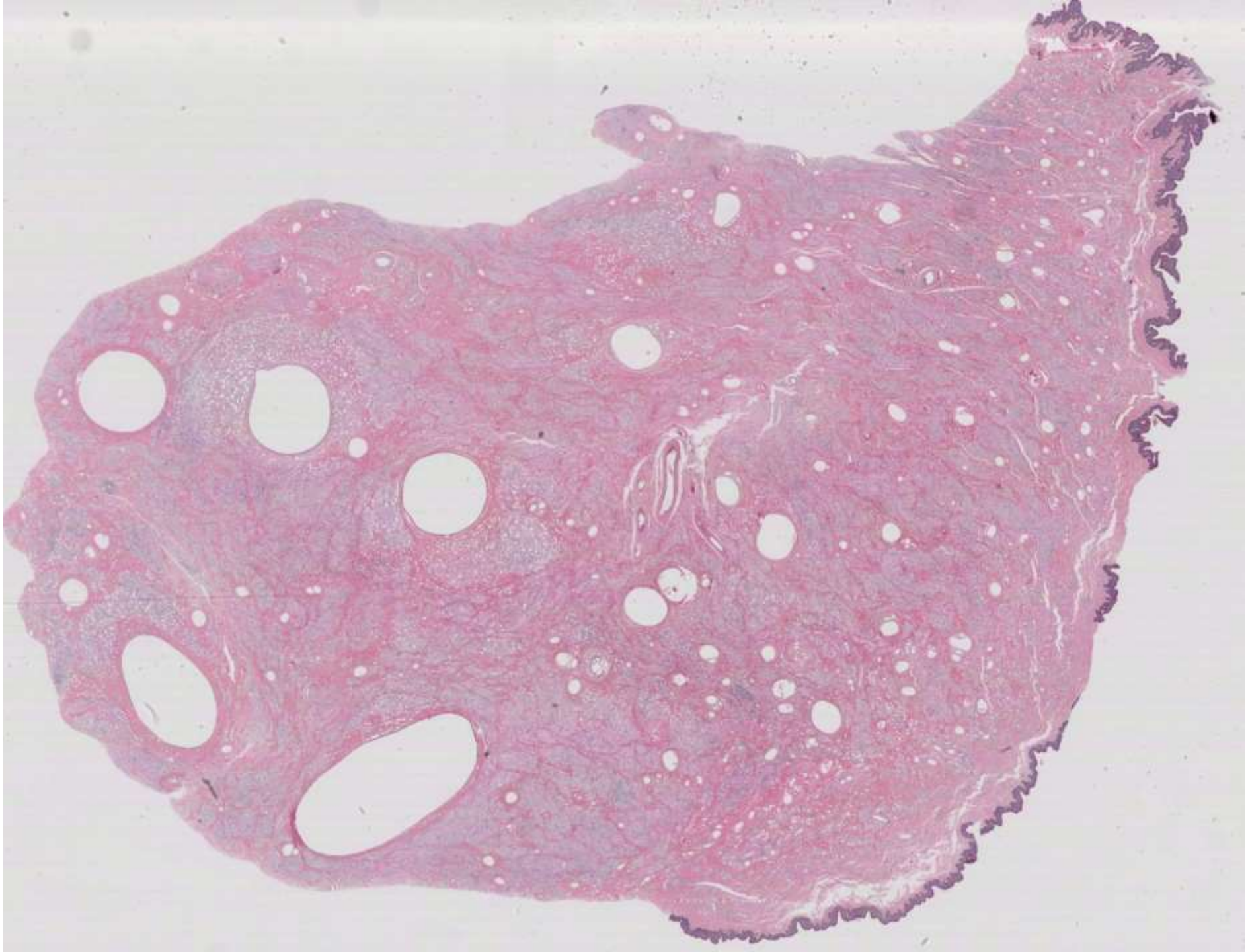
**EWSR1, partners, and tumours.**

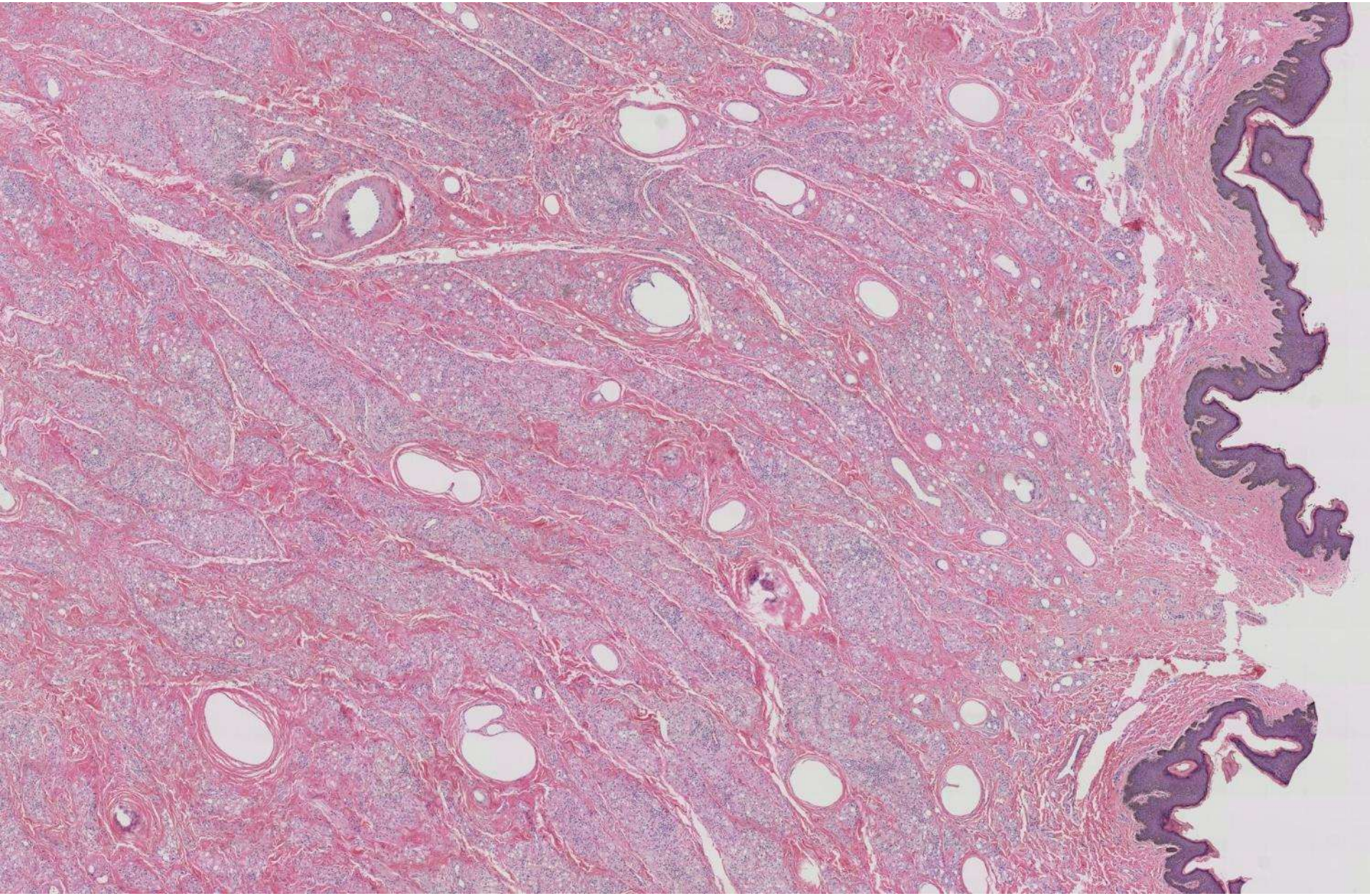
Jean Loup Huret 08/2010

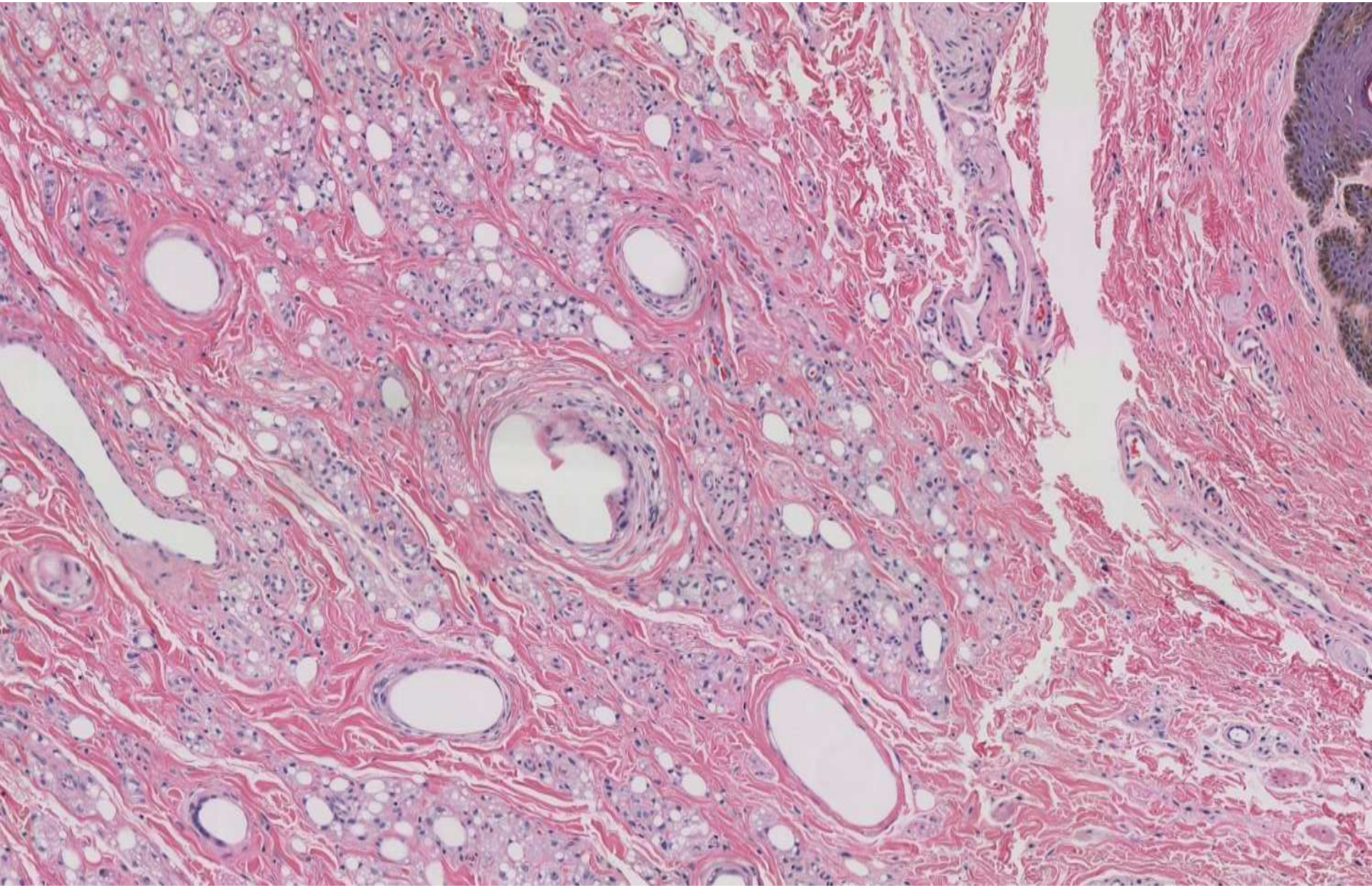
# 20-0103
# scanned slide available!

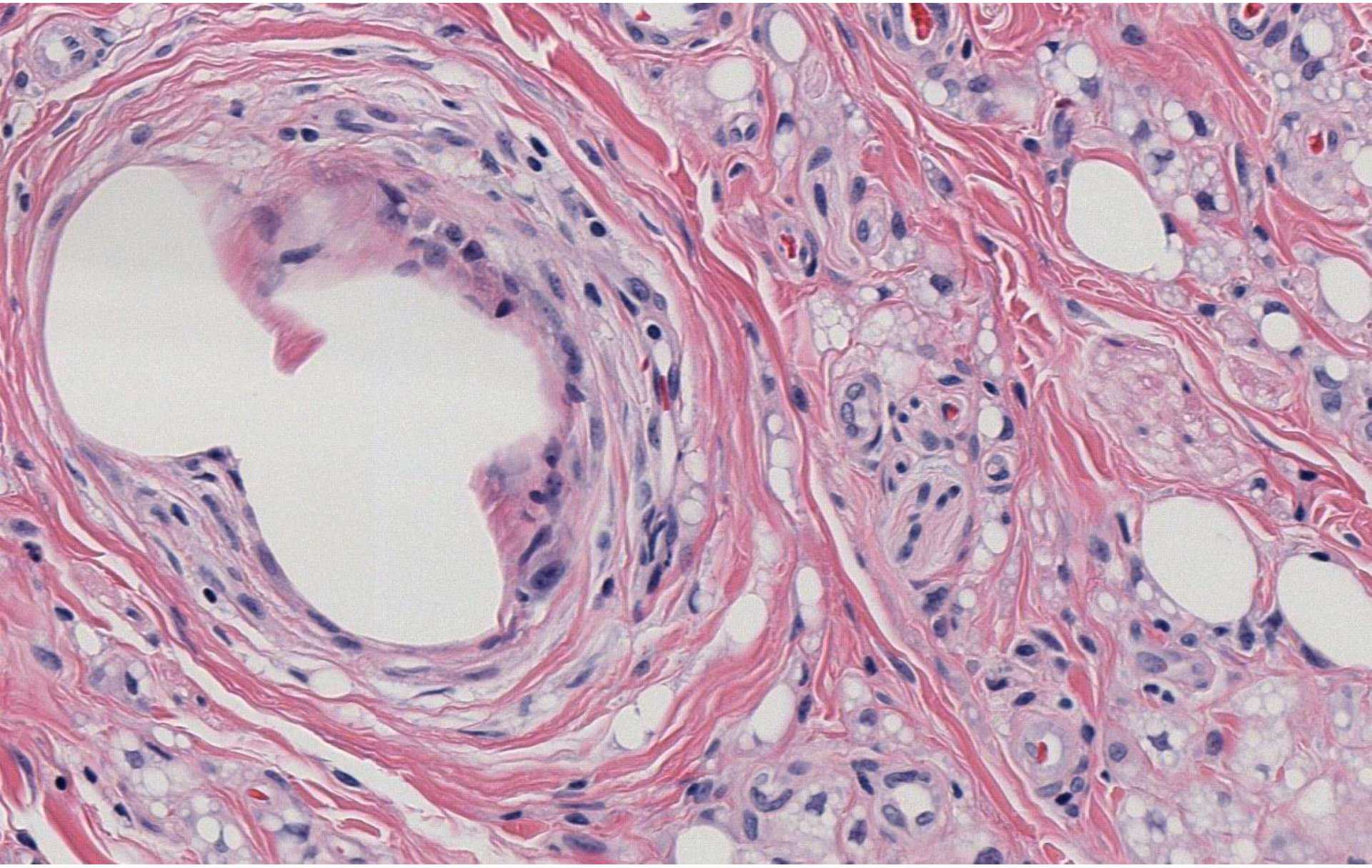
**Emily Chan/Marietya Lauw; UCSF**

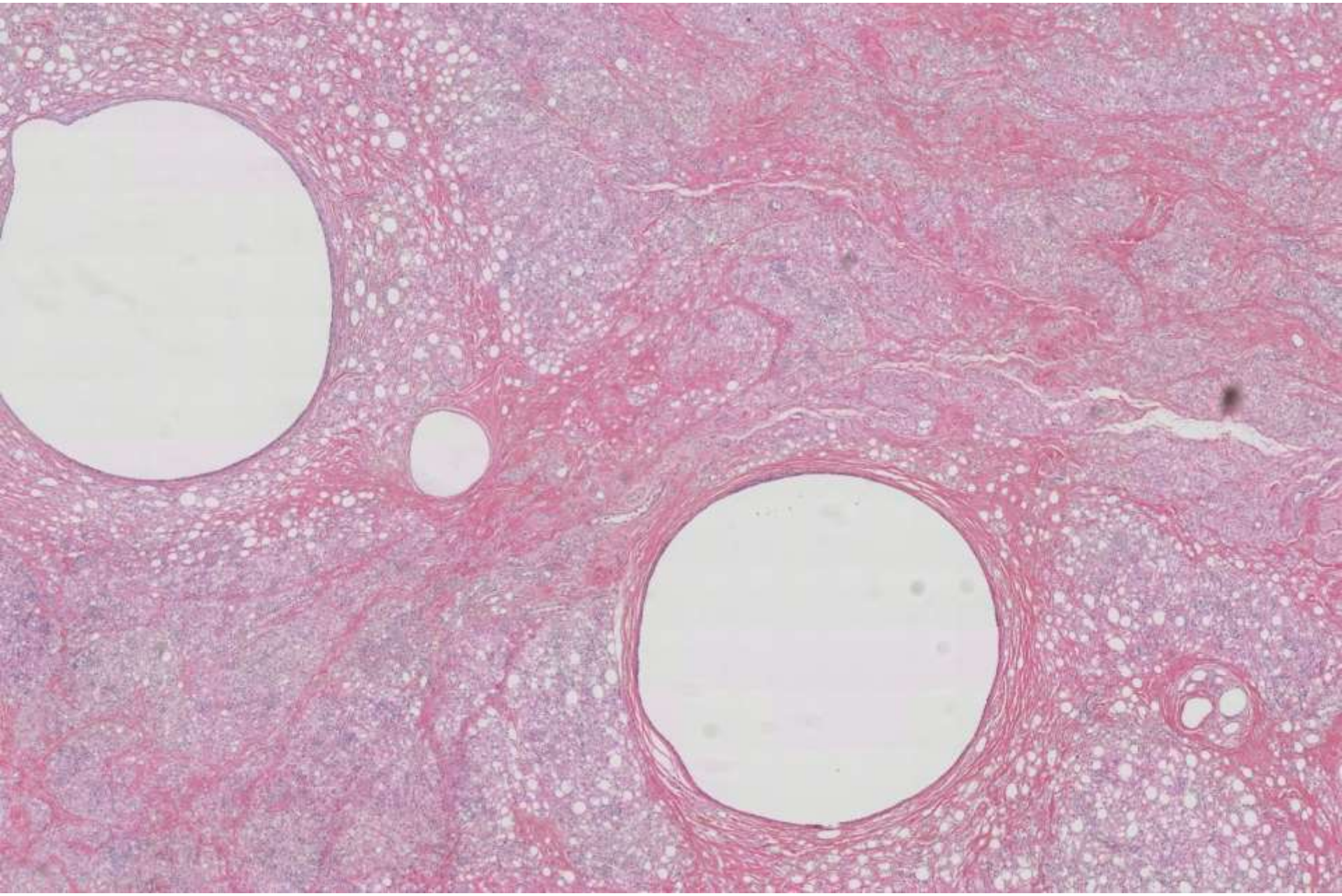
40-year-old M with a penile mass.

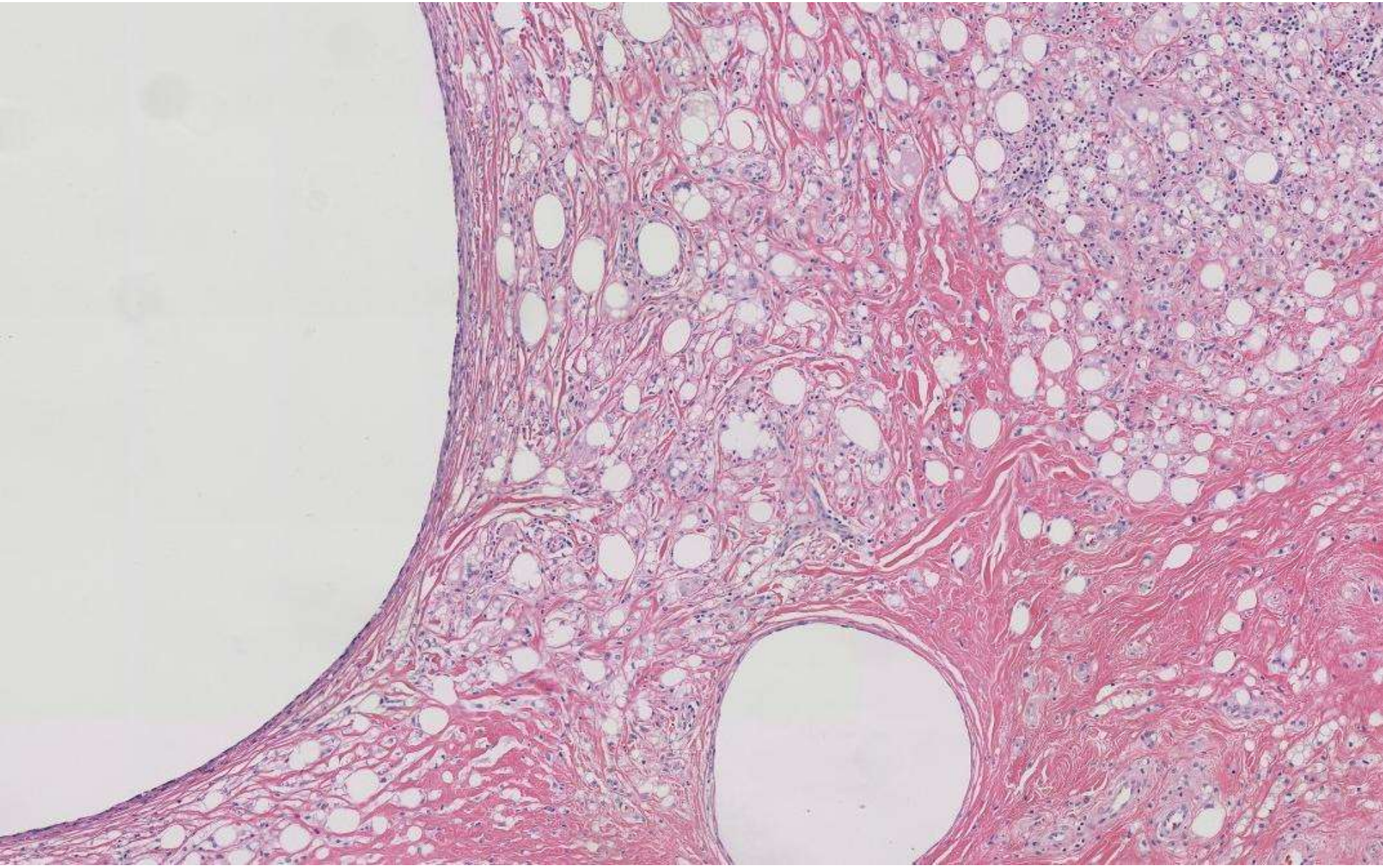


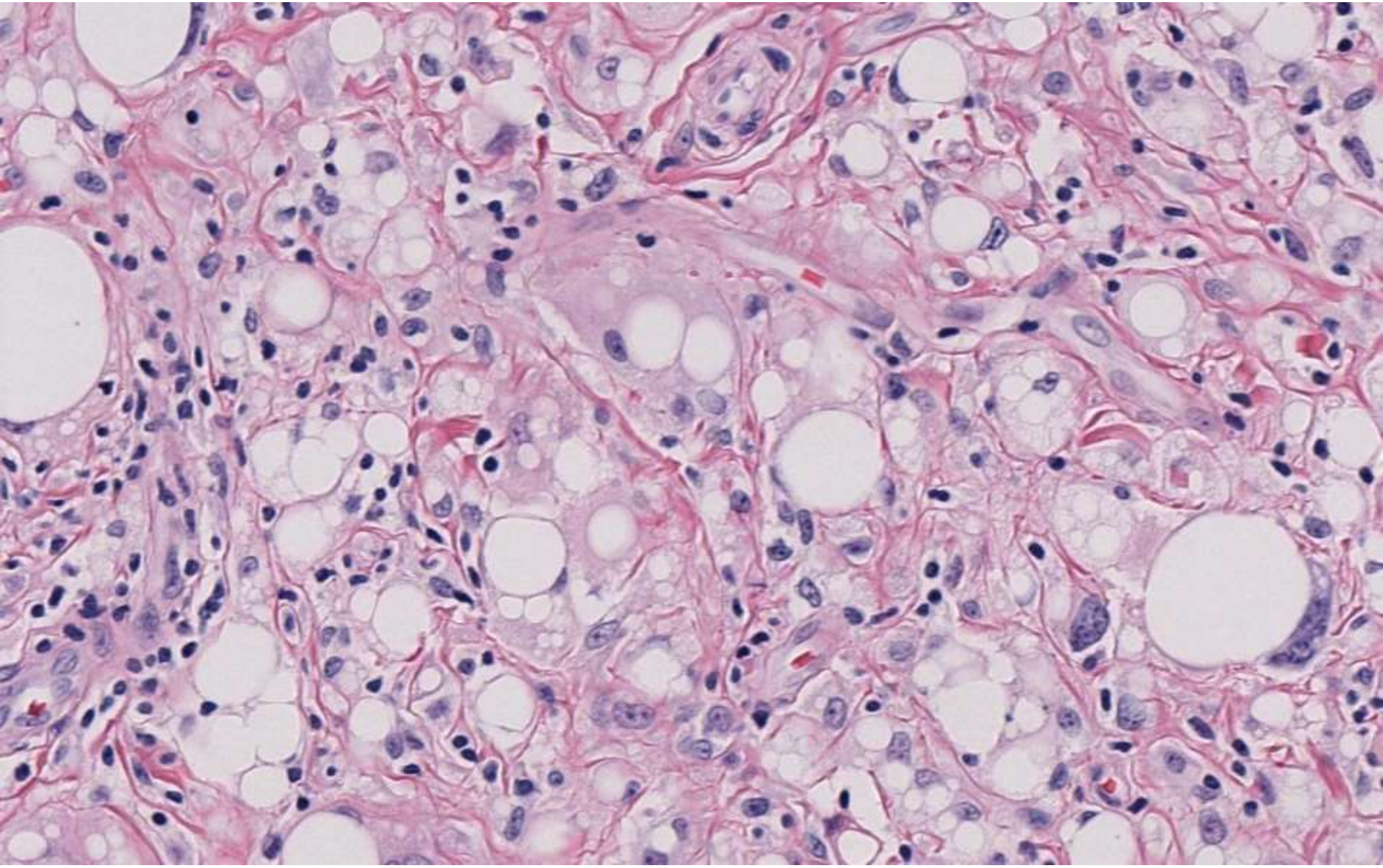




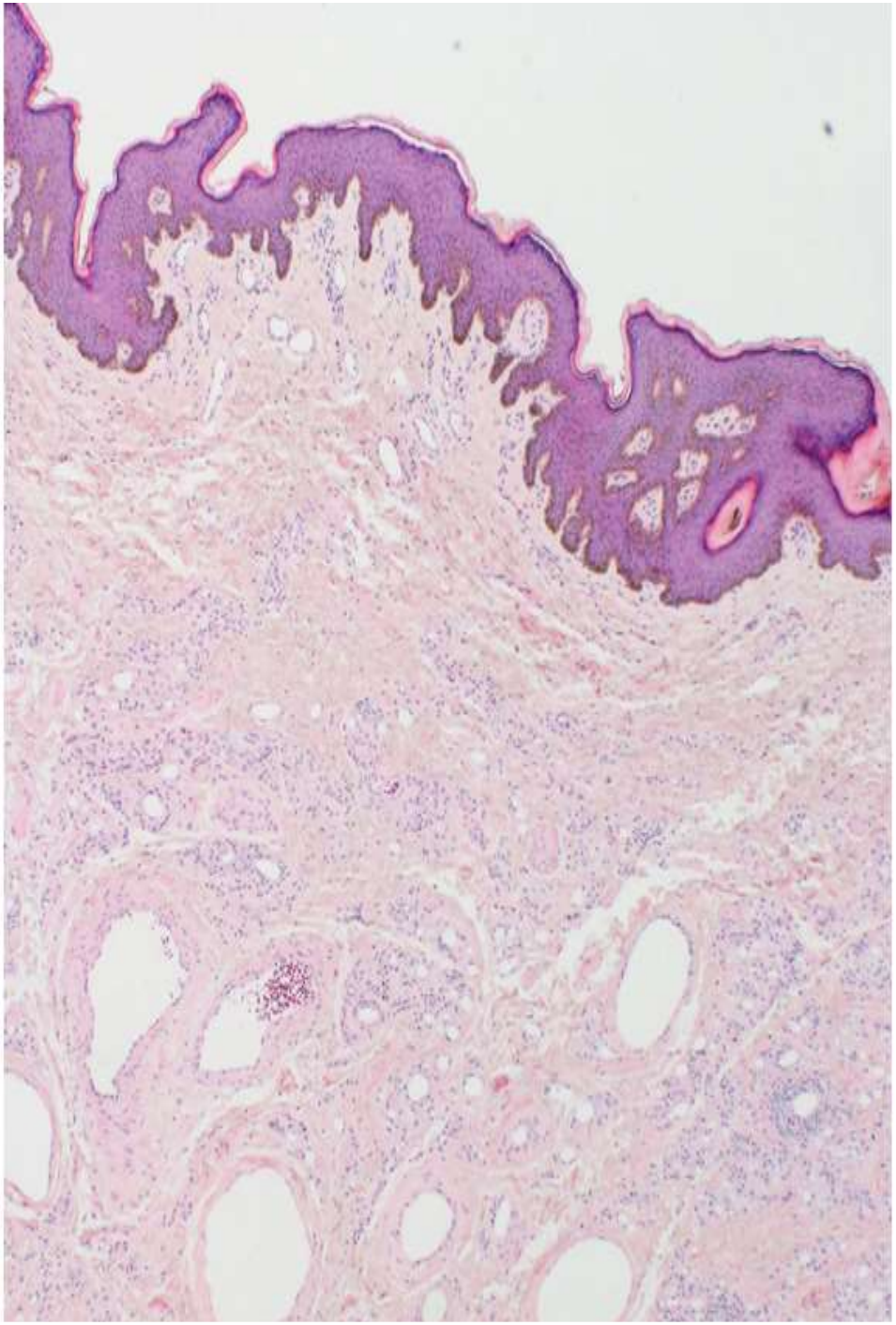


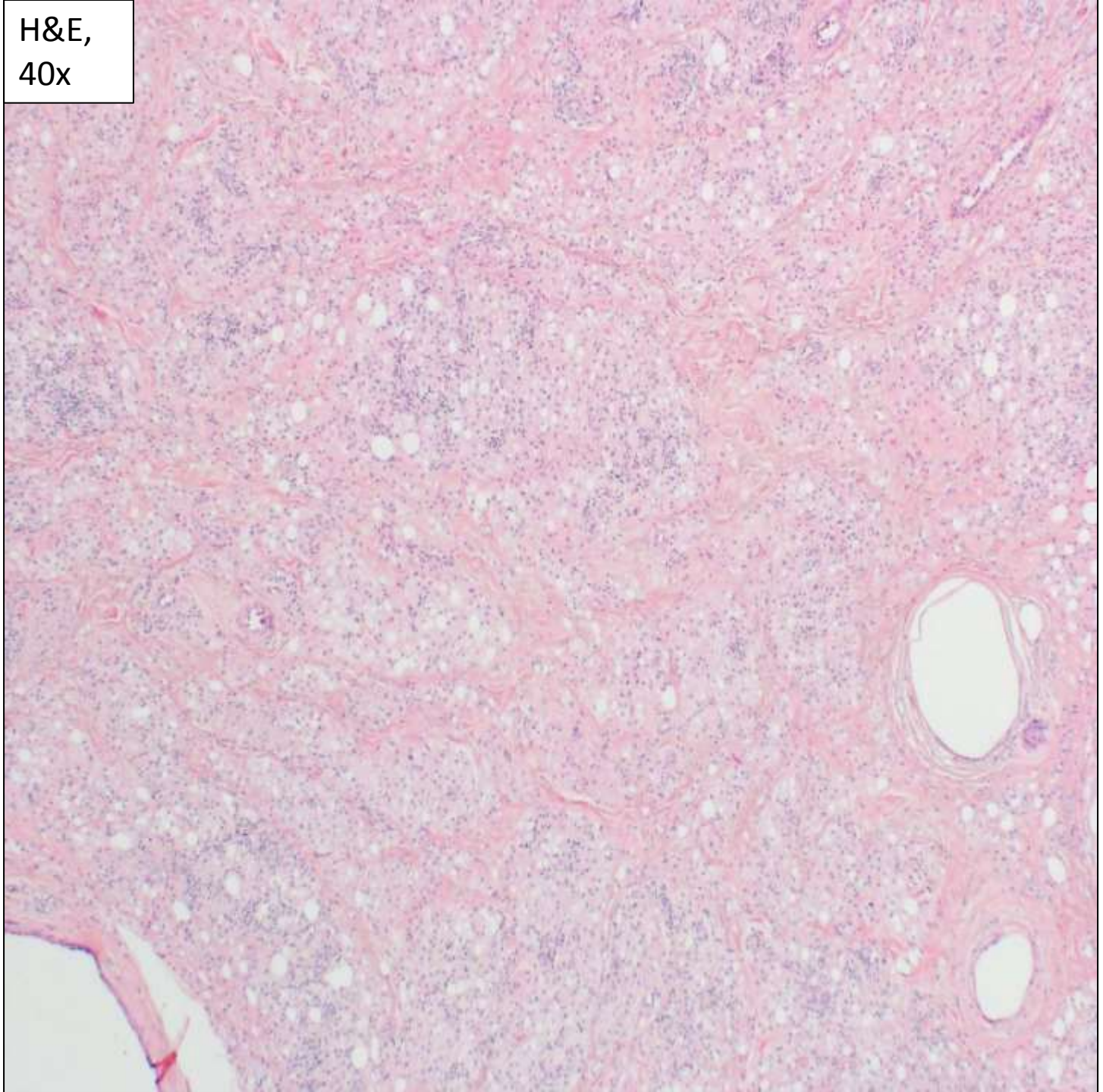


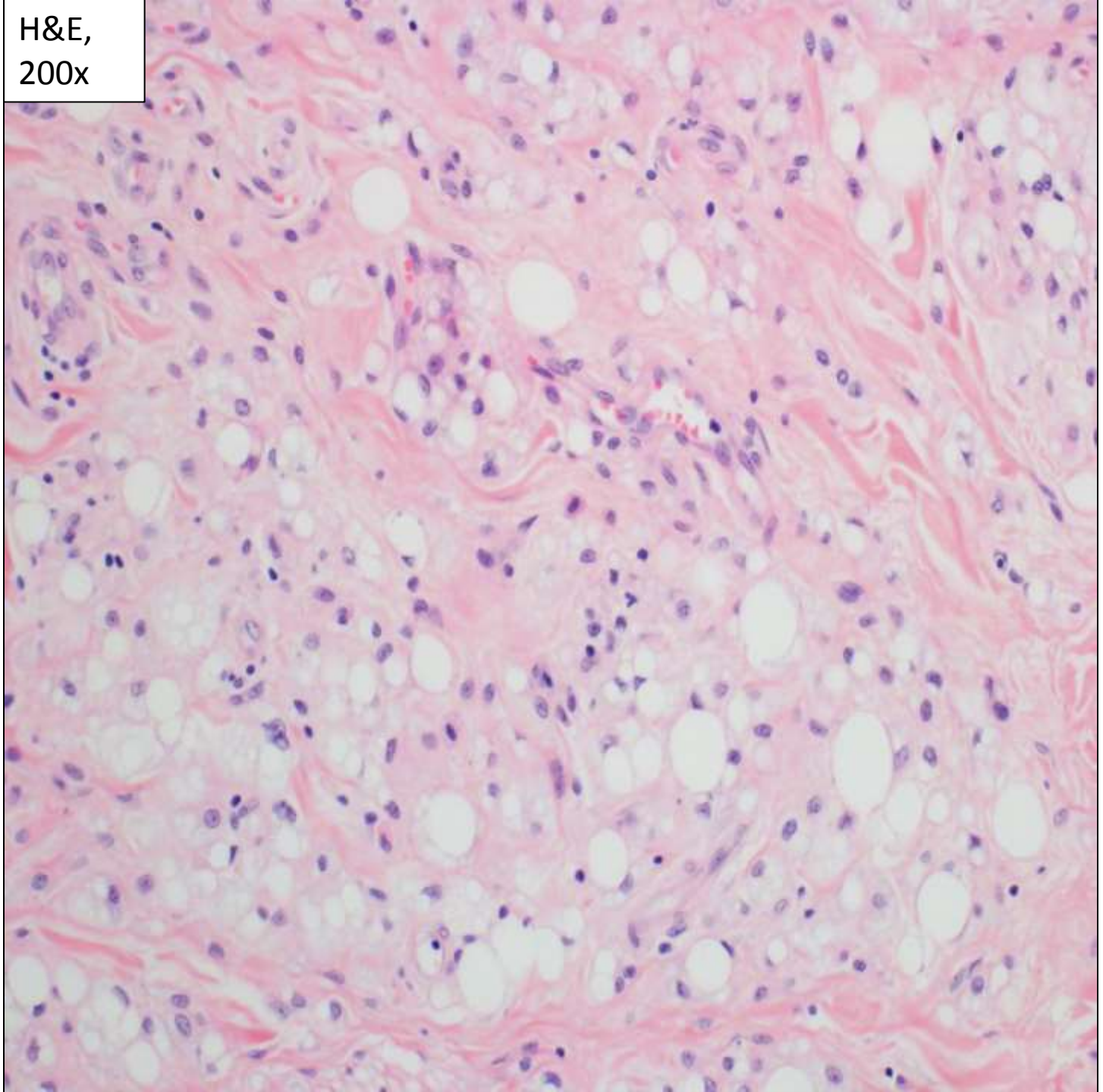


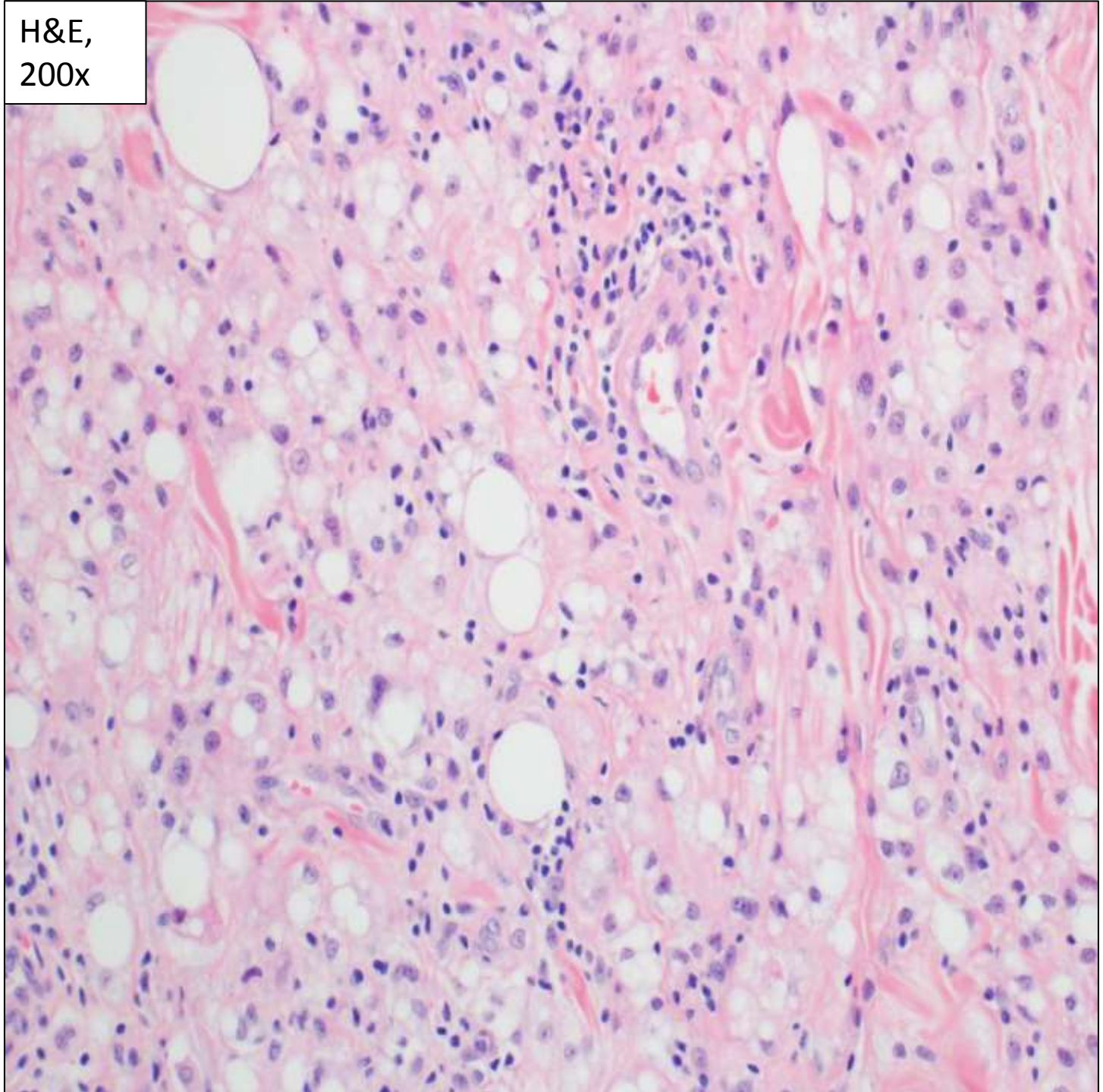


H&E,
40x




H&E,
40x


H&E,
200x


H&E,
200x

# Differential diagnoses

- Lipogranuloma
- Adenomatoid tumor
- Malakoplakia
- Lymphangioma
- Signet ring cell carcinoma
- Sclerosing liposarcoma

Less likely given lack of cytologic atypia

# Extra history

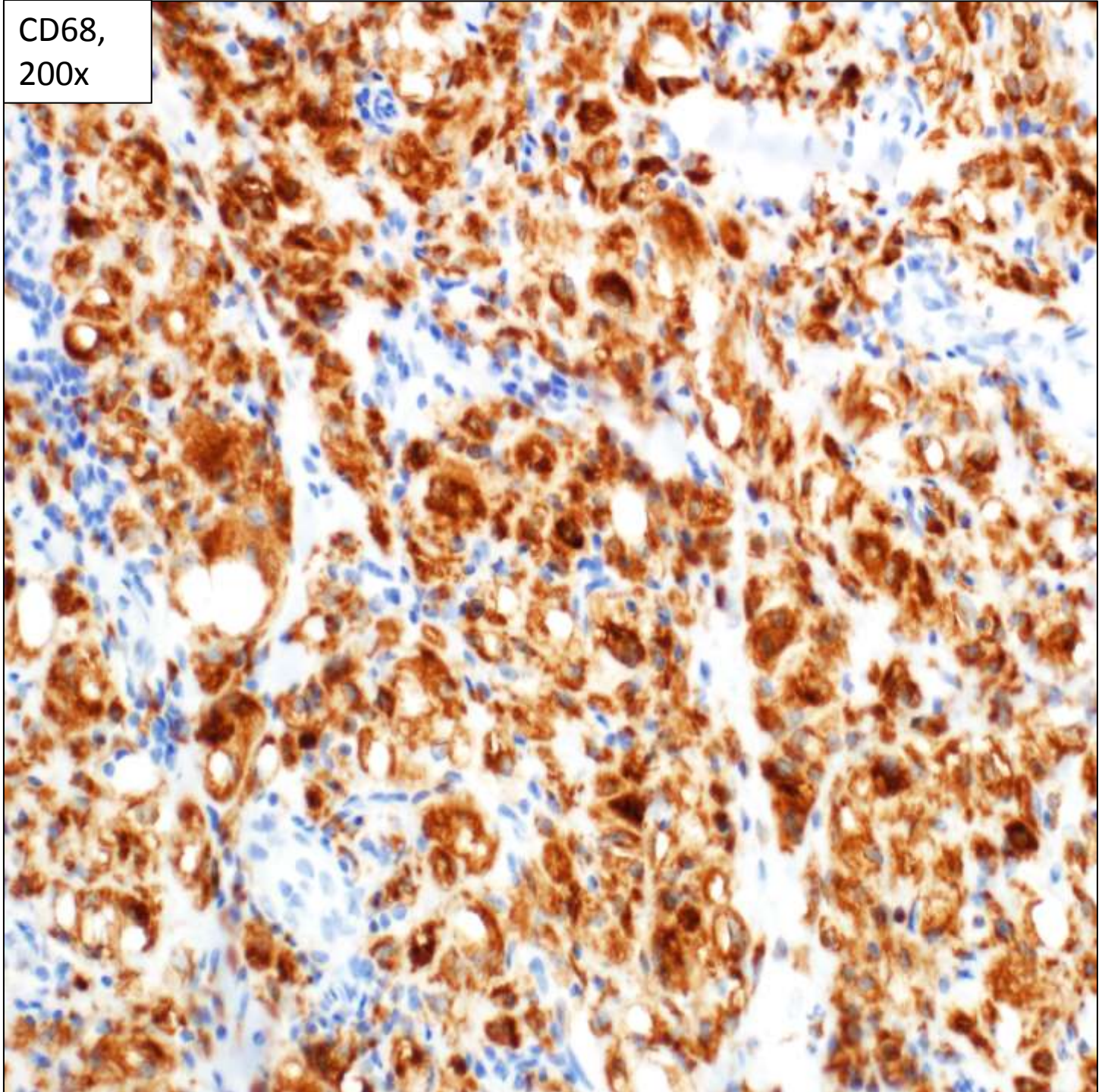
- The patient had a history of petroleum jelly injection to his penis.

# Diagnosis

- Skin, penis, excision:

  Lipogranuloma.

- Other names include Paraffinoma, Vaselinoma, oleoma, Tancho nodules.


CD68,
200x

# Penile implants

- Wide variety of implants:

  Solid: Glass, stone, bullets, ivory, gems, gold, plastic.

  Liquid: Silicone, paraffin, Vaseline, petroleum jelly, cod liver oil, nandrolone decanoate, waxes, and mineral oil.

- 1989: Robert Gersuny described injections of mineral oil as a medical procedure.
- Since then mineral oil injections have been used for a wide range of cosmetic purposes, i.e., cleft palate, wrinkles, face deformities, baldness, and muscle, breast and penile augmentation.
- 1906: Heidingsfeld presented the first report of adverse effects (disfiguring subcutaneous nodules) of human body oil injections.
- After several reports of serious adverse effects, these treatment modalities were omitted in traditional medicine.
- Still used by non-medical personnel or as self-injections mostly for cosmetic purposes.
- More commonly performed in Asia and Eastern Europe.

# Prevalence

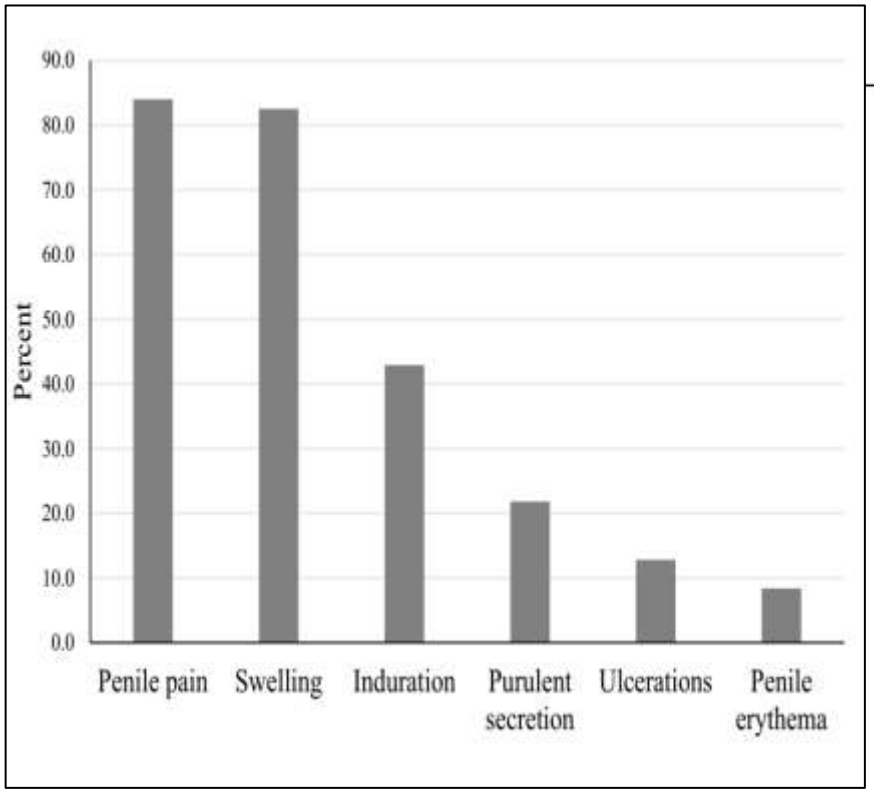
- High prevalence in certain male populations:

  - 7.5 % in a study of 639 Burmese fishermen in Thailand (Ohnmar, et al. Sex Health. 2009).

  - 15.7% in another study among Hungarian prisoners (Rosecker et al. J Sex Med. 2013).

# Clinical presenta

| Mild | Moderate | Severe | Life threatening |
|---|---|---|---|
| Penile pain | Phimosis | Induration | Fournier's gangrene |
| Swelling | Ulceration | Necrosis | Sepsis |
| Penile erythema | Purulent secretion | | |
| Itching at injection area | Pale penile skin colour change | | |
| Discharge | Dysuria | | |
| | Fever | | |
| | Atrophy | | |
| | Recurrent bleeding | | |




Svensøy JN, et al. World J Urol. 2018.

# Penile lipogranuloma

- Etiology:

  Primary: Unknown.

  Secondary: Injection of substances such as paraffin, silicone, oil, or wax into the penis.

- Histology:

  - Lipid vacuoles of varying sizes embedded in a sclerotic stroma.

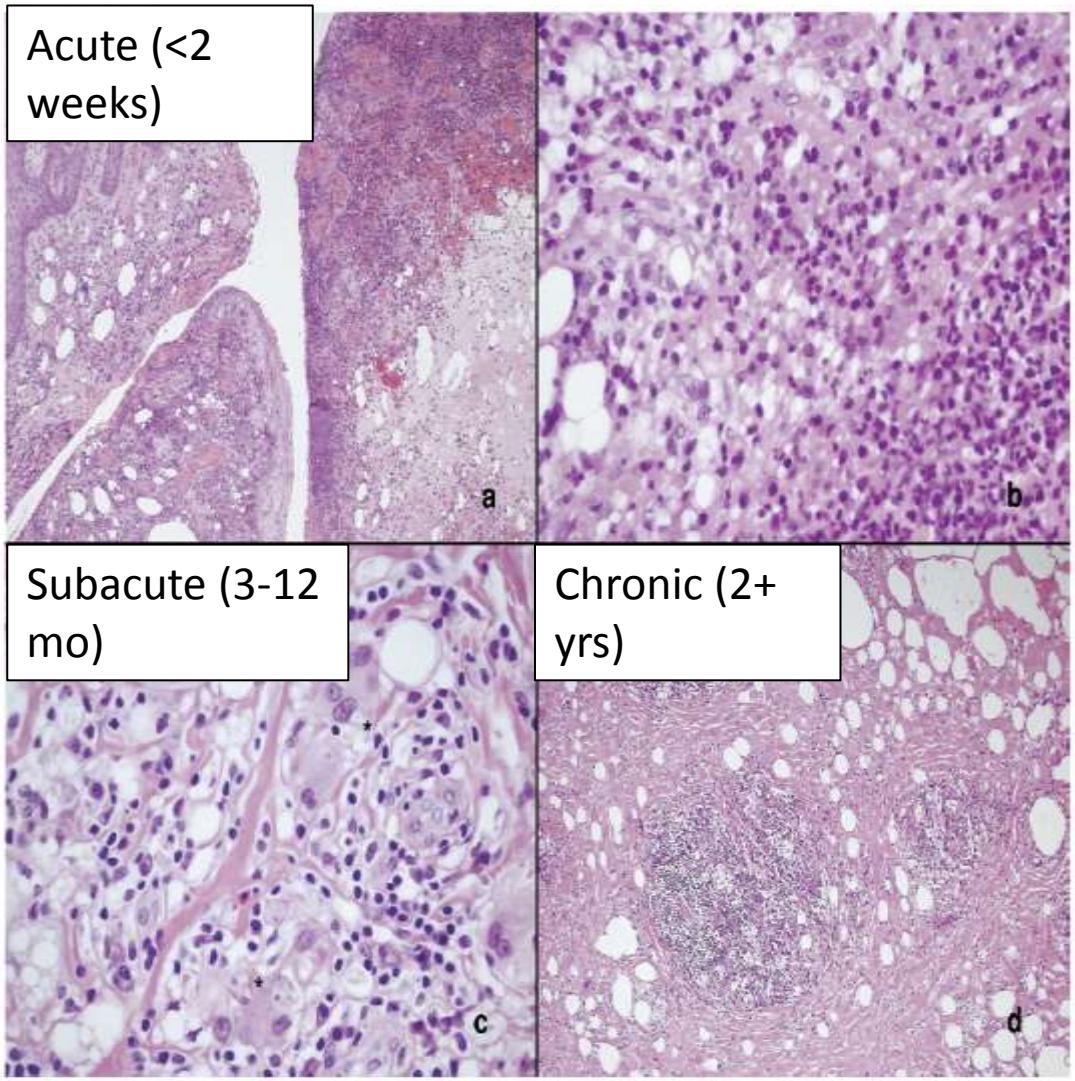
  - Usually accompanied by a histiocytic or foreign body granulomatous infiltrate with or without eosinophils.

  - No cytologic atypia.

  - CD68 staining is strongly positive in multinucleated giant cells and epithelioid histiocytic cells.

  - H&E diagnosis (with good history) in most cases.

# Acute, subacute and chronic phases of Vaseline injection




Nyirády P, at al. Urology. 2008 Jun;71(6):1132-7.

Treatment performed at the Mae Tao Clinic

| | Frequency | Percent |
|---|---|---|
| Surgical treatment | 507 | 74.6 |
| Conservative treatment | 173 | 25.4 |
| Total | 680 | 100 |

Svensøy JN, et al. World J Urol. 2018.

# Treatment

- Conservative

- Total or partial excision of the lesion

  *Purpose*: to excise all involved tissue

  without delay (if possible in the

  acute phase), preventing the

  chronic granulomatous processes

  that leads to necrosis and severe

  deformity of the penis.

# Summary

- Mineral oil injection in penis can produce disfiguring effects, sometimes mimicking a mass lesion and manifesting histologically as lipogranuloma.
- Histologic examination is important to exclude malignancy.
- History of foreign body injection is important to support the diagnosis.

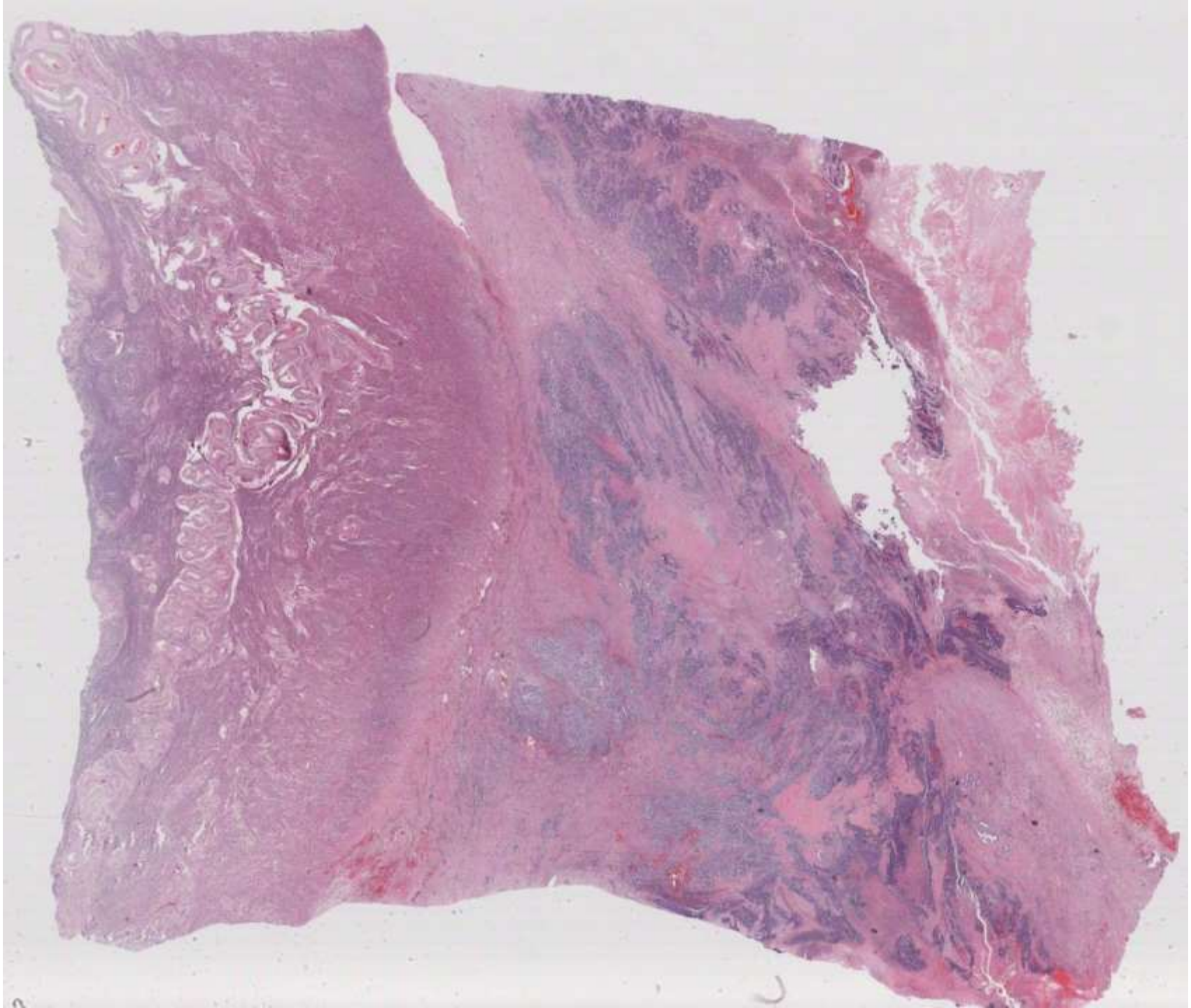
# Reference

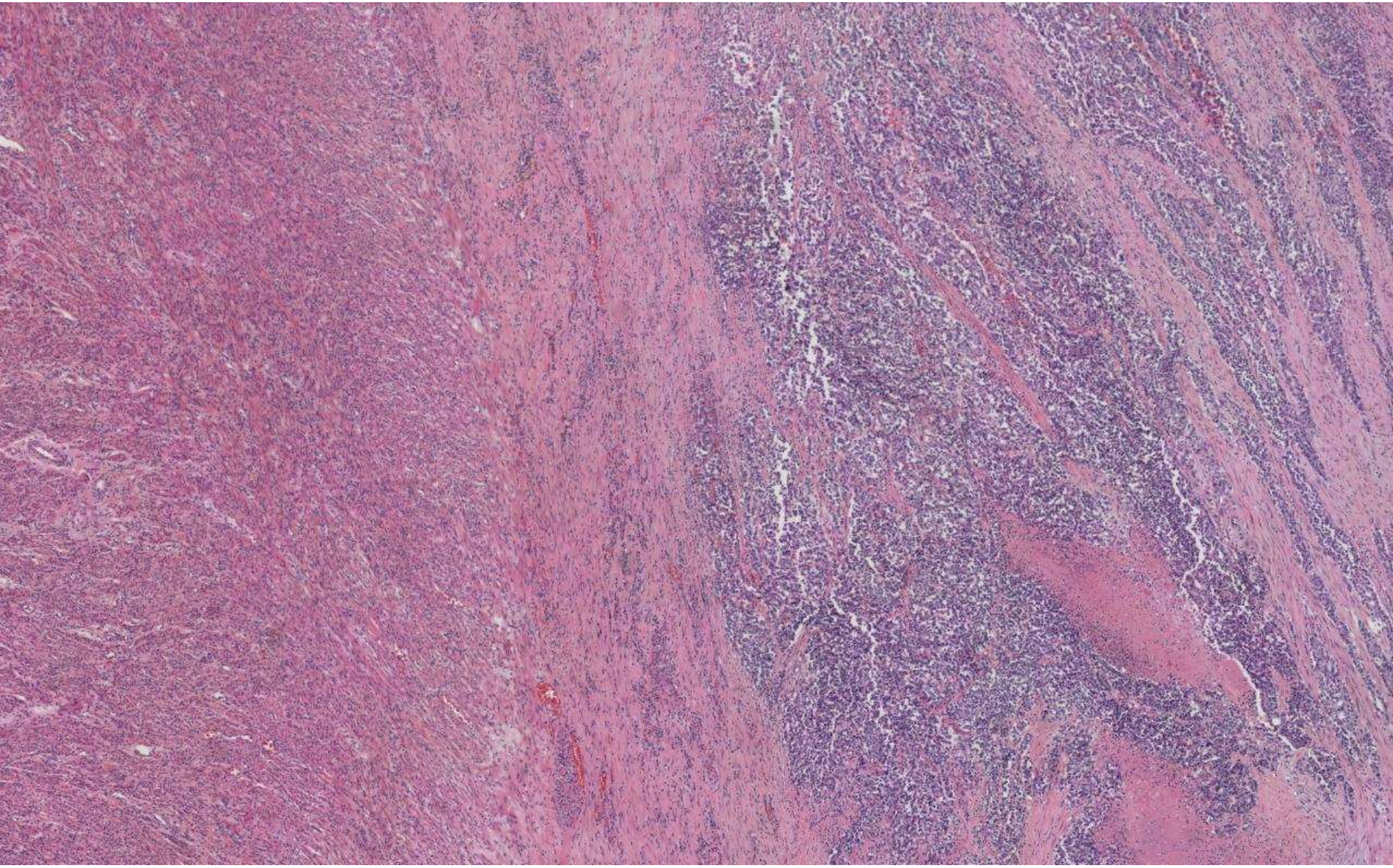

- Nyirády P, Kelemen Z, Kiss A, Bánfi G, Borka K, Romics I. Treatment and outcome of vaseline-induced sclerosing lipogranuloma of the penis. Urology. 2008 Jun;71(6):1132-7.
- Ro JY, et al. Urologic Surgical Pathology (Fourth Edition). 2020, Pages 853-901, 901.e1-901.e16
- Lawrentschuk N, Angus D, Bolton DM. Sclerosing lipogranuloma of the genitalia treated with corticosteroids. Int Urol Nephrol. 2006;38(1):97-9.
- Svensøy JN, Travers V, Osther PJS. Complications of penile self-injections: investigation of 680 patients with complications following penile self-injections with mineral oil. World J Urol. 2018 Jan;36(1):135-143.
- Ohnmar, Geater AF, Winn T, Chongsuvivatwong V. Penile oil injection, penile implantation and condom use among Myanmar migrant fishermen in Ranong, Thailand. Sex Health. 2009 Sep;6(3):217-21.
- Rosecker Á, Bordás N, Pajor L, Bajory Z. Hungarian "jailhouse rock": incidence and morbidity of Vaseline self-injection of the penis. J Sex Med. 2013 Feb;10(2):509-15.

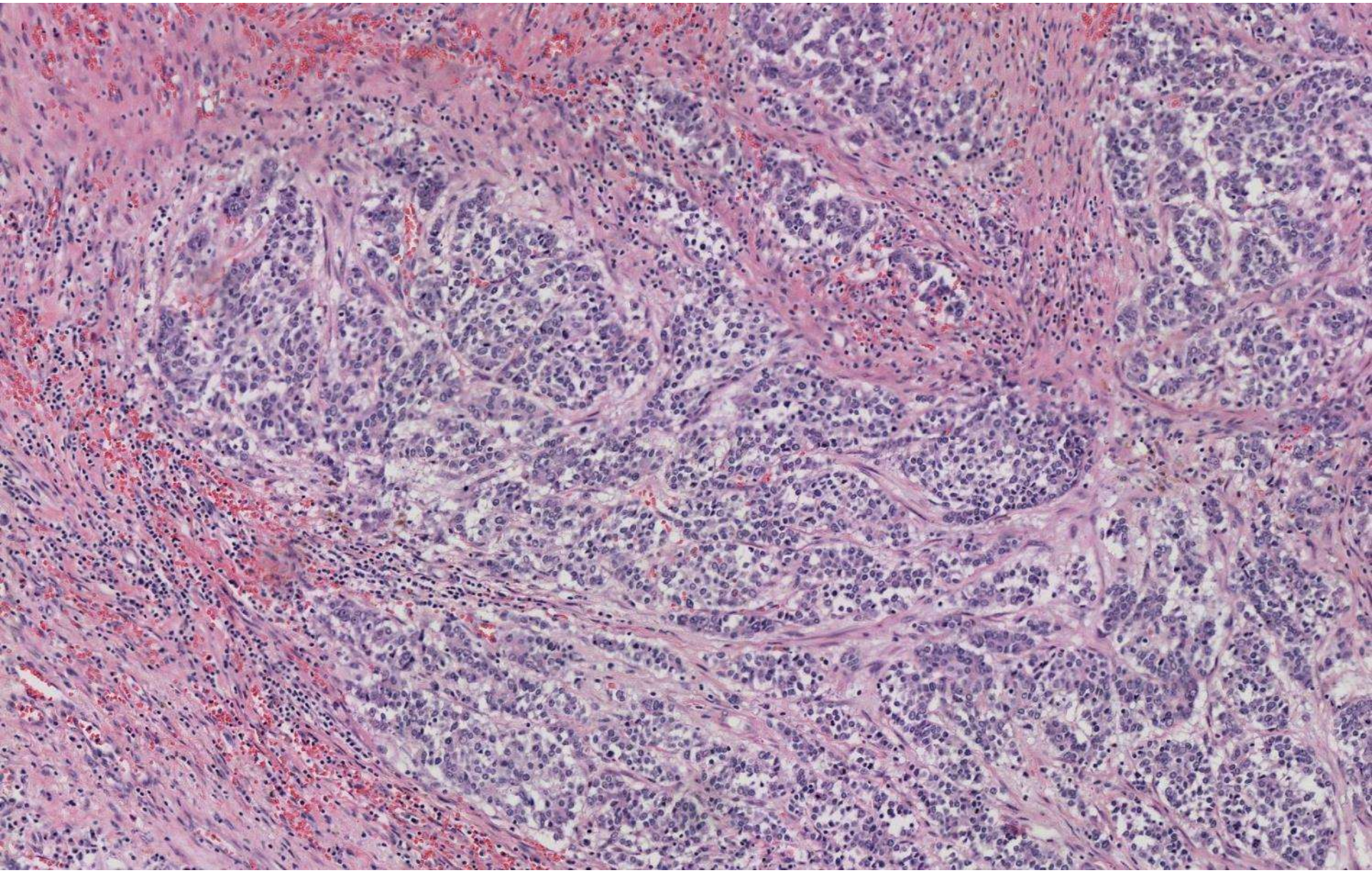
# 20-0104
# scanned slide available!

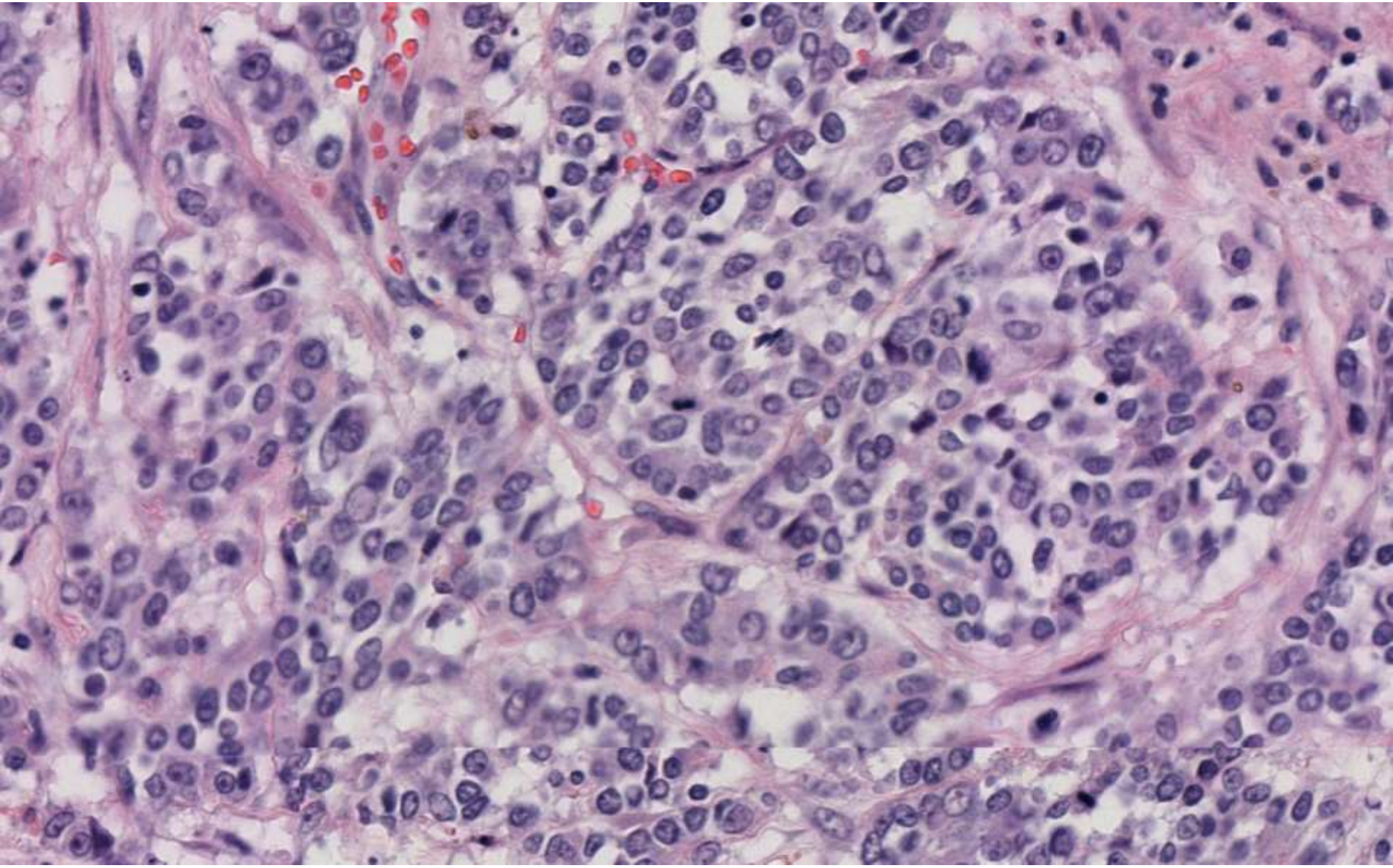
**Constance Chen/Emily Chan; UCSF**

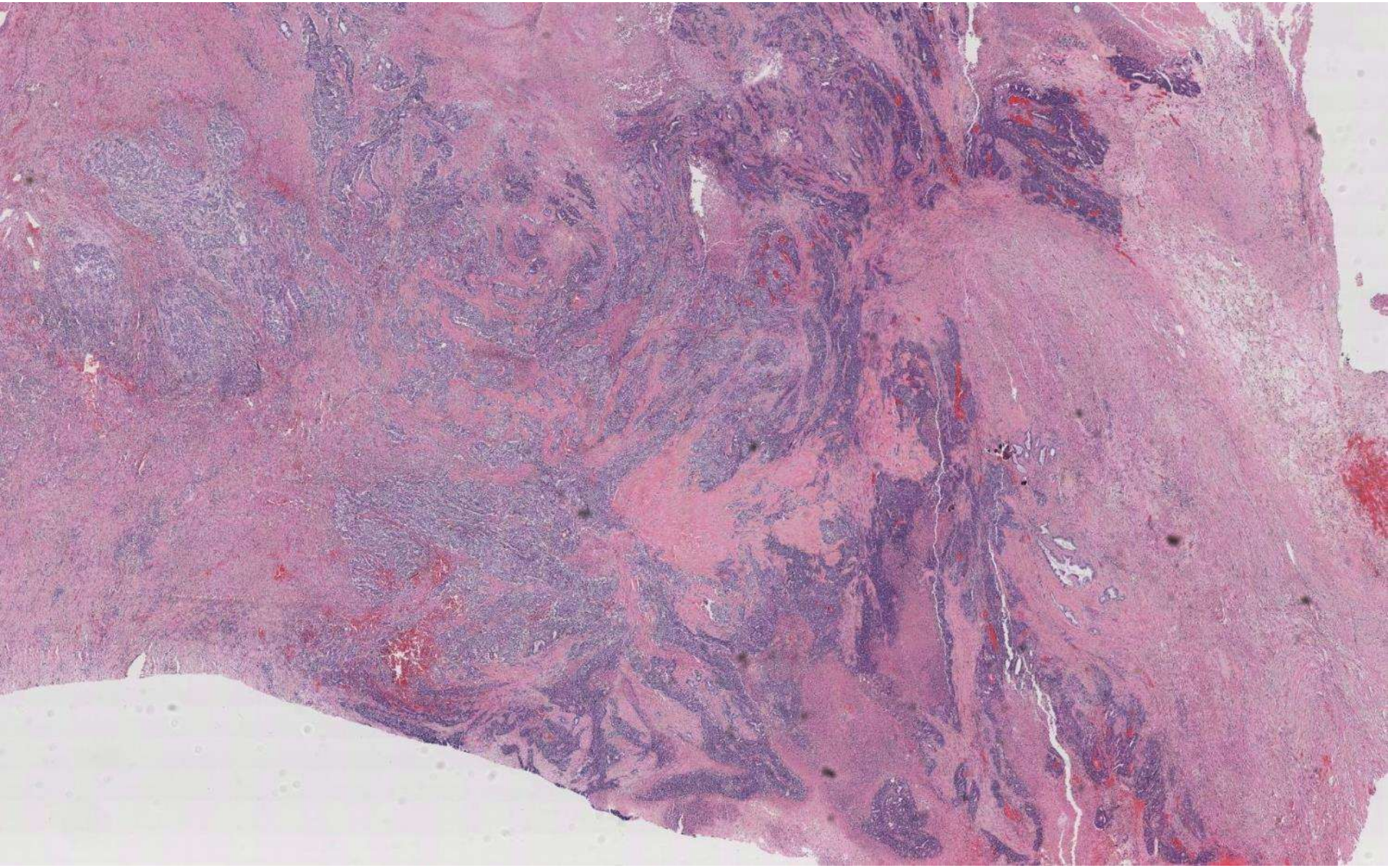
68-year-old F with a larger urinary bladder mass. She underwent radical cystectomy with hysterectomy. Her hysterectomy shows a superficial FIGO grade 1 endometrioid adenocarcinoma. Section of urinary bladder mass in relation to adhesed uterus provided.

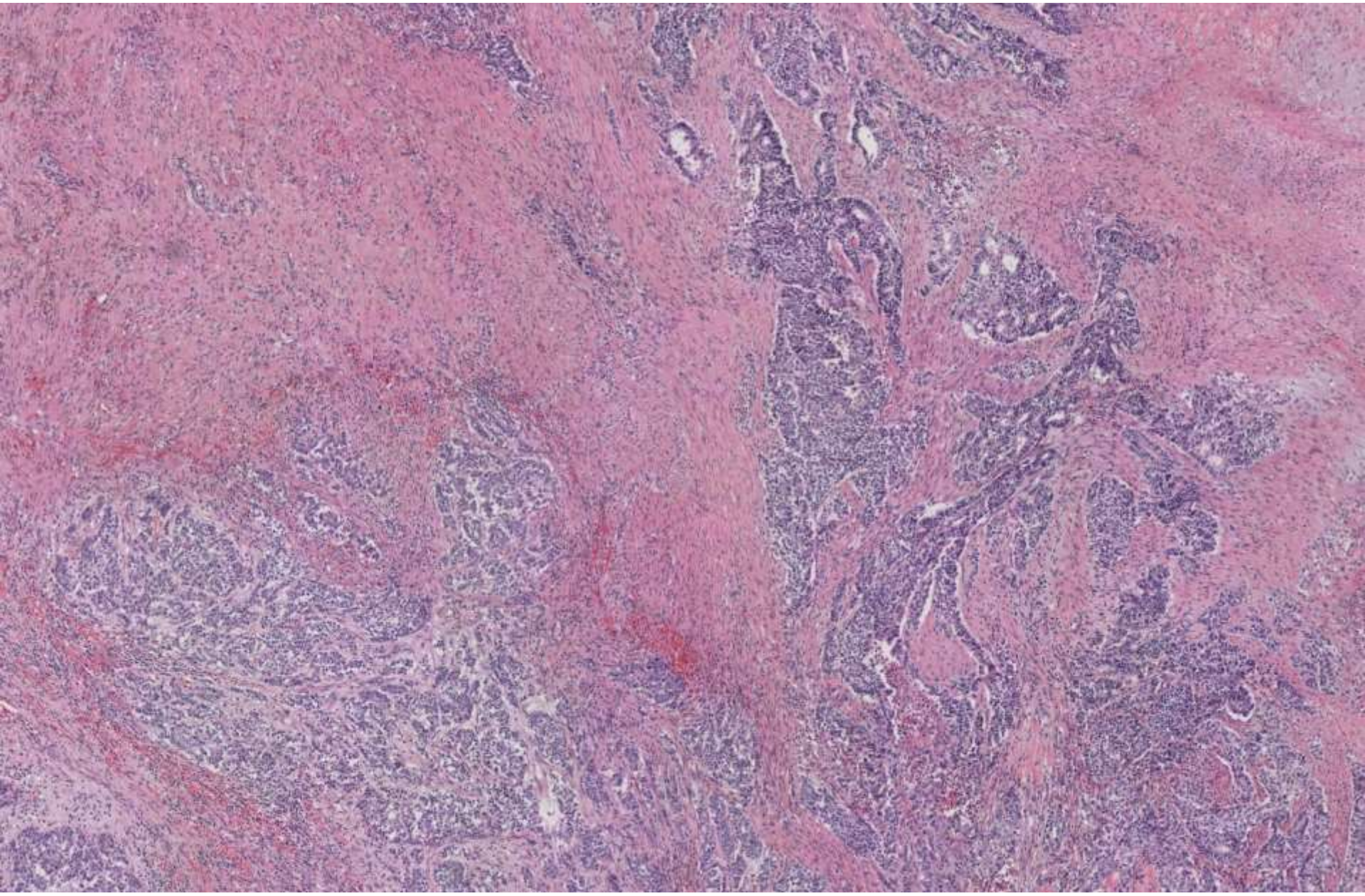


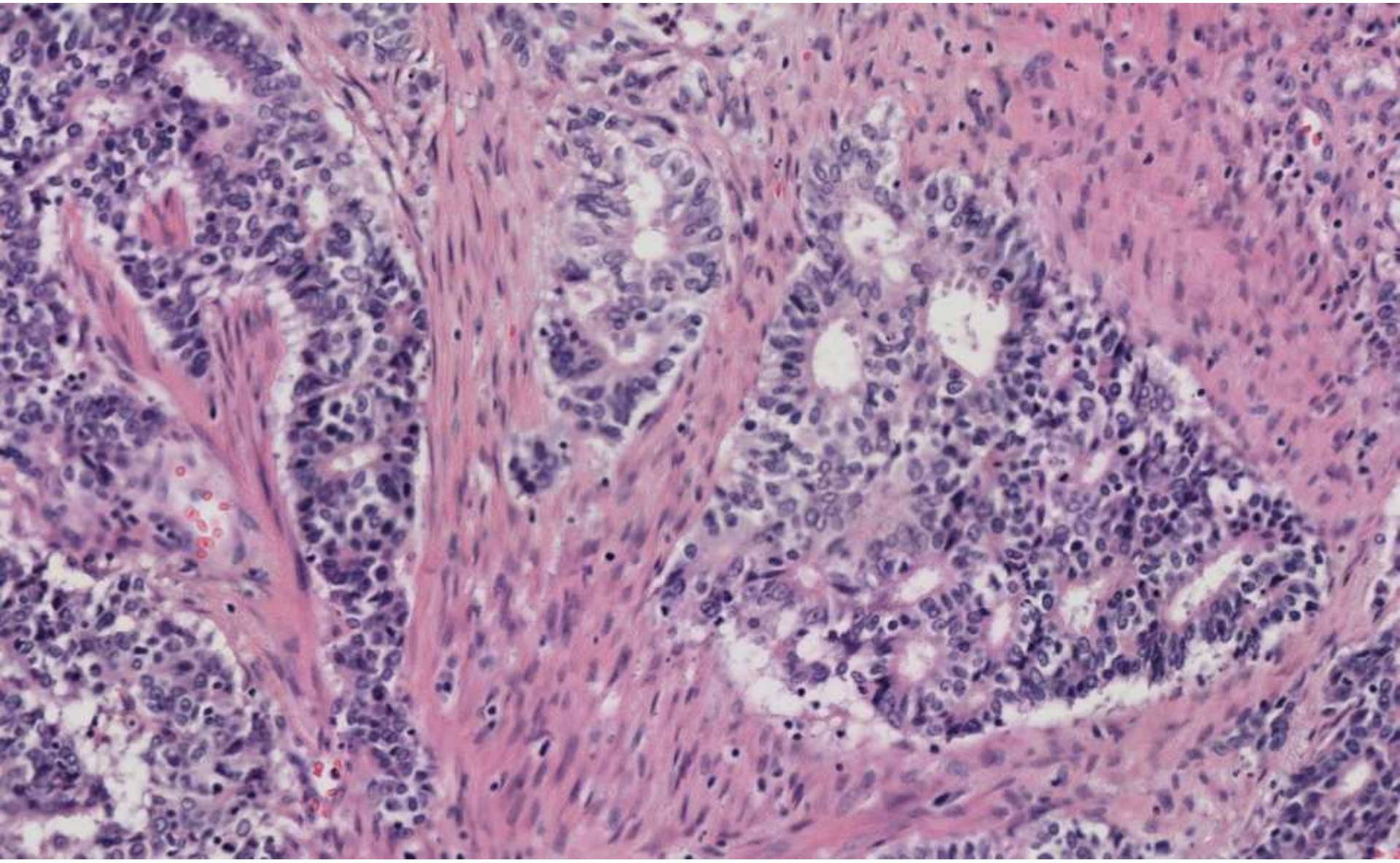


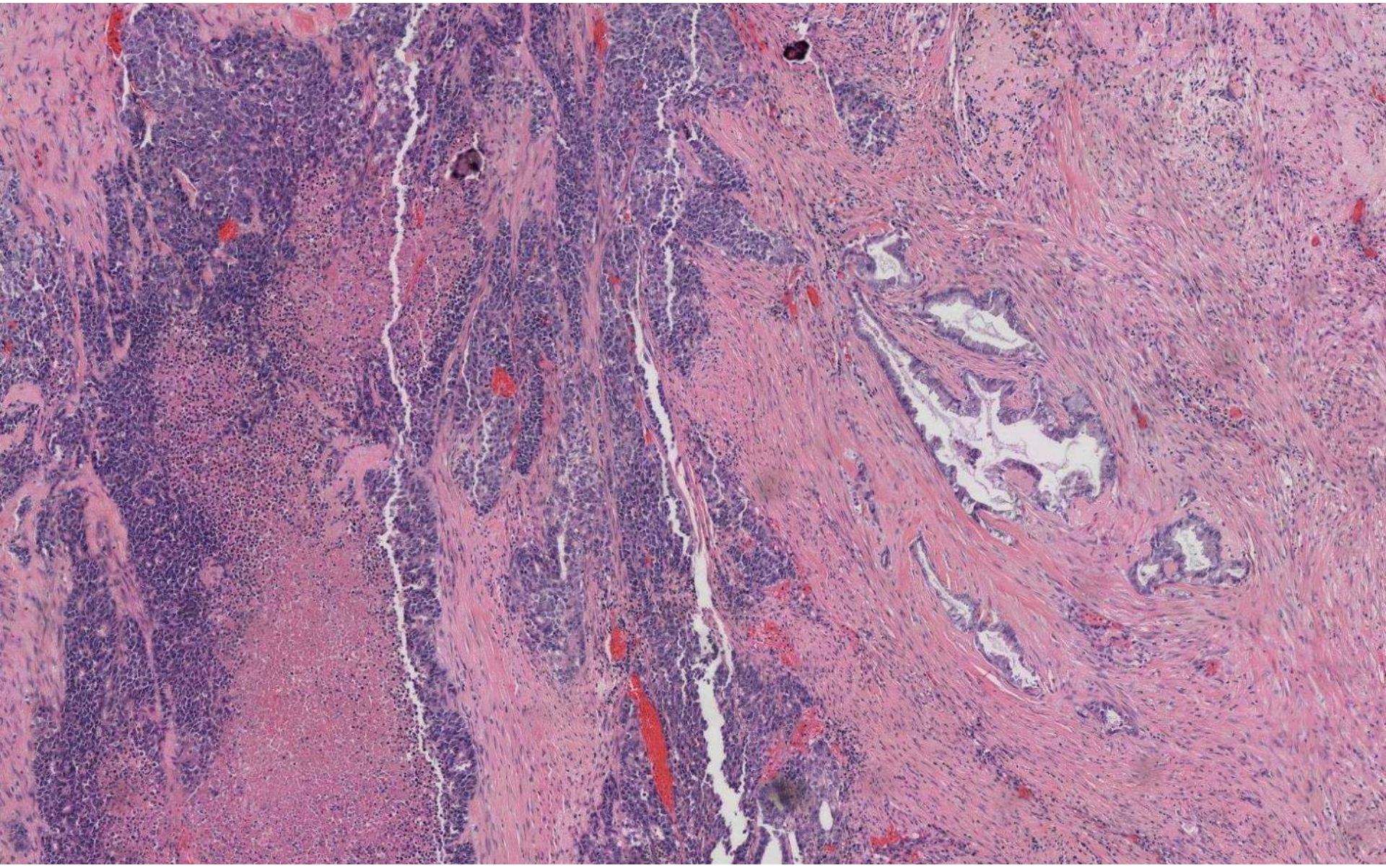


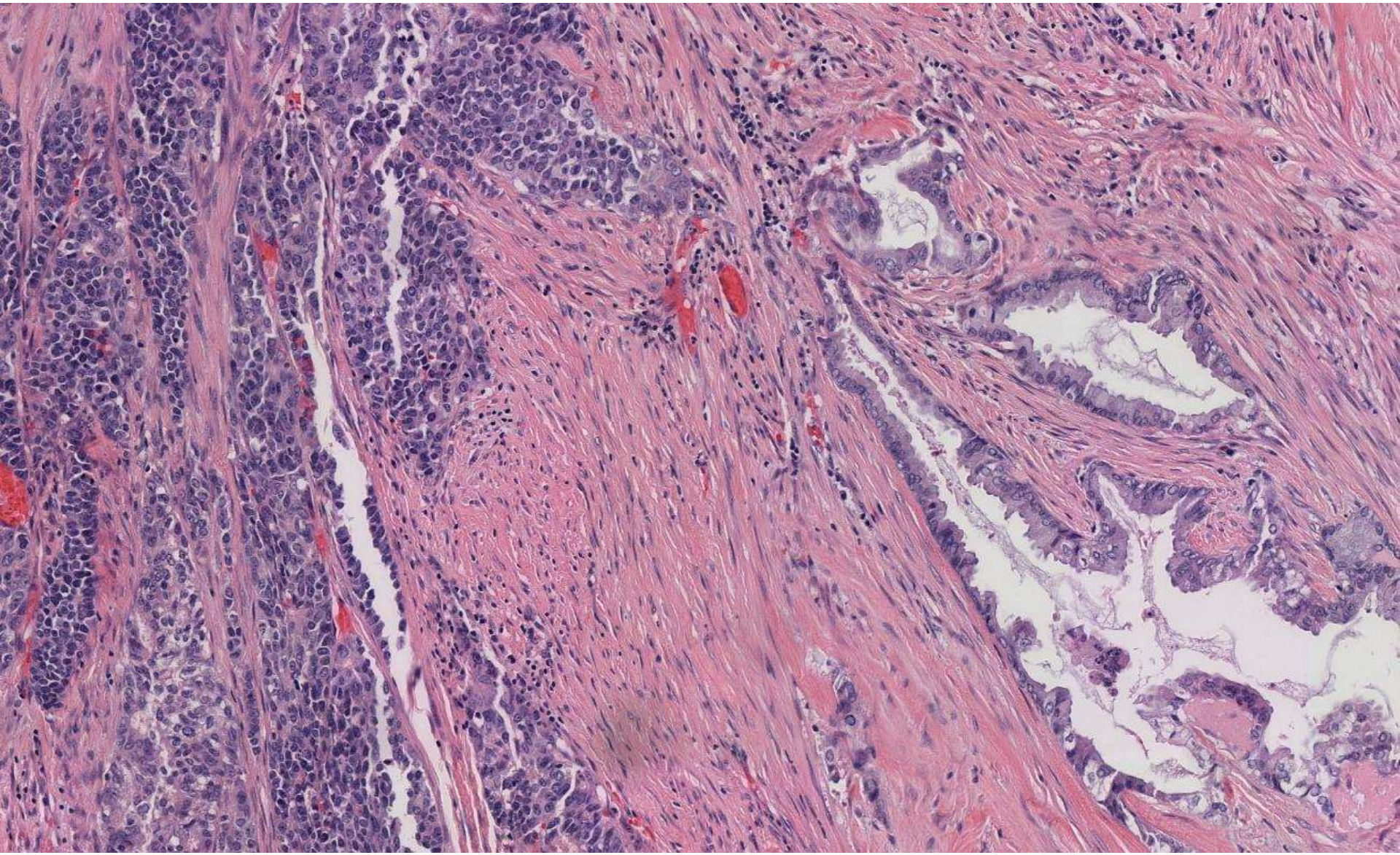


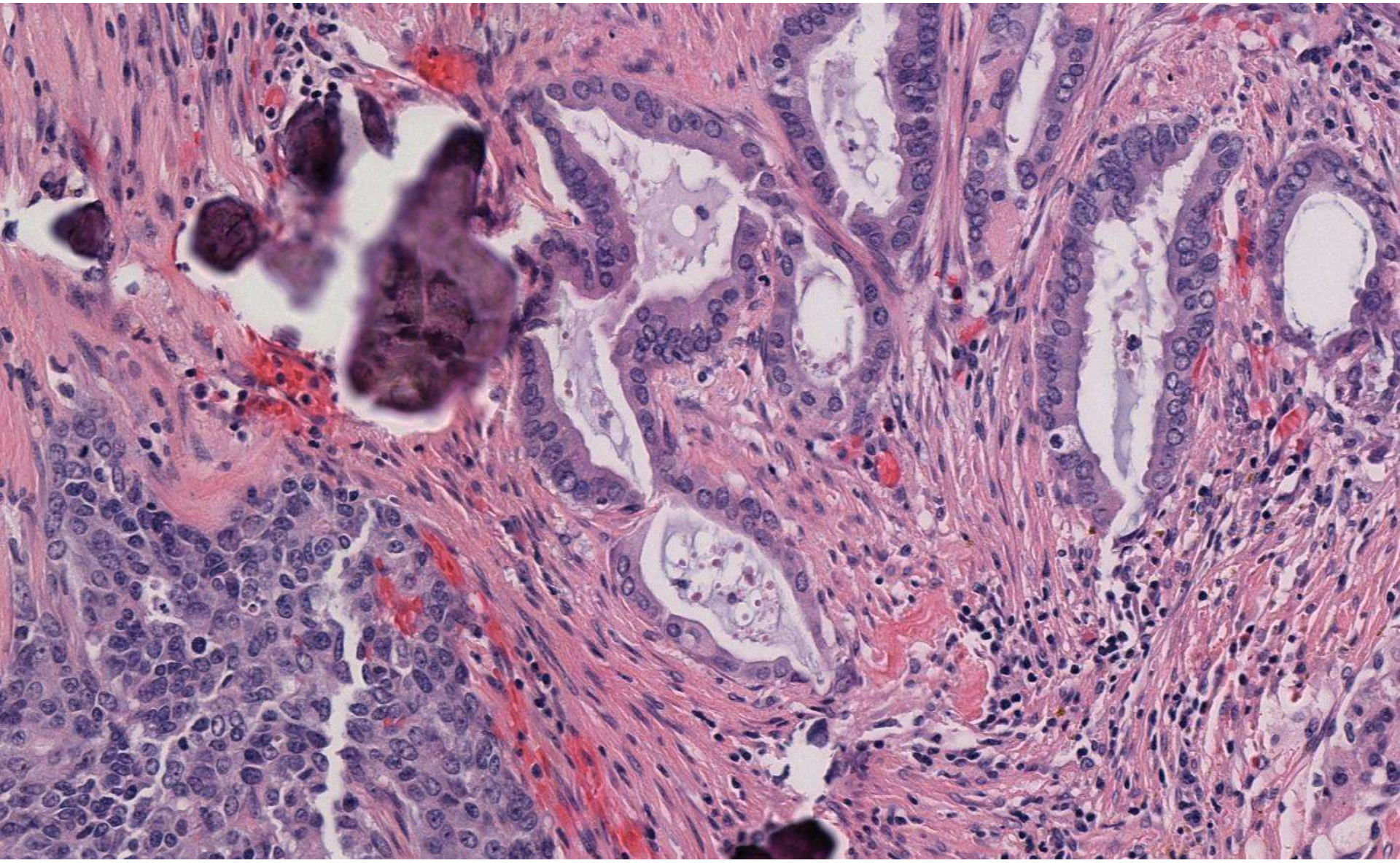


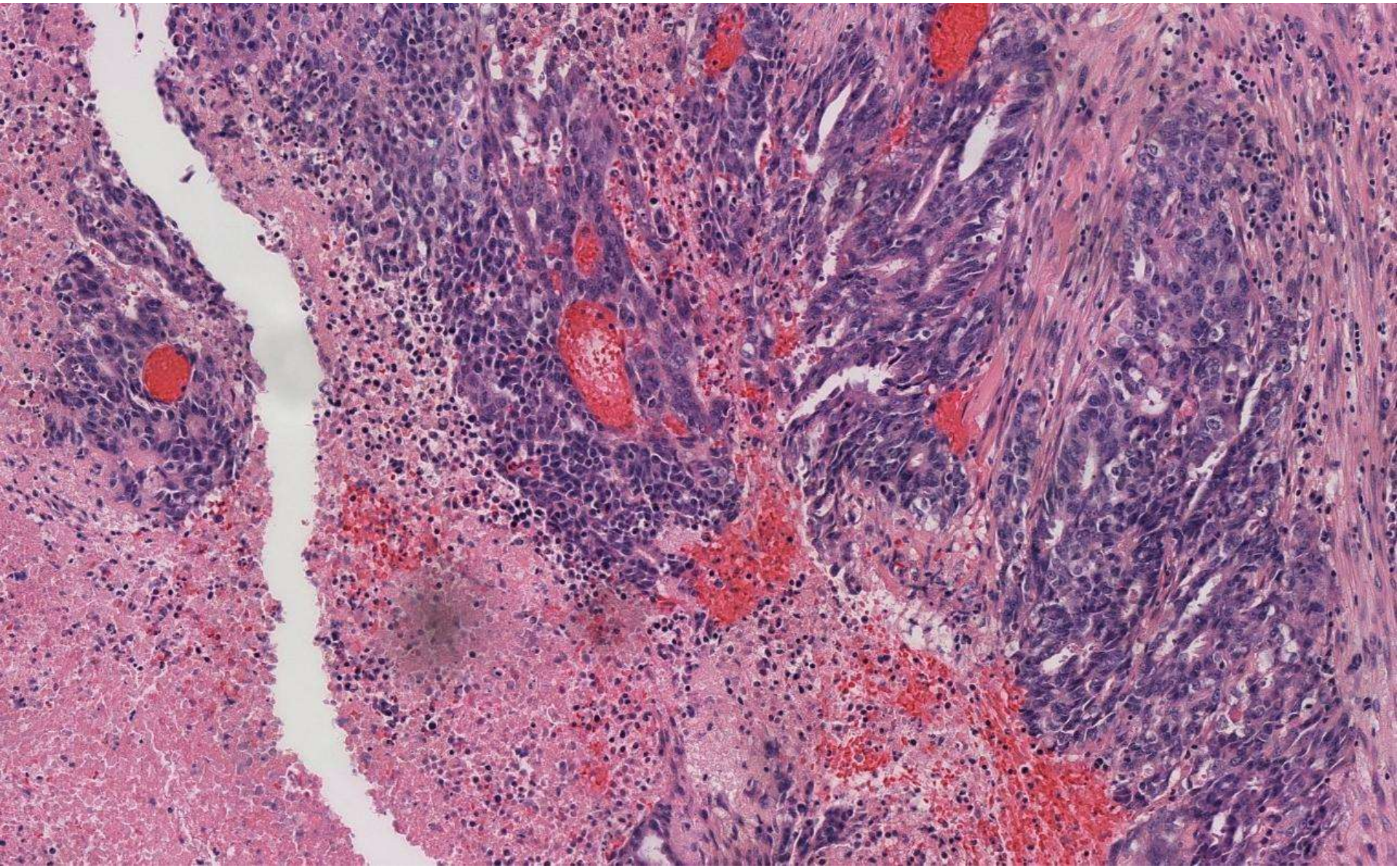












# 68-year-old woman with large urinary bladder mass

South Bay Meeting

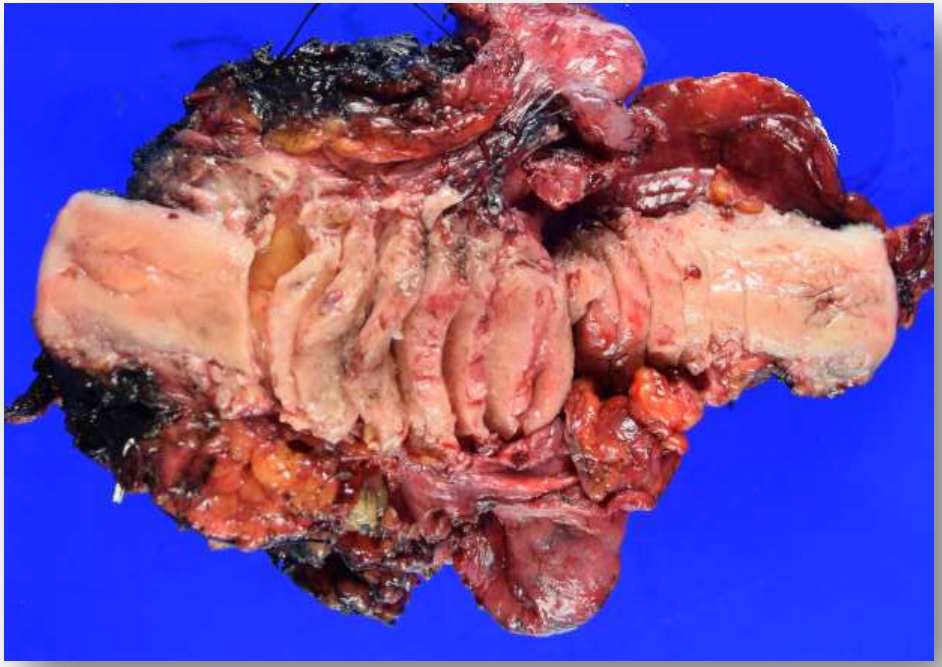
January 6, 2020

Connie Chen/Emily Chan; UCSF

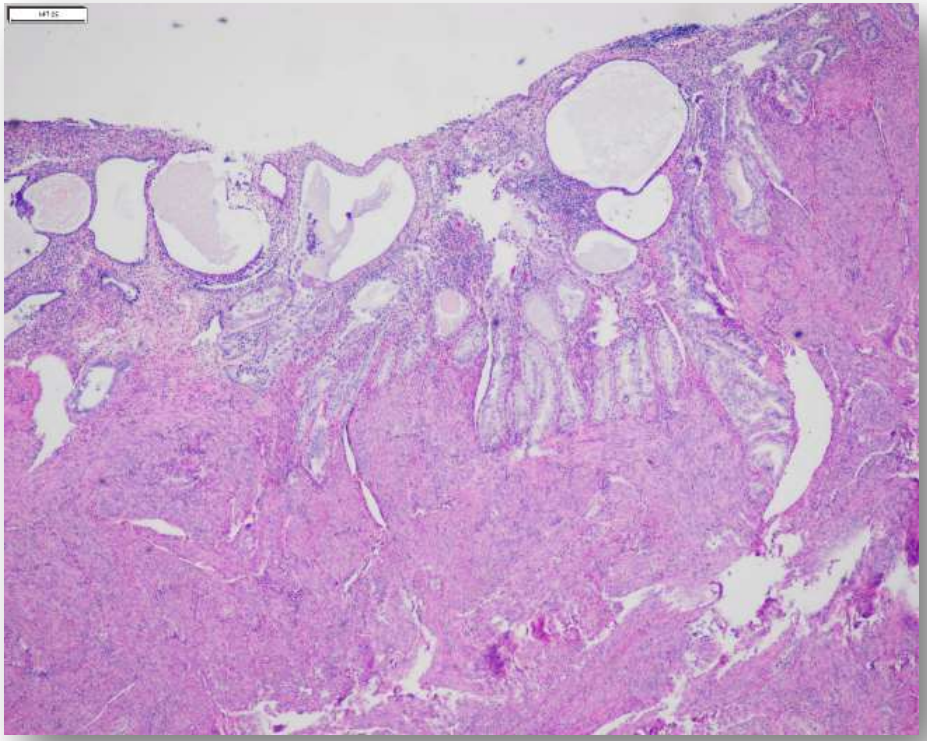
# CASE HISTORY

- 68 year-old woman with vaginal bleeding. Endometrial biopsy showed FIGO grade 1 endometrioid adenocarcinoma
- Further workup showed a large mass in the bladder
- Underwent neoadjuvant chemo followed by hysterectomy and cystectomy

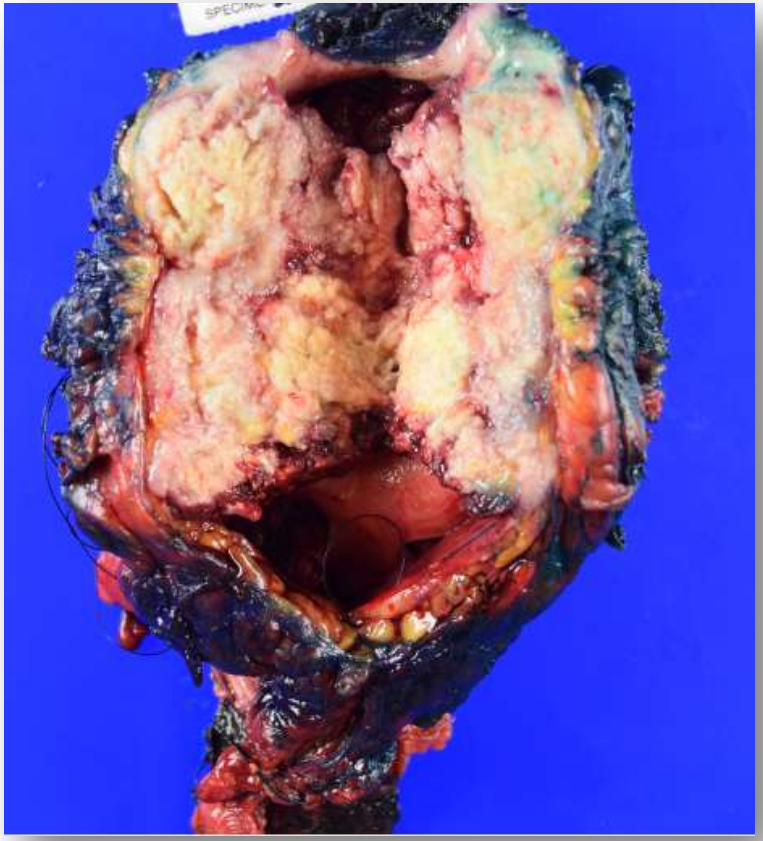
# GROSS - UTERUS



# ENDOMETRIAL TUMOR



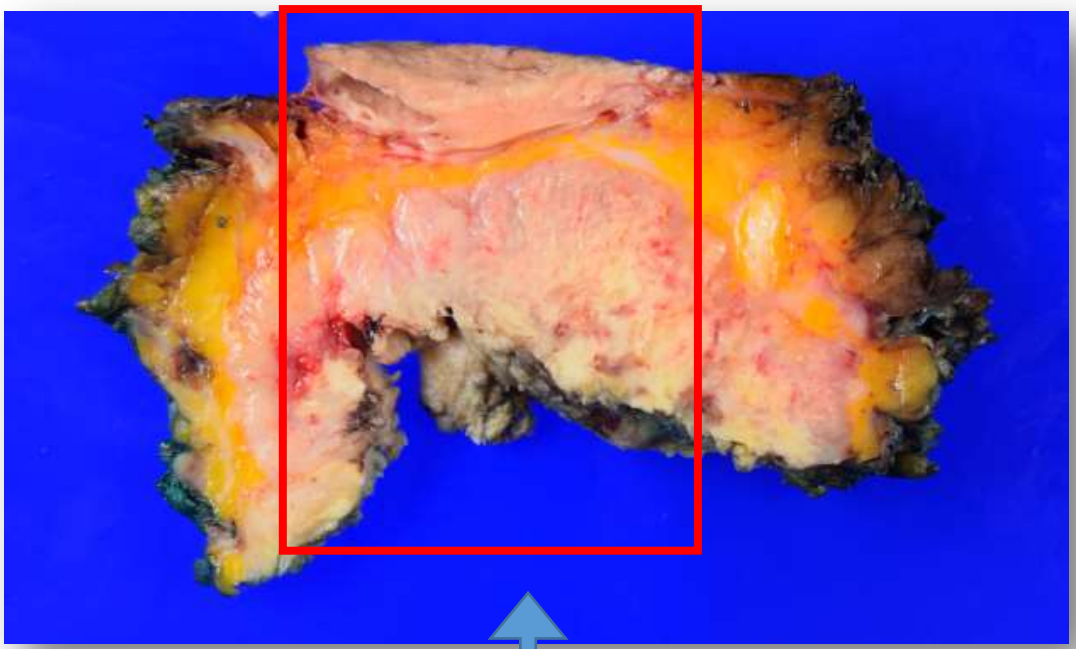
# GROSS - BLADDER



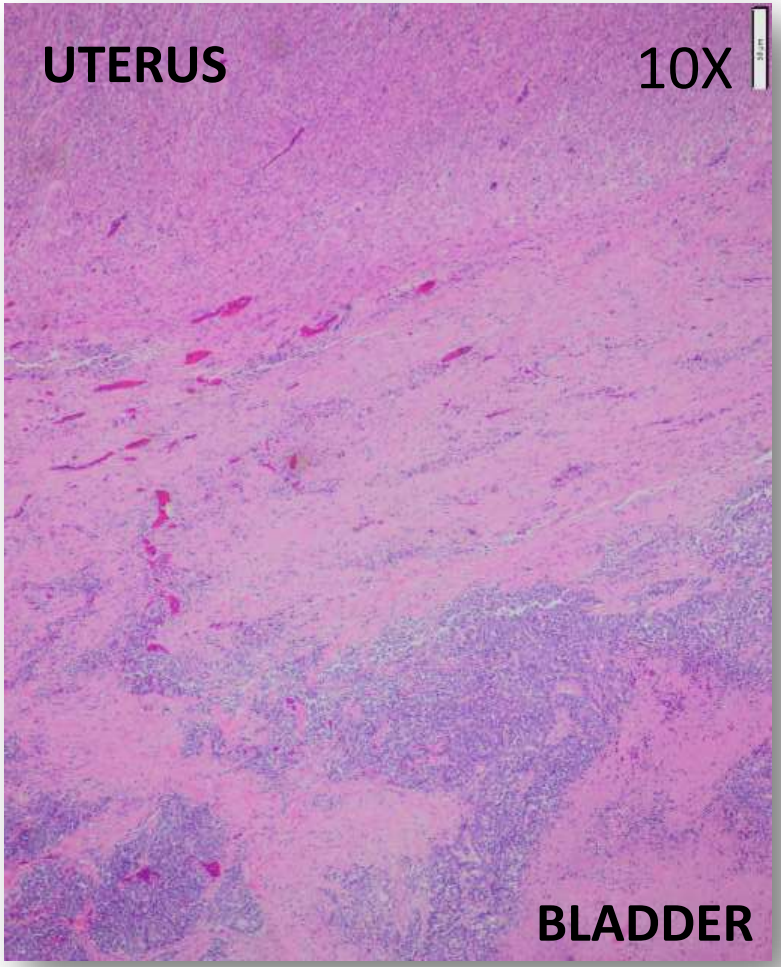
# DIFFERENTIAL DIAGNOSES

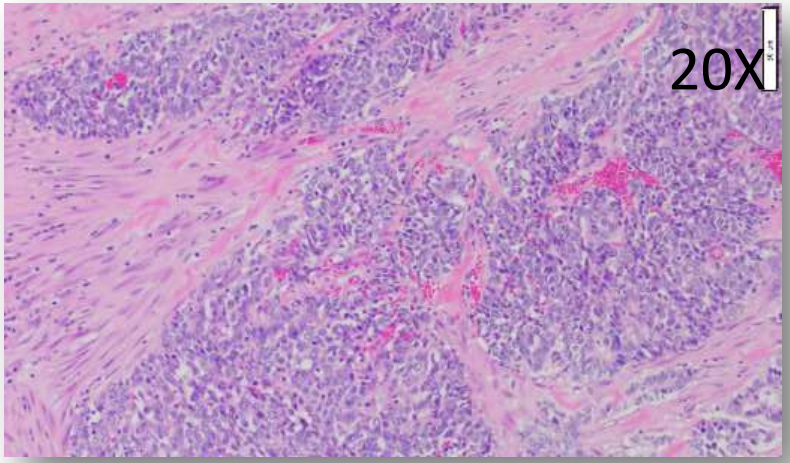
- Urothelial carcinoma (UC with glandular differentiation)
- Endometrioid adenocarcinoma
- Colonic adenocarcinoma

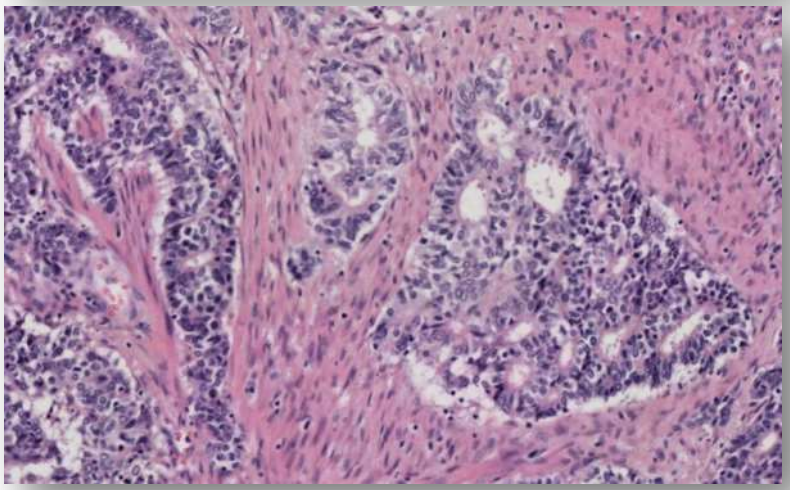
UTERINE FUNDUS



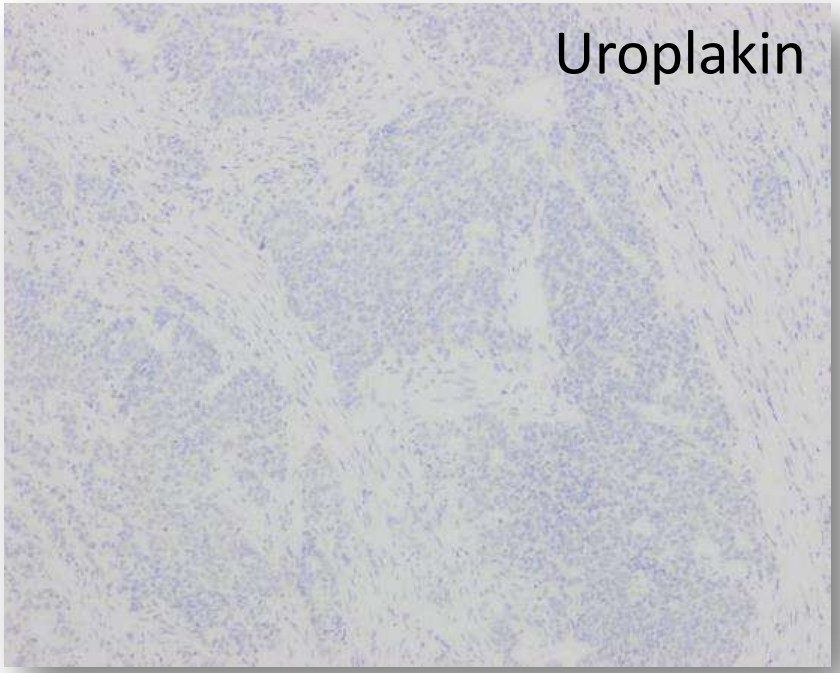
URINARY BLADDER

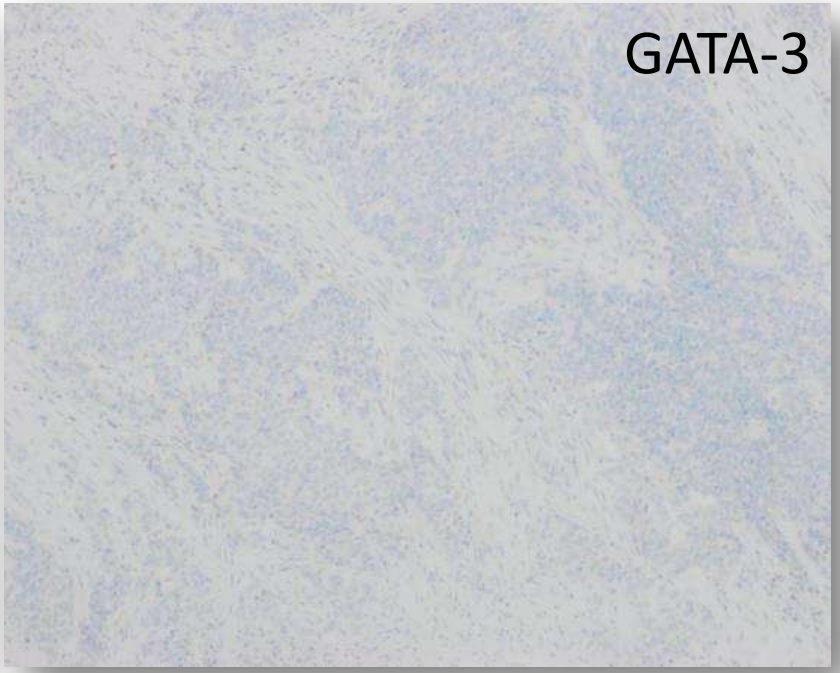

UTERUS
10X
BLADDER


20X

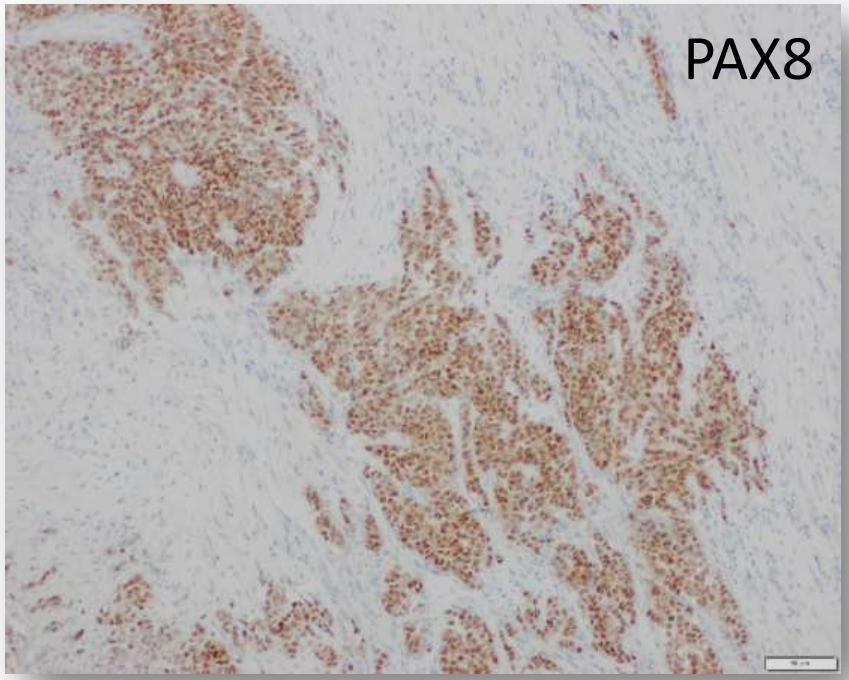


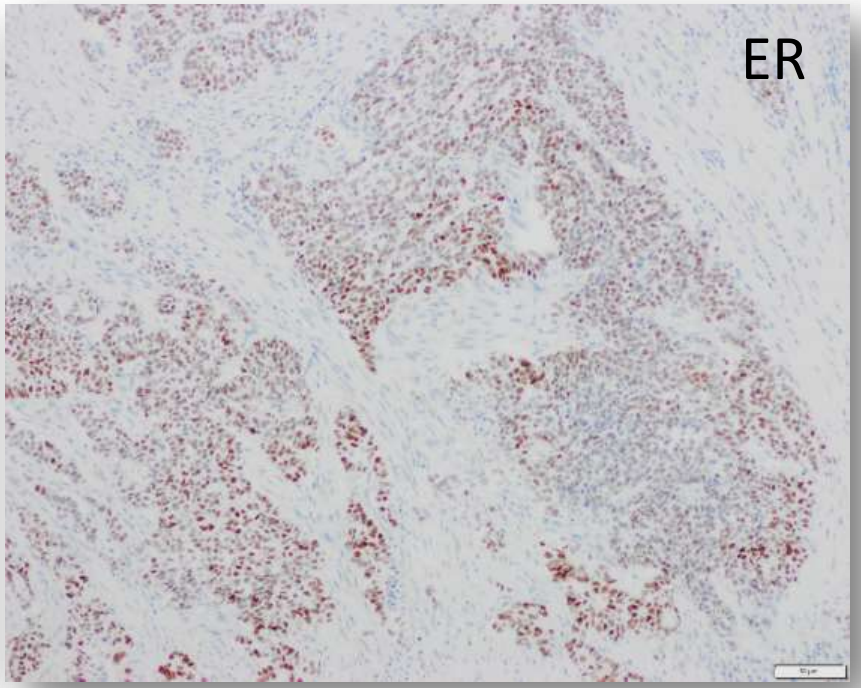
# IMMUNOHISTOCHEMICAL STAINS



# IMMUNOHISTOCHEMICAL STAINS



# FINAL DIAGNOSIS

URINARY BLADDER, UTERUS, FALLOPIAN TUBE AND OVARIES, COMPOSITE RESECTION WITH RADICAL CYSTECTOMY, HYSTERECTOMY, AND BILATERAL SALPINGO-OOPHORECTOMY:

-Urinary bladder:

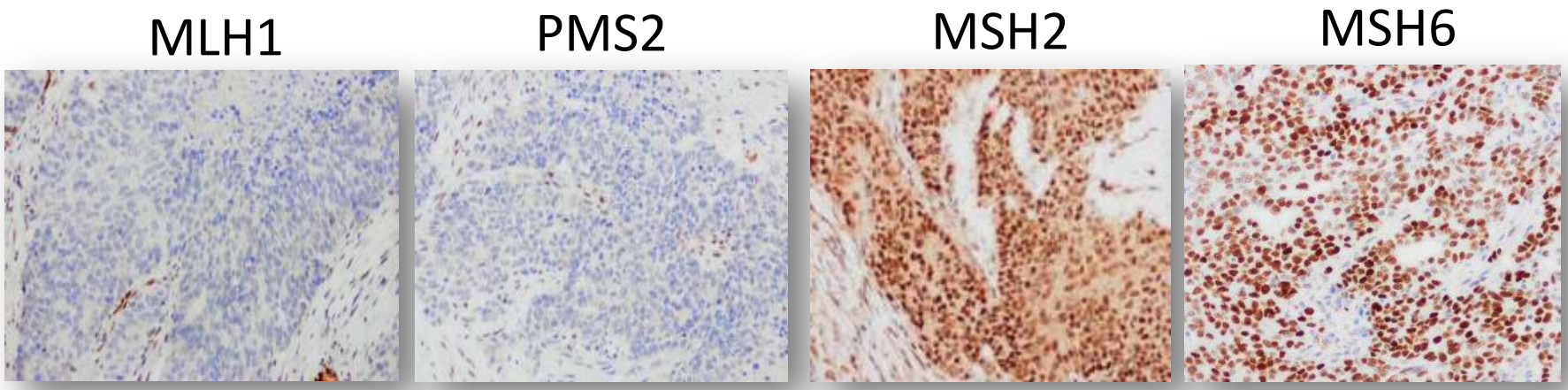
**Endometrioid adenocarcinoma, FIGO Grade 3, extensively involving urinary bladder**

-Endometrium:

**Endometrioid adenocarcinoma, FIGO Grade 1, invasion into inner-half of myometrium**

Other involved areas: Small intestine and colon

# DNA MISMATCH REPAIR PROTEIN EXPRESSION IN URINARY BLADDER TUMOR




DNA mismatch repair protein expression:

**Intact** in FIGO 1 endometrioid adenocarcinoma in endometrium

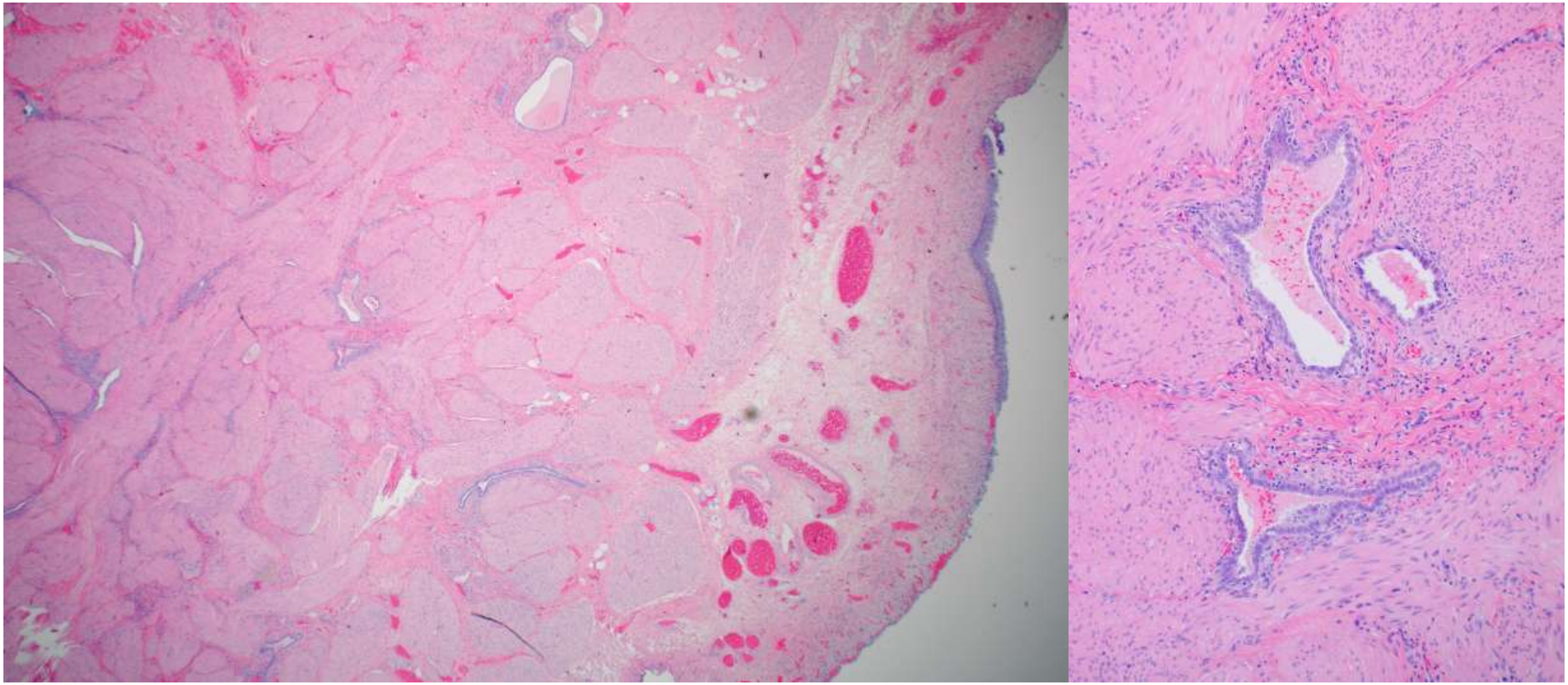
**Lost** in FIGO 3 endometrioid adenocarcinoma in bladder

UCSF Clinical Cancer Genomics Laboratory

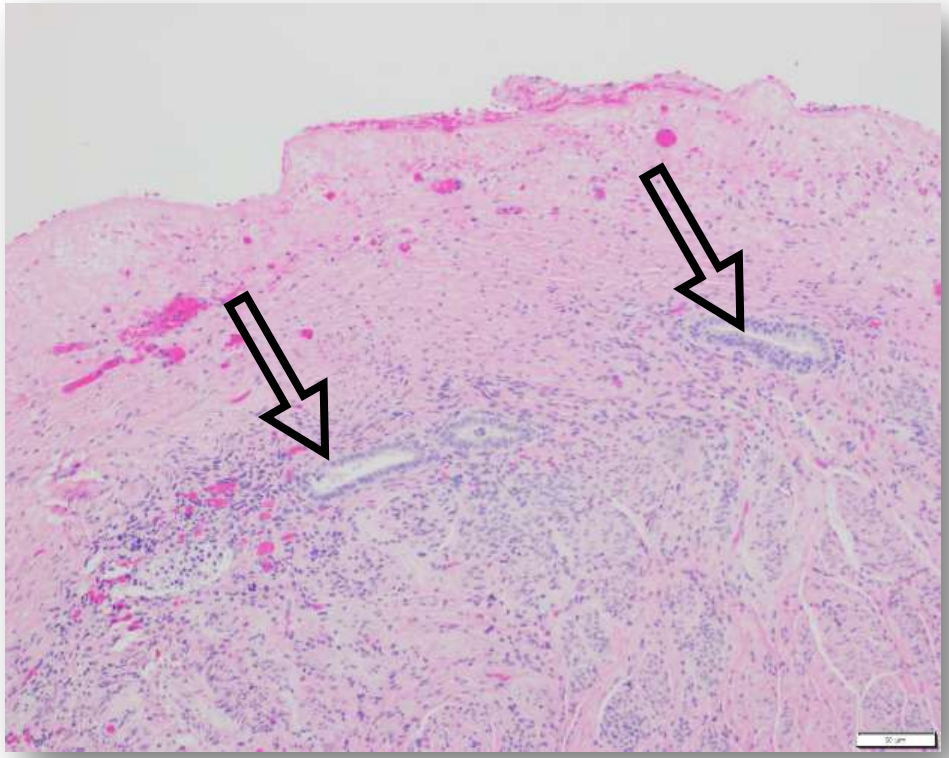
In this bladder tumor, UCSF500 was performed:

- More than 50 somatic mutations present ("hypermutated" genotype) in urinary bladder endometrioid adenocarcinoma
  - ARID1A, ARID1B, KMT2D, MSH3, PIK3R1, PTEN, TP53….
- Positive MLH1 promoter methylation

# EXAMPLE OF ENDOMETRIOSIS IN THE BLADDER



# ENDOMETRIOSIS IN UTERINE SEROSA



# MALIGNANT TRANSFORMATION

- Endometriosis occurs in 10-15% women of reproductive age
- Malignant transformation occurs in up to 0.7%-1.6% of women with endometriosis
- Rare cases of endometrial type cancers arising from endometriosis in the bladder have been reported, most commonly clear cell carcinoma followed by endometrioid adenocarcinoma

Kobayashi, IJGC 2007.
Tarumi, et al. Gynecol Oncol Rep, 2015.

# TAKE-HOME POINTS

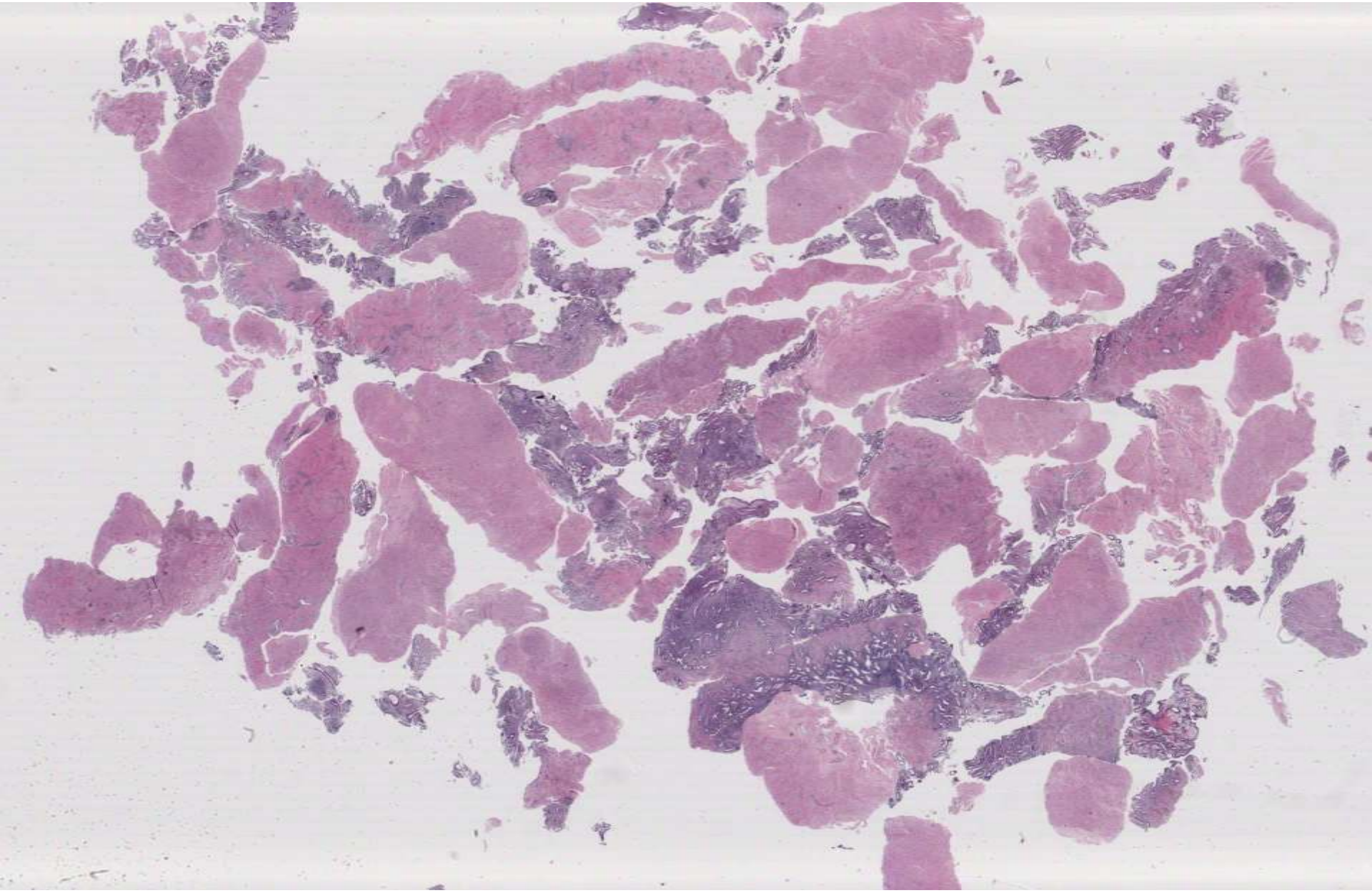
- Not all bladder tumors are urothelial carcinoma-consider other possibilities, particularly if no obvious urothelial or in situ component is seen

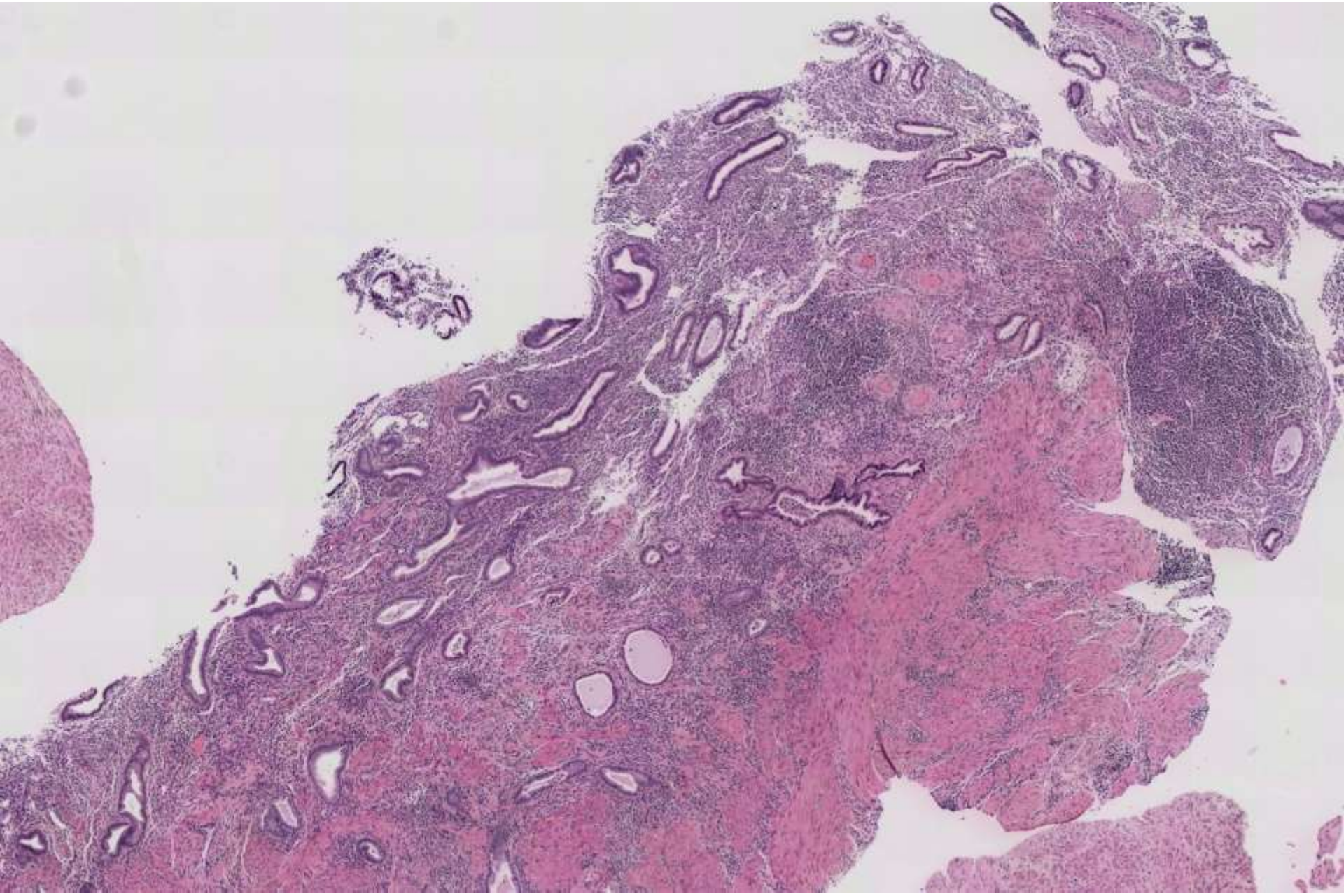
- Deep infiltrating endometriosis in the urinary bladder is rare, and malignant transformation is even rarer, but can occur-remember to exclude other primary sites.

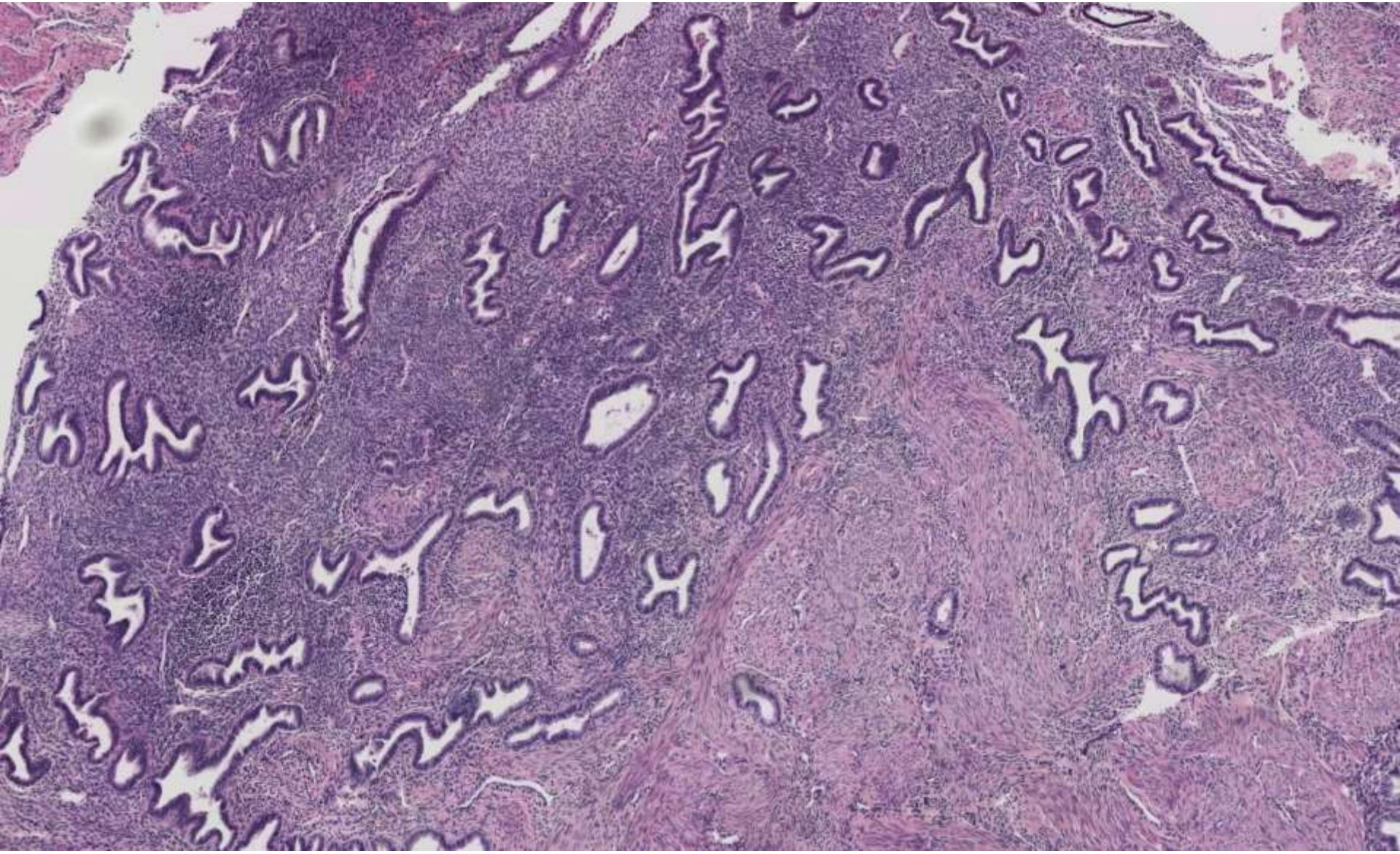
# 20-0105
# scanned slide available!

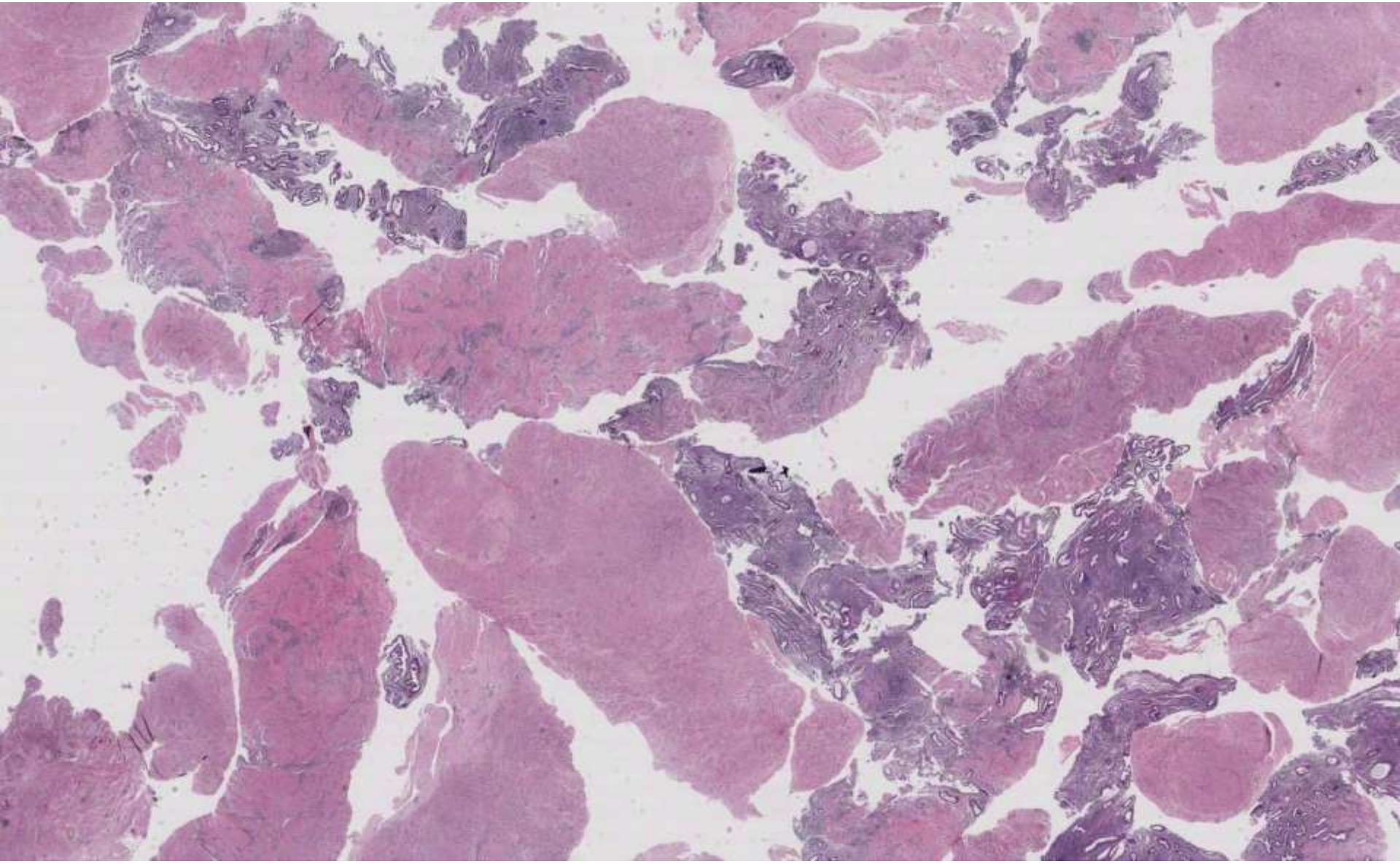
**Jordan Taylor/Charles Zaloudek; UCSF**

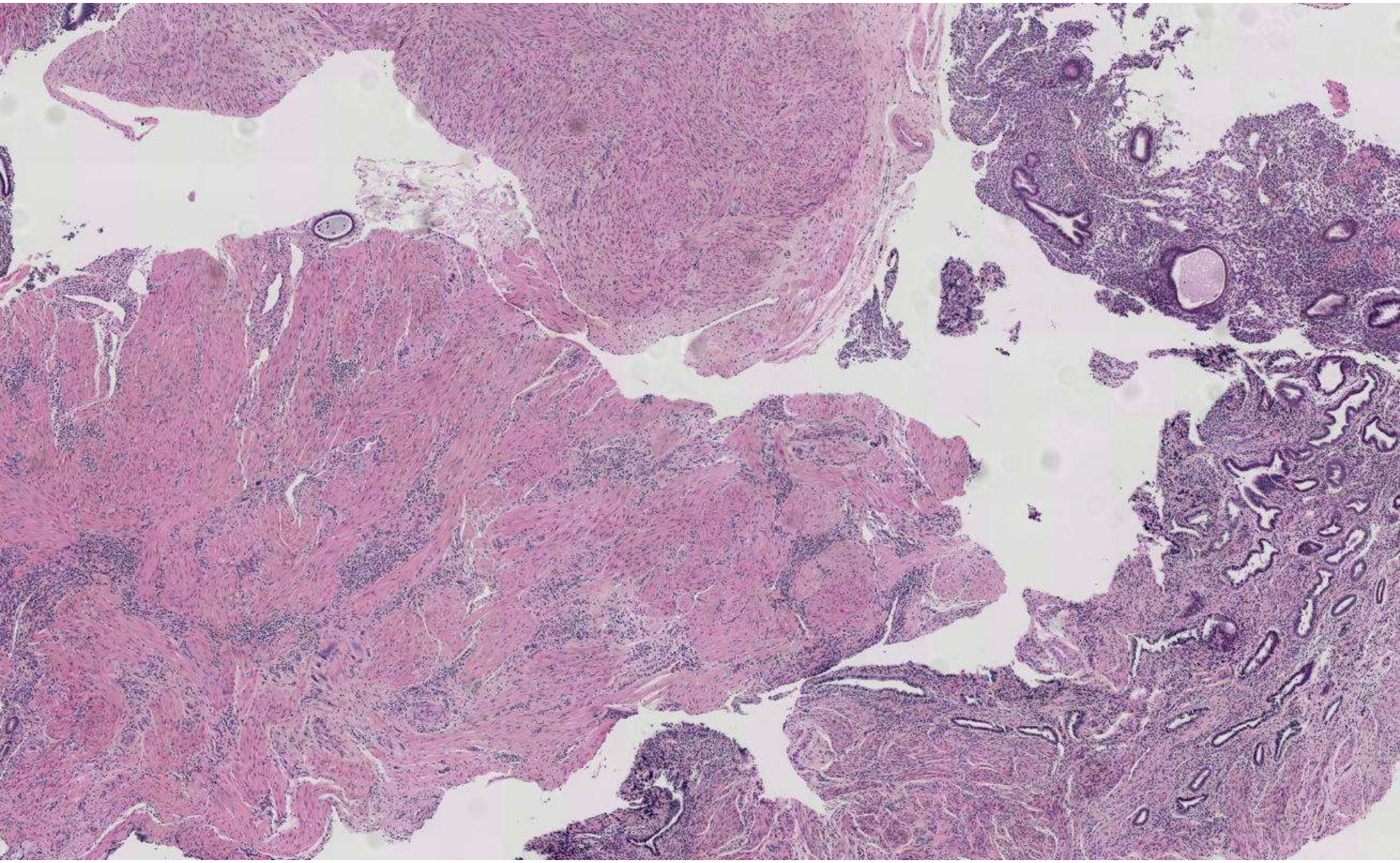
35-year-old F with fibroids, presented for hysteroscopic myomectomy.

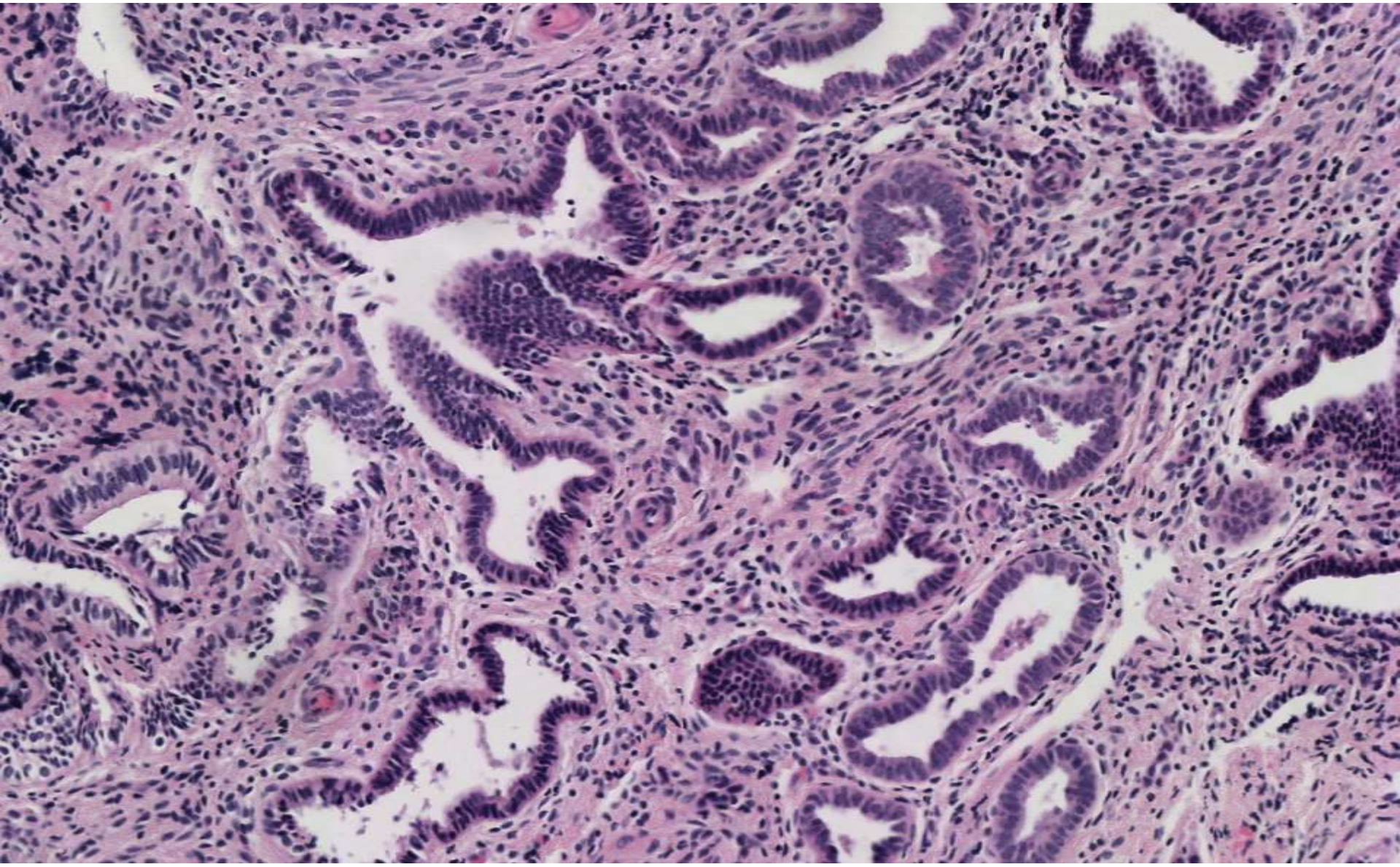


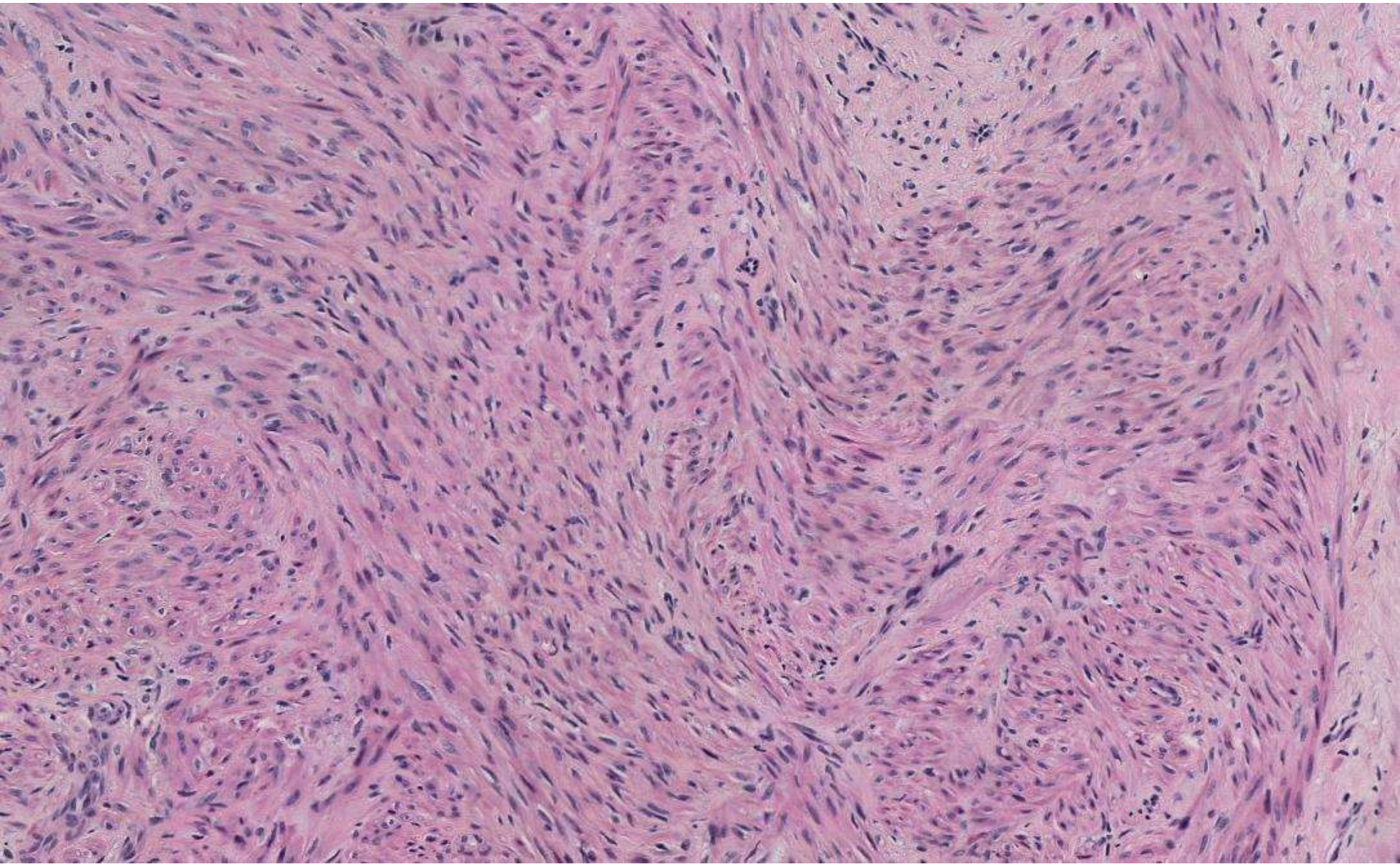


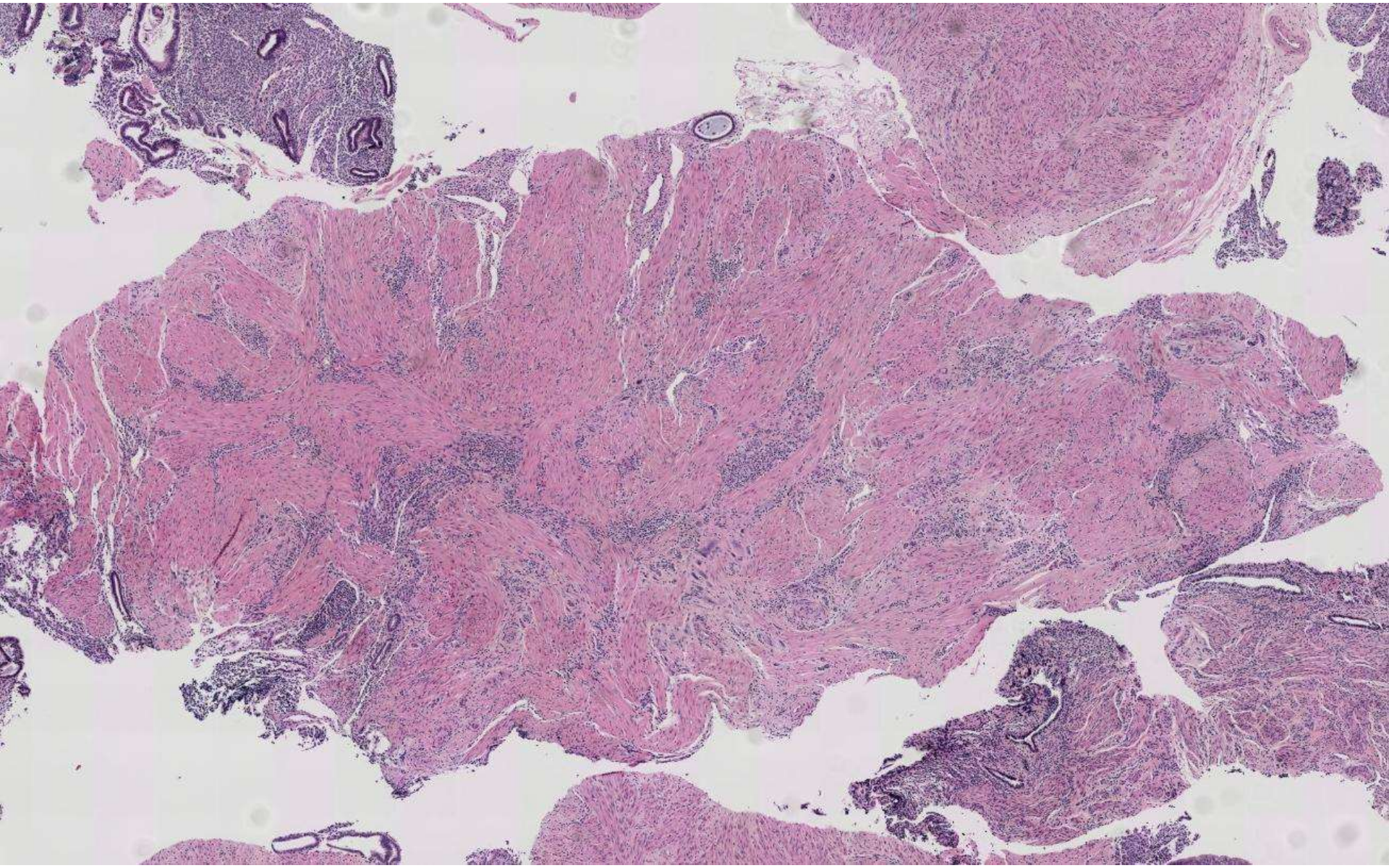


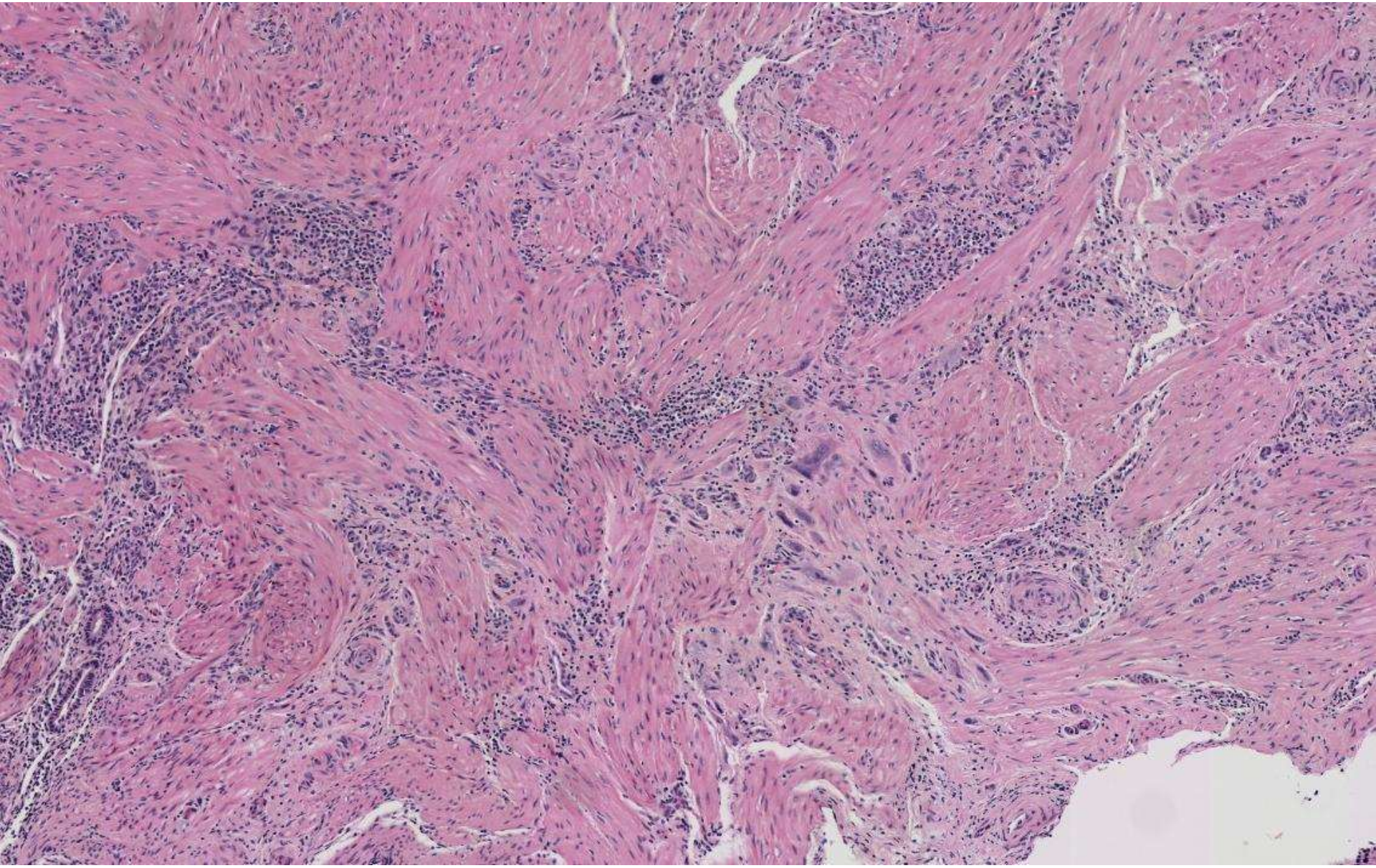


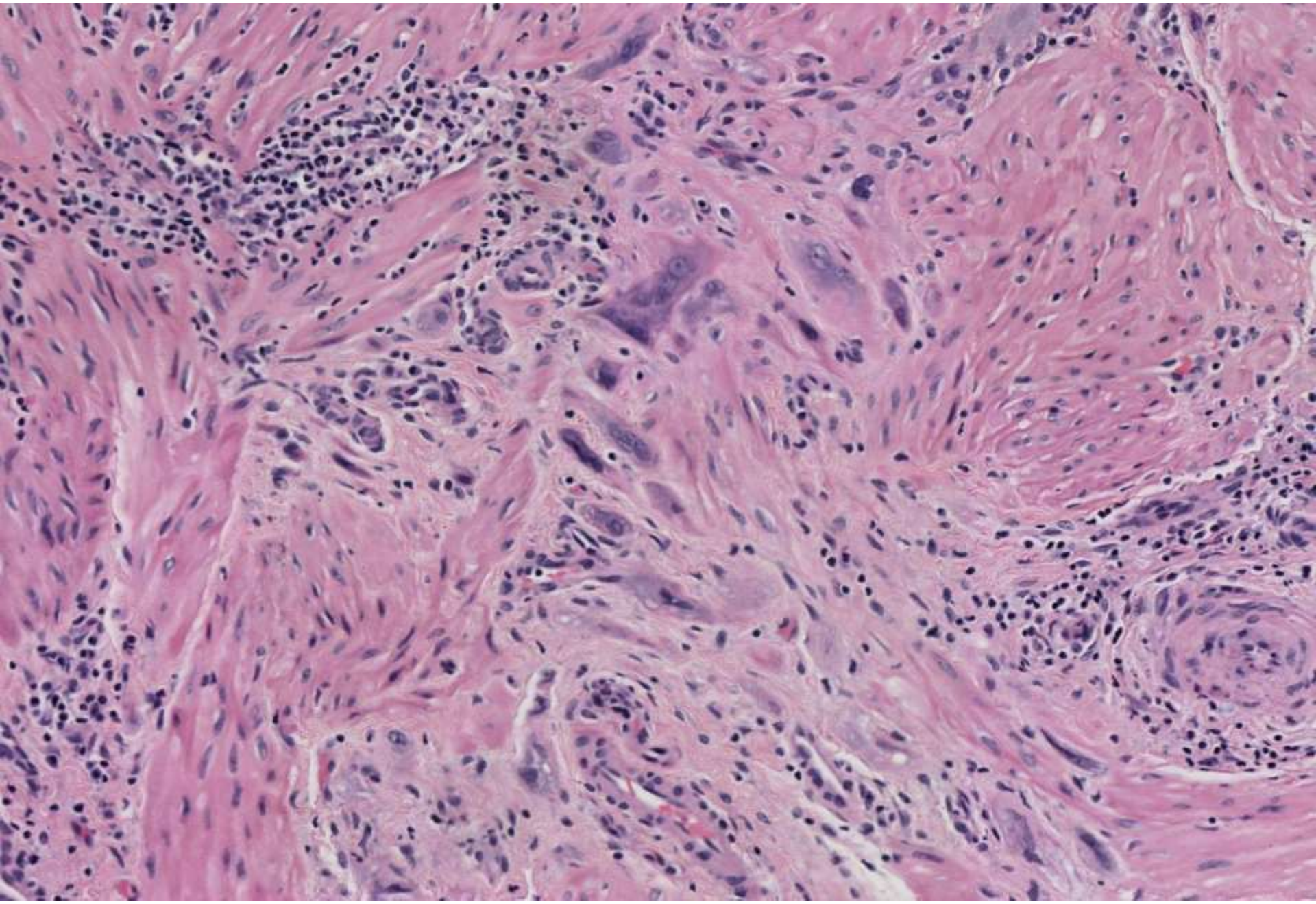


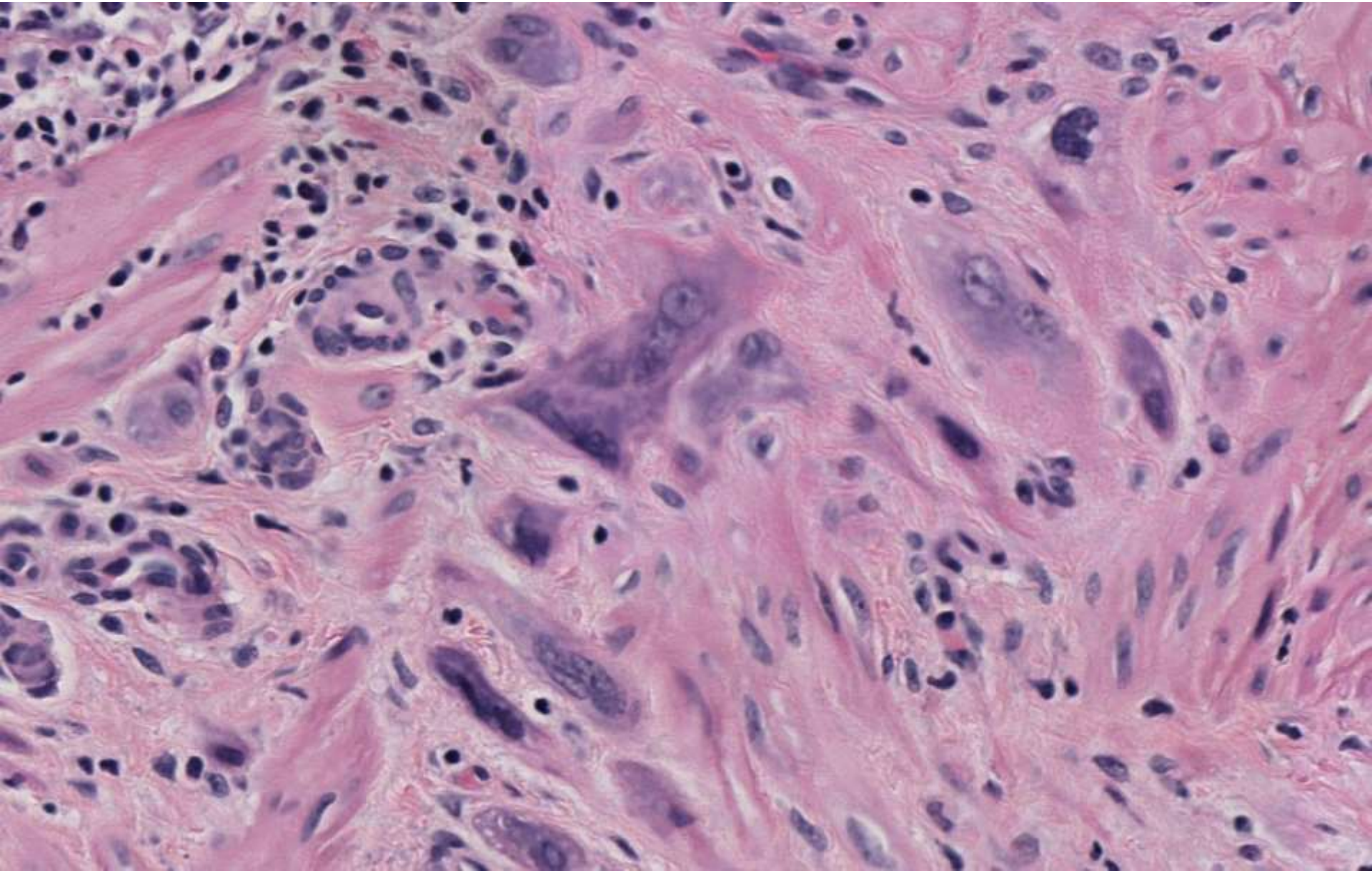


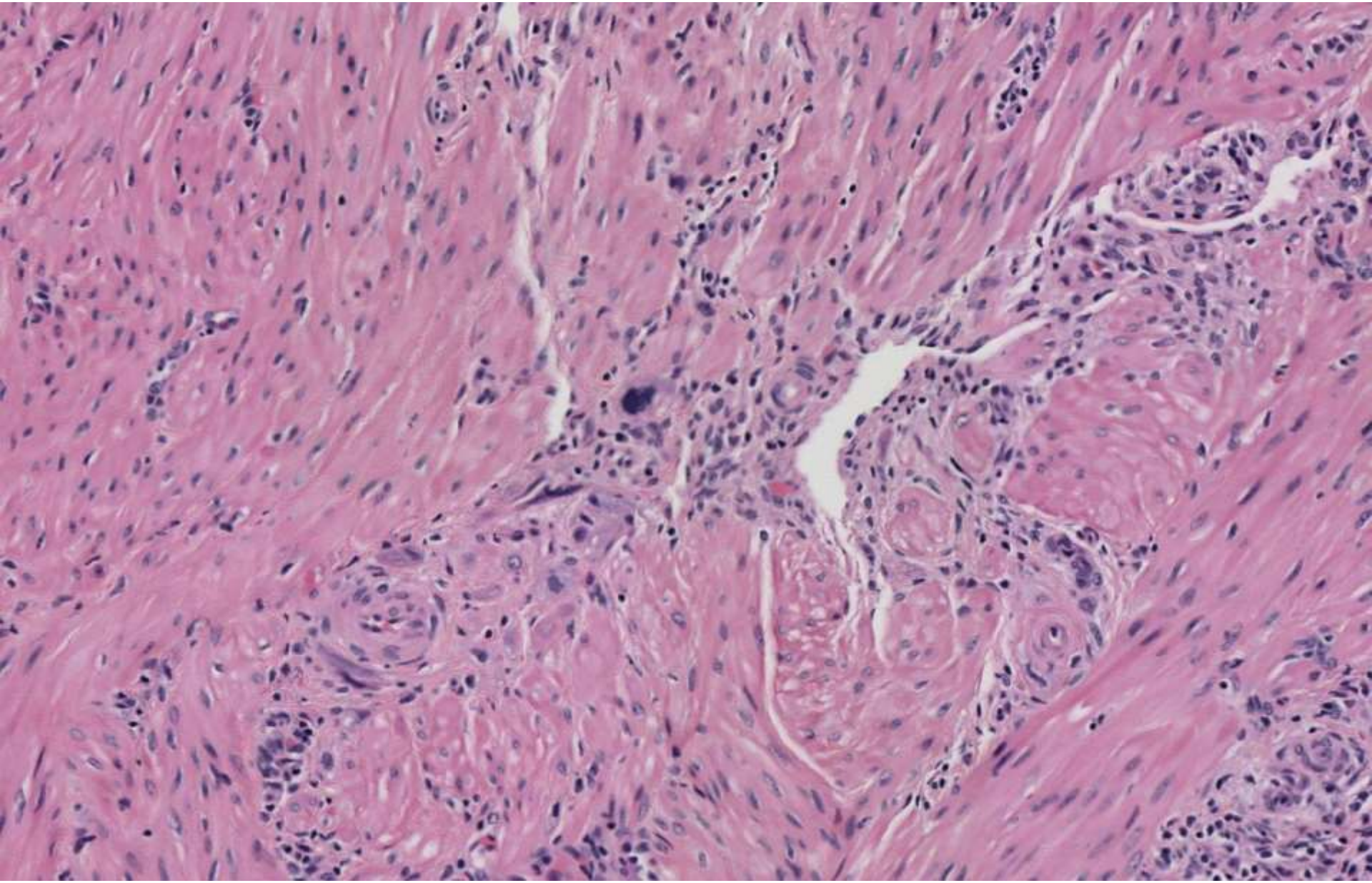


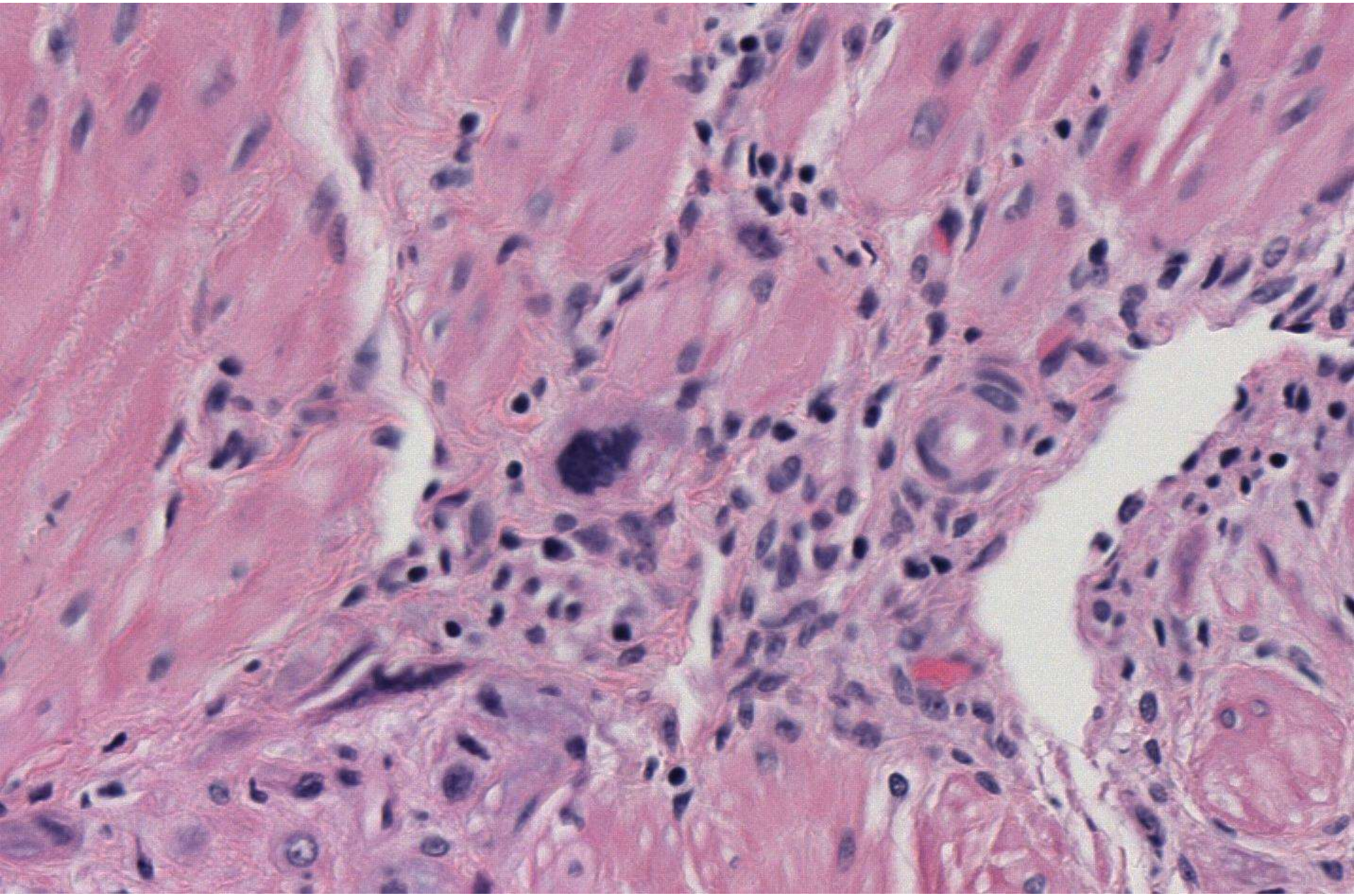








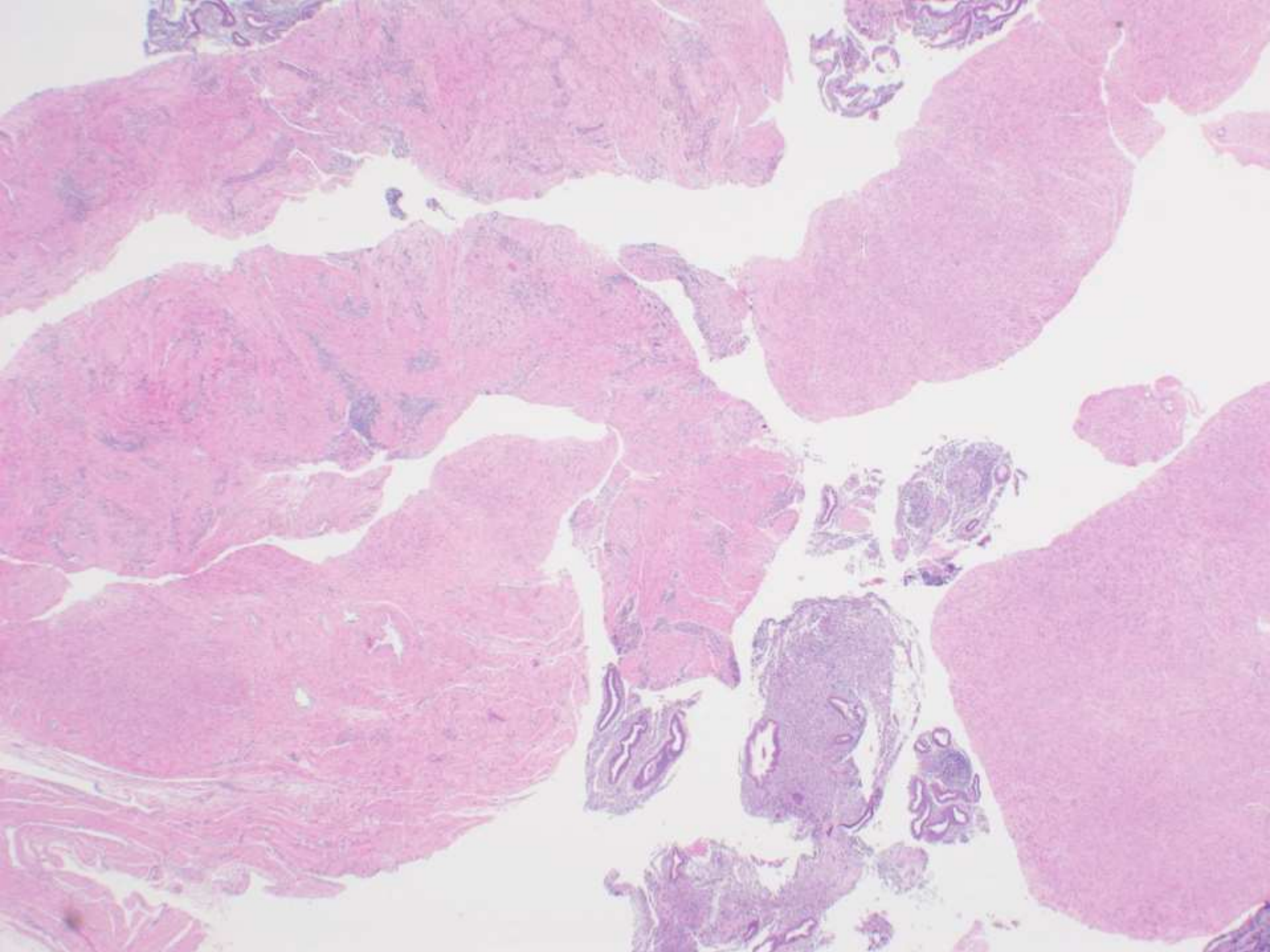


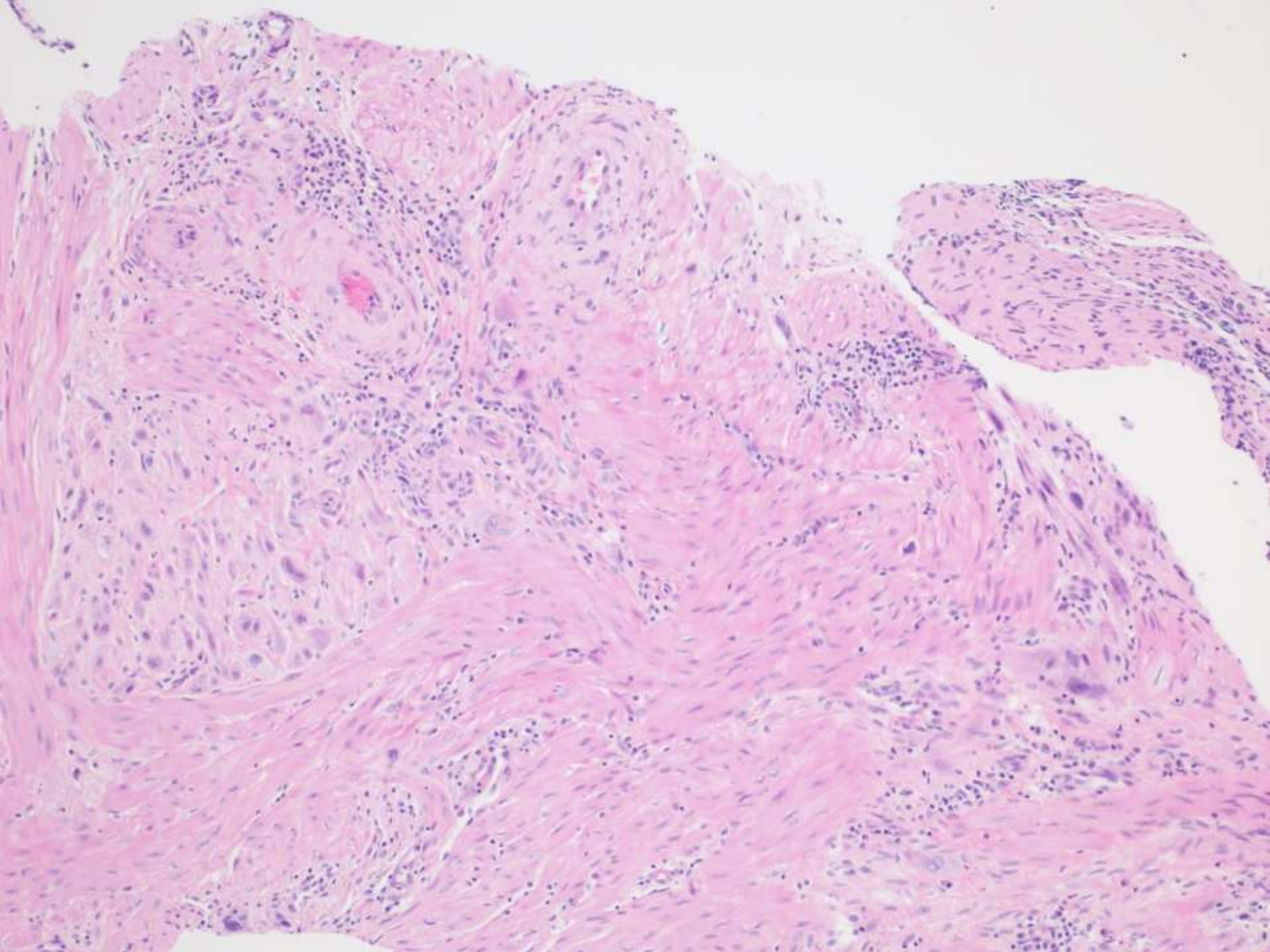


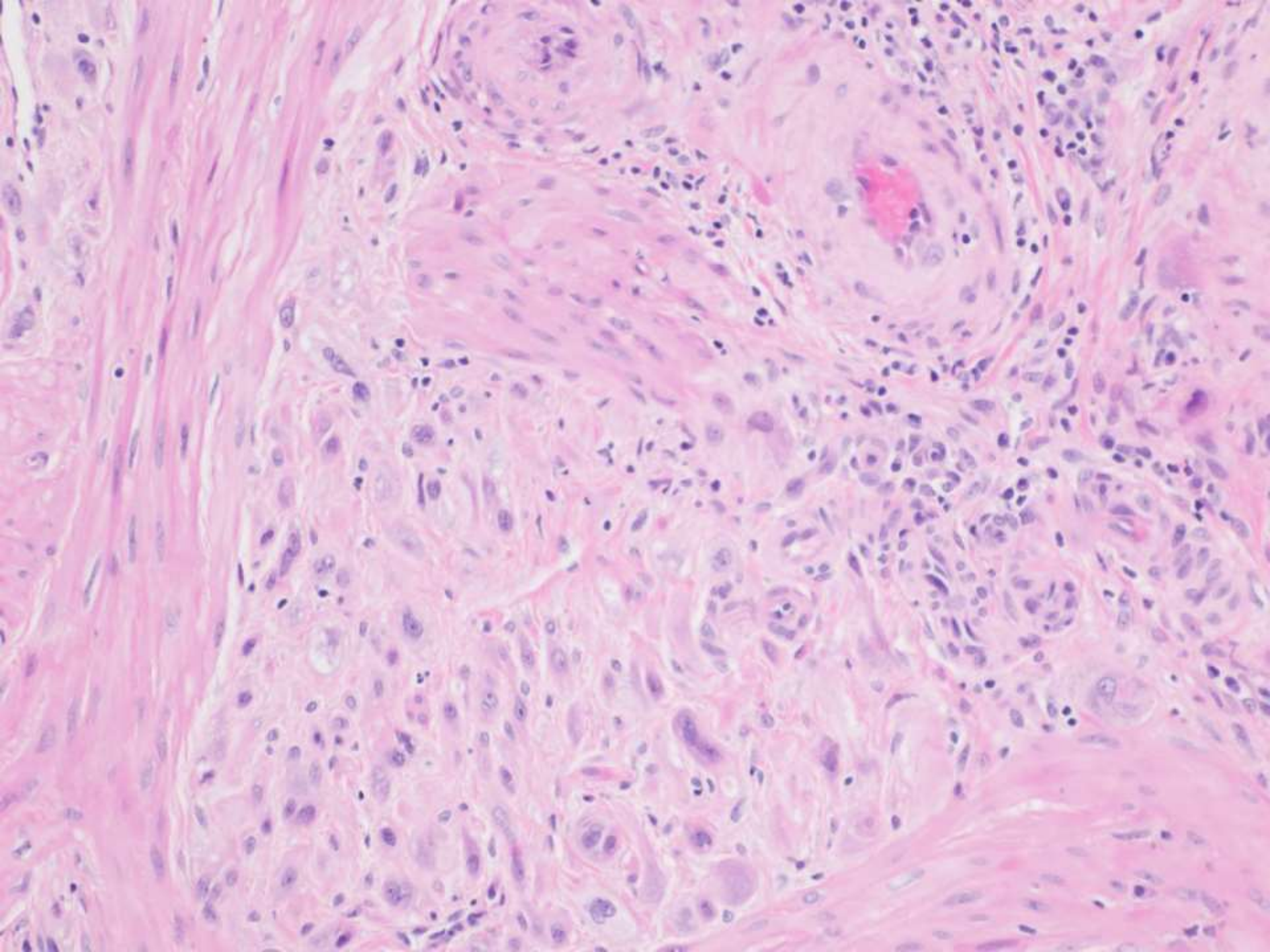
# 35-year-old woman with fibroids who presents for hysteroscopic myomectomy

Jordan Taylor/Charles Zaloudek/Ben Buelow

UCSF

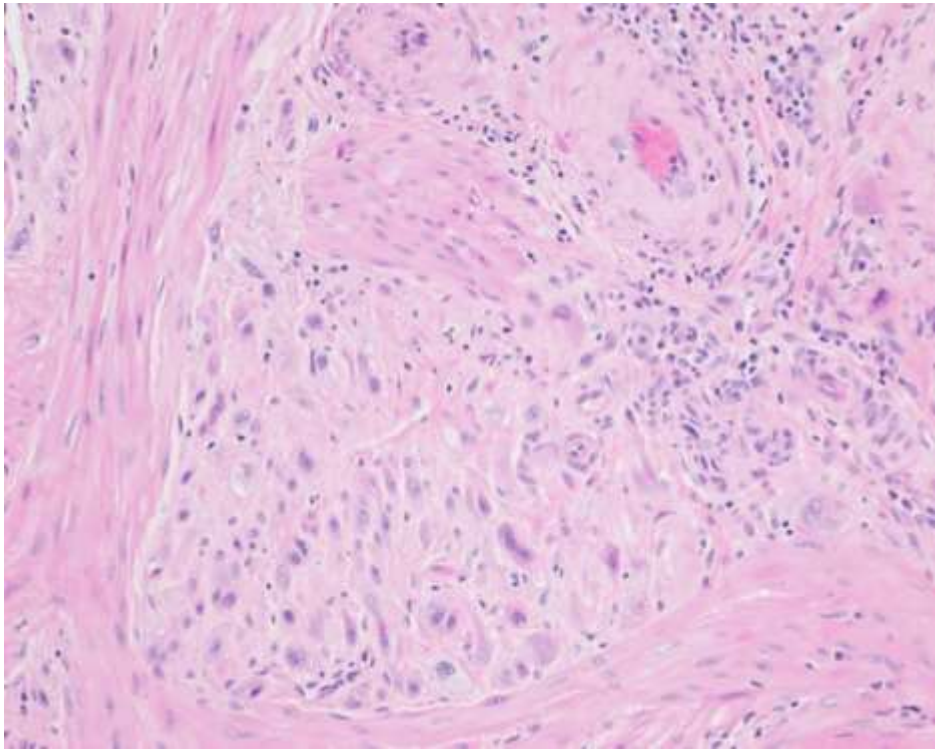




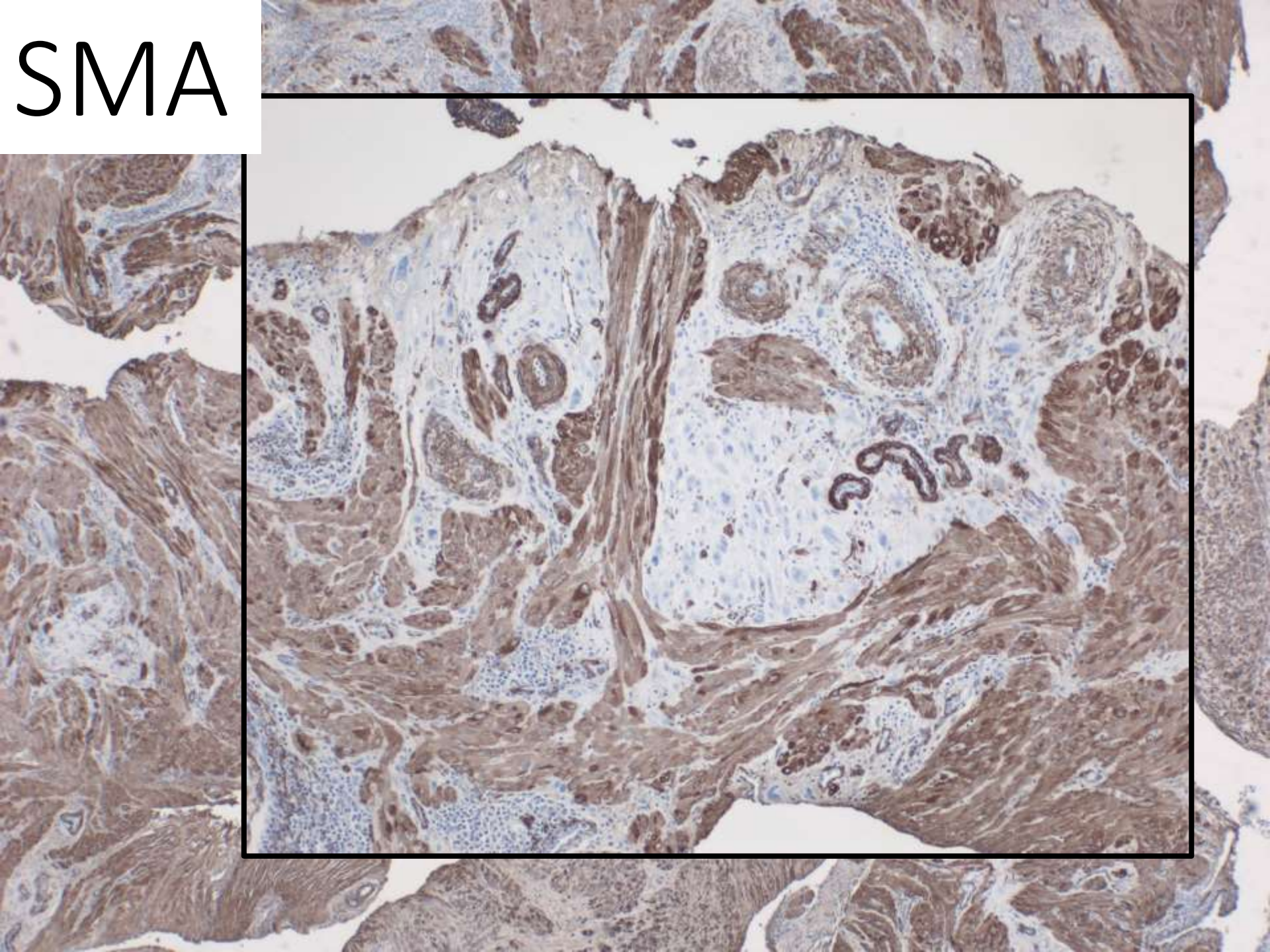


# Differential Diagnosis

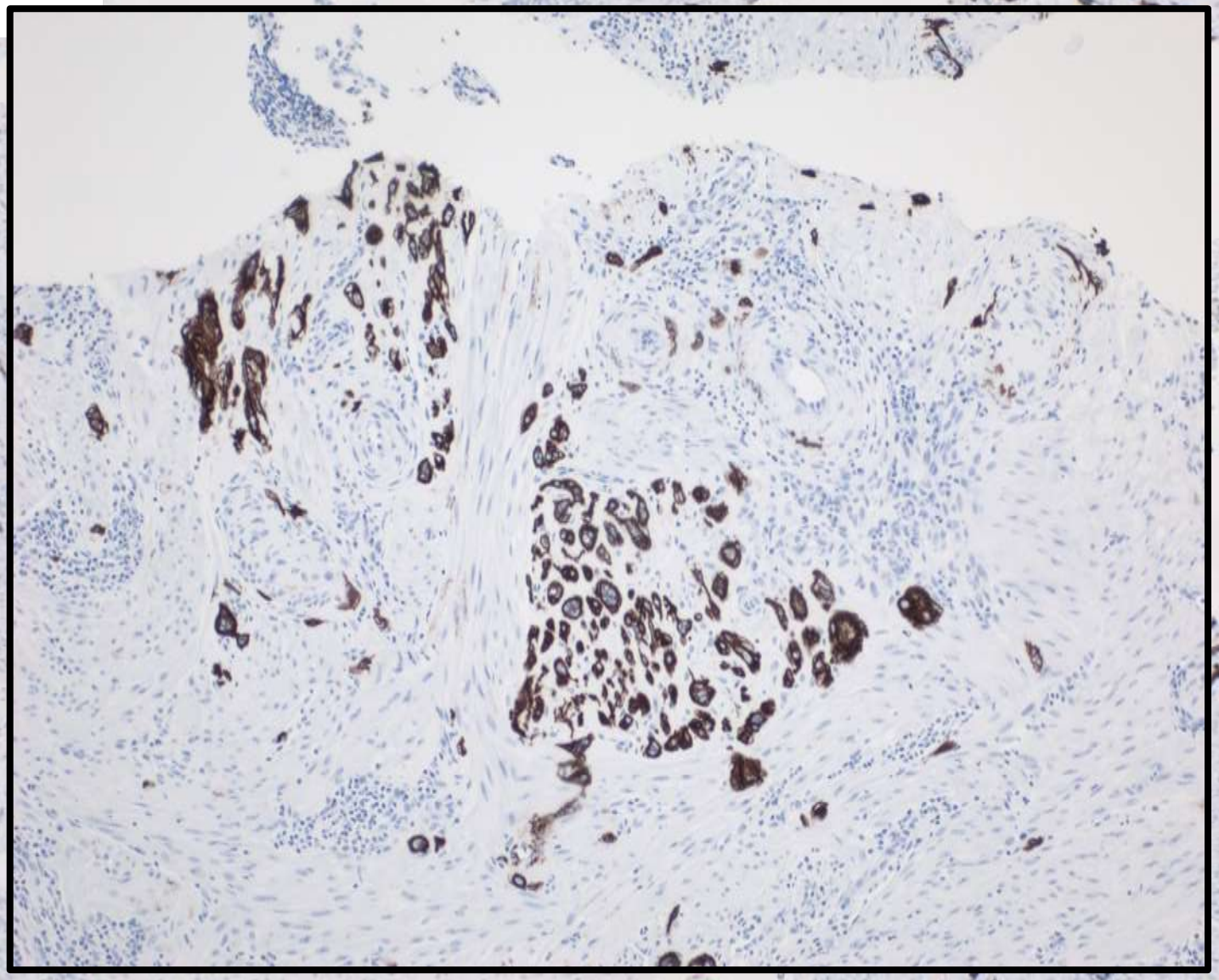
- Leiomyoma with bizarre nuclei
- Gestational trophoblastic disease
  - Exaggerated placental site
  - Atypical placental site nodule
  - Placental site nodule



# SMA



# Keratin



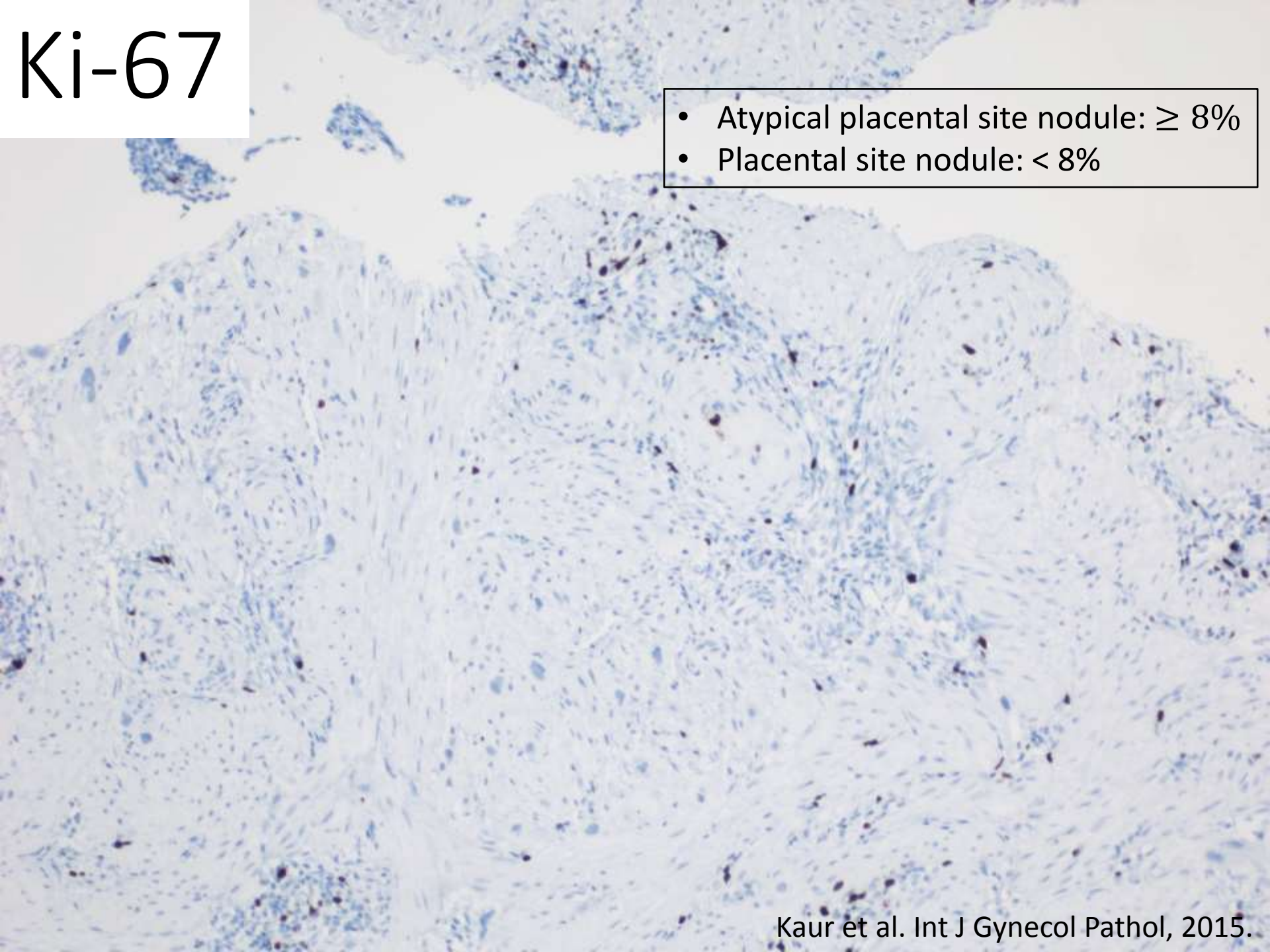
# Atypical Placental Site Nodule (APSN) and Association With Malignant Gestational Trophoblastic Disease; A Clinicopathologic Study of 21 Cases

Baljeet Kaur, F.R.C.Path., Dee Short, Rosemary A. Fisher, Ph.D., F.R.C.Path., Philip M. Savage, Ph.D., F.R.C.P., Michael J. Seckl, Ph.D., F.R.C.P., and Neil J. Sebire, F.R.C.Path.

- 21 cases of APSN identified over a 7.5 year period
- 3 (14%) developed malignant GTD
- Histologic features between typical PSN and PSTT/ETT

| Tumor type | Ki-67 | Other |
|---|---|---|
| Placental site nodule | <8% | <4 mm |
| Atypical placental site nodule | 8-10% | Moderate to severe atypia |
| Placental site trophoblastic tumor | >10% | Infiltrative growth |
| Epithelioid trophoblastic tumor | >10% | Nodular growth, geographic necrosis |

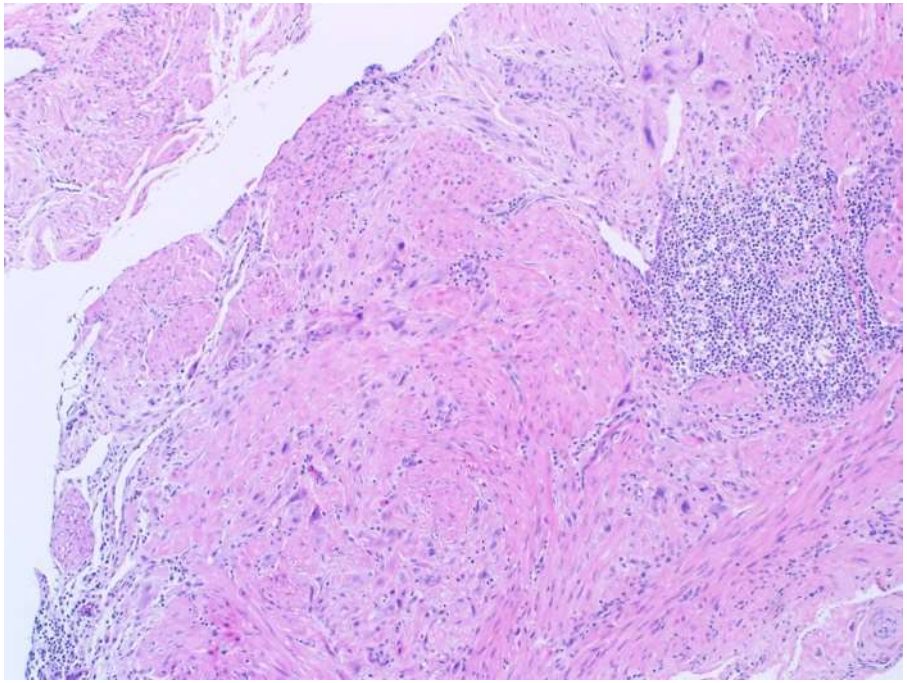
# Ki-67

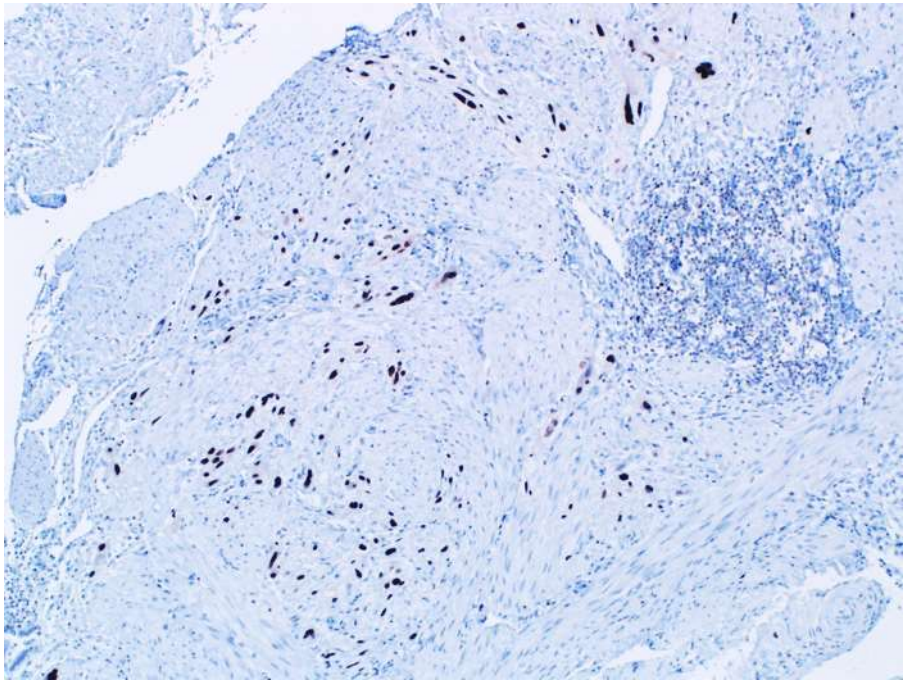


- Atypical placental site nodule: ≥ 8%
- Placental site nodule: < 8%

Kaur et al. Int J Gynecol Pathol, 2015.

# Other IHC for trophoblastic tissue: GATA3!



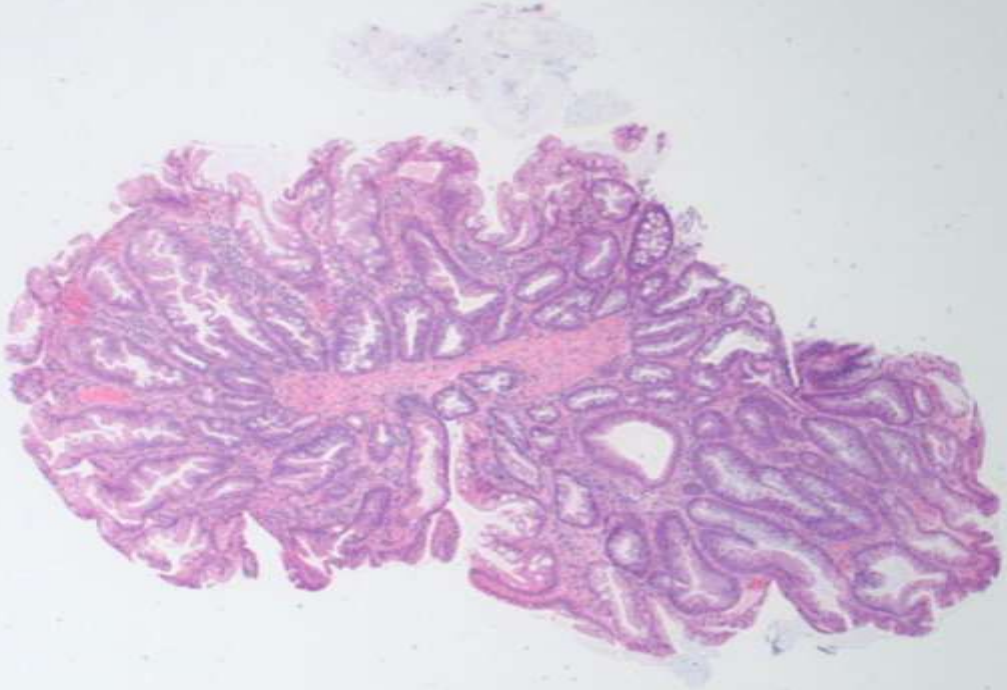


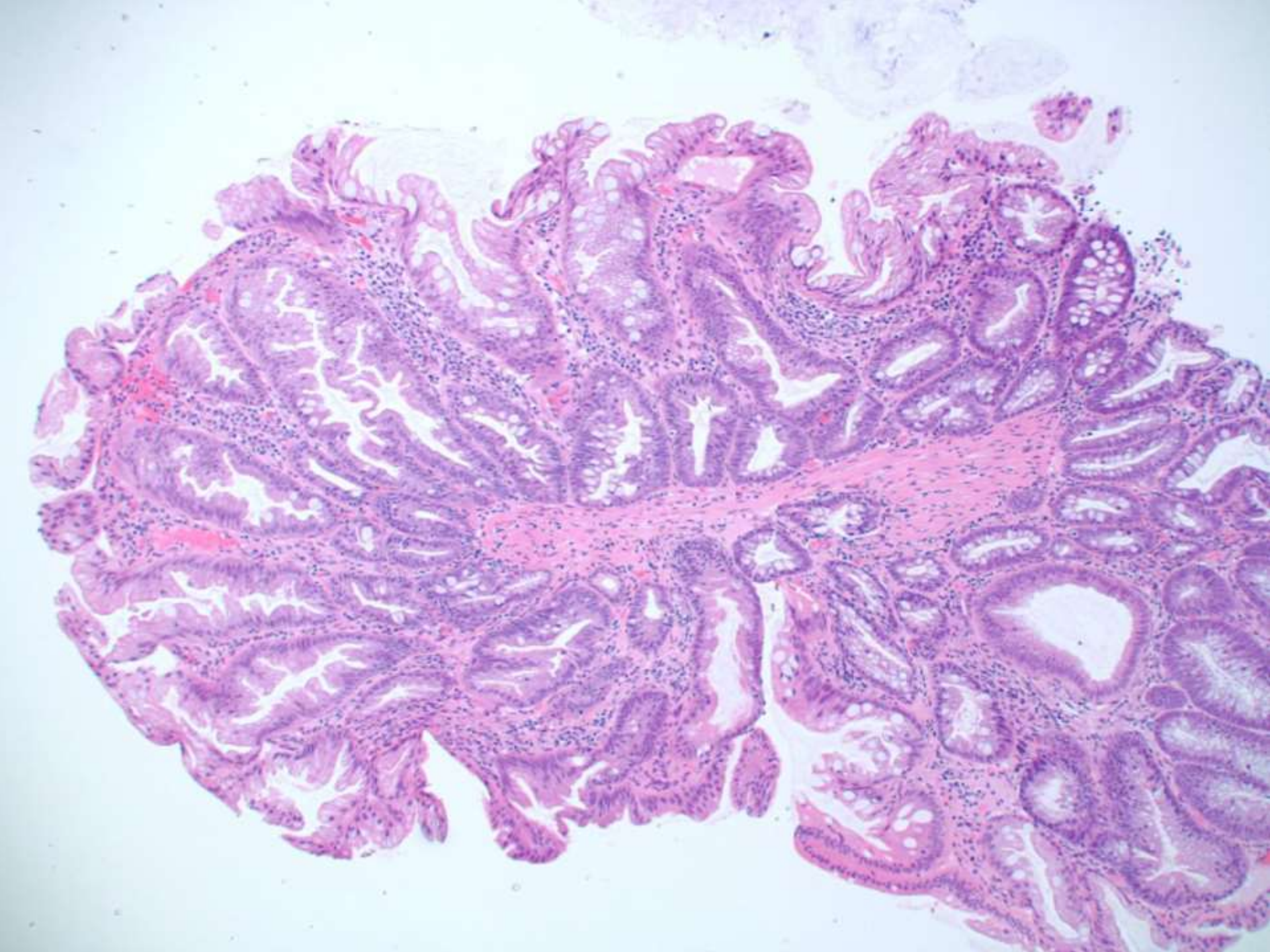
Mirkovic et al., Histopathology 2015

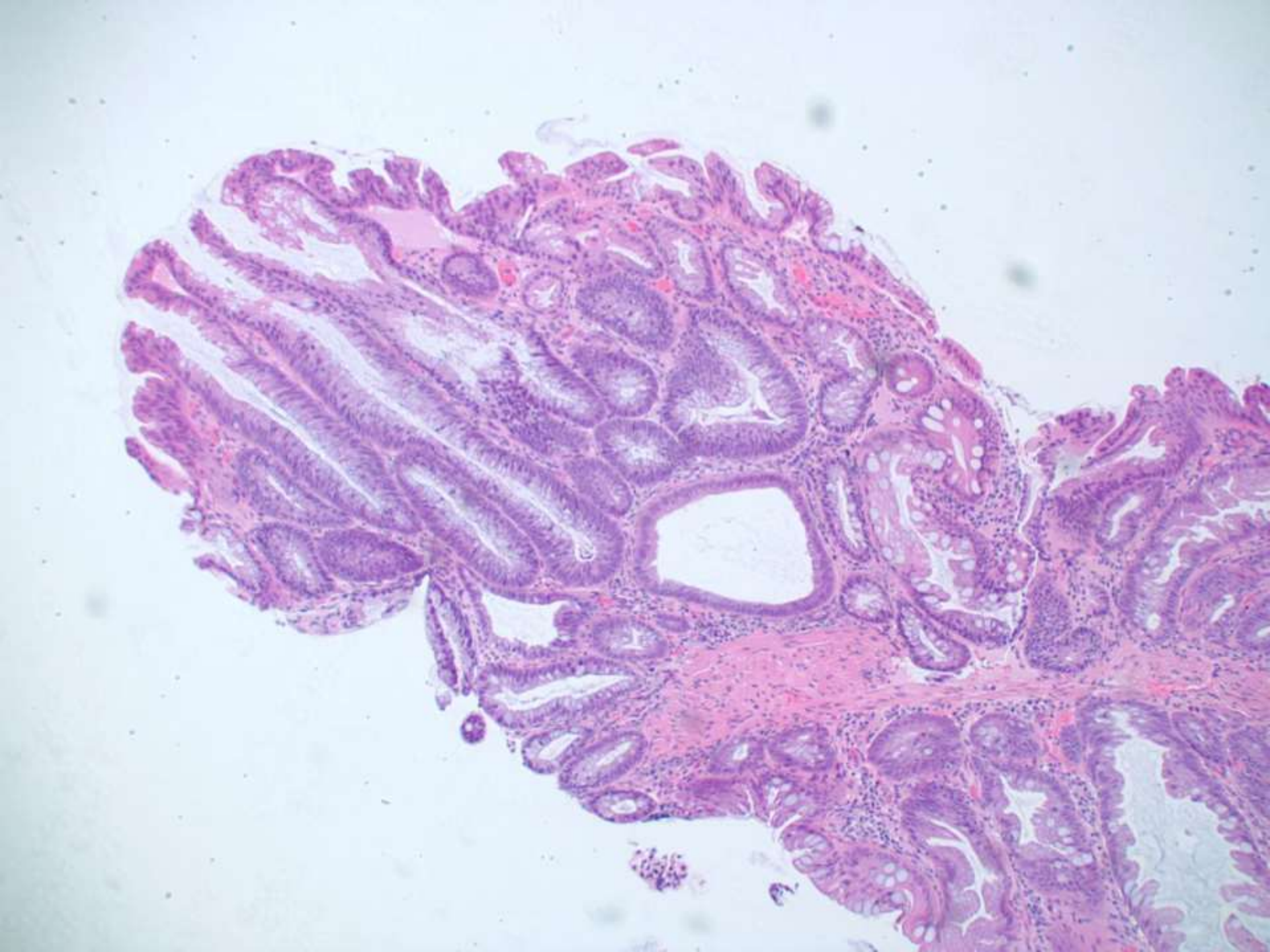
# 20-0106

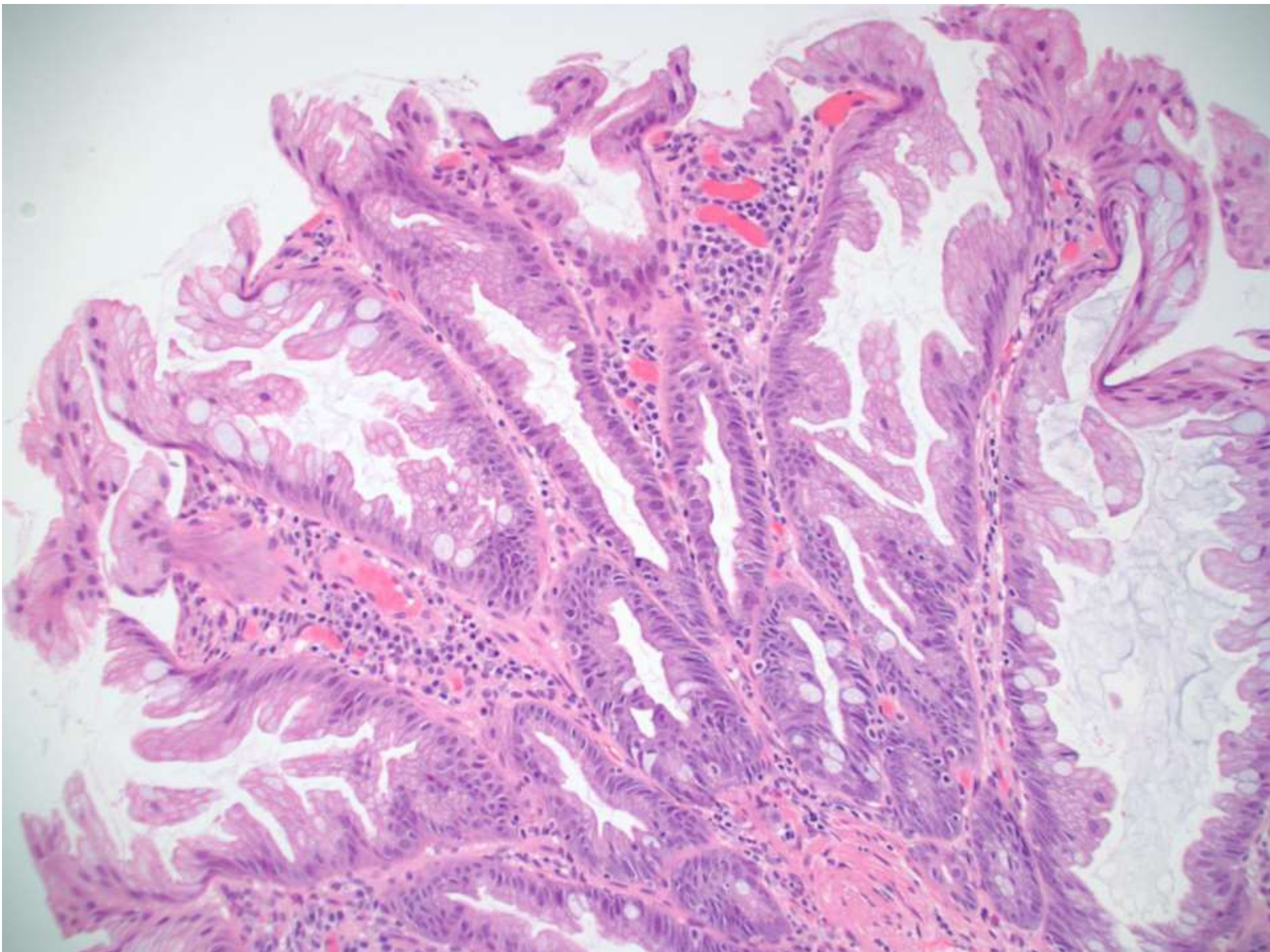
**Natalie Patel; El Camino Hospital**

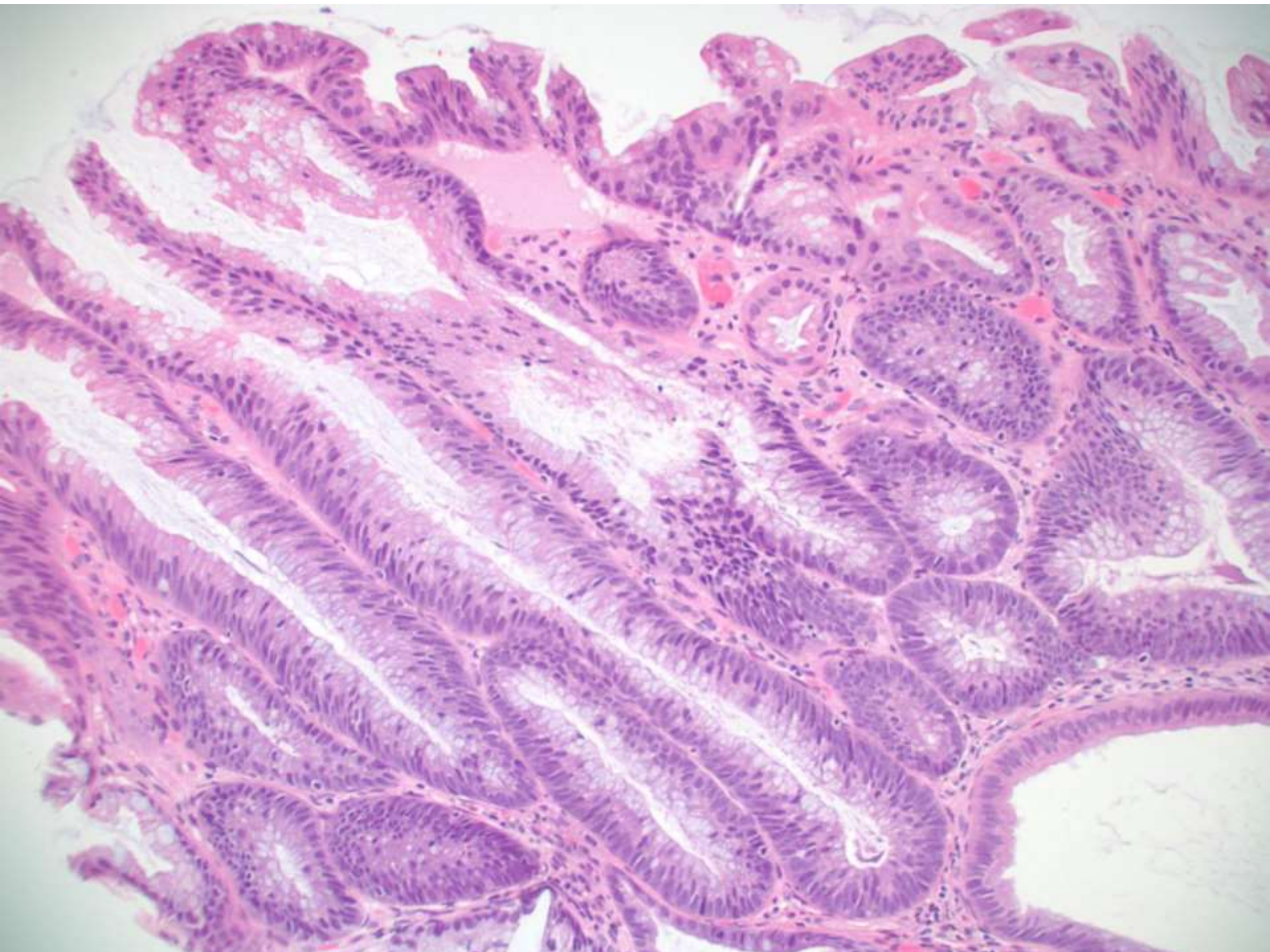
76-year-old F presents with distal ascending colon polyp on colonoscopy.

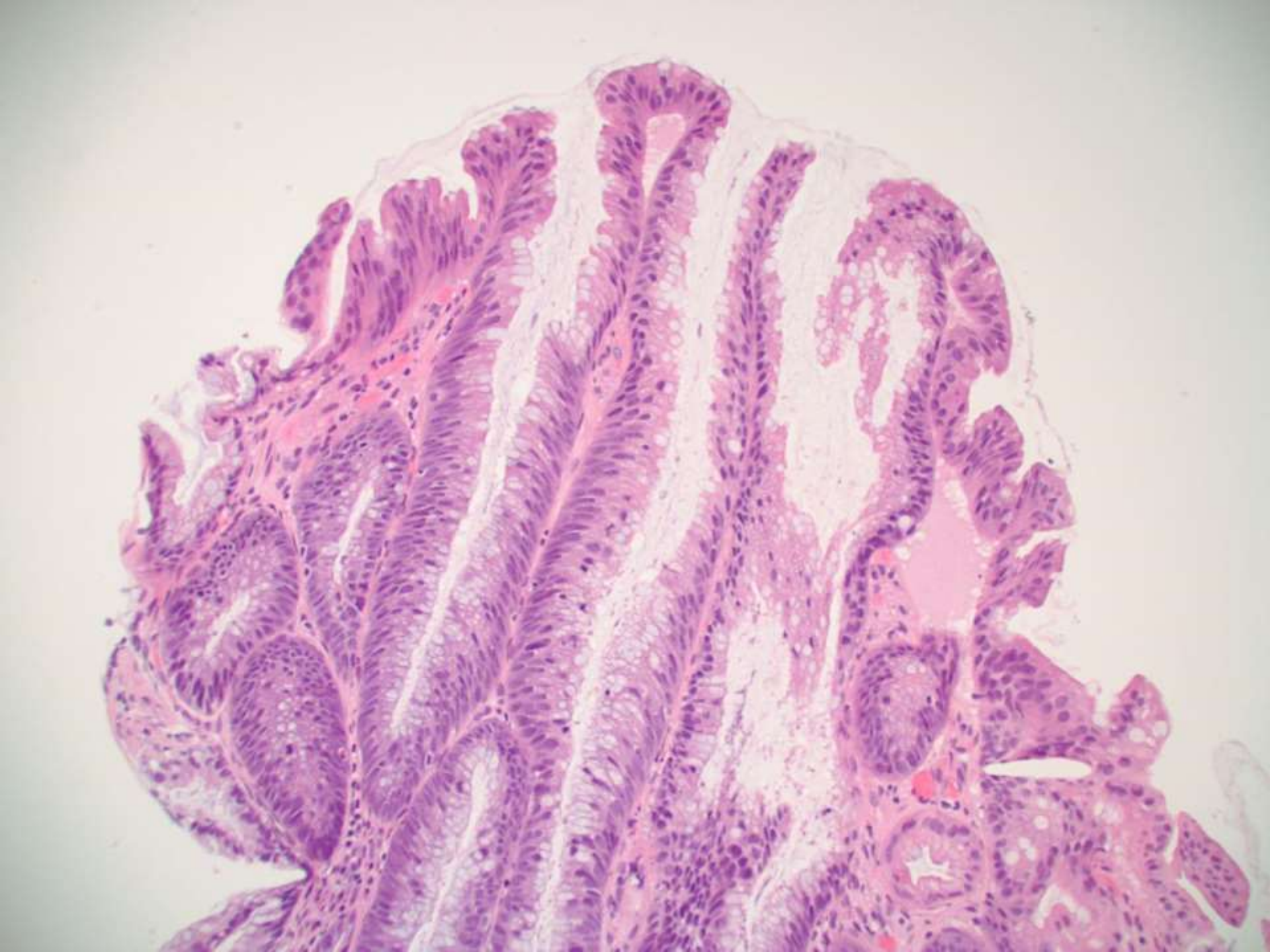


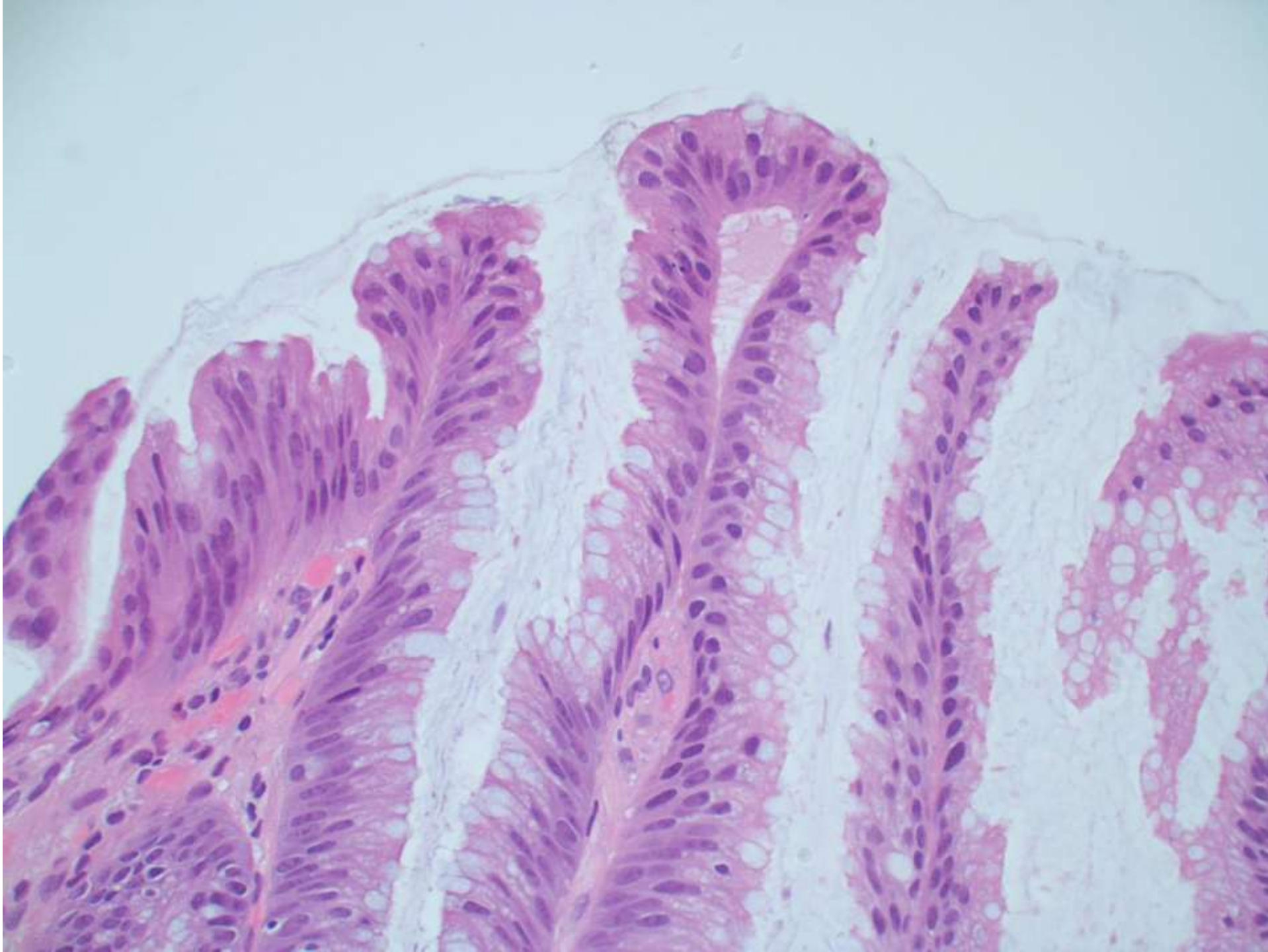






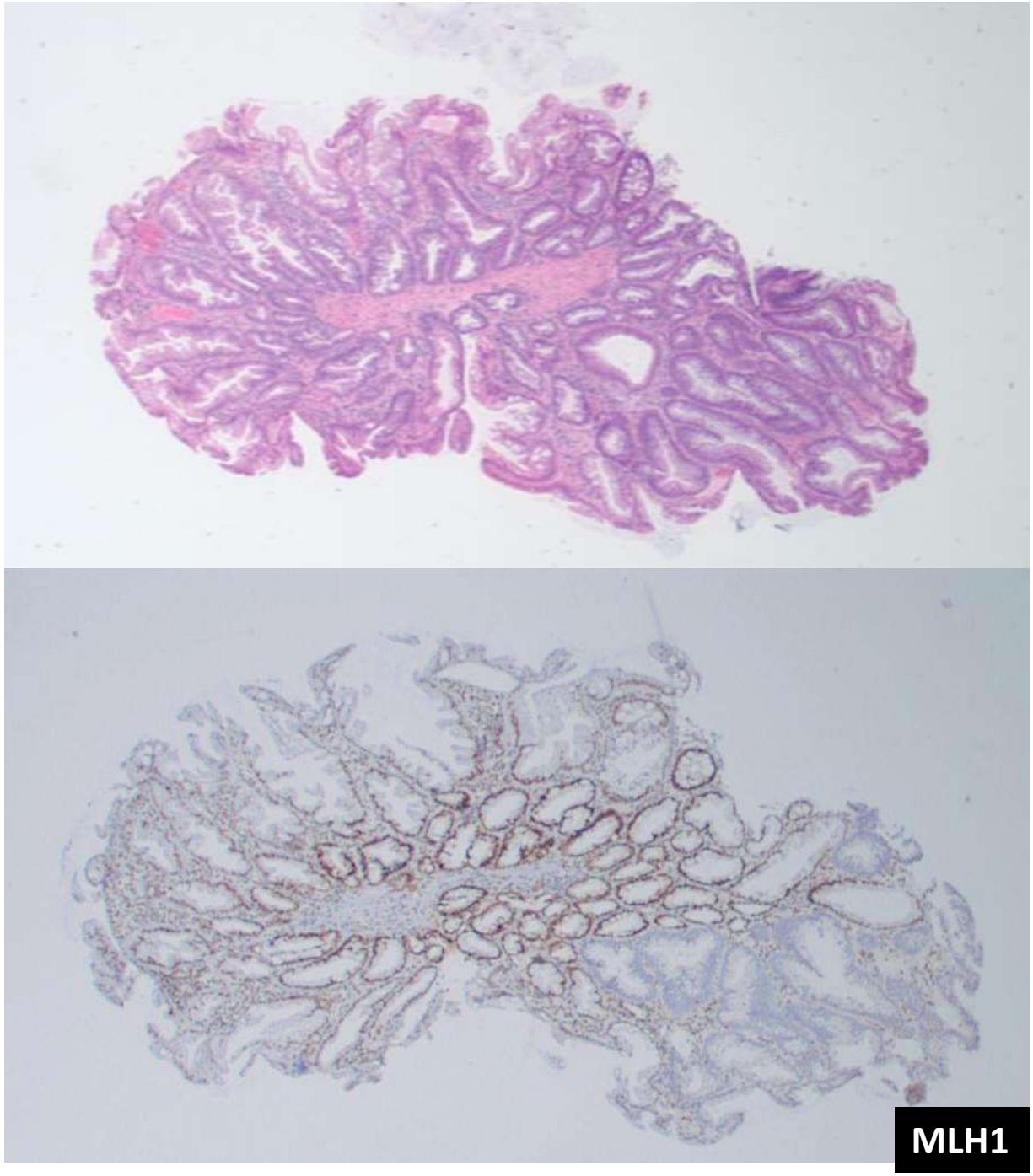


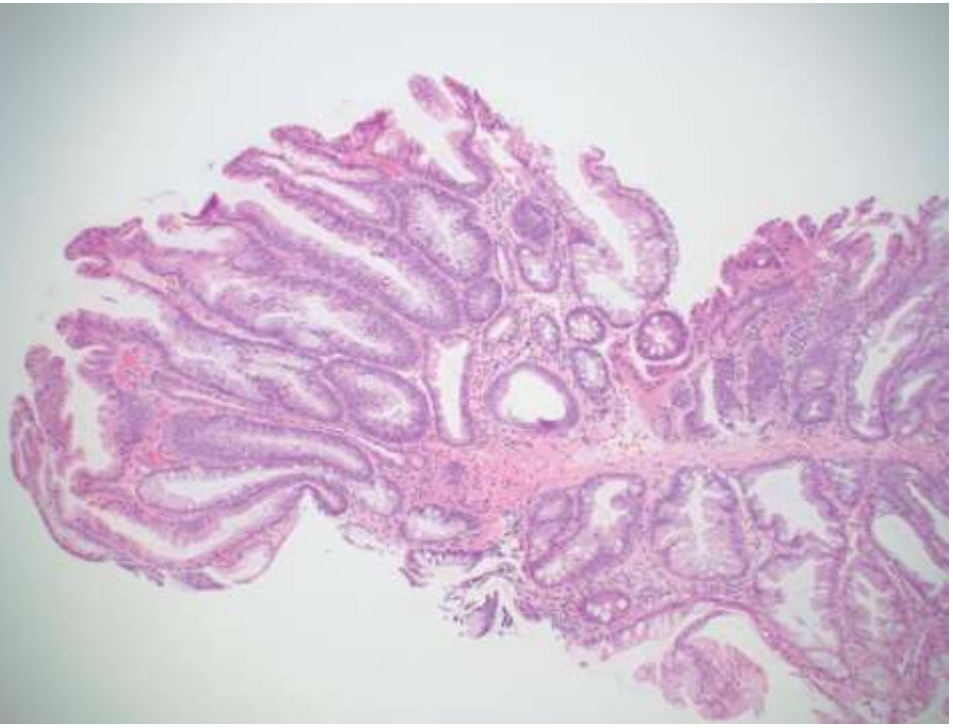


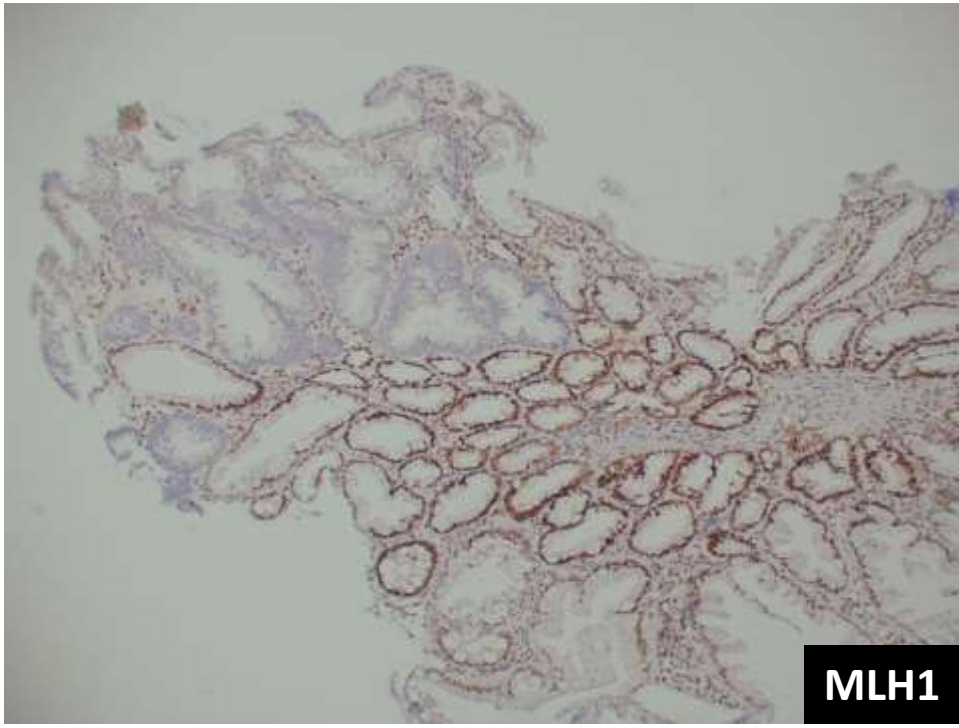


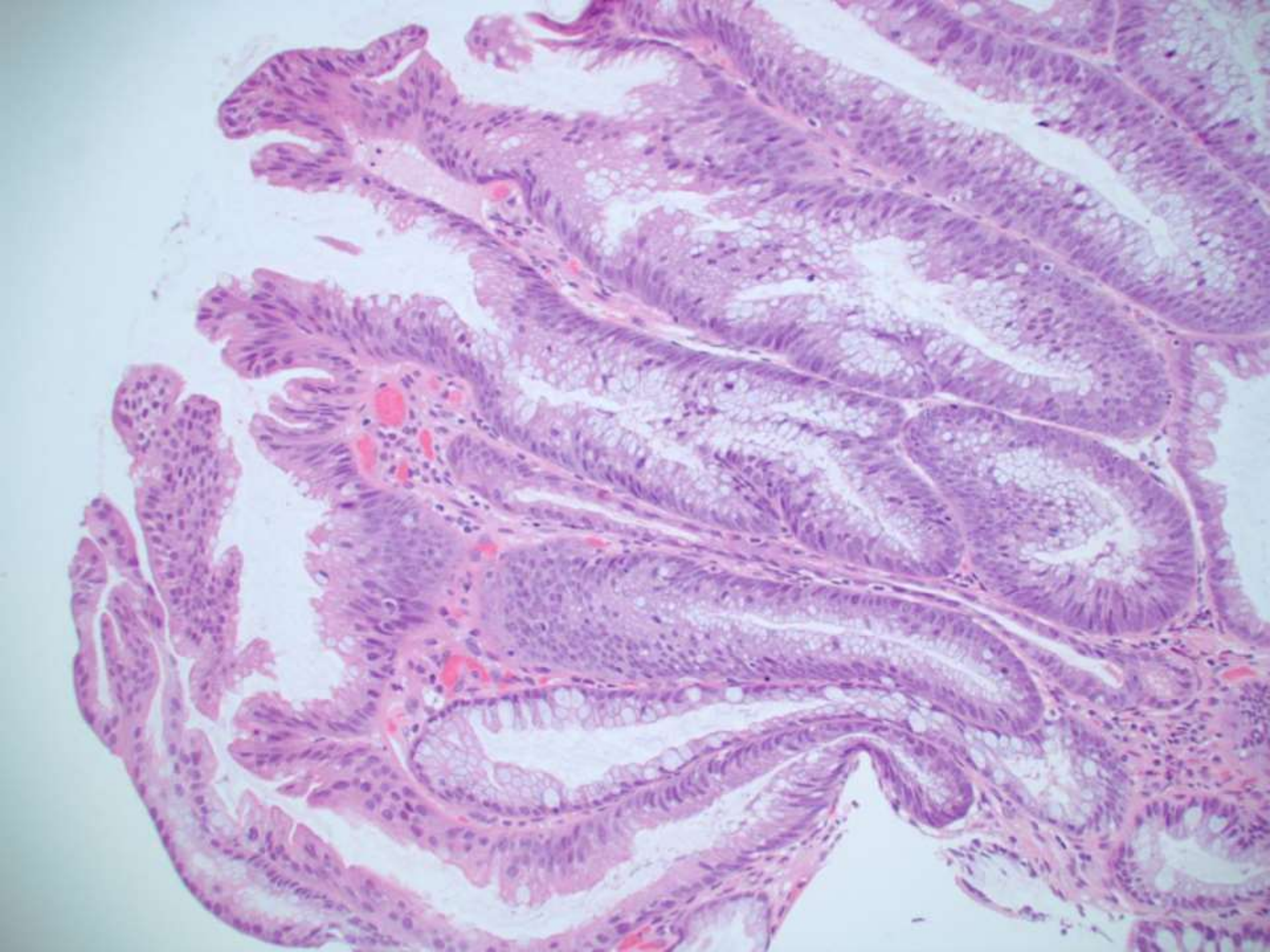
# Differential diagnosis

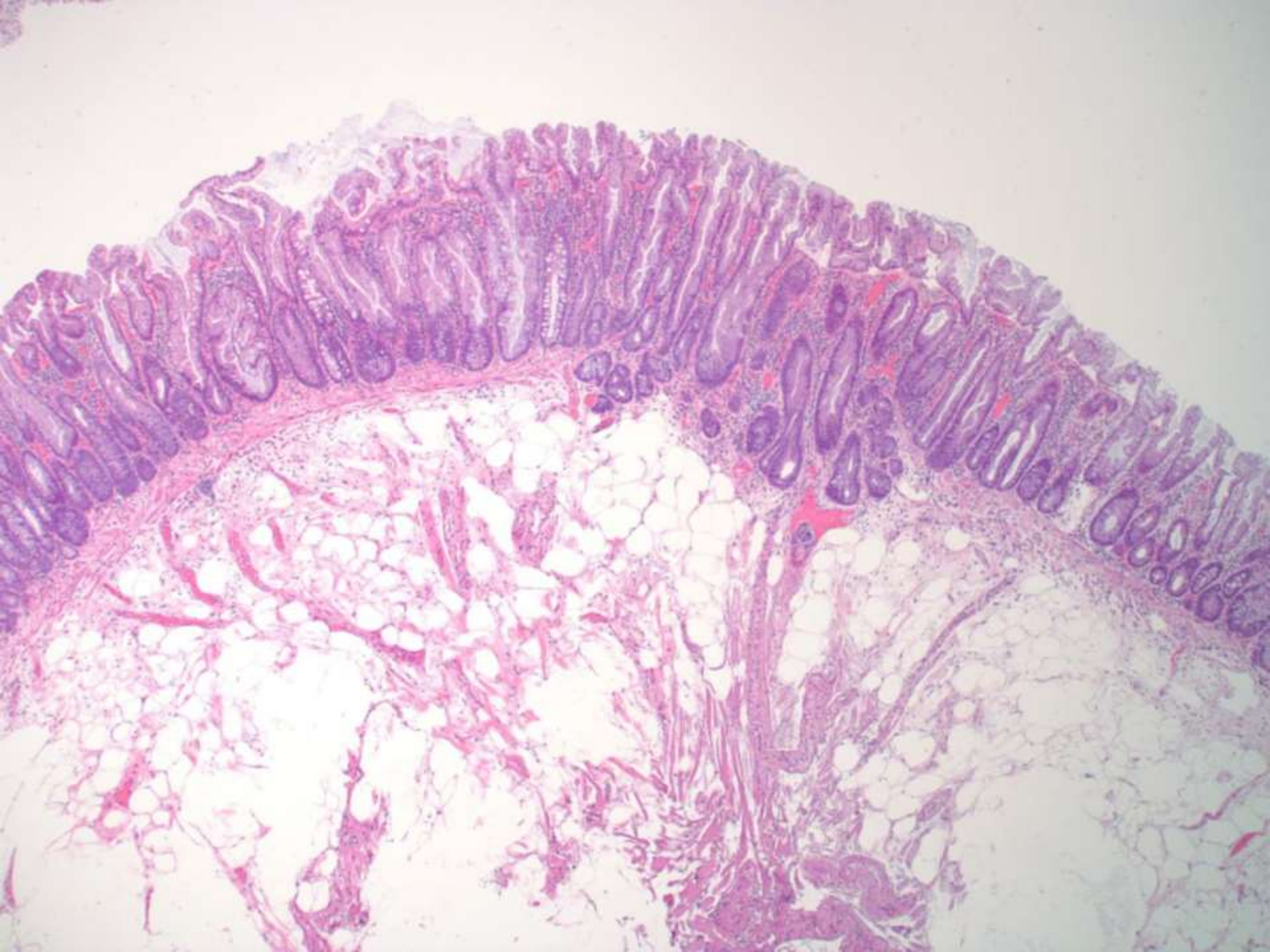
1. Hyperplastic polyp
2. Sessile serrated polyp
3. Sessile serrated polyp, dysplasia NOS
4. Sessile serrated polyp with adenomatous dysplasia
5. Sessile serrated polyp with serrated dysplasia
6. Sessile serrated polyp with minimal deviation
7. Sessile serrated polyp with some sort of dysplasia

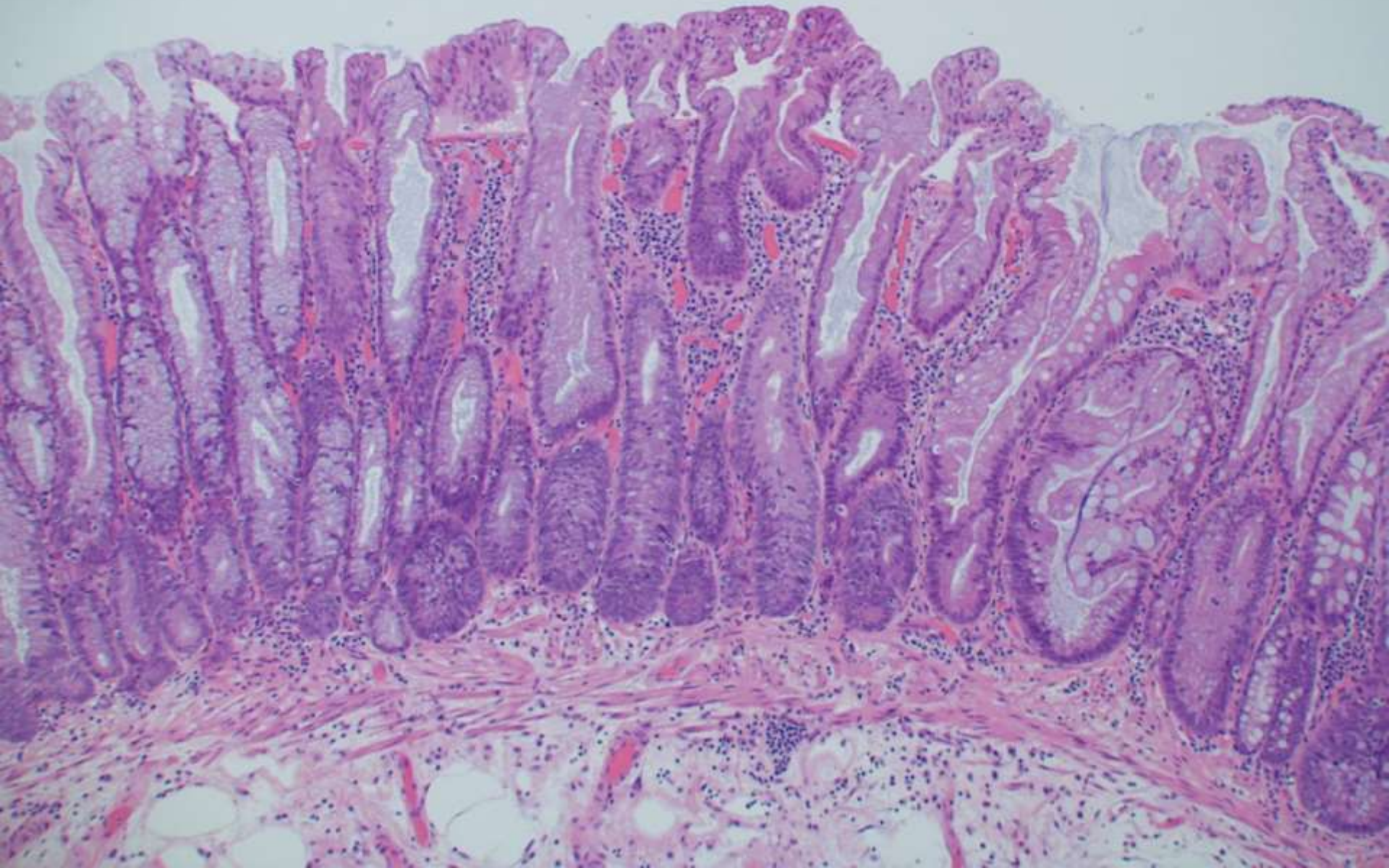

MLH1

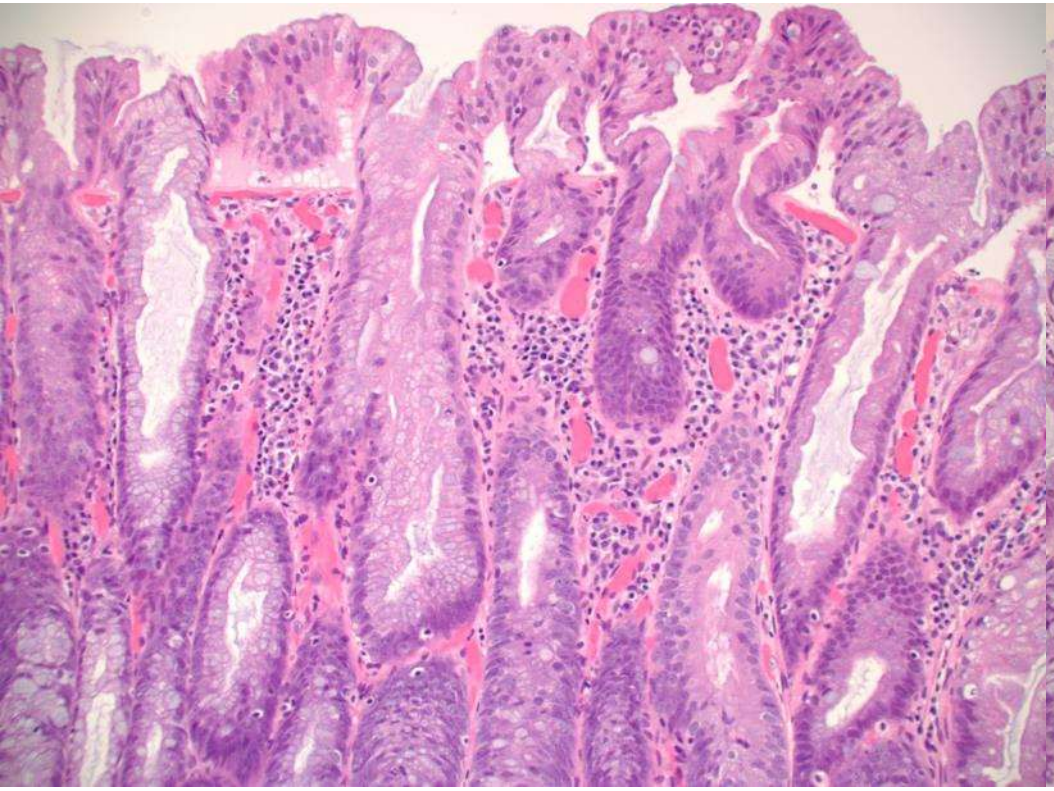
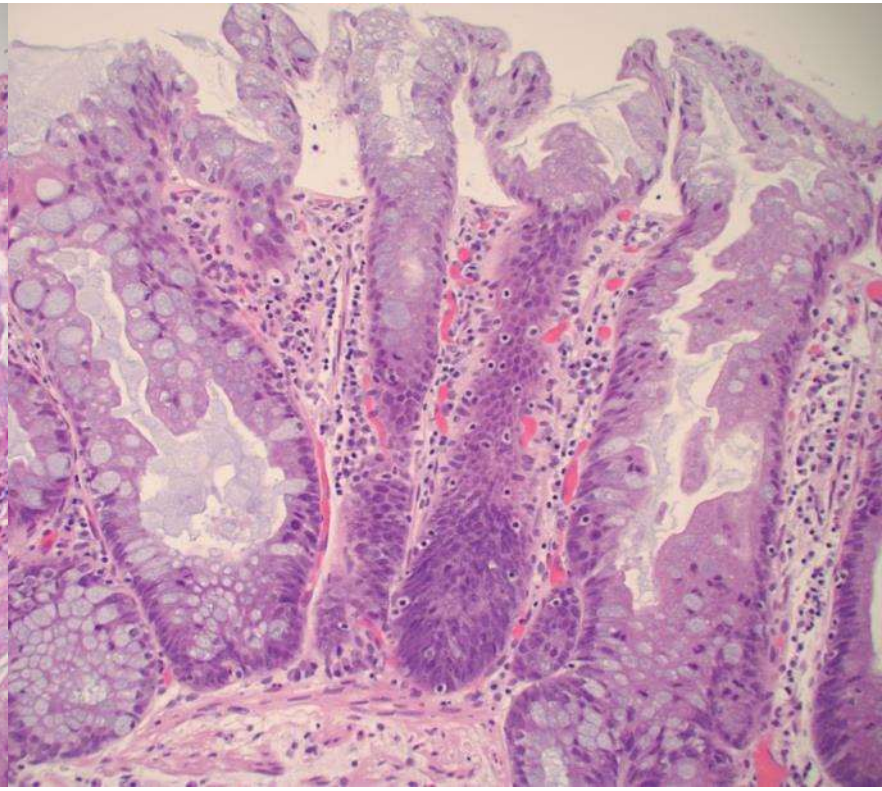



MLH1



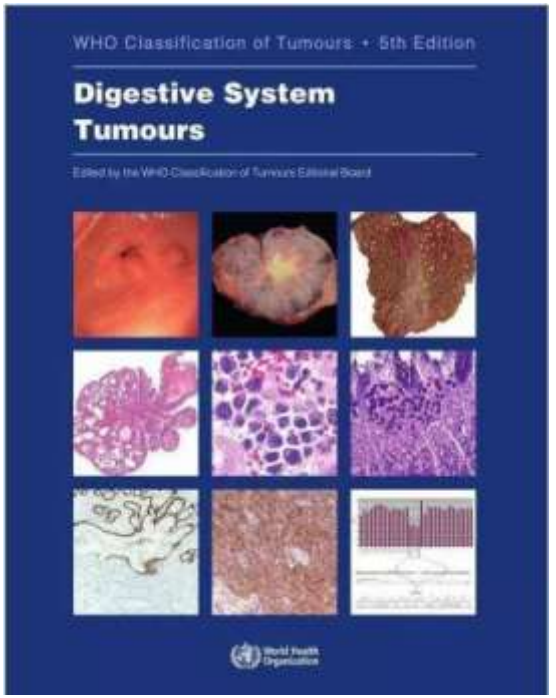




# **WHO 2019** Serrated polyp updates

- Nomenclature: Sessile serrated lesion
- Only **one** unequivocally distorted crypt is required
- Grading dysplasia is not performed
- Expanded the spectrum of dysplasia in SSP
  - (WHO 4th ed: 2 types: serrated and adenomatous)

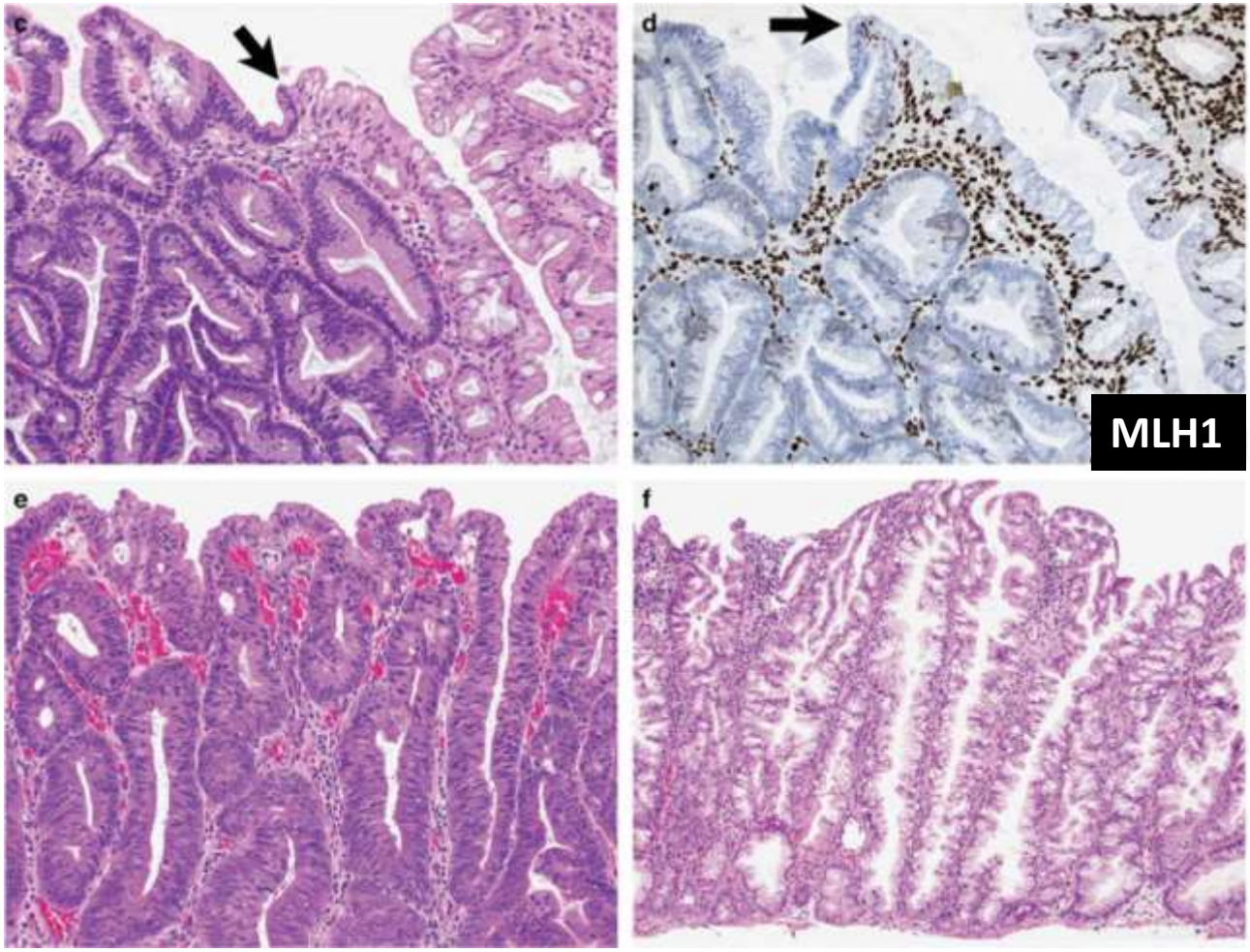


# SSL/P-basics

- Mixture of **both** goblet cells and microvesicular mucin droplets
- Distortion of the architecture from alterations of the proliferative zone leading to:
  - 1. Asymmetric proliferation
  - 2. Horizontal growth along the MM
  - 3. Serrations extending into the crypt base (contrast to HP-superficial)
  - 4. Dilation of crypt base (basal third of crypt)
    - Symmetric dilatation without deep serrations or lateral growth does not count
- Need any **ONE** of these features to qualify as distorted crypt **regardless of location or size**
- When in doubt, **LEVEL**

**Dysplasia (NOS) (79%)**

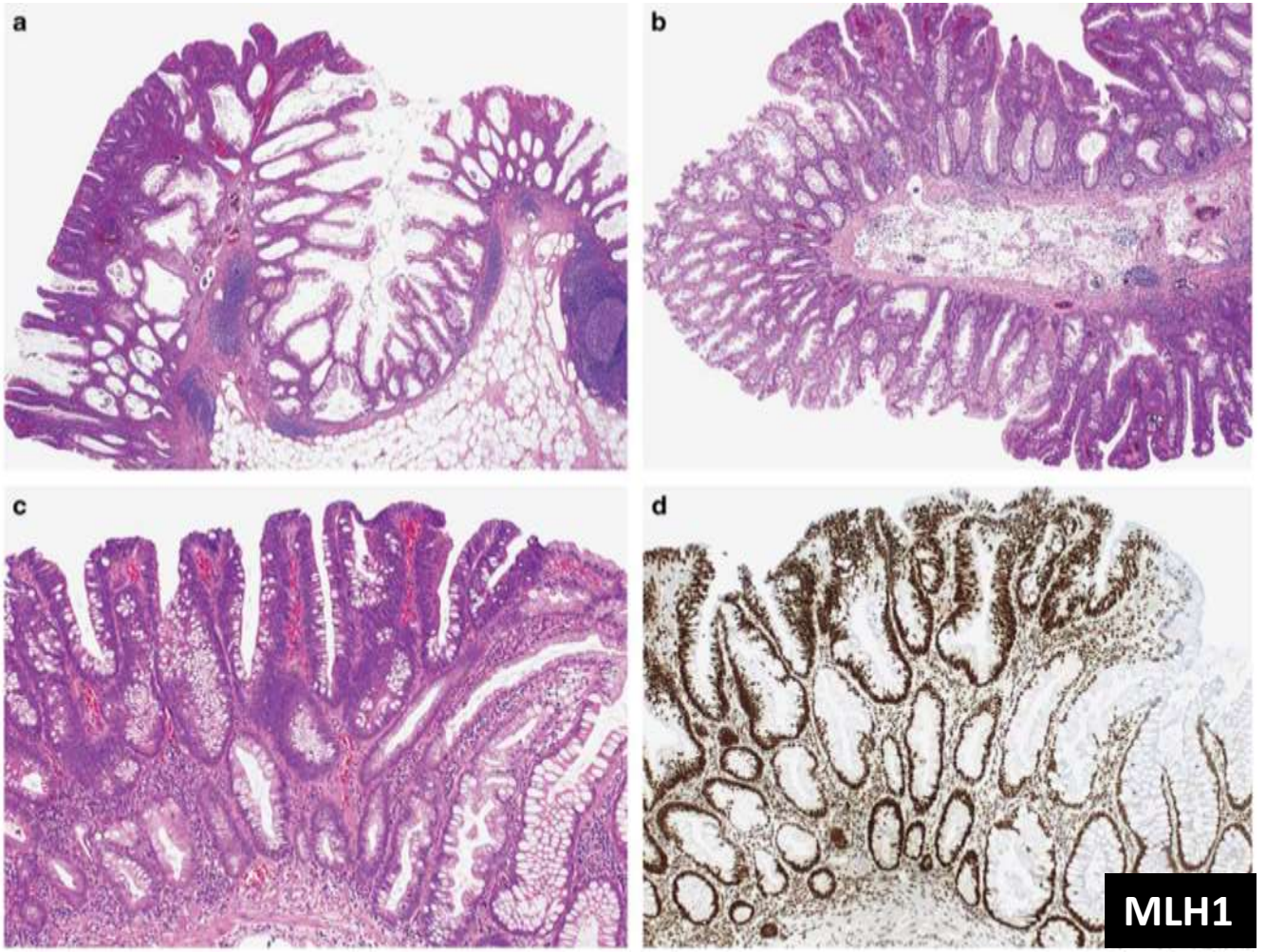
- Full depth
- Variable patterns
- Majority are MLH1 deficient




Liu C et al. Mod Pathol 2017;30:1728-1738

**Adenomatous dysplasia (21%)**

- Top down dysplasia
- Basophilic cytoplasm, penicillate nuclei
- Can have gastric foveolar appearance
- Most MLH1 proficient




Liu C et al. Mod Pathol 2017;30:1728-1738

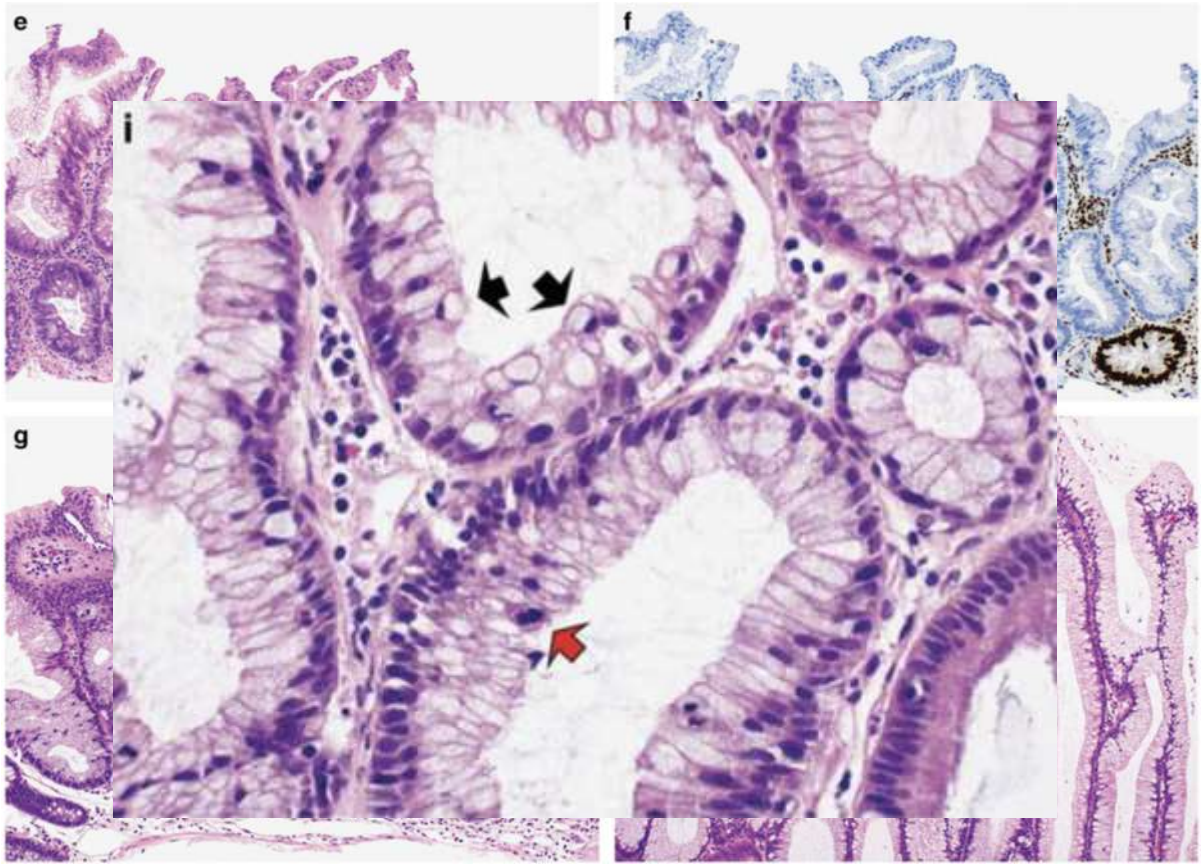
## Minimal Deviation Dysplasia (19%)

- Low Mag: Mild crypt disorganization, crypt crowding and reduced luminal serration
- May have hypermucinous appearance
- Less commonly, mildly eosinophilic cytoplasm with apical mucin
- Some nuclei with loss of polarity and mitotic figures
- Dystrophic mucus cells

**Subtle architectural and cytologic changes**

**+**

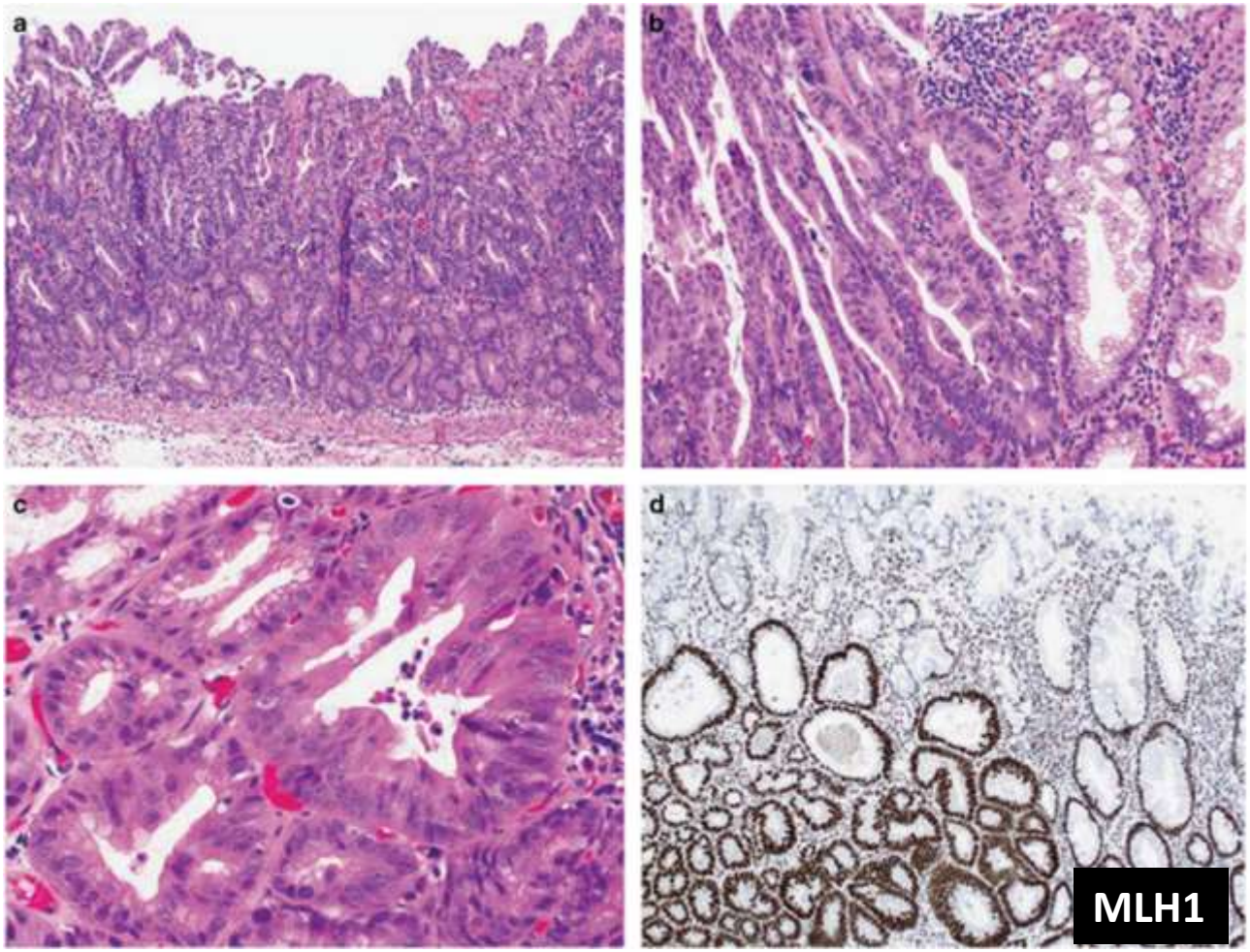
**loss of MLH1 ( by definition)**




Liu C et al. Mod Pathol 2017;30:1728-1738

## Serrated dysplasia (12%)

- Glands with large nuclei, prominent nucleoli, and eosinophilic cytoplasm
- Mitosis frequent
- Most MLH1 proficient dysplasia
- Most MLH1 proficient



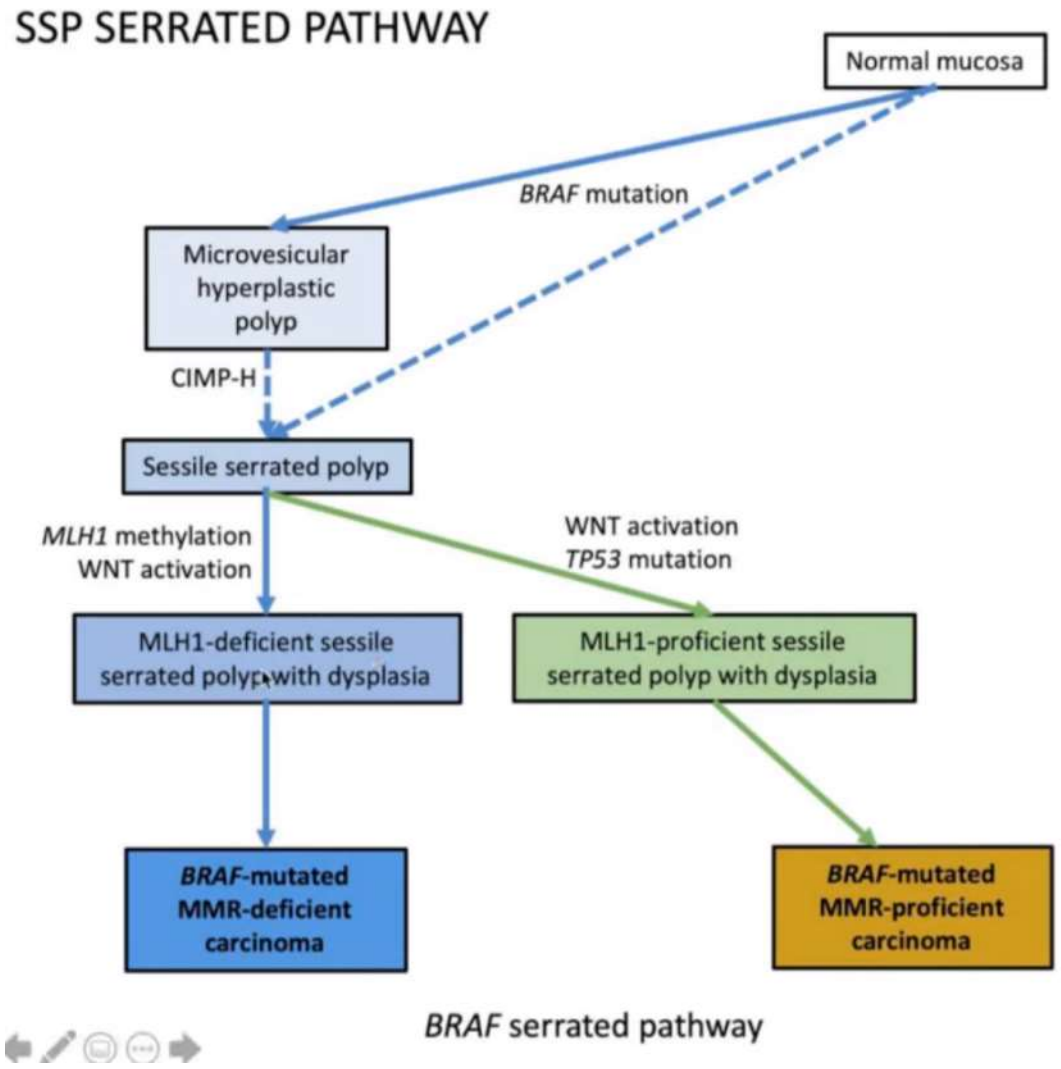

Liu C et al. Mod Pathol 2017;30:1728-1738

**Table 2** Morphologic patterns of dysplasia in sessile serrated polyps

| Patterns | Architectural changes | Cytologic features | MLH1 loss | Frequency[a] |
|---|---|---|---|---|
| Dysplasia not otherwise specified | Easily identifiable and varied in appearance: crypt elongation, crowding, complex branching, change in serration | Obvious atypia with amphophilic or eosinophilic cytoplasm, hyperchromatic nuclei with pseudostratification, frequent mitotic figures and loss of polarity | Frequent (>80%) | 79% |
| Minimal deviation | Subtle changes with crypt crowding, change in crypt branching pattern and often reduced serration | Cells with hypermucinous cytoplasm or slightly eosinophilic with gastric phenotype, basally located nuclei showing mild hyperchromasia and mitotic figures not restricted to the lower part of the crypts. | Required for the diagnosis | 19% |
| Serrated dysplasia | Closely packed small glands with reduced serration and cribriforming | Cuboidal cells with eosinophilic cytoplasm, frequent mitotic figures, marked nuclear atypia with vesicular nuclei and prominent nucleoli | Rare | 12% |
| Adenomatous dysplasia | Absence of crypt serration, same appearance as conventional adenomas; dysplastic component on the upper part of the lesion | Cells with amphophilic or basophilic cytoplasm, elongated hyperchromatic nuclei and variable amount of goblet cell differentiation resembling cells from conventional adenomas | Rare | 8% |

[a]Frequency of each pattern from Liu et al. [28] Multiple patterns can be present in a single lesion.

Pai R et al Mod Pathol 2019; 32: 1390-1415




## Important points

- SSPs probably develop from MVHPs (more commonly right colon)
- Serrated pathway is characterized by hypermethylation of CpG islands (CIMP-high) and BRAF mutations
- Two types of SSP with dysplasia
  - MLH1 deficient: 75%
  - MLH1 proficient: 25%

Pai R et al Mod Pathol 2019; 32: 1390-1415

# SSP with dysplasia

- Prevalence: rare, about 2-5% of SSPs
- WHO does not require separating into high and low grade
- See dysplasia in same fragment as SSP
- Do not need to subtype them in reports, just be aware of heterogeneity
- Low threshold for ordering MLH1 to detect Min. deviation dysplasia

# References

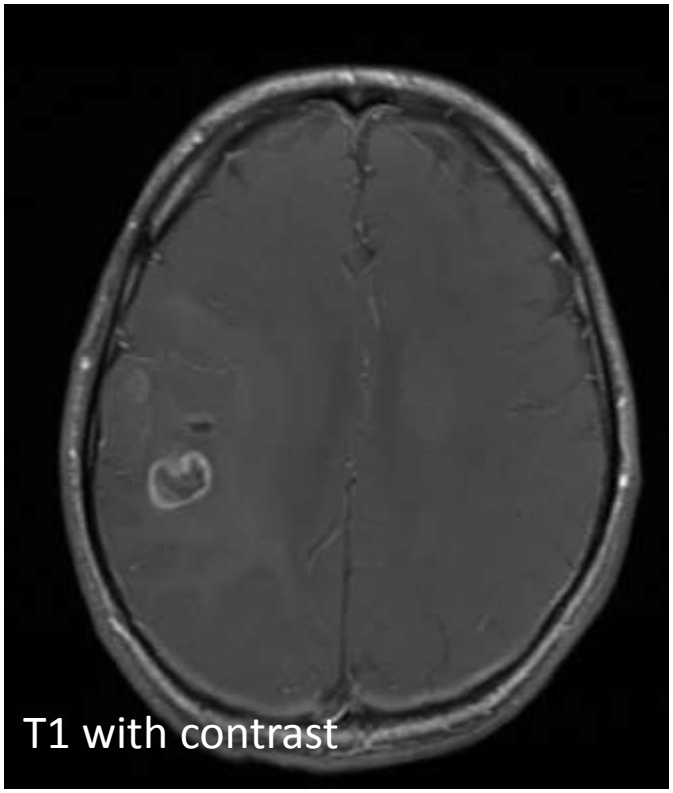

1. Pai, R.K., Bettington, M., Srivastava, A. and Rosty, C., 2019. An update on the morphology and molecular pathology of serrated colorectal polyps and associated carcinomas. *Modern Pathology*, p.1.
2. Liu, C., Walker, N.I., Leggett, B.A., Whitehall, V.L., Bettington, M.L. and Rosty, C., 2017. Sessile serrated adenomas with dysplasia: morphological patterns and correlations with MLH1 immunohistochemistry. *Modern Pathology*, *30*(12), p.1728.
3. Sheridan, T.B., Fenton, H., Lewin, M.R., Burkart, A.L., Iacobuzio-Donahue, C.A., Frankel, W.L. and Montgomery, E., 2006. Sessile serrated adenomas with low-and high-grade dysplasia and early carcinomas: an immunohistochemical study of serrated lesions "caught in the act". *American journal of clinical pathology*, *126*(4), pp.564-571.
4. Goldstein, N.S., 2006. Small colonic microsatellite unstable adenocarcinomas and high-grade epithelial dysplasias in sessile serrated adenoma polypectomy specimens: a study of eight cases. *American journal of clinical pathology*, *125*(1), pp.132-145.
5. Fujita, K., Yamamoto, H., Matsumoto, T., Hirahashi, M., Gushima, M., Kishimoto, J., Nishiyama, K.I., Taguchi, T., Yao, T. and Oda, Y., 2011. Sessile serrated adenoma with early neoplastic progression: a clinicopathologic and molecular study. *The American journal of surgical pathology*, *35*(2), pp.295-304.
6. Kim, K.M., Lee, E.J., Ha, S., Kang, S.Y., Jang, K.T., Park, C.K., Kim, J.Y., Kim, Y.H., Chang, D.K. and Odze, R.D., 2011. Molecular features of colorectal hyperplastic polyps and sessile serrated adenoma/polyps from Korea. *The American journal of surgical pathology*, *35*(9), pp.1274-1286.
7. Nagtegaal, I.D., Odze, R.D., Klimstra, D., Paradis, V., Rugge, M., Schirmacher, P., Washington, M.K., Carneiro, F. and Cree, I.A., 2019. The 2019 WHO classification of tumours of the digestive system. *Histopathology*.

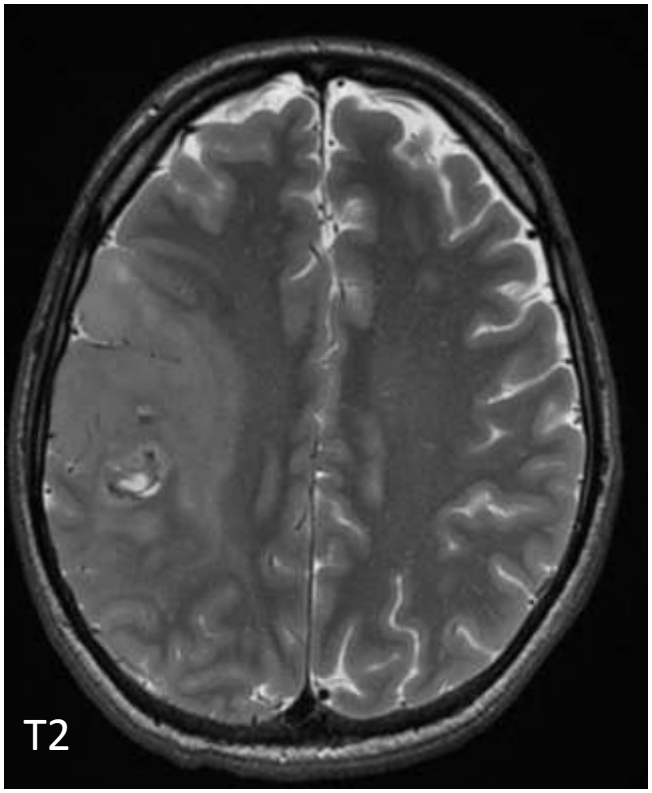
# 20-0107

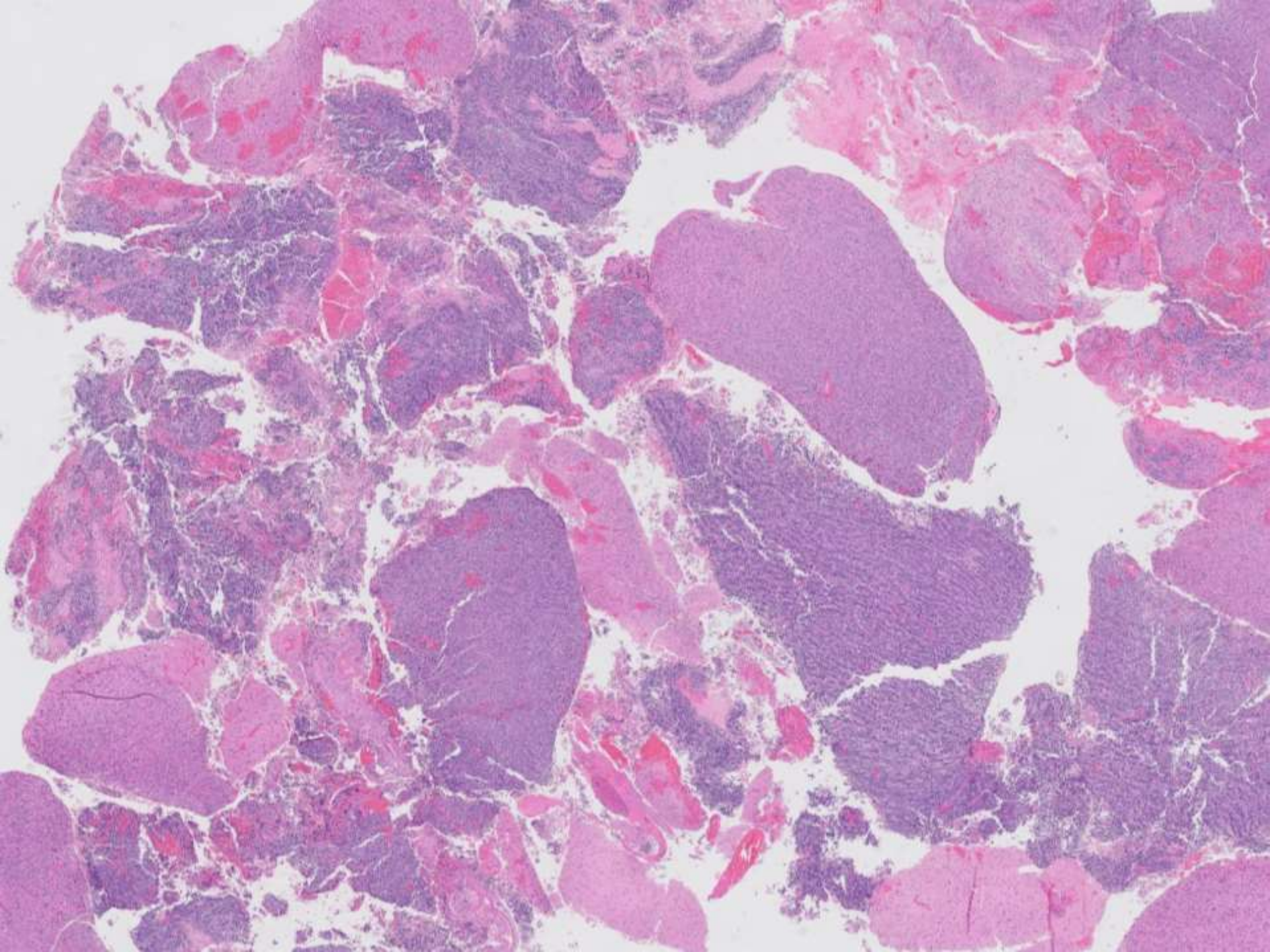
**Romain Cayrol/Hannes Vogel; Stanford**

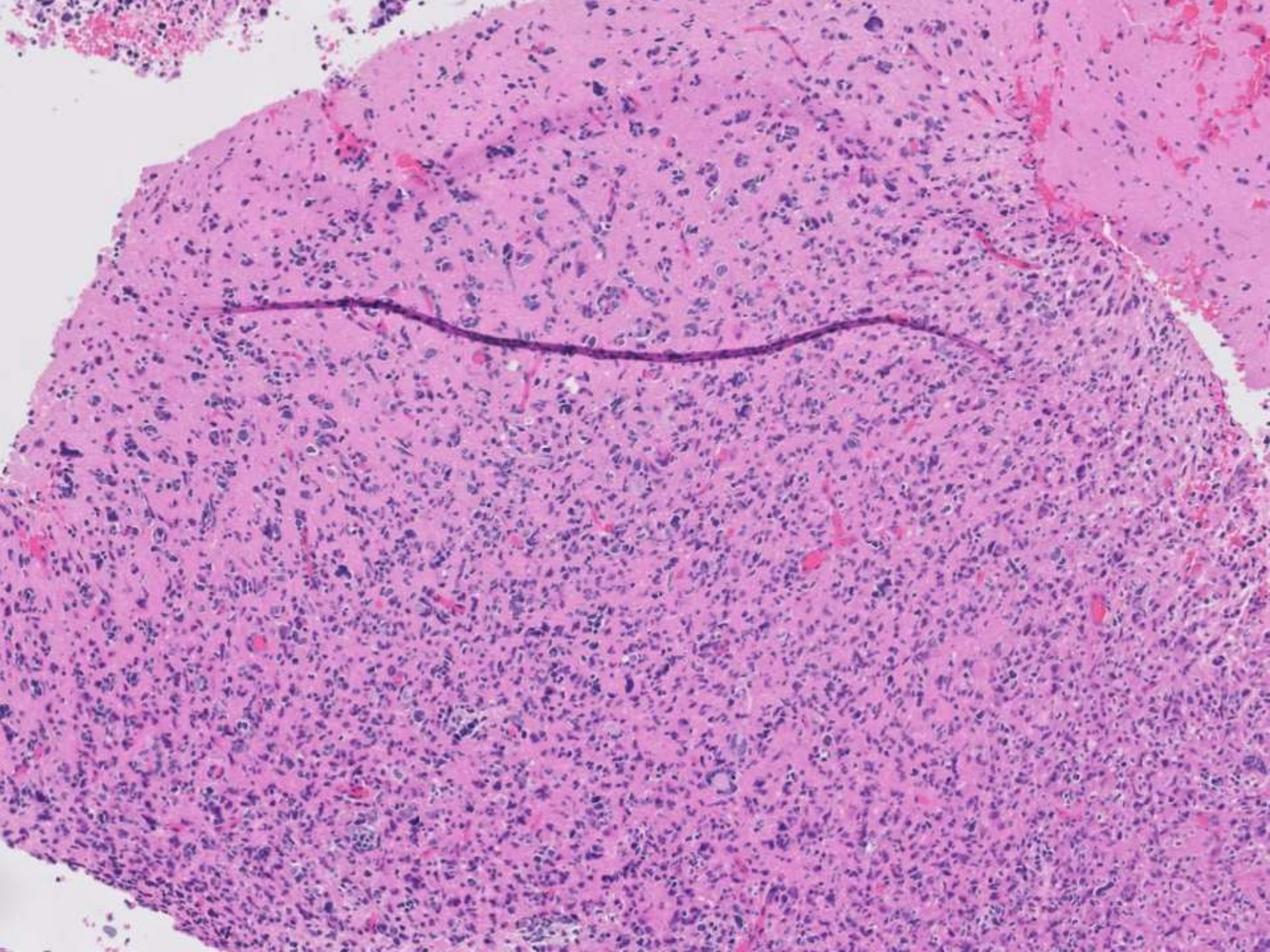
15-year-old M presents with seizures. Imaging revealed a ring-enhancing right front mass.

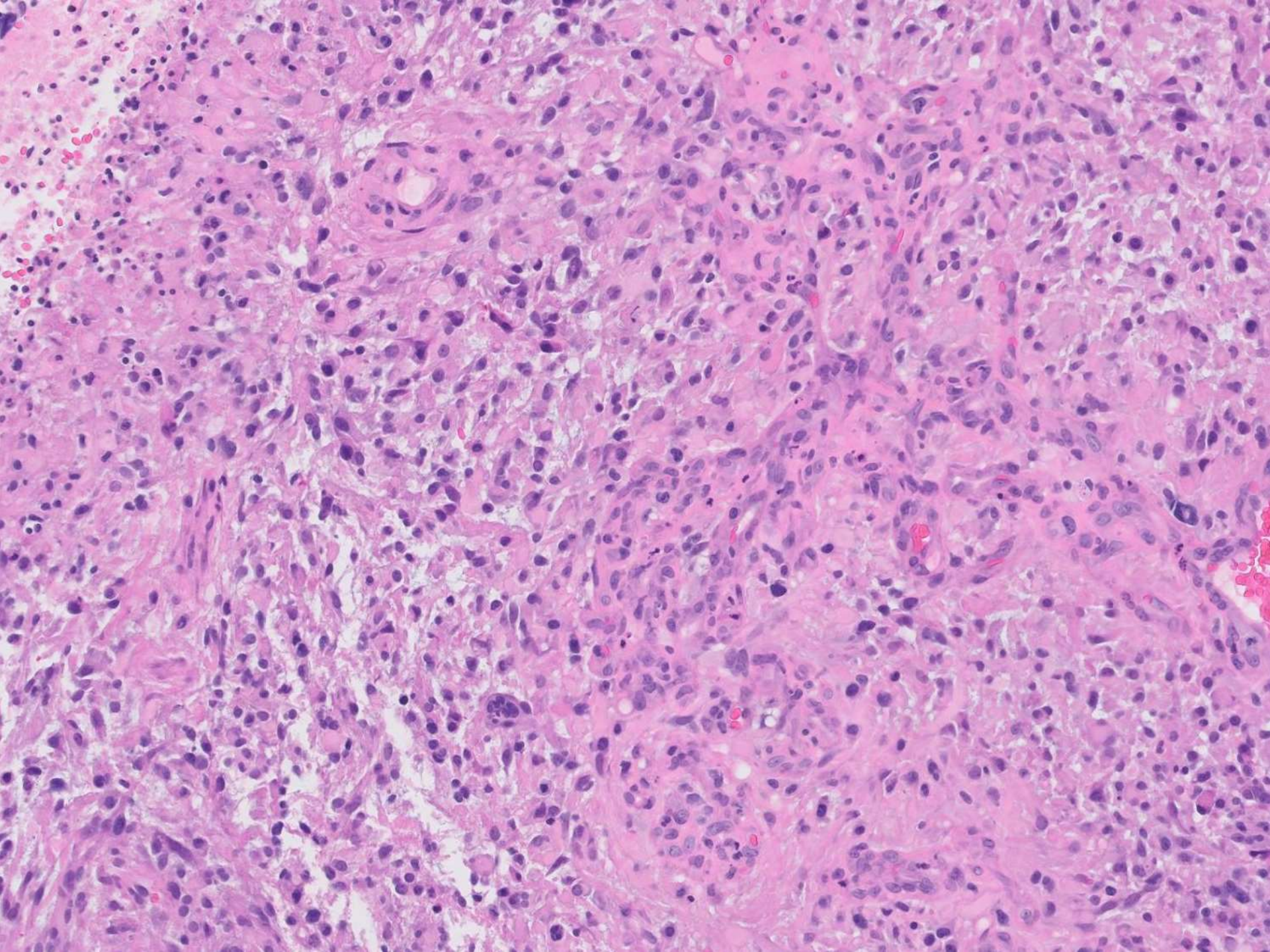
- 15 year old boy who presented with seizures
- Imaging revealed a ring-enhancing  right frontal mass

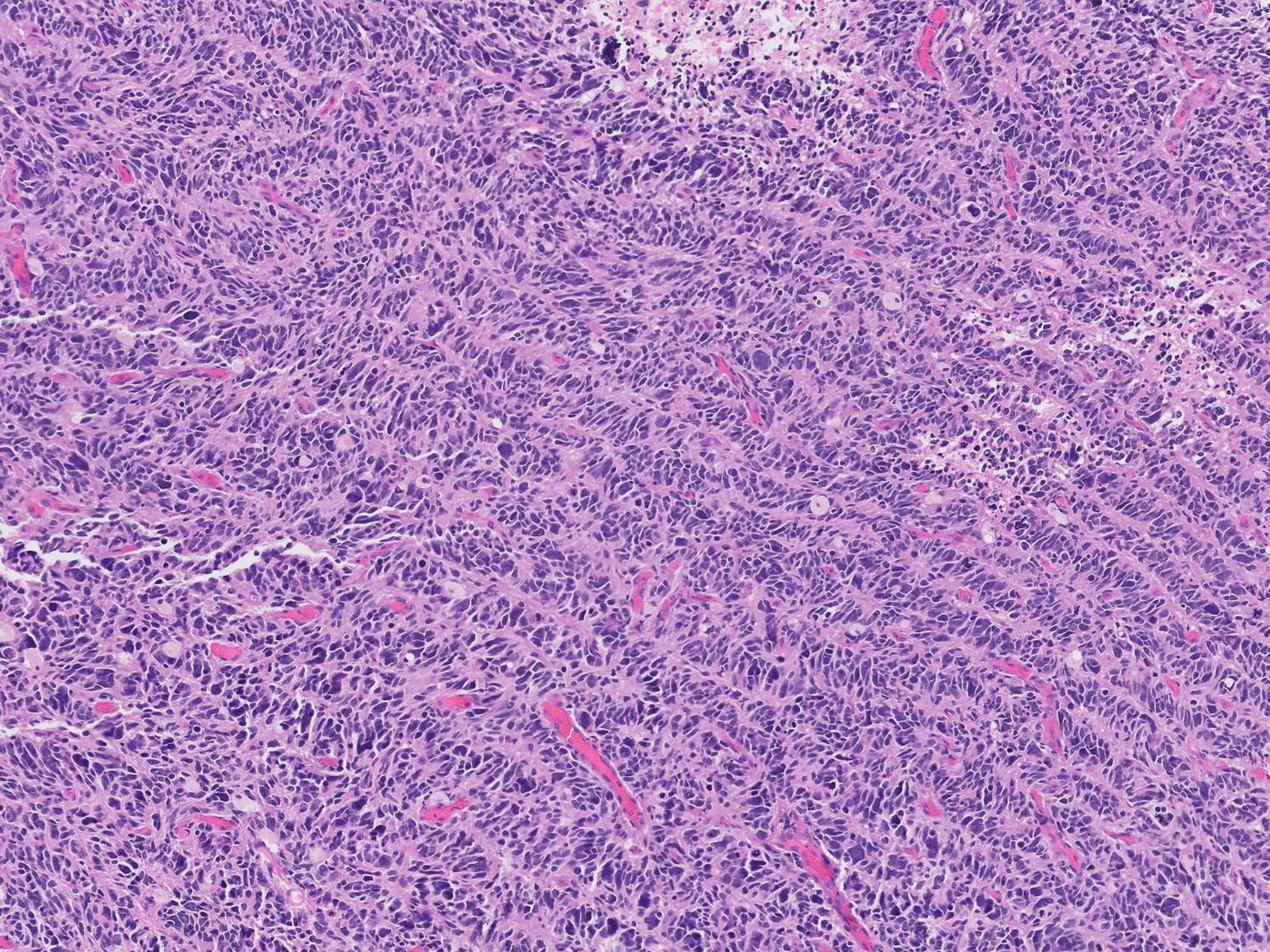


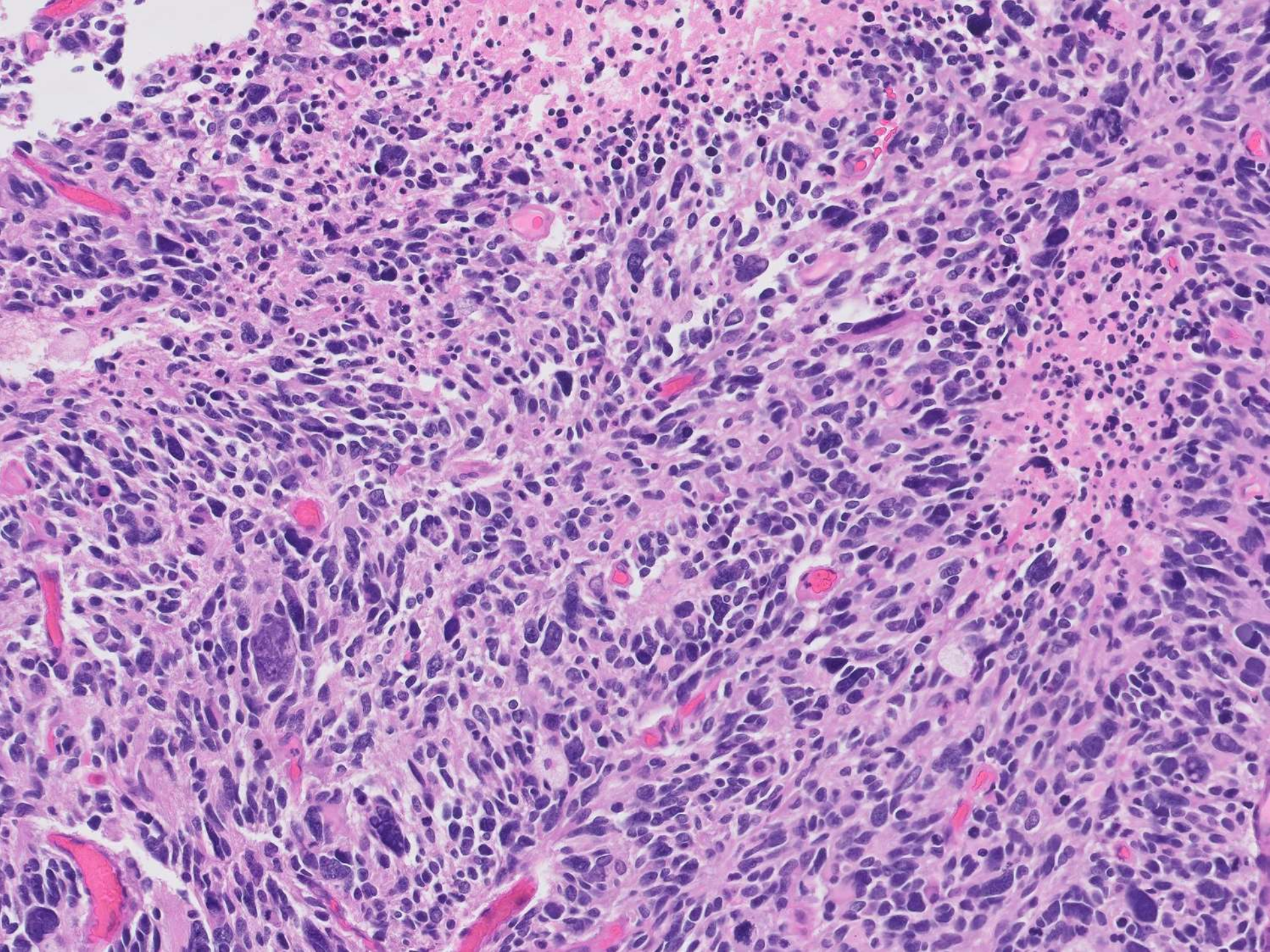







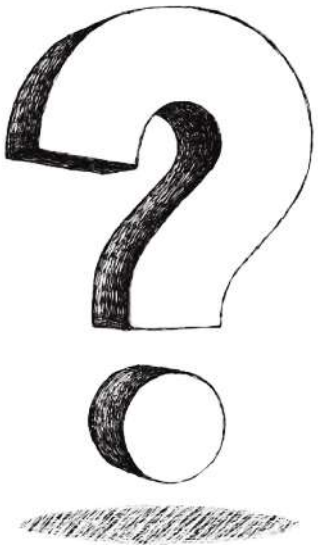






- Immunohistochemistry:
  - Positive: GFAP (focal and patchy), CD56, p53
  - Negative: IDH1 R132H, H3K27M, H3K27me3 (retained)
  - ATRX (patchy loss) equivocal

- DIAGNOSIS:
- A. BRAIN, ANTERIOR RIGHT FRONTAL TUMOR, RESECTION



- DIAGNOSIS:
- A. BRAIN, ANTERIOR RIGHT FRONTAL TUMOR, RESECTION
- -- *MALIGNANT NEUROEPETHELIAL NEOPLASM*
  - *St-Jude Children's Hospital: HIGH GRADE NEUROEPITHELIAL TUMOR*

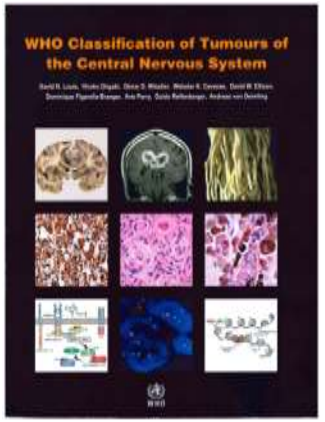
# Molecular studies

- BRAIN, RIGHT FRONTAL “ENHANCING” TUMOR, MUTATIONAL PROFILING BY FOUNDATION ONE CDx
  - -- *POSITIVE FOR H3F3 G35V MUTATION*
  - -- POSITIVE FOR ATRX EXONS 3-10 LOSS
  - -- POSITIVE FOR KDM6A EXONS LOSS 4-28
  - -- POSITIVE FOR TP53 G245S MUTATION
  - -- POSITIVE FOR TP53 R342* MUTATION
  - -- POSITIVE FOR AKT3 E17K MUTATION

- MGMT promoter methylated

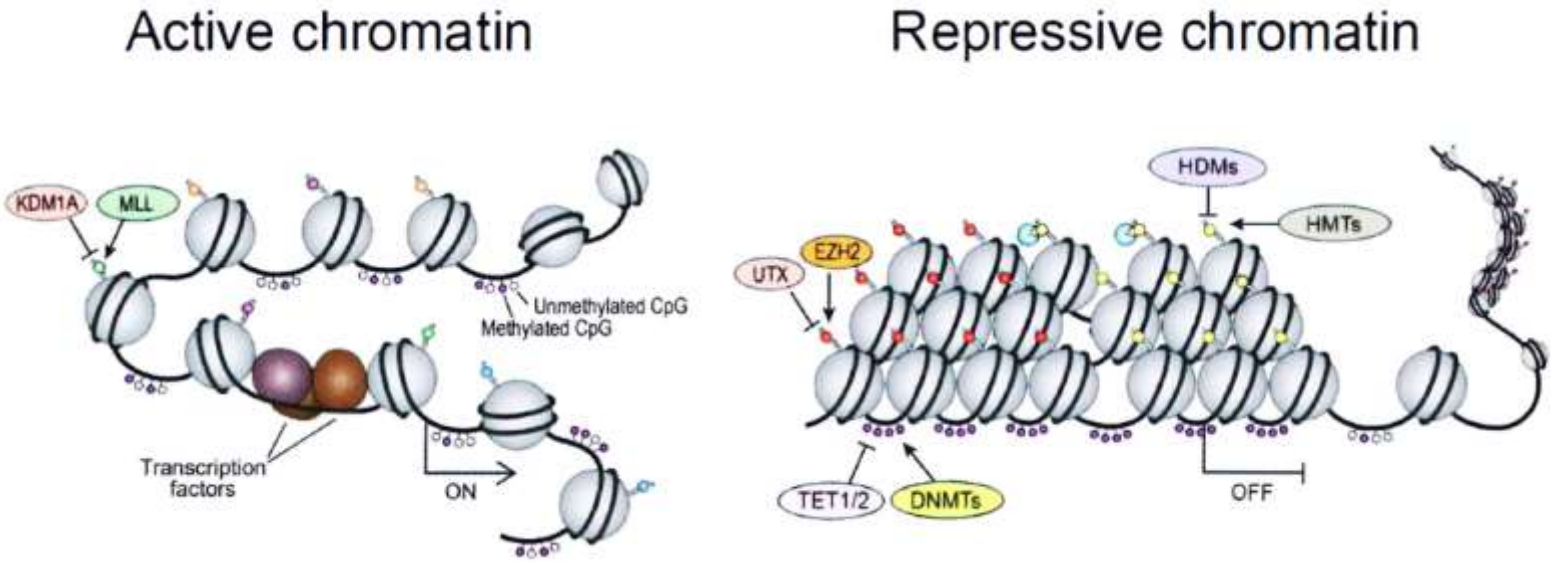
- DIAGNOSIS:
- A. BRAIN, ANTERIOR RIGHT FRONTAL TUMOR, RESECTION
- -- GLIOBLASTOMA, IDH WILDTYPE AND H3 G34/35 MUTANT, NOT ELSEWHERE CLASSIFIED (NEC), WHO GRADE IV

# Diffuse midline glioma, H3 K27M–mutant




- Infiltrative midline high-grade glioma with predominantly astrocytic differentiation and H3 K27M mutation H3F3A or HIST1H3B/C, WHO Grade IV

- Mutations result in decreased H3K27 methylation and alters chromatin regulation



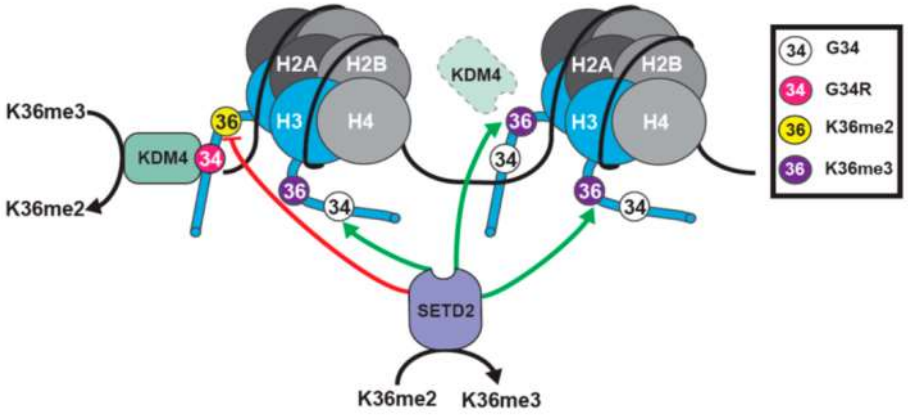
Acta Neuropathol (2016) 131:137–146
DOI 10.1007/s00401-015-1493-1

ORIGINAL PAPER

# Histologically distinct neuroepithelial tumors with histone 3 G34 mutation are molecularly similar and comprise a single nosologic entity

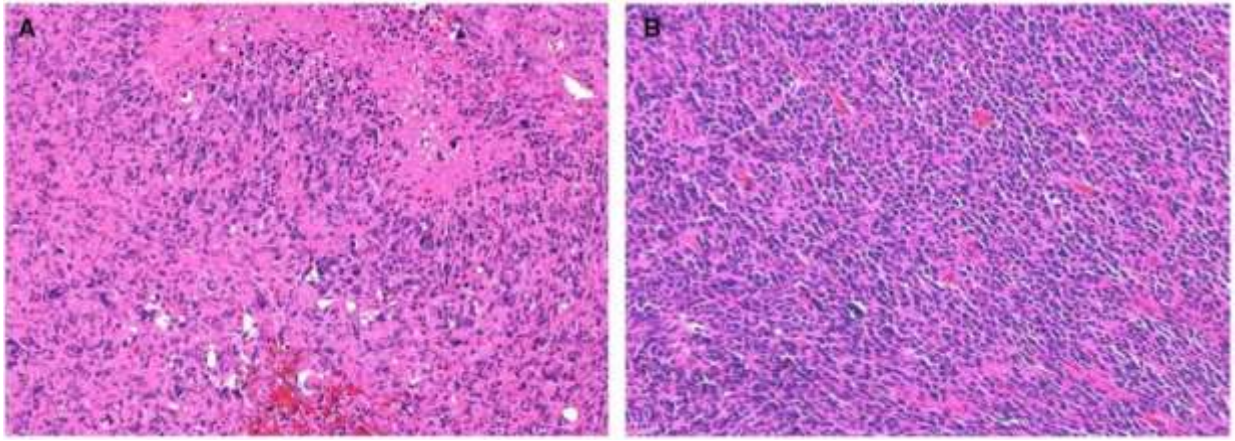
Andrey Korshunov[1,2,3] · David Capper[1,2,3] · David Reuss[1,2,3] · Daniel Schrimpf[1,2] · Marina Ryzhova[4] · Volker Hovestadt[5] · Dominik Sturm[6,7] · Jochen Meyer[1,2] · Chris Jones[8] · Olga Zheludkova[9] · Ella Kumirova[10] · Andrey Golanov[11] · Marcel Kool[3,6] · Ulrich Schüller[12] · Michel Mittelbronn[13] · Martin Hasselblatt[14] · Jens Schittenhelm[15] · Guido Reifenberger[16] · Christel Herold-Mende[17] · Peter Lichter[3,5] · Andreas von Deimling[1,2,3] · Stefan M. Pfister[3,6,7] · David T. W. Jones[3,6]

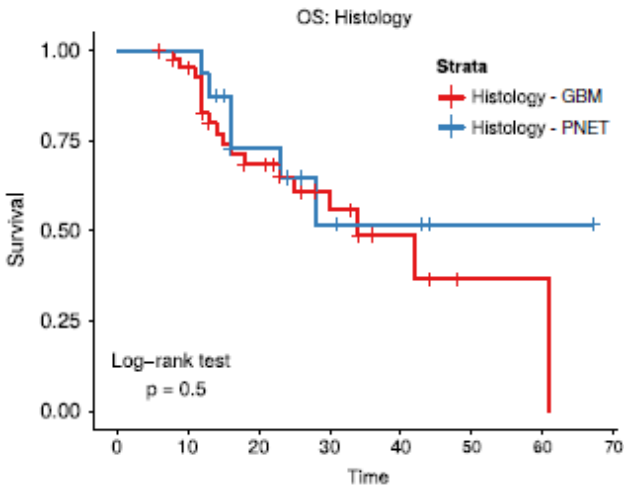
- Case series with 81 H3 G34/35 R/V mutant gliomas
- 9-51 years, mostly young adults (median 19 years old, 87% between 11 and 30)
- Cerebral hemispheres, predominantly temporal and parietal
- Median progression free survival 9 months, 88% has recurrence
- Mean overall survival 22 months



# H3 G34 glioma

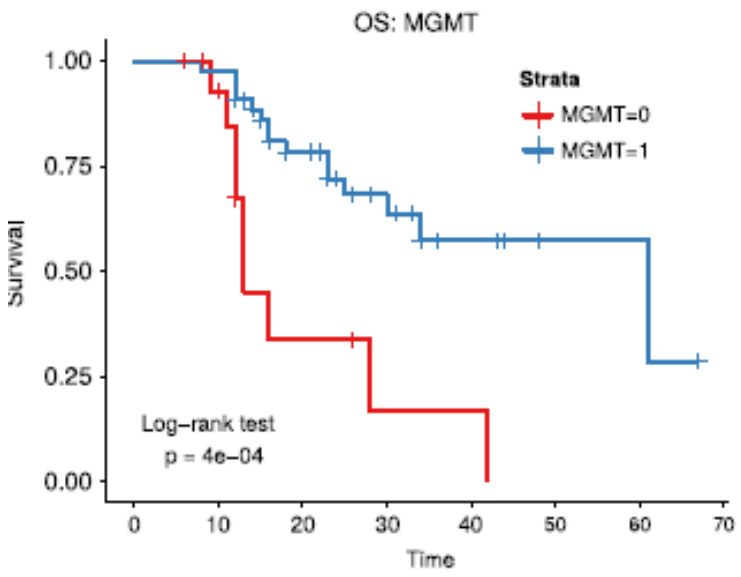
- Histology demonstrate high grade features (73% of cases, astrocytic lineage, mitoses, pleomorphism, microvascular proliferation-necrosis)
  - 30% demonstrate embryonal morphology or Primitive Neuroectodermal Tumor (PNET)-like
- GFAP+, olig2+, **p53+**, **ATRX loss**, MGMT promoter methylation
- Defined by the H3 glycine 34/35 mutation
  - p53 mutation (88%), ATRX loss (95%), MGMT methylation (75%)
  - 50% with oncogene amplification: PDGFRA, CCND2, CDK6
  - Loss 3q and/or 4q

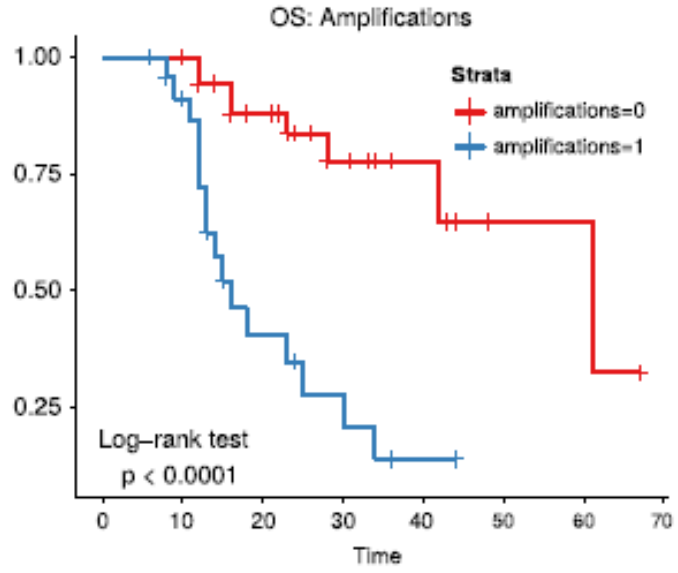


# H3 G34 glioma

- Multivariate analysis identified 2 independent prognostic factors
  - MGMT methylation, good prognosis
  - Oncogene amplification, bad prognosis



# Conclusion

- Malignant gliomas with heterogeneous histologic features defined by *H3 G34/35 R/V mutations*
  - Young adult, hemispheric
  - GBM and PNET-like histology
  - Molecularly distinct
    - p53, ATRX, oncogene amplification, MGMT promoter methylation
  - Not Elsewhere Classified since not yet included in the WHO classification of CNS tumors

# References


- Louis, DN, WHO Classification of Central Nervous System tumor, 2016

- Histologically distinct neuroepithelial tumors with histone 3 G34 mutation are molecularly similar and comprise a single nosologic entity Korshunov A, Capper D, Reuss D, Schrimpf D, Ryzhova M, Hovestadt V, Sturm D, Meyer J, Jones C, Zheludkova O, Kumirova E, Golanov A, Kool M, Schüller U, Mittelbronn M, Hasselblatt M, Schittenhelm J, Reifenberger G, Herold-Mende C, Lichter P, von Deimling A, Pfister SM, Jones DT. Acta Neuropathol. 2016 Jan;131(1):137-46

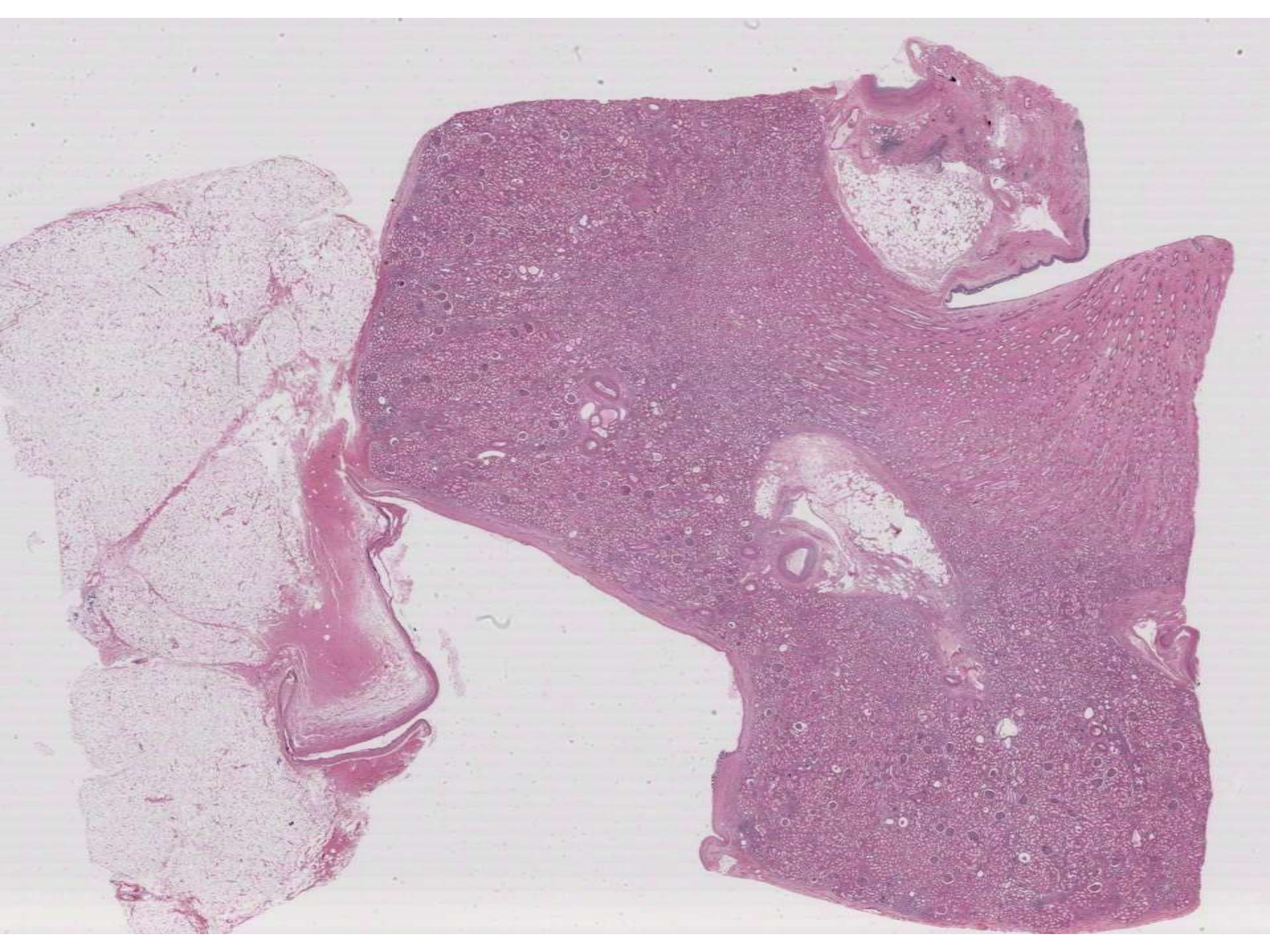
- K27/G34 versus K28/G35 in histone H3-mutant gliomas: A note of caution Leske H, Rushing E, Budka H, Niehusmann P, Pahnke J, Panagopoulos I. Acta Neuropathol. 2018 Jul;136(1):175-176

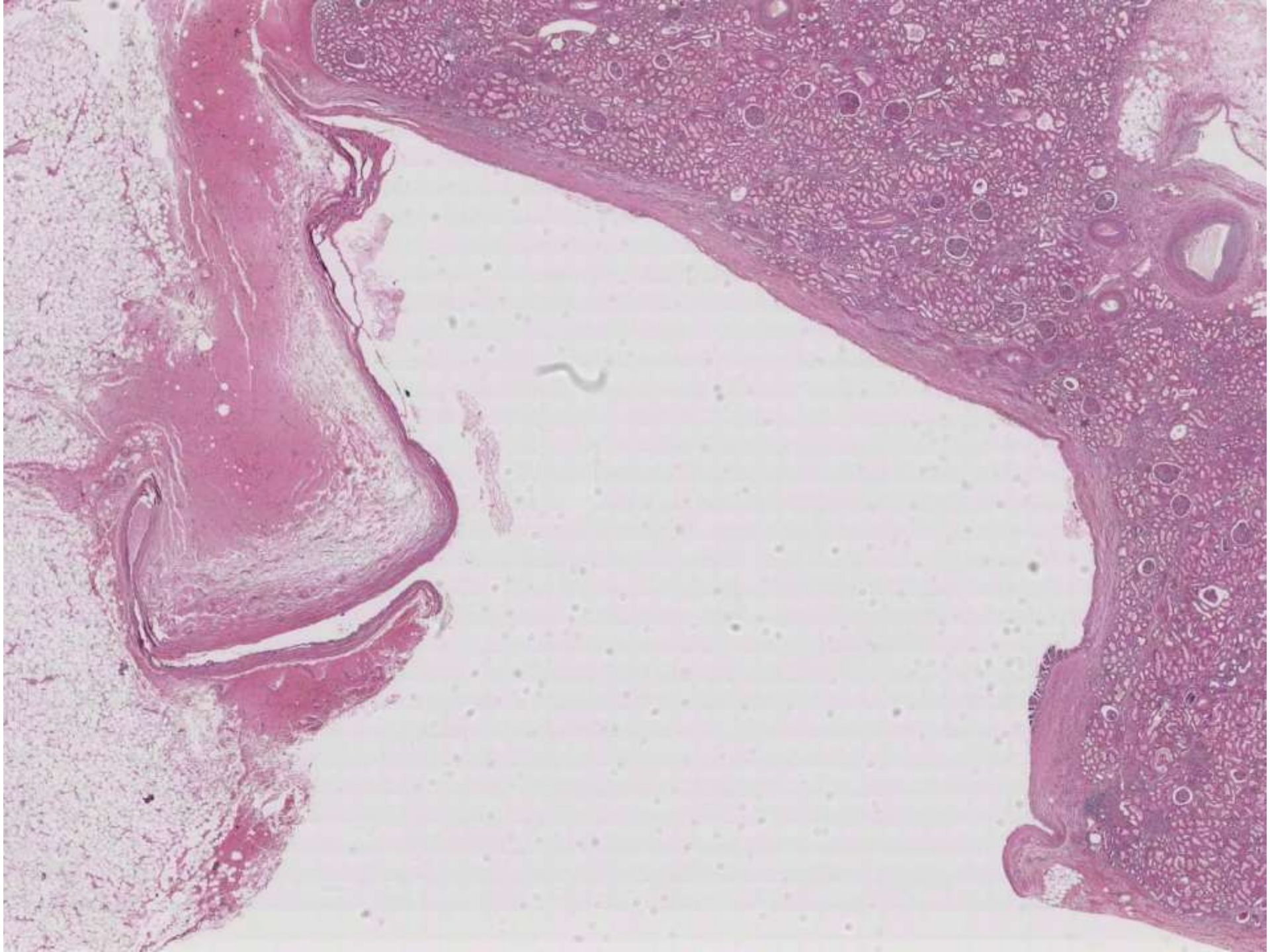
- Histone H3 Mutations: An Update on the Role in Chromatin Deregulation and Cancer Lowe BR, Maxham LA, Hamey JJ, Wilkins MR, Partridge JF. Cancers (Basel). 2019 May 13;11(5)

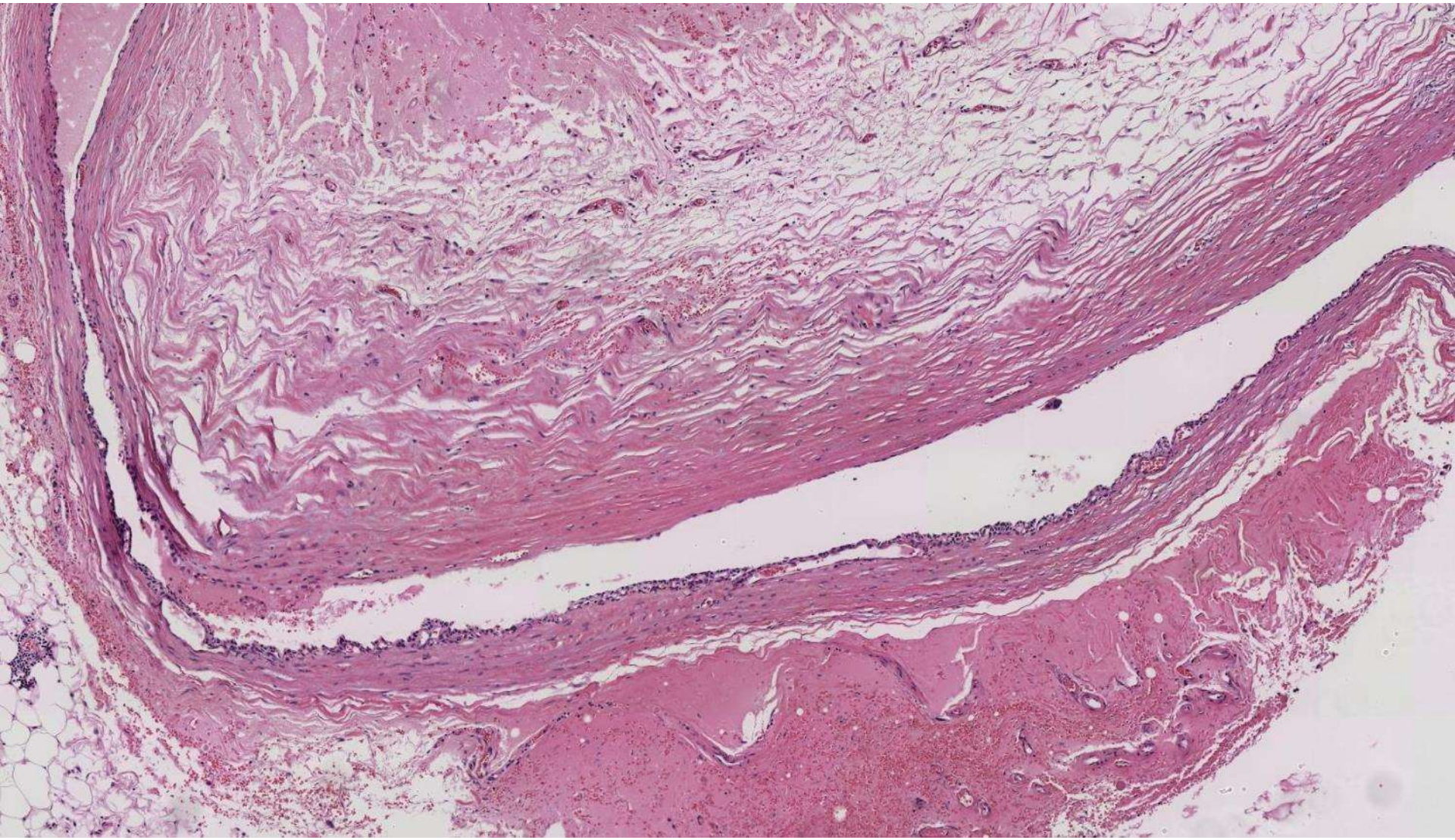

# 20-0108
# scanned slide available!

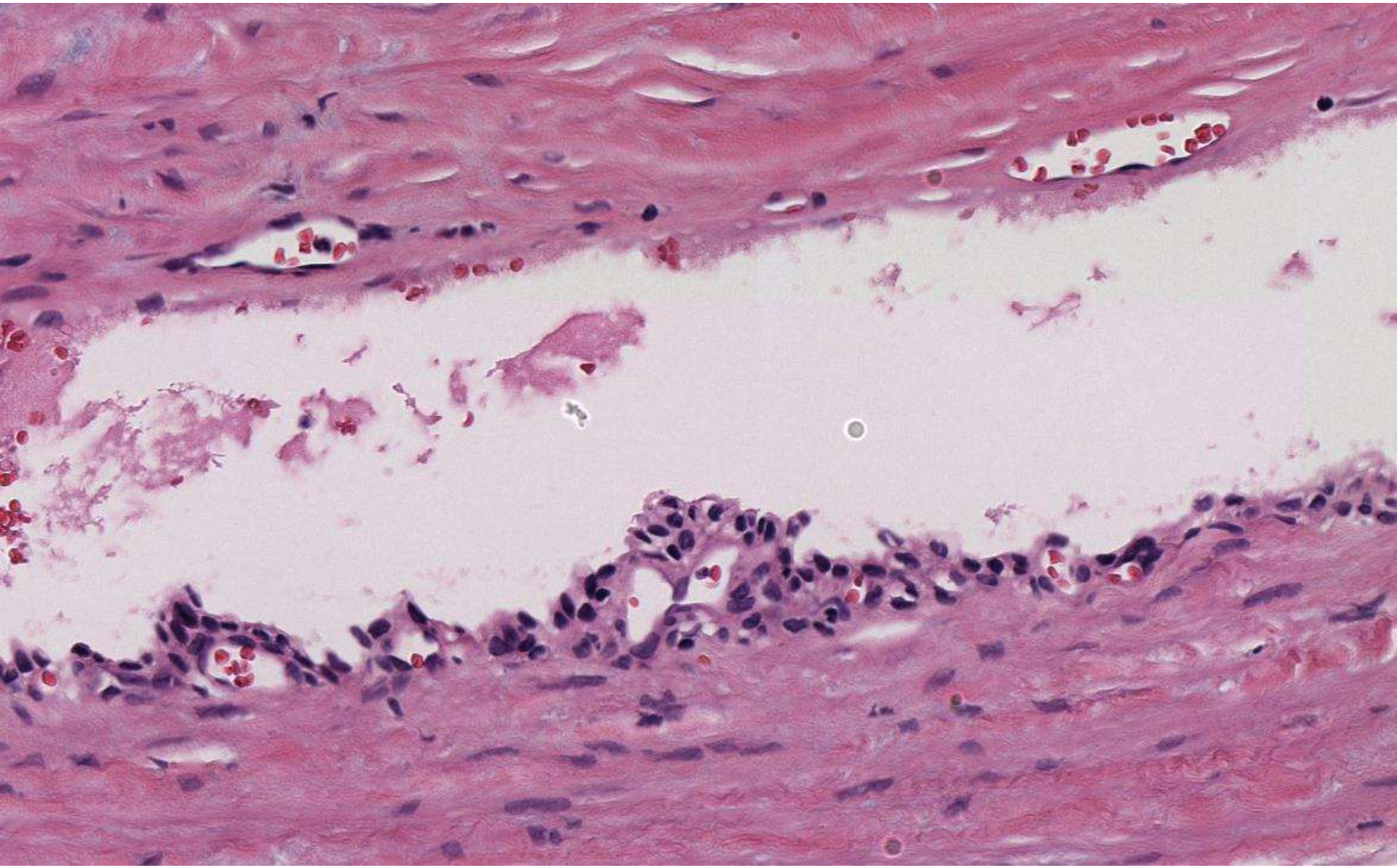
**Ankur Sangoi; El Camino Hospital**

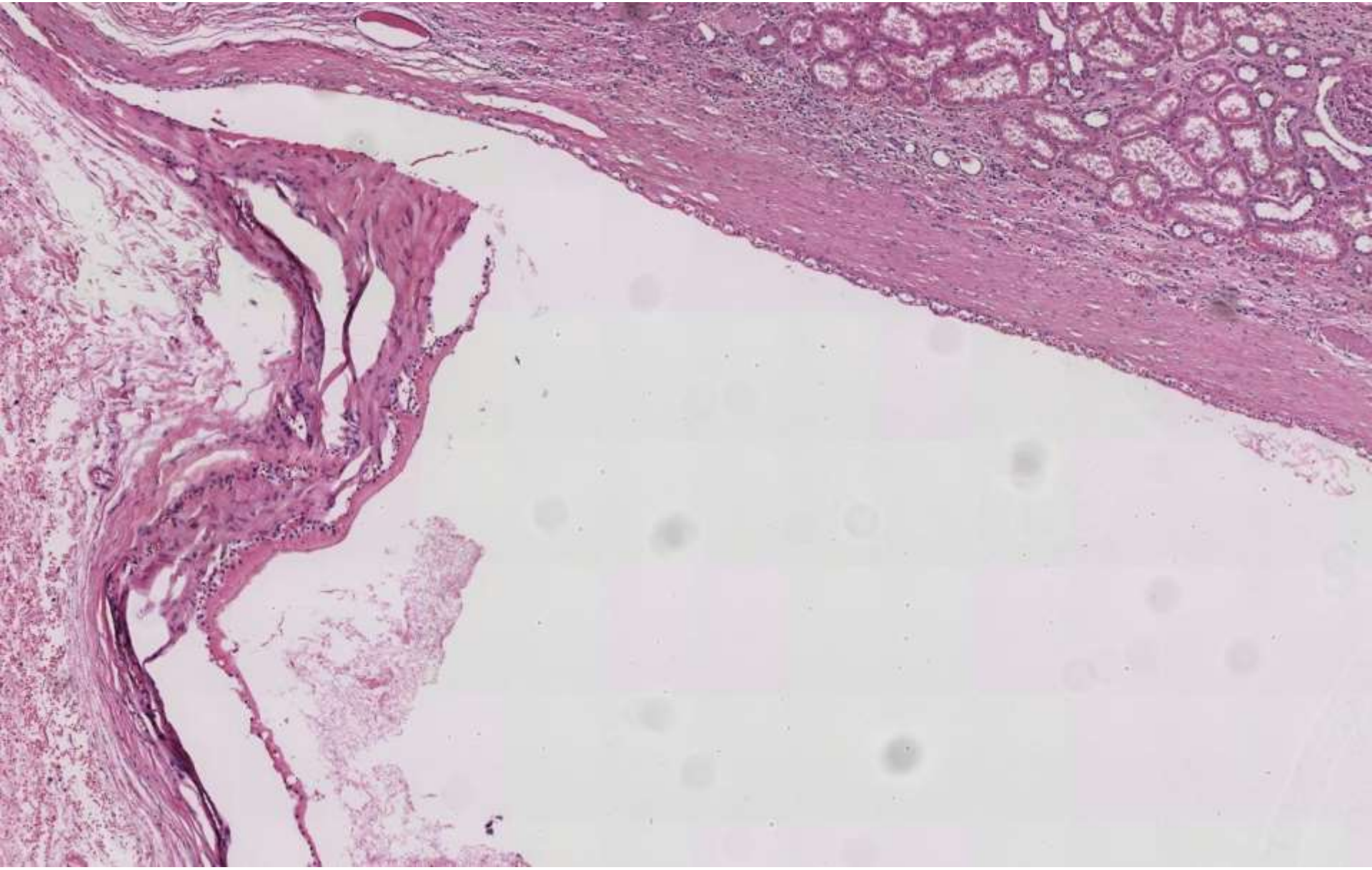
75-year-old F undergoes radical nephro-ureterectomy for renal pelvic papillary urothelial carcinoma. Background kidney away from renal pelvis shows 1.5cm cystic mass.

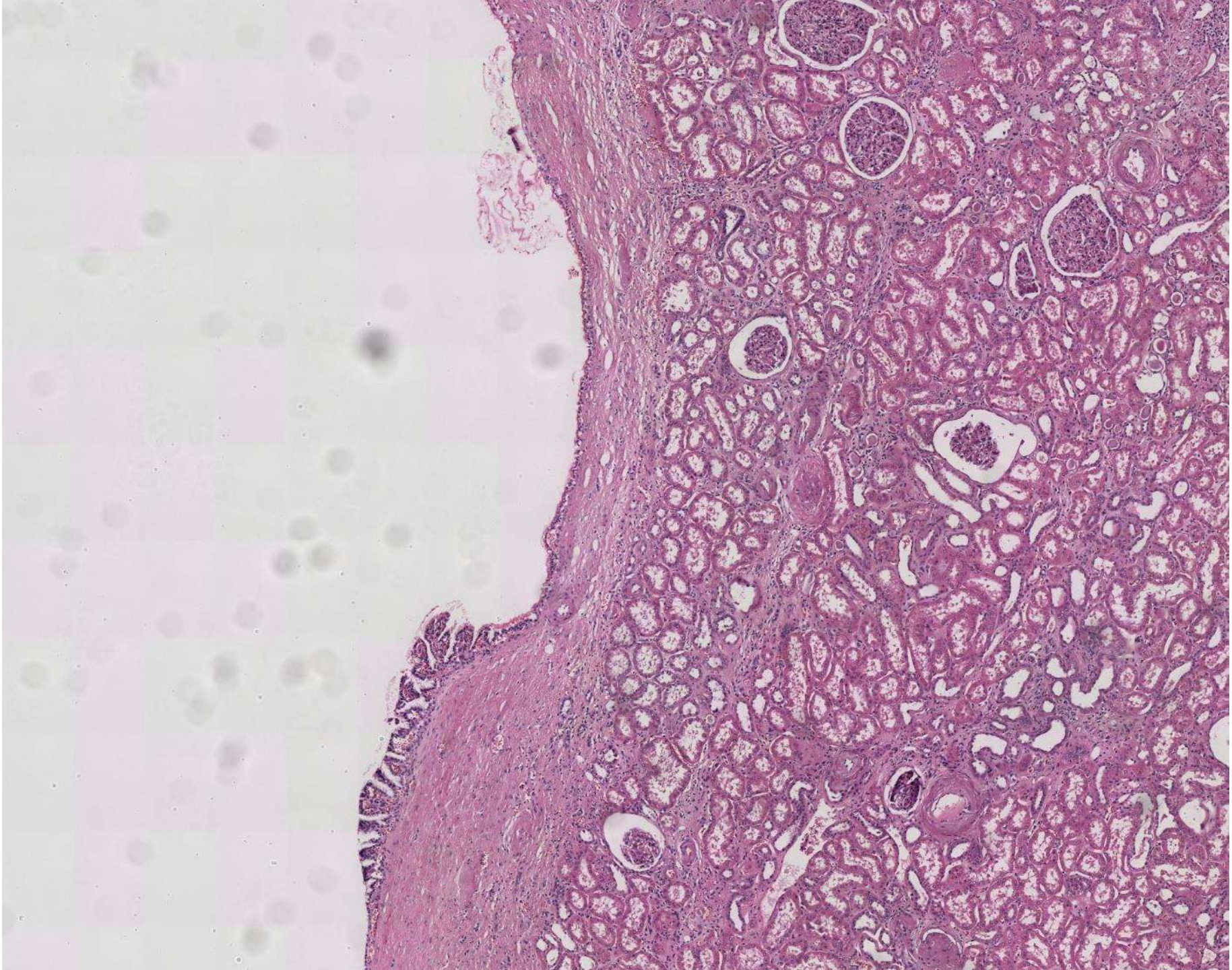


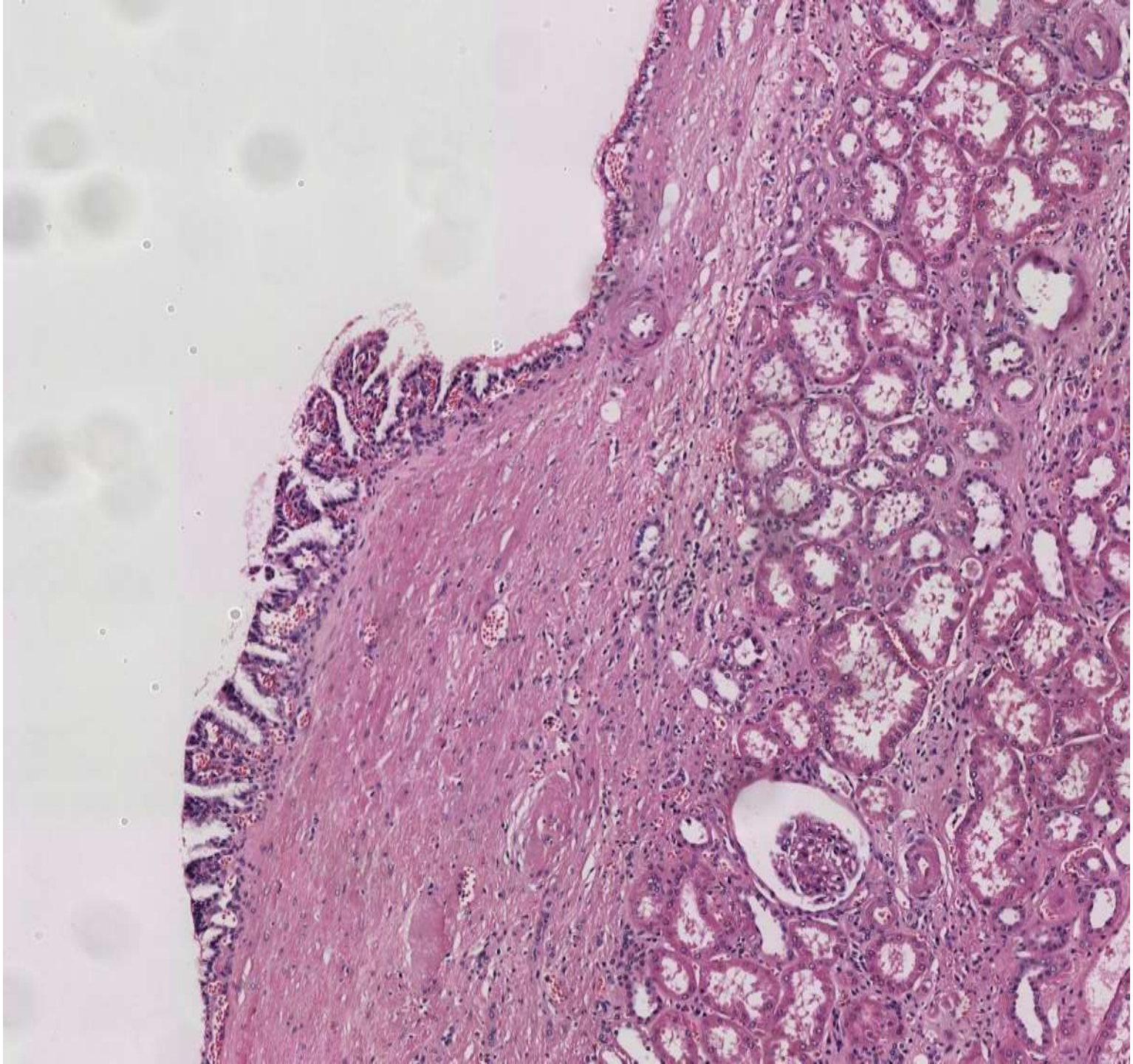


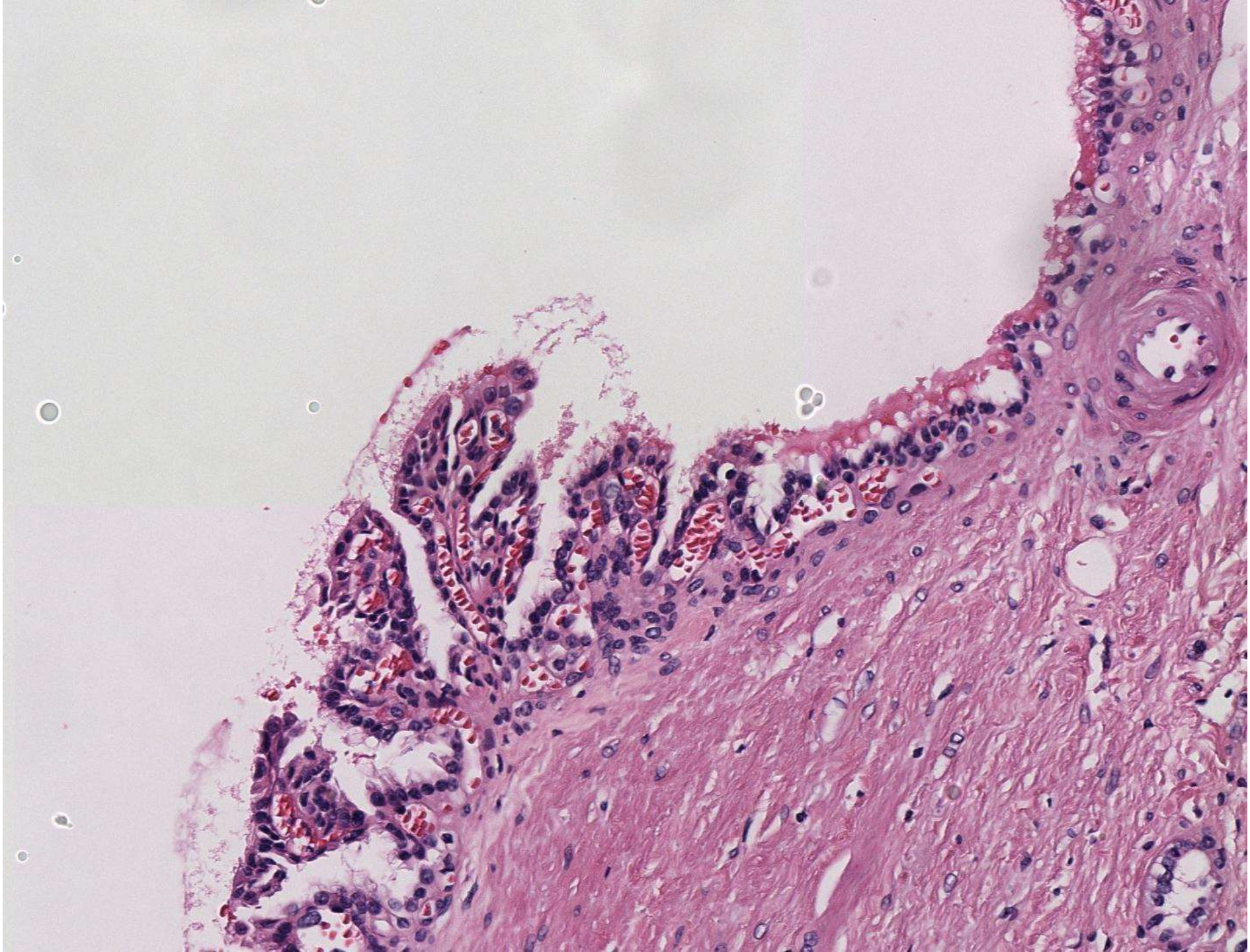


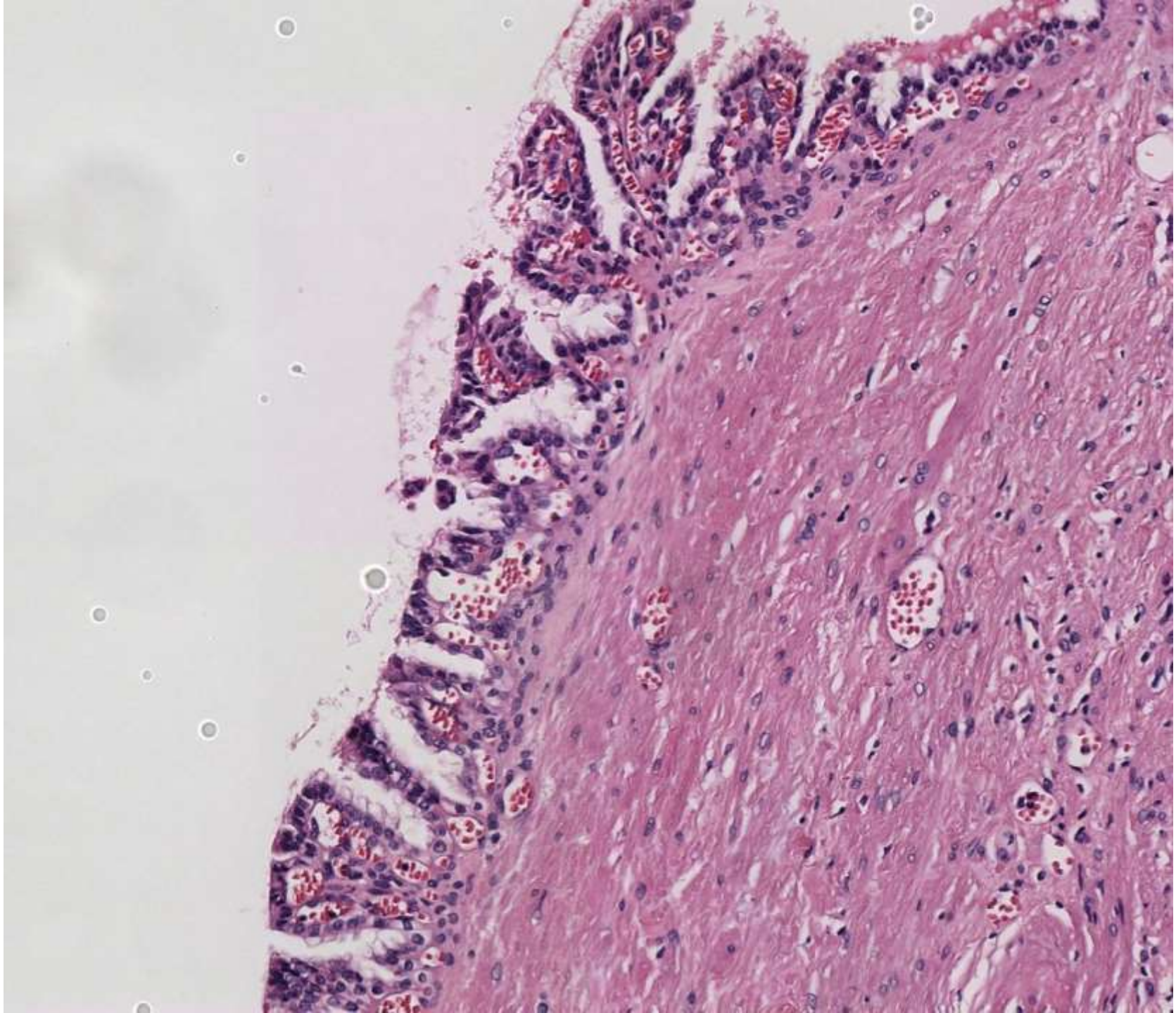


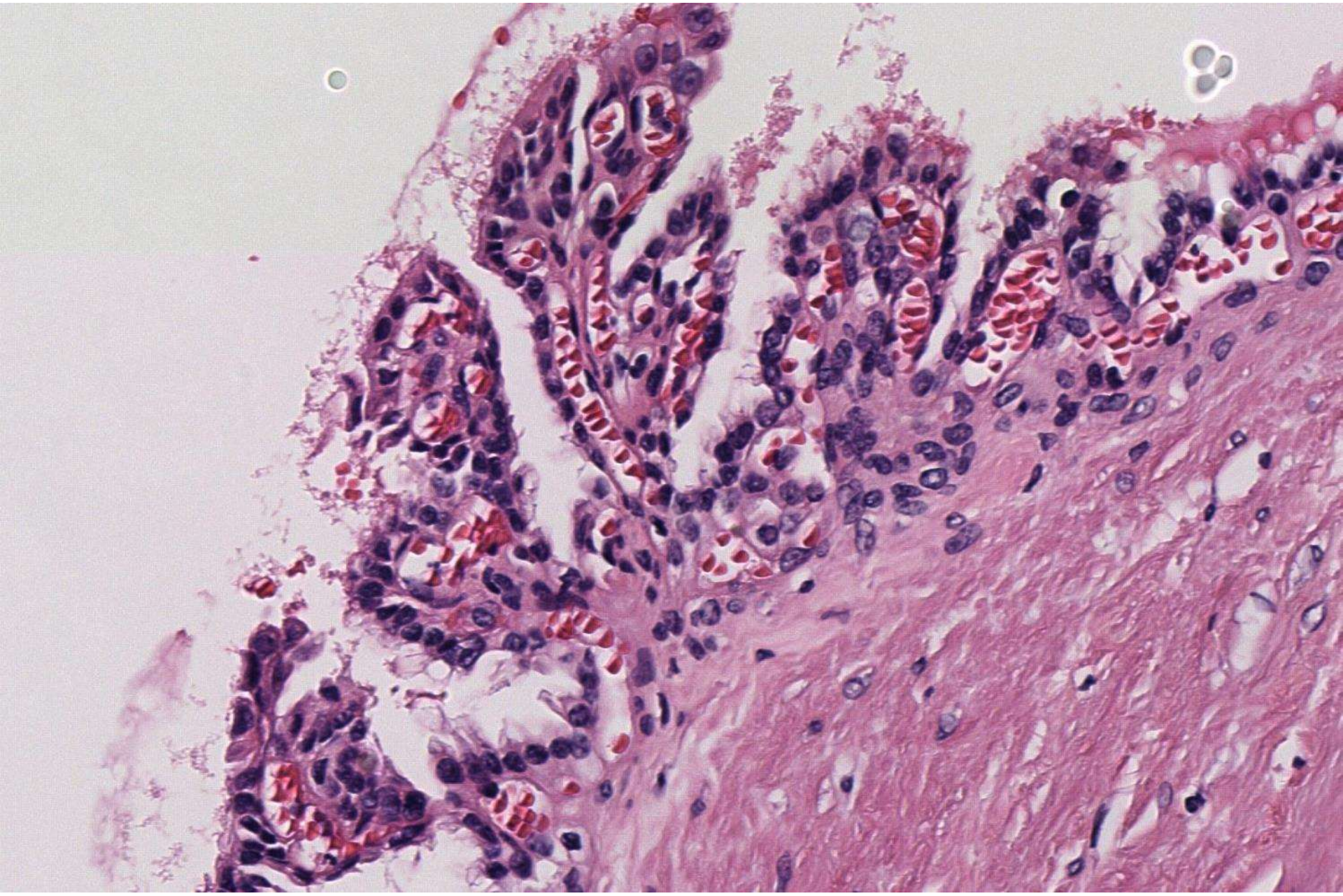






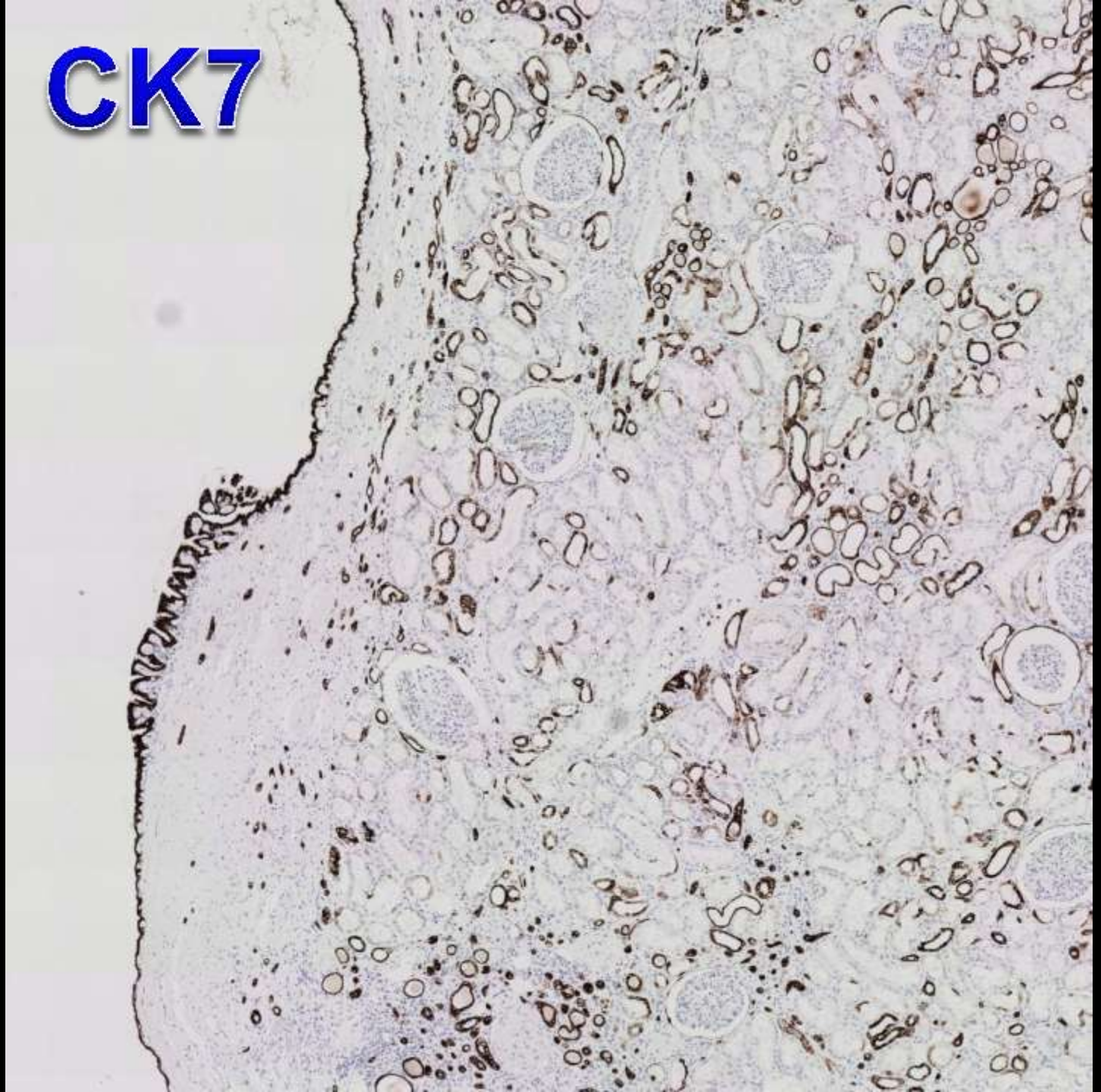


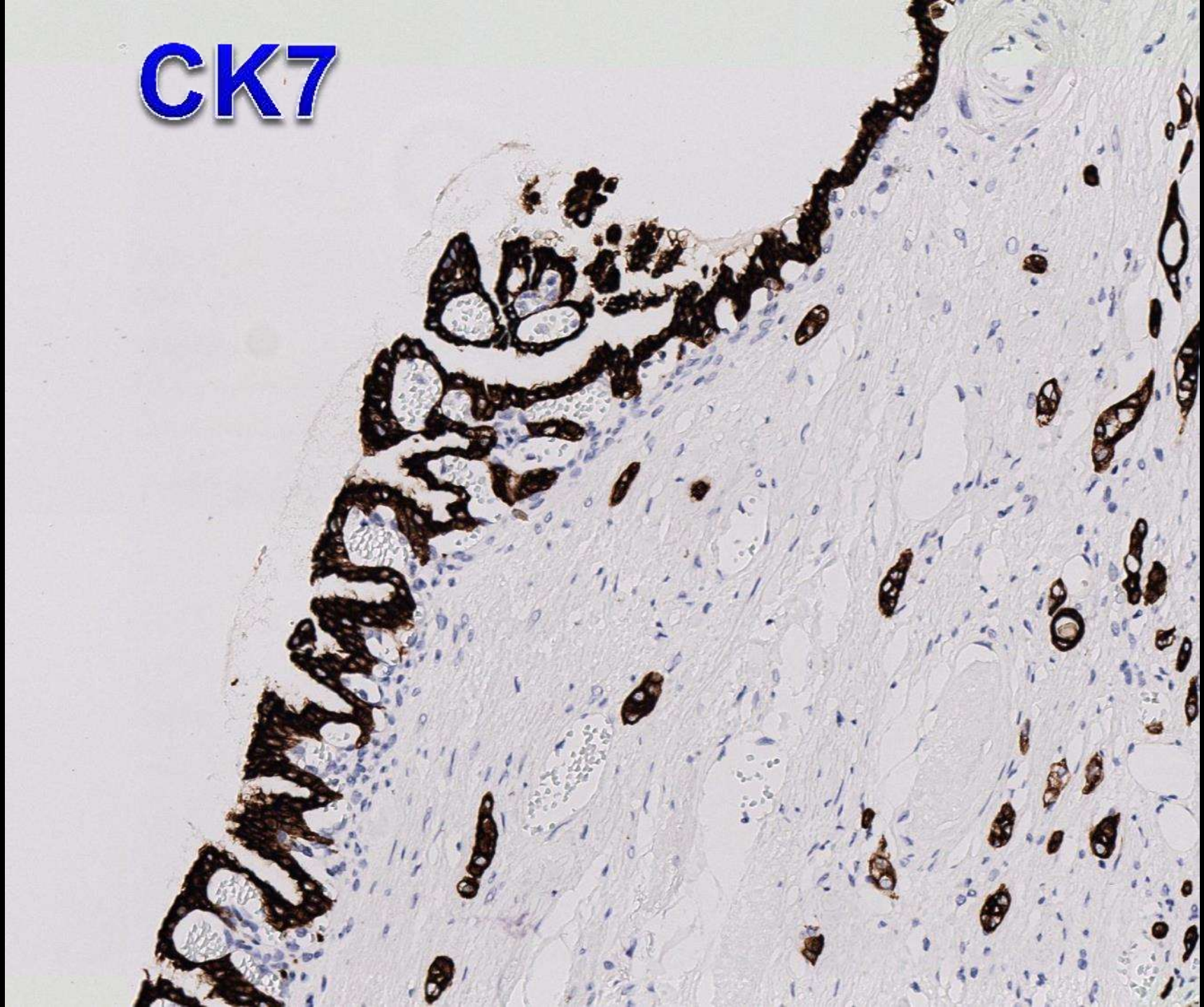




# DDx

- **MALIGNANT**
  - clear cell RCC
  - papillary RCC
  - clear cell papillary (tubulopapillary) RCC
  - MiTF/Xp11 RCC
- **BENIGN**
  - multilocular cystic renal neoplasm of LMP
  - papillary adenoma
  - cortical cyst


CK7


CK7

# IHC summary

- **CK7+++**
- **Variable CD10, CAIX, AMACR**

# Final Dx: atypical renal cyst

- **MALIGNANT**
  - clear cell RCC
  - papillary RCC
  - clear cell papillary (tubulopapillary) RCC
  - MiTF/Xp11 RCC
- **BENIGN**
  - multilocular cystic renal neoplasm of LMP
  - papillary adenoma
  - cortical cyst

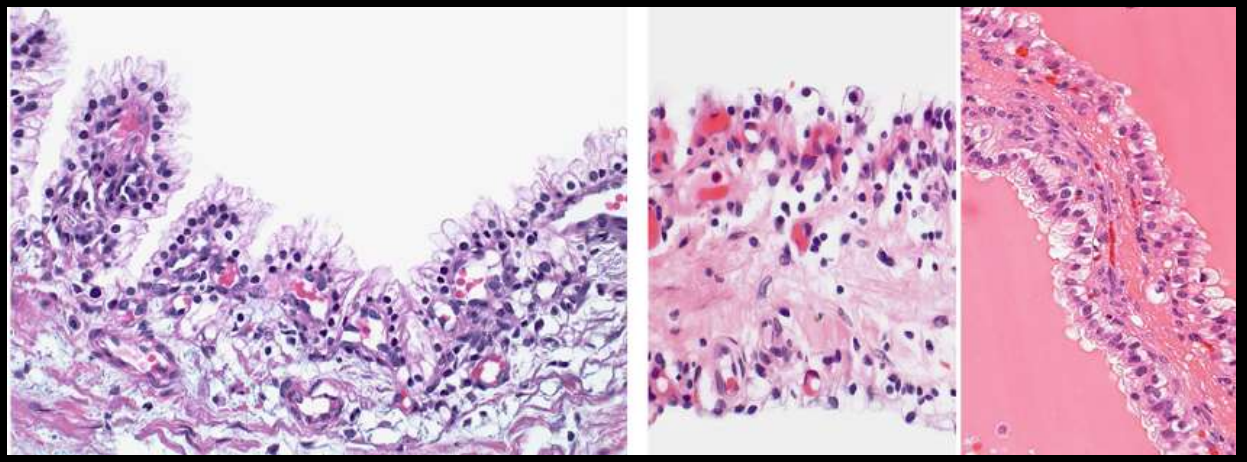
# Atypical Renal Cysts

## *A Morphologic, Immunohistochemical, and Molecular Study*

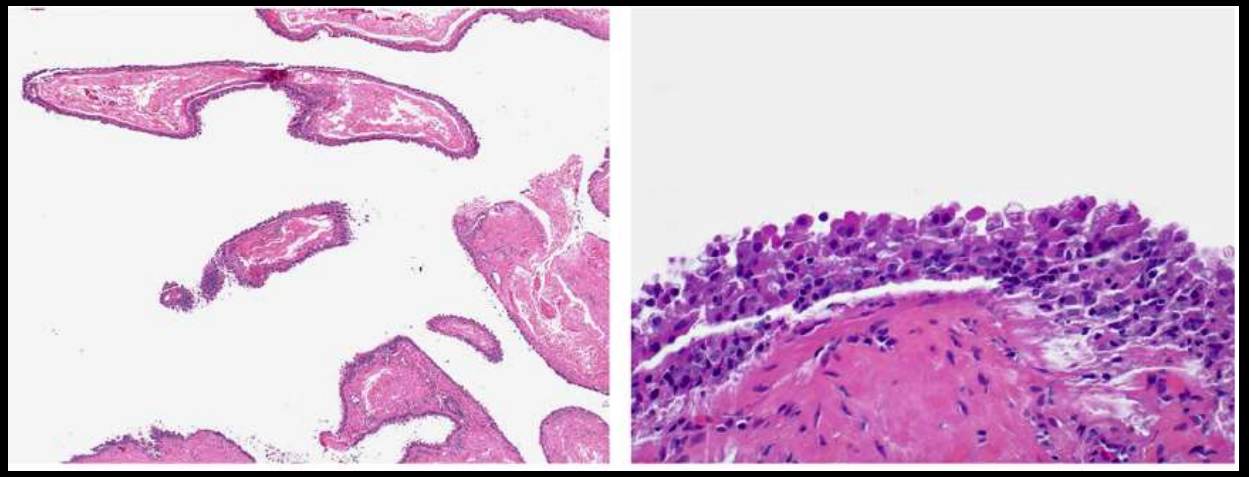
*Andres Matoso, MD,*† Ying-Bei Chen, MD, PhD,*‡ Vishal Rao, MD,* Lu Wang, MD, PhD,‡ Liang Cheng, MD,§ and Jonathan I. Epstein, MD*‖¶*

*Am J Surg Pathol* • Volume 40, Number 2, February 2016

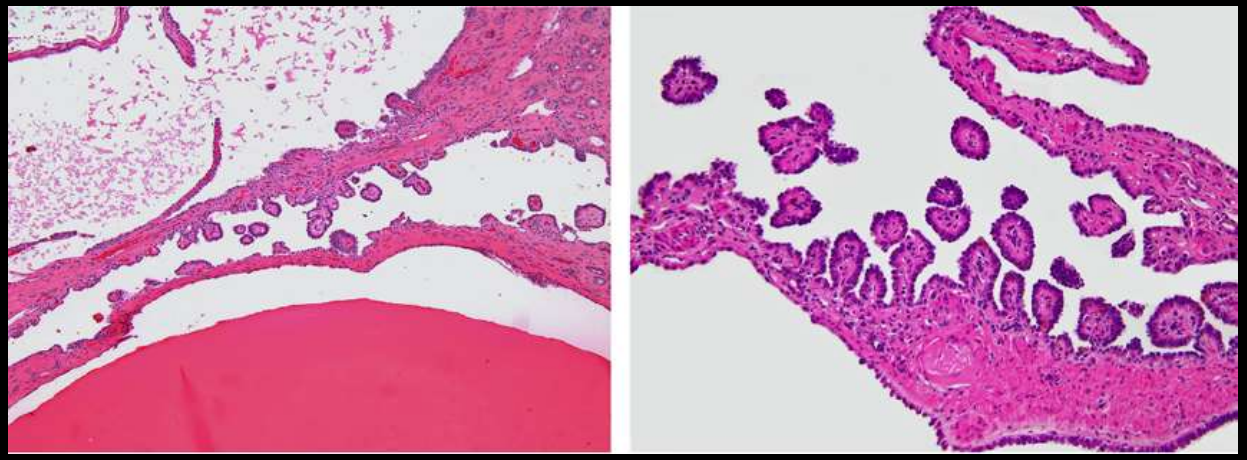
clear cell type



eosinophilic stratified type



eosinophilic papillary type



*Am J Surg Pathol* • Volume 40, Number 2, February 2016

# Atypical renal cysts

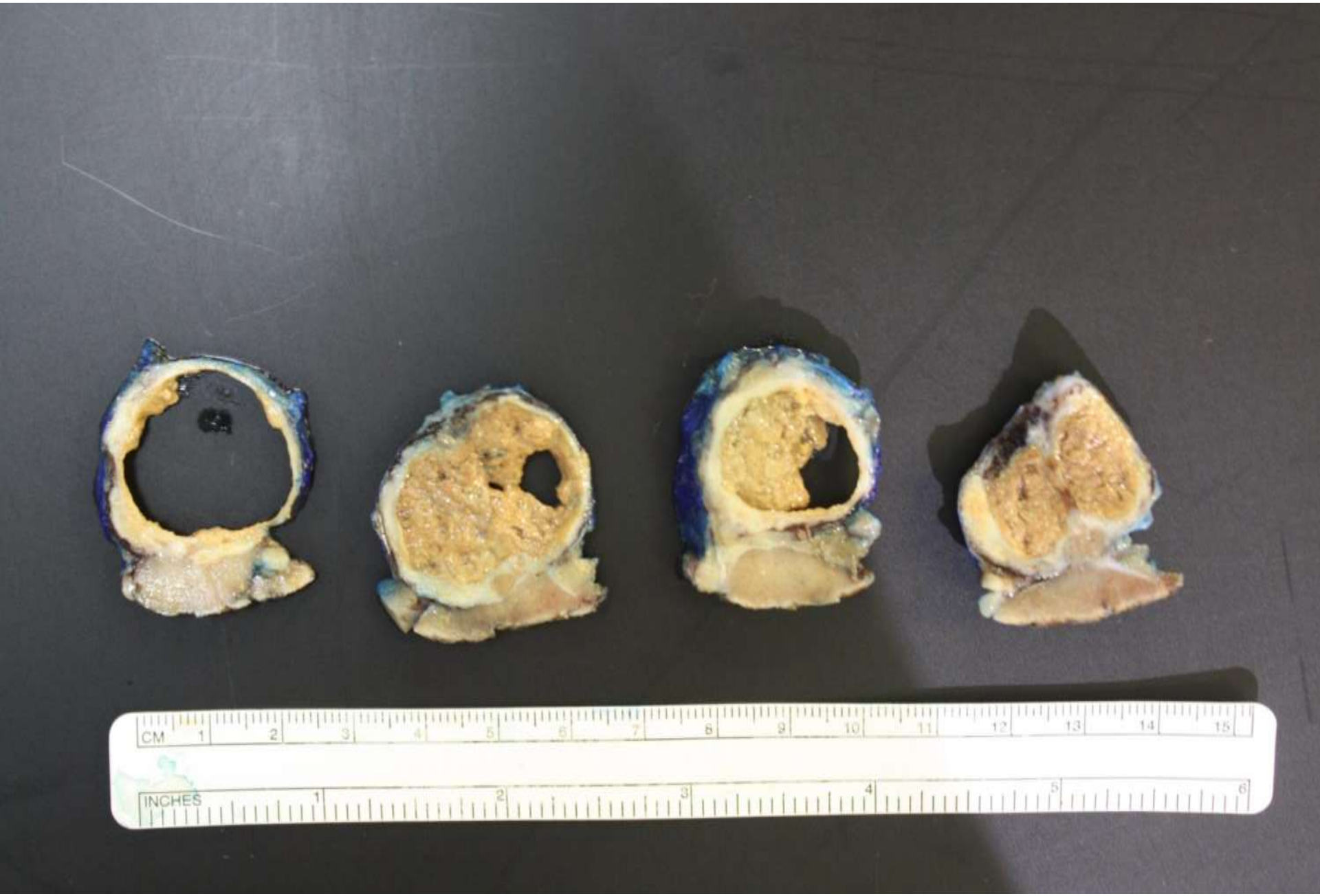
*Am J Surg Pathol* • Volume 40, Number 2, February 2016

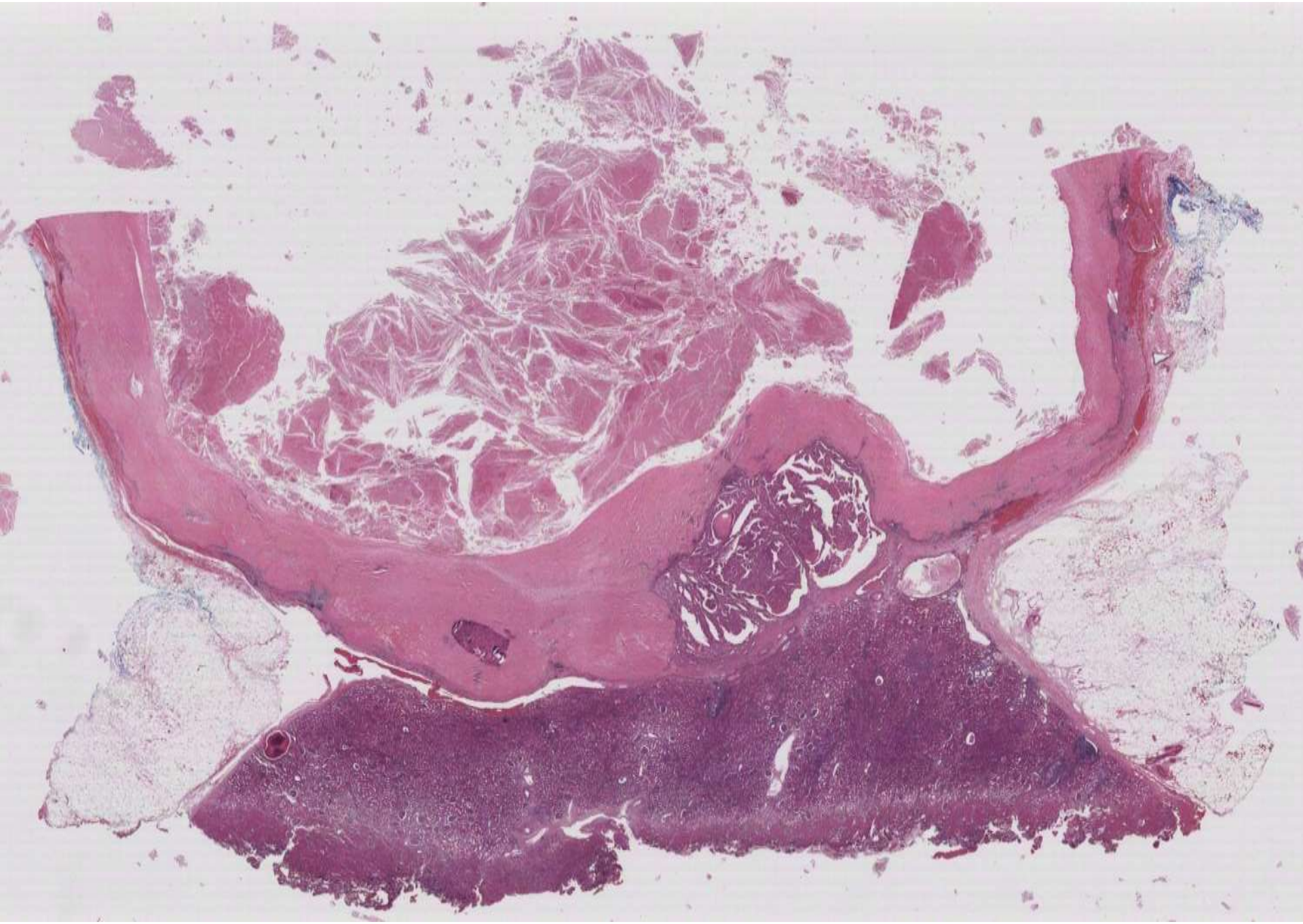
- **Can present as complex radiologic lesions, incidental/secondary lesions, or in background of chronic renal disease**
- **IHC: usually CK7+, variable AMACR, CD10, CAIX**
  - More aligned with papillary RCC
- **Molecular: trisomy 17, trisomy 7, 3p-**
  - May be precursors of RCC
- **Good outcome**
  - Avoid “carcinoma” label

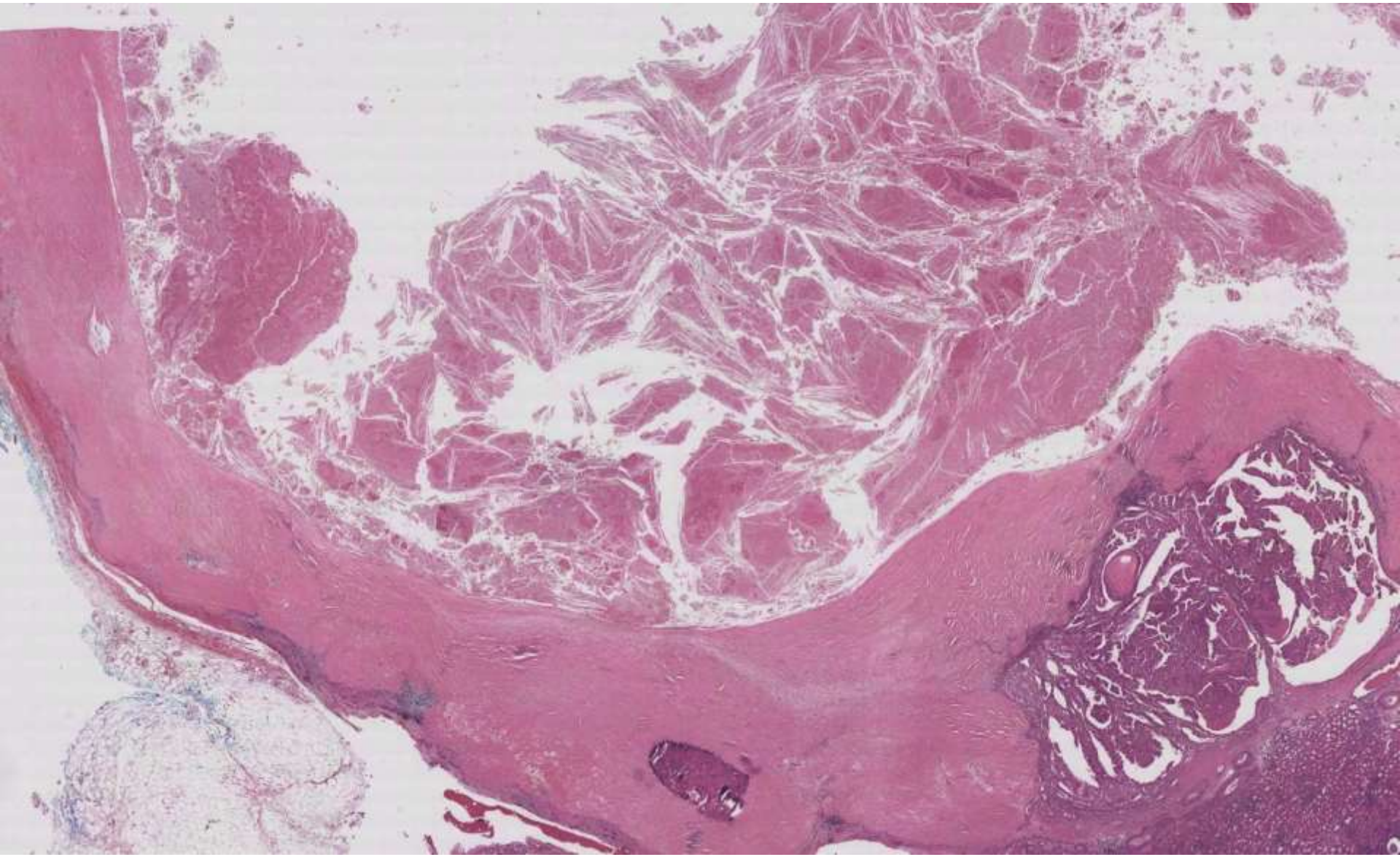
# 20-0109
# scanned slide available!

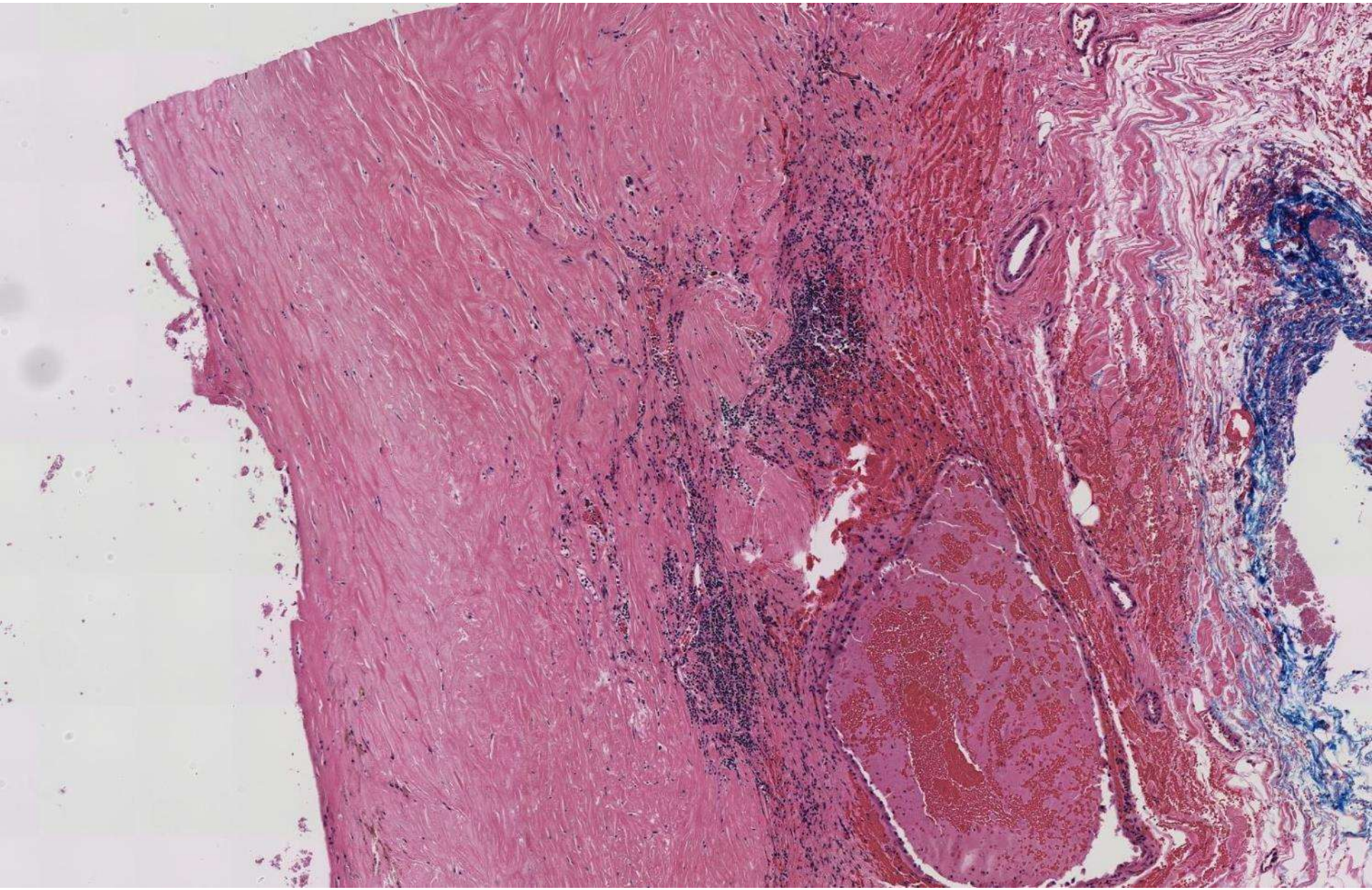
**Ankur Sangoi; El Camino Hospital**

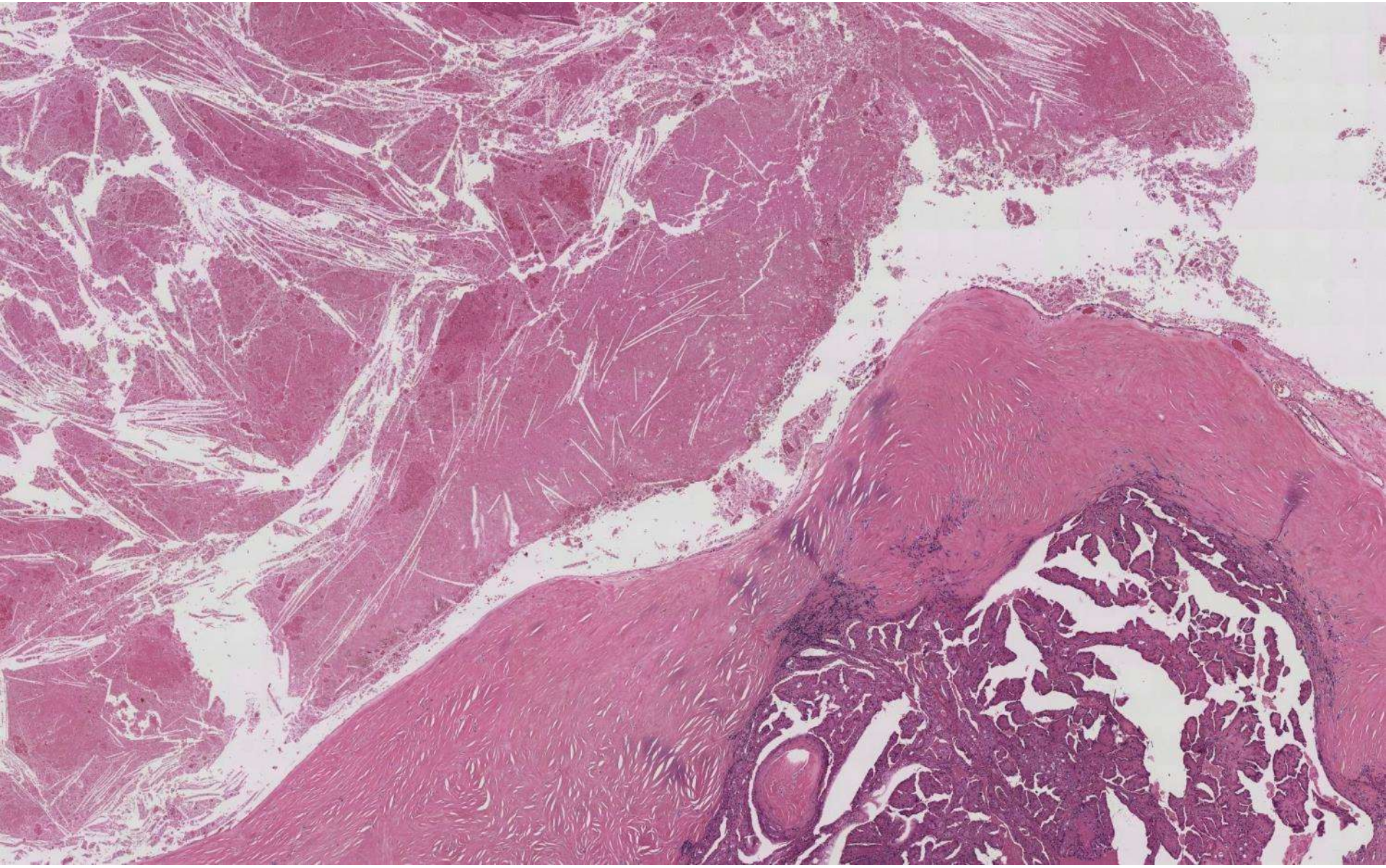
66-year-old M undergoes partial nephrectomy, found to have 3.2cm cystic mass.

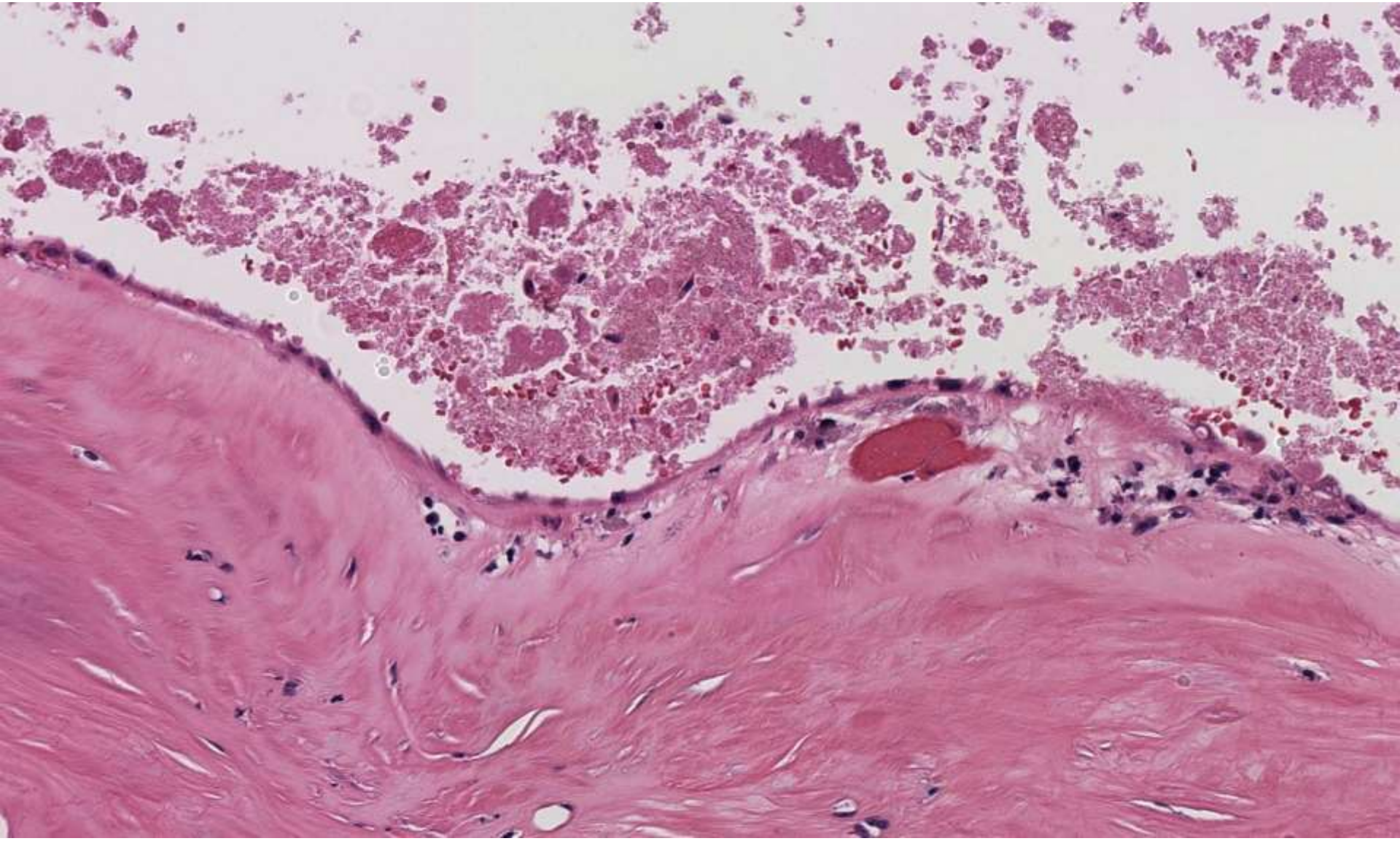

CM 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
INCHES 1 2 3 4 5 6

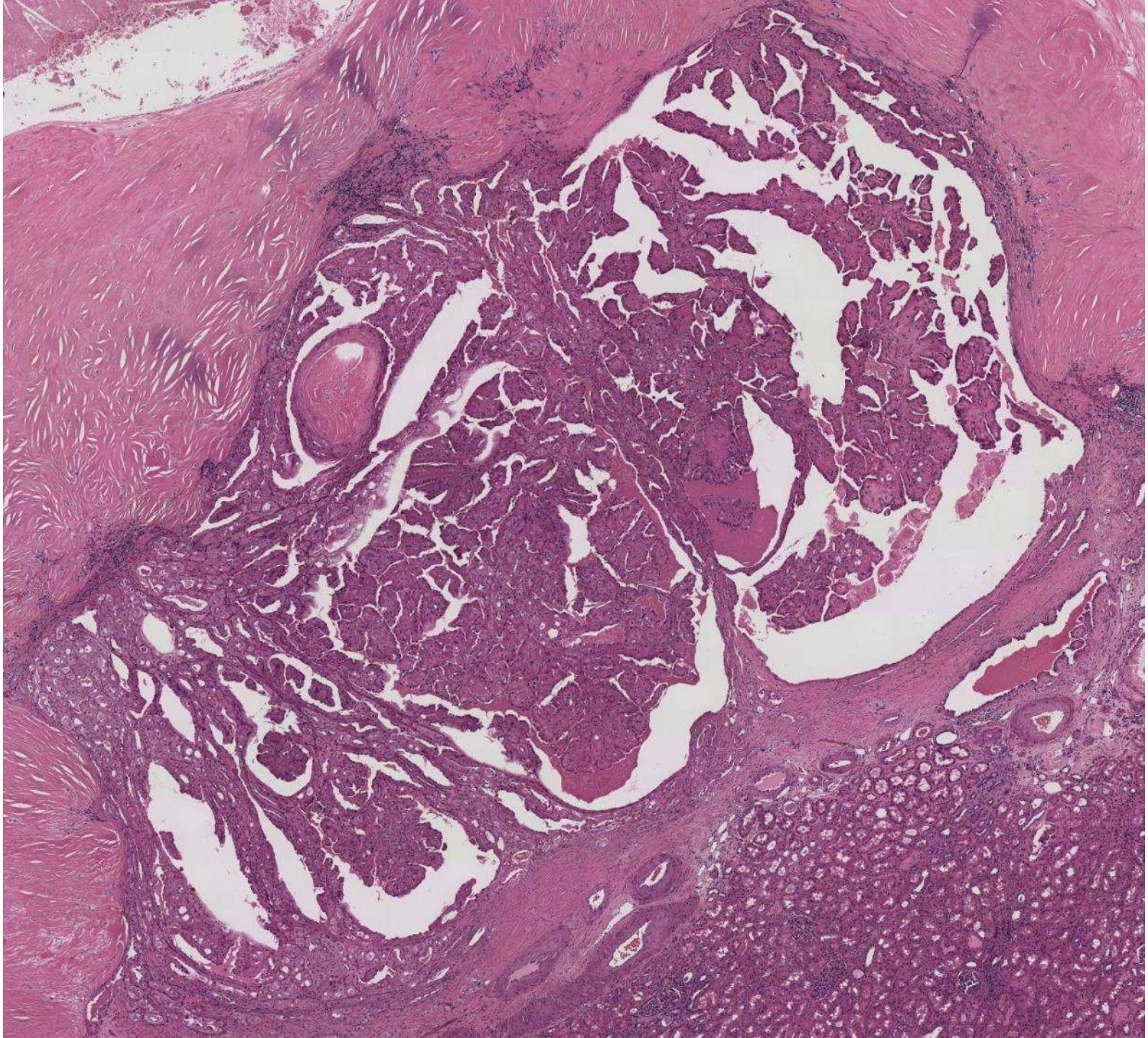


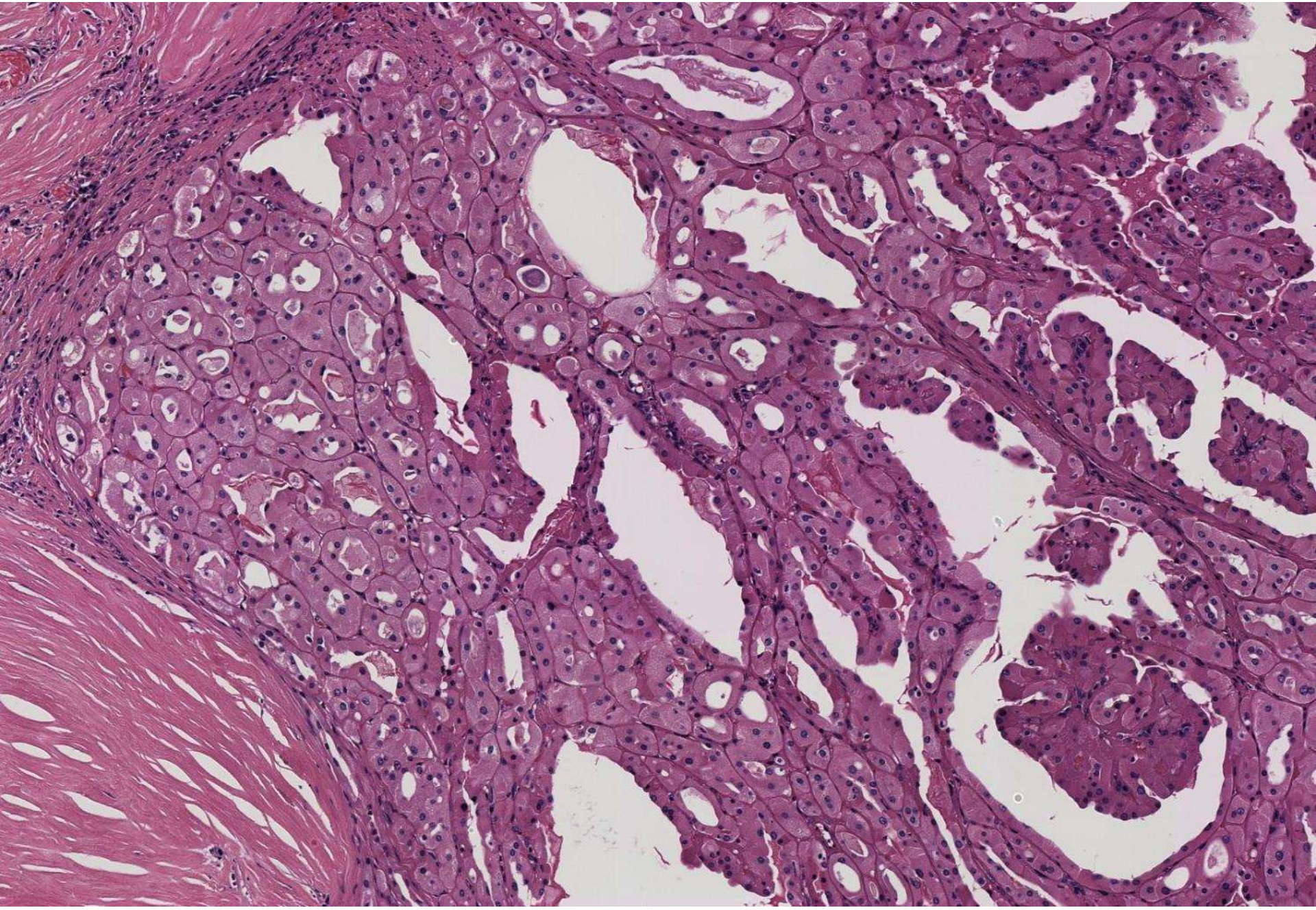


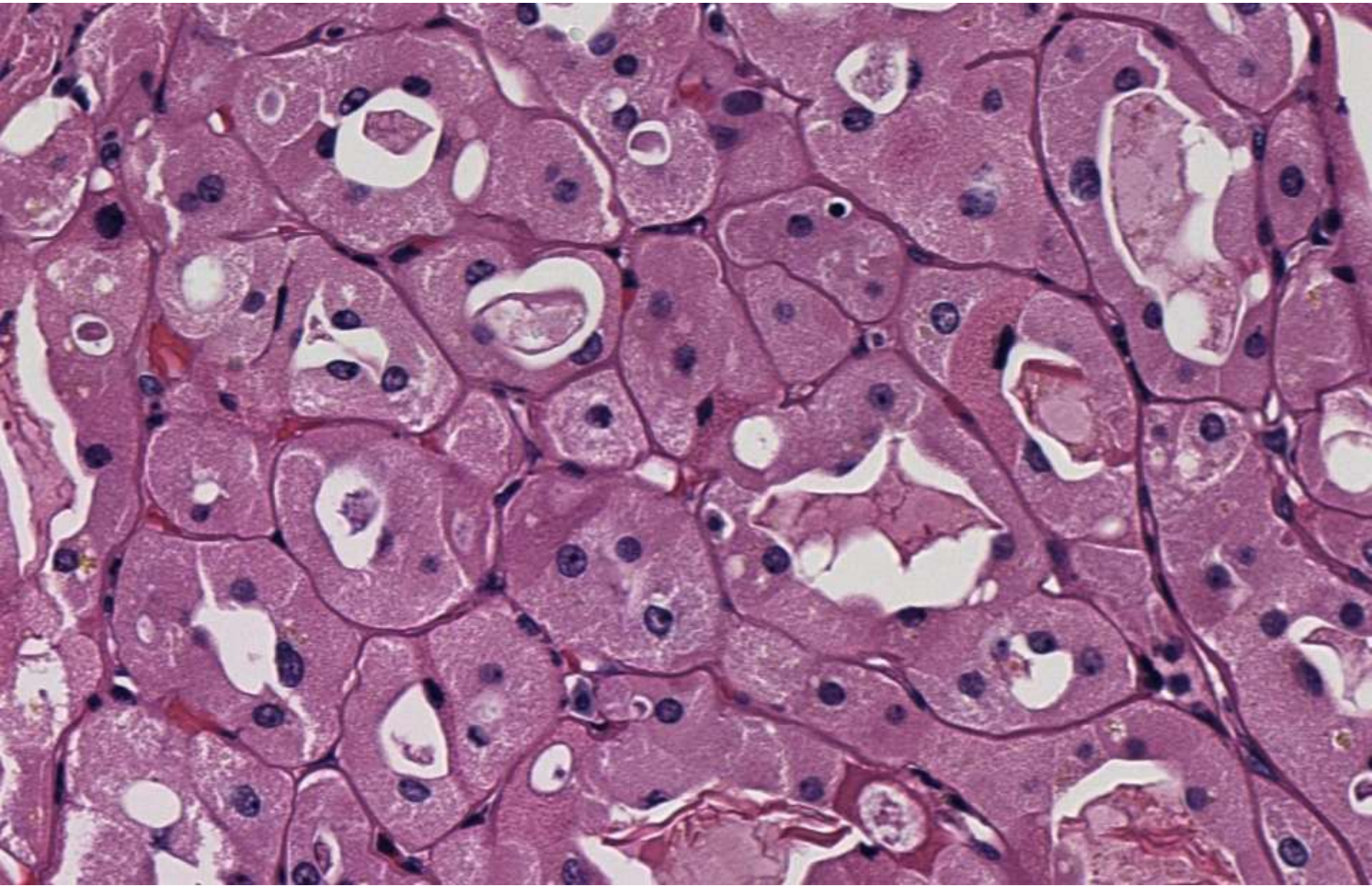


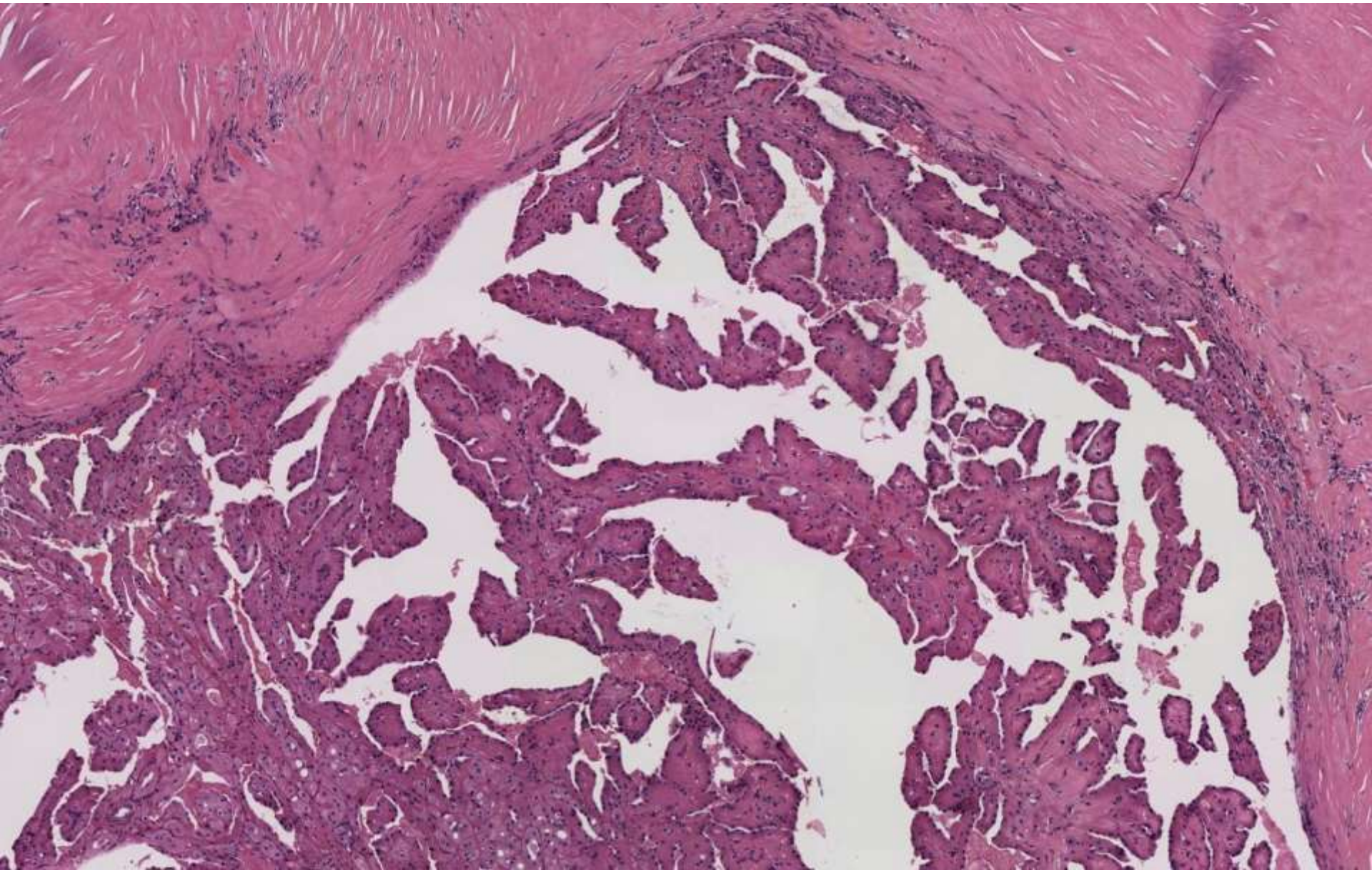


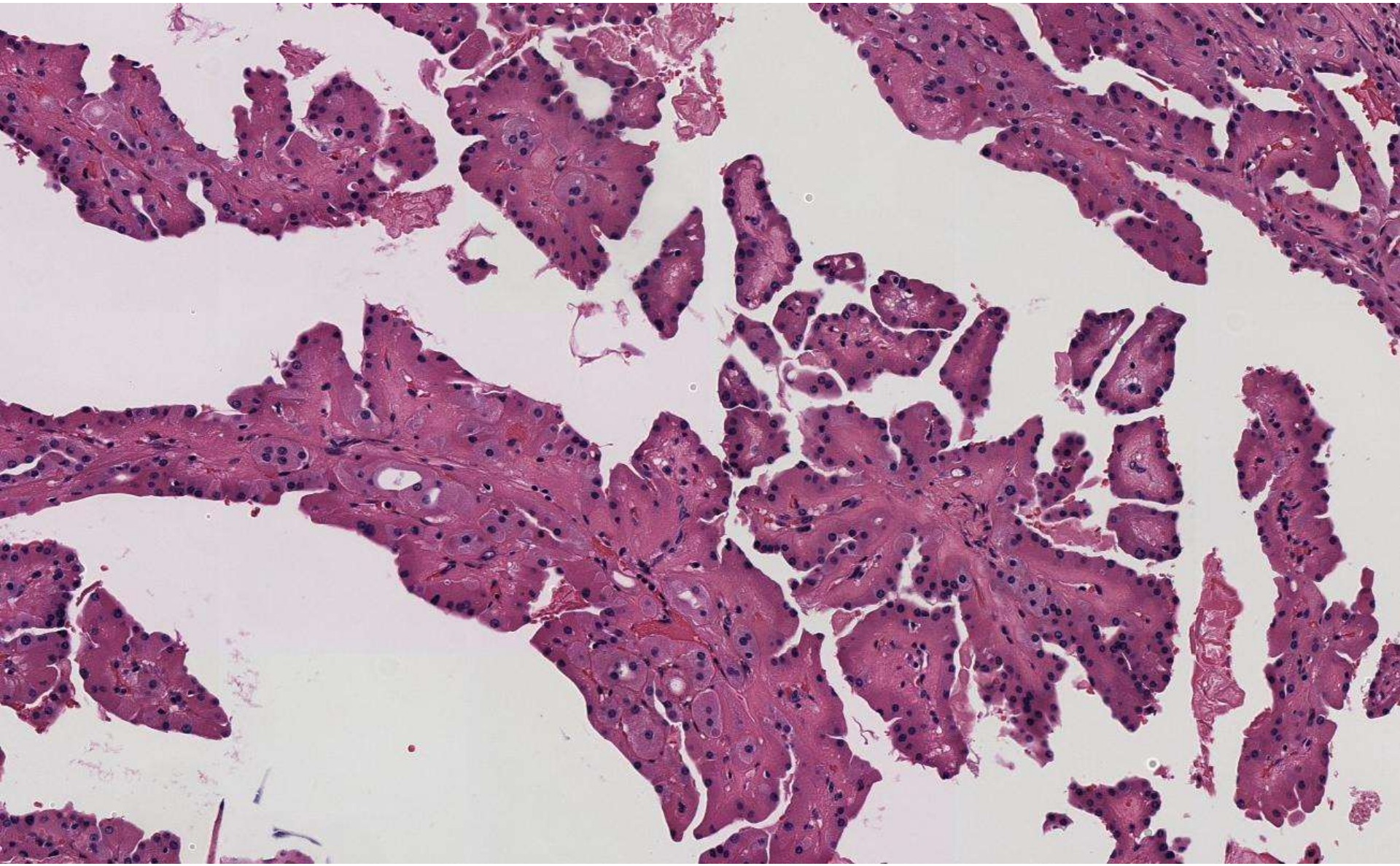


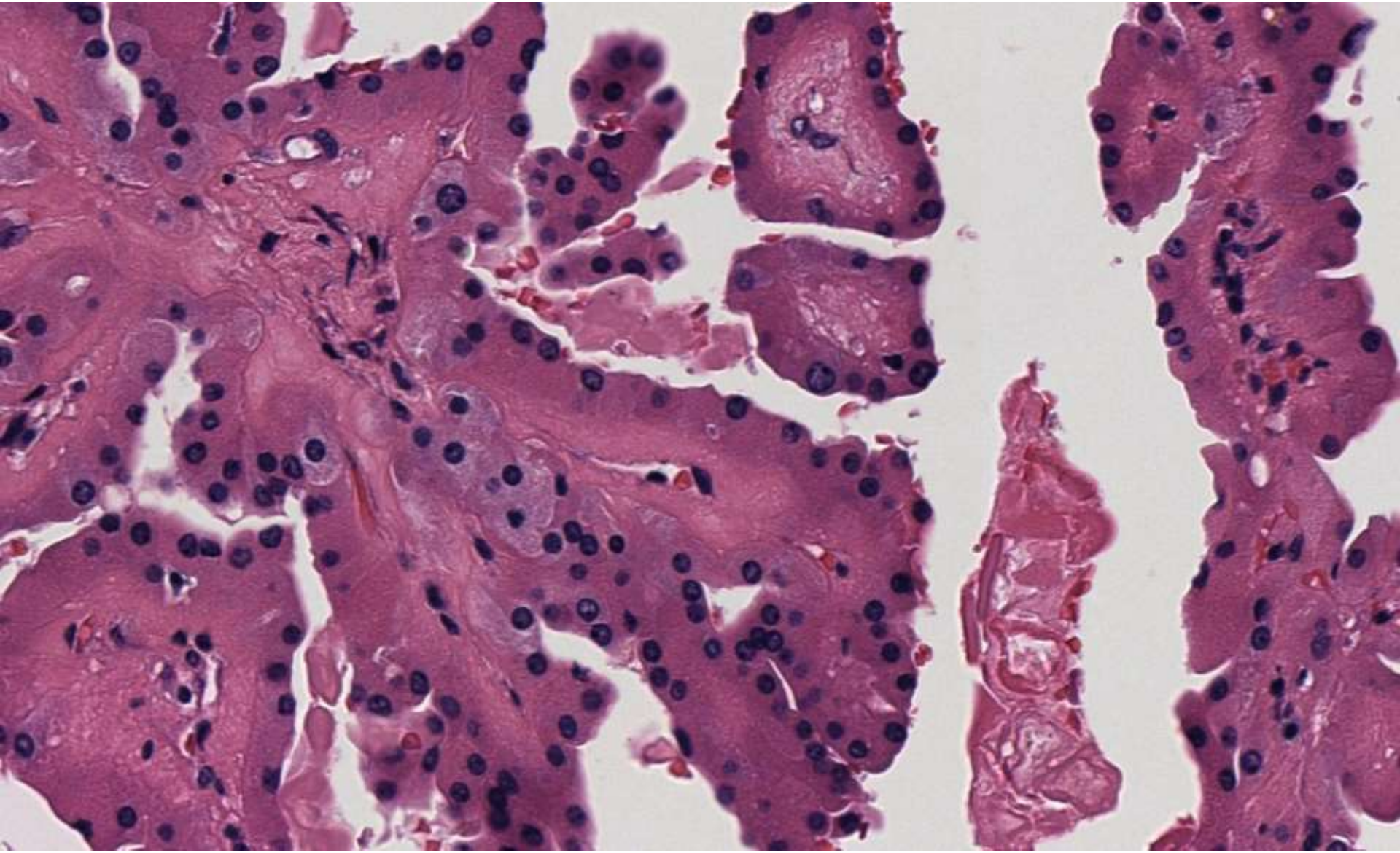






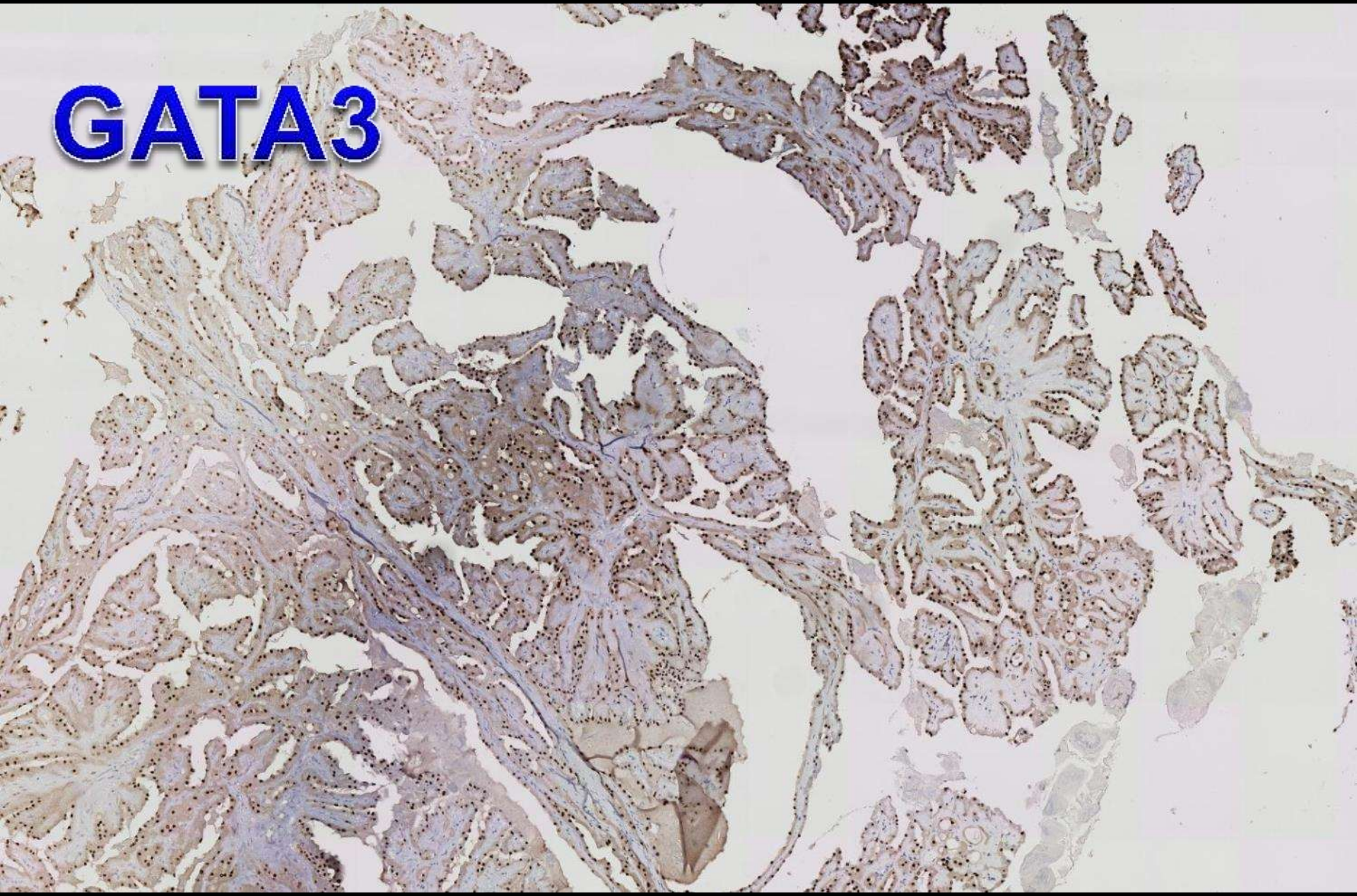


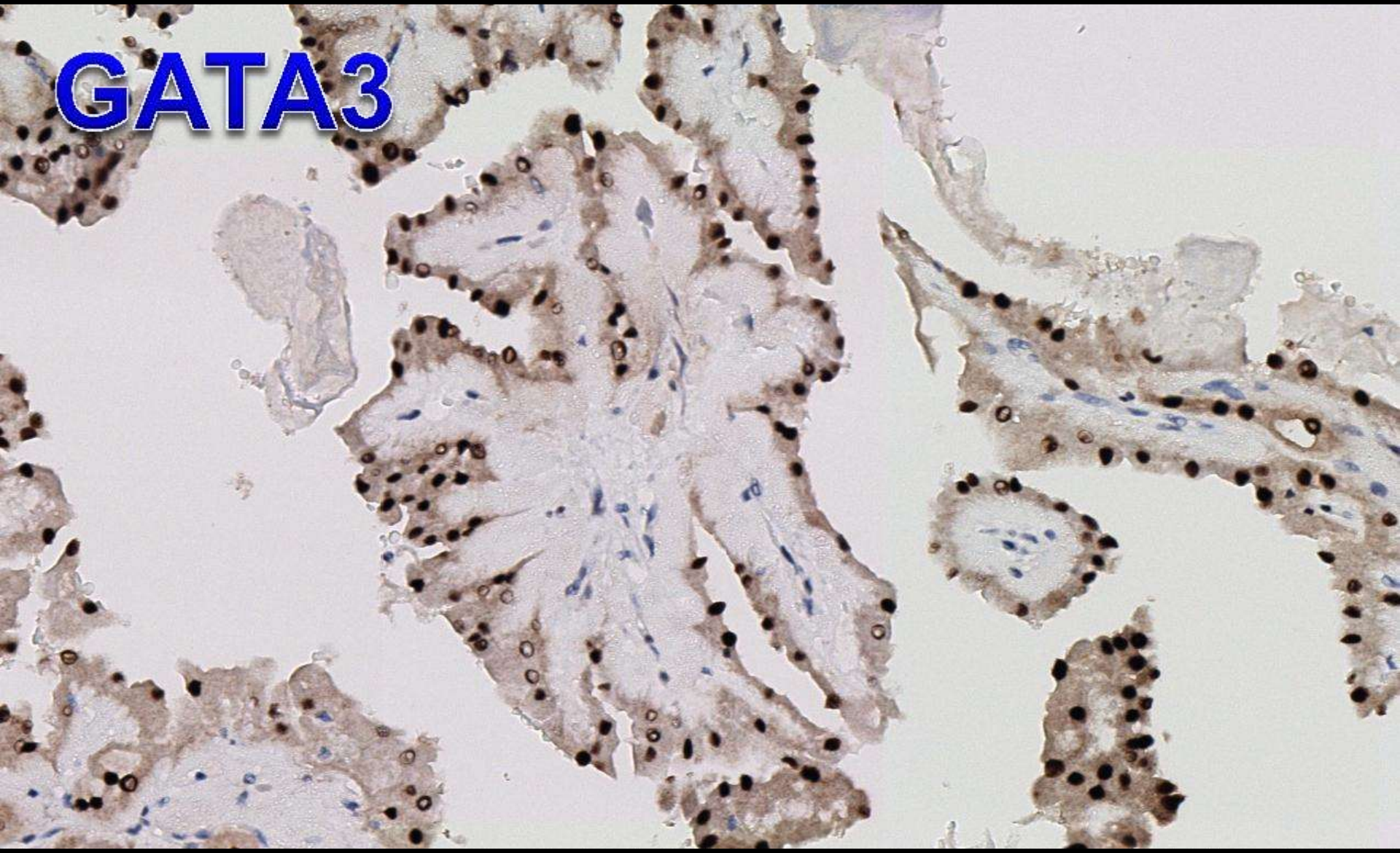




# DDx

- **MALIGNANT**
  - papillary RCC
    - type 2
  - clear cell papillary (tubulopapillary) RCC
  - tubulocystic RCC
  - MiTF/Xp11 RCC
  - FH-deficient RCC
- **BENIGN**
  - papillary adenoma
  - atypical renal cyst

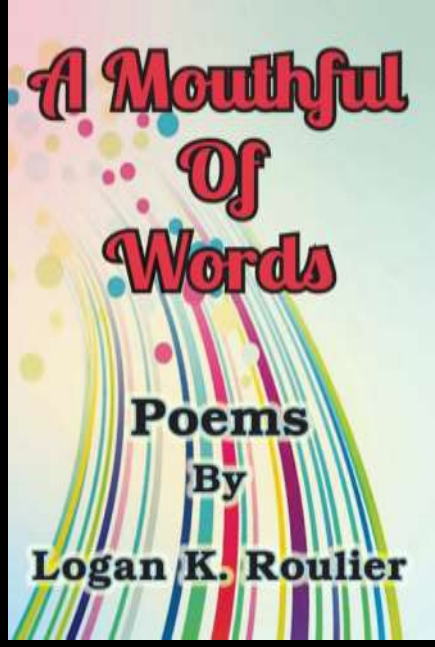

GATA3


GATA3

# IHC summary

PAX8: positive (diffuse strong)
CK7: positive (diffuse strong)
GATA3: positive (diffuse strong)
EMA: positive (diffuse strong)
CD10: positive (mostly diffuse moderate)
AMACR: positive (diffuse moderate)
vimentin: negative
CD117: negative
CK20: negative
cathepsinK: negative
CAIX: negative

# Final Dx




- Papillary renal cell neoplasm with reverse polarity

  =
- Oncocytic low grade papillary renal cell carcinoma

  =
- Type 4 papillary renal cell carcinoma

# Adult Papillary Renal Tumor With Oncocytic Cells

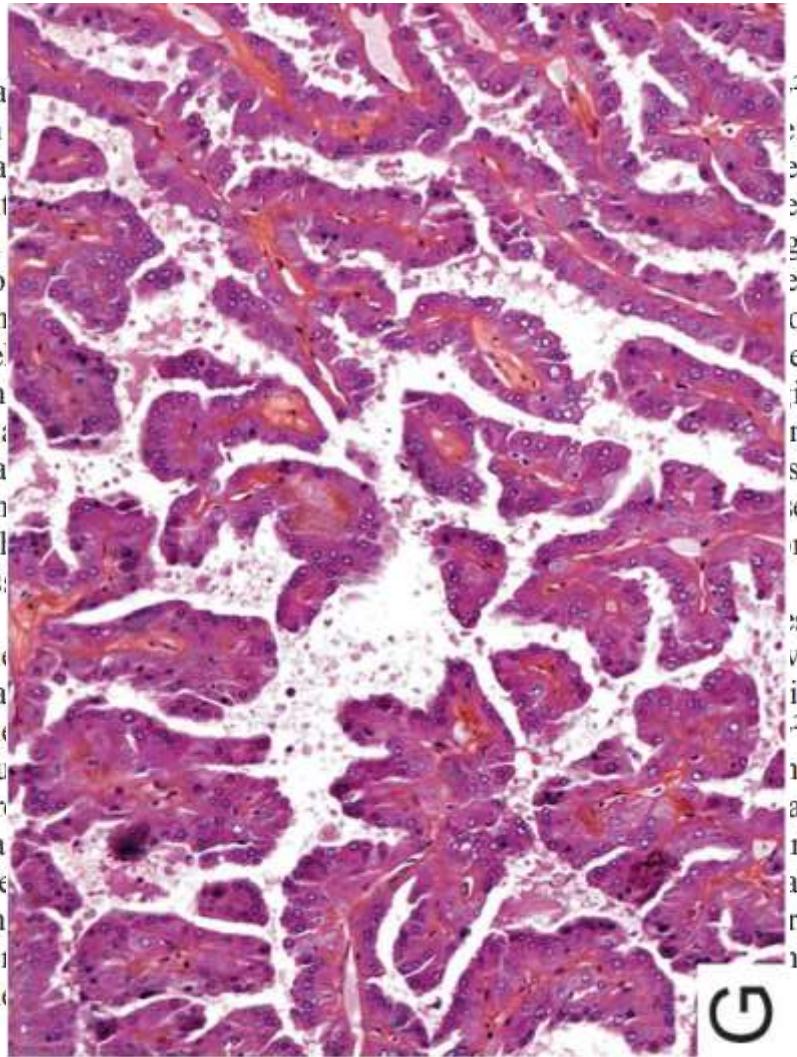
## *Clinicopathologic, Immunohistochemical, and Cytogenetic Features of 10 Cases*

*Marine Lefèvre, MD,* Jèrôme Couturier, MD,† Mathilde Sibony, MD, PhD,* Céline Bazille, MD,¶ Karine Boyer, MD,‡ Patrice Callard, MD,* Annick Vieillefond, MD,‡ and Yves Allory, MD*§‖*

**Abstract:** We report a series of 10 oncocytic renal papillary tumors, with the aim of determining their clinicopathologic features. All patients were male (median age, 71 years), treated by radical nephrectomy and free of recurrence or metastasis (median follow-up, 62 months). Tumors (median size, 3.3 cm) were intrarenal and well limited, with no extrarenal extension. They consisted of thin, nonfibrotic papillae lined by a single layer of oncocytic cells, with finely granular eosinophilic cytoplasm and round regular nucleus exhibiting central nucleolus (Fuhrman grade II, except for one grade III). Foci of necrosis were present in most cases. All tumors were immunoreactive for alpha-methylacyl-coenzyme A racemase, vimentin, and CD10; 4 expressed renal cell carcinoma antigen and 3 cytokeratin 7. There were a low number of cytogenetic changes in the 5 analyzed cases (median, 4; range, 1–7), with no trisomy 7 or 17. Papillary architecture, necrosis, and immunohistochemical profiles argued against the diagnosis of oncocytoma and suggested our cases to be part of the papillary renal cell carcinoma group. However, the cases were atypical for type 1 papillary carcinoma (due to oncocytic cells and absence of trisomy 17) and for type 2 (due to a good outcome). These results suggest that adult papillary renal tumors with oncocytic cells might be a distinct variant in the papillary renal cell carcinoma group.

**Key Words:** kidney, adult renal neoplasms, oncocytoma, papillary renal cell carcinoma, prognosis, racemase

(*Am J Surg Pathol* 2005;29:1576–1581)



# Toward Biological Subtyping of Papillary Renal Cell Carcinoma With Clinical Implications Through Histologic, Immunohistochemical, and Molecular Analysis

*Rola M. Saleeb, MD,*† Fadi Brimo, MD, FRCPC,‡ Mina Farag, MD,* Alexis Rompré-Brodeur, MD,§ Fabio Rotondo, BSc,* Vidya Beharry, BSc,* Samantha Wala, MSc,* Pamela Plant, PhD,* Michelle R. Downes, MD, FRCPC,†‖ Kenneth Pace, MD, MSc, FRCPC,¶ Andrew Evans, MD, PhD, FRCPC,†# Georg Bjarnason, MD, FRCPC(C),** John M.S. Bartlett, BSc, PhD,†† and George M. Yousef, MD, PhD, FRCPC (Path)*†*

**Abstract:** Papillary renal cell carcinoma (PRCC) has 2 histologic subtypes. Almost half of the cases fail to meet all morphologic criteria for either type, hence are characterized as PRCC not otherwise specified (NOS). There are yet no markers to resolve the PRCC NOS category. Accurate classification can better guide the management of these patients. In our previous PRCC study we identified markers that can distinguish between the subtypes. A PRCC patient cohort of 108 cases was selected for the current study. A panel of potentially distinguishing markers was chosen from our previous genomic analysis, and assessed by immunohistochemistry. The panel exhibited distinct staining patterns between the 2 classic PRCC subtypes; and successfully reclassified the NOS (45%) cases. Moreover, these immunomarkers revealed a third subtype, PRCC3 (35% of the cohort). Molecular testing using miRNA expression and copy number variation analysis confirmed the presence of 3 distinct molecular signatures corresponding to the 3 subtypes. Disease-free survival was significantly enhanced in PRCC1 versus 2 and 3 ($P=0.047$) on univariate analysis. The subtypes stratification was also significant on multivariate analysis ($P=0.025$; hazard ratio, 6; 95% confidence interval, 1.25-32.2). We propose a new classification system of PRCC integrating morphologic, immunophenotypical, and molecular analysis. The newly described PRCC3 has overlapping morphology between PRCC1 and PRCC2, hence would be subtyped as NOS in the current classification. Molecularly PRCC3 has a distinct signature and clinically it behaves similar to PRCC2. The new classification stratifies PRCC patients into clinically relevant subgroups and has significant implications on the management of PRCC.

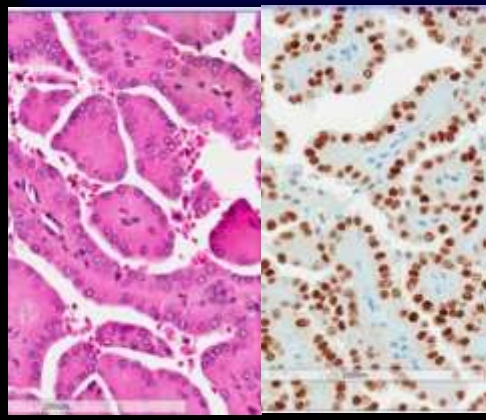
**Key Words:** papillary renal cell carcinoma, papillary renal cell carcinoma NOS, ABCC2

(*Am J Surg Pathol* 2017;41:1618–1629)

Papillary renal cell carcinoma (PRCC) has been recognized since 1976.[1] It was acknowledged as the second most common type of renal cell carcinoma (RCC) following clear cell RCC. Consistently thereafter, many publications

**TABLE 1.** Morphological Characteristics of the 4 PRCC Subtypes

| Features | PRCC1 | PRCC2 | PRCC3 | PRCC4/OLG |
|---|---|---|---|---|
| Cytoplasmic quantity | Scant, occasionally moderate | Abundant | Moderate | Abundant |
| Cytoplasmic color | Basophilic or eosinophilic or clearing | Eosinophilic or clearing | Eosinophilic, or clearing | Oncocytic eosinophilic |
| Cell size | Small to intermediate | Large | Intermediate | Large |
| Nucleolar prominence at ×10 | Inconspicuous, rarely prominent | Very prominent | Often prominent | Inconspicuous, rarely prominent |
| % nucleolar prominence at ×10 | If present <5 | 30-100 | 10-70 | If present <5 |
| Nuclear pseudostratification (presence or absence) | Absent | Mostly present, occasionally absent | Mostly absent, occasionally present | Absent. Linear. Nuclei arranged away from base of the cells |
| Nuclear size | Small | Large | Small to intermediate | Intermediate |
| Nuclear shape | Elongated oval (angulations and grooves) or round | Mostly round | Round or elongated | Round |
| Chromatin (open or closed) | Closed or open | Open vesicular nuclei, rarely focal areas with closed chromatin | Open, rarely closed | Open |
| ISUP nucleolar grade | 1-2, very rarely focal 3 | Mostly 3 | Mostly 3 | 1-2 |
| Foamy macrophages | Present or absent | Present or absent | Present or absent | Absent |
| ABCC2 IHC | Negative | Strong diffuse positive | Weaker patchy positive | Strong diffuse positive |
| CA9 IHC | Negative | Positive Golgi pattern (perinuclear dot) | Negative | Negative |
| GATA3 IHC | Negative | Negative | Negative | Positive |



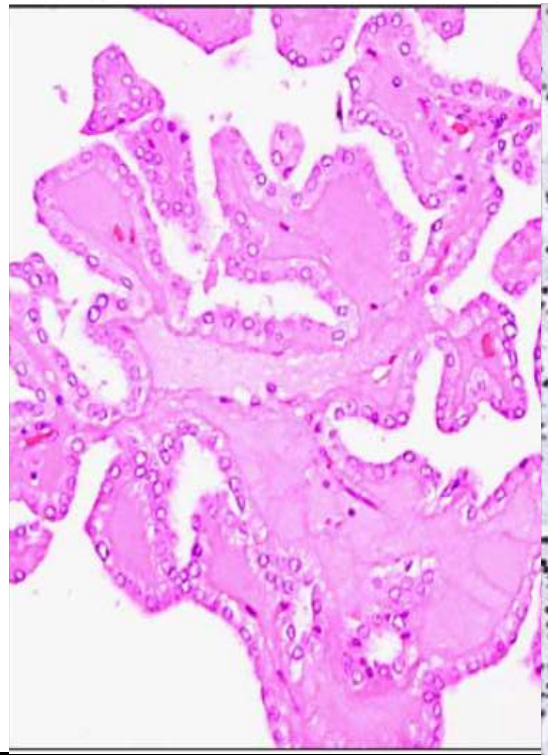
*Am J Surg Pathol* • Volume 41, Number 12, December 2017

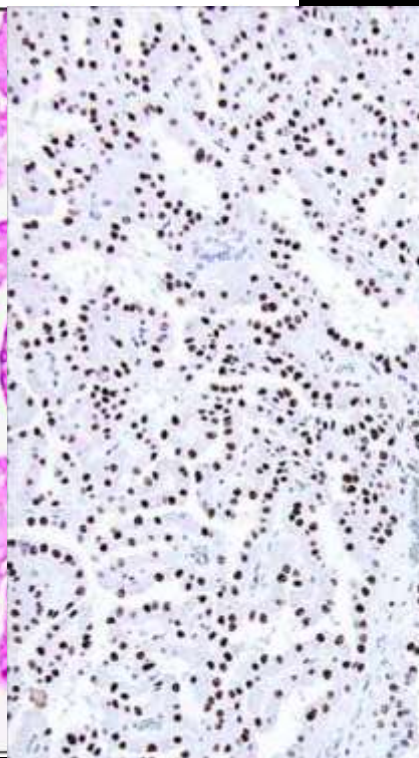
# Papillary Renal Neoplasm With Reverse Polarity

## *A Morphologic, Immunohistochemical, and Molecular Study*

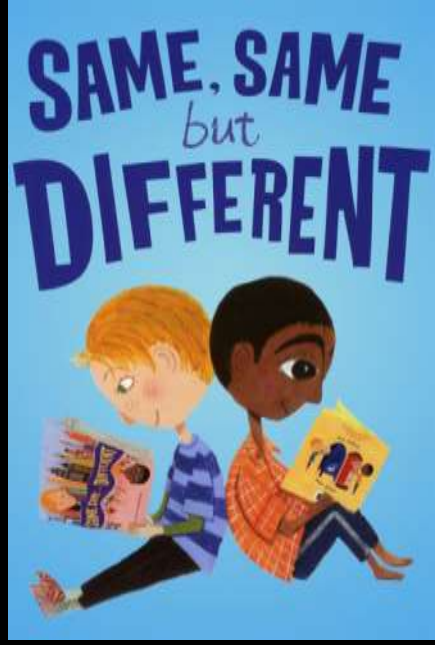
*Khaleel I. Al-Obaidy, MD,* John N. Eble, MD,* Liang Cheng, MD,* Sean R. Williamson, MD,† Wael A. Sakr, MD,‡ Nilesh Gupta, MD,† Muhammad T. Idrees, MBBS,* and David J. Grignon, MD**

**Abstract:** We evaluated the clinicopathologic and chromosomal characteristics of a distinct subset of papillary renal tumors and compared them to a control series of papillary renal cell carcinoma types 1 and 2. Of the 18 patients, 9 were women and 9 were men, ranging in age from 46 to 80 years (mean, 64 y; median, 66 y). The tumors ranged in diameter from 0.6 to 3 cm (mean, 1.63 cm; median, 1.4 cm). Fourteen tumors were WHO/ISUP grade 2 and 4 were grade 1. All were stage category pT1. The tumors had branching papillae with thin fibrovascular cores, covered by cuboidal to columnar cells with granular eosinophilic cytoplasm, smooth luminal borders, and mostly regular and apically located nuclei with occasional nuclear clearing and inconspicuous nucleoli. Tubule formation and clear cytoplasmic vacuoles were observed in 5 and 9 tumors, respectively. Ten tumors had pseudocapsules. Psammoma bodies, necrosis, mitotic figures and intracellular hemosiderin are absent from all tumors. In contrast, papillary renal cell carcinoma type 1 consisted of delicate papillae covered by a single layer of cells with scanty pale cytoplasm with nuclei generally located in a single layer on the basement membrane of the papillary cores, while type 2 tumors had broad papillae covered by pseudostratified cells with eosinophilic cytoplasm and more randomly located nuclei. Both had occasional psammoma bodies, foamy macrophages and intracellular hemosiderin. Immunohistochemically, all were positive for pancytokeratin AE1/AE3, epithelial membrane antigen, MUC1, CD10, GATA3, and L1CAM. Cytokeratin 7 was positive in 16 tumors (1 had <5% positivity). CD117 and vimentin were always negative. α-methylacyl-CoA-racemase (AMACR/p504s) showed variable staining (range, 10% to 80%) in 5 tumors. However, all tumors in the control group were negative for GATA3 and positive for AMACR/p504s and vimentin immunostains. Fluorescence in situ hybridization analysis of the study group demonstrated chromosome 7 trisomy in 5 tumors (33%), trisomy 17 in 5 tumors (33%), and trisomy 7 and 17 in 3 tumors (20%). Chromosome Y deletion was found in 1 of 7 male patients and chromosome 3p was present in all tumors. No tumor recurrence or metastasis occurred. In summary, we propose the term papillary renal neoplasm with reverse polarity for this entity.





# Take home points

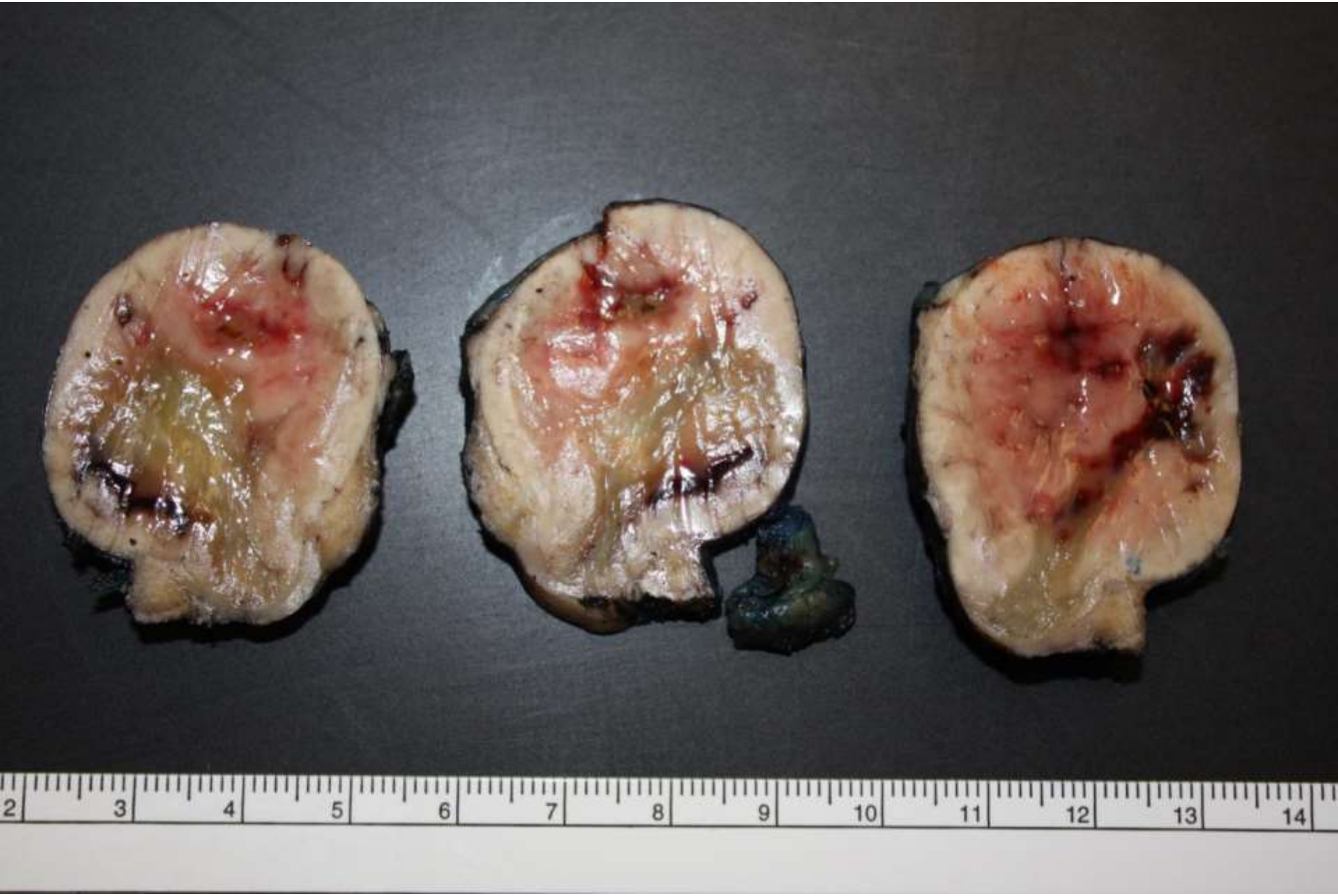


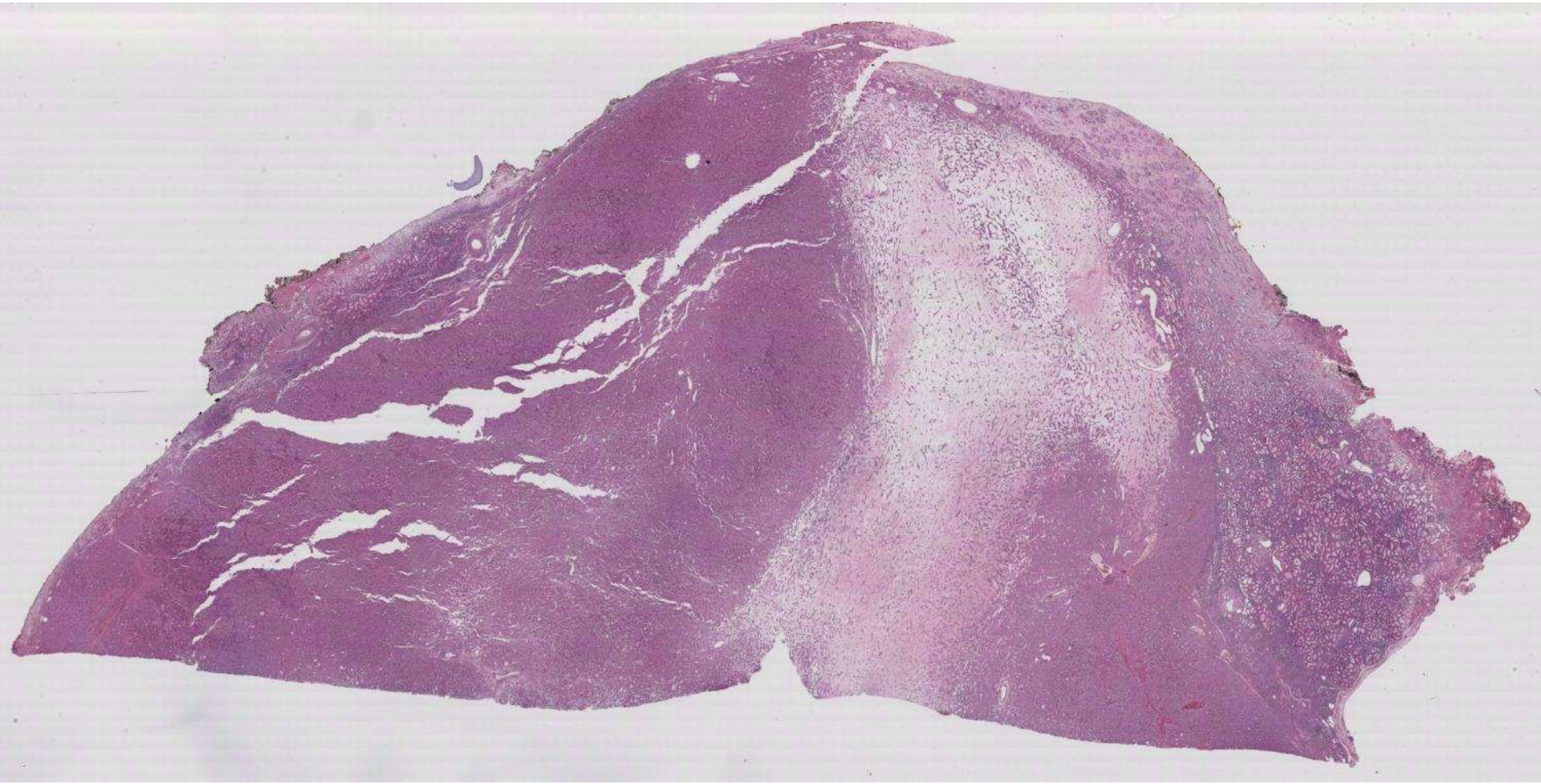

- **Typically small size, low stage, low WHO/FIGO grade**
- **Branching papillae, eosinophilic cytoplasm, "reverse-apical" nuclei**
  - Usually ABSENT: psammoma bodies, necrosis, mitoses, intracellular hemosiderin, tight clusters of foamy mac's
- **IHC: CK7+ GATA3+ vimentin – variable AMACR**
- **Good prognosis**

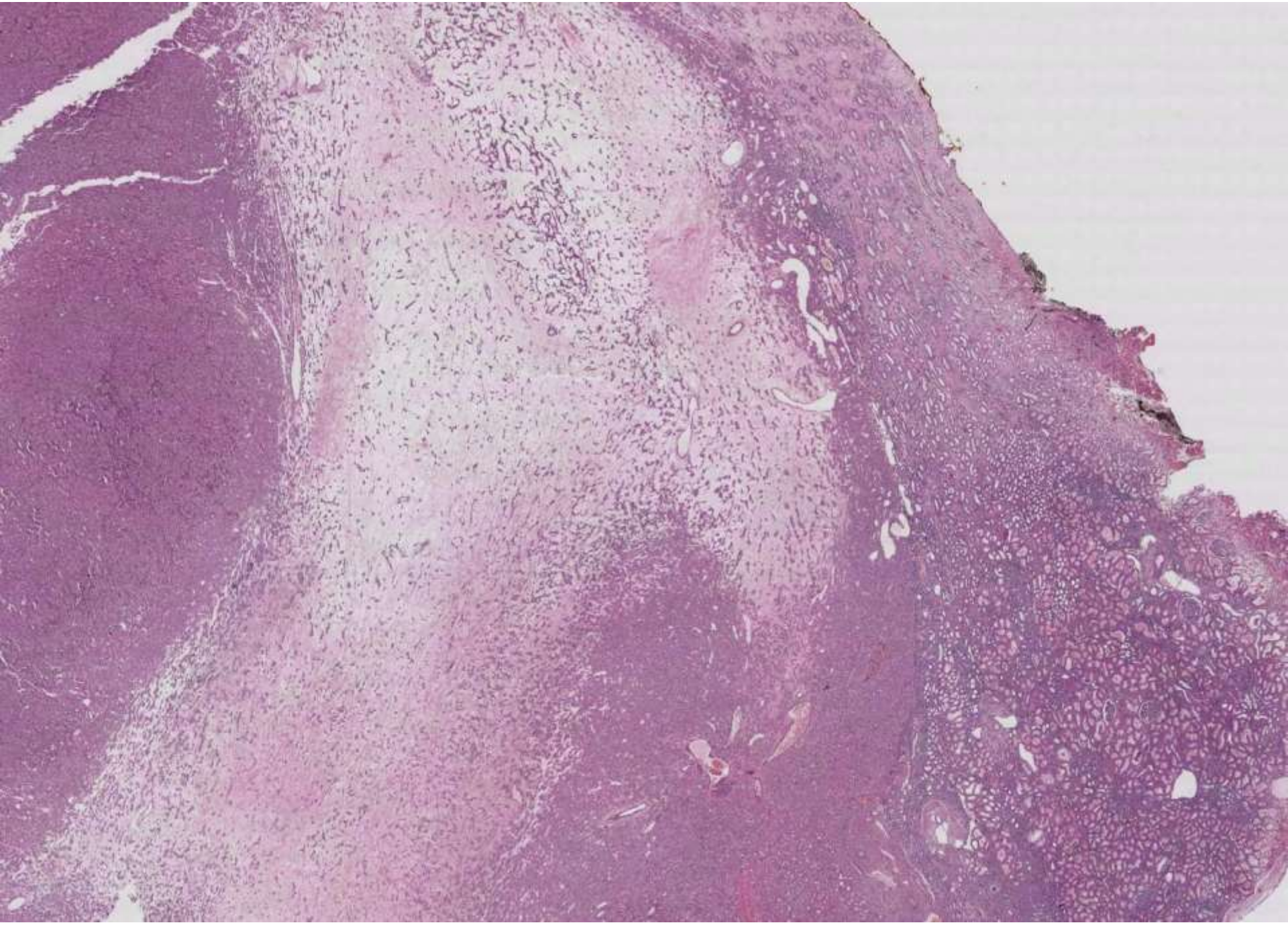
# 20-0110
# scanned slide available!

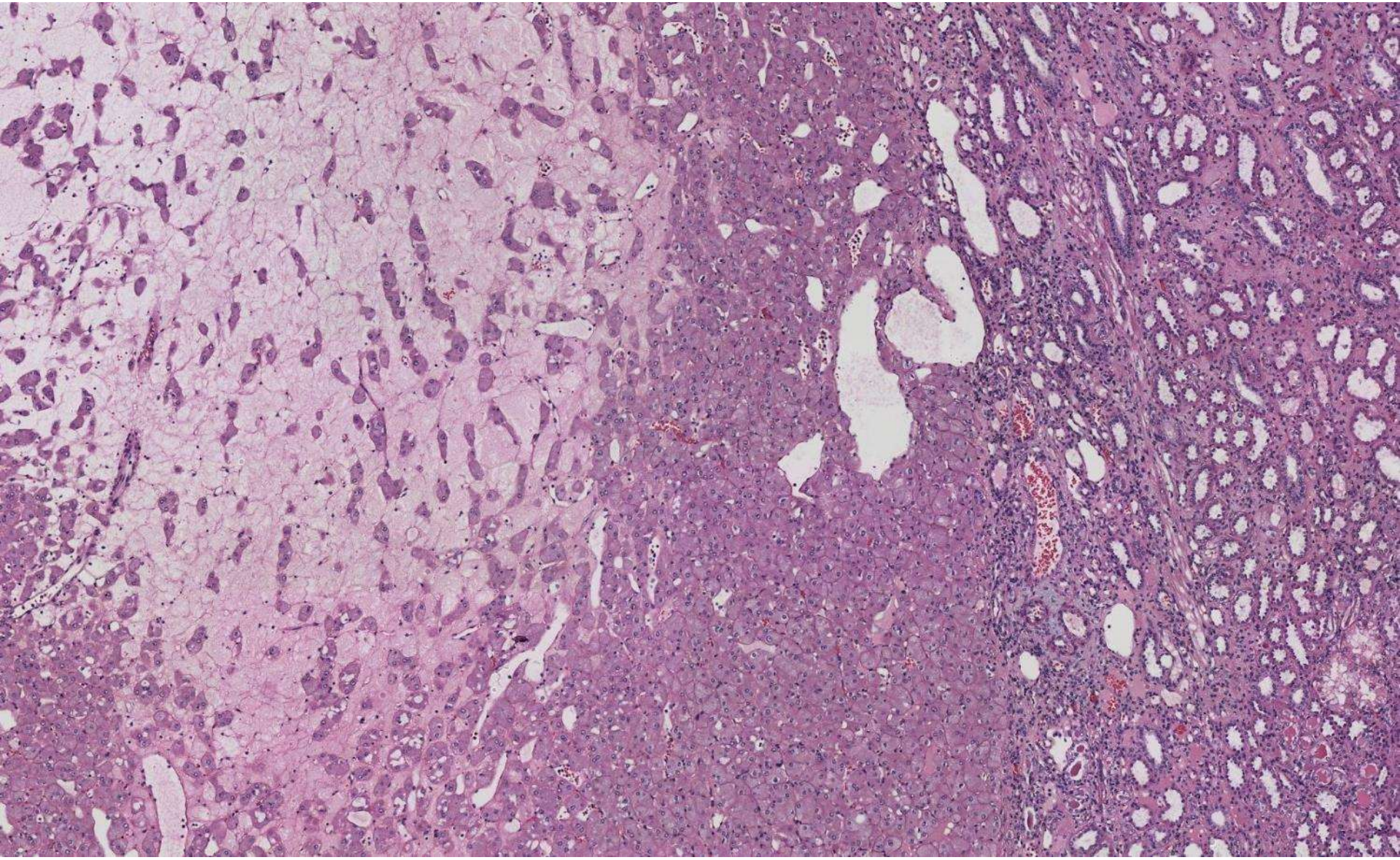
**Ankur Sangoi; El Camino Hospital**

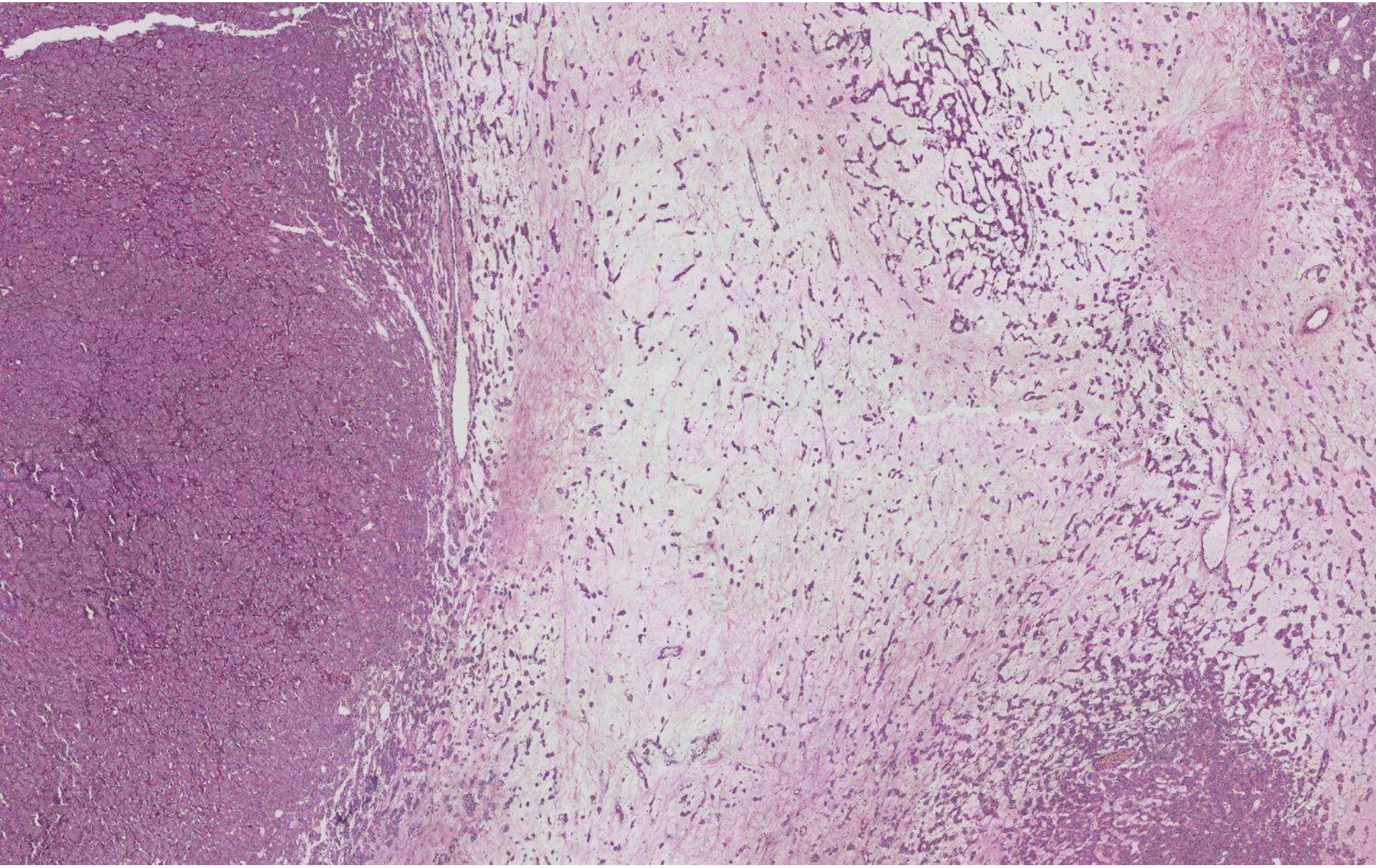
55-year-old F undergoes radical nephrectomy, found to 5.5cm solid/cystic mass.

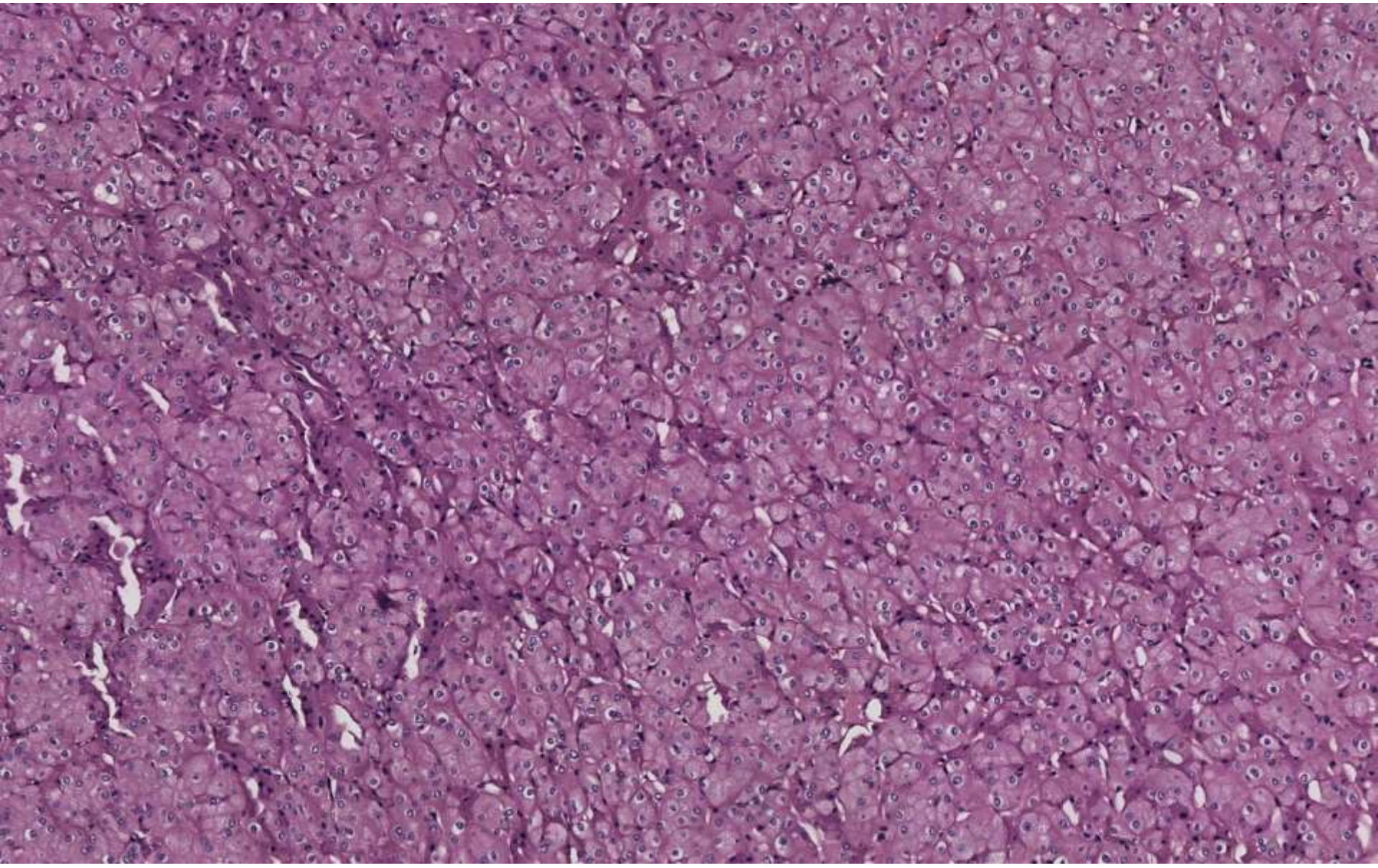

2
3
4
5
6
7
8
9
10
11
12
13
14

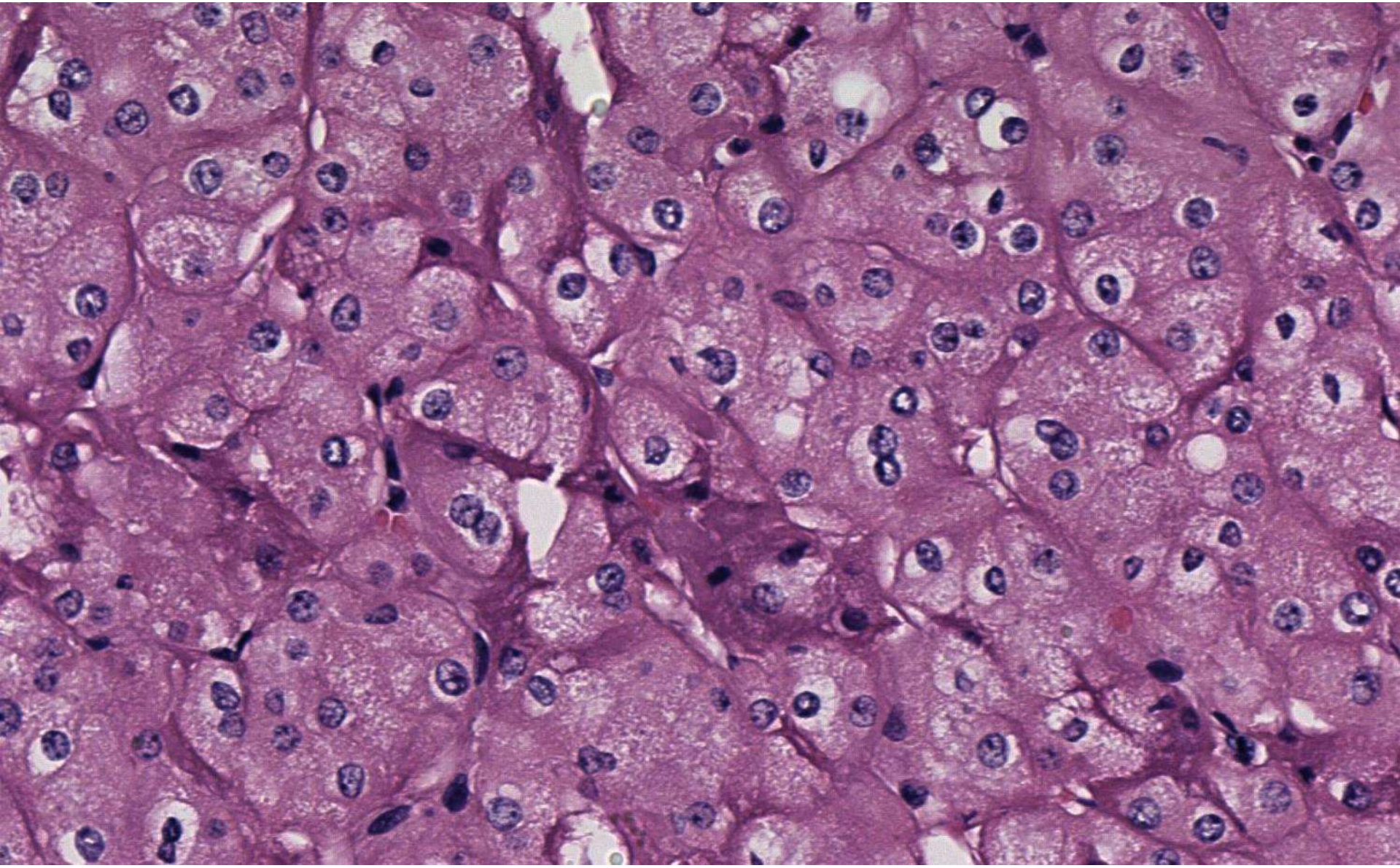


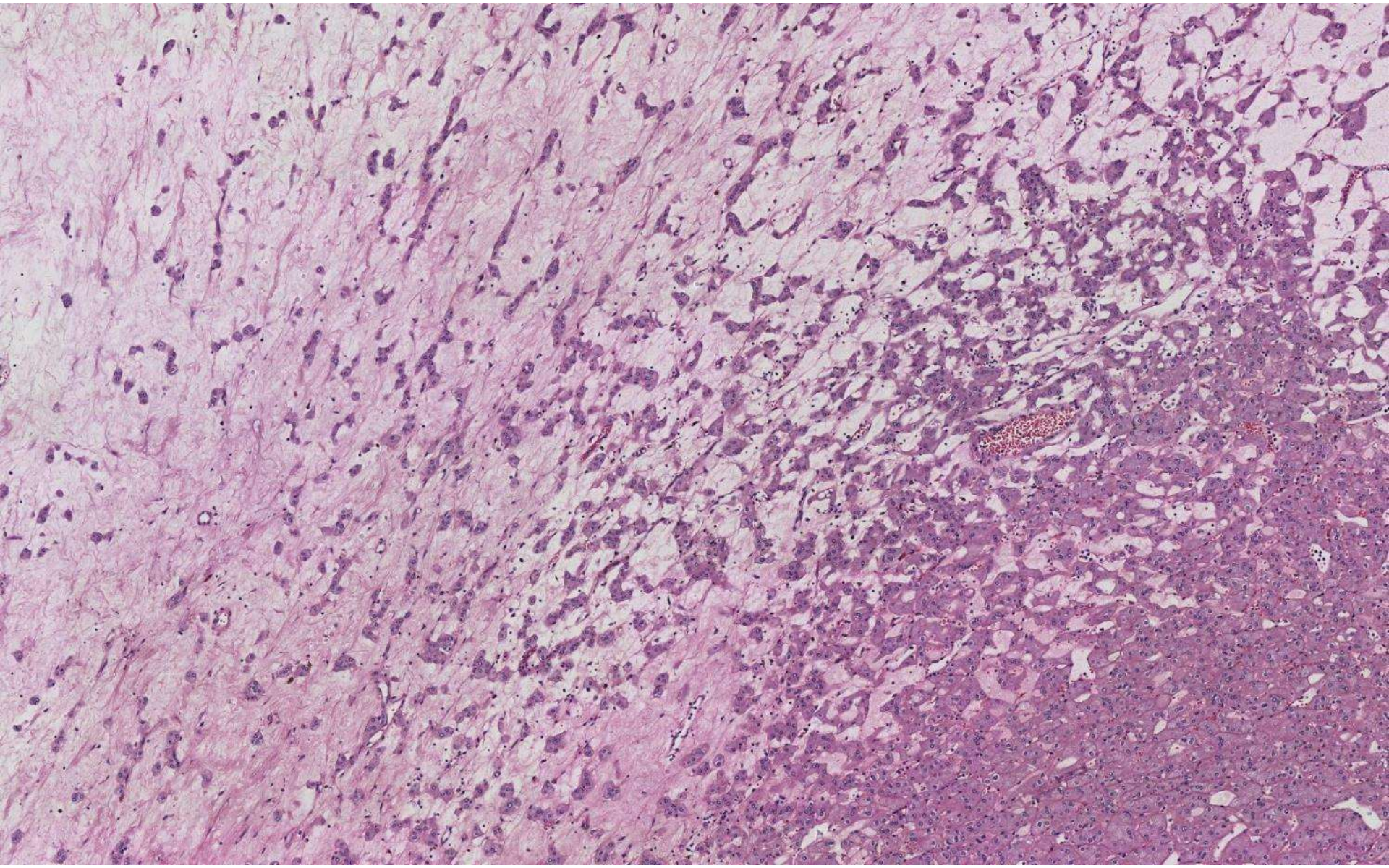


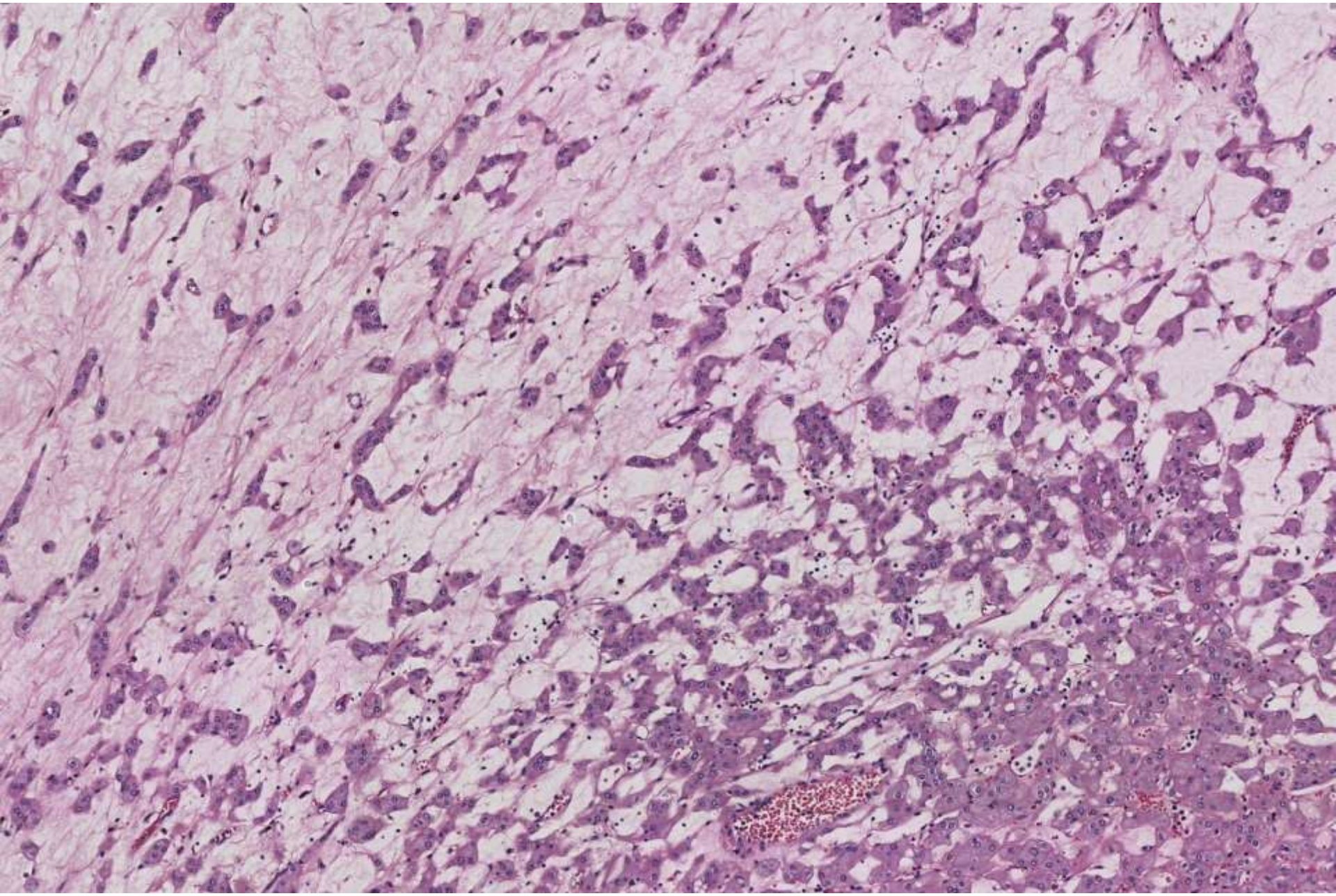


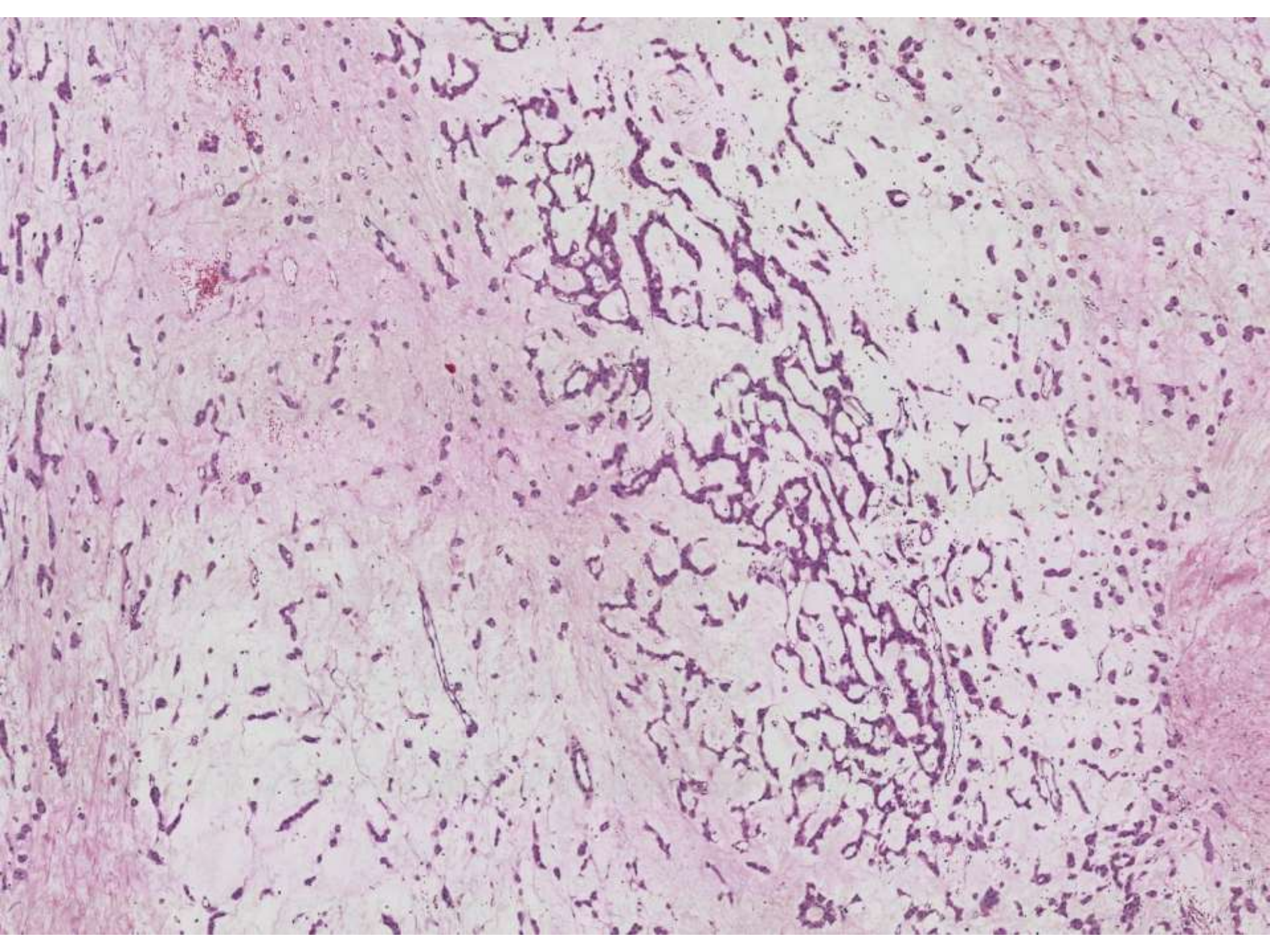


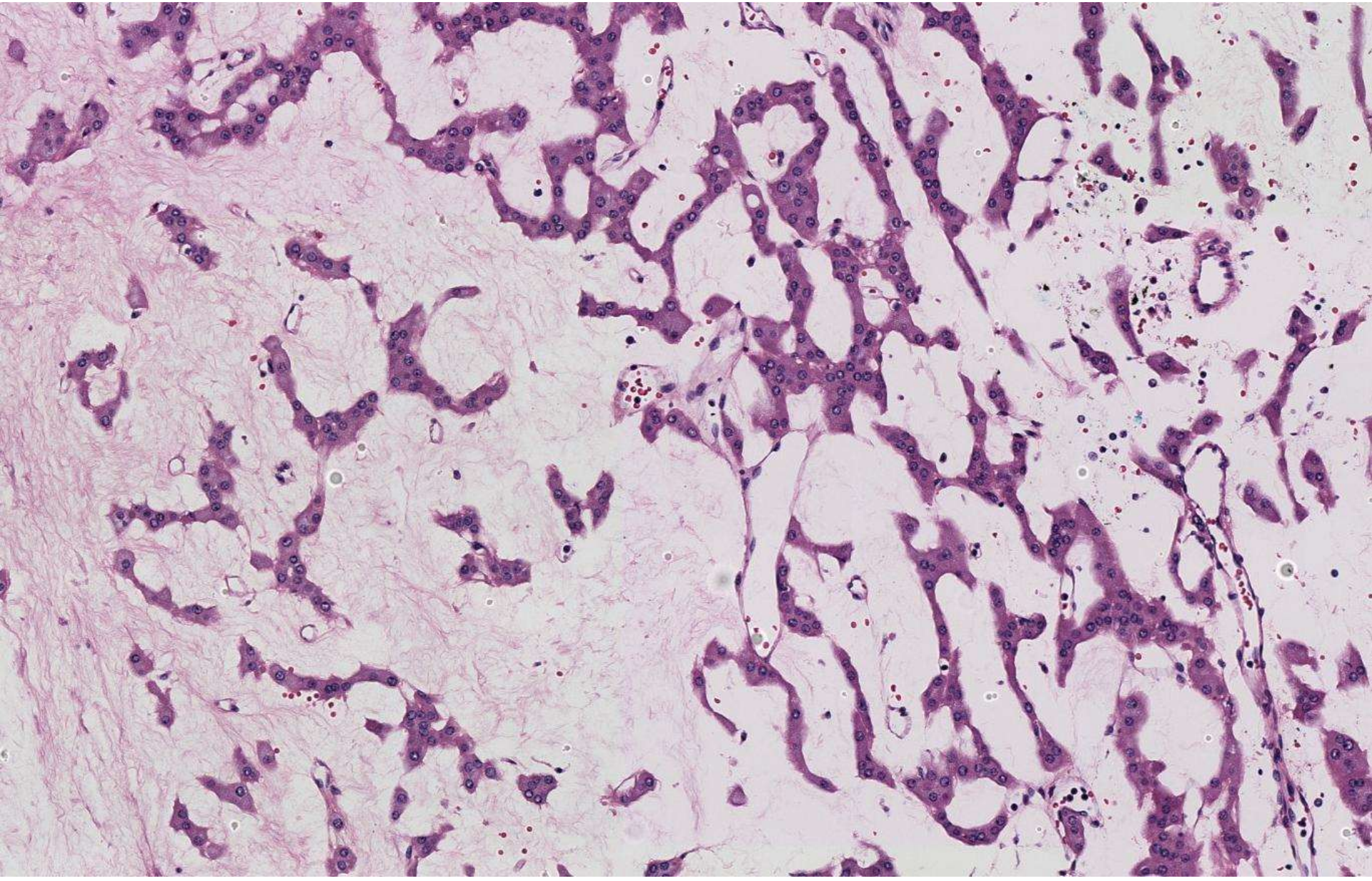


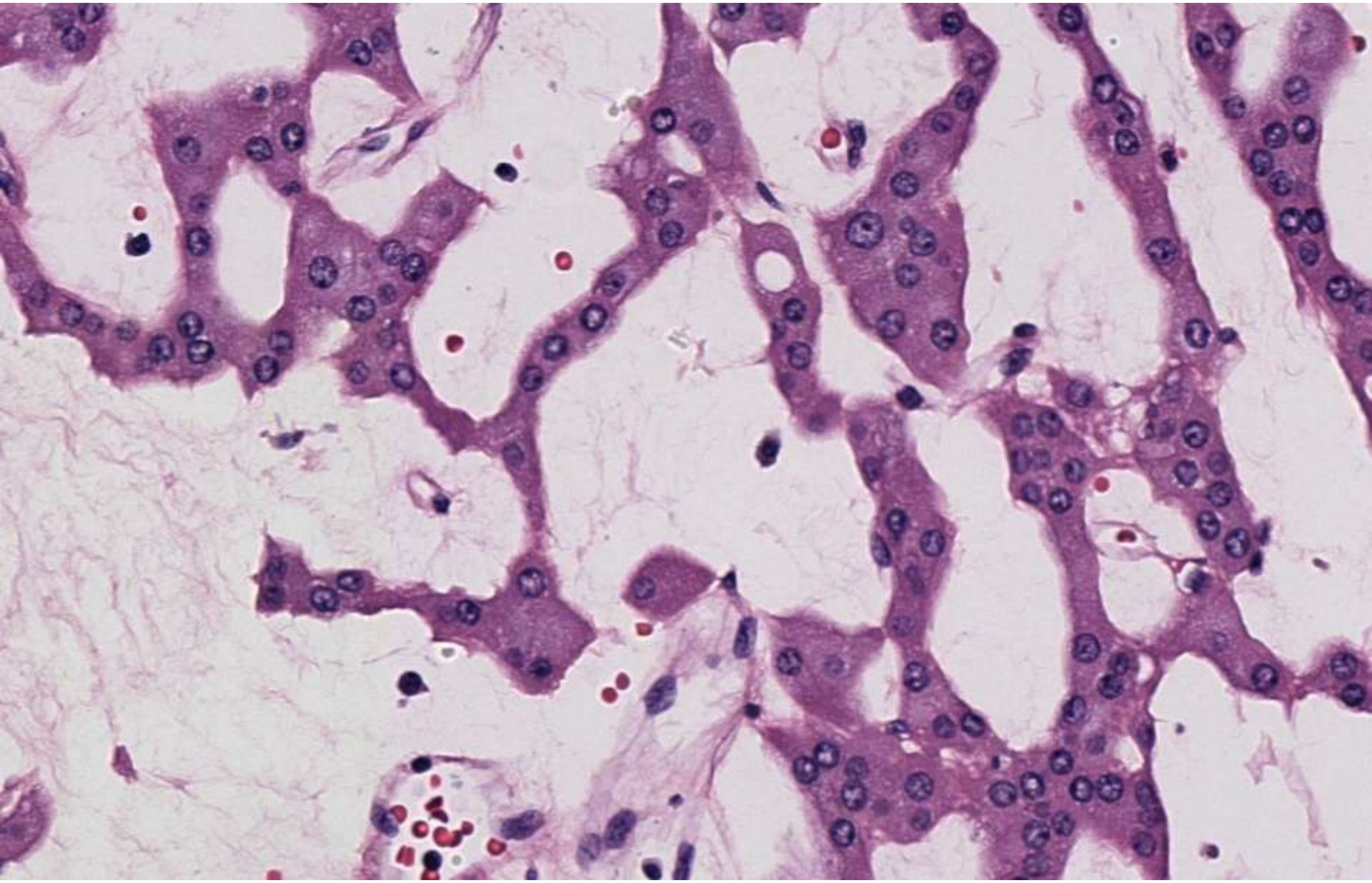


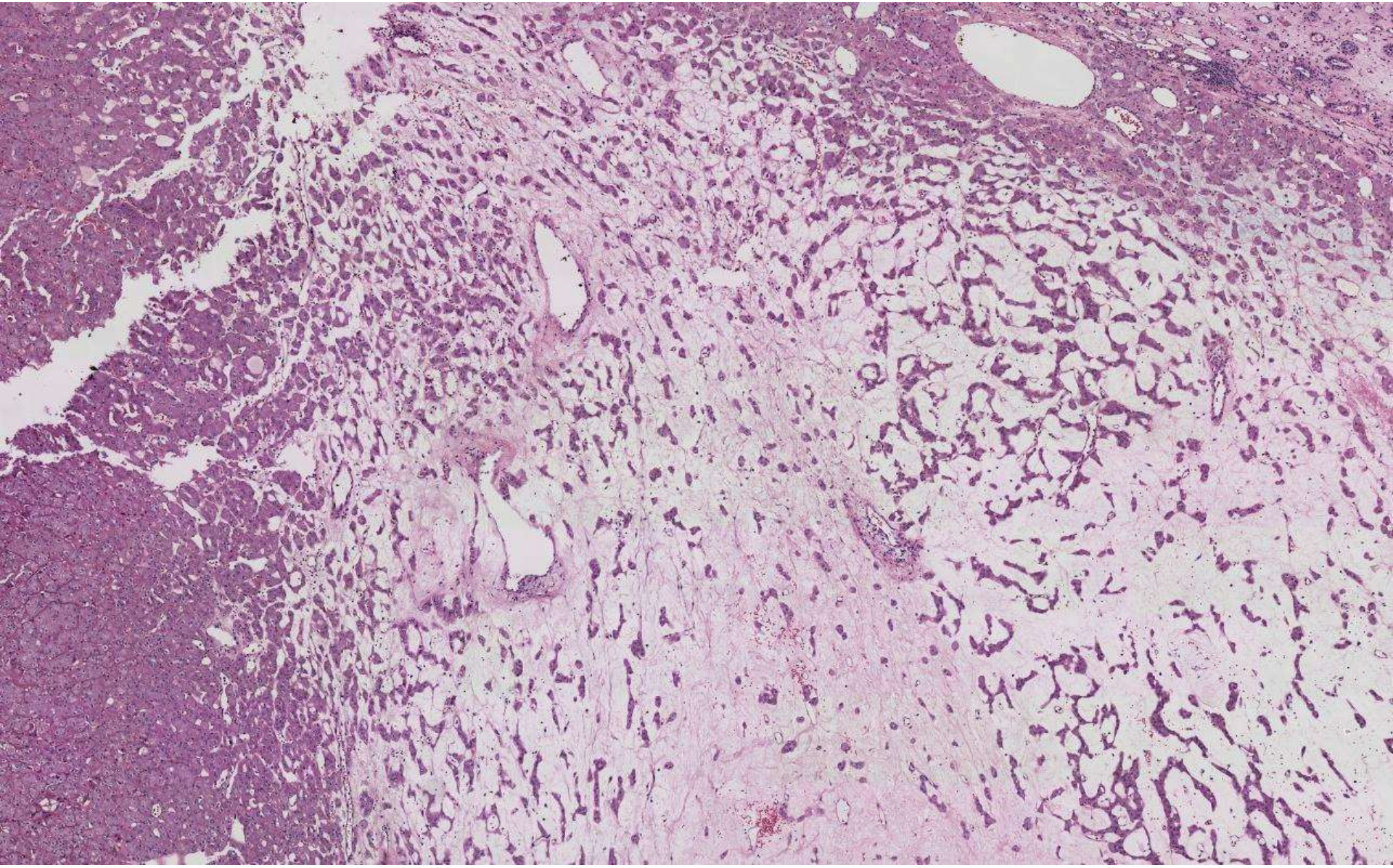








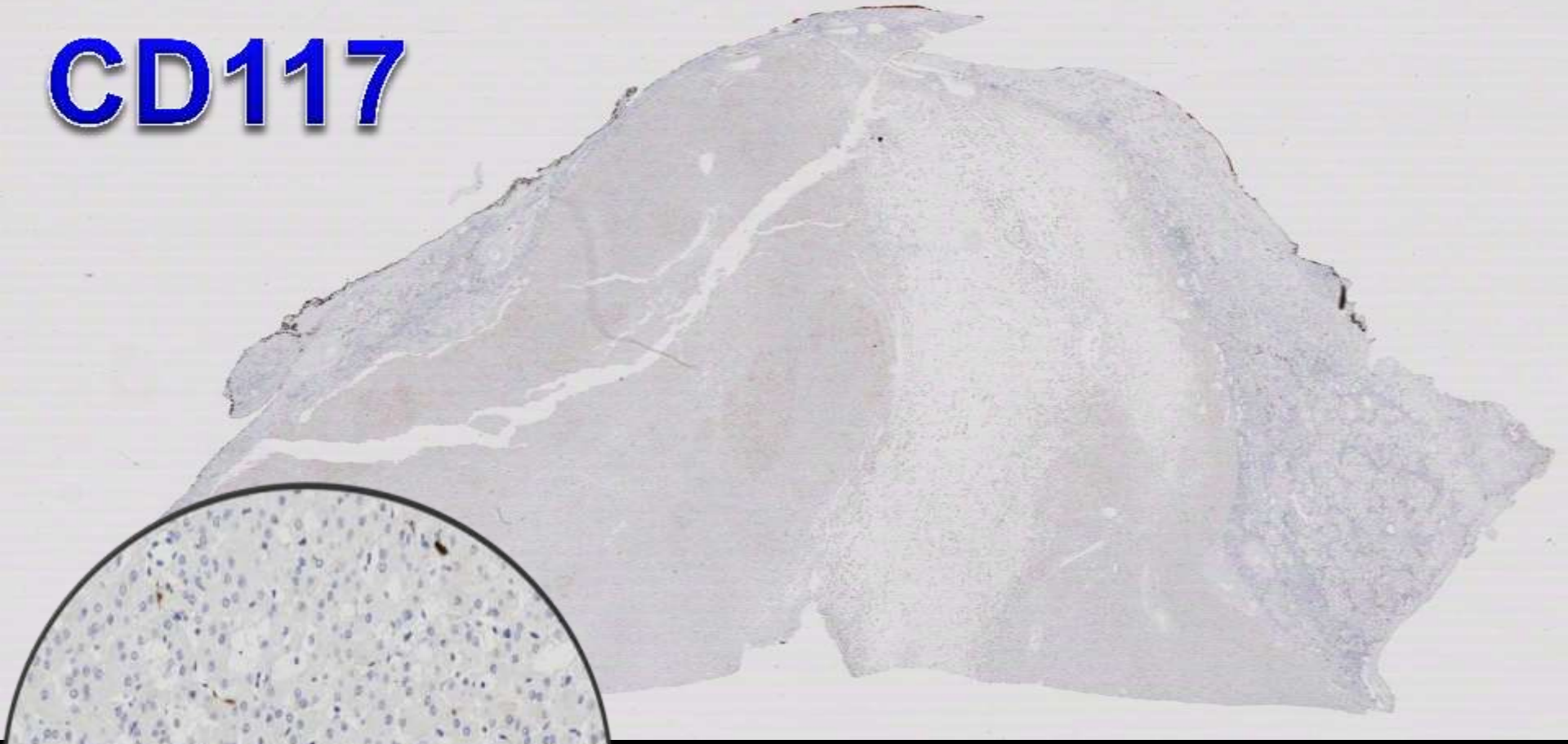


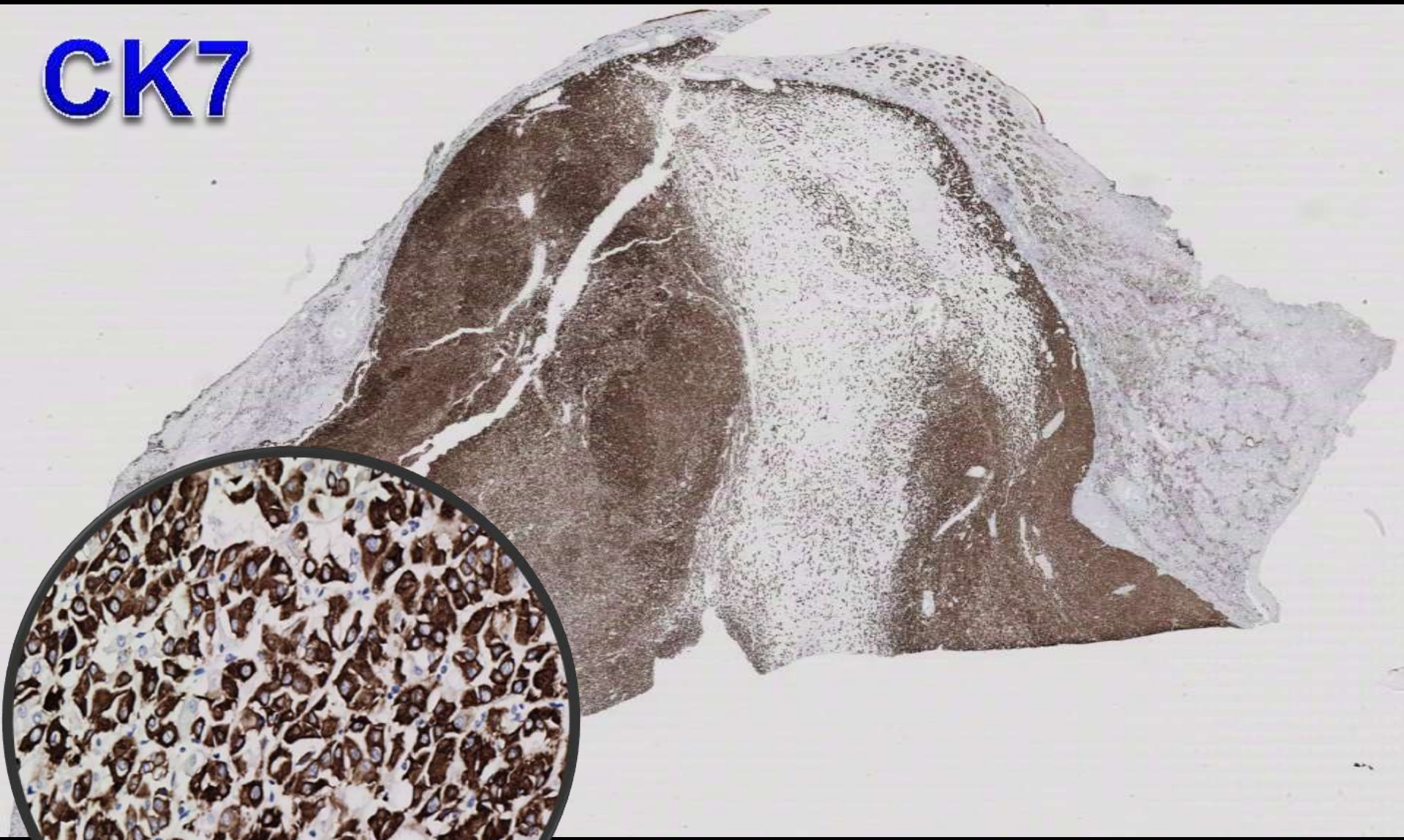


# DDx

- Oncocytoma
- Chromophobe RCC (eosinophilic)
- Clear cell RCC (eosinophilic)
- Papillary RCC (oncocytic)
- Epithelioid AML
- Eosinophilic, solid, & cystic RCC
- SDH deficient RCC

# CD117




CK7

# IHC profile

**POSITIVE**

PAX8

CK7

**NEGATIVE**

CD117

cathepsinK

Vimentin

CK20

CAIX

FH (retained/normal)

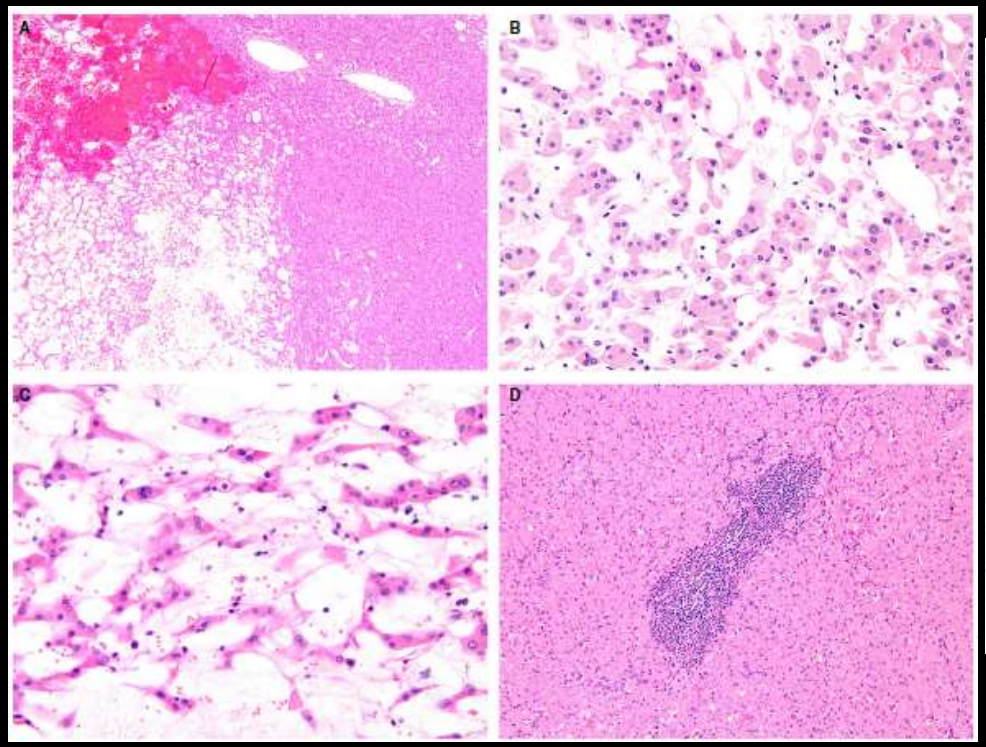
# DDx

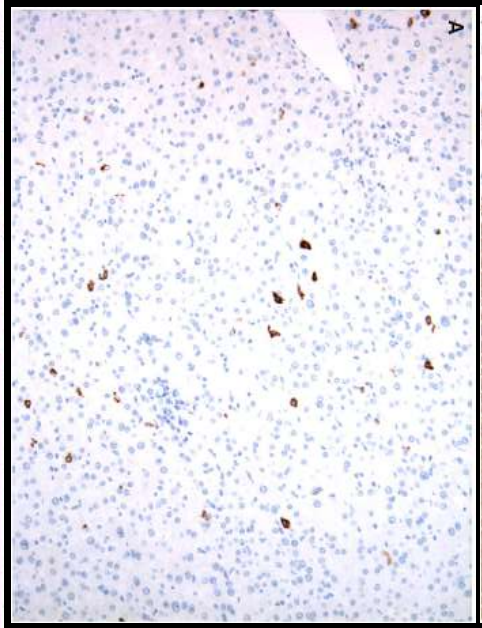
- Oncocytoma
- Chromophobe RCC (eosinophilic)
- Clear cell RCC (eosinophilic)
- Papillary RCC (oncocytic)
- Epithelioid AML
- Eosinophilic, solid, & cystic RCC
- SDH deficient RCC

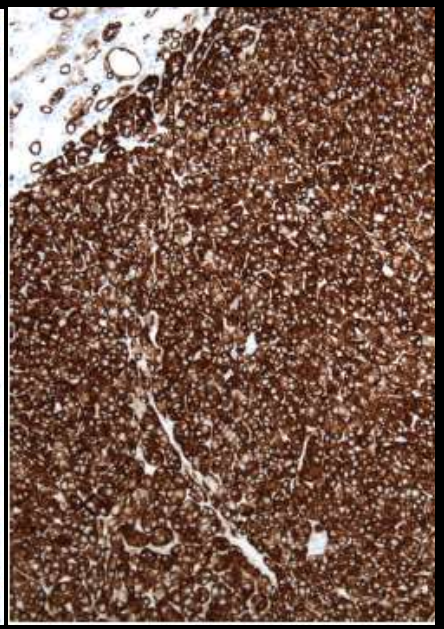
*Histopathology* 2019, 75, 174–184. DOI: 10.1111/his.13865

# Low-grade oncocytic tumour of kidney (CD117-negative, cytokeratin 7-positive): a distinct entity?

Kiril Trpkov[1] Sean R Williamson,[2] Yuan Gao,[1] Petr Martinek,[3] Liang Cheng,[4] Ankur R Sangoi,[5] Asli Yilmaz,[1] Cheng Wang,[6] Pilar San Miguel Fraile,[7] Delia M Perez Montiel,[8] Stela Bulimbasić,[9] Joanna Rogala[10] & Ondrej Hes[3]

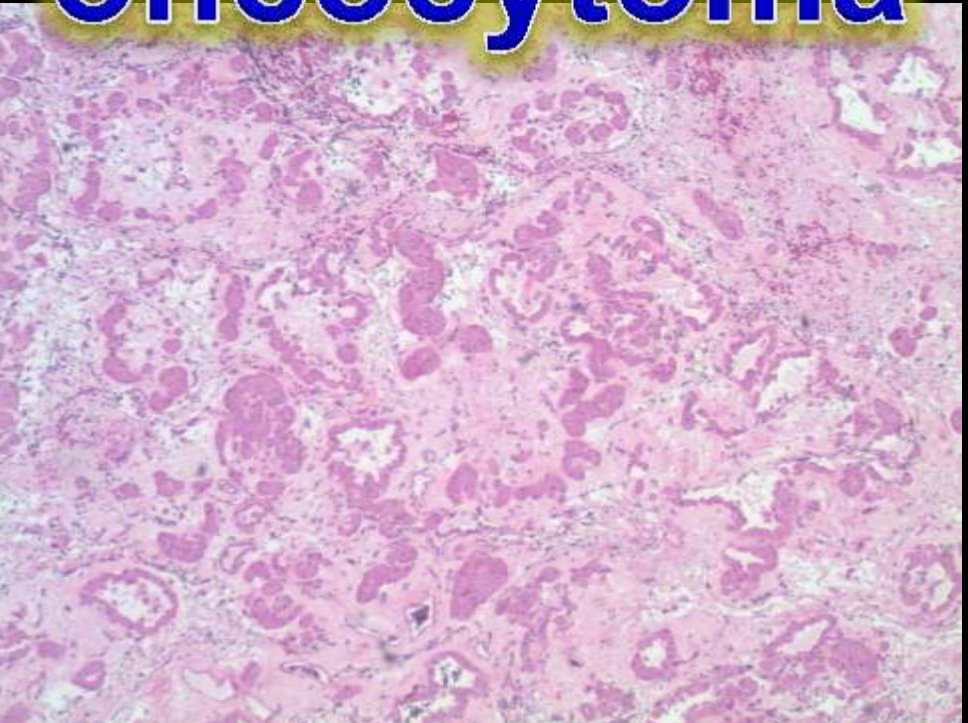


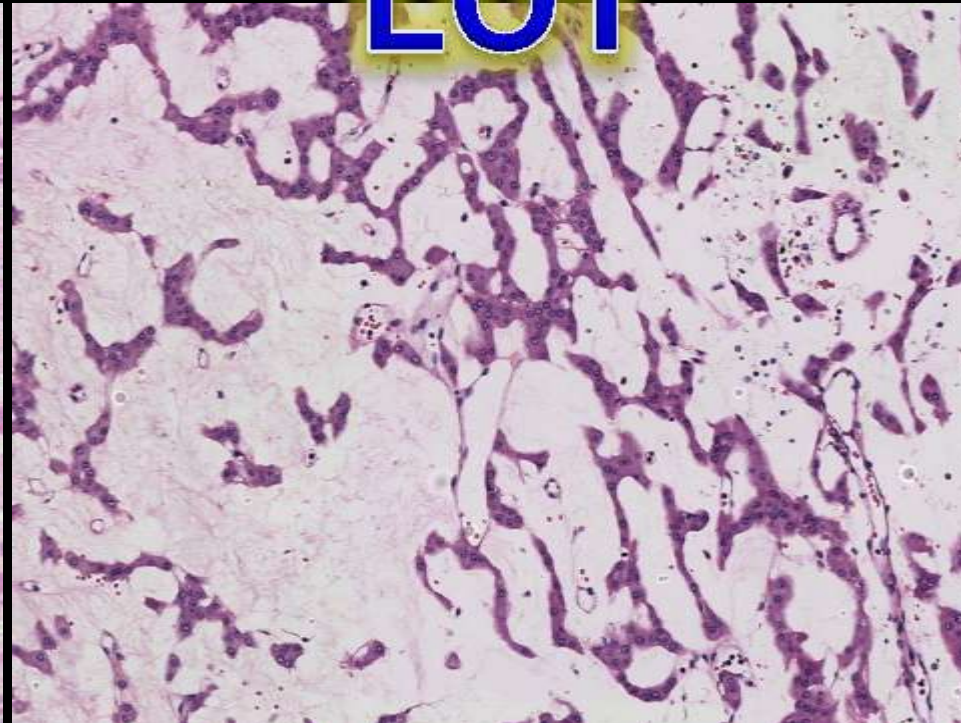




oncocytoma


LOT





# Low grade oncocytic tumor

| | |
|---|---|
| Clinical | Older patients, non-syndromic, M: F = 1:1.8, relatively small size, good prognosis |
| Gross | Tan-brown and solid, single tumours |
| Light microscopy | Architecture: non-encapsulated, solid, compact nested or focal tubular and tubuloreticular growth. Frequent oedematous stromal areas with irregular and loose reticular, cord-like and individual cell growth. Focal lymphocytic aggregates can be seen |
| | Cytology: homogeneous oncocytic cytoplasm, round to oval nuclei, without significant irregularities. Delicate perinuclear halos focally present |
| Immunohistochemistry | Positive: CK7, PAX-8, E-cadherin, AE1/AE3, BerEP4, MOC 31 |
| | Negative: CD117 (rare cases focal weak+), CA9, CK20, Vimentin, CD10 (−/focal+), AMACAR (−/focal+), CK5/6, p63, HMB45, Melan A, CD15 |
| Special stains | Muller – Mowry colloidal iron: negative or apical, bar or blob-like positive |
| aCGH | Frequent deletions at 19p13.3 (7/9), 1p36.33 (5/9) and 19q13.11 (4/9); some disomic (2/9). No other consistent chromosomal gains or losses |

(2019) *Histopathology* 75, 174–184.

# DDx

| | | |
|---|---|---|
| Low-grade oncocytic tumour | Solid sheets and compact nests, with gradual transition to trabecular areas; sharply delineated oedematous stromal areas with loose cell growth | CD117−, CK7+ |
| Chromophobe RCC, eosinophilic | Solid growth, more prominent cell membranes, irregular (raisinoid) nuclei, perinuclear halos, loose stromal areas lacking | CD117+, CK7+ |
| Oncocytoma | Can show more tubulocystic growth, lacks perinuclear halos, central stromal 'archipelaginous' areas are present, however lacks areas of loose and irregular cell growth | CD117+, CK7 −/+ |
| Clear cell RCC, eosinophilic | At least focal clear cell areas, delicate vasculature in the background | CA9+, CD117− |
| Papillary RCC, oncocytic | Papillary growth | AMACR+, CD10+, Vimentin + |
| Epithelioid angiomyolipoma | Epithelioid cells, may be pleomorphic, lacks perinuclear halos | PAX8−, HMB45+, AE1/AE3−, CK7− |
| Eosinophilic, solid and cystic RCC | Great majority females, solid and cystic growth, cytoplasmic stippling, lacks perinuclear halos | CK20+, CK7−, CD117− |
| SDH-deficient RCC | Flocculent cytoplasm and vacuoles; lacks perinuclear halos | CD117−, SDH−, AE1/AE3− (often) |

(2019) *Histopathology* 75, 174–184.