Aug 2019 DIAGNOSIS LIST

19-0801: favor perineurioma (kidney; GU pathology)
19-0802: Mesonephric-like adenocarcinoma (uterus; GYN pathology)
19-0803: endometrioid adenocarcinoma with POLE mutation (uterus; GYN pathology)
19-0804: gliomatosis peritonei with increased cellularity (pelvis; GYN pathology)
19-0805: Q-fever with fibrin ring granuloma (liver/non-neoplastic liver pathology)
19-0806: Gallbladder epithelial inclusions mimicking parasitic infection (gallbladder; GI pathology)
19-0807: endometrial stromal sarcoma (large bowel; GYN pathology)
19-0808: pulmonary alveolar proteinosis (lung; non-neoplastic lung pathology)
19-0809: acanthamoeba keratitis (eye; infectious disease pathology)
19-0810: NUT carcinoma (lung; soft tissue pathology)

Disclosures
Aug 5, 2019

The following planners and presenters had disclosures:

Ankur Sangoi	Google	Consultant
Christine Louie	Grail	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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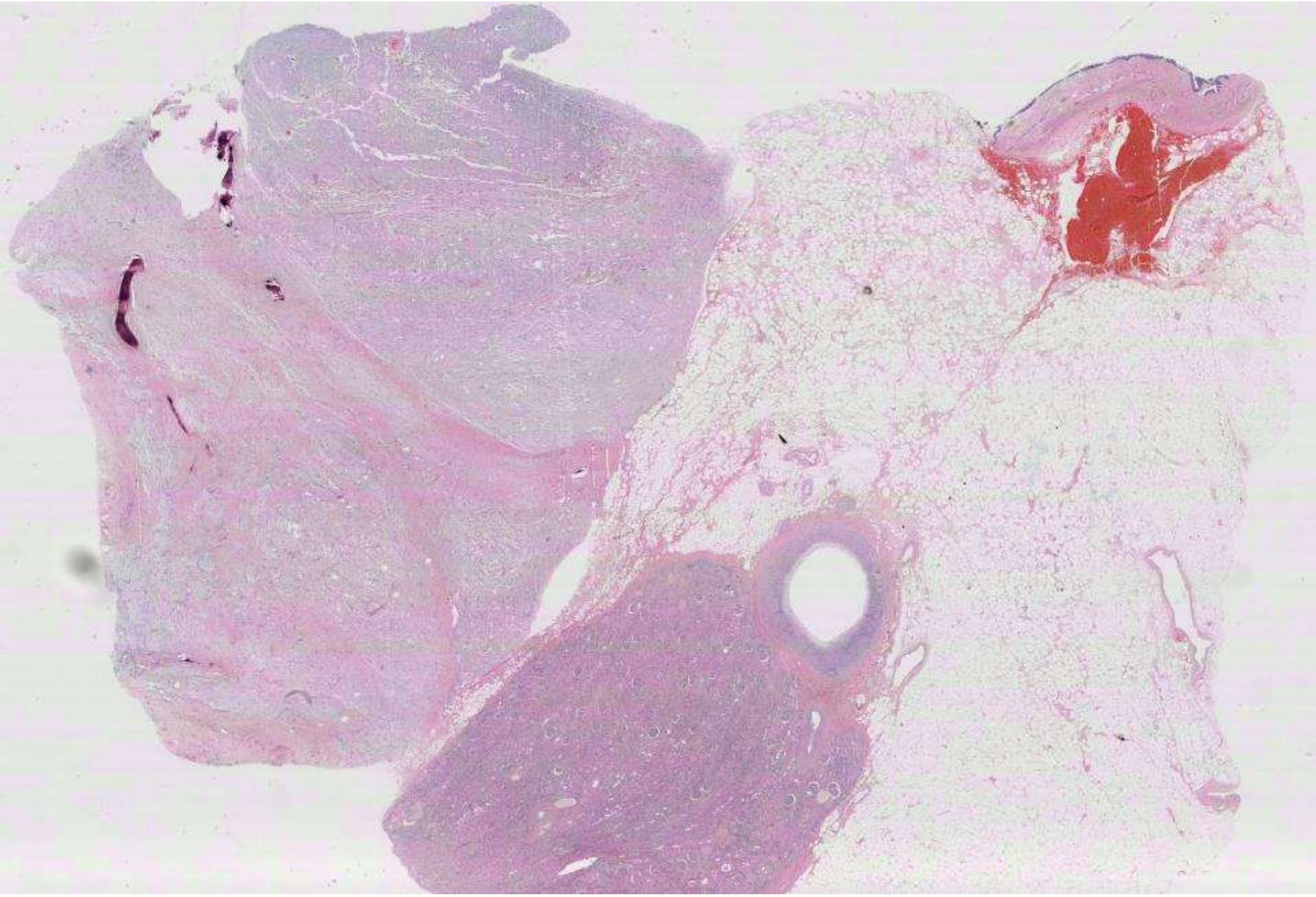
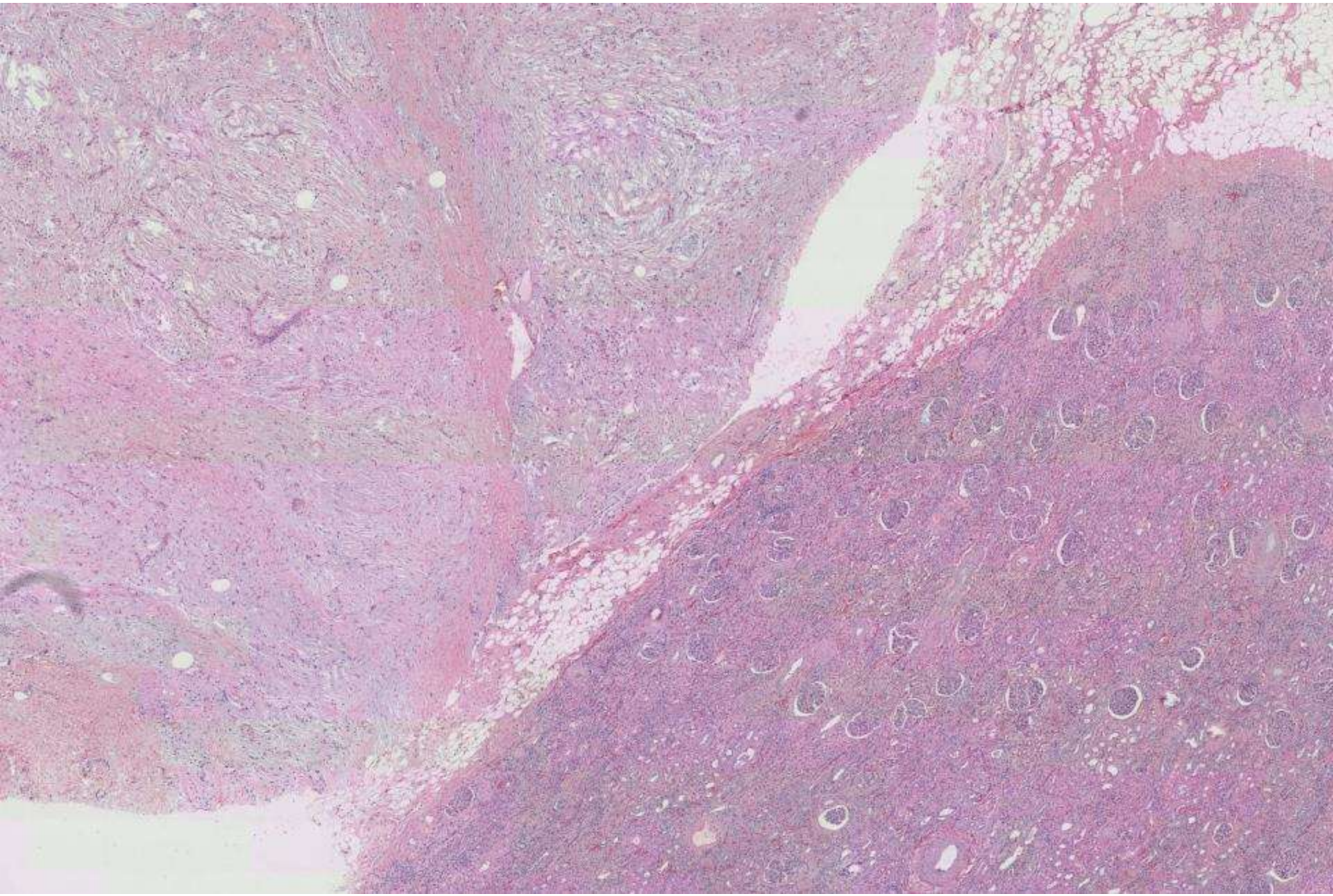
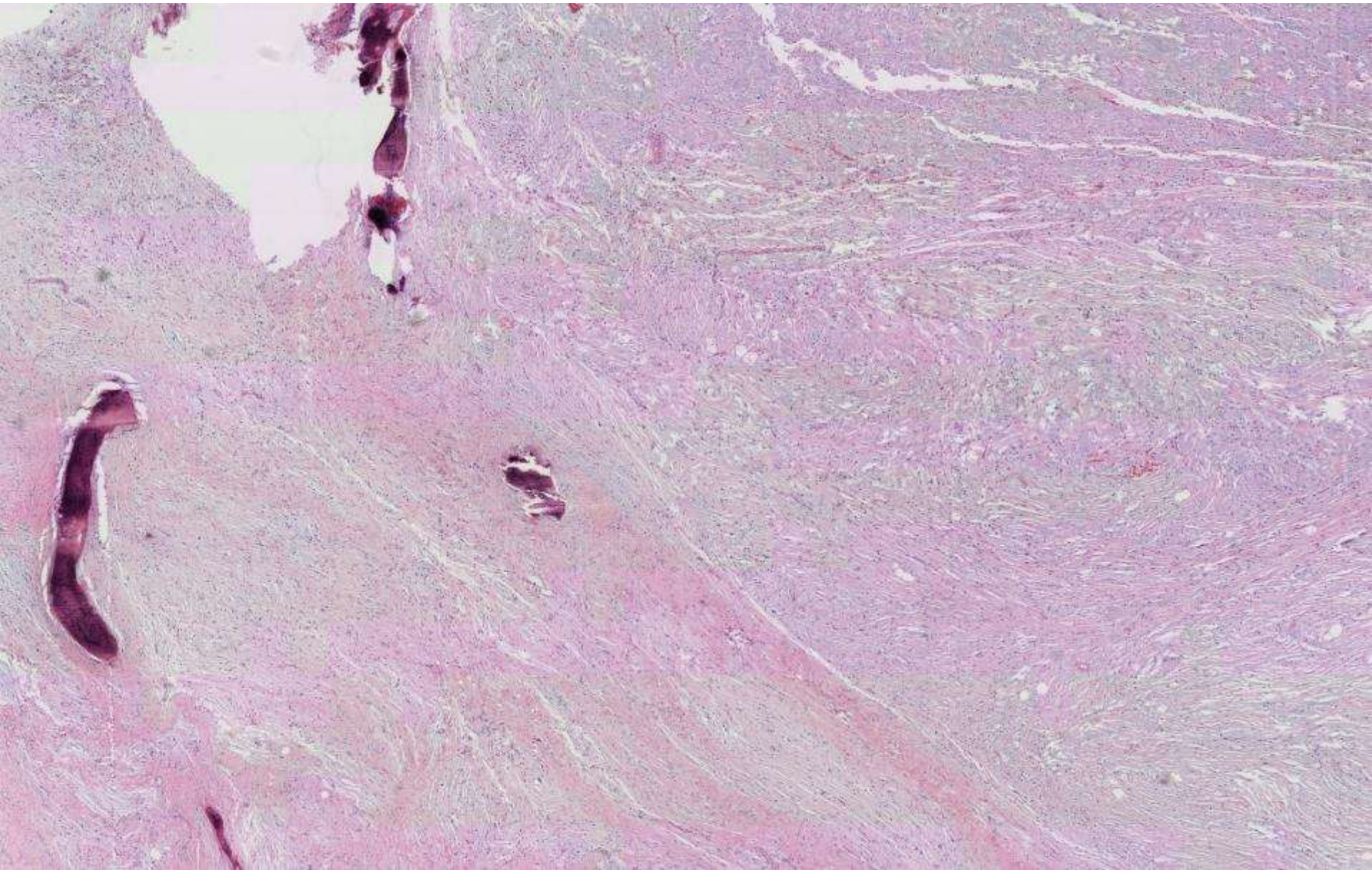
19-0801
(scanned slide available)

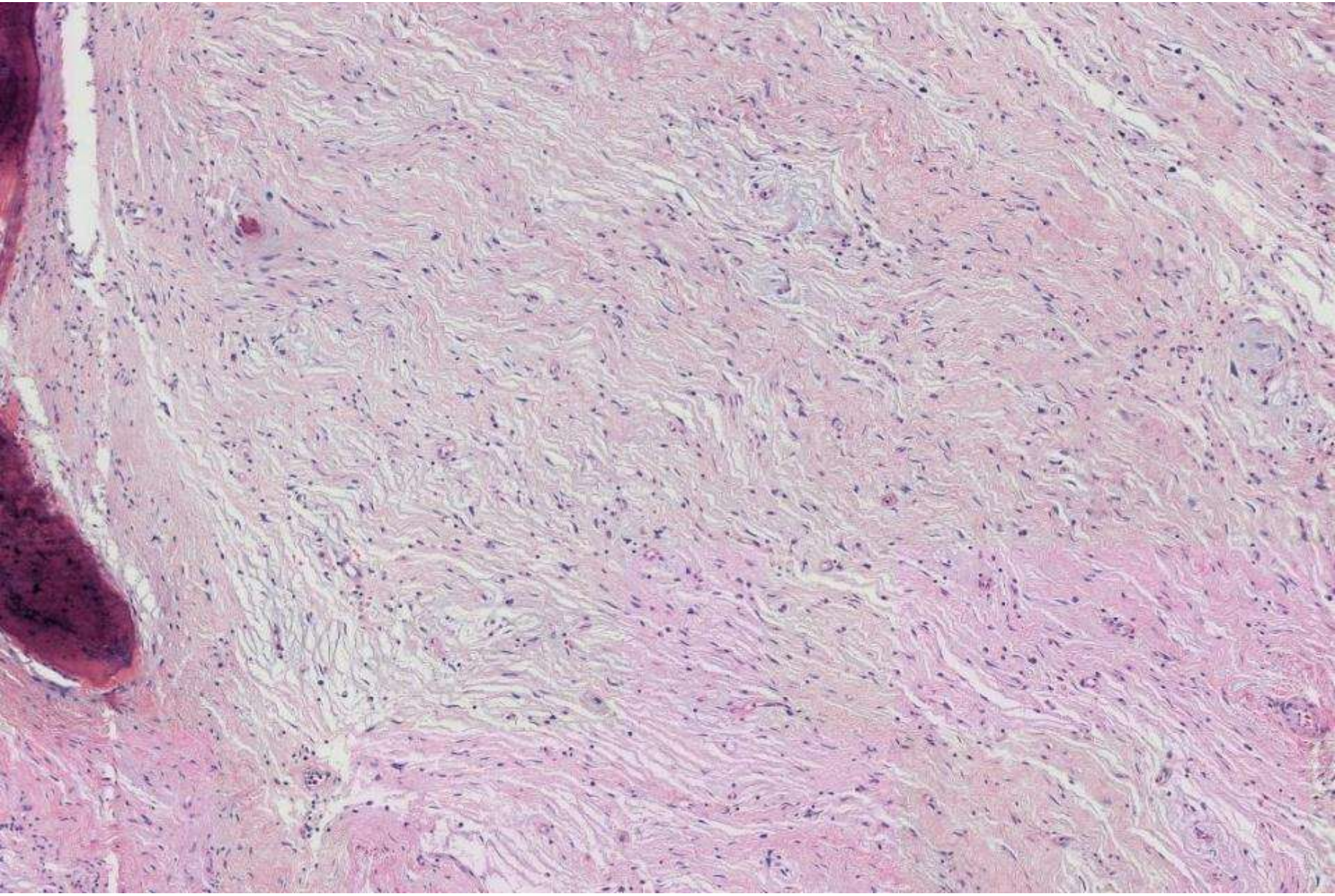
Emily Chan, UCSF

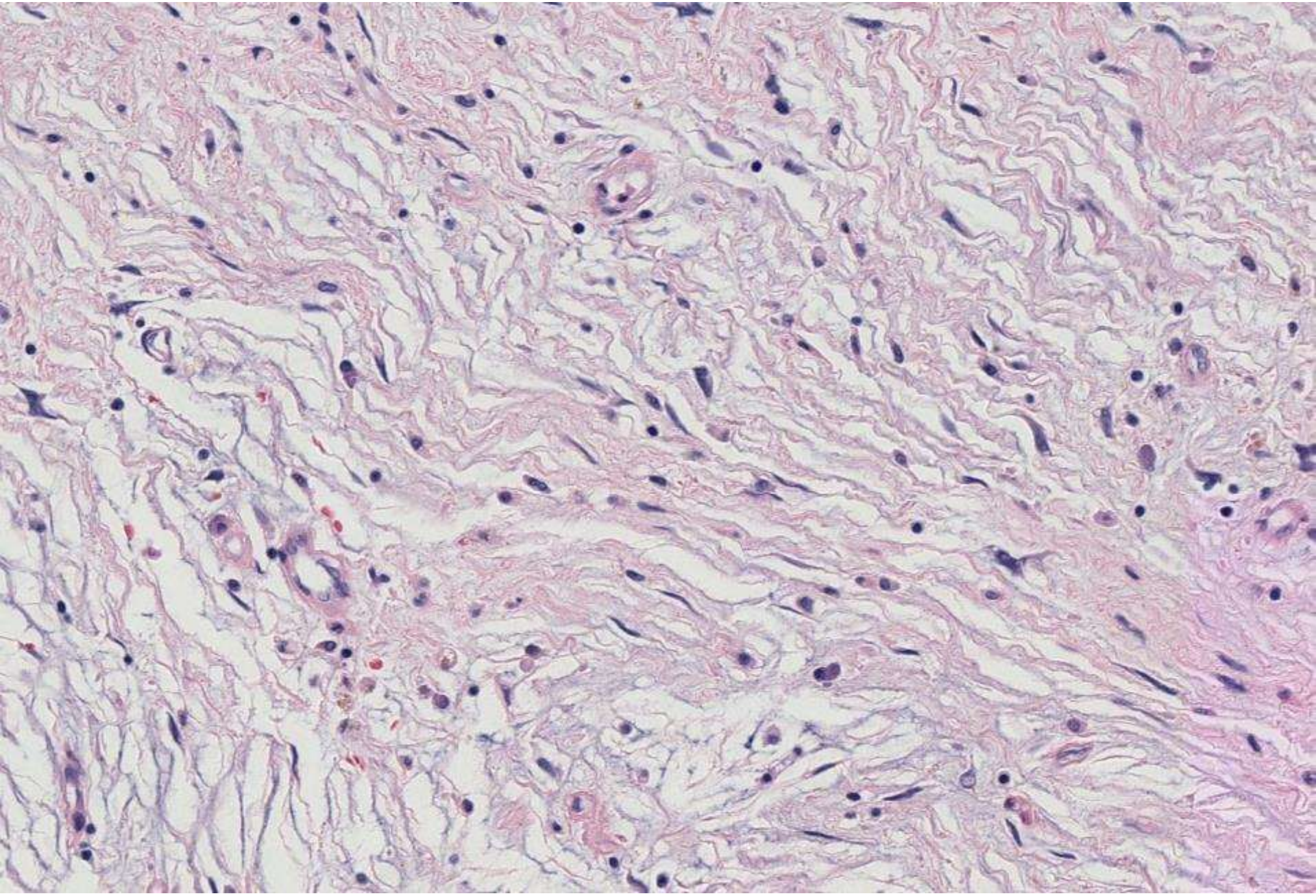
57-year-old man with 5.2cm left upper pole/para-pelvic renal mass.

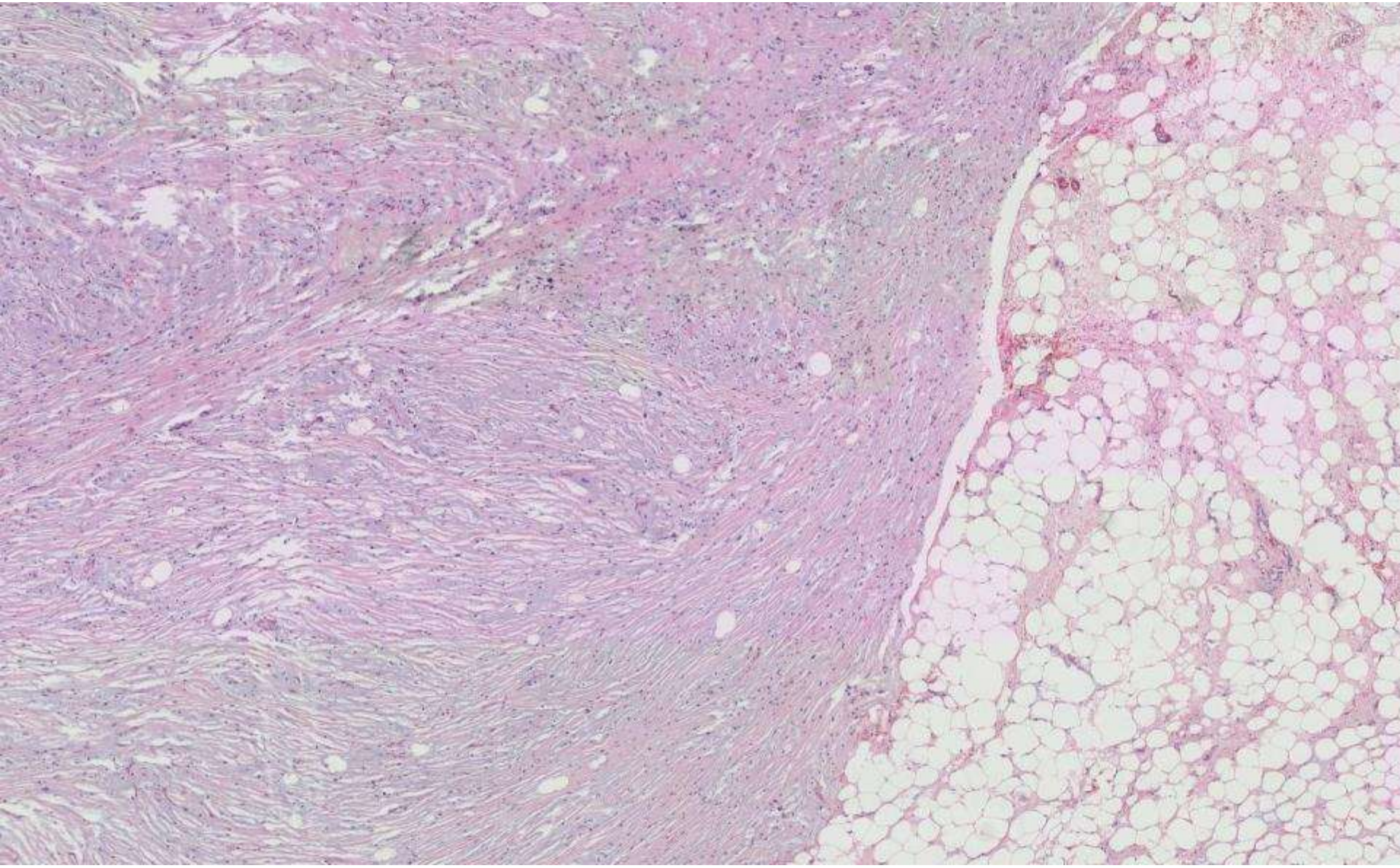


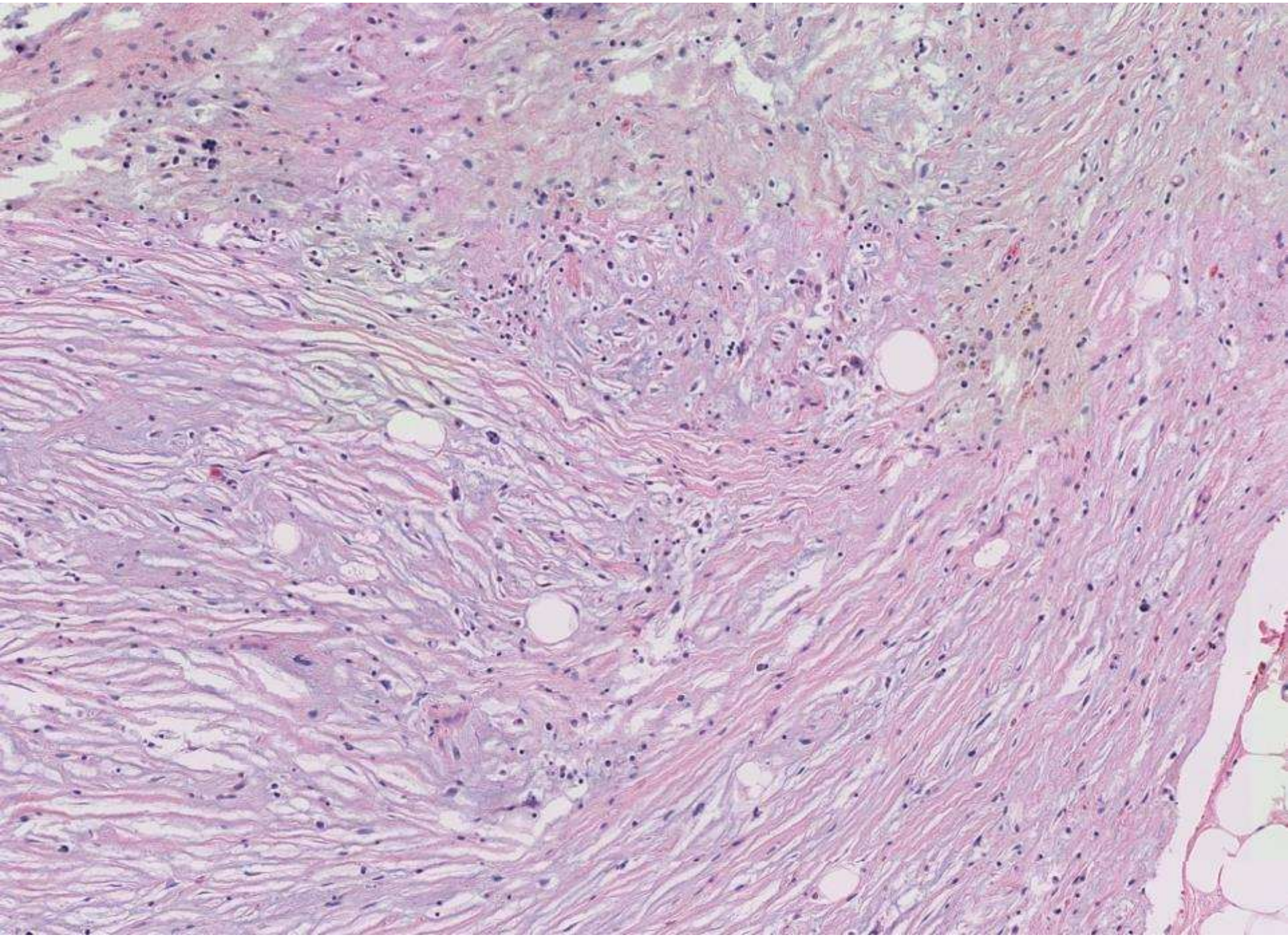


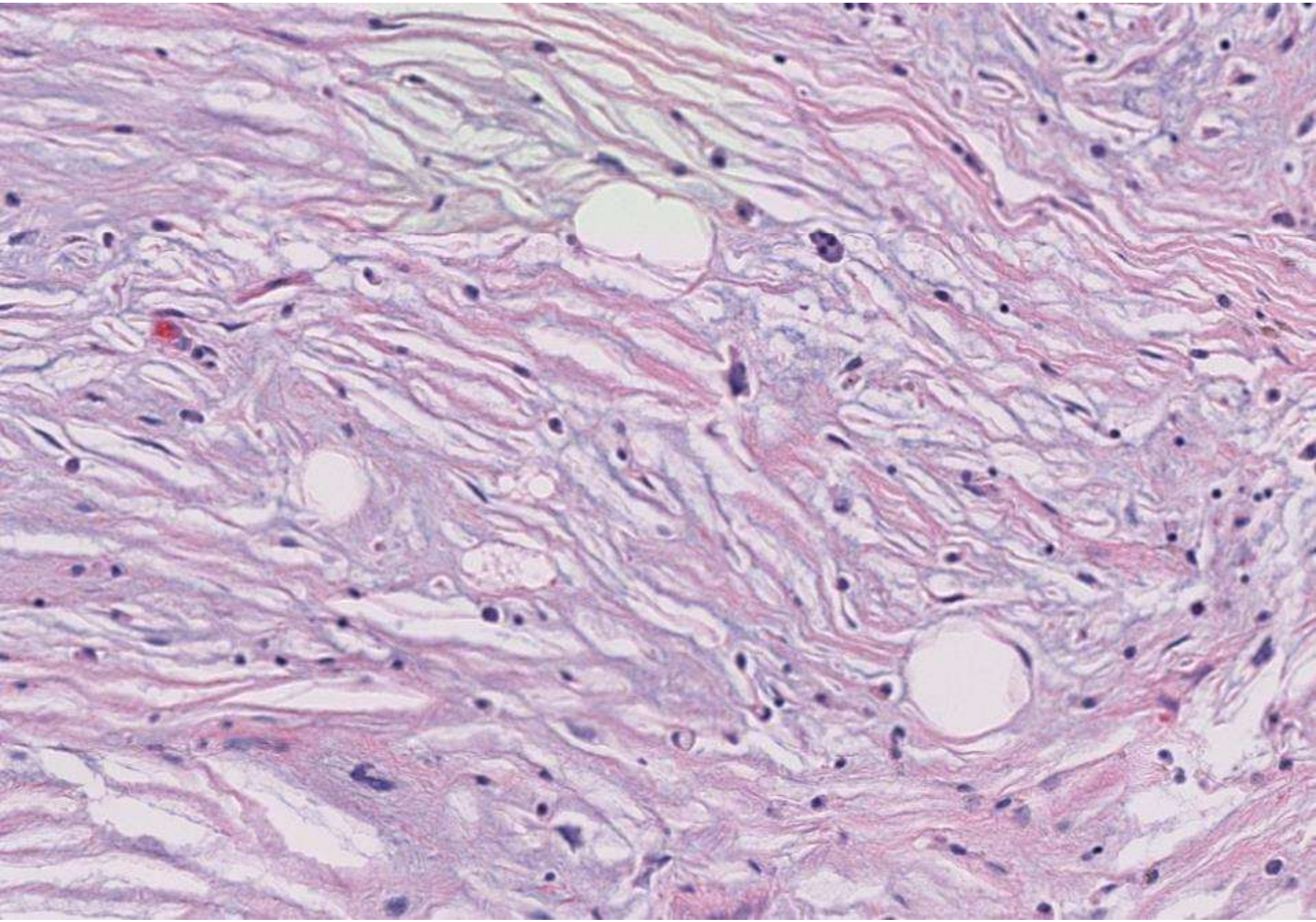


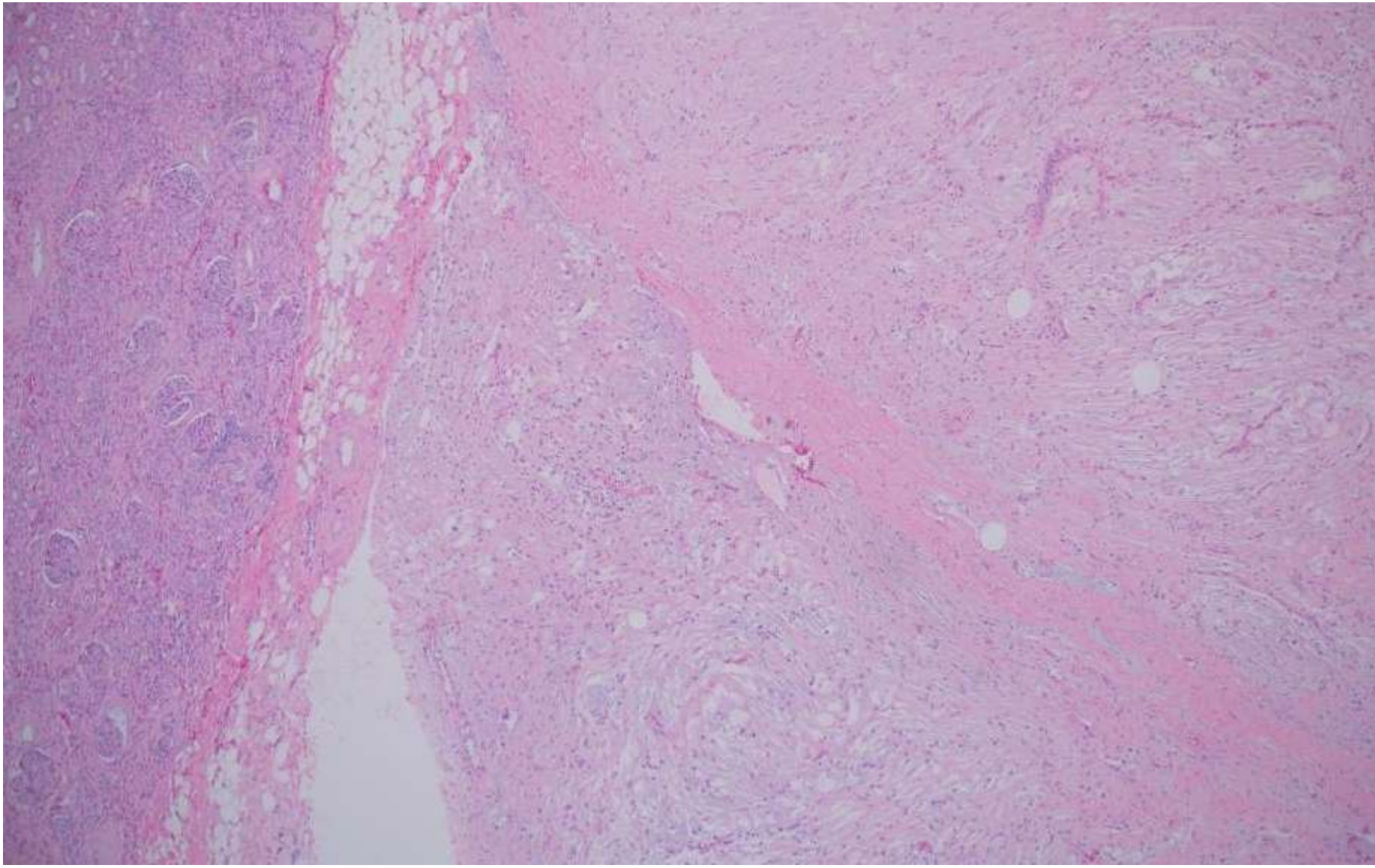


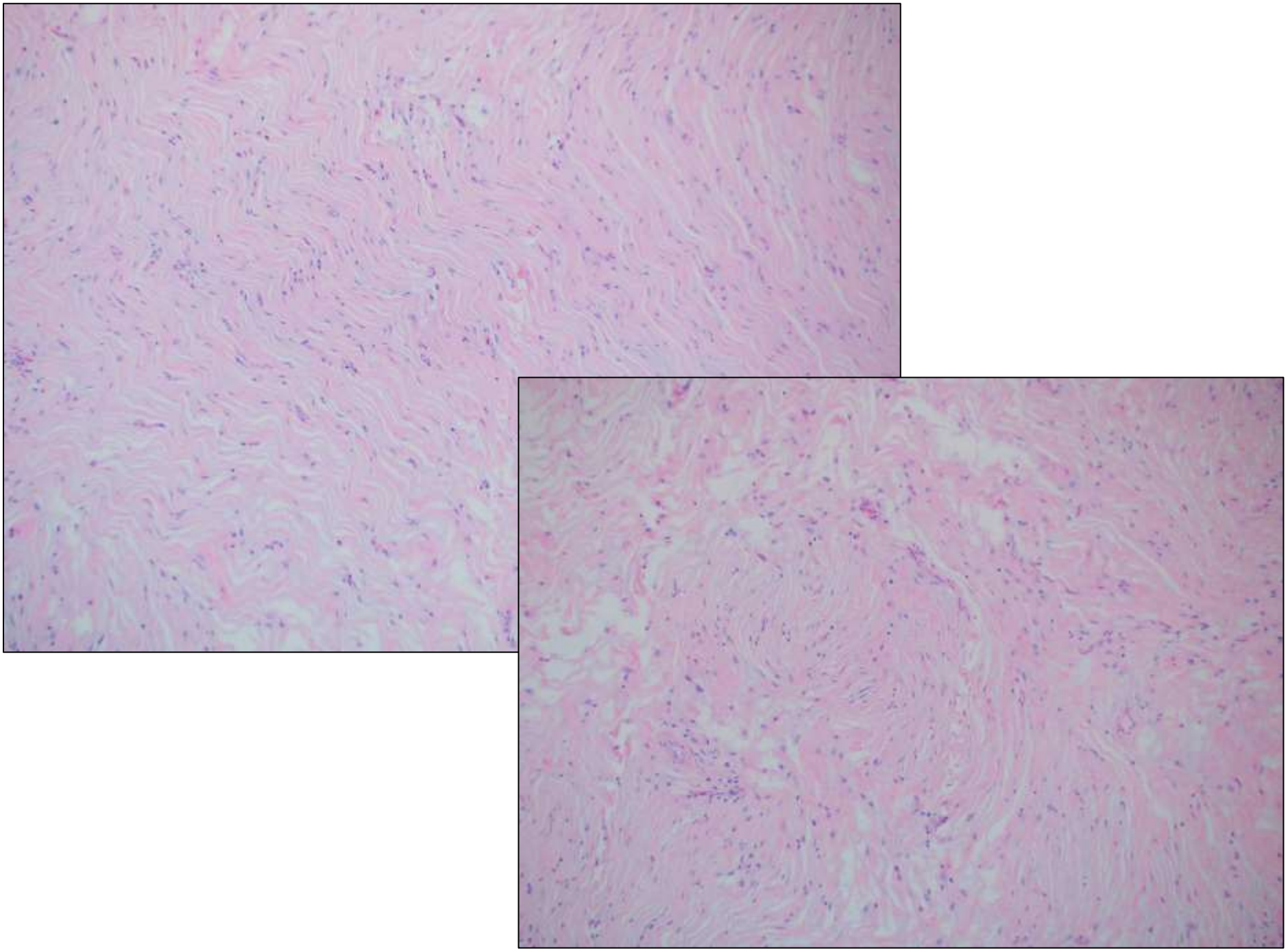








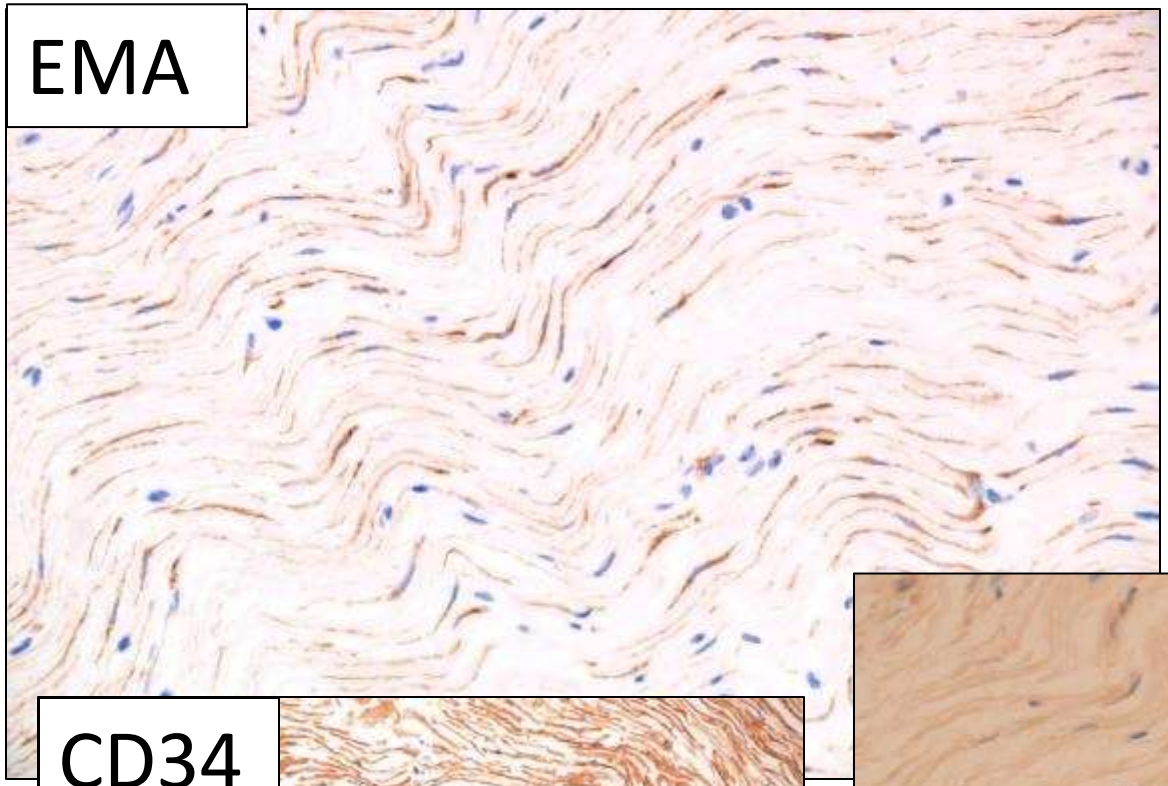




Differential Diagnosis

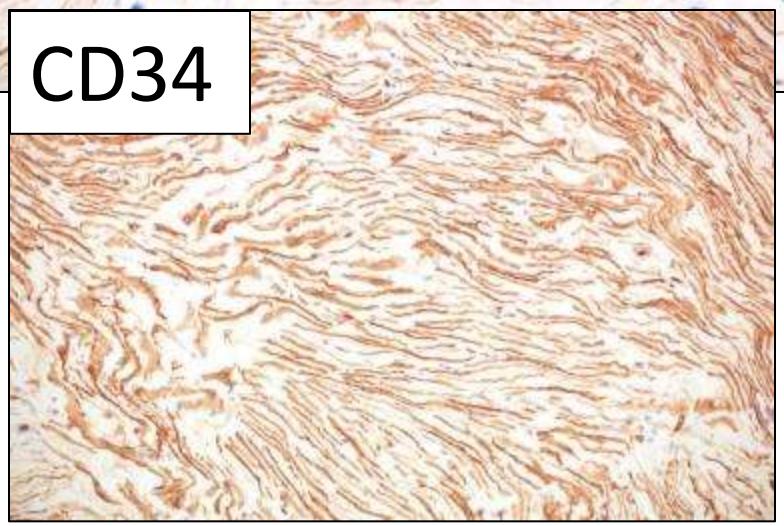
- Schwannoma/neurofibroma
- Perineurioma
- GIST
- SFT
- Desmoid
- Leiomyoma
- Inflammatory myofibroblastic tumor
- Cellular myxoma
- Low-grade myxofibrosarcoma
- Low-grade fibromyxoid sarcoma
- Low-grade liposarcoma

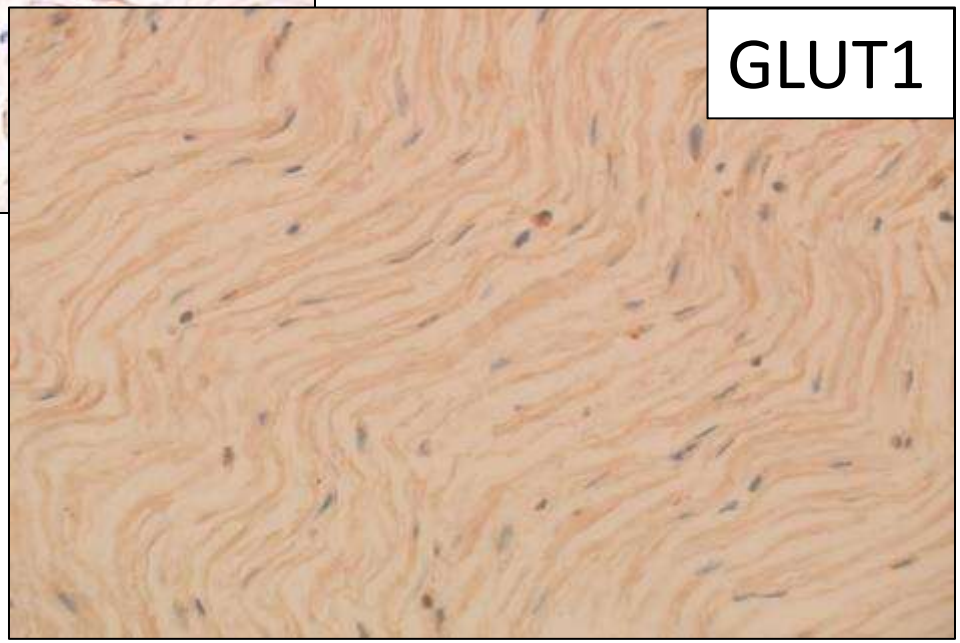
Immunohistochemistry



Negative stains:

- Pankeratin
- S100
- STAT6
- DOG1
- B-catenin
- MDM2/CDK4
- ALK
- MUC4
- CD117
- Desmin





Soft Tissue Perineurioma

- Benign neoplasm composed of perineurial cells
- Microscopic: Storiform, whorled, fascicular with collagenous and myxoid stroma, bland wavy nuclei, delicate elongated bipolar cytoplasmic processes
- IHC: EMA, GLUT1 positive, and to lesser extent claudin-1 and CD34

Soft Tissue Perineurioma

Hornick and Fletcher, Clinicopathologic analysis of 81 cases… AJSP 2005

Location	# cases
Lower limb/limb girdle	36
Upper limb/limb girdle	19
Trunk	15
Head and neck	7
Retroperitoneum	3
Paratesticular	1

- Majority superficial
- 14 called “atypical” (pleomorphism, increased cellularity, infiltration), but did not behave worse
- 5% local recurrence (these had + margin), no metastases

Perineurioma in the Kidnev

Arch Pathol Lab Med. 1993 Jun;117(6):654-7.

Perineurioma of the kidney. Report of a case with histologic, immunohistochemical and ultrastructural studies.

Kahn DG[1], Duckett T, Bhuta SM

Autho

Abstract

We report evaluati hypertensi a was

CASE REPORT

Bilateral Renal Myxoid Perineuriomas

MD, Victor Chia-Hsiang Lin, MD and Tsan-Jung Yu, MD

ELSEVIER

Myxoid Perineurioma in a Transplanted Kidney

V.H.L. Gan, W.K. Wan, and Y.H. Tan

ABSTRACT

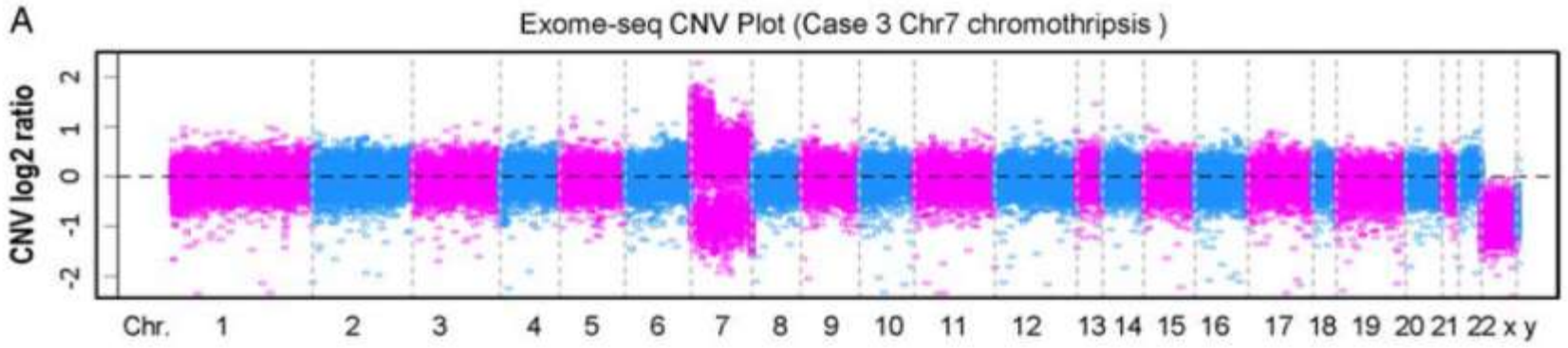
South Bay Pathology Society

5805	SFT,Soft Tissue	Sessile serrated adenoma with dysplasia, perineurioma, and lipoma	Matsukuma
5237	GU,Kidney	Perineurioma of kidney	Sangoi
4578	Neuro,Soft tissue	Perineurioma, right thigh	Latner
4577	Neuro,Soft tissue	Sclerosing perineurioma, left finger	Latner

Start another a ivity (Alt)

Soft Tissue Perineurioma: Genetics

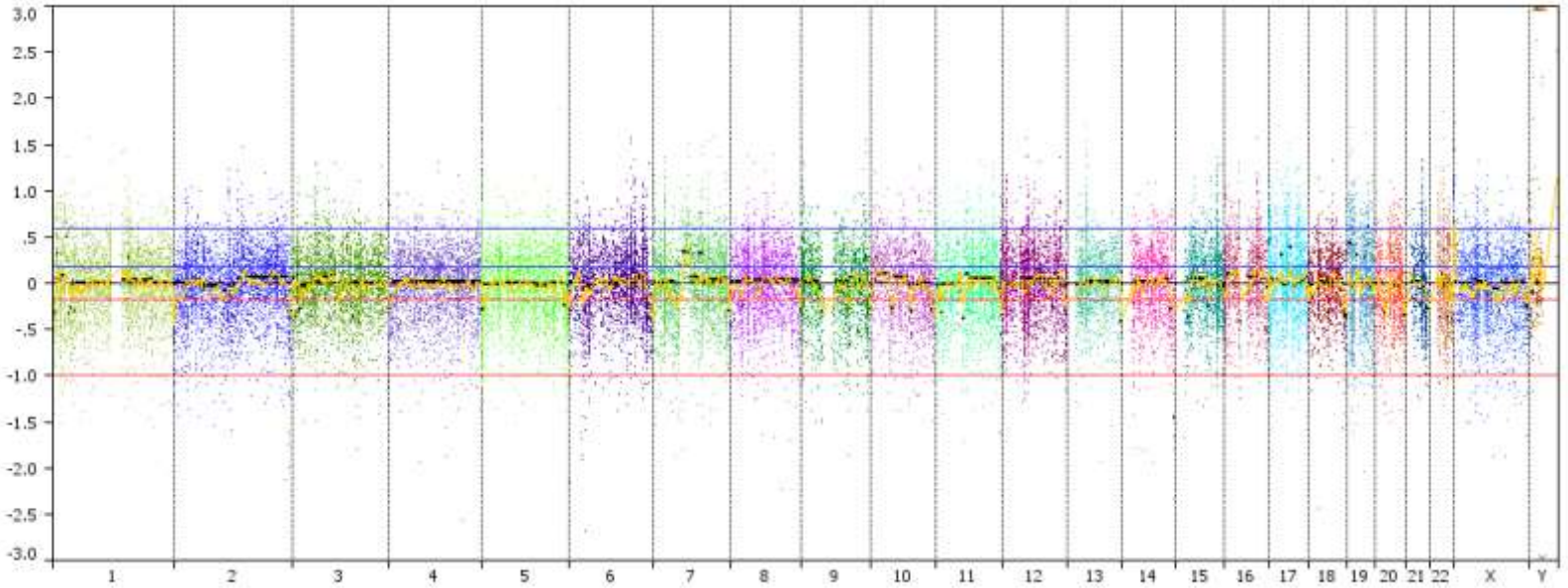
- WES of 14 cases
- No TRAF7 mutations (unlike intraneural perineuriomas)
- Multiple large chromosomal abnormalities, frequently:
  - Losses in Ch22q including NF2 (n = 6 cases)
  - Losses 17q including NF1 (n= 4 cases)



Carter et al, Recurrent genomic alterations in soft tissue perineuriomas, AJSP 2018

UCSF500 Next Generation Sequencing Assay performed on our case:

- No mutations



Final diagnosis: Morphologically bland fibromyxoid tumor, favor perineurioma

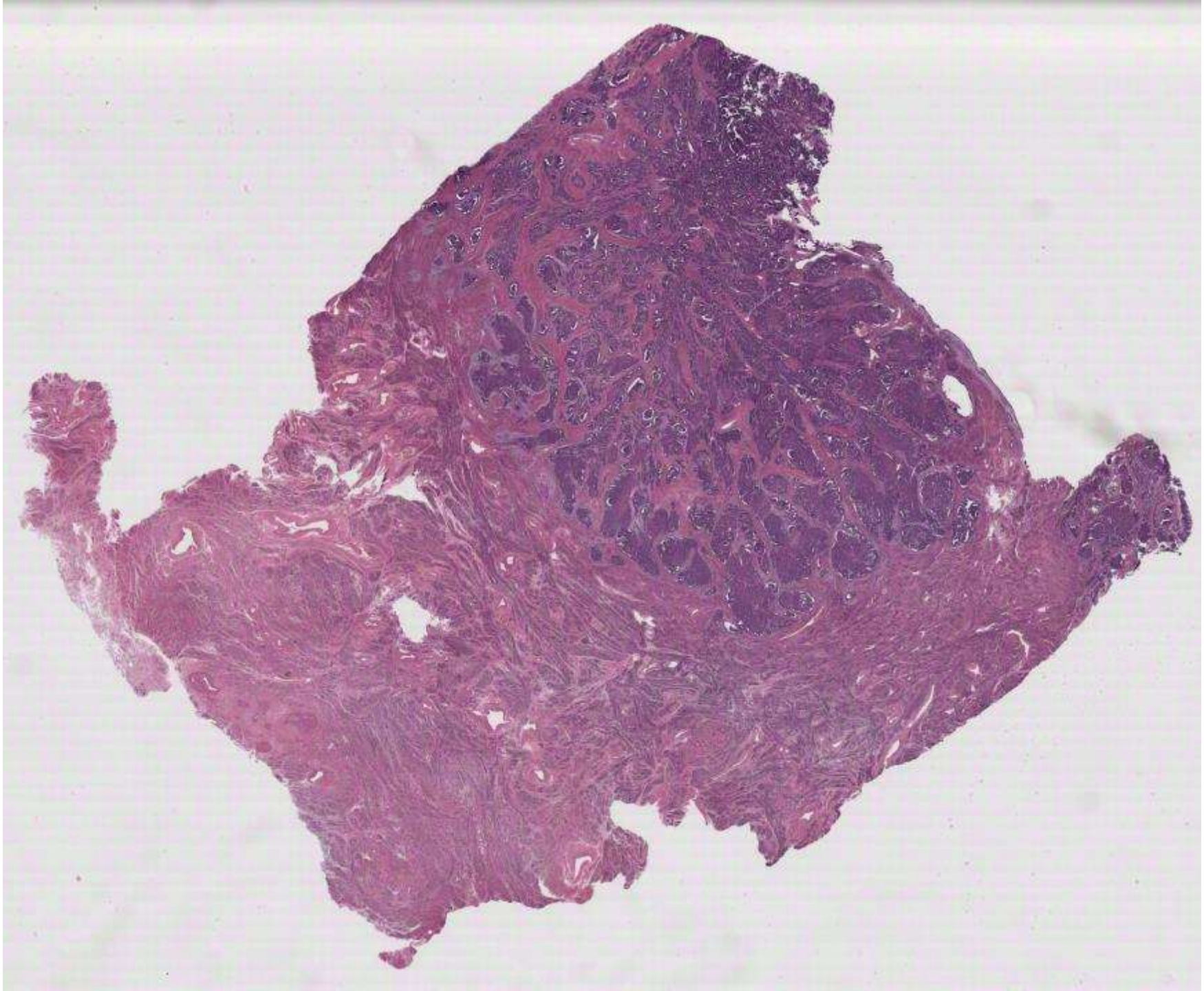
Take home points

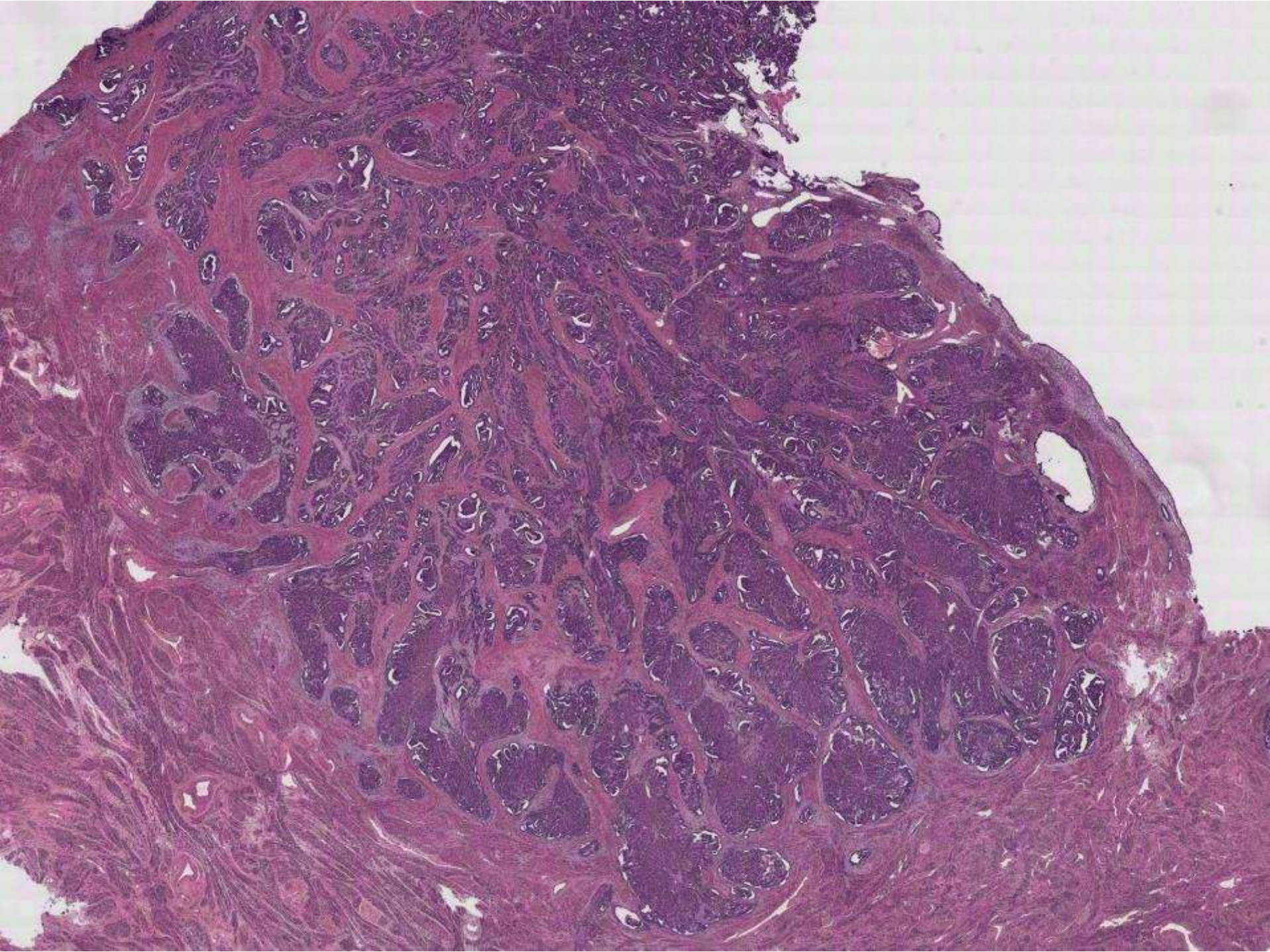
- Perineurioma can occur in the kidney
- Positive EMA and negative S100, pankeratin stains (and other markers in bland spindle cell differential) can clue you in
- Exclude malignant possibilities
- Soft tissue perineurioma has genomic profile that is distinct from intraneural perineurioma

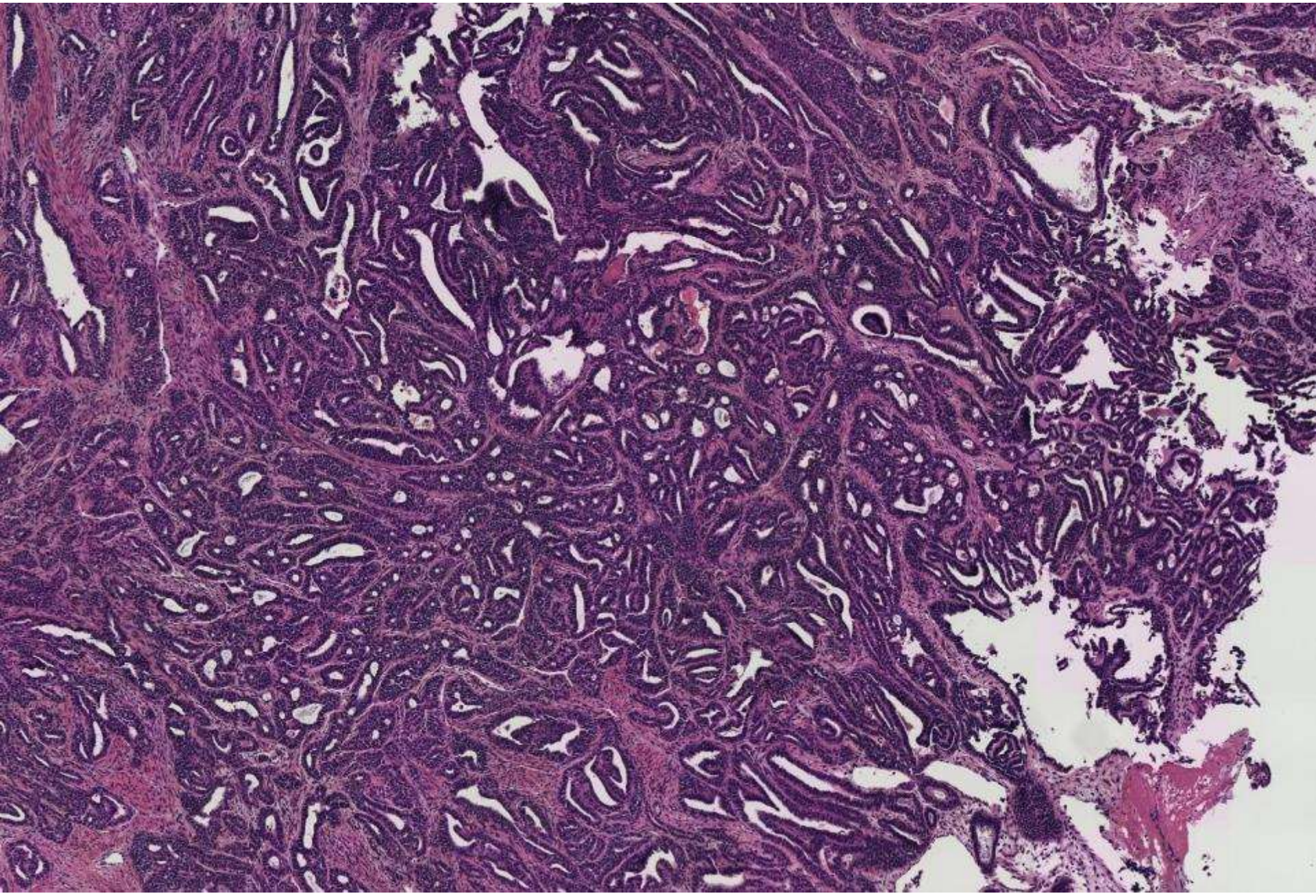
19-0802
(scanned slide available)

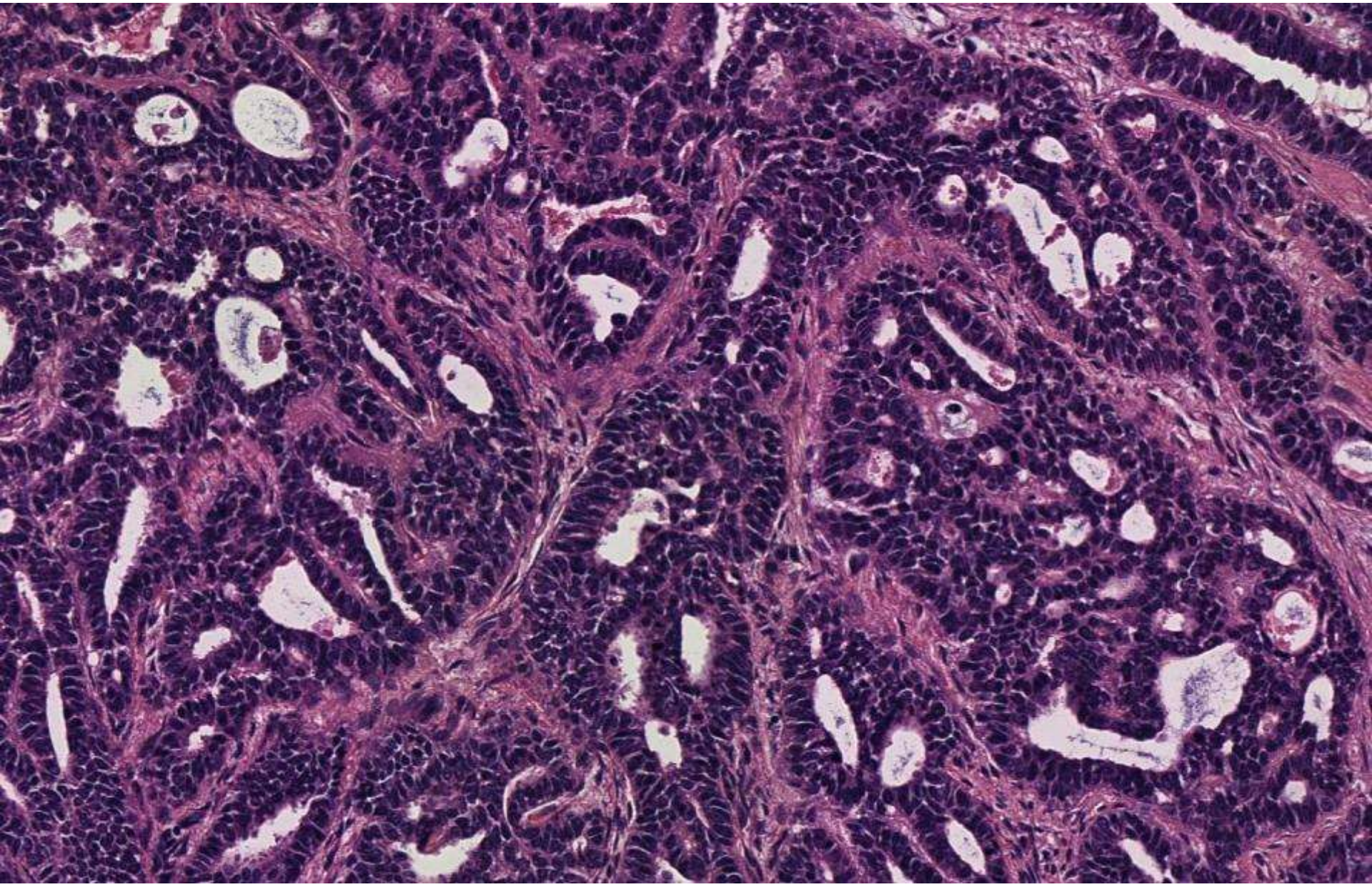
Ankur Sangoi, El Camino Hospital

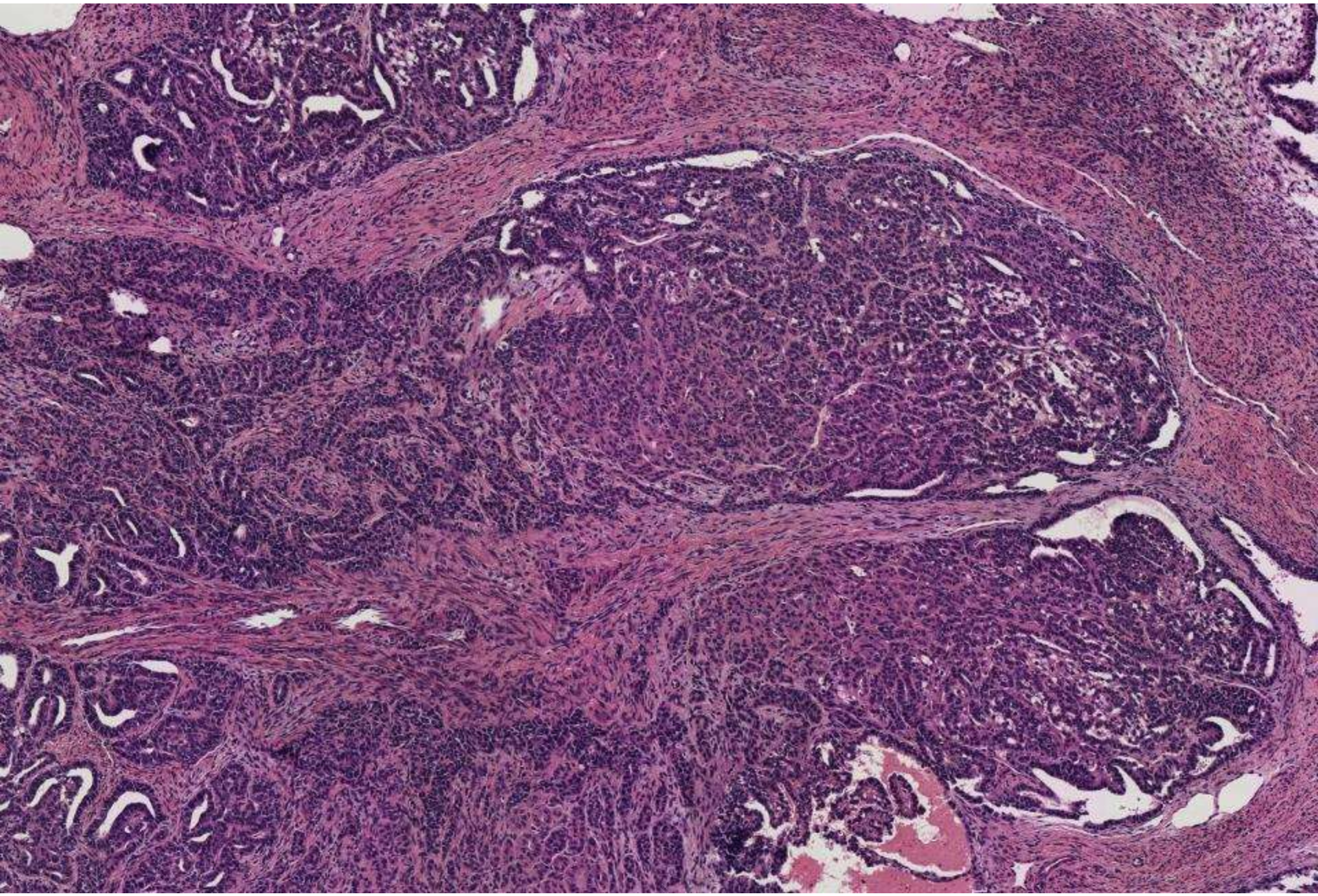
54-year-old woman with endometrial mass. TAH performed.

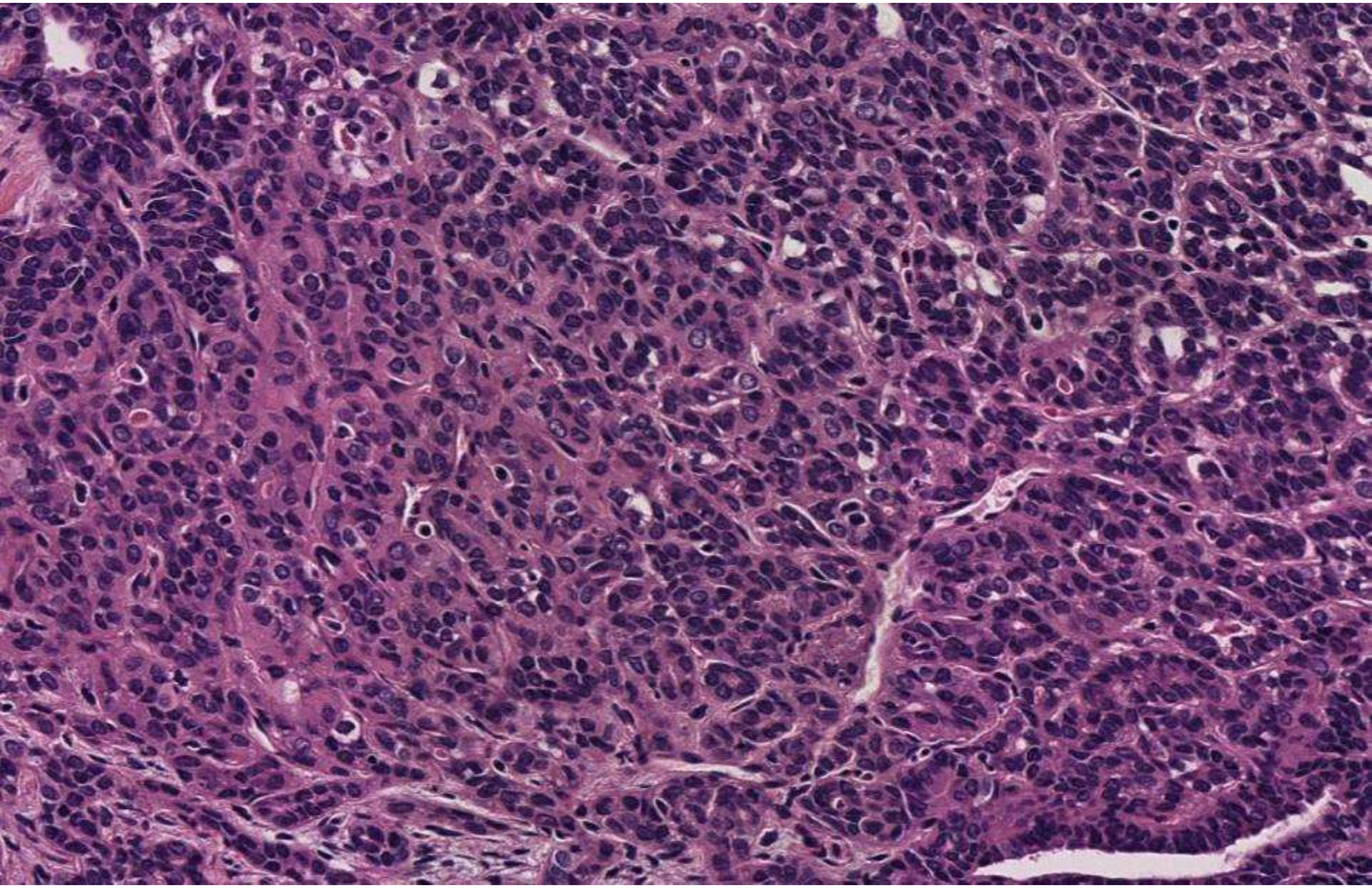


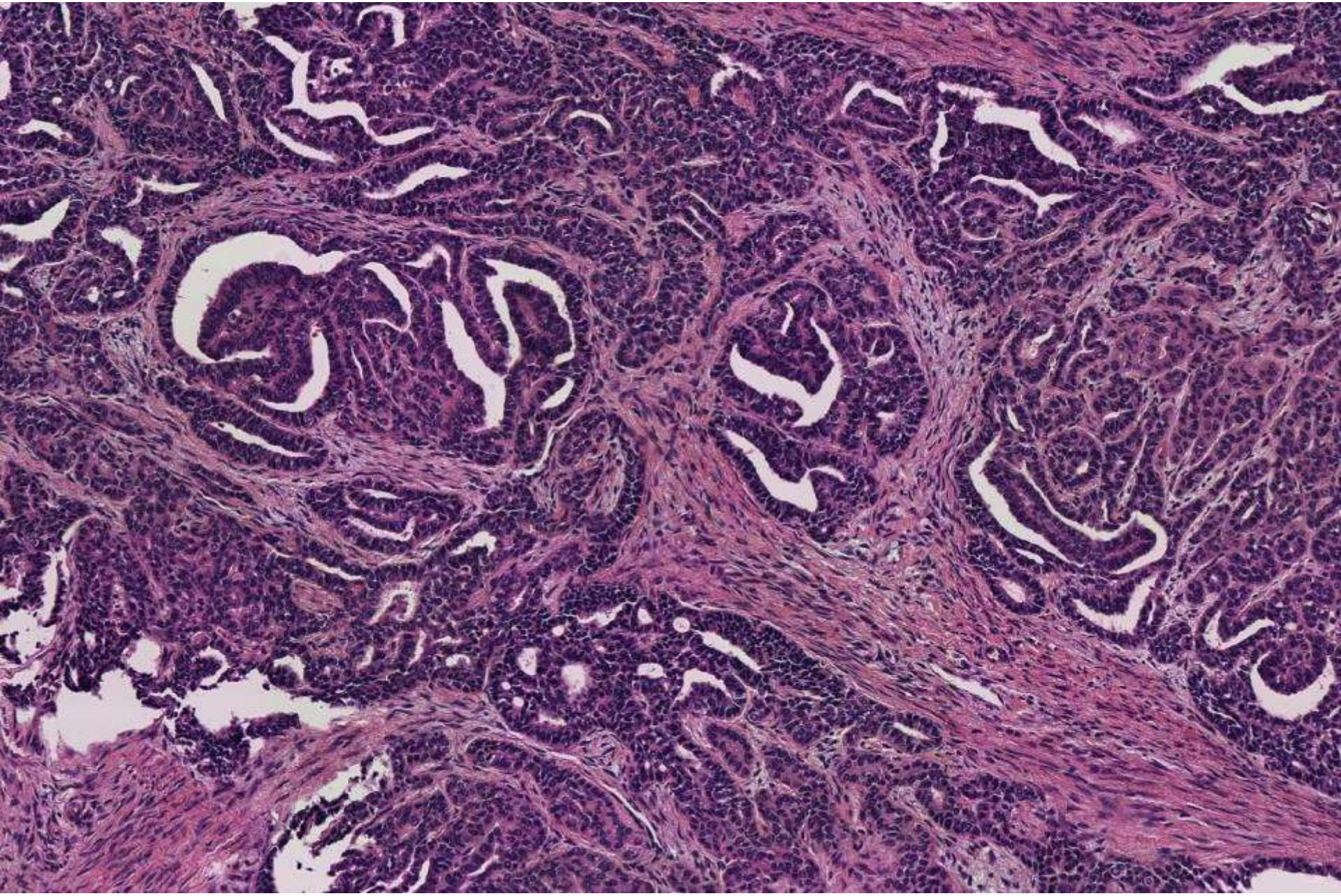


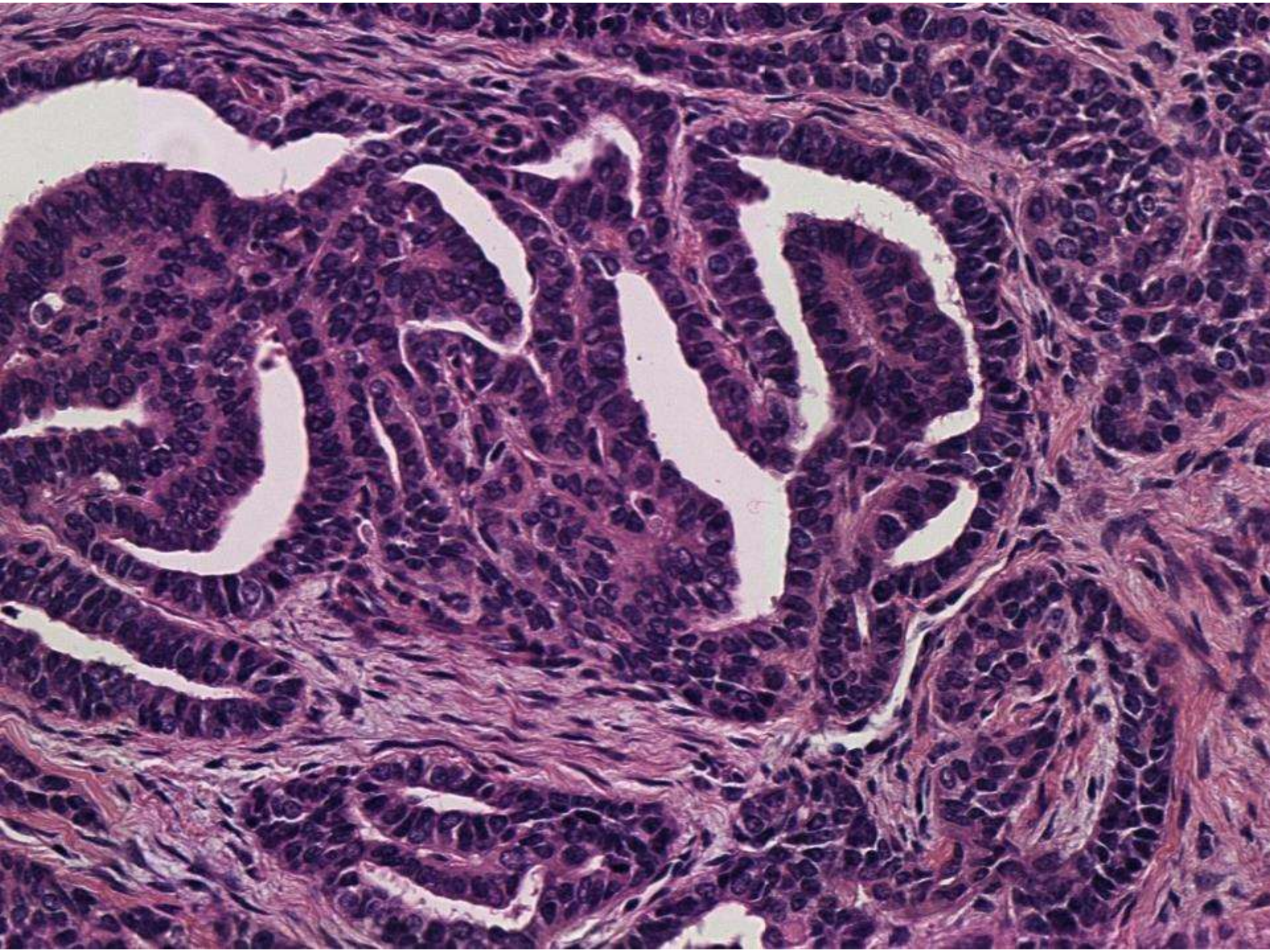


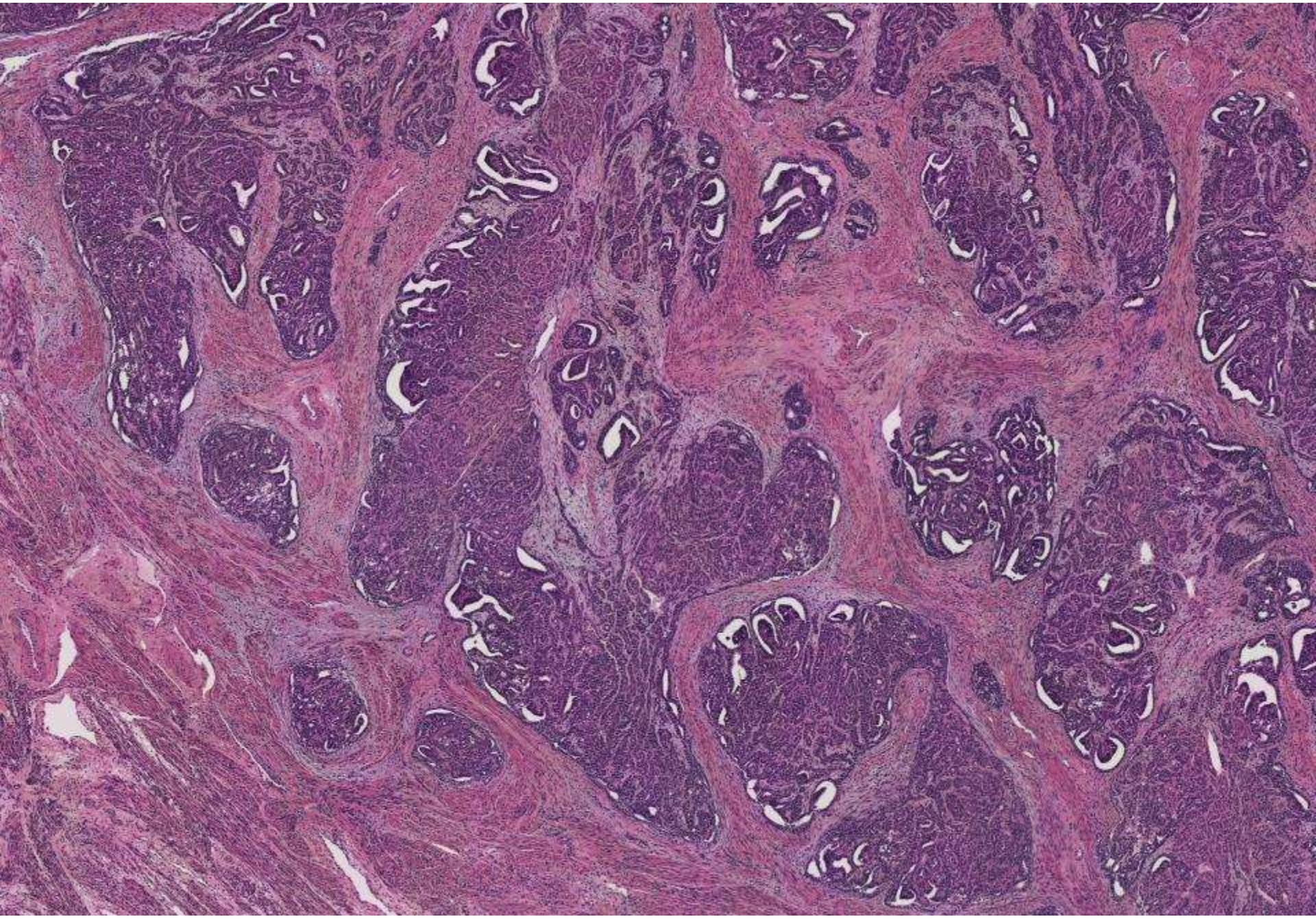


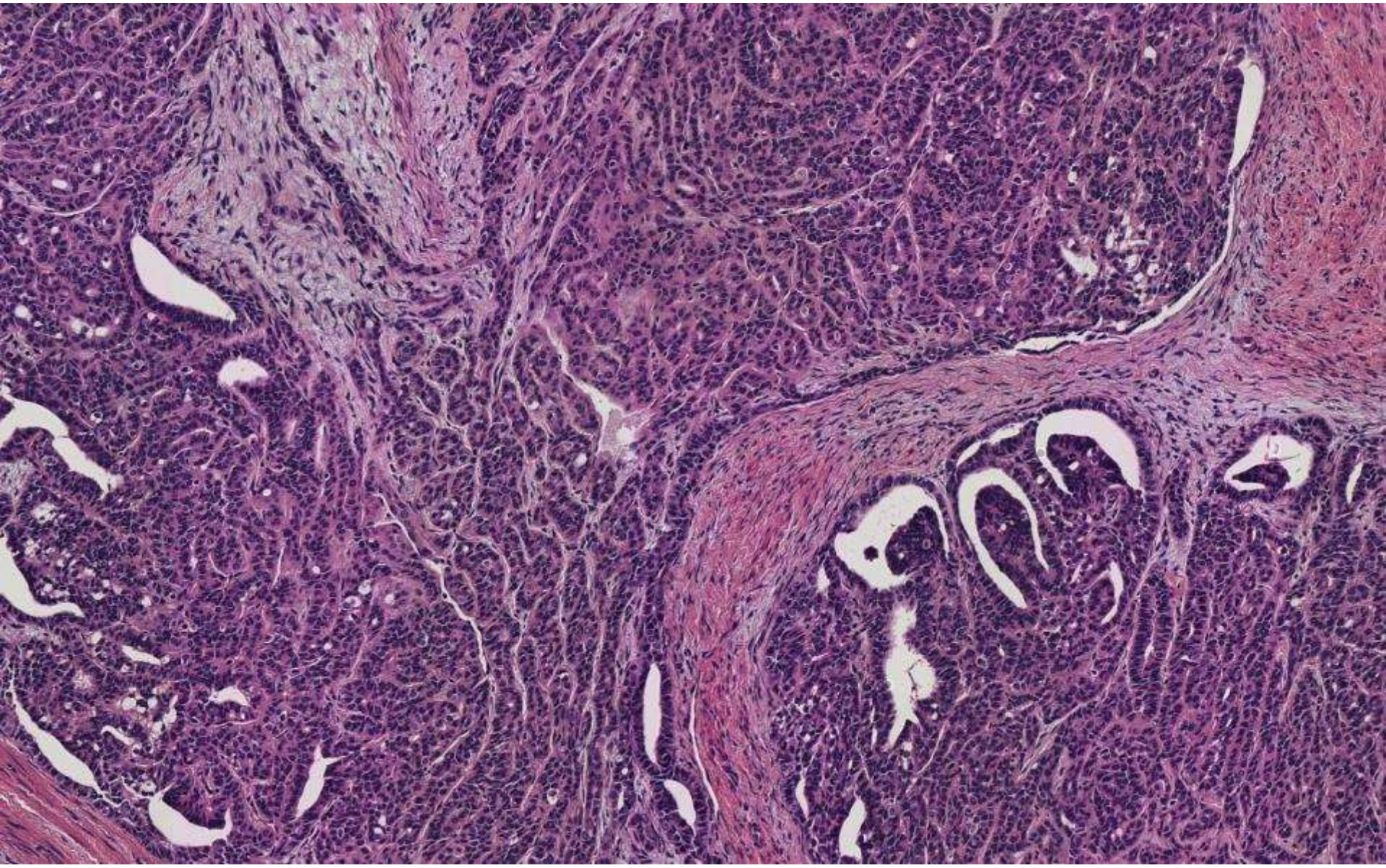


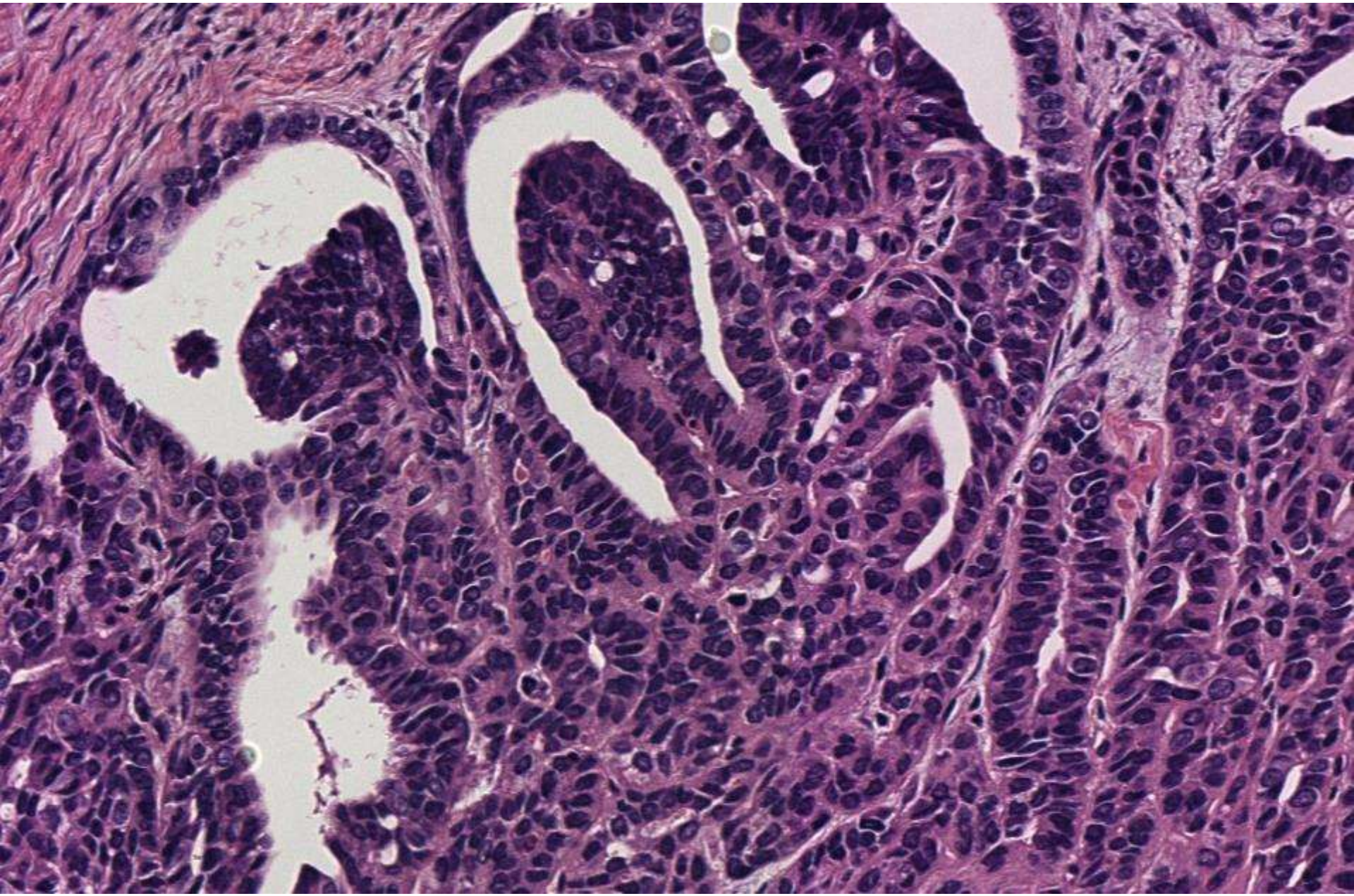


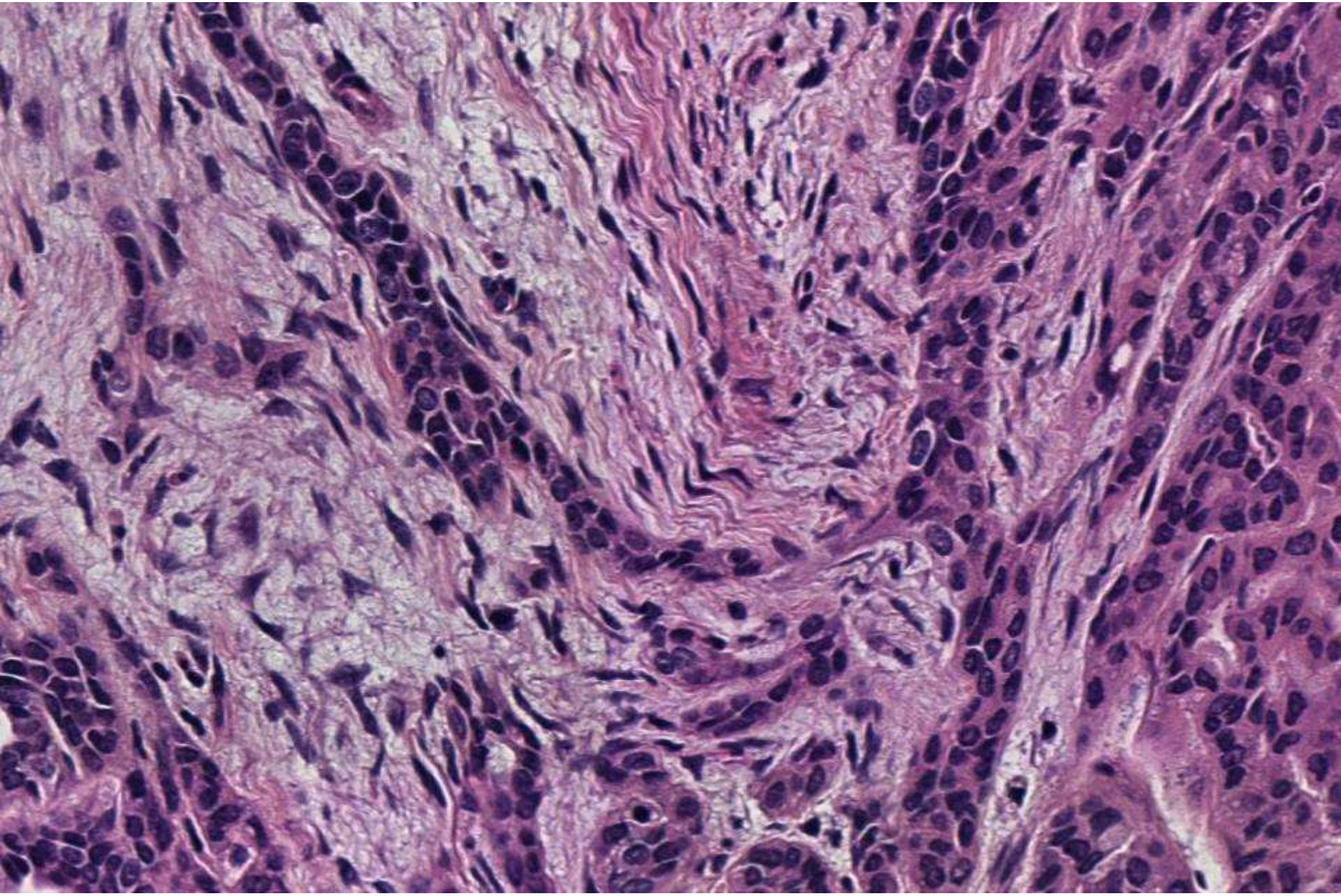






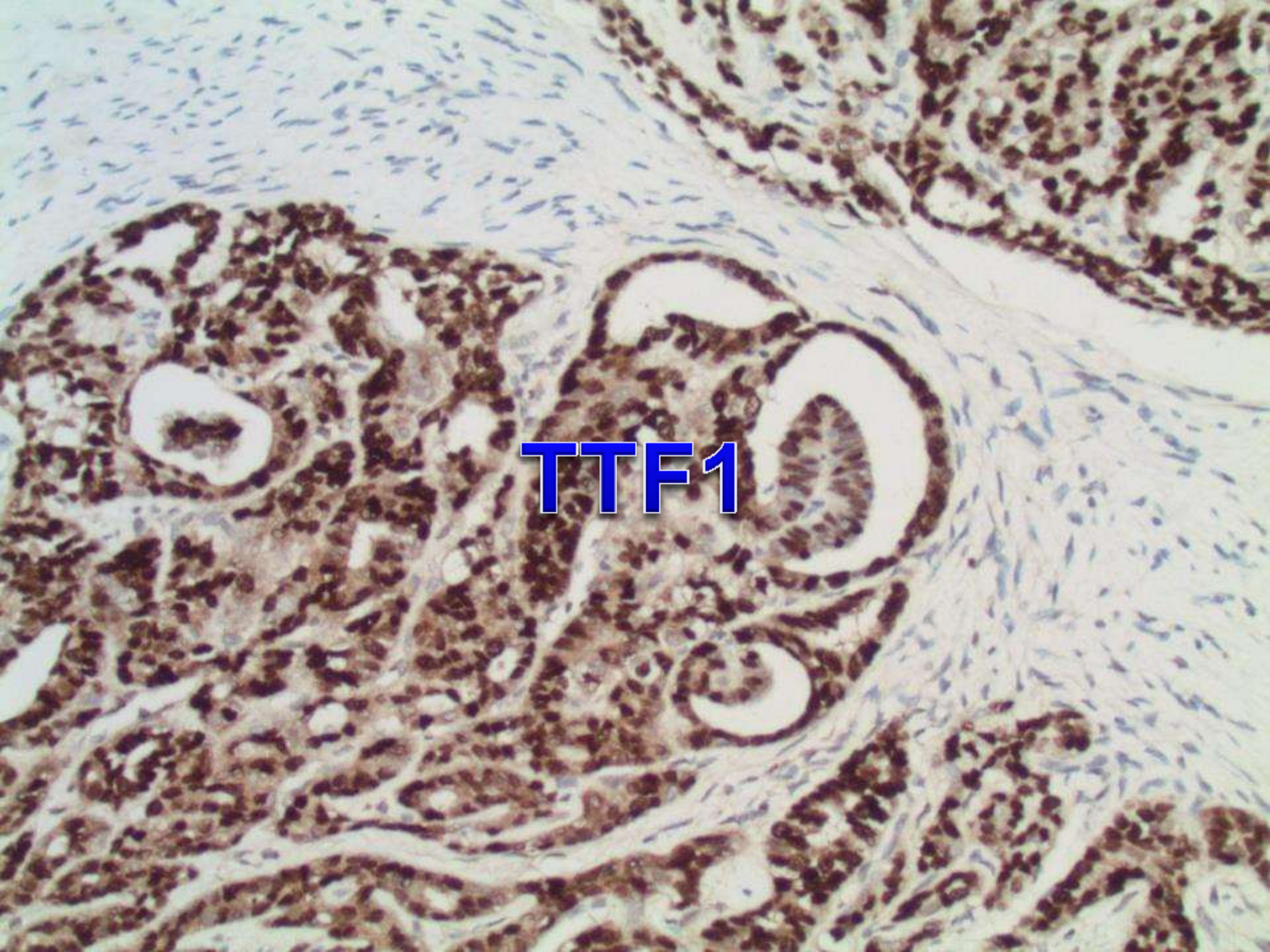


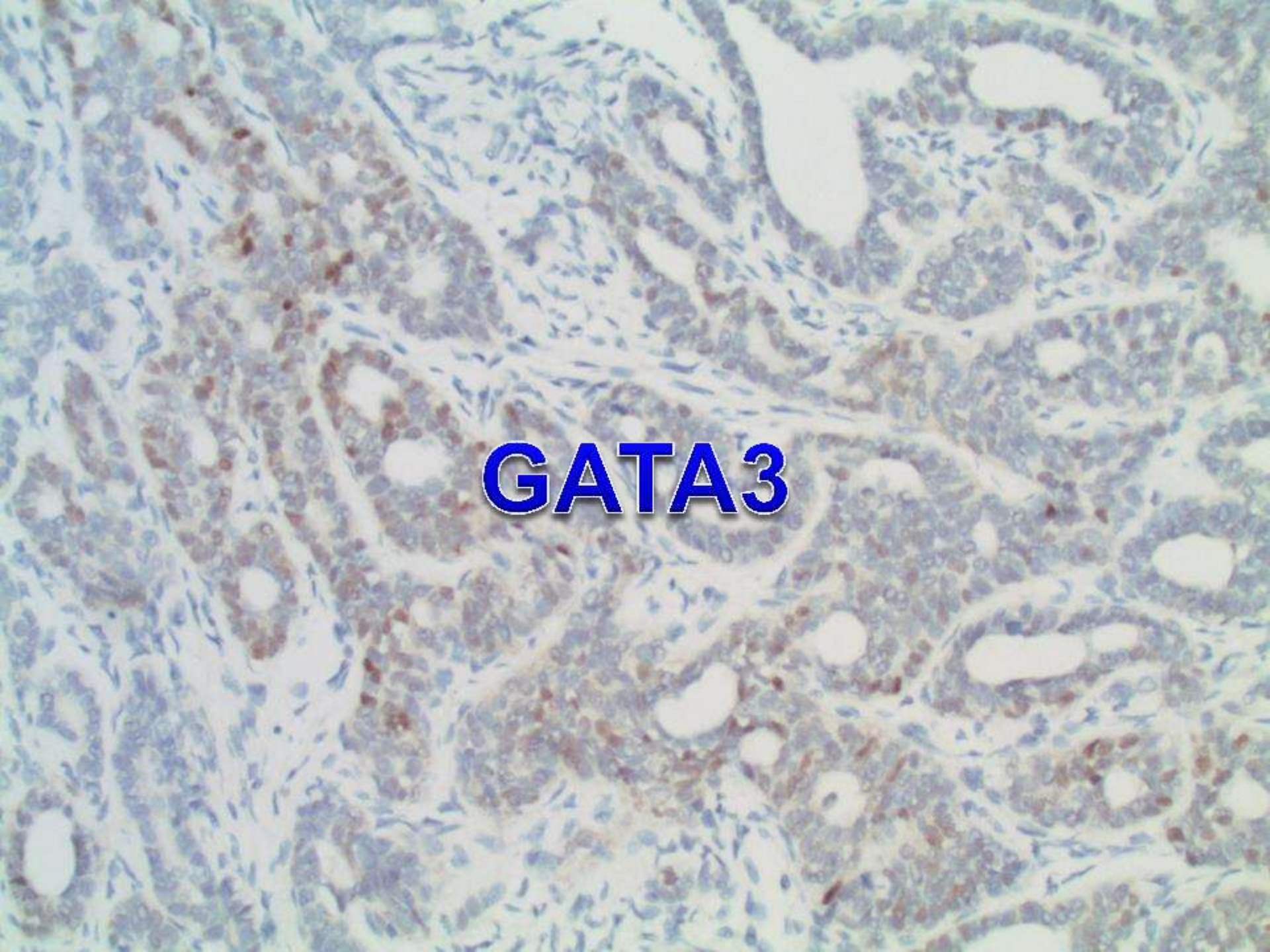


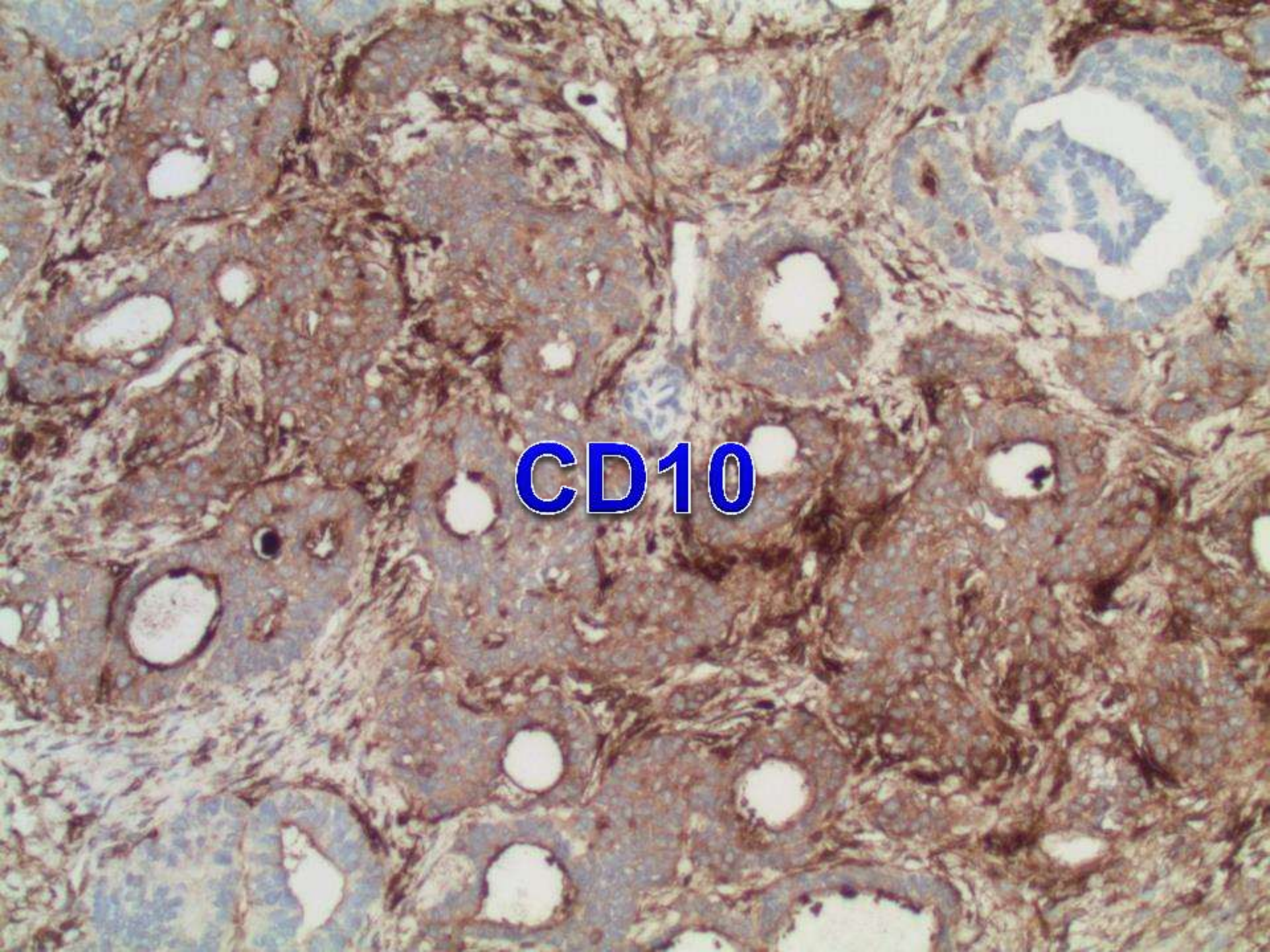


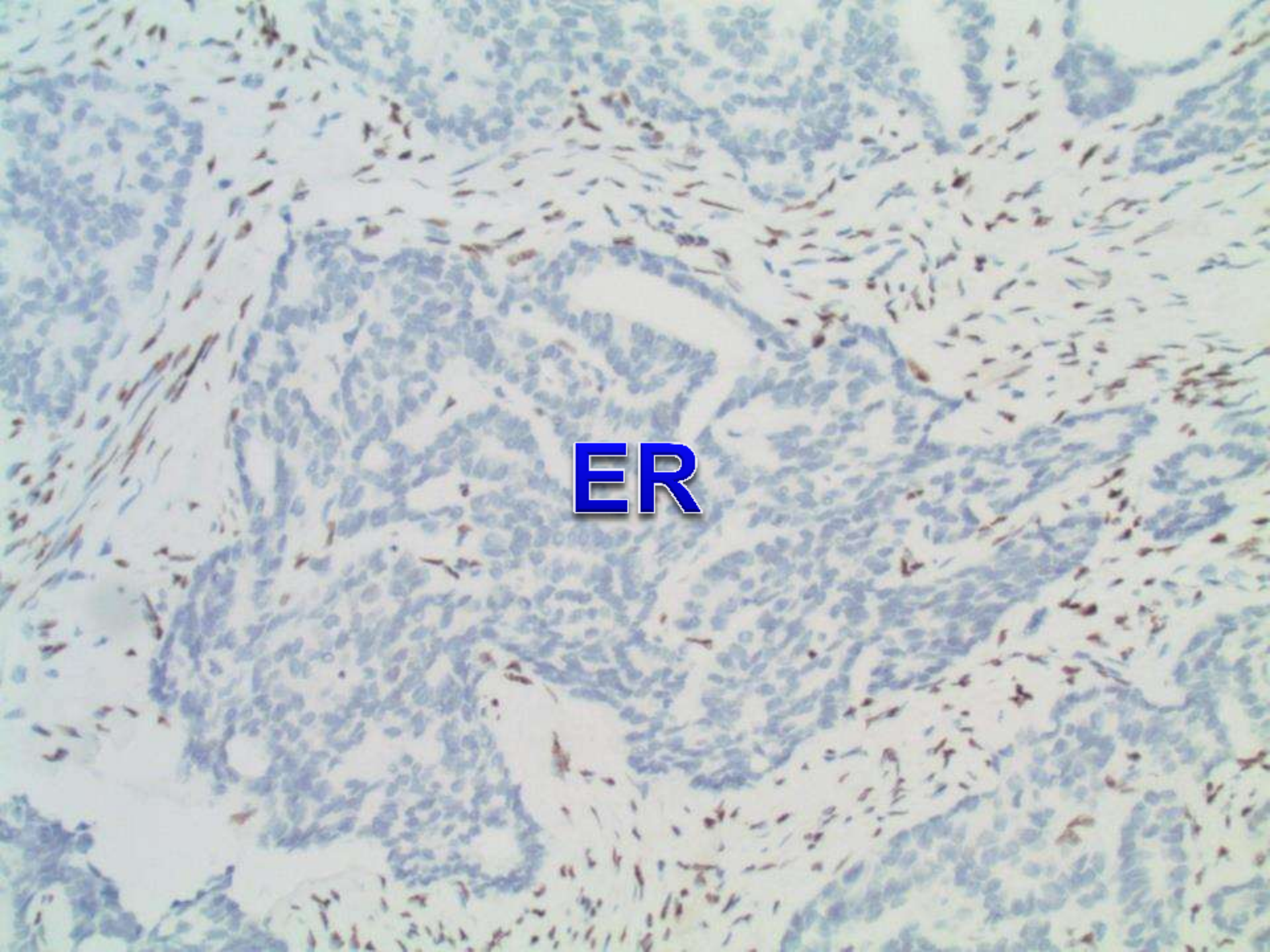
DDx

- **Mesonephric-like adenocarcinoma**
- **Endometrioid adenocarcinoma**
- **Uterine serous carcinoma**
- **Colonization/metastasis from:**
  - Tubo-ovarian serous carcinoma
  - endocervical adenocarcinoma
- **Distant metastatic adenocarcinoma**


TTF1


GATA3


CD10


ER

MSI by IHC intact
(no pics)

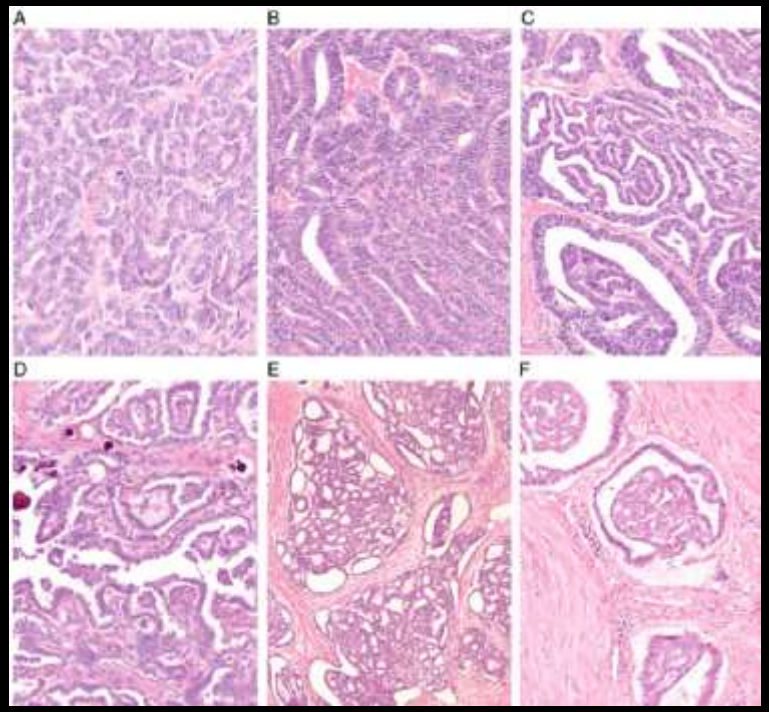
DIAGNOSIS

- **Mesonephric-like adenocarcinoma of the endometrium**
  - Location outside of cervix
  - No mesonephric remnants/hyperplasia
  - Mixed data on prognosis
    - Uterine nephrogenic adenocarcinoma may have more aggressive behavior than cervical mesonephric adenocarcinoma and endometrial endometrioid adenocarcinoma of similar grade

A Comparison of GATA3, TTF1, CD10, and Calretinin in Identifying Mesonephric and Mesonephric-like Carcinomas of the Gynecologic Tract

Jennifer Pors, MD, Angela Cheng, BSc,† Joyce M. Leo, MD,‡ Mary A. Kinloch, MD,§ Blake Gilks, MD,*† and Lynn Hoang, MD*†*

Am J Surg Pathol • Volume 42, Number 12, December 2018



Diagnosis	No. Cases	GATA3(+) TTF1(+)	GATA3(+) TTF1(−)	GATA3(−) TTF1(+)	GATA3(−) TTF1(−)
Uterine carcinomas					
Endometrioid carcinoma, FIGO grade 1-2	193	0	1 (0.5)	1 (0.5)	191 (99)
Endometrioid carcinoma, FIGO grade 3	130	0	5 (4)	2 (2)	123 (94)
Serous carcinoma	95	0	4 (4)	1 (1)	90 (95)
Clear cell carcinoma	30	1 (3)	1 (3)	0	28 (94)
Carcinosarcoma	113	1 (0.9)	22 (19)	0	90 (80)
Mixed carcinoma	12	0	0	0	12 (100)
Other*	12	0	0	0	12 (100)
Cervical adenocarcinomas†					
HPVA—usual type	63	0	6 (10)	0	57 (90)
HPVA—villoglandular	5	0	0	0	5 (100)
HPVA—mucinous, NOS	17	0	0	0	17 (100)
HPVA—mucinous, intestinal type	3	0	0	0	3 (100)
HPVA—mucinous, signet ring cell type	0	0	0	0	0
HPVA—invasive SMILE	1	0	0	0	1 (100)
NHPVA—gastric type	4	0	0	0	4 (100)
NHPVA—minimal deviation adenocarcinoma	3	0	0	0	3 (100)
All mesonephric (uterine and cervical)‡	11	5 (45)	6 (55)	0	0
Total	692	7 (1)	45 (7)	4 (<1)	636 (92)

TABLE 4. Comparison of GATA3, TTF1, CD10, and Calretinin Performance in Distinguish Mesonephric Carcinomas From Other Endometrial and Endocervical Adenocarcinomas*

	GATA3 (%)	TTF1 (%)	CD10 (%)	Calretinin (%)
Sensitivity	91	45	73	36
Specificity	94	99	83	89

*Excludes mesonephric carcinomas occurring in the vagina and ovary.

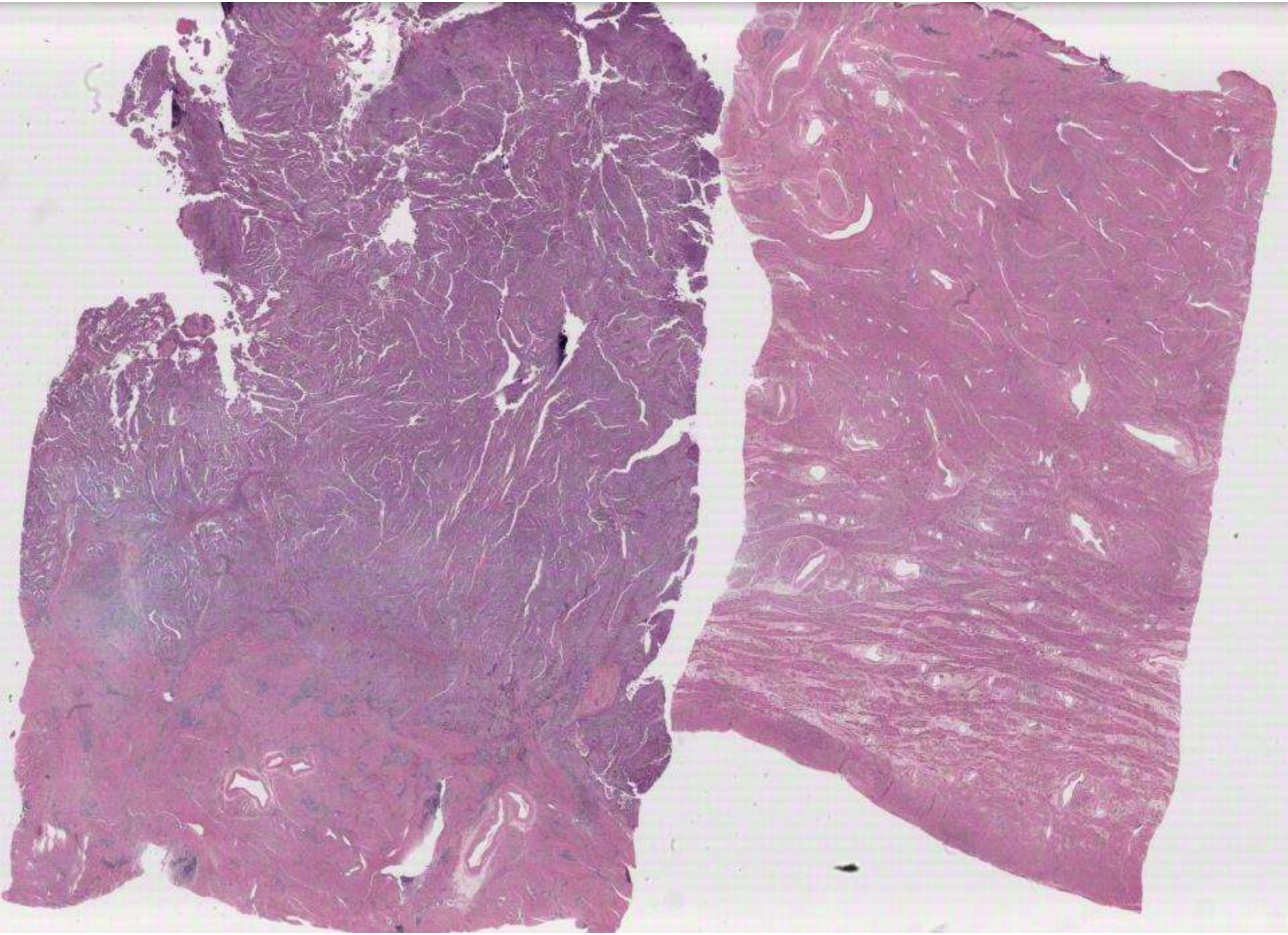
Caveats

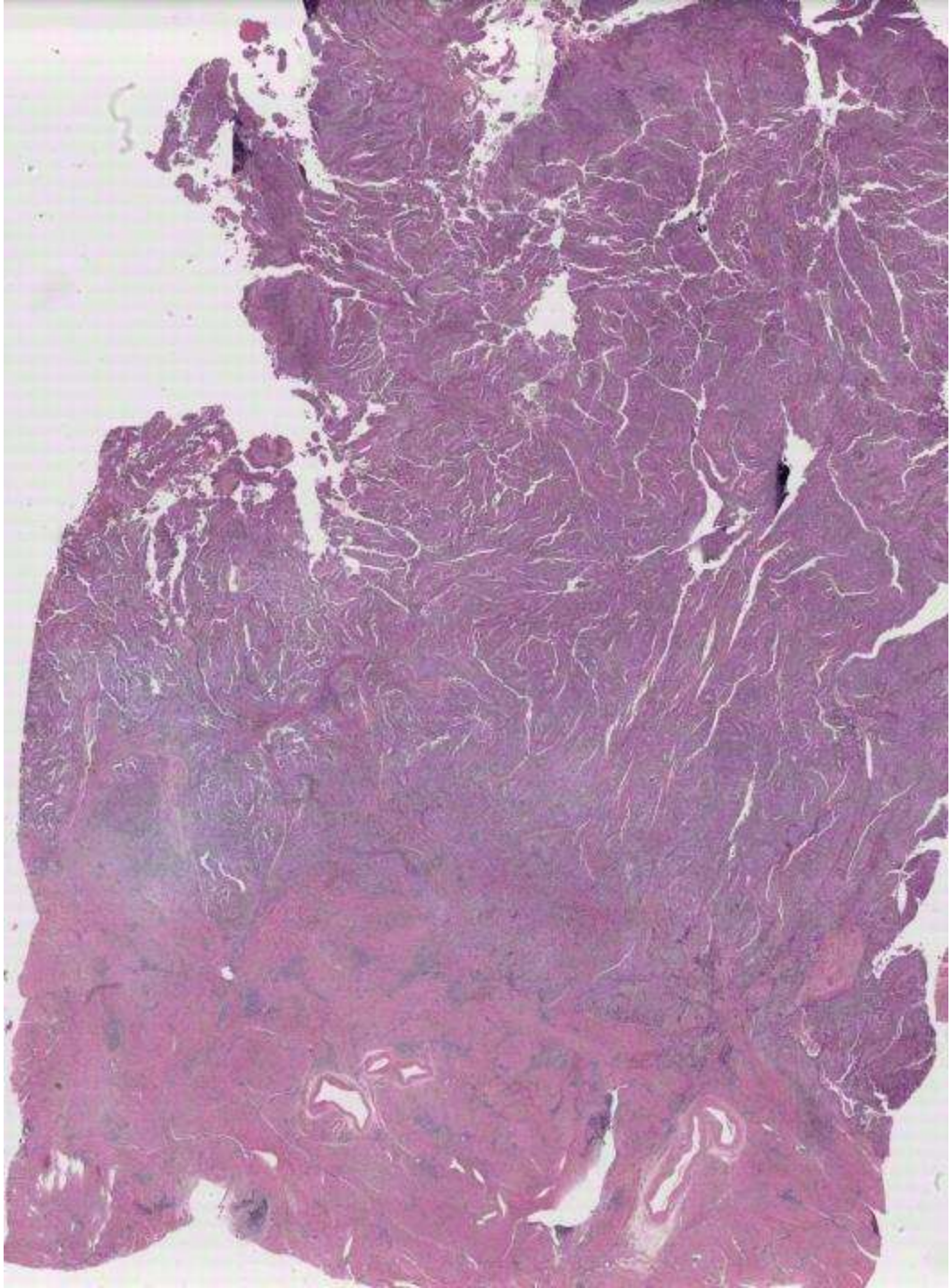
- **GATA3 can be + in Mullerian type carcinosarcomas**
  - Either carcinoma/sarcoma component
  - Usually weak
- **Often inverse staining with GATA3 & TTF1**
  - USE BOTH!

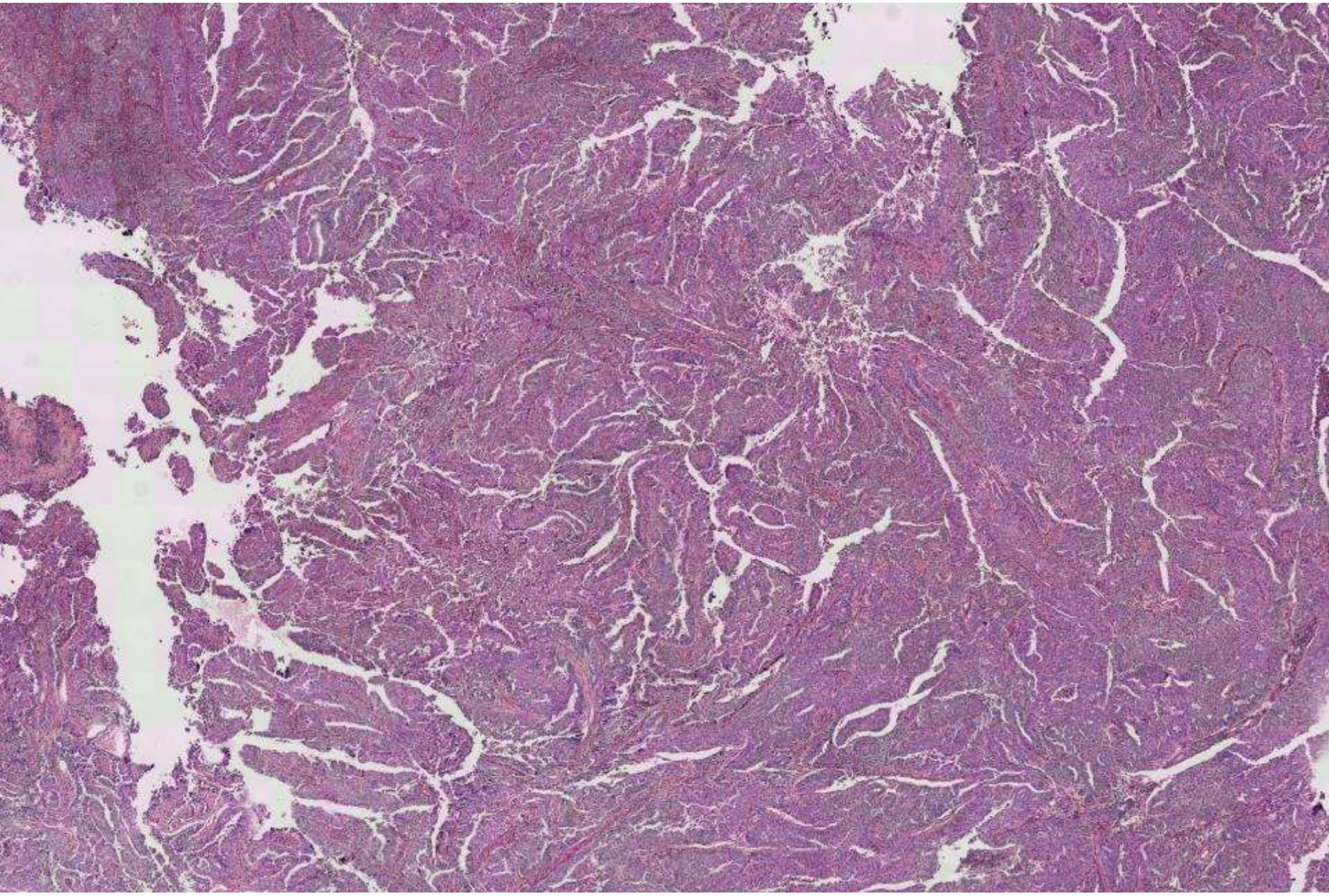
19-0803
(scanned slide available)

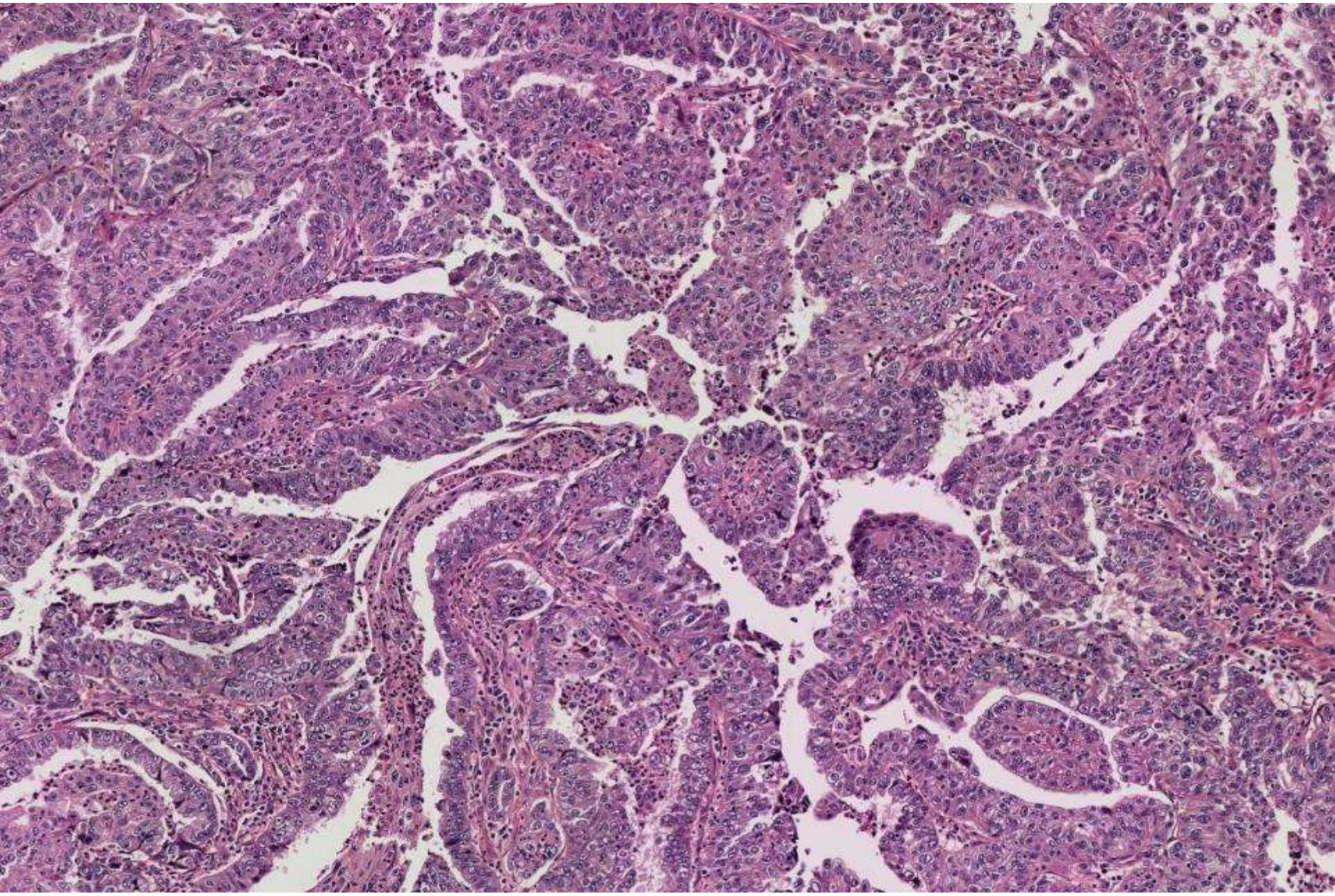
Ankur Sangoi, El Camino Hospital

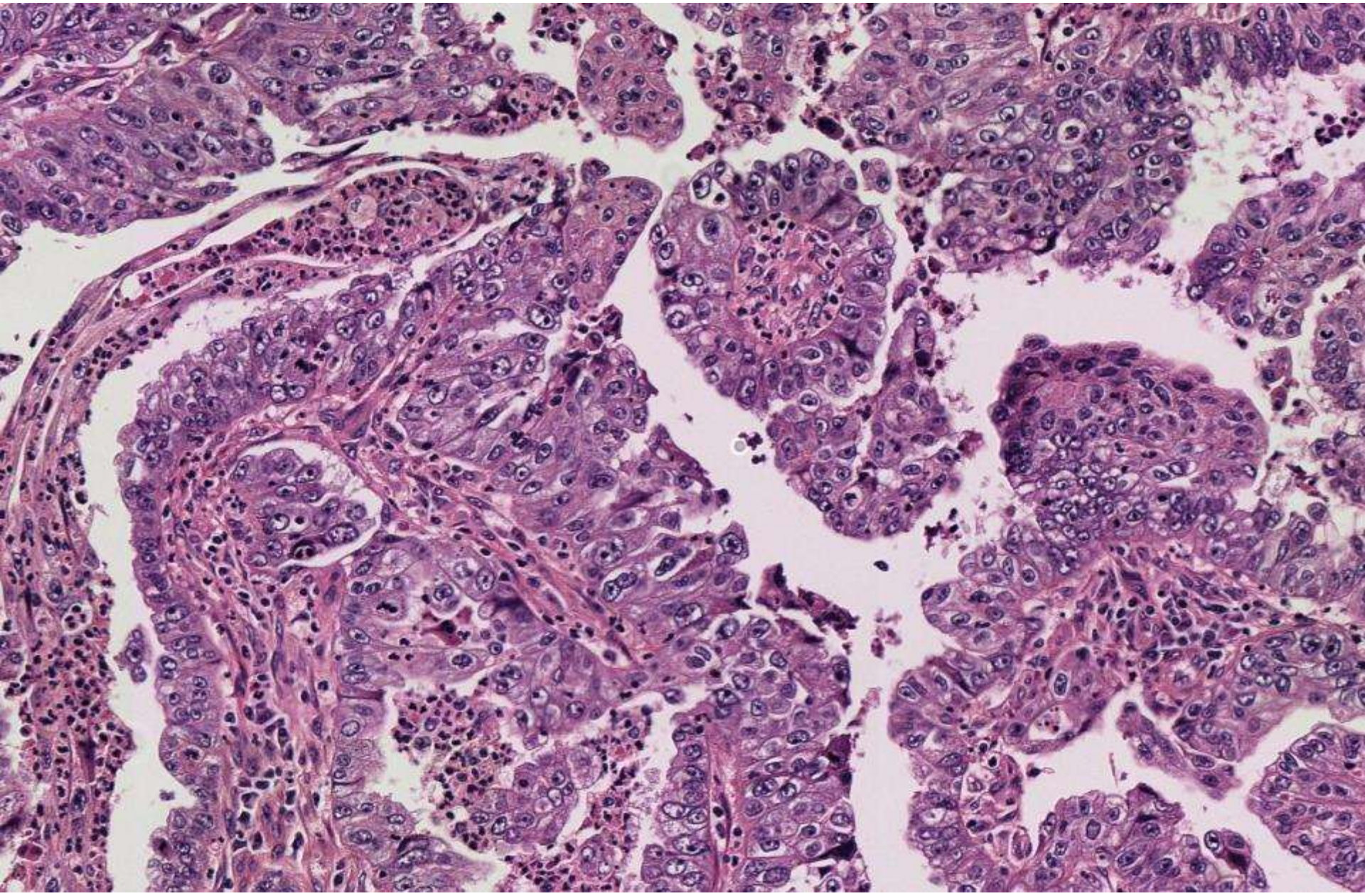
(Different!) 54-year-old woman with endometrial mass. TAH performed.

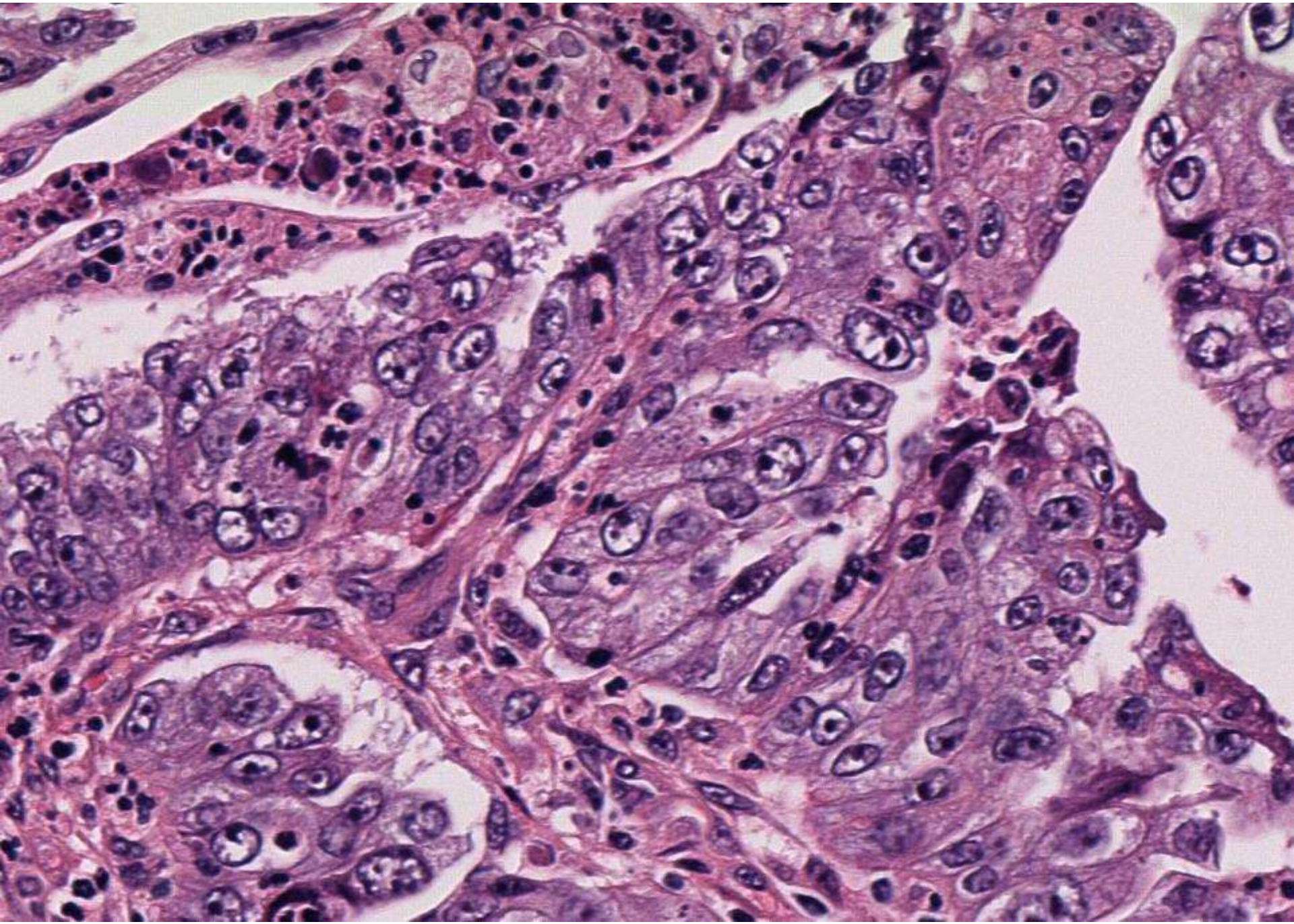


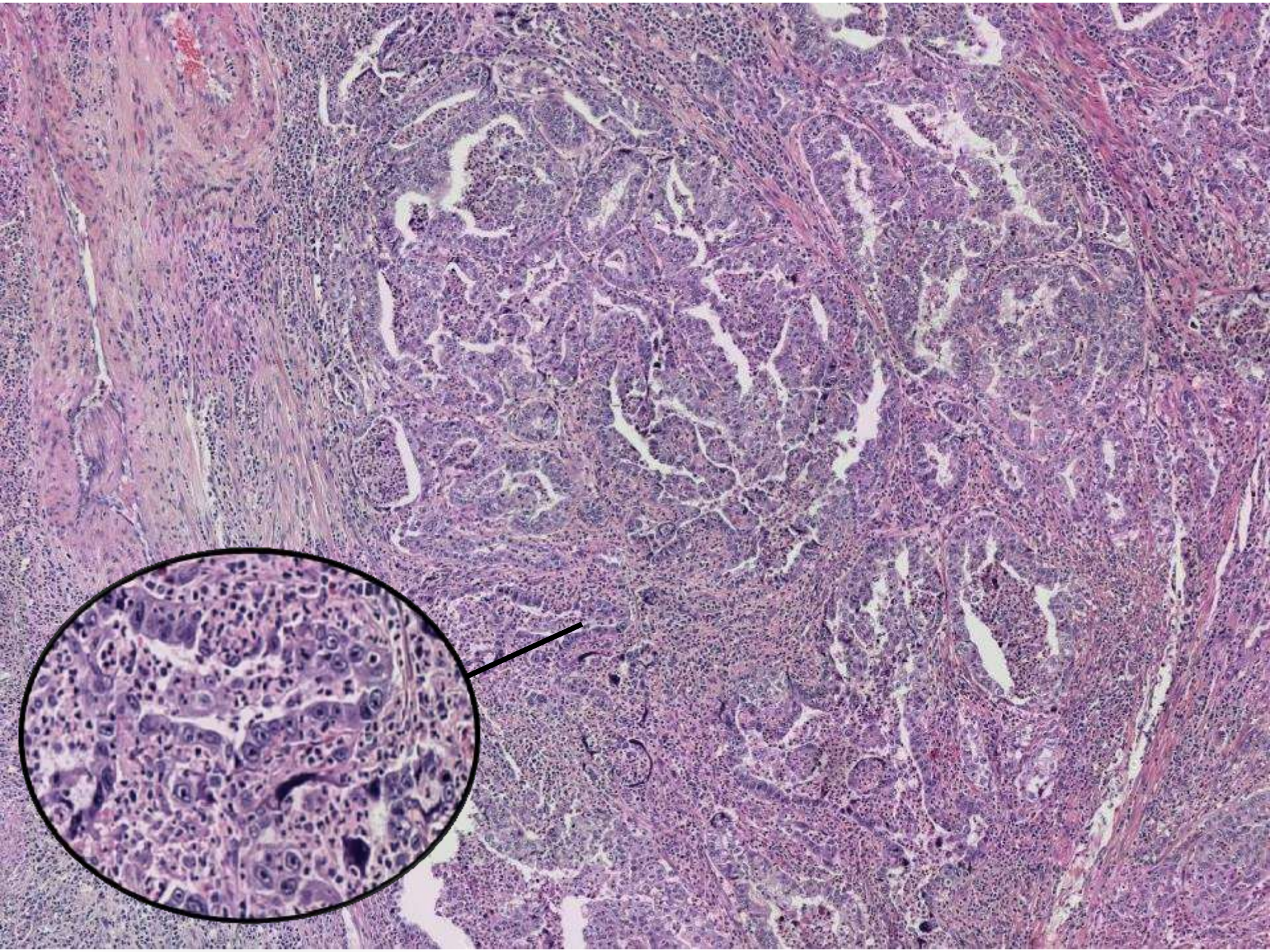


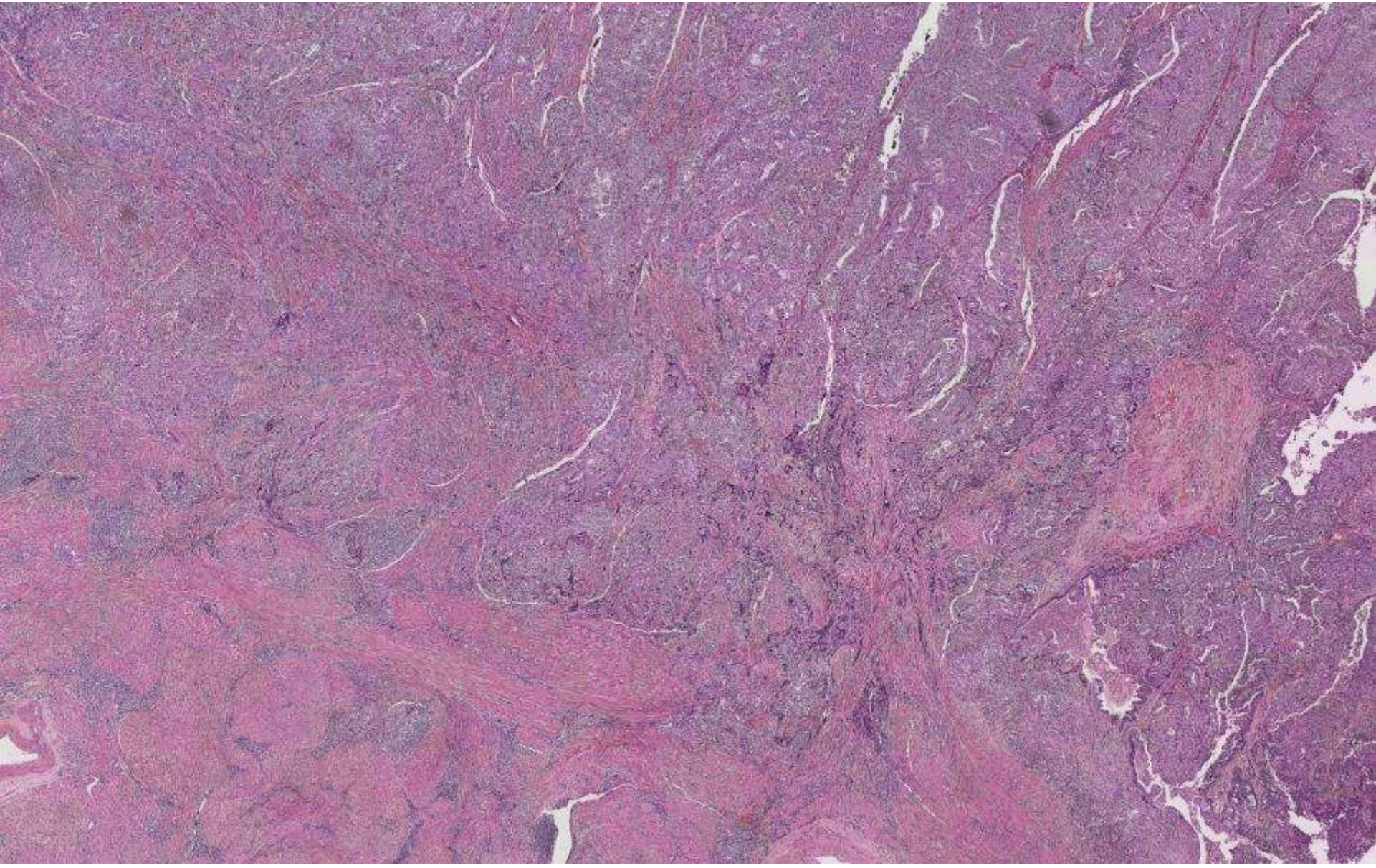


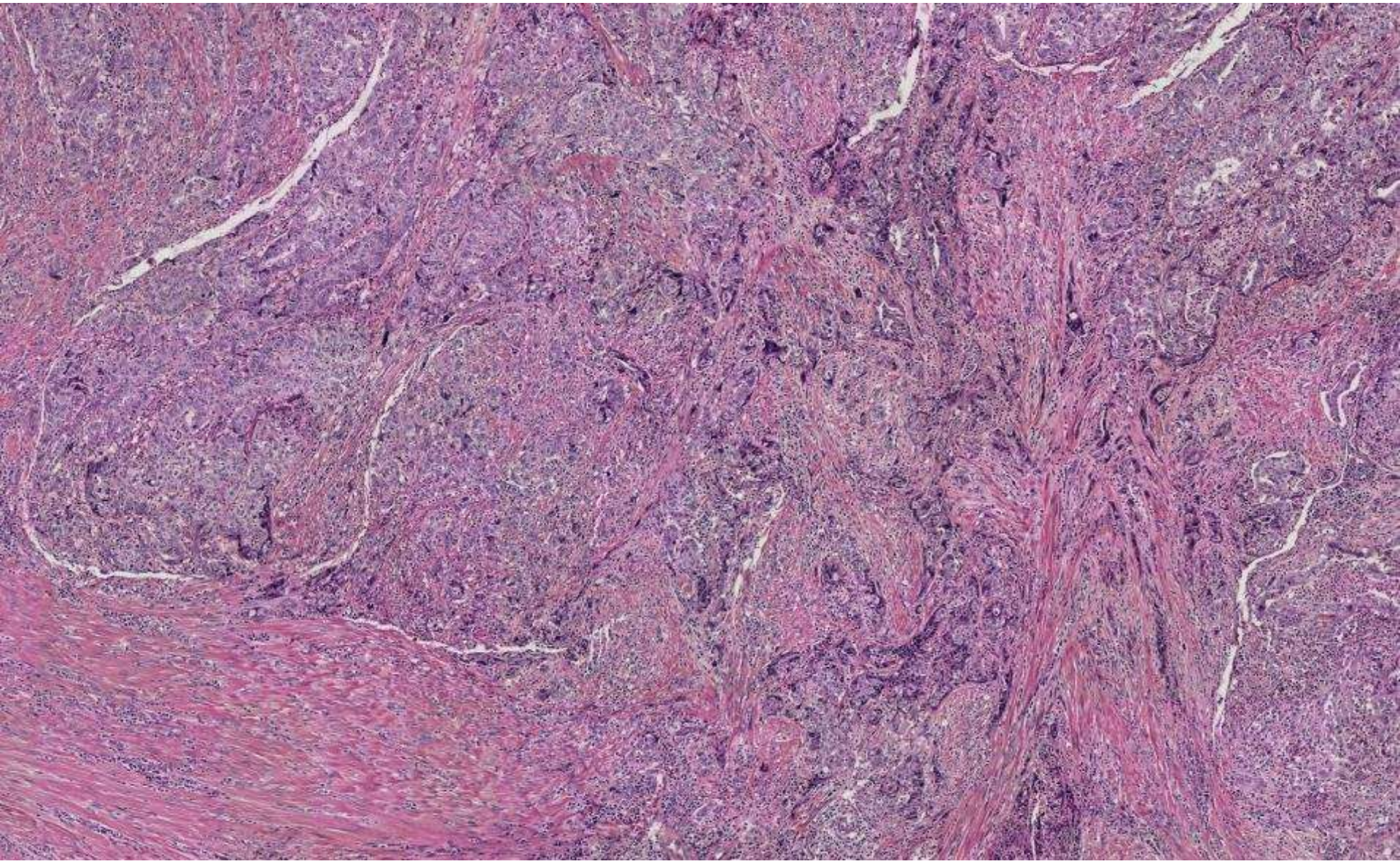


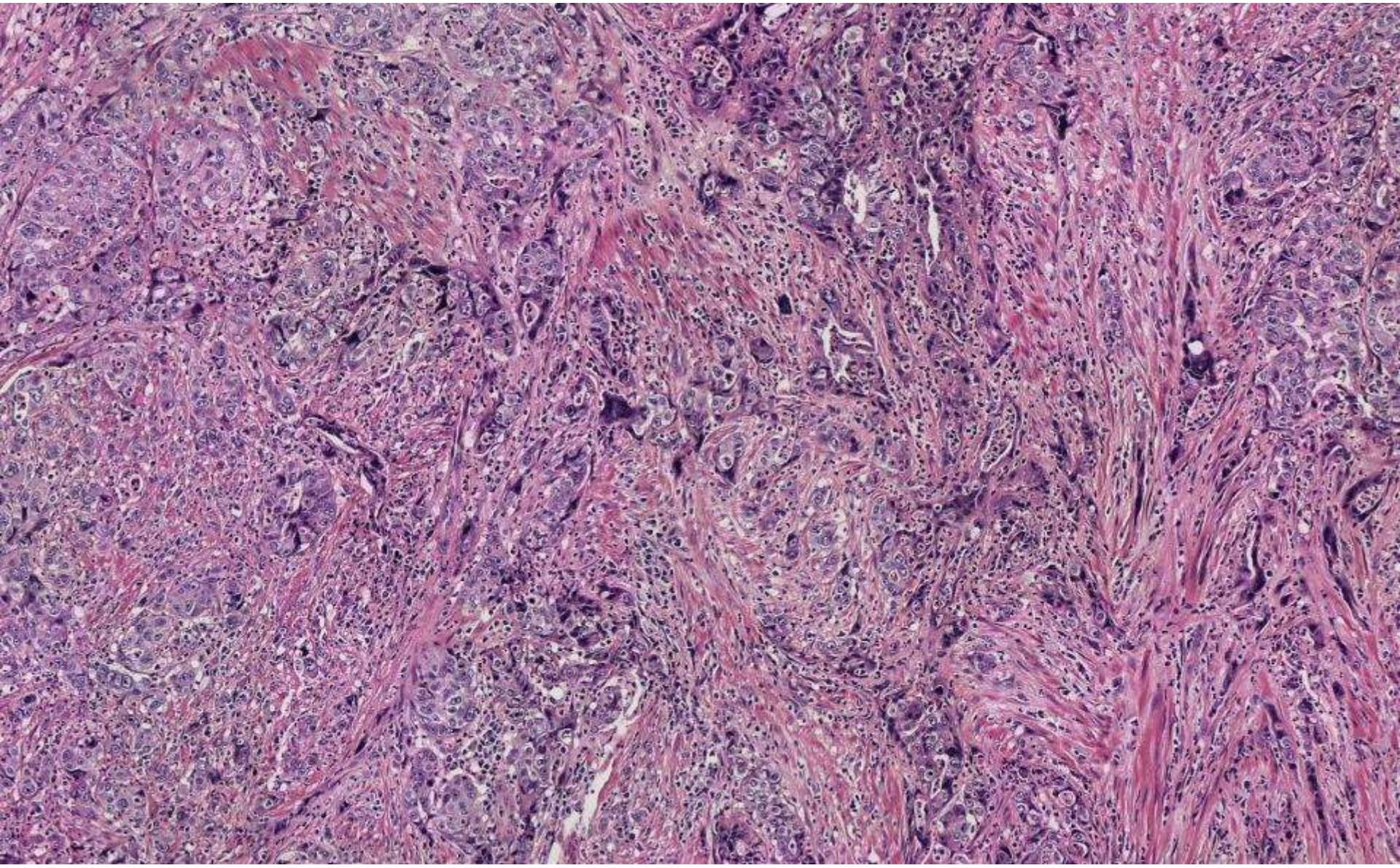


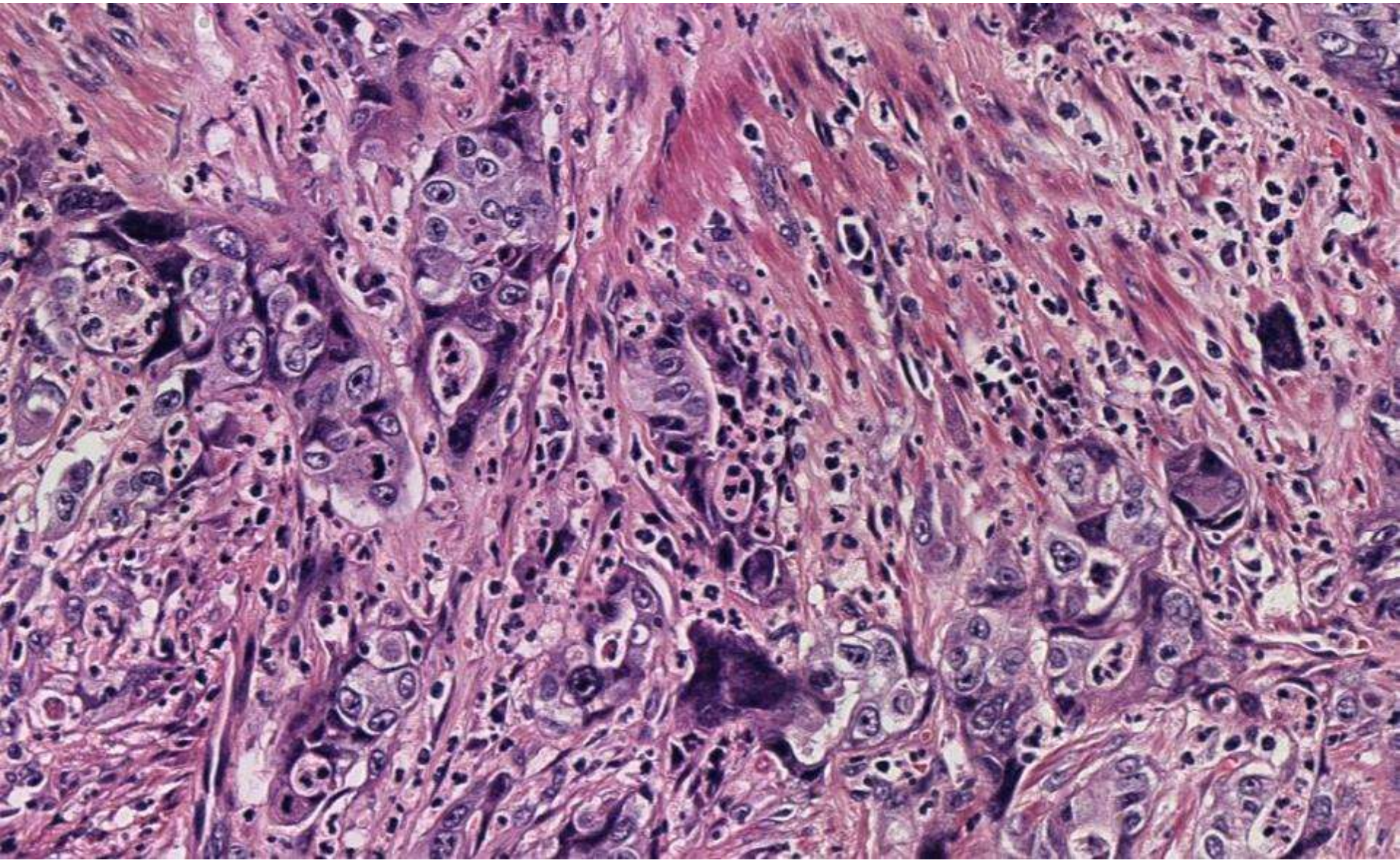


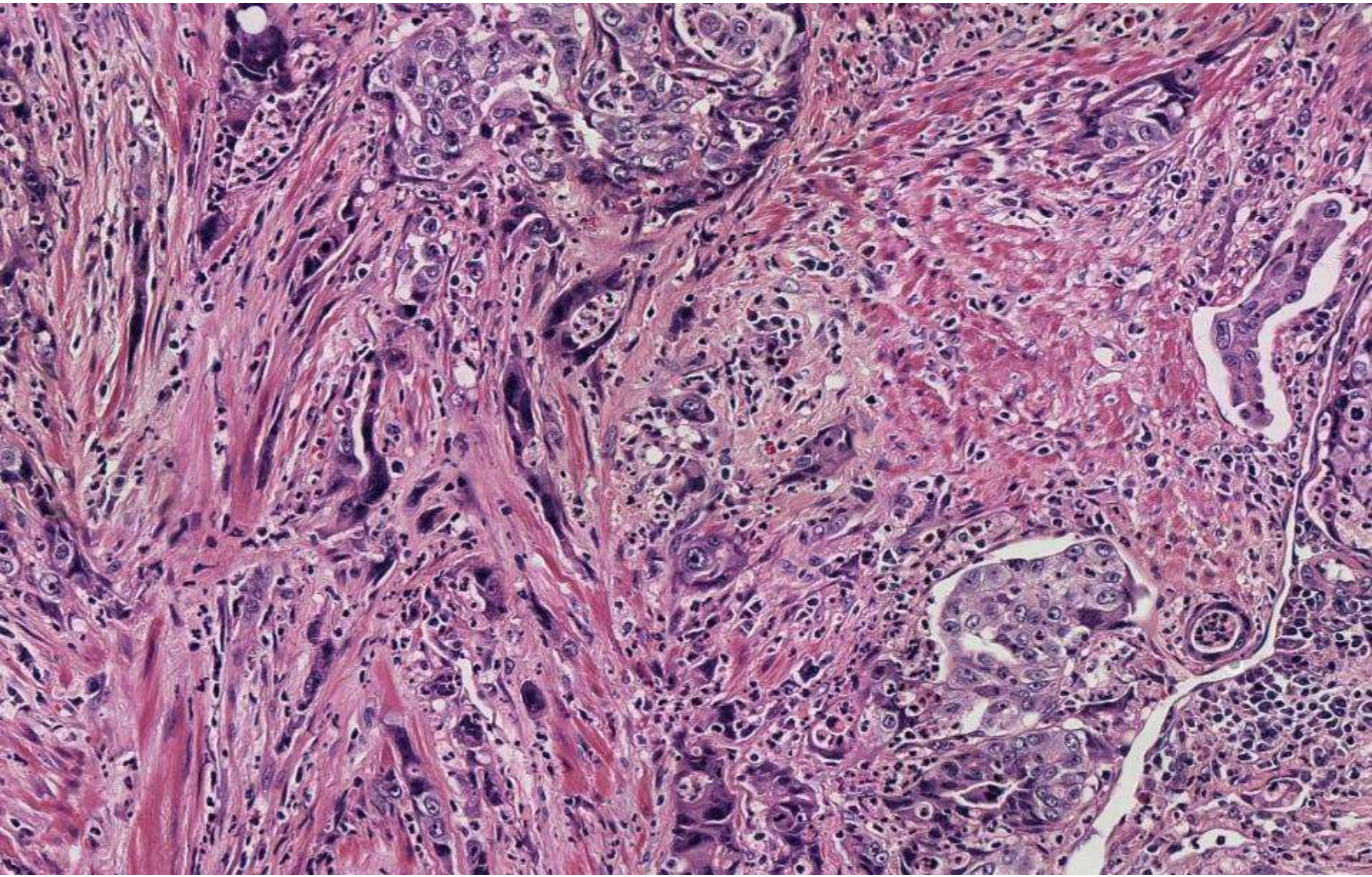












DDx

- **High grade endometrioid adenocarcinoma**
- **Uterine serous carcinoma**
- **Mesonephric-like adenocarcinoma**
- **Colonization/metastasis from:**
  - Tubo-ovarian serous carcinoma
  - endocervical adenocarcinoma

IHC summary

p53 wild type

ER, PR, NapsinA, HNF1b, p16 negative

ARID1a, PTEN, MSI retained/normal

HMGA2 patchy/weak

Molecular send out testing

- **Positive for POLE mutation**

- **FINAL DIAGNOSIS:**
  - High grade endometrioid adenocarcinoma with POLE mutation
  - Stage IA

Review Article

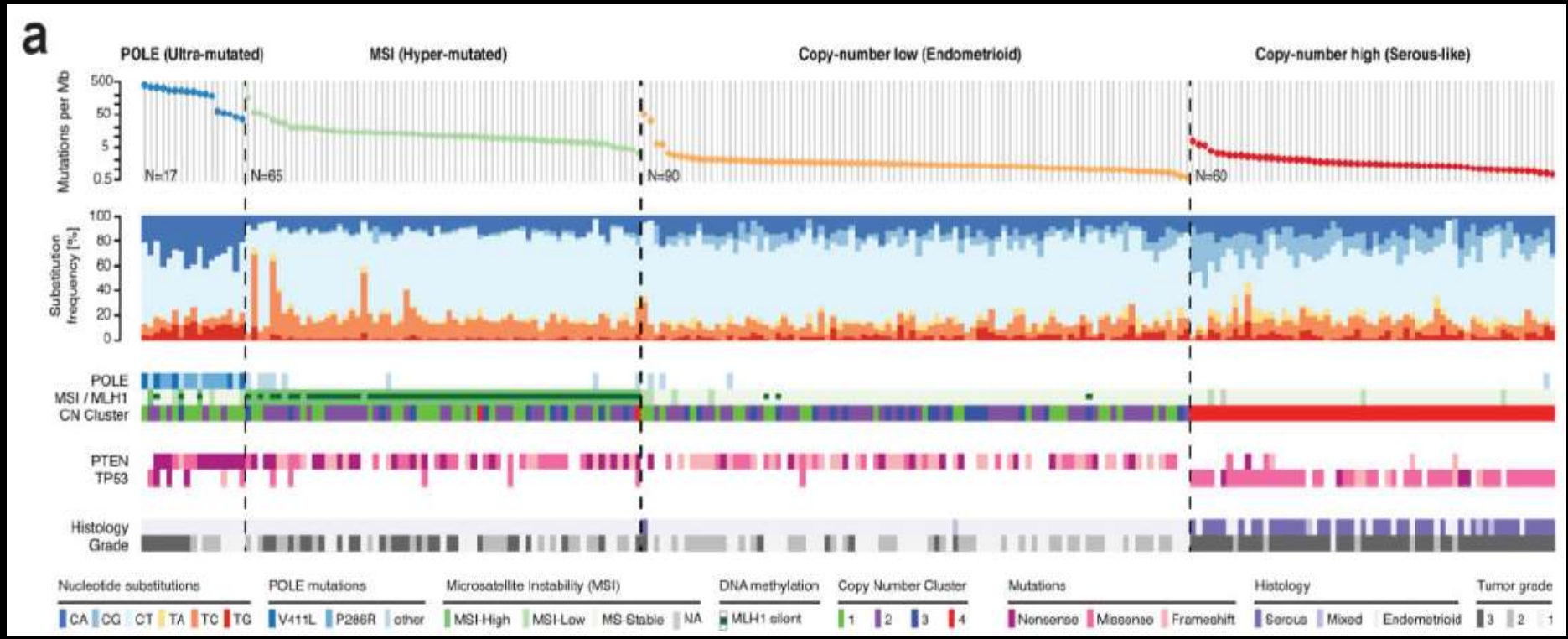
Endometrial Cancer: Not Your Grandmother's Cancer

Jessica N. McAlpine, MD[1]; Sarah M. Temkin, MD[2]; and Helen J. Mackay, MBChB, MD, MRCP[3]

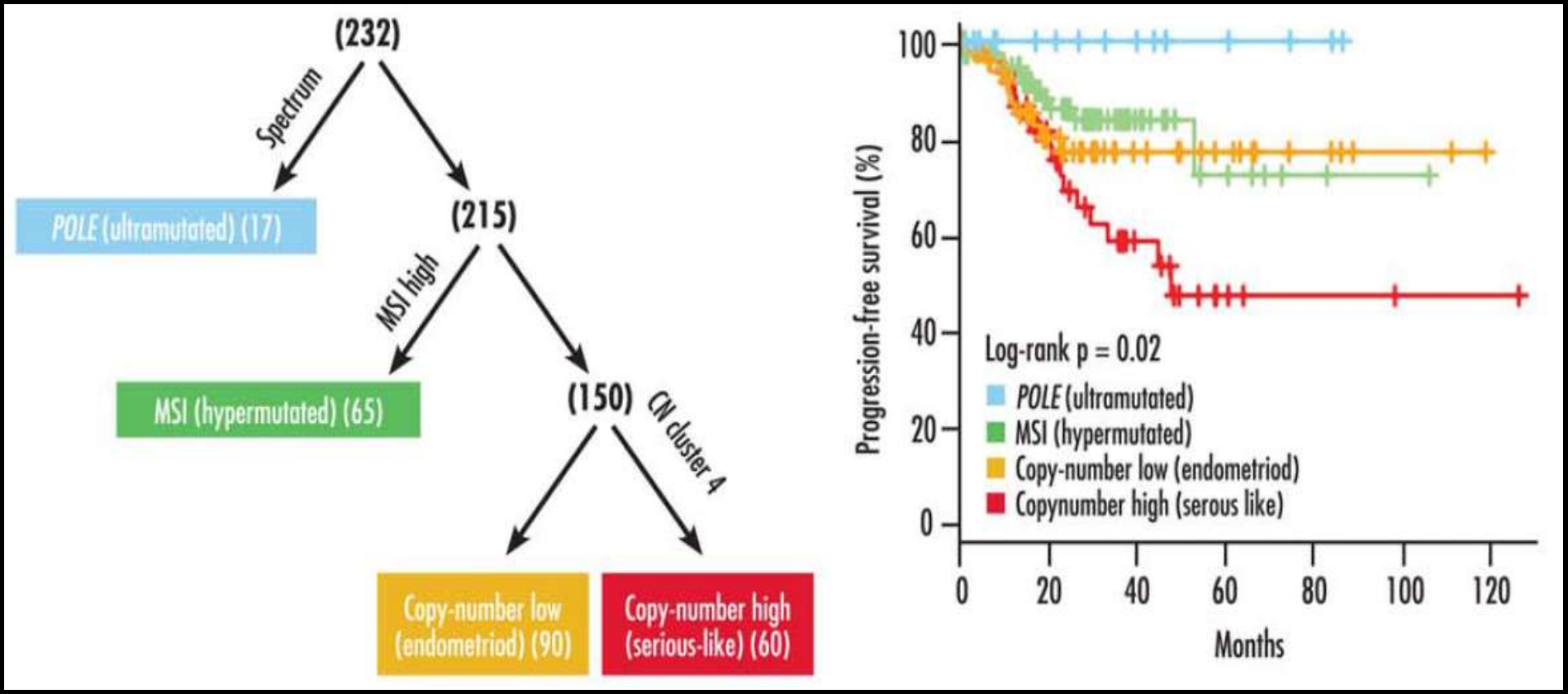
TABLE 1. Milestones in the Treatment of Endometrial Cancer

Year	Advance	Reference(s)
1961	Progesterone suggested to successfully treat EC	Kelley & Baker 1961[96]
1976	Unopposed estrogen linked to increasing EC rates	Gordon 1977[97]
1979	Doxorubicin with demonstrated activity in EC	Thigpen 1979[98]
1980	Pelvic radiotherapy shown to decrease pelvic recurrences without changing survival	Aalders 1980[99]
1983	Type I and type II EC defined	Bokhman 1983[49]
1987	GOG-33 establishes that grade, depth of myometrial invasion, and vascular invasion are correlated to metastasis	Creasman 1987[100]
1988	FIGO recommends surgical staging for EC	Shepherd 1989[101]
1993	Combination chemotherapy (doxorubicin plus cisplatin) improves response rates to chemotherapy in advanced EC	Barett 1993[102]
1997	High-dose progesterone in fertility-sparing treatment for EC described	Kim 1997[103]
2000	PORTEC trial demonstrates no survival benefit to adjuvant radiation in early stage disease	Creutzberg 2000[31]
2004	Progesterone plus tamoxifen for active in the treatment of EC	Fiorica 2004,[104] Whitney 2004[105]
2004	Paclitaxel added to cisplatin and doxorubicin improves PFS and OS	Fleming 2004[106]
2005	Endometrial cancer identified as the more common "sentinel cancer" among women with HNPCC	Lu 2005[73]
2006	Chemotherapy (doxorubicin plus cisplatin) shown superior to whole abdominal radiation	Randall 2006[34]
2009	Laparoscopy shown to be equivalent to laparotomy for surgical staging	Walker 2009[25]
2011	mTOR inhibition shows promise in the treatment of recurrent, advanced EC	Oza 2011[107]
2011	Antiangiogenic therapy (bevacizumab) shows promise in the treatment of EC	Aghajanian 2011[90]
2014	TCGA defines four molecular subgroups of ED	TCGA Research Network 2013[64]
2015	TransPORTEC and Vancouver research teams refine molecular classification: 4 prognostic subgroups identified using pragmatic methodologies	Stelloo 2015,[65] Talhouk 2015[66]

TCGA Integrated Genomic Analysis of Endometrial Carcinoma



Nature. 2013 May 2; 497(7447): 67–73.



Nature. 2013 May 2; 497(7447): 67–73.

POLE-mutated endometrial carcinoma

HISTOLOGIC FEATURES

- **Usually high grade**
  - Often heterogenous, haphazard atypia
- **Eosinophilic cytoplasm**
- **TILs/PTLs**

CLINICOPATH FEATURES

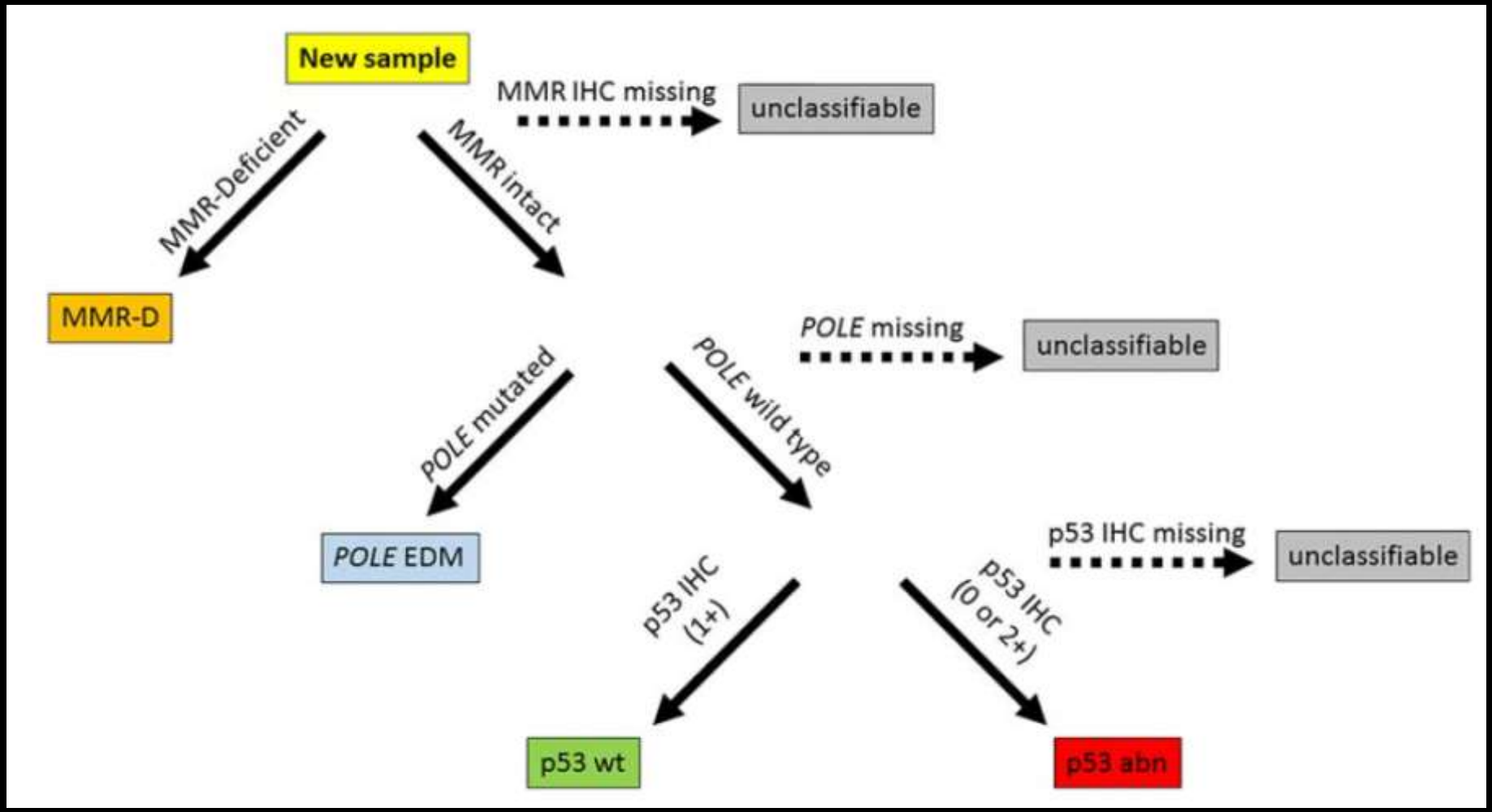
- **Often FIGO stage I**
- **Often have LVI**
- **Excellent prognosis**
  - Low rate mets/recurrence
- **Mean age 54-64y**
- **5-10% of endometrial ca**
  - 15-20% of grade 3 EC

Table 4 Clinicopathological features distinct between ultramutated endometrial carcinomas harboring *POLE* exonuclease domain mutation and serous carcinoma

	EC-POLE	*Serous carcinoma*
Clinical		
Average age, years	54 (33–87)	69 (45–87)
Clinical outcome	Favorable	Worse
Morphology		
SC-like features	Focal/patchy	Diffuse
Confirmatory EMC features	+	–
TILs/PTLs	+	–
Molecular		
TP53 mutation	35%	>90%
PTEN and *ARID1A* mutation	94% and 76%	17% and 8%
SCNAs	Low	High

Modern Pathology (2015) 28, 505–514

Proactive Molecular Risk Classifier for Endometrial Cancer (ProMisE)



Cancer 2017;123:802-13.

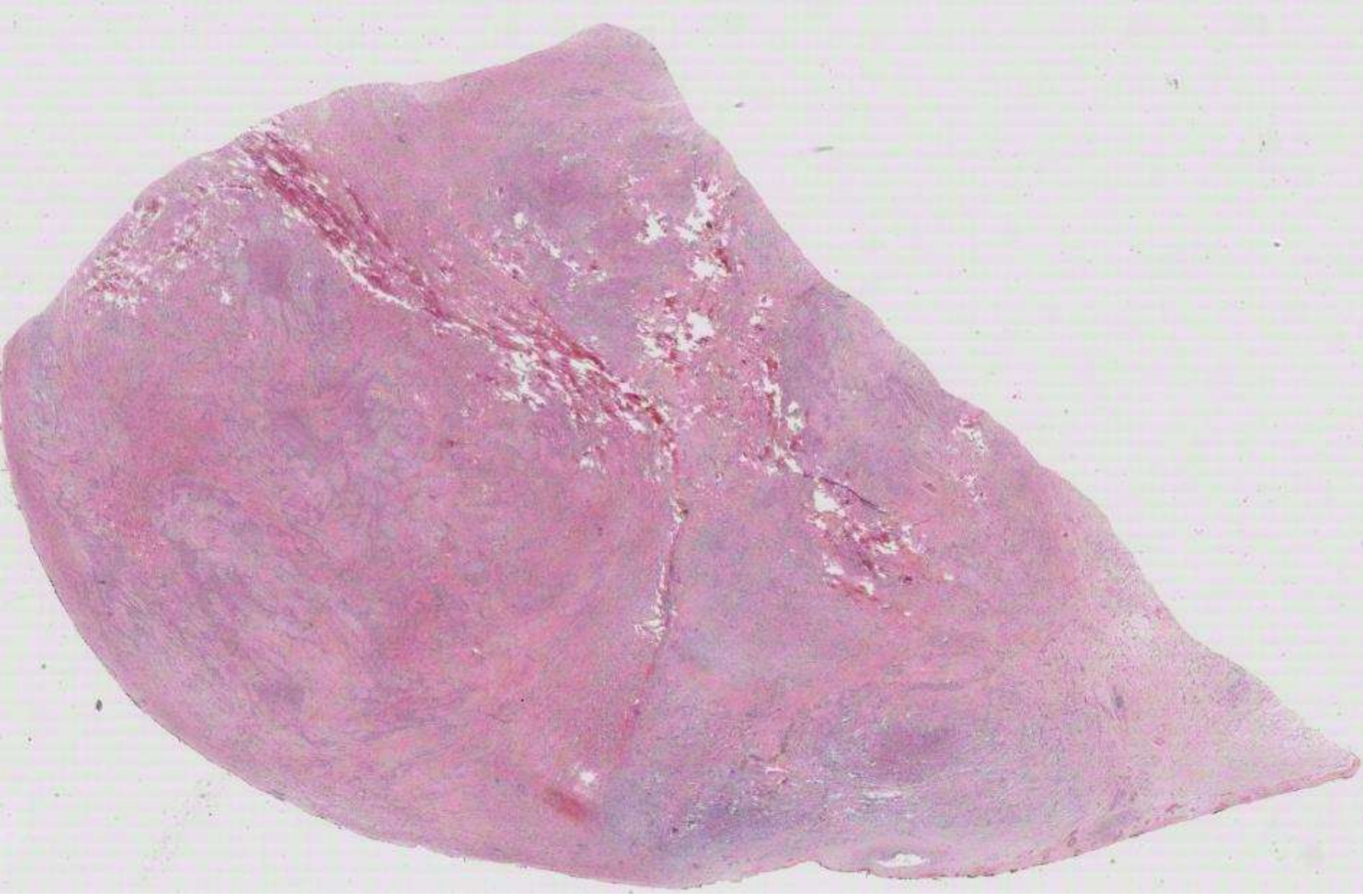
Biomarker Reporting?

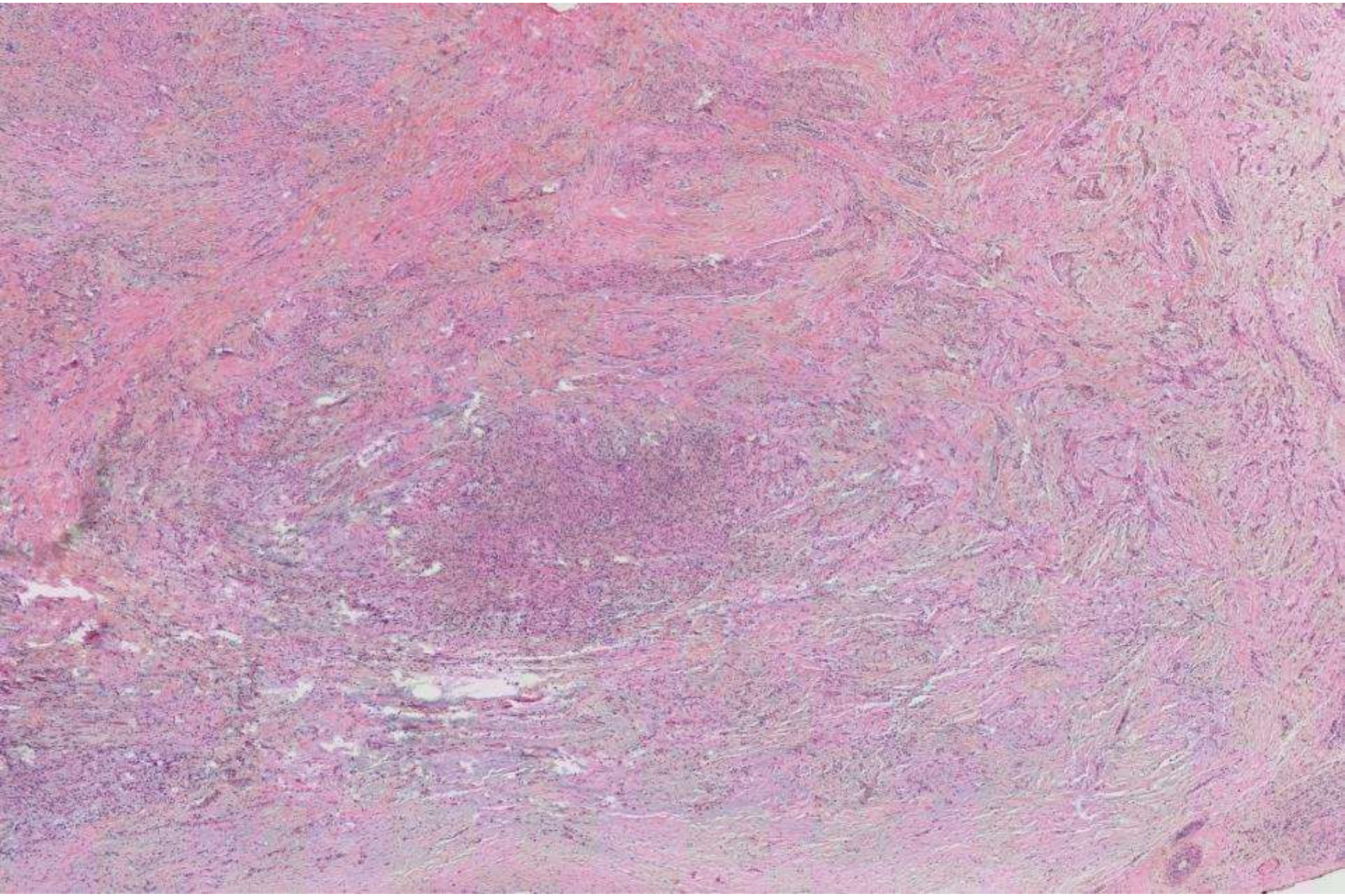
- **MSI**
  - Loss = likely good prognosis
- **POLE mutation**
  - Good prognosis
- **p53 (surrogate TP53 mutation)**
  - Positive result (3+ or null) = likely bad prognosis
- **Beta-catenin (surrogate CTNNB1 exon 3 mutation)**
  - Nuclear staining = likely bad prognosis

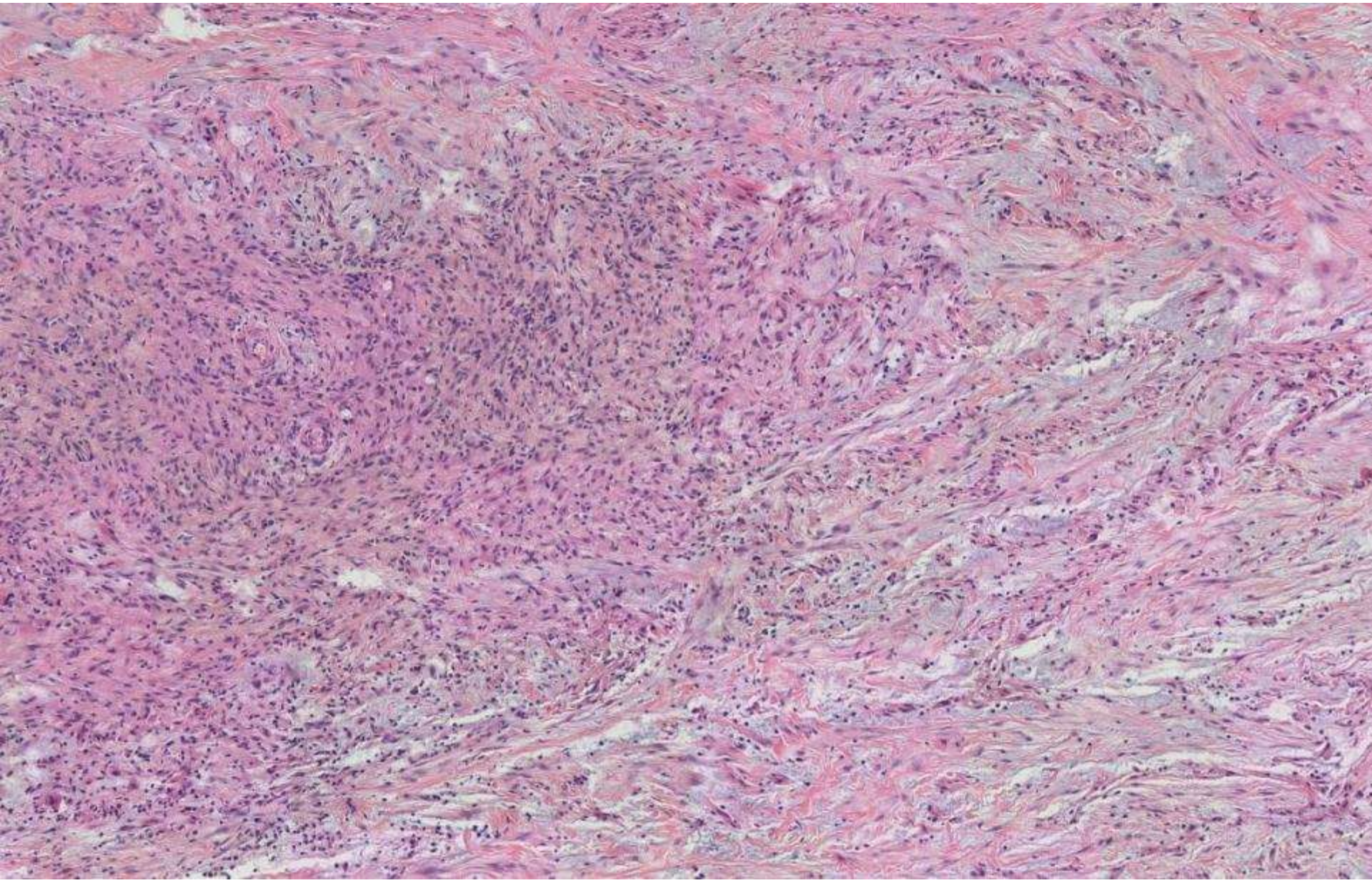
19-0804
(scanned slide available)

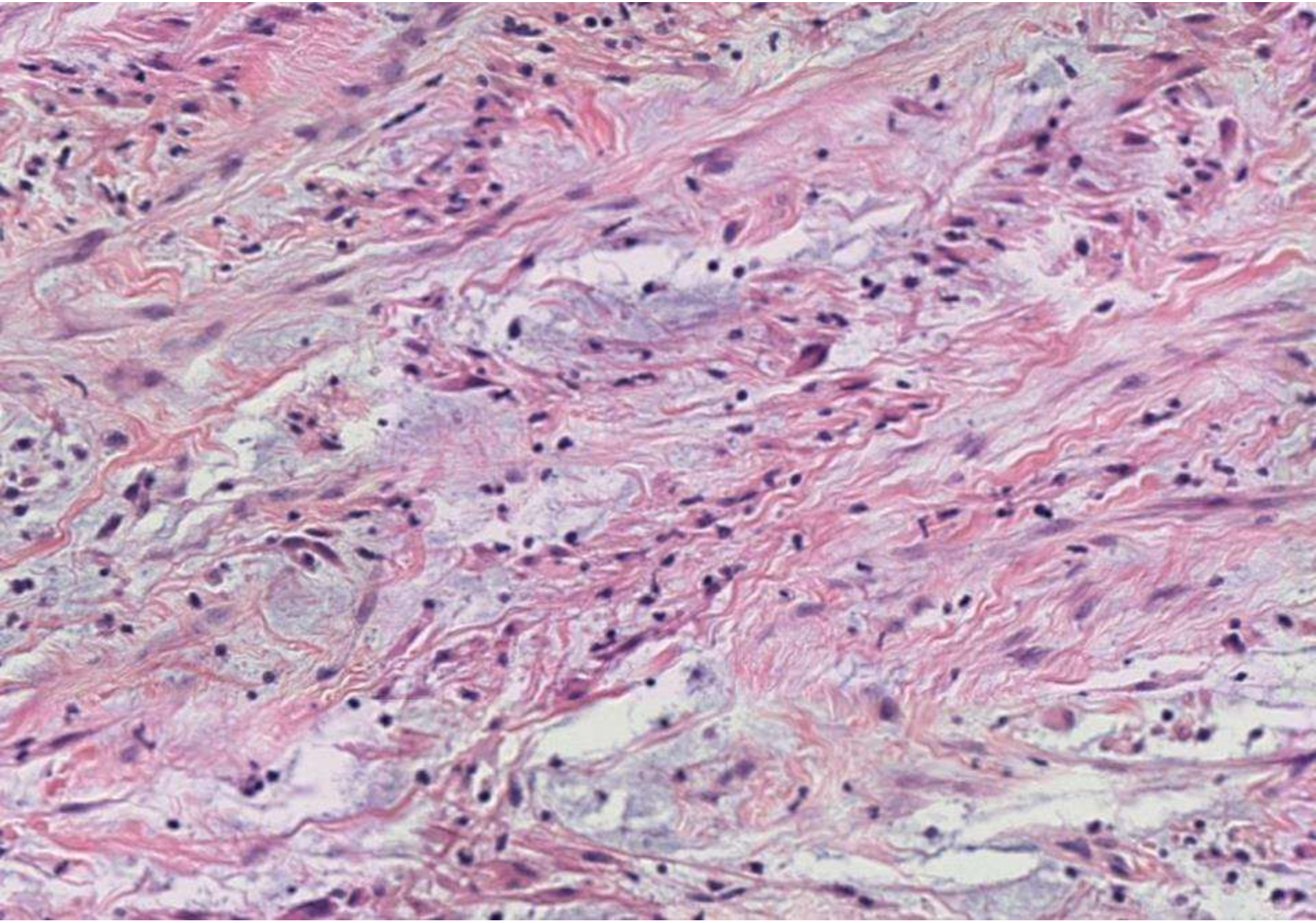
Nicole Croom/Karuna Garg; UCSF

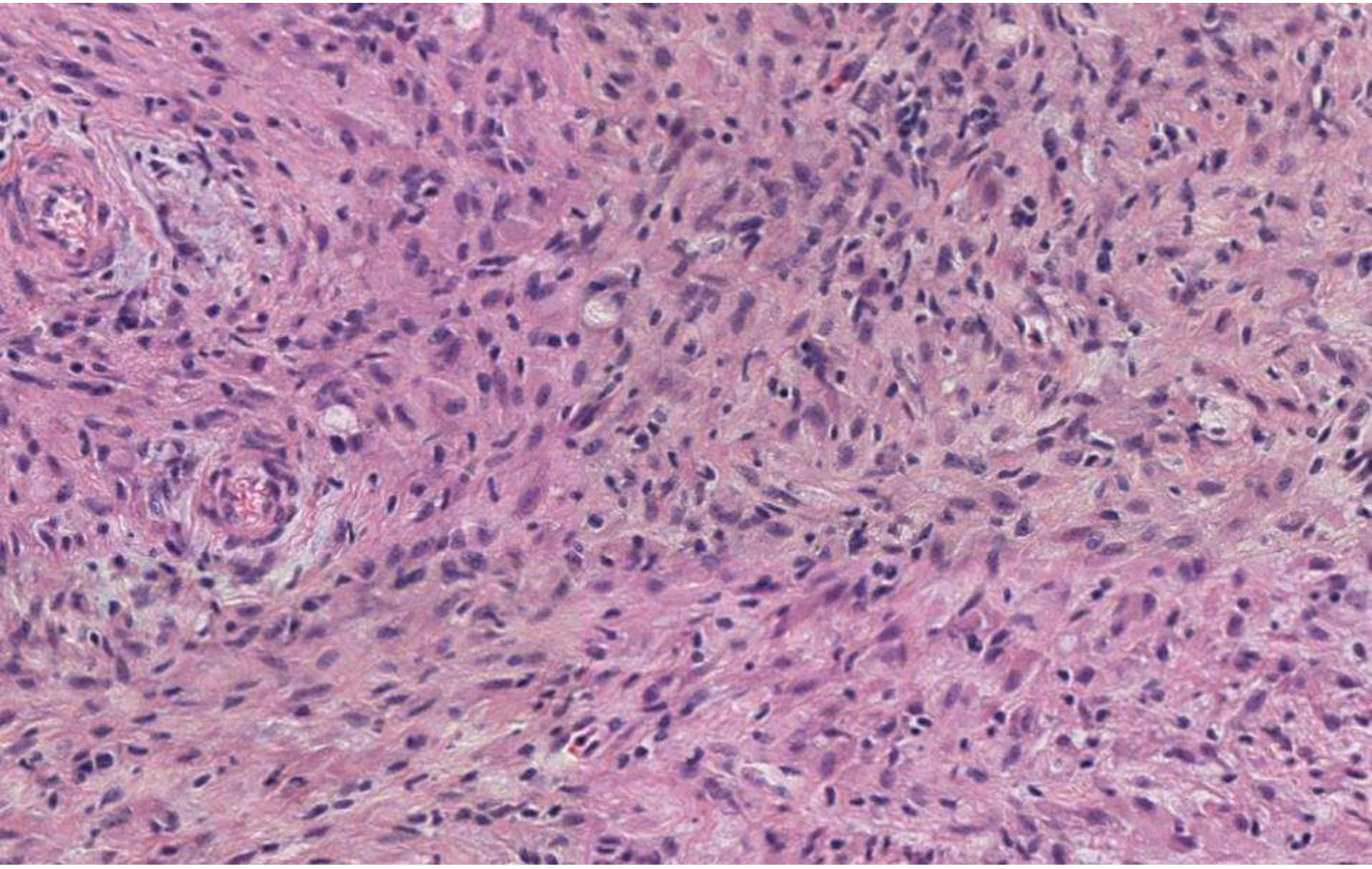
10-year-old girl with h/o immature pelvic teratoma s/p resection now with 7cm Pouch of Douglas mass.

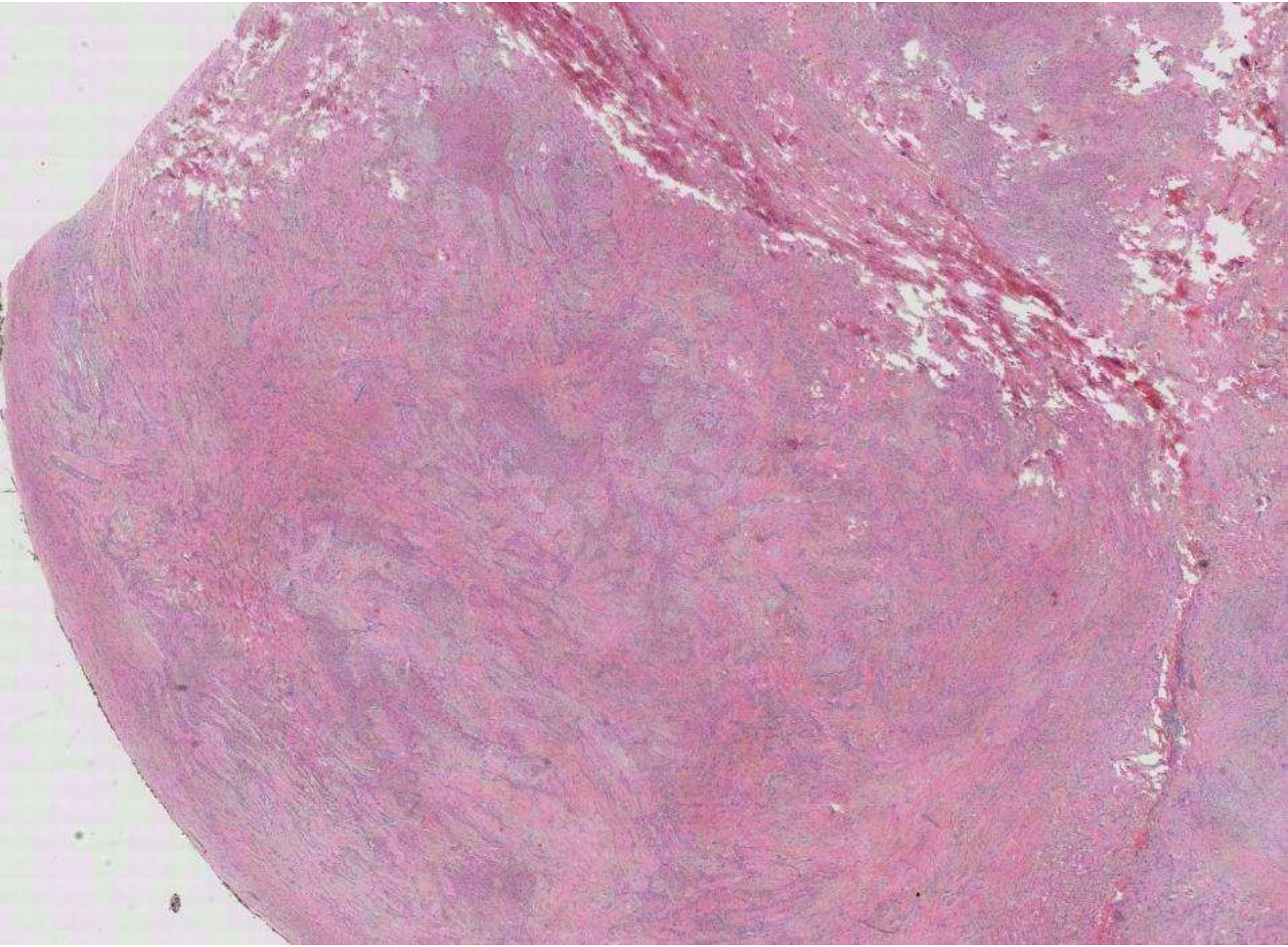


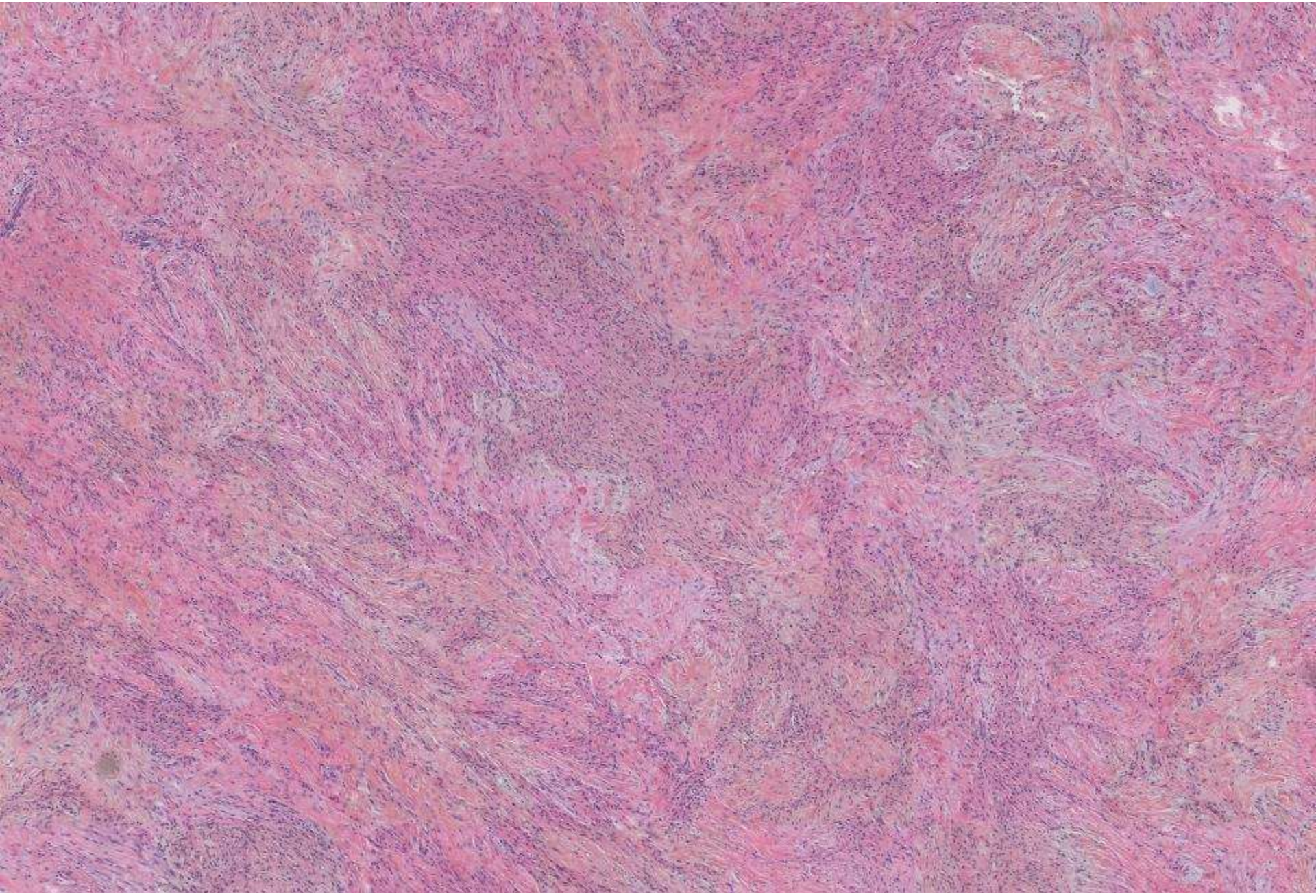


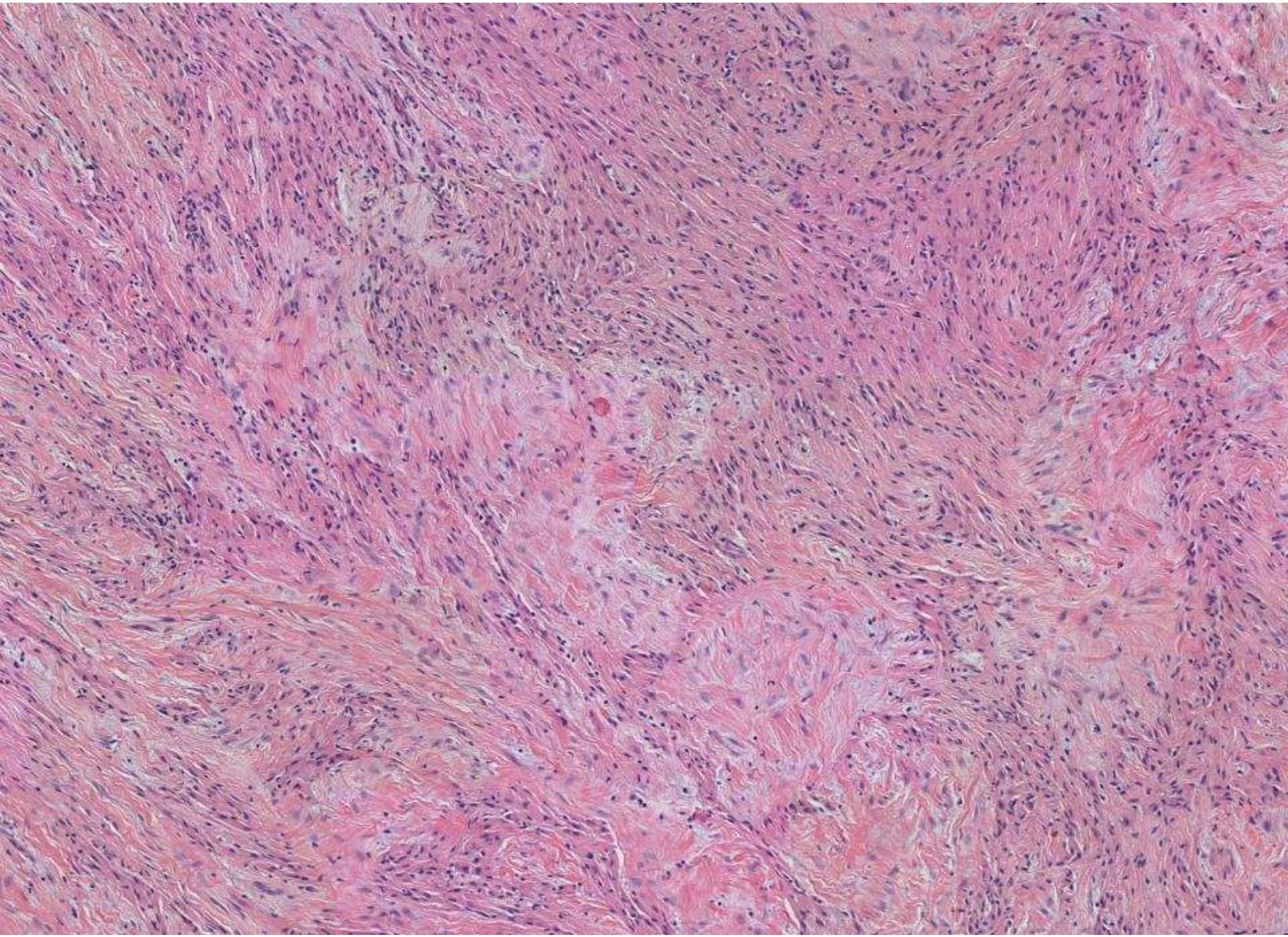


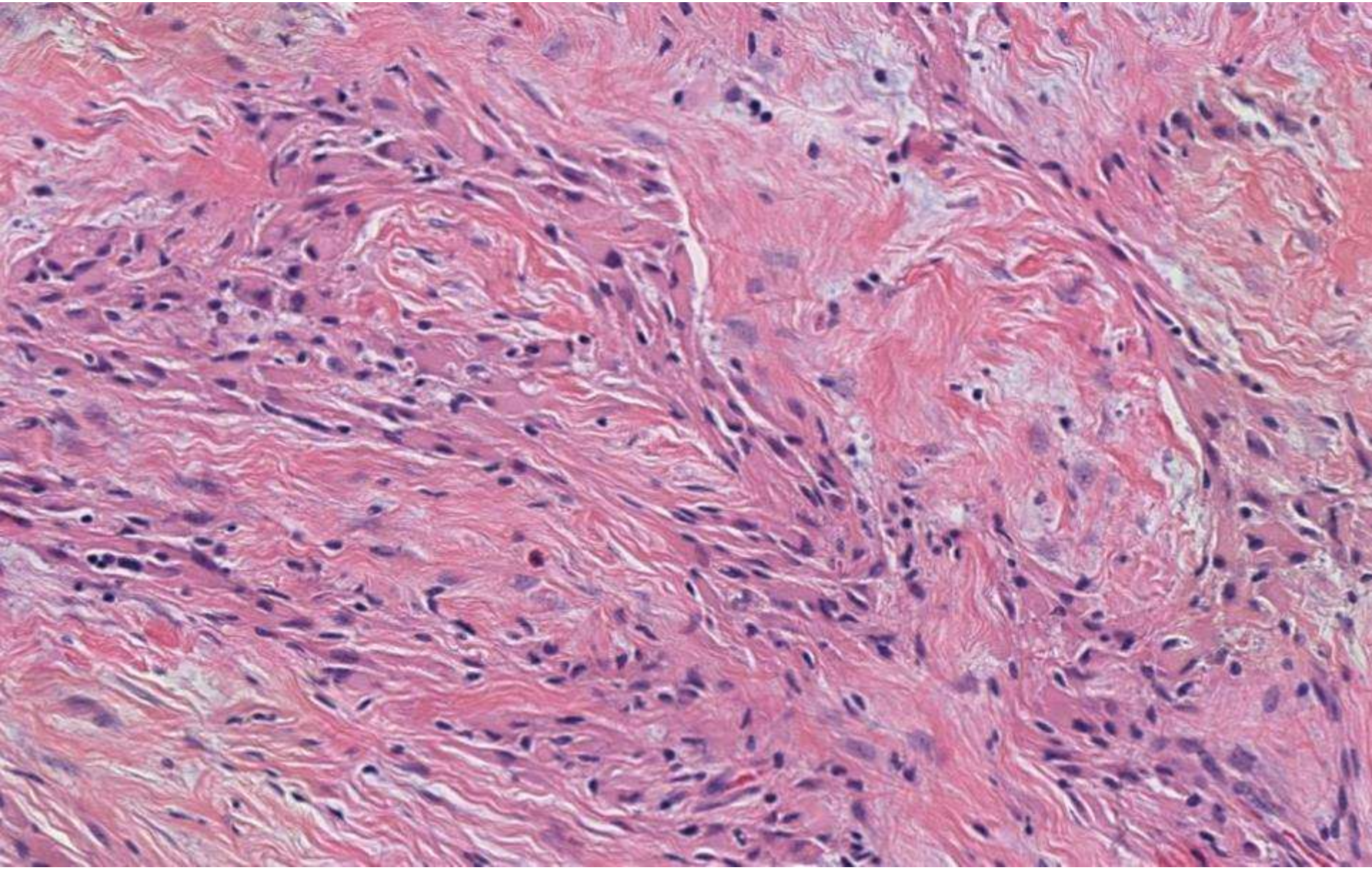






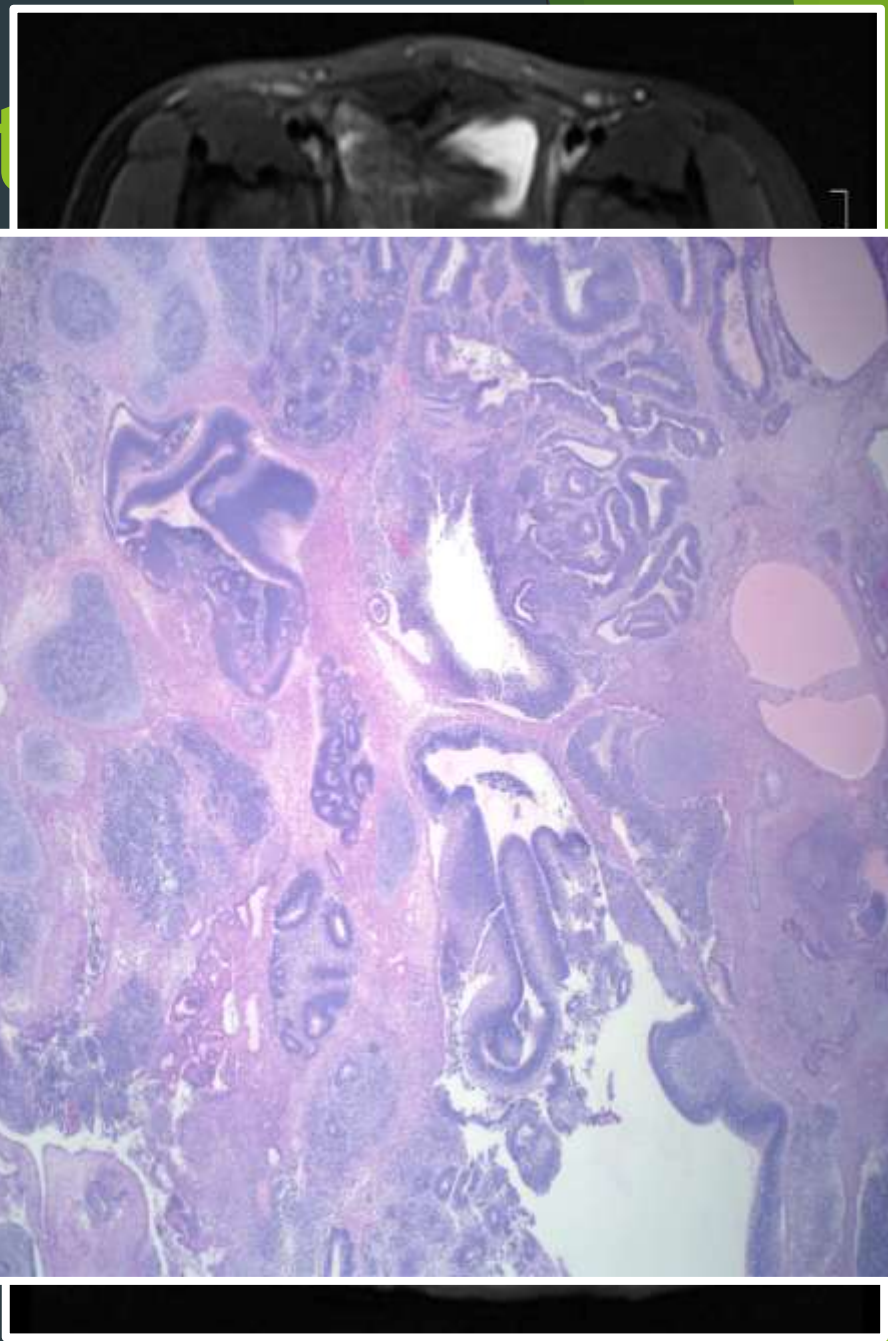


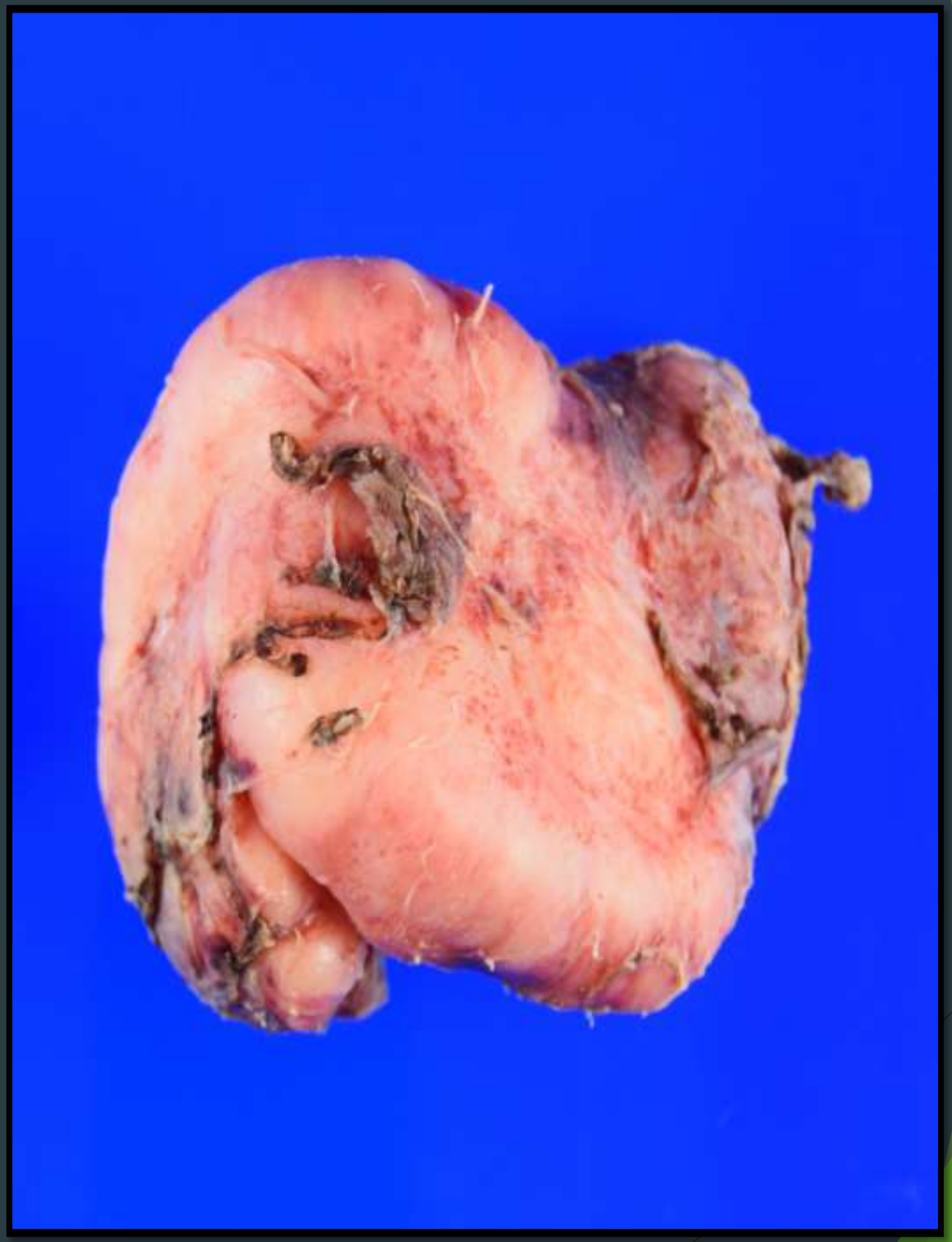


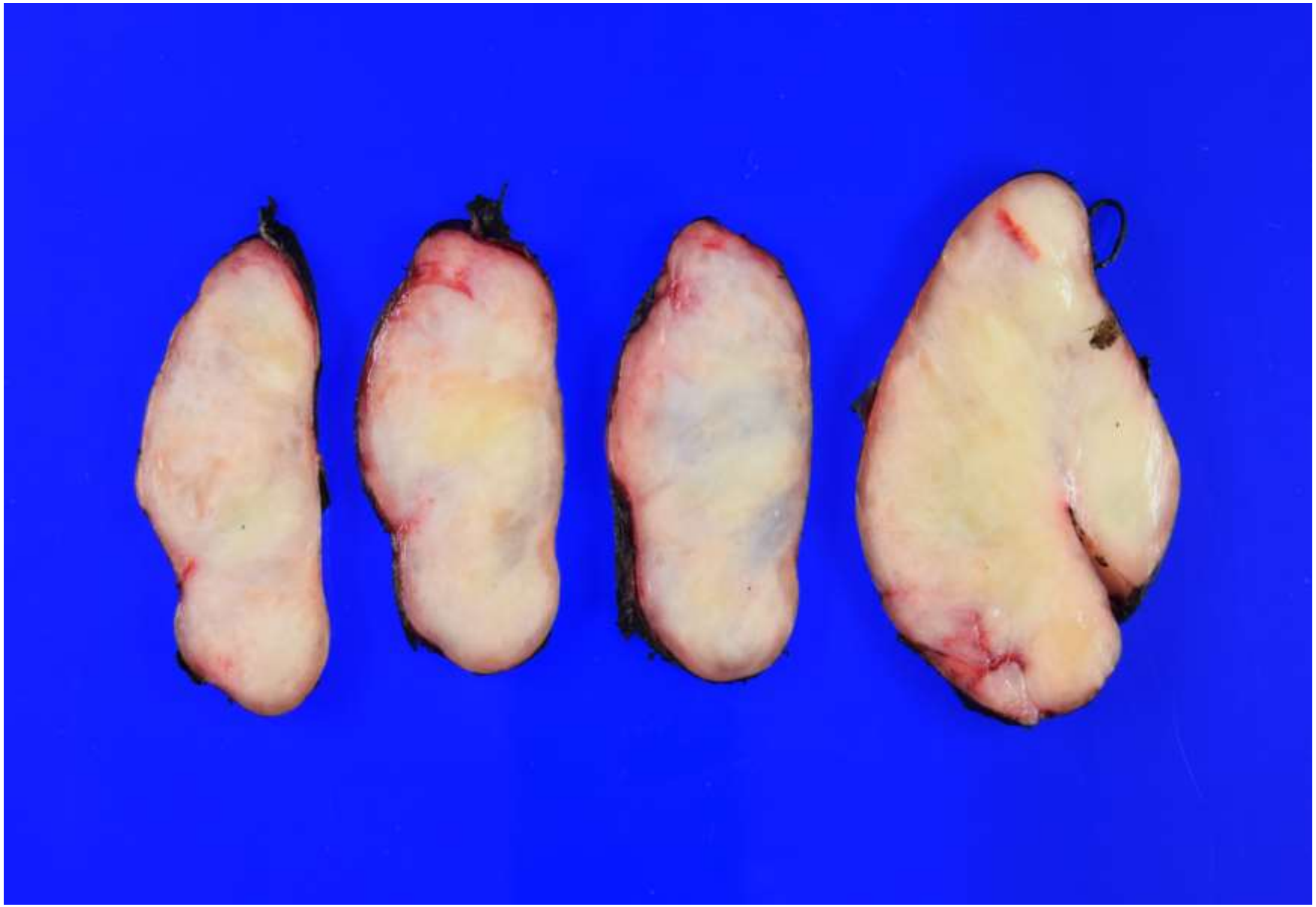


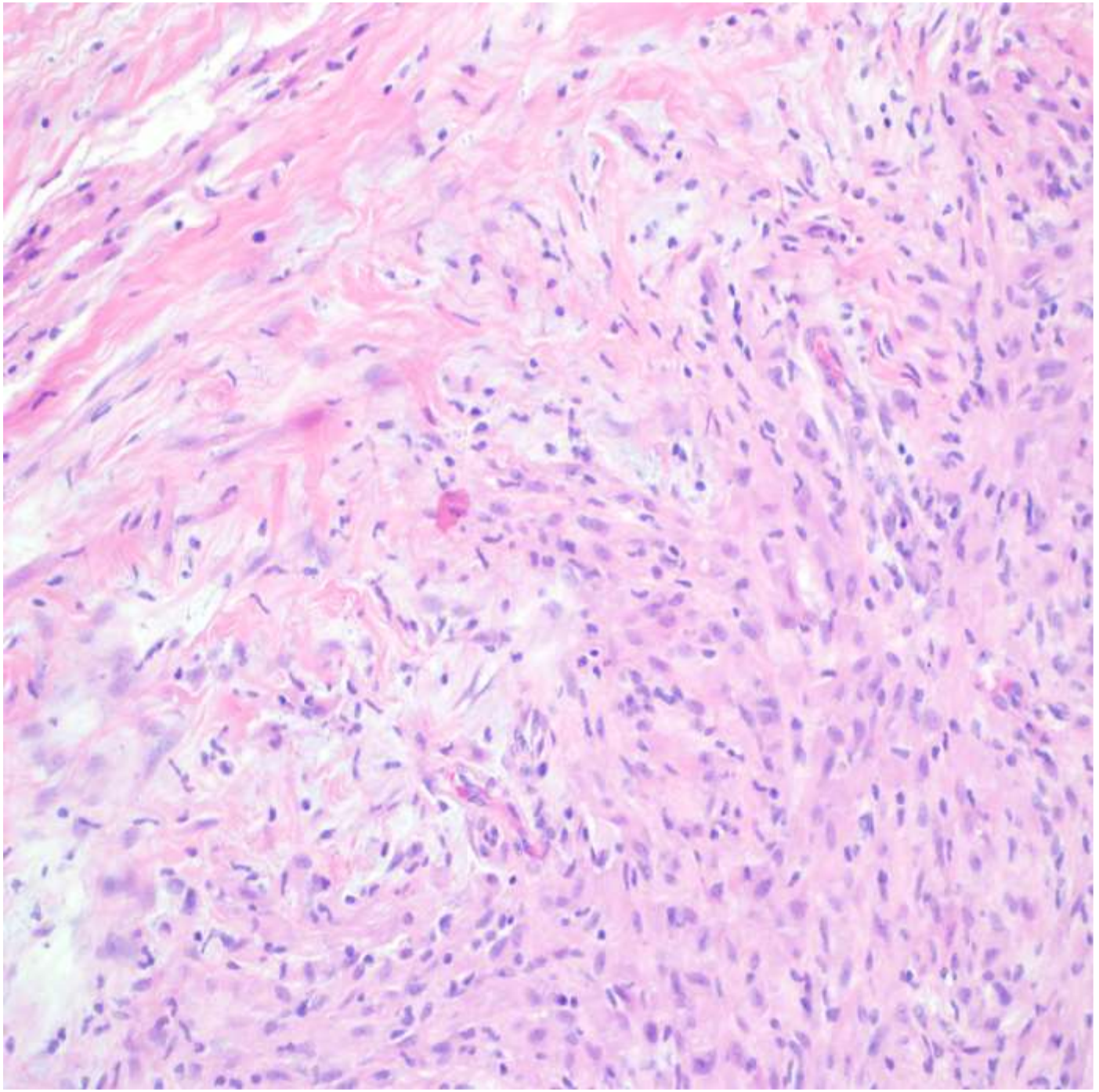
Case Presentat

- 10F with history of immature pelvic teratoma status post resection with new difficulty defecating
- Imaging: Hyperintense mass (7.7 x 7.4 x 6.2 cm) in



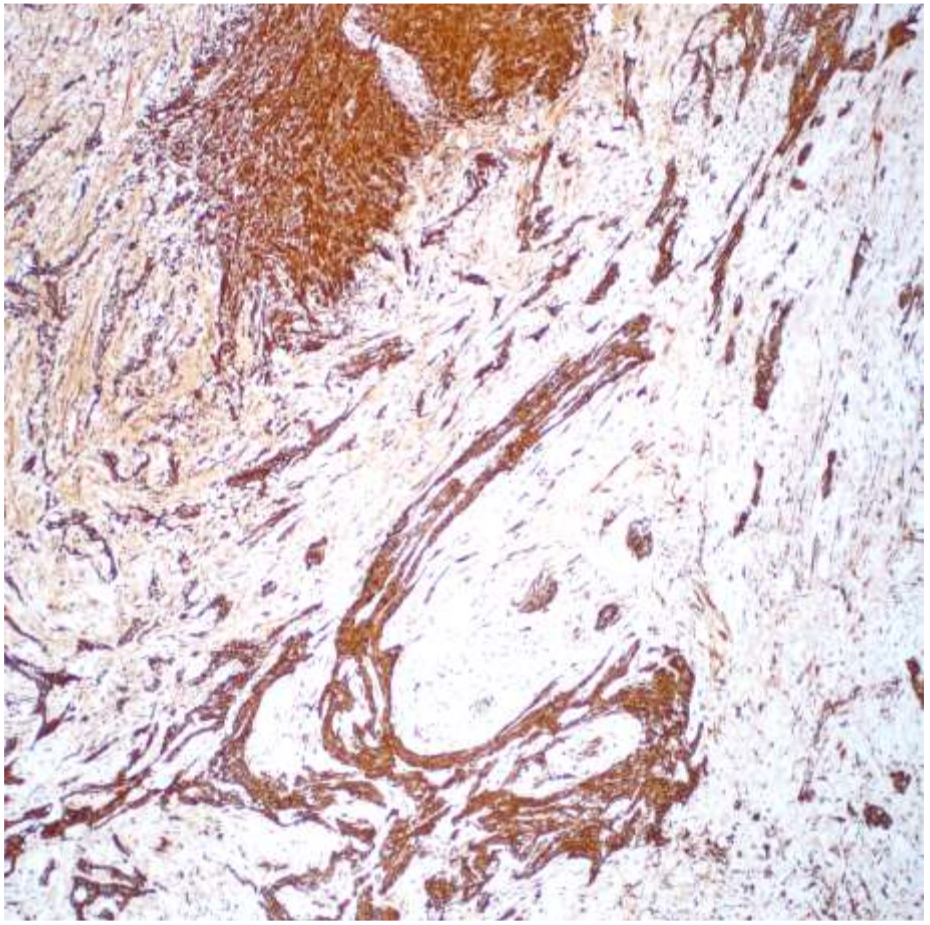




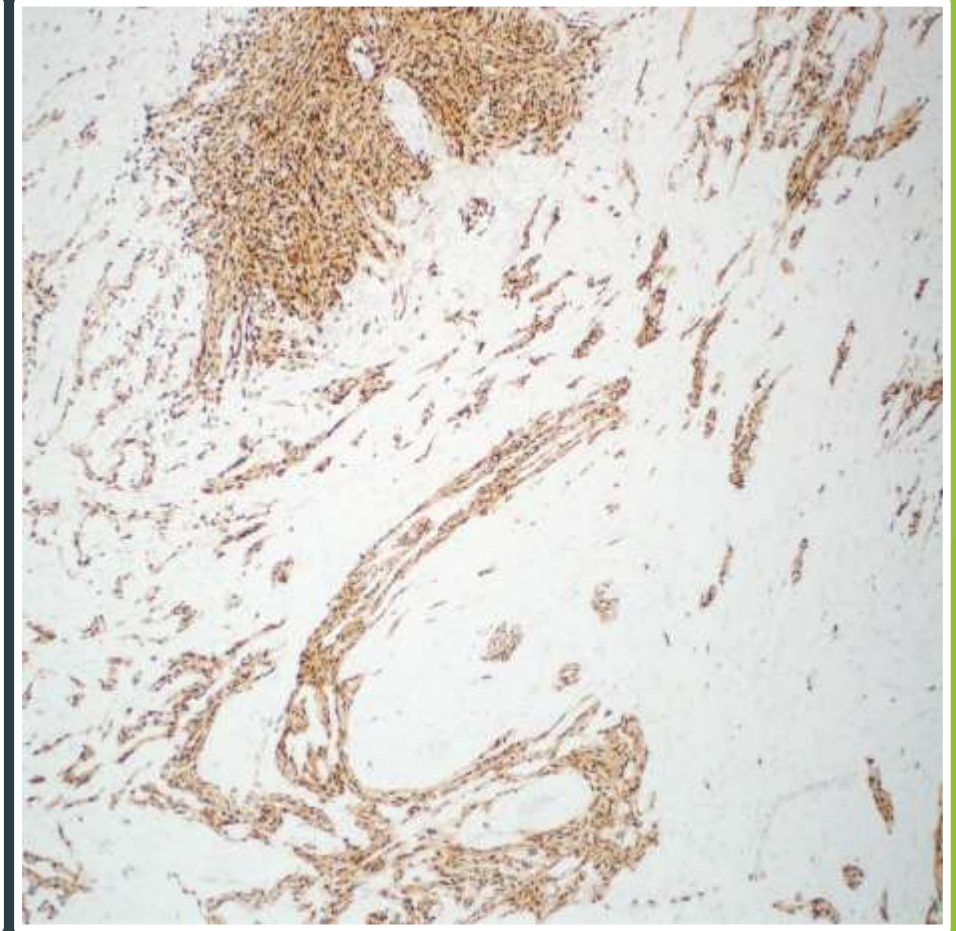


Differential Diagnosis

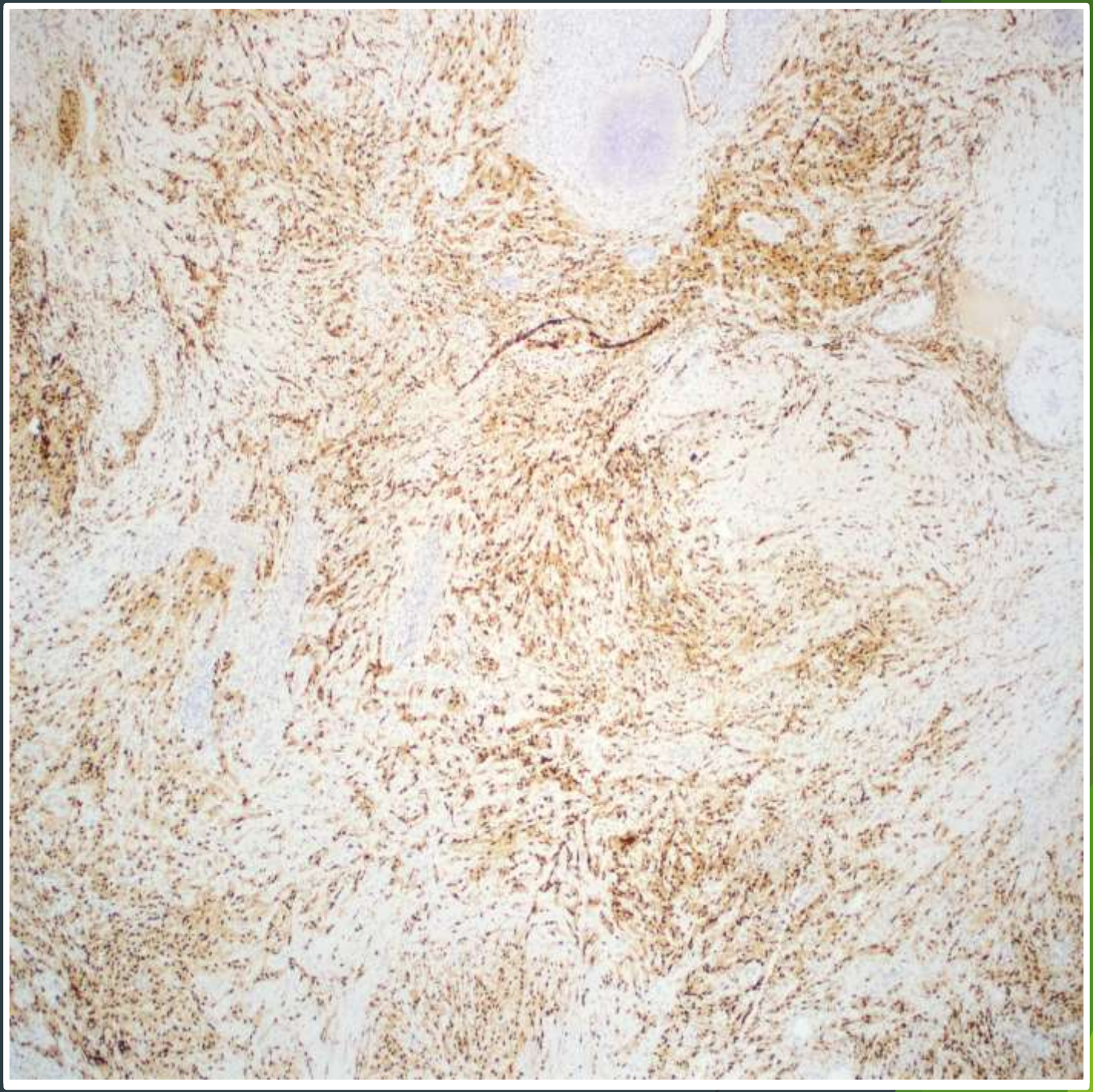
- Fibromatosis (desmoid tumor)
- Leiomyoma
- Gliomatosis peritonei



GFAP

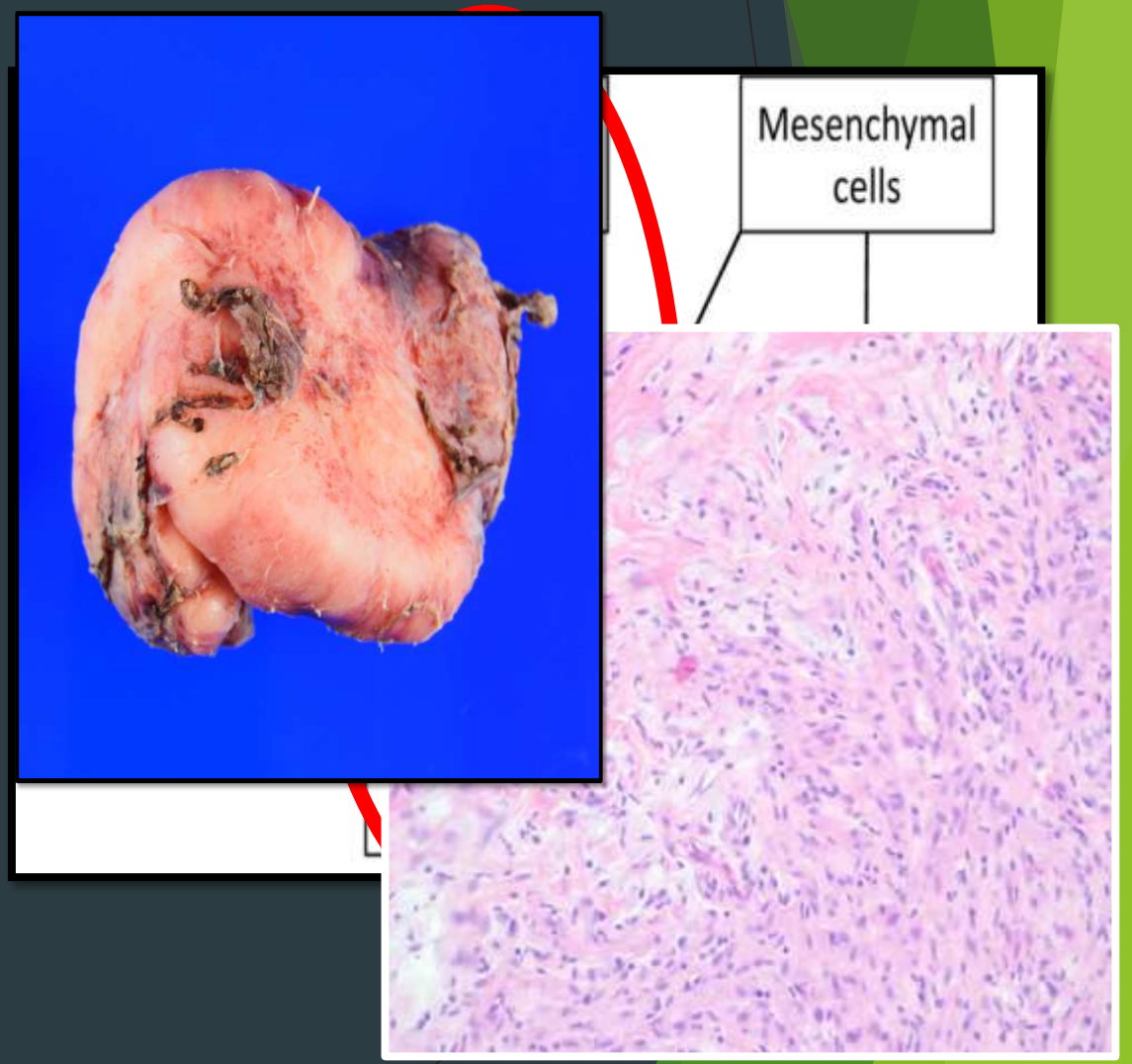


SOX2



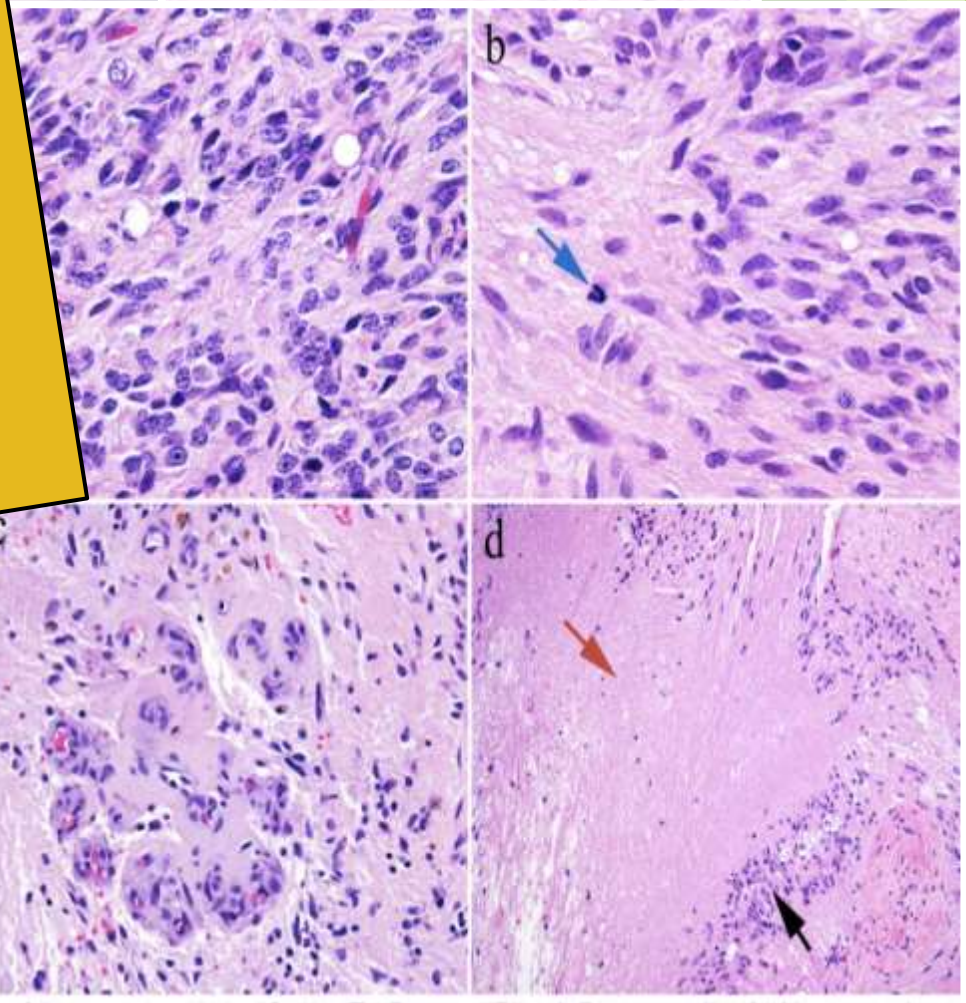
Gliomatosis Peritonei (GP)

- Presence of mature glial tissue in the peritoneum
- Associated with immature teratoma
- Favorable prognosis*
- Pathogenesis poorly understood
- IHC: SOX2+/OCT4-/NANOG-



Transformation to glioma:
Increased cellularity
+
Atypia
Mitoses
Endothelial proliferation
Necrosis

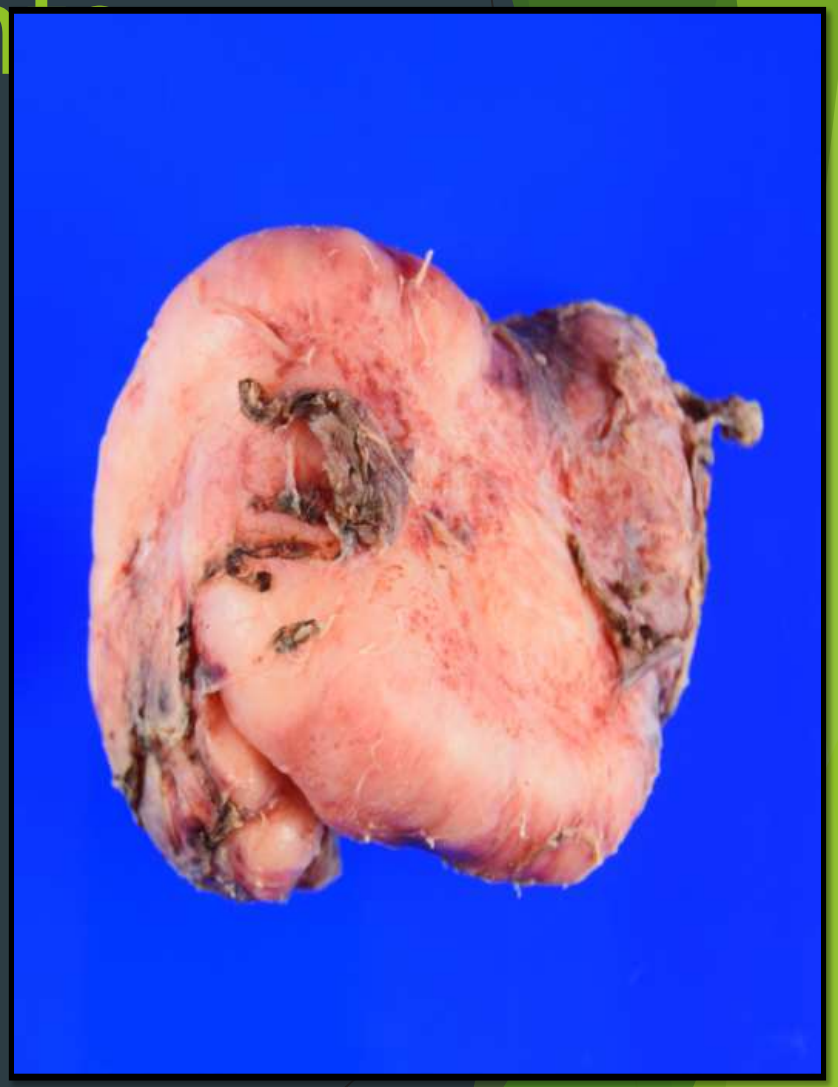
Ruleout glioma



Sample adequately to ruleout teratoma

Take Home Points

- Gliomatosis peritonei can present as a mass-like lesion
- IHC: GFAP+/SOX2+
- Important to sample adequately in order to rule out immature teratoma and transformation to glioma
  - Rosettes
  - Increased cellularity
  - AMEN



Resources

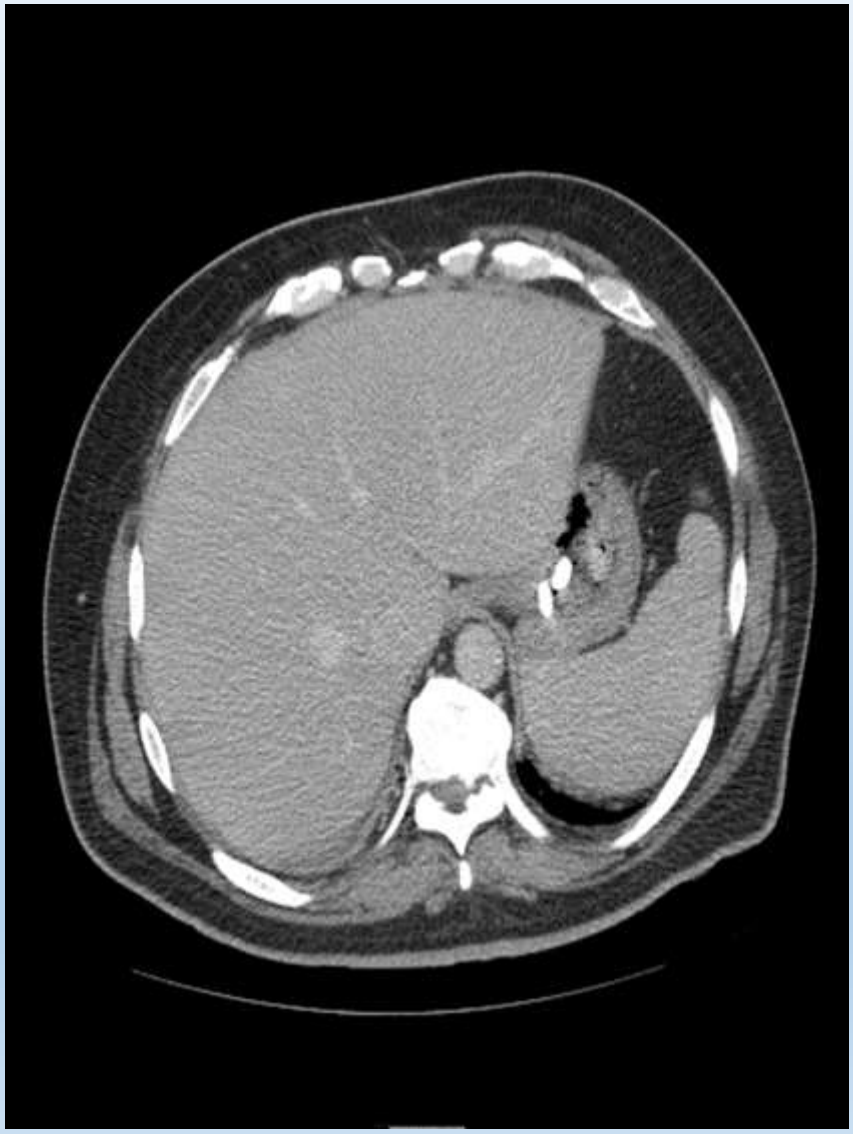
- Liang et al. Gliomatosis peritonei: a clinicopathologic and immunohistochemical study of 21 cases. Mod Pathology. 2015 Dec; 28(12): 1613-1620.
- Francisco F. Nogales, Isabel Dulcey, and Ovidiu Preda (2014) Germ Cell Tumors of the Ovary: An Update. Archives of Pathology & Laboratory Medicine: March 2014, Vol. 138, No. 3, pp. 351-362.

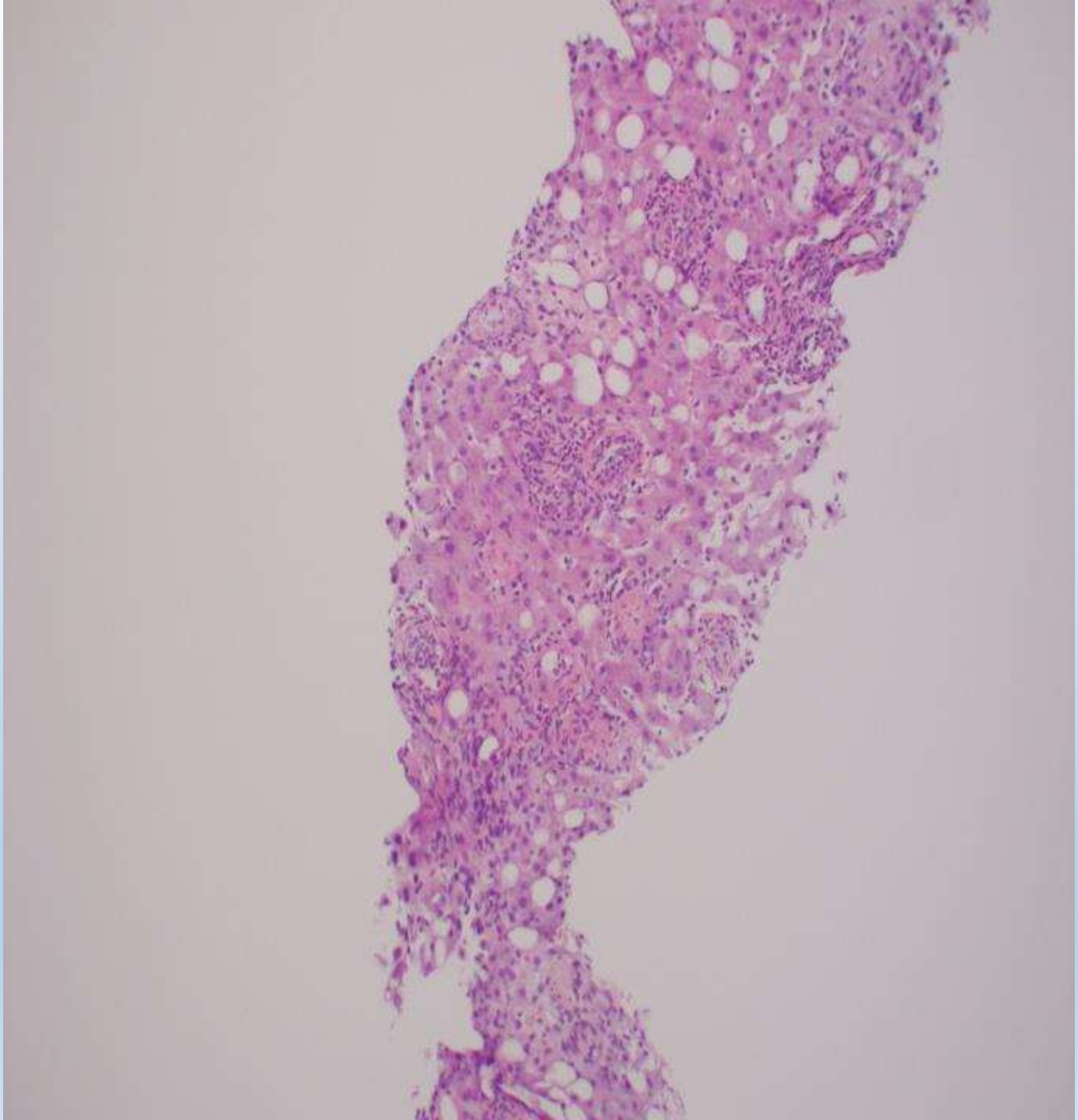
19-0805
(scanned slide available)

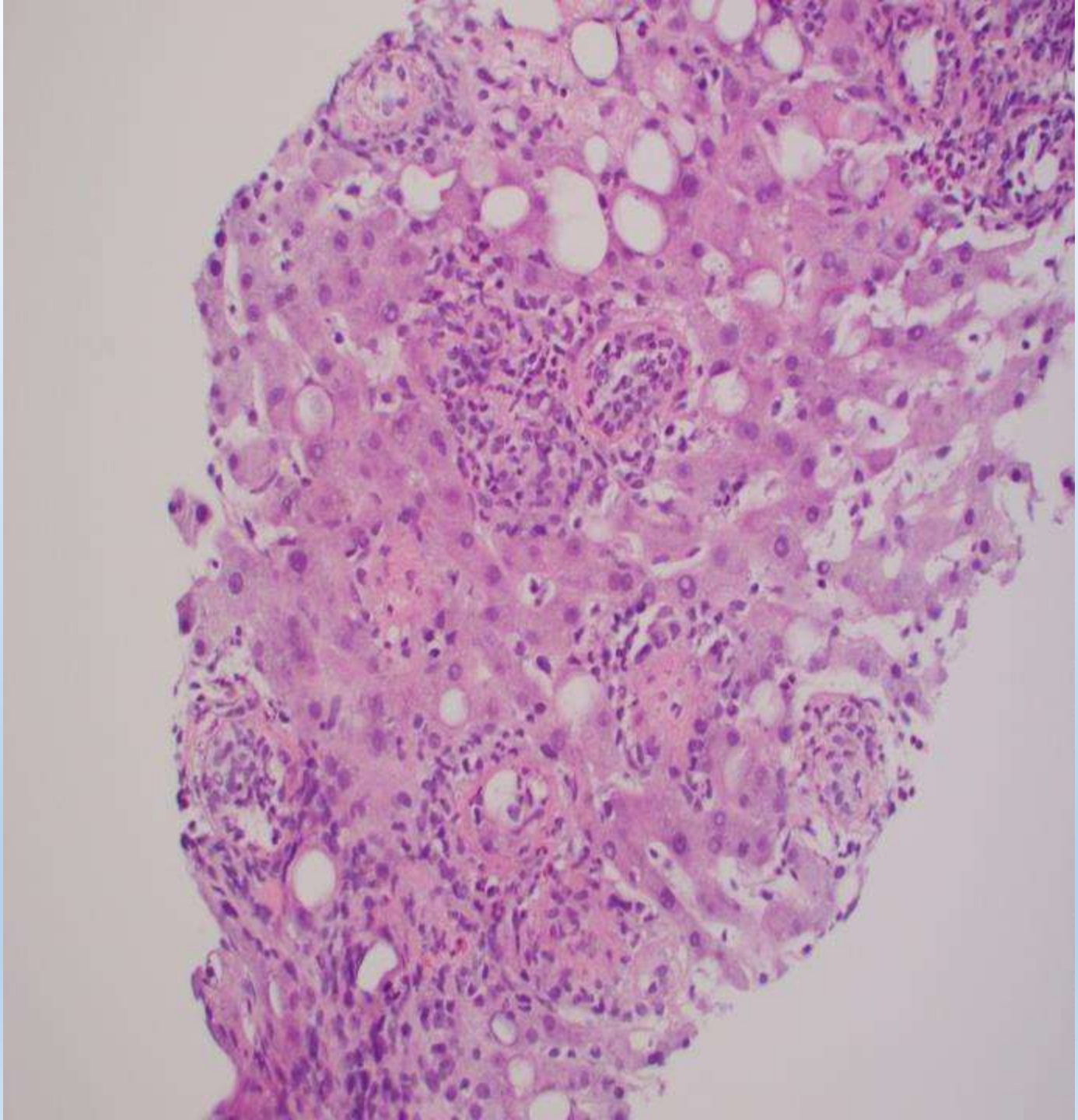
Sava Grujic; Kaiser San Jose

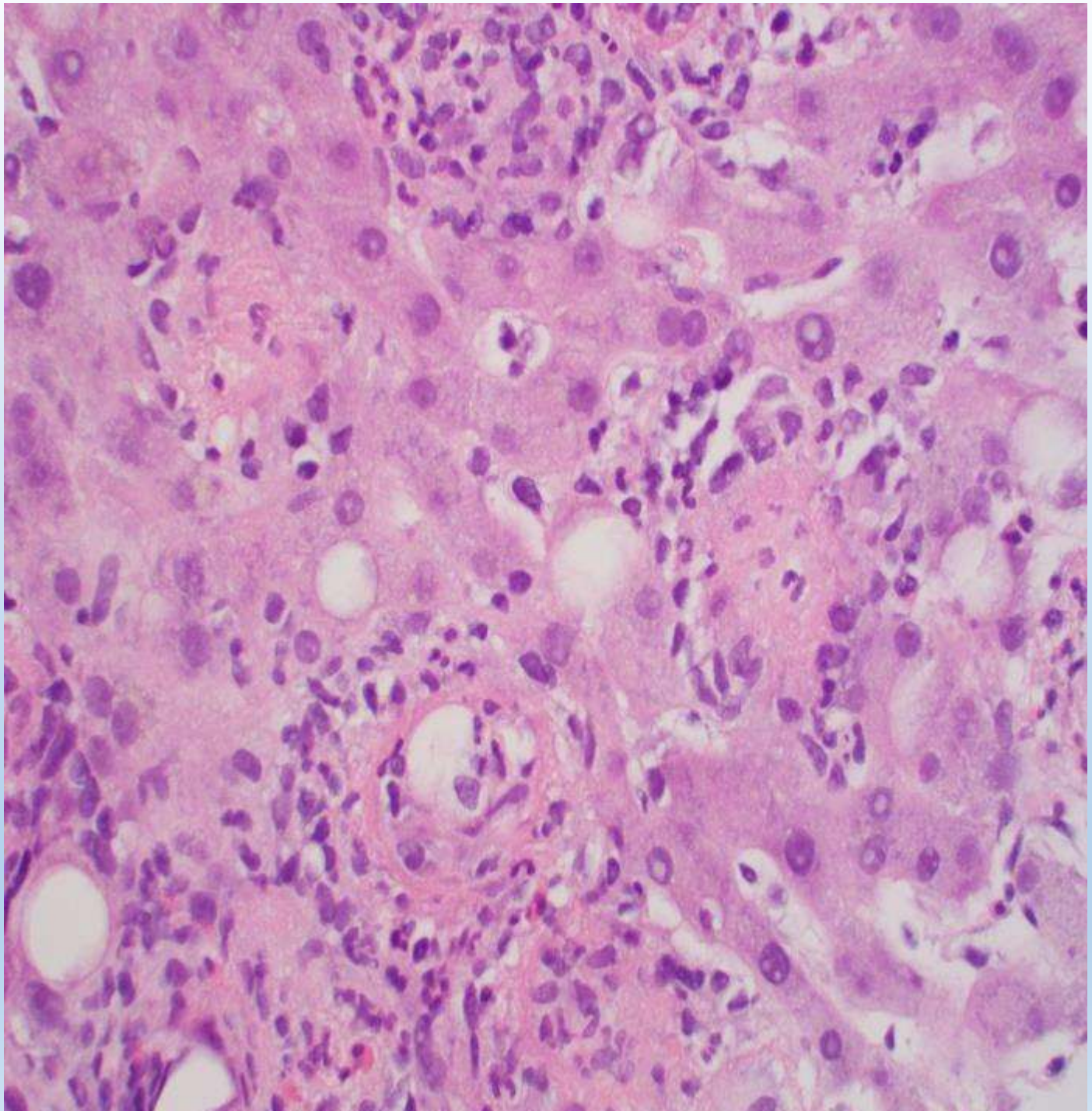
48-year-old man with fever and hepatosplenomegaly. Liver biopsy submitted.

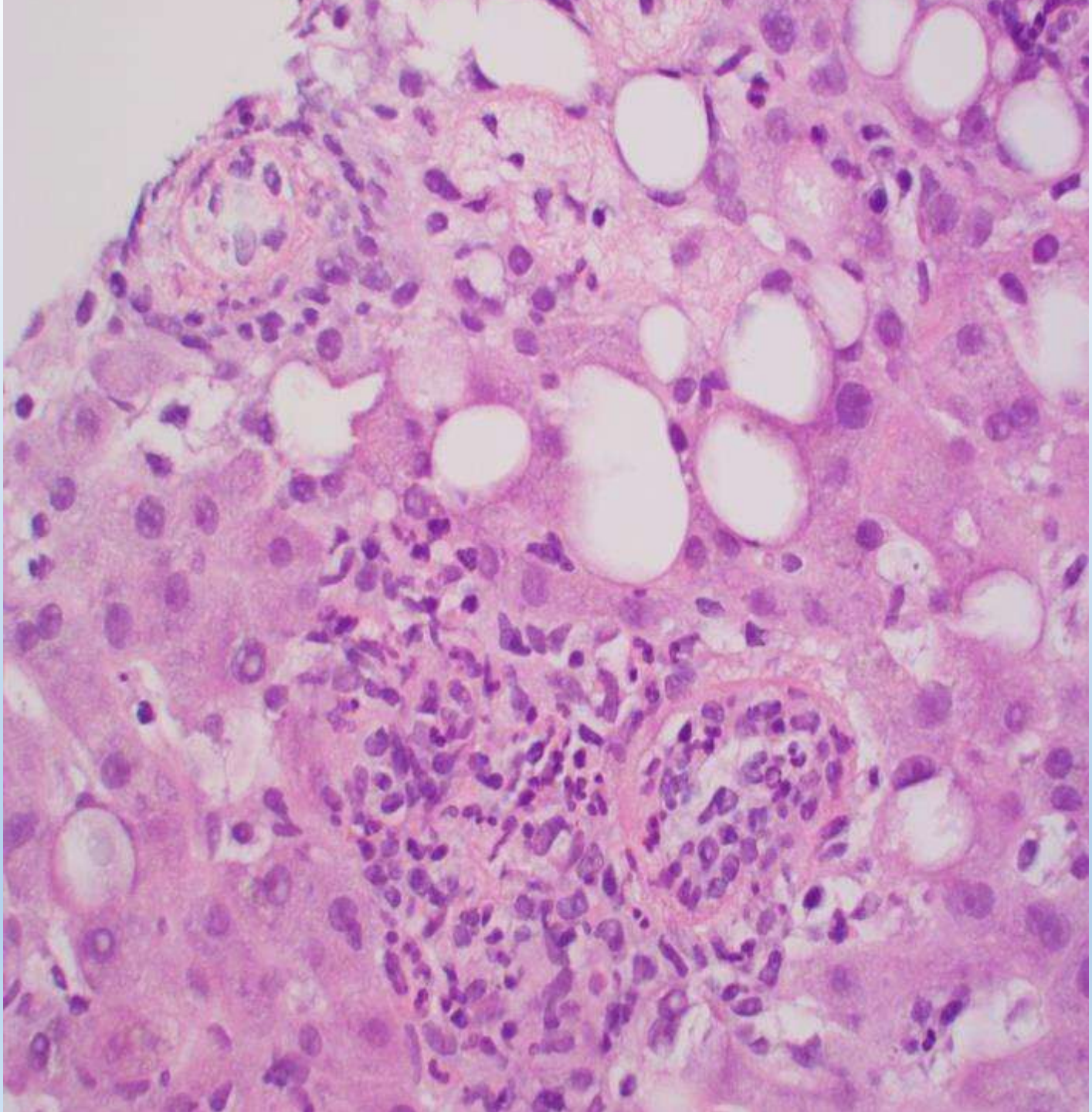
48 y/o male with fever and hepatosplenomegaly
Initial serology was nonconclusive, liver bx was performed

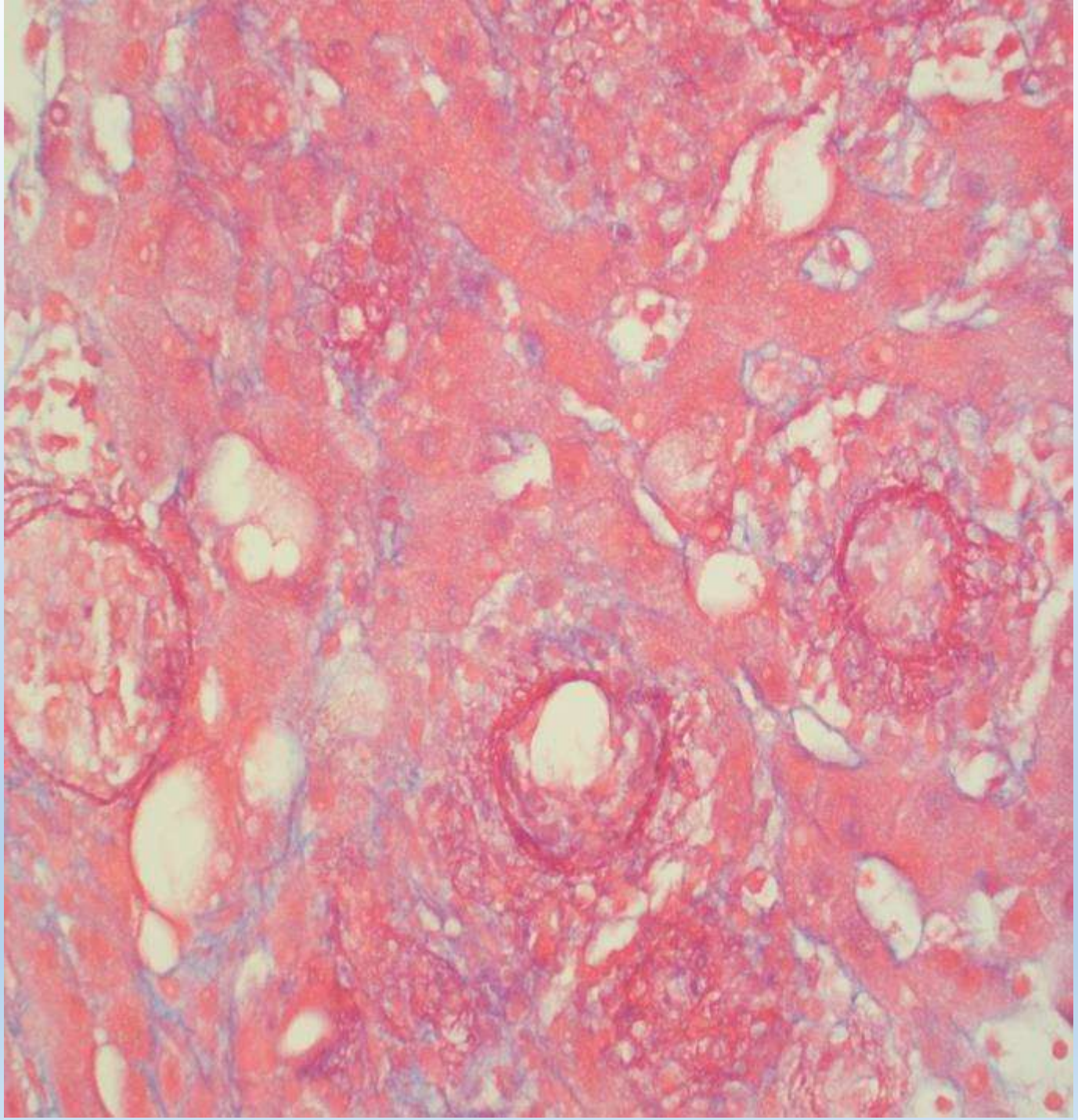


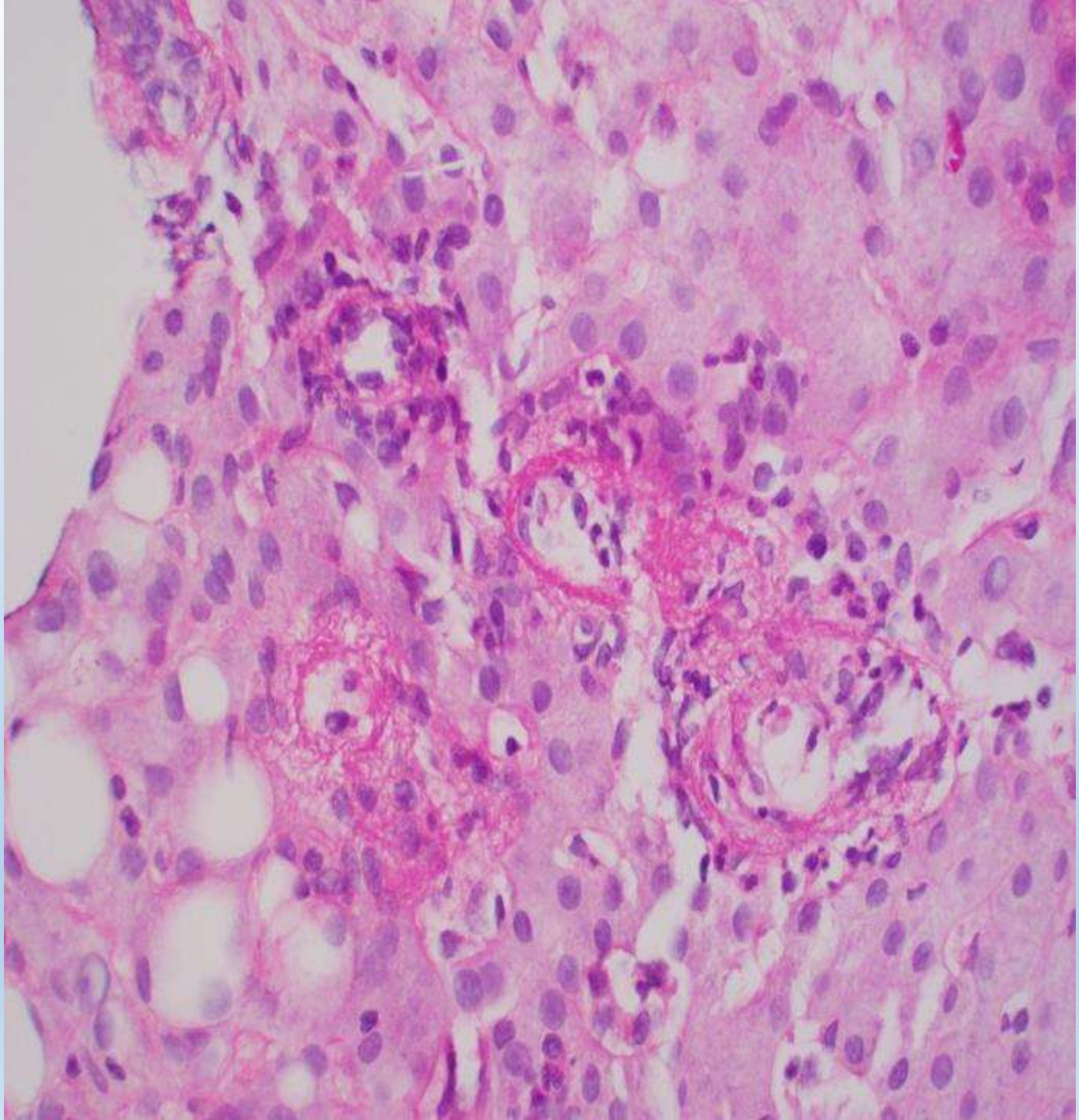












Final Diagnosis **Date Signed Out:** 12

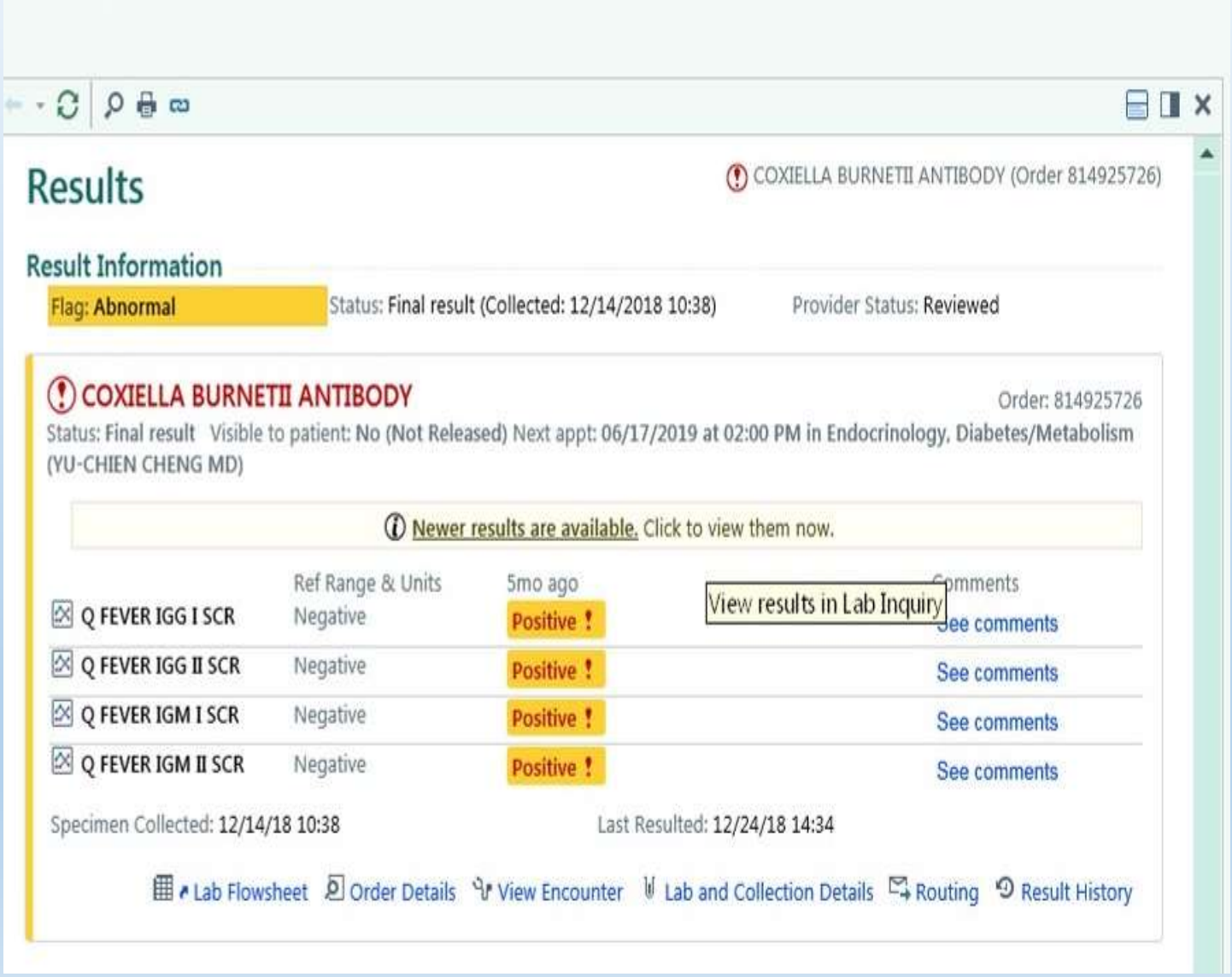
LIVER BIOPSY:

- LOBULAR HEPATITIS WITH FIBRIN RING GRANULOMAS, SEE COMMENT

Diagnosis Comment

Fibrin ring granulomas were initially described in association with Q-fever (Coxiella burnetii) but they are nonspecific and can be seen in various infectious and noninfectious conditions including EBV, hepatitis A, hepatitis C, Rickettsia conorii, toxoplasmosis, CMV, Leishmaniasis, MAI, typhoid fever, Allopurinol toxicity, giant cell arteritis, Hodgkin's disease and lupus. Clinical and serologic correlation is required. AFB stain is pending and will be reported in addendum.

Repeat serology for Coxiella Burnetii



Results

COXIELLA BURNETII ANTIBODY (Order 814925726)

Result Information

Flag: Abnormal Status: Final result (Collected: 12/14/2018 10:38) Provider Status: Reviewed

COXIELLA BURNETII ANTIBODY Order: 814925726

Status: Final result Visible to patient: No (Not Released) Next appt: 06/17/2019 at 02:00 PM in Endocrinology, Diabetes/Metabolism (YU-CHIEN CHENG MD)

Newer results are available. Click to view them now.

	Ref Range & Units	5mo ago	Comments
Q FEVER IGG I SCR	Negative	Positive !	See comments
Q FEVER IGG II SCR	Negative	Positive !	See comments
Q FEVER IGM I SCR	Negative	Positive !	See comments
Q FEVER IGM II SCR	Negative	Positive !	See comments

View results in Lab Inquiry

Specimen Collected: 12/14/18 10:38 Last Resulted: 12/24/18 14:34

Lab Flowsheet Order Details View Encounter Lab and Collection Details Routing Result History

Epidemiology

- Q fever was first recognized as a human disease in Australia in 1935 and in the United States in the early 1940s.
- The “Q” stands for “query” and was applied at a time when the cause was unknown.
- Q fever is a zoonosis caused by *Coxiella burnetii,* an obligate gram-negative intracellular bacterium.
- Cattle, sheep, and goats are commonly infected and people often become exposed by breathing in dust contaminated by infected animal body fluids.
- People in direct contact with animals during birthing, such as veterinarians and farmers may be at higher risk for infection.
- *C. burnetii* can survive for long periods of time in the environment and may be carried long distances by wind.

Signs and symptoms

- The three main clinical presentations of acute Q fever are:
- Self-limited, influenzalike febrile illness of abrupt onset, often accompanied by headache, myalgia, chills, fatigue and sweats
- Pneumonia, usually mild in nature or as an incidental radiographic finding; when there is respiratory involvement, patients have a dry, nonproductive cough, dyspnea. Occasionally can progresses to ARDS.
- Hepatitis, usually with mild elevation of transaminases (2-3 times the reference range) and may be associated with antismooth muscle, antiphospholipid, or antinuclear antibodies; jaundice and acute gastrointestinal symptoms (nausea and vomiting, diarrhea)
- Chronic Q fever - Endocarditis with negative culture findings and seropositivity is the main clinical presentation.

Diagnosis and treatment

- The diagnosis of Q fever relies on a high index of suspicion as suggested by the epidemiologic features and is proven by serologic analysis (indirect immunofluorescence is the method of choice)
- Doxycycline is the treatment of choice for acute Q fever, and 2 weeks of treatment is recommended for adults and children aged 8 years or older
- Chronic Q fever is difficult to treat and a prolonged antimicrobial regimen is recommended. The most current recommendation for endocarditis is combination of doxycycline and hydroxychloroquine for at least 18 months to eradicate any remaining *C burnetii* and prevent relapses.

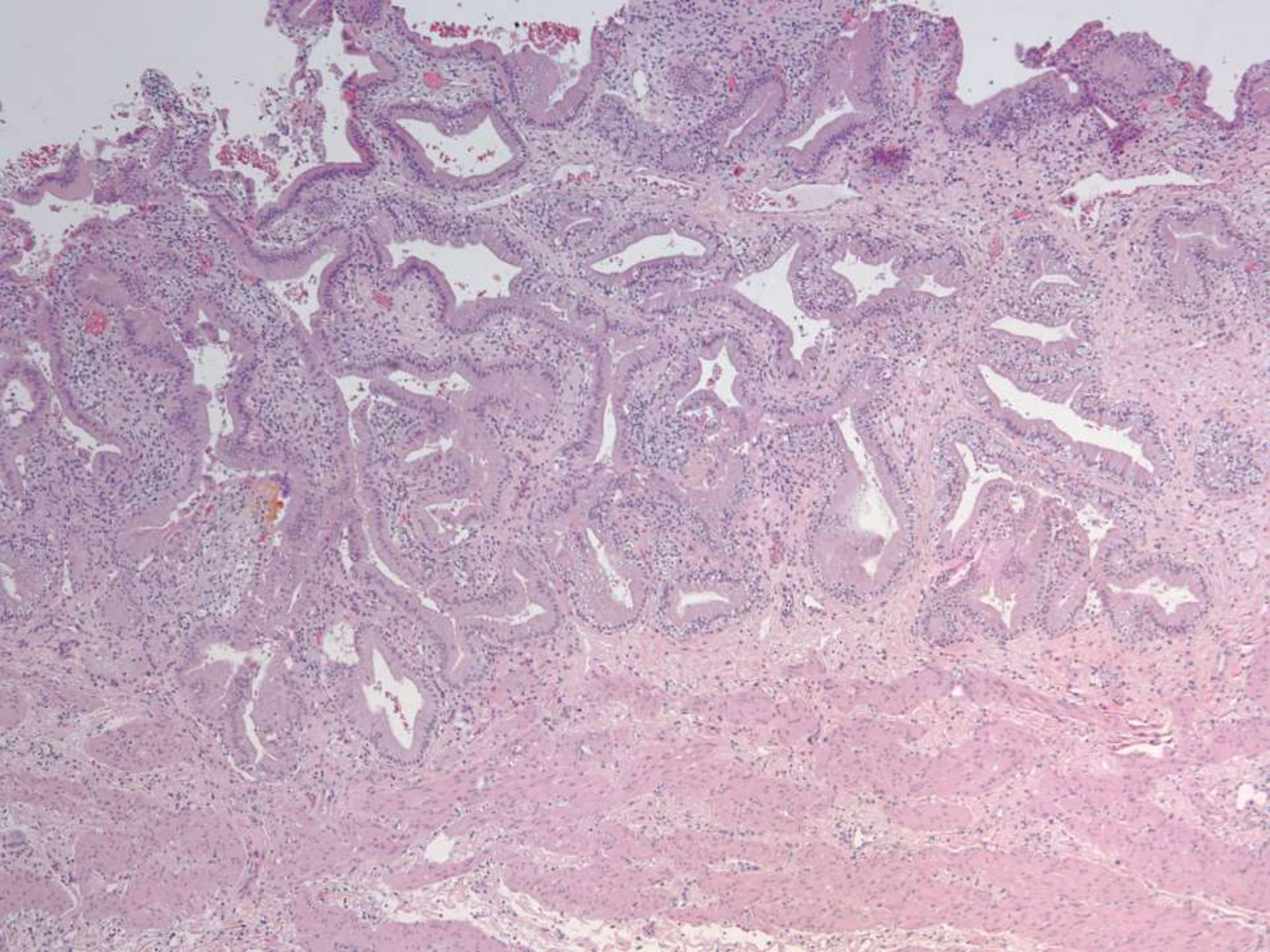
Considerations for Intentional Release

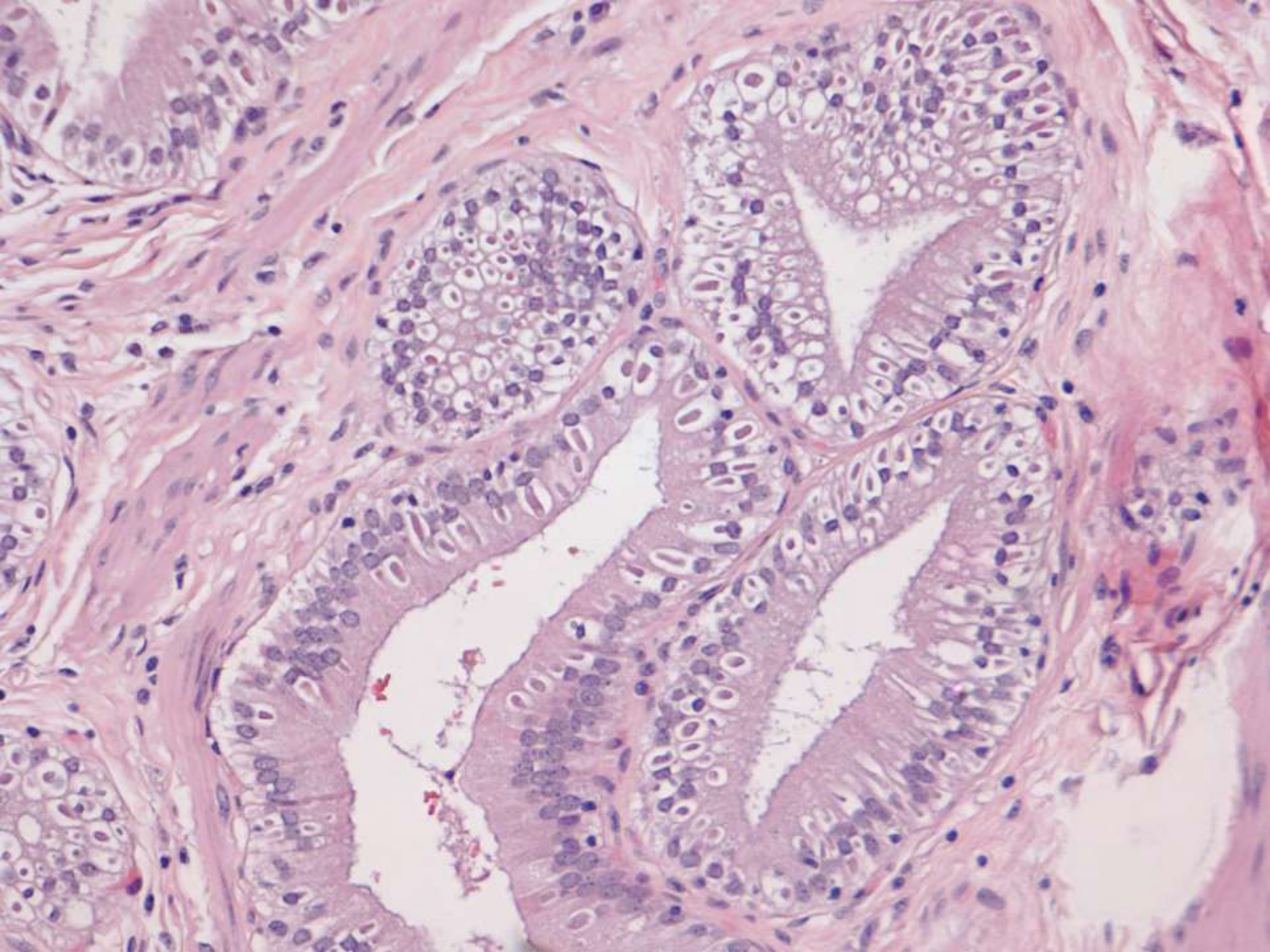
- *C. burnetii* is a highly infectious agent that is resistant to heat, drying, and many common disinfectants.
- It can be aerosolized and inhalation is the primary route of infection for people.
- As few as 1-10 *C. burnetii* organisms may cause disease in a susceptible person.
- This agent has been previously weaponized for use in biological warfare and is considered a potential terrorist threat.
- The World Health Organization has estimated that if 50 kg of *C. burnetii* were aerosolized over an urban area with 500,000 inhabitants, there would be 125,000 cases of acute illness, 9,000 cases of chronic Q fever, and 150 fatalities

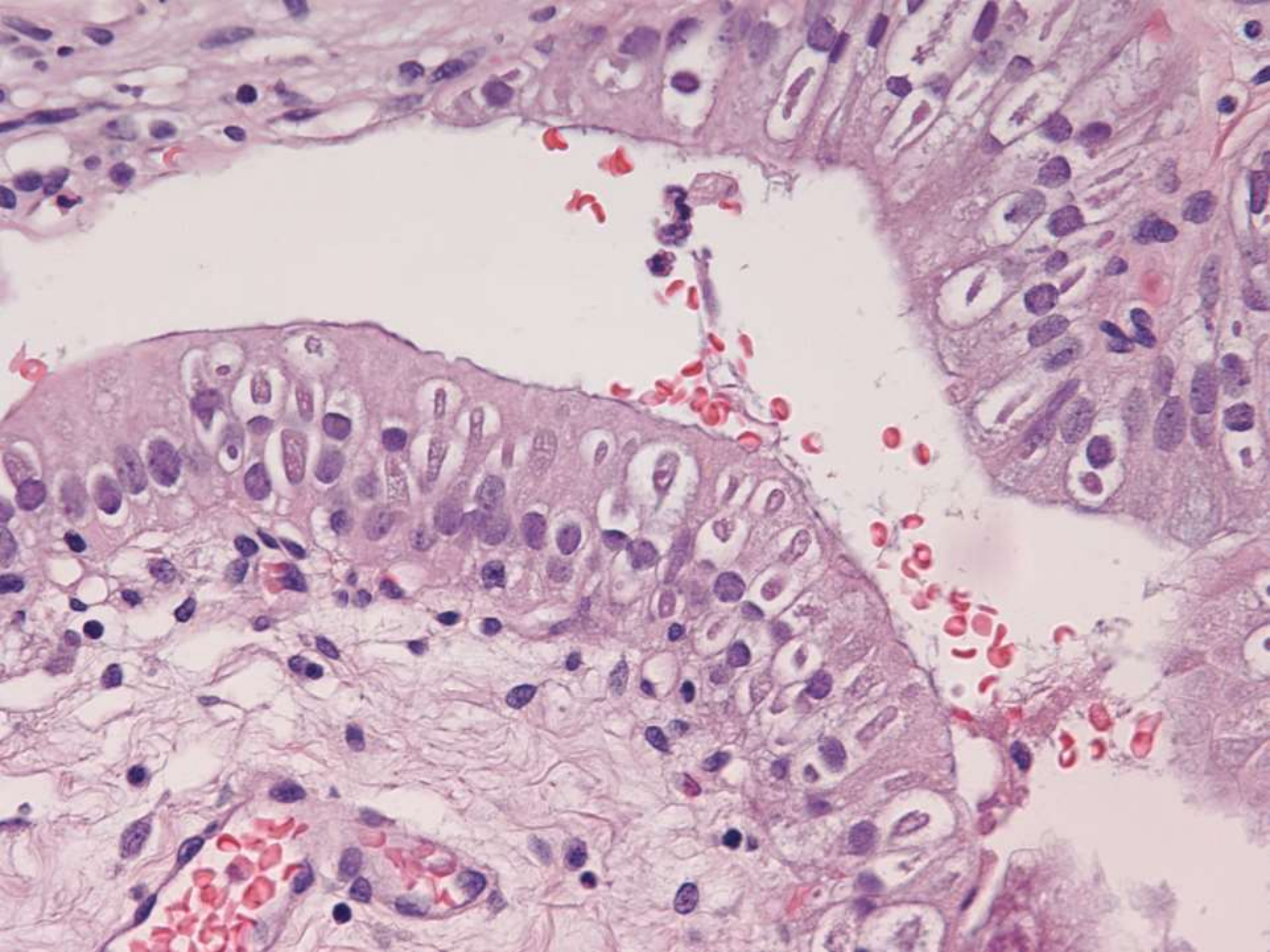
19-0806

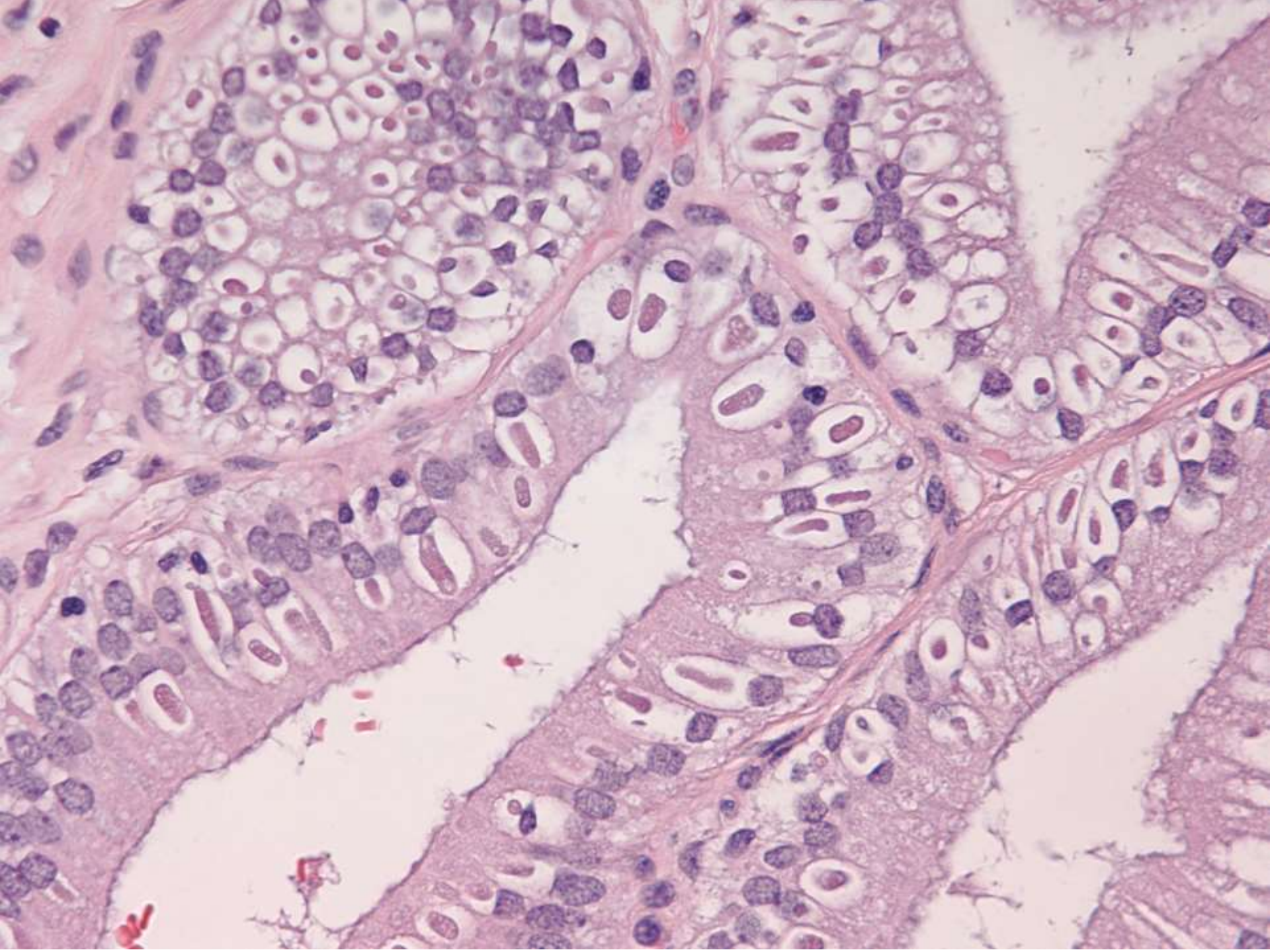
Greg Charville; Stanford

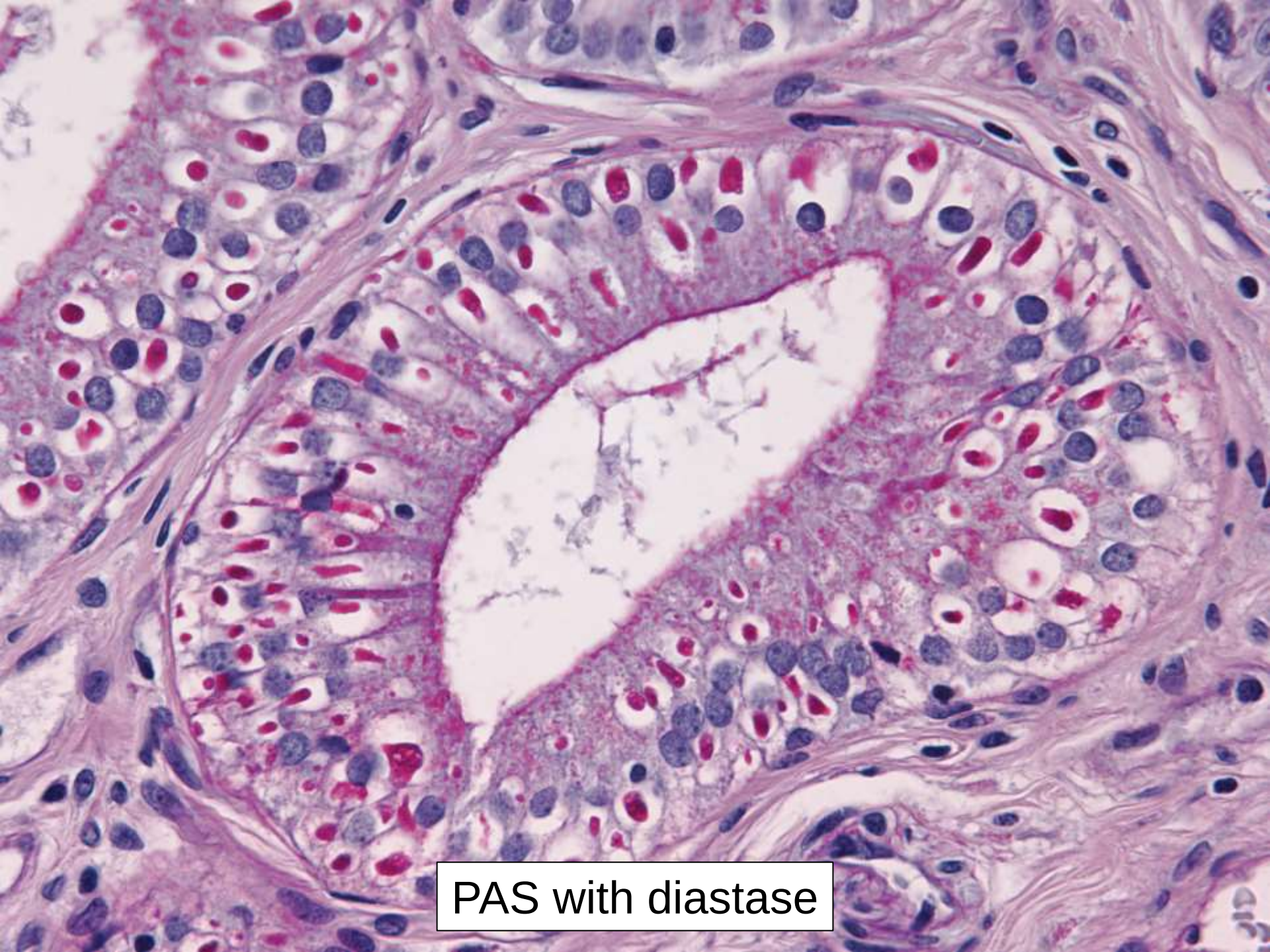
71-year-old undergoing liver transplant for Hepatitis C cirrhosis complicated by HCC. Persistent diarrhea developed 6 days post-transplant. Donor gallbladder specimen submitted.









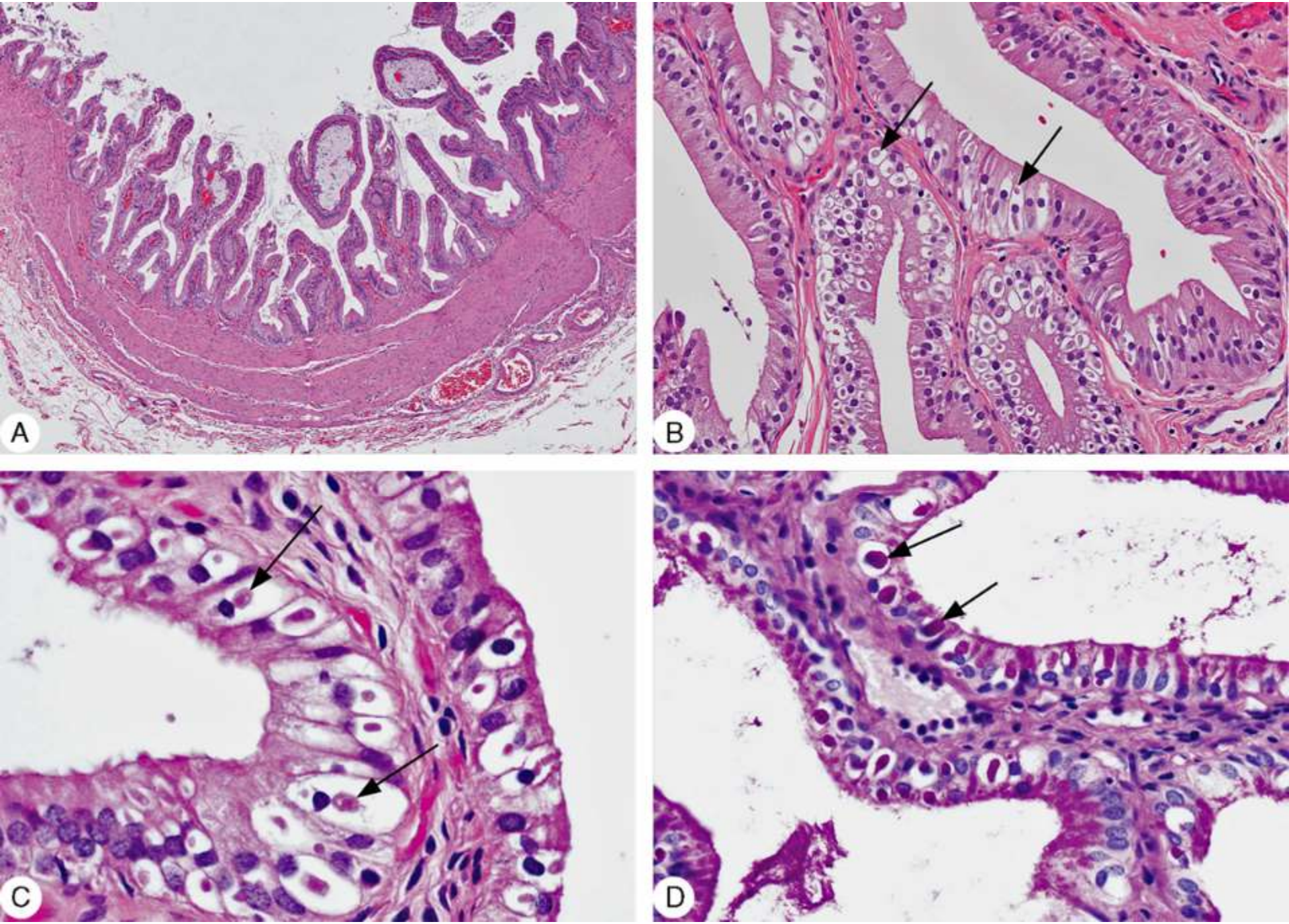

PAS with diastase

Cystoisospora belli Infection of the Gallbladder in Immunocompetent Patients

A Clinicopathologic Review of 18 Cases

Am J Surg Pathol • Volume 40, Number 8, August 2016

- Eosinophilic, oval or banana-shaped intraepithelial parasites
- Most cases showed epithelial disarray and minimal intraepithelial lymphocytosis
- 2 cases represented donor gallbladders from transplant
- Of the 11 cases with an average follow-up of 15 months, none had evidence of disease related to Cystoisospora infection within the biliary tract or elsewhere in the gastrointestinal tract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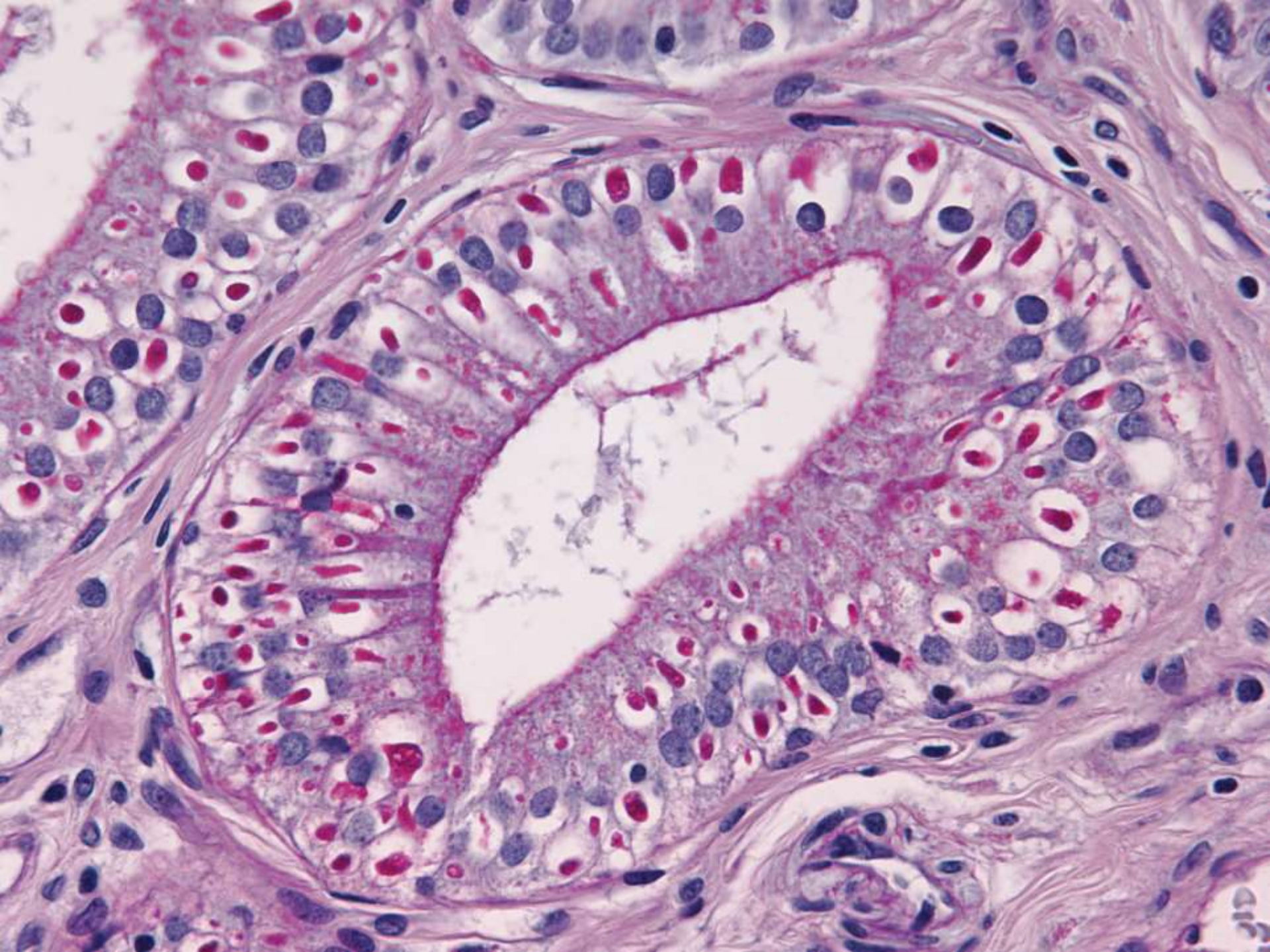
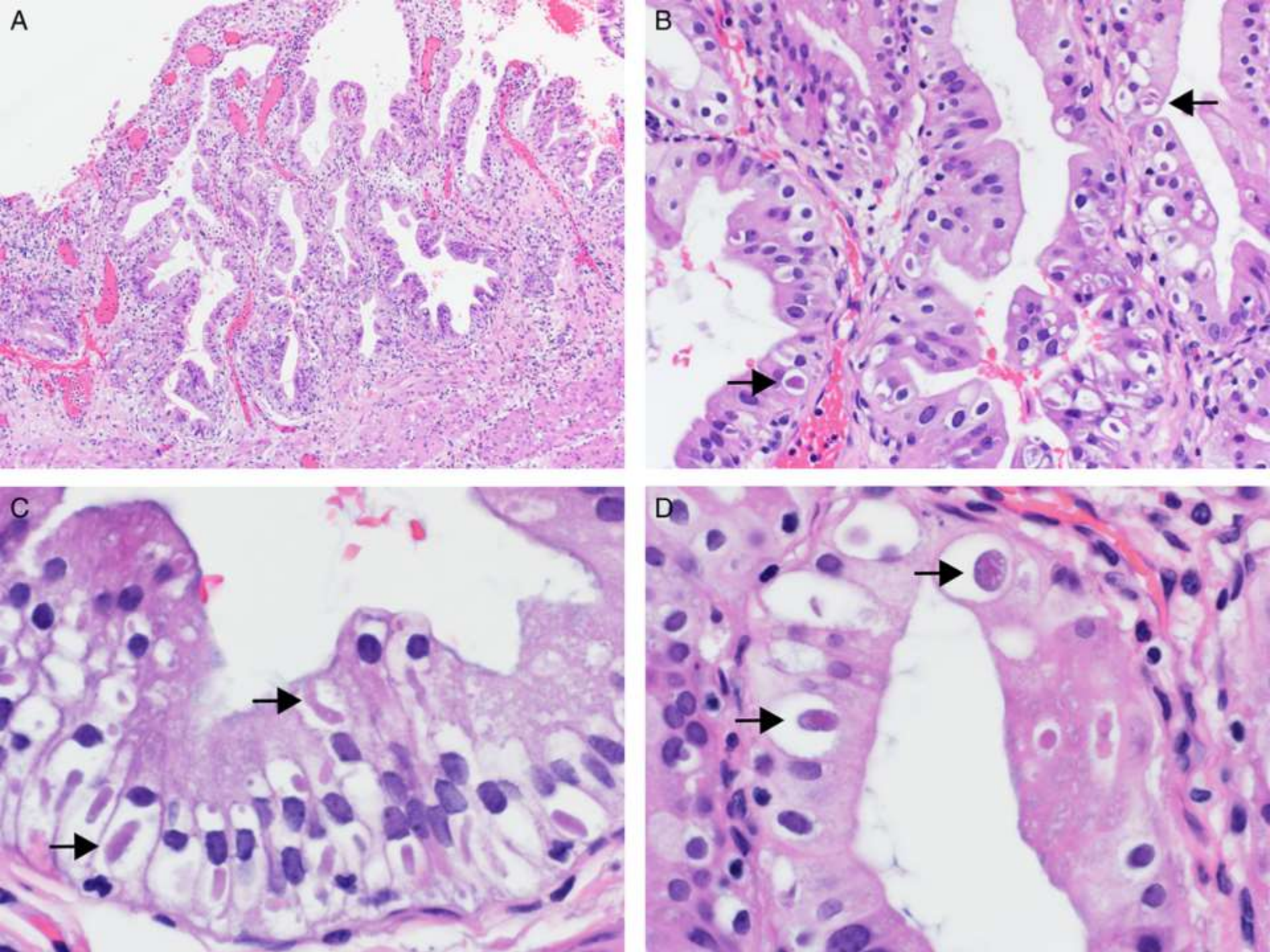


Epithelial Inclusions in Gallbladder Specimens Mimic Parasite Infection

Histologic and Molecular Examination of Reported Cystoisospora belli Infection in Gallbladders of Immunocompetent Patients

Am J Surg Pathol • Volume 42, Number 10, October 2018

- 8 cases with presumed C belli infection, 3 positive controls
- All 8 gallbladder cases were negative for C belli by PCR
- Epithelial inclusions stained positive by GMS/PAS-D, C belli were GMS-negative and had a distinct staining pattern on PAS-D
- Artifact of epithelial cytolysis related to tissue preservation – may be more common in gallbladders that remain intact for longer periods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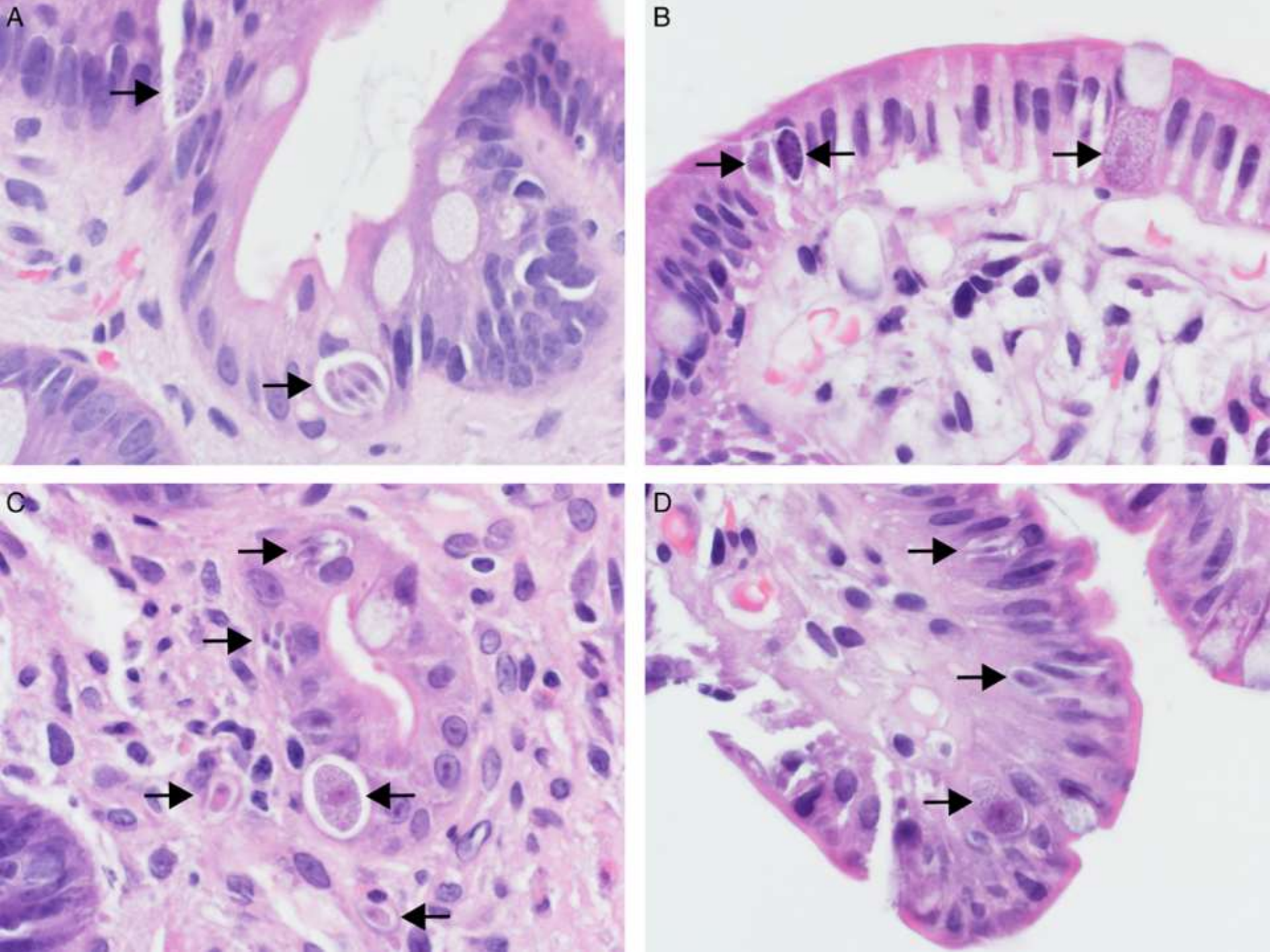
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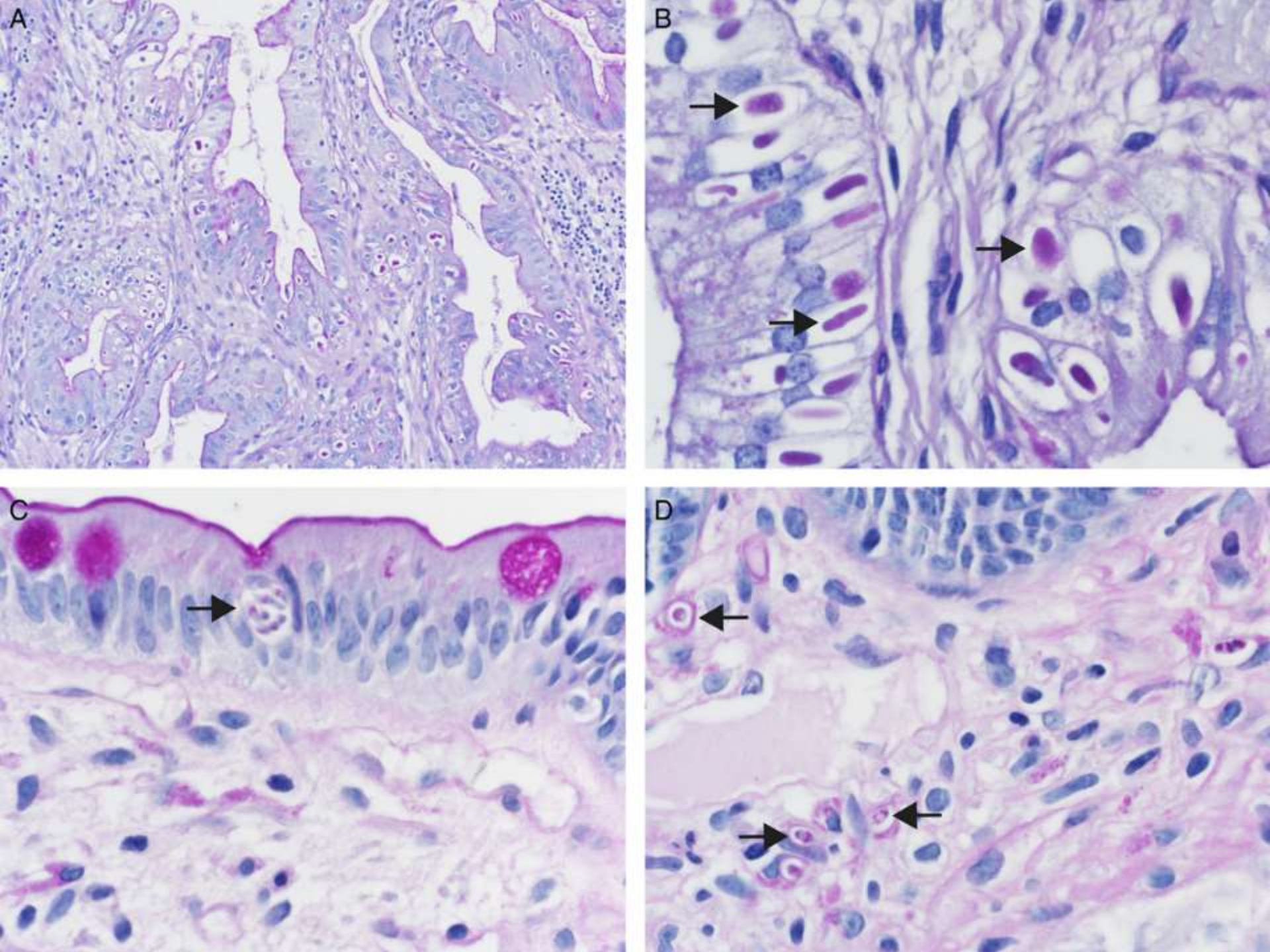
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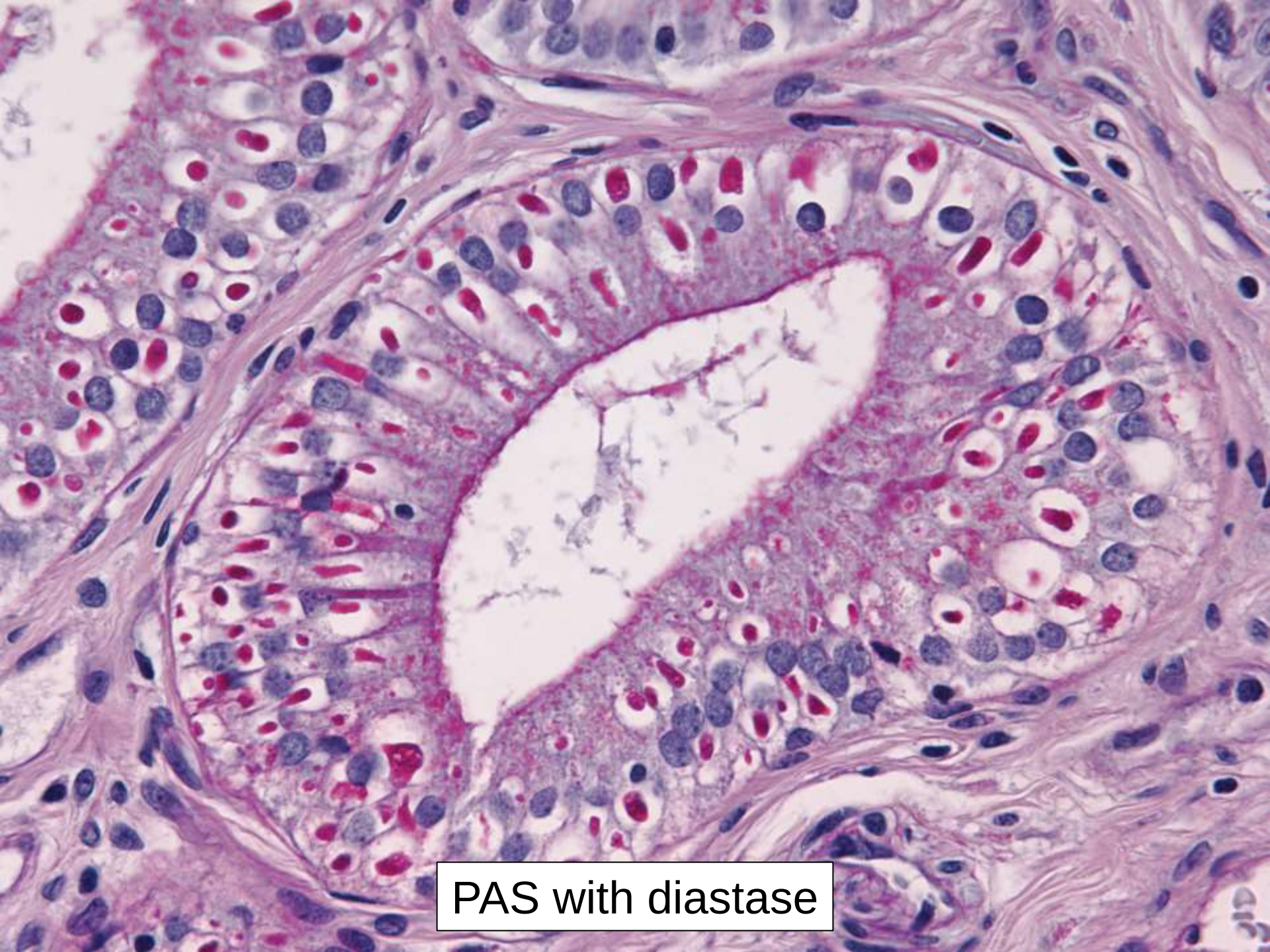
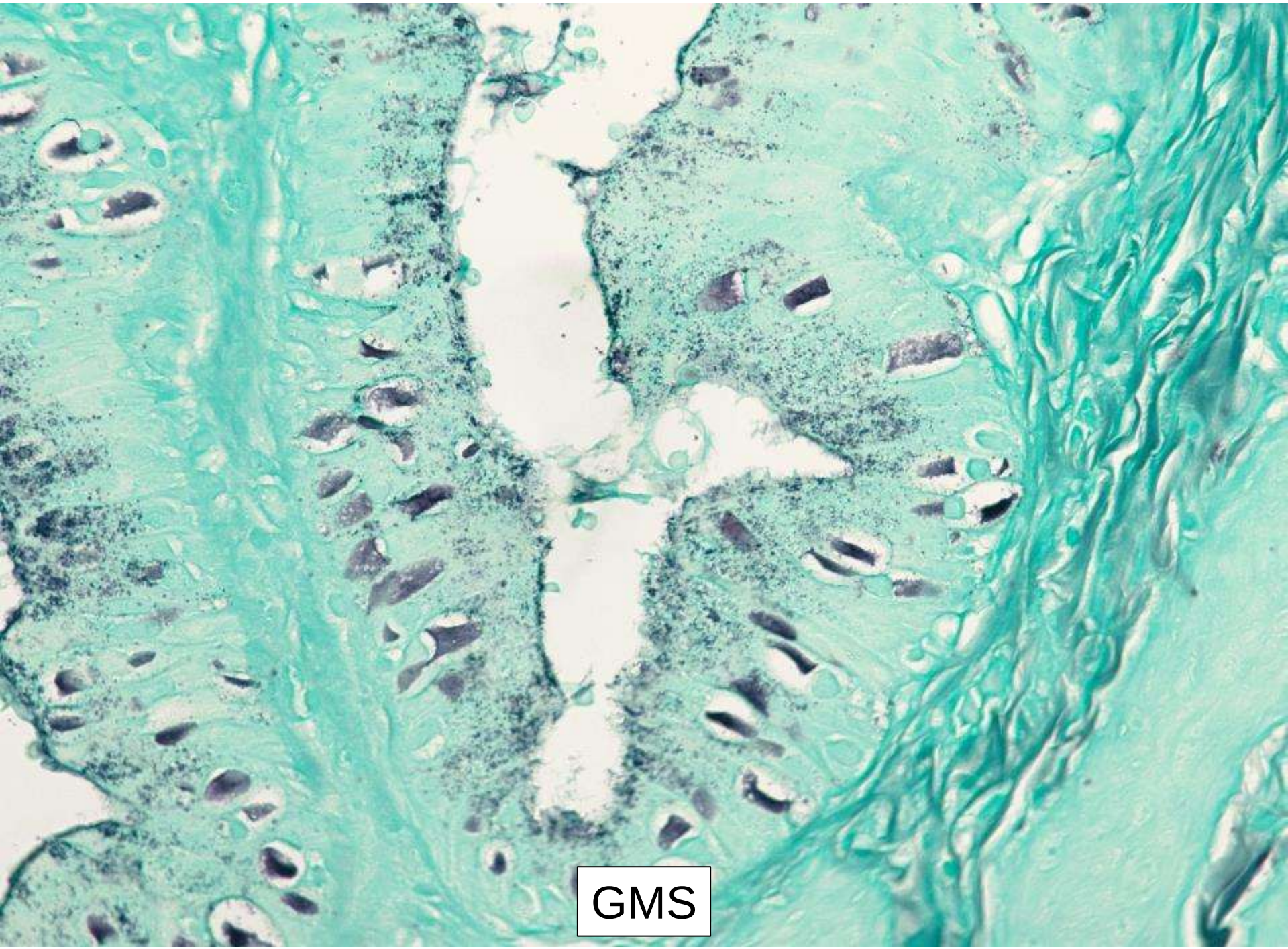

PAS with diastase


GMS

Gallbladder epithelial inclusions mimicking parasites

- Diagnosis: chronic cholecystitis
- Follow-up: Patient had *C. difficile* infection
  - Treated with antibiotics and diarrhea resolved
- Epithelial inclusions in the gallbladder should be interpreted with caution

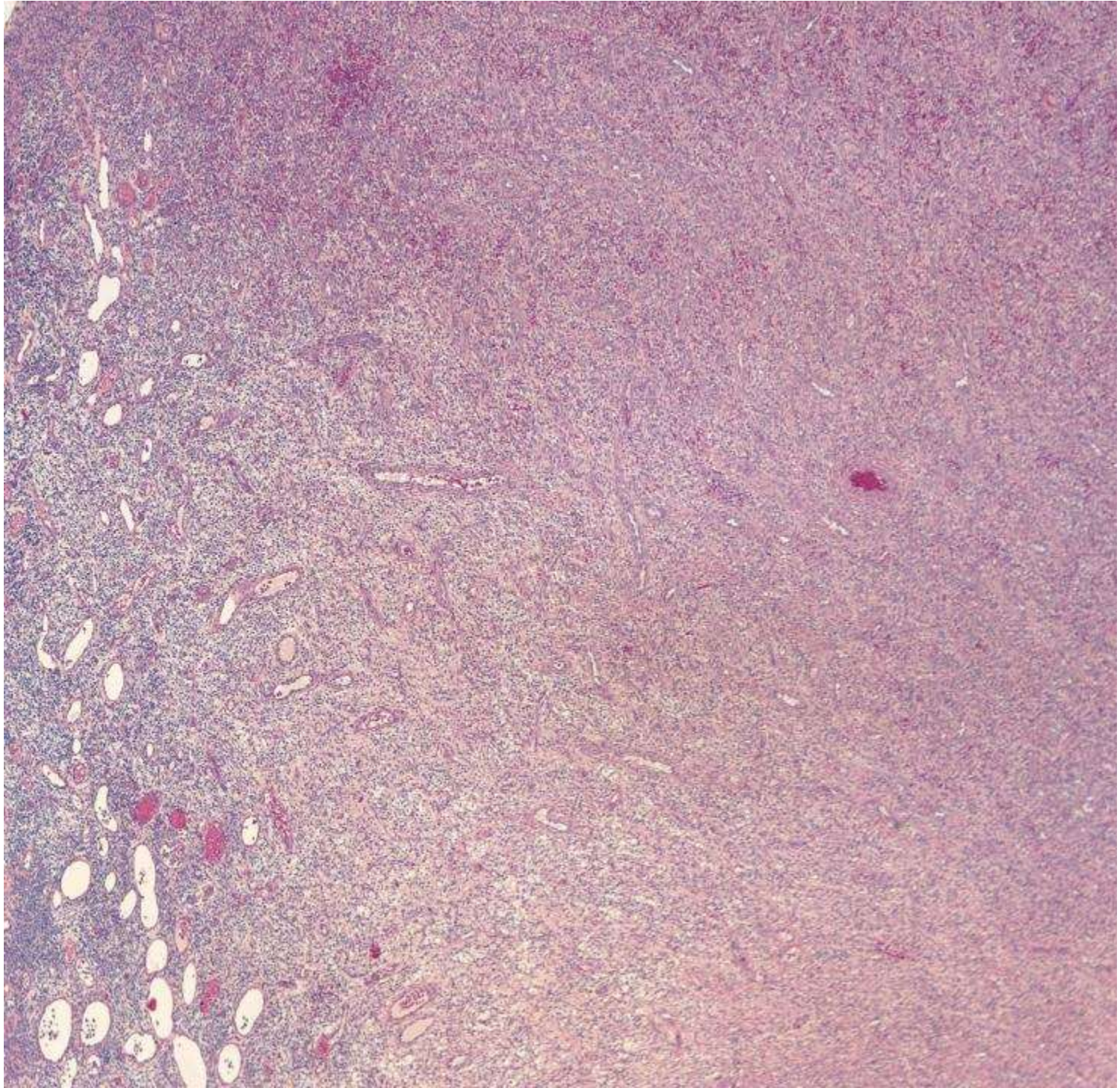
19-0807

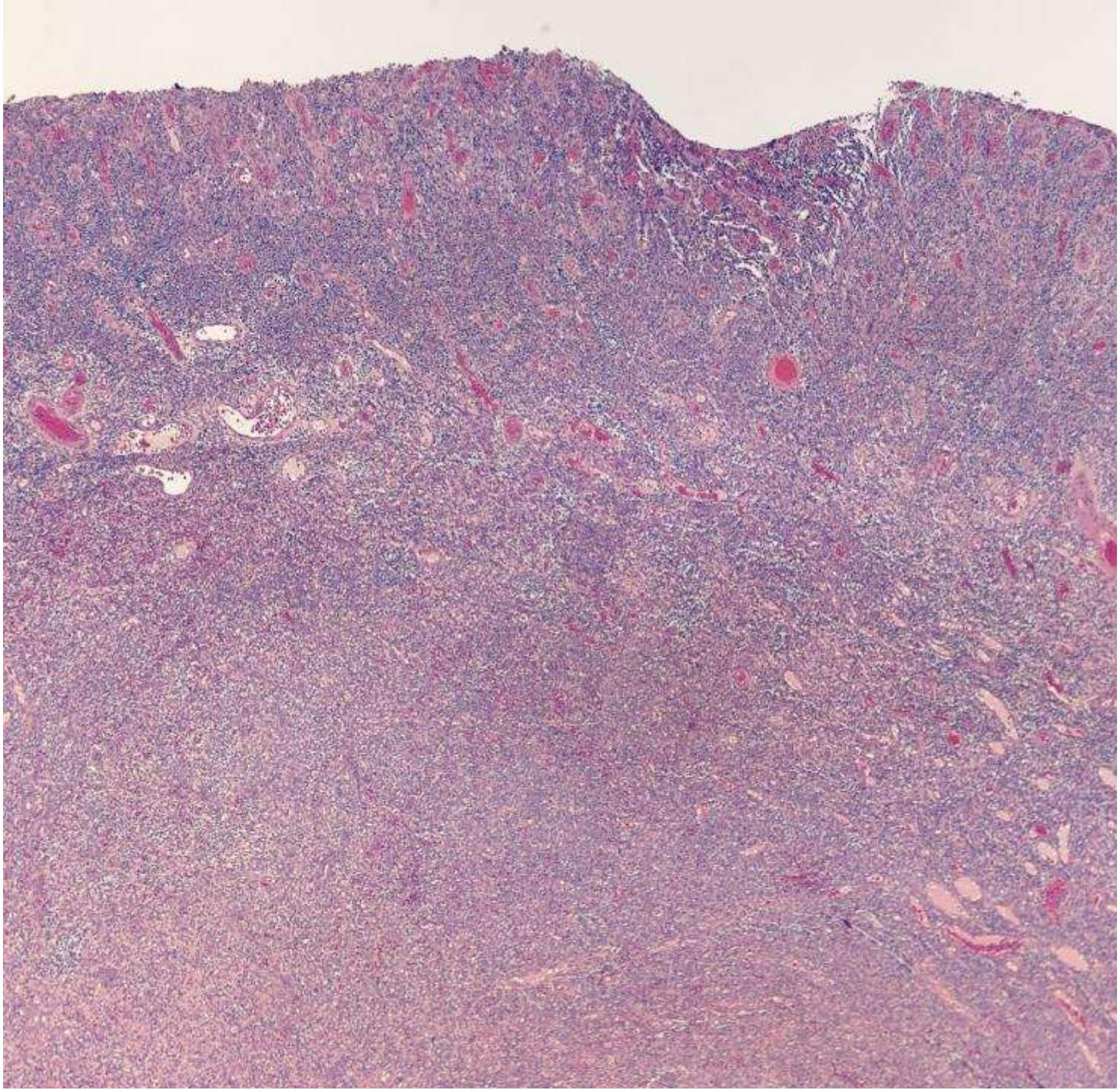
Shyam Raghavan/Greg Charville; Stanford

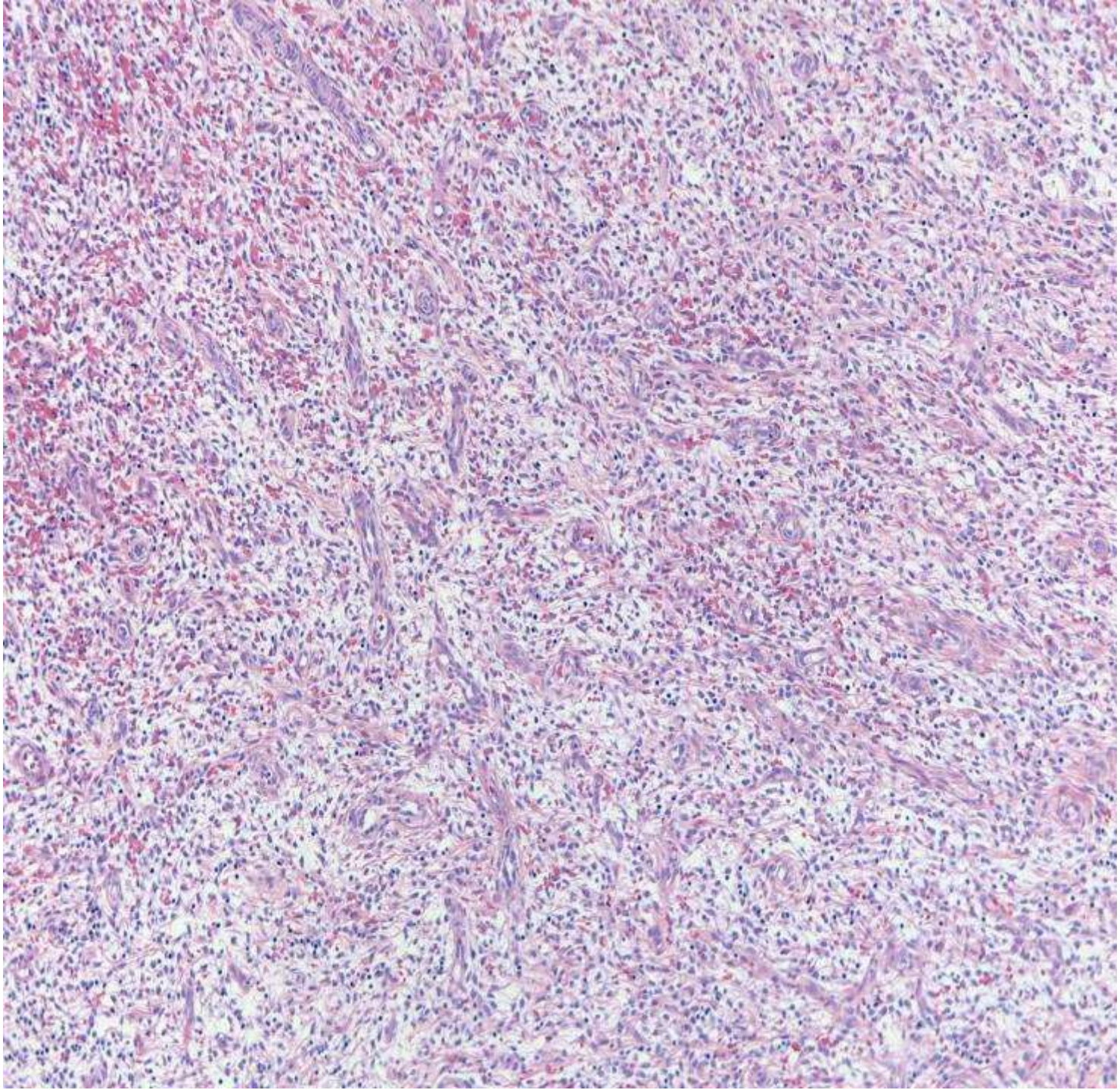
68-year-old woman with sessile sigmoid colon mass.

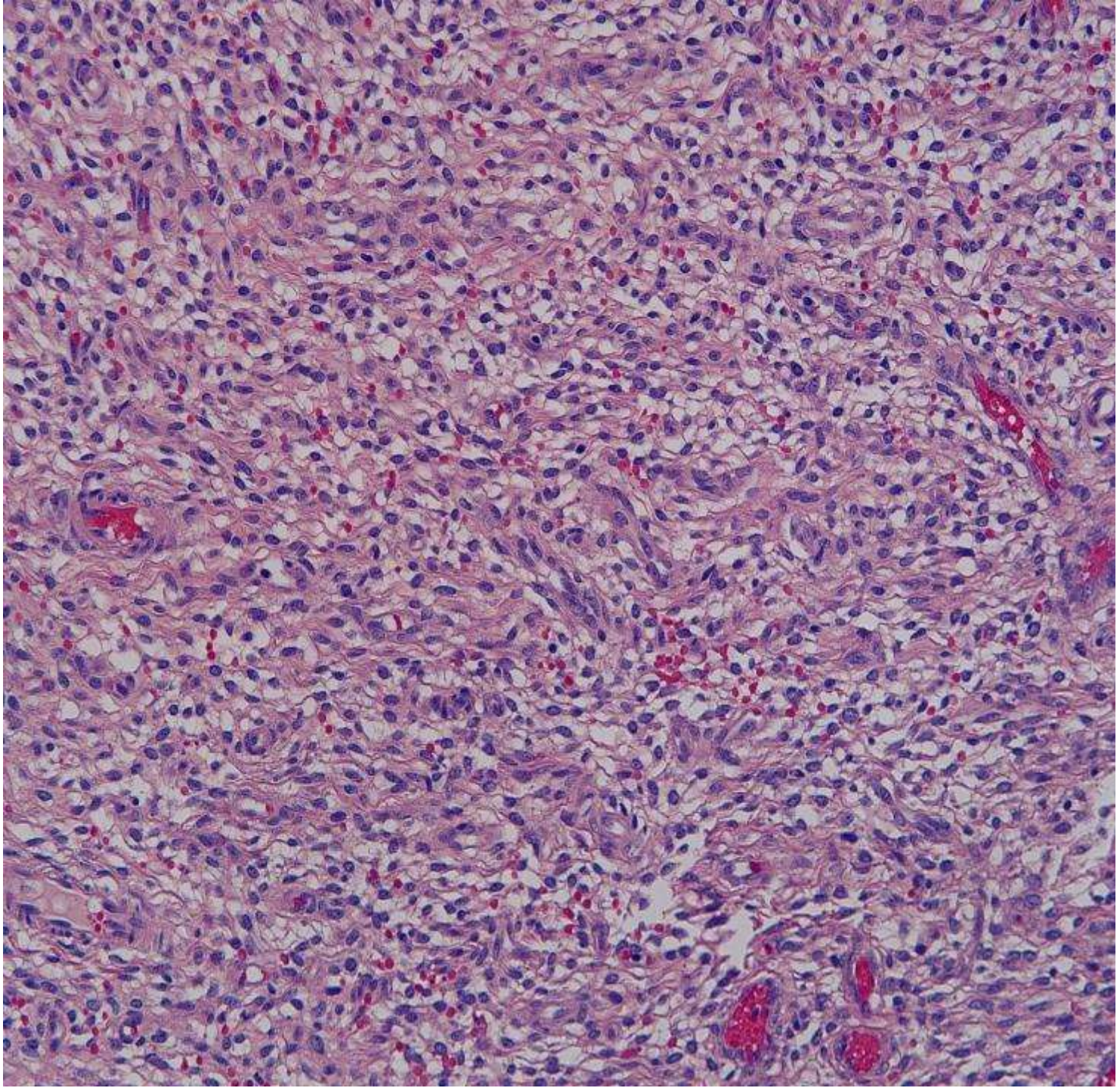
Clinical History

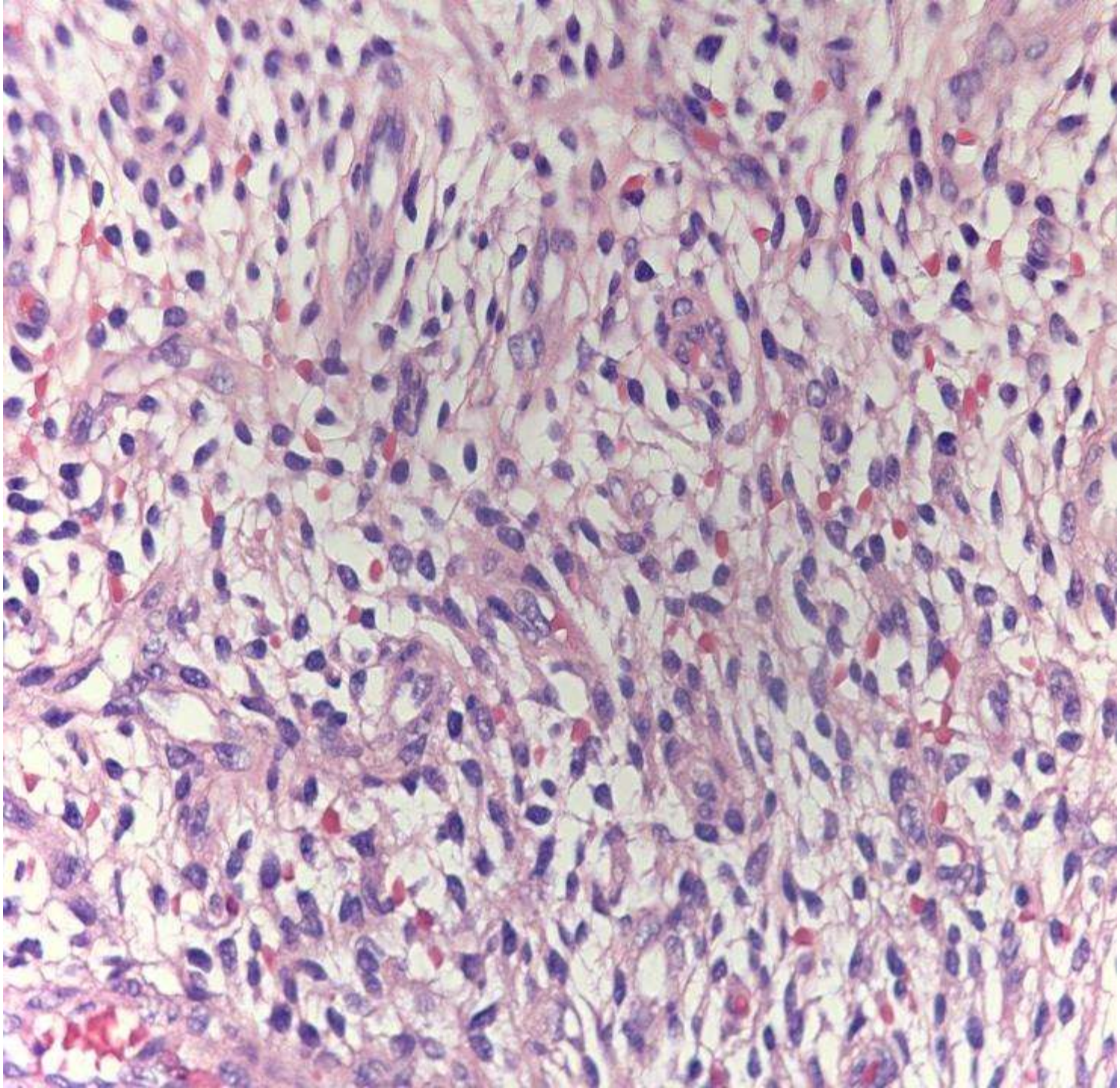
- 68 year old female with a rectosigmoid mass, identified on routine screening colonoscopy
- No relevant PMH, PSH, Meds
- Endoscopically appeared a sessile broad based partially ulcerated mass

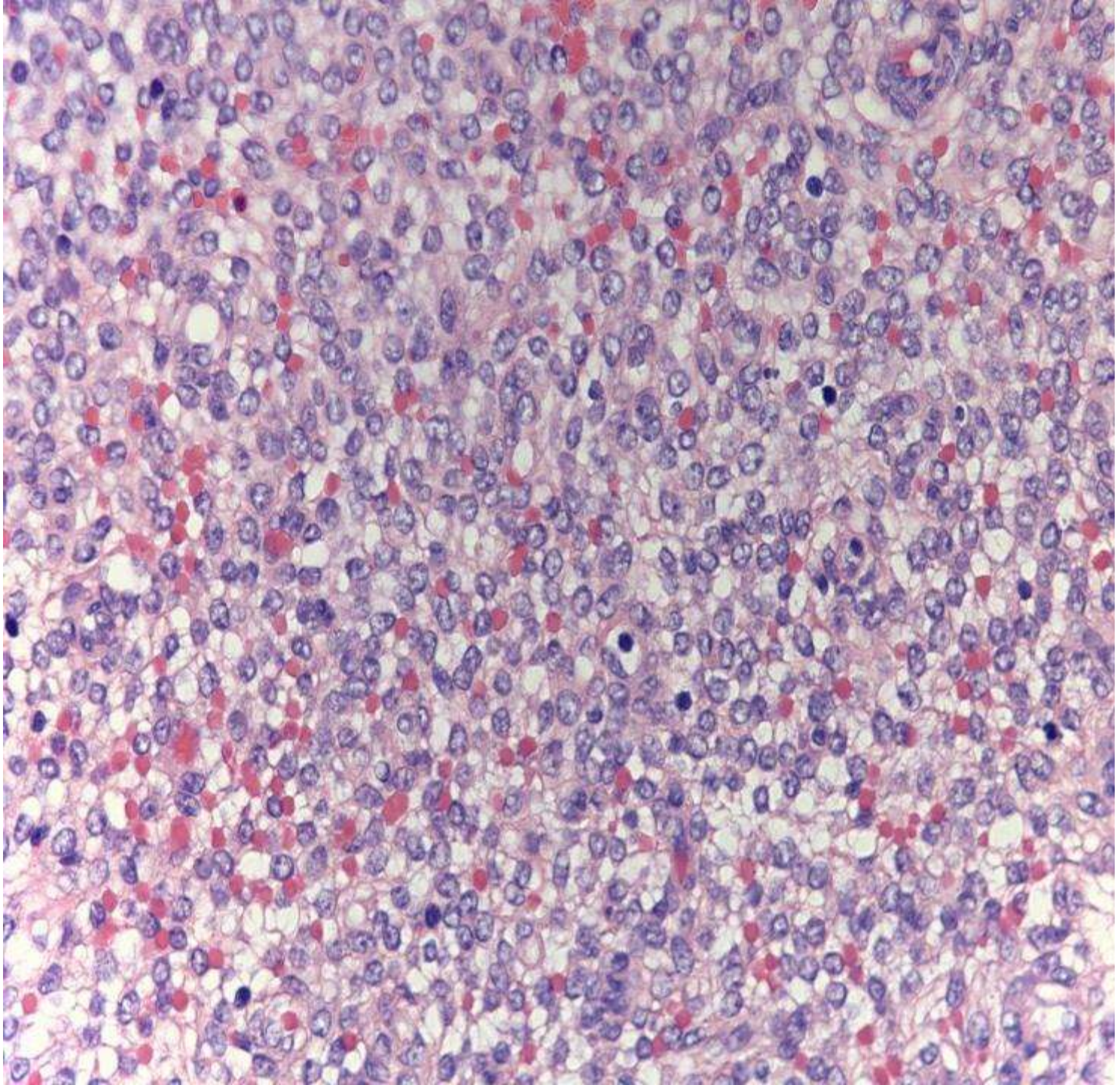


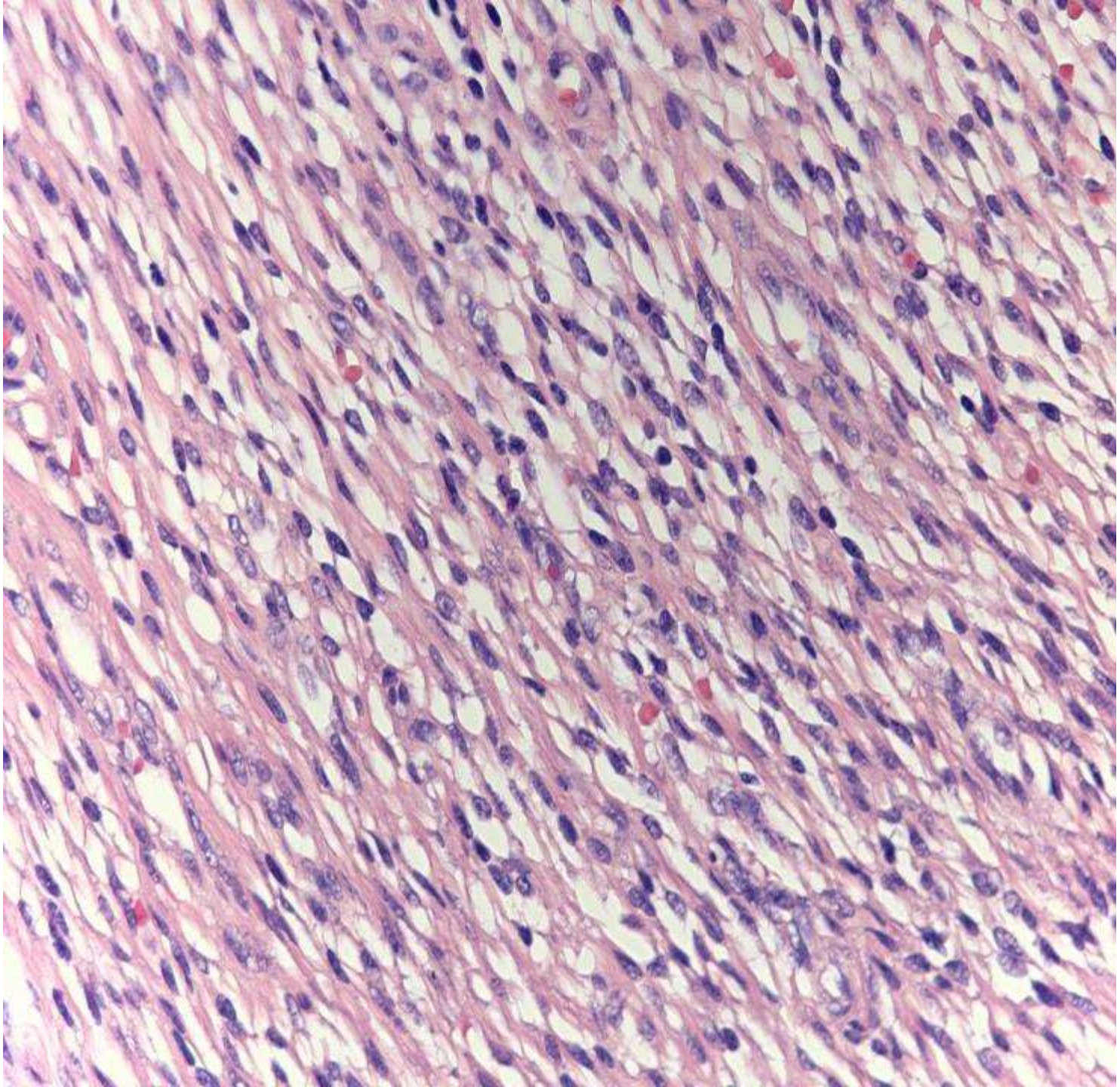


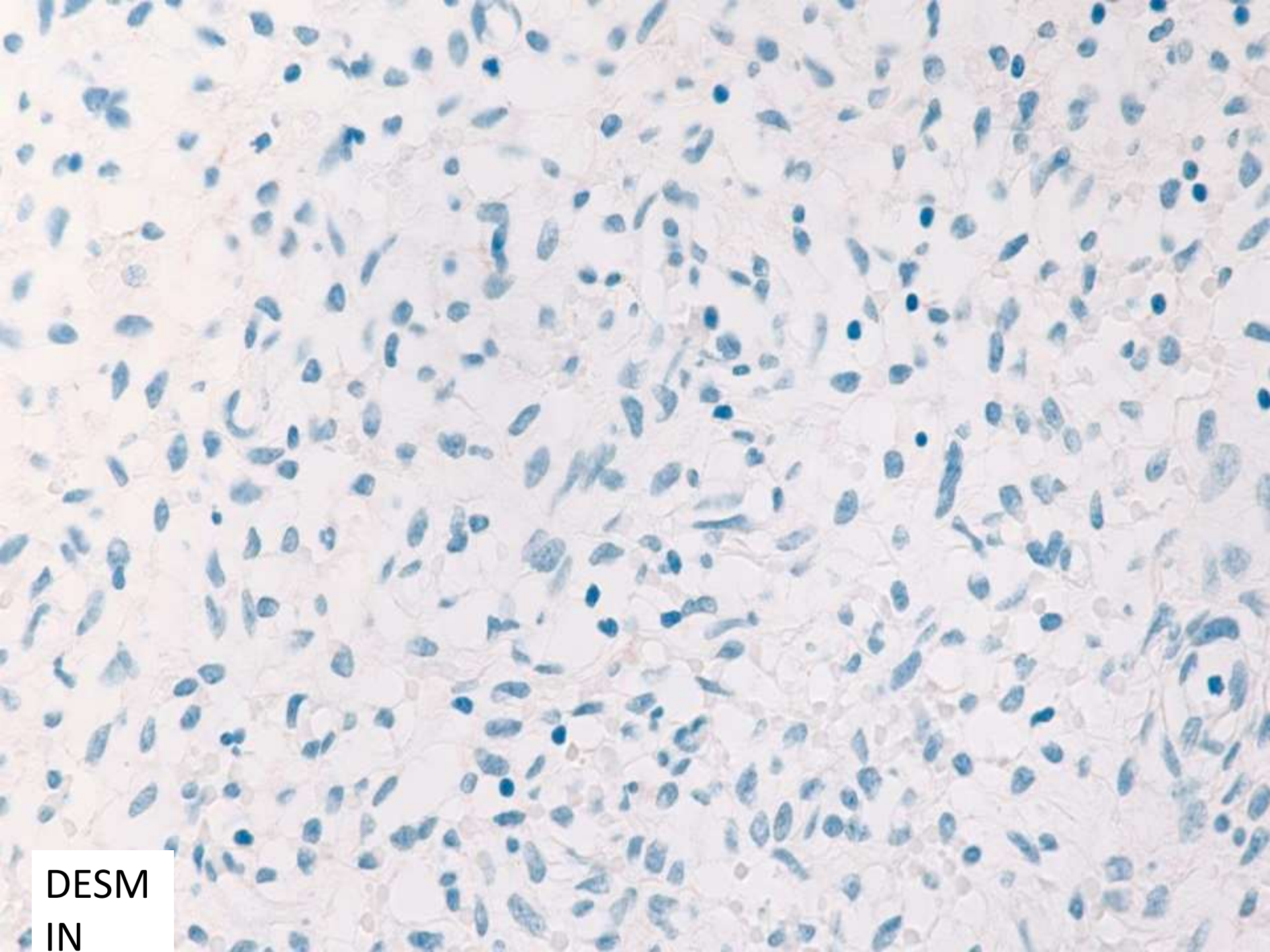


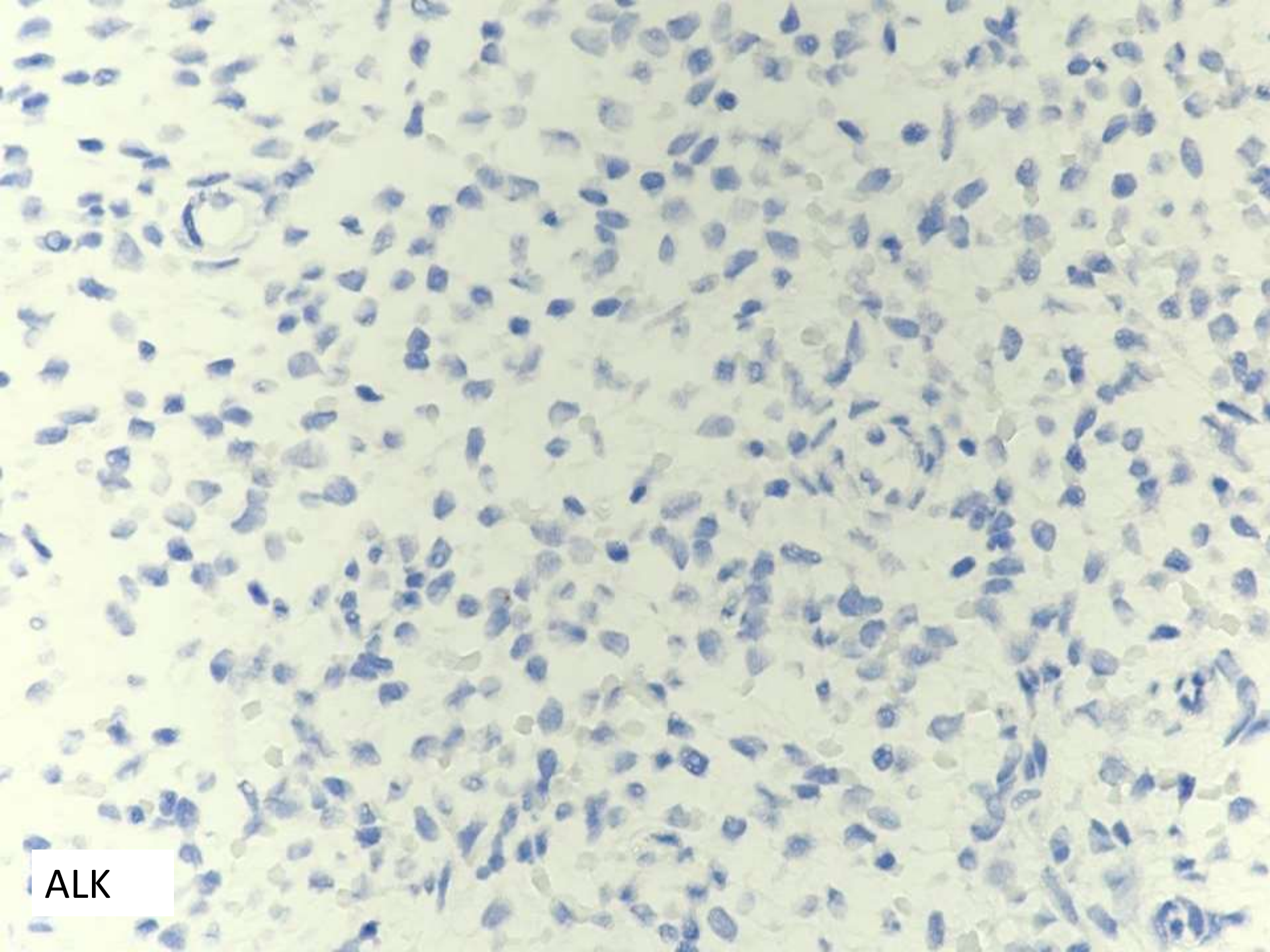


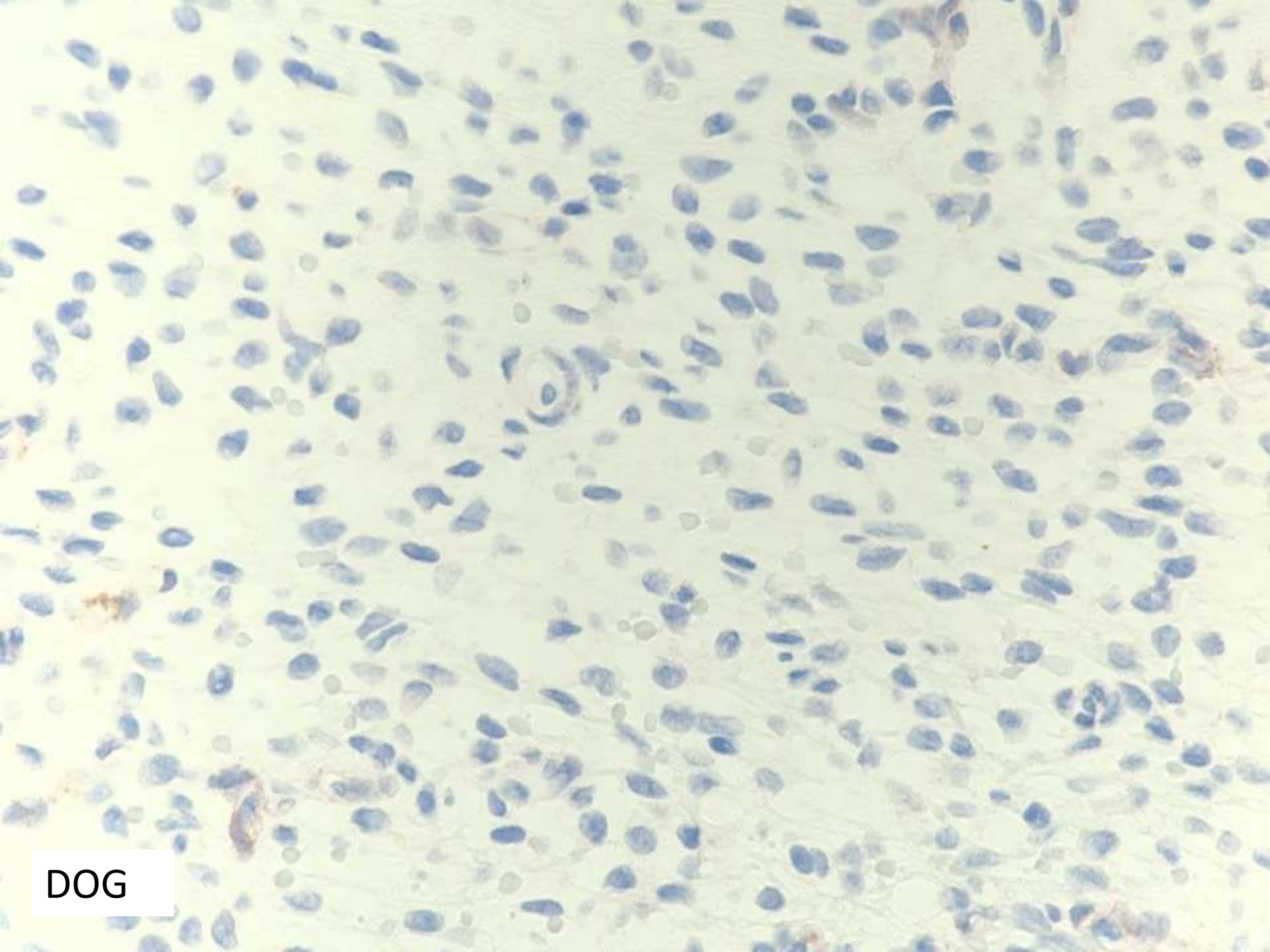


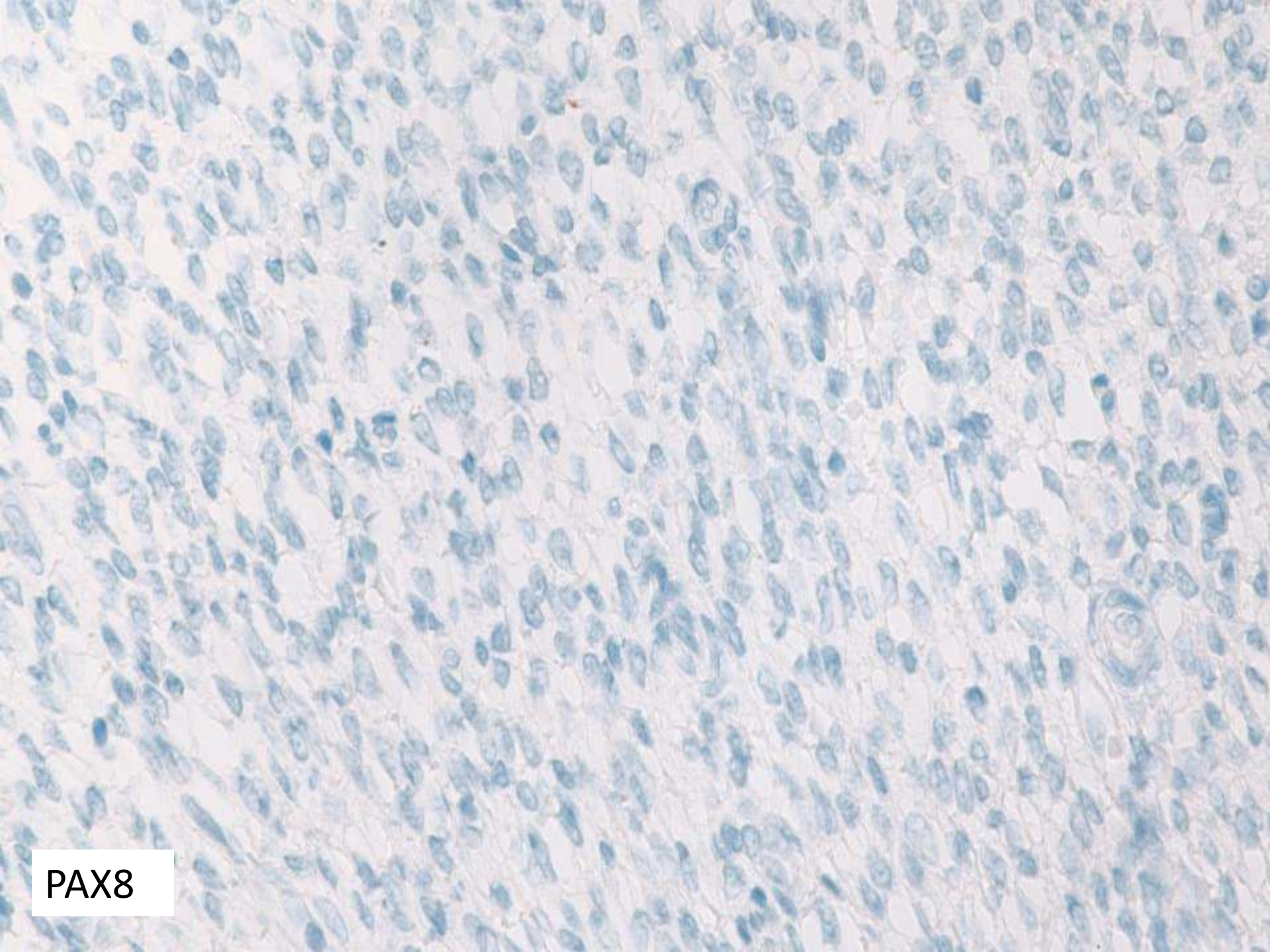





DESM
IN


ALK


DOG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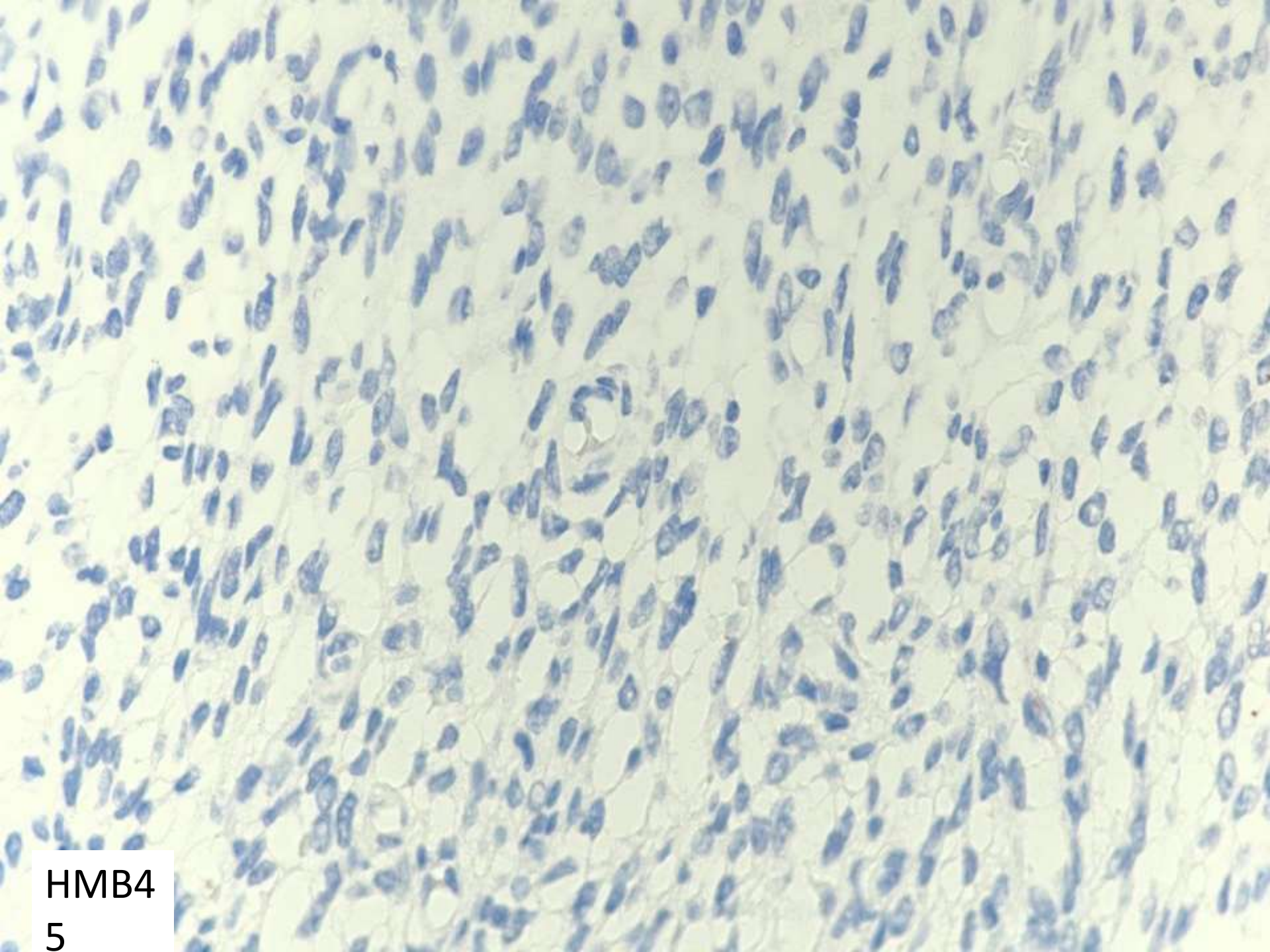
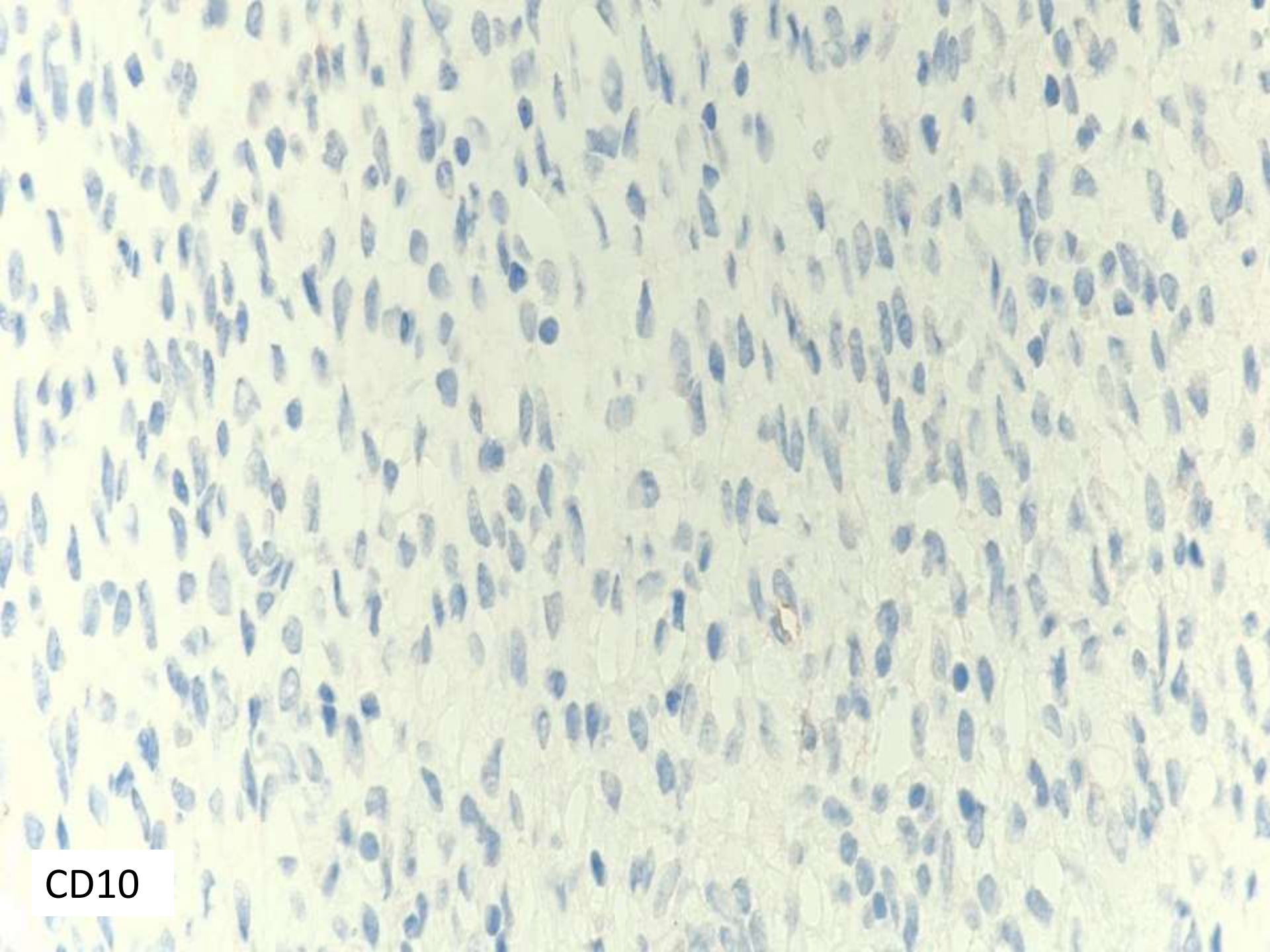
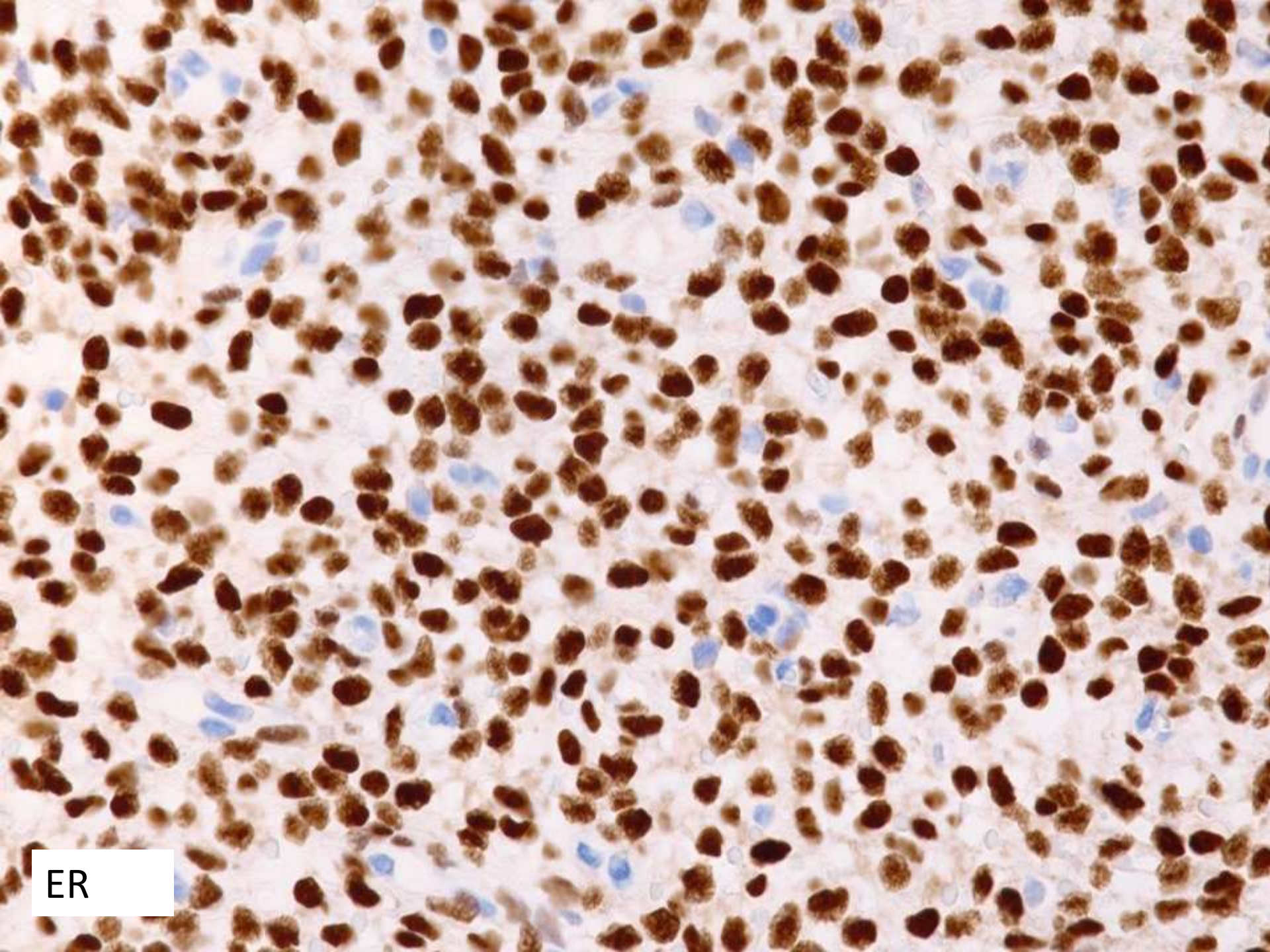

HMB4
5


CD10


ER

Diagnostics

- Rearrangement in JAZF1 (95%)
- No re-arrangmenet in PHF1
- **INVOLVED BY LOW GRADE ENDOMETRIAL STROMAL SARCOMA**

Frequency of Known Gene Rearrangements in Endometrial Stromal Tumors

Sarah Chiang, MD, Rola Ali, MD,† Nataliya Melnyk, BS,† Jessica N. McAlpine, MD,‡ David G. Huntsman, MD,† C. Blake Gilks, MD,† Cheng-Han Lee, MD, PhD,† and Esther Oliva, MD**

Low grade endometrial Stromal Sarcoma

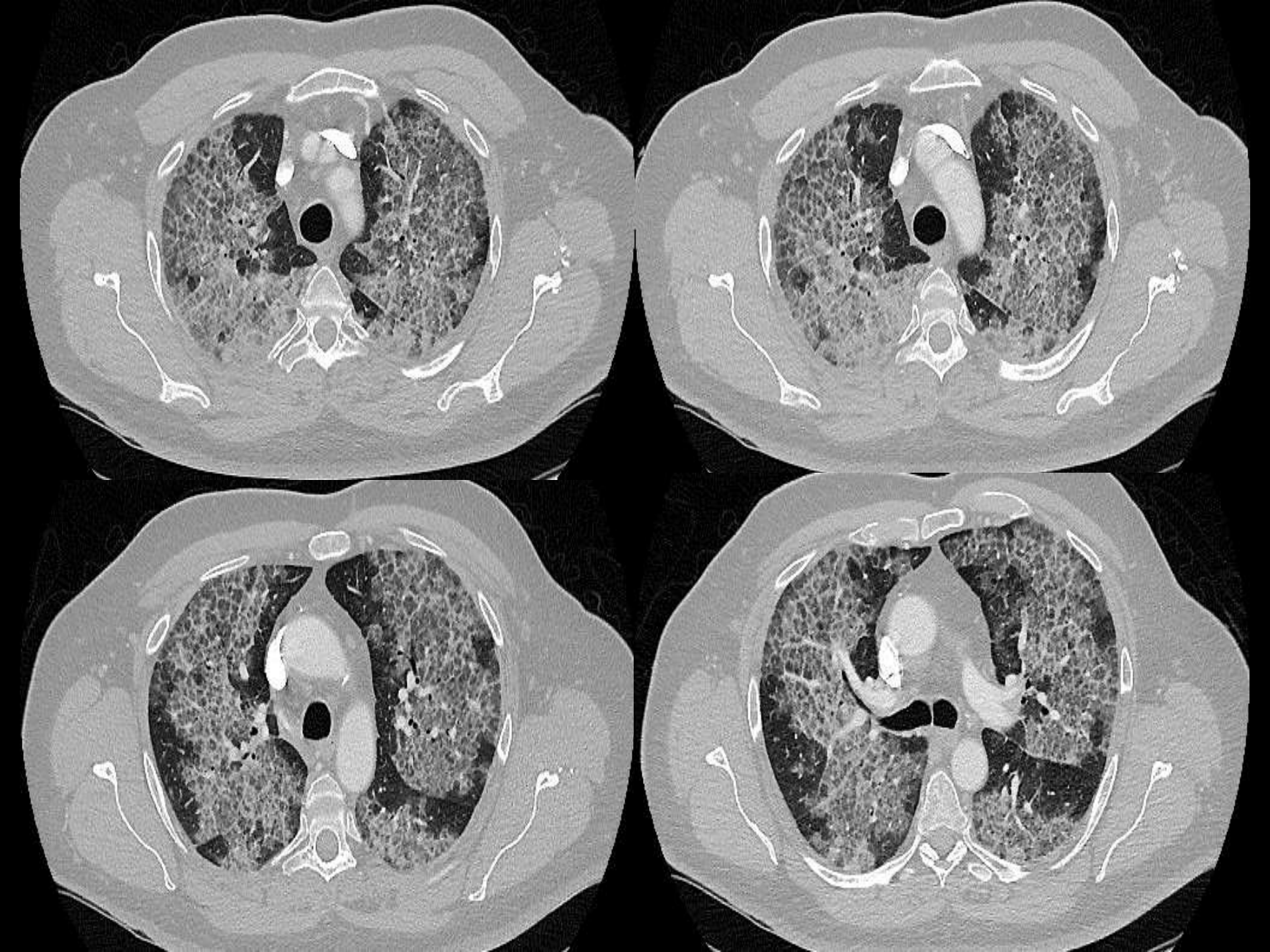
- Typically show rearrangements in *JAZF1, SUZ12 or PHF1*
- Diffuse CD10+ (usually)
- Diffuse ER+ and PR+
- Usually occur in women in the 4^{th}-5^{th} decade and often presents as a painless intrabdominal mass.
- They can extend through direct extension or through vascular metastasis.
- High-grade: *YWHAE and BCOR* translocations.

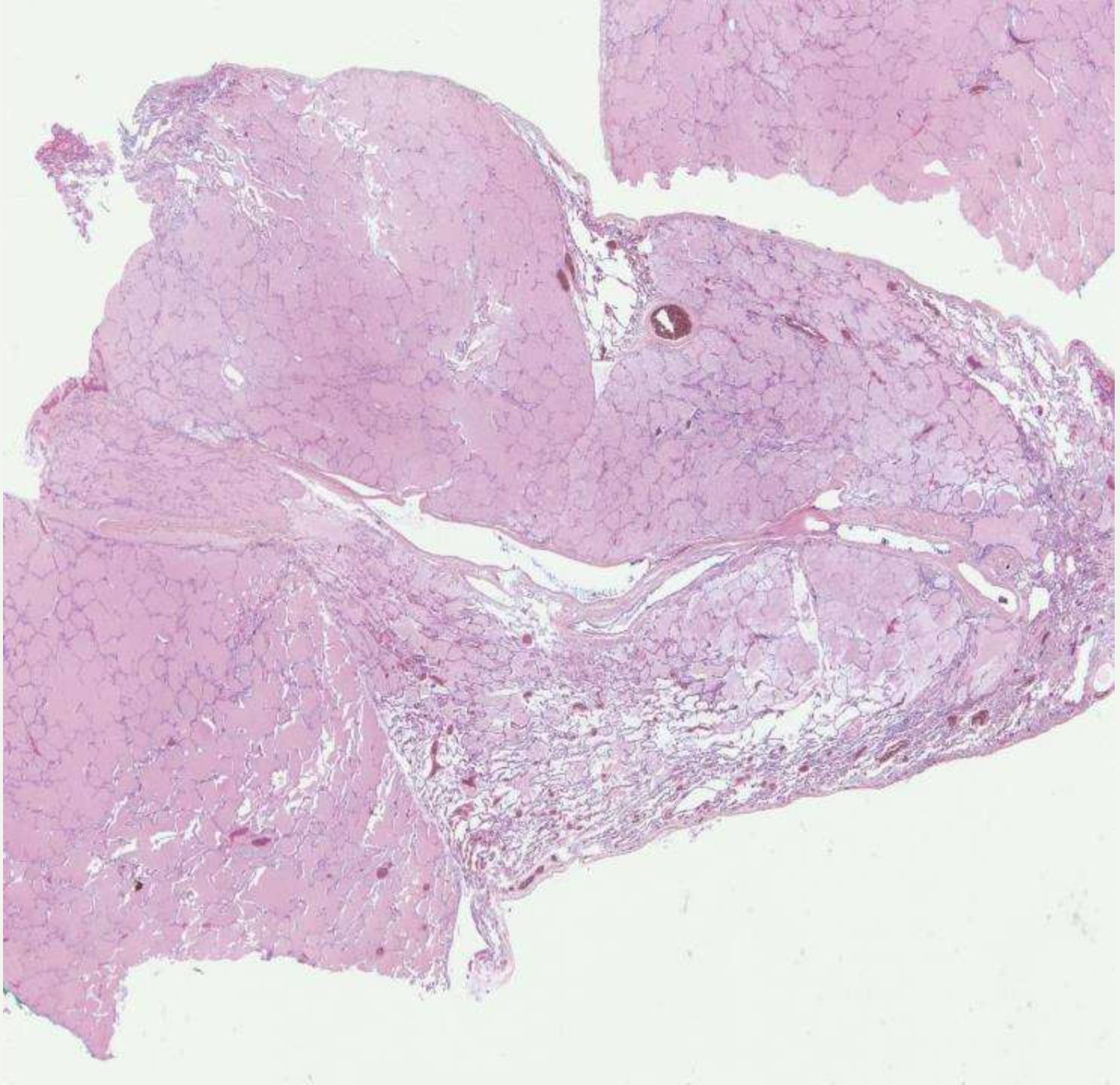
19-0808

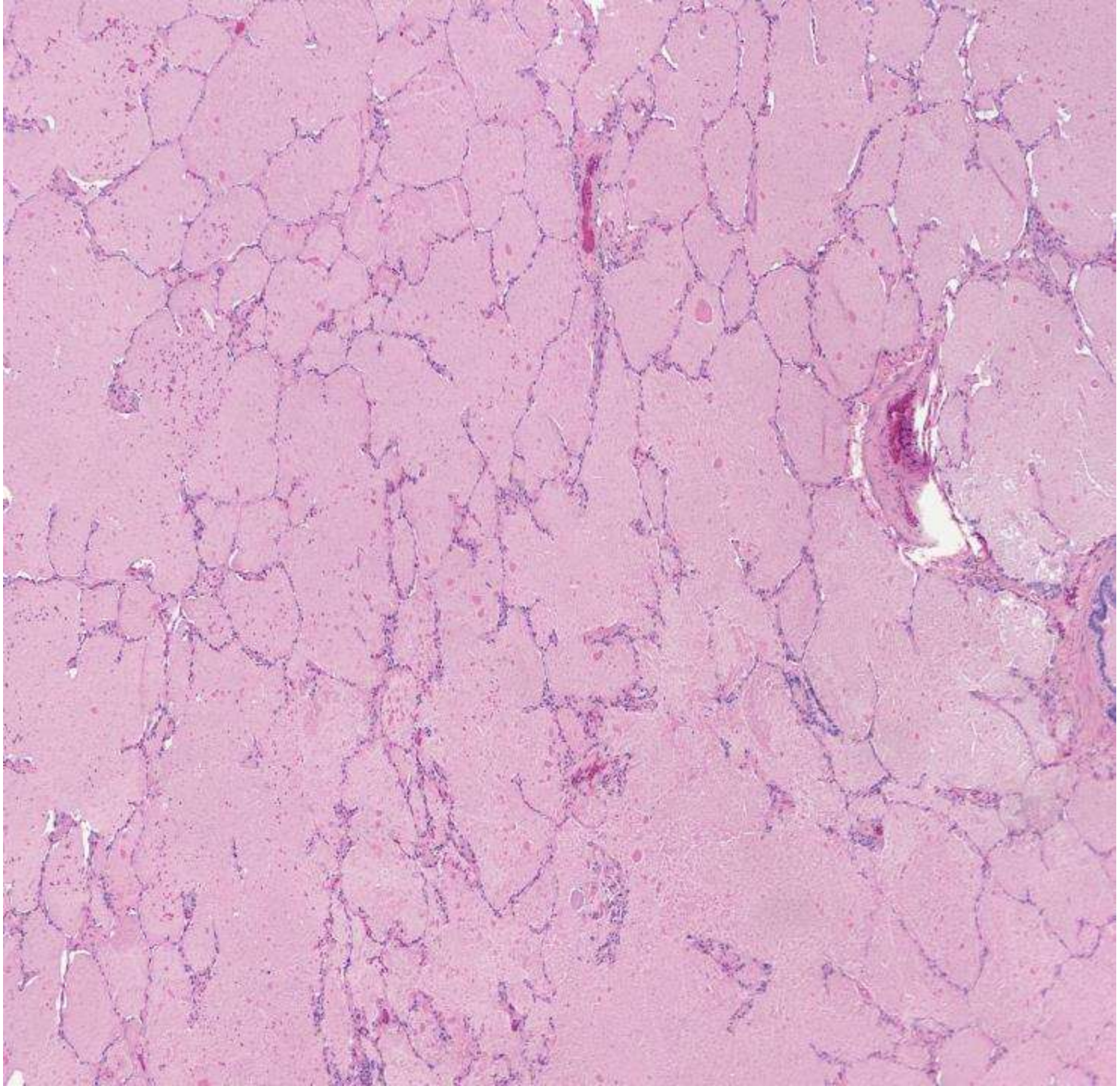
Kevin Kolahi/Kristin Jensen/Christine Louie; VA Hospital Palo Alto

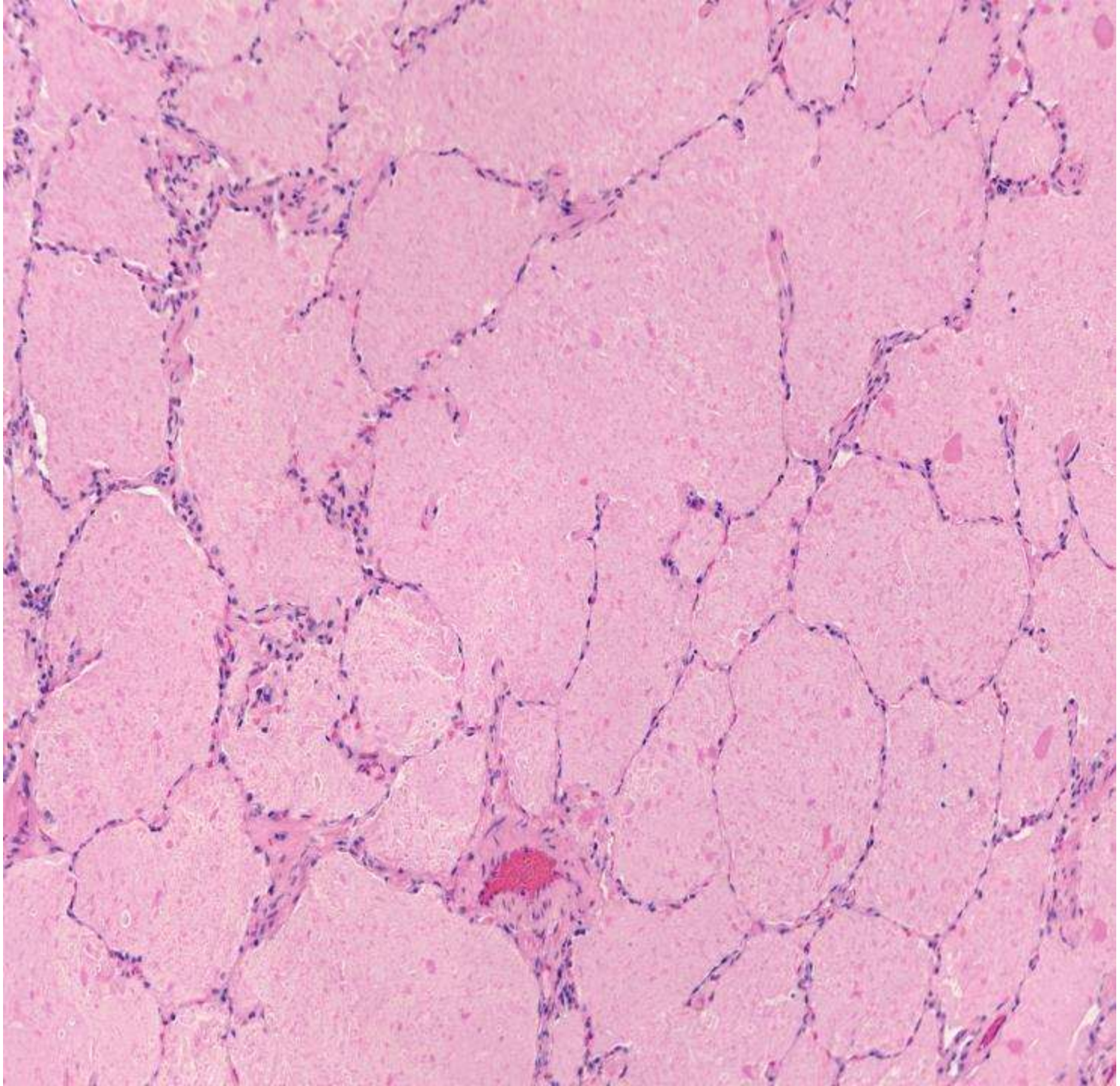
65-year-old with slowly progressive dyspnea on exertion and bilateral lung opacities discovered on chest CT.

L
78

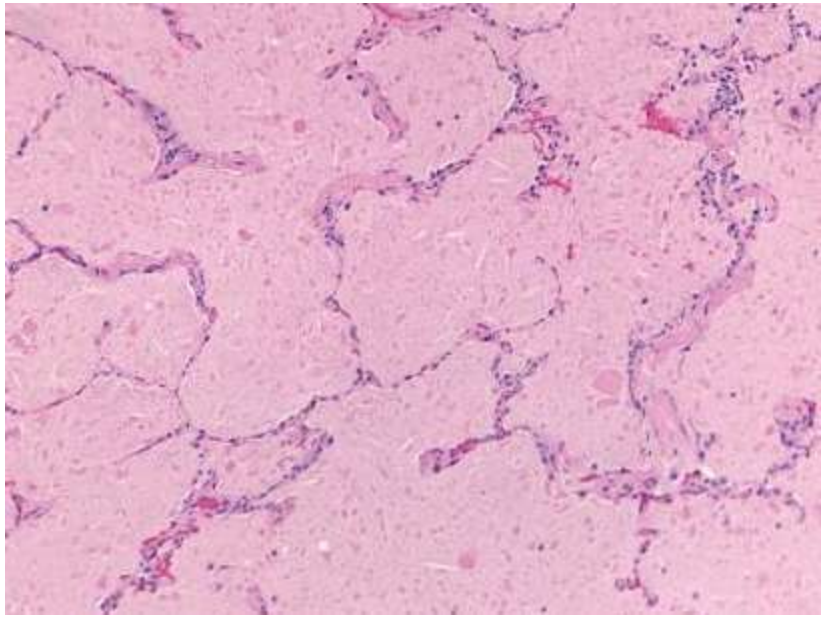




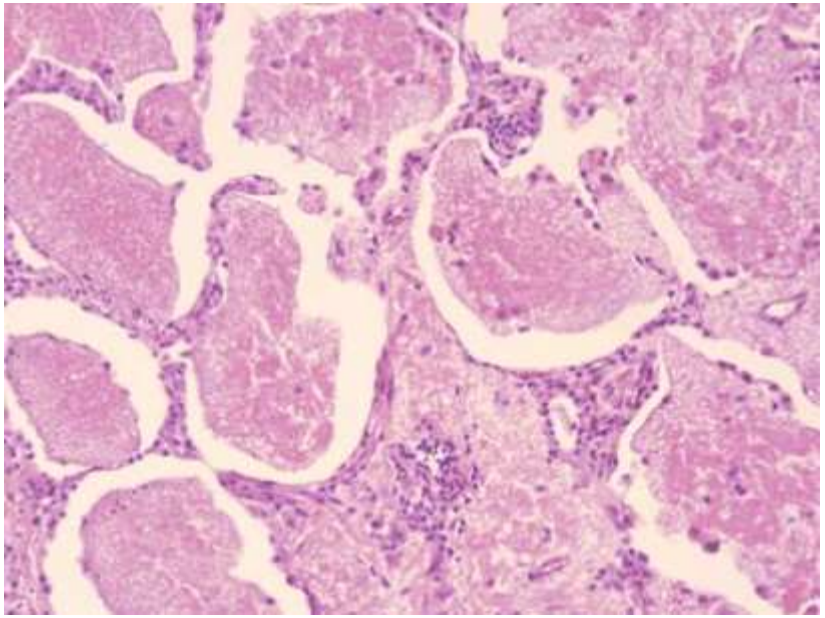




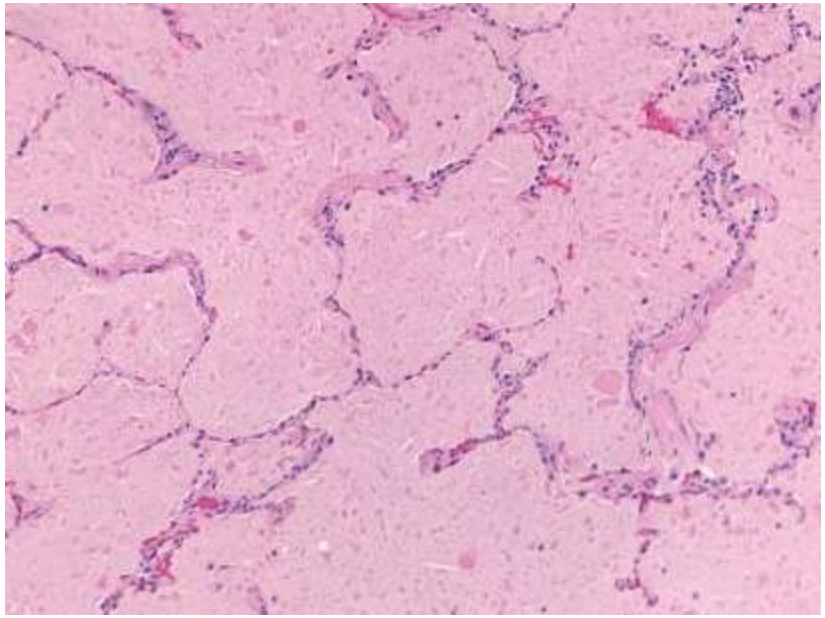
Pulmonary Alveolar Proteinosis



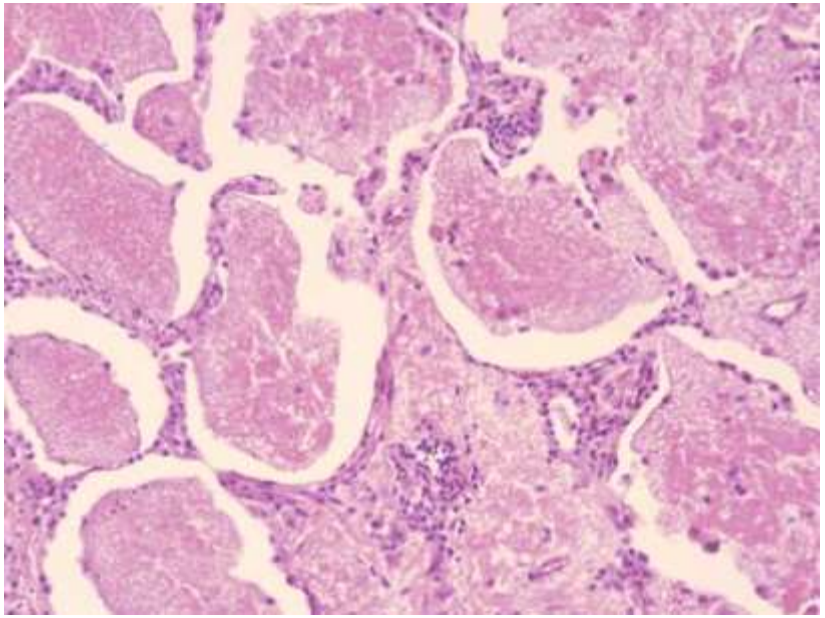
Pneumocystis Pneumonia

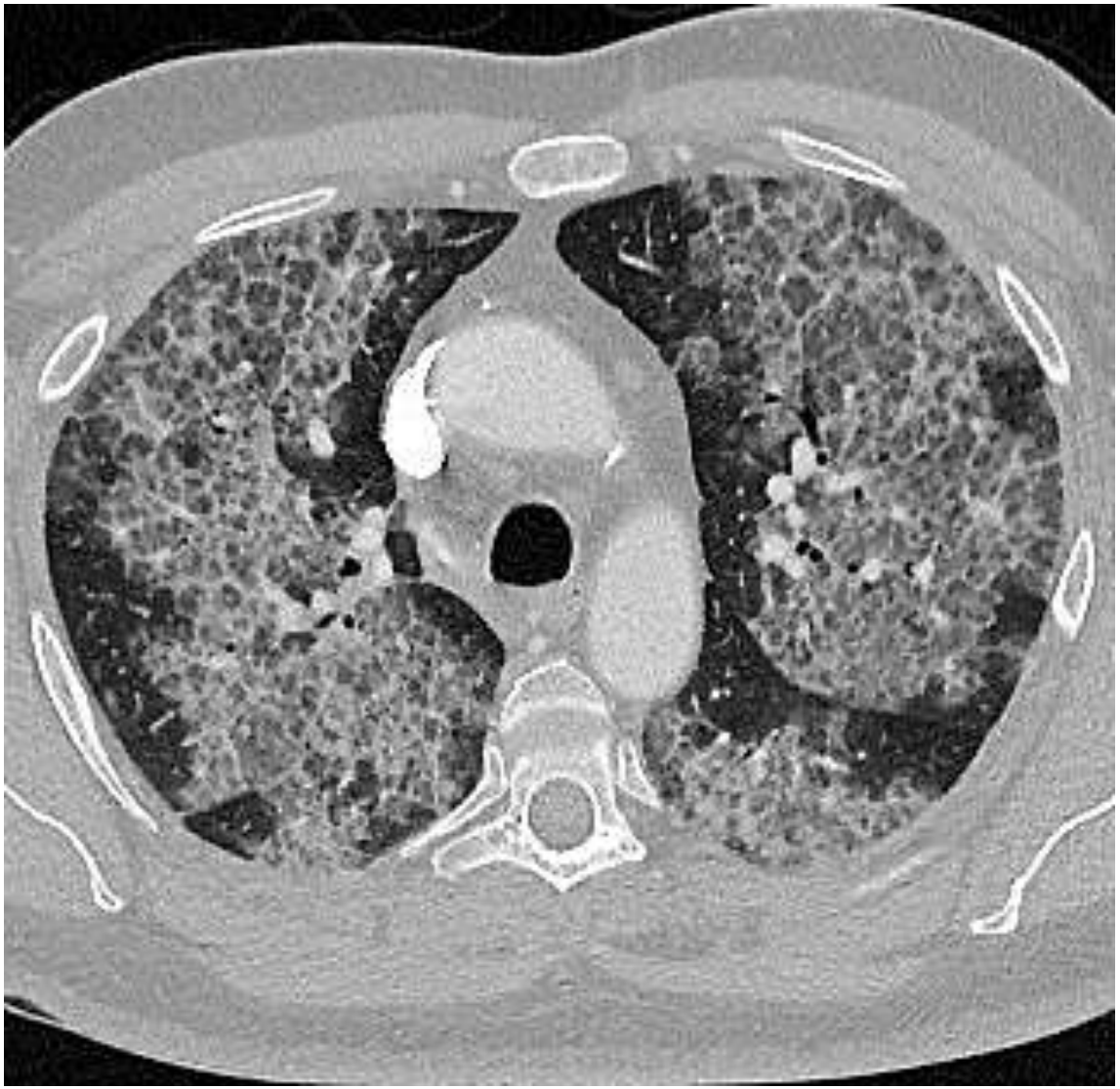


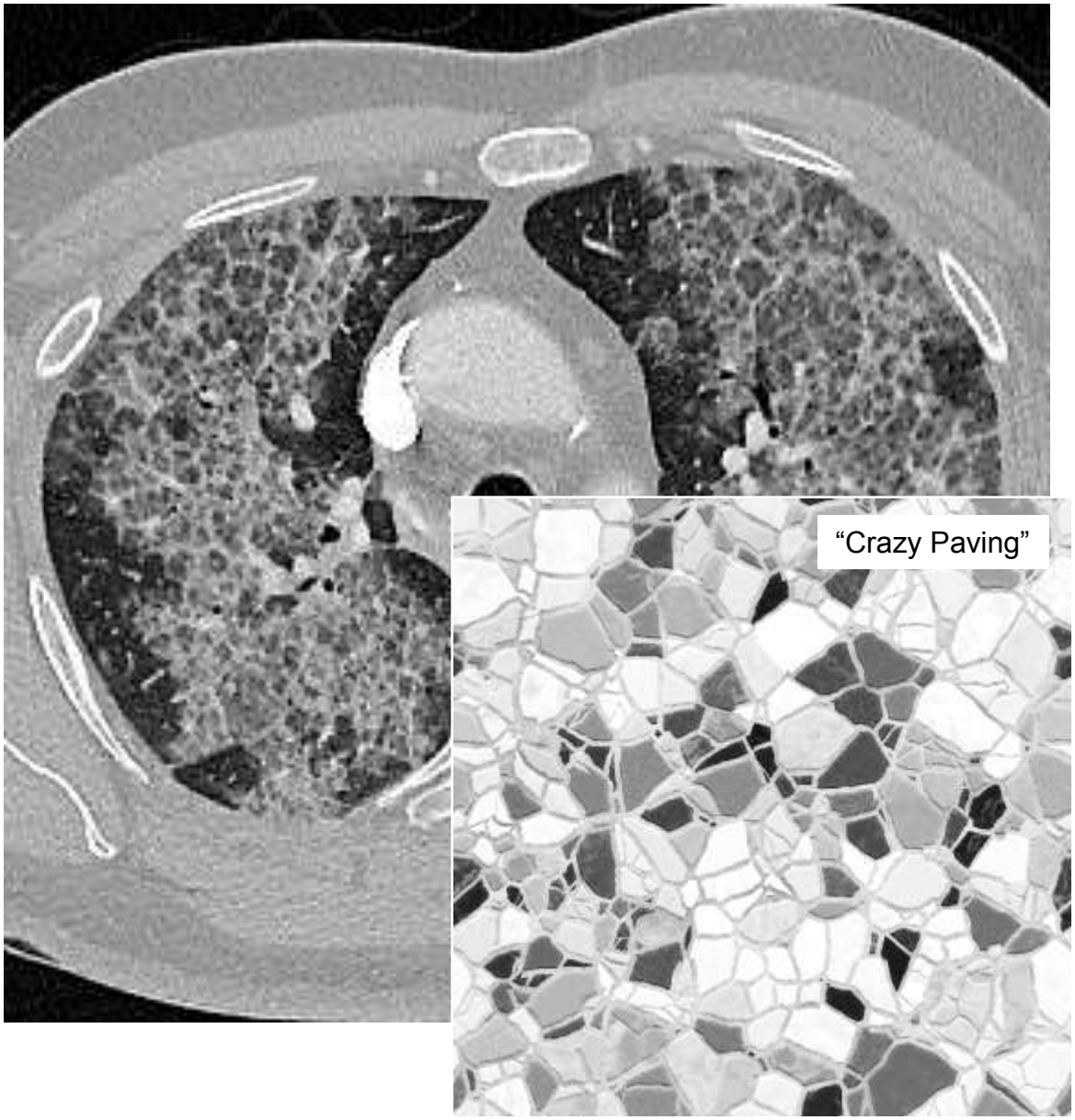
Pulmonary Alveolar Proteinosis

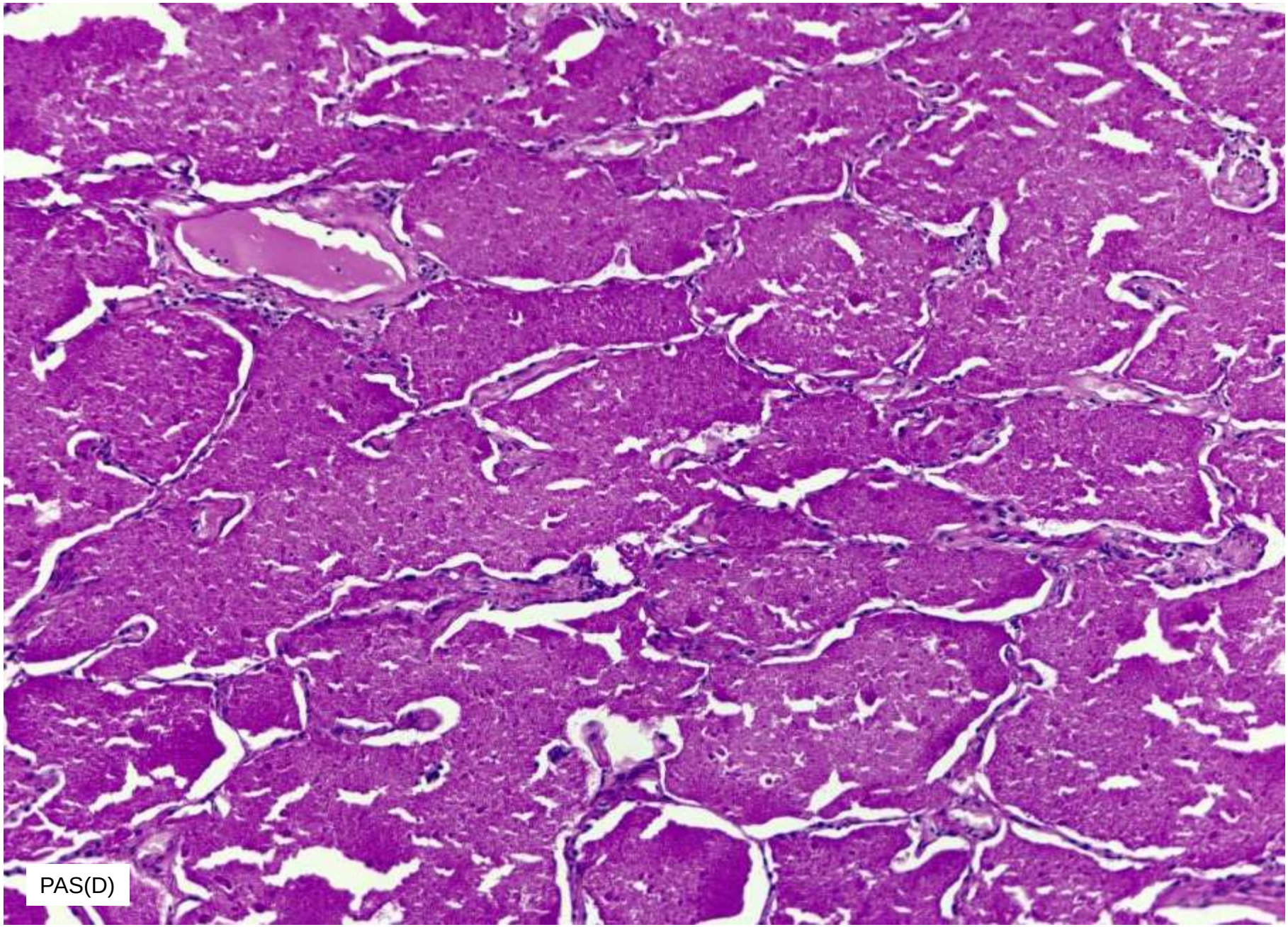


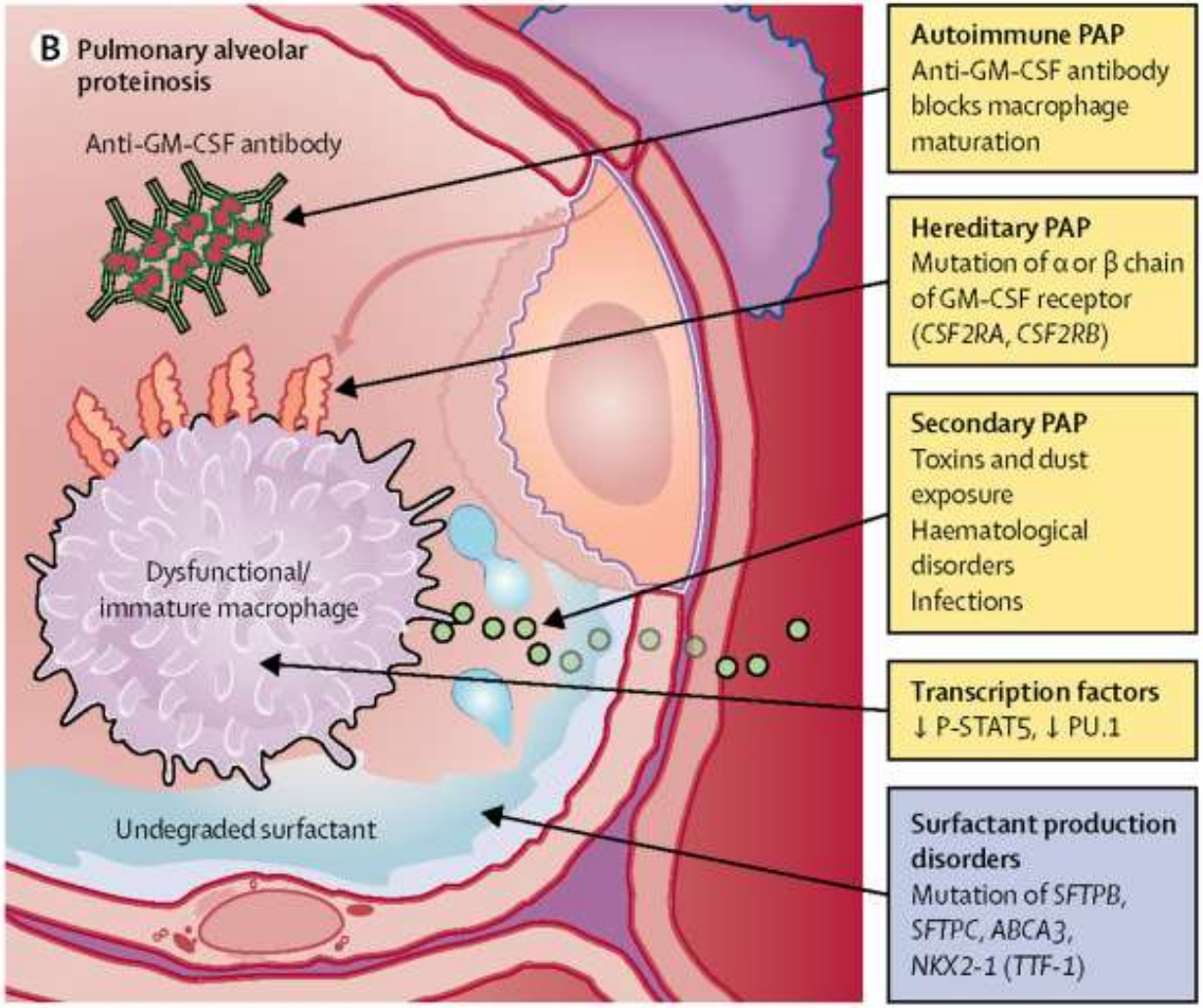
Pneumocystis Pneumonia






“Crazy Paving”


PAS(D)



Lancet Respir Med. 2018 Jul;6(7):554-565.

19-0809

Romain Cayrol/Don Born; Stanford

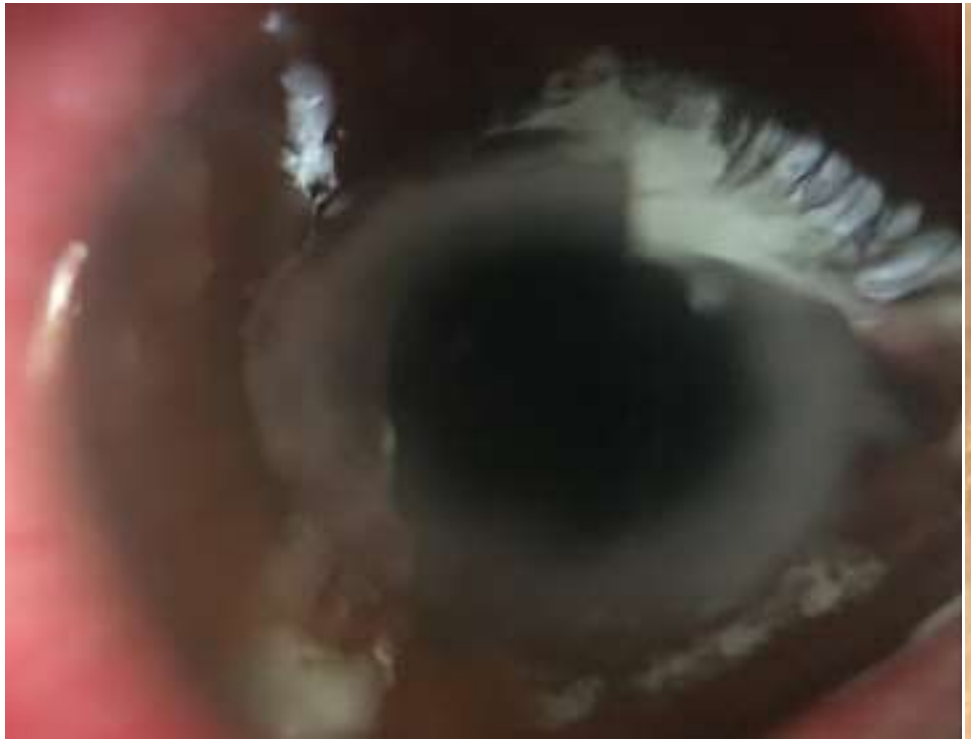
25-year-old female presents with acute pain and redness in left eye.

Clinical History

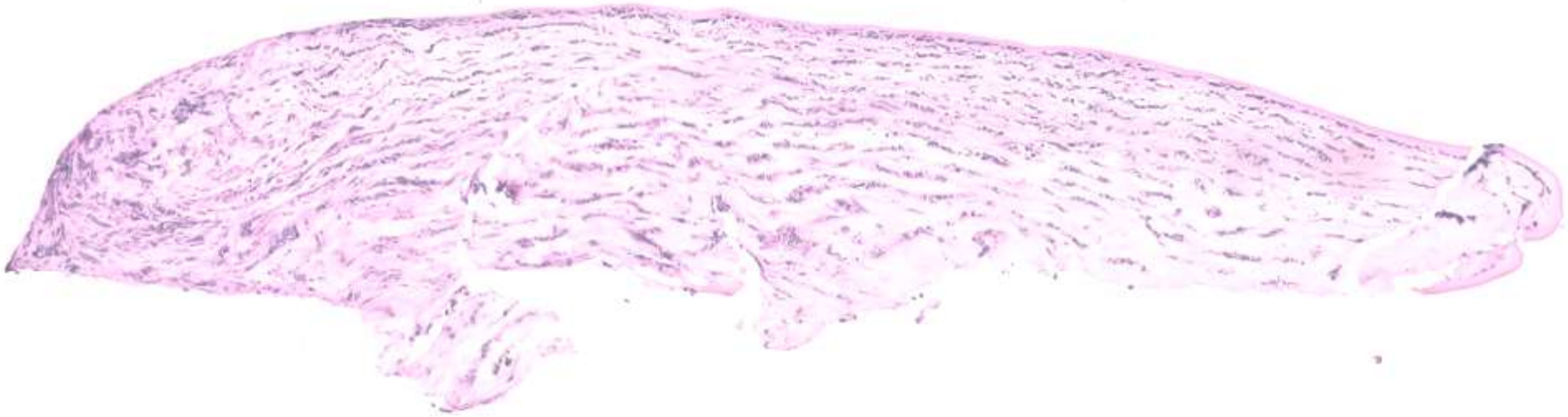
- 25-year-old female with acute (24-48h) worsening left eye pain, redness and discharge
- In January she developed pain and redness in her left eye, the clinical examination showed a Wessly immune ring
- The clinical diagnosis was herpes keratitis and she started Zylet (loteprednol/tobramycin), difluperdnate, topical ganciclovir, besifloxacin, fluoromethalone and valacyclovir
- The symptoms improved at the time, no cultures were taken
- Worked on a farm from November through February
  - Chickens, pigs, goats, one alpaca, and in close proximity to the farm's well system
- She wears glasses and used to wear rigid gas permeable lenses, but stopped wearing them in December due to irritation

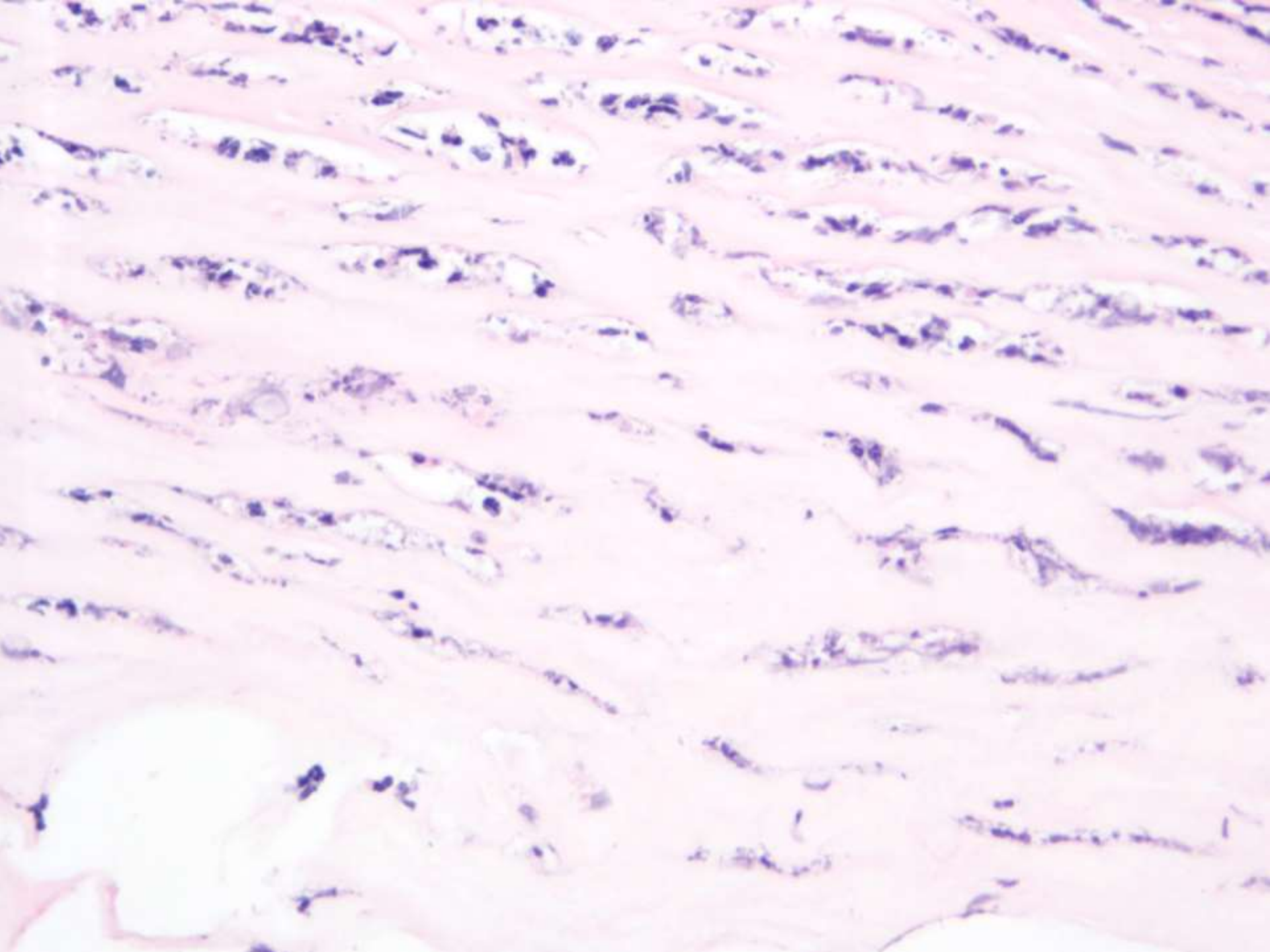
Clinical Examination

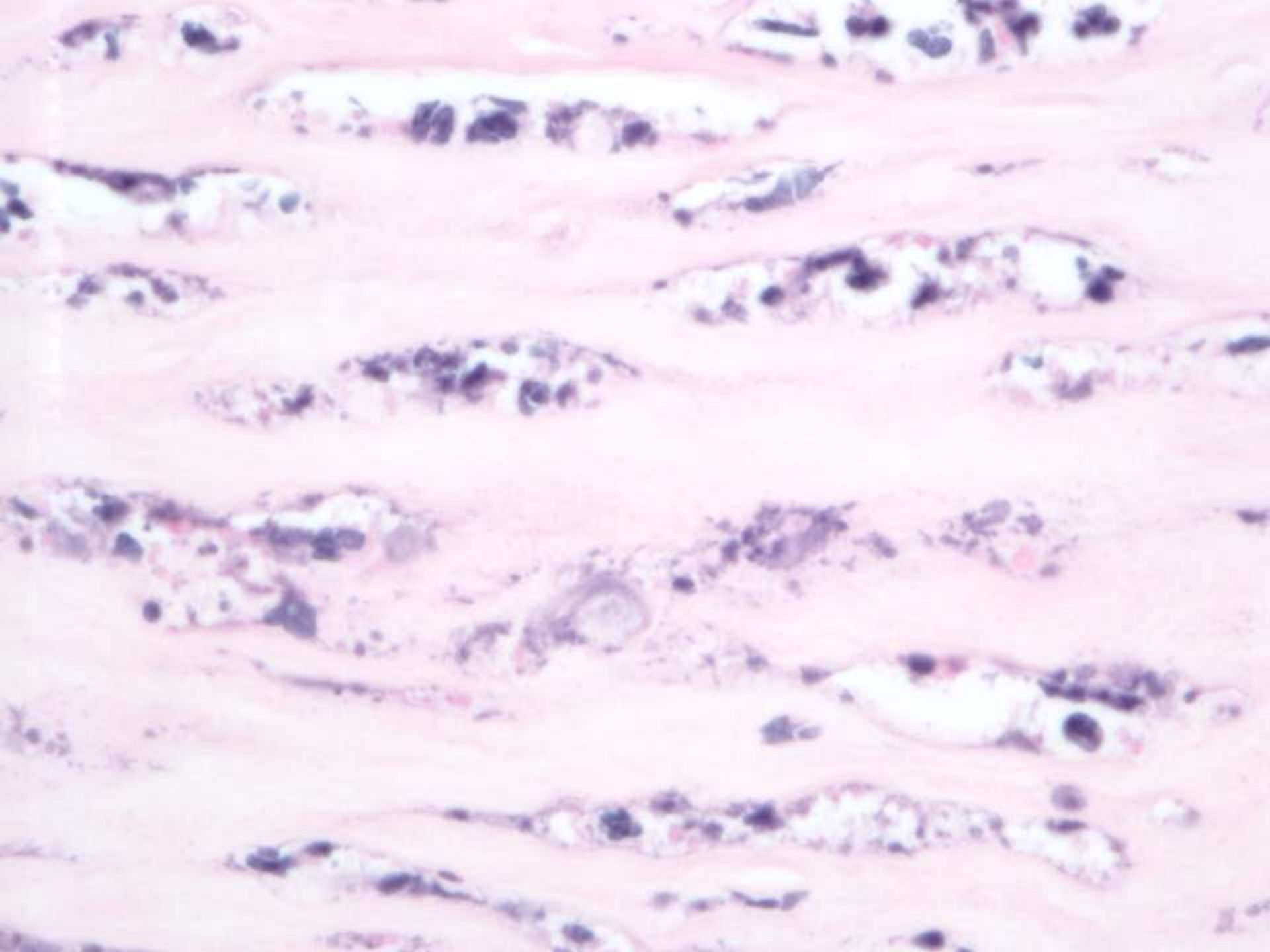
- Corneal haze, small epithelial ulcerations, anterior corneal stroma white ring infiltrate



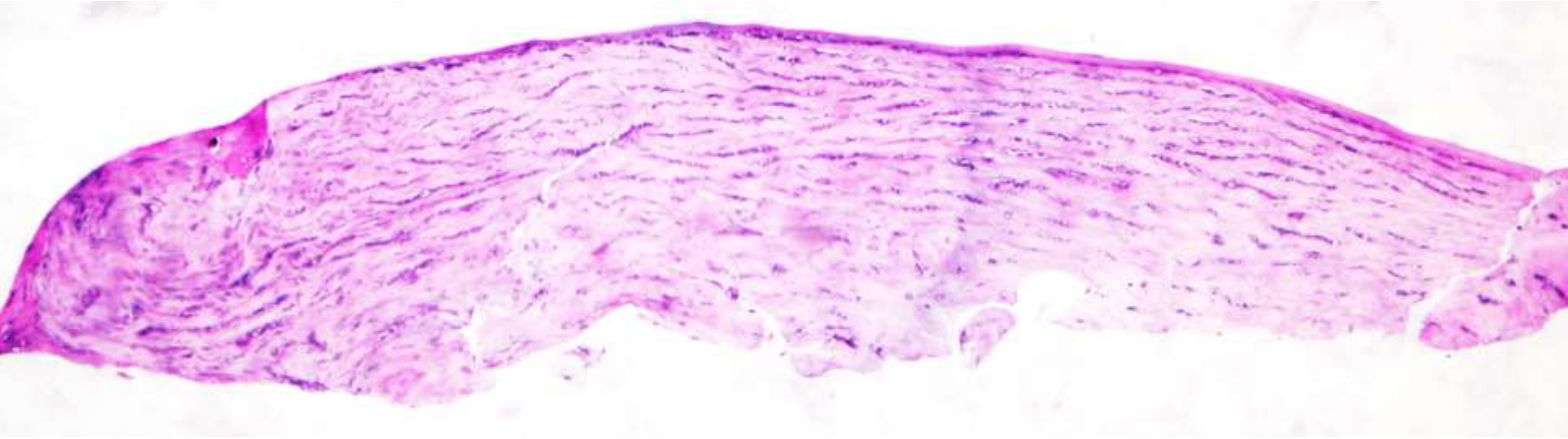
H&E

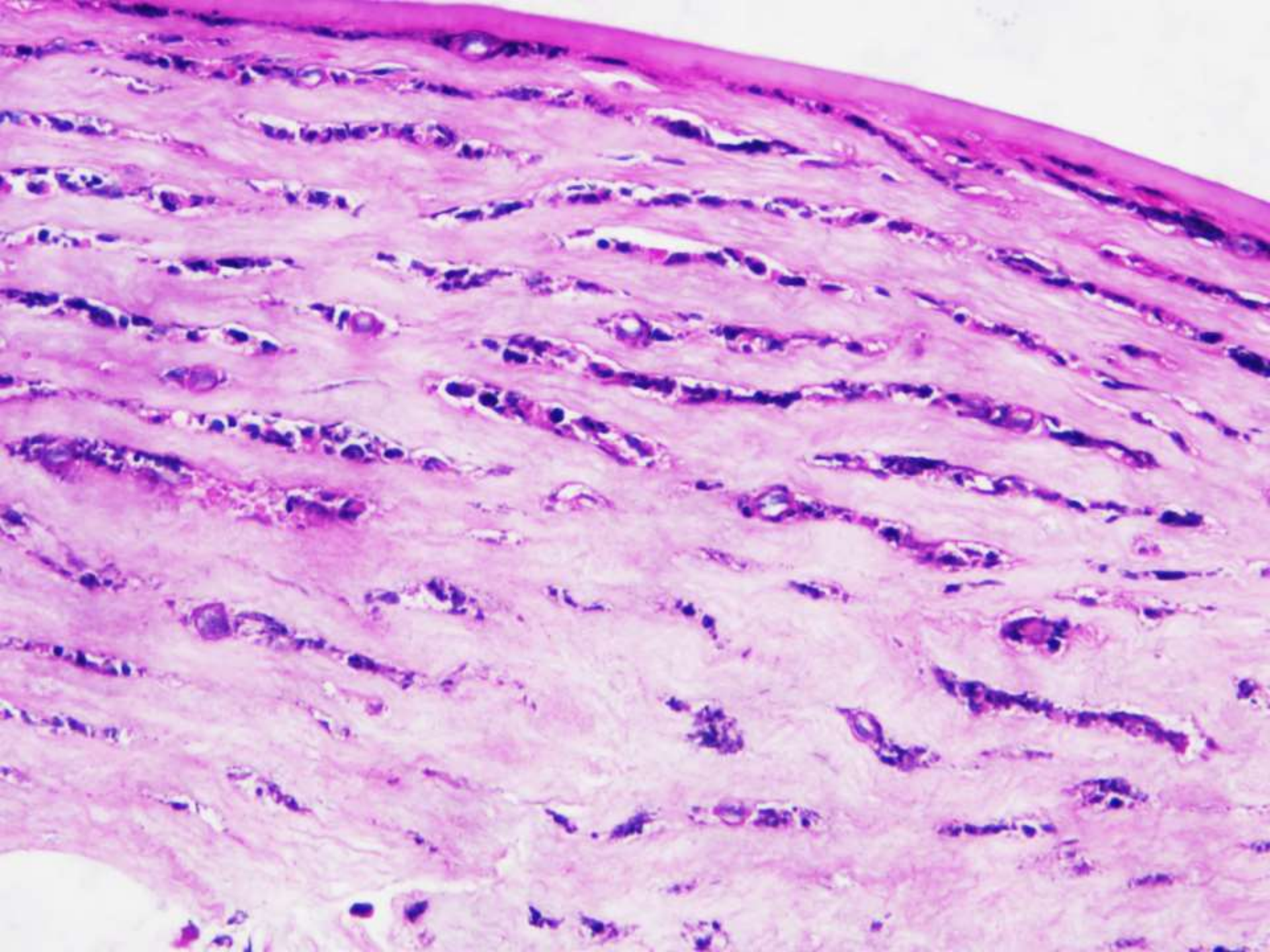


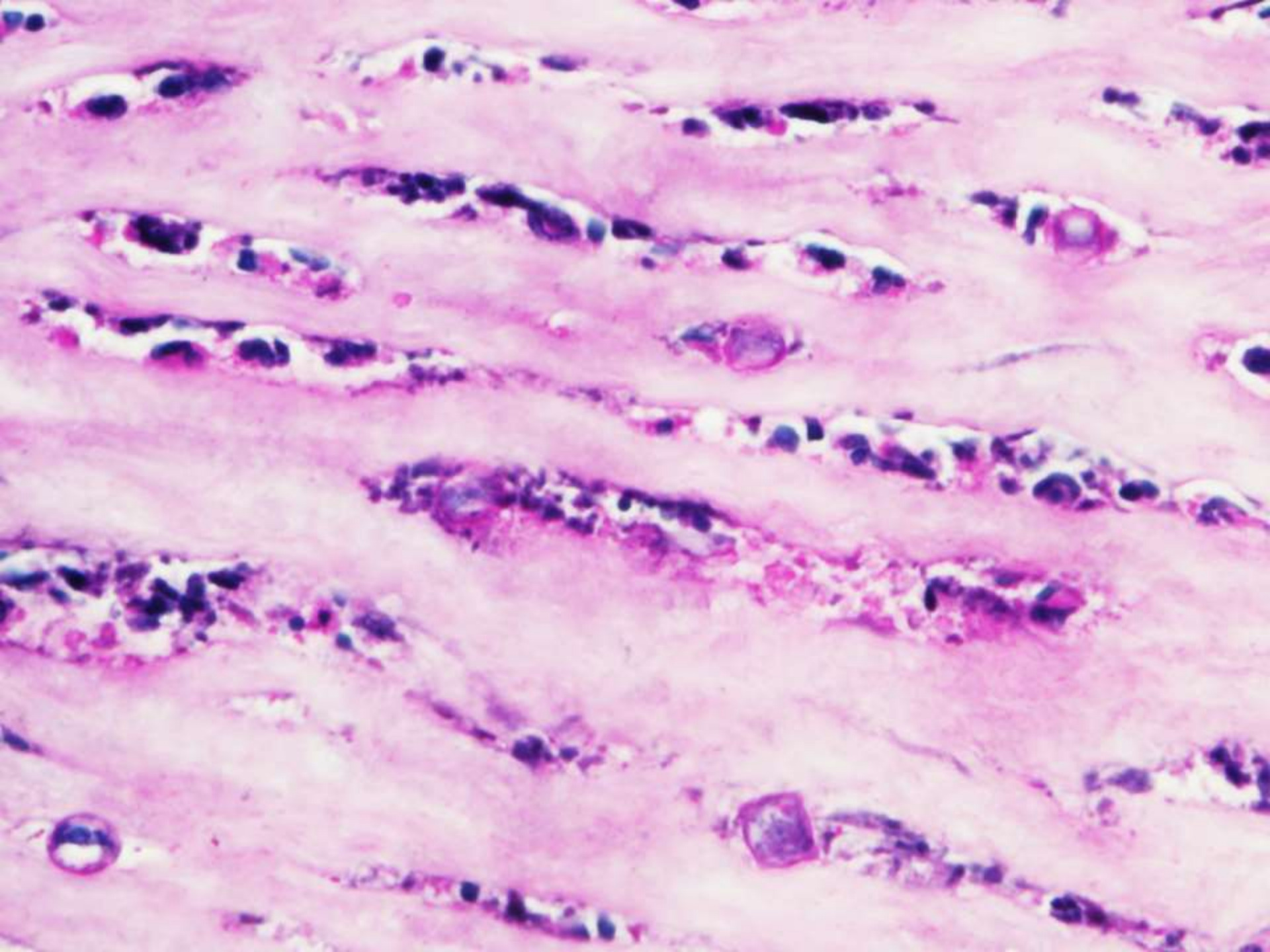




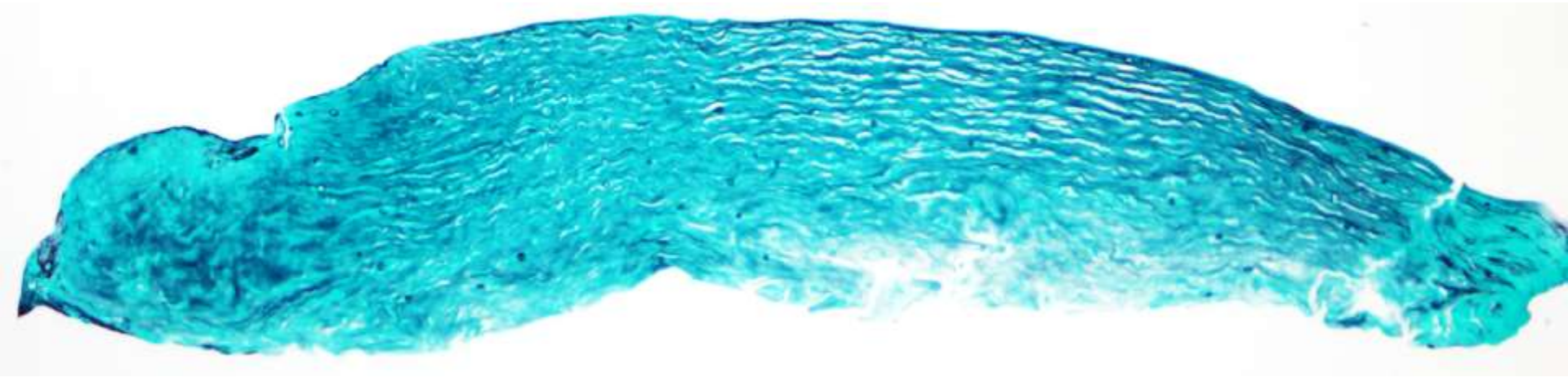
PASD

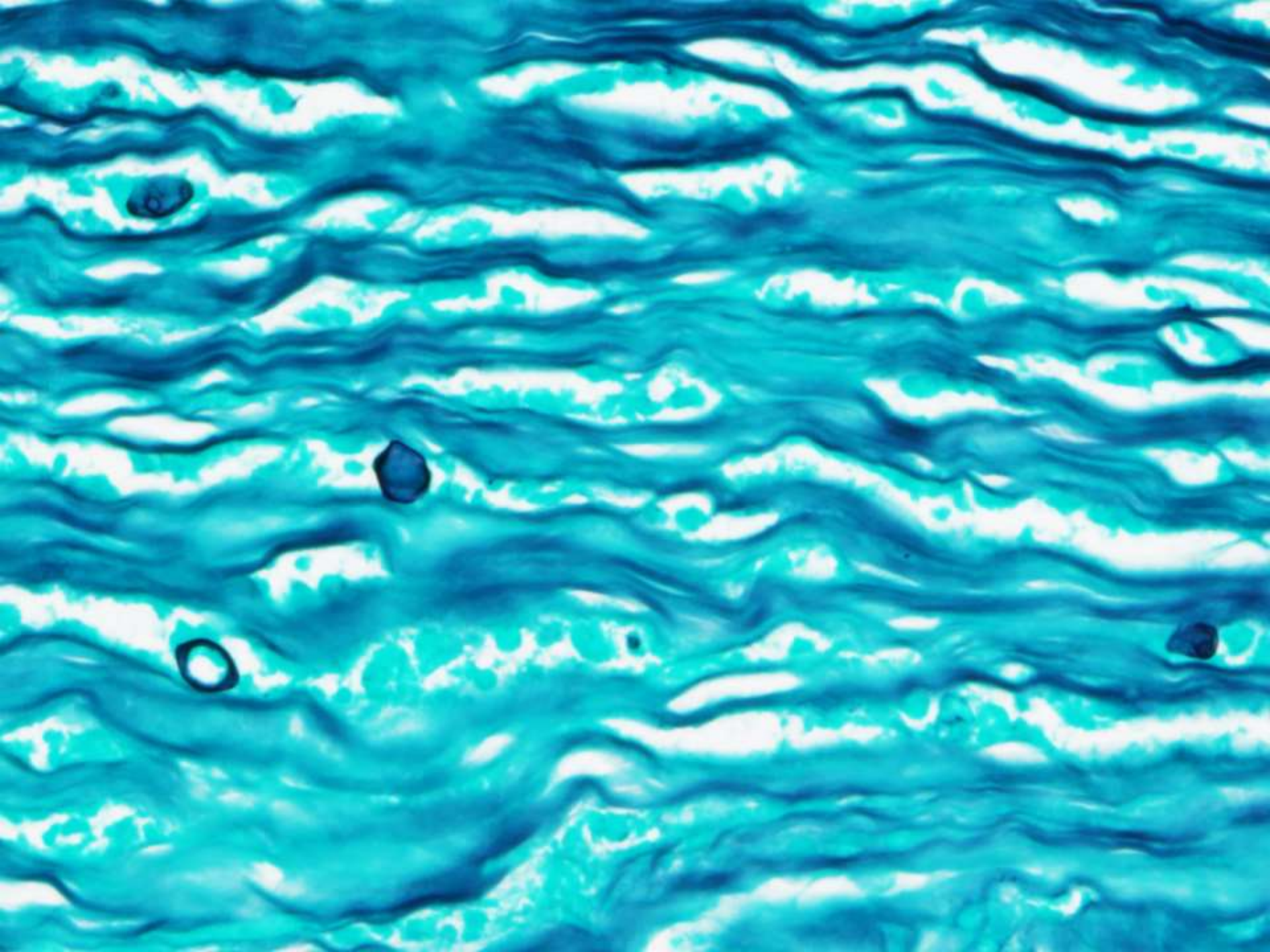






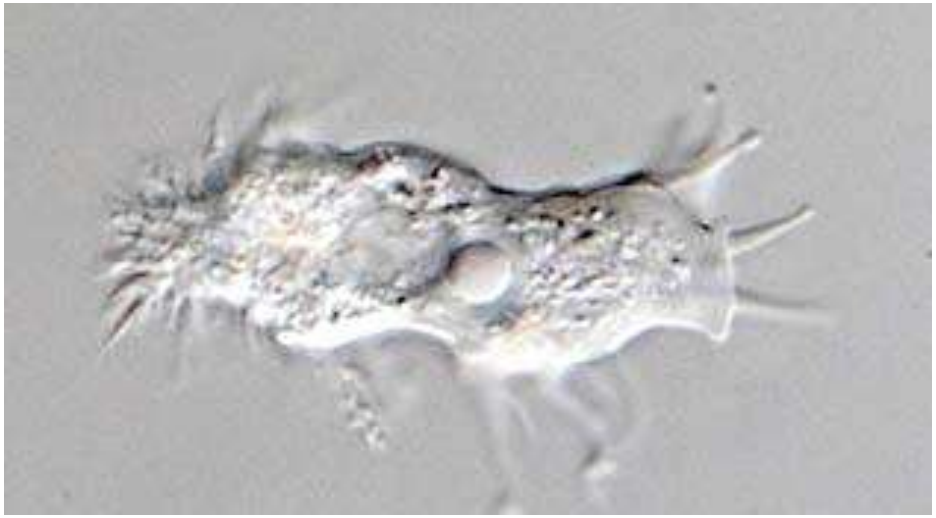
GMS





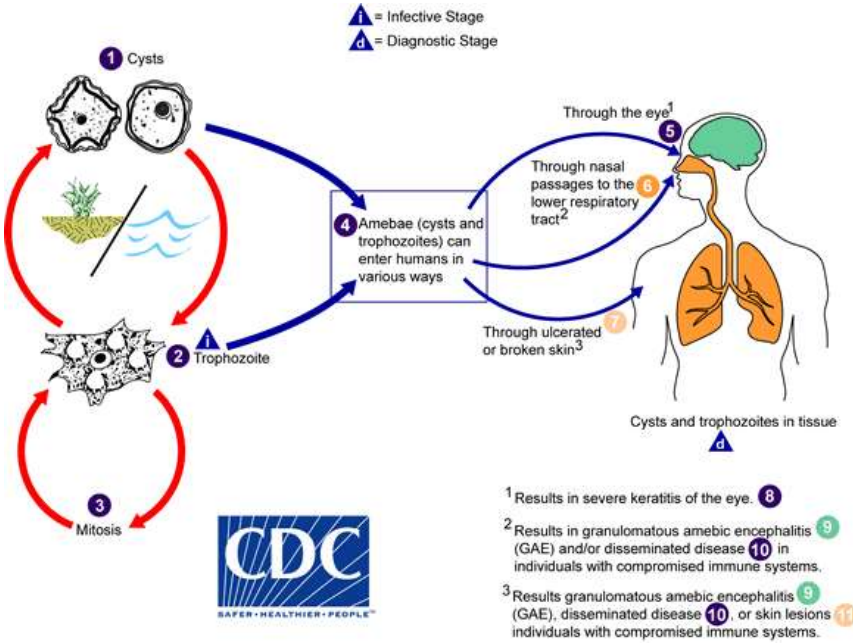
DIAGNOSIS

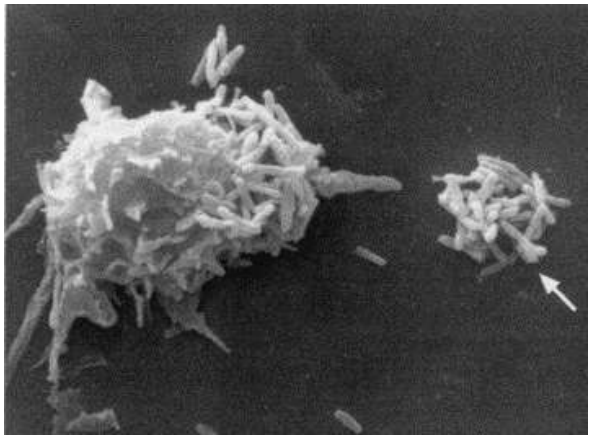
- A. EYE, LEFT CORNEA, BIOPSY
  - Acanthamoeba keratitis

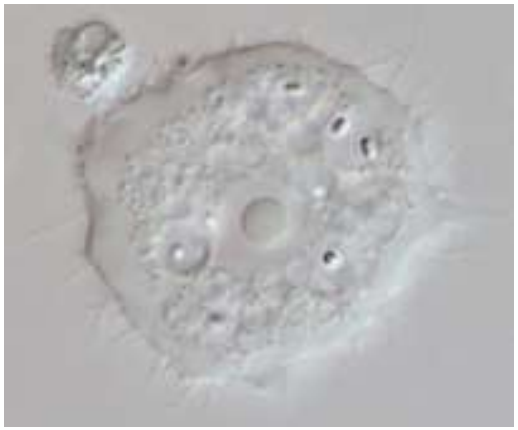


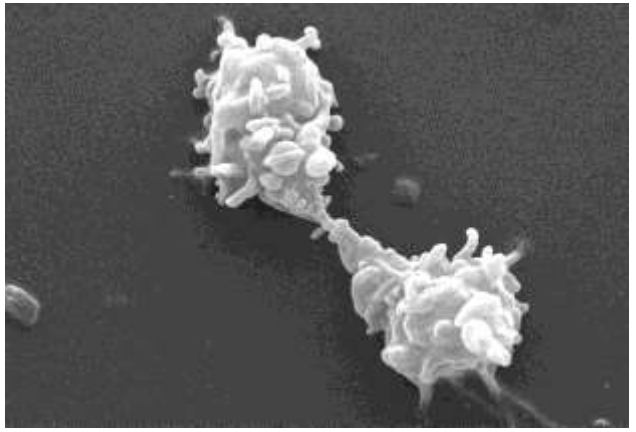
Acanthamoeba

- Microscopic, free-living ameba (or amoeba), single-celled living organism
- Worldwide in the environment, water and soil
- Bacteria is the main food source
- Rare, but severe infections of the eye, skin, and central nervous system
  - Brain and spinal cord infections are usually fatal

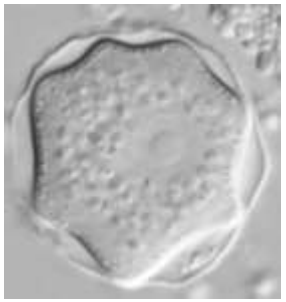








Acanthamoeba keratitis

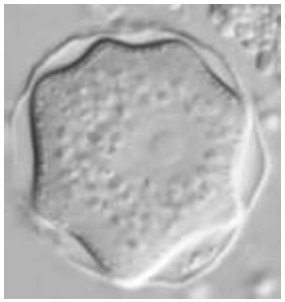


- Eye infection is associated with contact lens use, cuts, or skin wounds
  - 1-33 per million contact lens user
    - Improper storing and handling
    - Improper lens disinfection (hydrogen peroxide)
    - Swimming, hot tubs and showering with lens
    - Contaminated water
    - Trauma to the cornea
  - Symptoms: pain, redness, epiphora, conjunctival hyperhemia, photophobia, ring infiltrate
  - Diagnosis: in vivo confocal microscopy, PCR, histopathology, microbiology cultures

Diagnostic method	Analyzed material	Sensitivity
In-vivo confocal microscopy	In vivo corneal examination	Above 90% with experienced examiner
Polymerase-chain reaction (PCR)	Corneal scrapings (epithelum) or corneal biopsy + contact lense case and cleaning solution	84–100%
In-vitro culture	Corneal scrapings (epithelum) or corneal biopsy + contact lense case and cleaning solution	0–77%
Histopathological analysis	Corneal scrapings or excision or explanted tissue from keratoplasty	31–65%

Szentmary N et al, J. Current Ophthalmology (2019) 31: 16-23

Acanthamoeba keratitis



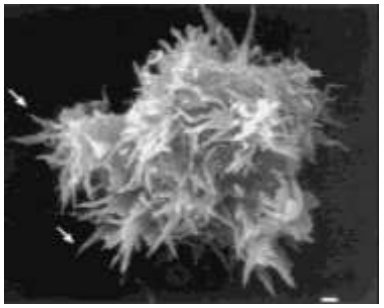
- Eye infection
  - Binds epithelial Mannose Binding Protein, activation of proteases (serine and cysteine proteases, MMPs) for stromal invasion
  - Infection can be mixed (virus, bacteria or fungi)
  - Can lead to visual impairment and blindness
    - Anterior synechia, secondary glaucoma, iris atrophy, cataract, corneal atrophy and endothelial cell defect, uveitis, chorioretinitis
  - Infection is difficult to treat
    - Corneal stroma has no blood vessels
    - Diamidines (propamidine-isethionate) and biguanides (chlorhexidine) topical solutions, neomycin +/- antifungals, +/- corticosteroids
    - Surgical treatment: epithelial abrasion removes organism and allow a better corneal penetration of the topical solutions, +/- cryotherapy, +/- keratoplasty with amniotic membrane graft

Clinical symptoms and their timely presentation in acanthamoeba keratitis.

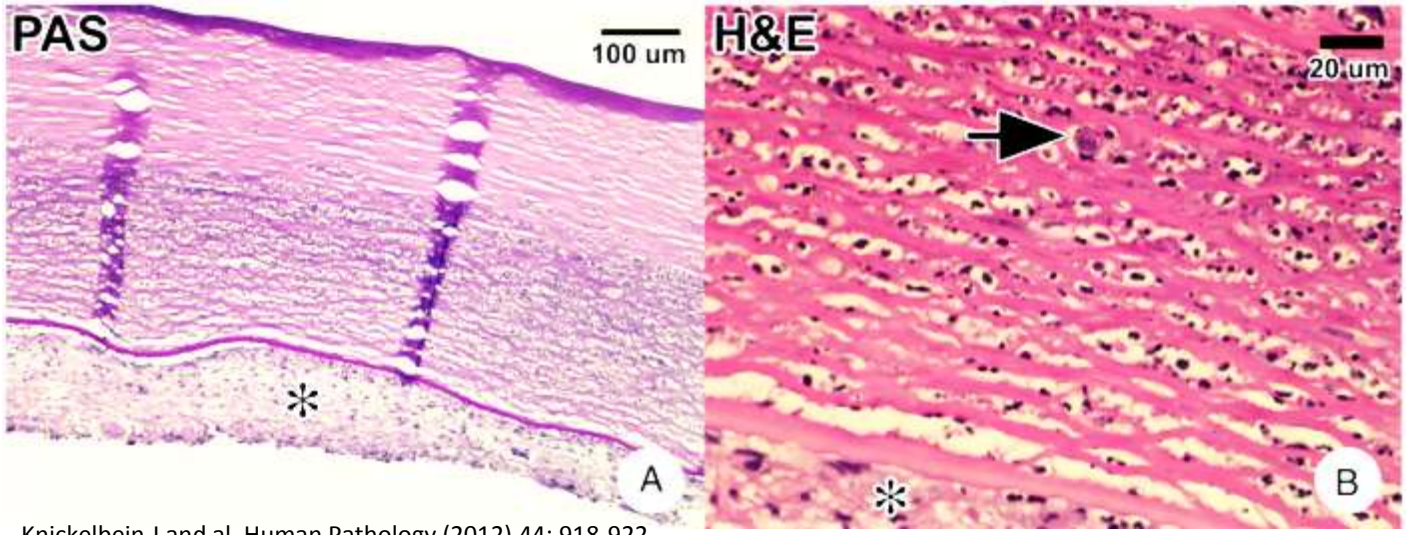
Clinical symptom	Time	Special properties
Chameleon-like epithelial changes ("dirty epithelium") (Fig. 1A)	Within the first 2 weeks in 50% of the patients	Grey epithelial opacities, pseudodendritiformic epitheliopathy, epithelial microerosions or microcysts
Multifocal stromal infiltrates (Fig. 2A)	Within the first 2 weeks	Mostly central and paracentral
Ringinfiltrate/Wessely immune ring (Figs. 1B and 2A)	In the first month in 20% of the patients	From polymorphonuclear leukocytes, antigen-antibody-komplex and complement; incidence increases with time
Perineural infiltrate (Fig. 3)	In the first month of the disease in 2.5–63% of the patients	Radial, from limbus to middle stroma, results in loss of corneal nerve fibers
Sterile anterior uveitis, scleritis, broad-based anterior synechiae, secondary glaucoma, iris atrophie, mature cataract (Fig. 4), chorioretinitis, retinal vasculitis	Late symptoms, following months	Rare Reason unknown (treatment or disease?).[50,57]

Szentmary N et al, J. Current Ophthalmology (2019) 31: 16-23

Acanthamoeba keratitis



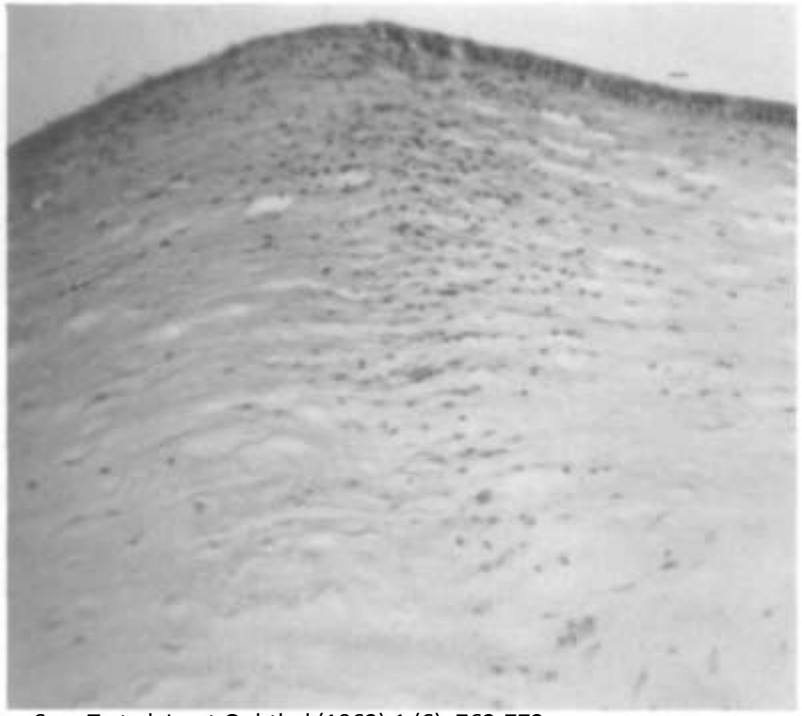
- Eye infection is through contact lens use, cuts, or skin wounds
  - Corneal infiltration by neutrophils, lymphocytes and macrophages often in close proximity to the acanthamoeba
  - Polygonal 13-20 um cysts, 25-40 um trophozoite
  - Seen on H&E, highlighted by PASD and GMS
- Differential diagnosis: acute keratitis
  - Infectious viral (herpetic keratitis), bacterial and fungal, auto-immune, drugs



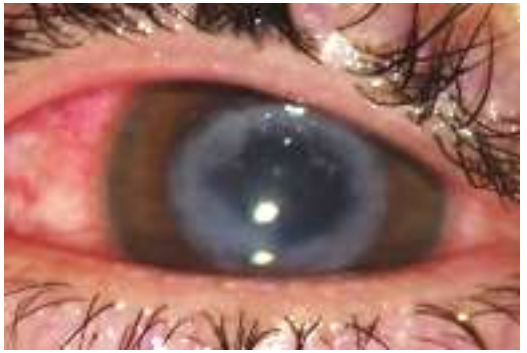
Knickelbein J and al, Human Pathology (2012) 44: 918-922

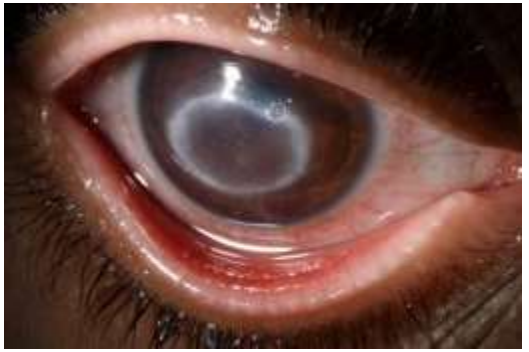
Wessely Immune Ring

- Non-specific, ring-shaped corneal stroma infiltrate, known as a Wessely ring, associated with a strong reaction to an antigen
- Immune cell infiltration within the corneal stroma
  - Infections (viral, bacterial, fungal, parasites), autoimmune diseases (Behcet's), chronic trauma (contact lens), topical ointments

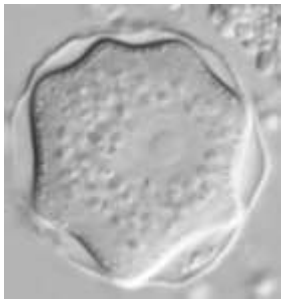


Sery T et al, Ivest Ophthal (1962) 1 (6): 762-772





Conclusions



- Acanthamoeba keratitis is a rare but sight threatening infection caused by an opportunistic pathogen and should be treated as a medical emergency with prompt diagnosis and adequate treatment
  - Main risk is the use of contact lens
  - Diagnosis is by confocal microscopy, PCR, microbiology and histology
- Treatment is topical application of a cocktail of drugs, +/- surgical intervention

- Clinical follow up
  - Culture positive for acanthamoeba
  - Patient is slowly improving on treatment (diamidine, biguanide, antibiotic and low dose corticosteroid) , epithelial defect is getting smaller at each visit
  - No progressive corneal thinning

References

- Szentmary N et al, J. Current Ophthalmology (2019) 31: 16-23
- Knickelbein J and al, Human Pathology (2012) 44: 918-922
- Sery T et al, Ivest Ophthal (1962) 1 (6): 762-772
- Center for Disease Control (CDC, https://www.cdc.gov/)

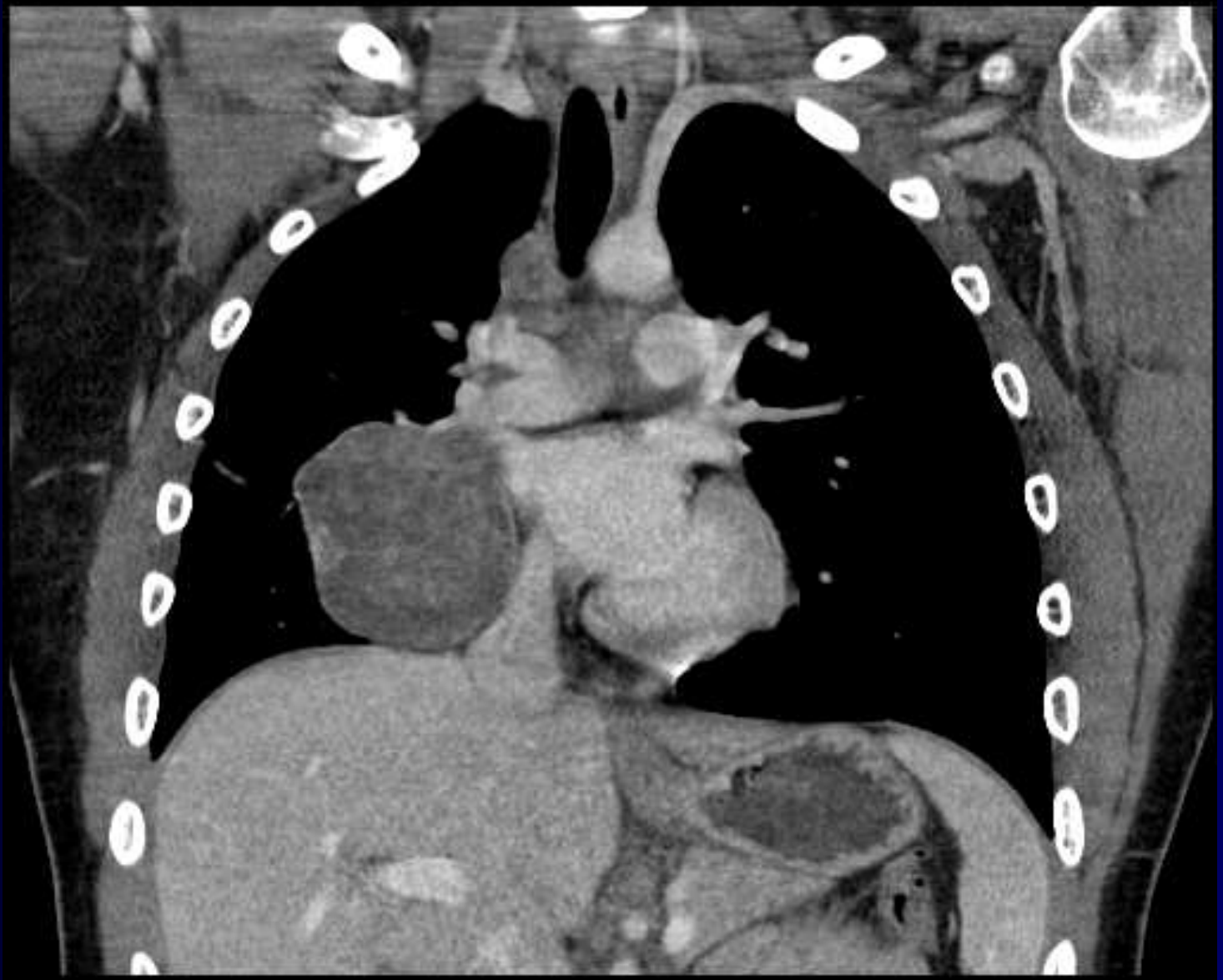
19-0810

Liping Song; Kaiser Permanente Oakland Medical Center

16-year-old female with a history of mild asthma, evaluated for abnormal chest imaging for cough, chest discomfort, and SOB.. She is from California but lived in Arizona for 1.5 years. Chest X-ray showed right lung mass. CT showed 6.3cm right lung mass with large subcarinal adenopathy. Clinically concern for Coccidioides infection, she was started on fluconazole. Over the past week she has continued to have chest discomfort and required norco administration.

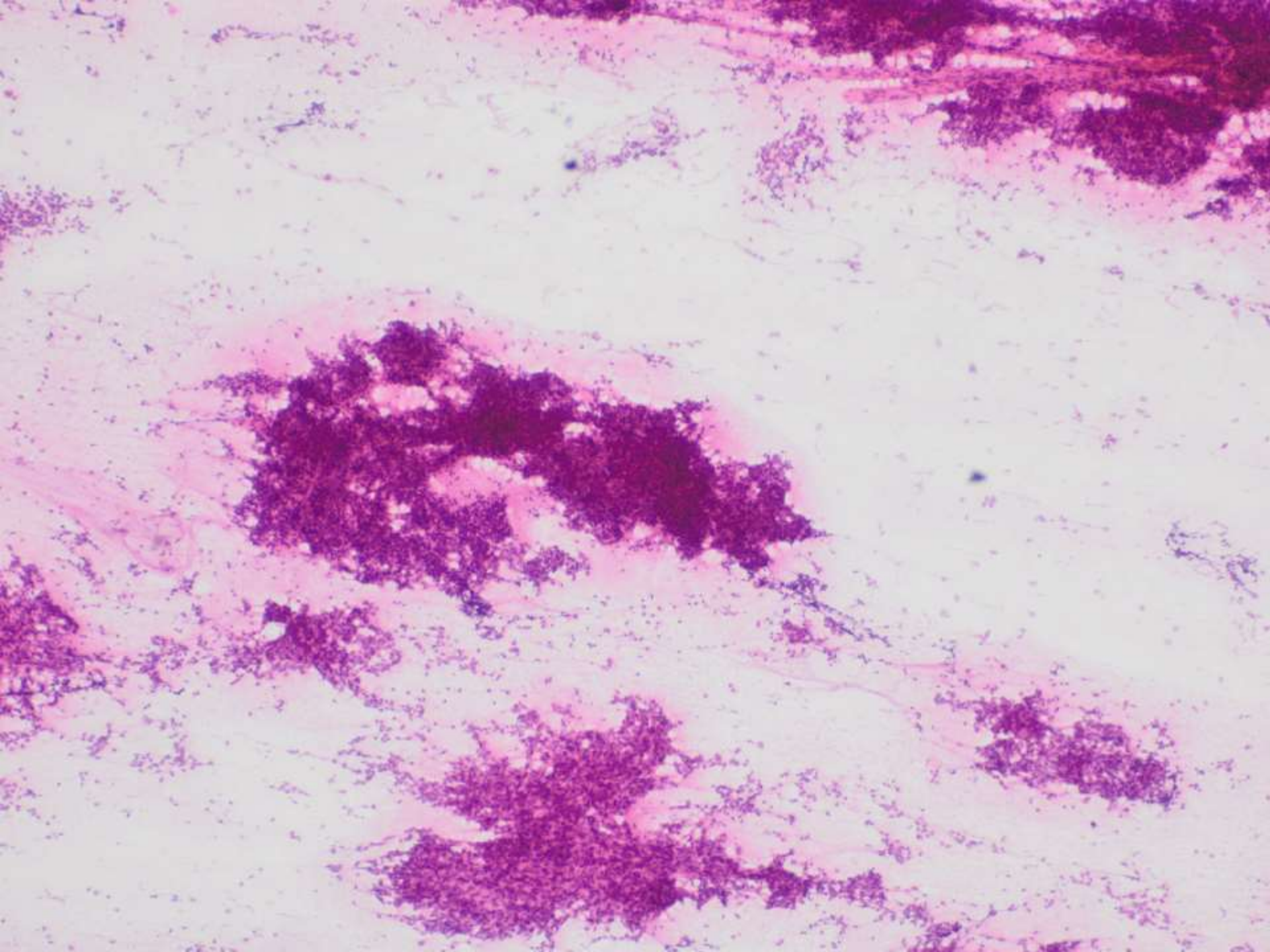
After hour frozen call

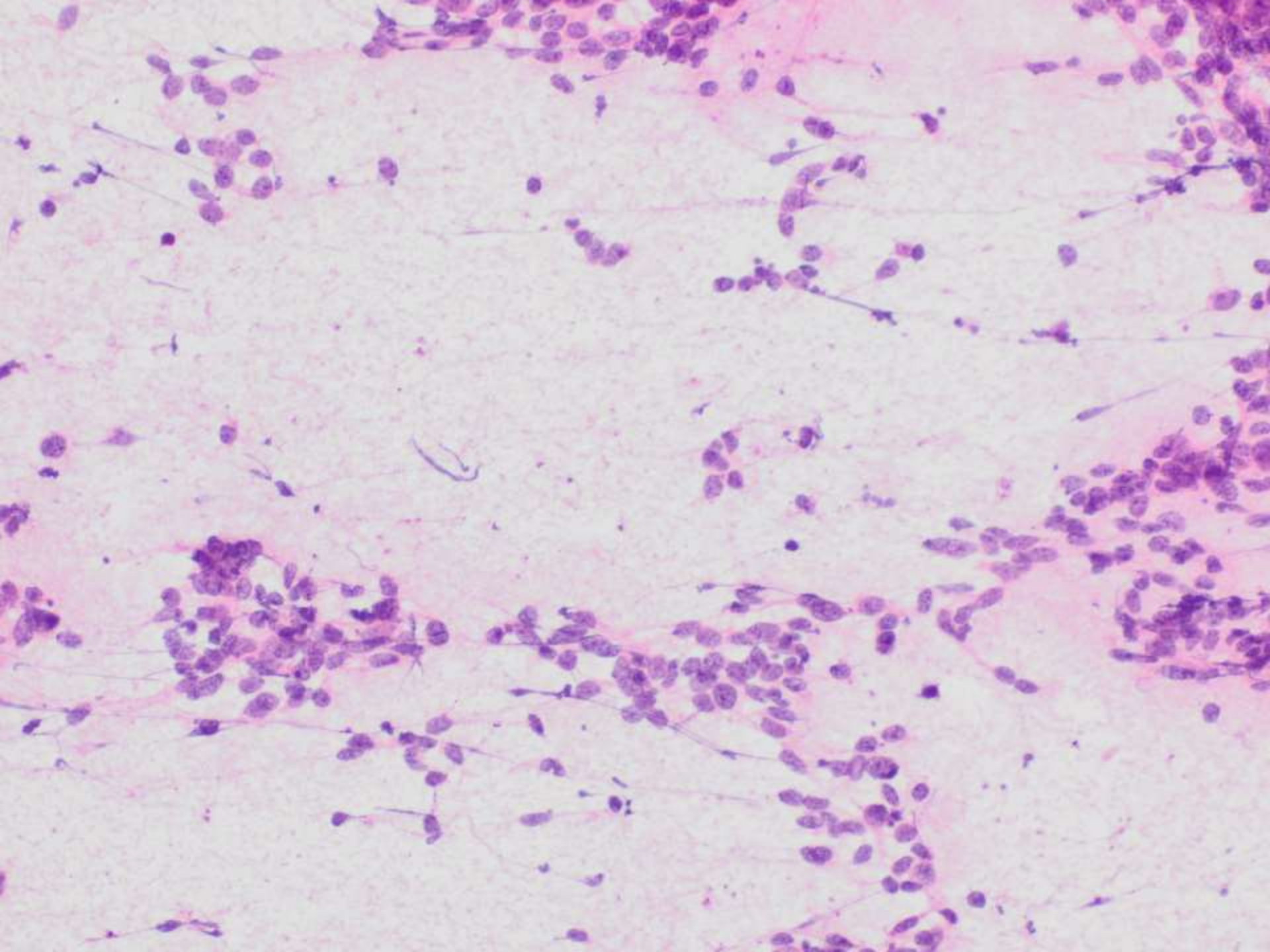
16 year old girl clinically concern for coccidioides infection (lived in Arizona for 1.5 years). she was started on fluconazole. Over the past week she has continued to have chest discomfort and is requiring norco administration

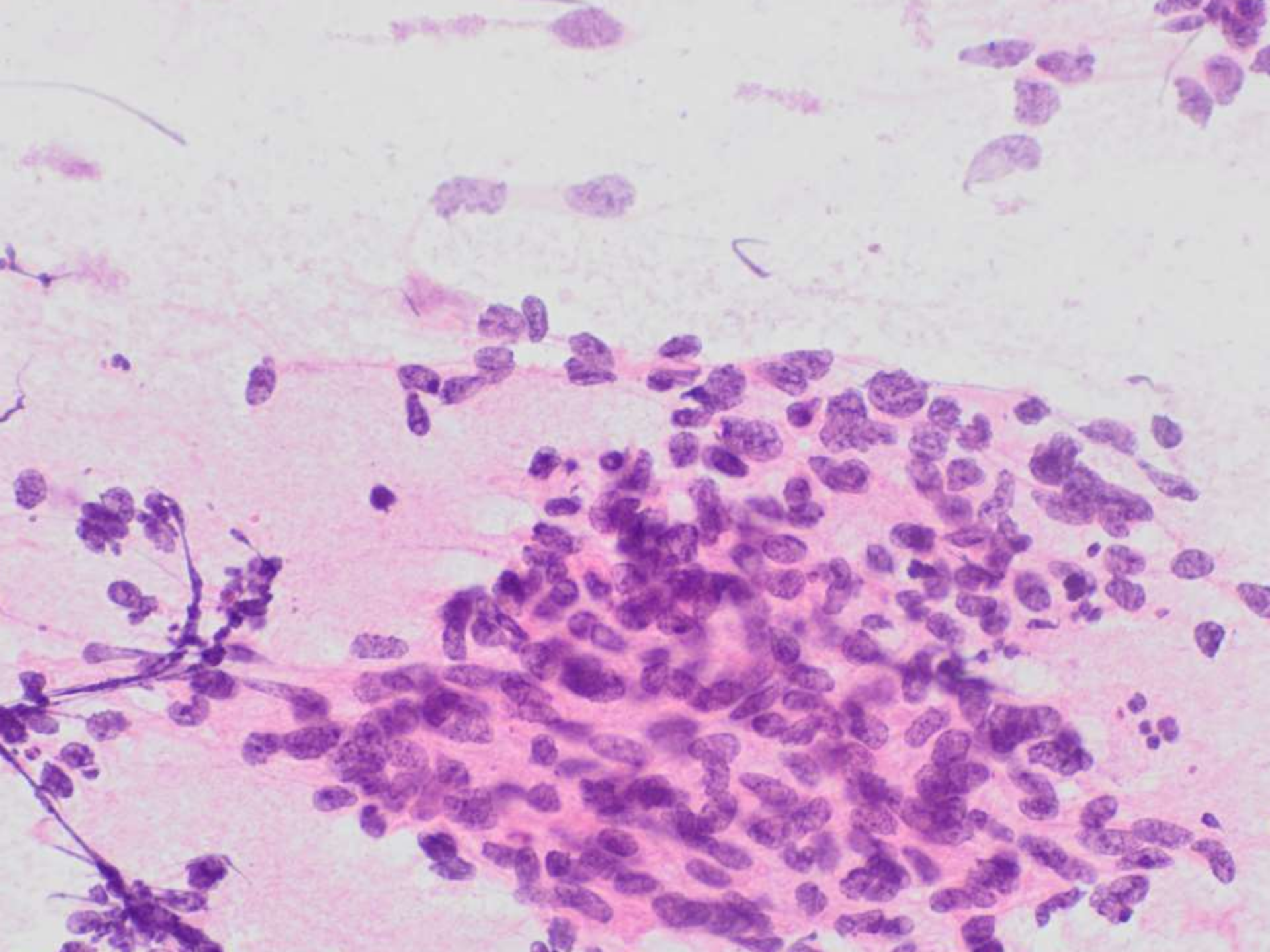


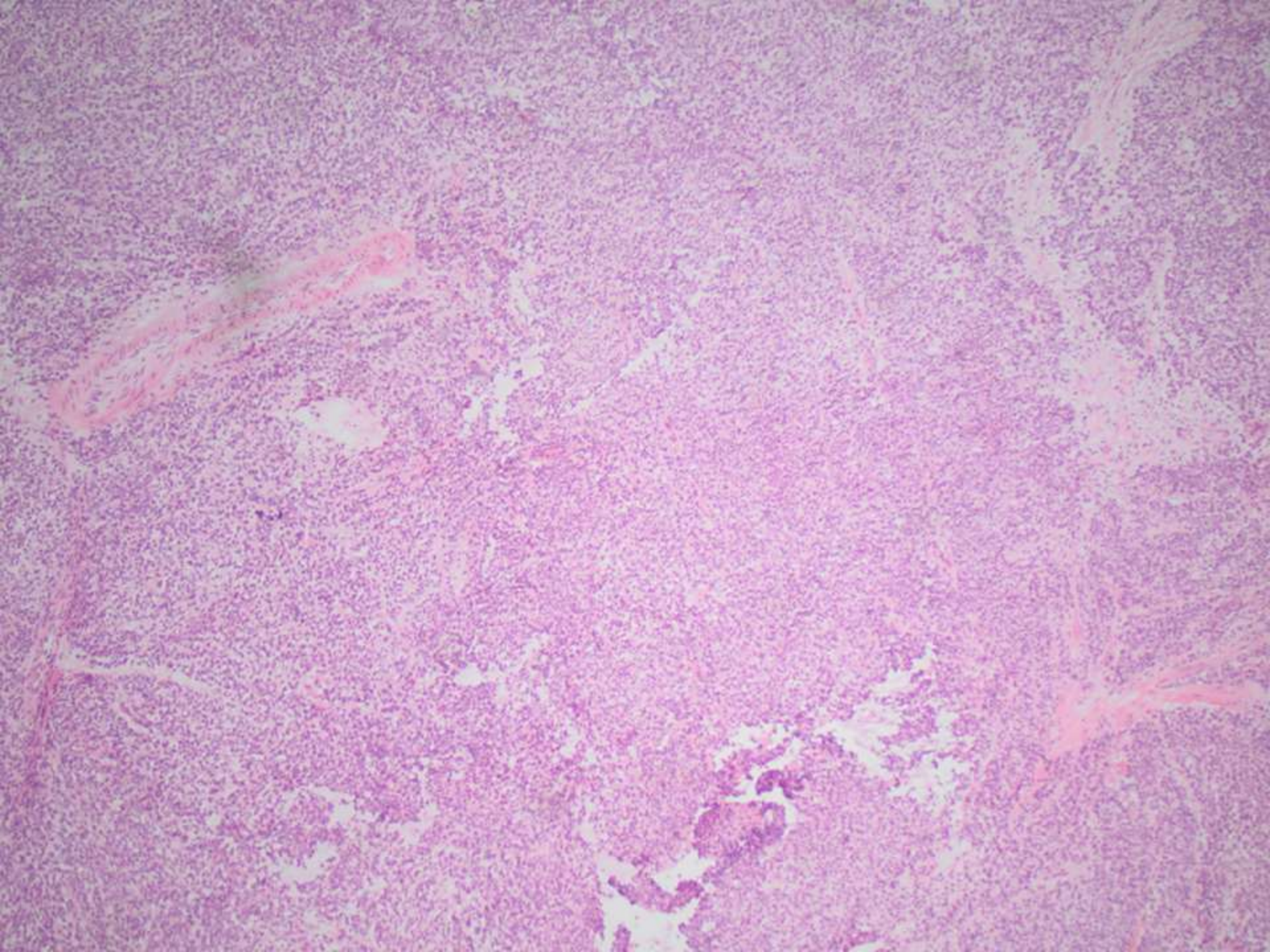
CT report

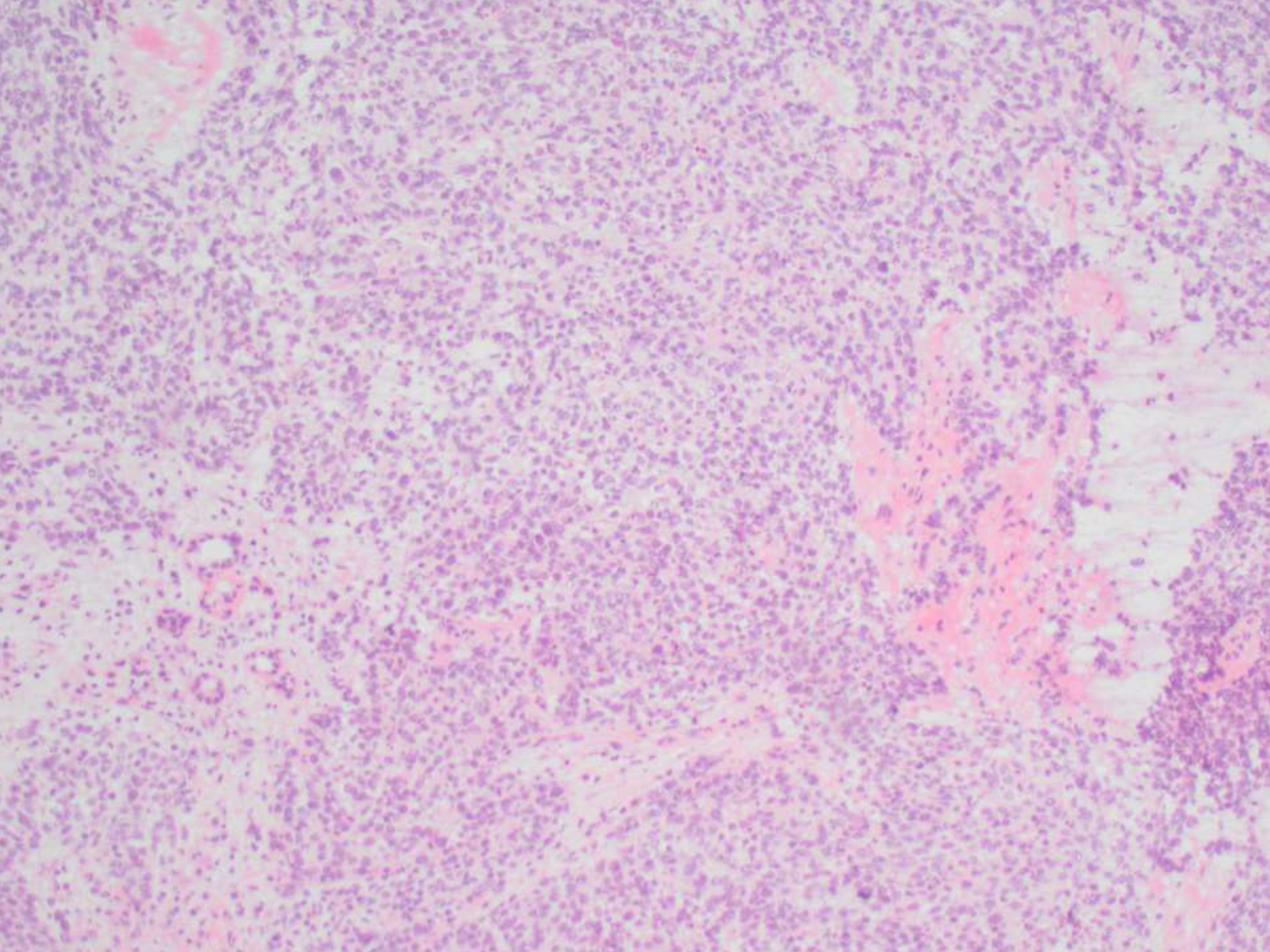
- 11/19/18 CT Large (6.3 cm) masslike right infrahilar lung consolidation with mediastinal adenopathy, including large subcarinal adenopathy. There is obstruction of the right middle lobe bronchus with some right middle lobe consolidation, likely post compressive atelectasis. Given the predominantly hypodense appearance, an atypical infectious process (i.e. coccidiomycosis though TB or other atypical infections can also be considered) is favored. A true neoplastic mass seems less likely, though is difficult to exclude. Possibly infectious or inflammatory pulmonary nodule(s).

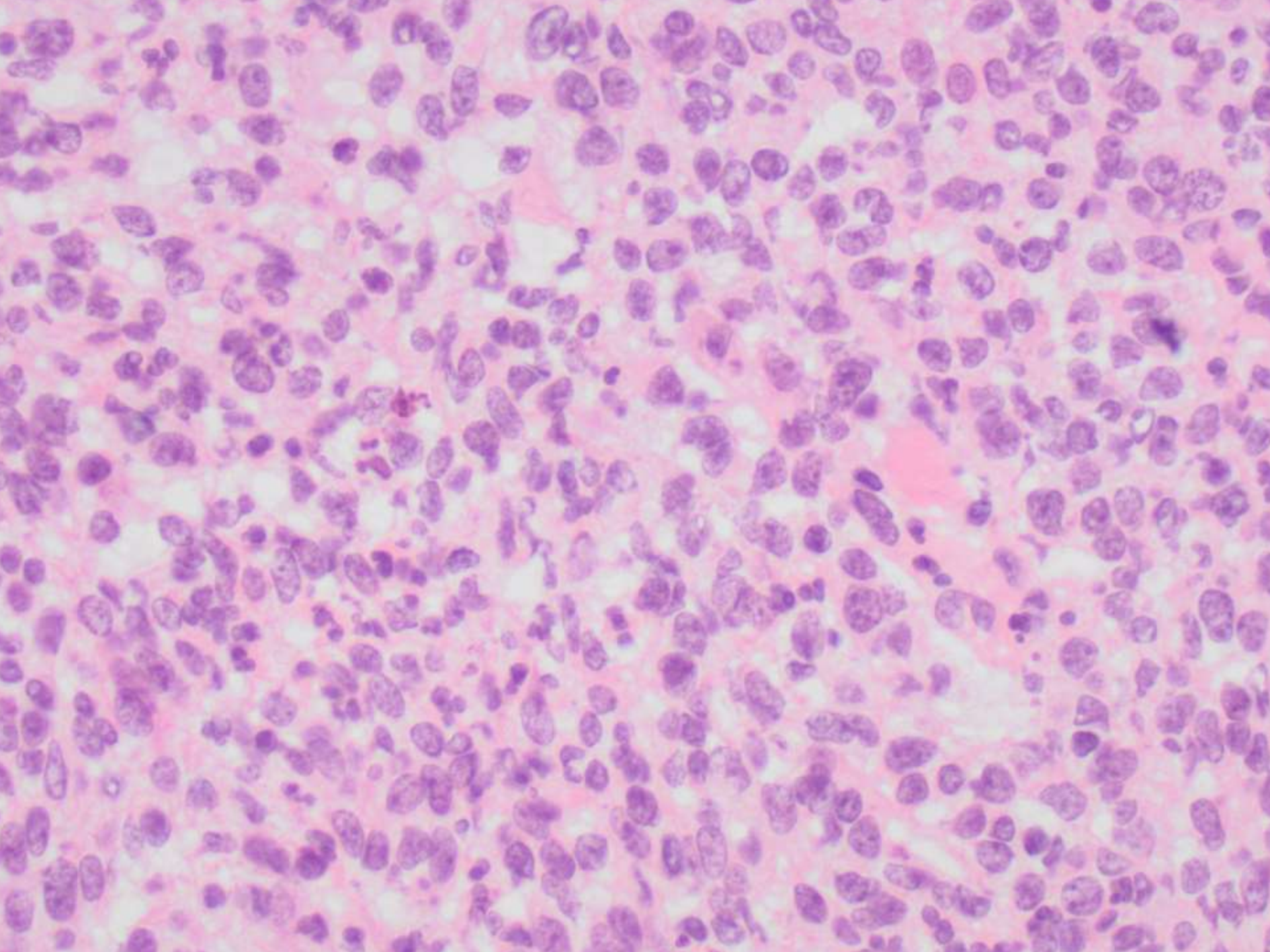




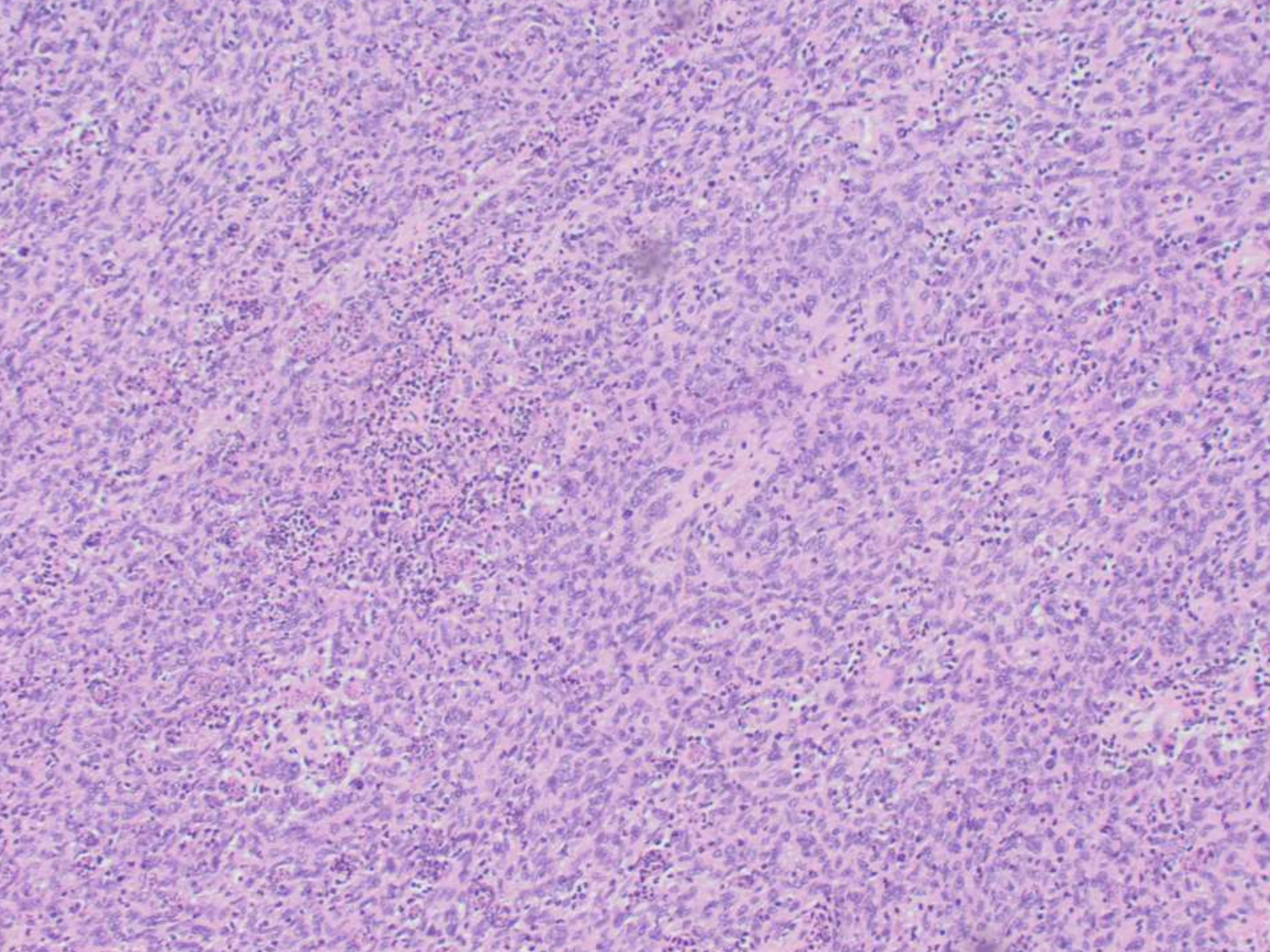


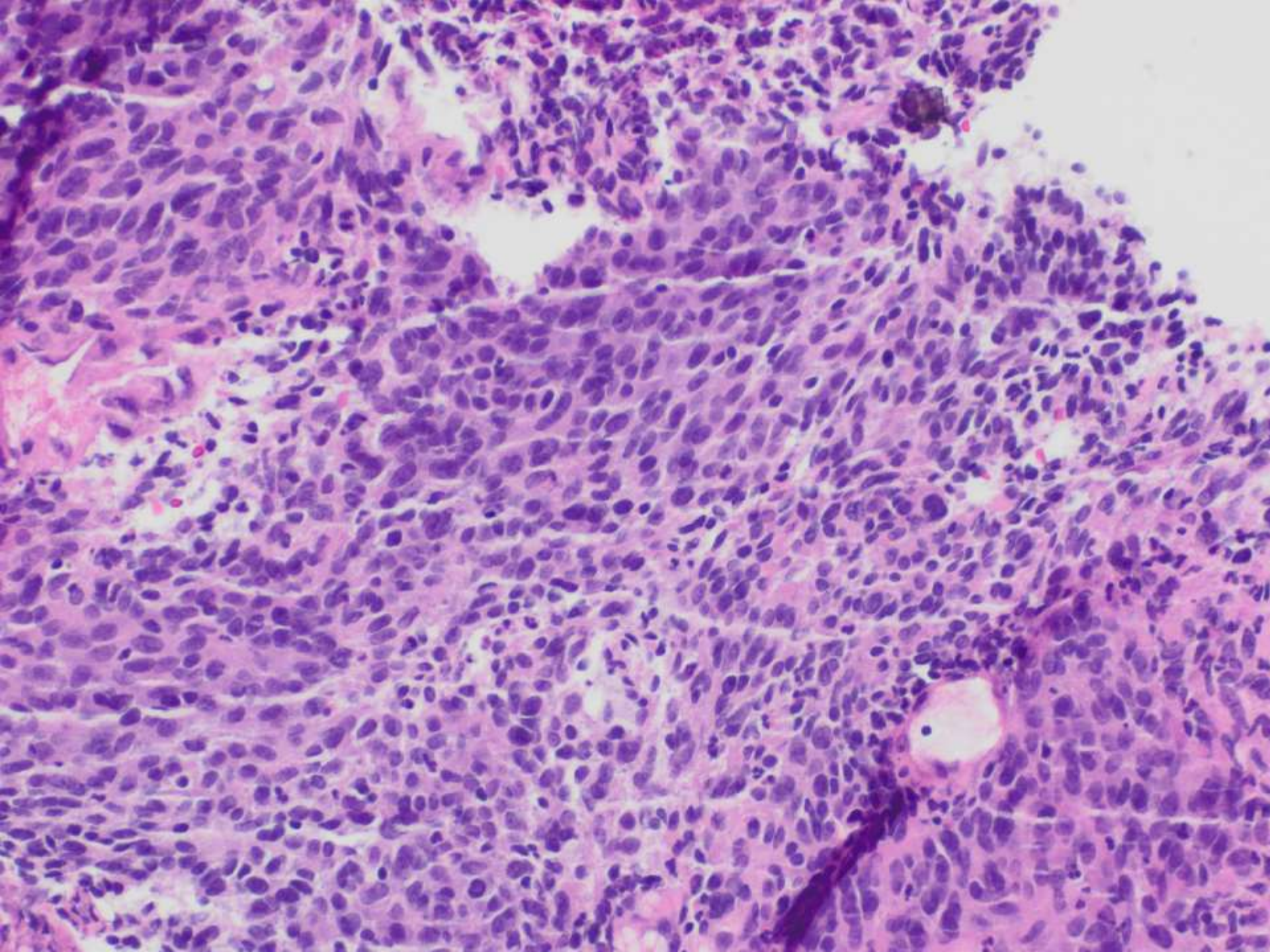


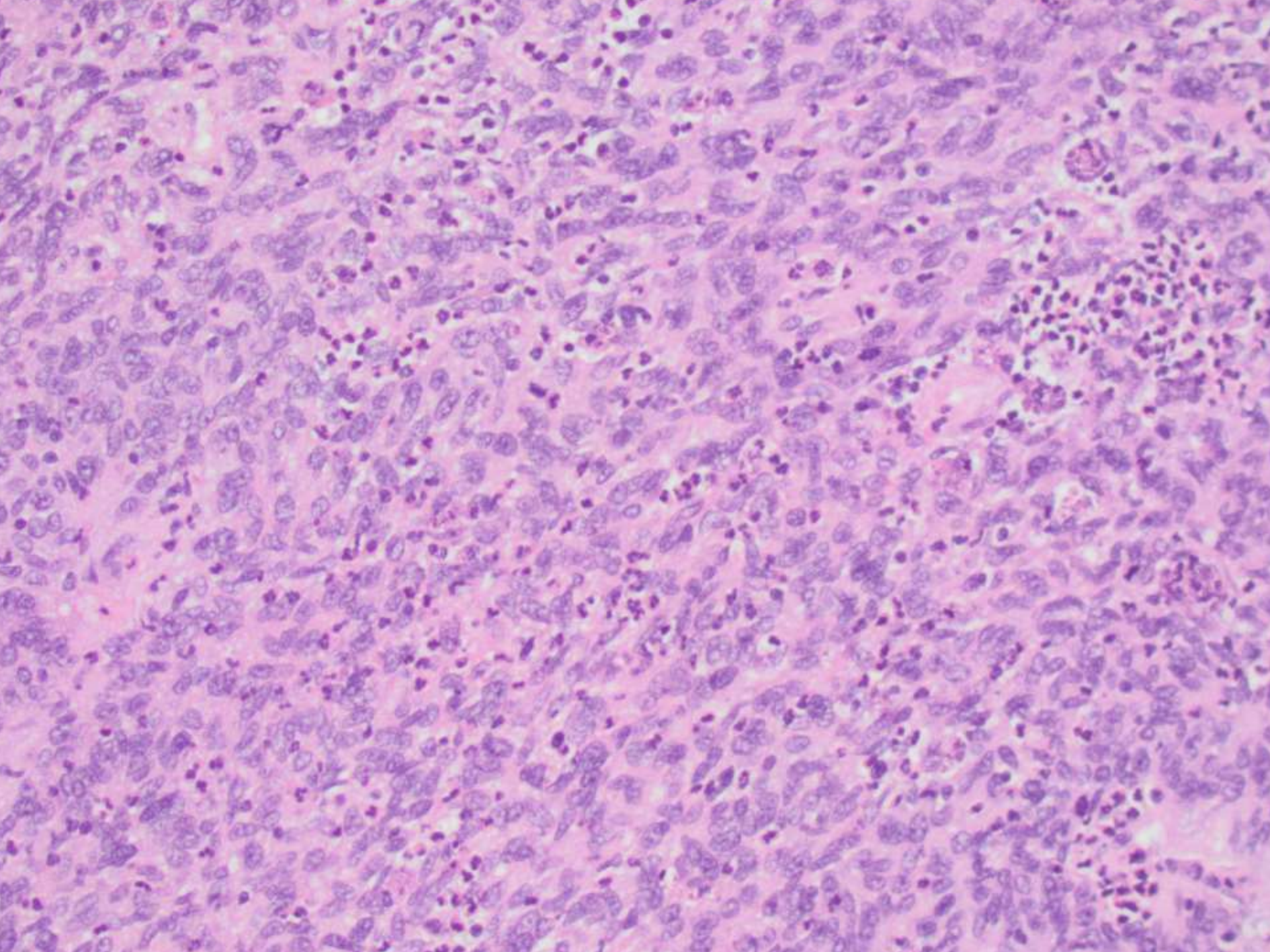


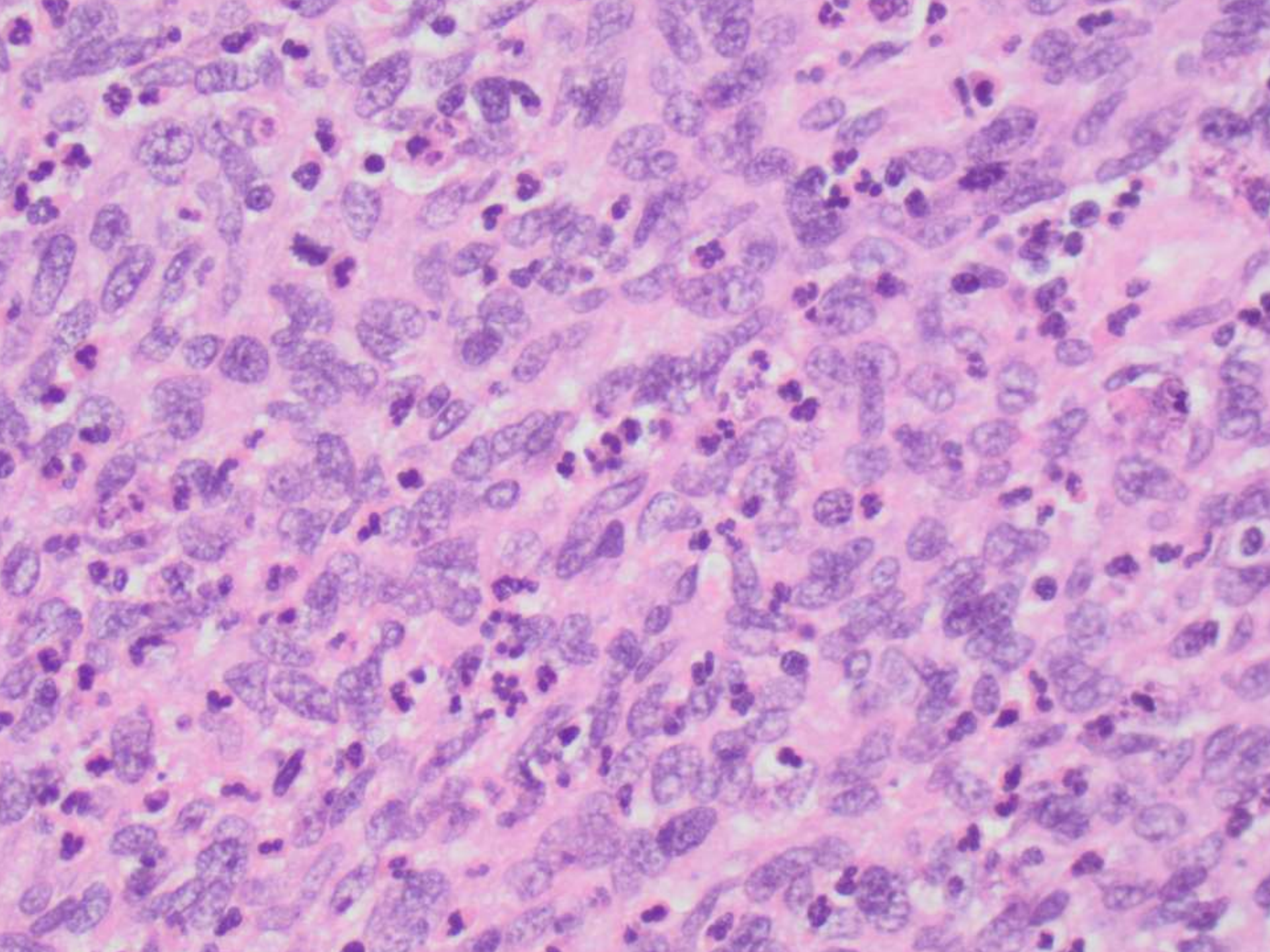


PERMANENT



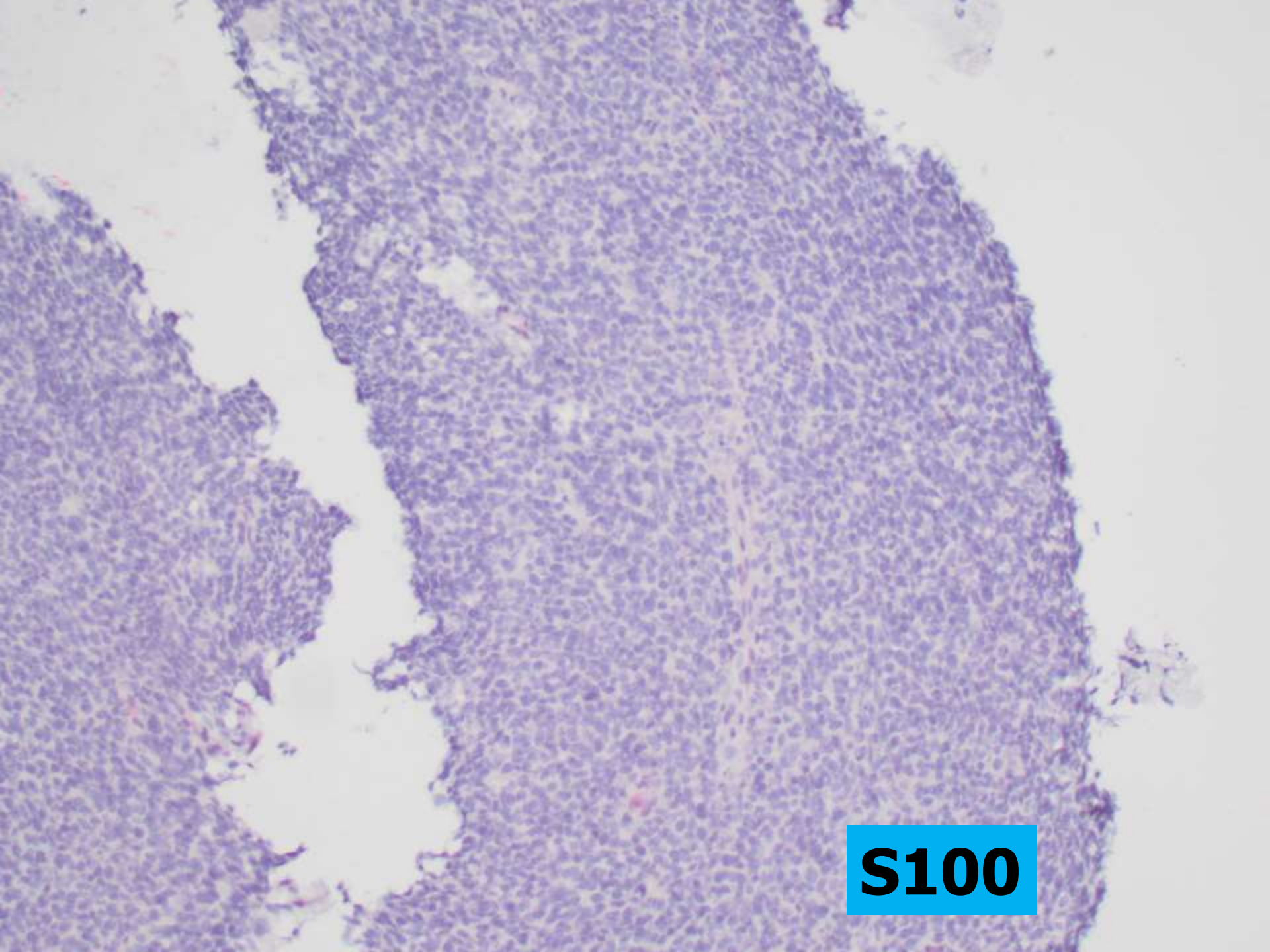


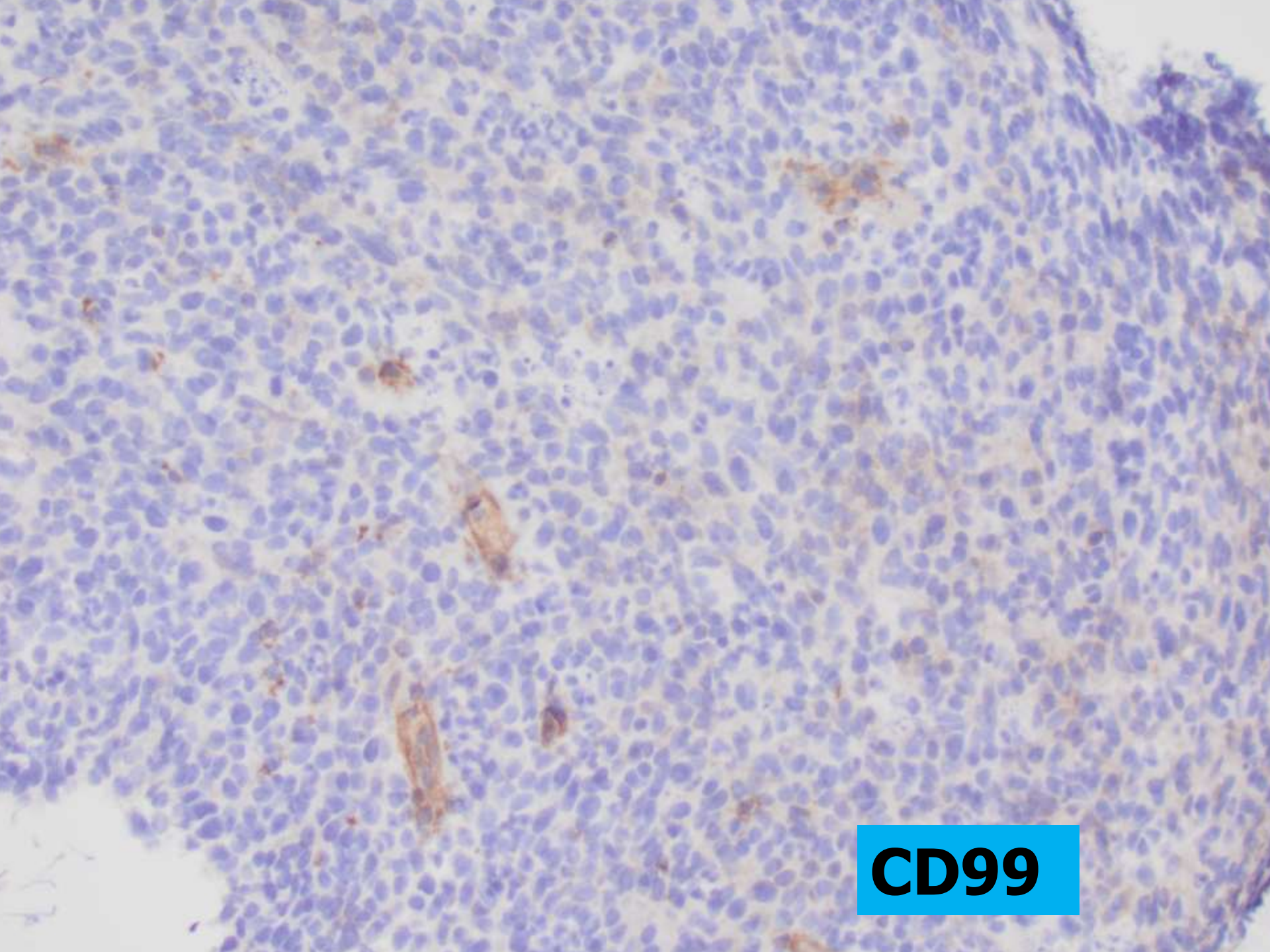


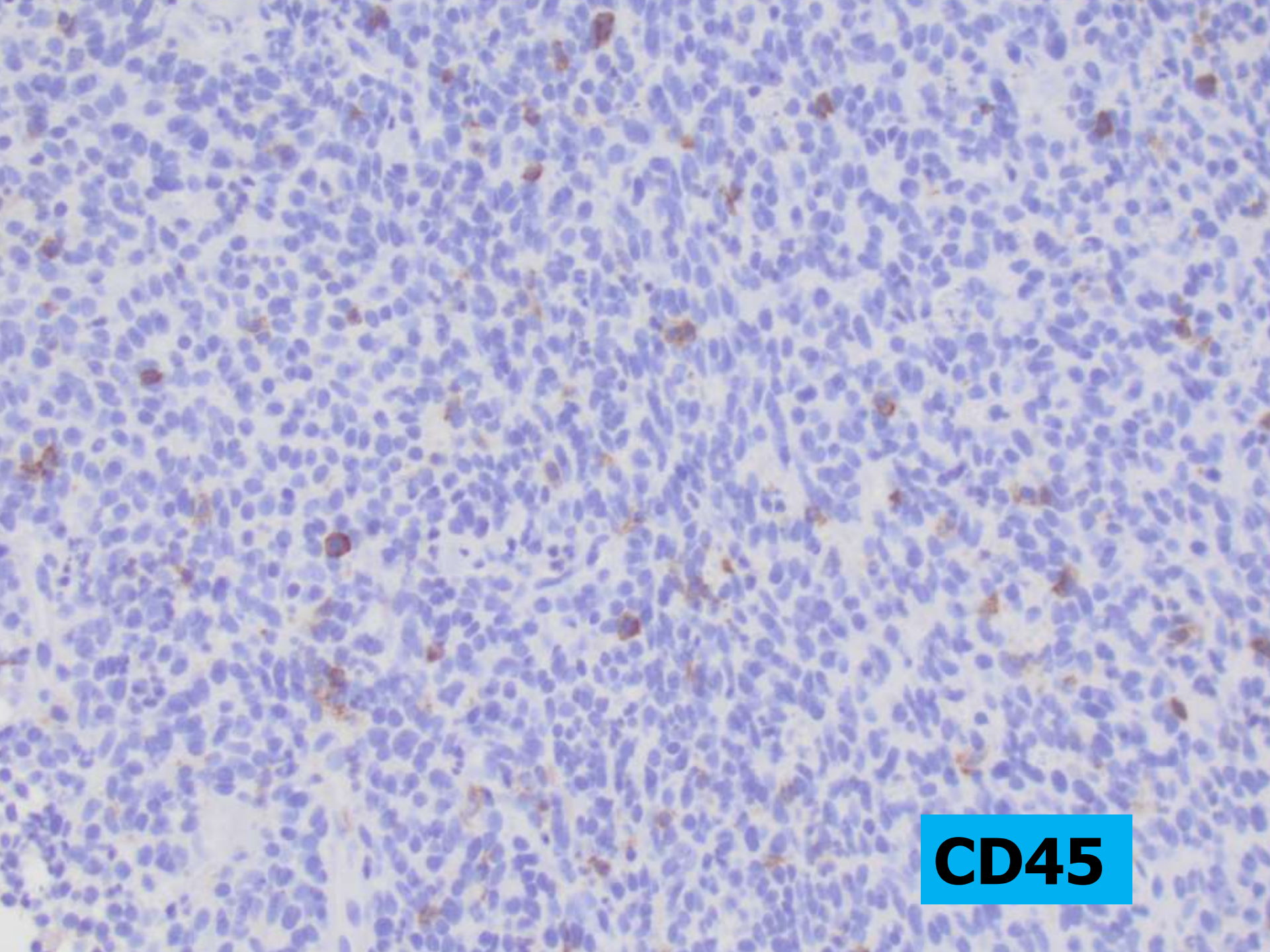


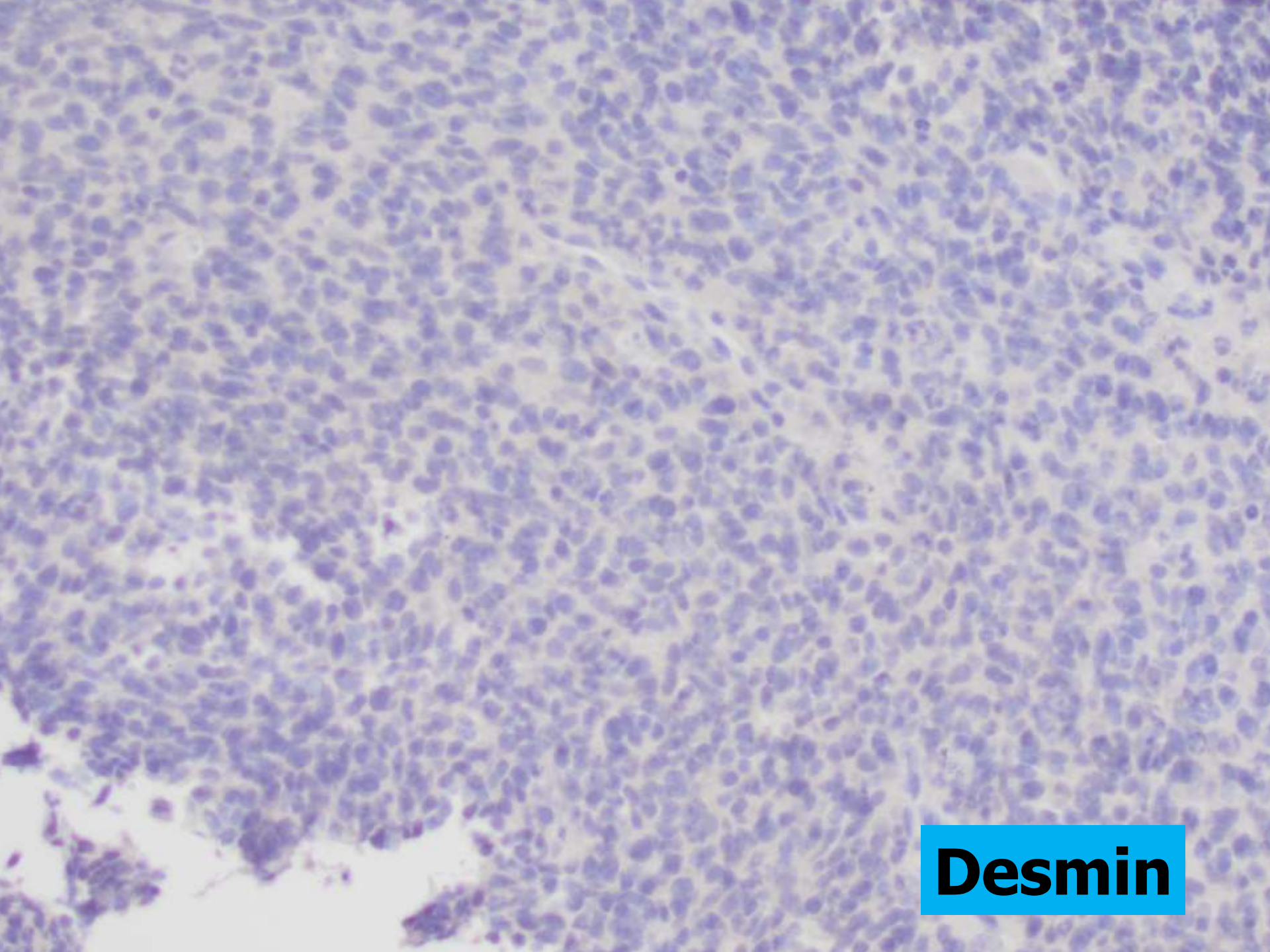
Your differential diagnosis?

- Melanoma?
- Neuroendocrine carcinoma?
- Squamous cell carcinoma (met, primary)?
- SMARCB1-deficient carcinoma?
- Lymphoma?
- Ewing sarcoma?
- Alveolar rhabdosarcoma?
- Others?


S100


CD99


CD45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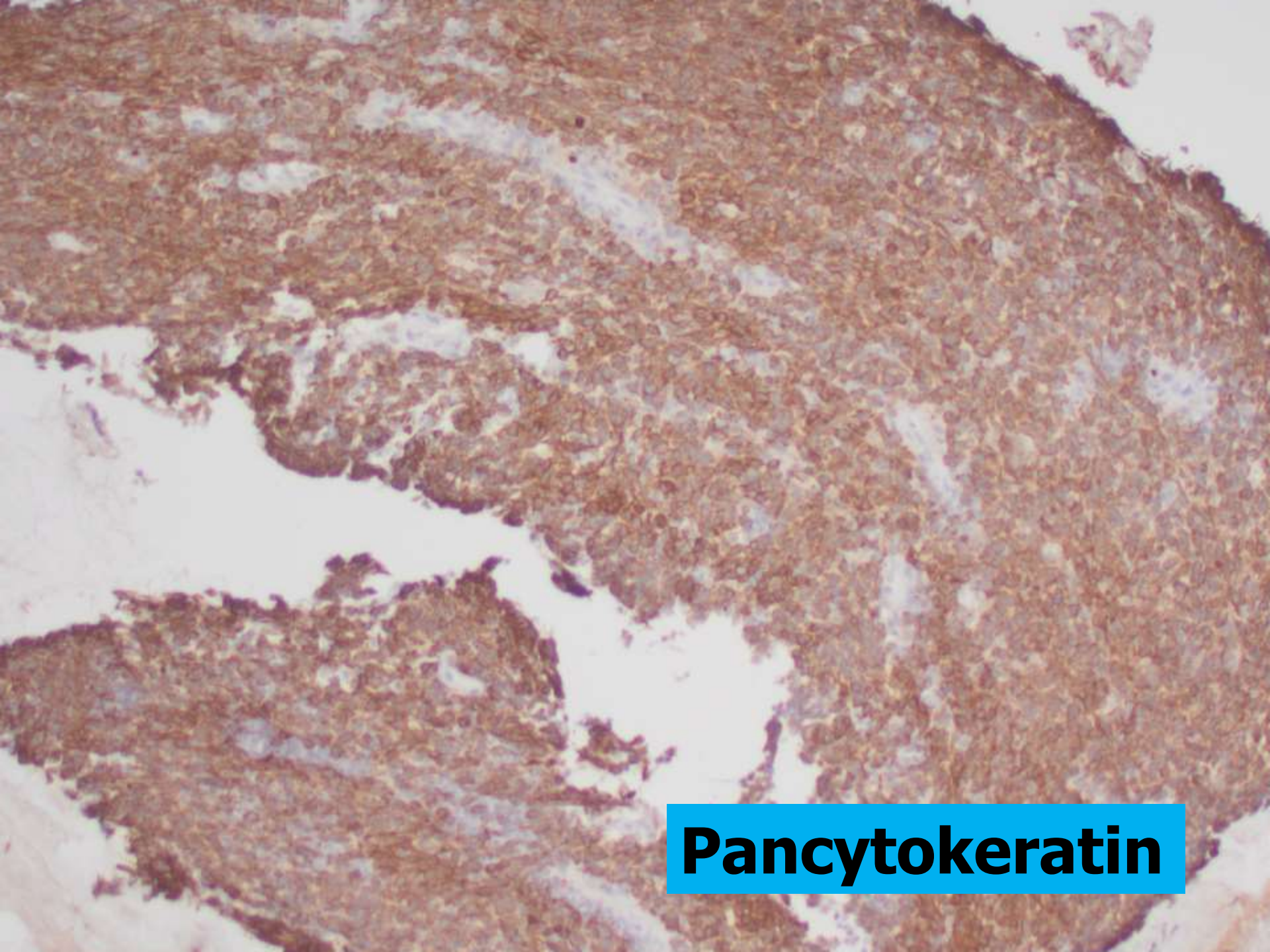
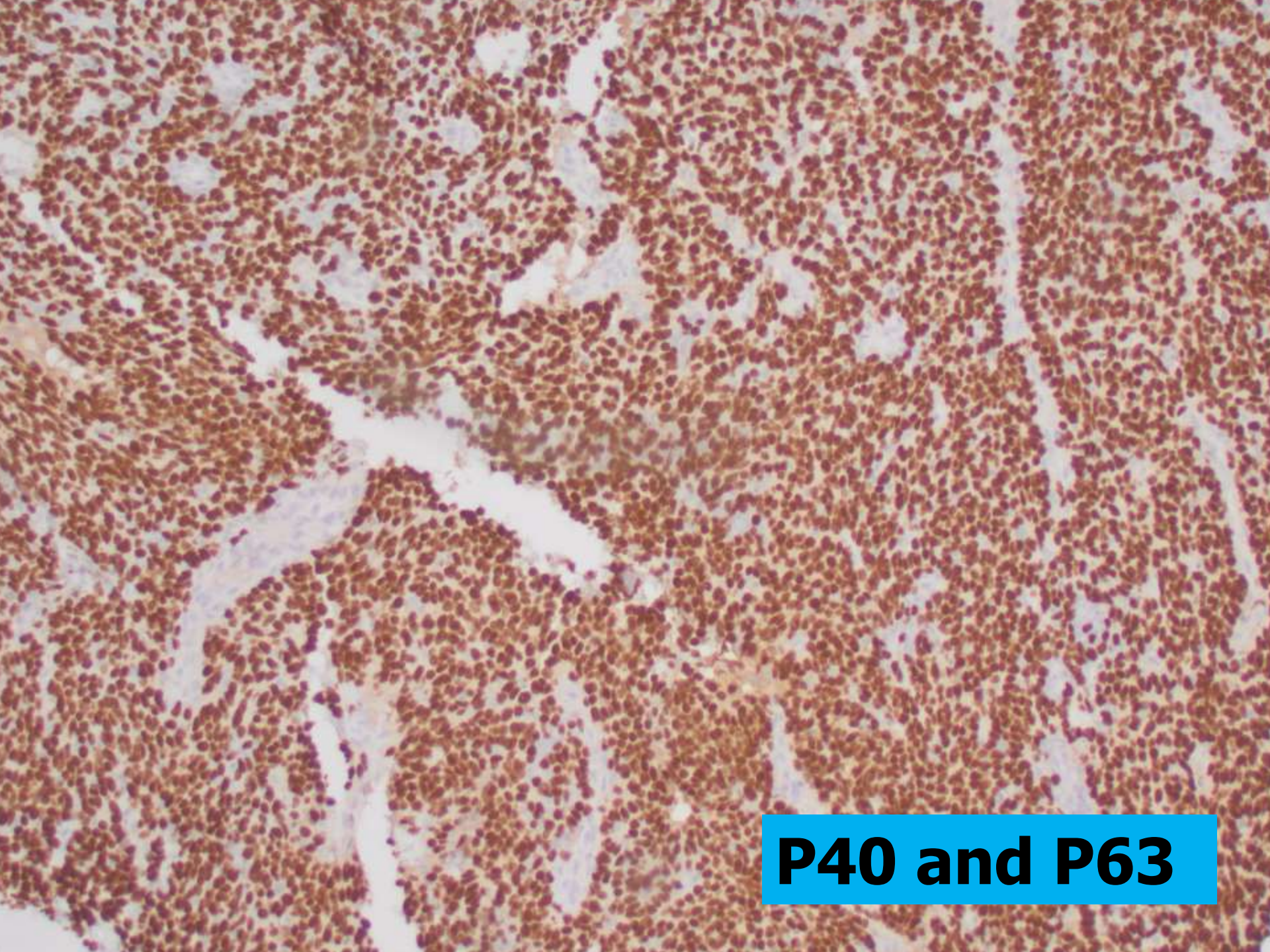
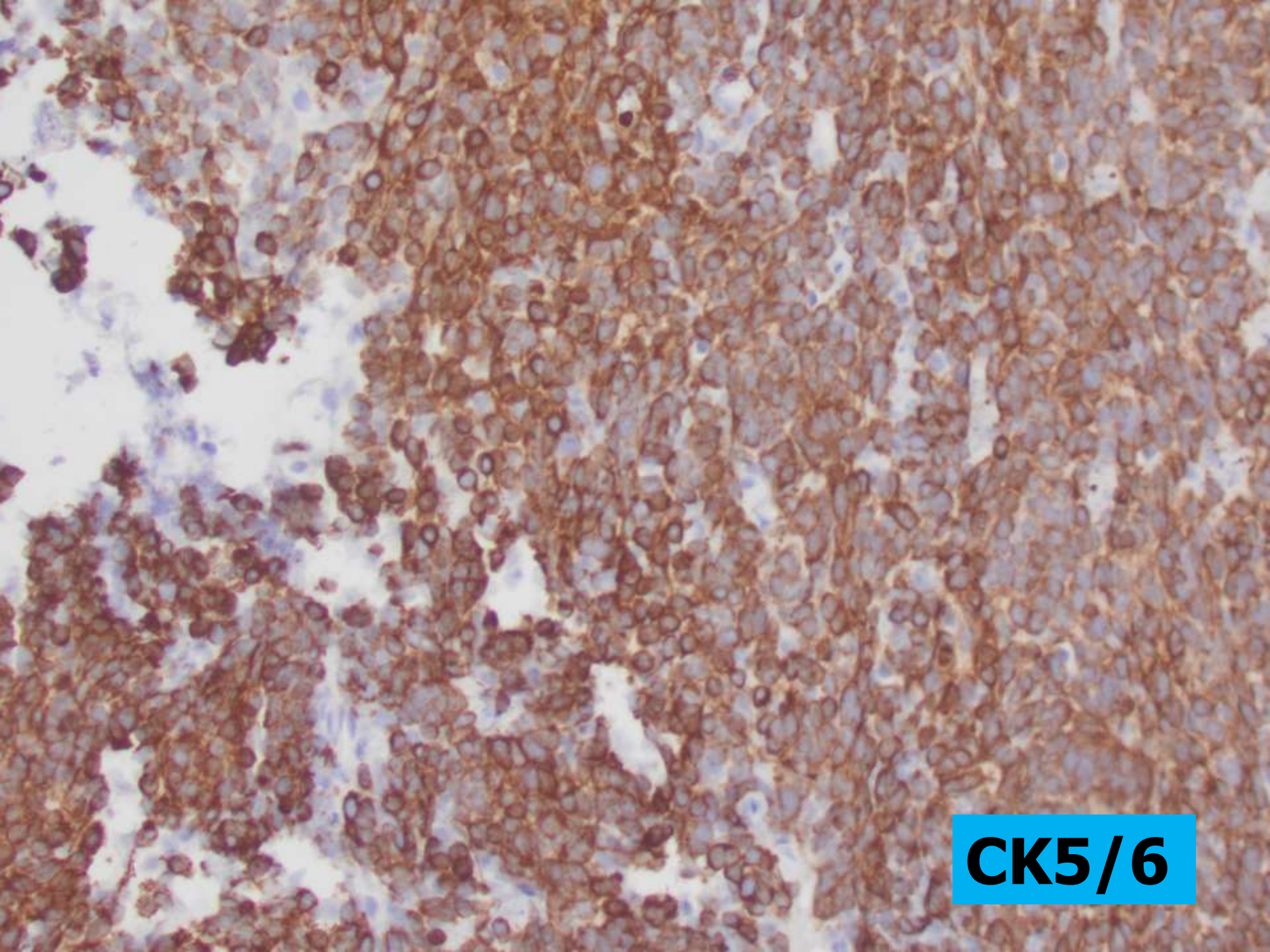
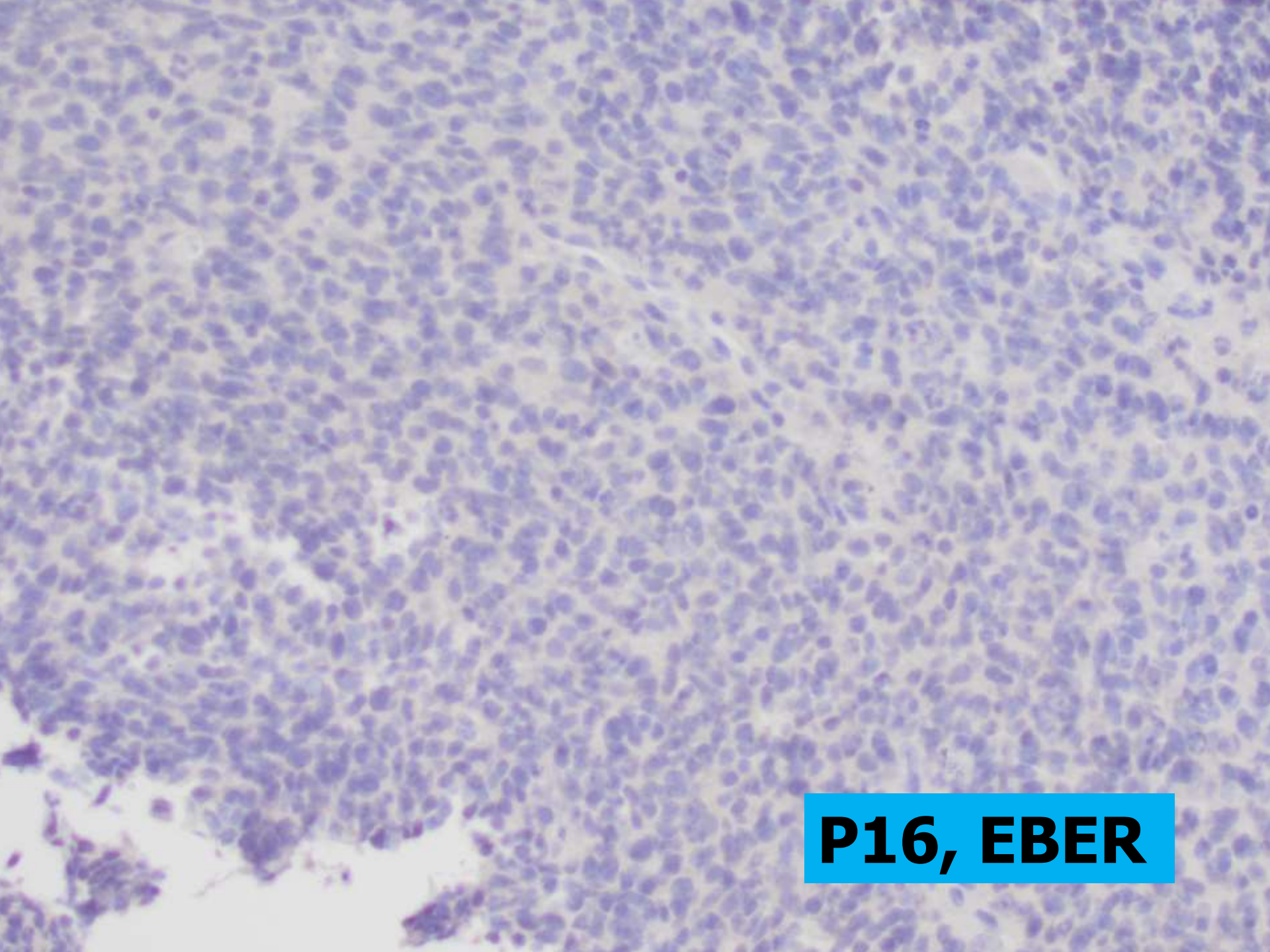
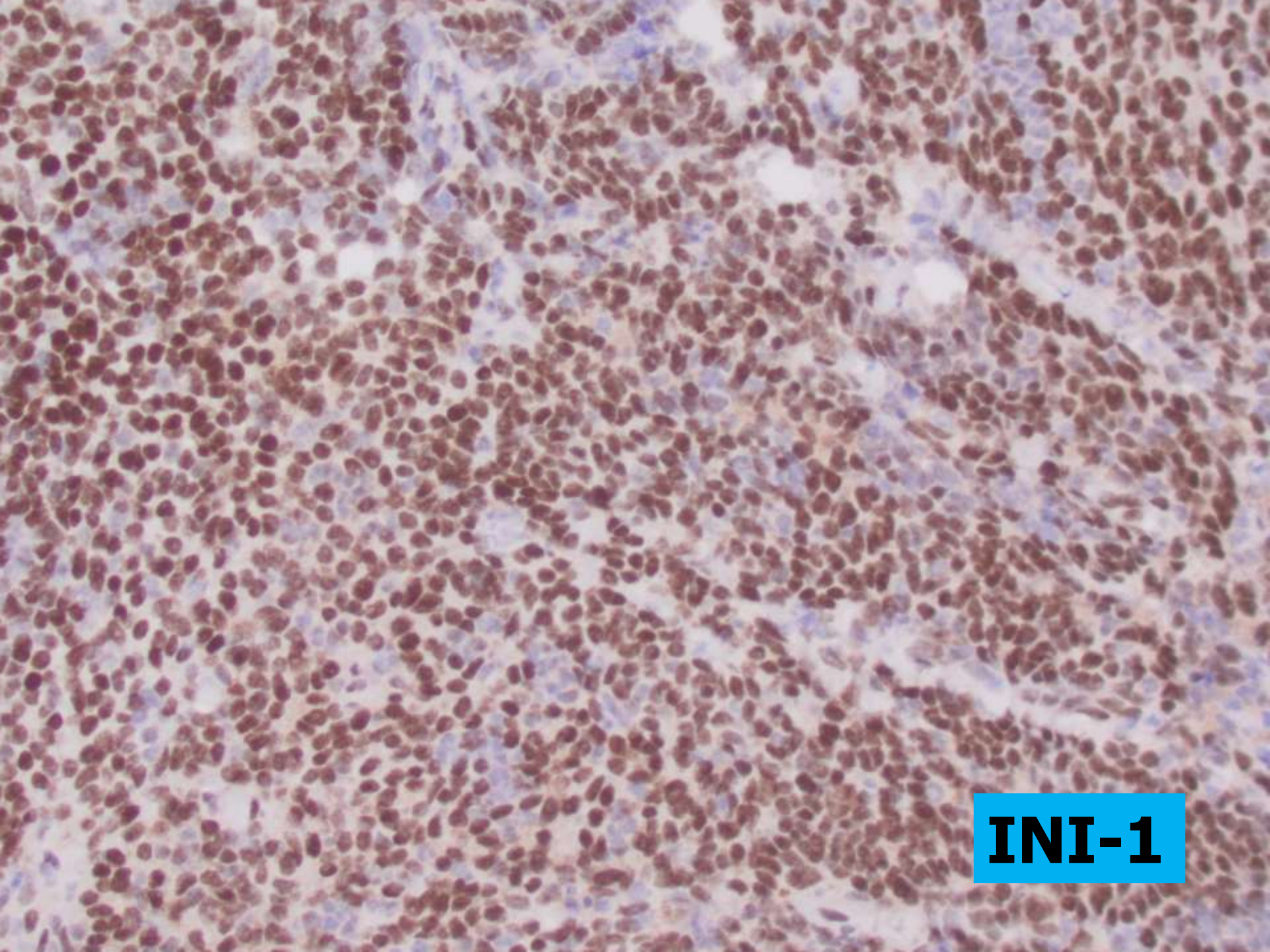

Pancytokeratin


P40 and P63


CK5/6

POORLY DIFFERENTIATED SQUAMOUS CELL CARCINOMA OF LUNG!? IN A 16 YEAR OLD NON-SMOKER GIRL?

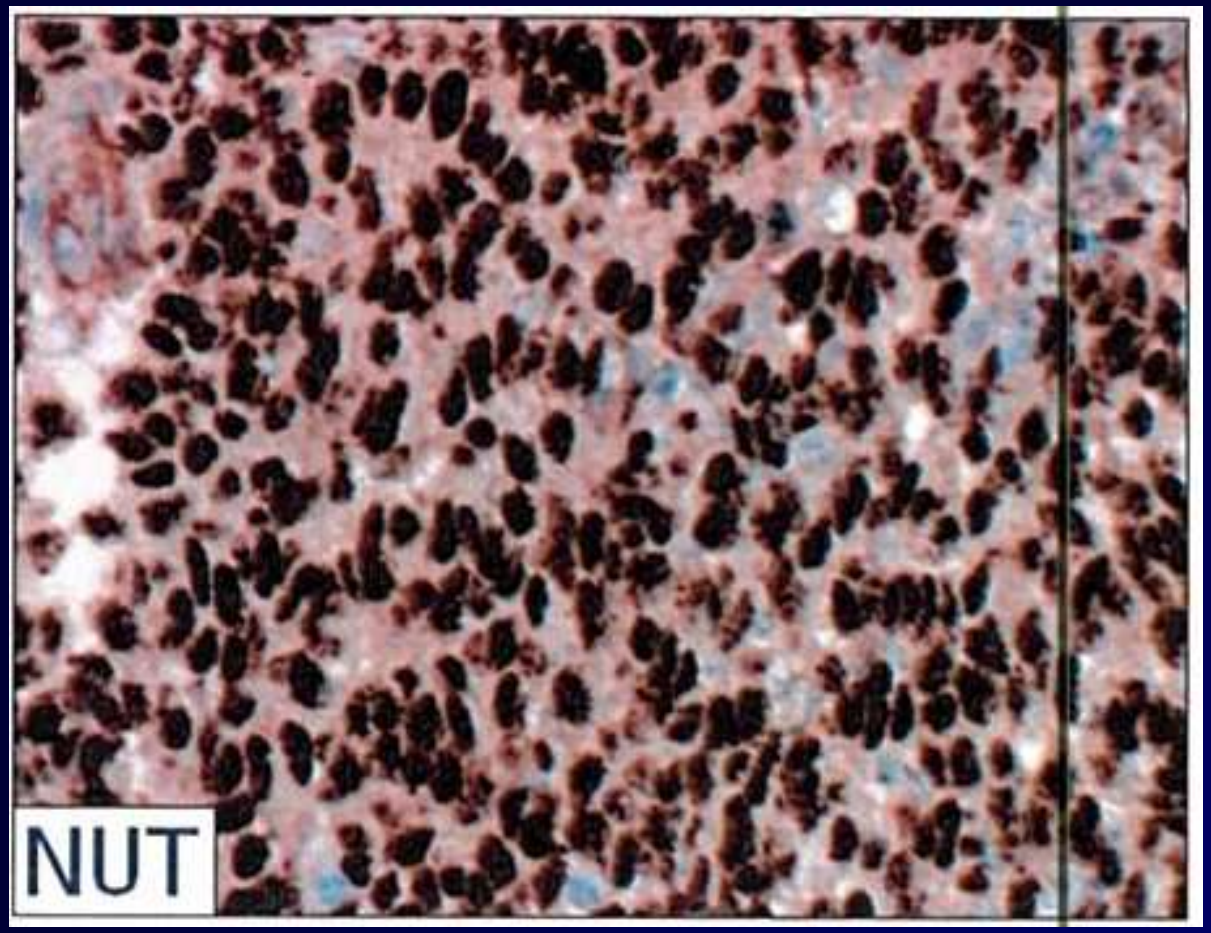

P16, EBER


INI-1

OTHER MARKERS

NEGATIVE FOR:

SALL4, MYOGENIN, WT-1, CD34, STAT-6, CD3, CD20,
ERG, CHROMOGRANIN, SYNAPTOPHYSIN


NUT

Final diagnosis

- Nut carcinoma.
- FISH: BRD4-NUTM1 rearrangement was observed in 70% of nuclei.

FOLLOW UP

- PET scan revealed metastasis to distant bone (left humerus, left fibula).
- Received 2 courses of intensive multiagent chemotherapy of VAI and PAI
- Palliative XRT to sites of pain
- Molebrisib (Bet inhibitor). This was associated with thrombocytopenia and elevation of ALT and INR so it was held.
- Hospice and patient diseased on 7/6/2019.