SEPT 2019 DIAGNOSIS LIST

19-0901: Dengue fever (atypical lymphocytosis mimicking lymphoma); peripheral blood/hematopathology and infectious disease pathology
19-0902: infarcted myelolipoma; adrenal gland/endocrine pathology
19-0903: follicular lymphoma, grade 1-2, with plasmacytic differentiation; lymph node/hematopathology
19-0904: typical carcinoid; lung/neoplastic lung pathology
19-0905: solitary fibrous tumor; pleural/soft tissue pathology
19-0906: cranial fasciitis; soft tissue/soft tissue pathology
19-0907: gastrointestinal stromal tumor with rhabdoid morphology; stomach; GI pathology
19-0908: reactive follicular hyperplasia (positive for syphilis); lymph node/hematopathology and infectious disease pathology
19-0909: invasive ductal carcinoma, focal DCIS associated with papilloma; breast/breast pathology
19-0910: malakoplakia; prostate/GU pathology

19-0901

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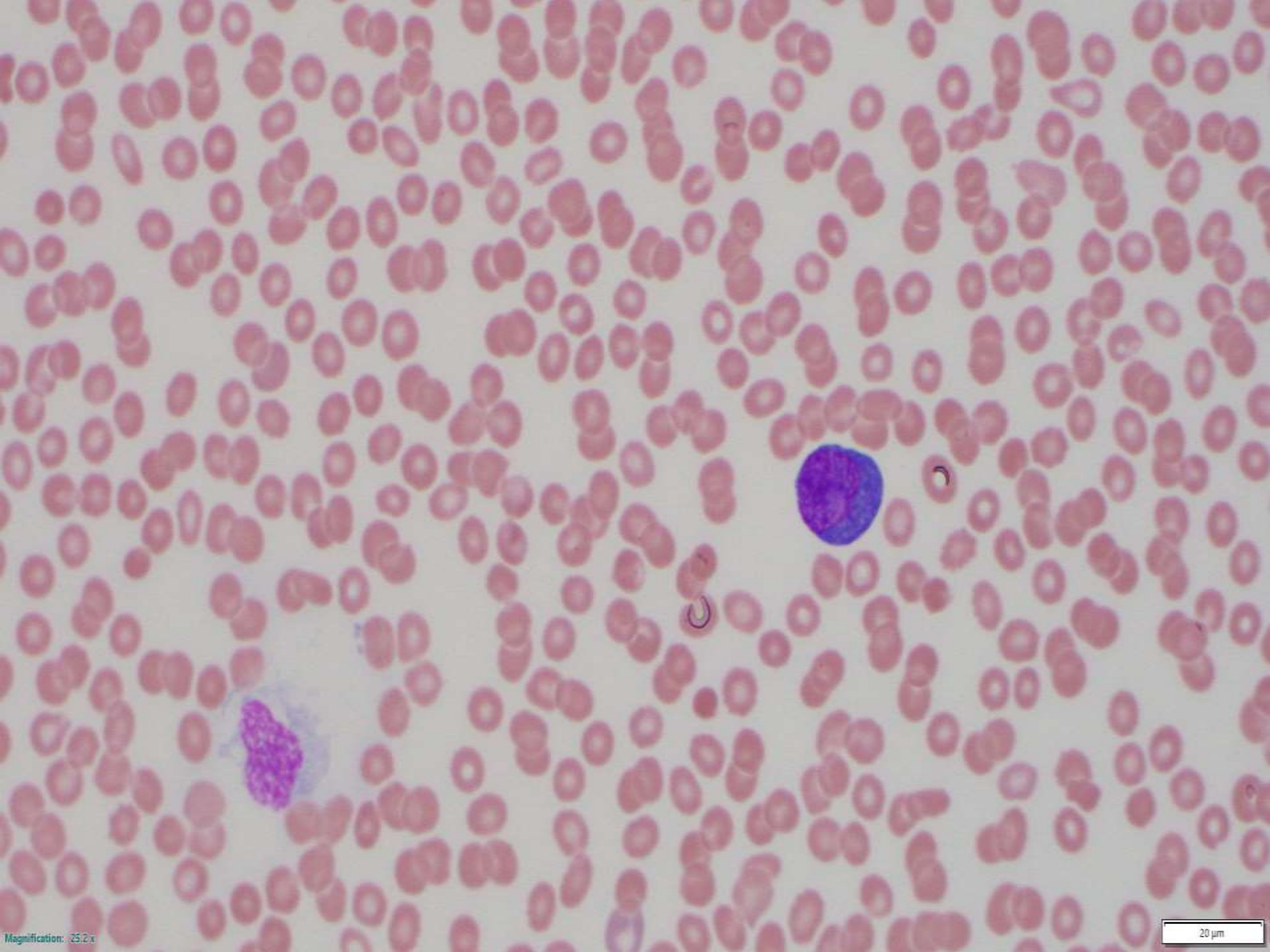
Deborah Dayhoff/Dean Fong; Kaiser San Rafael

History

- 56 year old female. Presented to the ER with fevers.
- CBC:
  - WBC 7.6
  - H/H 13.6/42.7
  - PLT 24
  - Diff
    - PMNs 17%
    - Lymphs 35%
    - Bands 1%
    - Mono 8%
    - Baso 2%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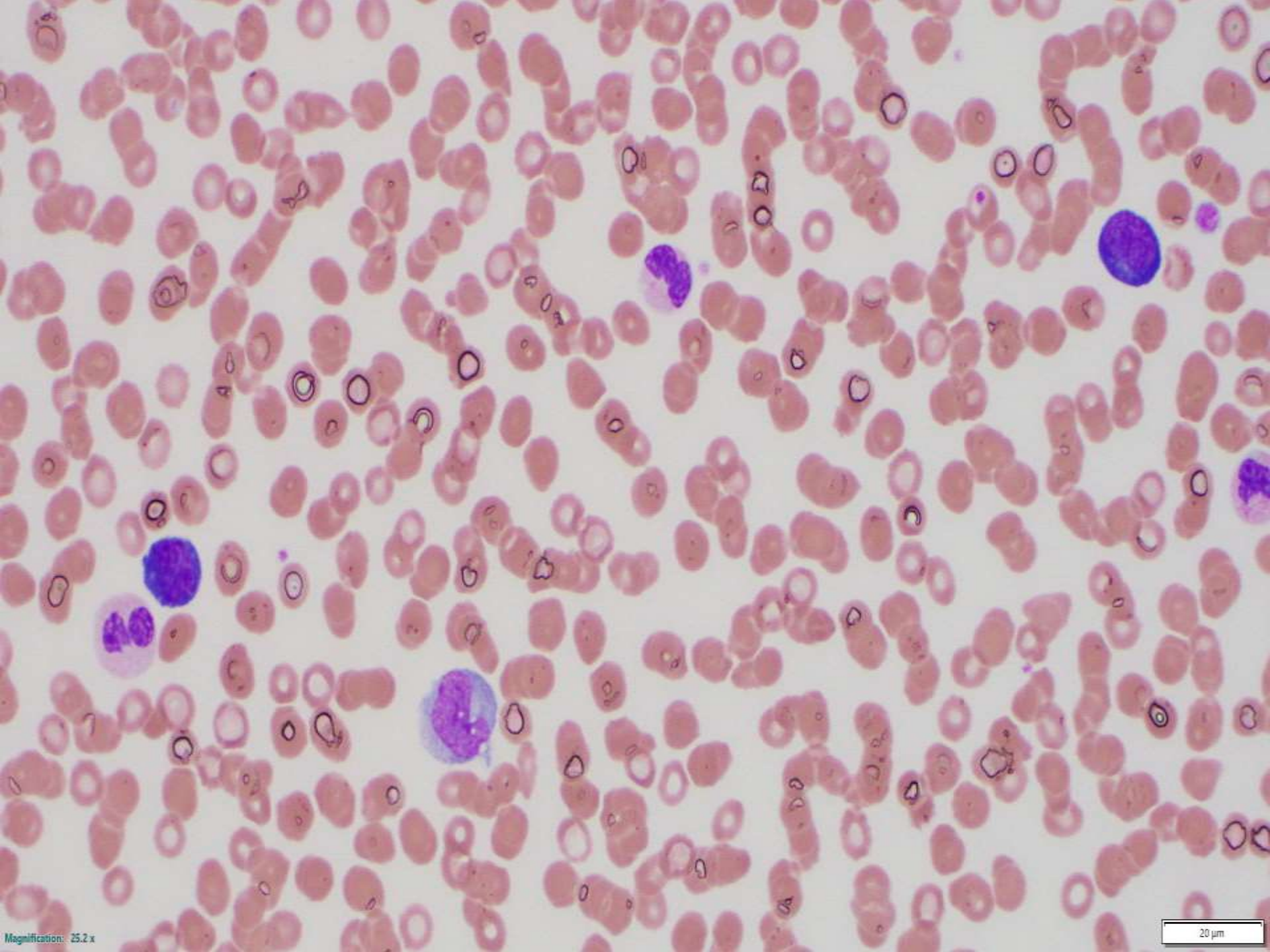
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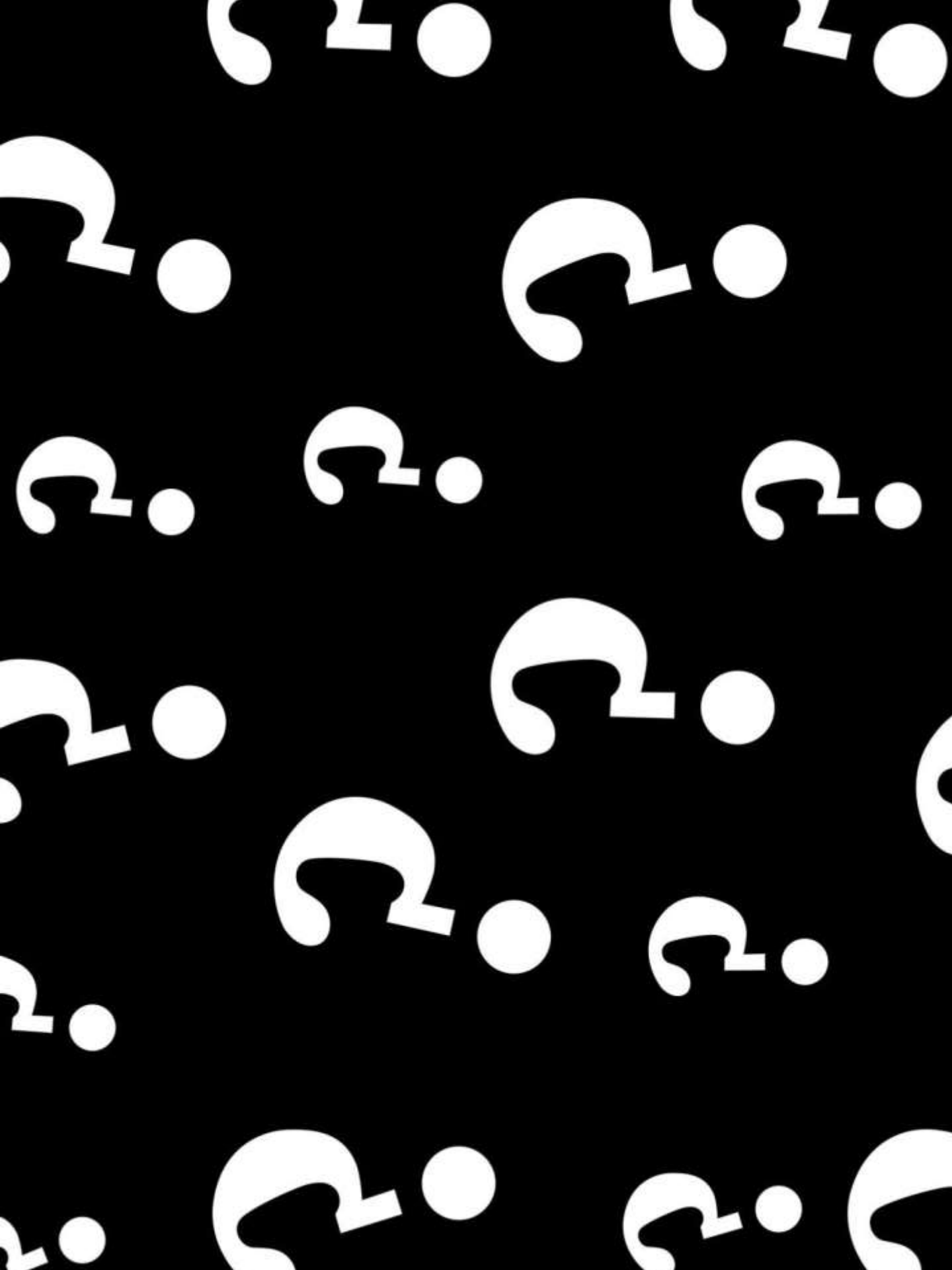


19-0901

Deborah Dayhoff, MD, and Dean Fong, DO

Kaiser Permanente San Rafael

Further Evaluation

- Petechial of the oral palate and extremities
- LFTs
  - ALT 104 ↑ (11-66)
  - AST 128 ↑ (14-36)
  - AP 61
  - Lipase 210
  - D. Bili 0.6
- Flow cytometry of peripheral blood
  - Increased plasma cells, 23%, with slight lambda predominance

Infectious Disease Work-up

- Recent travel to Philippines → her and her family had multiple mosquito bites
- Dengue IgG 13.55 (< 1.64)
- Dengue IgM 3.51 (< 1.64)

Diagnosis

- Atypical Plasmacytosis associated with Dengue Fever

Dengue Fever

- *Flavivirus* family
  - Positive single-stranded enveloped RNA viruses
  - Mosquitoes-transmitted virus: Yellow fever, Dengue Fever, Japanese encephalitis, West Nile virus, Zika virus
  - Ticks-transmitted virus: Tick-borne Encephalitis (TBE), Kyasanur Forest Disease (KFD) and Alkhurma disease, and Omsk hemorrhagic fever.
- Febrile illness caused by infection of 1 of 4 dengue virus of the genus *Flavivirus* (DENV-1, DENV-2, DENV-3, DENV-4)
- Primary versus Secondary infection
  - Approximately 95 percent of all severe/hospitalized cases of dengue are associated with second dengue virus infection.

Transmission

***Aedes aegypti* mosquito**

***Aedes albopictus* mosquito**

These mosquitoes also spread chikungunya and Zika viruses.

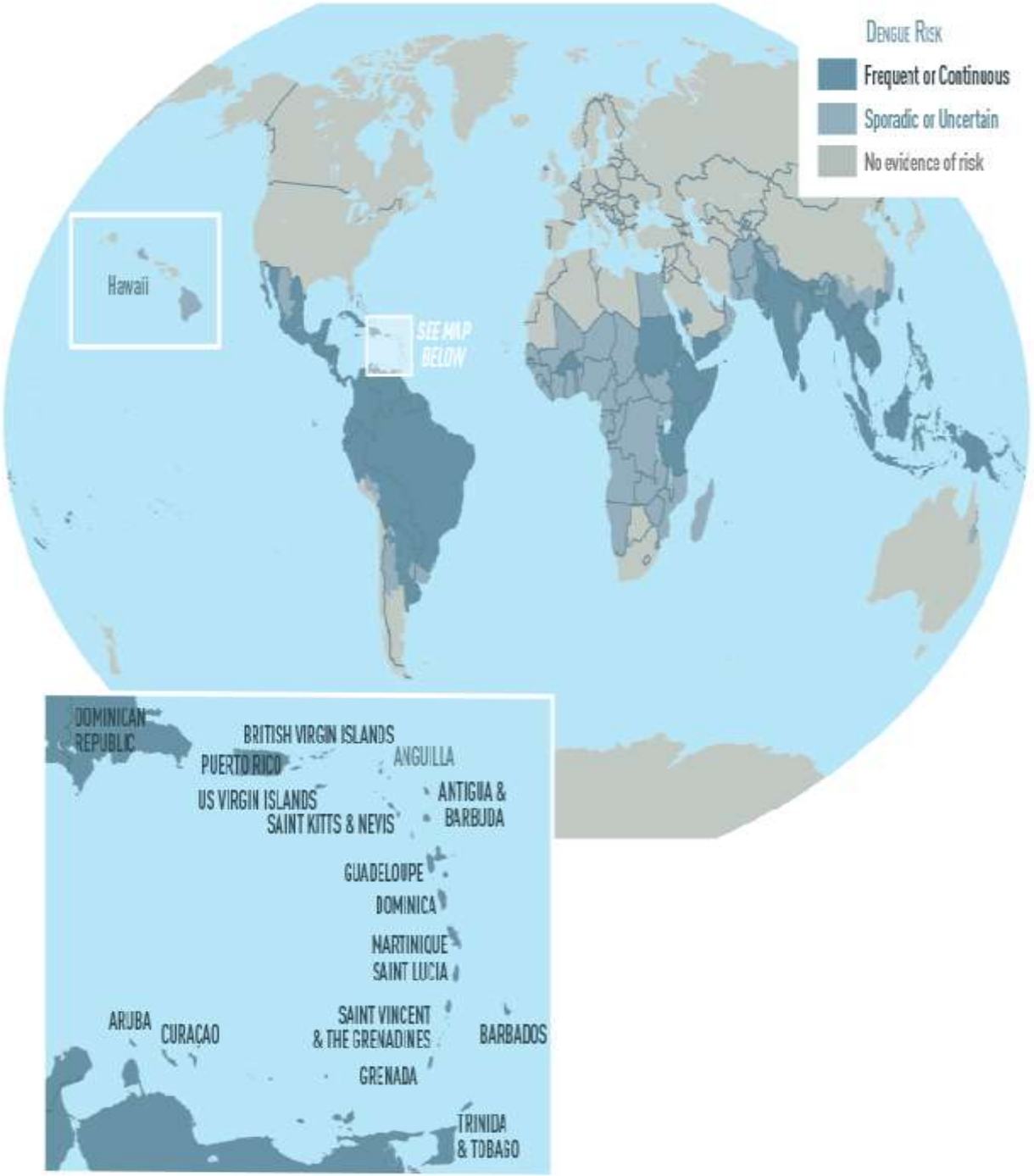
Mother-to-child (also test for Zika)

Through infected blood, organ transplant or needle stick

→ RARE

Epidemiology

- Records of dengue-like illness date back more than 200 years
  - Viral etiology of dengue virus was established in the 1940s
- Infection remains largely uncontrolled worldwide → hyperendemic throughout the tropics
- Estimates of 390 million infections worldwide each year; 96 million clinically apparent; and over 2.5 billion individuals at risk for infection
  - Increasing incidences in recent decades
- Approximately 500K develop dengue hemorrhagic fever → 20,000 deaths, primarily among children
- *Ae. aegypti* → widely distributed in tropical and subtropical areas
- *Ae. albopictus* → more tolerant of the cold and have a wider geographic distribution than *Ae. Aegypti*
  - Less likely to transmit since they do not feed on humans as frequently
- WHO → neglected tropical disease


Dengue Risk
Frequent or Continuous
Sporadic or Uncertain
No evidence of risk
Hawaii
SEE MAP BELOW
DOMINICAN REPUBLIC
BRITISH VIRGIN ISLANDS
PUERTO RICO
ANGUILLA
US VIRGIN ISLANDS
ANTIGUA & BARBUDA
SAINT KITTS & NEVIS
GUADELOUPE
DOMINICA
MARTINIQUE
SAINT LUCIA
ARUBA
CURACAO
SAINT VINCENT & THE GRENADINES
BARBADOS
GRENADA
TRINIDA & TOBAGO

Provisional data* as of August 7, 2019

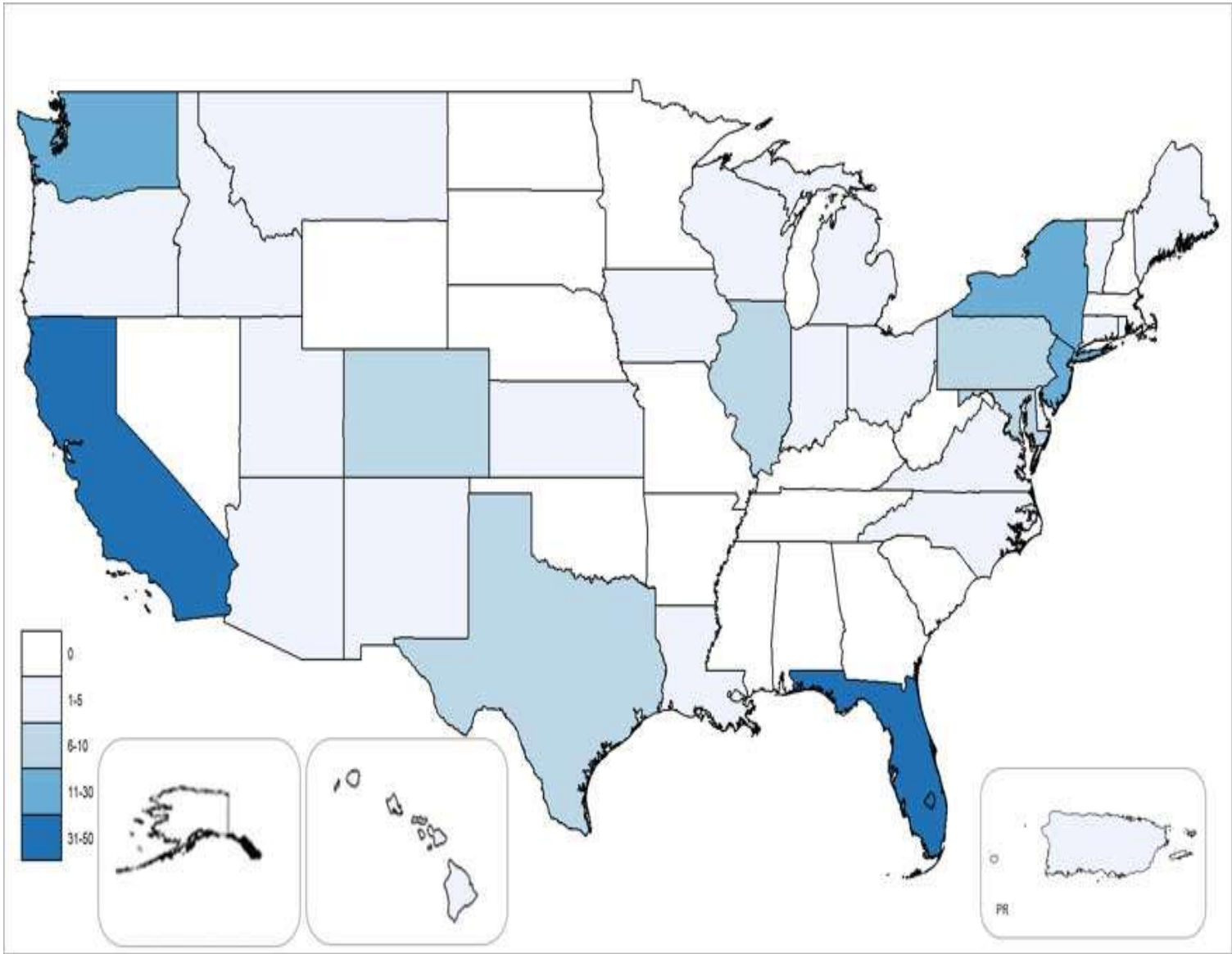
- This webpage contains provisional data reported to ArboNET for **2019**.

US States

- 216 dengue cases reported

US Territories

- 3 dengue cases reported



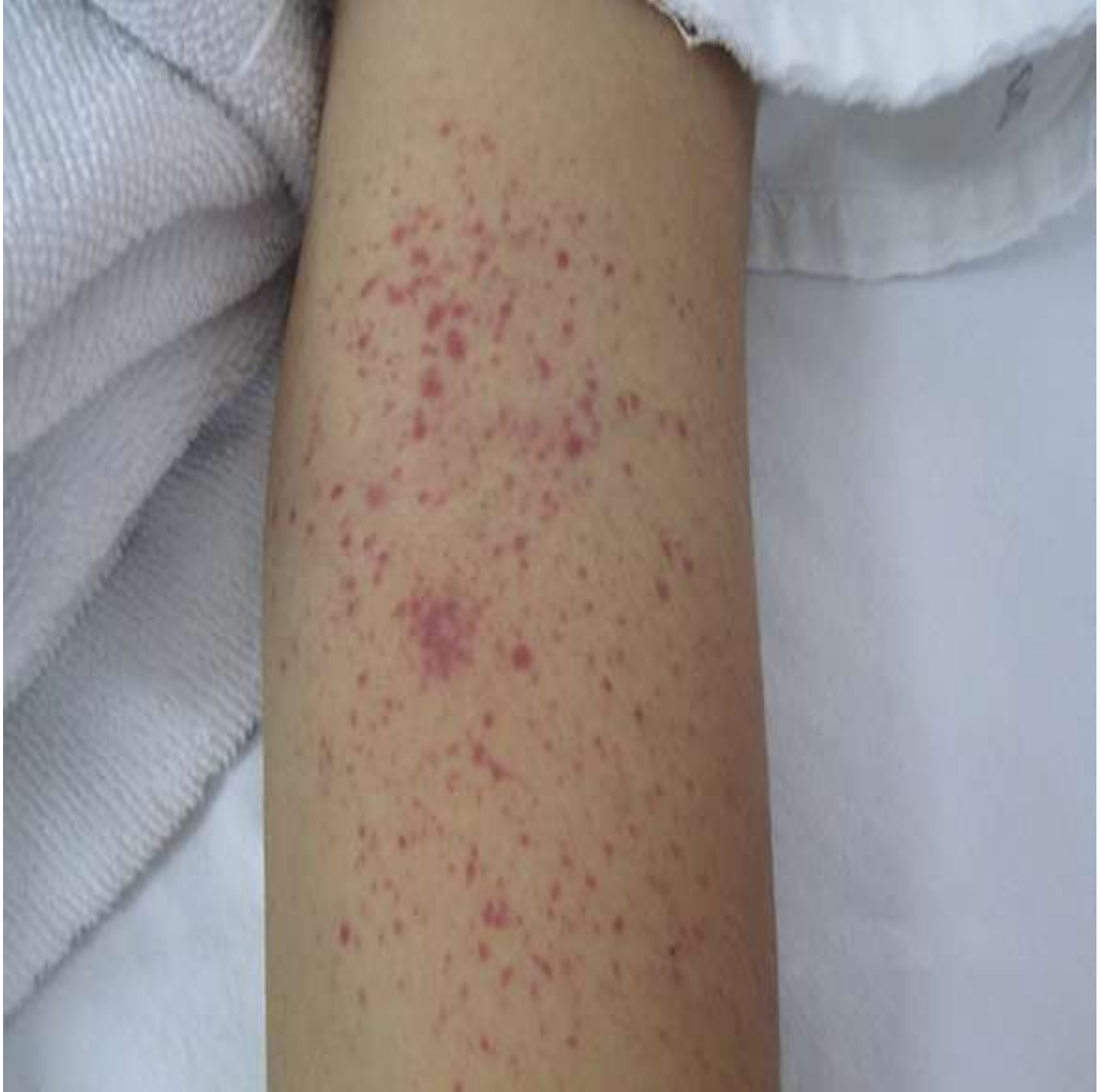
Classification

WHO 1997

- Dengue Fever
  - “Break-bone fever”
- Dengue Hemorrhagic Fever
  - Plasma leakage
  - Tourniquet or blood pressure cuff test
- Dengue Shock Syndrome
  - Marked plasma leakage leading to shock

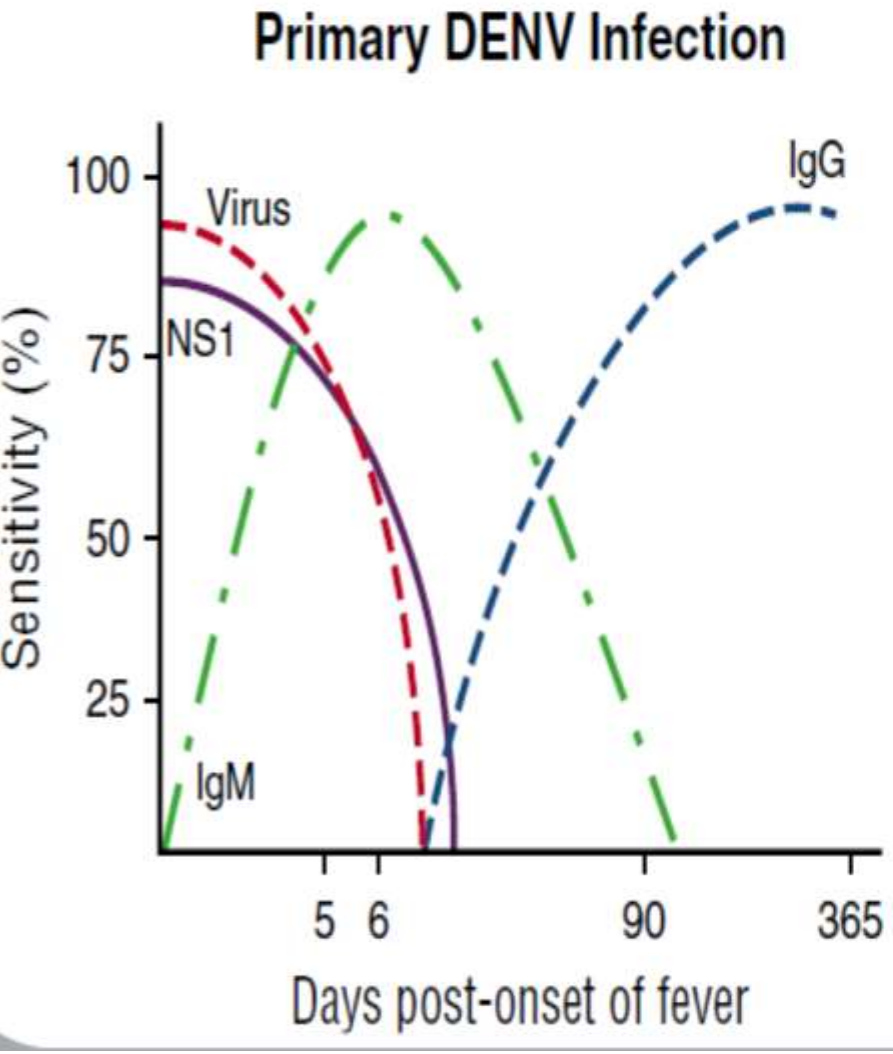
WHO 2009

- Dengue Without Warning Signs
- Dengue With Warning Signs
- Severe Dengue

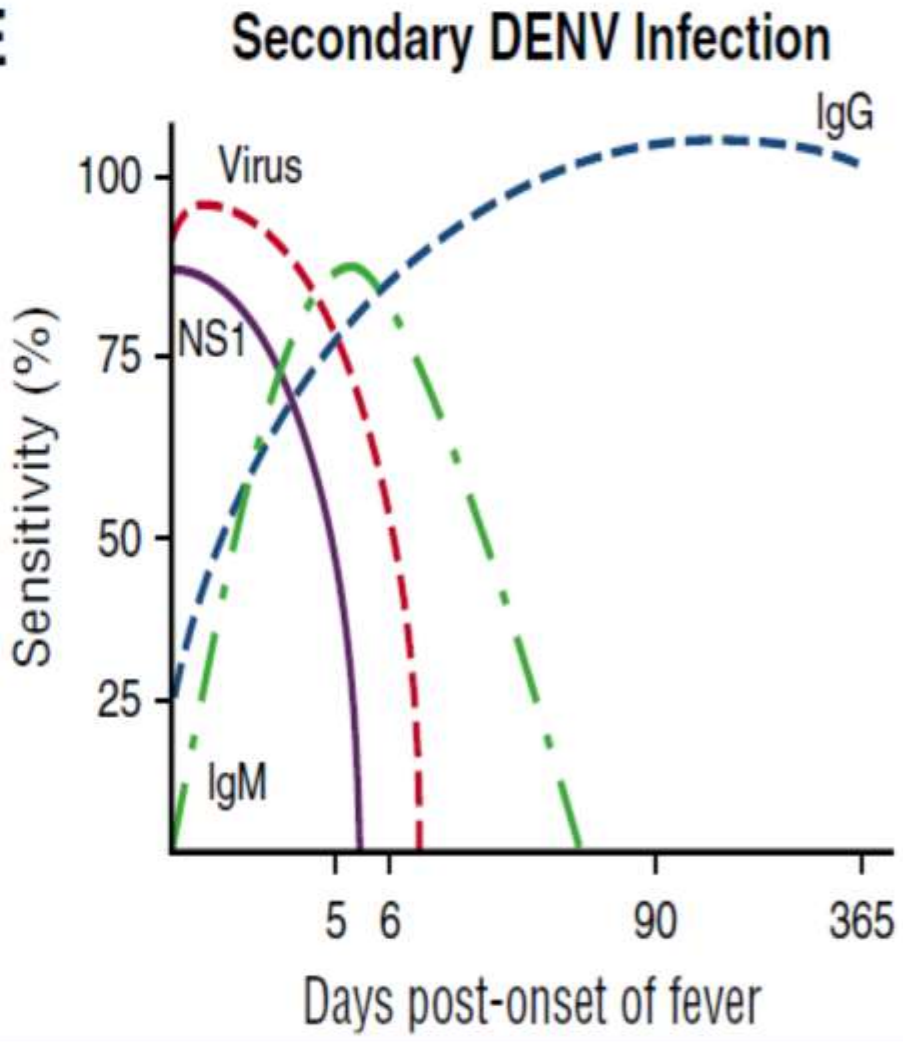


Clinical Manifestation

- Incubation period → 3-14 days; symptoms develop between 4-7 days after bite
- Phases of Infection
  - Febrile → high grade fevers ≥38.5°C, HA, eye pain, joint pain, rash
    - Hemorrhagic manifestations may be observed
    - Leukopenia and thrombocytopenia common; AST levels are frequently elevated
  - Critical → defervescence (3-7 days of infection) → a small proportion of patients (typically children and young adults) develop a systemic vascular leak syndrome
    - The critical phase lasts for 24 to 48 hours.
    - Hemorrhagic manifestations may be observed
  - Recovery → lasts two to four days; adults may have profound fatigue for days to weeks after recovery
- Usual manifestations → encephalitis, hepatitis, myocarditis, splenomegaly, etc.


Primary DENV Infection
100
75
50
25
Sensitivity (%)
Virus
NS1
IgM
IgG
5
6
90
365
Days post-onset of fever

E


Secondary DENV Infection
100
75
50
25
Sensitivity (%)
Virus
NS1
IgM
IgG
5
6
90
365
Days post-onset of fever

CDC recommends dengue virus testing for:

- Anyone who lives in or traveled to areas where dengue virus is transmitted and has recently experienced signs and symptoms of dengue illness.
  - Signs and symptoms of dengue may include fever, headache, rash, body aches, and bleeding manifestations. Symptoms may be mild or severe. Severe dengue often requires hospitalization. Dengue can occasionally present with signs and symptoms of aseptic meningitis or encephalitis.
- Symptomatic pregnant women with possible dengue or Zika virus exposure*

Dengue virus testing is **not** recommended for:

- Asymptomatic patients
- Preconception screening

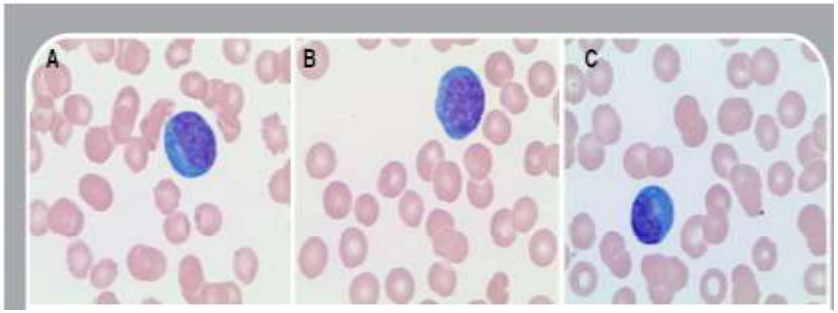
Diagnostic Tests for Dengue and Specimens

Diagnostic Test	≤7 Days After Symptom Onset	>7 Days Post Symptom Onset	Specimen Types
Molecular Tests	✓	—	Serum, plasma, whole blood, cerebrospinal fluid*
Dengue Virus Antigen Detection (NS1)	✓	—	Serum
Serologic Tests	✓	✓	Serum, cerebrospinal fluid*
Tissue Tests	✓	✓	Fixed tissue

* Testing cerebrospinal fluid is recommended in suspect patients with central nervous system clinical manifestations such as encephalopathy and aseptic meningitis.

bloodwork
IMAGES IN HEMATOLOGY

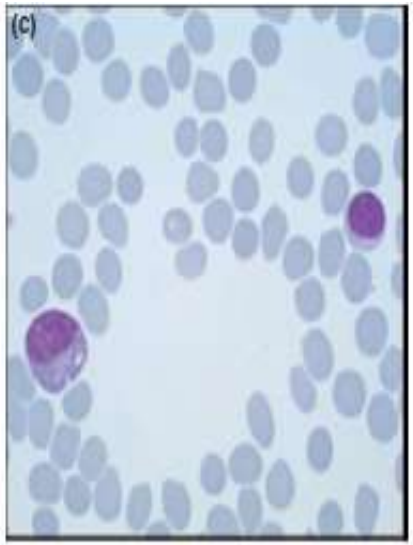
Plasmacytoid lymphocytes: a clue to dengue diagnosis



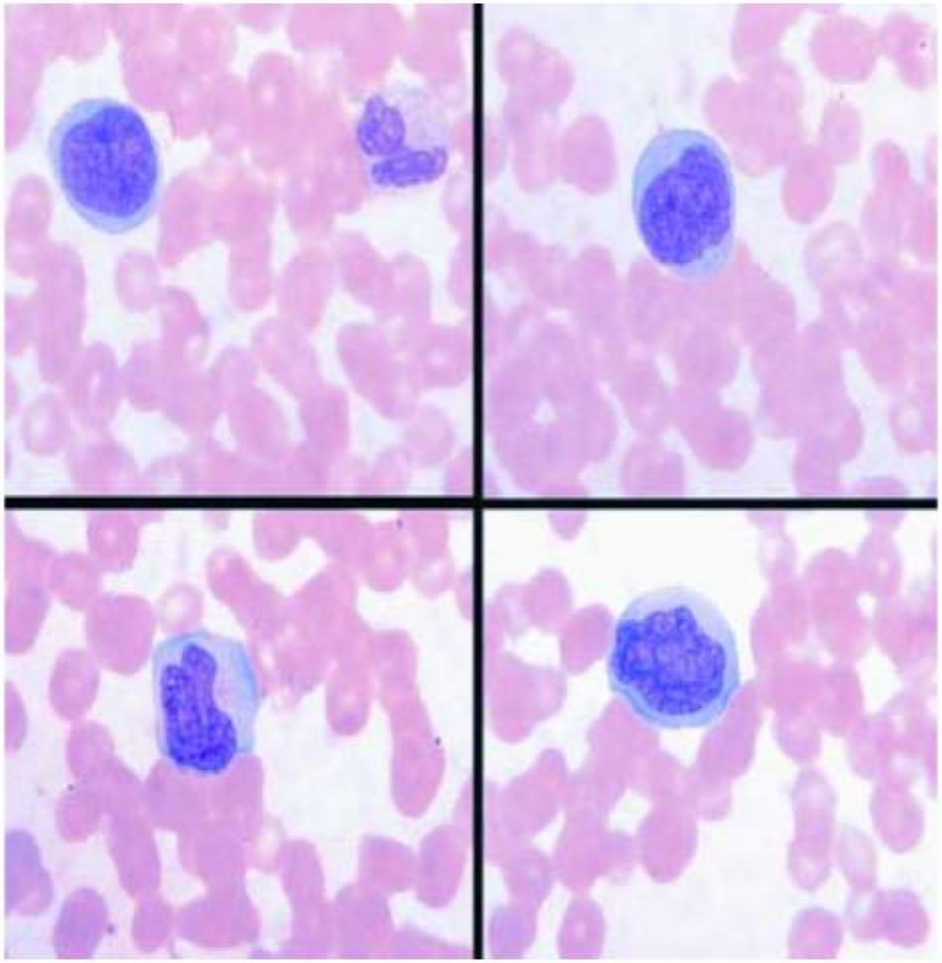
High incidence of peripheral blood plasmacytosis in patients with dengue virus infection

Clinical Microbiology and Infection, Volume 17 Number 12, December 2011

K. T. D. Thai[1,2], J. A. Wismeijer[1], C. Zumpolle[1], M. D. de Jong[2,3], M. J. Kersten[1] and P. J. de Vries[1,2]



LABMEDICINE ■ Volume 38 Number 1 ■ January 2007



Cell Host Microbe. 2014 July 9; 16(1): 115–127.

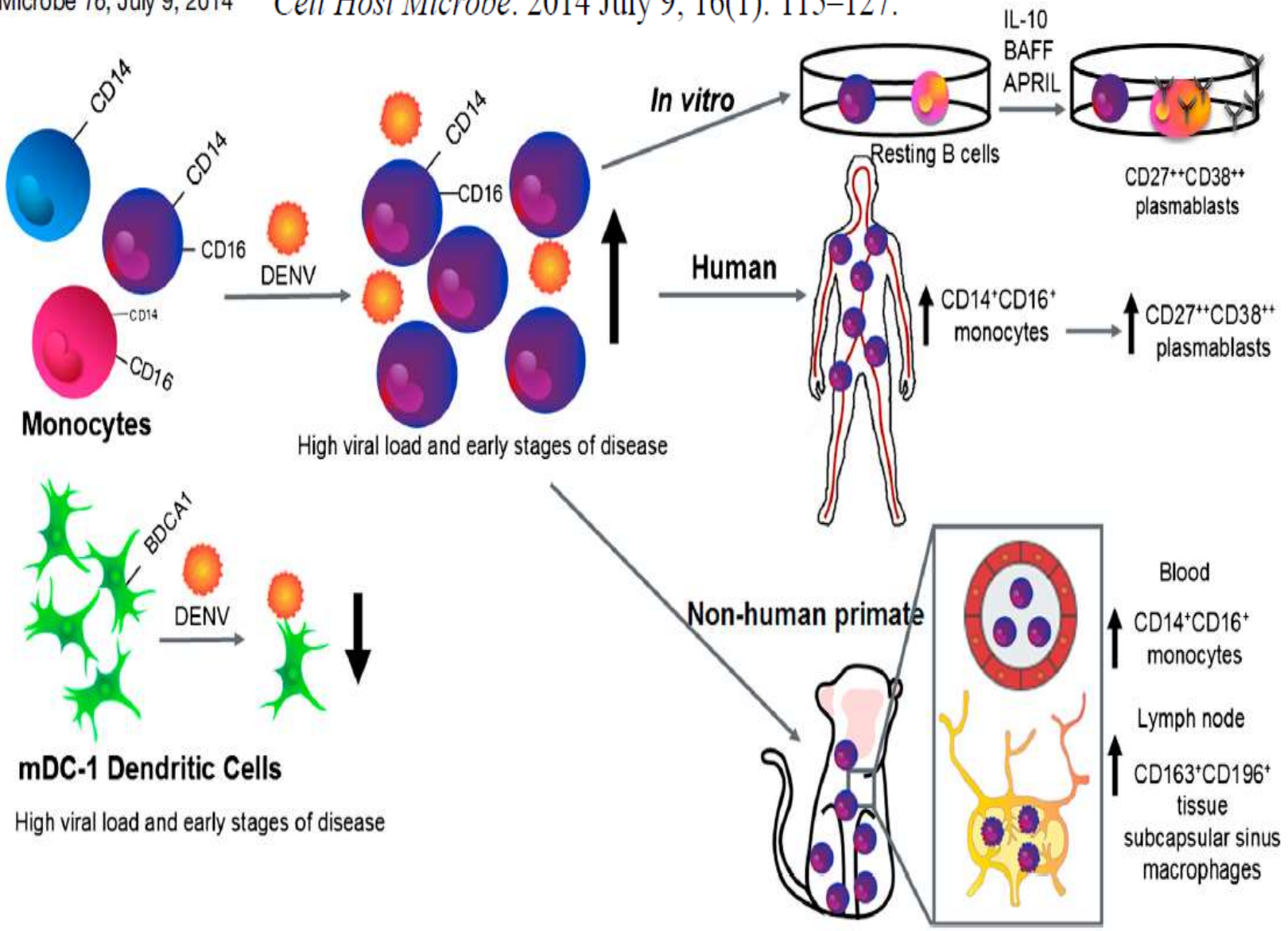


Figure 1. Identification of CD14$^+$CD16$^+$ Monocytes Involved in Plamablast Differentiation

CD14$^+$CD16$^+$ monocytes increase in humans and nonhuman primates following DENV infection. This monocyte population migrates to the lymph node and expresses markers of subcapsular sinus macrophages, which are capable of activating antigen-specific B cells. CD14$^+$CD16$^+$ monocytes stimulate plasmablast formation in vitro, driven by BAFF, APRIL, and IL-10. Illustrated by Sara Watson.

Dengue Fever Mimicking Plasma Cell Leukemia

John M. Gawoski, MD; Winnie W. Ooi, MD

(*Arch Pathol Lab Med.* 2003;127:1026–1027)

Peripheral Blood Plasmacytosis Not Associated With Hematologic Malignancy in Which Plasmactyosis or Combined Plasma Cells and Plasmacytoid Cells Exceeded 10% of Circulating White Blood Cells*

Diagnosis	Plasma Cells		Plasmacytoid Cells		Reference
	%	Absolute ($\times 10^3/\mu L$)	%	Absolute ($\times 10^3/\mu L$)	
Sickle cell anemia, parvovirus B19	~50	~15	. . .	. . .	Koduri and Naides[4]
Mononucleosis-like syndrome	38	3.84	. . .	. . .	Komiya and Kuriya[5]
Serum sickness (equine tetanus antitoxin)	30	4.83	. . .	. . .	Barnett et al[6]
Azathioprine toxicity	23	3.6	. . .	. . .	Kathol and Hamilton[7]
Serum sickness (diphtheria antitoxin)	21	. . .	. . .	. . .	Schmidt et al[8]
This case	19	1.1	9	0.52	. . .
Rubella (multiple cases)	13	0.9	0.5	0.03	Hickling[9]
Streptokinase therapy	9	1.01	13	2.2	Gorden et al[10]
Alcoholic liver disease	8	1.34	11	1.89	Moake et al[11]
Sulfisoxazole therapy	6	0.82	14	1.9	Moake et al[11]
Hyperimmunization (tetanus toxoid)	6	1	5	0.84	Moake et al[11]
Pokeweed ingestion (multiple cases)	. . .	. . .	10.8	. . .	Barker et al[12]

* Where multiple cases are noted, the most extreme is shown.

Dengue Vaccine

- A vaccine to prevent dengue (Dengvaxia®, live attenuated vaccine) is licensed and available in some countries for people ages 9-45 years old. WHO recommends that the vaccine only be given to persons with confirmed prior dengue virus infection.
- **The vaccine manufacturer, Sanofi Pasteur, announced in 2017 that people who receive the vaccine and have not been previously infected with a dengue virus may be at risk of developing severe dengue if they get dengue after being vaccinated.**
- Dengue Vaccine in the United States
  - In May 2019, Dengvaxia® was approved by the U.S. FDA in USA for use in children 9-16 years old living in an area where dengue is common (the US territories of American Samoa, Guam, Puerto Rico and the US Virgin Islands), with laboratory confirmed prior dengue virus infection.

Take Home Points

- Dengue fever global public health threat
- Clinical History – especially travel
- Not all plasmacytosis are neoplastic
- Bring mosquito repellent!!!

19-0902

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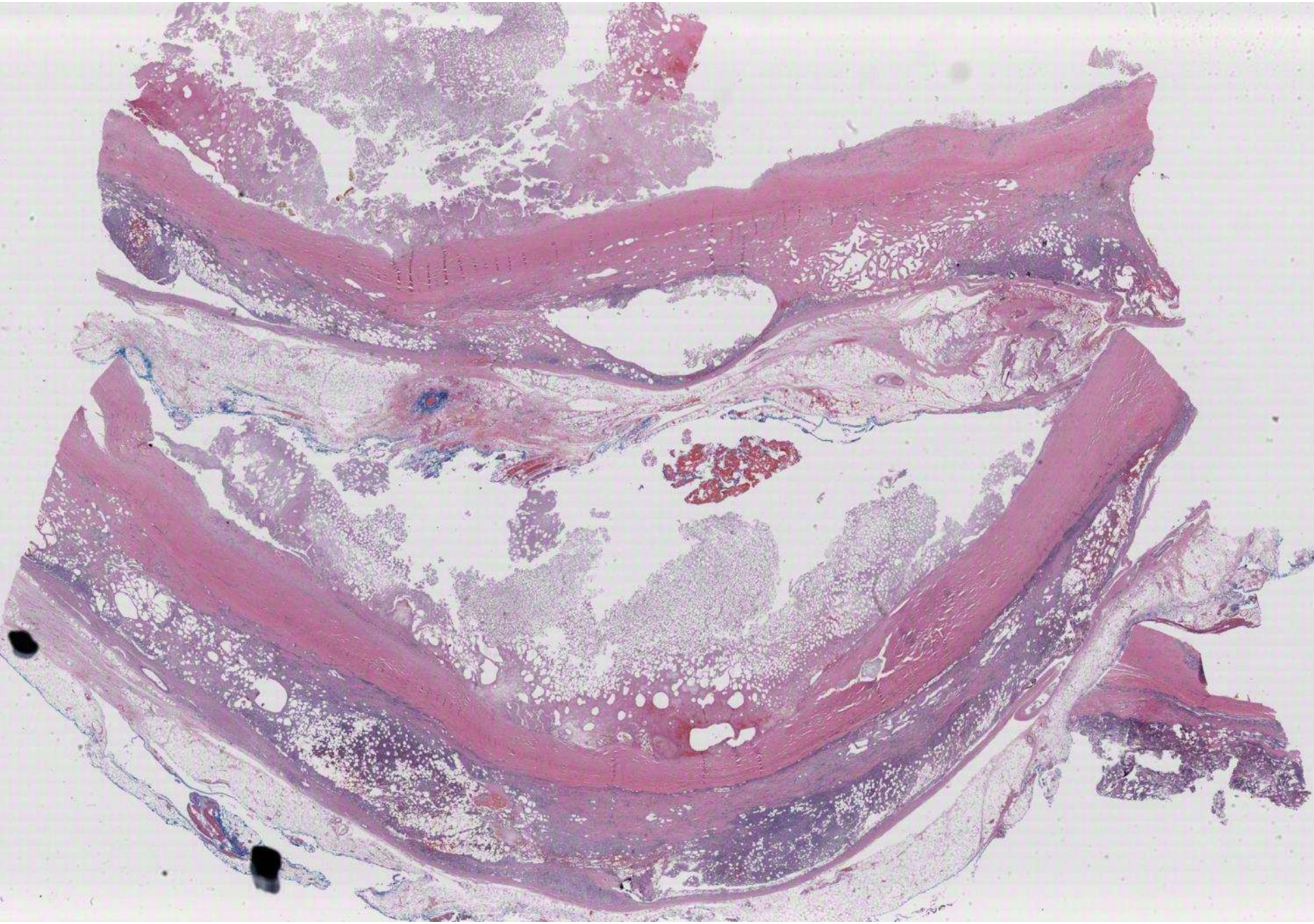
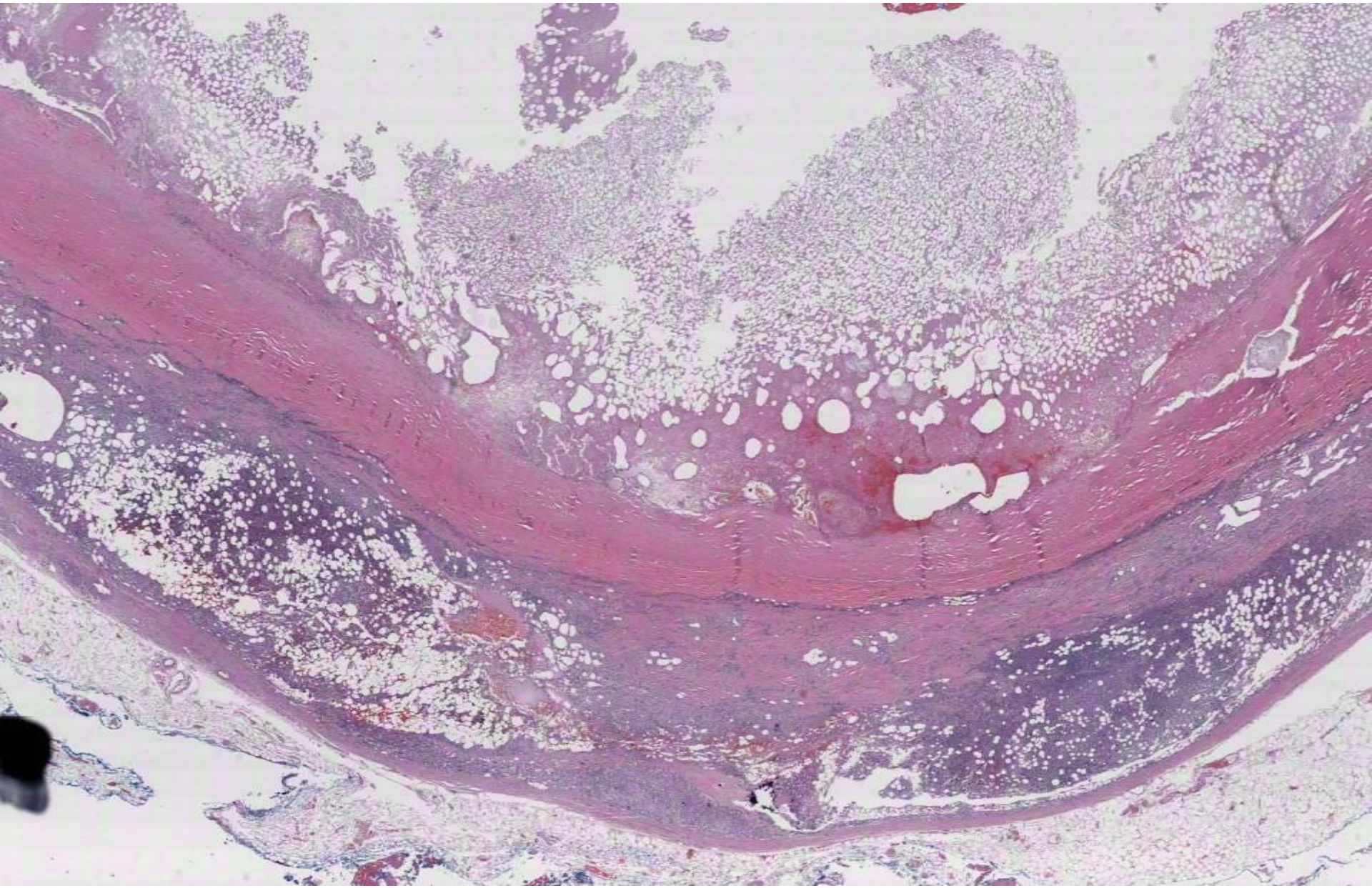
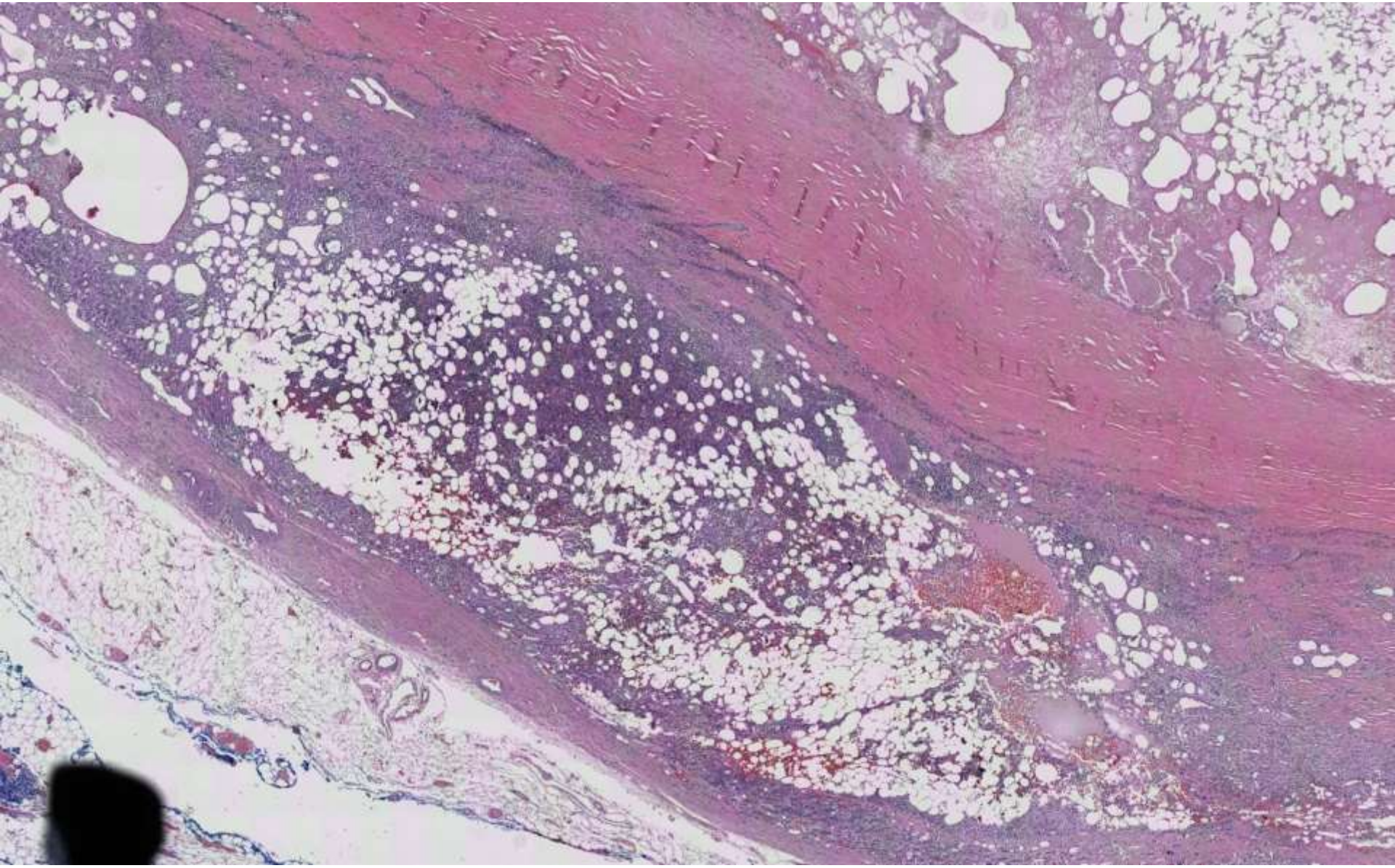
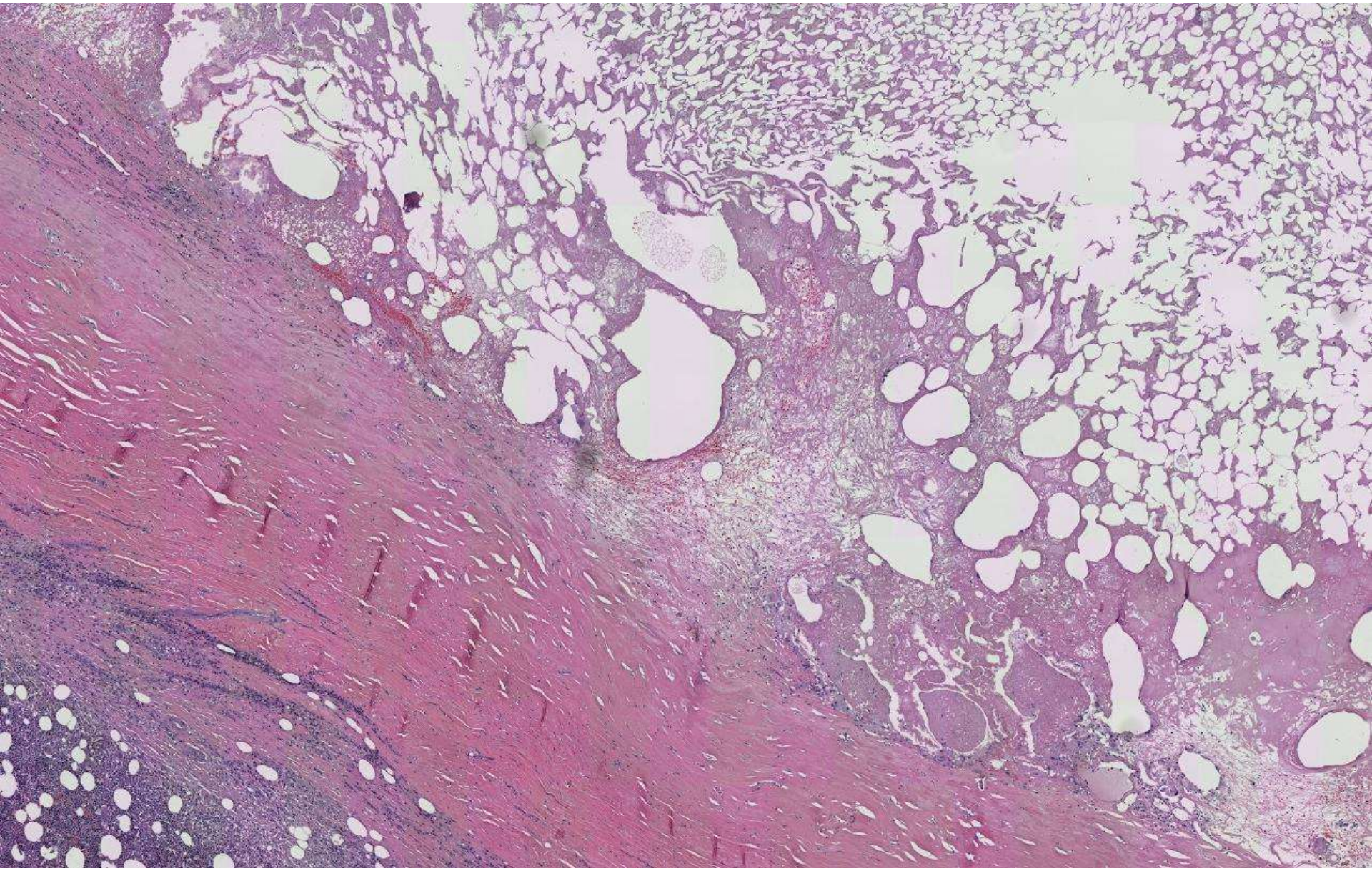
Mahendra Ranchod; Good Samaritan Hospital

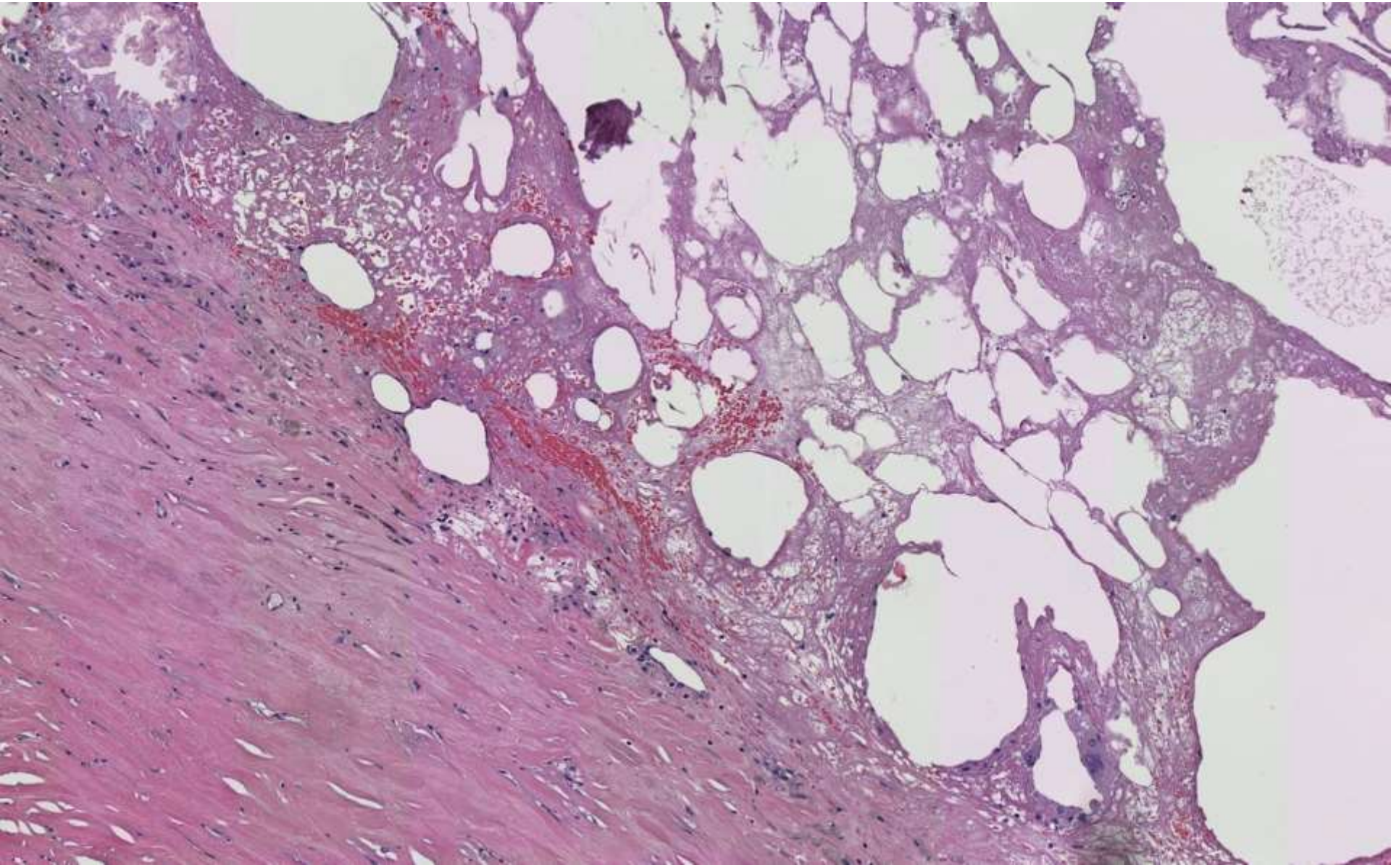
41-year-old male presented with abdominal pain. CT scan showed 9cm circumscribed mass in retroperitoneum superior to right kidney.

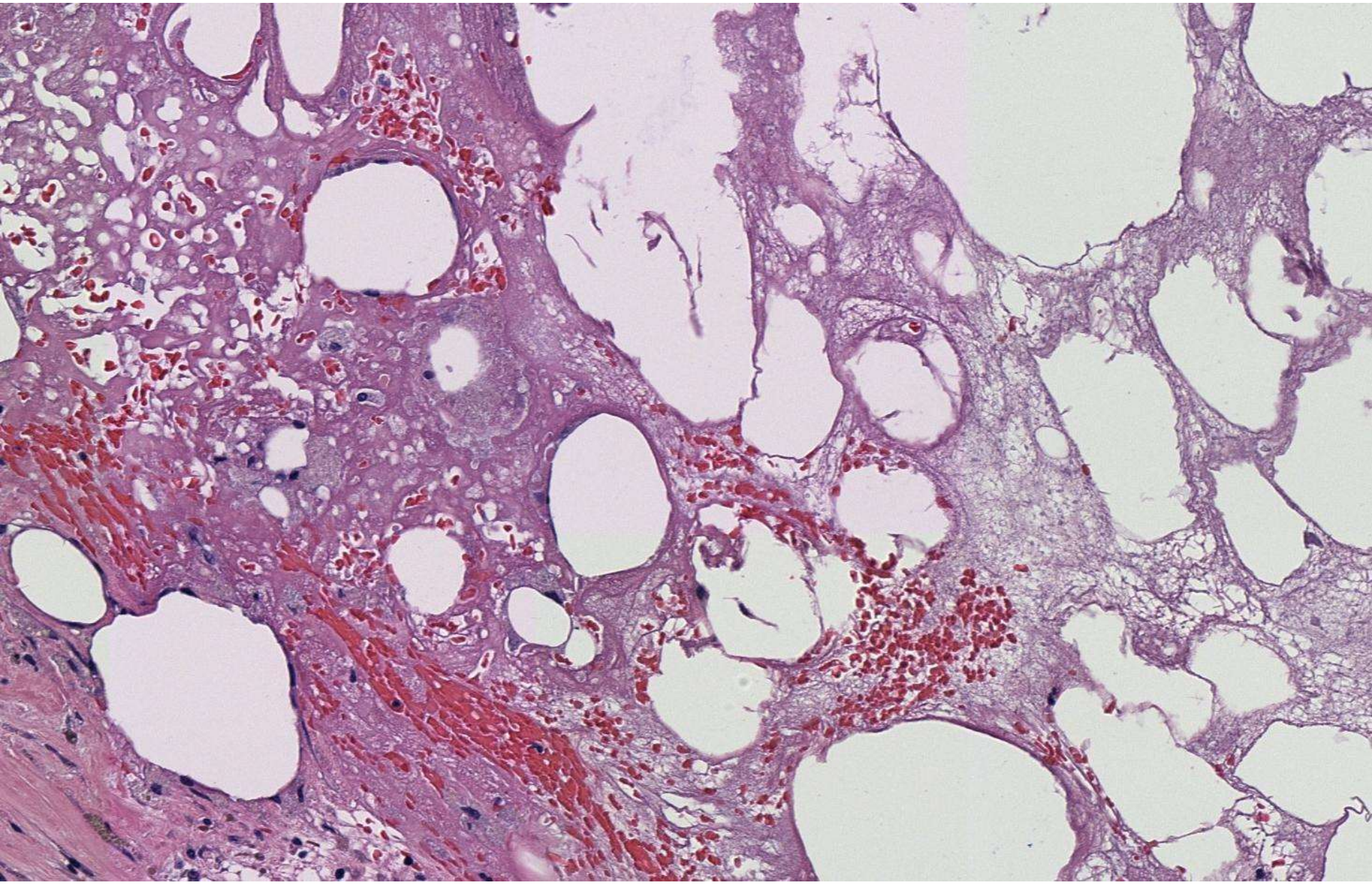


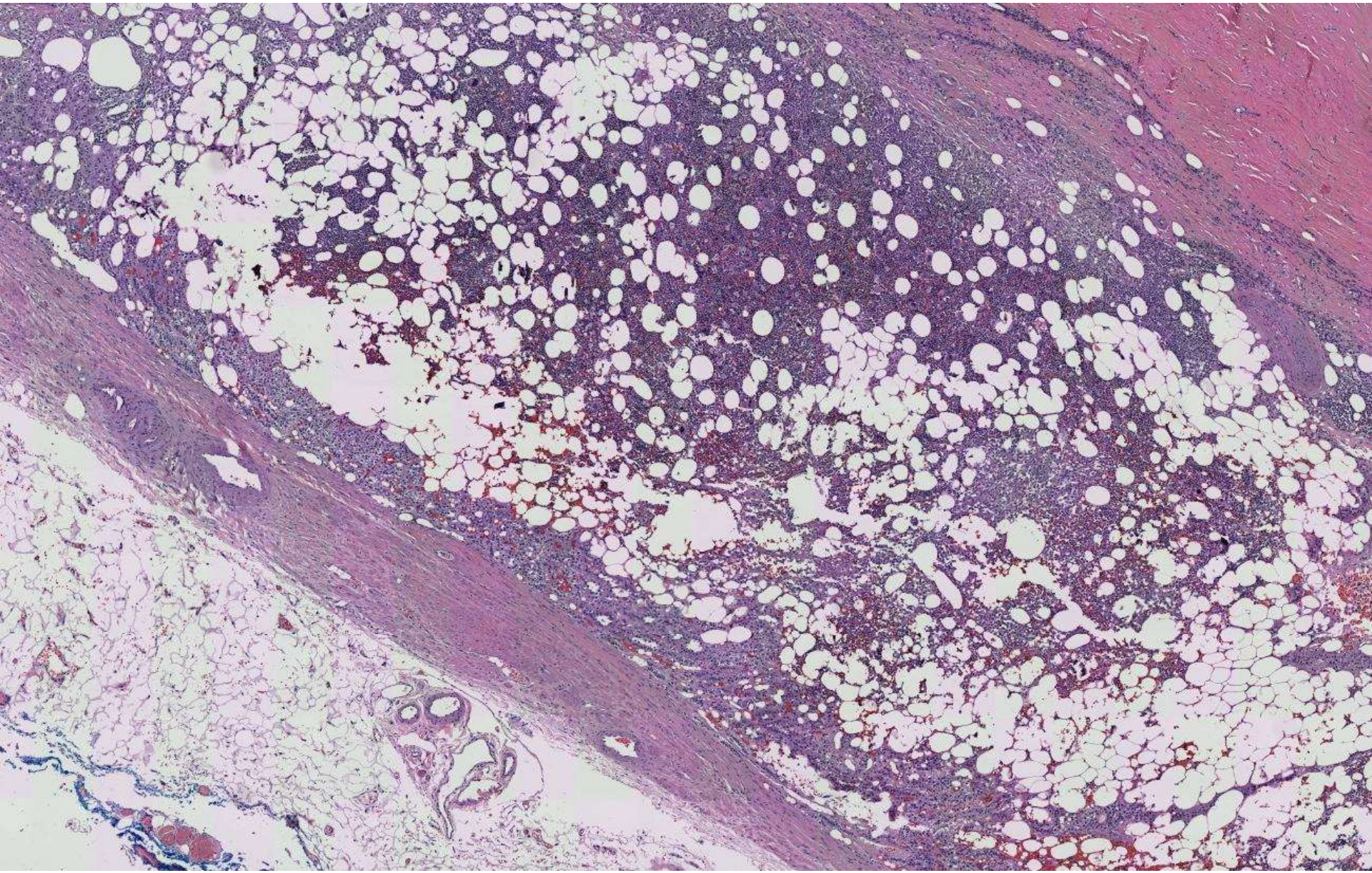


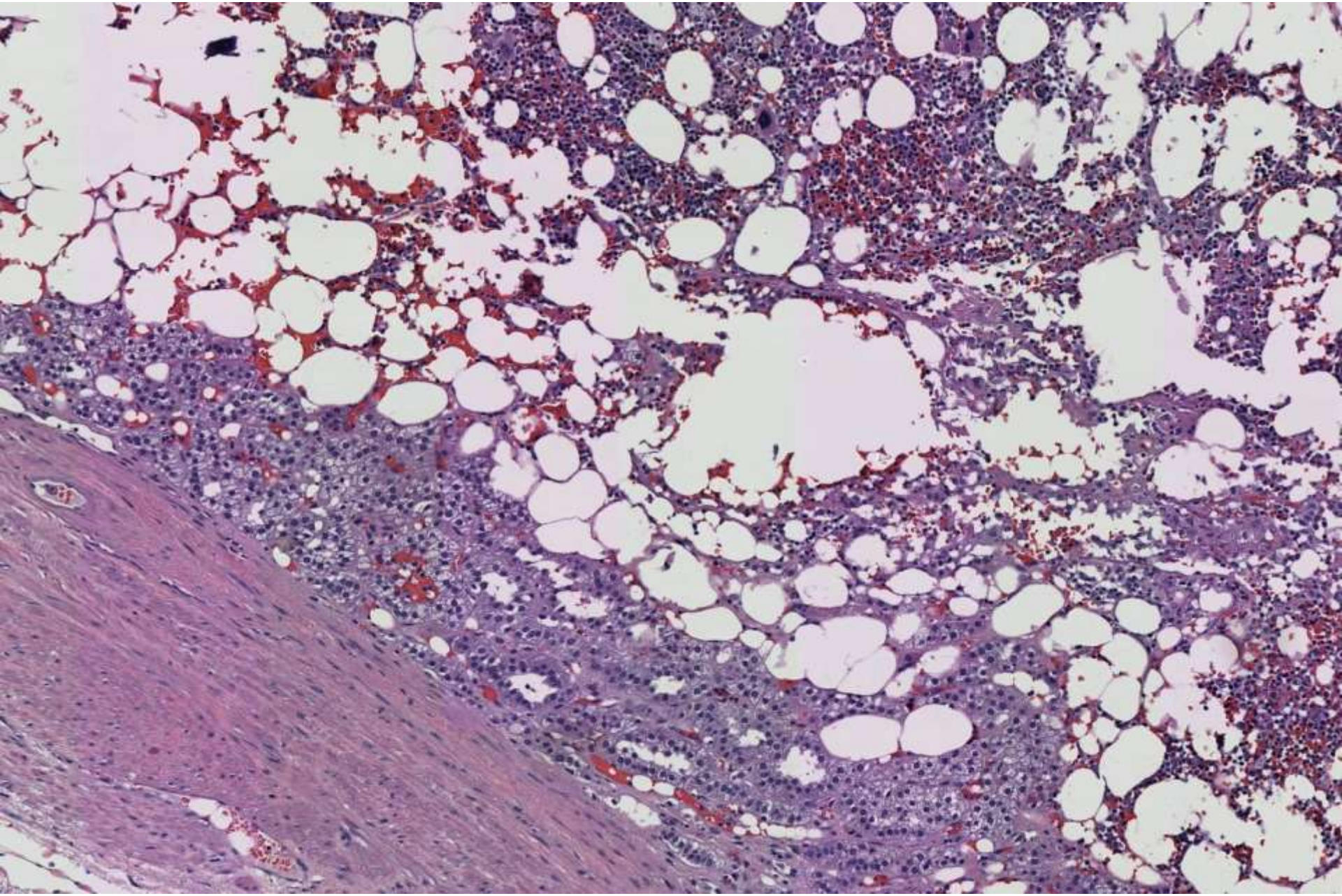


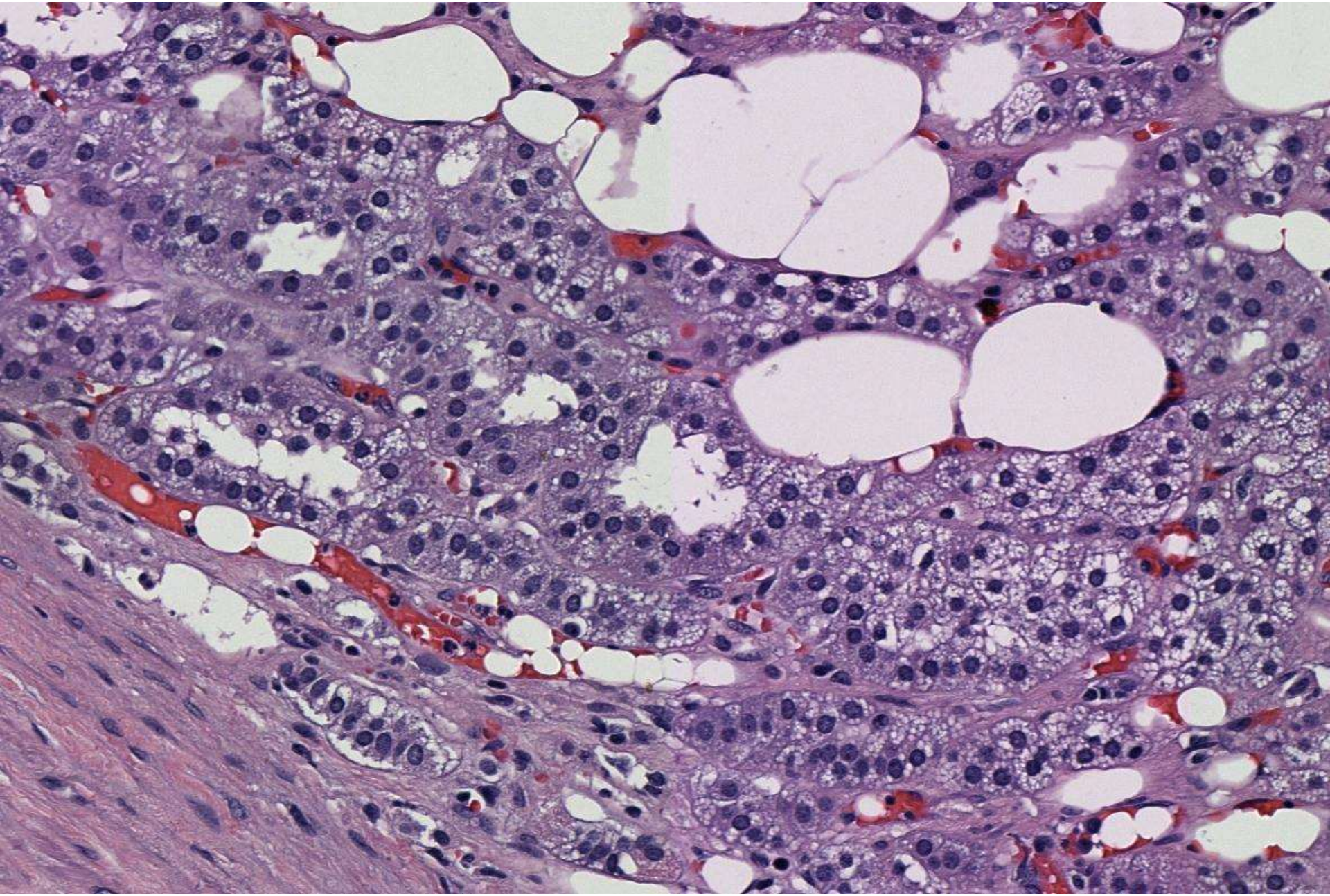


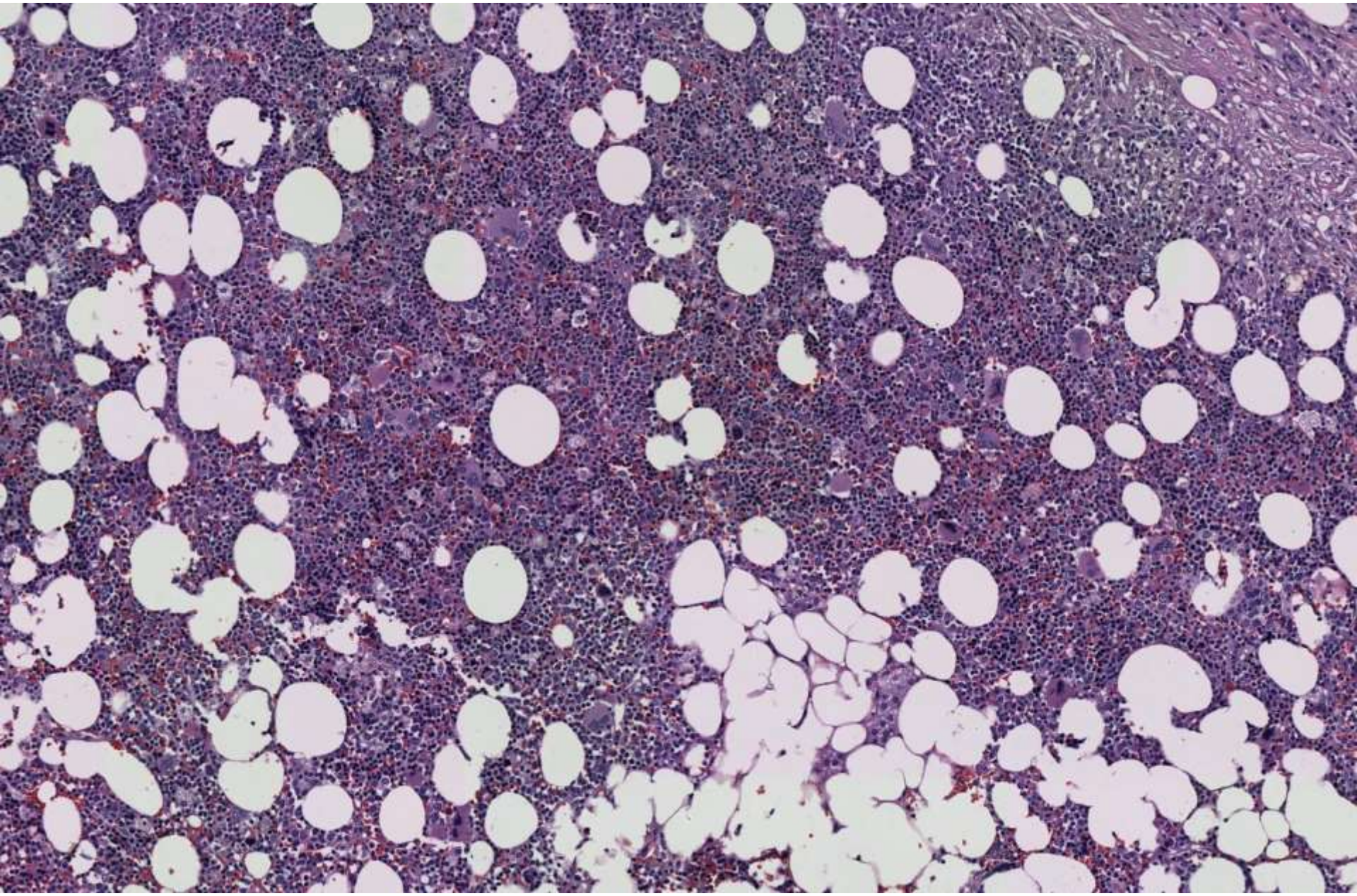


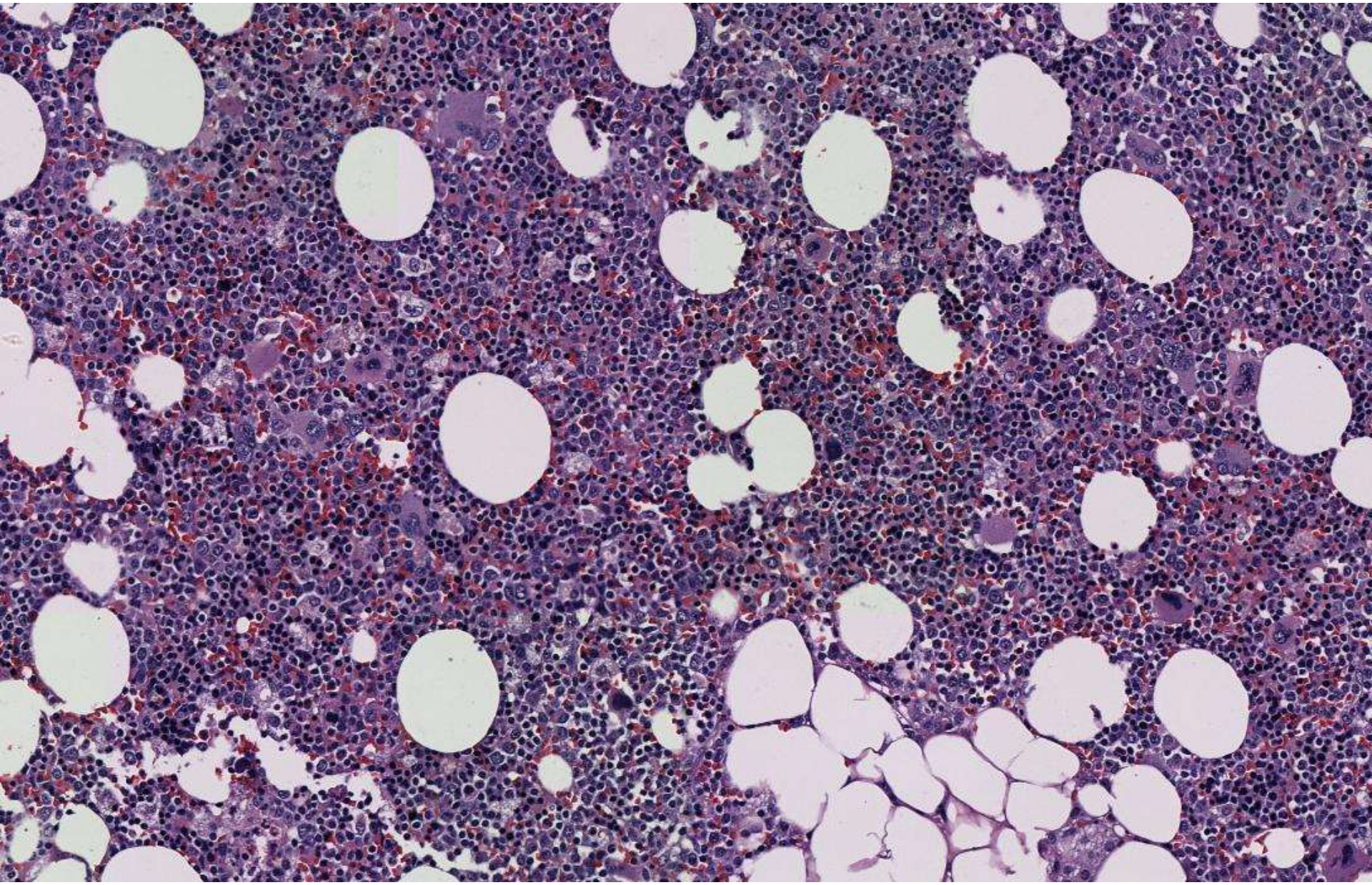


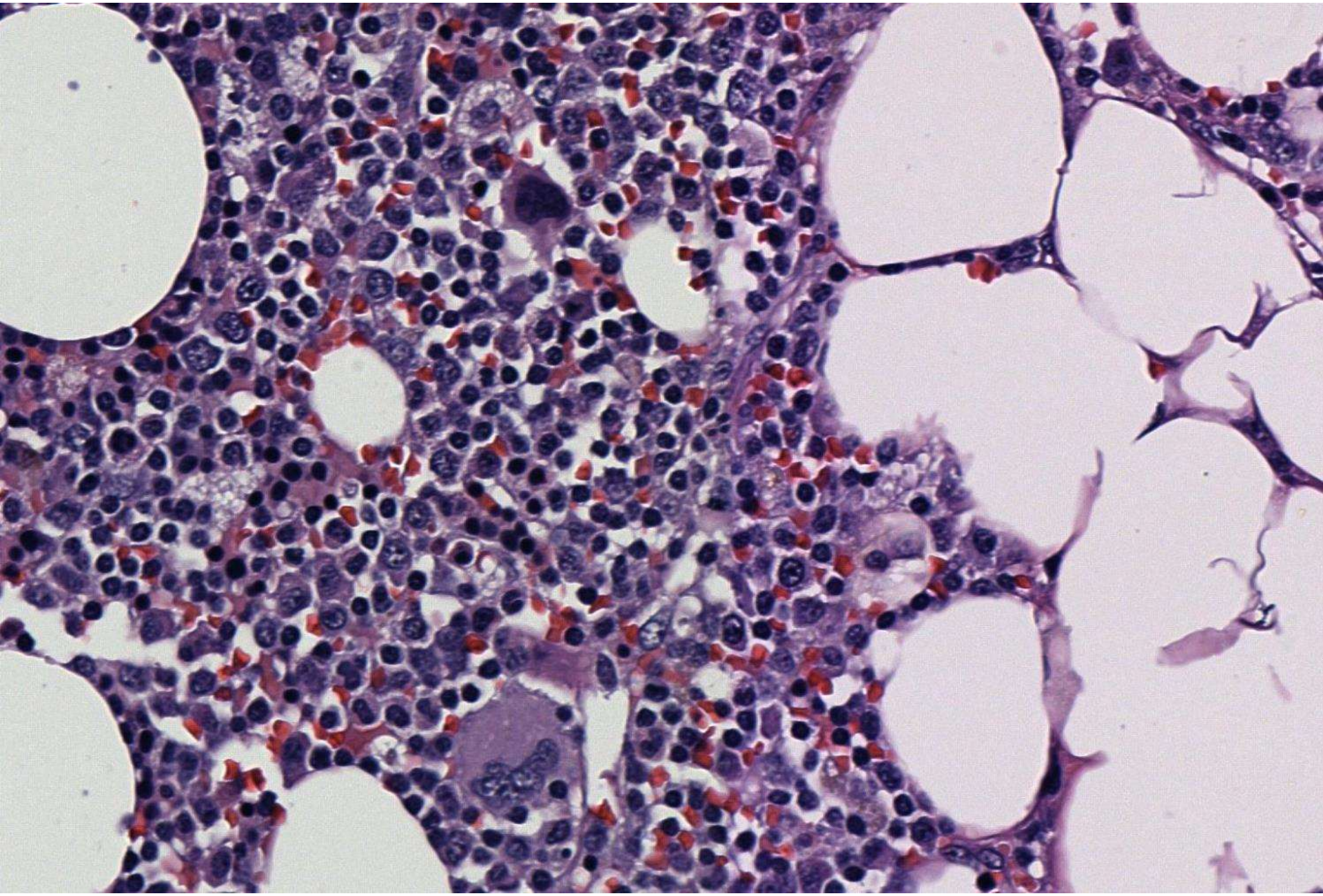


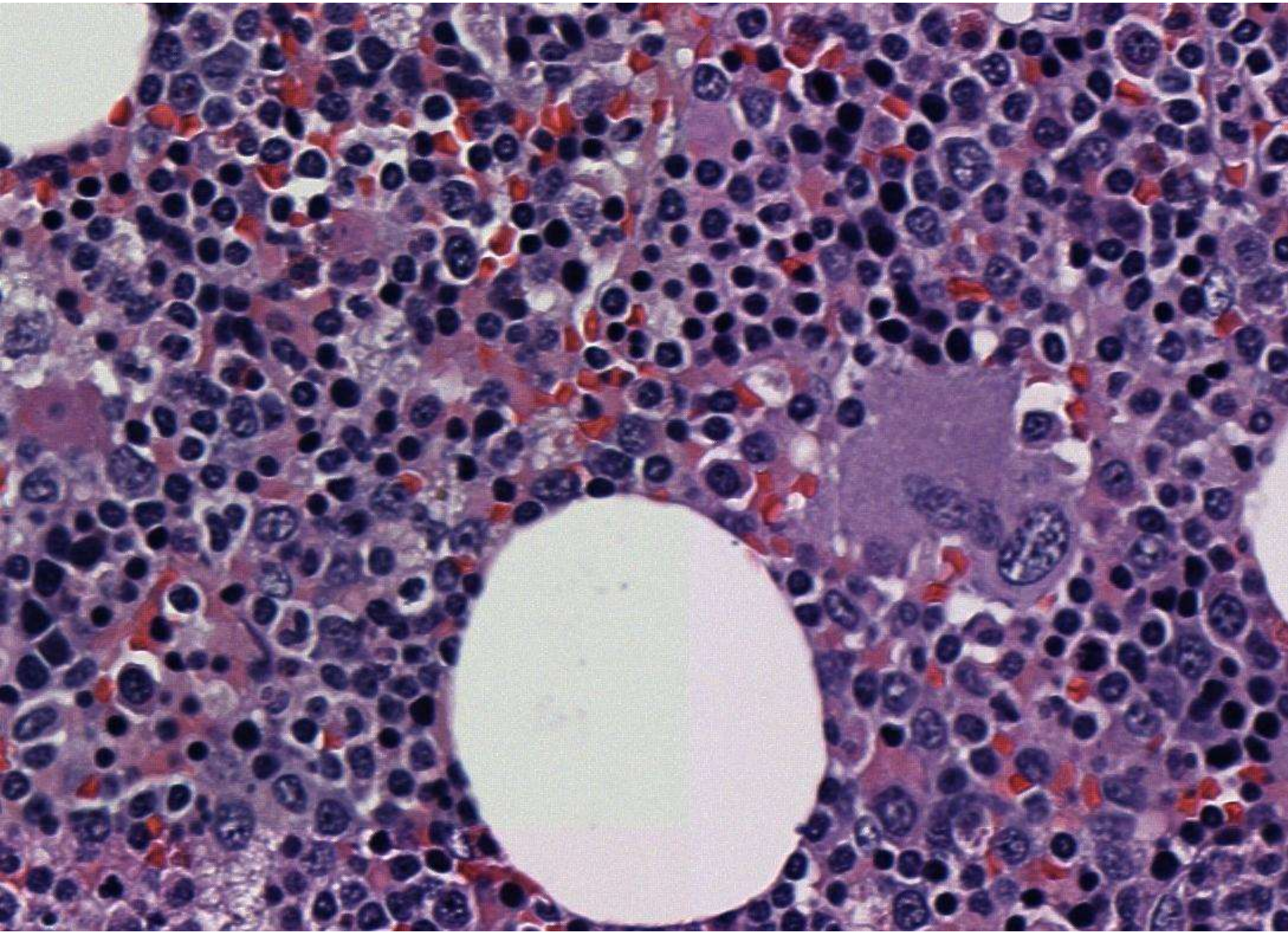


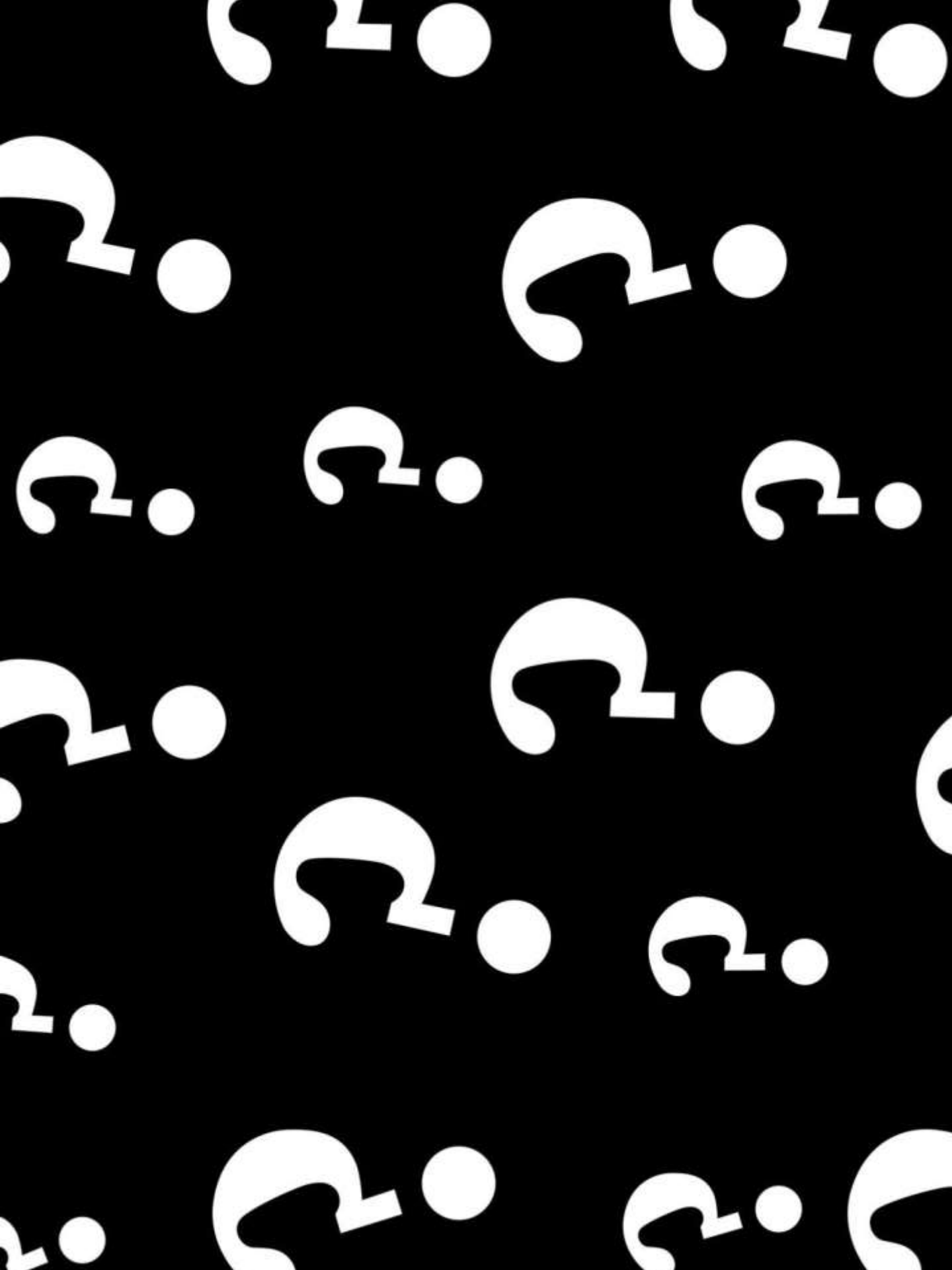


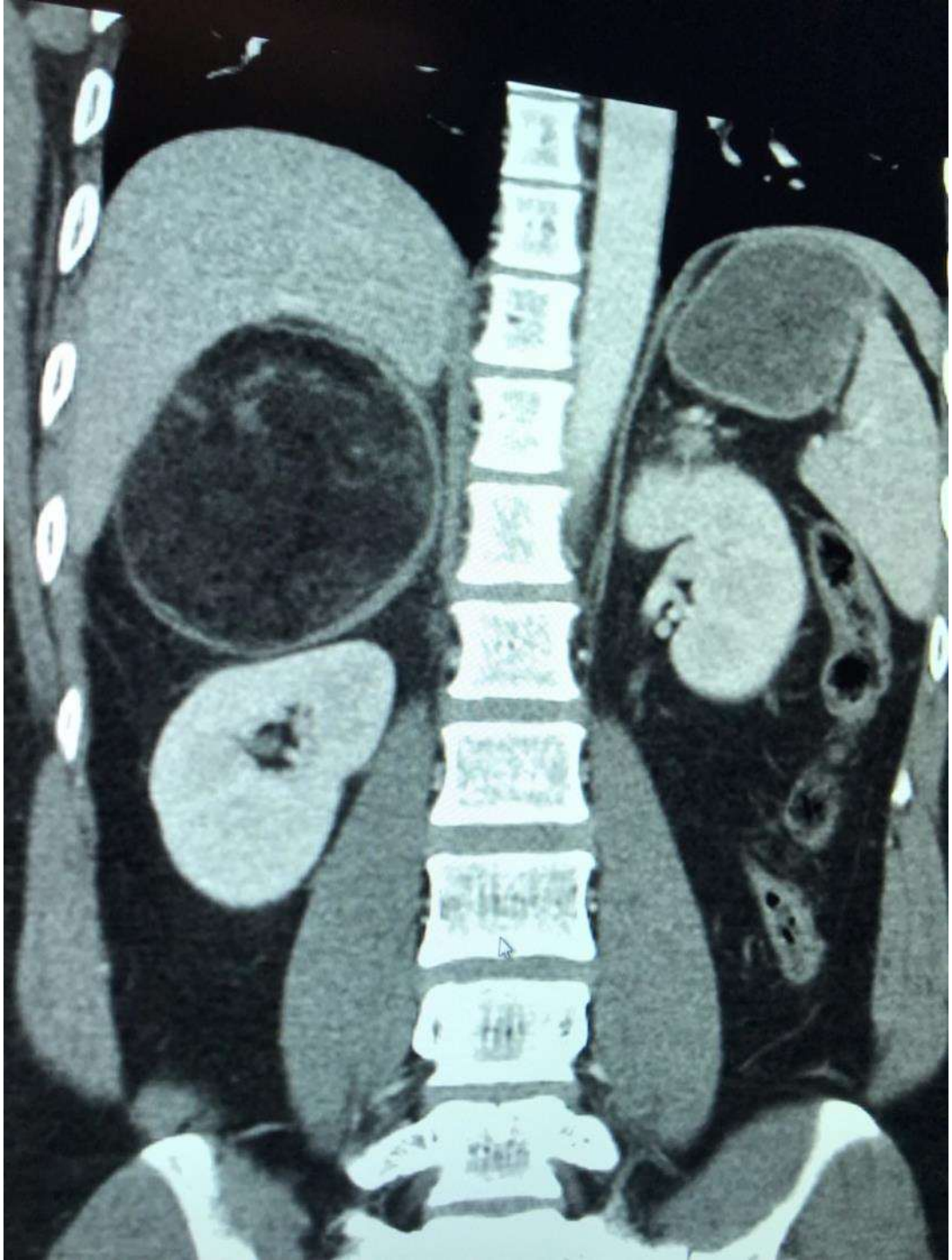


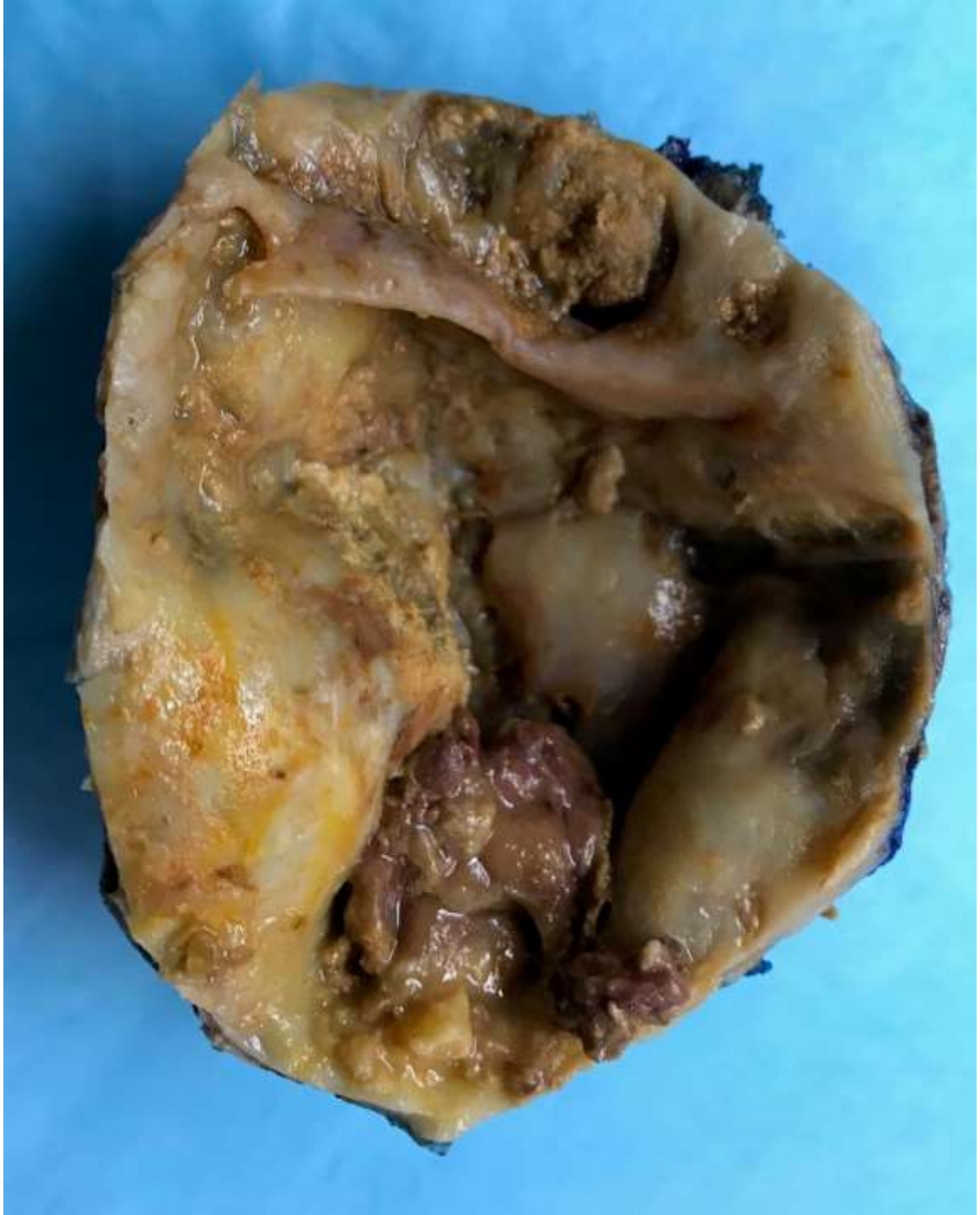












Myelolipoma

Adrenal

Kidney

Liver

Retroperitoneum

Mediastinum

Thyroid gland

Lung

Nasal Cavity

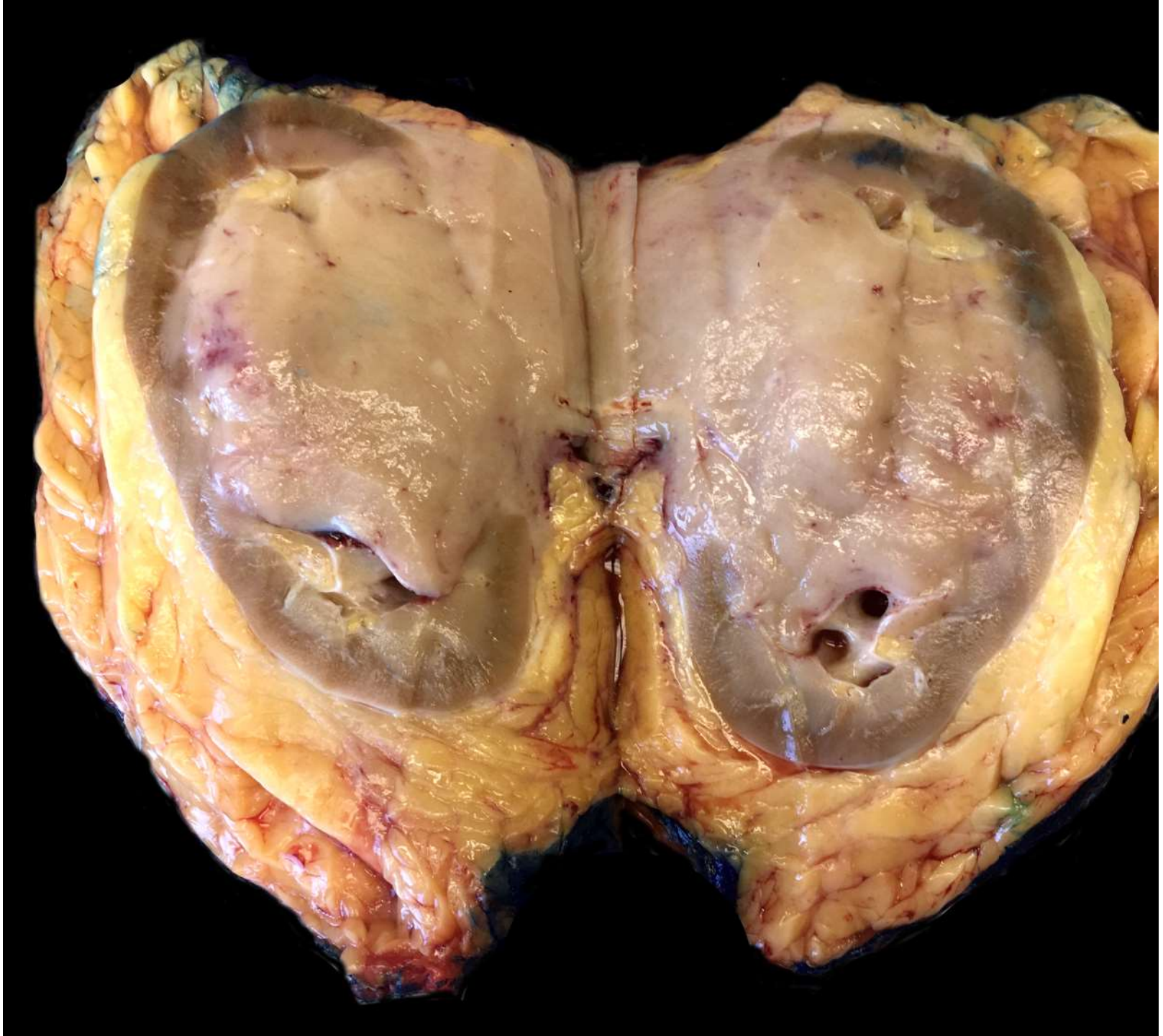
Myelolipoma

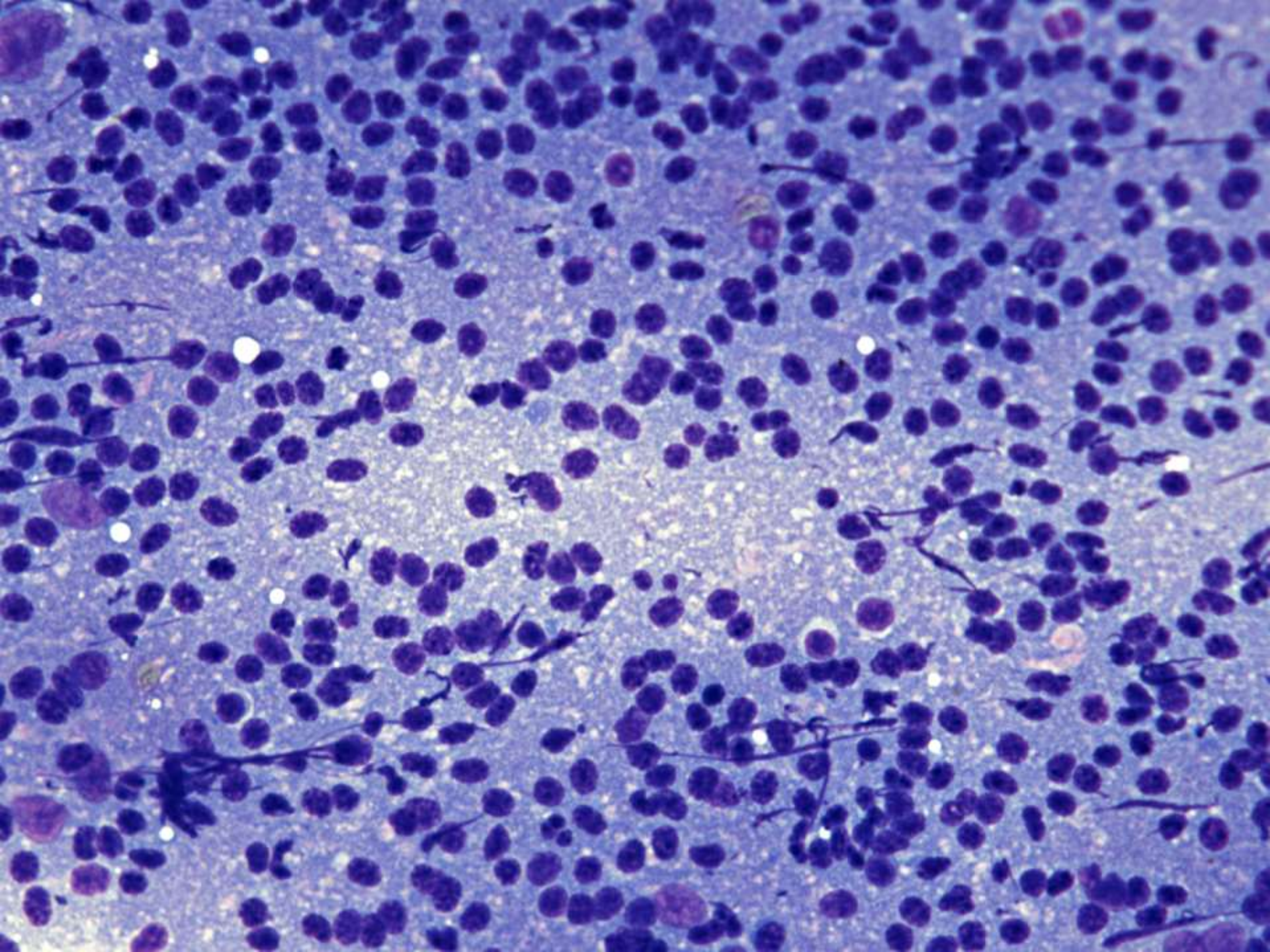
- Small lesions are asymptomatic
- Large tumors (up to 30cm) symptomatic because of:
    - Infarction of the tumor
    - Infarction with hemorrhage and cystic change
    - Extra-tumoral hemorrhage
    - Extensive cystic change uncommon and due to resorption of blood

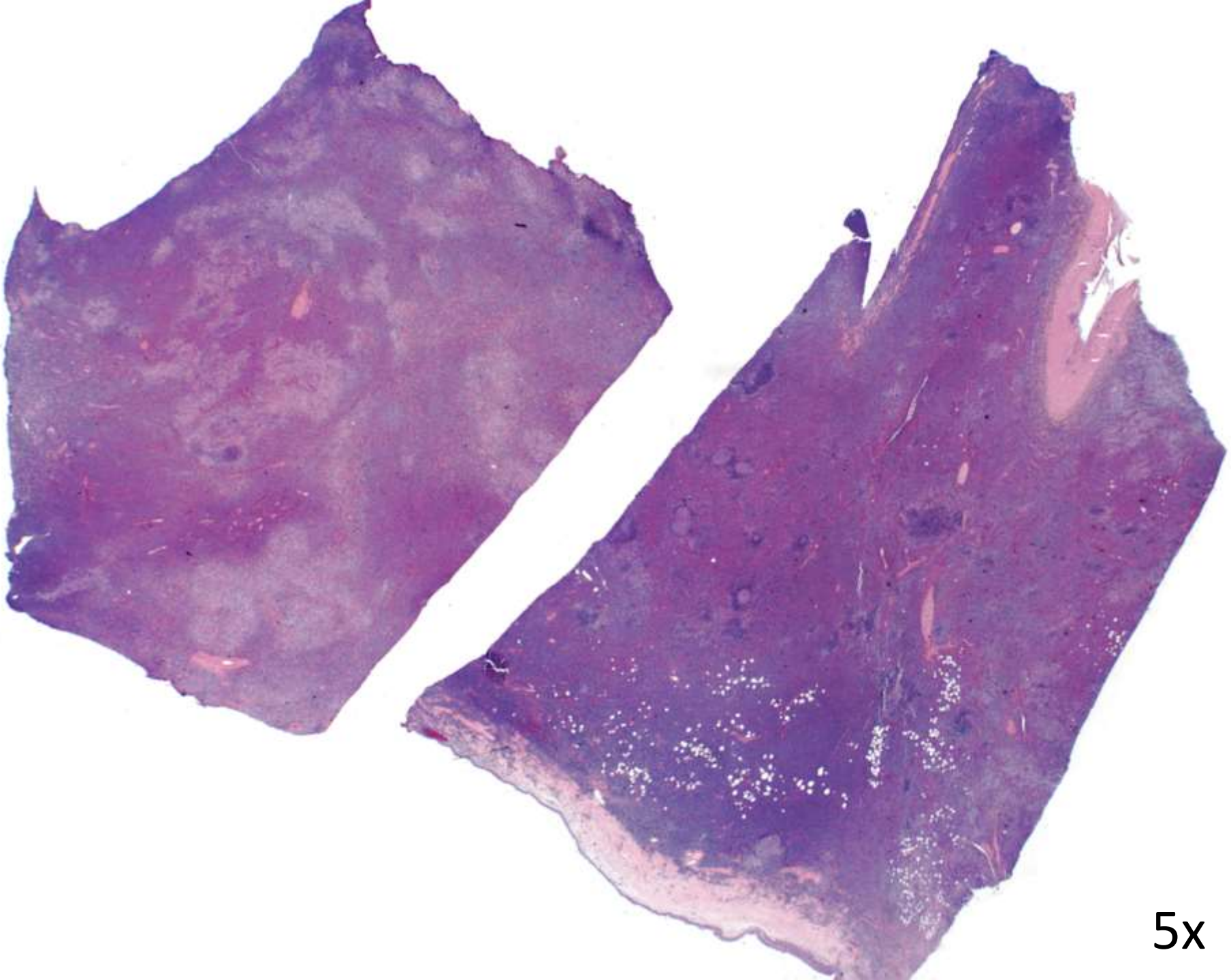
19-0903
(scanned slide avail 2 slides)

Rebekah Wieland/Melissa Clark/Dean Fong; PAVA

70-year-old male with past medical history of HTN, HLD, afib, hypothyroidism, and anemia with recent pneumonia and incidentally found 8cm left renal mass on CT encasing vasculature with para-aortic lymph nodes. IR guided biopsy was non-diagnostic. Radical nephrectomy with pelvic lymph node dissection performed.



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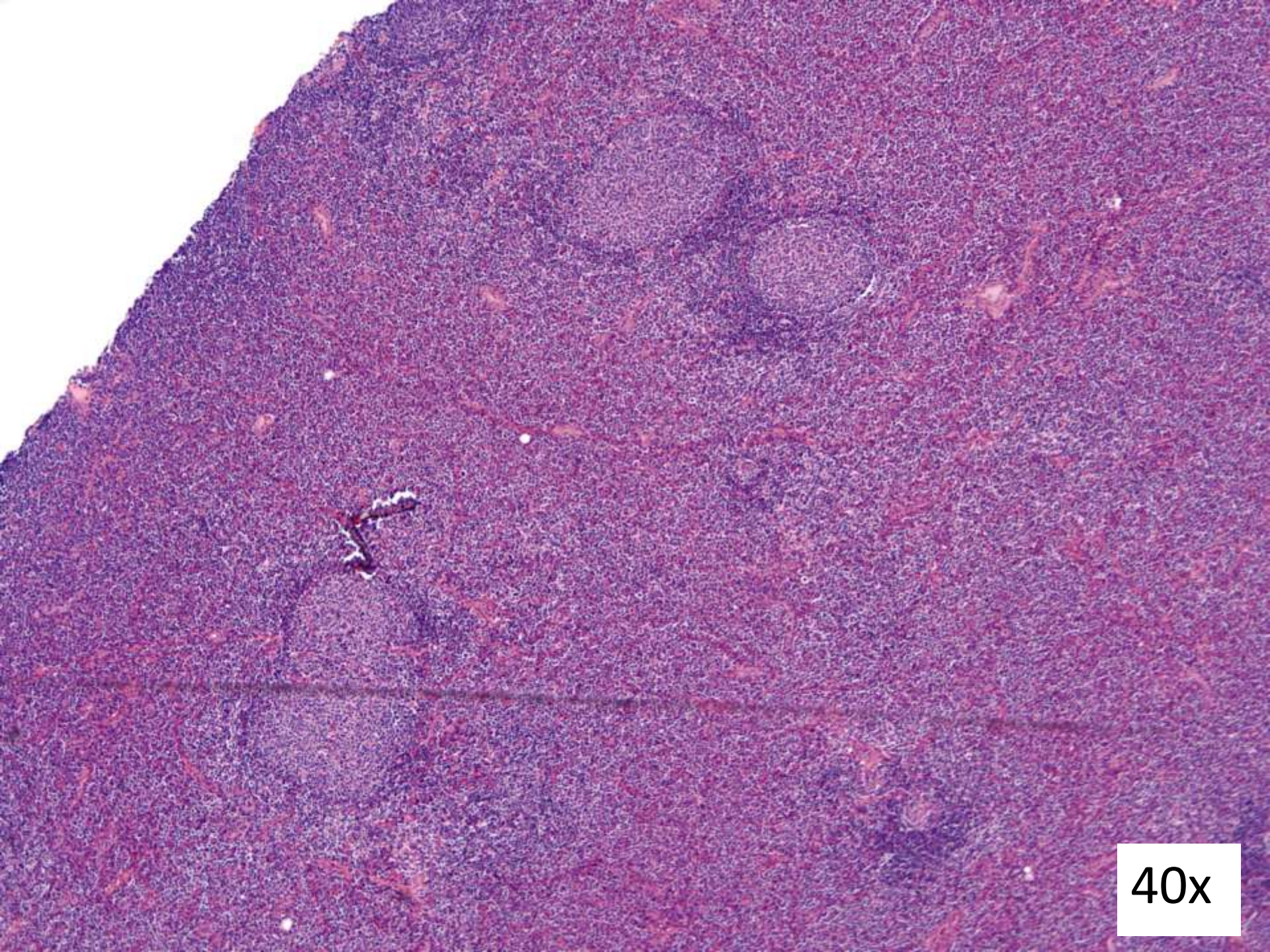
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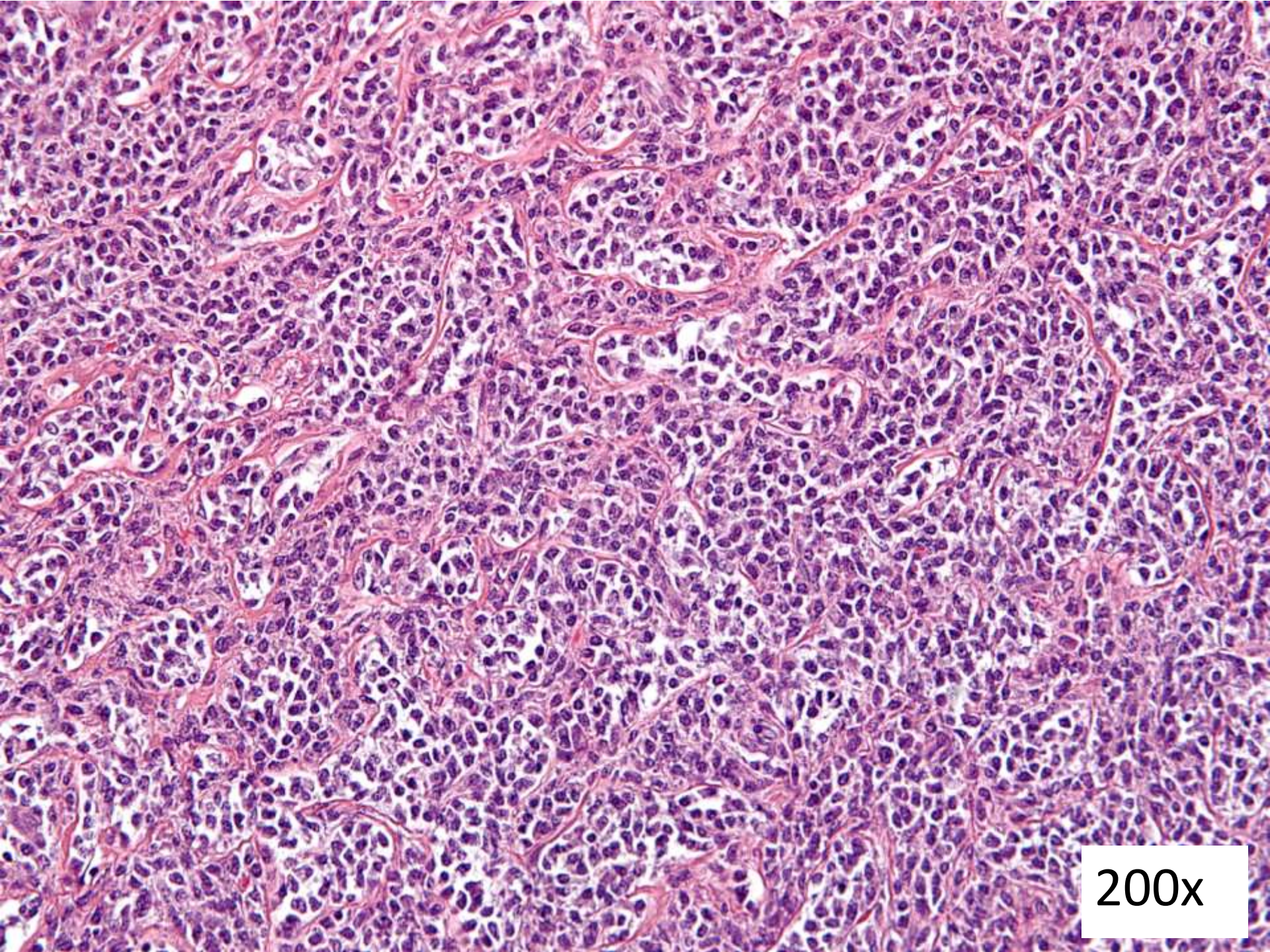
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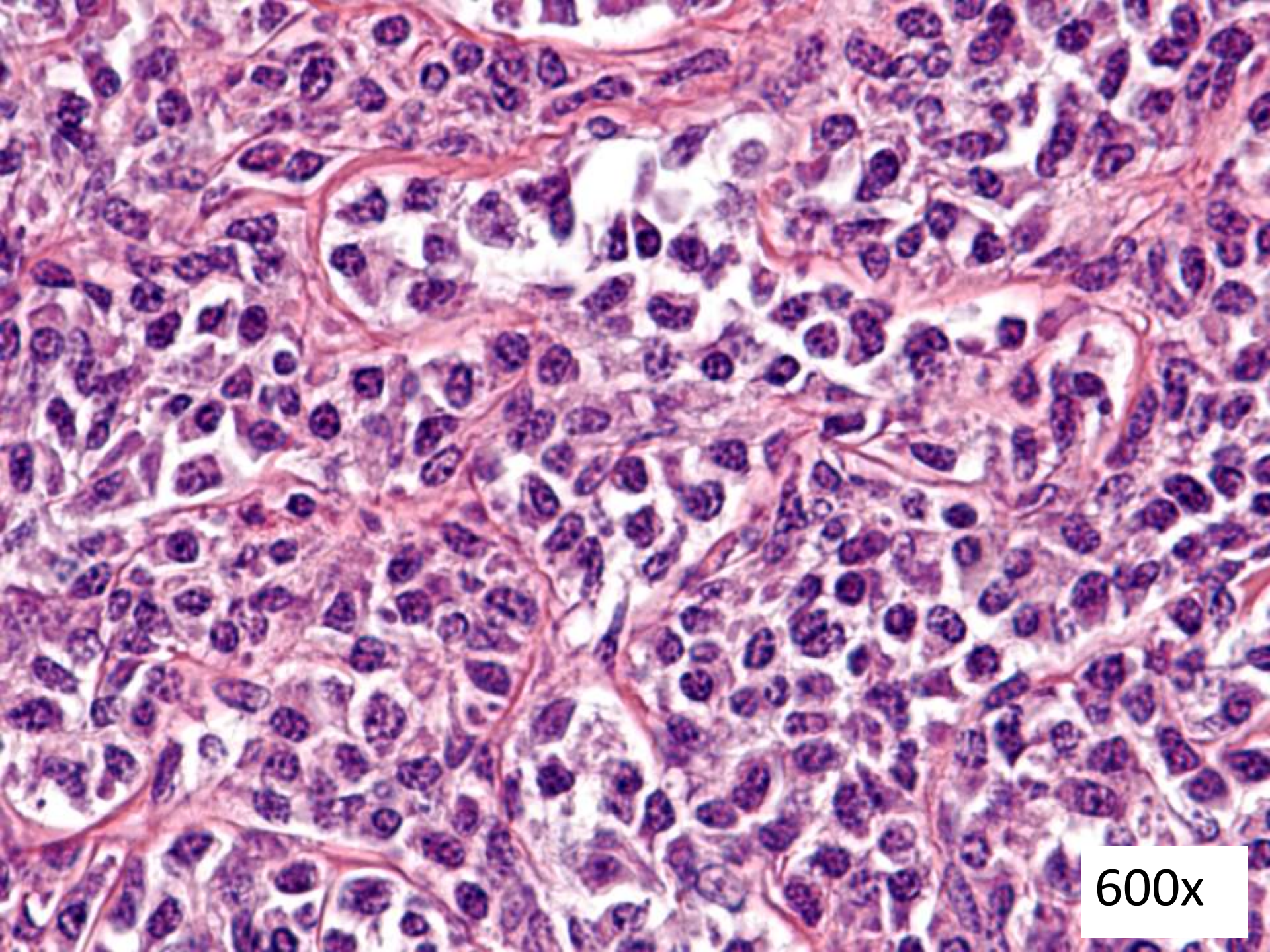
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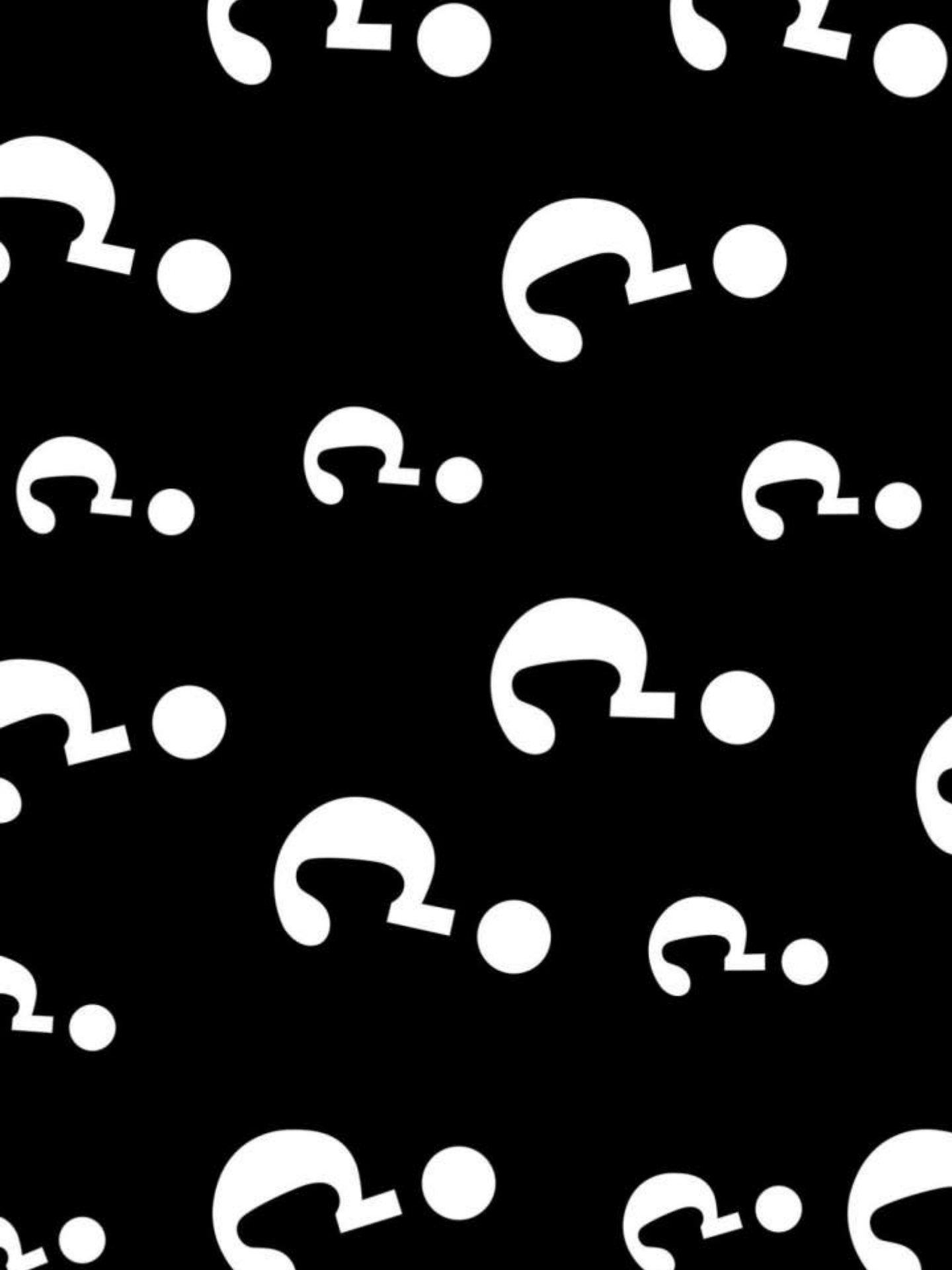


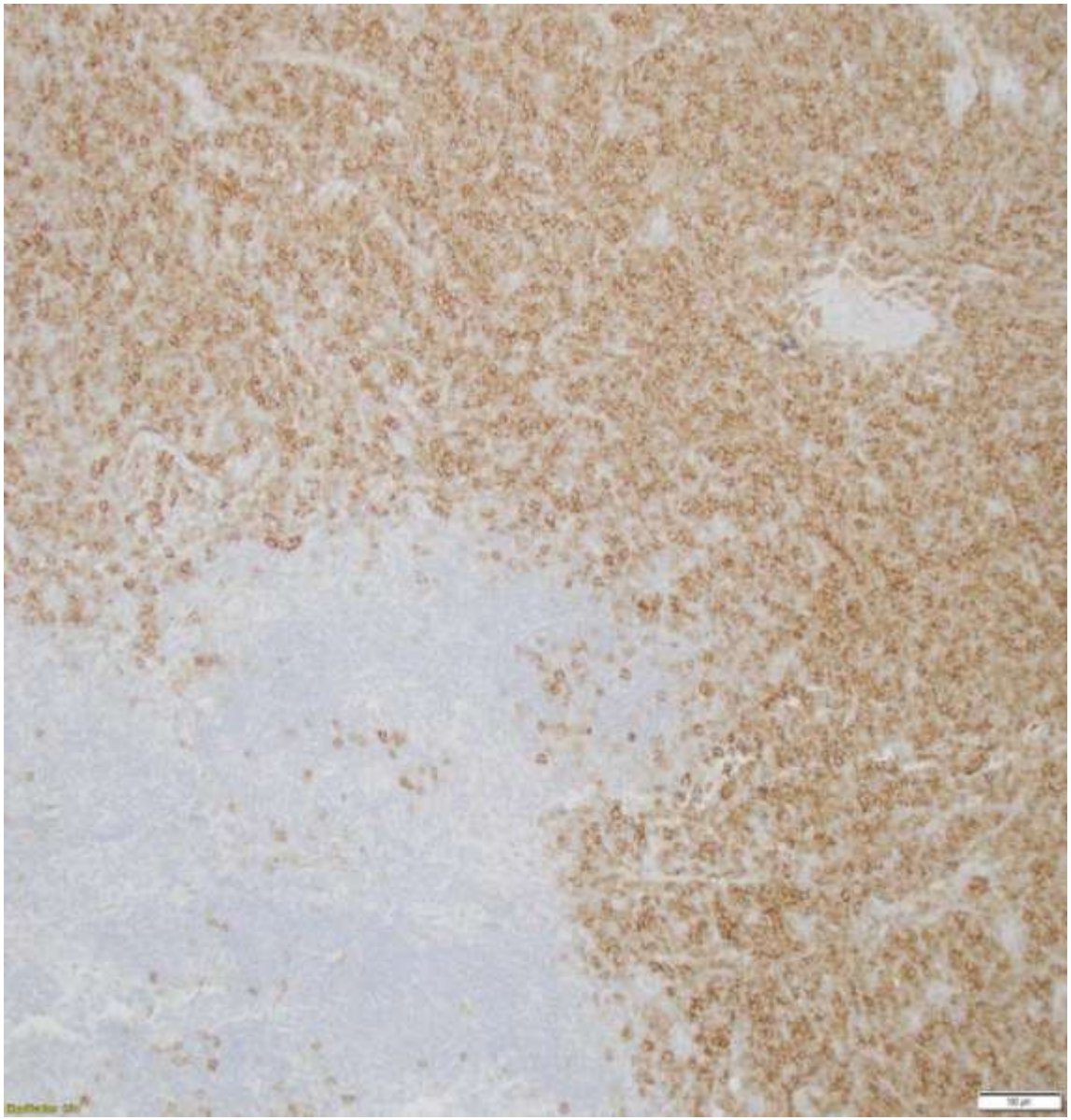
19-0903

Rebekah Wieland, MD, Melissa Clark, MD, Dean Fong, DO

VA Palo Alto

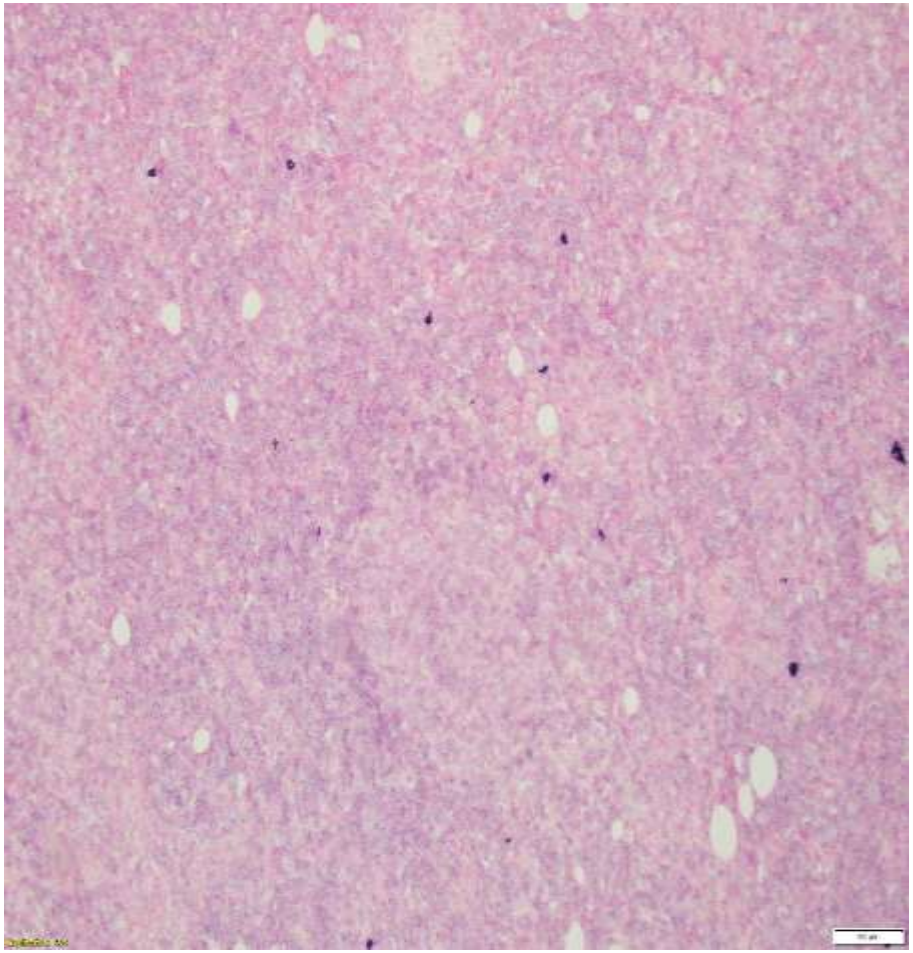
Kidney

CD1
38

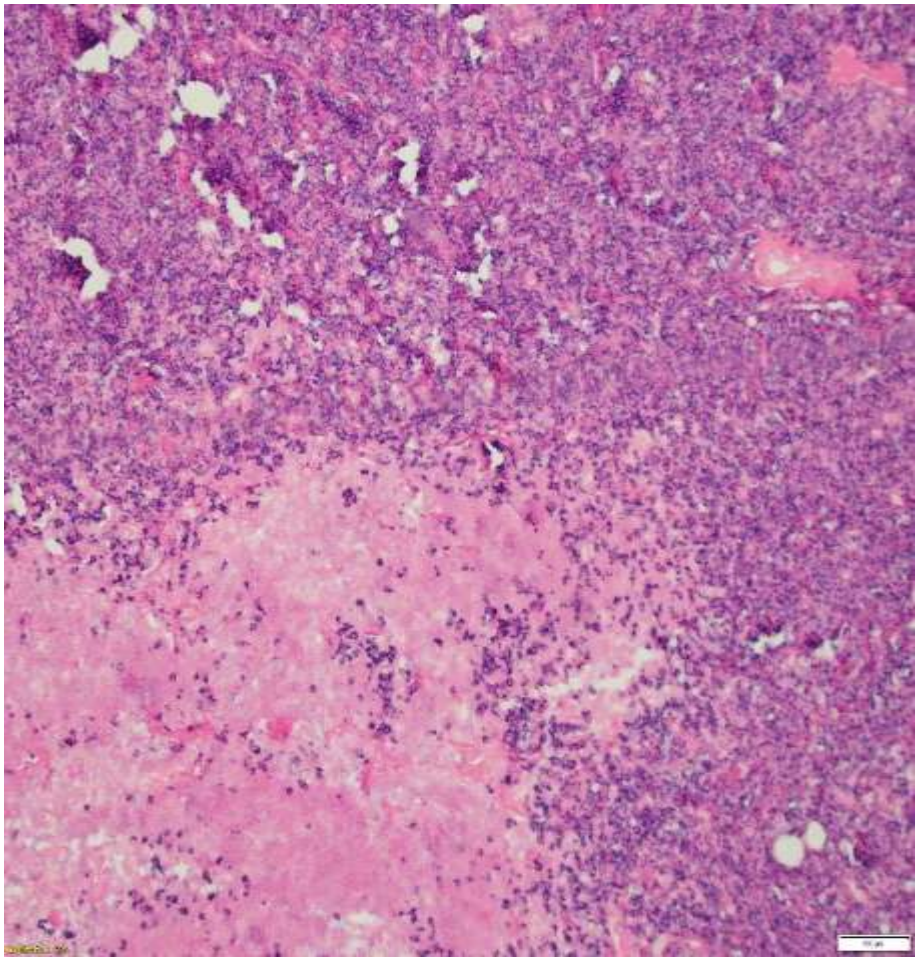


Kidney

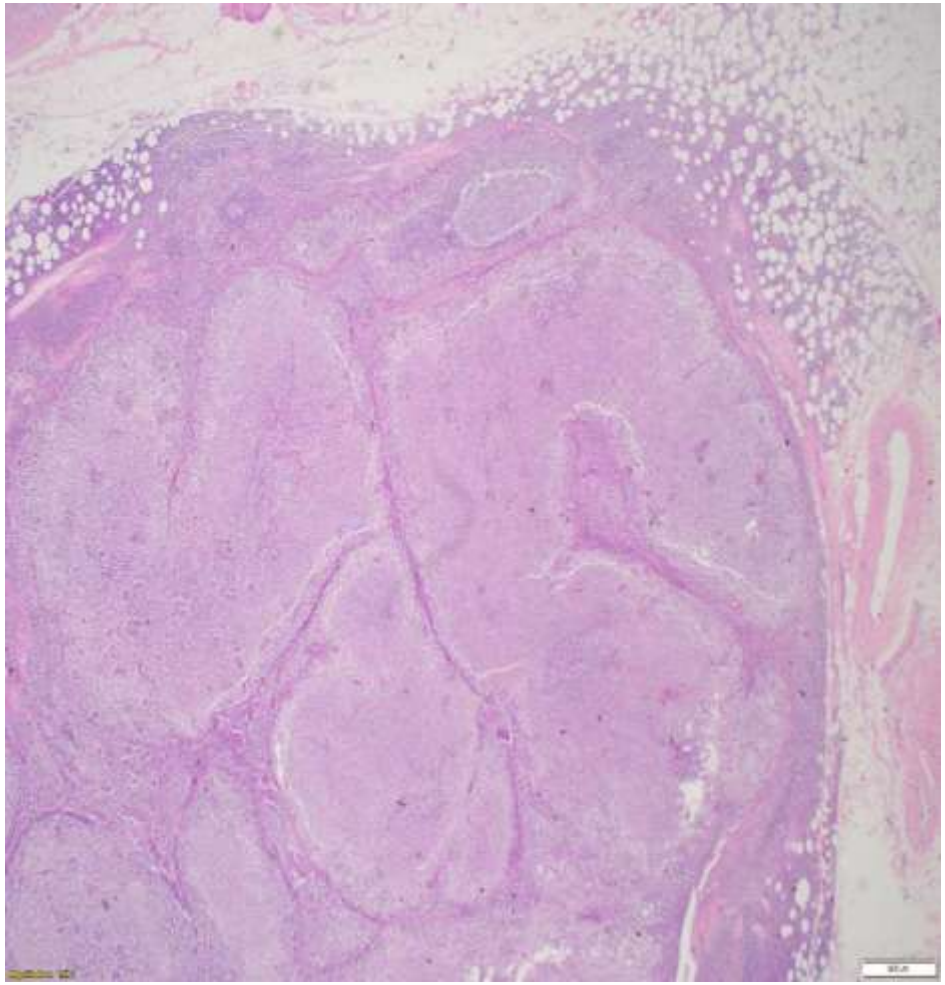
Kappa ISH

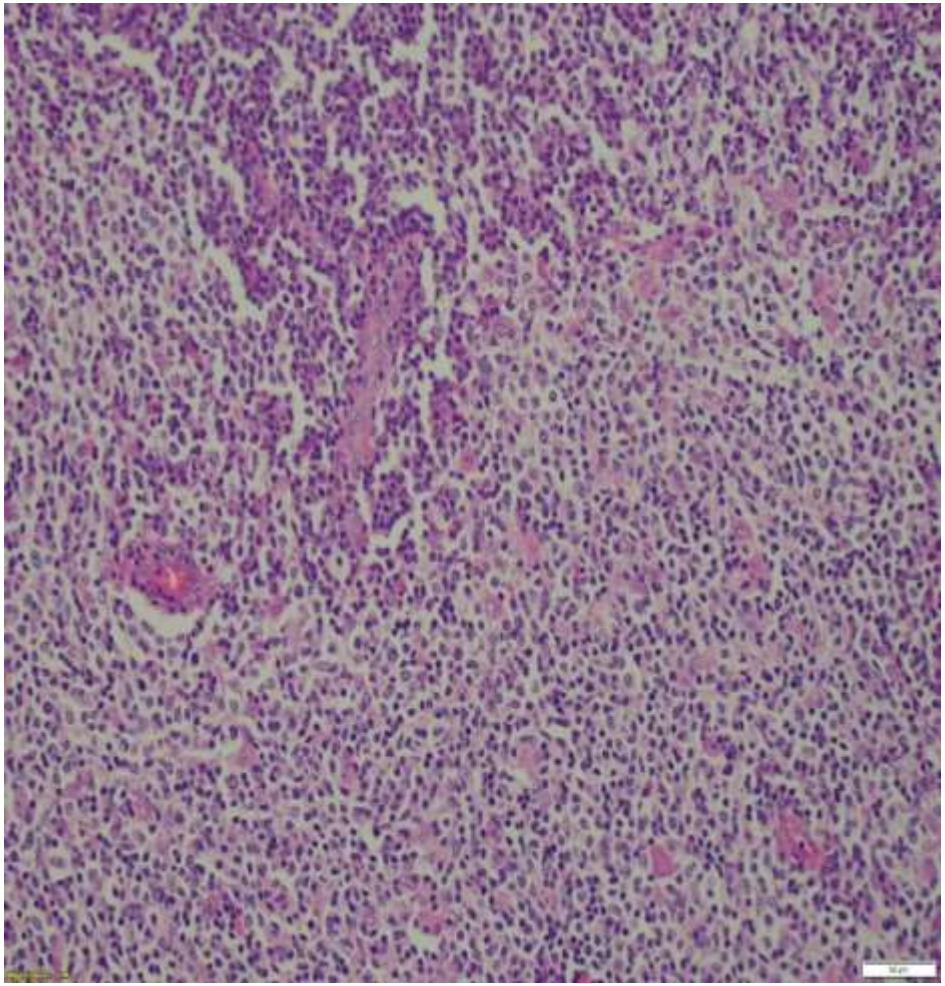


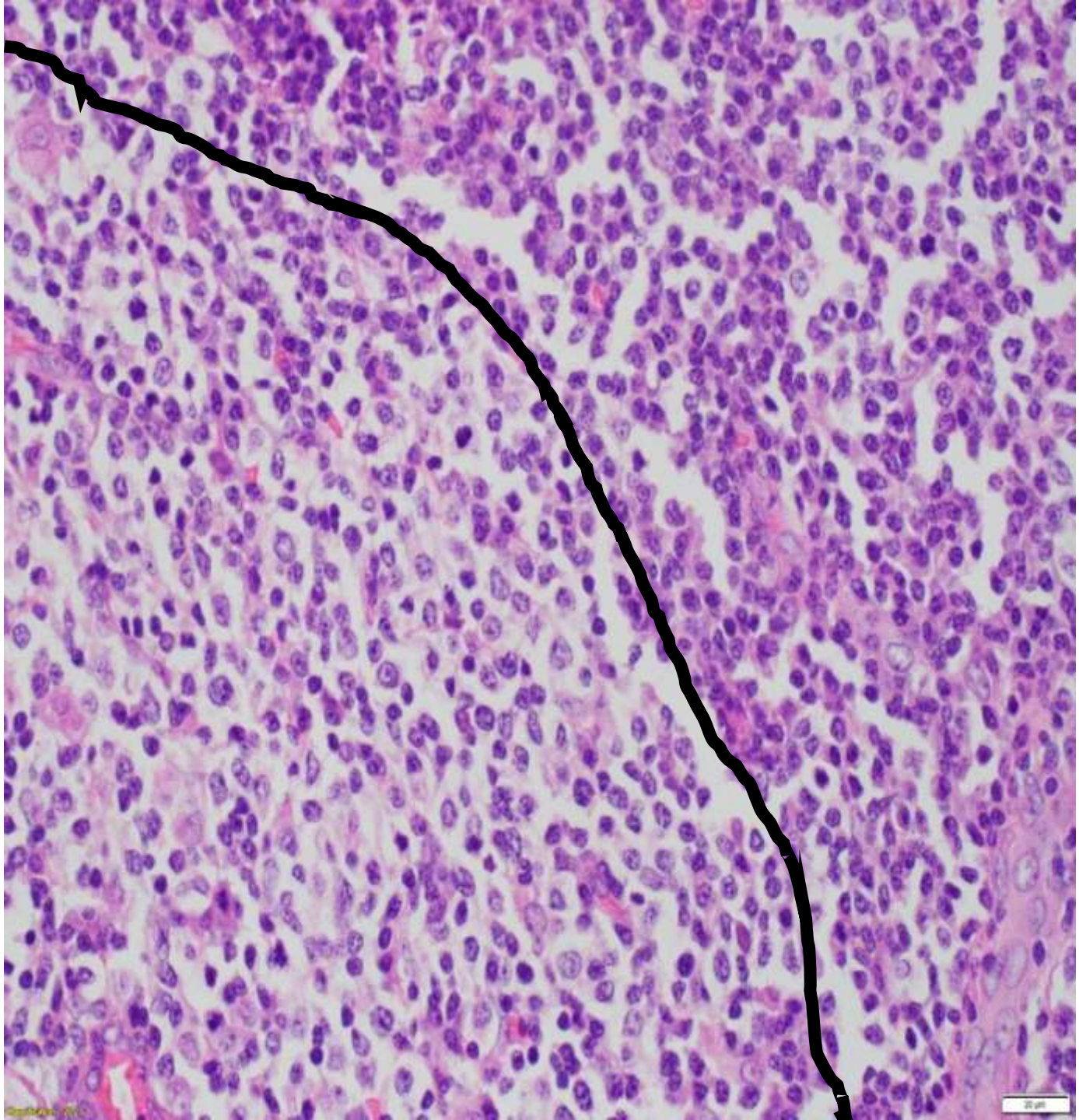
Lambda ISH



Lymph Node

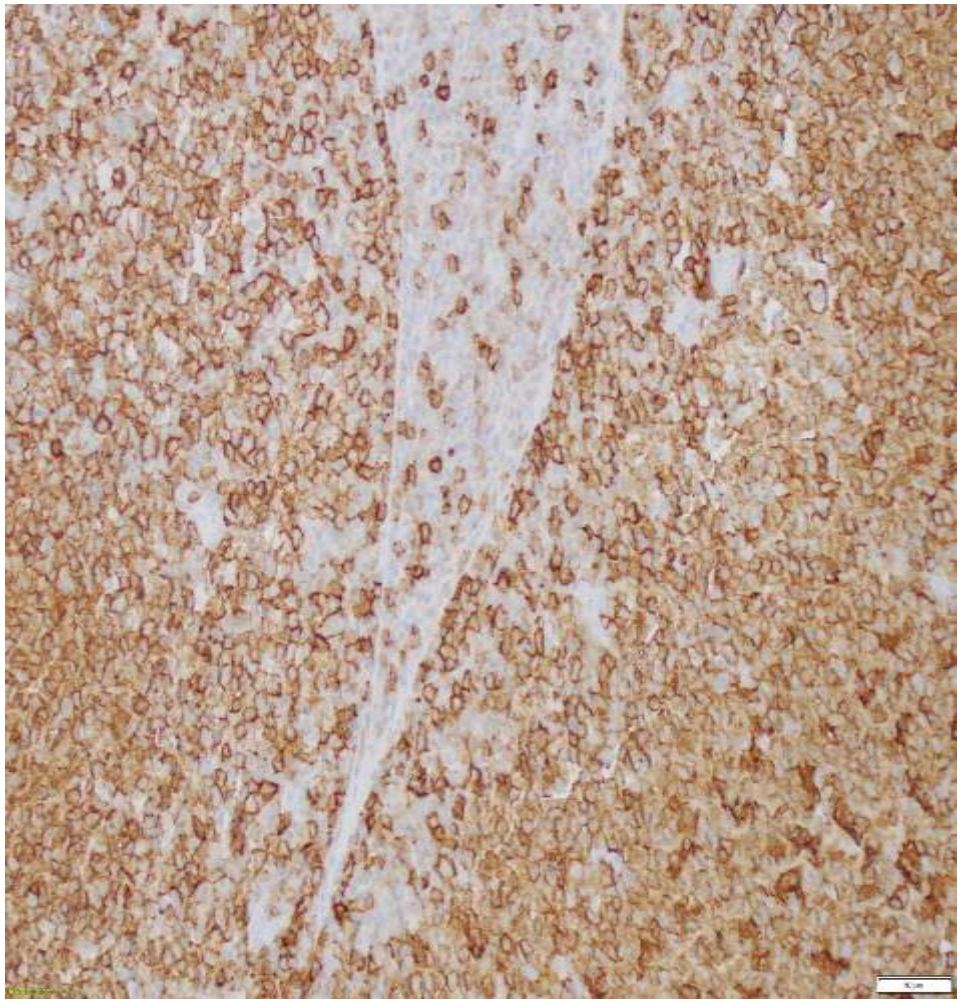




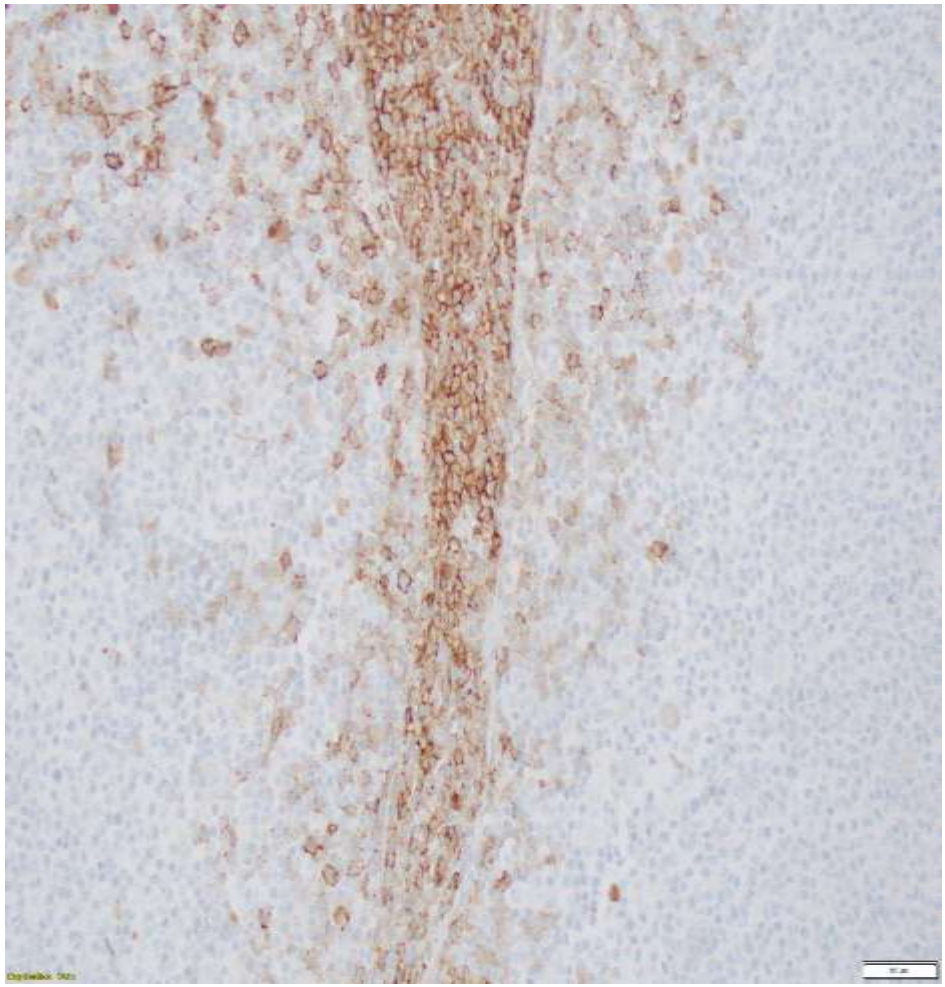


Lymph Node

CD20

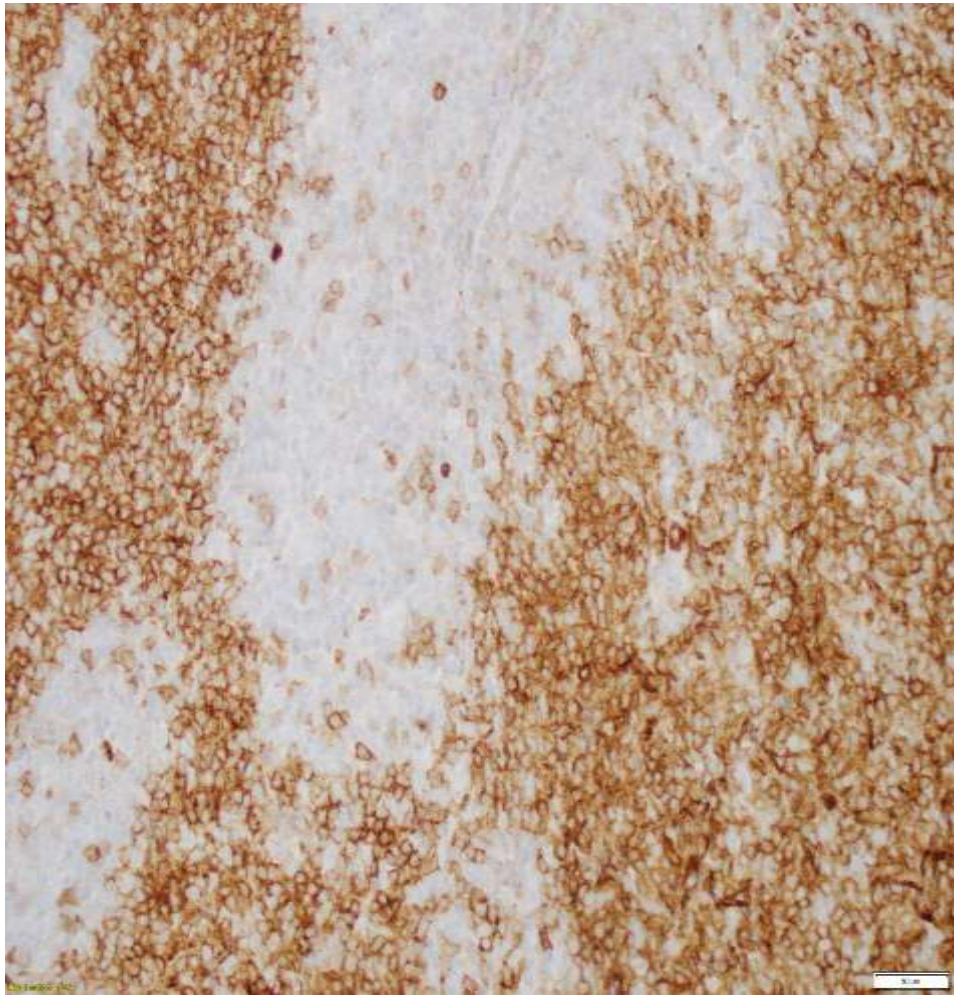


CD138

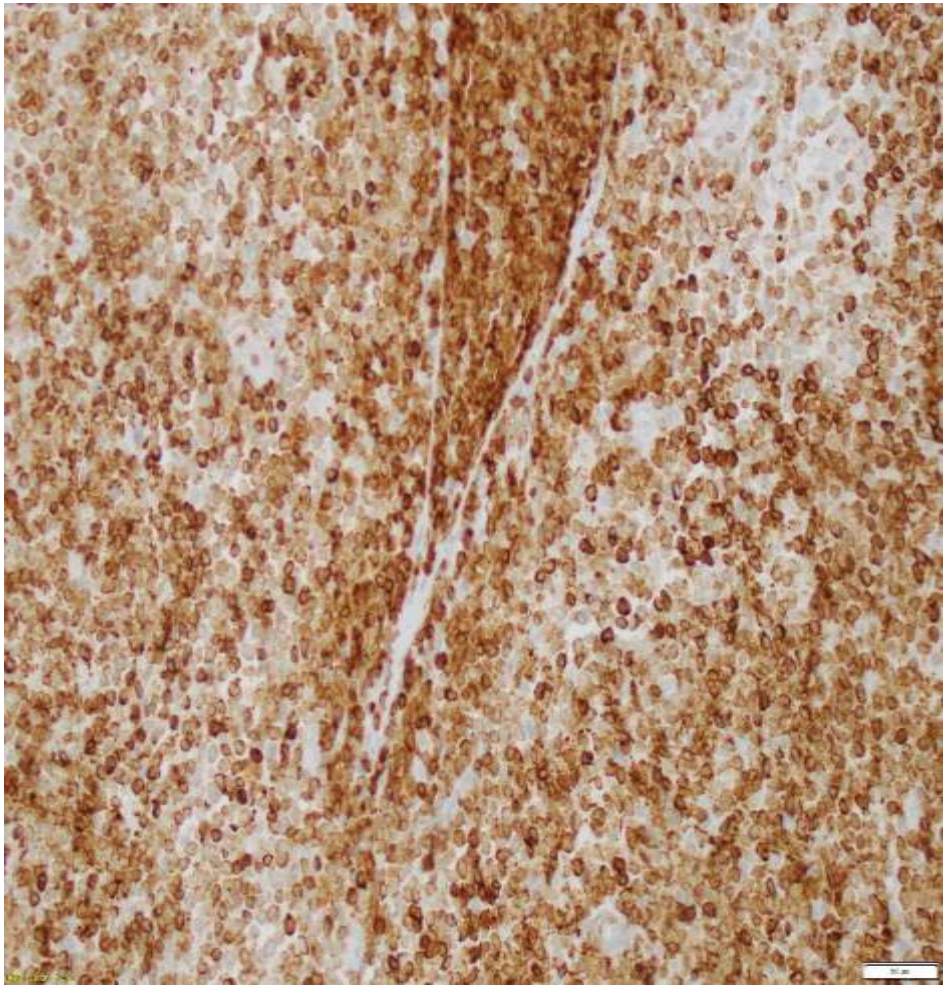


Lymph Node

CD10

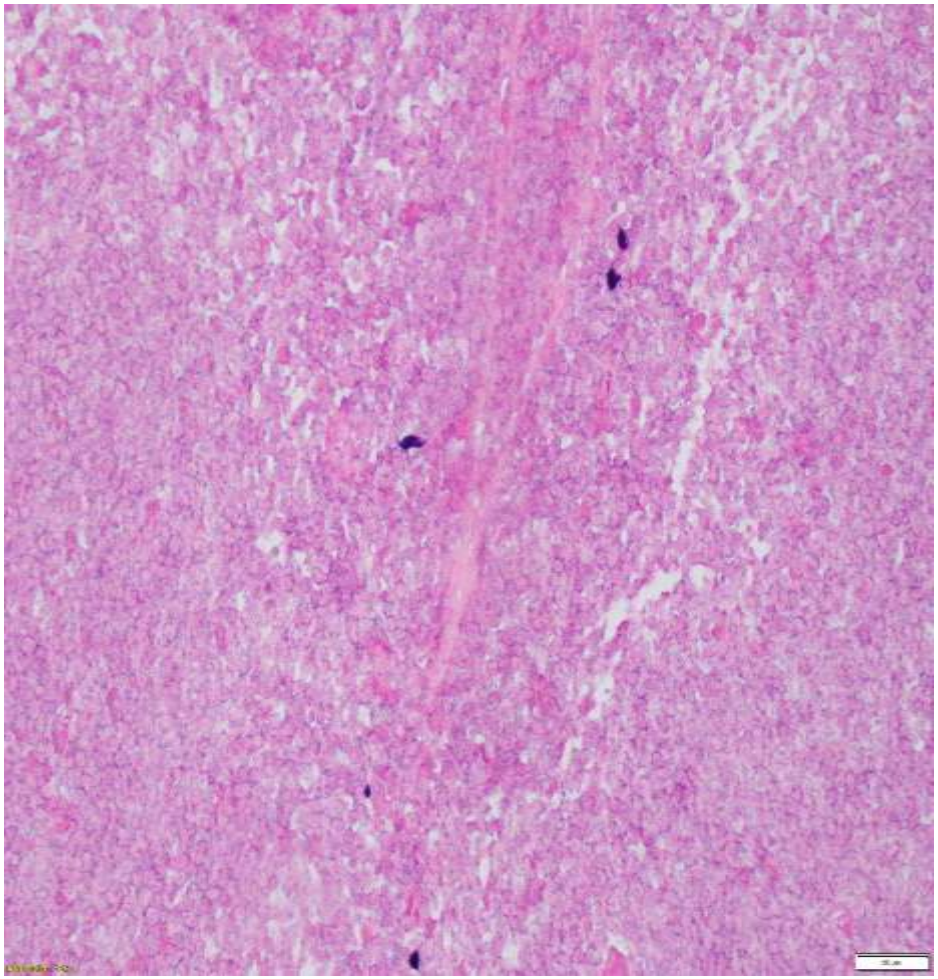


BCL2



Lymph Node

Kappa ISH



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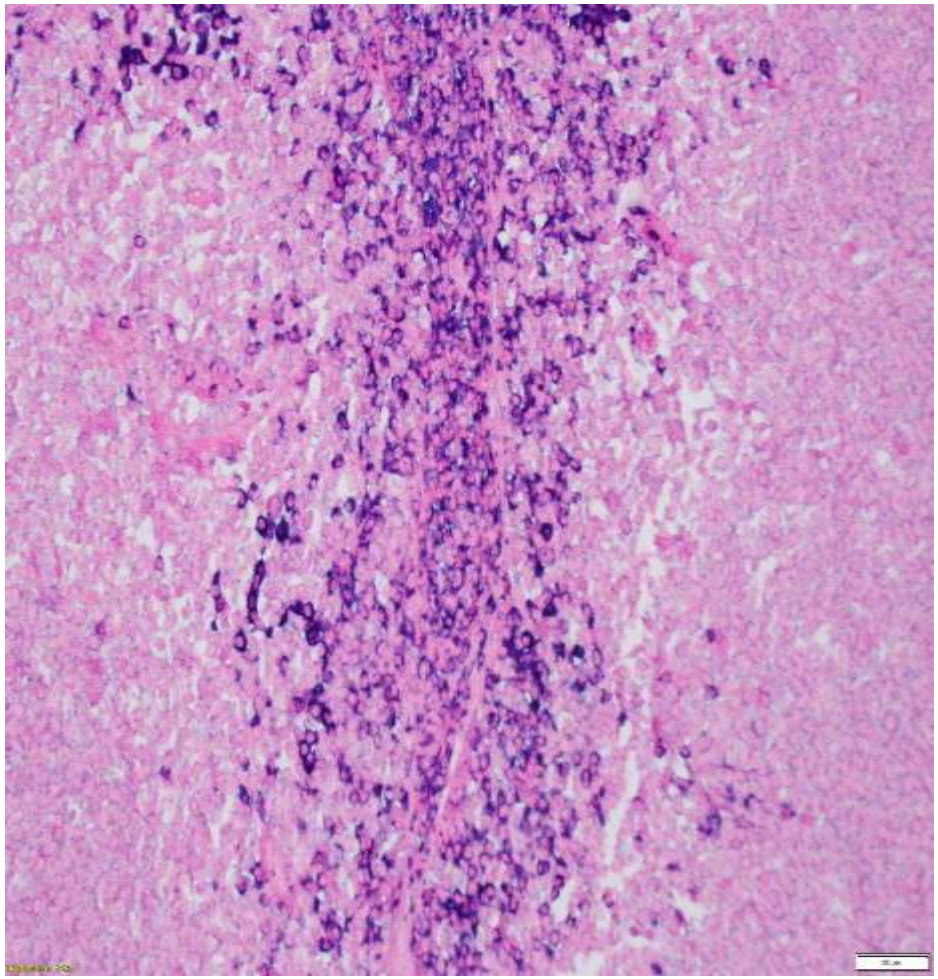
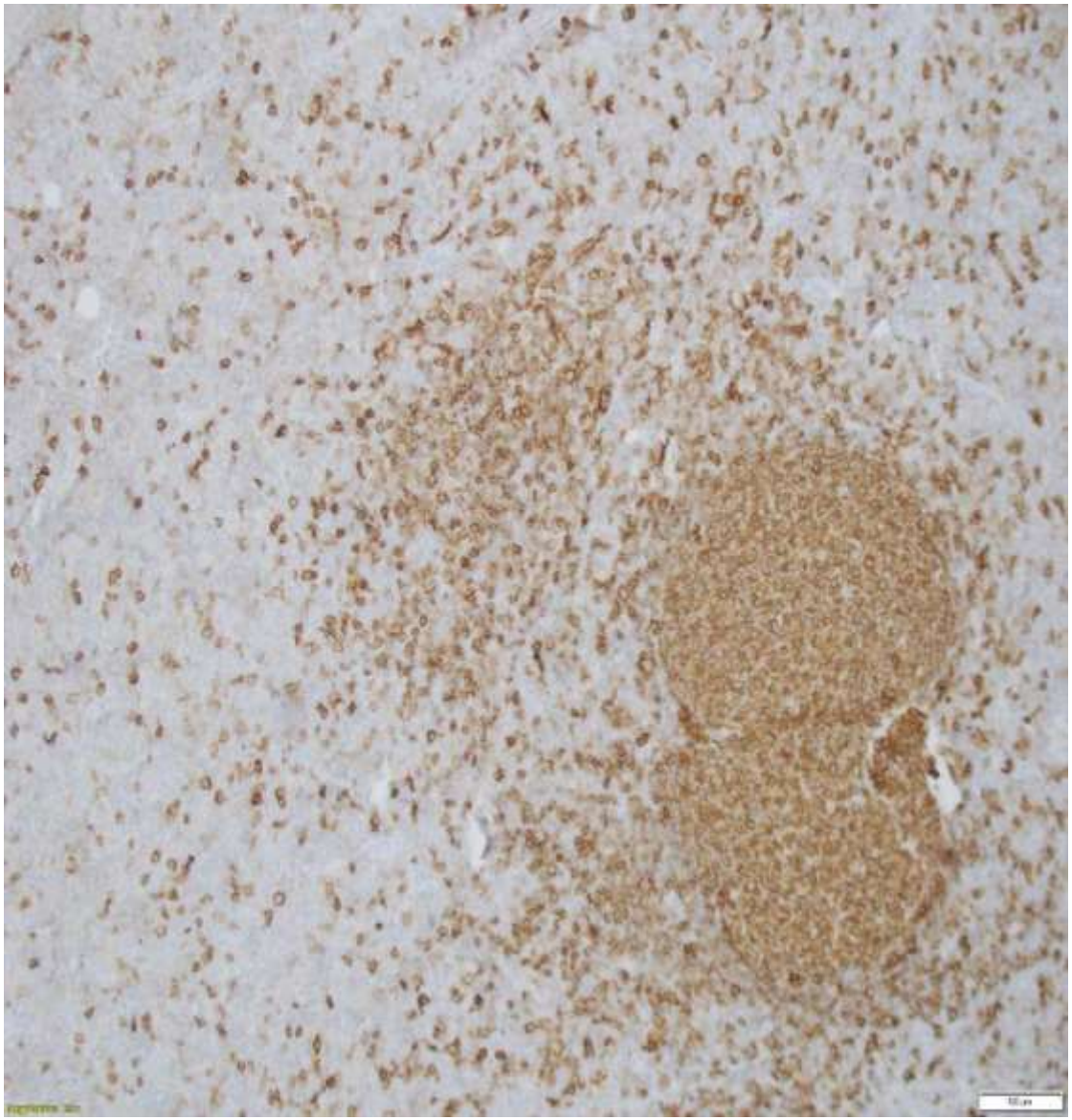


Back to the Kidney…

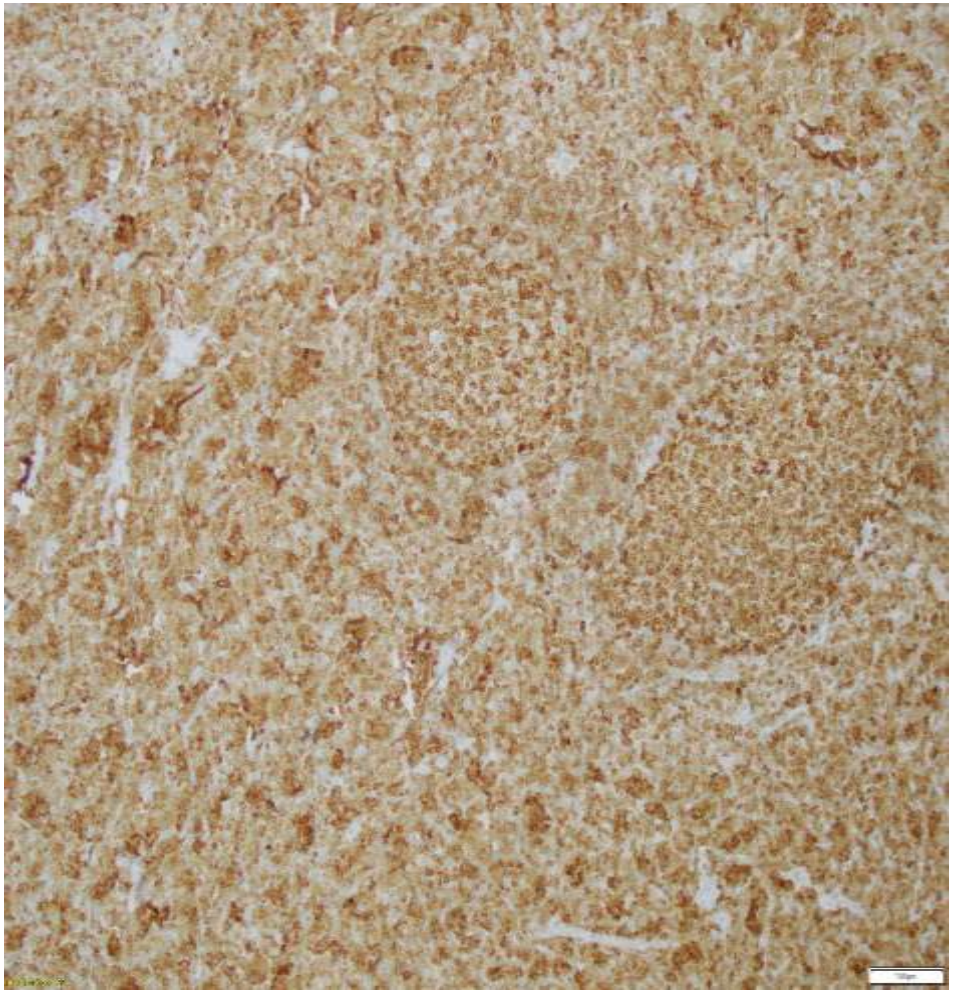
CD2
0



Kidney

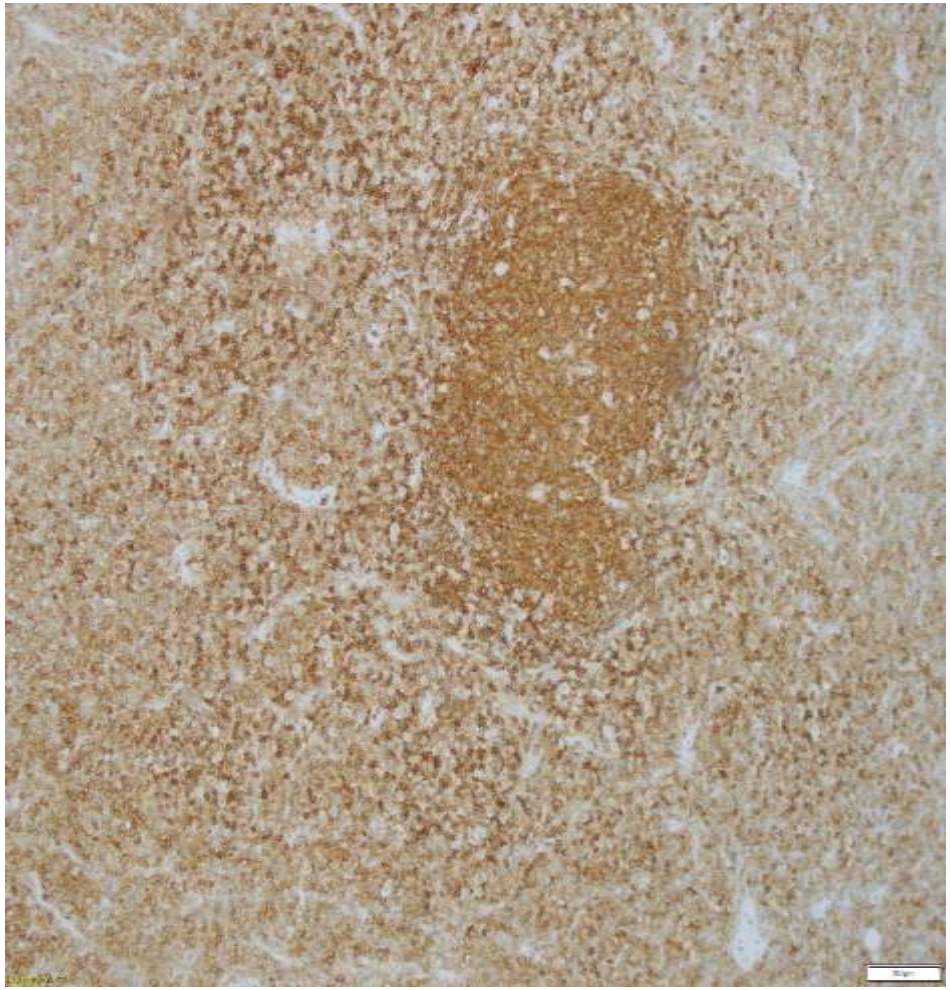
CD10

BCL2

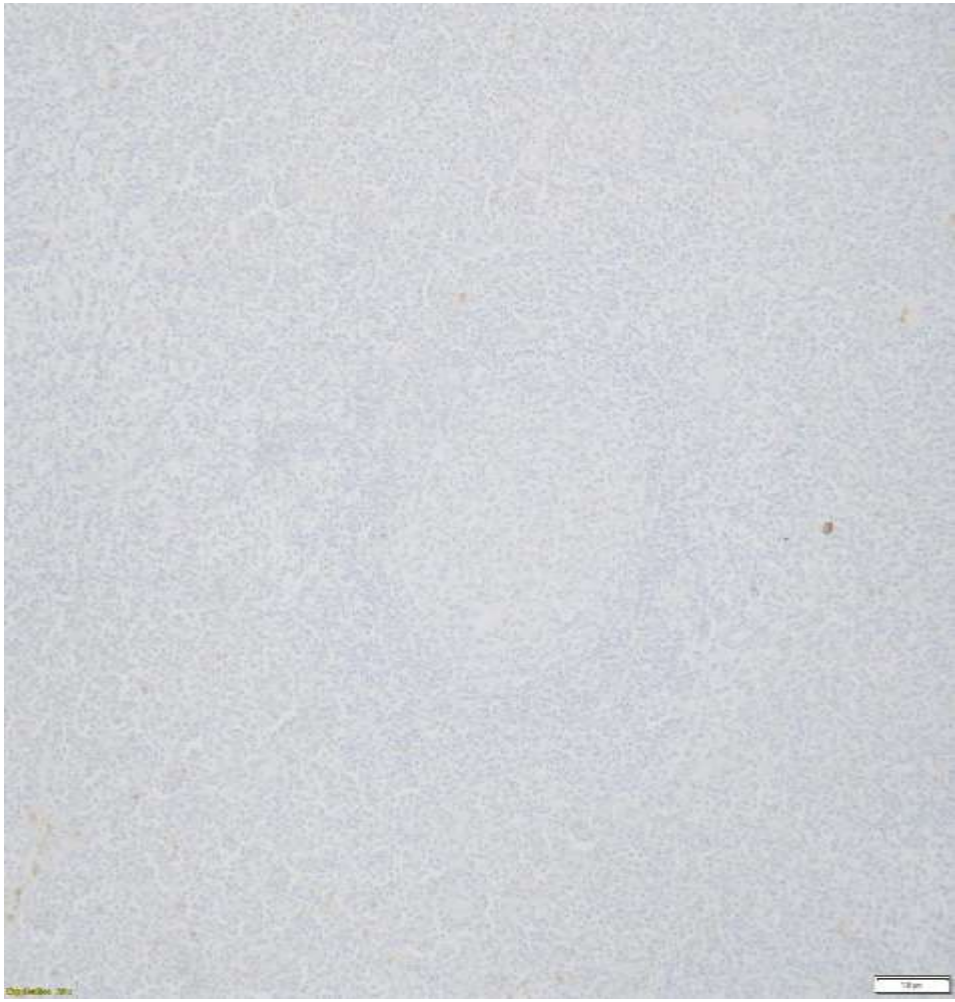


Kidney

CD45



CD117



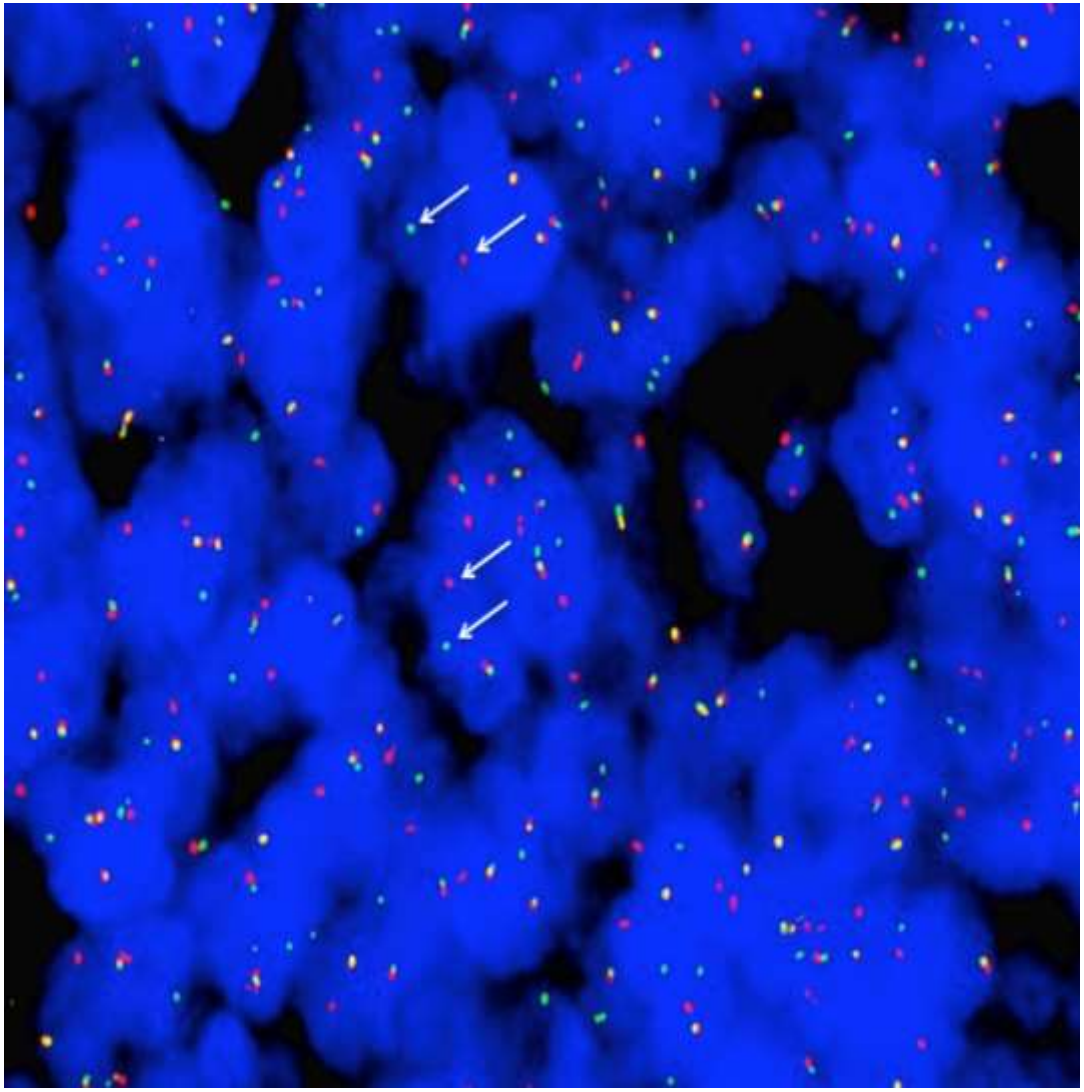
Differential Diagnosis

- 2 versus 1 ?
- Multiple myeloma and follicular lymphoma
- Marginal zone lymphoma with plasmacytic differentiation
- Lymphoplasmacytic lymphoma
- Follicular lymphoma with plasmacytic differentiation

Diagnosis

- B-cell lymphoproliferative disorder with plasmacytic differentiation
  1. Pending FISH for BCL2
- Recommend…
  1. Bone marrow biopsy
  2. Bone survey
  3. Serologies…Ca+2, SPEP/UPEP, free light chains, immunoglobulin levels

BCL2: Both lymphocytic and plasmacytic areas



Final Diagnosis:

Favor follicular lymphoma,
WHO grade 1-2, with plasmacytic differentiation

Follicular lymphoma with plasmacytic differentiation

- Rare morphologic variant of follicular lymphoma
- First series described by Keith et al in 1985: identified 198 cases of follicular lymphoma
  - 17 (8.6%) large numbers of plasma cells
  - 7 (3.5%) monotypic
- Frizzera et al 1986 had 6 cases FL with monotypic plasmacytic differentiation
  - 4 disseminated disease, 3 extranodal disease, 4 serum paraproteins
  - Median survival 40 months
  - Survival and clinical features closer to LPL than follicular lymphoma
- Gradowski et al 2010 examined 14 cases
  - Plasma cells and lymphoid cells separated: BCL2 shared in 7/14 cases

Further Work-Up

- Bone marrow biopsy:
  - Plasma cell neoplasm, lambda IgA restricted plasma cells 60% marrow cells
- PET scan no osseous involvement
- SPEP positive for abnormal proteins, lambda chains >5000 and IgA >2000
- Hypercalcemia
- Treat for multiple myeloma first with CyBORD (cyclophosphamide, bortezomib, and dexamethasone)
- Follow-up therapy follicular lymphoma with rituximab plus lenalidomide

Final Diagnosis

- ??????

- Follicular lymphoma present
- ? Relationship to plasma cells neoplasm and multiple myeloma

Take Home Lessons

- Plasmacytic neoplasms have a diverse differential diagnosis
  - Treatment implications
  - Due to follicular lymphoma bone marrow transplant ineligible
- Clinical, laboratory and pathologic correlation required for definitive WHO classification

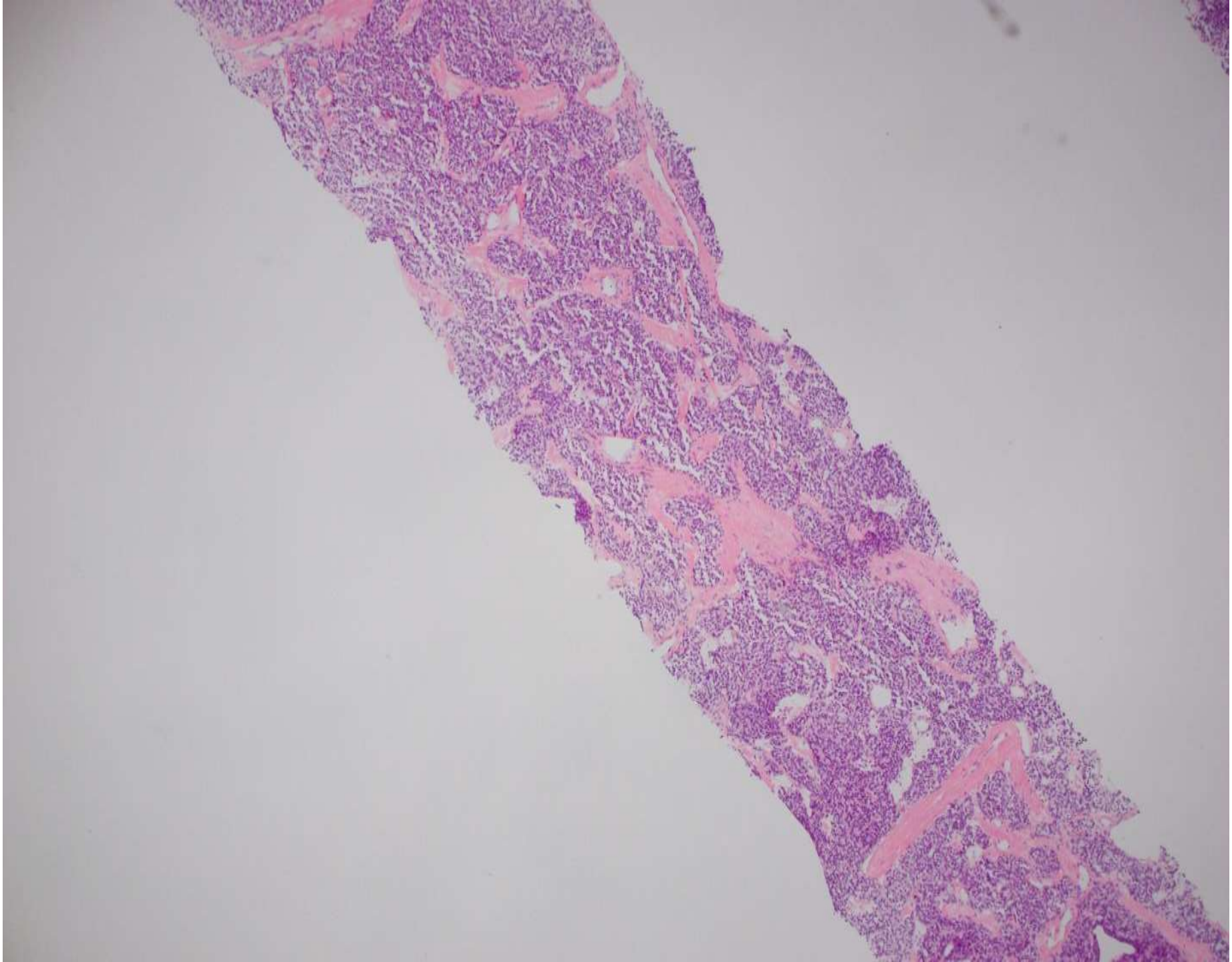
References

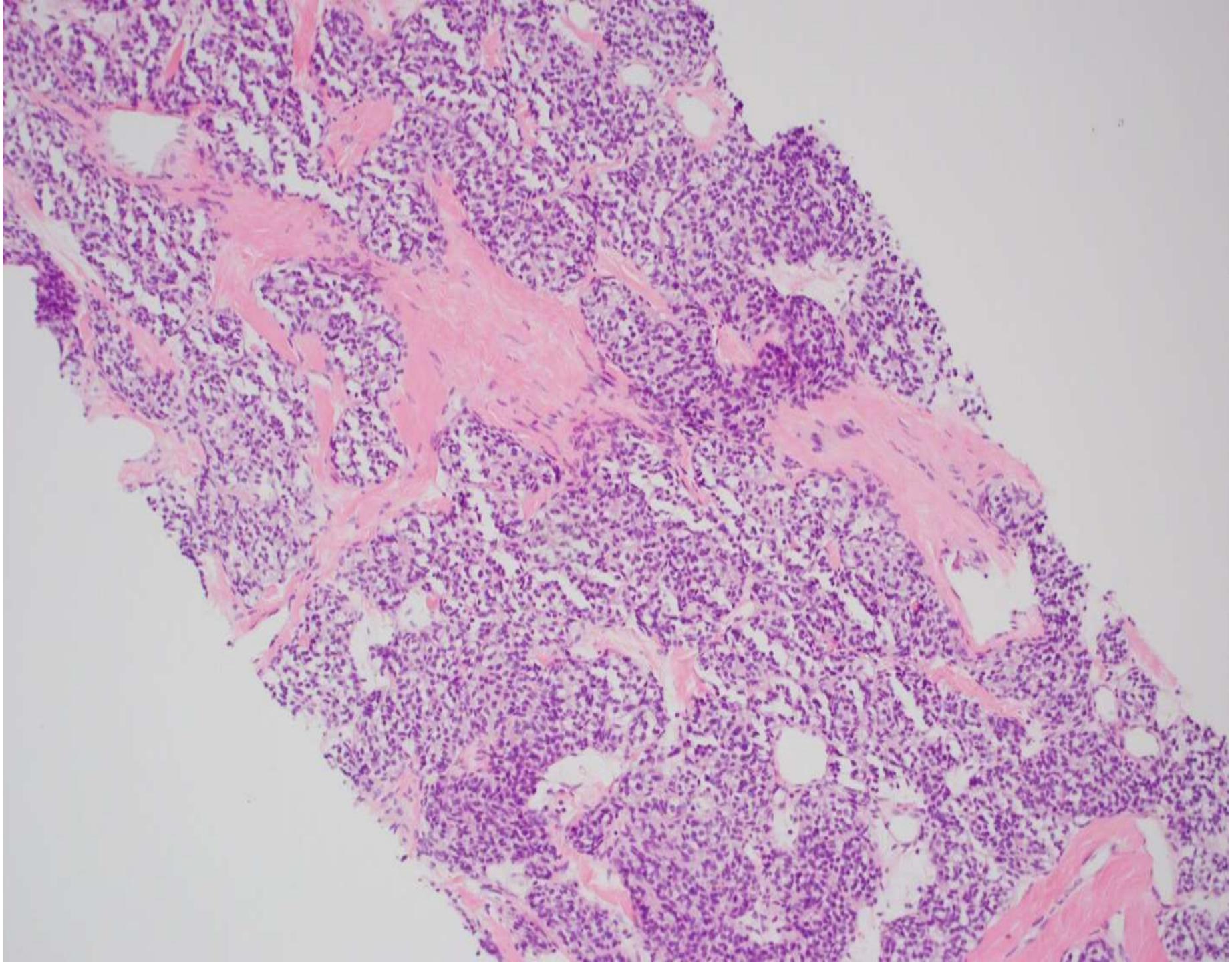
- Frizzera, G., Anaya, J. S., & Banks, P. M. (1986). Neoplastic plasma cells in follicular lymphomas. Clinical and pathologic findings in six cases. *Virchows Arch A Pathol Anat Histopathol, 409*(2), 149-162.
- Gradowski, J. F., Jaffe, E. S., Warnke, R. A., Pittaluga, S., Surti, U., Gole, L. A., & Swerdlow, S. H. (2010). Follicular lymphomas with plasmacytic differentiation include two subtypes. *Mod Pathol, 23*(1), 71-79.
- Keith, T. A., Cousar, J. B., Glick, A. D., Vogler, L. B., & Collins, R. D. (1985). Plasmacytic differentiation in follicular center cell (FCC) lymphomas. *Am J Clin Pathol, 84*(3), 283-290.

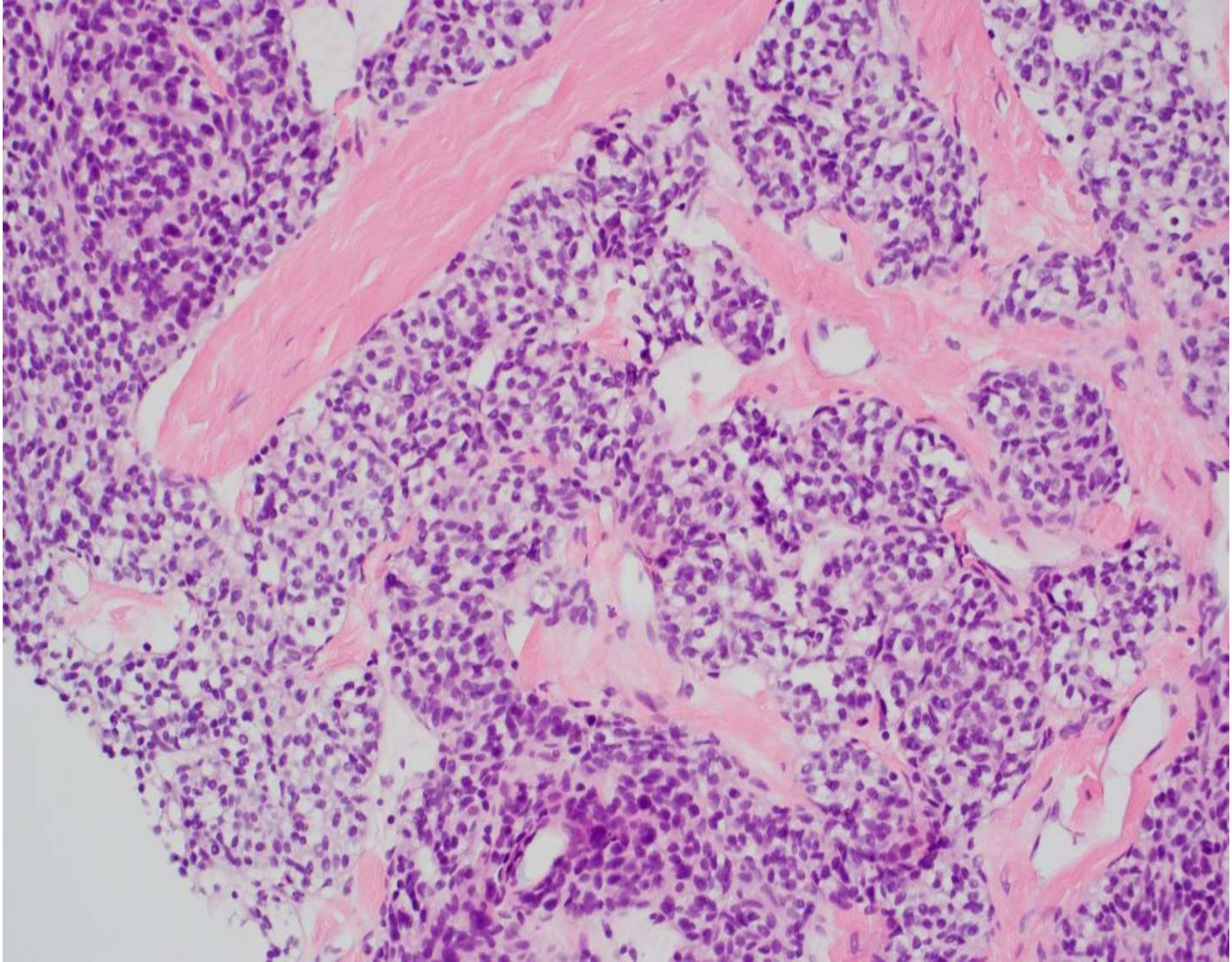
19-0904

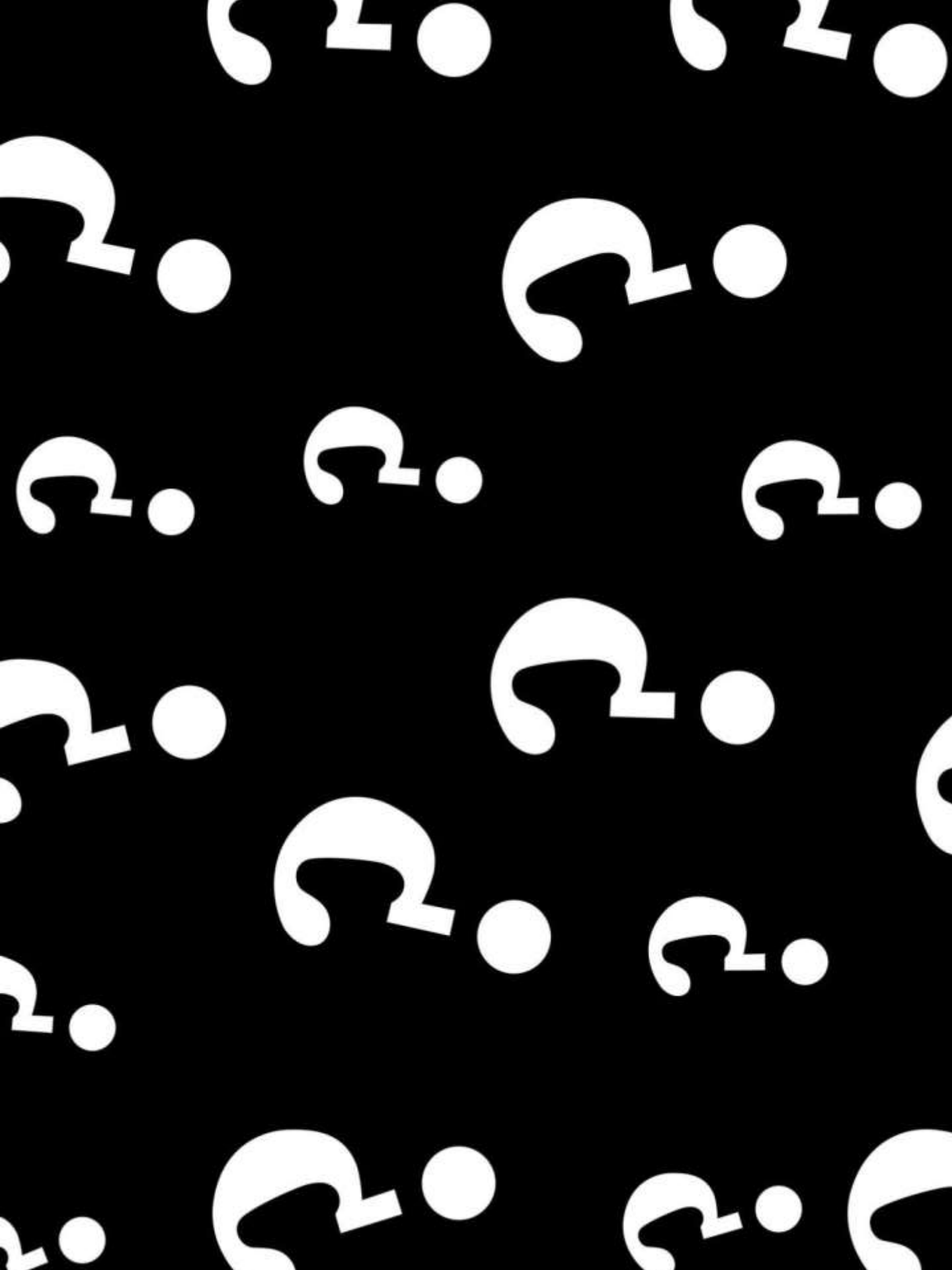
Sarah Cherny; Kaiser SF

71-year-old female with 4cm mass incidentally discovered on CXR. Indeterminate on imaging for mediastinal origin vs pleural/pulmonary origin.





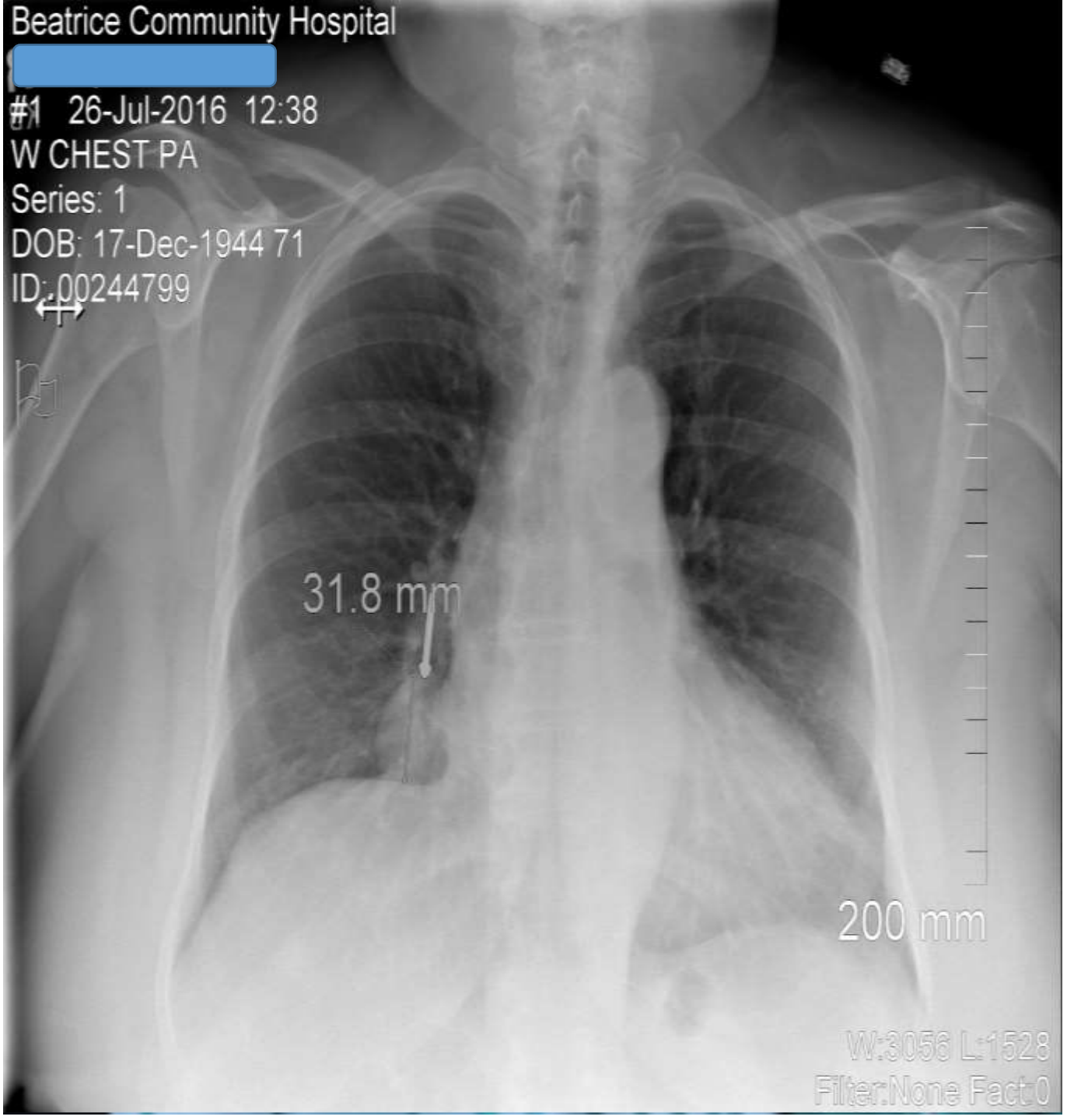




Case 19-0904

Sarah Cherny, MD

Kaiser SF


Beatrice Community Hospital
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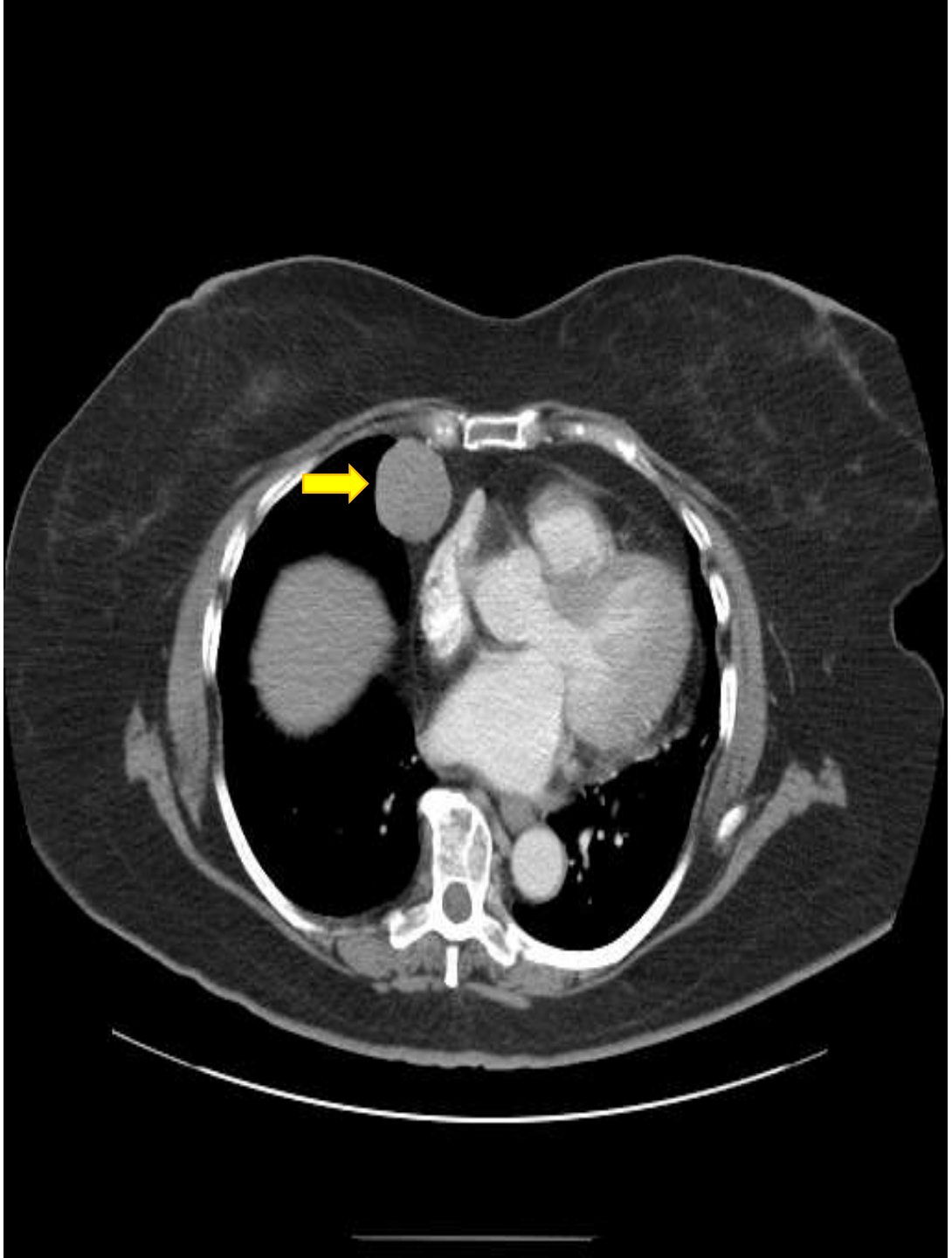
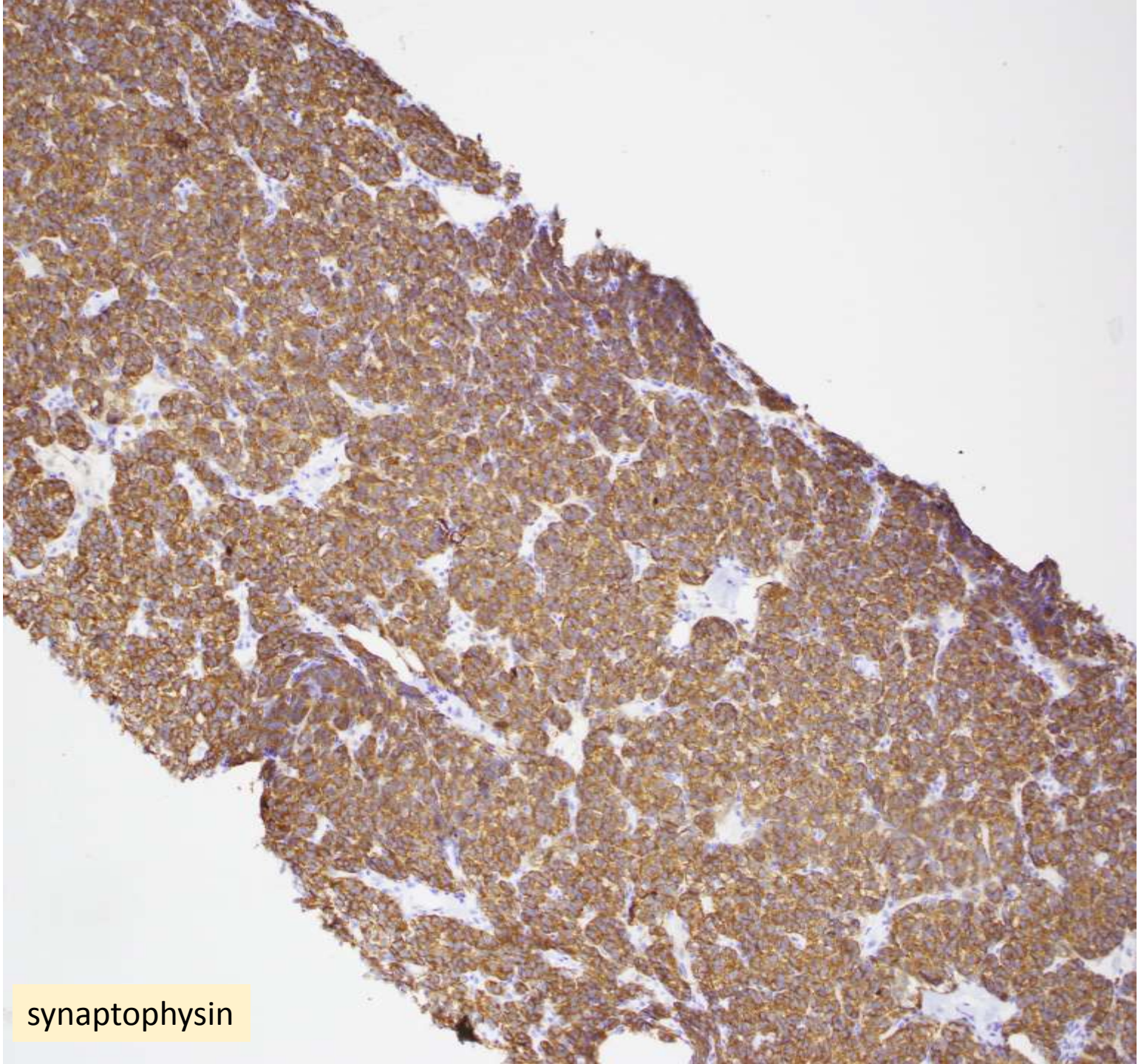
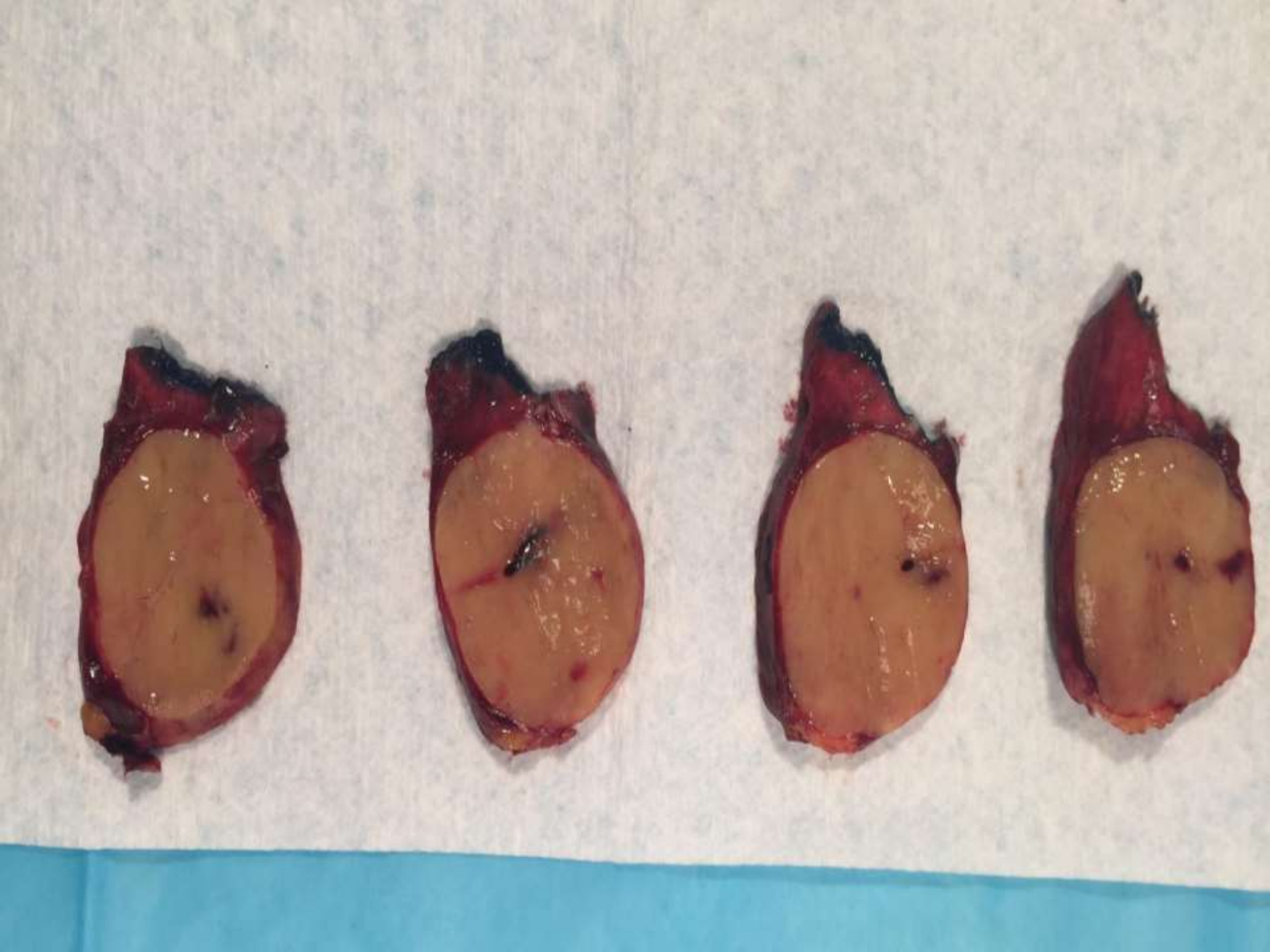


Ddx

- Carcinoid
- Cellular solitary fibrous tumor


synaptophysin

- Diagnosis: Typical Carcinoid Tumor



Pulmonary Carcinoid

- Incidence
  - ~1 case per 100,000 people
  - comprise 1-2% of all primary lung neoplasms
- Epidemiology
  - women > men
  - Median age: mid 50s (range: teens to 80s)
  - Caucasian > non-Caucasian
- Risk factors
  - family history of carcinoid tumors
  - *MEN1* gene mutation

Pulmonary Carcinoid

- Typical carcinoid:
  - <2 mitoses / 2 square mm
  - lack necrosis
  - ~90% of pulmonary carcinoids
- Atypical carcinoid:
  - 2-10 mitoses per 2 square mm
  - foci of necrosis – usually punctate
  - ~10% of pulmonary carcinoids
- 1/3 arise in peripheral lung
  - Usually asymptomatic
  - Uncommonly associated with clinical syndrome due to peptide production
    - e.g., Carcinoid syndrome, Cushing syndrome

- Terminology: IARC / WHO recently proposed classifying pulmonary carcinoid tumors as well differentiated NETs
  - Rindi G, Klimstra DS, et al. "A common classification framework for neuroendocrine neoplasms: an International Agency for Research on Cancer (IARC) and World Health Organization (WHO) expert consensus proposal." *Mod Pathol*. Dec 2018; 31: 1770-1786

Pulmonary Carcinoid

- Prognosis:
  - Typical carcinoids amenable to complete resection - excellent prognosis
  - Atypical carcinoids
    - higher recurrence rate, higher mortality than typical carcinoids
    - Almost half recur / metastasize within 5 years

The American Journal of Surgical Pathology. 43(9):1291–1296, SEPTEMBER 2019
DOI: 10.1097/PAS.0000000000001268, PMID: 31094922
Issn Print: 0147-5185
Publication Date: September 2019

The Prognostic Significance of the 8th Edition TNM Staging of Pulmonary Carcinoid Tumors: A Single Institution Study With Long-term Follow-up

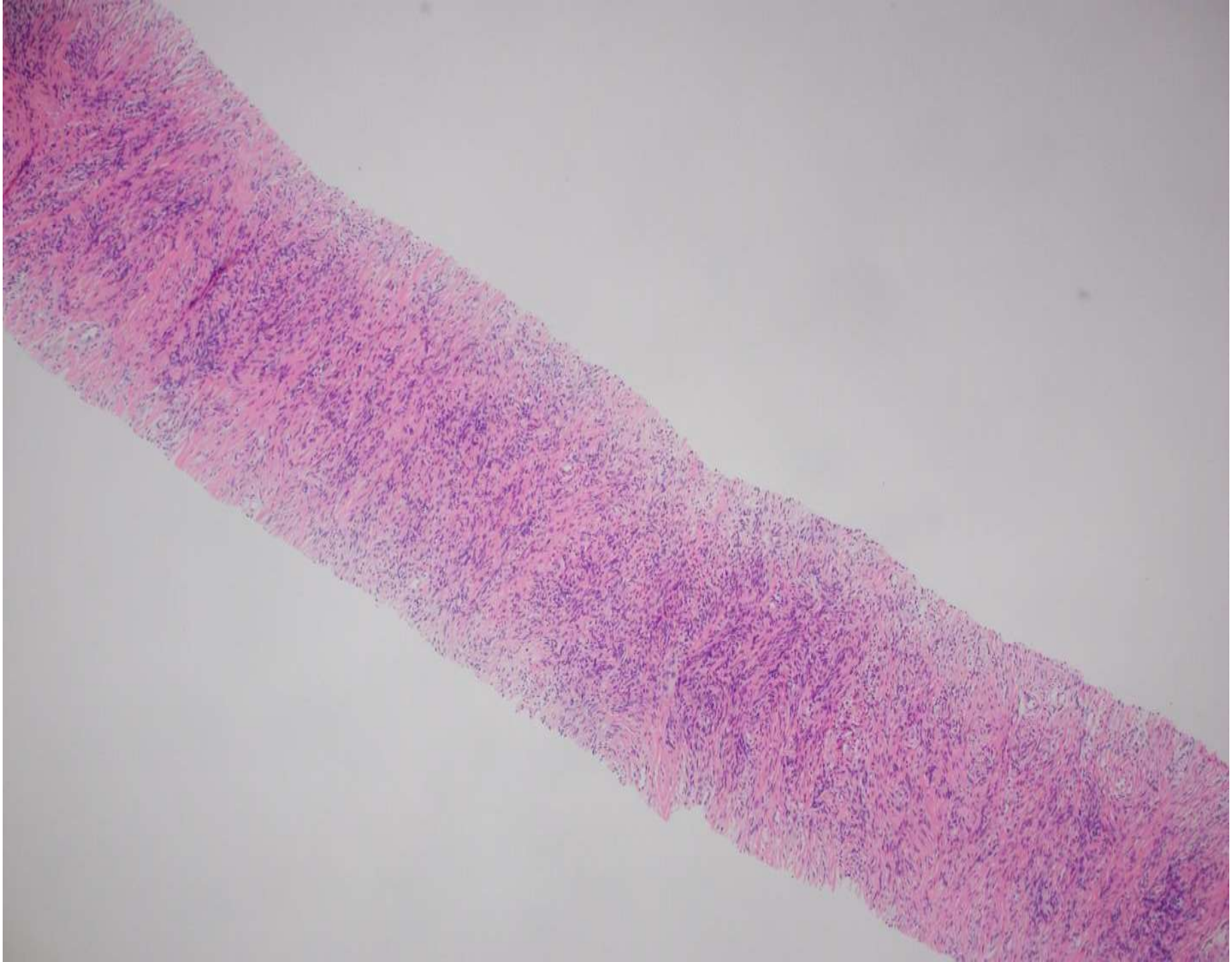
Josephine Dermawan;Carol Farver;

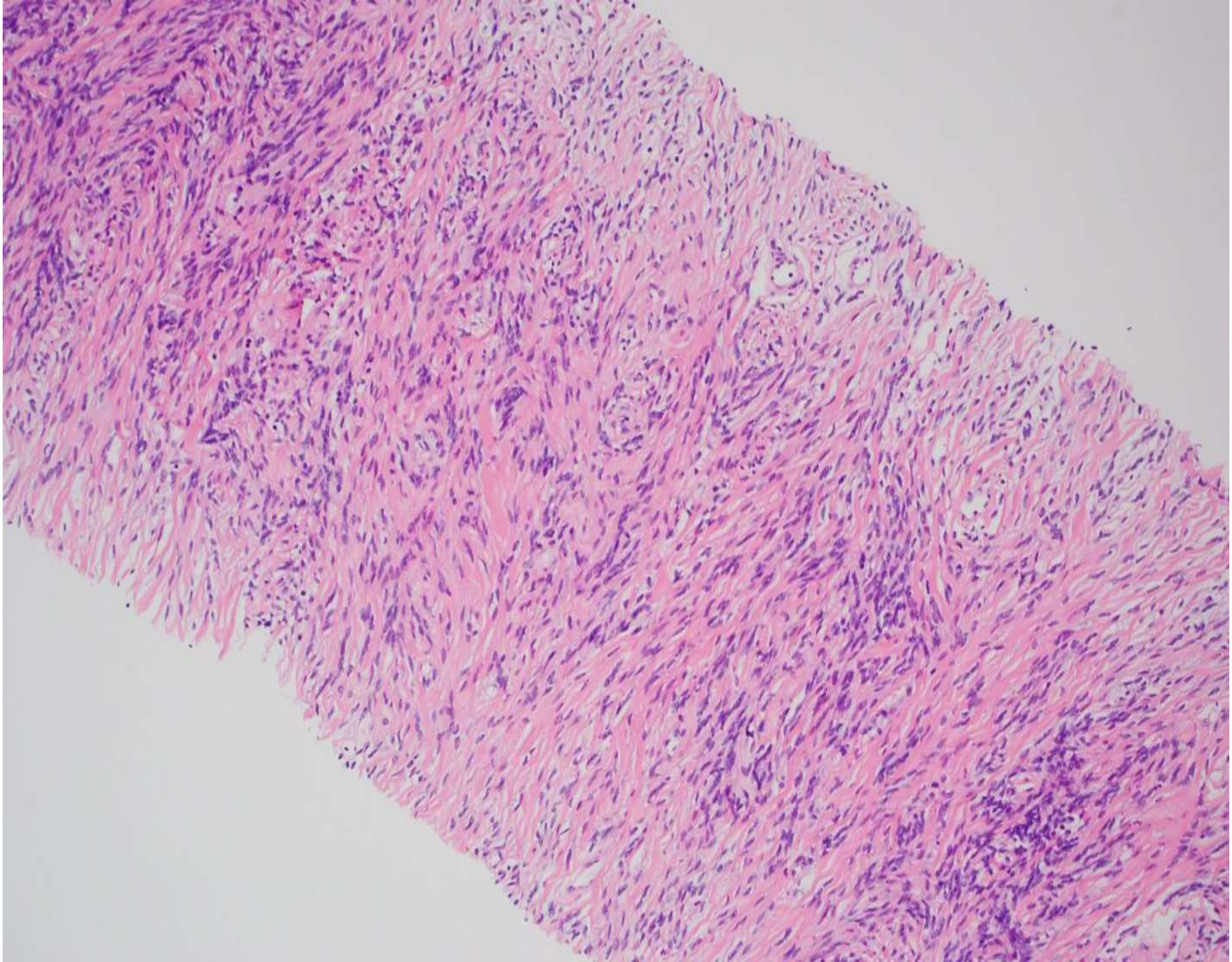
- Reviewed all typical (188) and atypical (17) pulmonary carcinoids from 1995 – 2016 at Cleveland Clinic
- Compared 7th ed with 8th ed of TNM stage with regards to strength in predicting outcome
- TNM 8th edition
  - upstages carcinoid tumors compared with 7th edition
  - better predictor of prognosis than 7th edition
- Histology (typical vs atypical) – remains equally powerful predictor

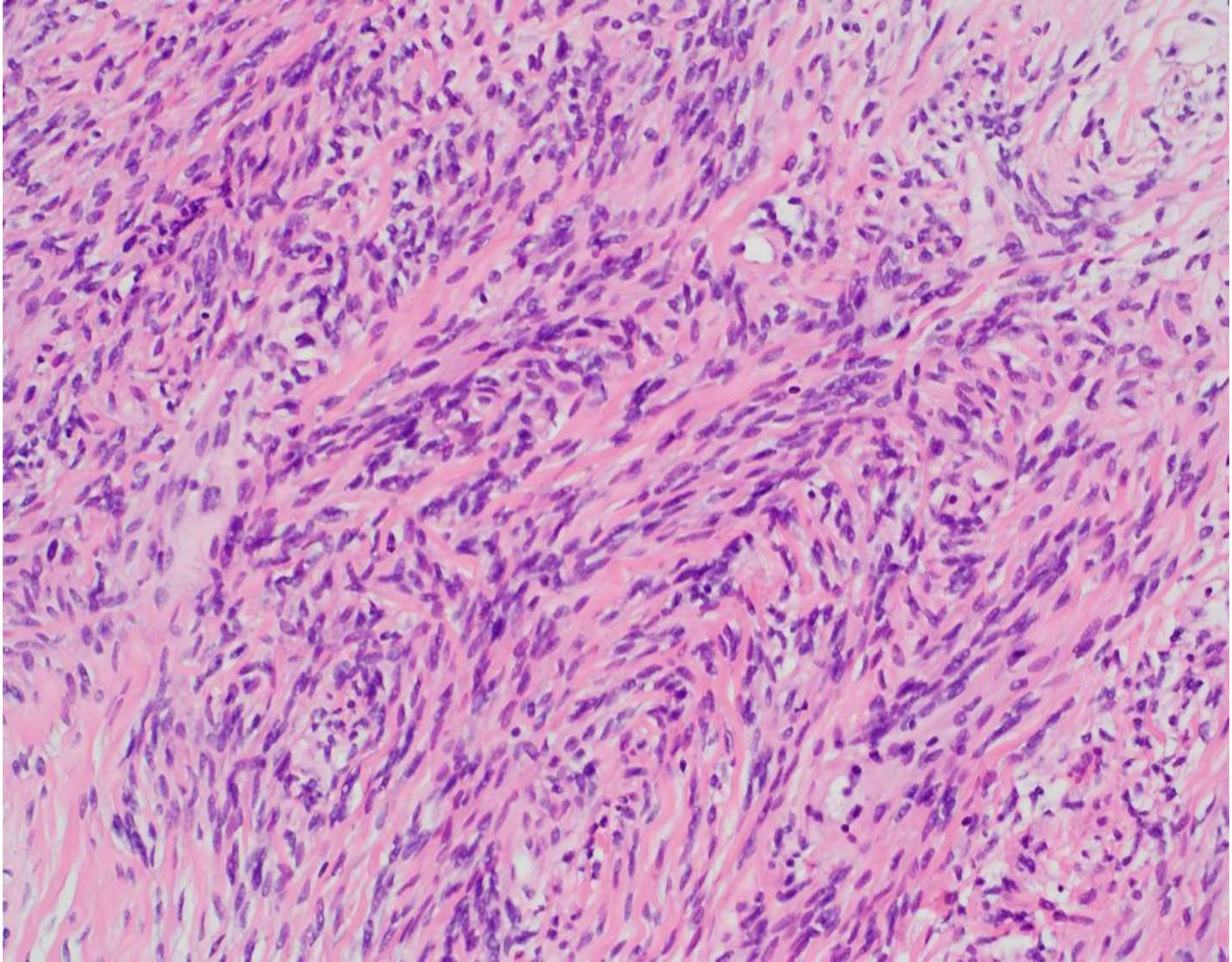
19-0905

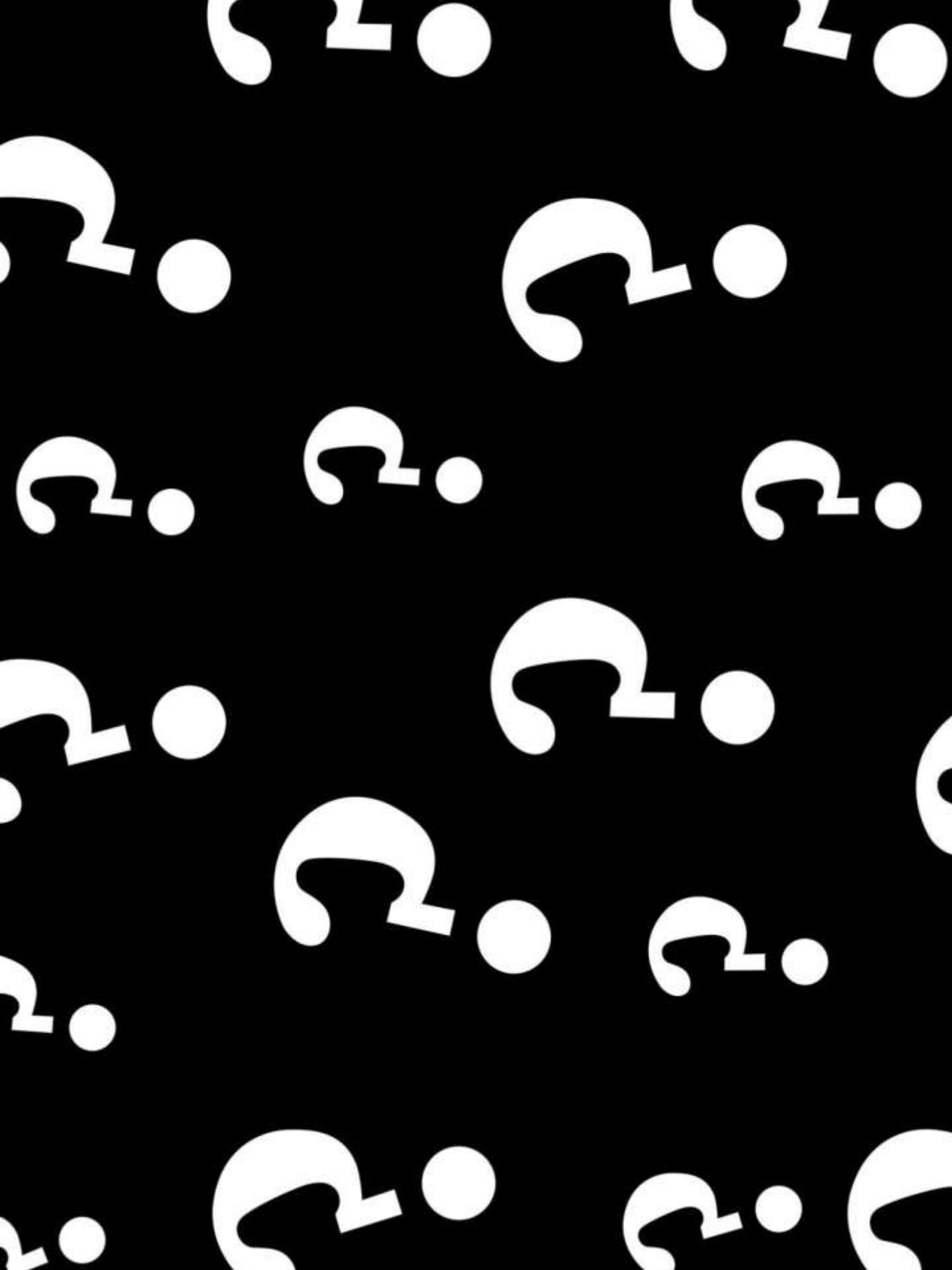
Sarah Cherny; Kaiser SF

50-year-old female with 4cm mass incidentally discovered on CXR. Favored to be pleural-based.









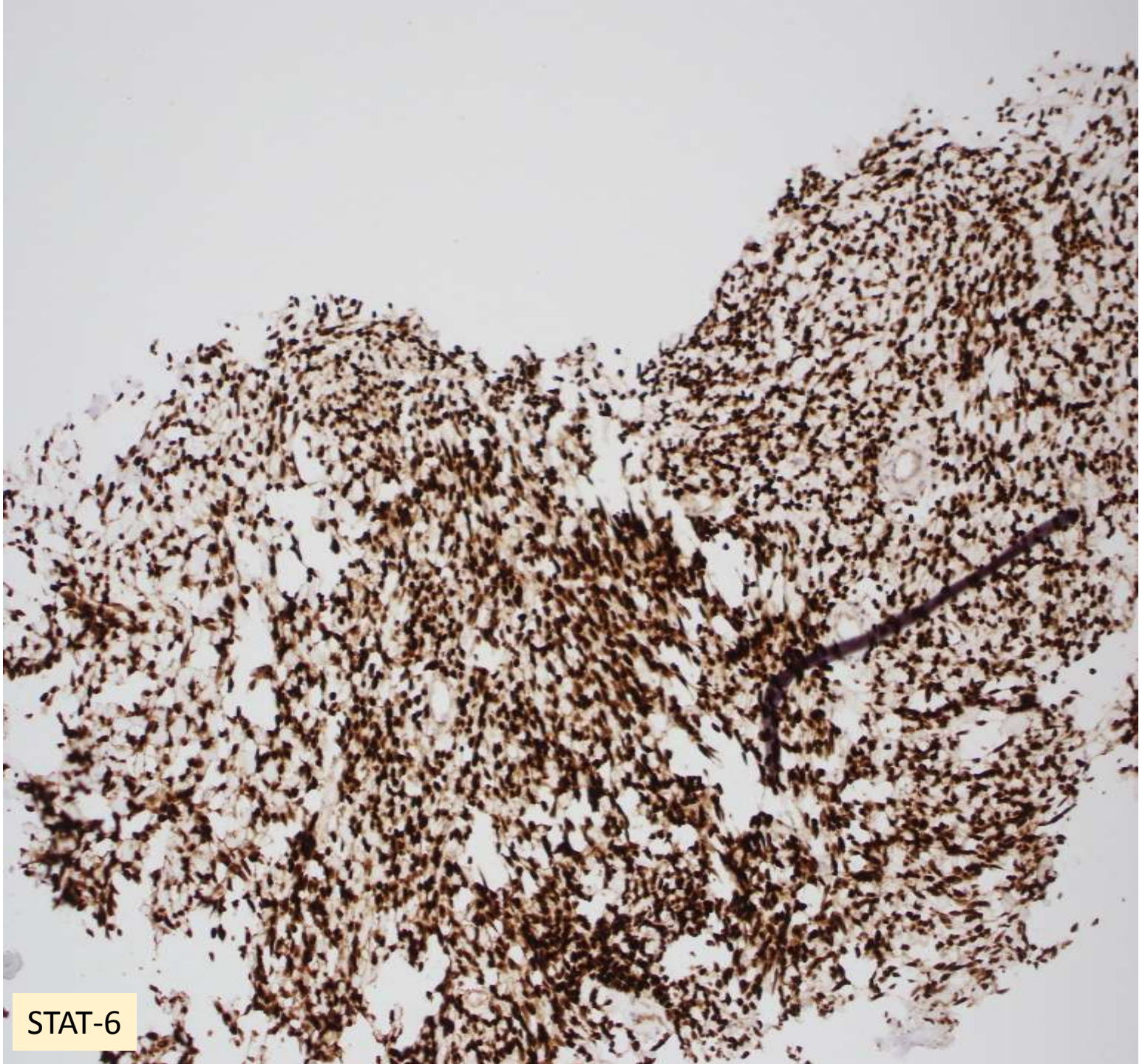
Case 19-0905

Sarah Cherny, MD

Kaiser SF

Ddx

- Solitary Fibrous Tumor
- Mesothelial?


STAT-6

Solitary Fibrous Tumor

- Incidence
  - ~2-3 cases per 100,000 people
  - comprise ~5% of all primary pleural tumors
- Epidemiology
  - women = men
  - 50s-60s
- Risk factors
  - None known

Solitary Fibrous Tumor

- Gross:
  - well-circumscribed, predominantly solid pleural-based masses
  - often greater than 10 cm
- Micro:
  - uniform spindle cells
  - branching HPC-like / staghorn vessels
  - variably prominent stromal hyalinization
  - STAT6: positive in >95% cases

Solitary Fibrous Tumor

- Genetics:
  - Characteristic gene fusion *NAB2-STAT6* -> overexpression of STAT6
- Prognosis / predictive factors:
  - Large majority are associated with excellent prognosis
  - ~10% recur locally
  - 5-10% metastasize
    - Mitotic rate of >4 per 2 square mm is most reliable indicator of aggressive behavior
    - Tumor size, cytologic atypia, and necrosis are much less predictive

19-0906

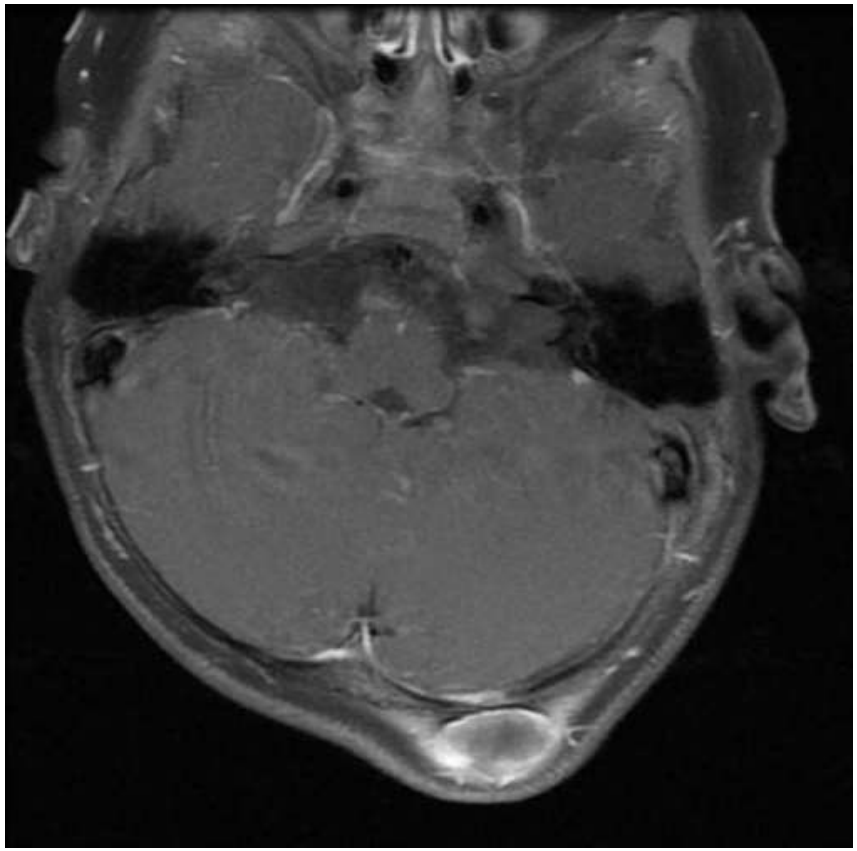
Saman Ahmadian/Romain Cayrol/Don Born; Stanford

15-month-old male infant referred for non-painful, non-tender, discrete area of swelling of the occipital scalp. No history of head trauma to the area.

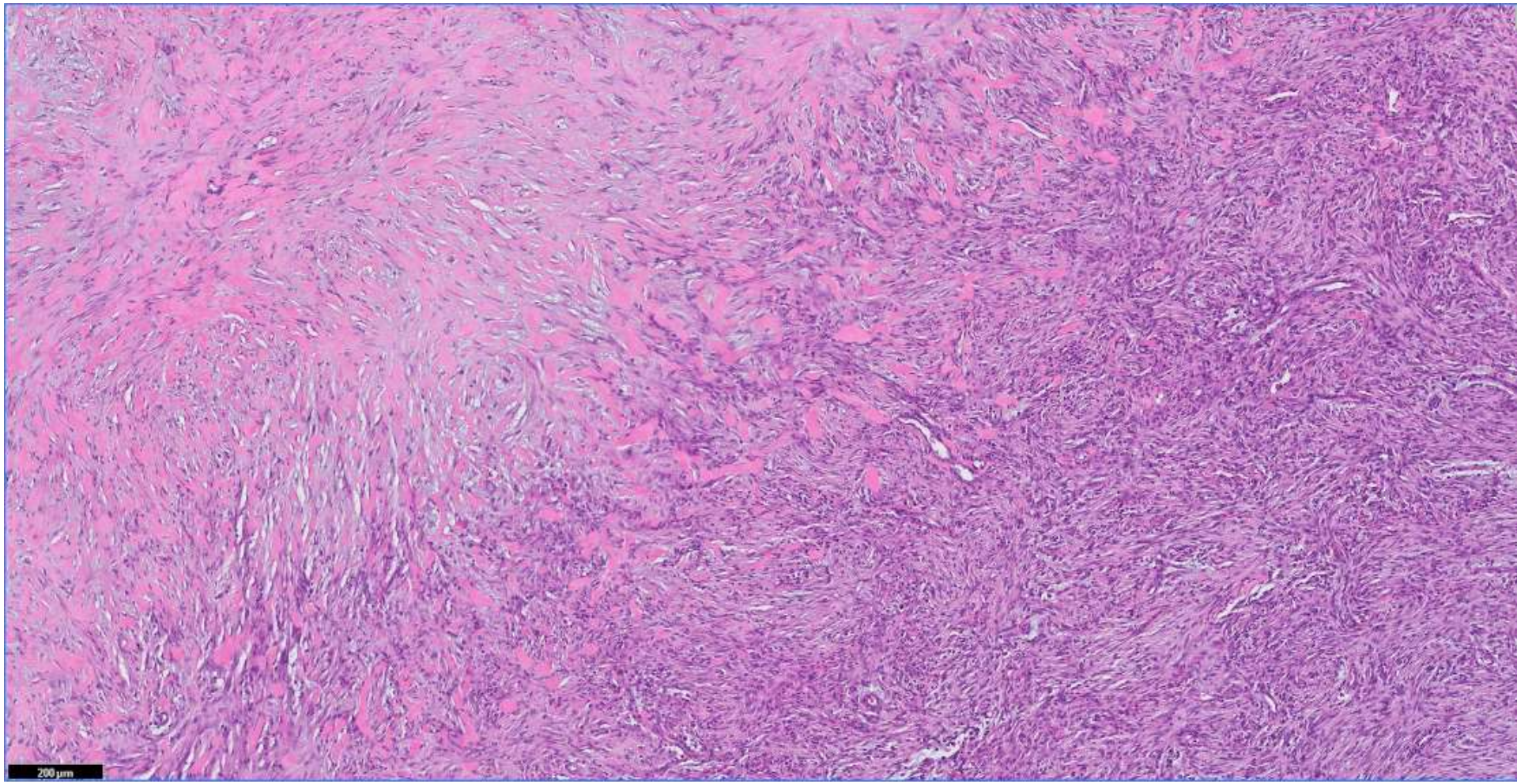
History and Radiology

- A 15-month-old male infant referred for non-painful, non-tender, discrete area of swelling of the occipital scalp. No history of head trauma to the area.

MRI with contrast



Pathology



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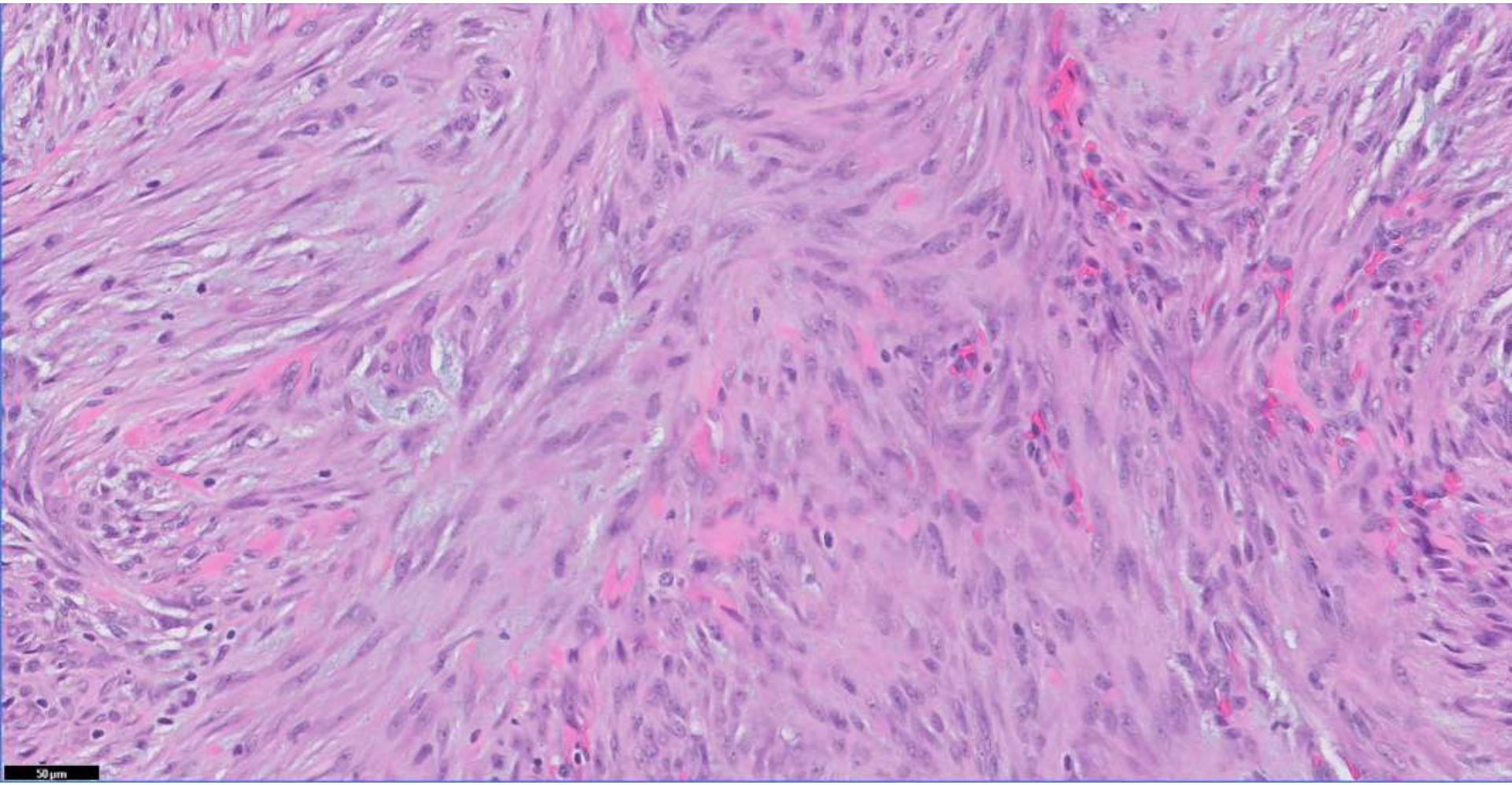

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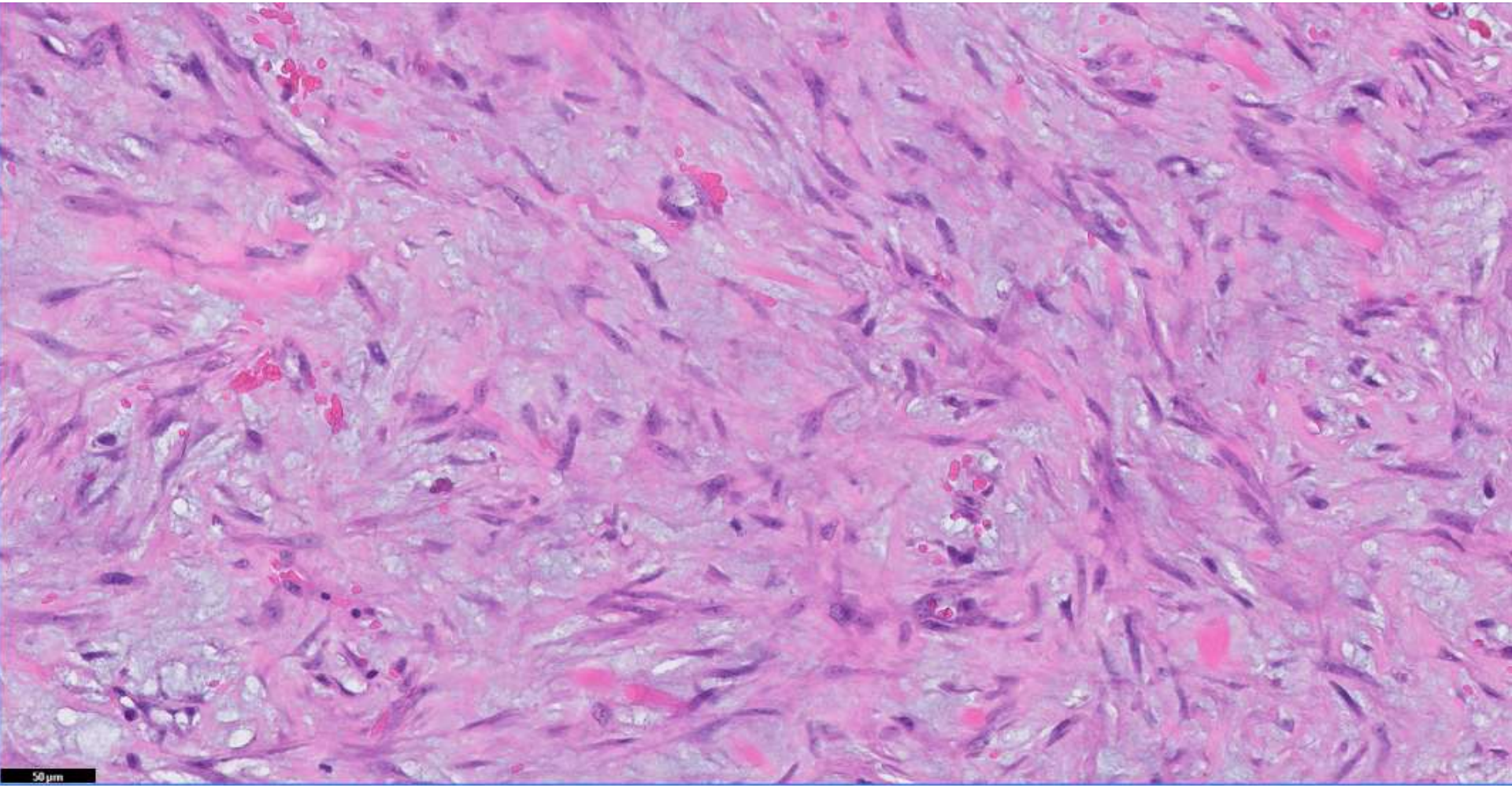

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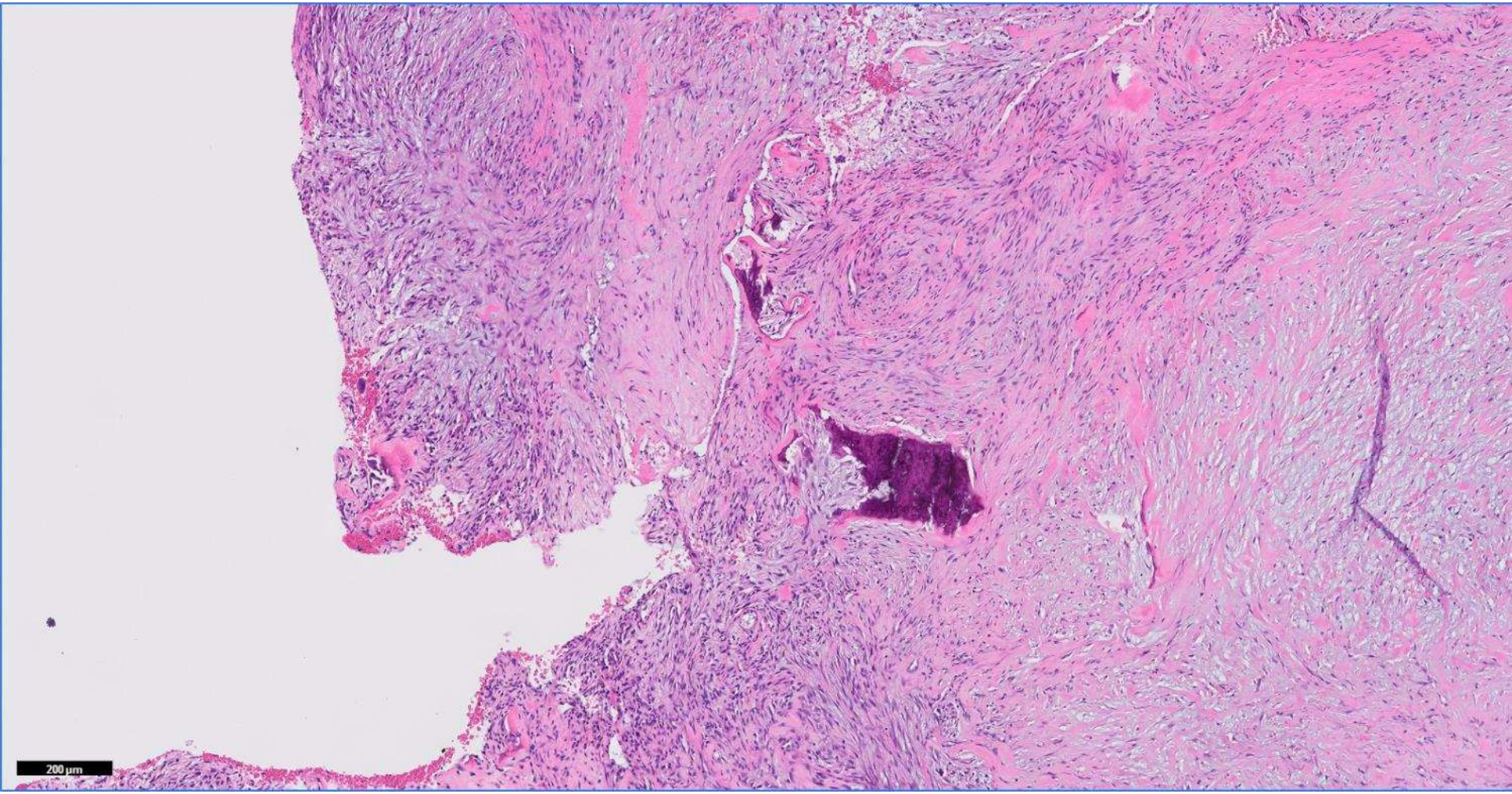

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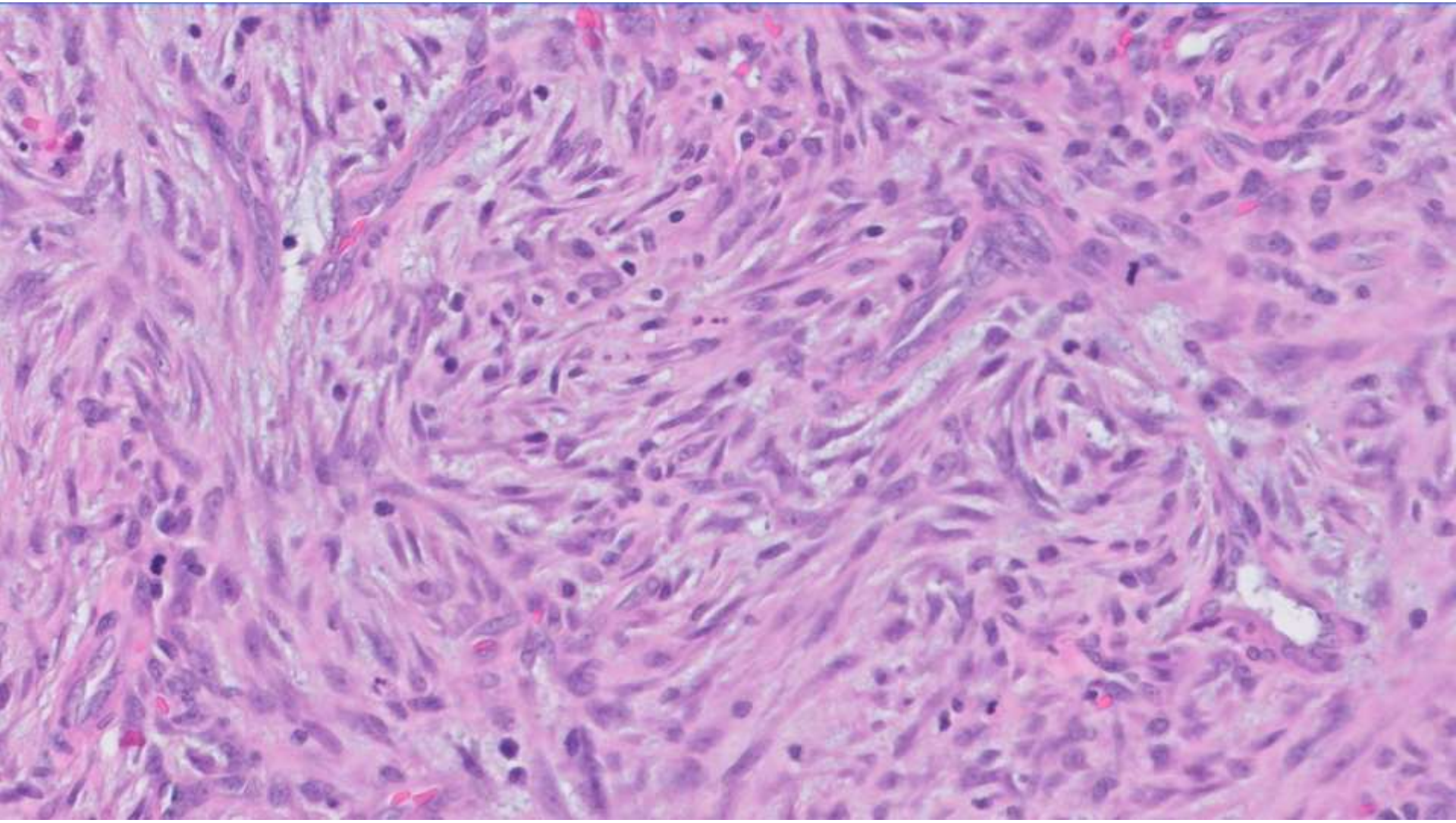
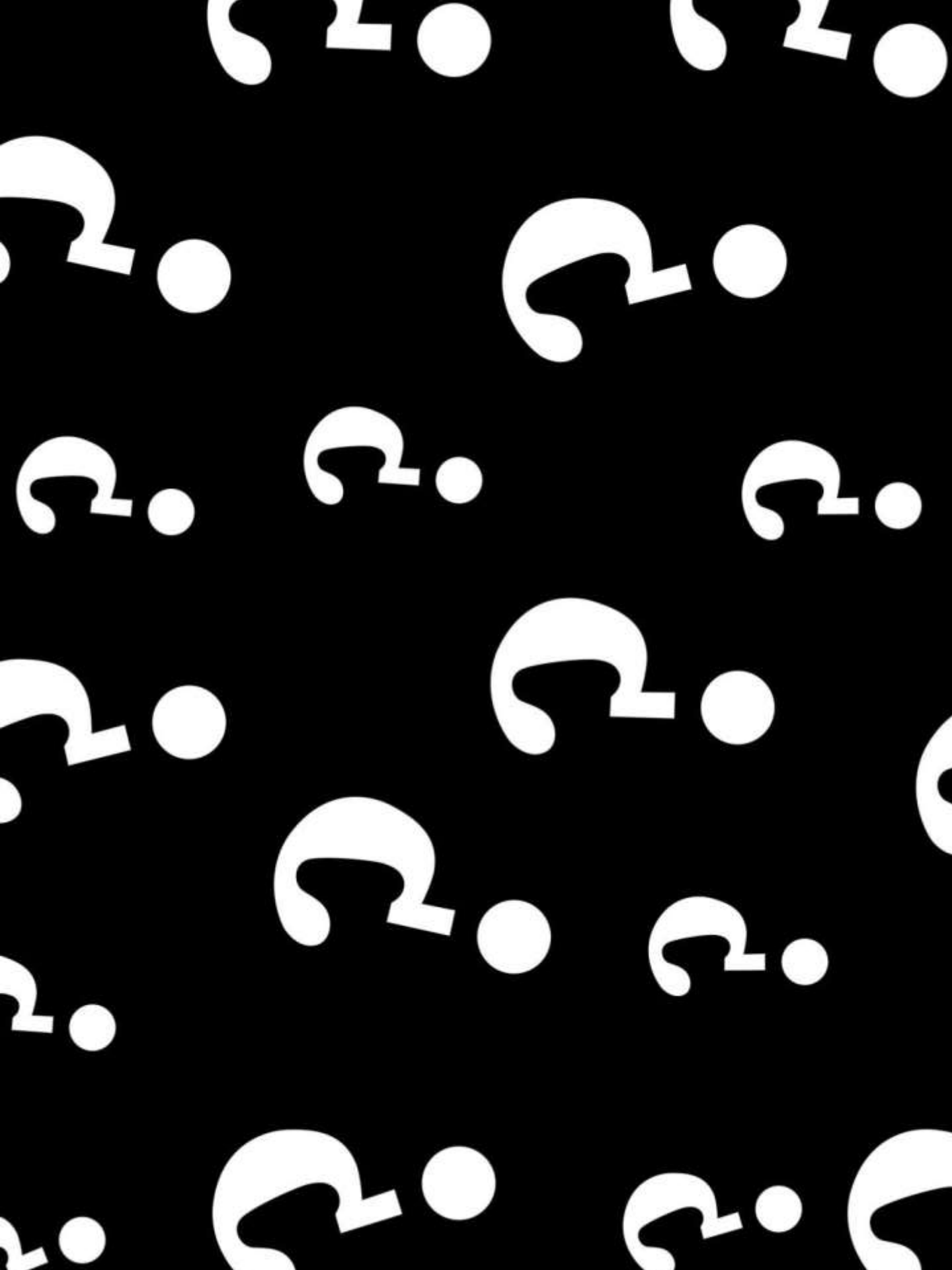


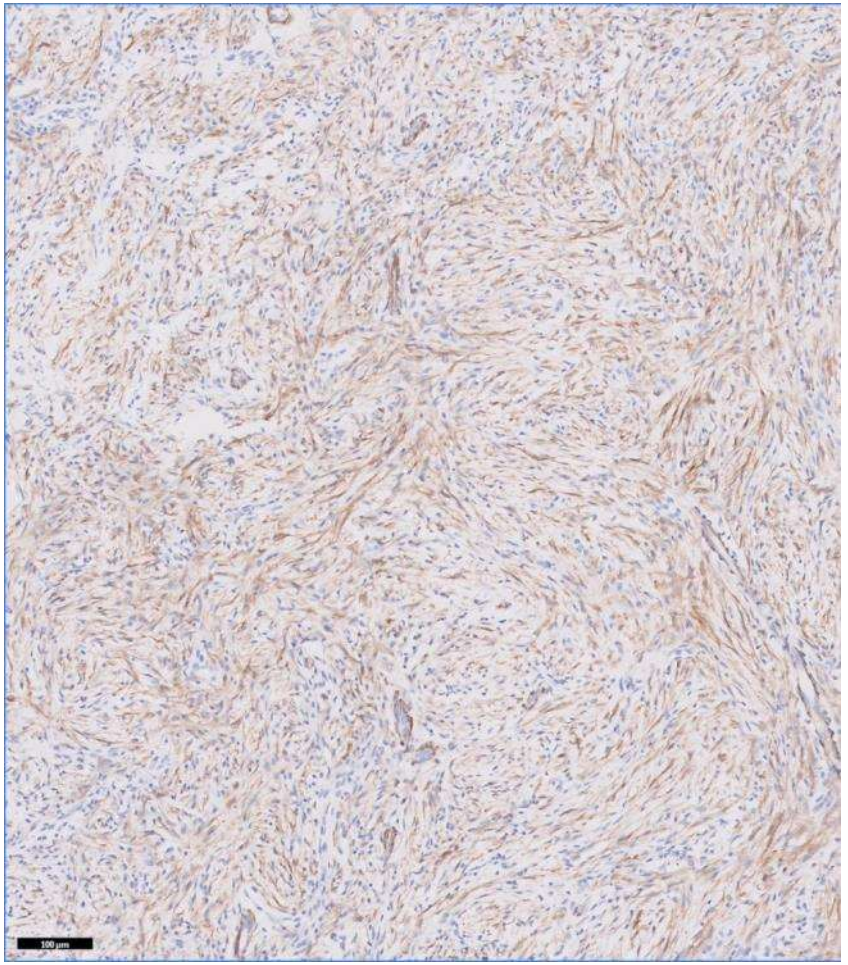


Differential Diagnosis

- Fibrous meningioma
- Schwannoma
- Solitary fibrous tumor
- Cranial fasciitis
- Langerhans cell histiocytosis
- Infantile fibrosarcoma

Immunohistochemistry

- Positive:
  - Muscle actin, smooth, skeletal & cardiac (HHF35)
- Negative:
  - S100,
  - EMA,
  - CD34,
  - STAT6



Summary of Findings

- 15-month-old infant with a scalp lesion
- Proliferation of loose cells with uniform spindled nuclei arranged in a storiform pattern with a “tissue-culture”-like appearance.
- Abundant myxoid/collagenous stroma
- Occasional mitosis; no necrosis
- Positive IHC for Muscle actin, HHF35 (reacts with skeletal muscle cells, cardiac muscle cells, smooth muscle cells, pericytes, and myoepithelial cells)

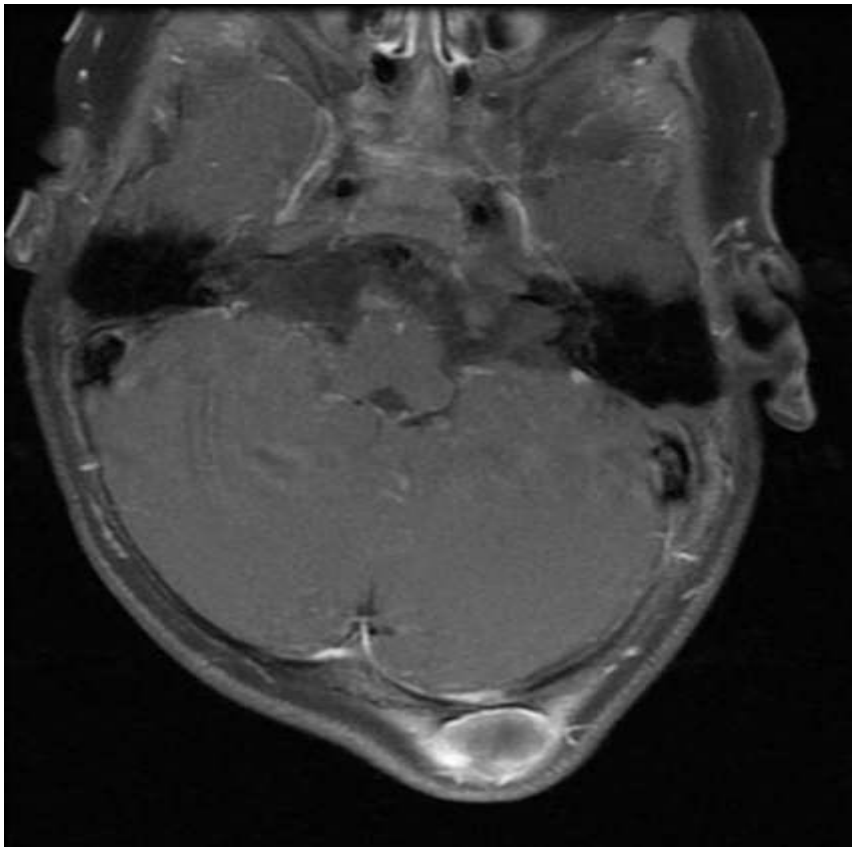
Cranial Fasciitis (CF)

- First described as a subset of nodular fasciitis in a study of nine cases in 1980 by Lauer and Enzinger
- 72 cases have been reported in the English literature until 2018
- Typically presents as a rapidly growing, single palpable, painless scalp mass in a child (median 21 months old)
- Usually localized to the subcutaneous tissue or galea aponeurotica. While CF may develop anywhere on the cranium, the most frequently anatomical sites of occurrence are temporal (39%) and parietal (25%) regions.
- The most common cause of the disease is idiopathic, and the role of trauma is not clearly established

CF Radiology

- CT scan usually shows a single lytic defect in the calvaria with an associated soft tissue mass.

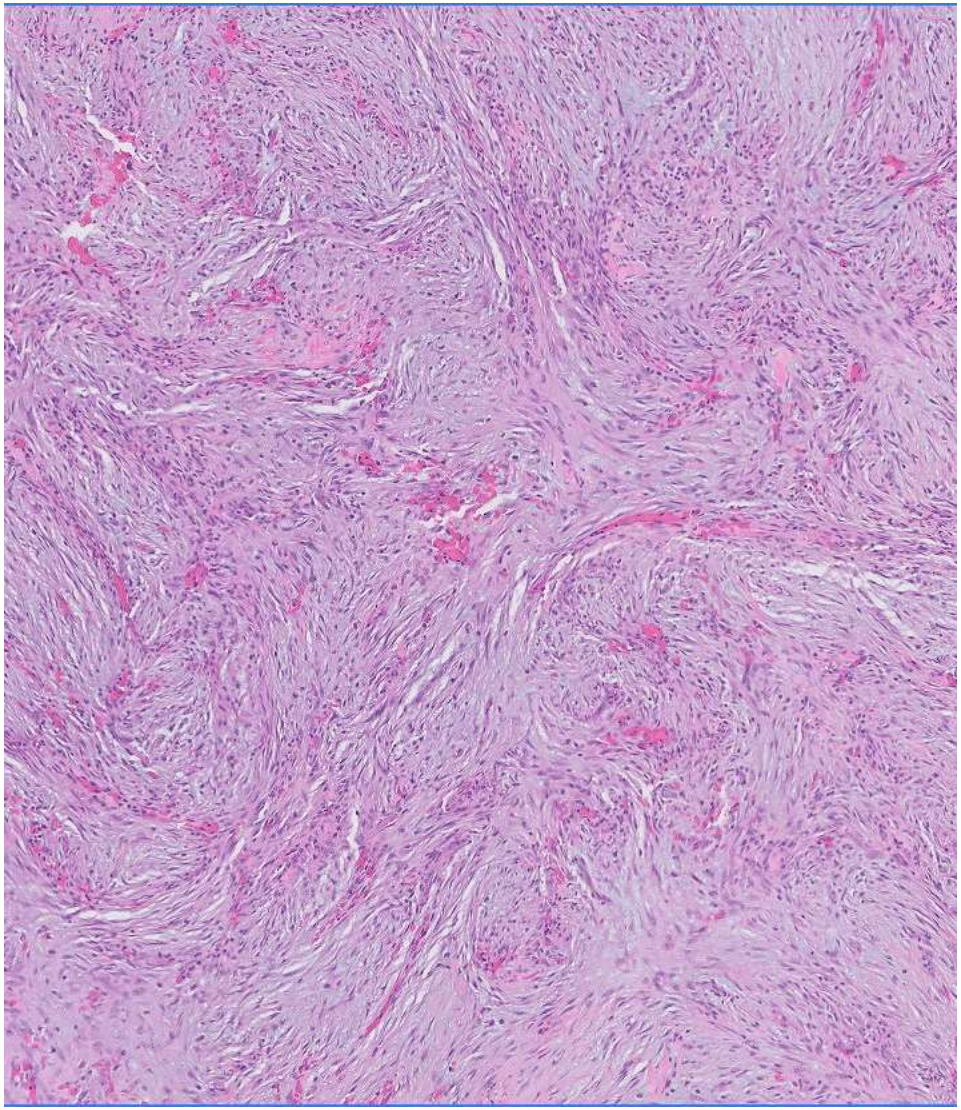
- MRI classically demonstrates hypointensity and vivid enhancement with a non-enhancing central region within the scalp mass.



Cranial Fasciitis

- Macroscopically can be circumscribed or infiltrative.

- Microscopic features include
  - Variable cellularity
  - Predominance of plump immature myofibroblasts arranged in short fascicles (tissue culture-like pattern)
  - Myxoid background (early lesions)
  - Hyalinization prominent in older lesions
  - Extravasation of red blood cells
  - Chronic inflammation
  - Osteoclast-like giant cells
  - Osseous metaplasia
  - Mitotic figures usually present



CF Molecular Genetic

- *USP6* gene rearrangement (17p13) in the majority of cases, most common *USP6-MYH9* fusion (60-80% of cases)
- USP6 rearrangement is not specific; it may also be identified in aneurysmal bone cysts and myositis ossificans.
- Many other fusion partners identified, including *RRBP1*, *COL6A2*, *CTNNB1*
- In this case, *USP6-COL6A2* fusion was identified

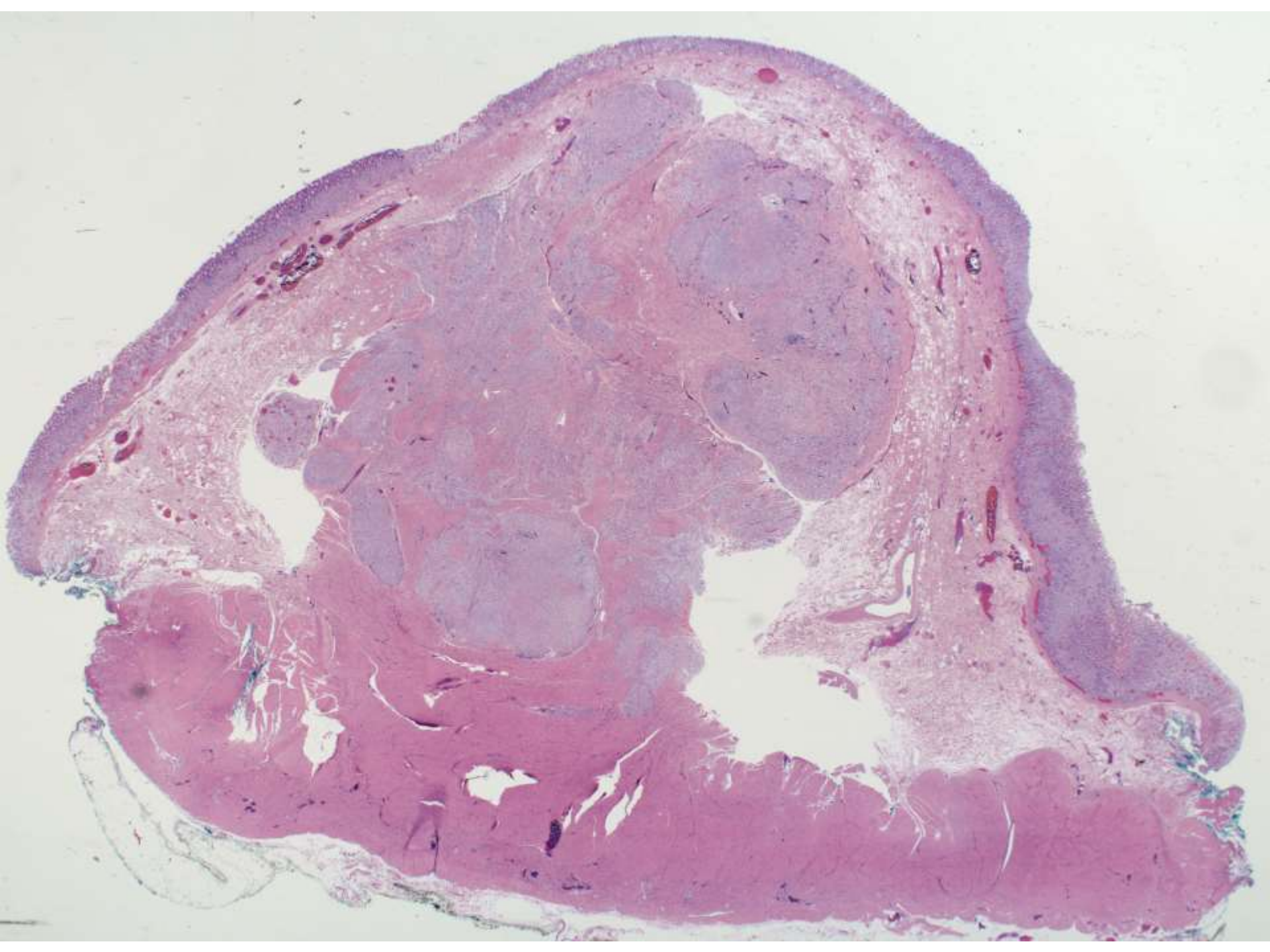
CF Treatment & Prognosis

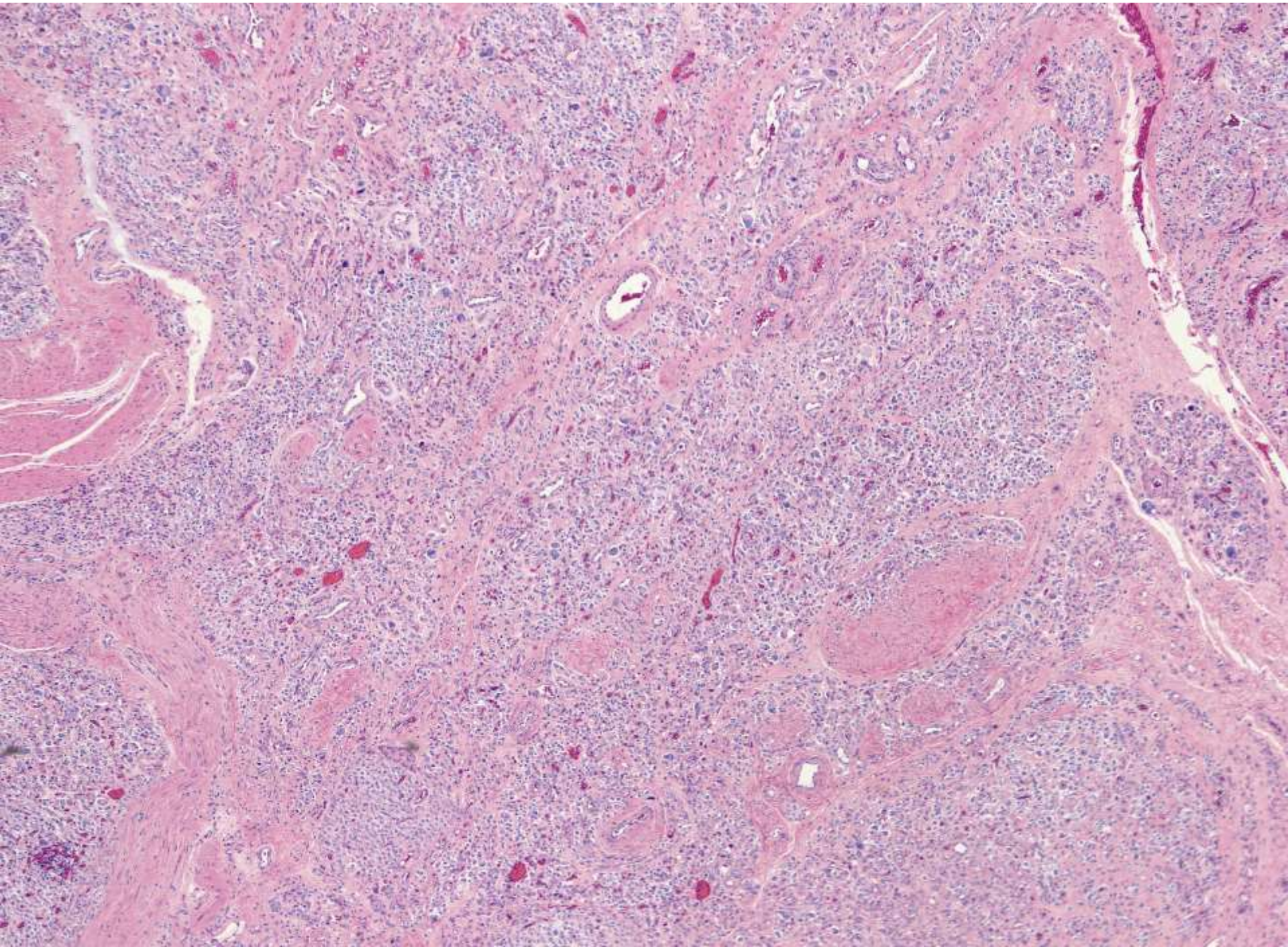
- Treatment
  - Surgical approaches
- Prognosis
  - Excellent
  - Rarely recur, even following incomplete excision
  - Metastases do not occur

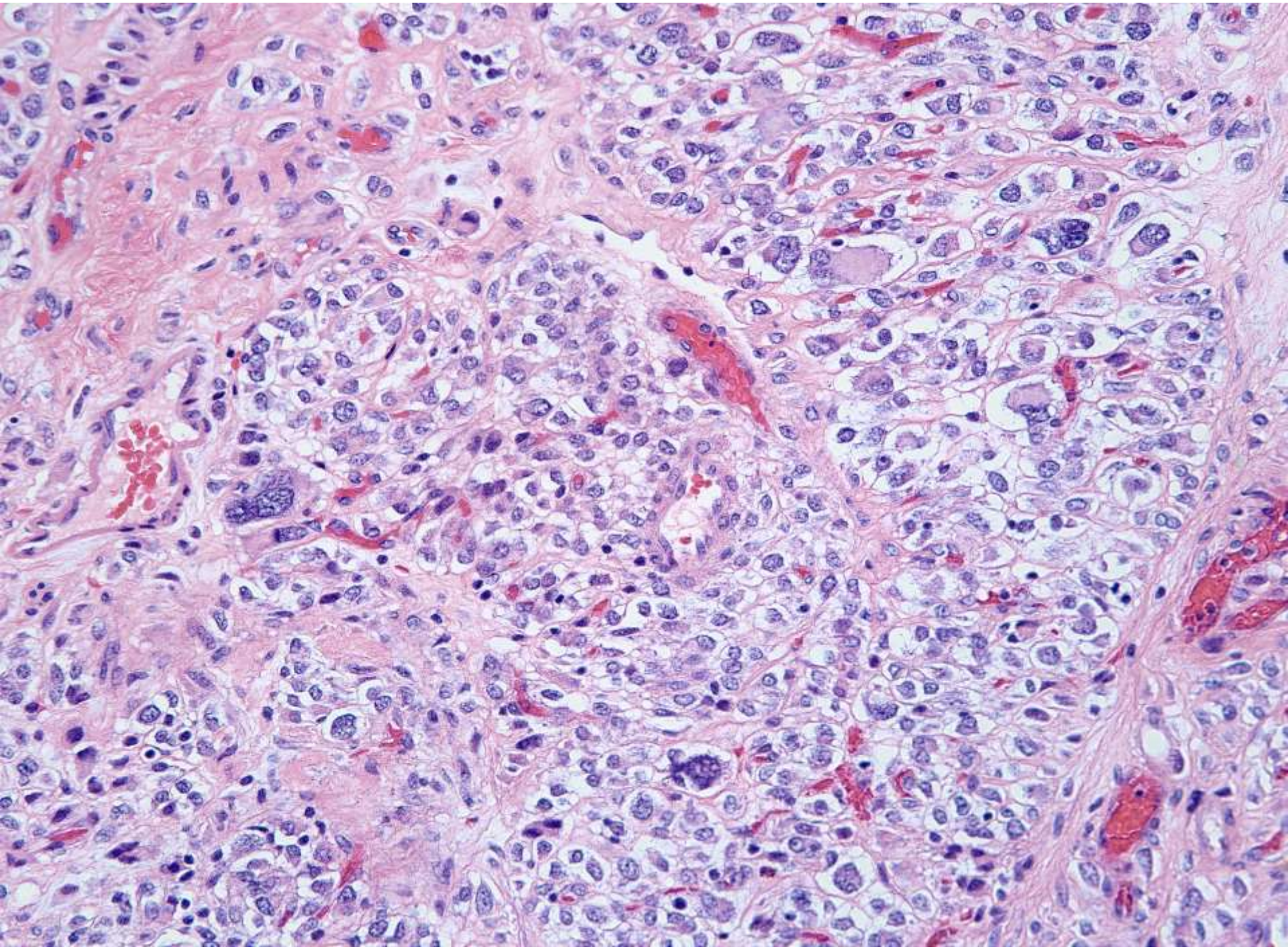
19-0907

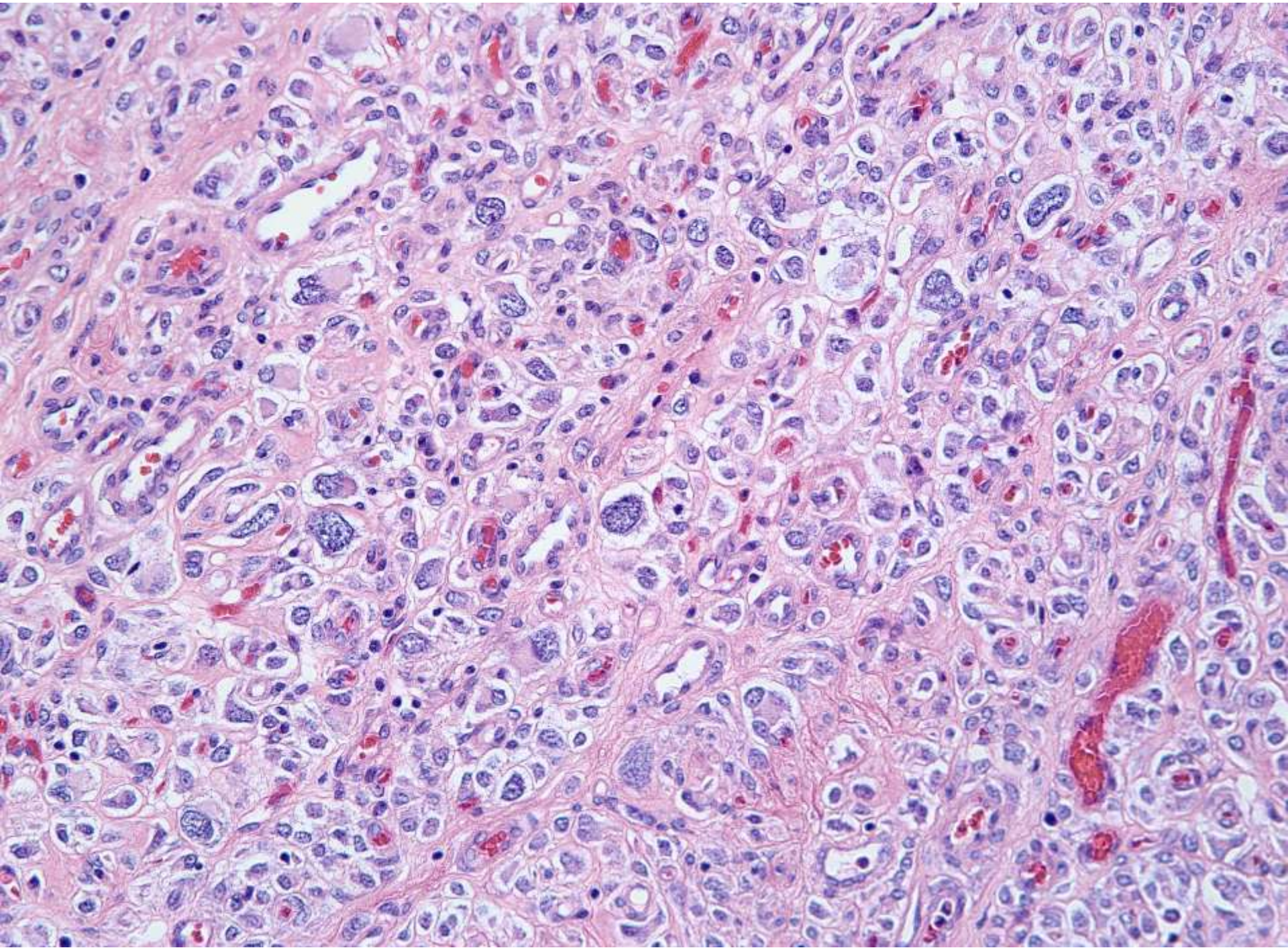
Greg Charville; Stanford

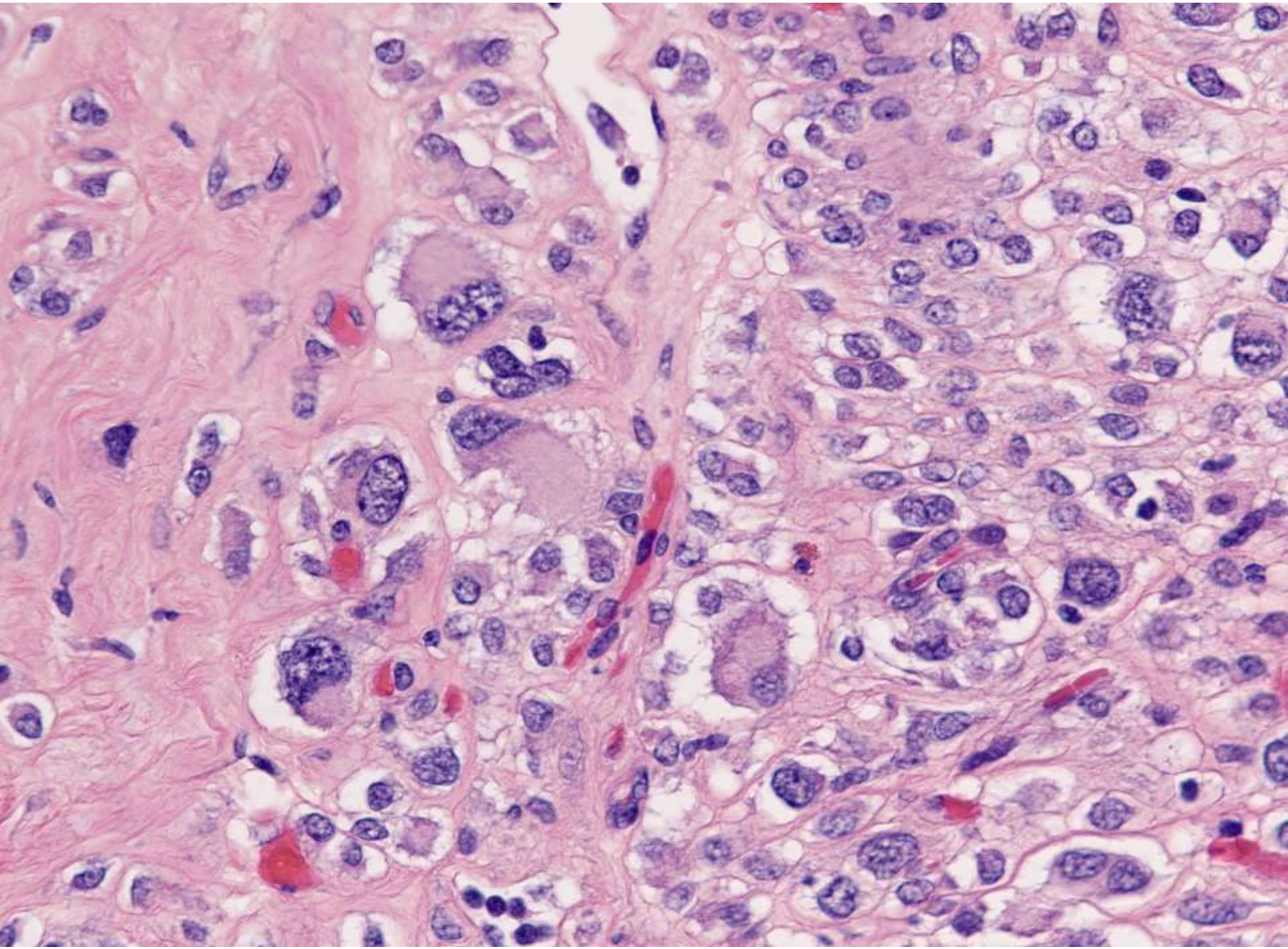
55-year-old female with a h/o cutaneous melanoma, found to have 2.9cm mass in gastric antrum on imaging for f/u of a pancreatic cyst. Partial gastrectomy performed.

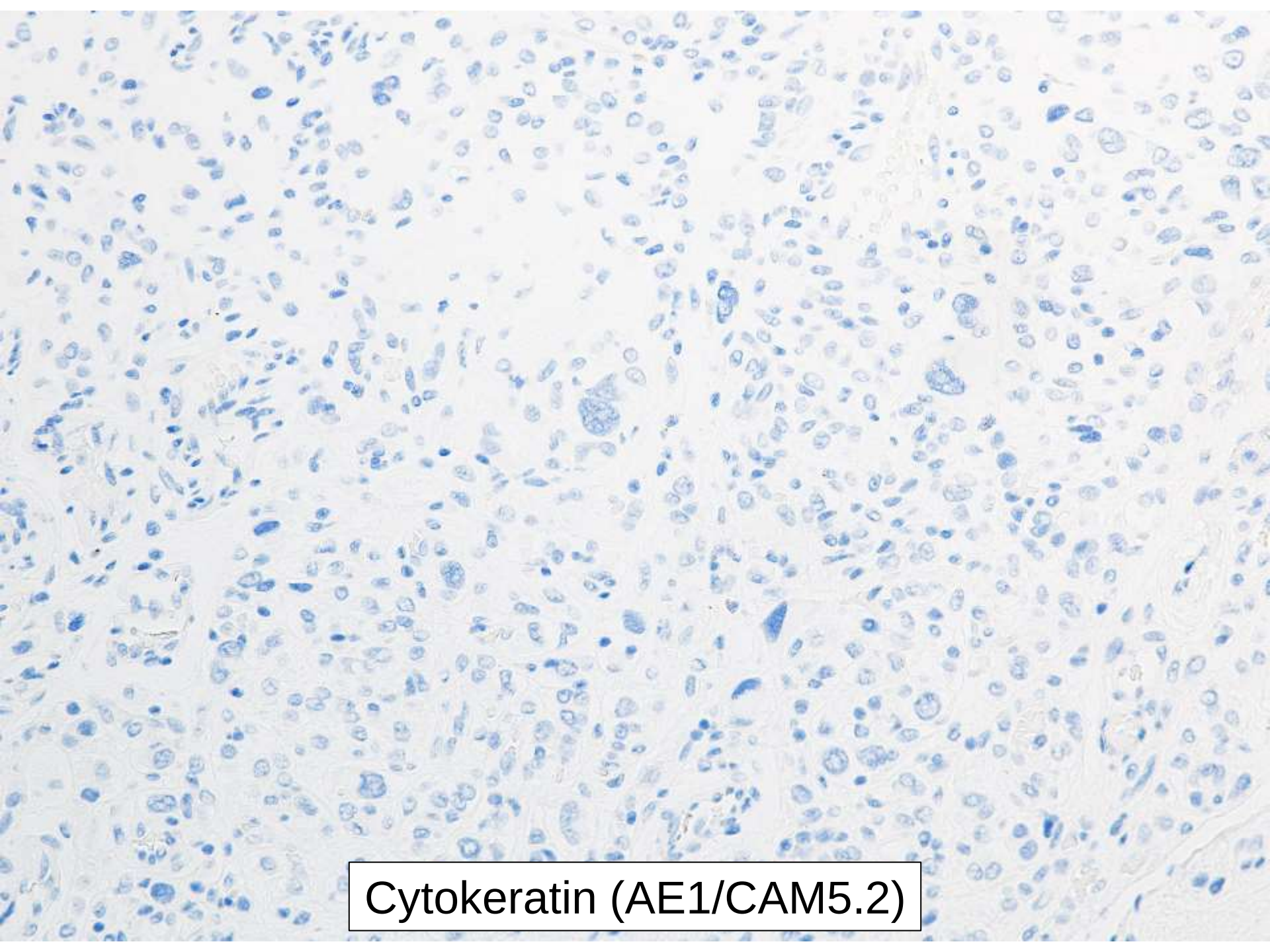


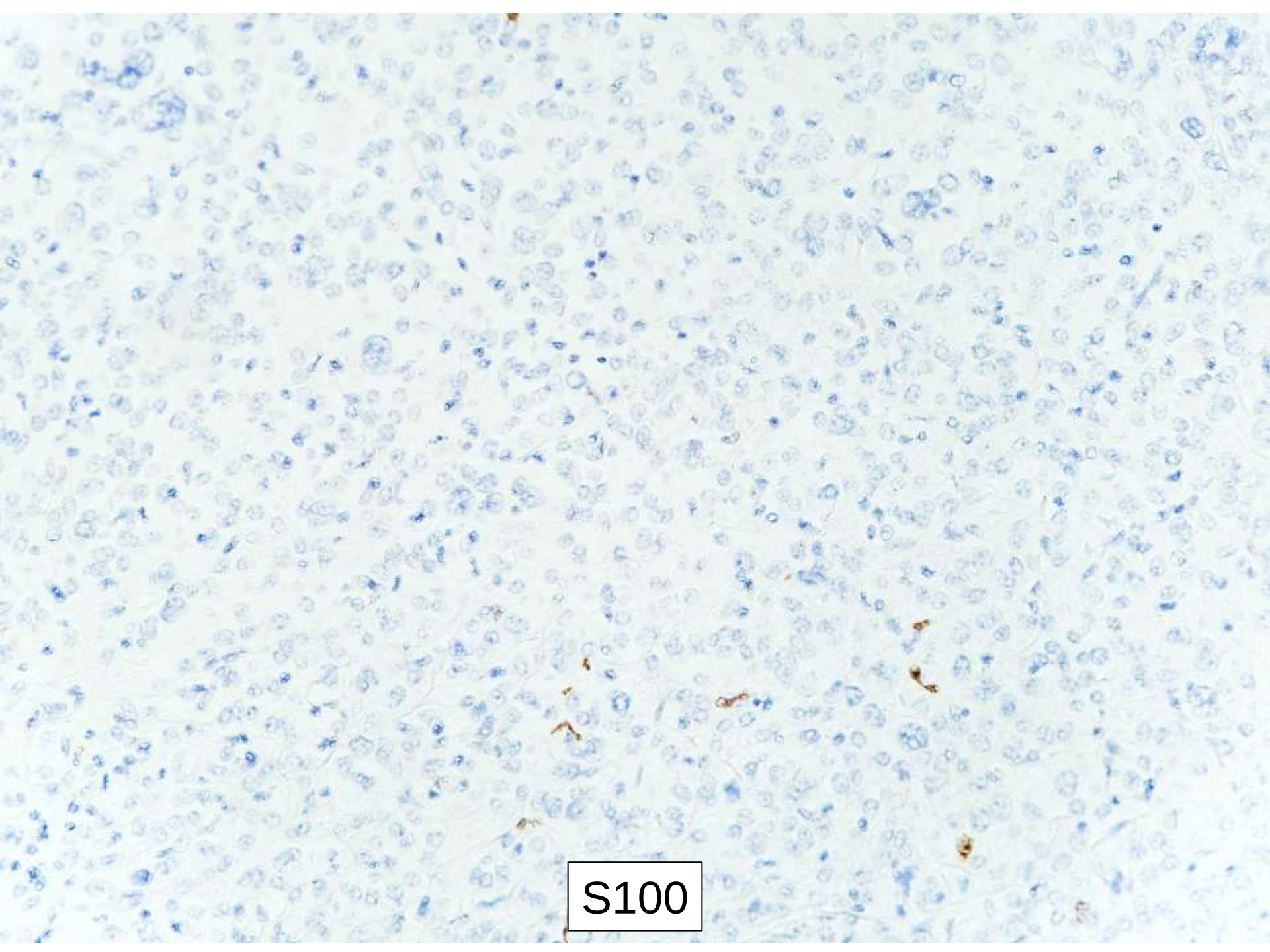


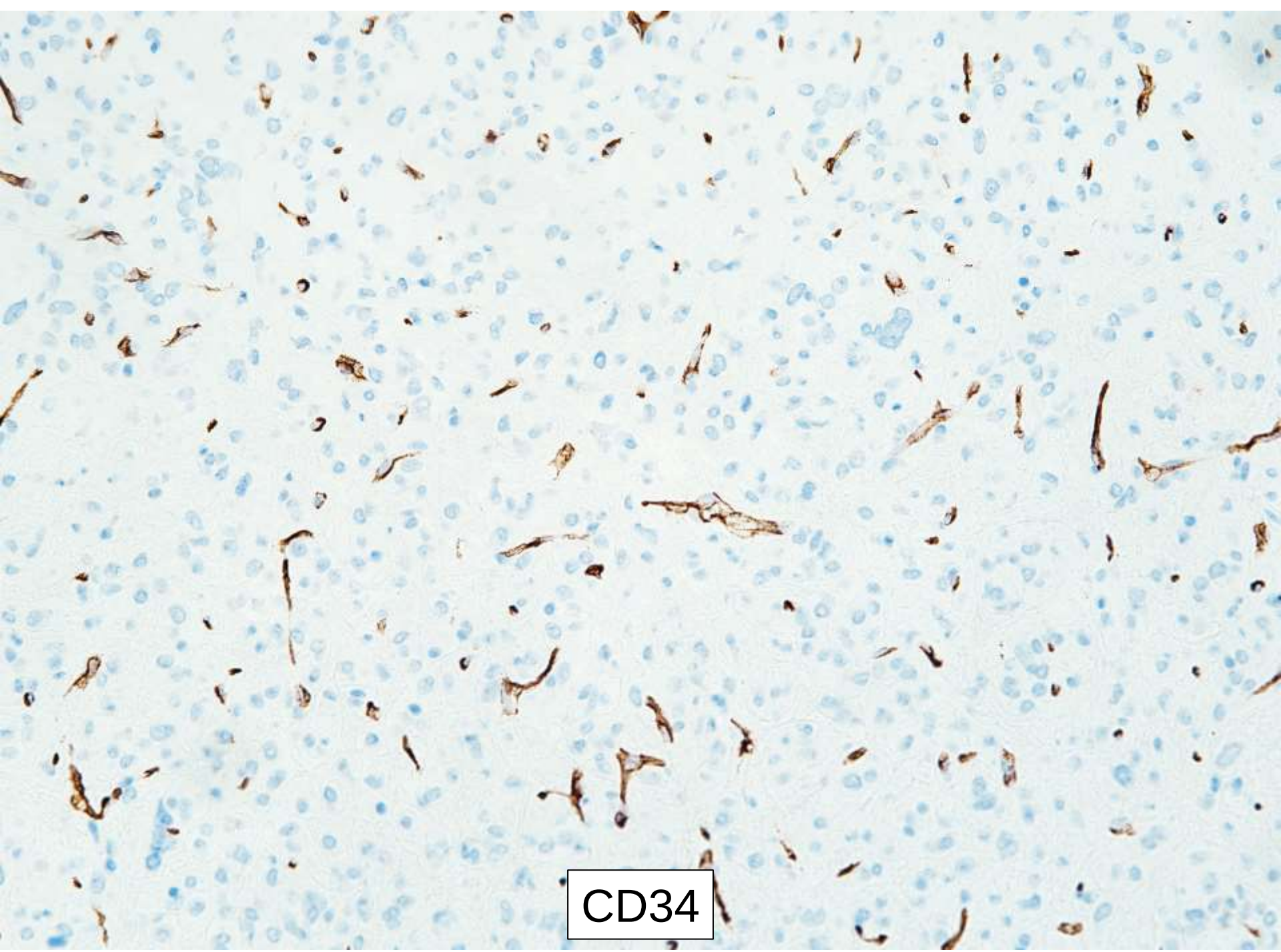


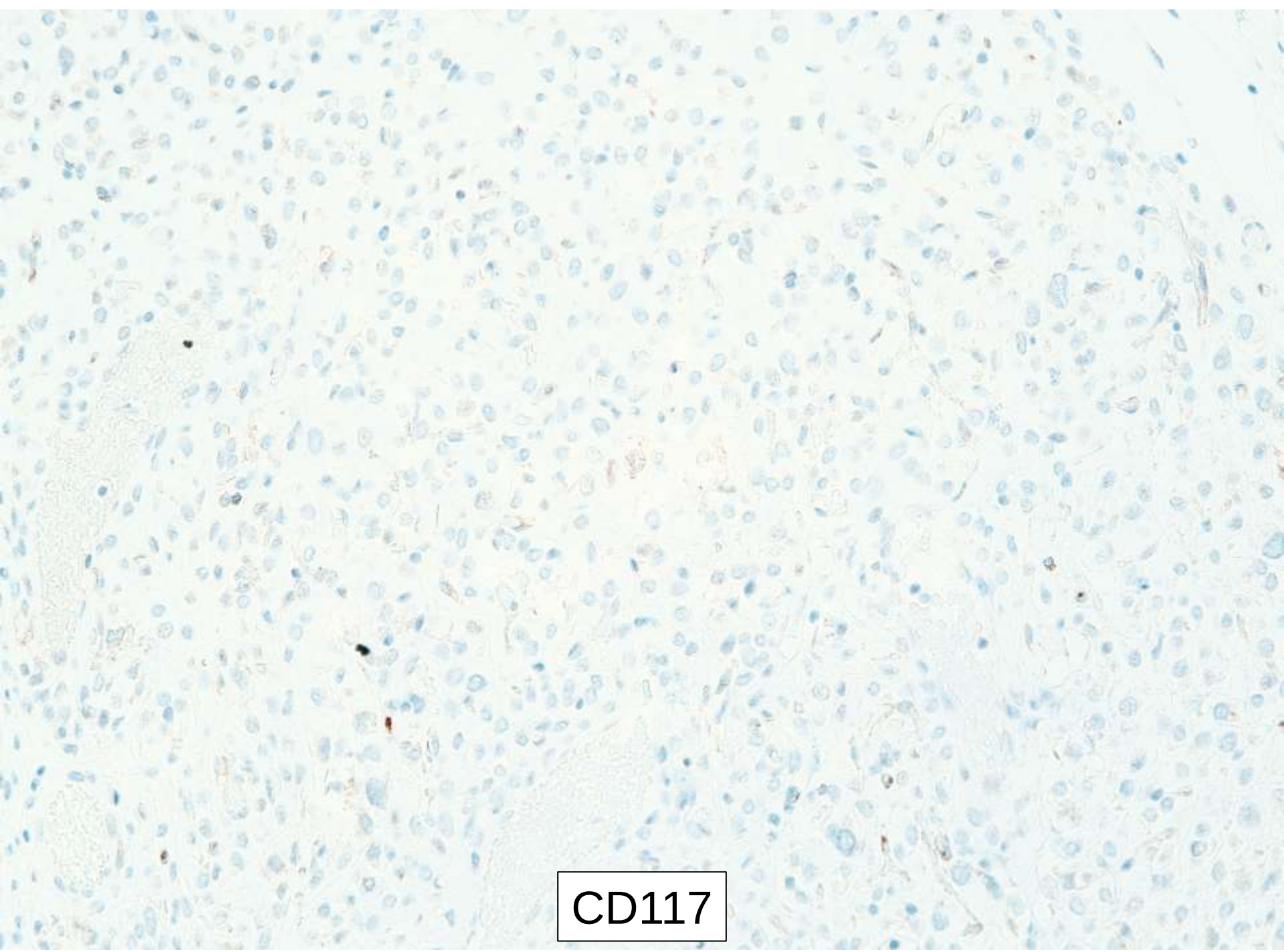


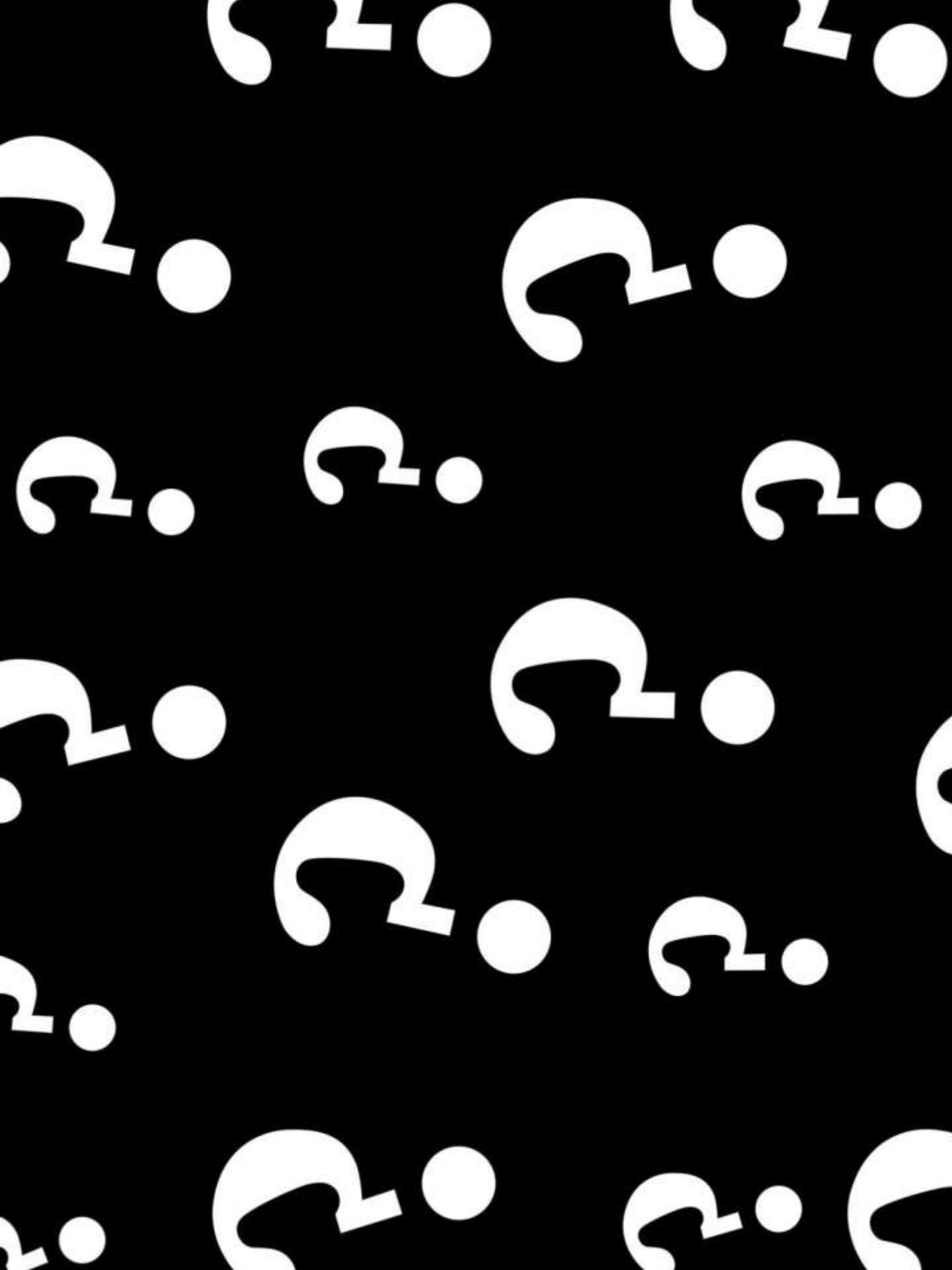



Cytokeratin (AE1/CAM5.2)


S100

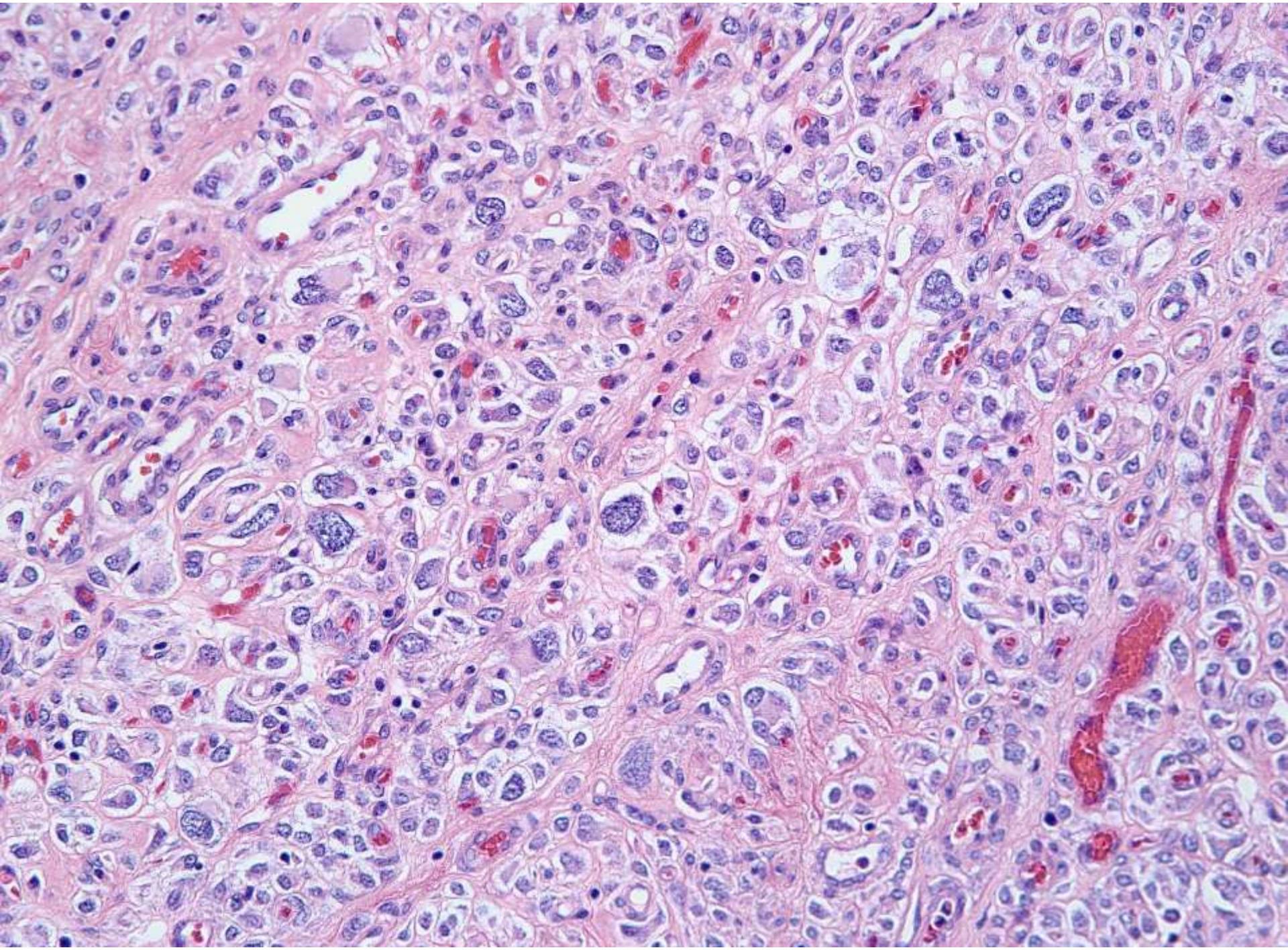

CD34

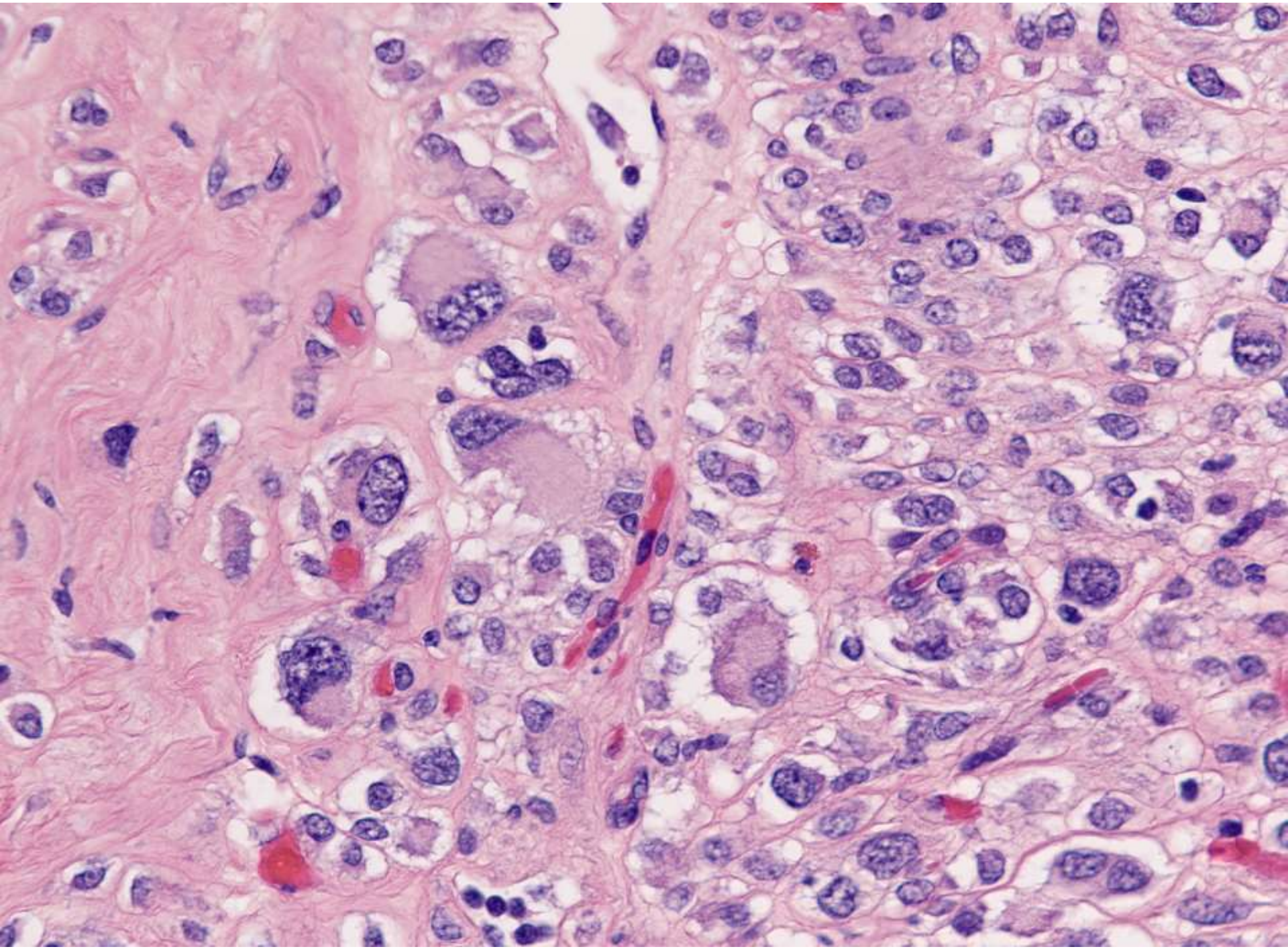

CD117



65 year-old female with a history of cutaneous melanoma who was found to have a 2.9-cm mass of the gastric antrum on imaging for follow-up of a pancreatic cyst. A partial gastrectomy is received.

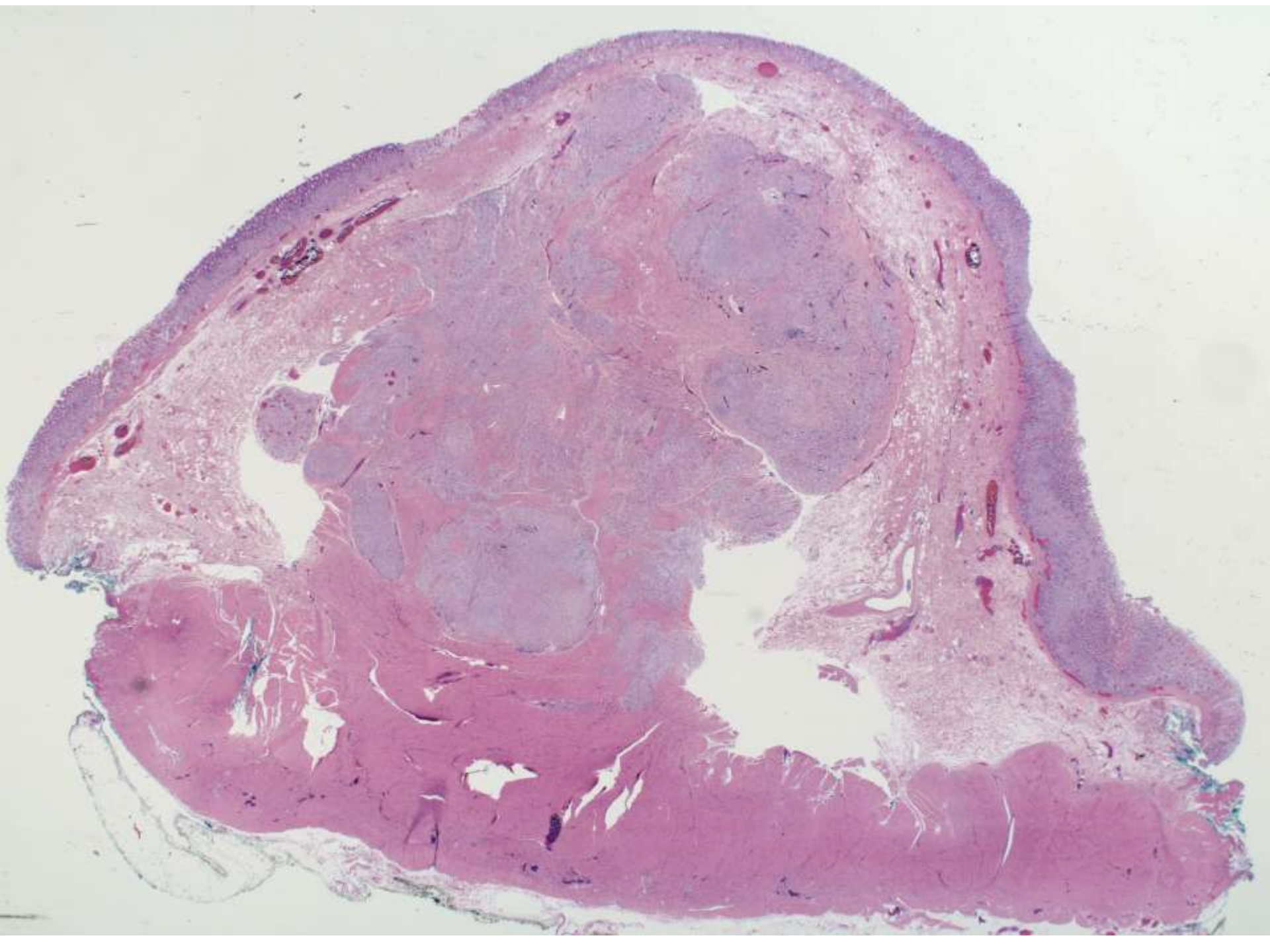
Greg Charville
Stanford

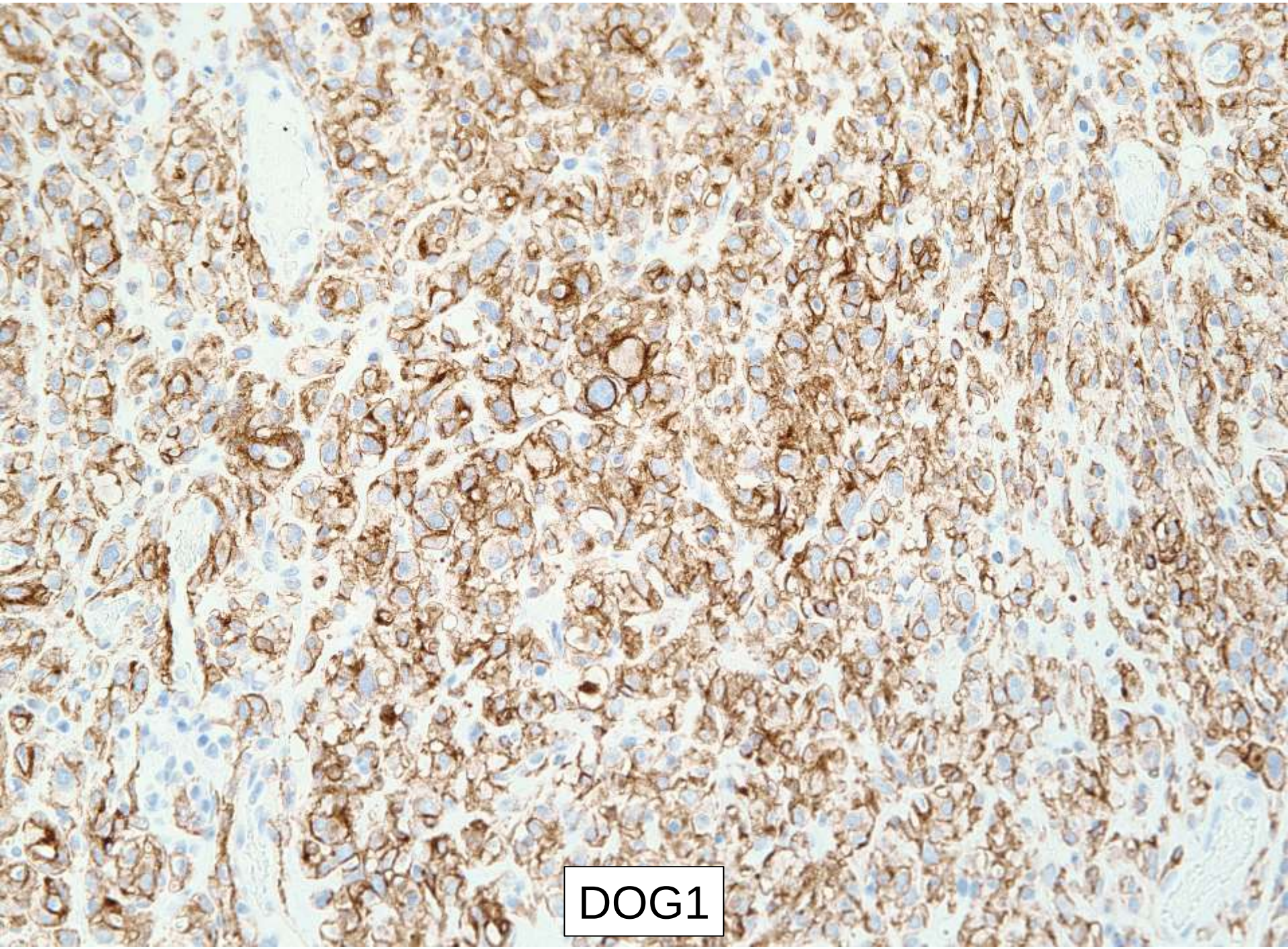


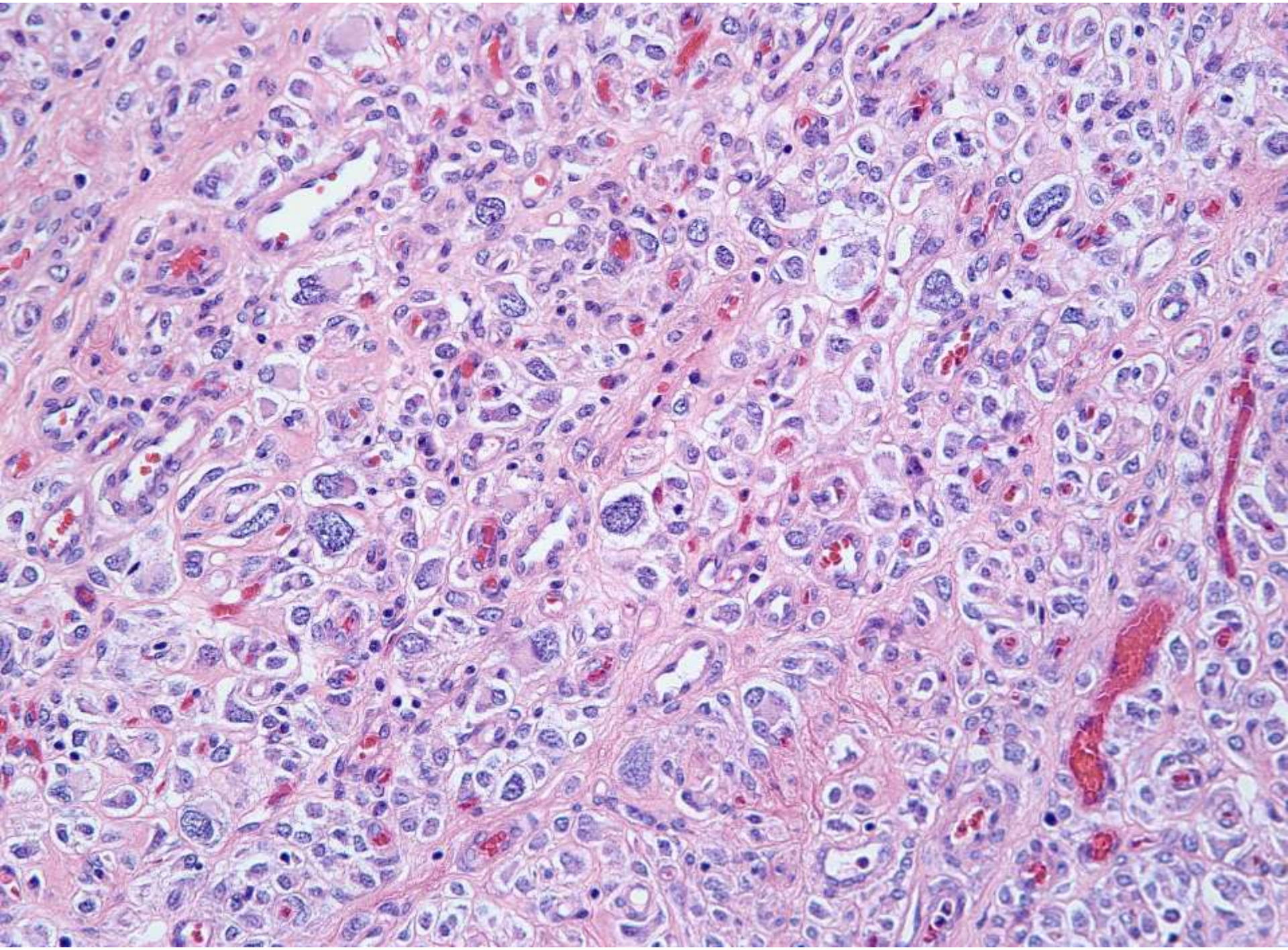


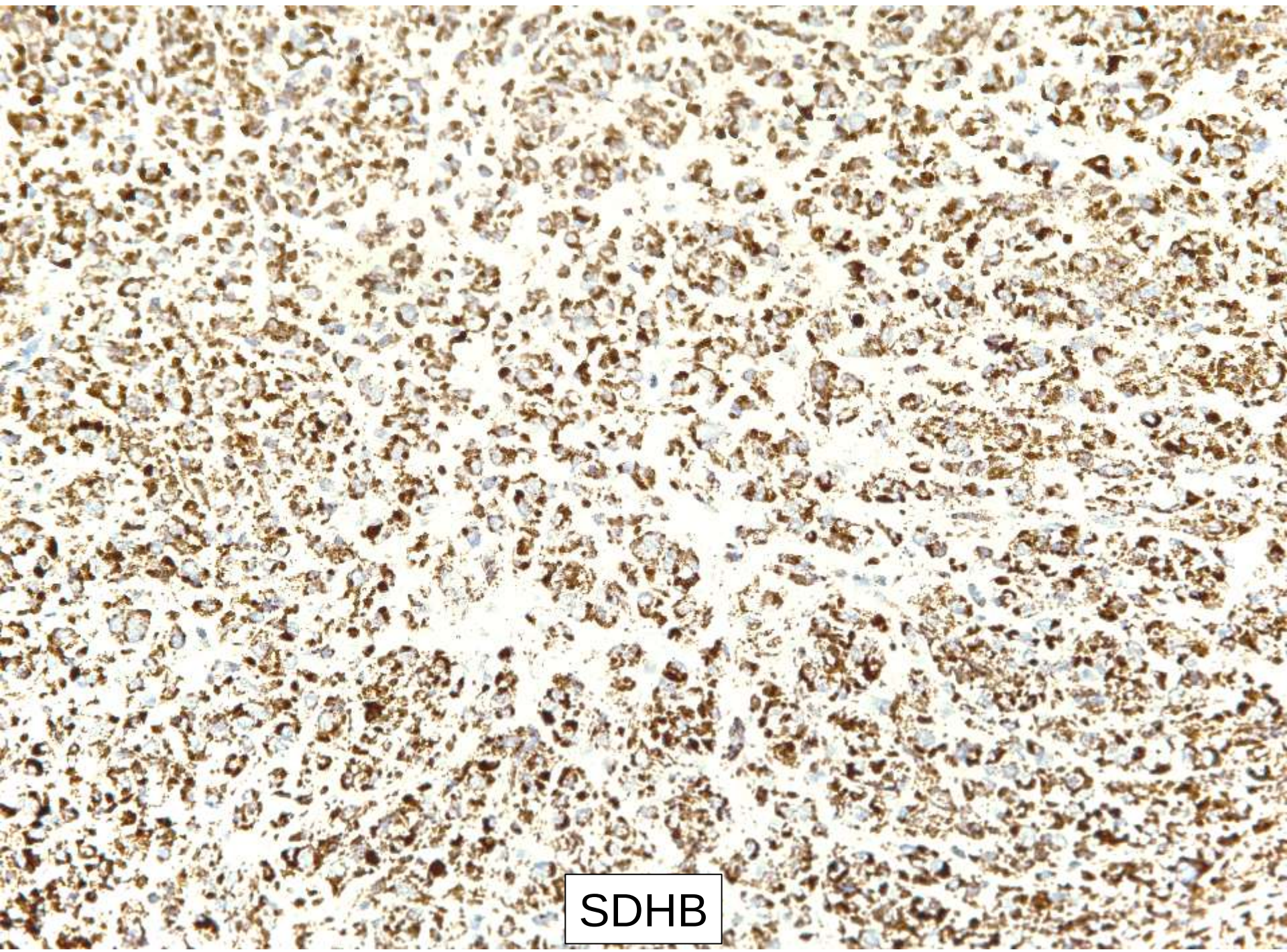
Diagnostic considerations

- Rhabdomyosarcoma (desmin positive)
- Poorly differentiated carcinoma (cytokeratin positive)
- GIST (CD34 and CD117 positive)
- Malignant melanoma (S100 positive)
- INI1 deficient epithelioid malignancy (cytokeratin positive)
- PEComa (desmin positive, HMB45 positive)




DOG1

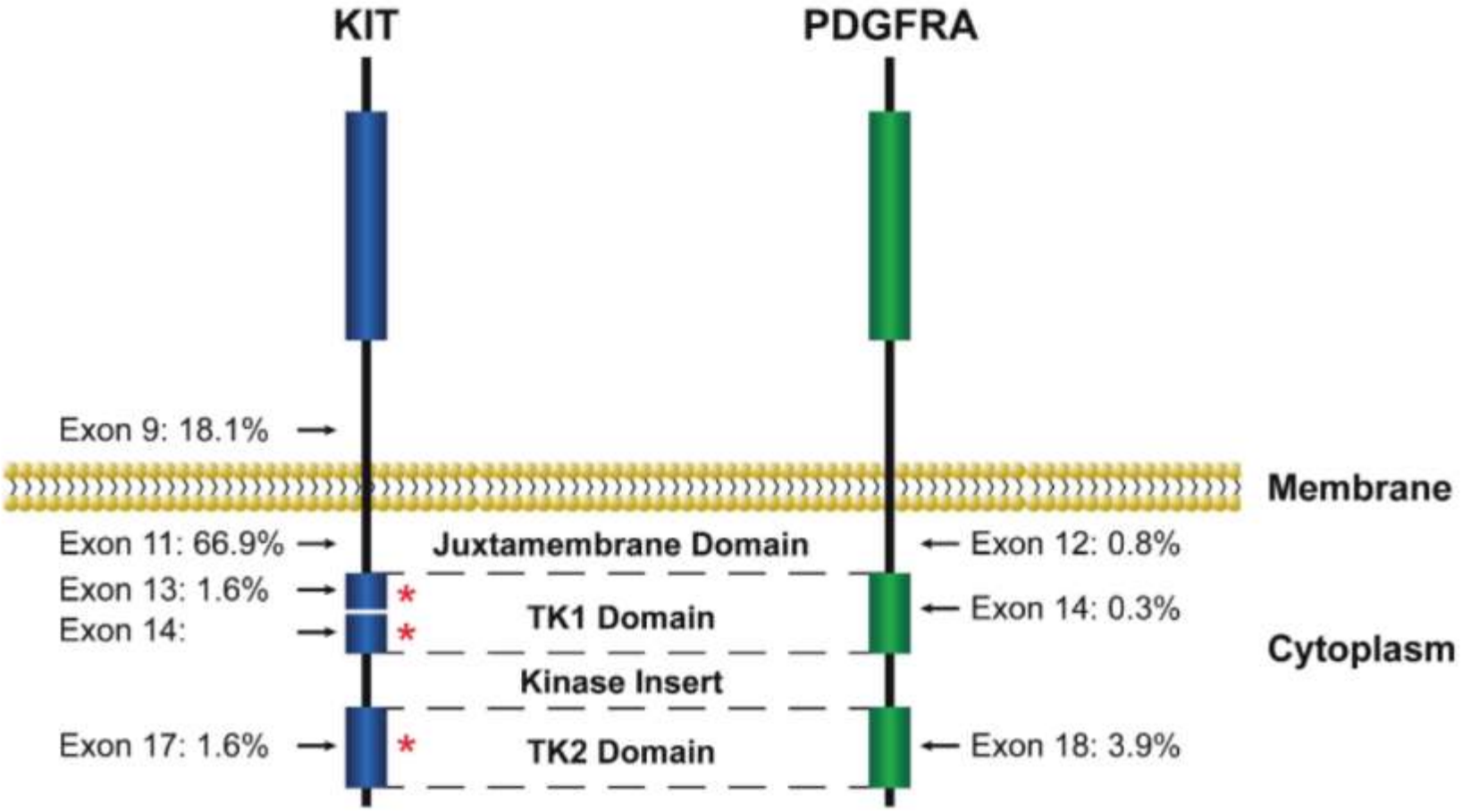



SDHB

American Journal of Pathology, Vol. 165, No. 1, July 2004

The Novel Marker, *DOG1*, Is Expressed Ubiquitously in Gastrointestinal Stromal Tumors Irrespective of *KIT* or *PDGFRA* Mutation Status

- 97.8% of all GISTs are DOG1-positive
- All PDFRA-mutant GISTs are DOG1-positive
- PDGFRA-mutant GISTs are often CD117-negative


KIT
PDGFRA
Exon 9: 18.1%
Membrane
Exon 11: 66.9%
Juxtamembrane Domain
Exon 12: 0.8%
Exon 13: 1.6%
Exon 14:
TK1 Domain
Exon 14: 0.3%
Cytoplasm
Kinase Insert
Exon 17: 1.6%
TK2 Domain
Exon 18: 3.9%
p. D842V

Histopathology

Histopathology 2014, **64**, 421–430. DOI: 10.1111/his.12265

Rhabdoid morphology in gastrointestinal stromal tumours (GISTs) is associated with *PDGFRA* mutations but does not imply aggressive behaviour

- Rhabdoid morphology is associated with epithelioid GISTs driven by PDGFRA mutations
- Rhabdoid component may represent genetic and biologic evolution from epithelioid component
- Rhabdoid morphology has no clear relationship to clinical outcome
- All (6) cases expressed CD117 and DOG1, 5/6 expressed CD34

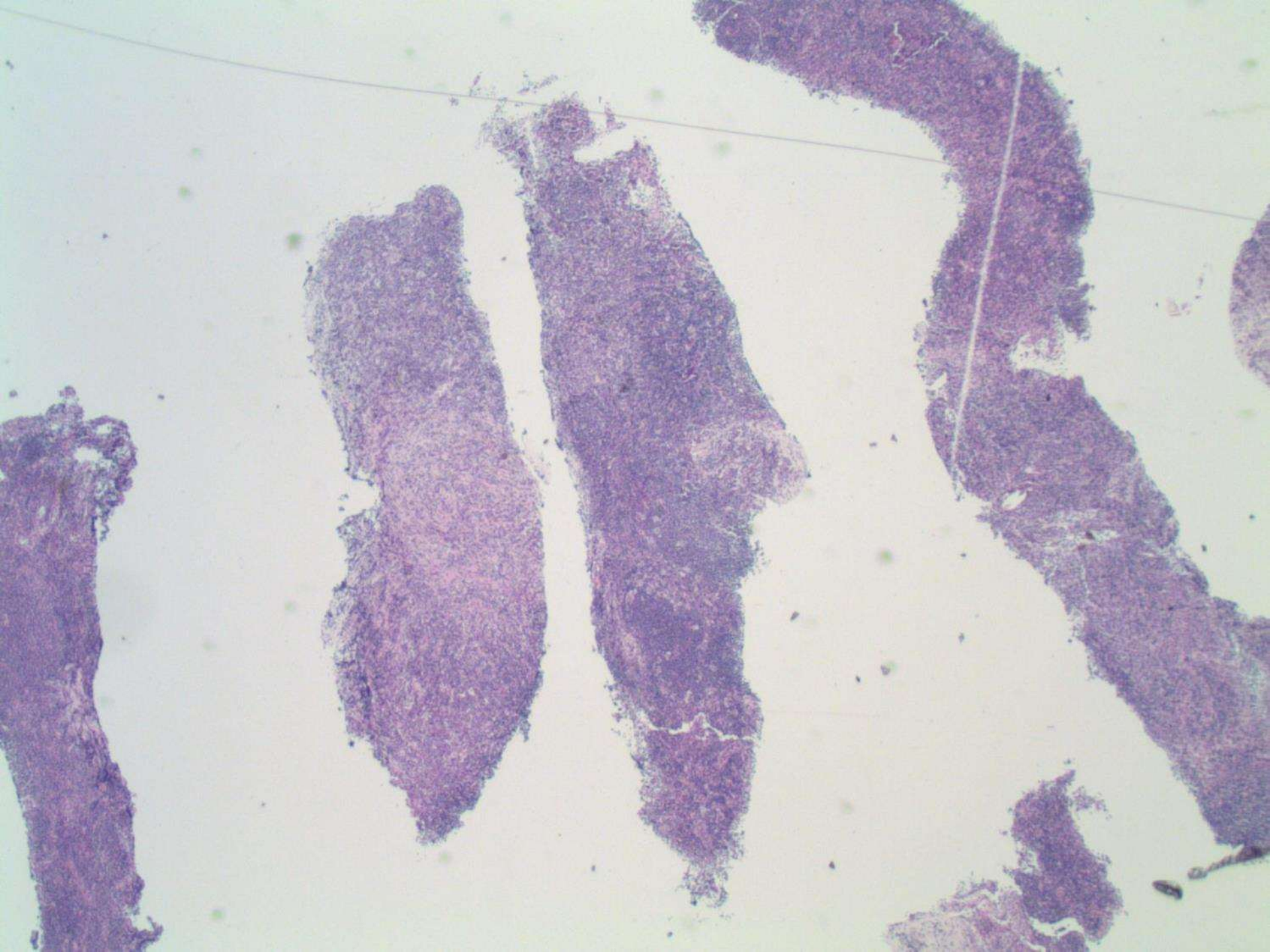
Gastrointestinal stromal tumor with rhabdoid morphology

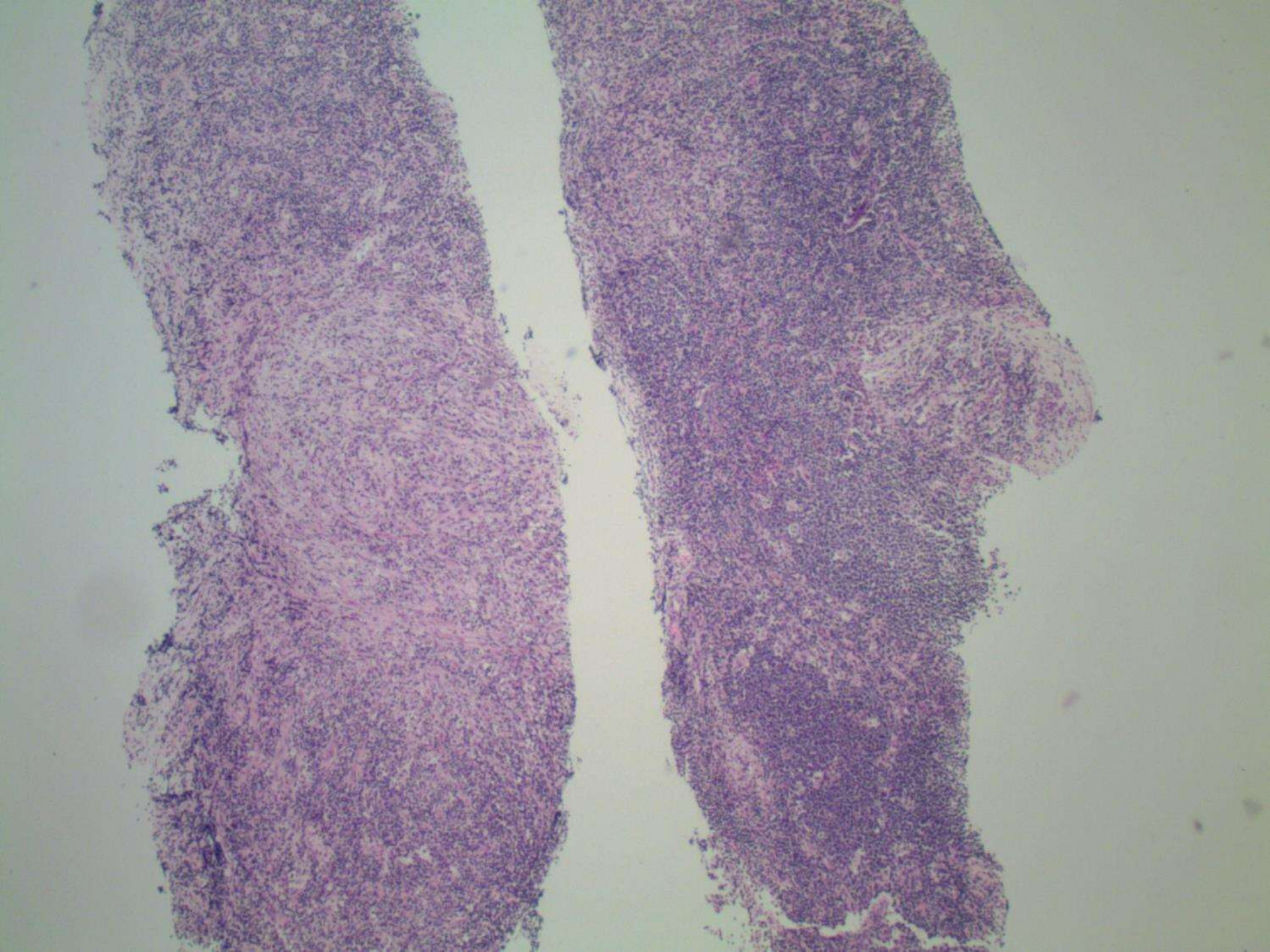
- Diagnosis of GIST can be especially challenging in the setting of unusual morphologic and immunohistochemical features
- DOG1 has particular value as a diagnostic marker of CD117-negative, PDGFRA-mutant GISTs
- Rhabdoid morphology appears to represent evolution of GIST, but without clear clinical significance
- Identification of the molecular driver can be helpful in confirming the diagnosis of GIST and guiding adjuvant therapy

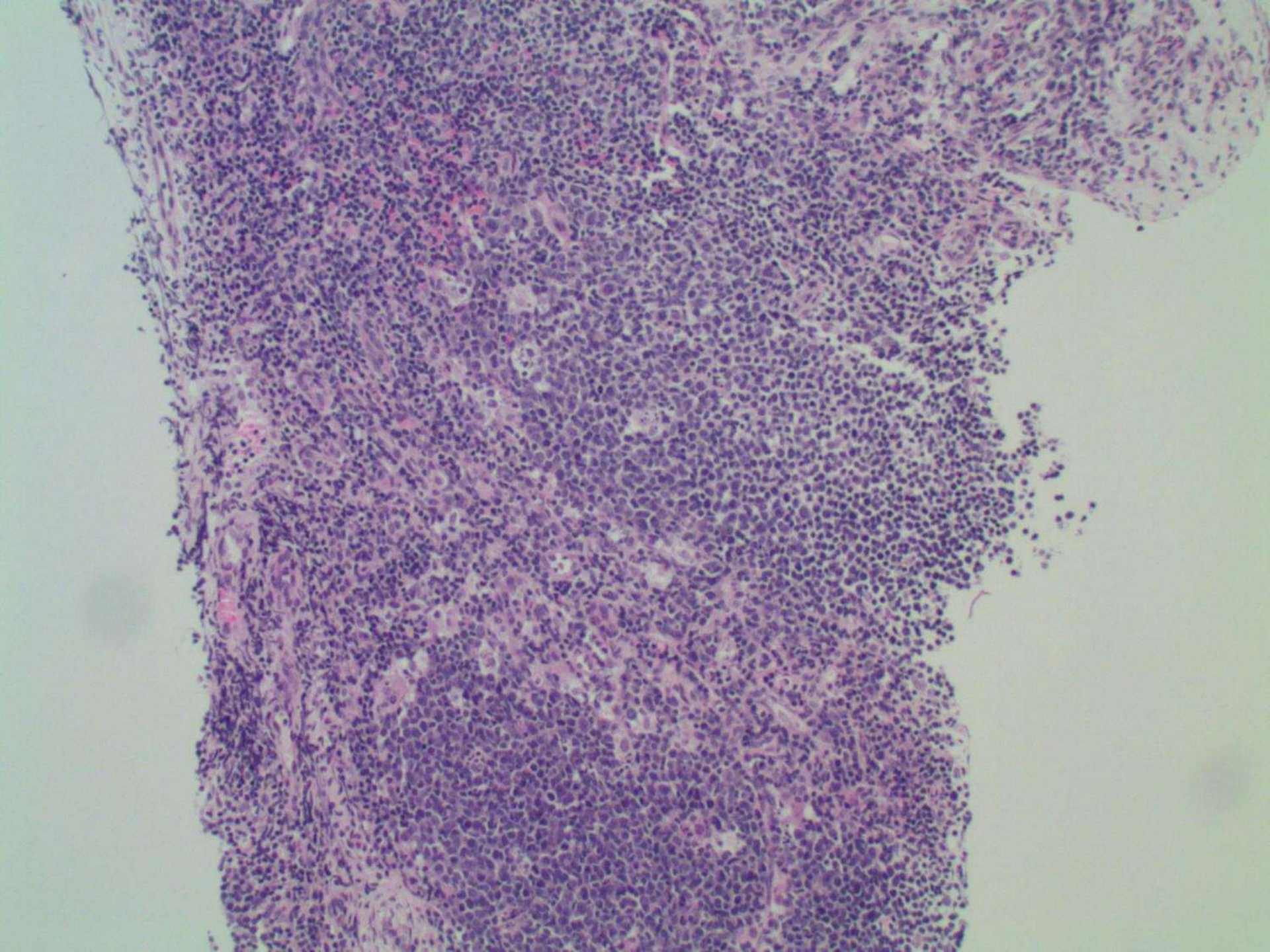
19-0908

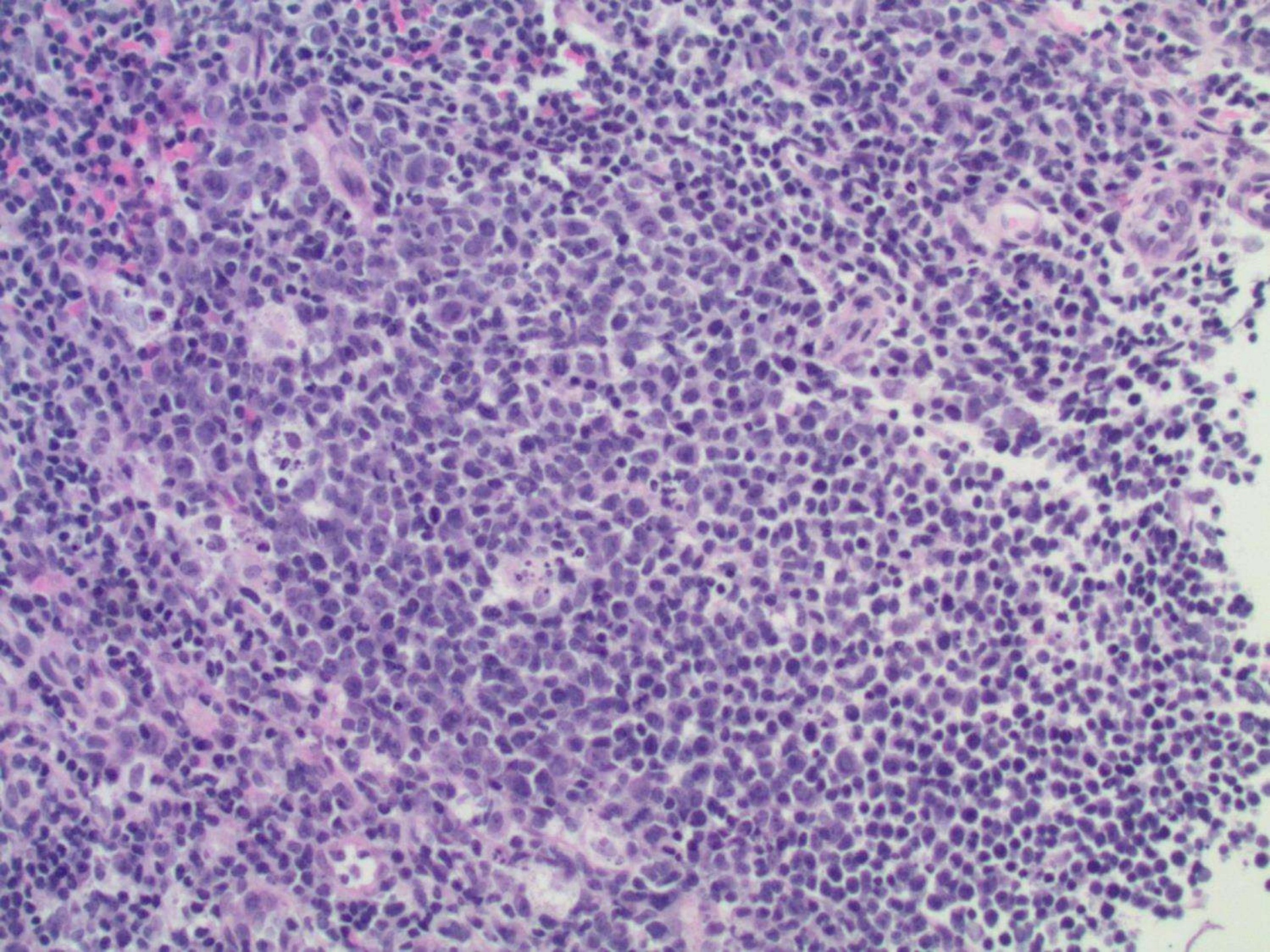
Caroline Temmins; Santa Clara Valley Medical Center

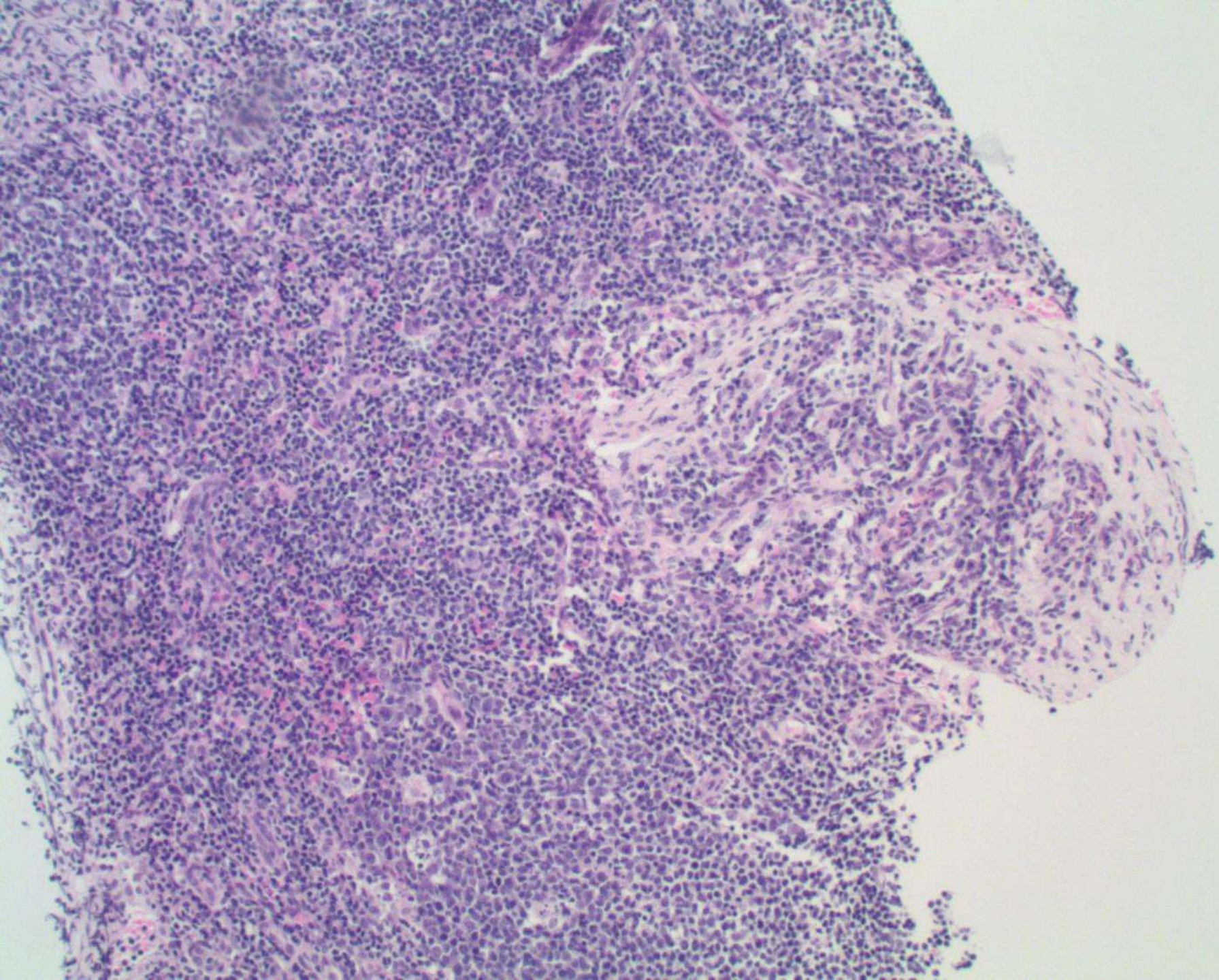
54-year-old female with 2-month h/o bilateral inguinal lymphadenopathy.

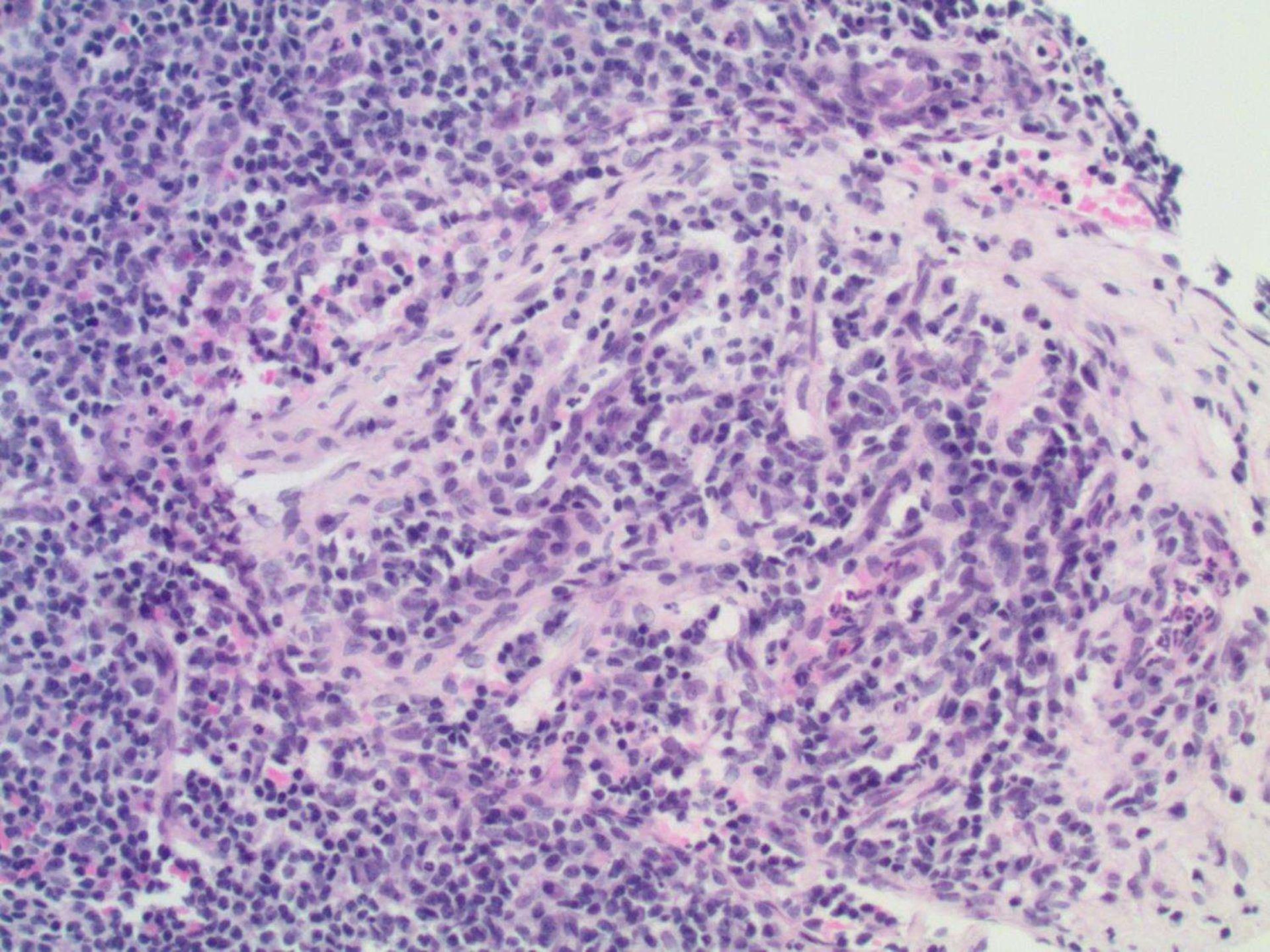


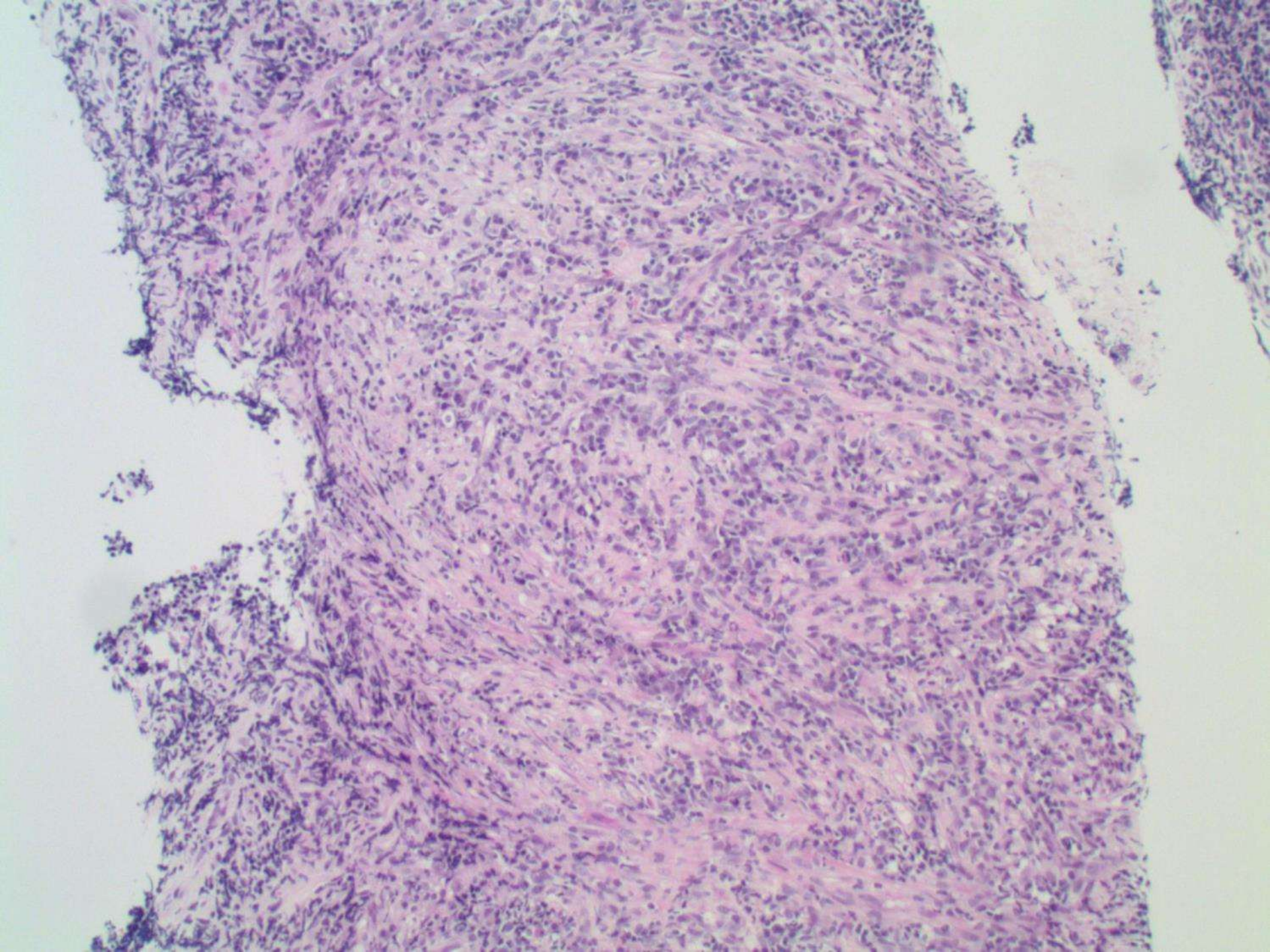


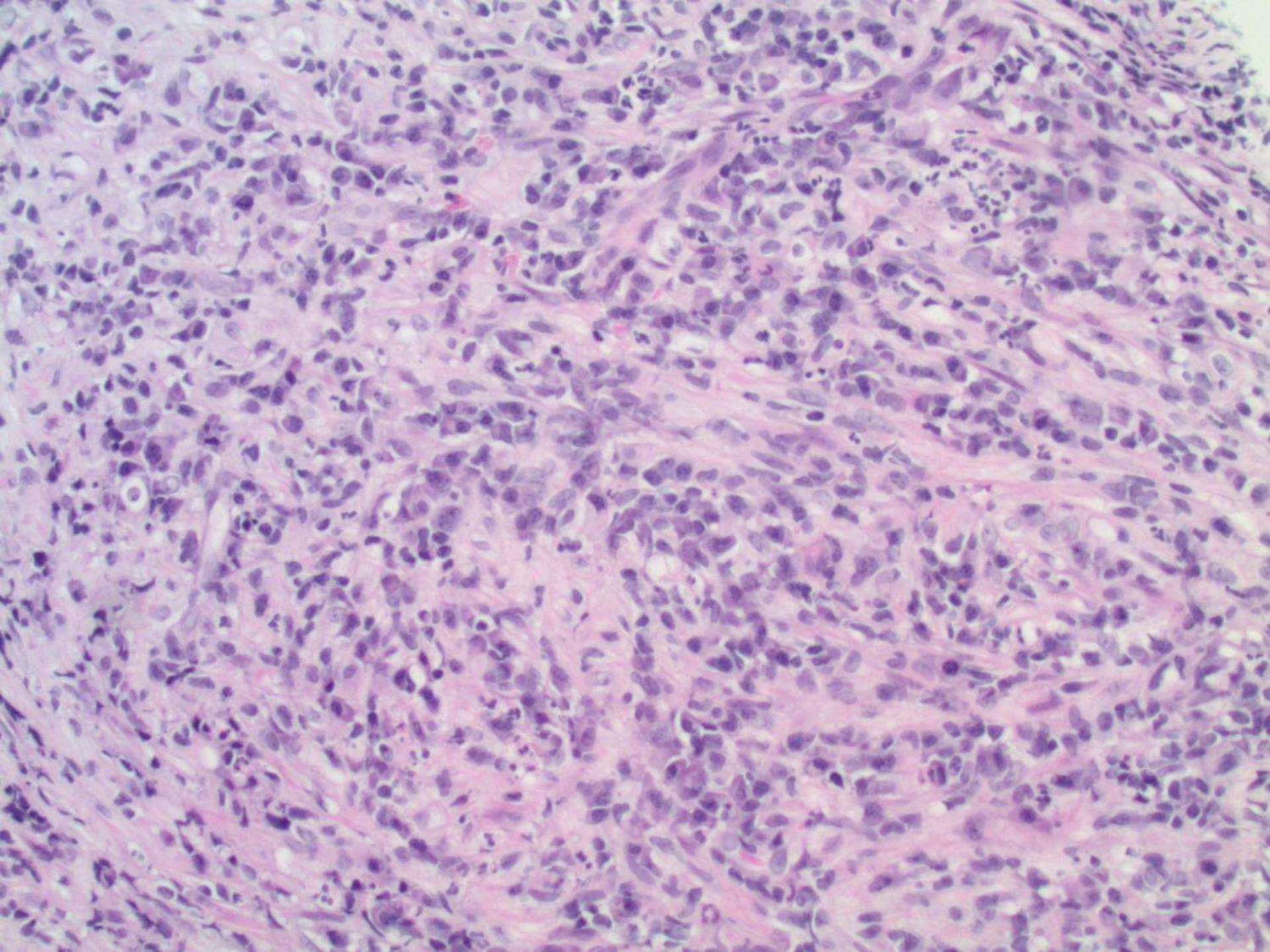


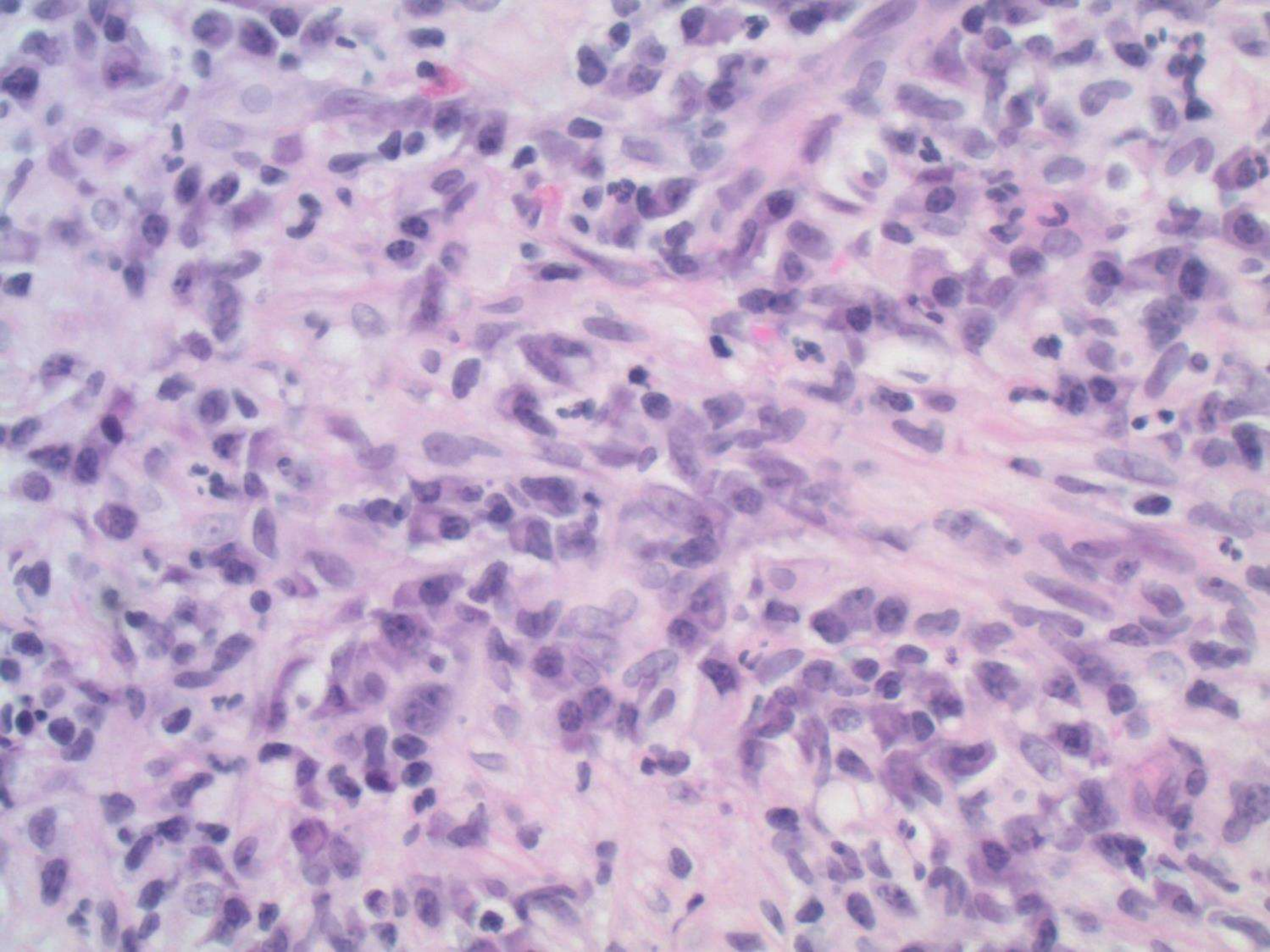


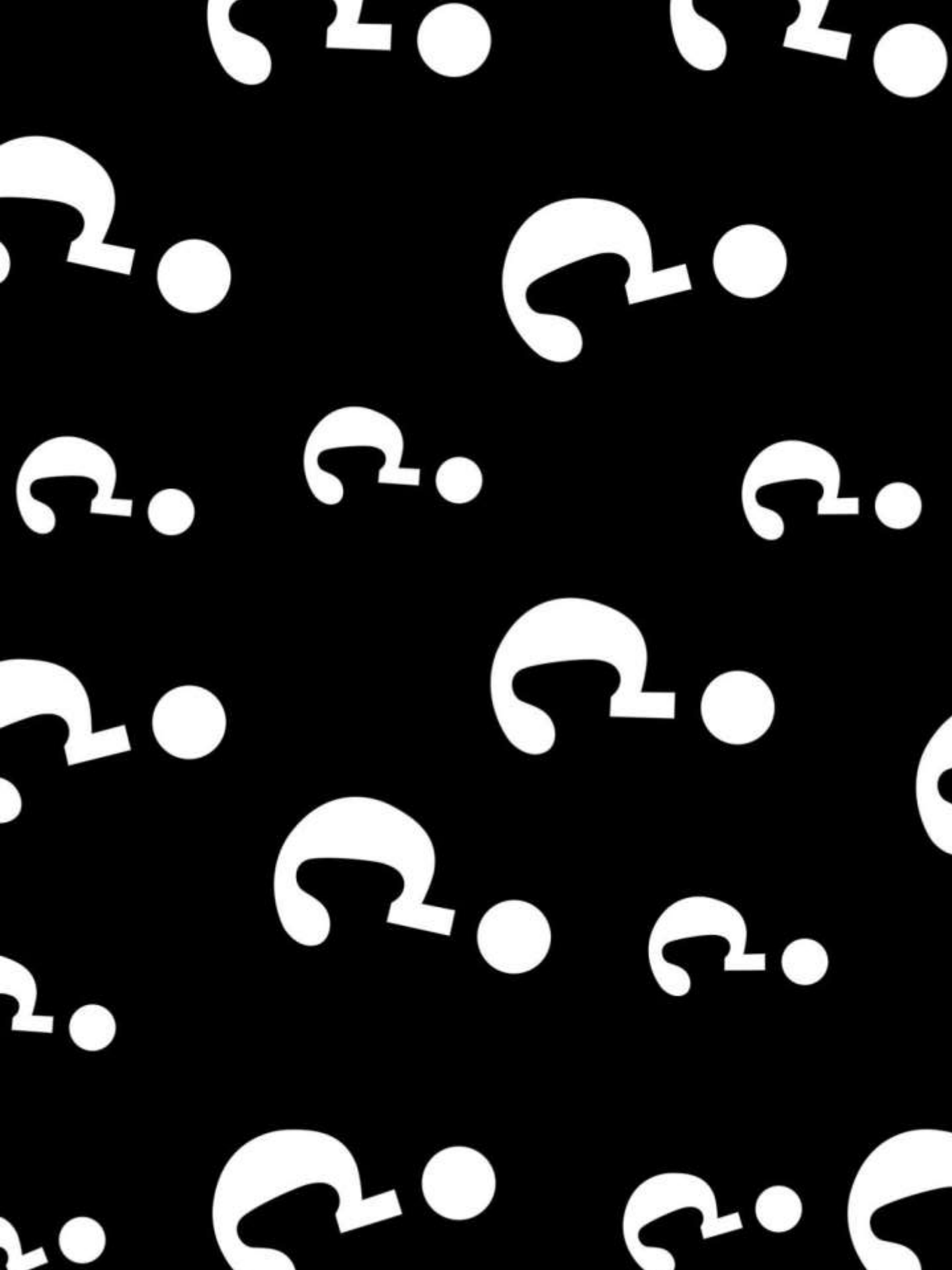












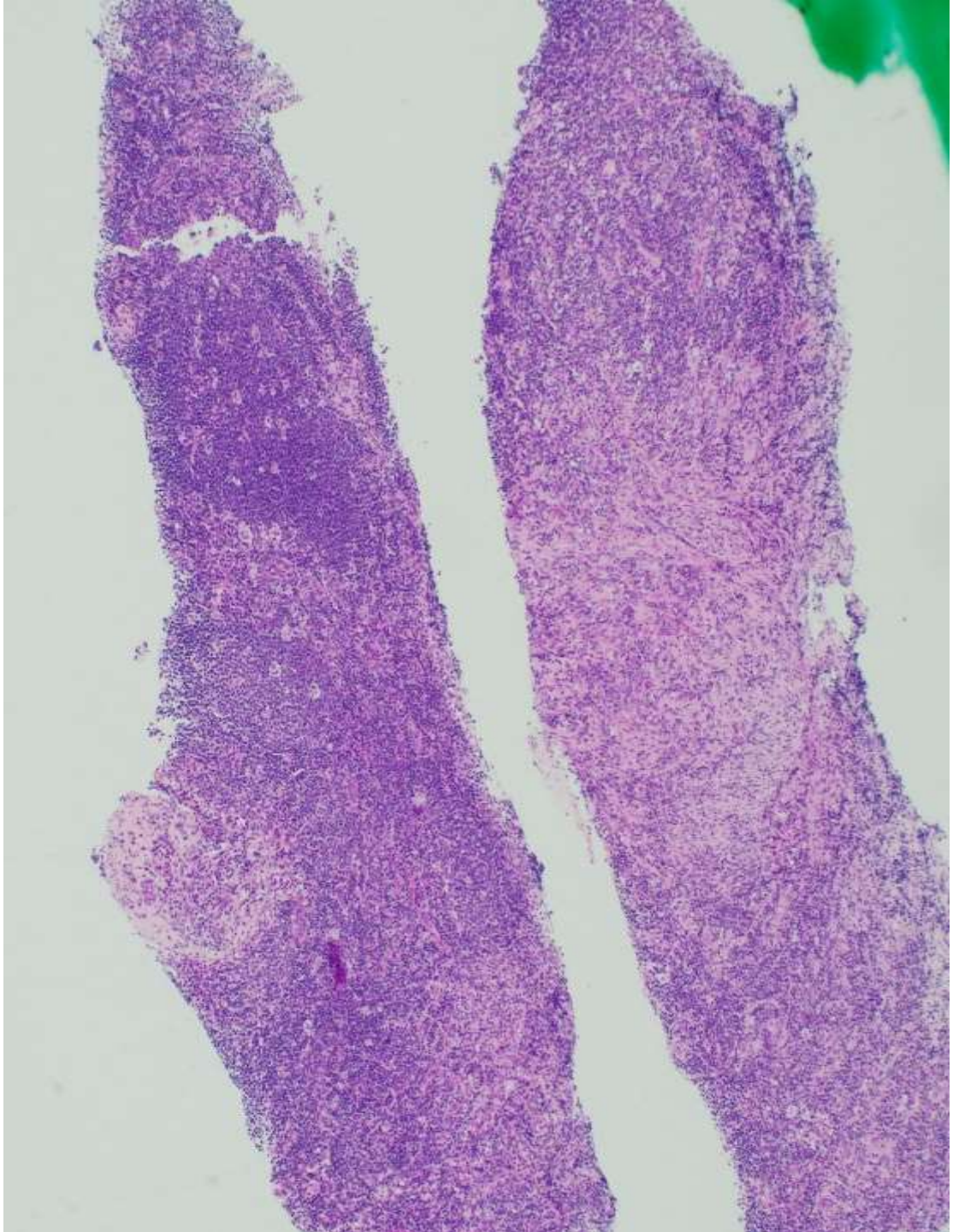
Southbay 19-908

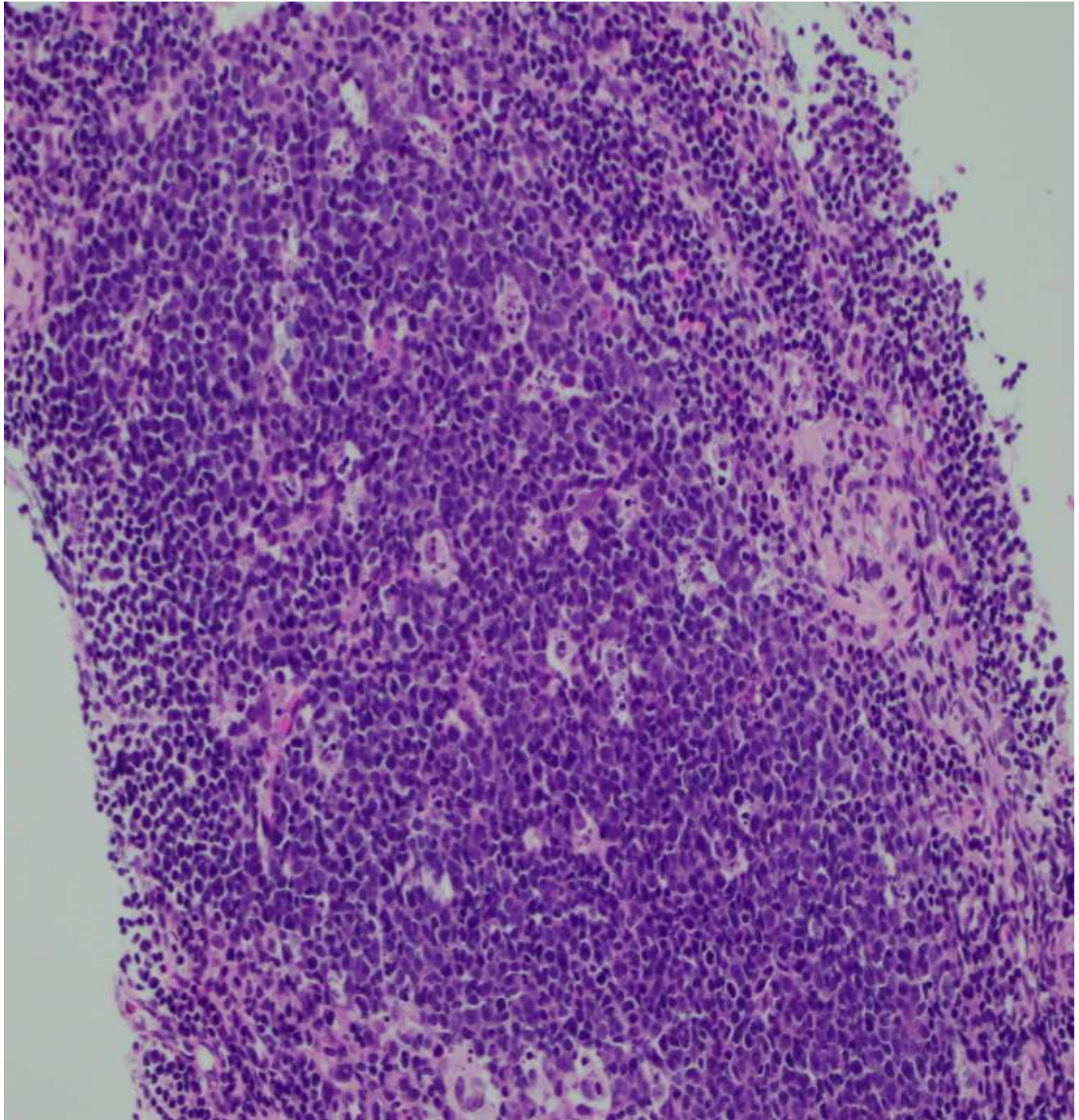
9/9/2019

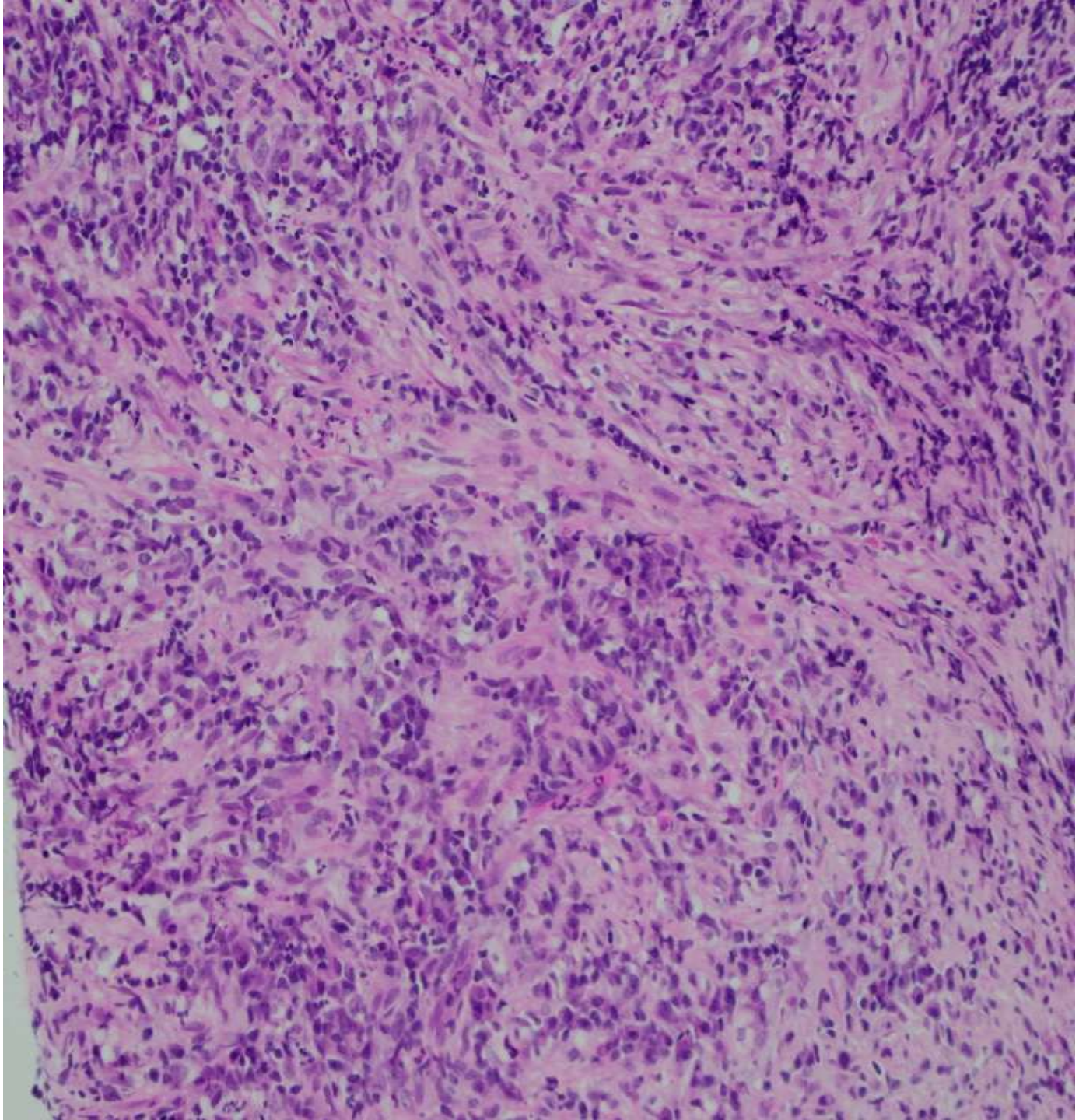
Caroline Temmins

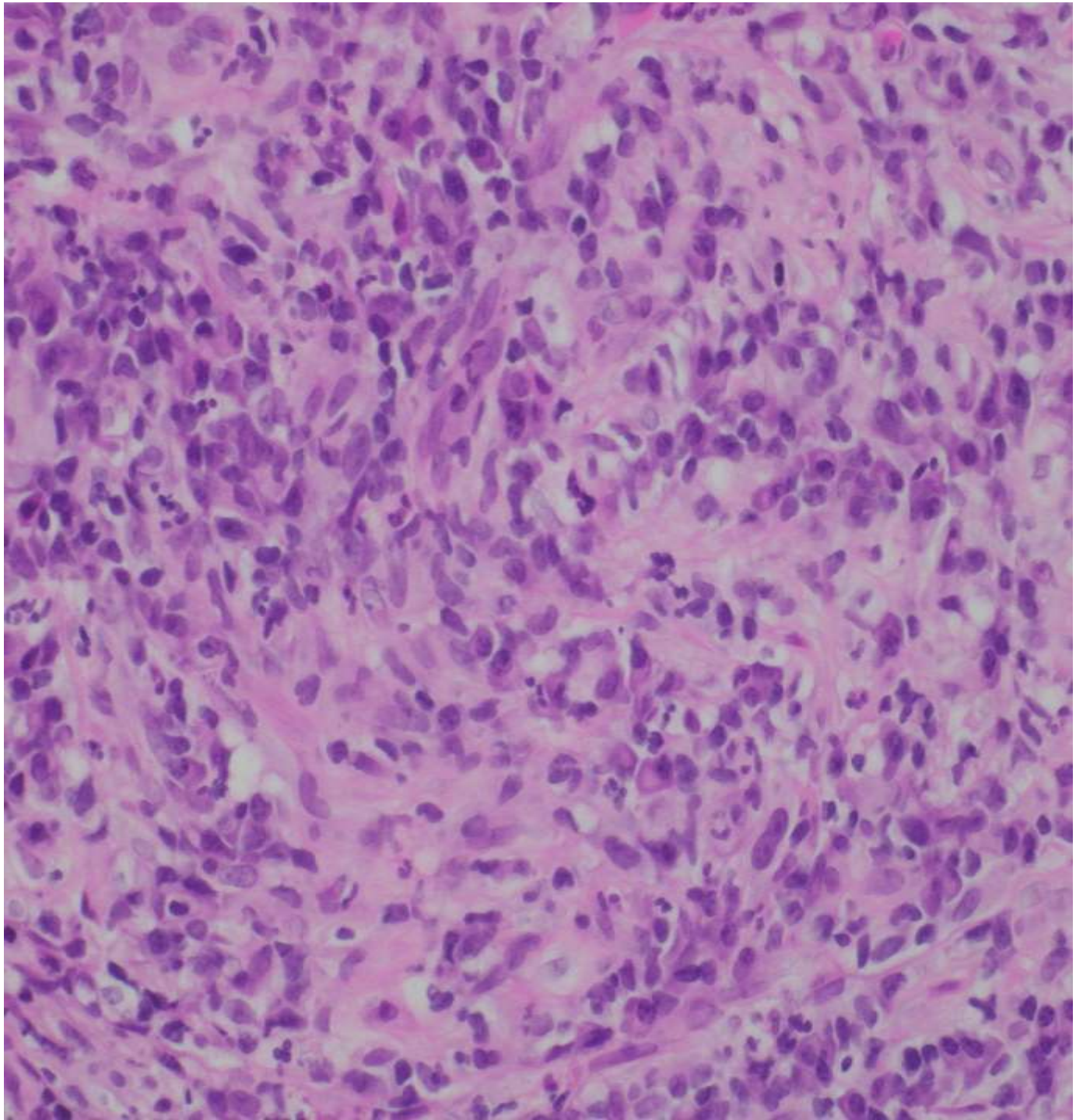
SCVMC

- 54-year-old female with 2-month history of bilateral inguinal lymphadenopathy.
- Ultrasound showed enlarged bilateral lymph nodes 2.4 x 1.2 x 1.3 cm left, 1.2 x 1.2 x 1.2 cm right.
- Ultrasound-guided FNA and core biopsy performed of left inguinal lymph node, submitted for flow cytometry and microbiology cultures.









Biopsy 5/17/2019
Physician note 5/21/2019:

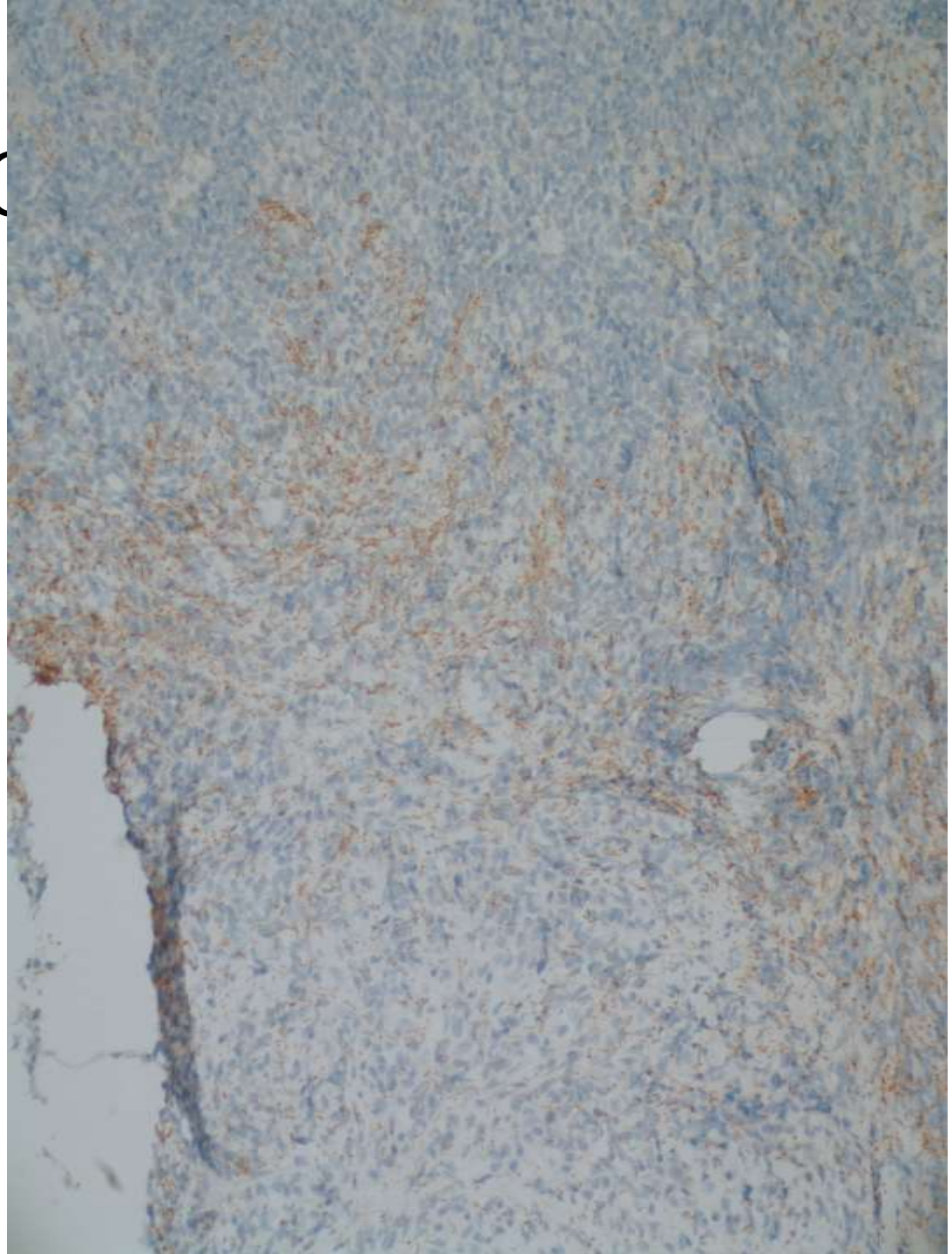
- **Syphilis RPR, quantitative**

- Order: 106020019 - Reflex for Order 105921242
- Status: Final result Visible to patient: No (Not Released) Dx: Screening examination for STD (sexual...
-
- **Ref Range**
- Syphilis RPR, Quant <1 256High

- Syphilis RPR, Interpretation
- Non-Reactive ReactiveAbnormal

-

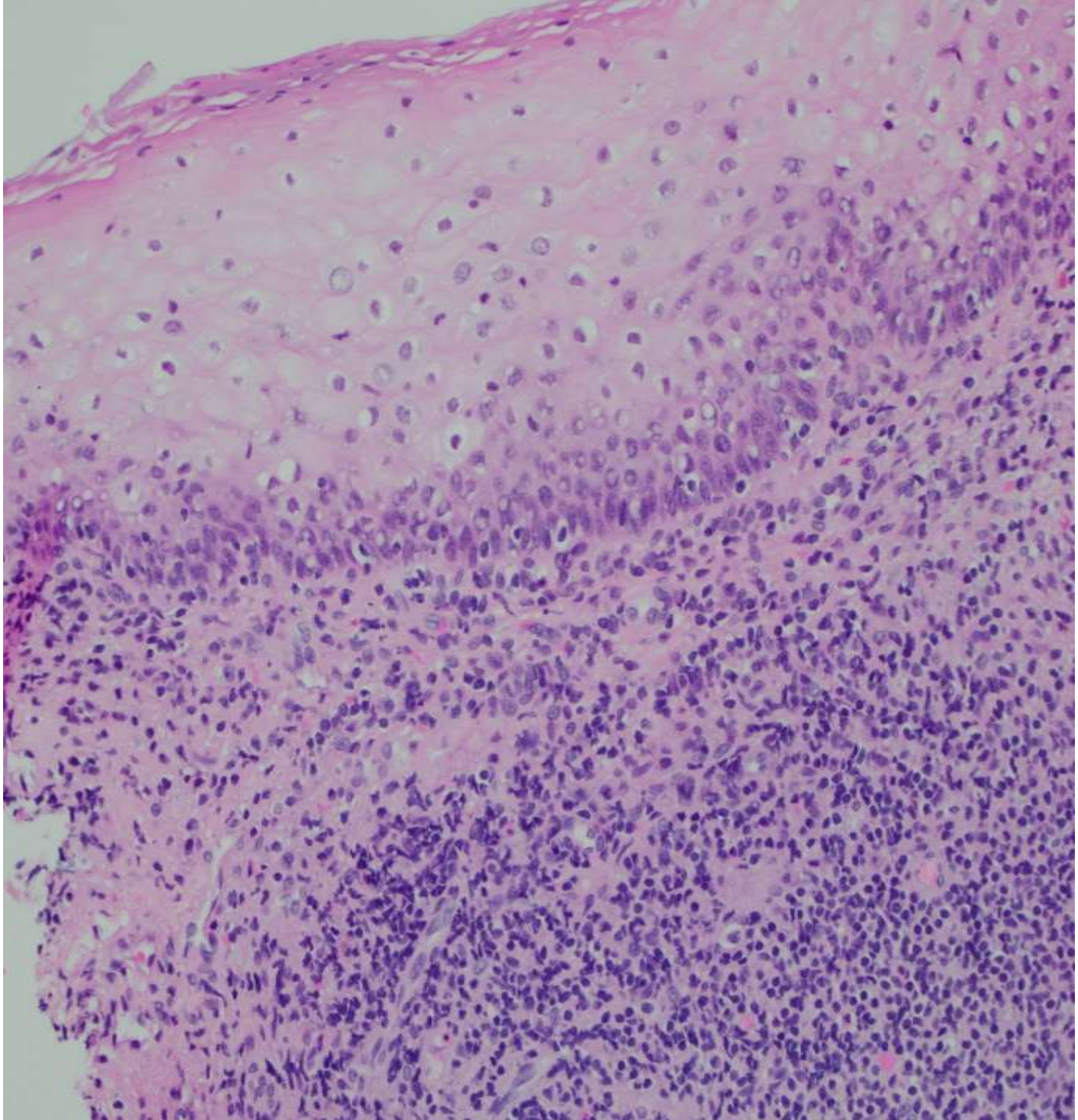
Spirochete IPC

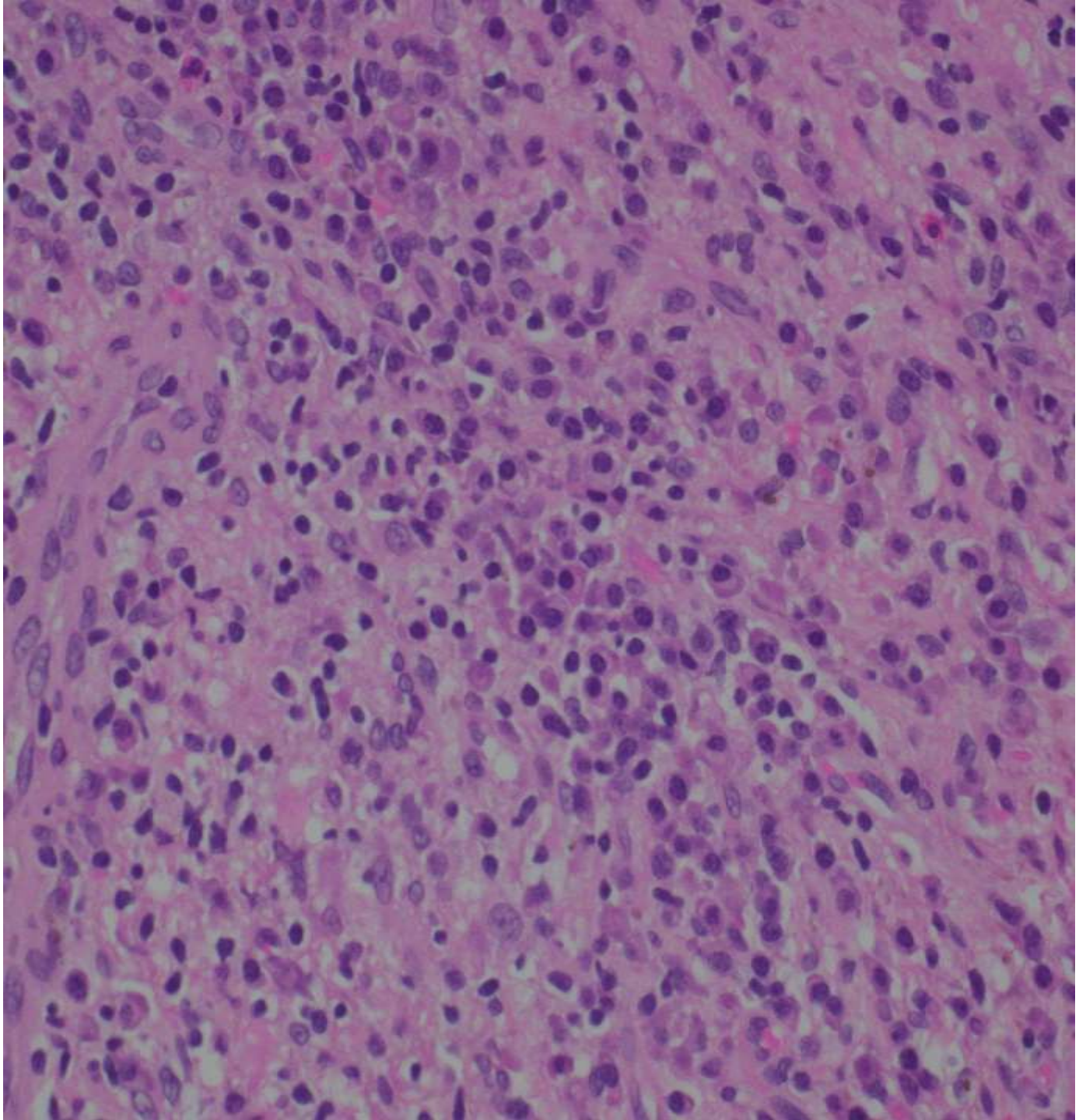


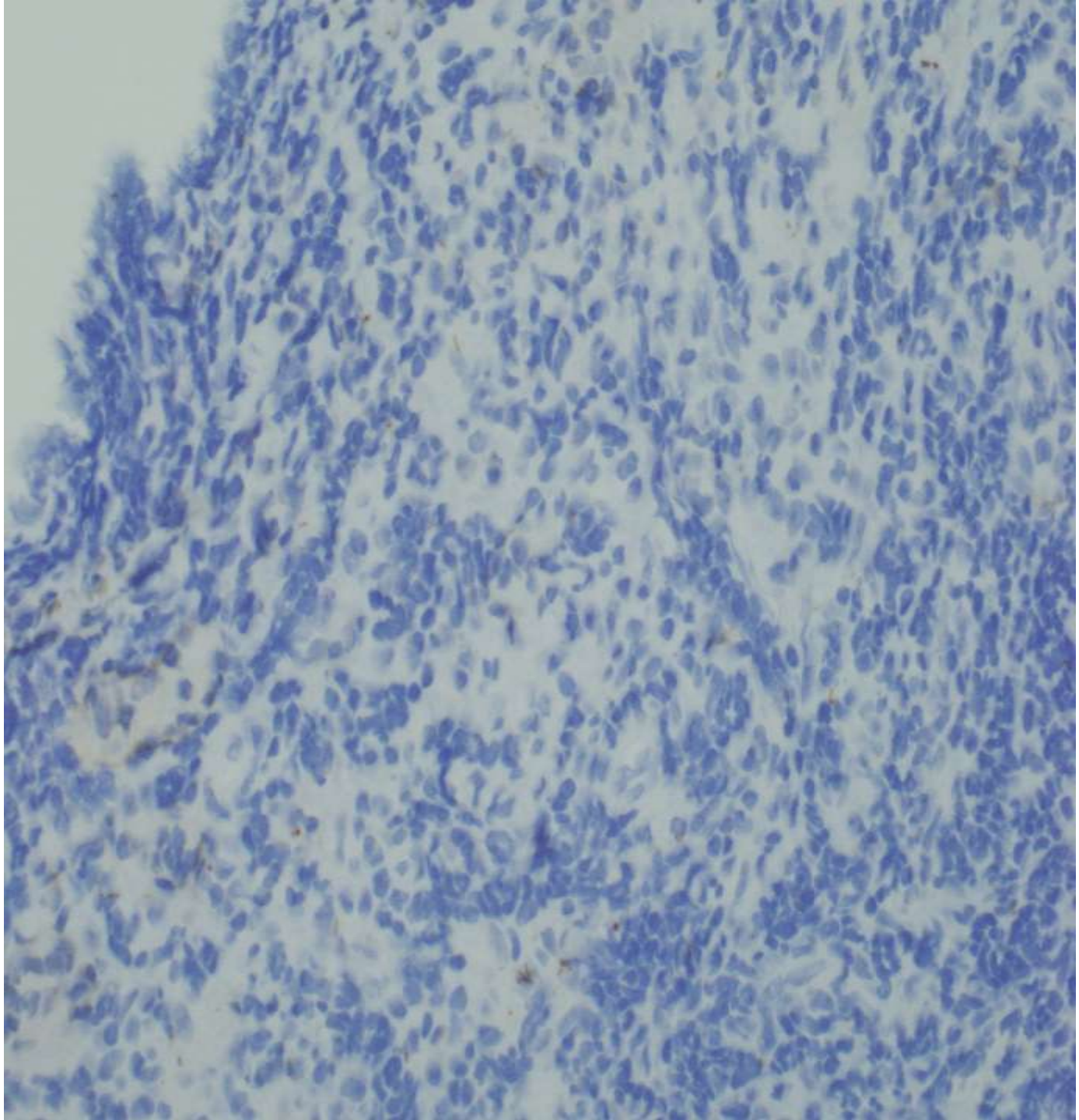
Syphilis in lymph node biopsies

- Rarely seen – patients usually diagnosed prior to biopsy with VDRL and RPR screening tests
- Often a history of a prior skin or mucosal lesion
- Lymph node: Prominent reactive follicular hyperplasia
- Prominent perilymphadenitis with thickening of the capsule, infiltration by plasma cells, and frequent endarteritis and phlebitis
- Paracortical area often shows plasmacytosis, particularly in a perivenular distribution
- Warthin-Starry or immunostains show spirochetes, particularly within and around the walls of venules, sometimes within germinal centers

Vulvar biopsy
~ 2 weeks
later



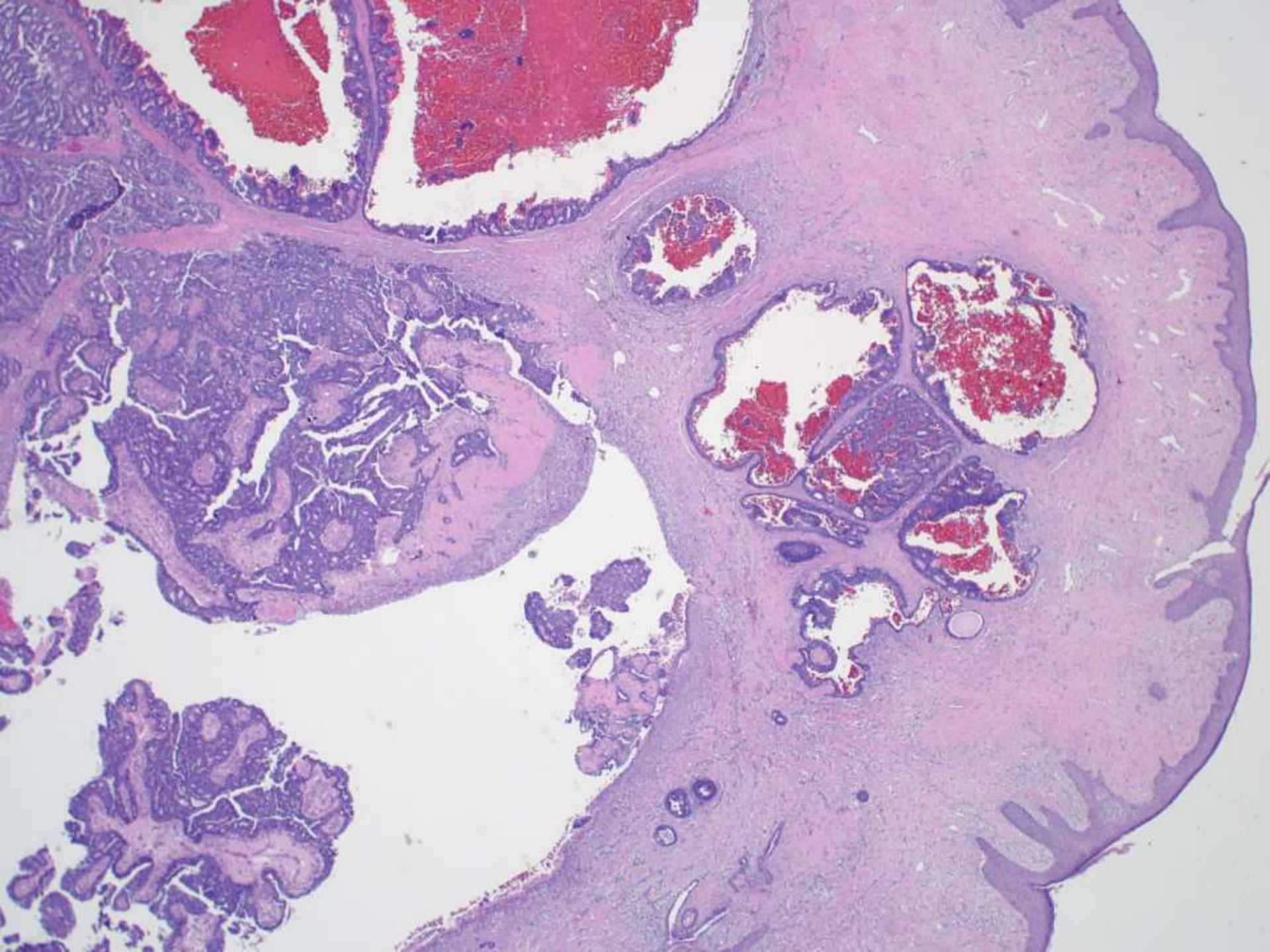


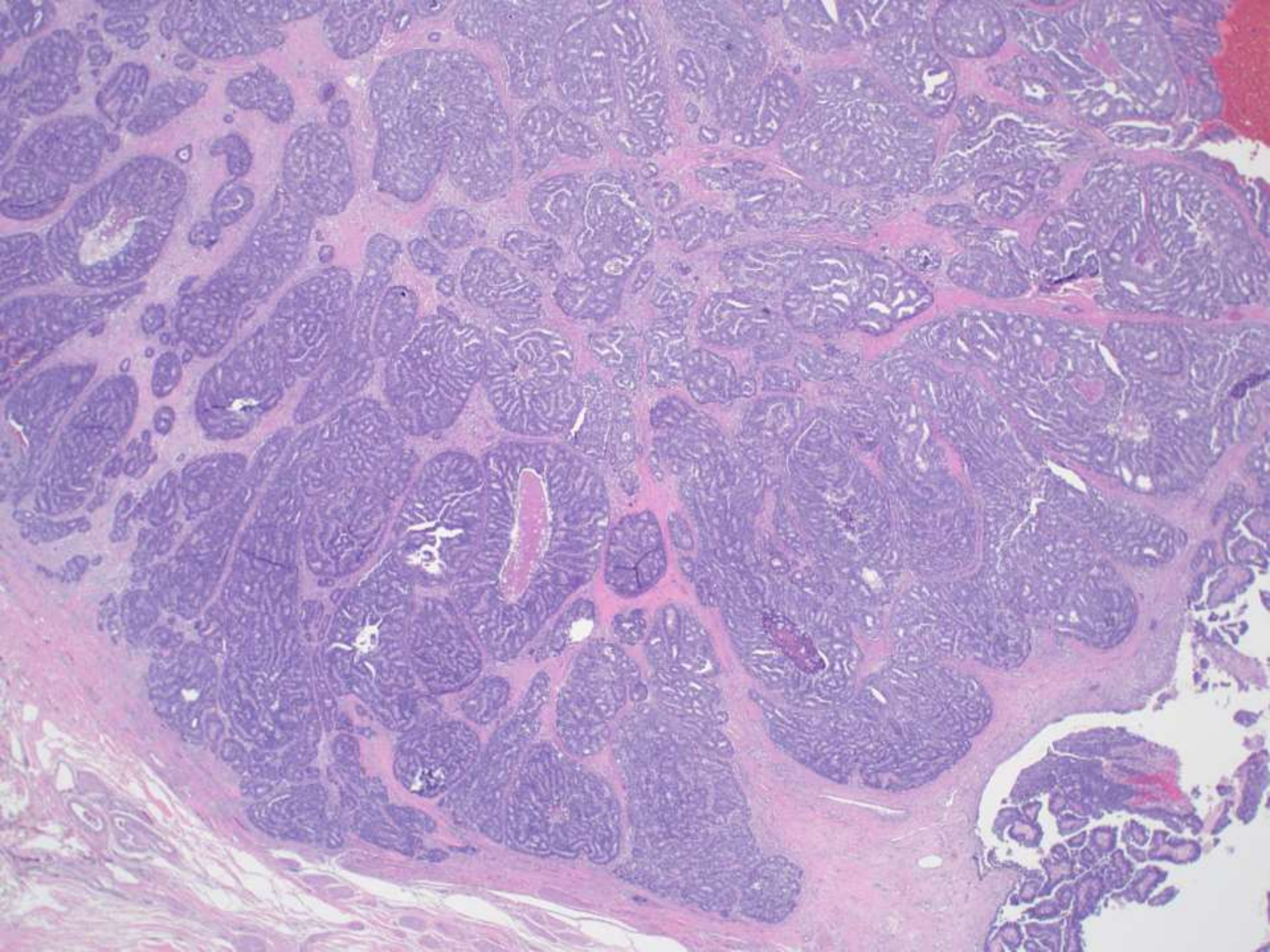


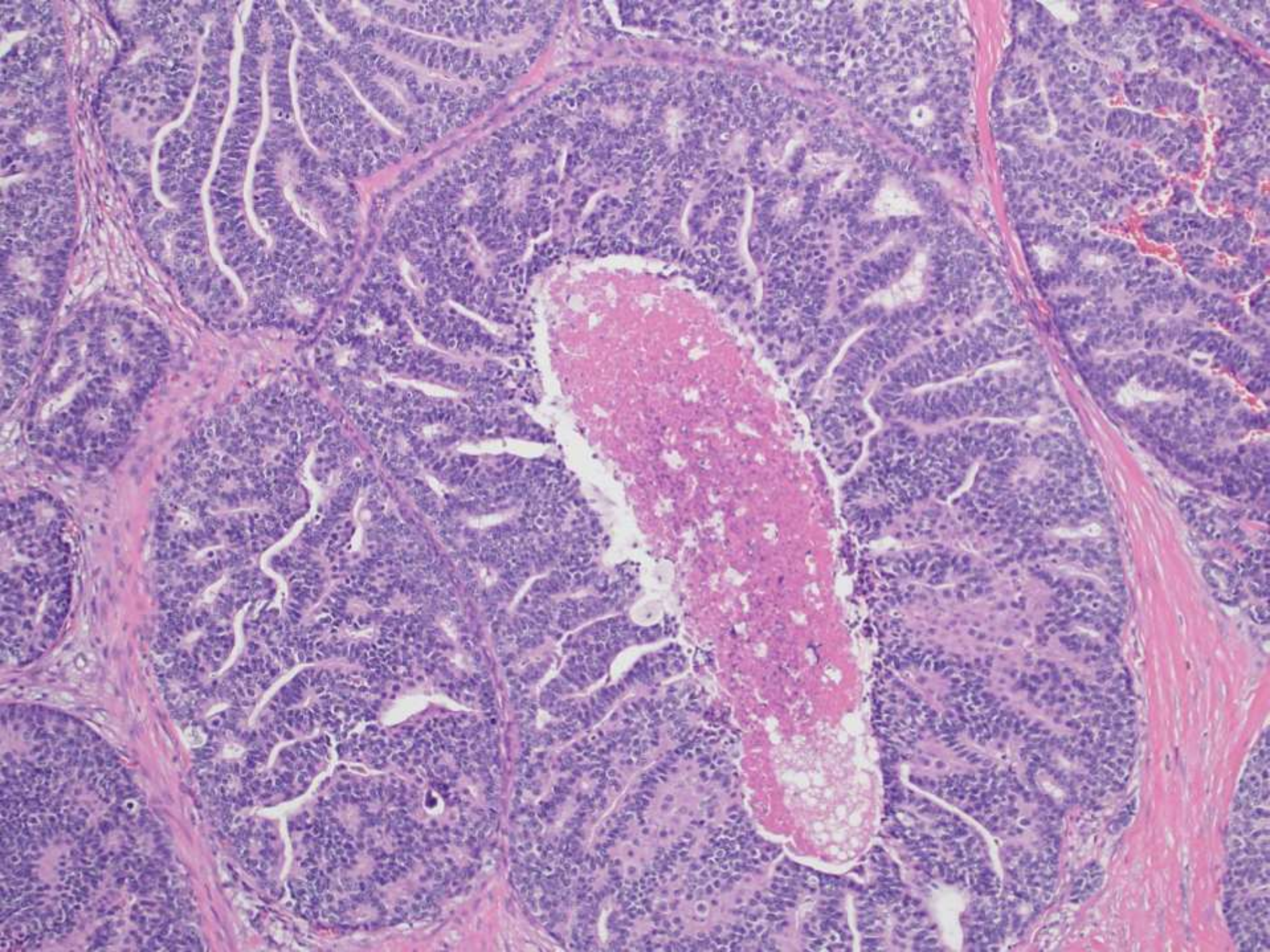
19-0909

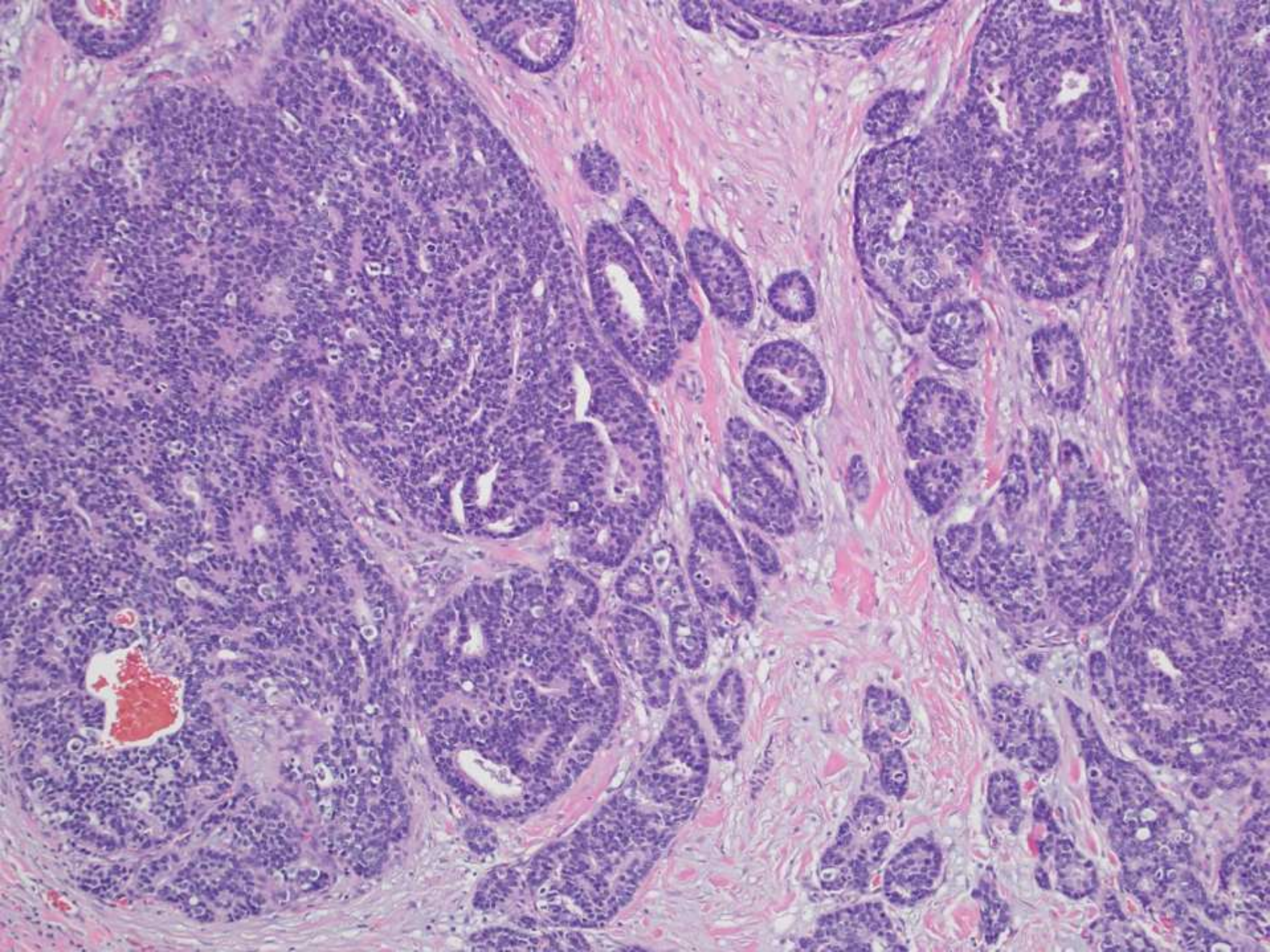
Megan Troxell; Stanford

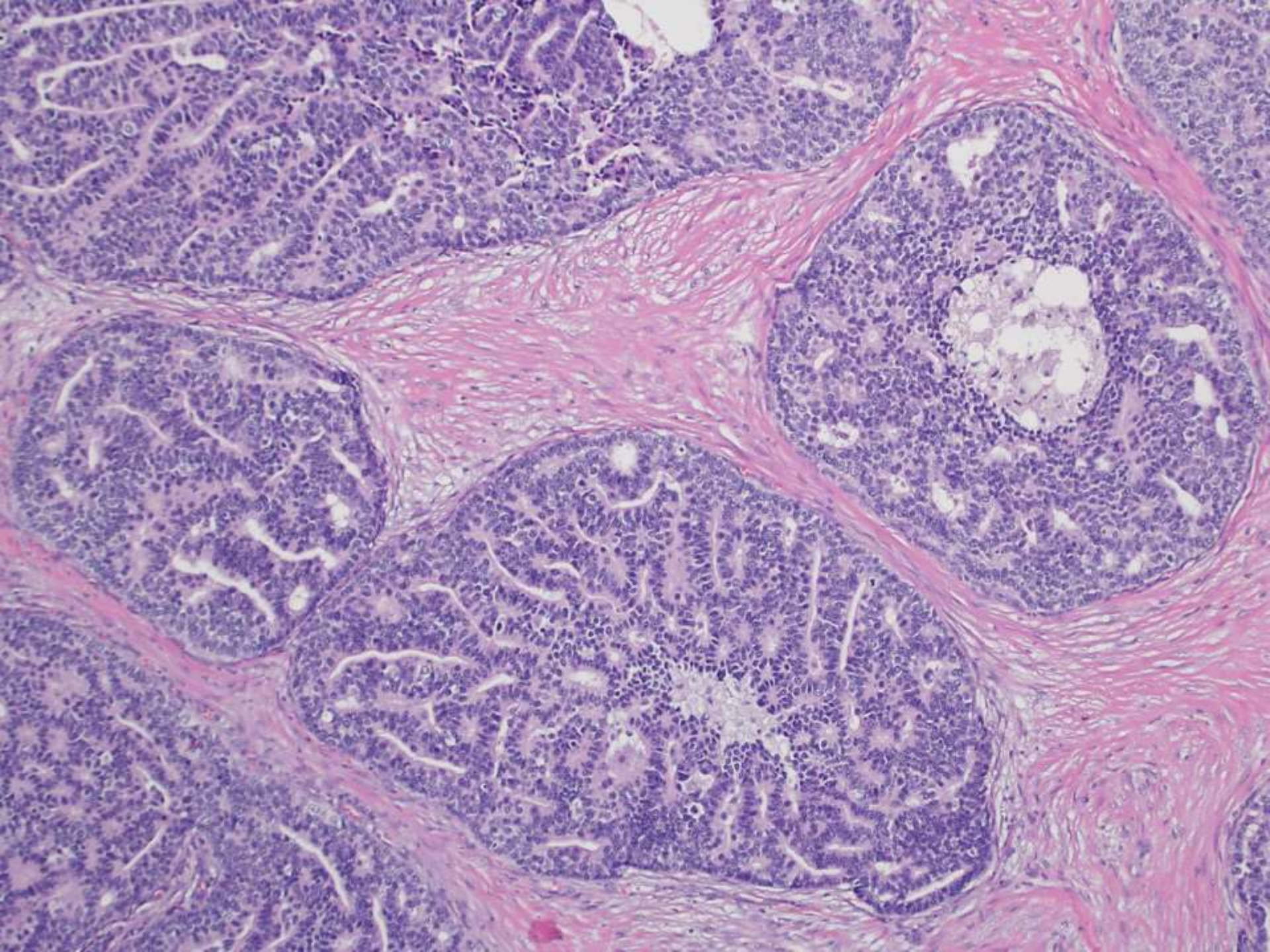
Elderly man with breast mass.

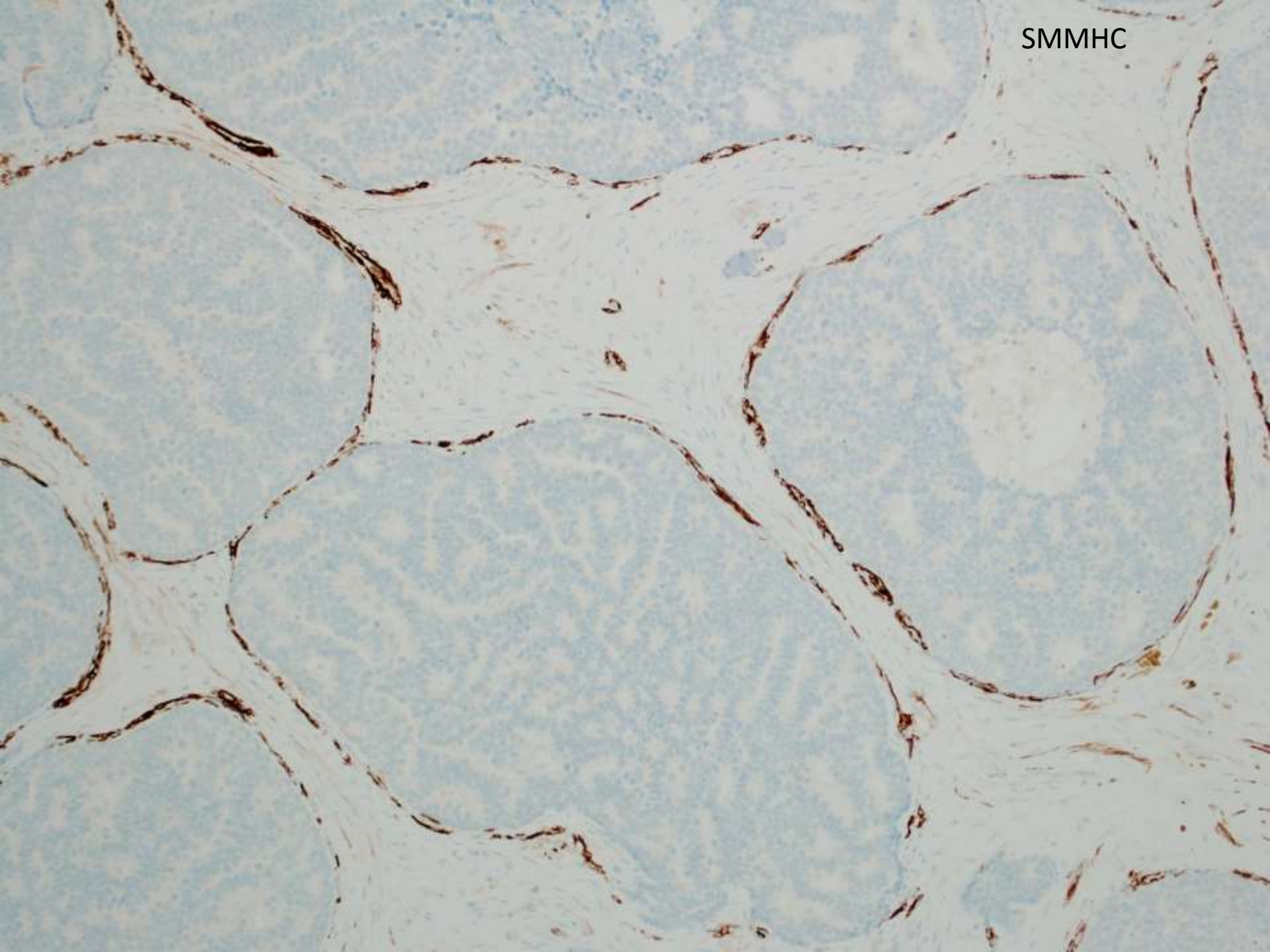








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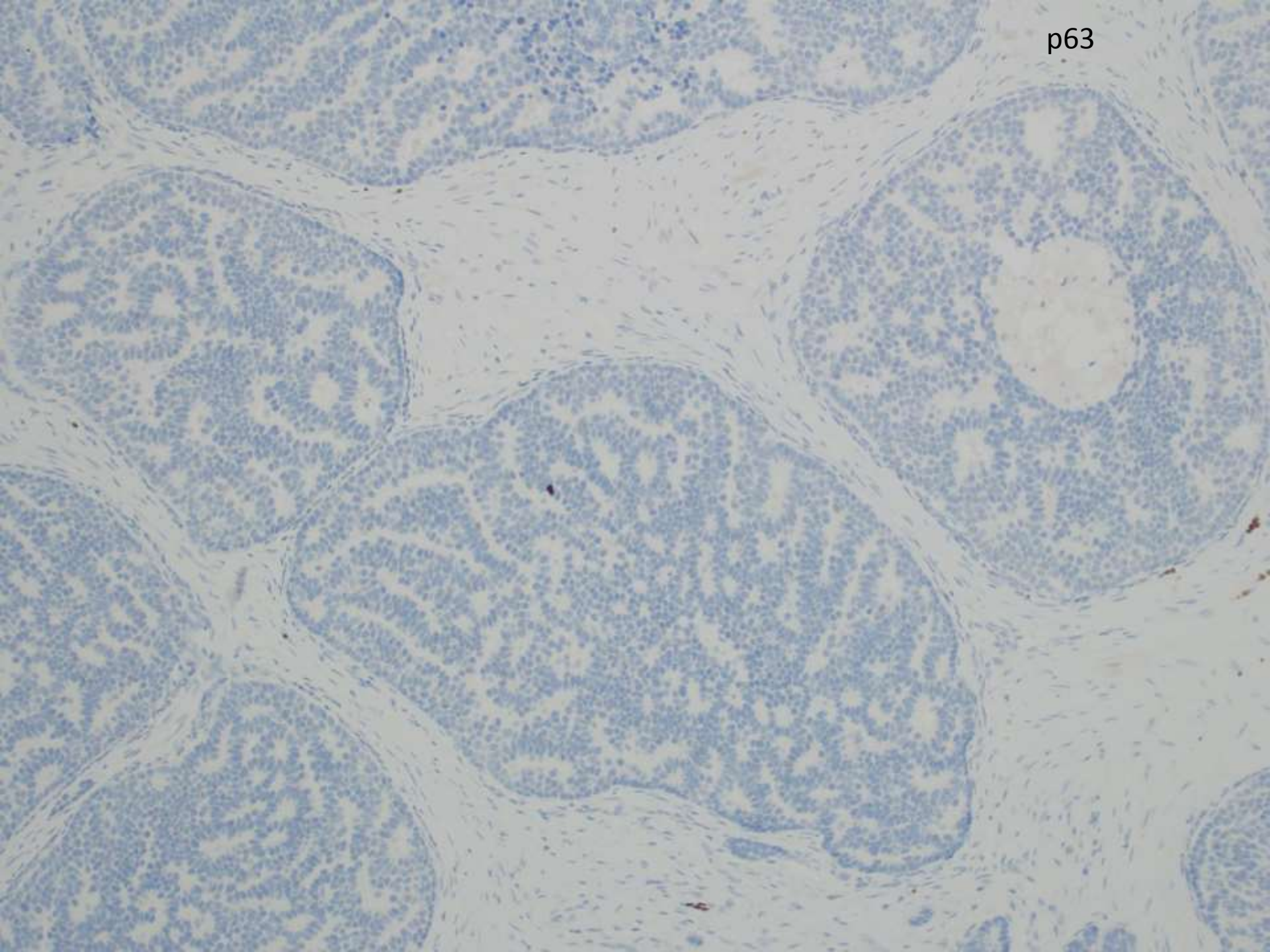
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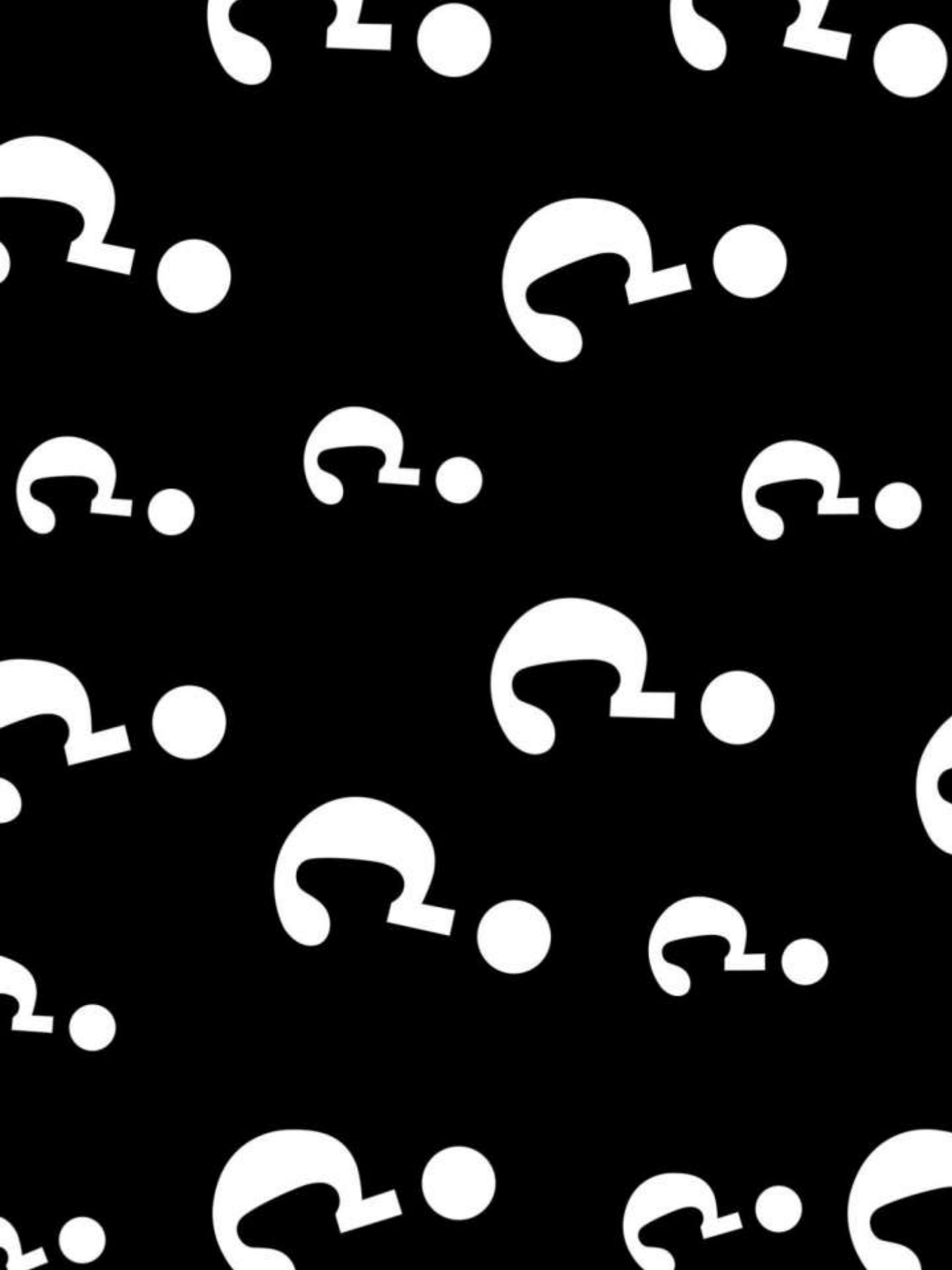

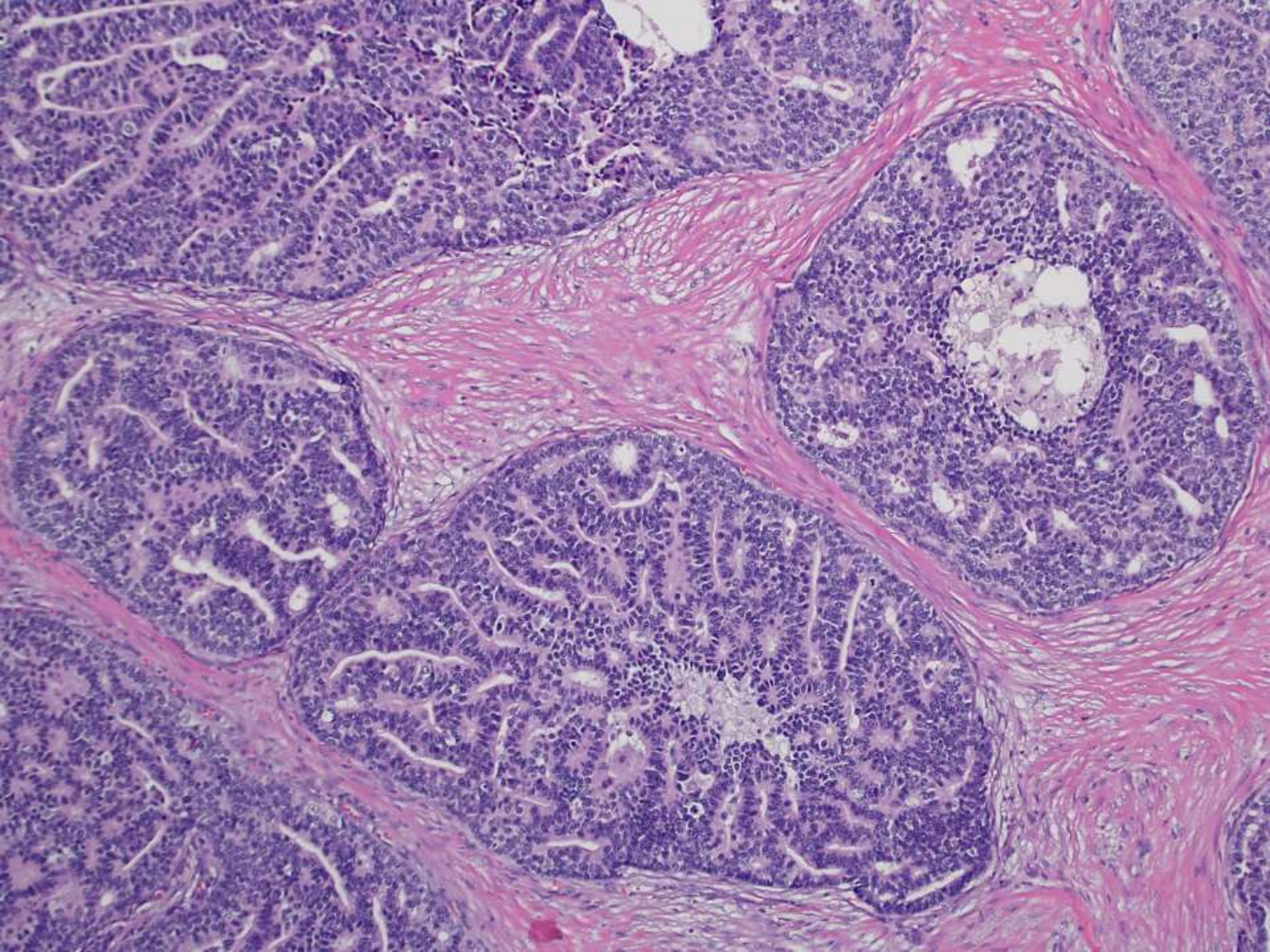

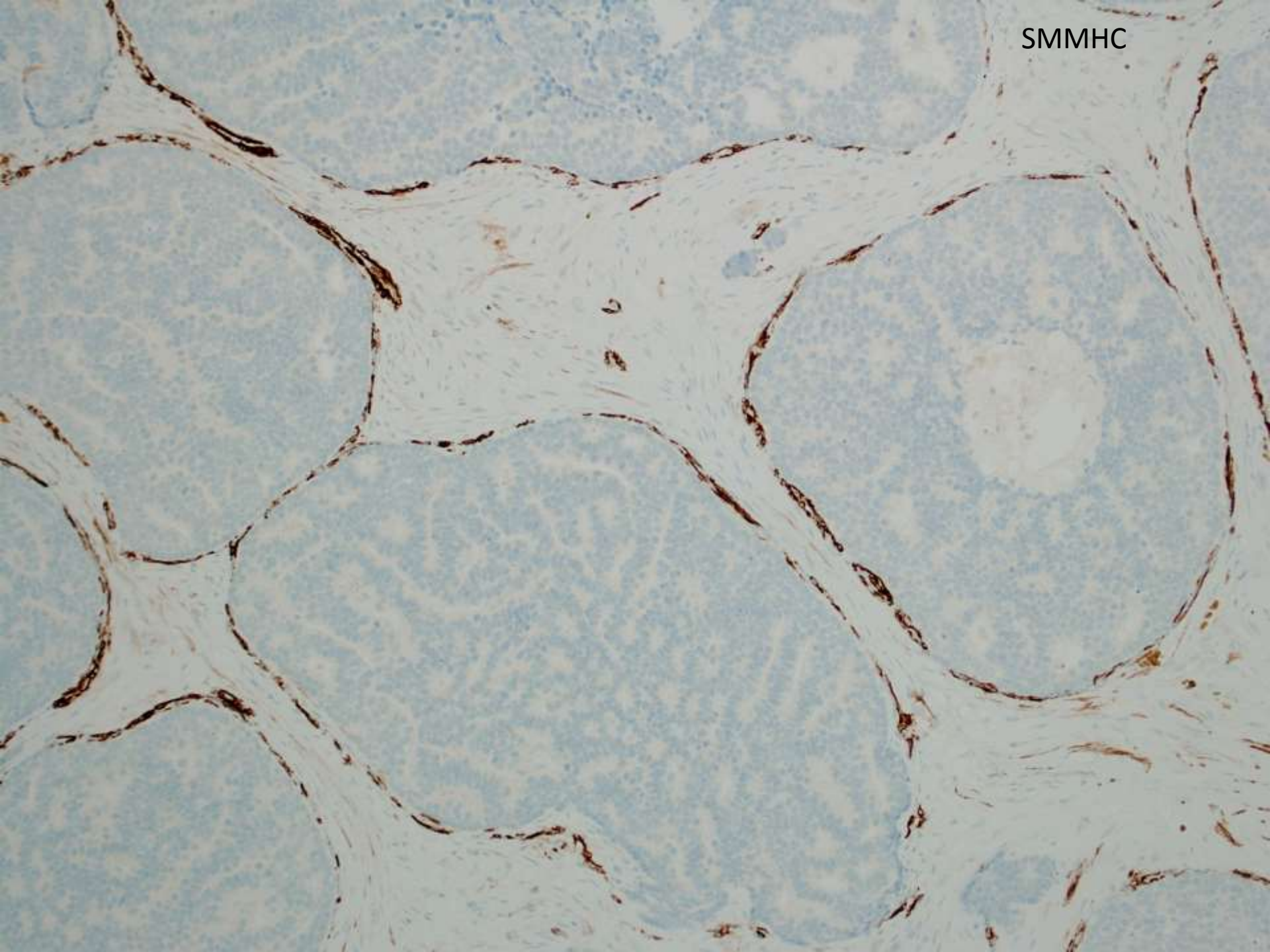
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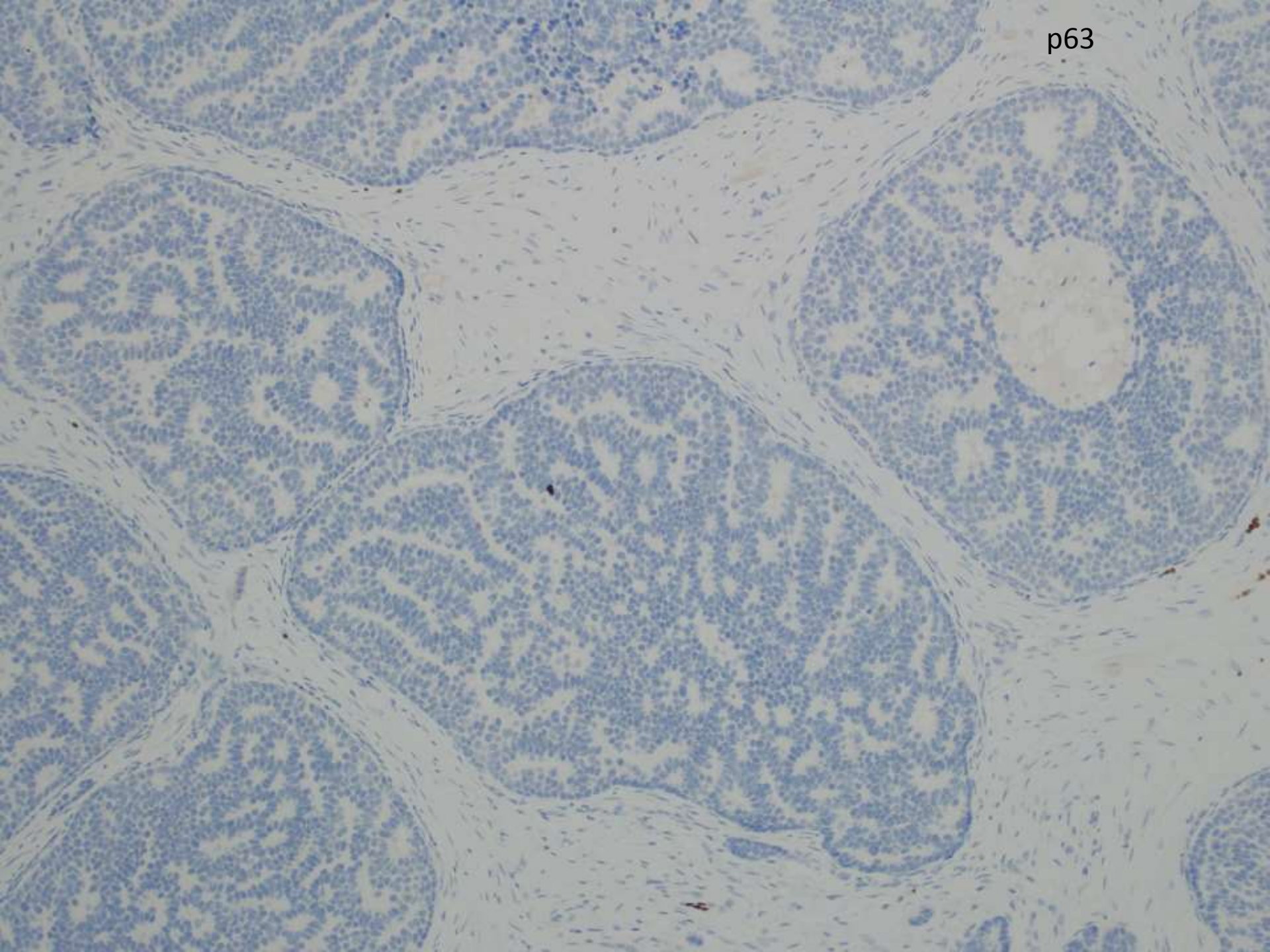
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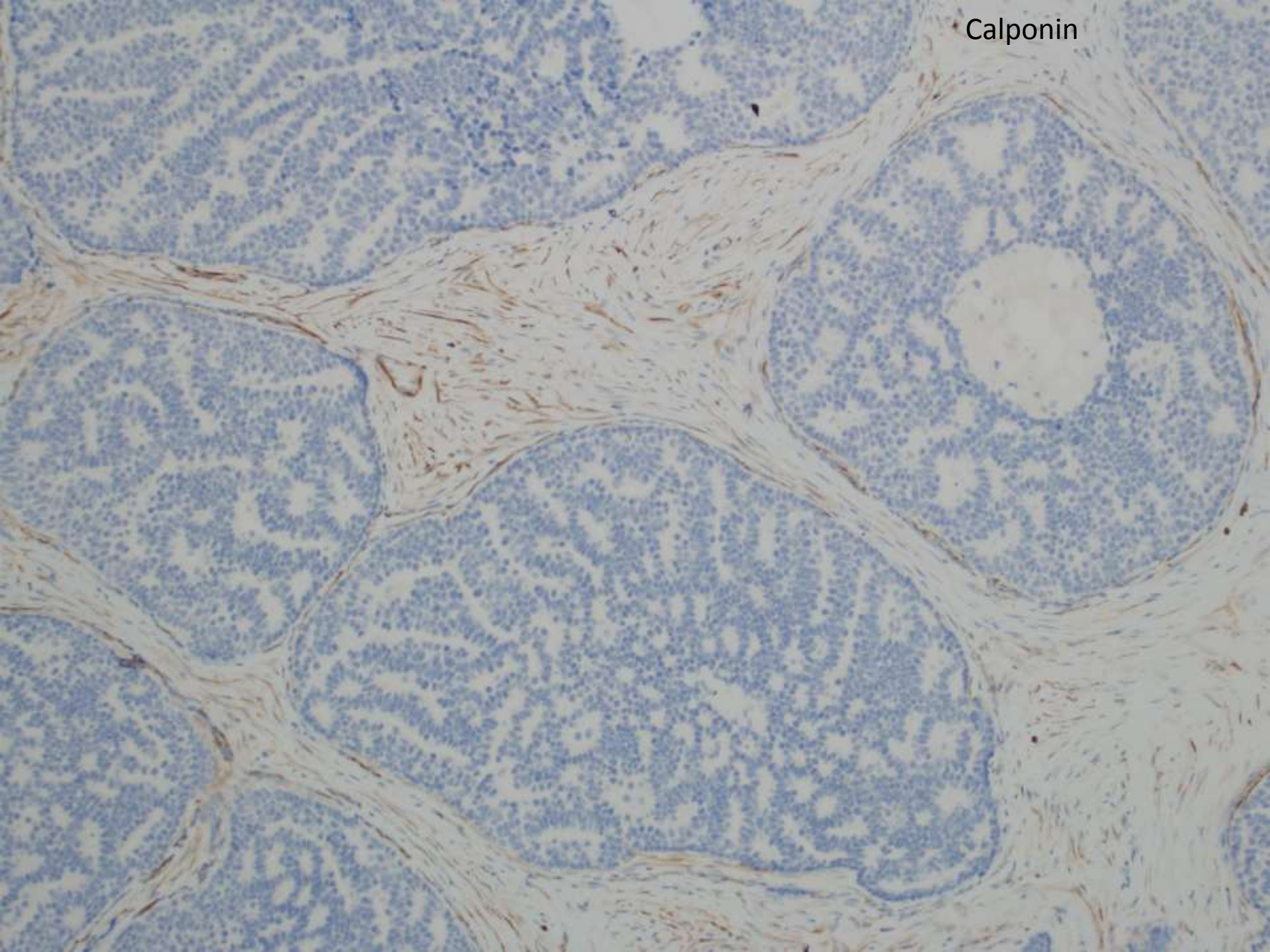
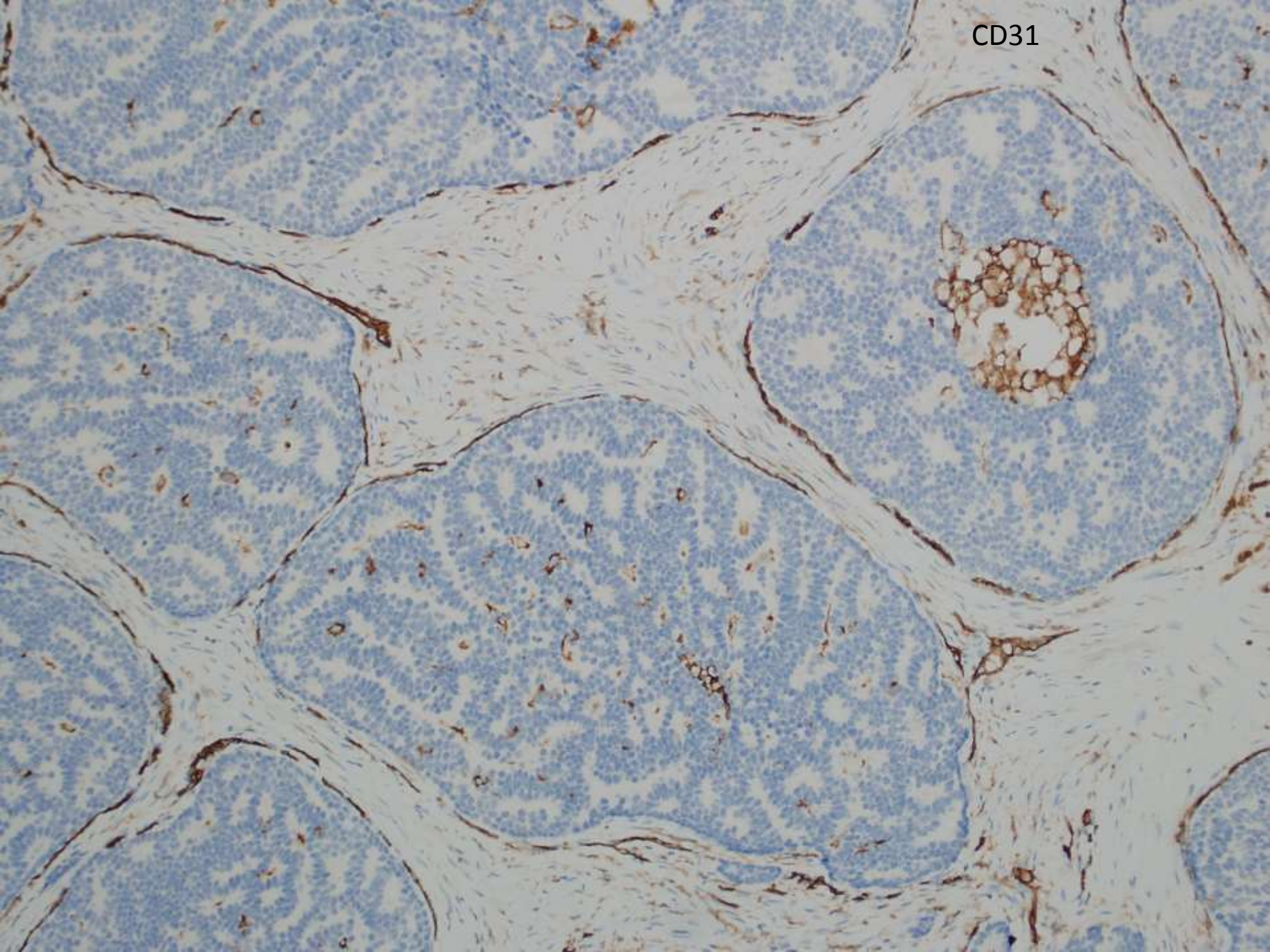
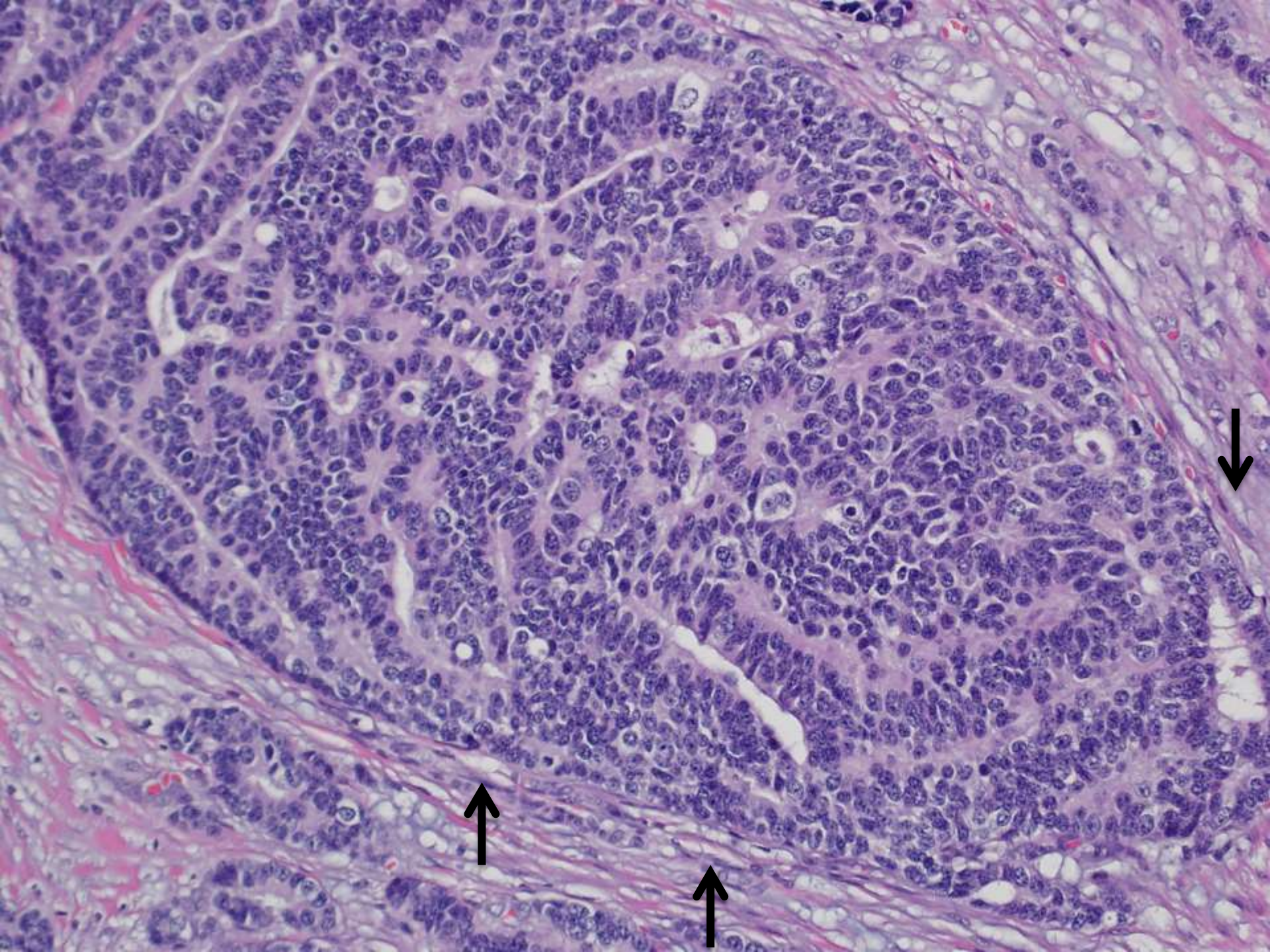
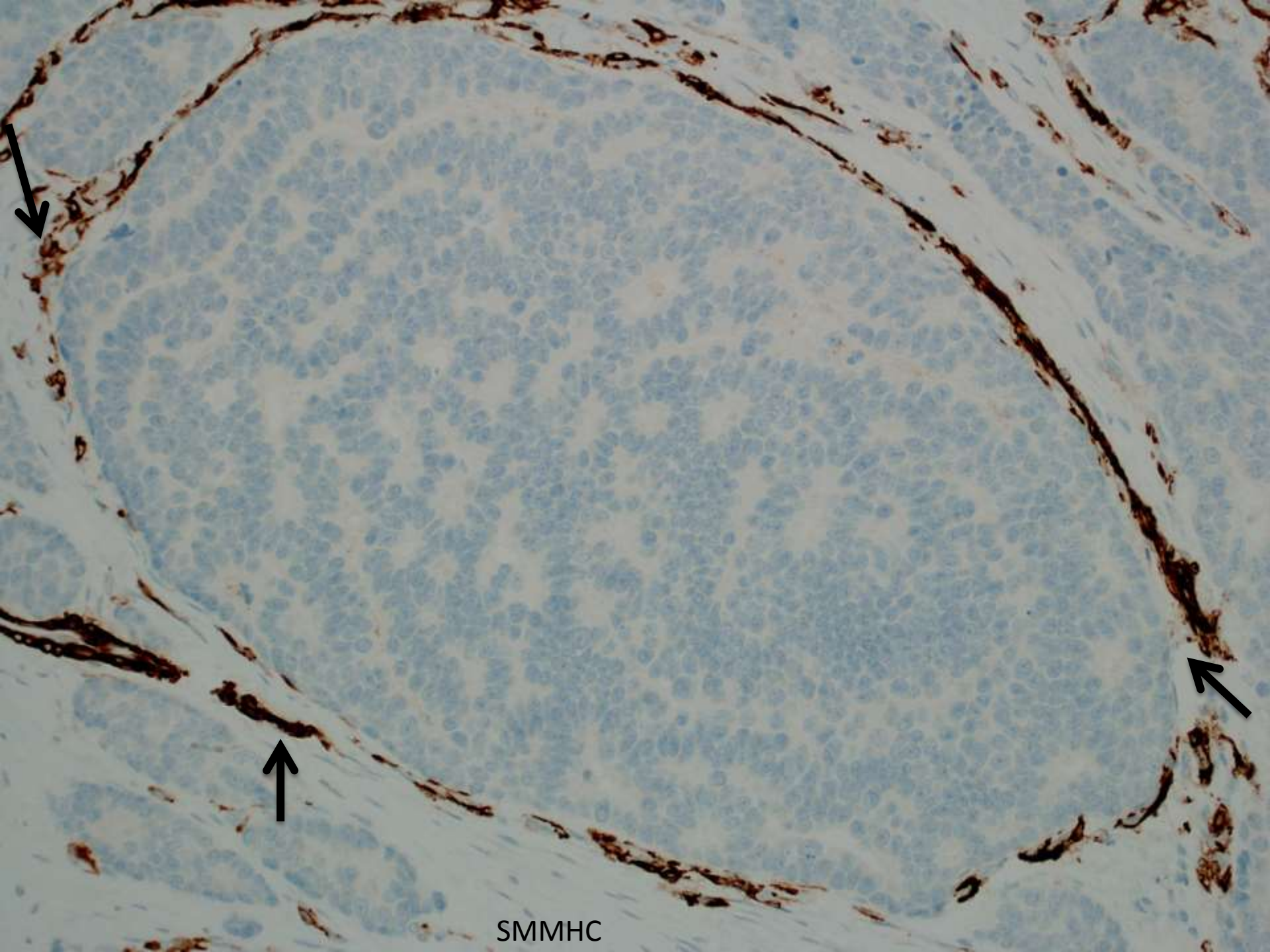

Calponin


CD31

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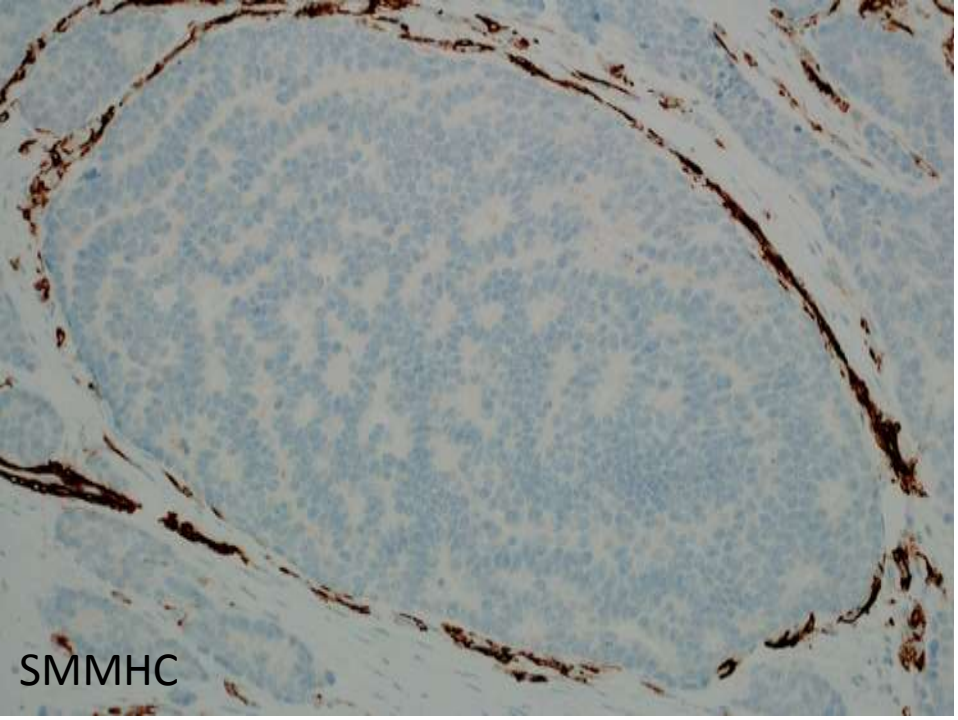
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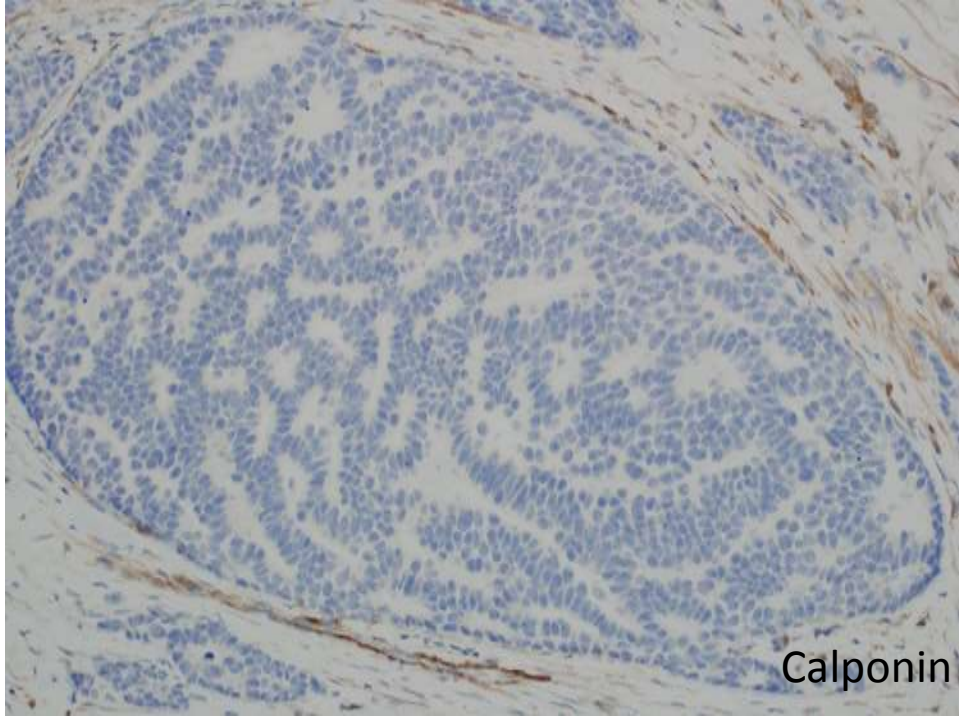
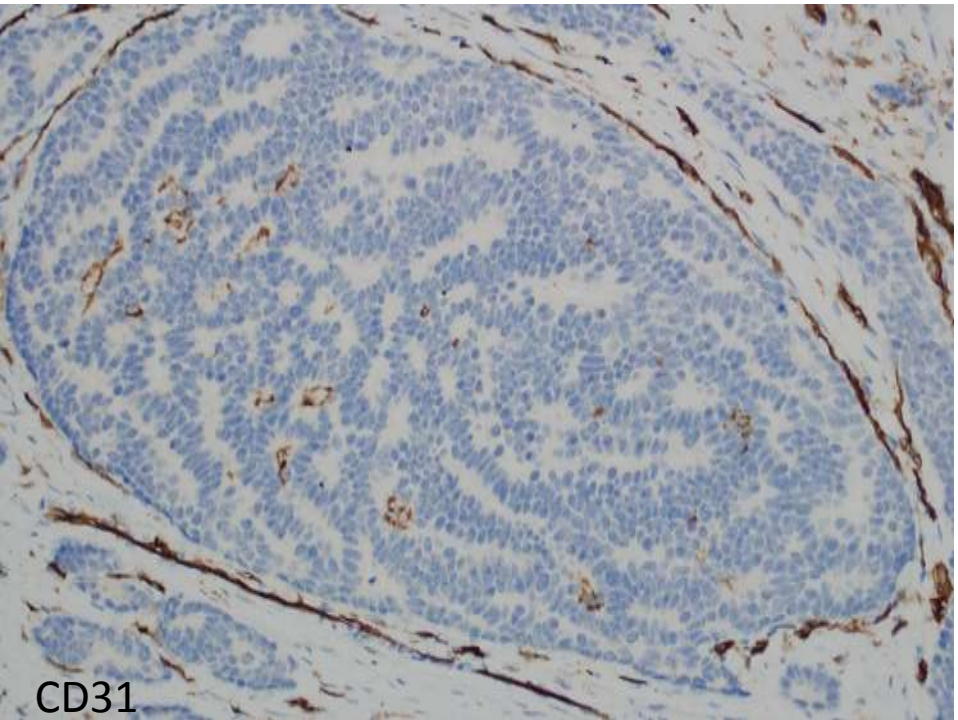
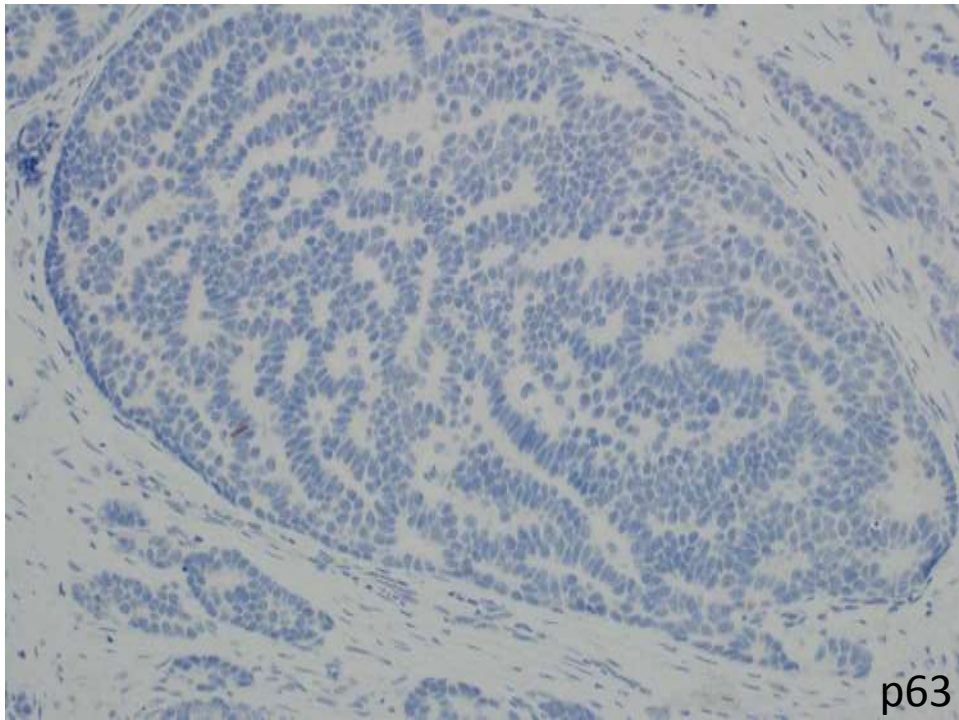

Calponin

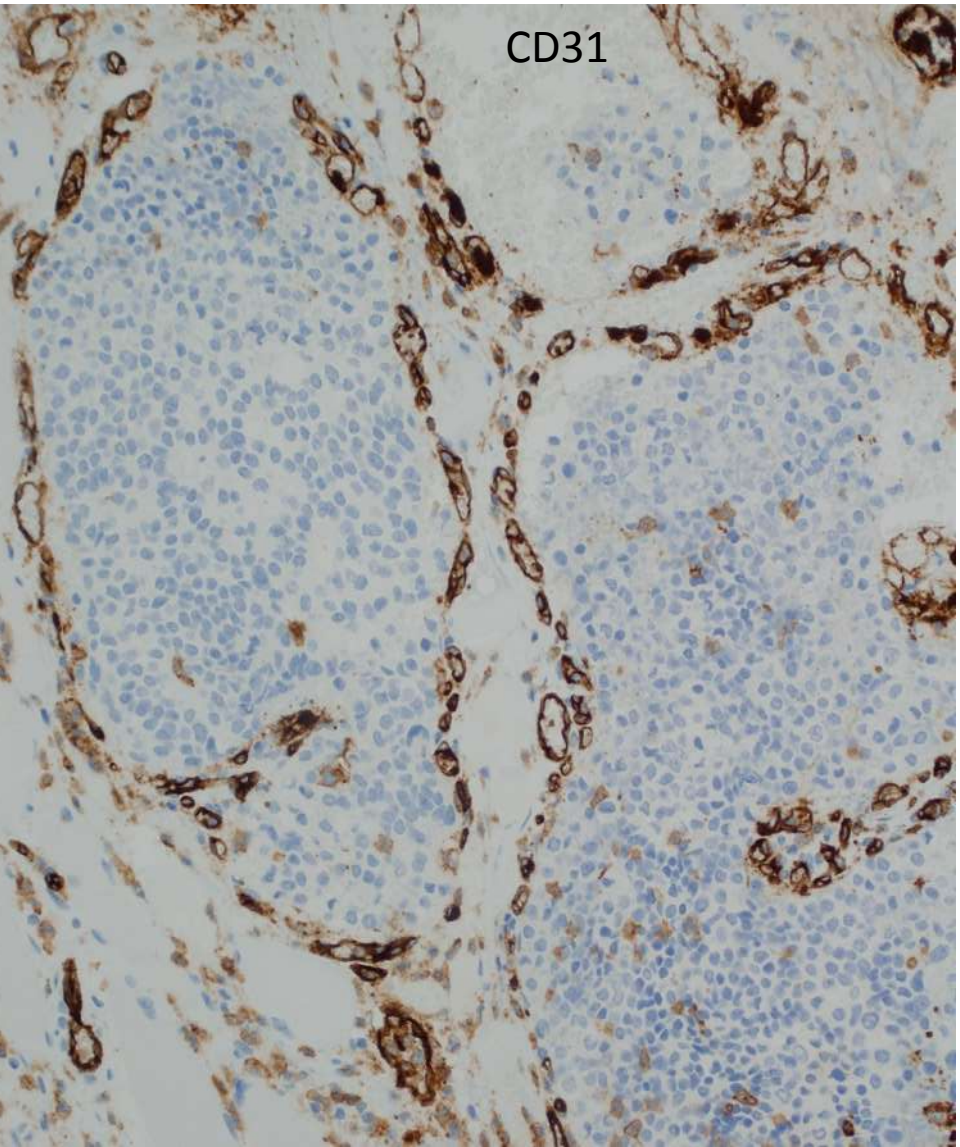

CD31

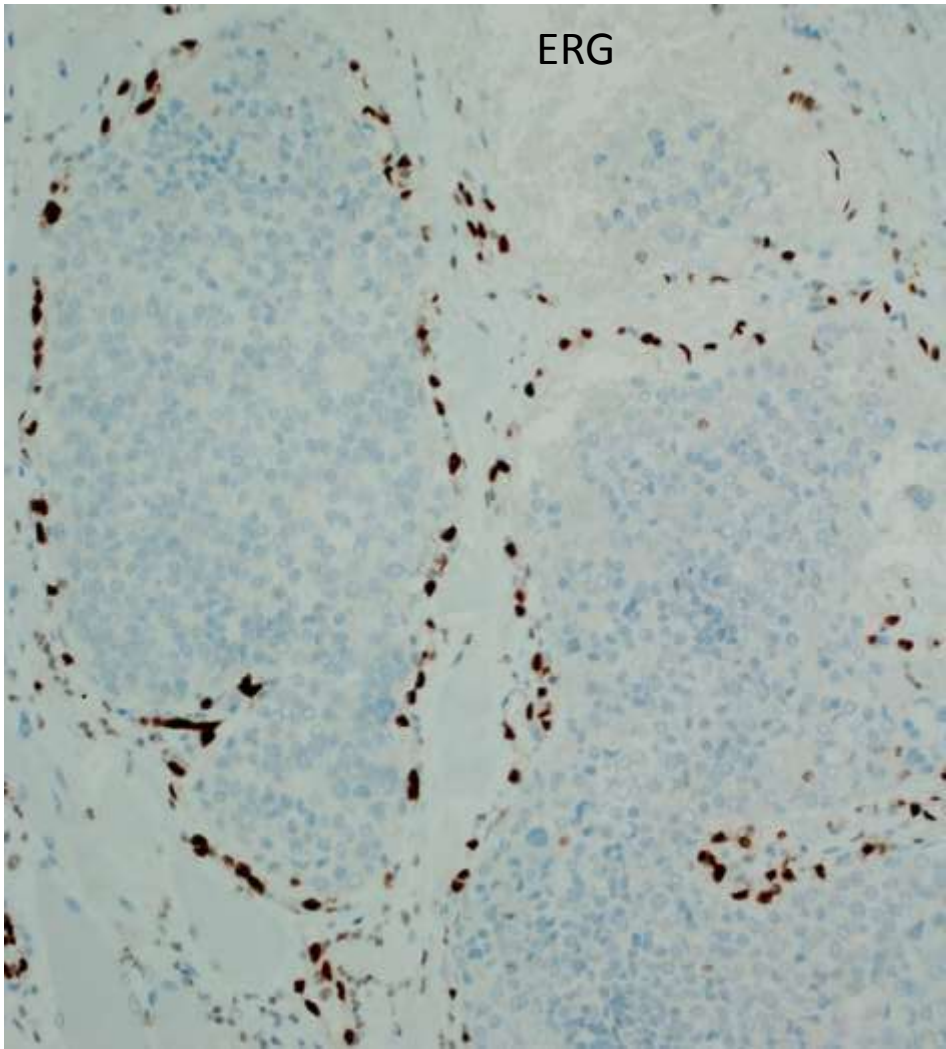

p63

Diagnosis

- Invasive ductal carcinoma
- Ductal carcinoma in situ, focal
  - DCIS involving papilloma

Different case





Immunohistochemical Distinction of Invasive From Noninvasive Breast Lesions

A Comparative Study of p63 Versus Calponin and Smooth Muscle Myosin Heavy Chain

Am J Surg Pathol 27(1): 82–90, 2003.

Robert W. Werling, M.D., Harry Hwang, M.D., Hadi Yaziji, M.D., and Allen M. Gown, M.D.

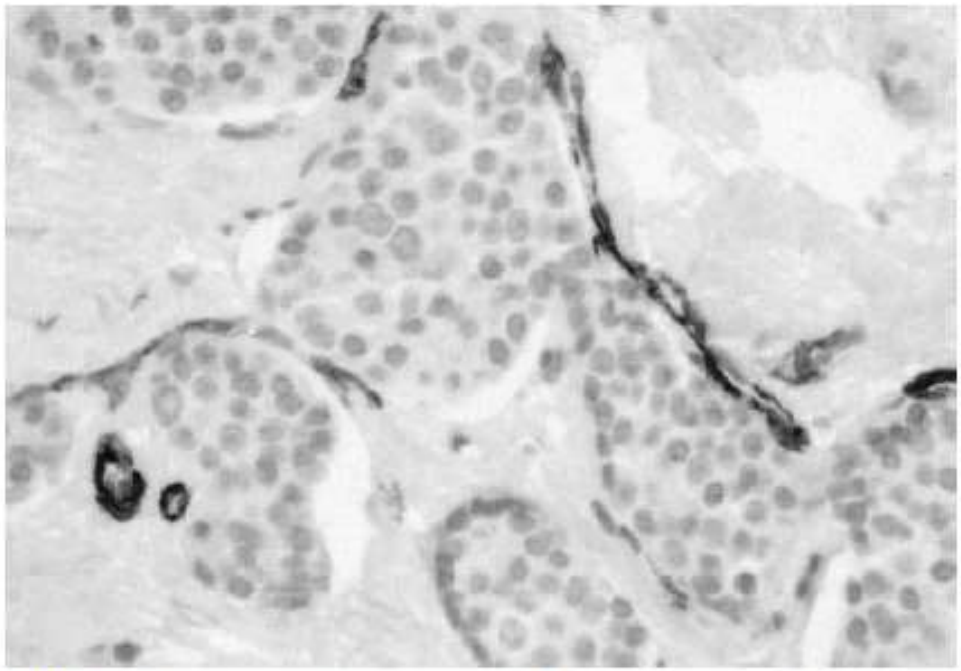
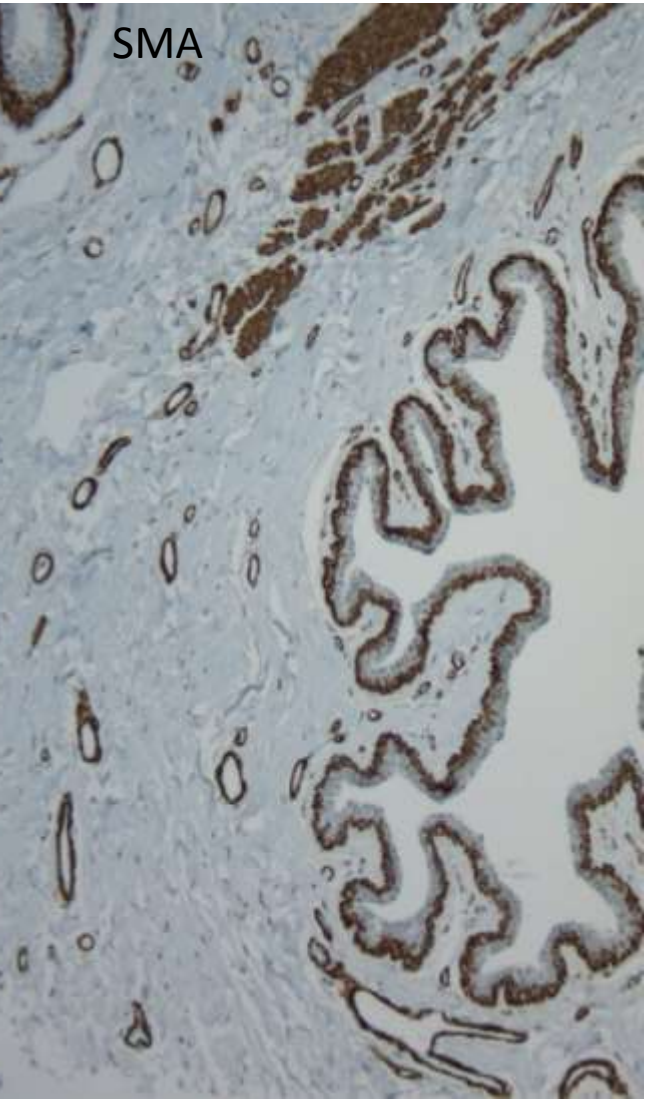
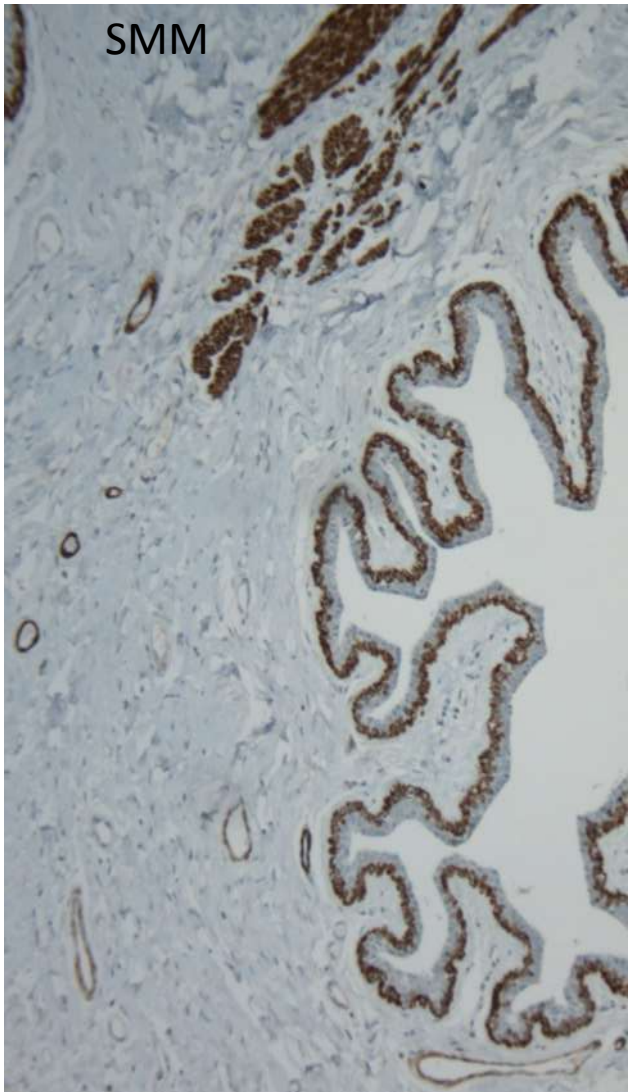


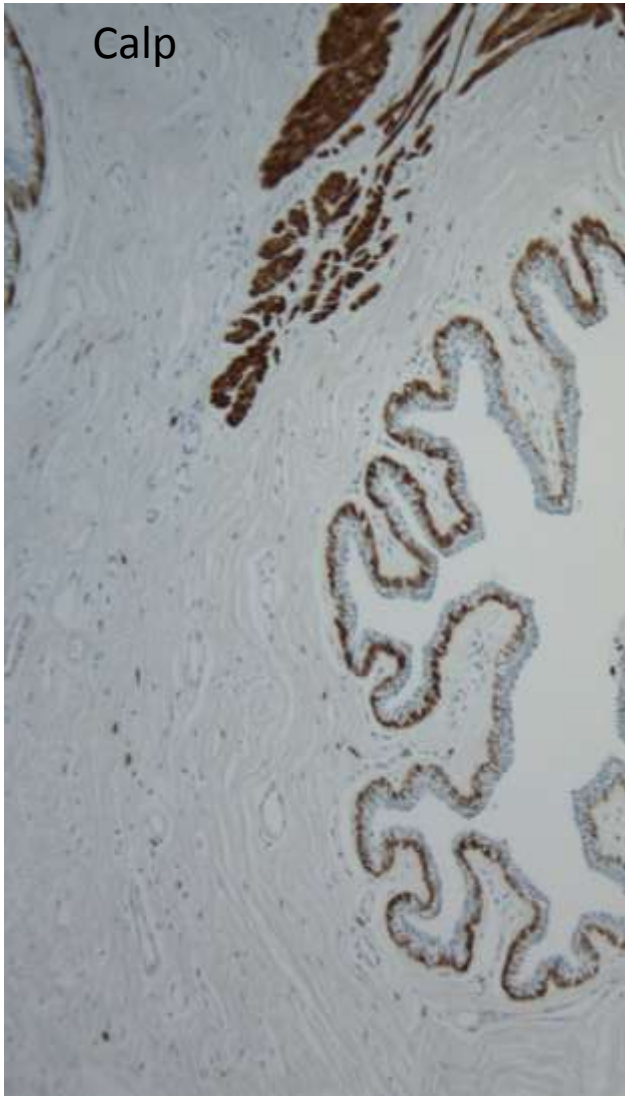
FIG. 4. Nests of infiltrating ductal carcinoma with closely apposed small vessels (upper right), which react with antibodies to SMM-HC, in a pattern that can simulate the myoepithelium present in DCIS. p63 immunostains in this case were negative (not shown).

"We also identified a subset of cases in which vascular smooth muscle cells, positive for expression of SMM-HC and calponin … closely approximated foci of infiltrating ductal carcinoma"

Vessels: SMA>SMM>Calp



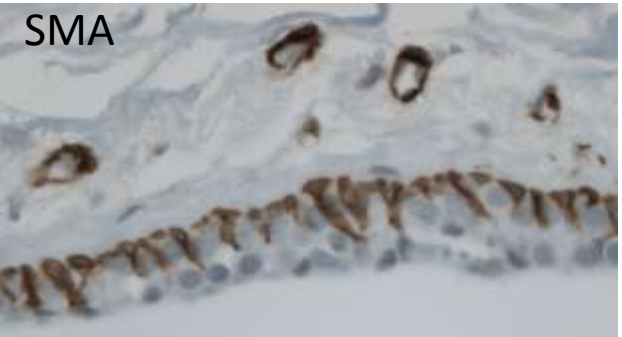


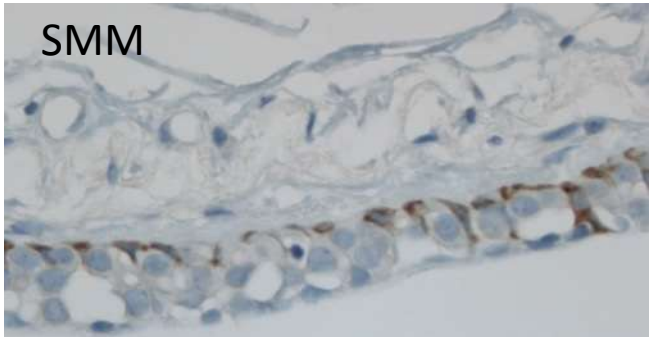


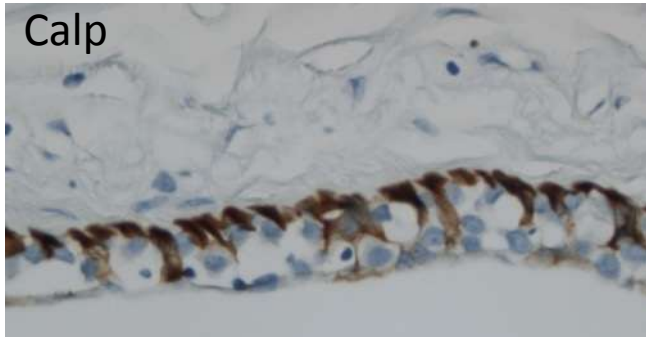
Myoepithelial stains

Protein	Myofibroblast	Vessel	% cases diminished^		Comments
			DCIS	sclerosing	
P63 Nuclear	No	No	13%	9%	Discontinuous
SMM HC	Yes-less	Yes (!)	76%	21%	
Calponin	Yes	Yes	17%	6%	
CK HMW	No	No	30%	32%	CK5 Inconsistent
SMA	Yes-most	Yes-most	1%	0%	
CD10	No	No	34%	15%	Less sensitive
D2-40	No	Lymphatic			

^Hilson, Schnitt & Collins. AJSP. 2010;34:896–900; Hilson, Schnitt & Collins. AJSP. 2009;33:227–2



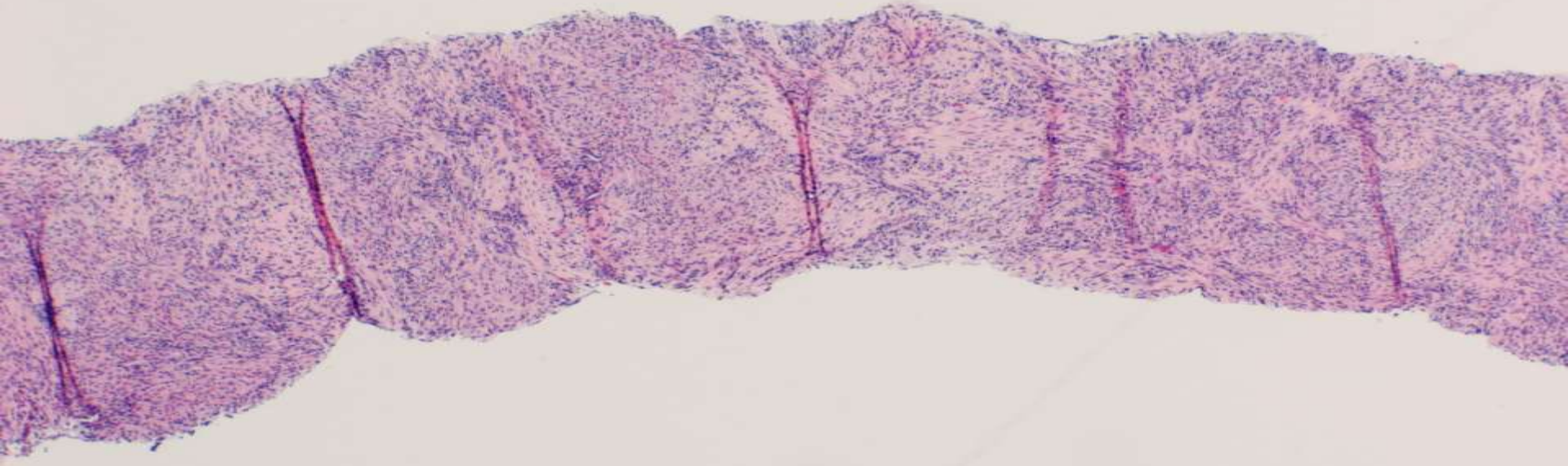


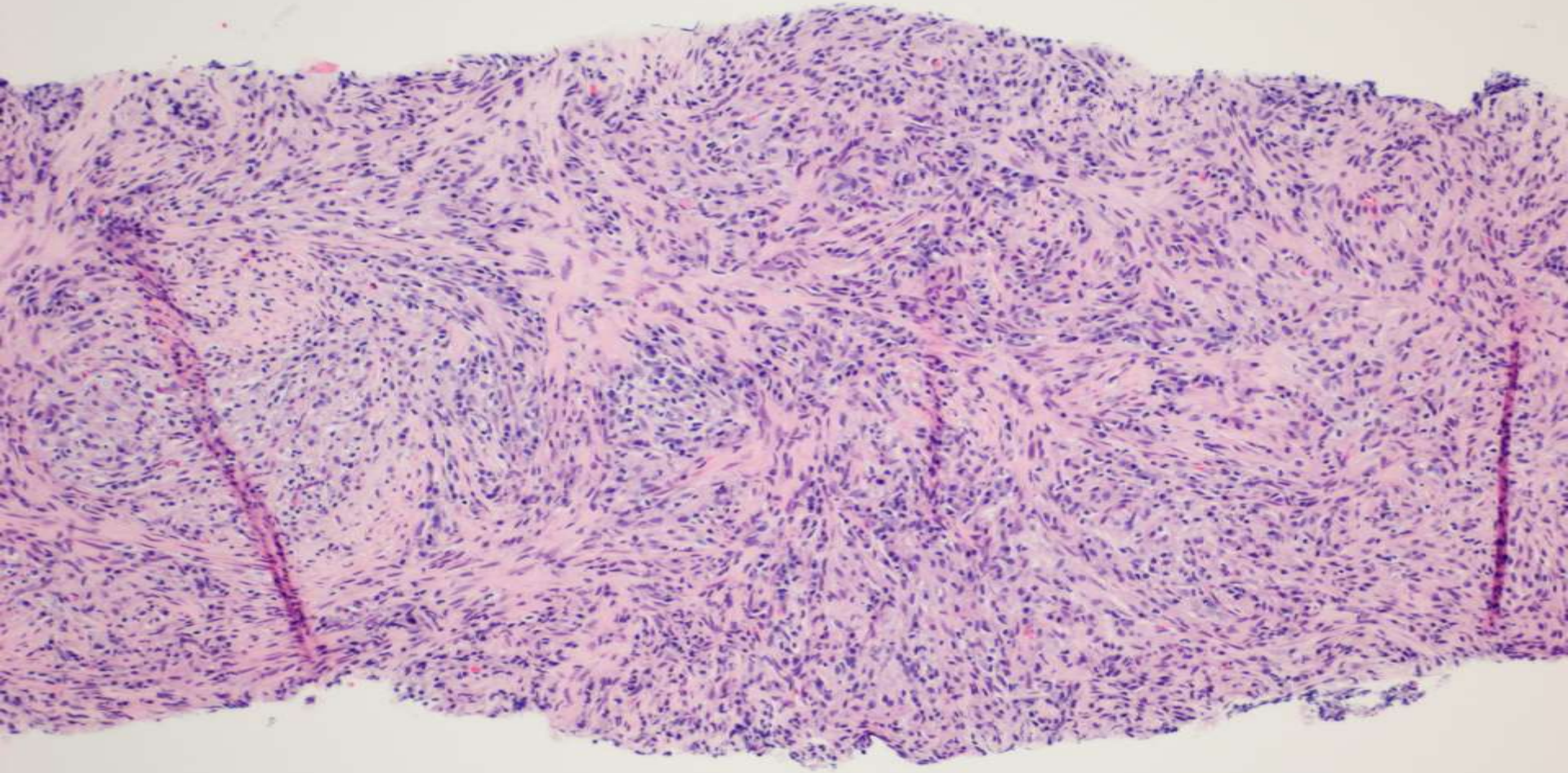


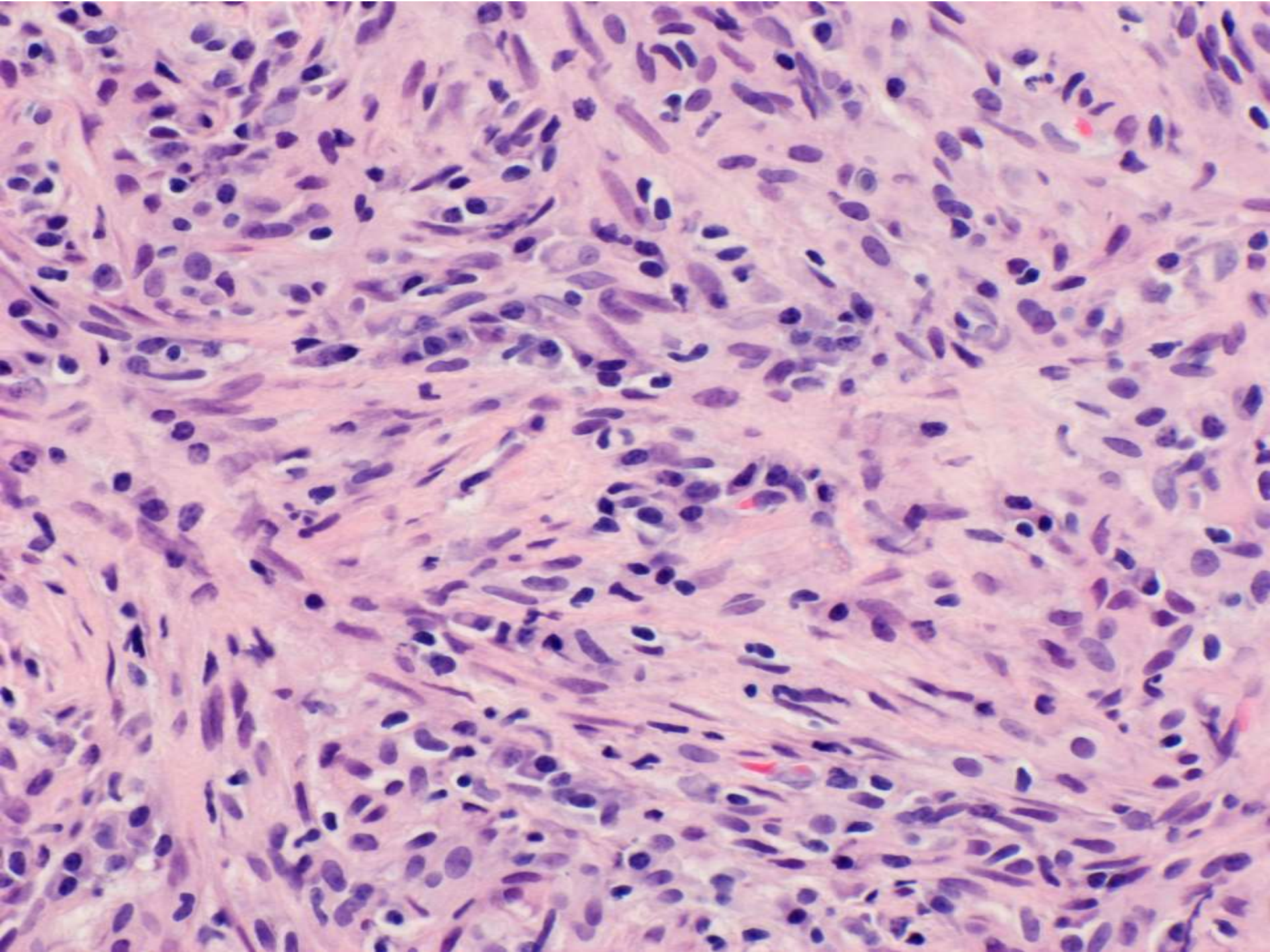
19-0910

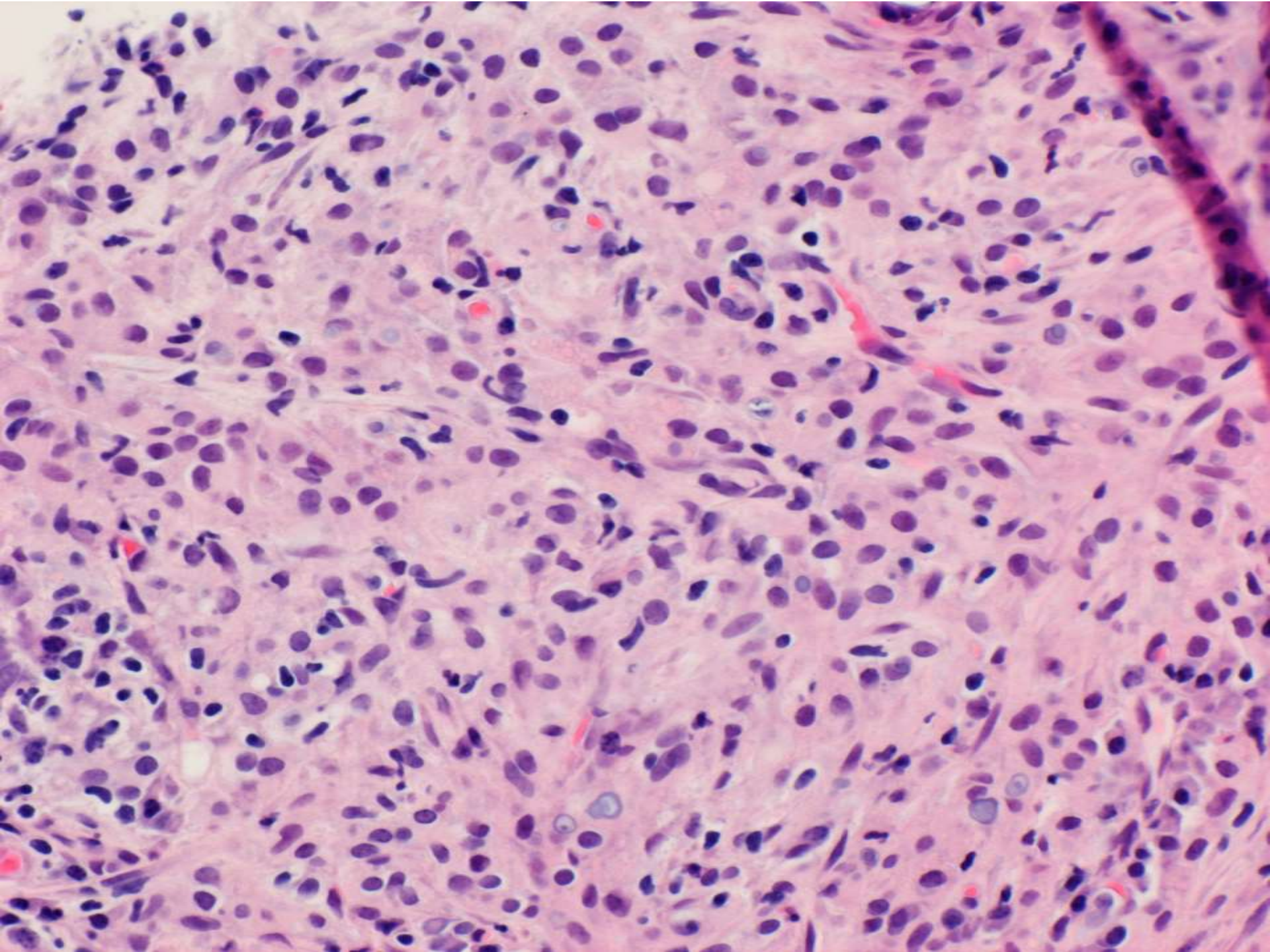
Nicholas Ladwig/Charles Zaloudek/Jeff Simko

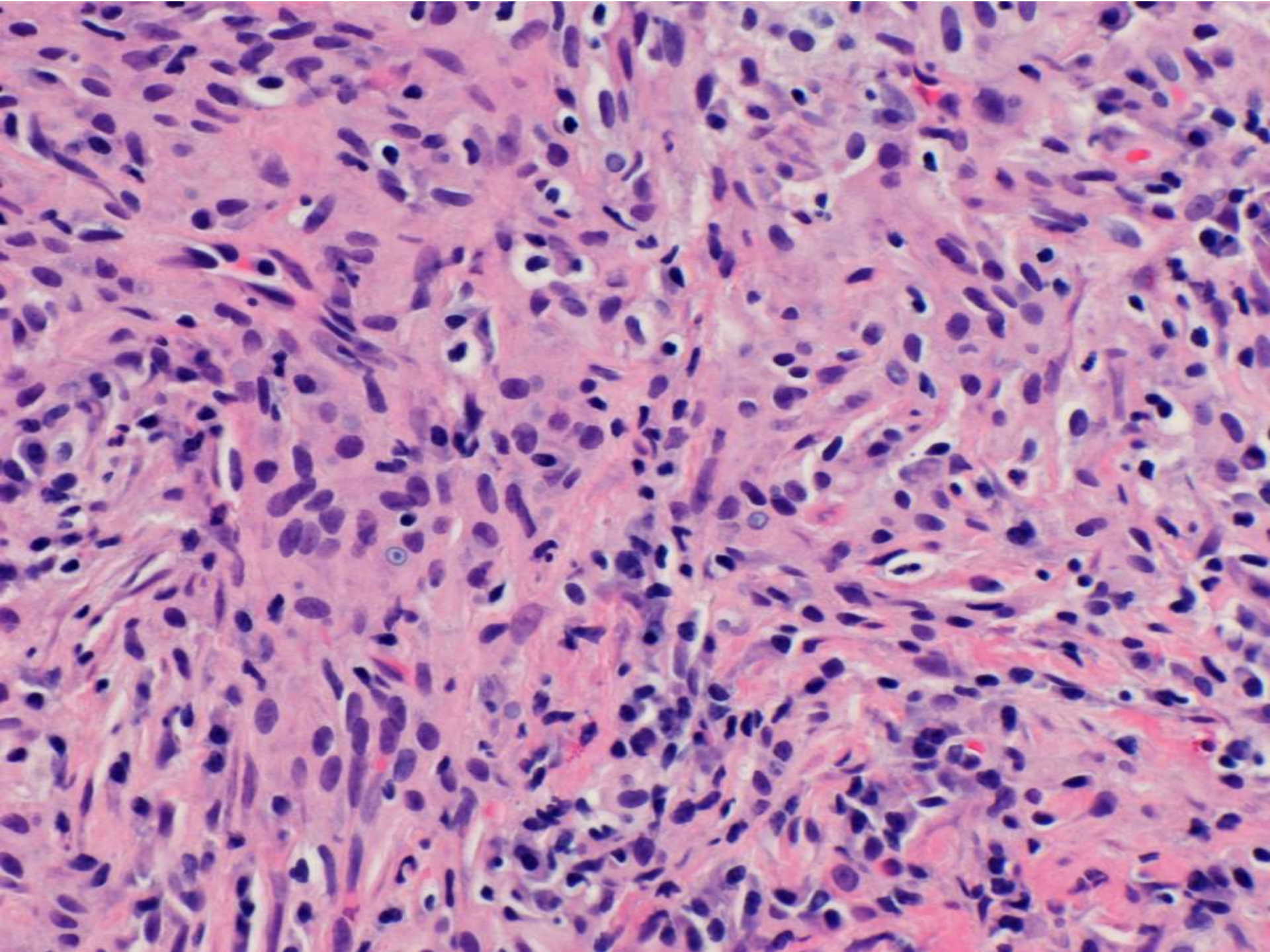
64-year-old male with elevated PSA. Prostate biopsy performed.

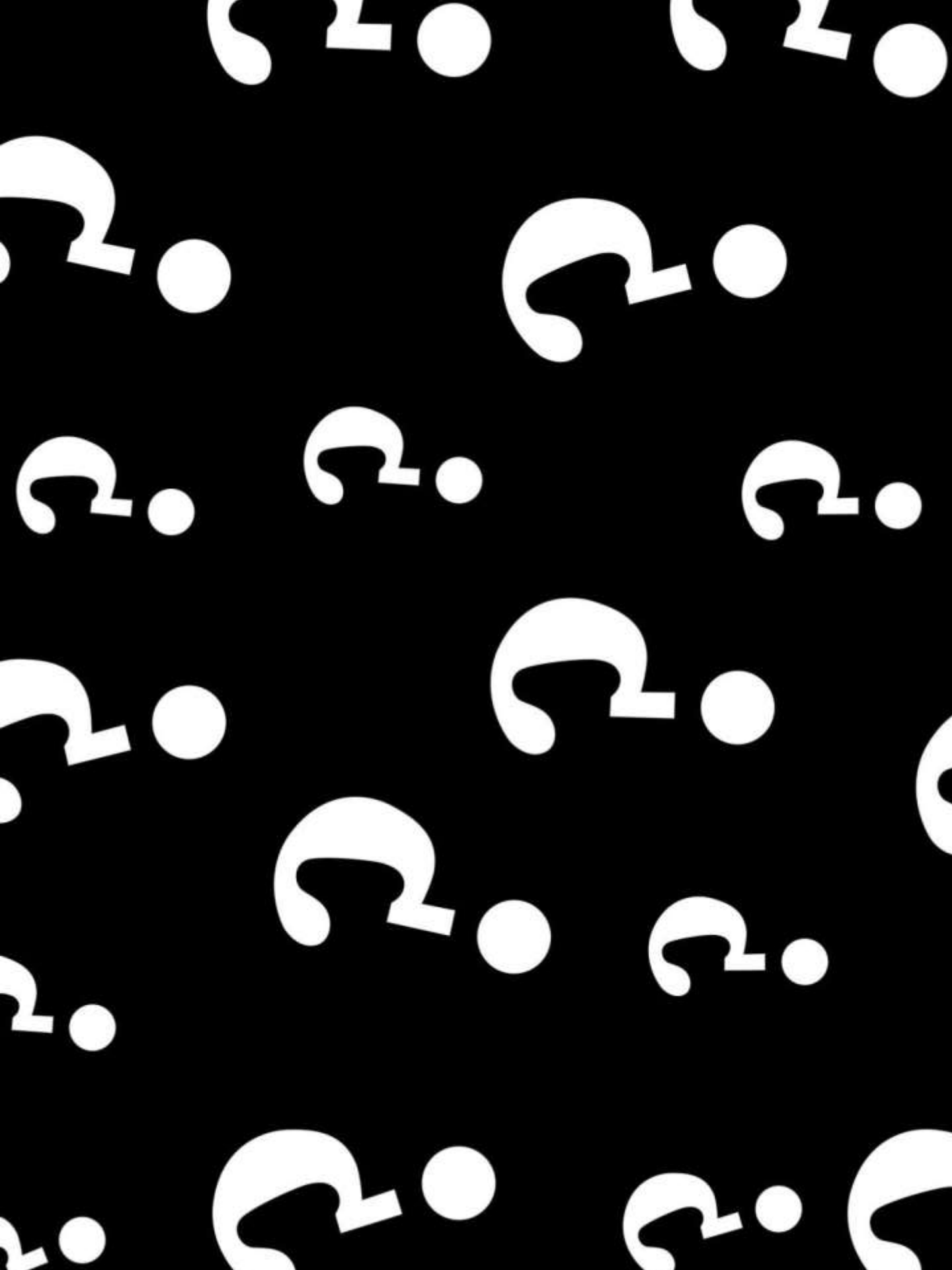








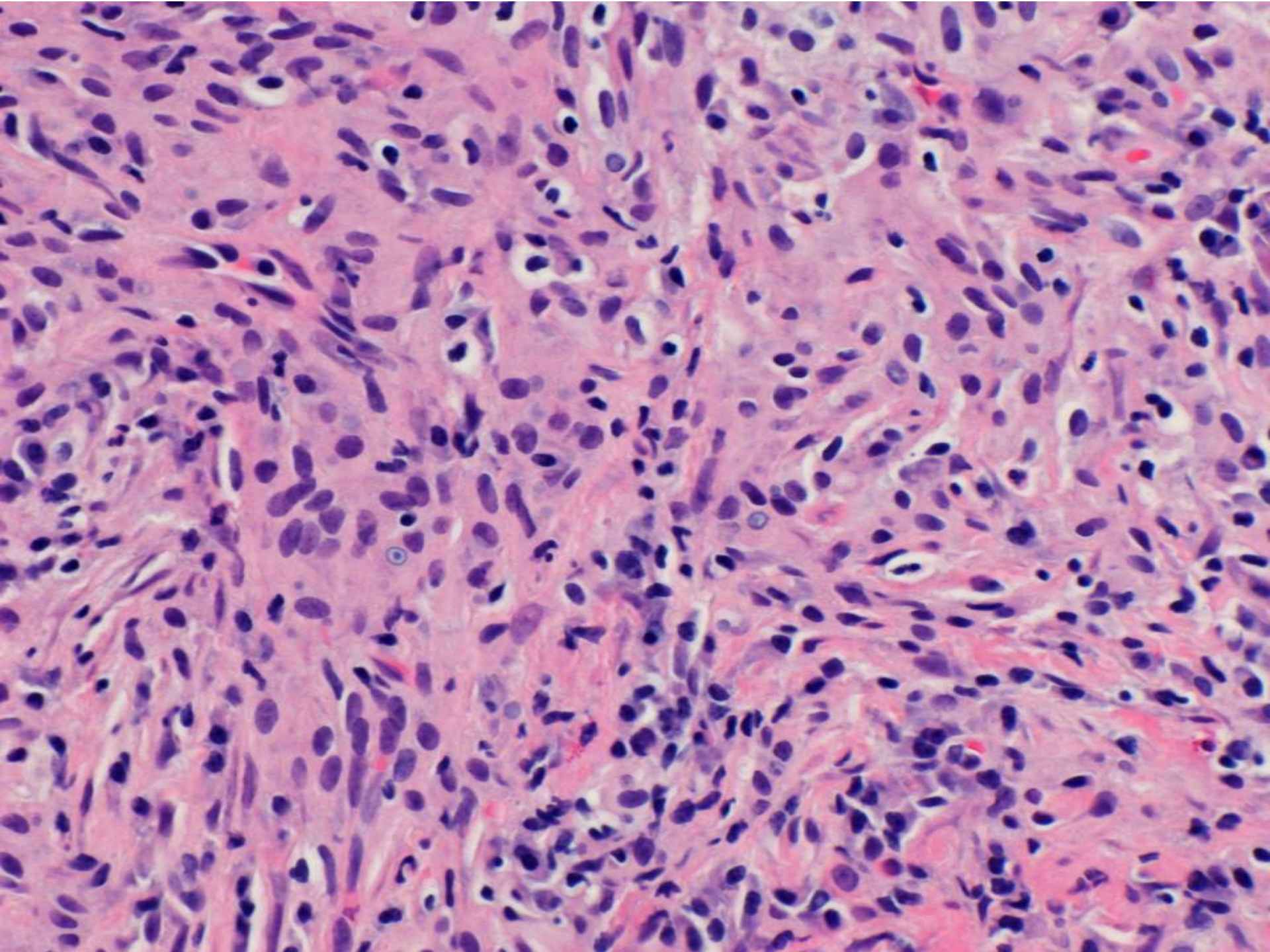




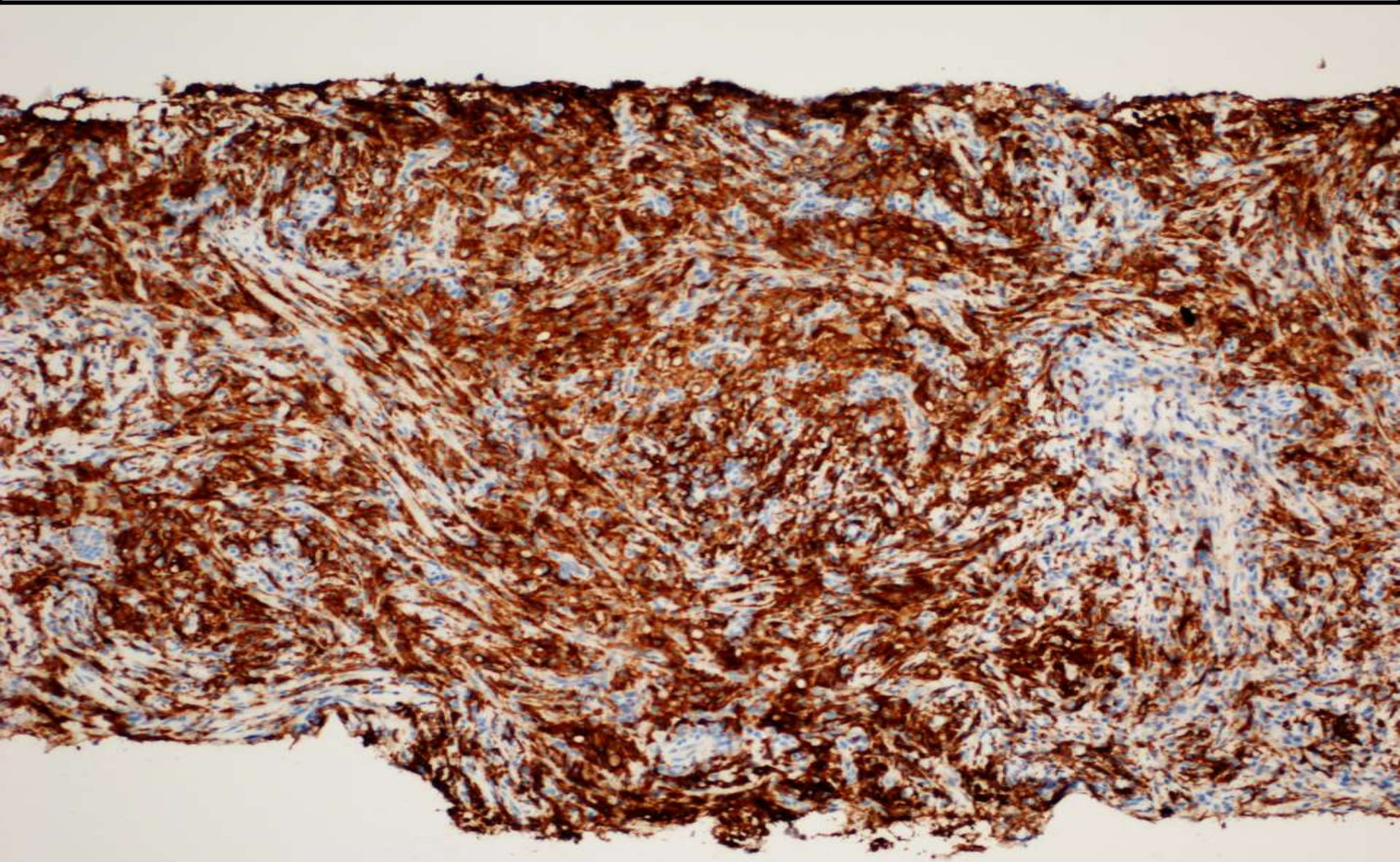
South Bay Case Discussion
Case 19-0910

Nicholas Ladwig / Charles Zaloudek / Jeff Simko
Sep 9, 2019

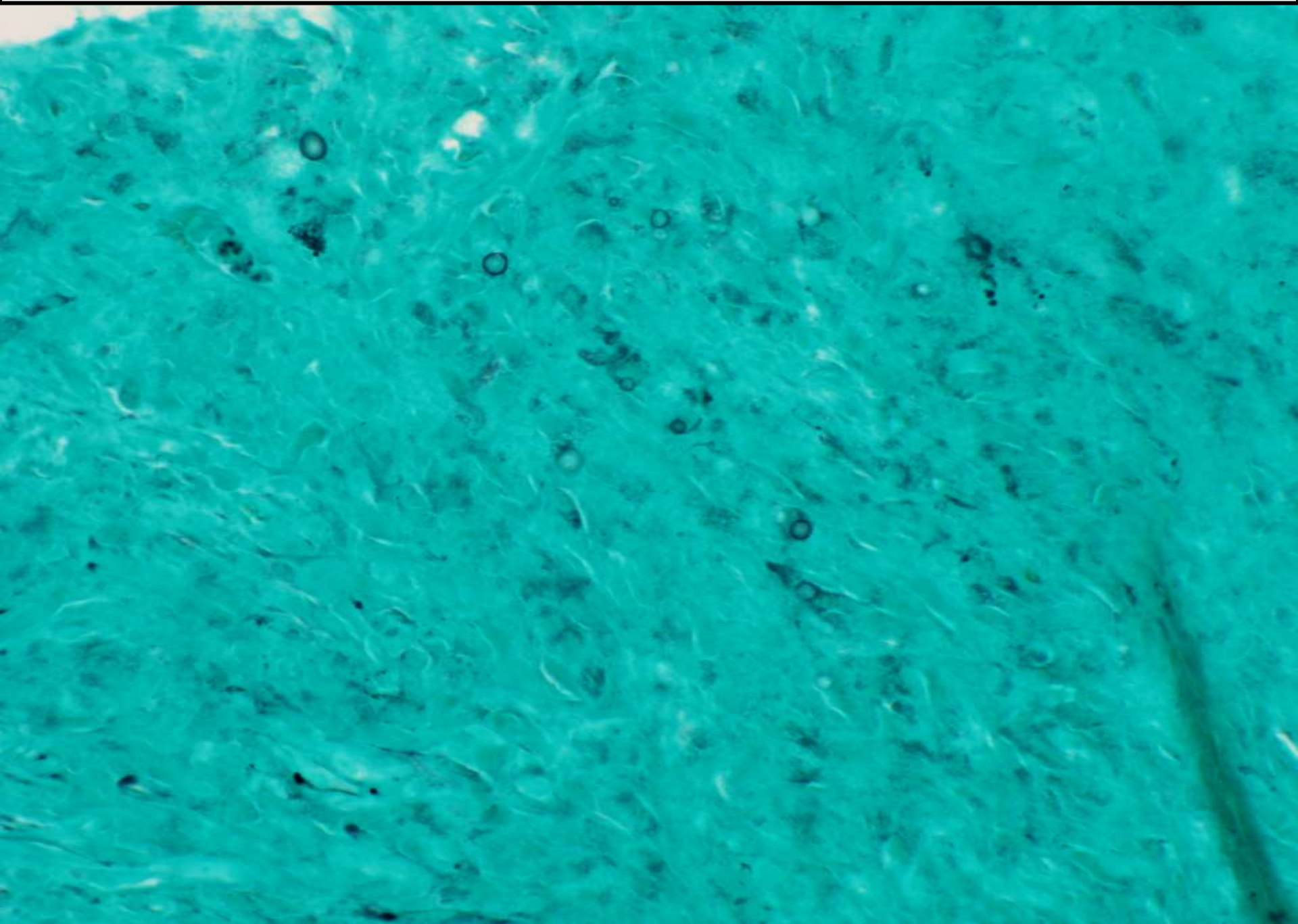
(Case presented with approval from Dr. Kenneth Hadler)



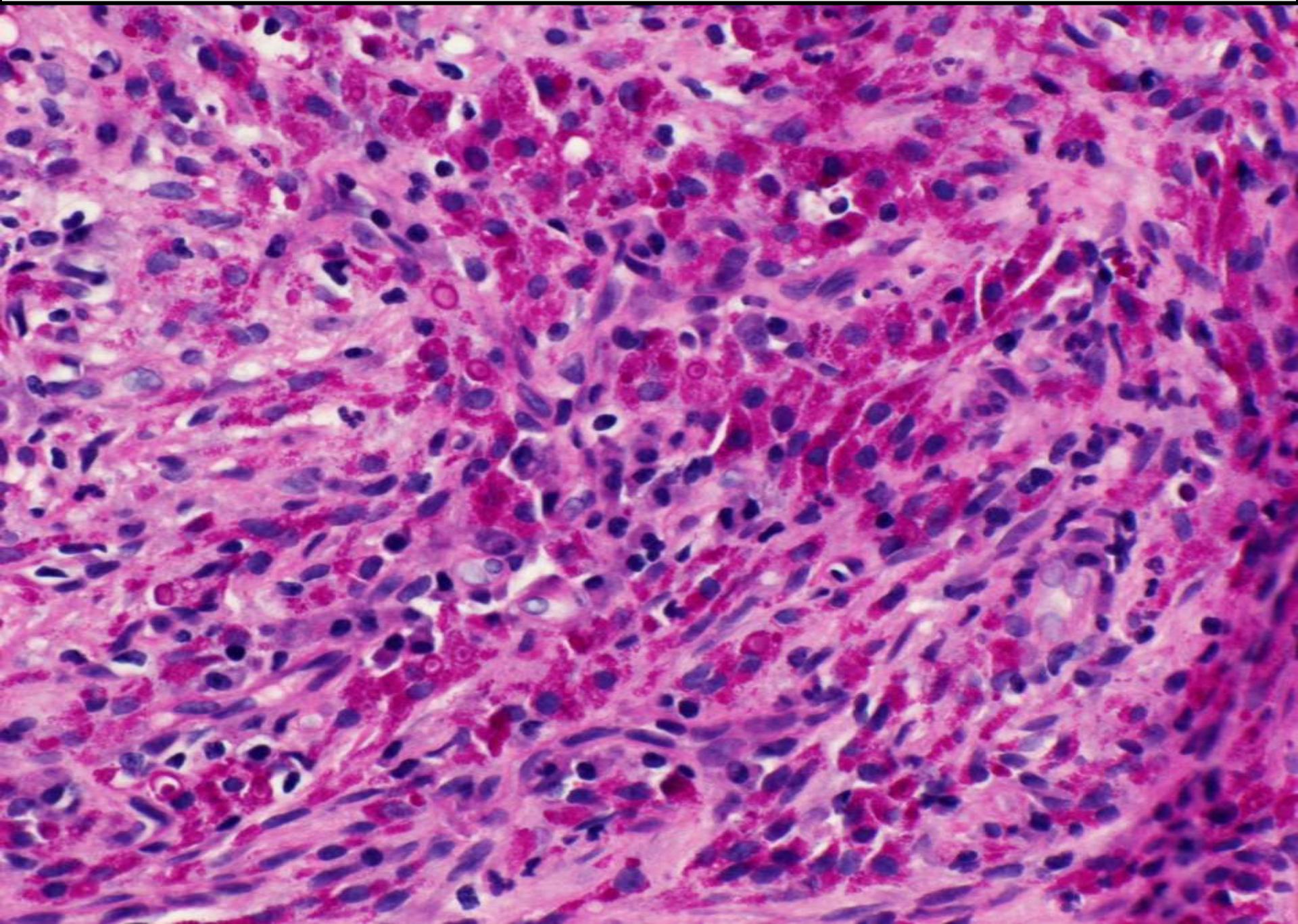
CD163



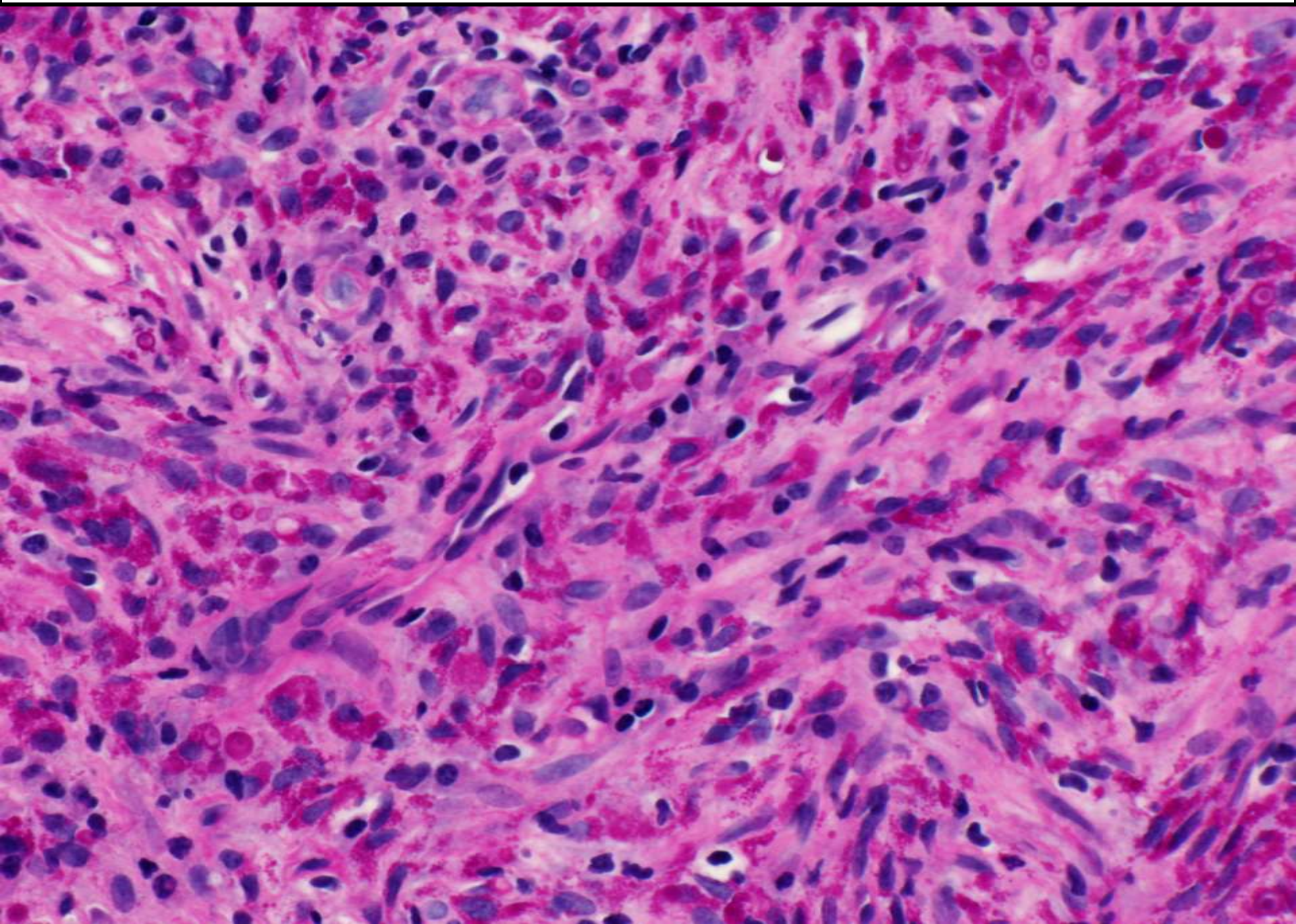
GMS



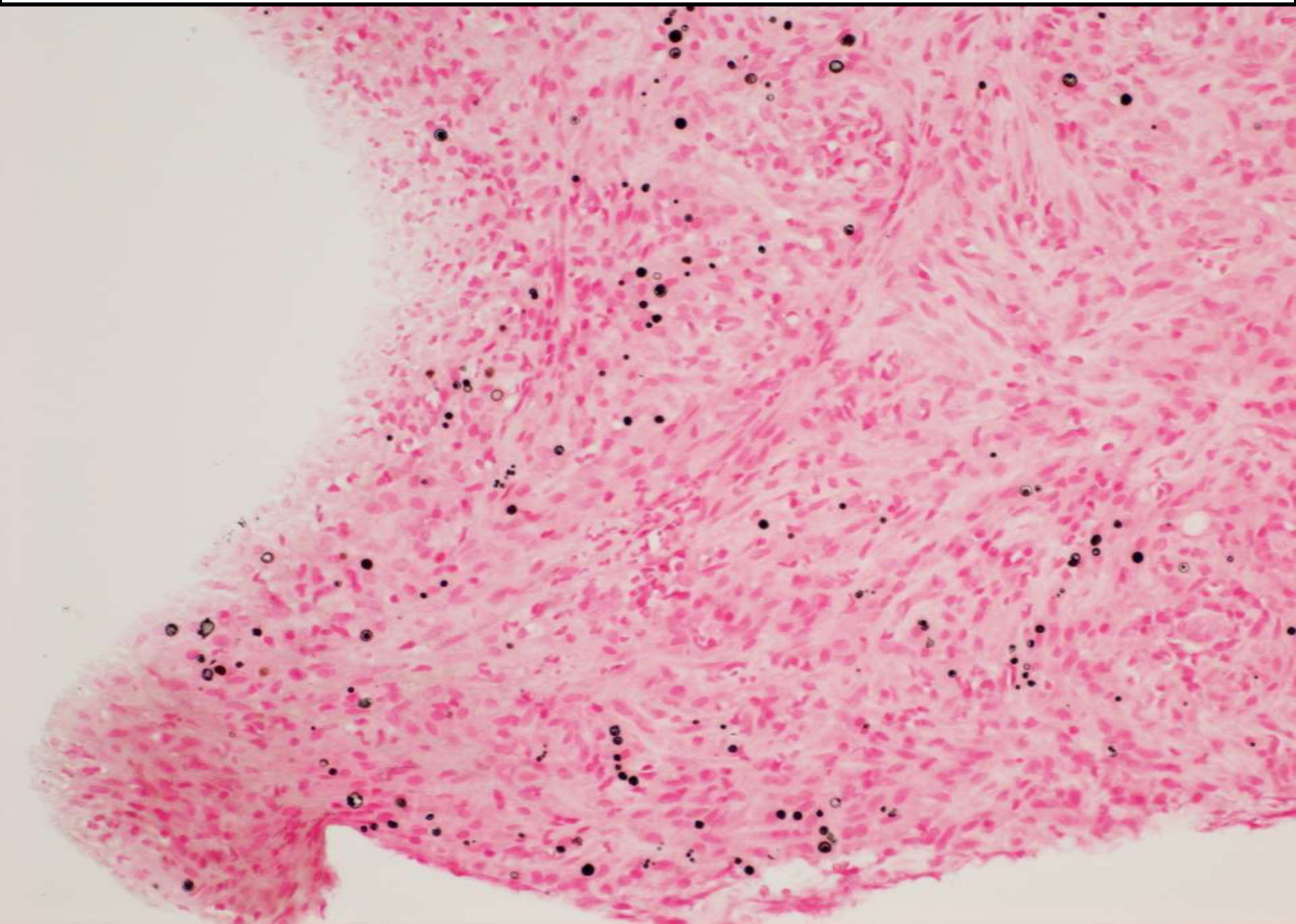
PAS-D



PAS-D



Von Kossa



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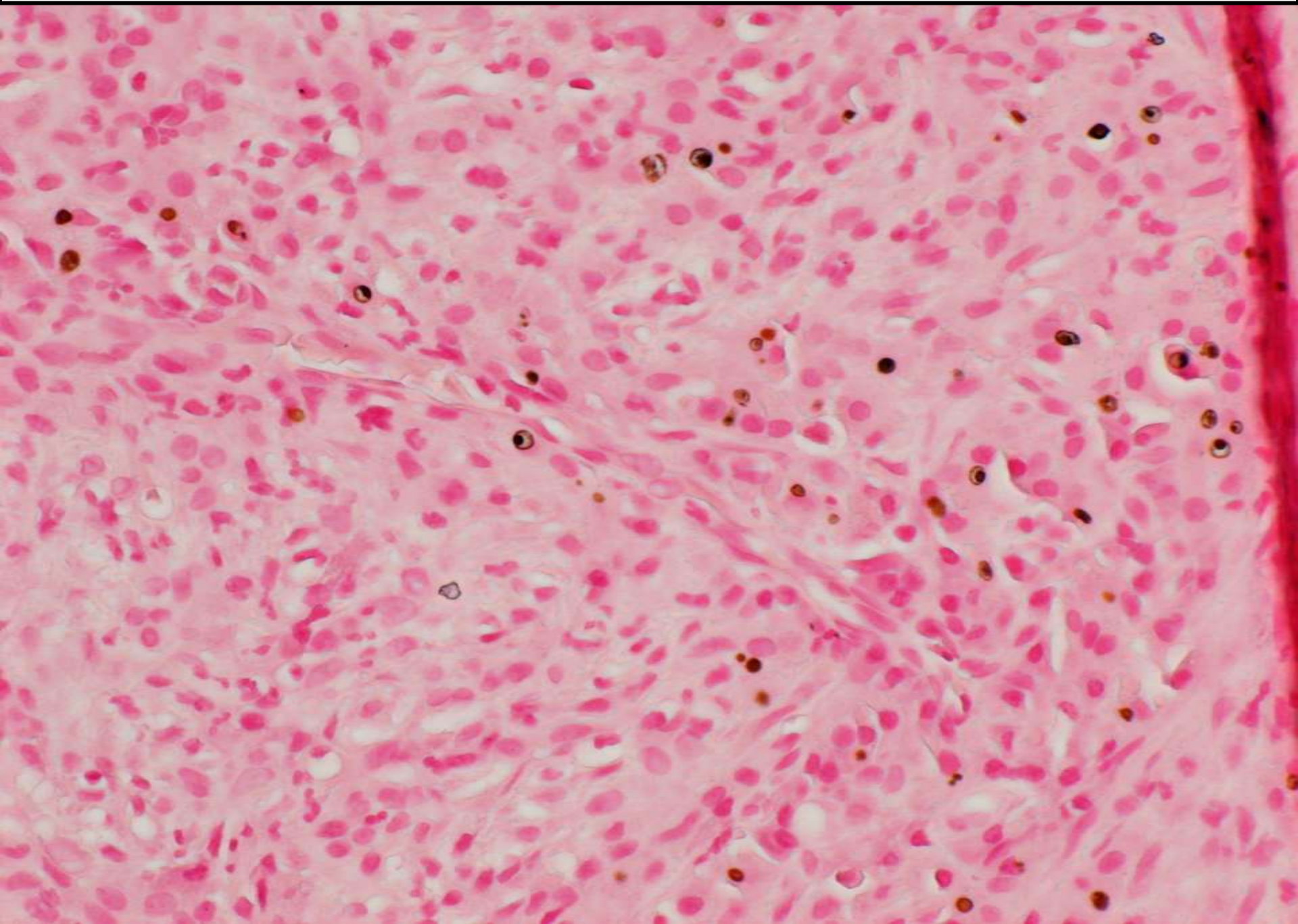
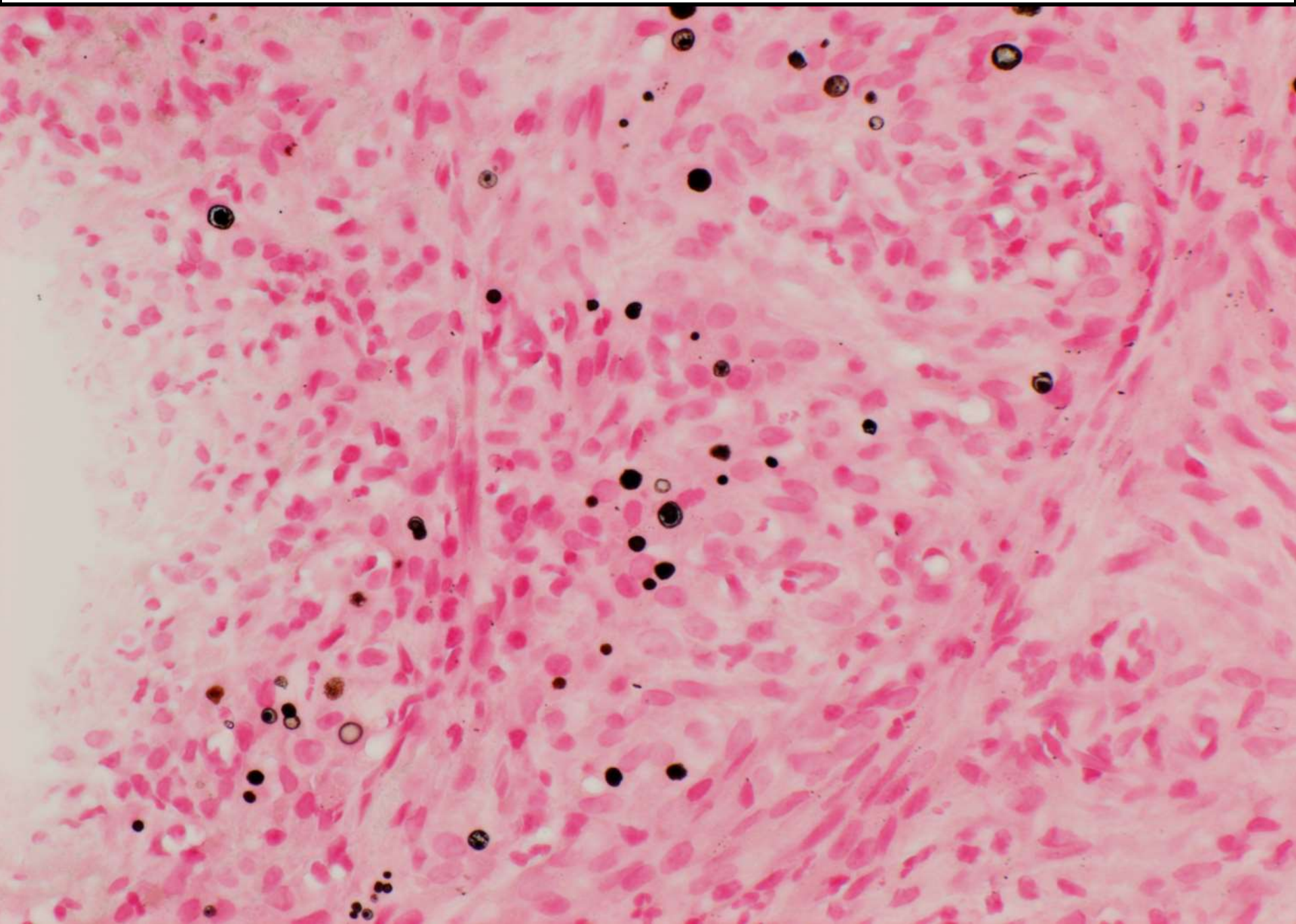


Von Kossa



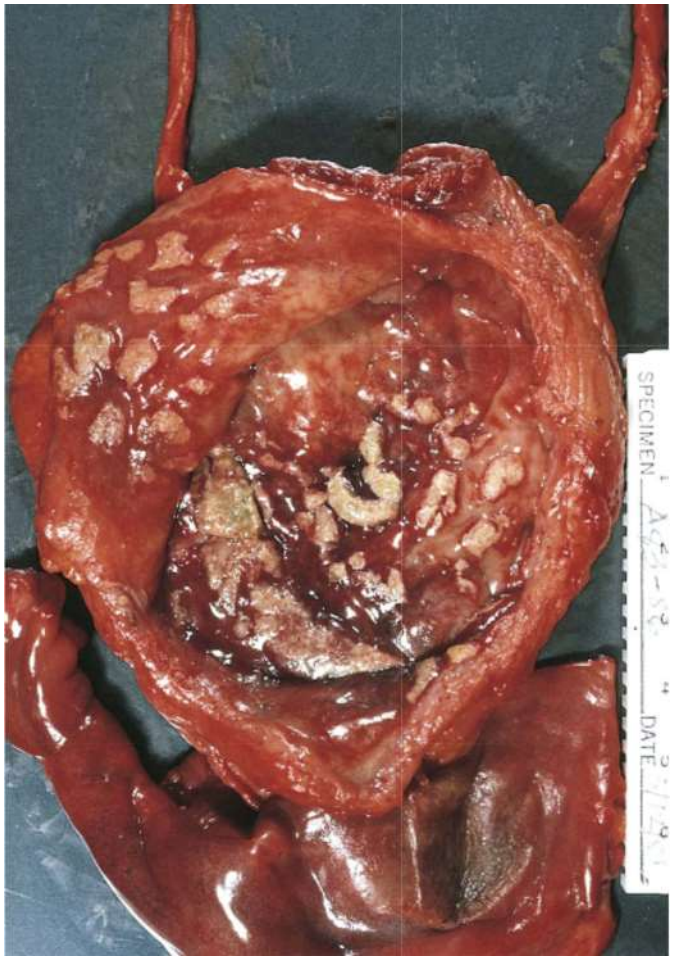
Final Diagnosis:

Malakoplakia of the prostate

Malakoplakia - General

- Malakoplakia:
  - "Malakos" = soft
  - "Plakos" = plaques

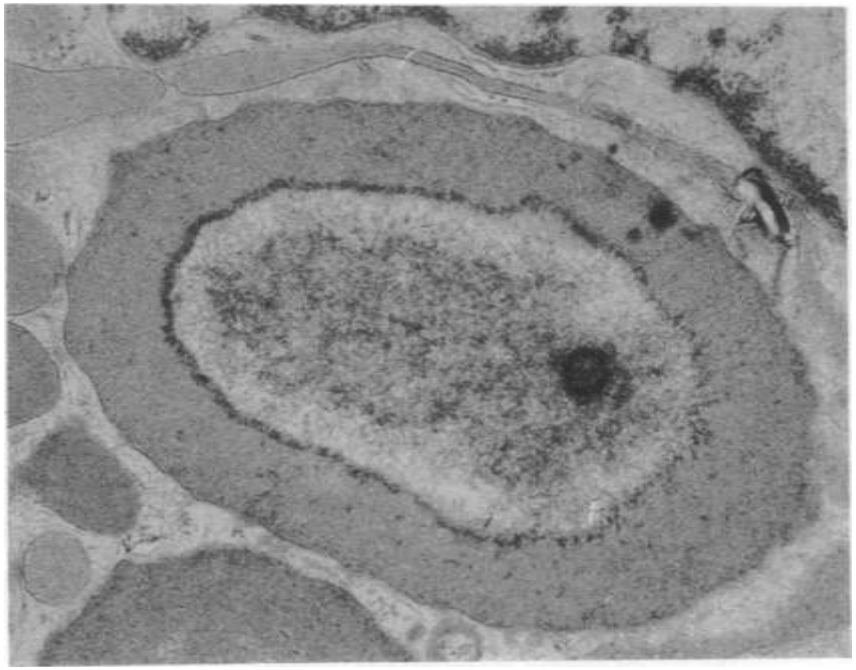
- Sites on involvement:
  - GU organs most common (F>M)
    - Urinary bladder: >70%
    - Rarely prostate
  - GI tract
  - Can involve any site



Source: Robbins and Cotran pathologic basis of disease (Ninth edition.)

Malakoplakia - Mechanism

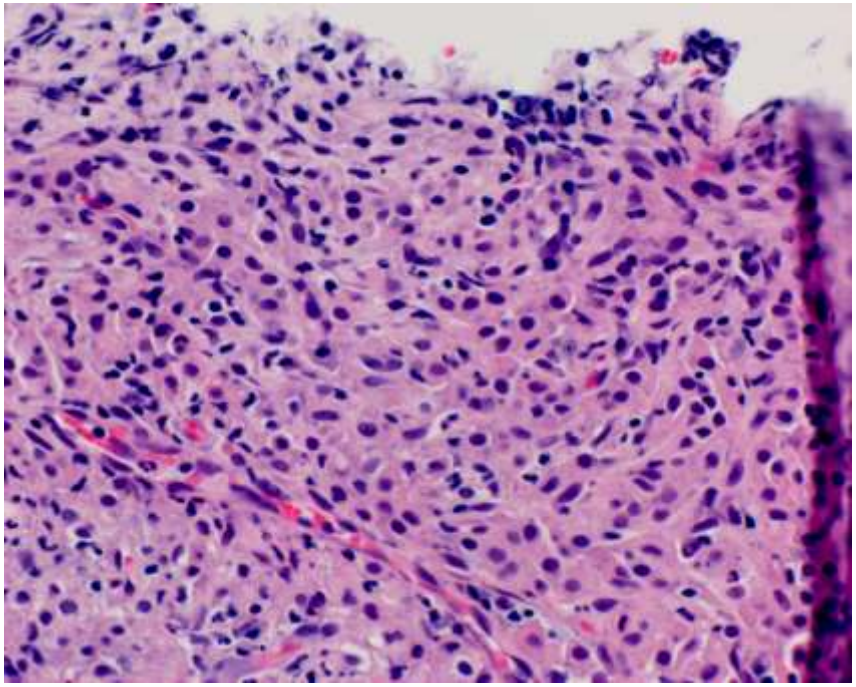
- Histiocyte disorder
  - Defective phagocytosis or elimination of bacteria
    - E. Coli & Klebsiella
  - Chronic inflammatory state leads to pathology
  - Lysosomes become mineralized
- Three stages:
  1. Inflammatory stage
  2. Classical stage
  3. Fibrotic stage



Source: Charney et al. Arch dis child. 1985

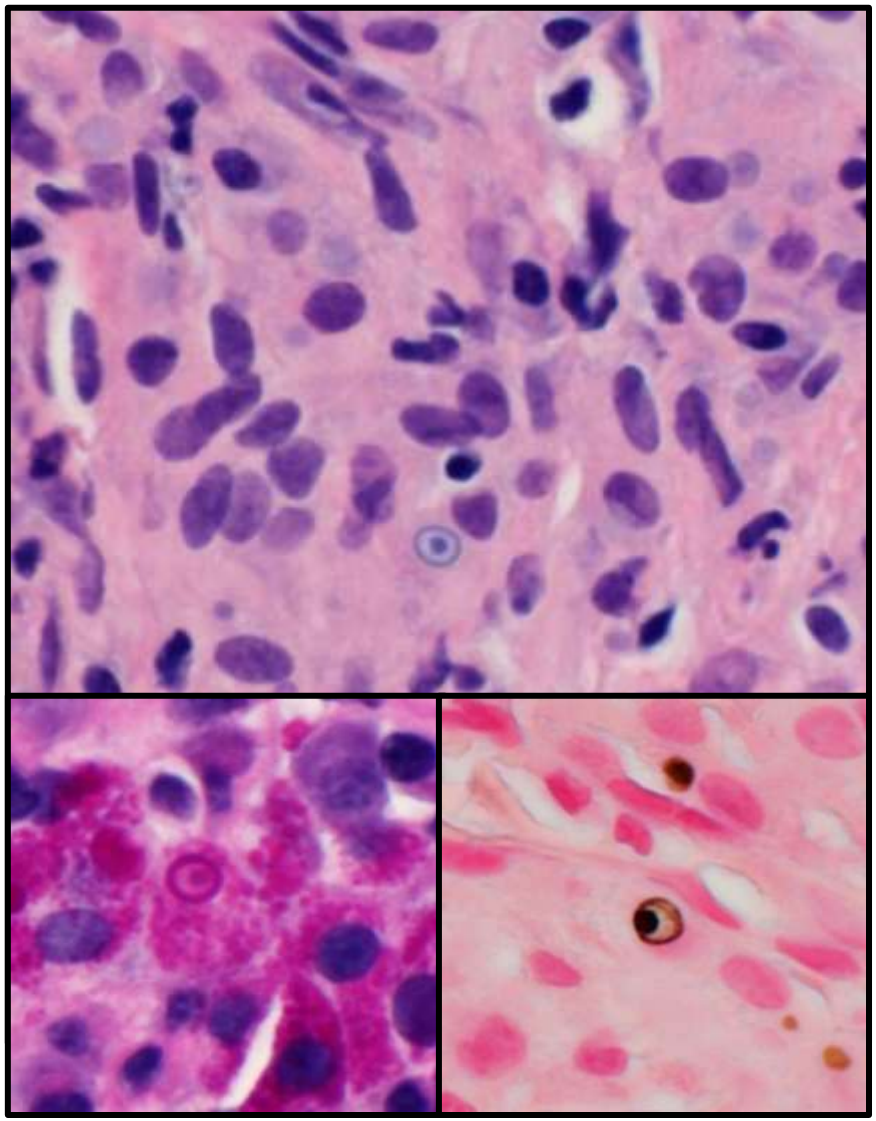
Malakoplakia - Diagnosis

- Sea of pink histiocytes
  - <10% of granulomatous prostatitis is due to malakoplakia
- Chronic inflammation



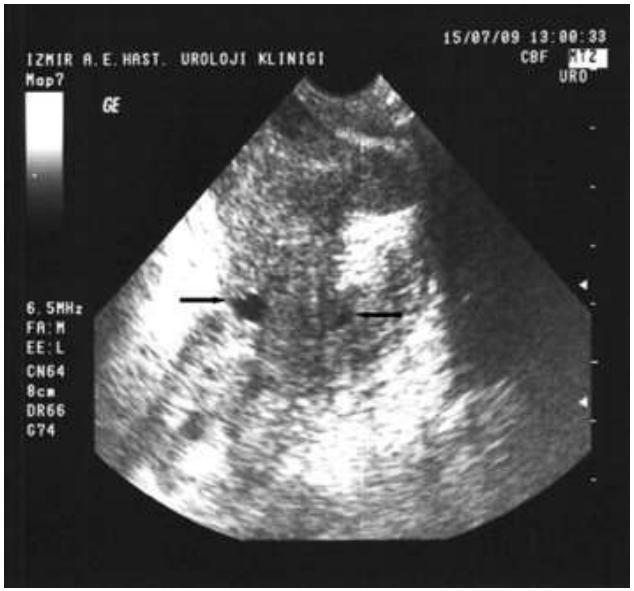
Malakoplakia - Diagnosis

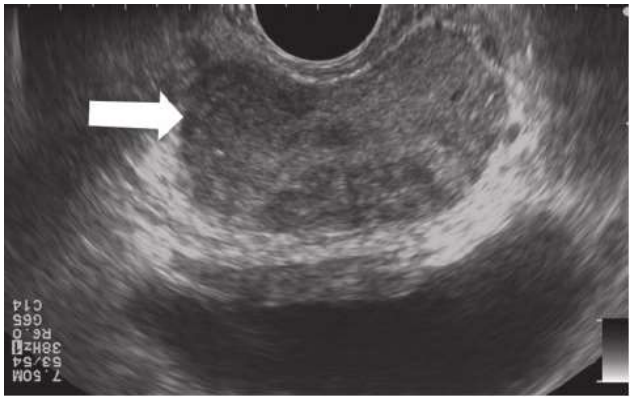
- Sea of pink histiocytes
- Chronic inflammation
- Michaelis-Gutmann bodies:
  - Targetoid intracytoplasmic inclusions
  - PAS-D (+)
  - Von-kossa (+)
  - Iron (+)
  - GMS (-)



Malakoplakia mimics malignancy

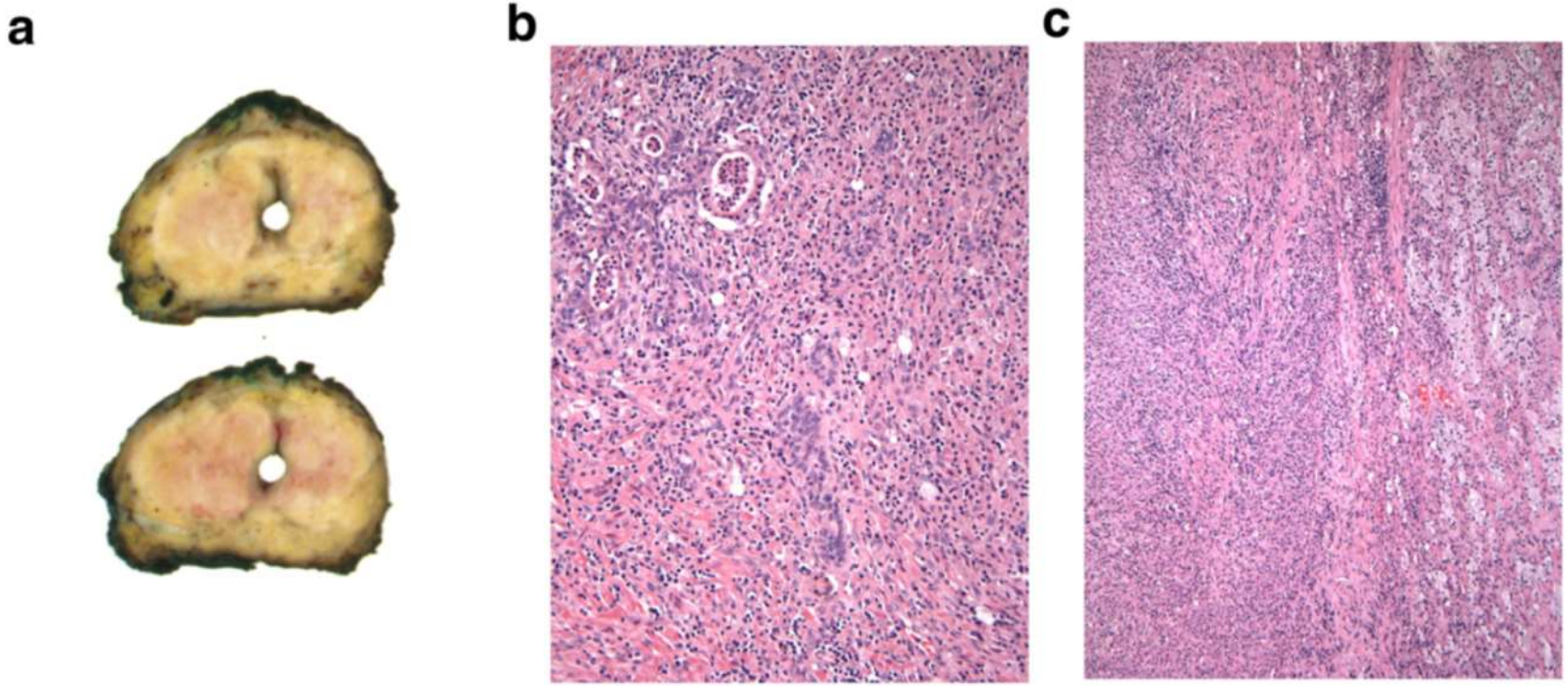
- Prostatic malakoplakia
  - 50+ y/o M
  - Elevated PSA
  - LUTS symptoms
  - Firm nodules/masses
  - Hypoechoic on US
  - MRI cannot resolve
  - Requires biopsy for diagnosis
  - Mass lesion may not resolve after antibiotics
  - Additional biopsies may exacerbate disease!





Source: Kitzing et al. Radiographics. 2016

Malakoplakia can occur with malignancy



Source: Medlicott et al. Ann Diag Pathol. 2016

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4. Kitzing YX, Prando A, Varol C, et al. Benign Conditions That Mimic Prostate Carcinoma: MR Imaging Features with Histopathologic Correlation. *Radiographics.* 2016;36:162-175.
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7. Mohan H, Bal A, Punia RP, et al. Granulomatous prostatitis--an infrequent diagnosis. *Int J Urol.* 2005;12:474-478.
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