

## **MARCH 2021 DIAGNOSIS LIST**

21-0301: primary meningeal melanoma (brain; neuropath)

21-0302: embolic cardiac myxoma (brain; neuropath and soft tissue path)

21-0303: consistent with synthetic marijuana associated lung injury (lung; nonneoplastic lung path)

21-0304: ectopic prostate tissue (cervix; GYN path)

21-0305: pseudomembranous collagenous colitis (colon; GI path)

21-0306: clear cell meningioma (dura; neuropath)

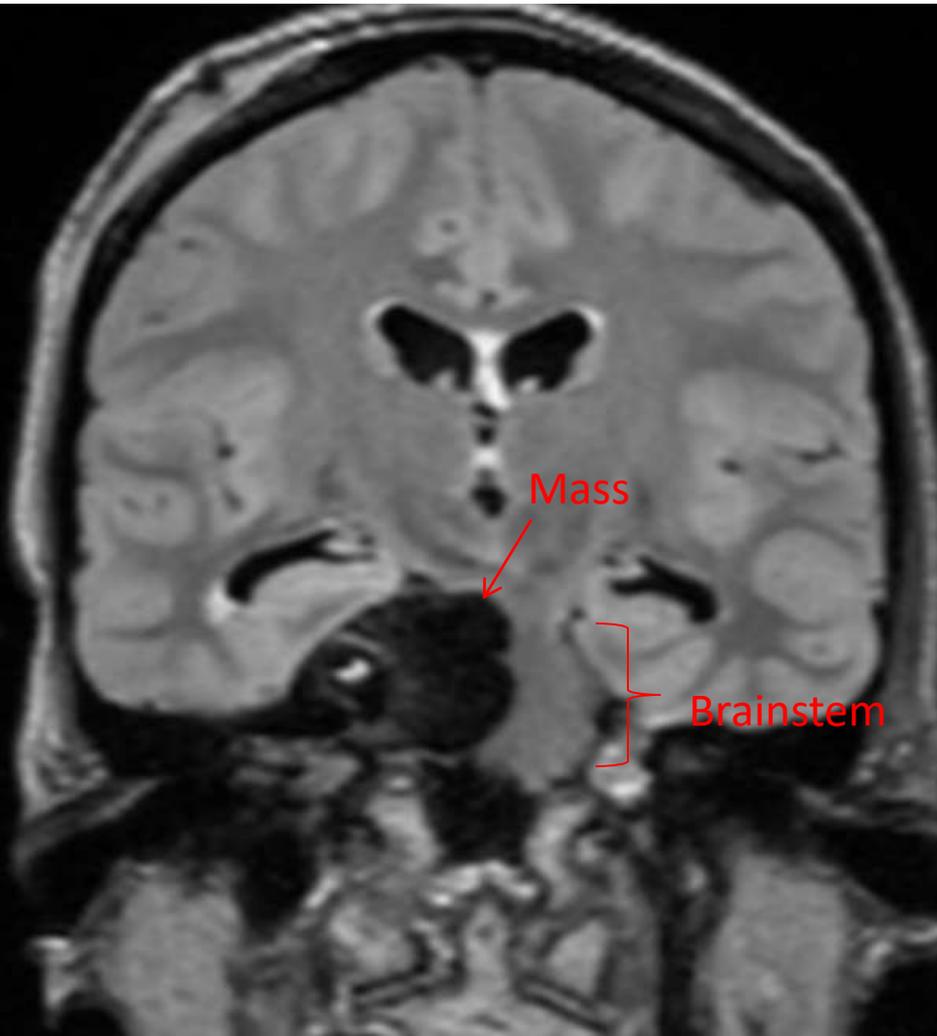
21-0307: BAP1-inactivated melanocytic tumor (skin; dermpath)

# 21-0301

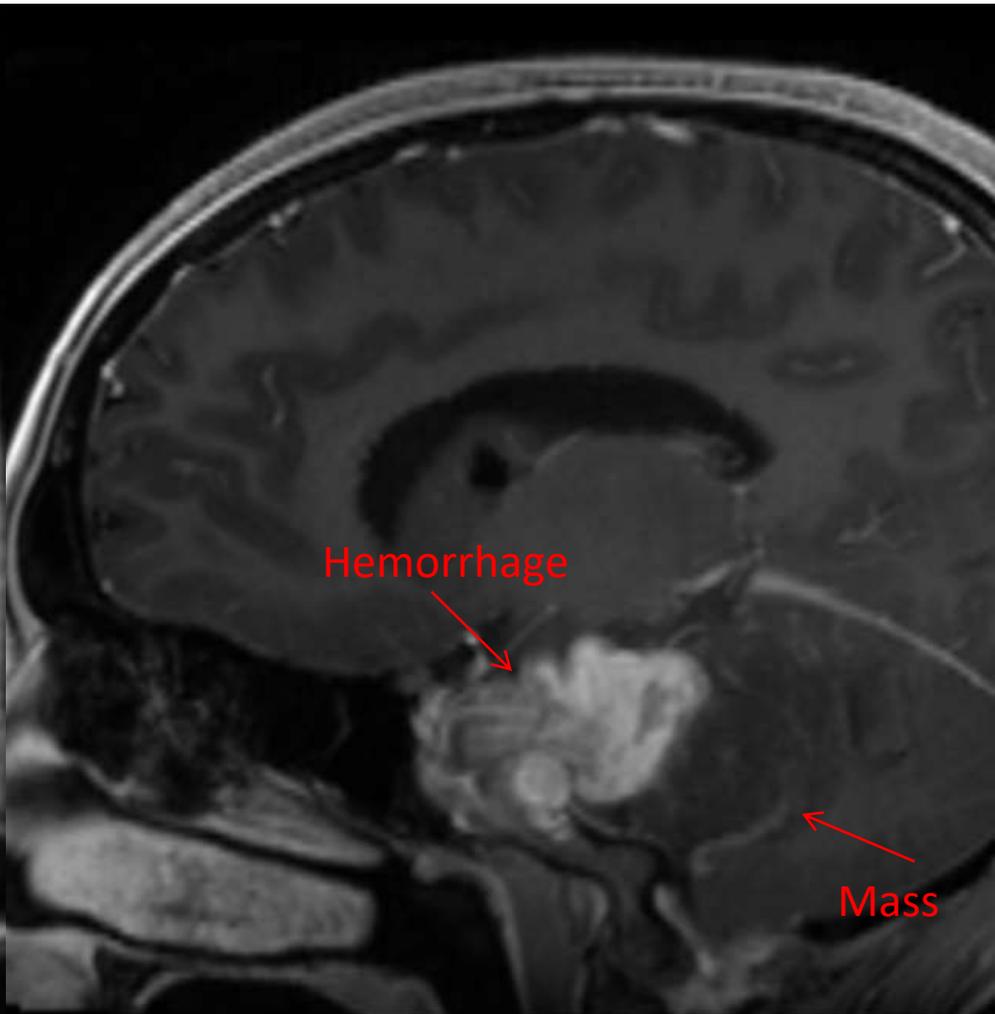
**Angus Toland/Hannes Vogel; Stanford**

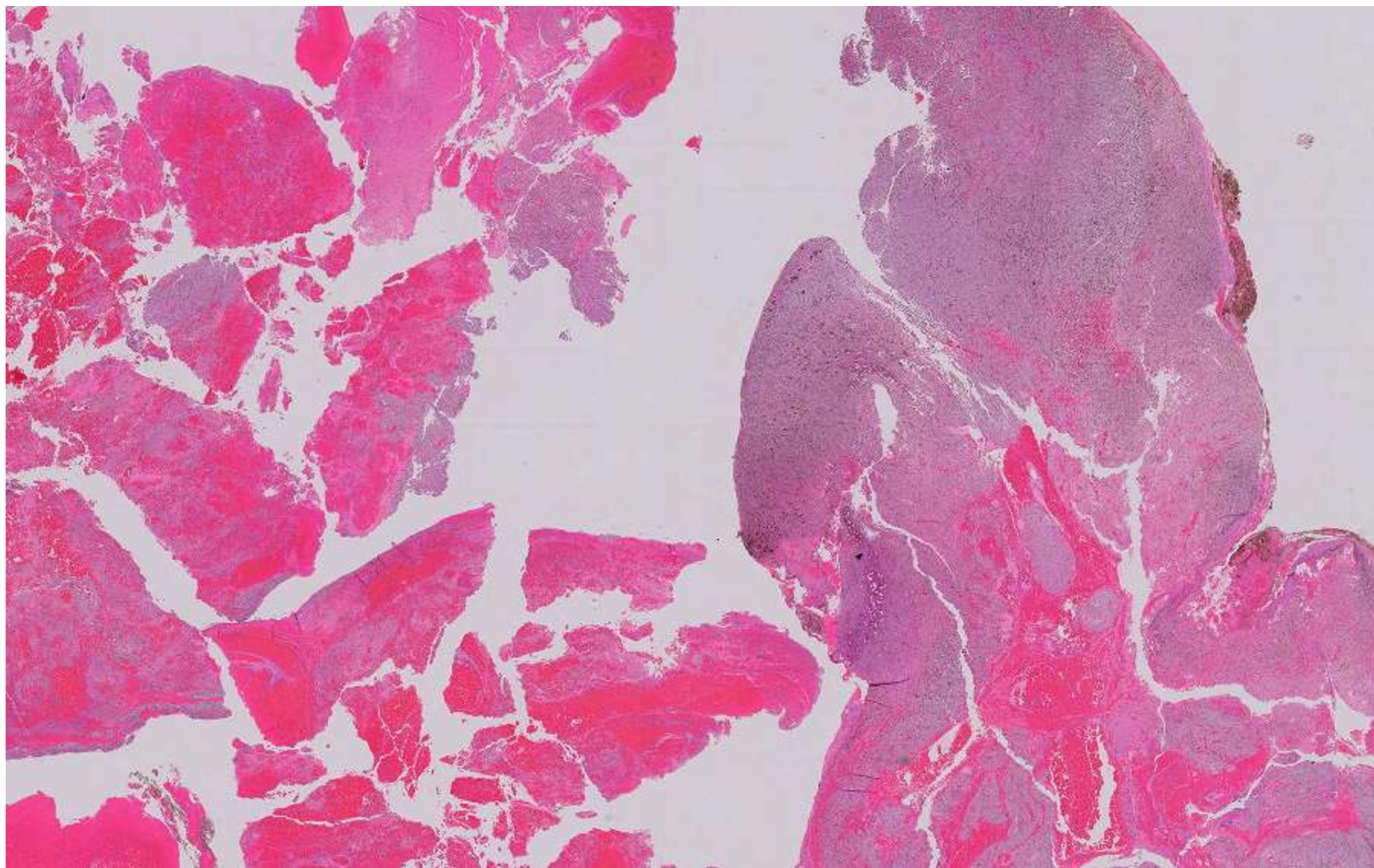
19-year-old F who presented with sudden onset headache and rapid deterioration of mental status. MRI showed 5cm hemorrhagic mass in the posterior and middle fossae.

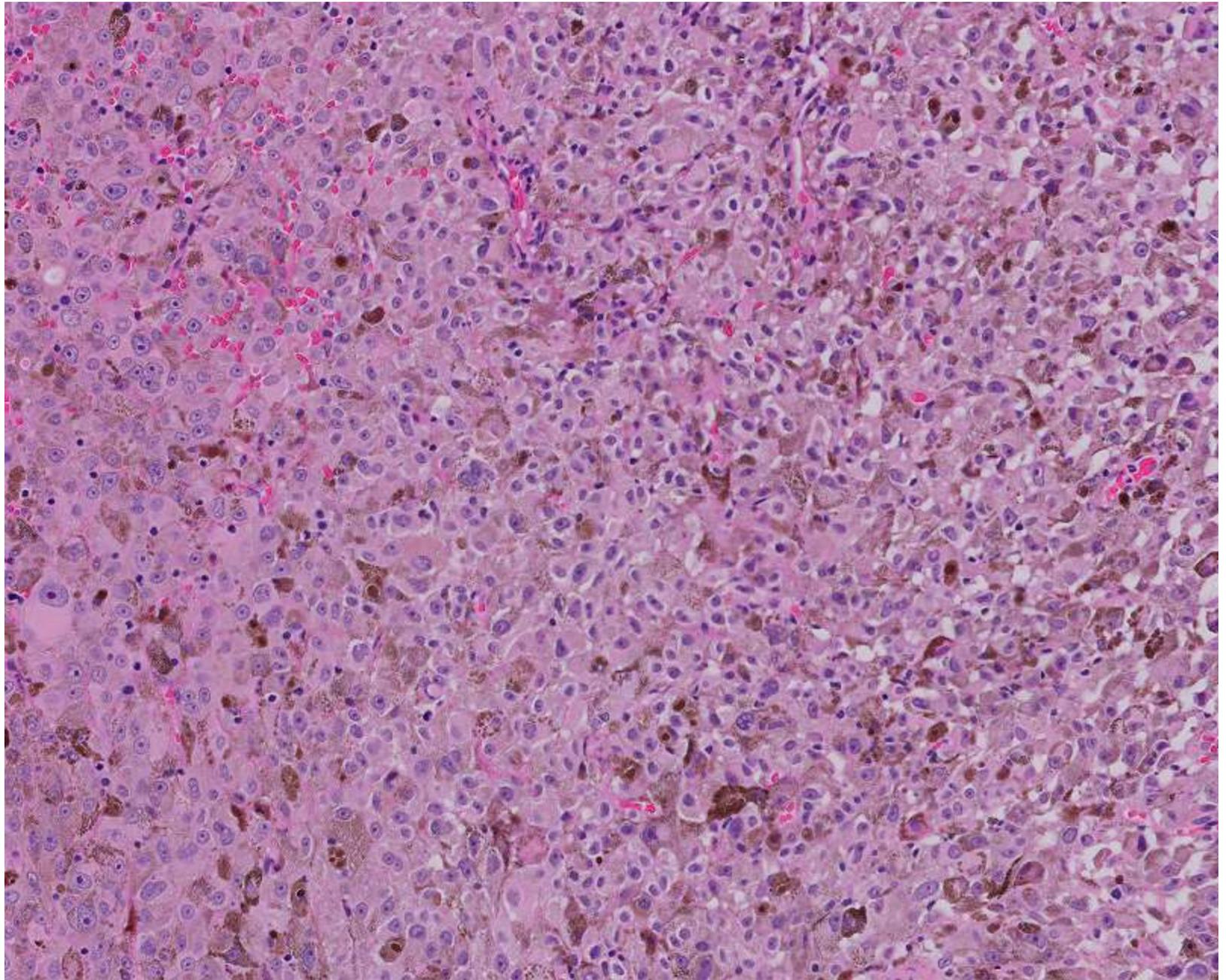
T2 FLAIR

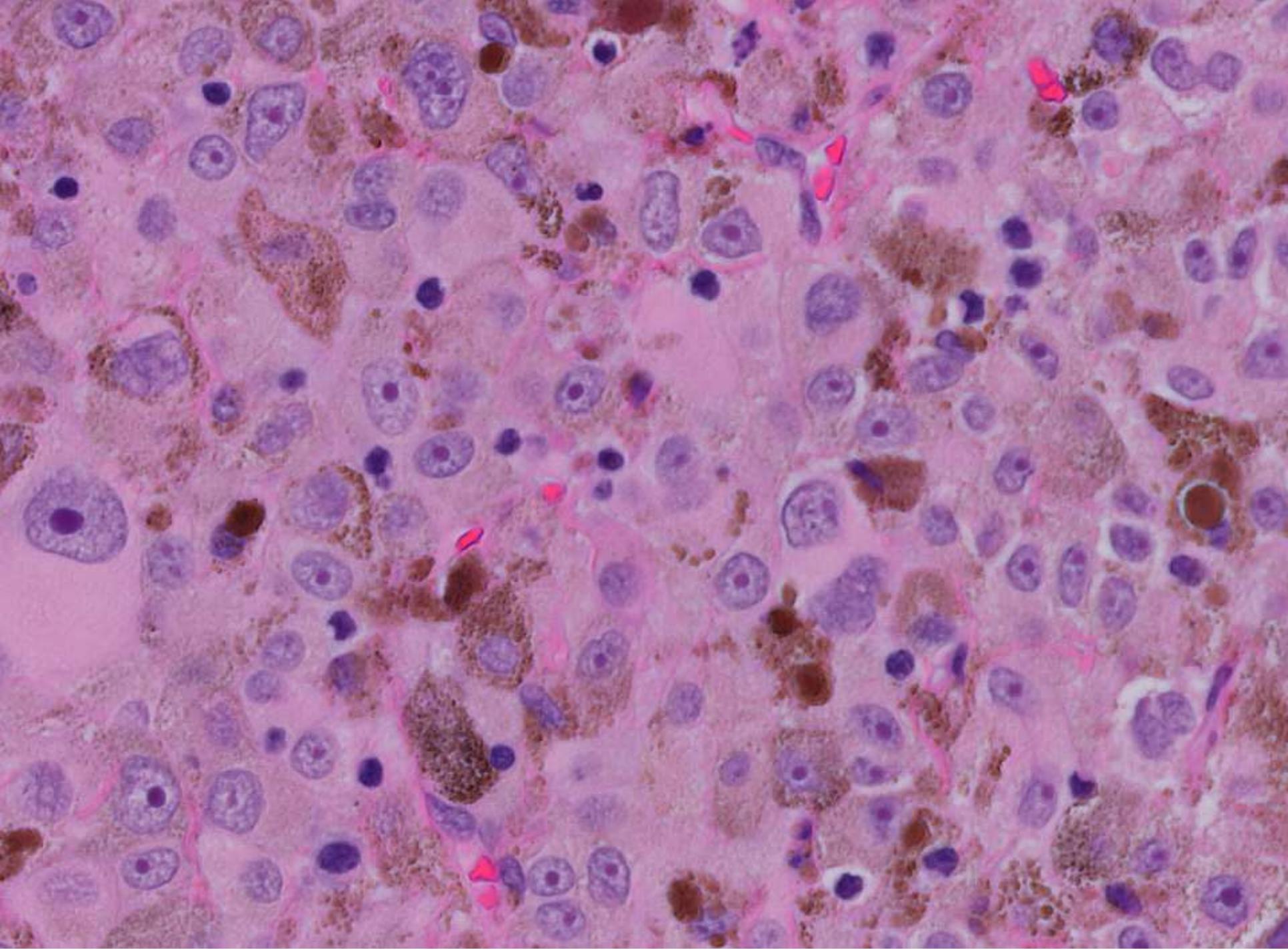


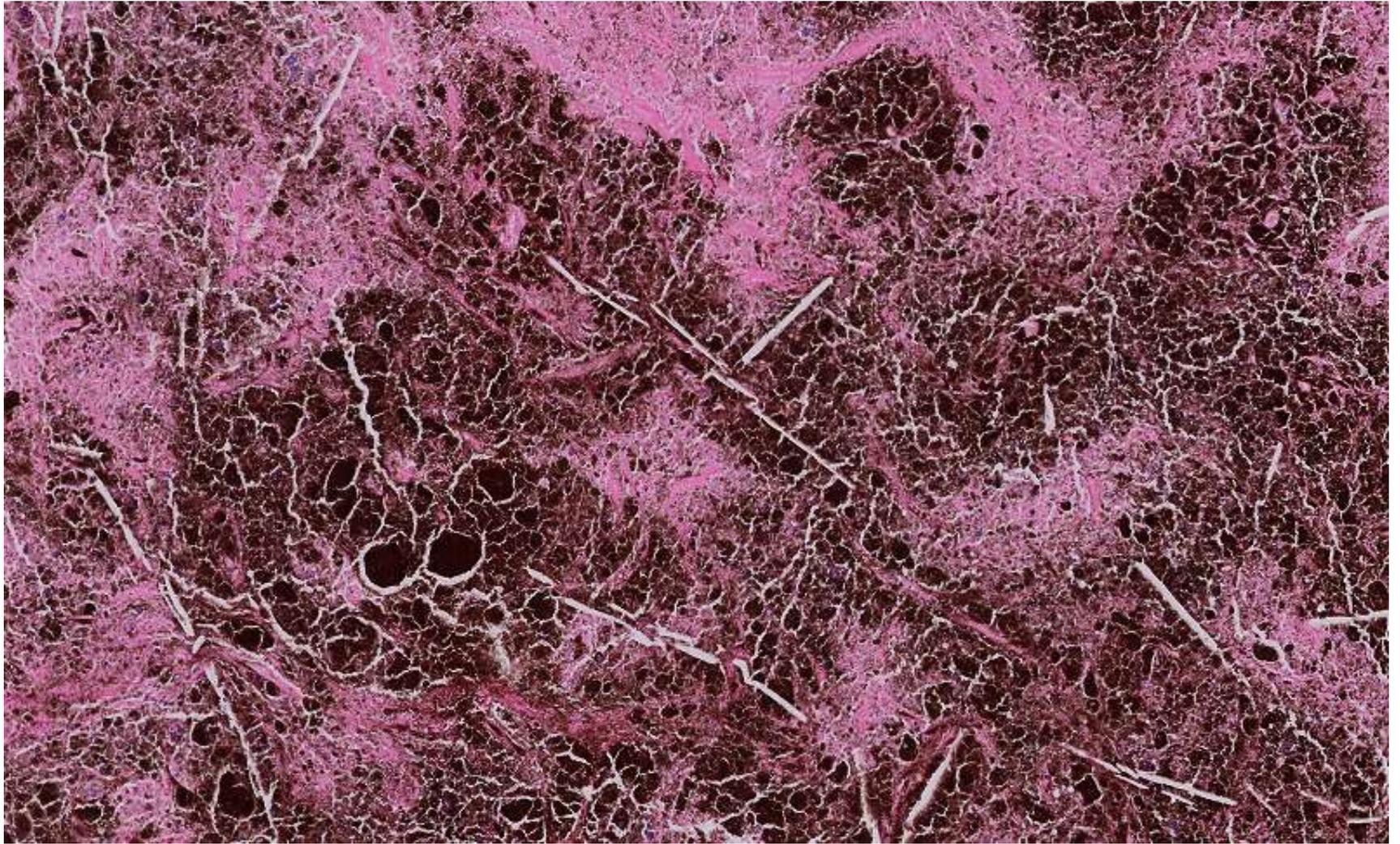
T1 with contrast

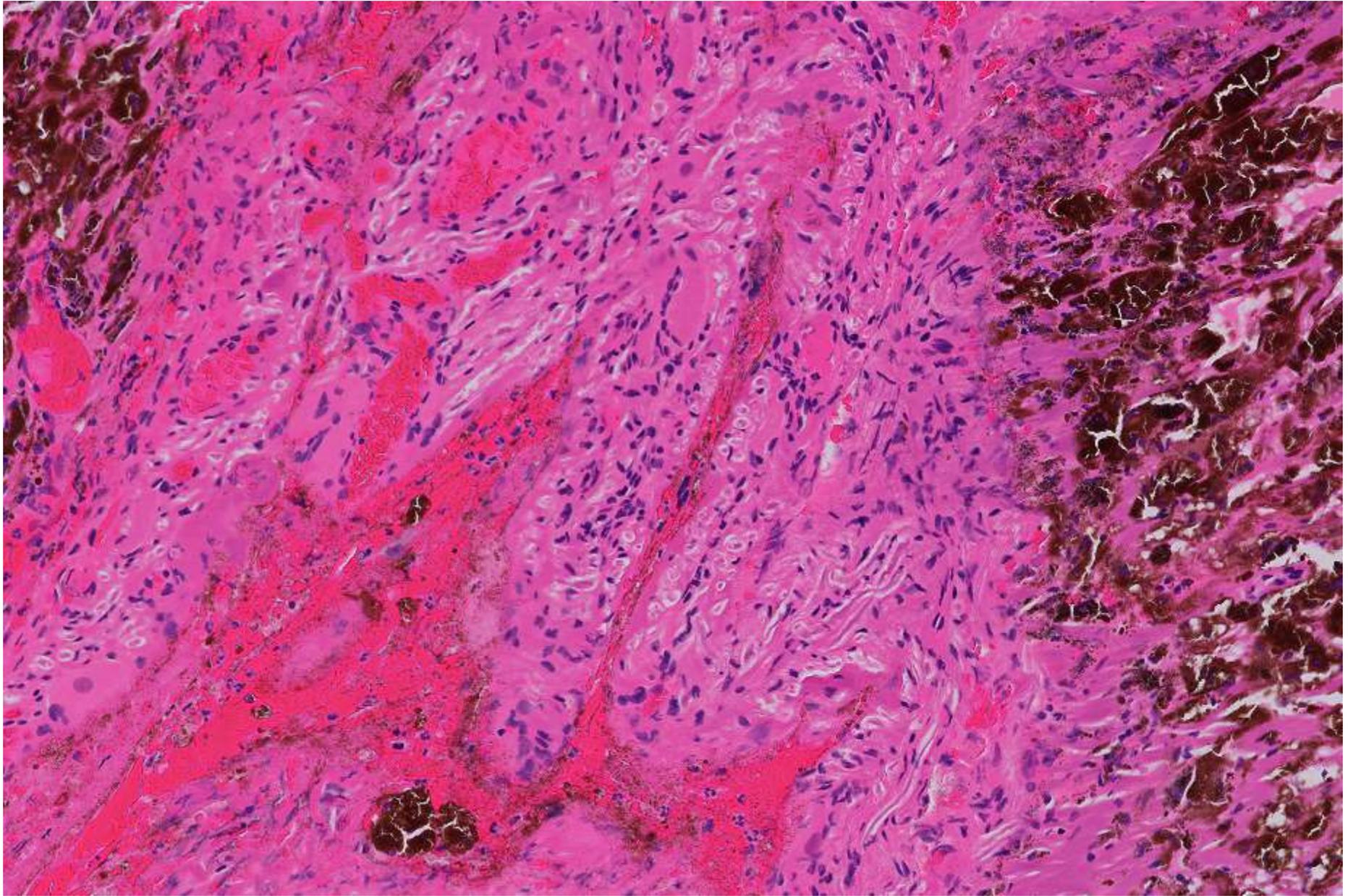


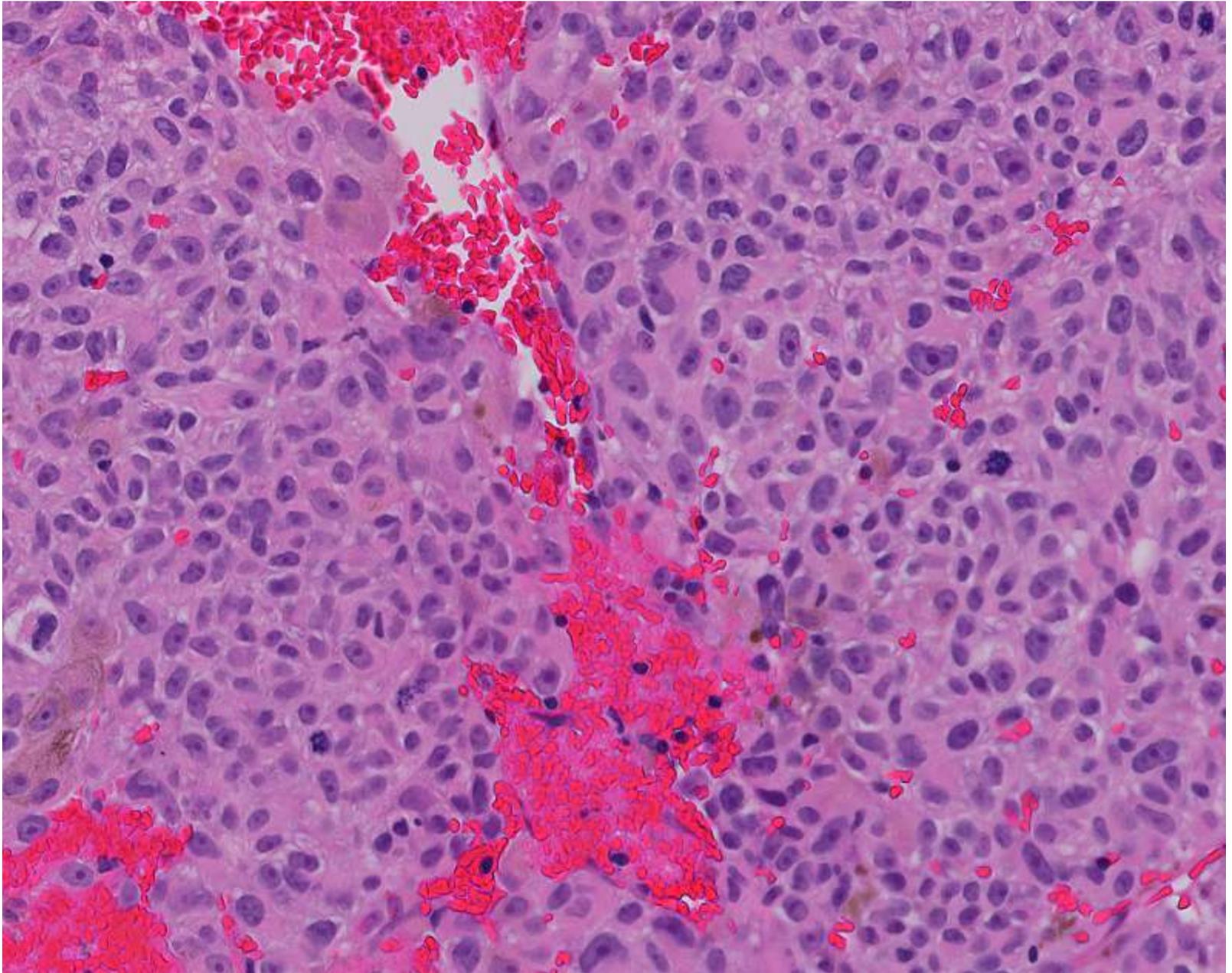


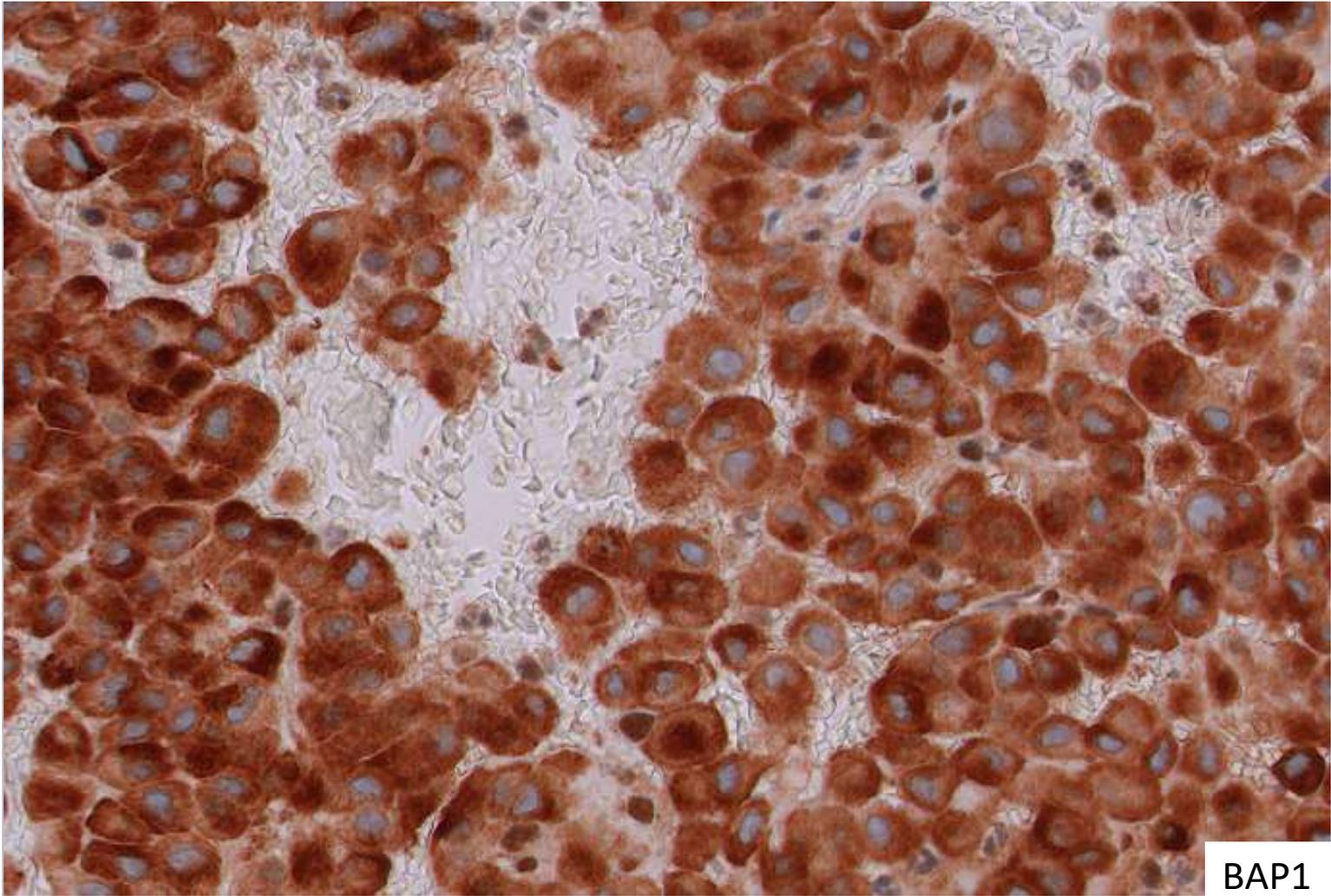












BAP1

# Primary Leptomeningeal Melanoma

- Average annual incidence of ~22 diagnoses in U.S.\*
- Median age at diagnosis: 57 years
- 2016 WHO: Melanocytic lesion with increased mitotic activity, unequivocal tissue invasion, and coagulative necrosis
- Frequently harbor mutations in *GNA11* or *GNAQ*
  - *BAP1* loss is a later event
  - *TERT* promoter, *BRAF* V600E, and *NRAS* mutations uncommon; likely suggest metastasis from cutaneous primary

# *BAP1*

- BRCA1-associated protein1
  - Ubiquitin hydrolase involved in DNA repair and chromatin modification through interactions with BRCA, histone H2B, and other proteins involved in DNA damage repair and cell cycle regulation
- Located at 3p21.1; frequently lost due to deletion
- Germline mutations associated with:
  - Melanoma (cutaneous and uveal)
  - Mesothelioma
  - Meningioma (often rhabdoid)
  - Clear cell renal cell carcinoma

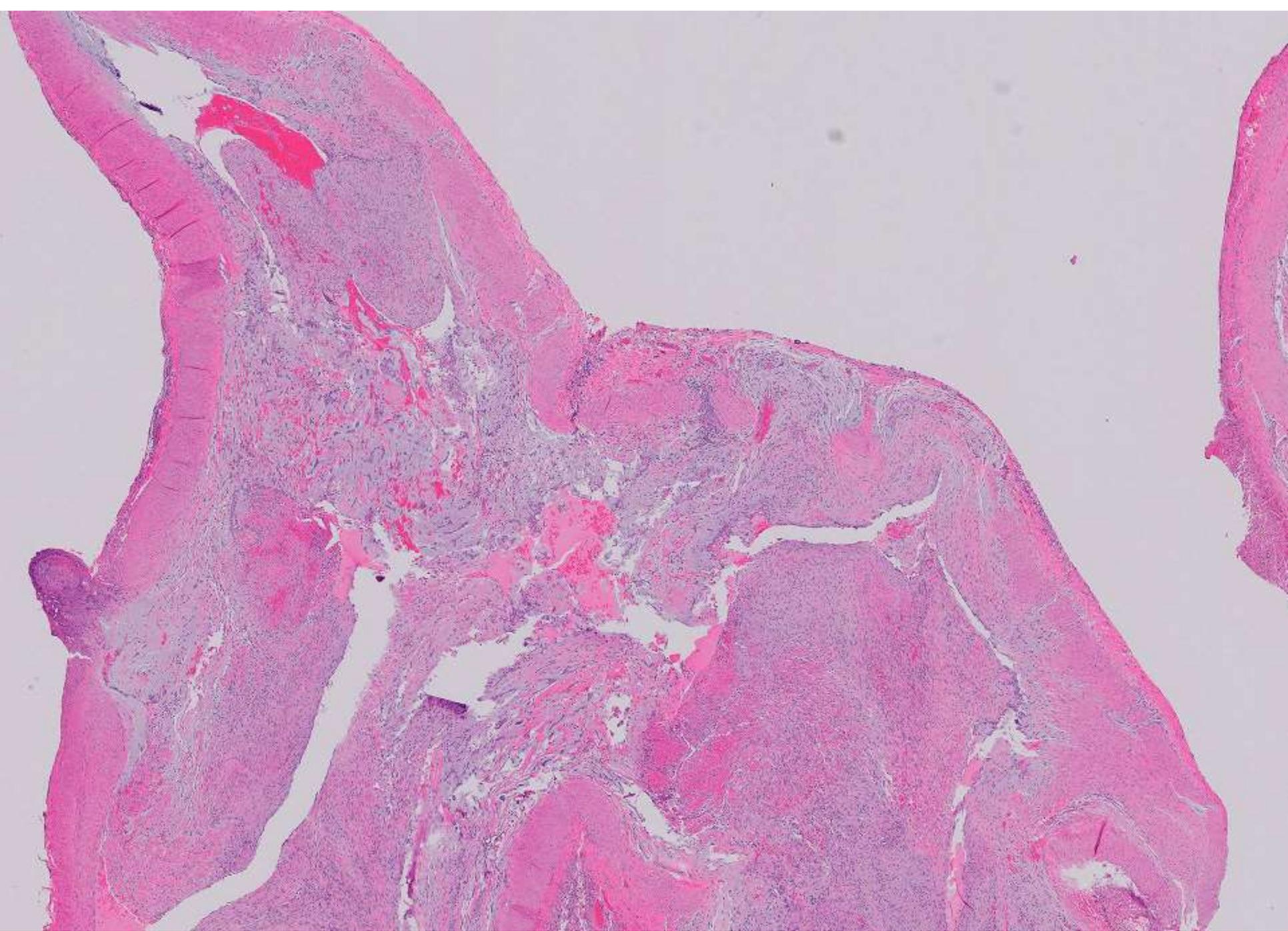
# References

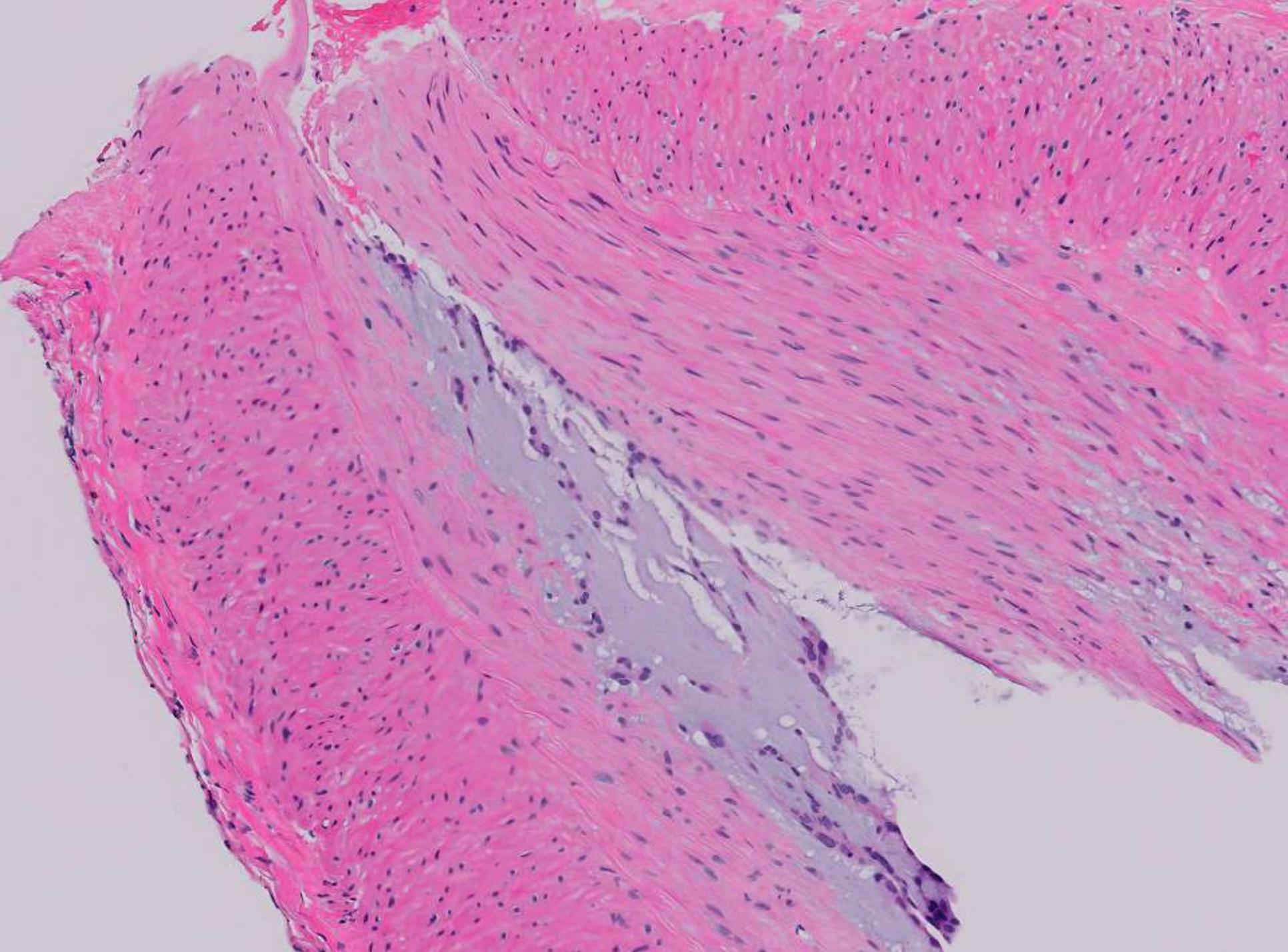
- Ostrom QT, Cioffi G, Gittleman H, Patil N, Waite K, Kruchko C, Barnholtz-Sloan JS. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2012-2016. *Neuro Oncol.* 2019 Nov 1;21(Suppl 5):v1-v100.
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- van de Nes J, Gessi M, Sucker A, Möller I, Stiller M, Horn S, Scholz SL, Pischler C, Stadtler N, Schilling B, Zimmer L, Hillen U, Scolyer RA, Buckland ME, Lauriola L, Pietsch T, Waha A, Schadendorf D, Murali R, Griewank KG. Targeted next generation sequencing reveals unique mutation profile of primary melanocytic tumors of the central nervous system. *J Neurooncol.* 2016 May;127(3):435-44.

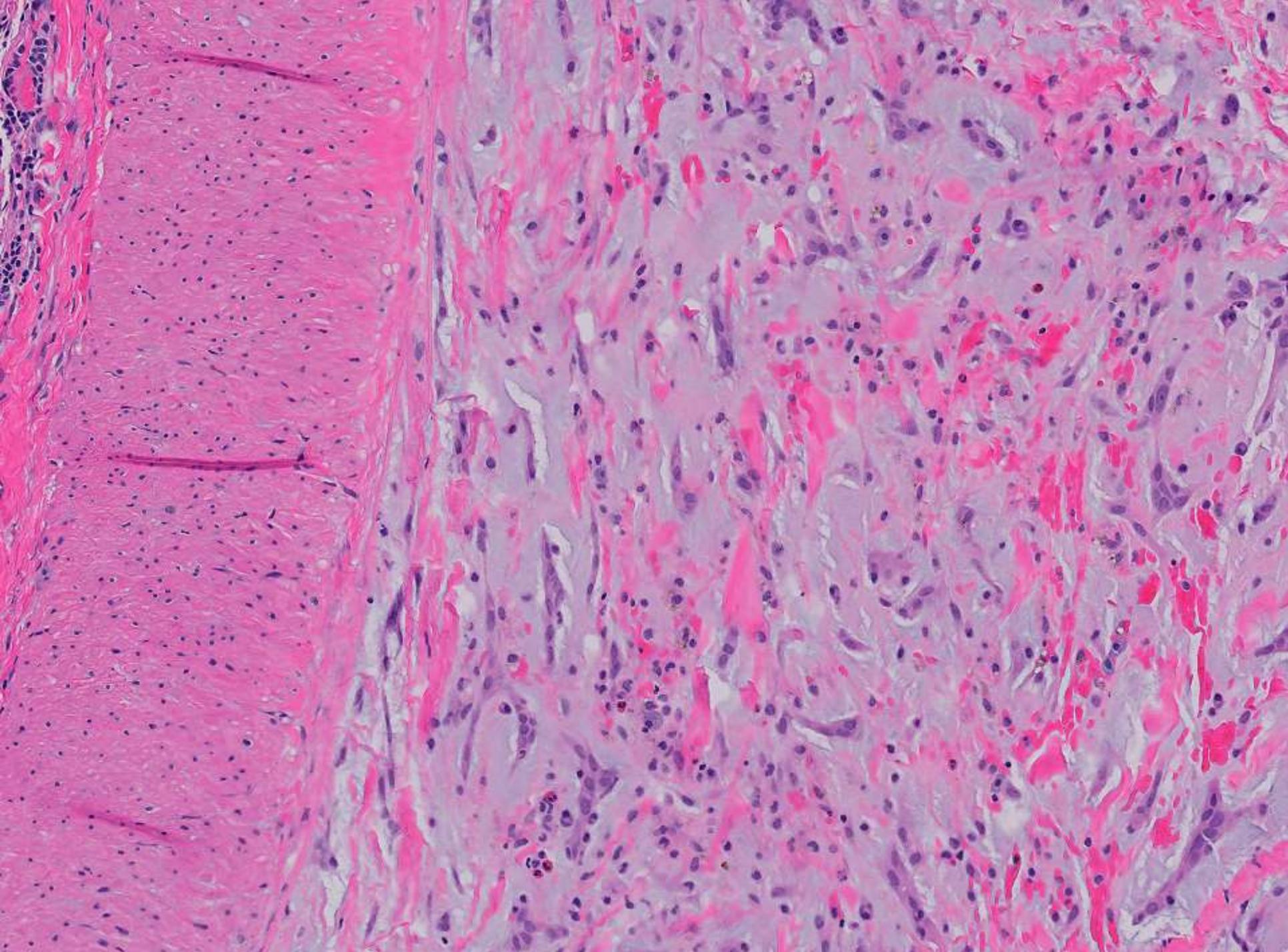
# 21-0302

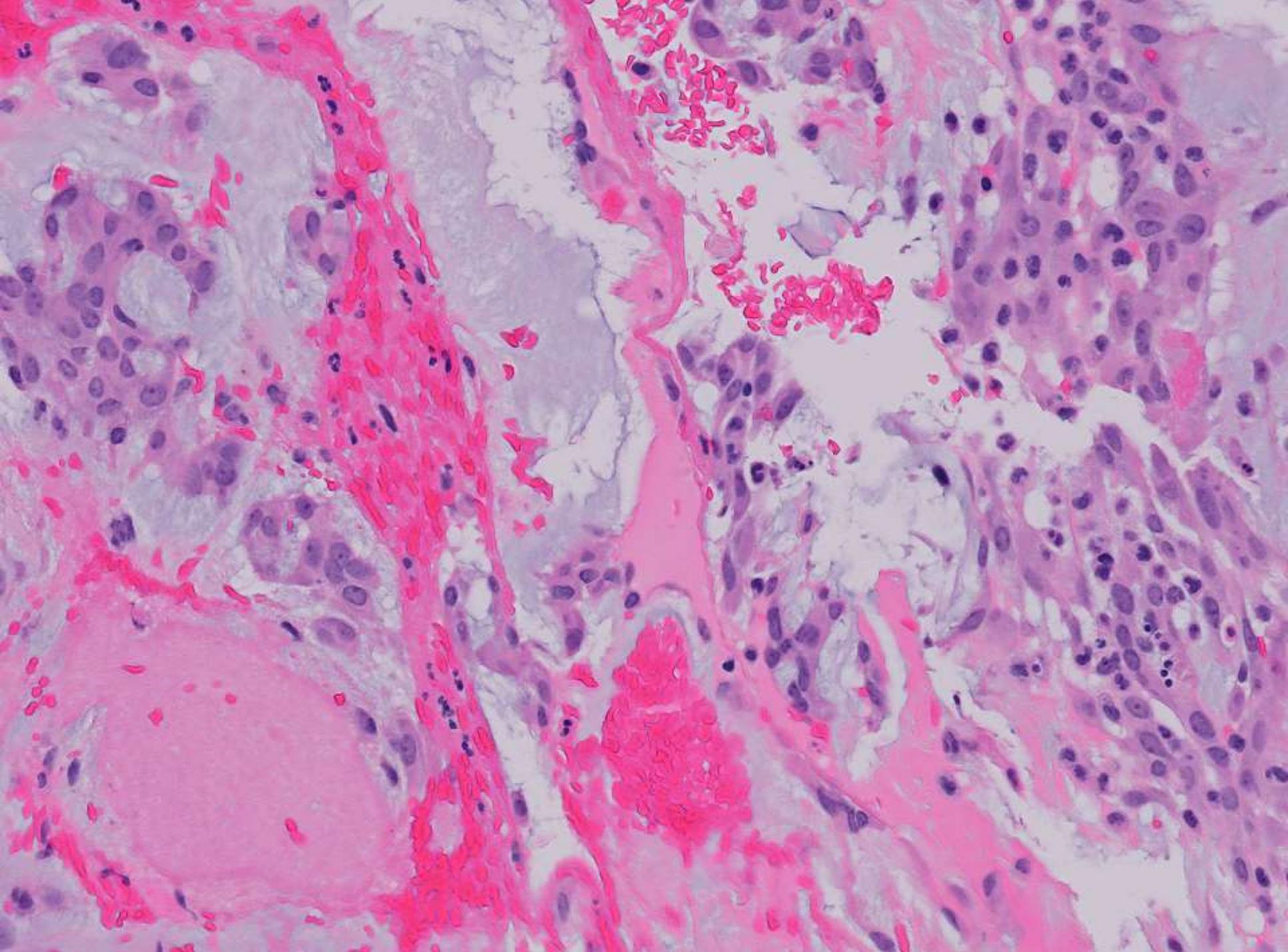
**Angus Toland/Hannes Vogel; Stanford**

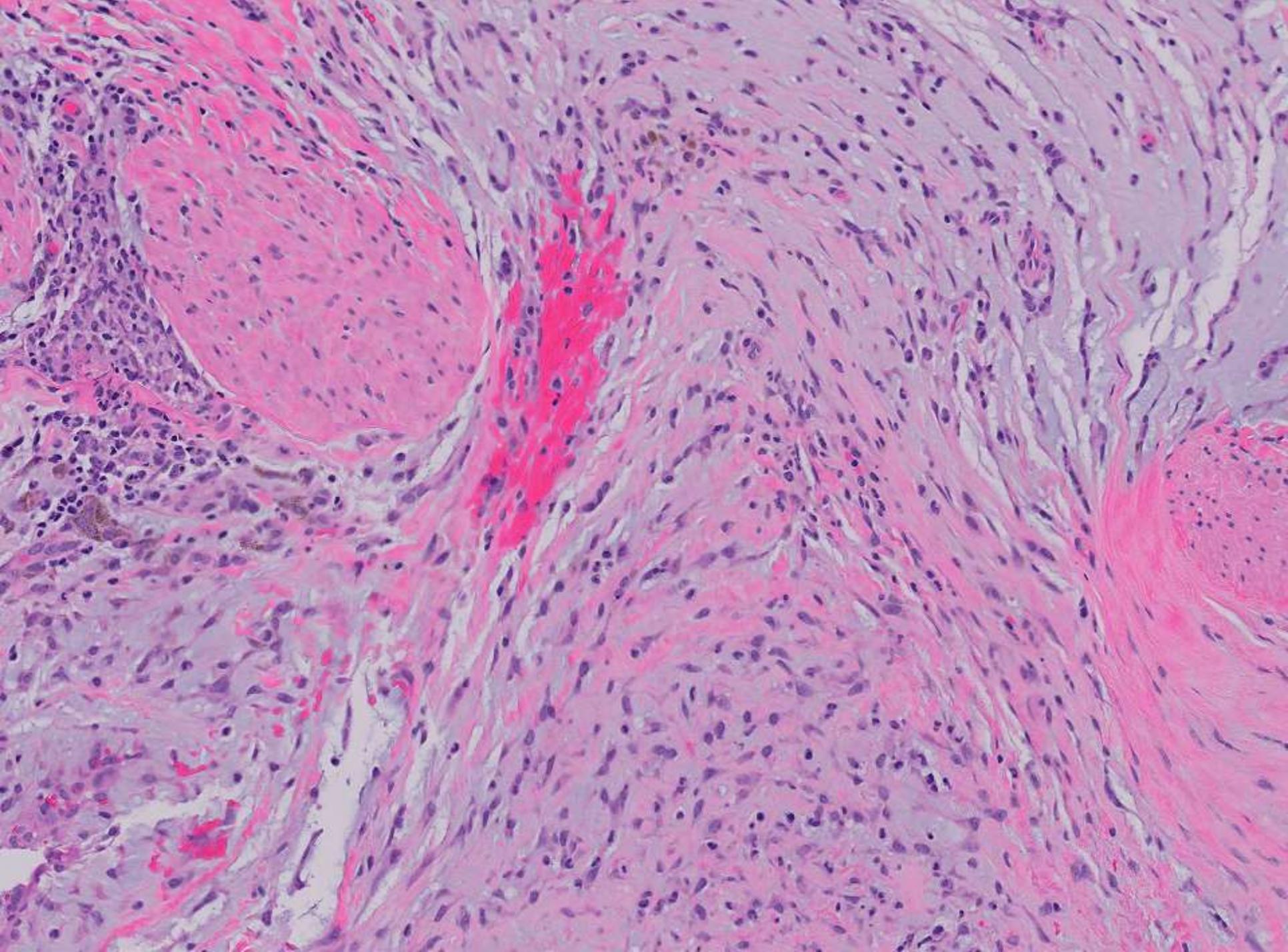
40-year-old F with a h/o right frontal subarachnoid hemorrhage in 2018 and small intraparenchymal hemorrhage in 2019. Imaging demonstrated multiple aneurysms of the distal middle cerebral arteries.

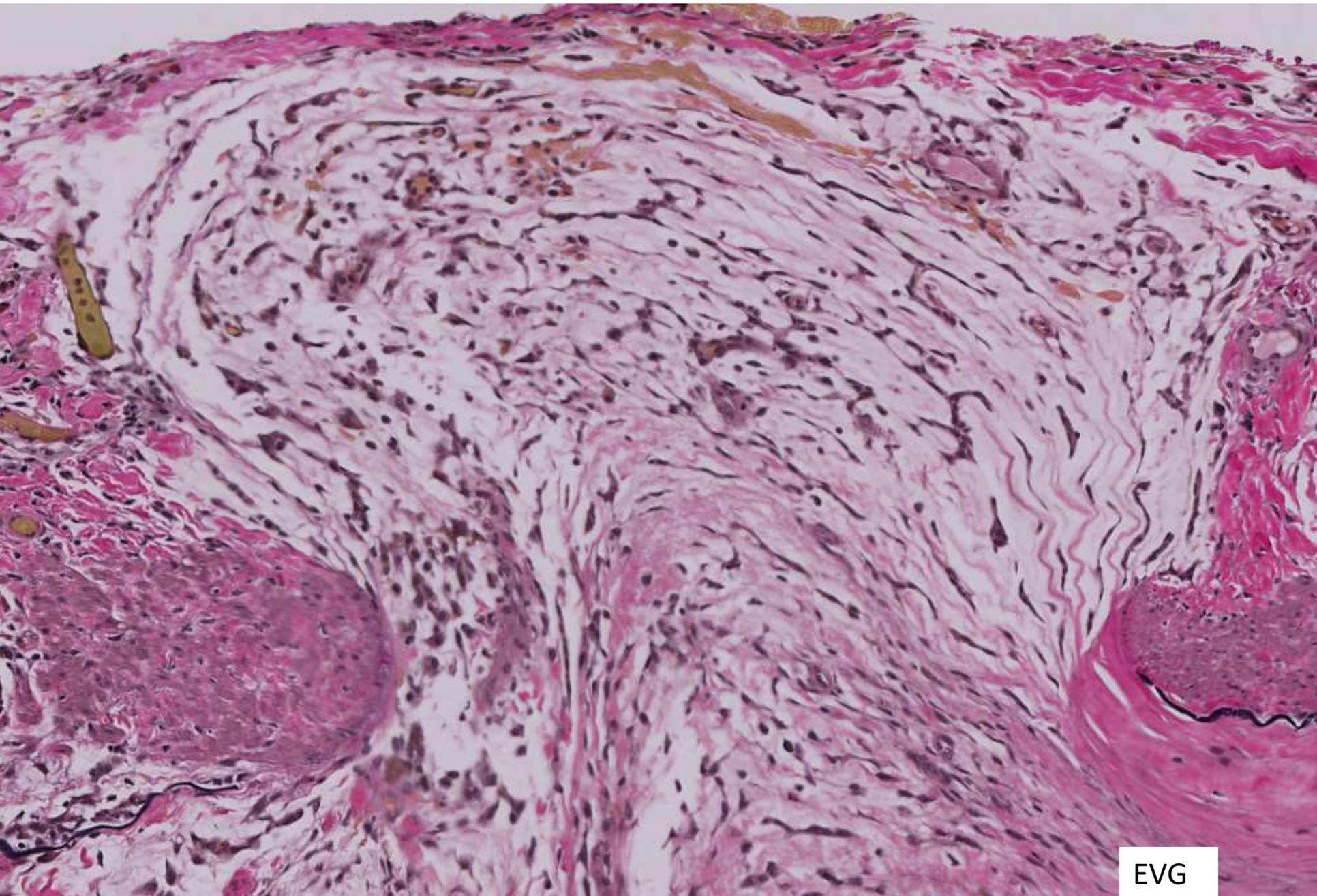




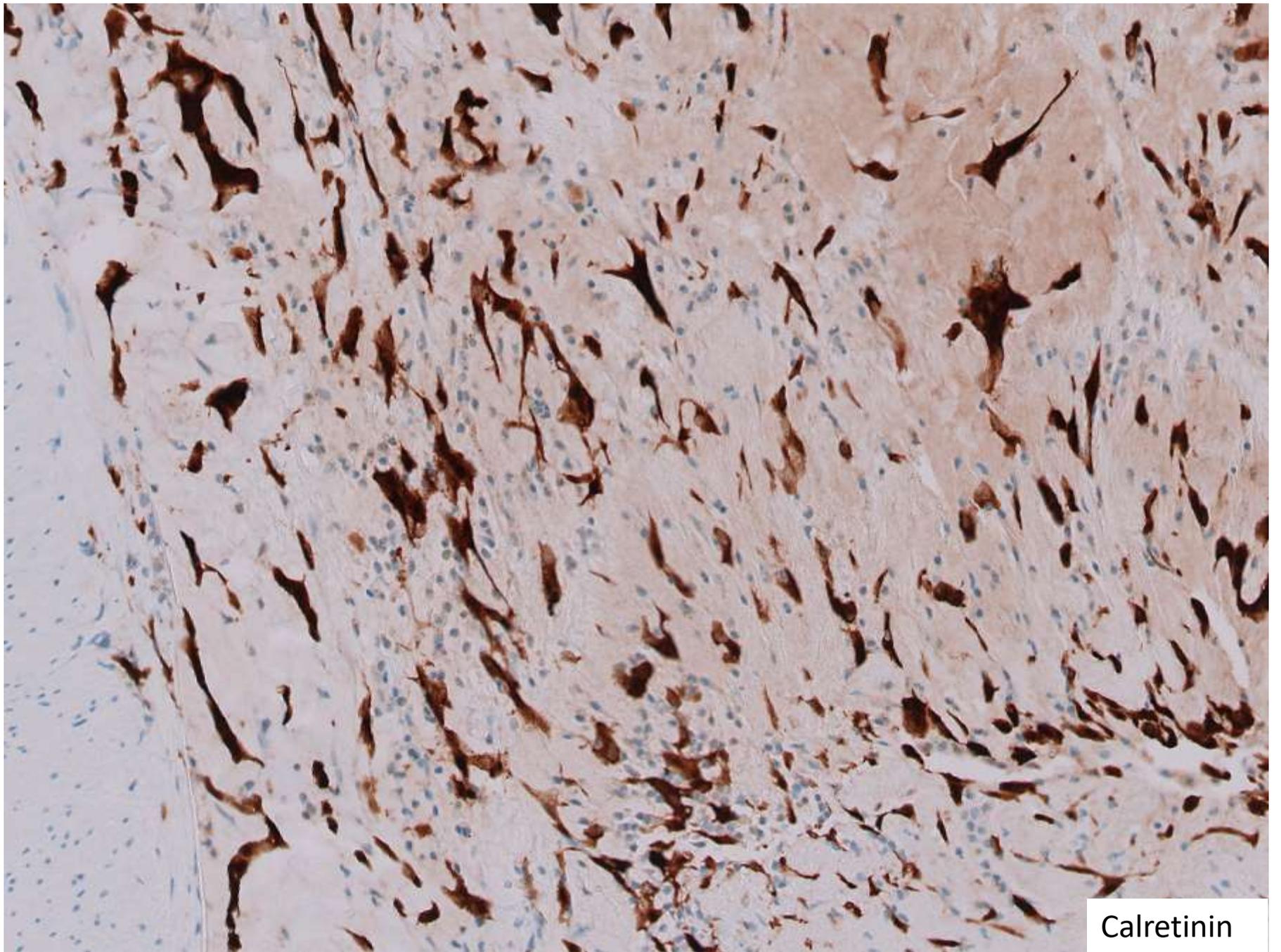








EVG



Calretinin

# Embolic Atrial Myxoma

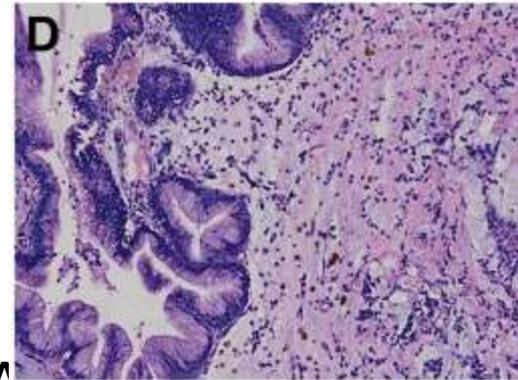
TABLE 1. Clinical and laboratory features of left atrial myxoma (112 cases)

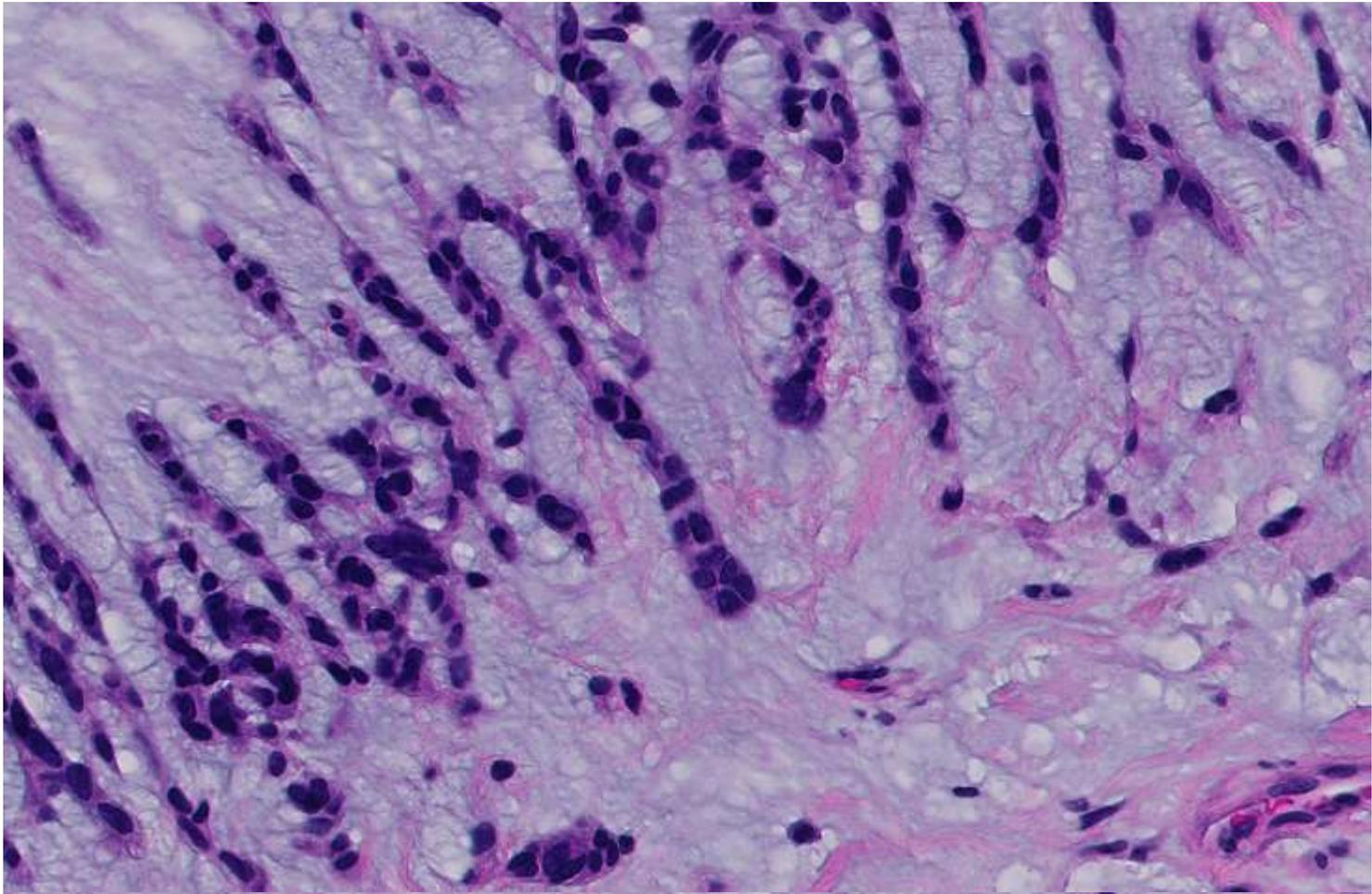
Feature	No. of Patients (%)
Cardiac signs	75 (67)
Cardiac failure	48 (43)
Malaise or syncope	16 (14)
Thoracic pain, palpitations, myocardial infarction, cough	34 (30)
Systemic signs	38 (34)
Fever	22 (20)
Decreased general status (asthenia, weight loss, etc.)	20 (18)
Pseudo-connective tissue disease	6 (5)
Embolic signs	33 (29)
1 emboli	25 (22)
2 or more emboli	8 (7)
Cerebral emboli	24 (21)
Peripheral (limbs) emboli	15 (13)
Coronary emboli	4 (3.5)
Neurologic signs	29 (26)
Neurologic deficiency (stroke)	23 (20.5)
Other (vertigo, epilepsy, coma, pseudo-multiple sclerosis)	9 (7.5)
Other symptoms	8 (7)
Endocarditis or meningitis	2
Hepatic symptoms	3
Abdominal pain or hemoptysis	3
Cardiac auscultation abnormalities	72 (64)
Pseudo-mitral auscultation	60 (54)
Tumor plop	17 (15)
Serologic abnormalities	42 (37)
Increased sedimentation rate	36 (32)
Anemia	15 (13)
Leukocytosis or thrombocythemia	6 (5)
Electrocardiogram abnormalities	69 (62)
Left atrial hypertrophy	39 (35)
Rhythm disorders	10 (9)
Repolarization disorders	24 (21)
Conduction disorders	13 (11)
Other	27 (24)
Chest film abnormalities	56 (50)
Pulmonary edema or heart failure	30 (27)
Cardiomegaly	35 (31)
Pleural effusion	8 (7)
Left atrial hypertrophy	12 (10)
Visible myxoma (calcifications)	10 (9)

- Most common cardiac neoplasm
  - Median age: 53 (range 12-84); F:M=~2:1
  - ~70-90% occur in the left atrium; Rarely present in ventricles
  - ~20% found incidentally; symptoms depend on location
    - Left side
      - Systemic embolization → strokes, myocardial infarction, other end organ embolization/infarction
        - » Aneurysms late complication following disruption of the vessel wall
      - Mitral valve obstruction
    - Right side
      - Pulmonary embolization; systemic involvement requires communication to left side of heart
      - Tricuspid valve obstruction

# Histology

- Myxoid stroma with scattered cells showing eosinophilic cytoplasm and round to spindle nuclei arranged as nests and cords
  - Occasional multinucleated and ring nuclei present
  - May show glandular differentiation
  - Perivascular cuffing
  - Mitoses infrequent
- IHC
  - Positive: CD31, CD34, +/- calretinin, SMA
  - Negative: Cytokeratins (usually), EMA, MUC4





# References

- Pinede L, Duhaut P, Loire R. Clinical presentation of left atrial cardiac myxoma. A series of 112 consecutive cases. *Medicine (Baltimore)*. 2001 May;80(3):159-72.
- Wang JG, Wang B, Hu Y, Liu JH, Liu B, Liu H, Zhao P, Zhang L, Li YJ. Clinicopathologic features and outcomes of primary cardiac tumors: a 16-year-experience with 212 patients at a Chinese medical center. *Cardiovasc Pathol*. 2018 Mar-Apr;33:45-54.

# 21-0303

## **Charles Lombard; El Camino Hospital**

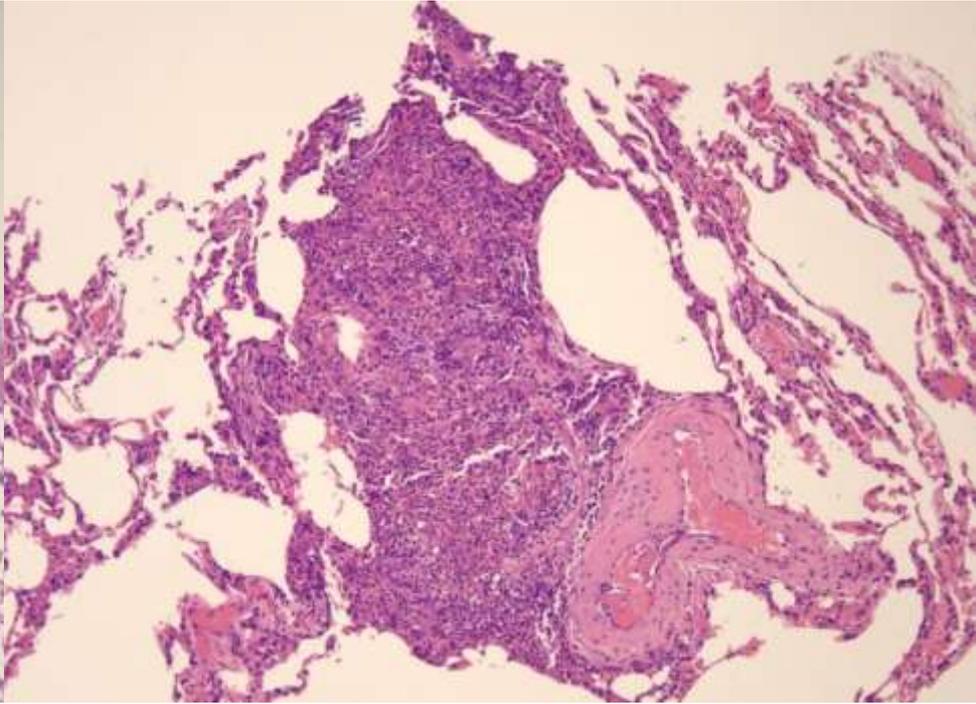
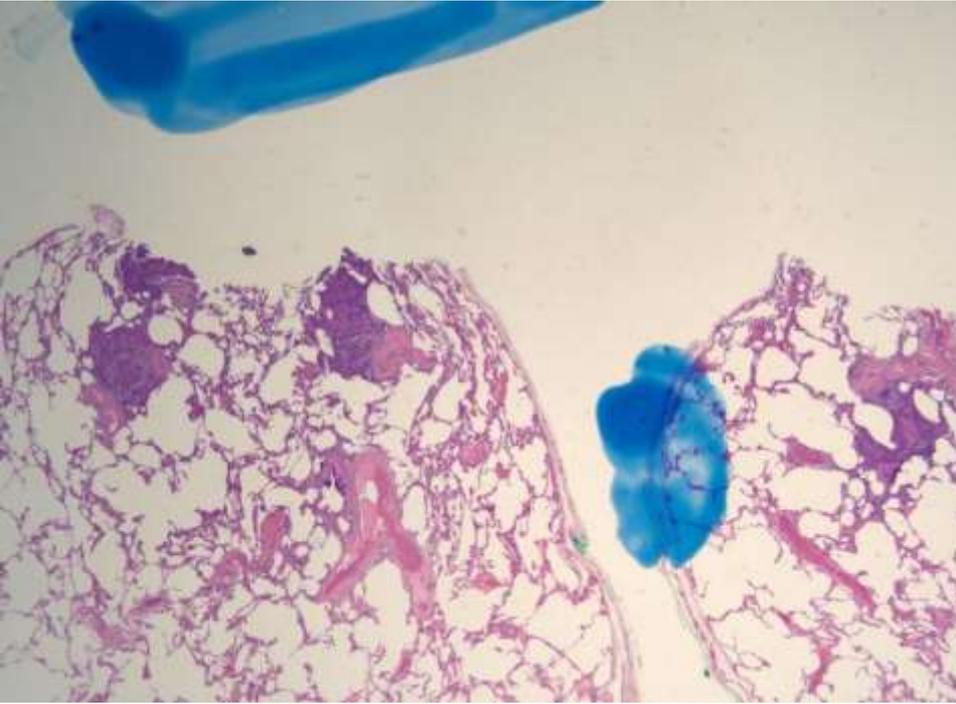
61-year-old M with acute respiratory failure. Previously healthy (prior cryo biopsy showed incidental granular cell tumor of bronchus). No history of IBD, sinus disease, or renal disease. Lung wedge biopsies performed.

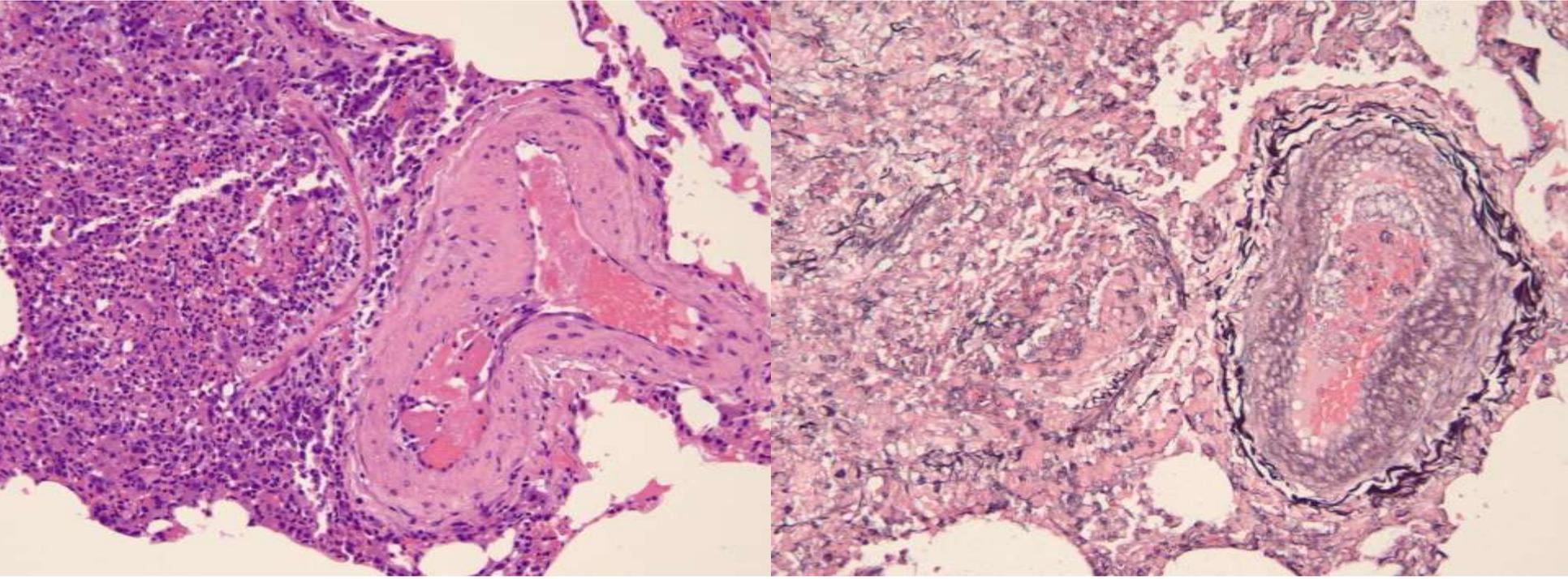




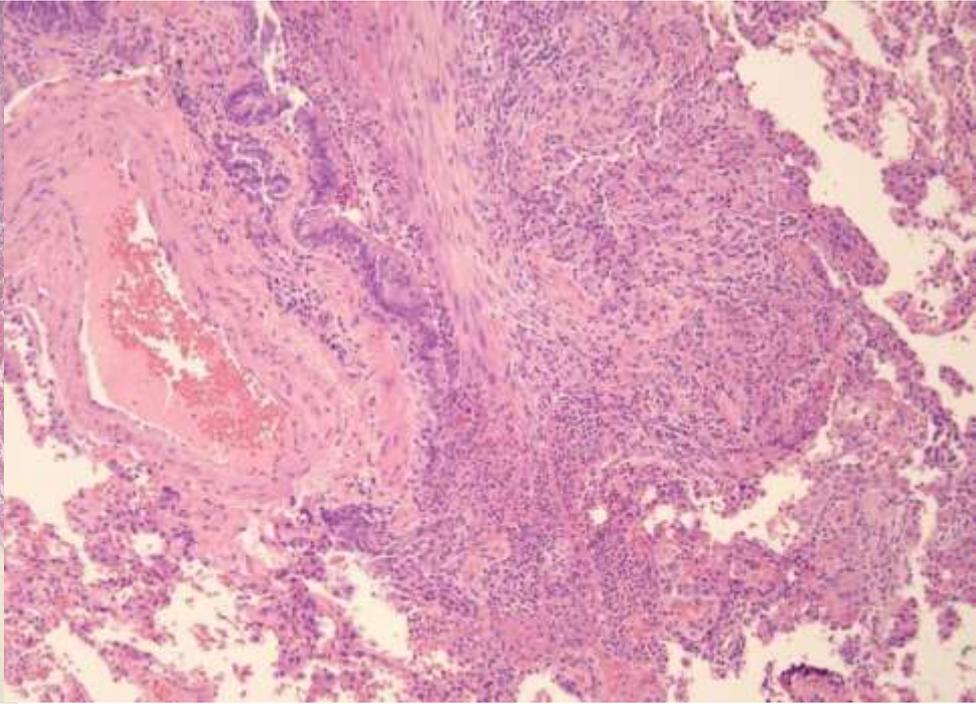
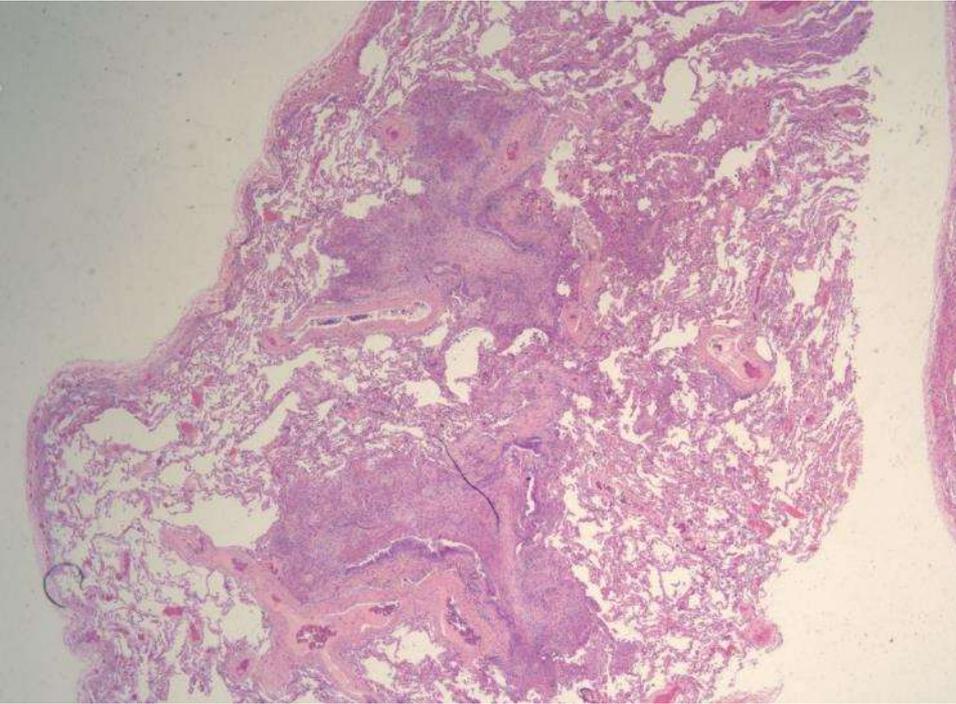


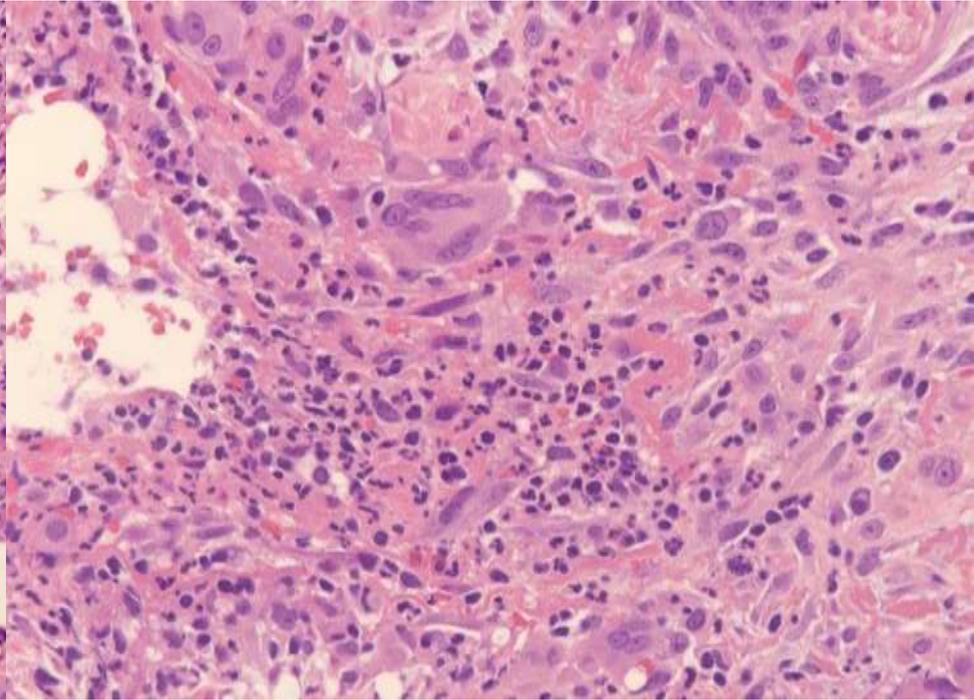
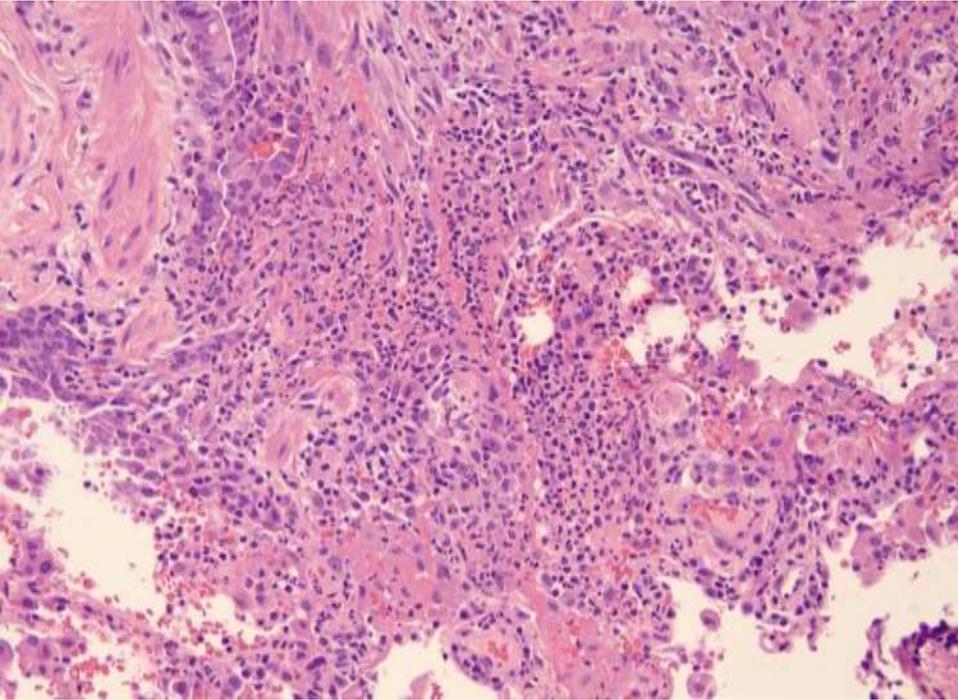
Right Lower Lobe



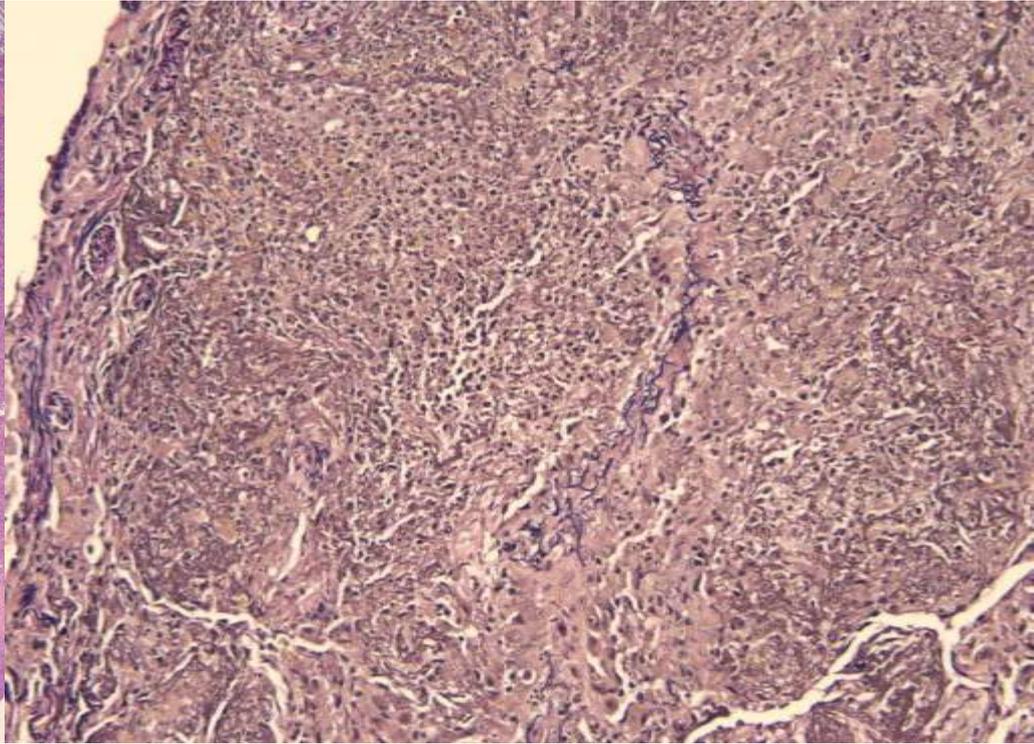
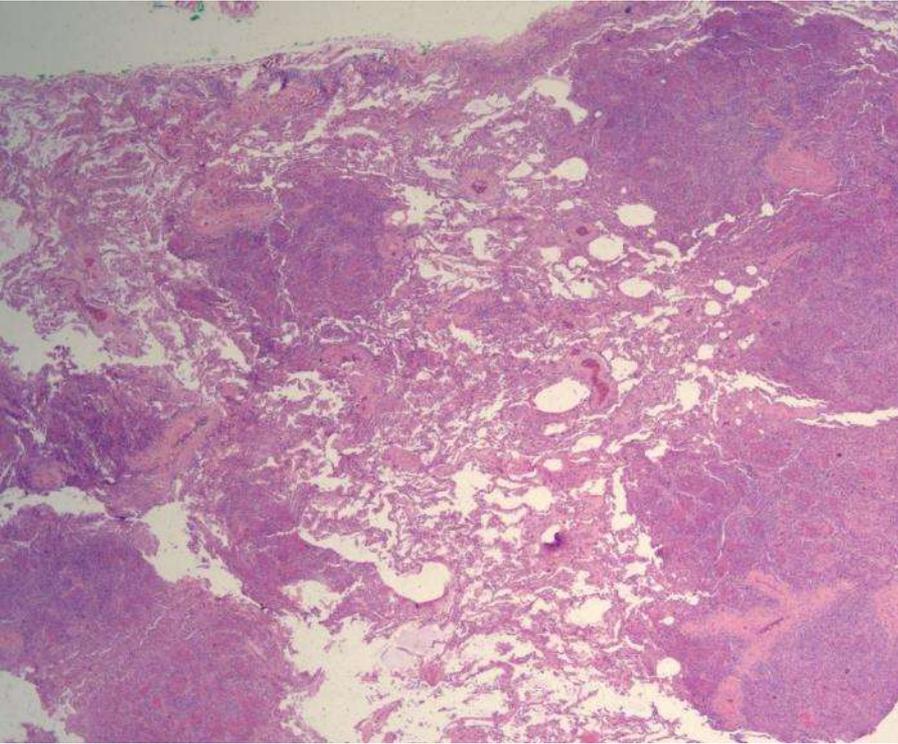


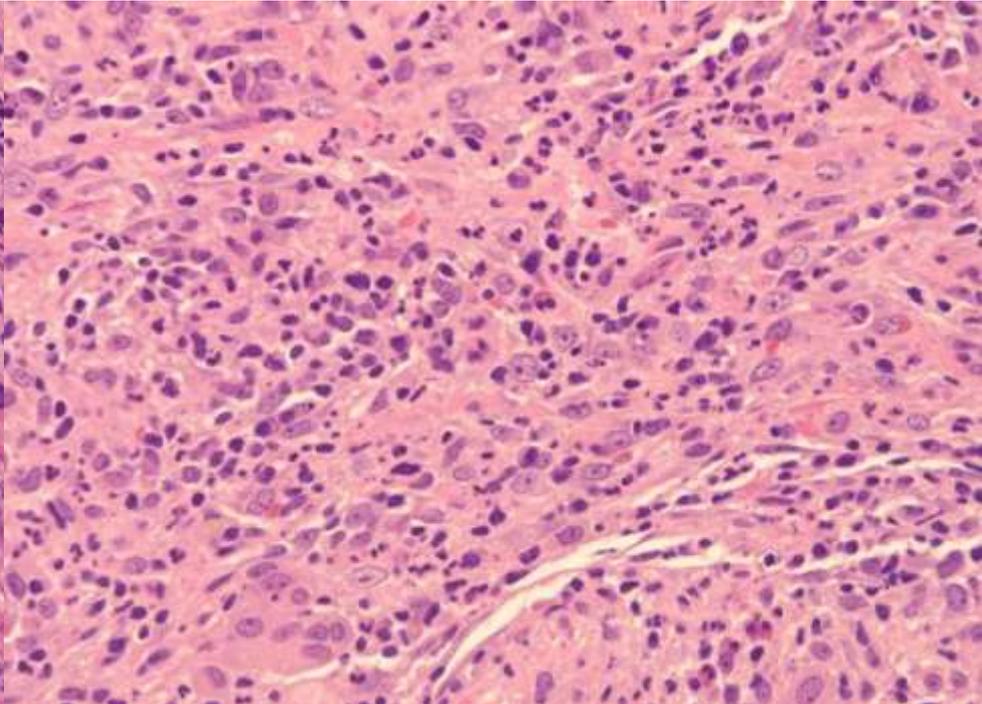
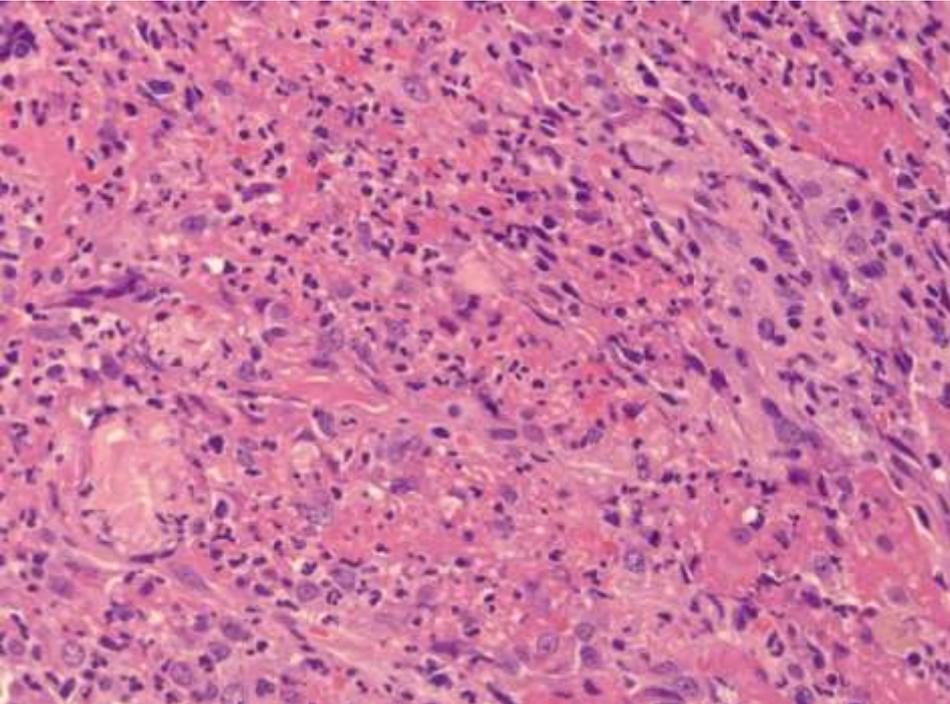
Right middle lobe

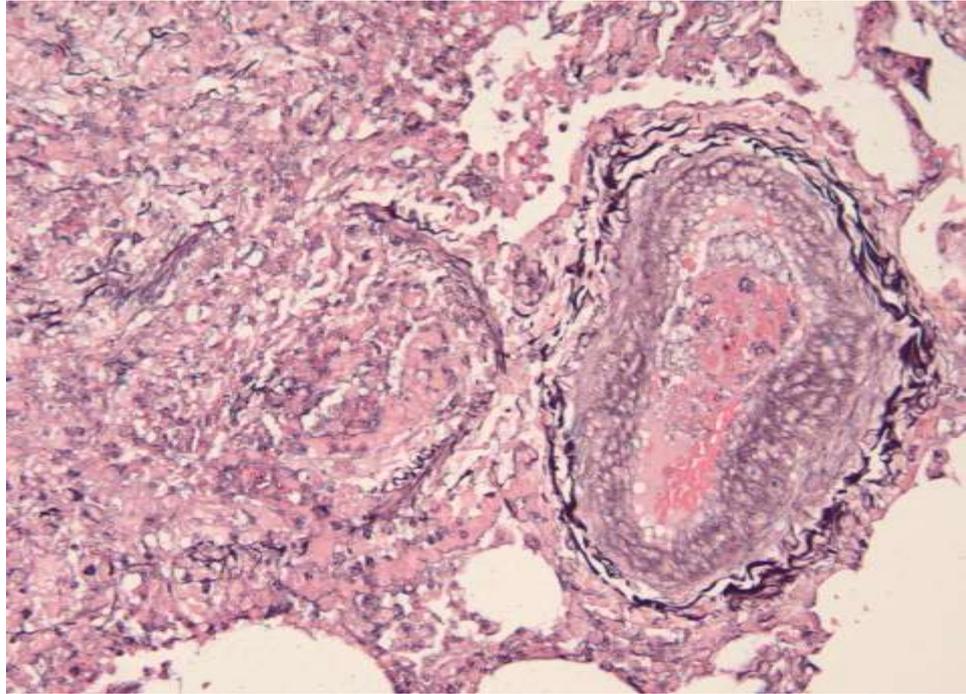
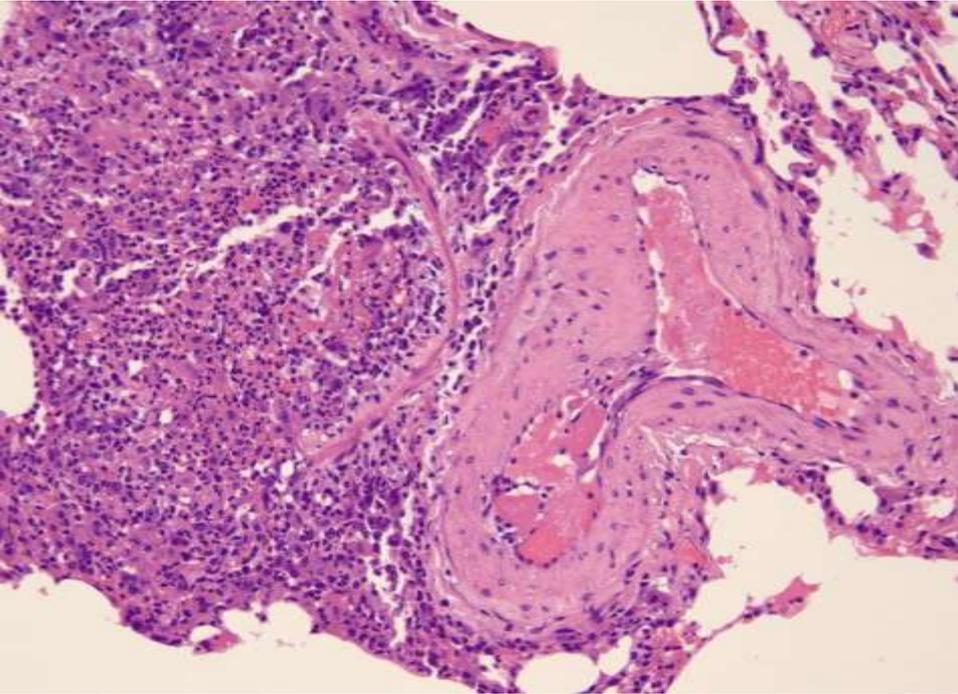


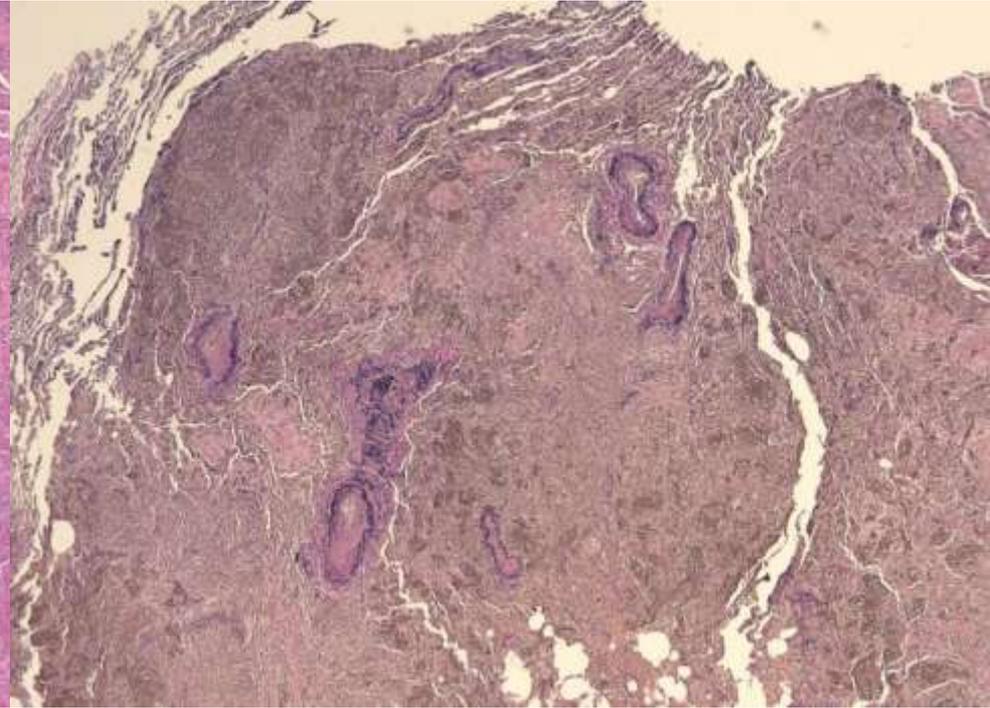
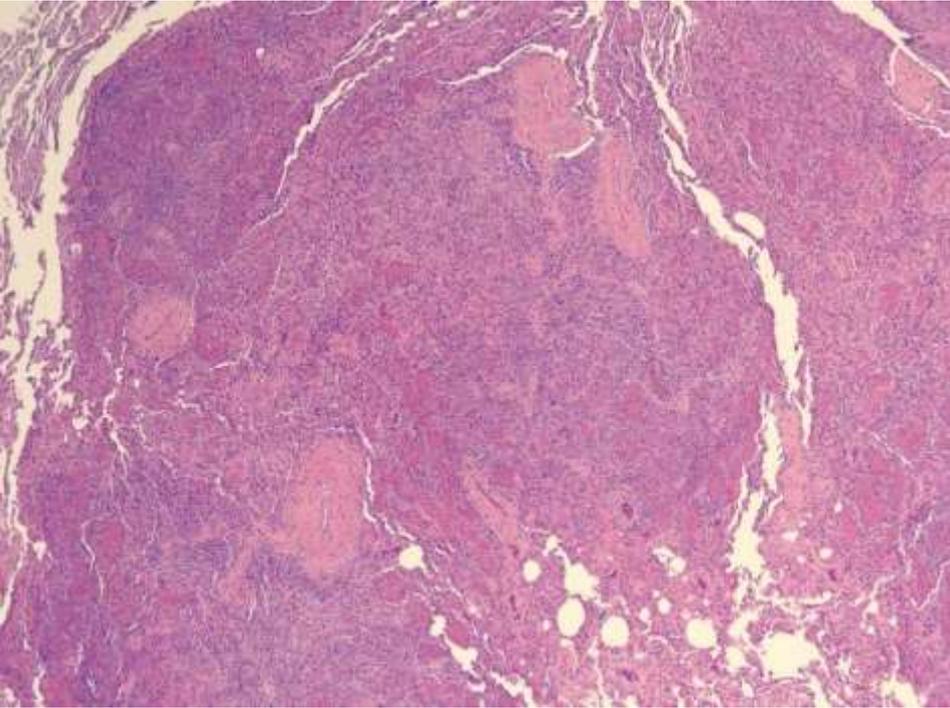


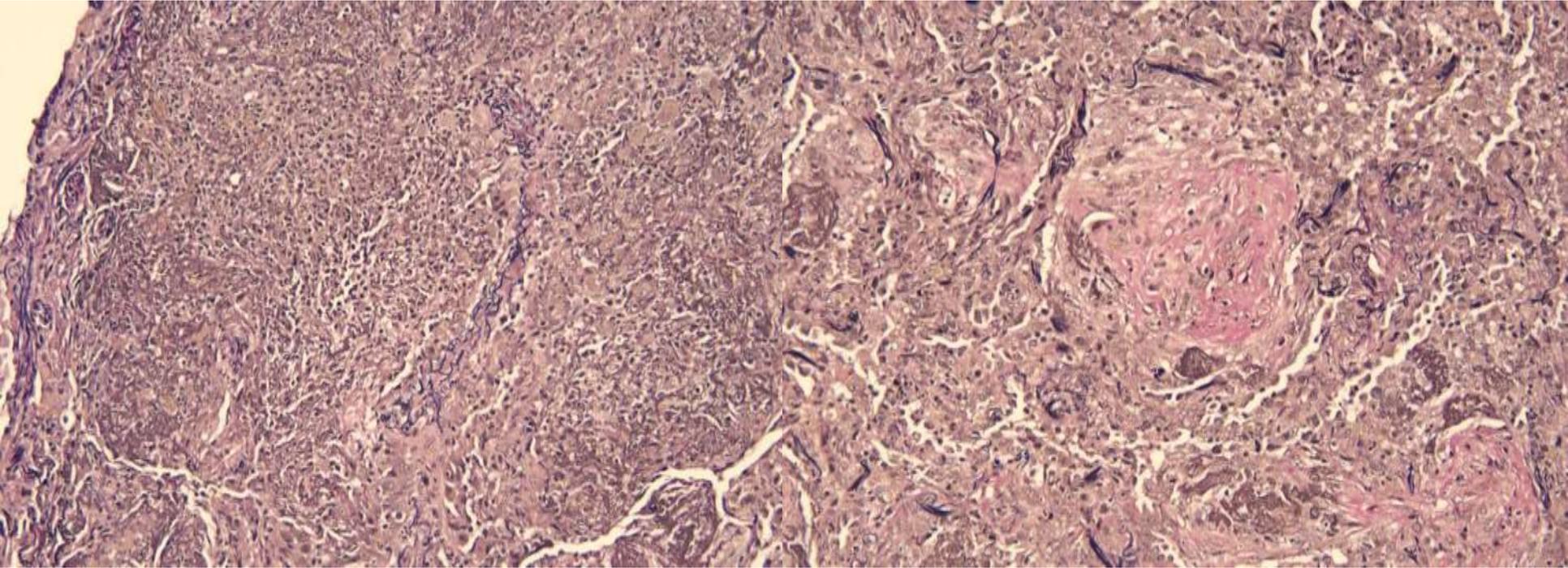
Right upper lobe

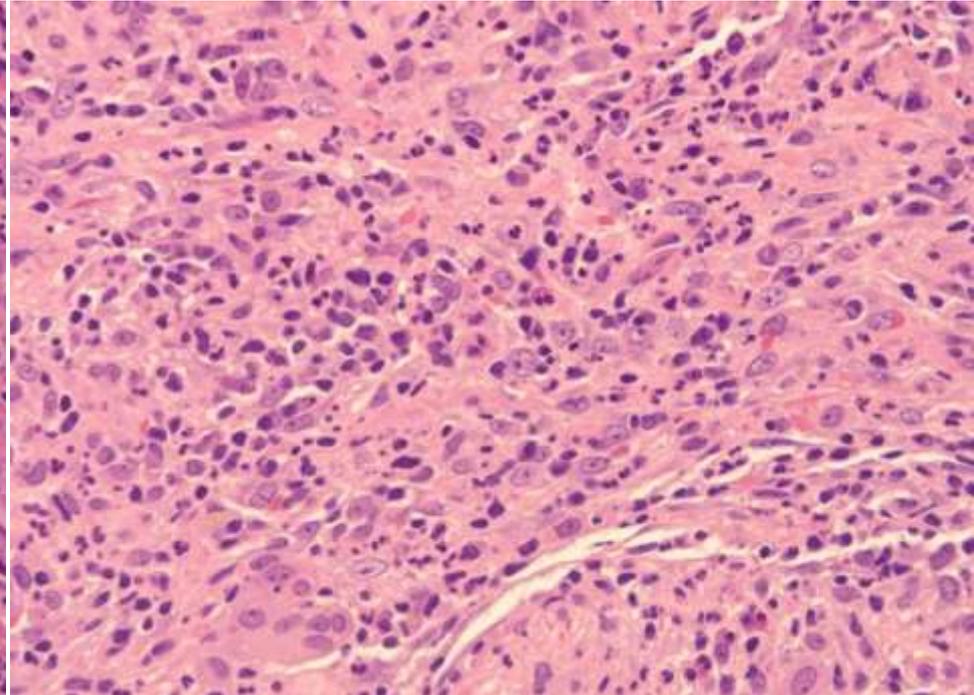
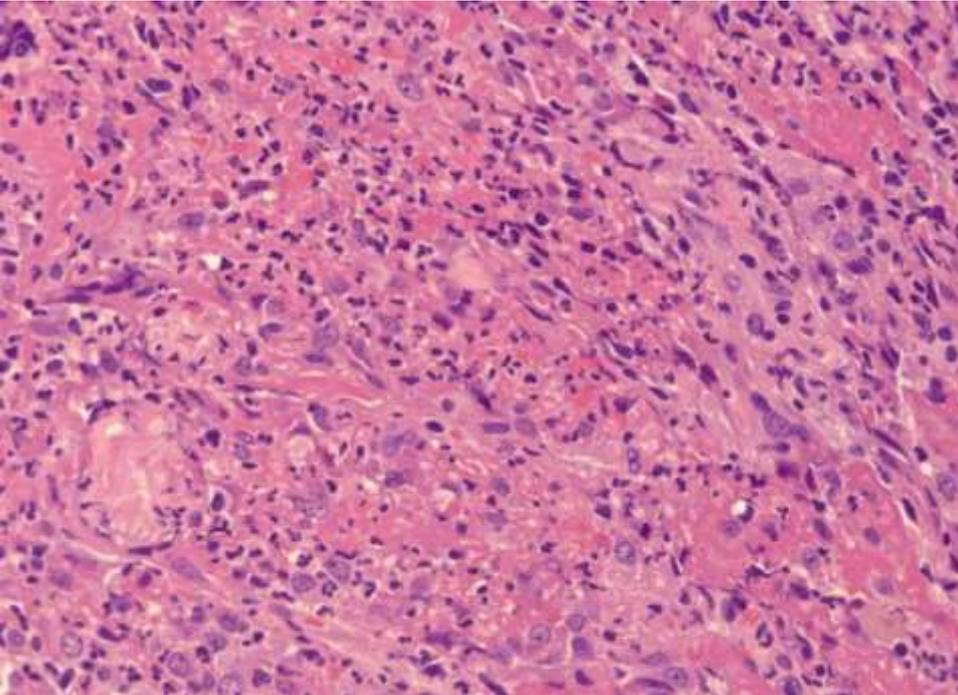












Patient smoked “synthetic  
marijuana” prior to developing  
lung disease.

His son brought the product home and said:  
“Hey Dad... Smoke this!!!”

Reference:

Berkowitz et al. “Pulmonary effects of synthetic marijuana:  
chest radiography and CT findings.  
Am J Roent 2015; 204: 750-757.

**Our patient smoked it for 5-7 days prior to getting sick**

# Synthetic marijuana

- Synthetically produced cannabanoids which are sprayed onto plants and herbs to mimic the appearance of cannabis and can be smoked.
- They have a different chemical structure from THC, they are readily available across the US, and their use is increasing.
- Potency ranges from 4 to 660 times more potent than THC.
- Effects vary from mood elevation and relaxation to anxiety, panic, hallucinations, paranoia, psychosis, suicidal ideation, and paralysis.
- May also induce: tachycardia, hypertension, arrhythmias, myocardial ischemia, spasms, seizures, tremors, nausea and vomiting.
- It is not picked up on normal urine drug tests but there are special tests available which detect up to 22 synthetic cannabinoid compounds

# Bronchiolocentric acute and chronic inflammatory infiltrates with associated bronchiolitis obliterans

- CT scan:
  - Diffuse centrilobular nodules
    - Tree in bud pattern
- Follow up CT scans:
  - Show evidence of bronchiolitis obliterans
- Pathology:
  - Patchy organizing pneumonia with striking bronchiolocentric distribution
  - Bronchiolitis obliterans
  - Patchy peribronchiolar fibrosis
  - Fibrinous pneumonitis
  - Scattered eosinophils
  - +/- giant cells

# Differential diagnosis for tree in bud pattern of miliary nodular infiltrates in the lung

- Infectious disease
  - Mycobacterial infection
  - Fungus
  - Mycoplasma/viral
- Congenital airway disease
  - CF
  - Dyskinetic cilia syndromes
  - Bronchiectasis
- Toxic fume inhalation
- Aspiration
- Connective Tissue disease
  - Sjogren's/follicular bronchiolitis
  - RA/follicular bronchiolitis
- Idiopathic
  - COP/BOOP
  - Panbronchiolitis
- ABPA
- Neoplastic
  - Carcinoma
  - Leukemia/lymphoma

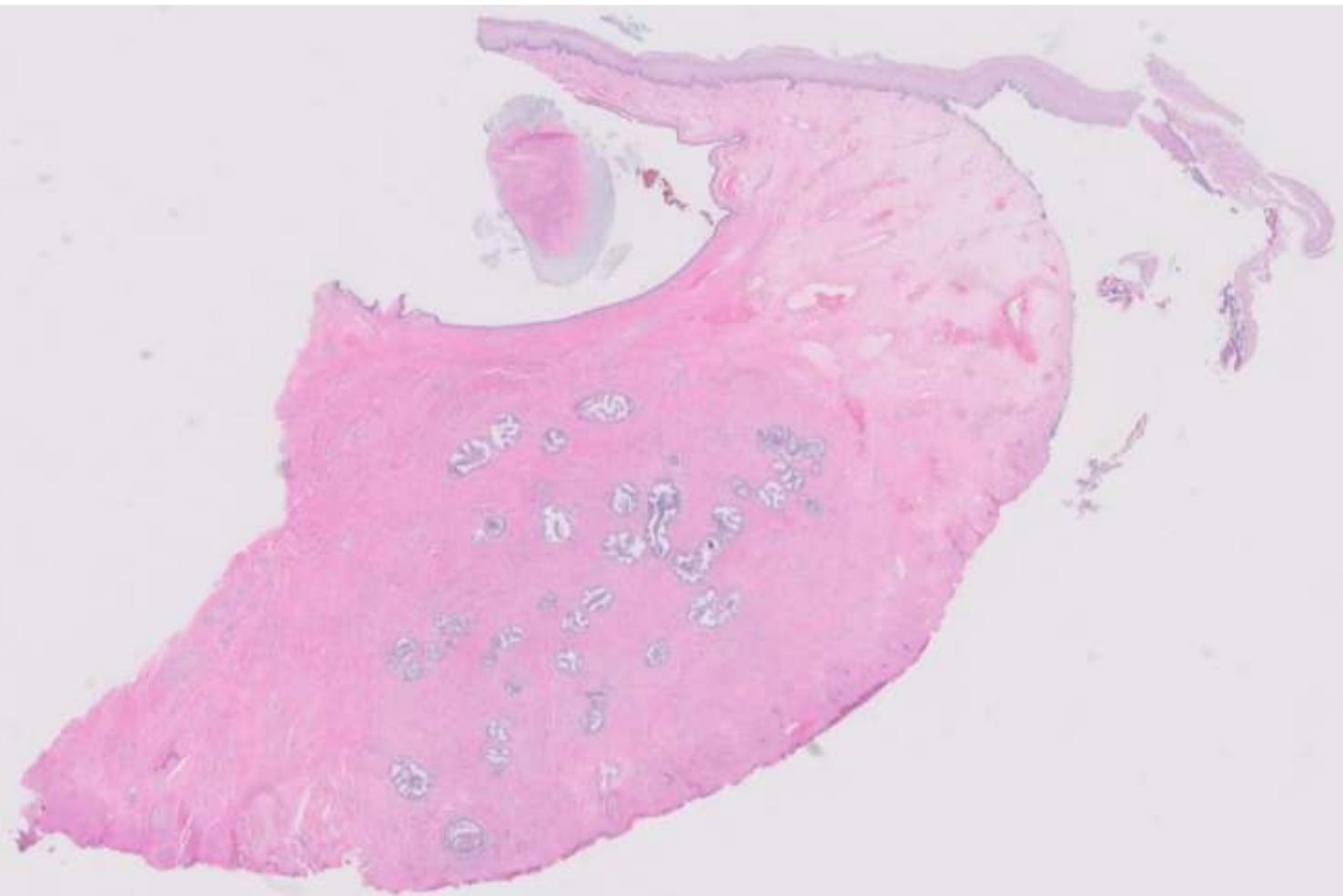
# Follow of patients:

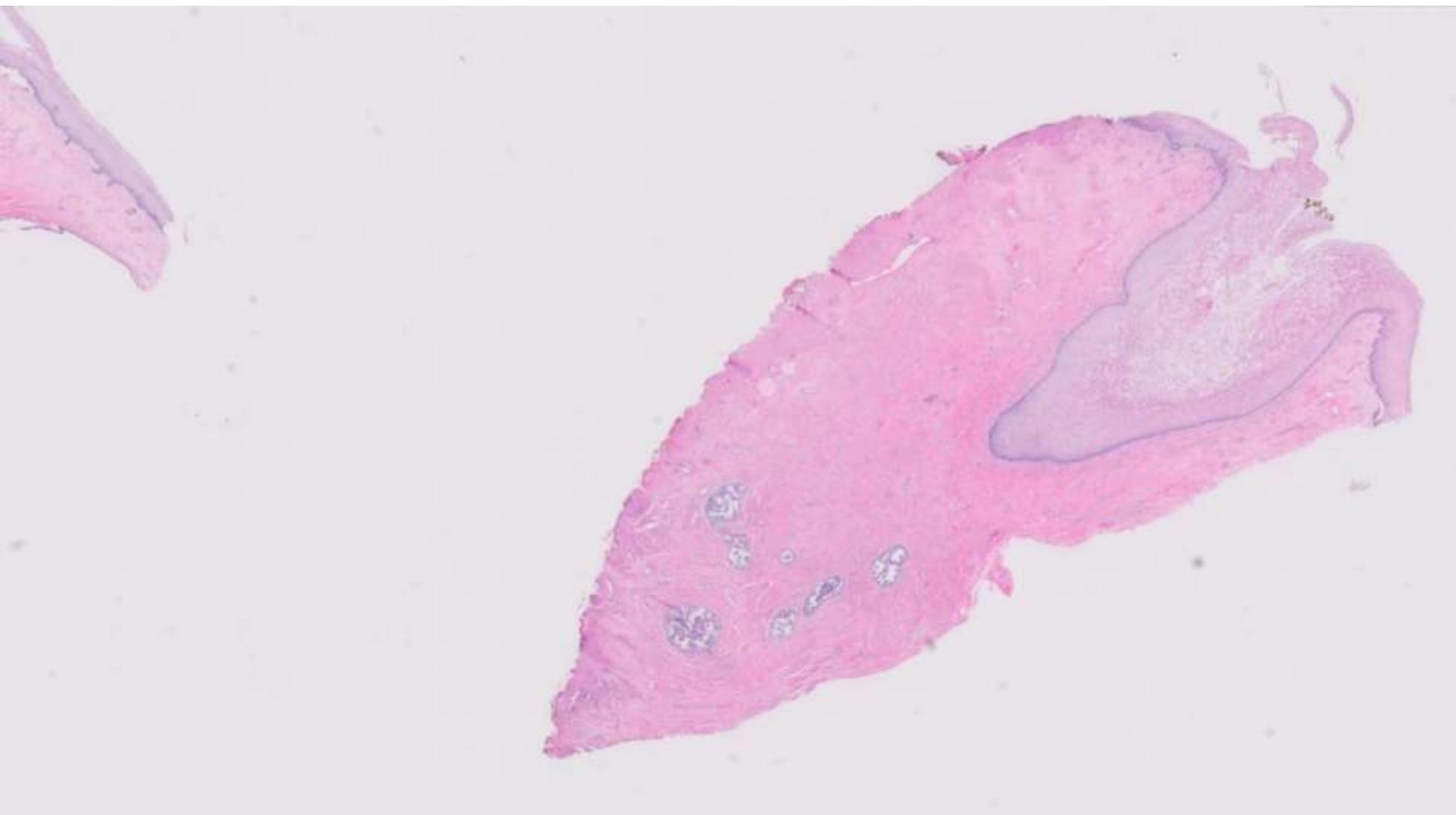
- One reported death: ARF
  - Others with persistent chronic dyspnea and cough
  - Exercise intolerance
  - PFT's with moderate to severe airflow obstruction
  - Mild to Moderate decrease in diffusion capacity
- Our patient:
    - Pending

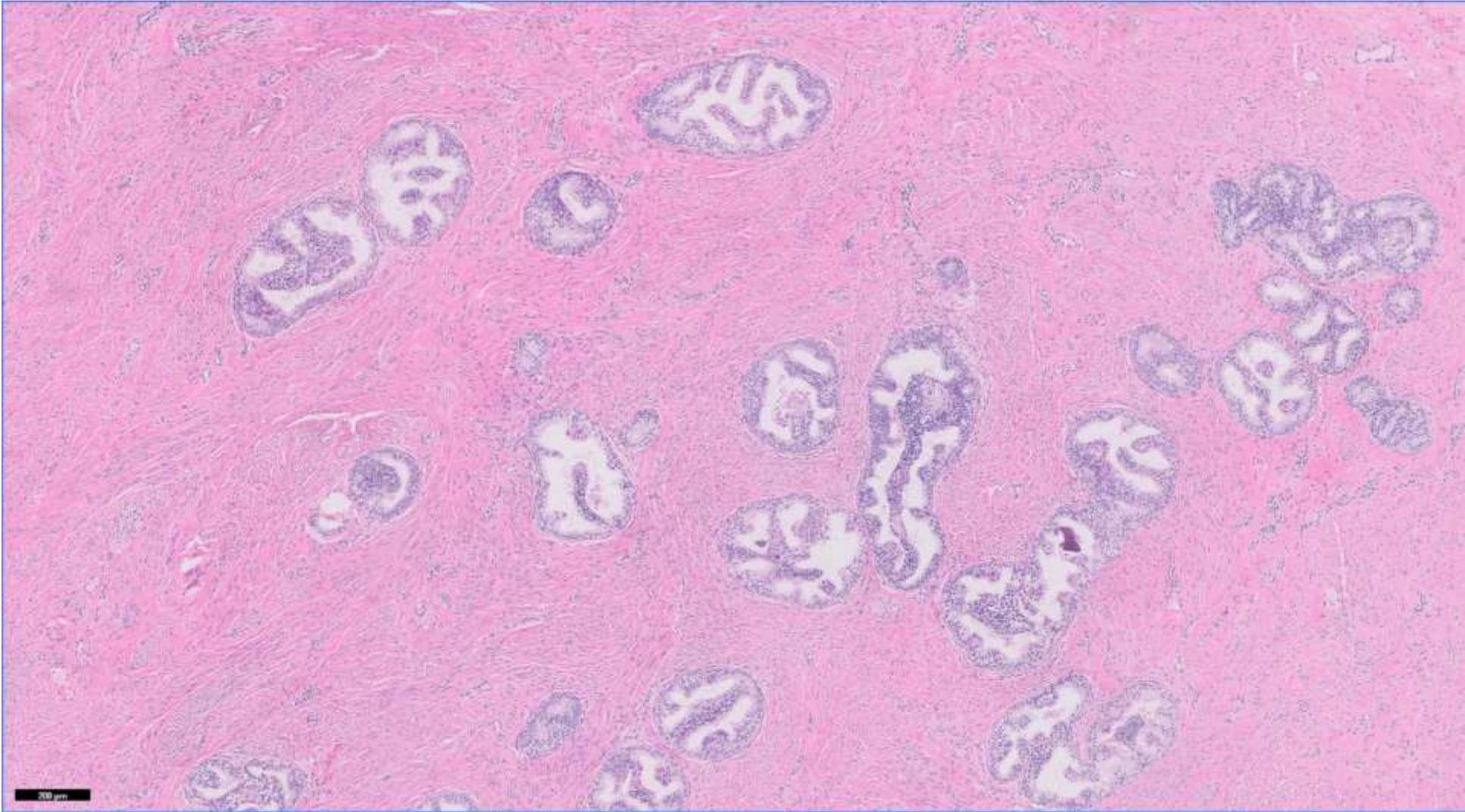
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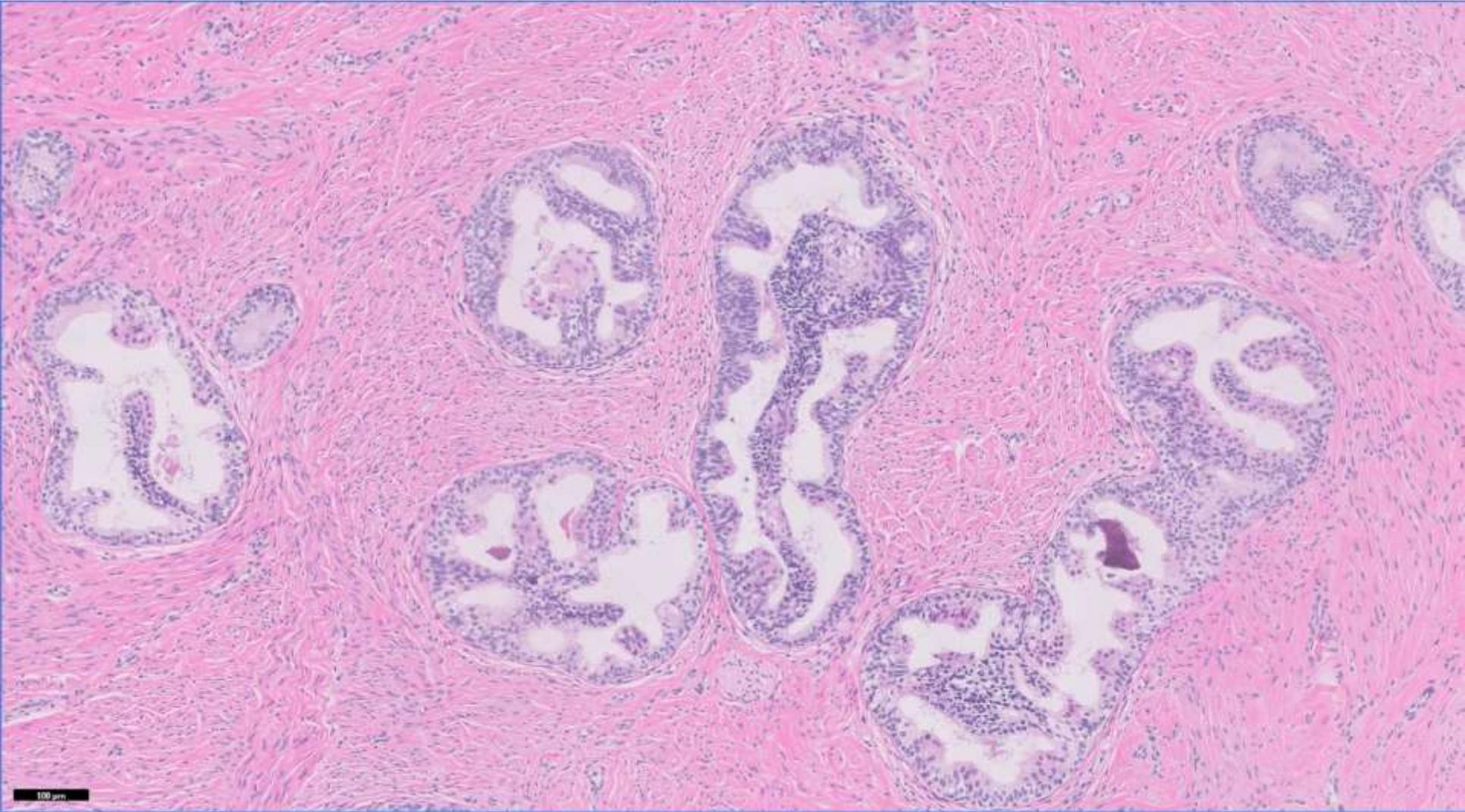
**Neslihan Kayraklioglu/Nick Ladwig; UCSF**

36-year-old F cervical HSIL and a recent Dx of ductal carcinoma of breast, undergoes cervical LEEP.

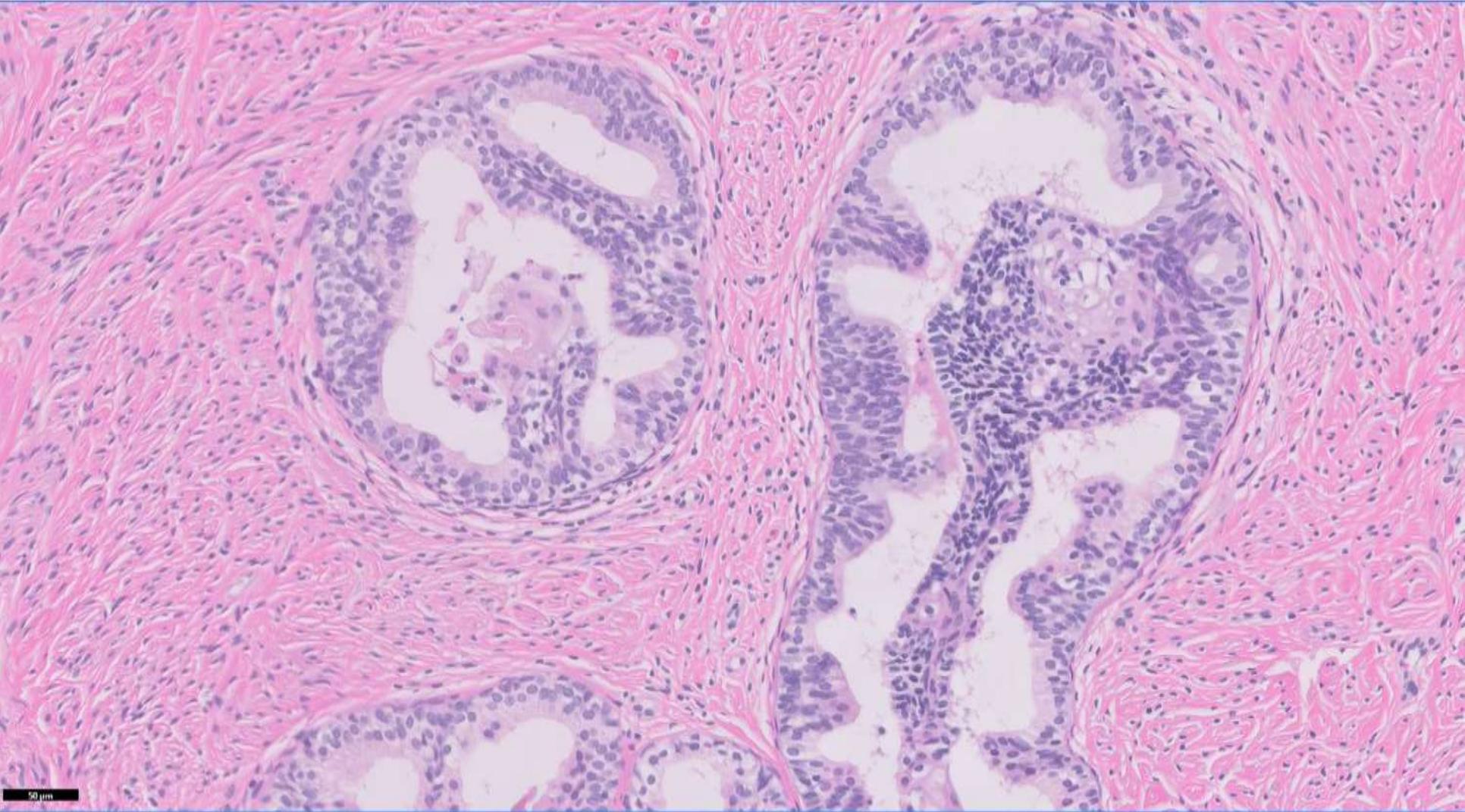




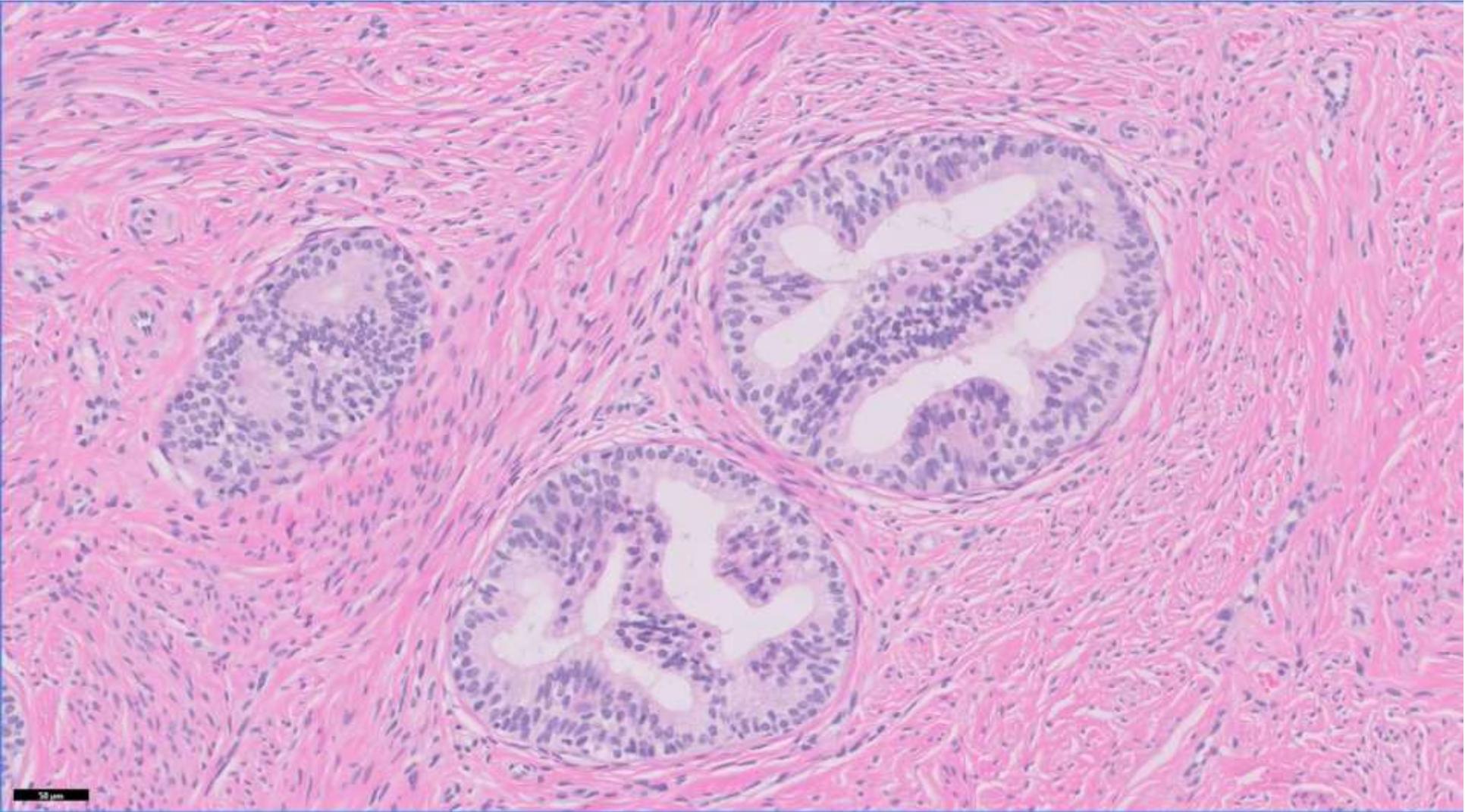




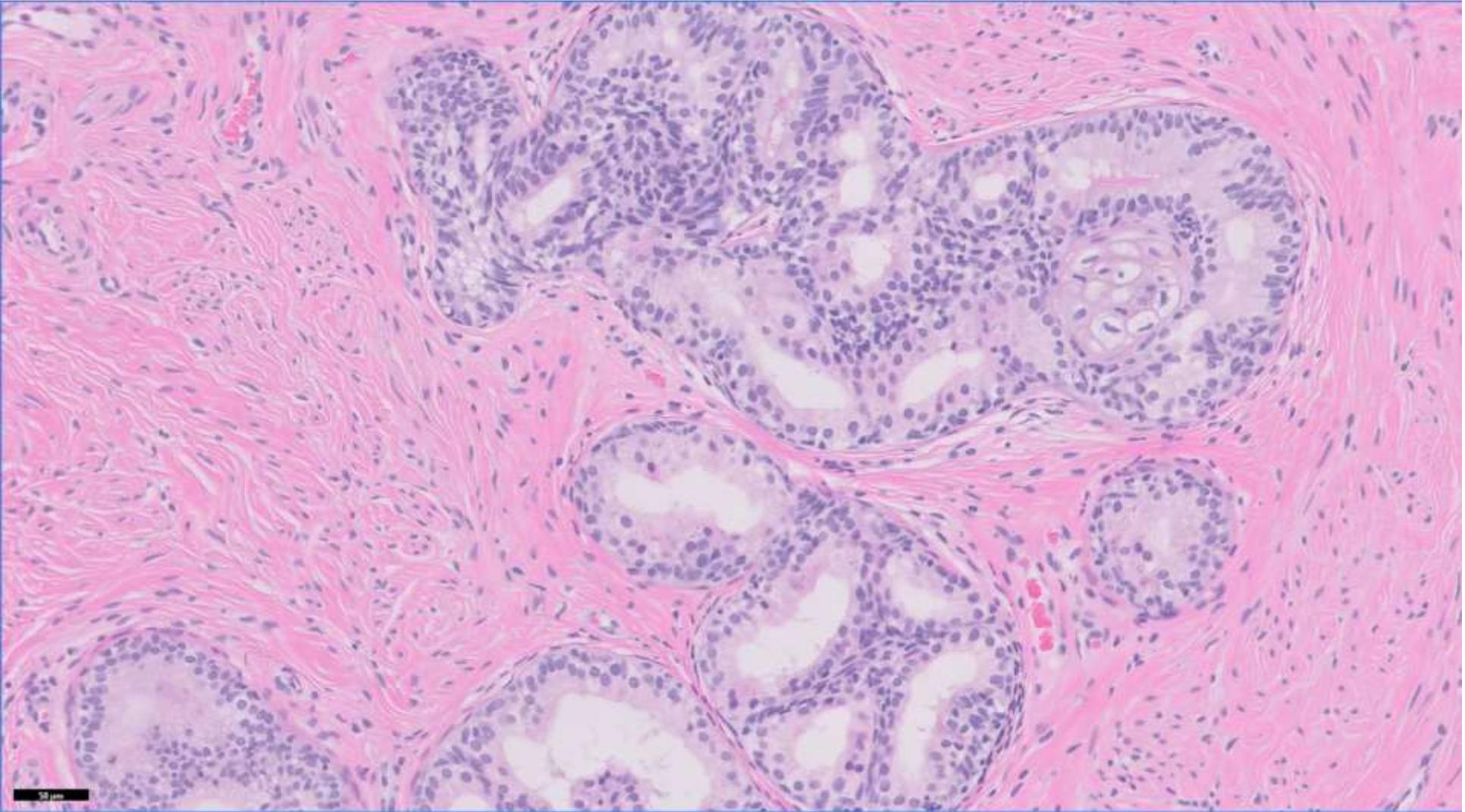
100  $\mu$ m



50  $\mu$ m



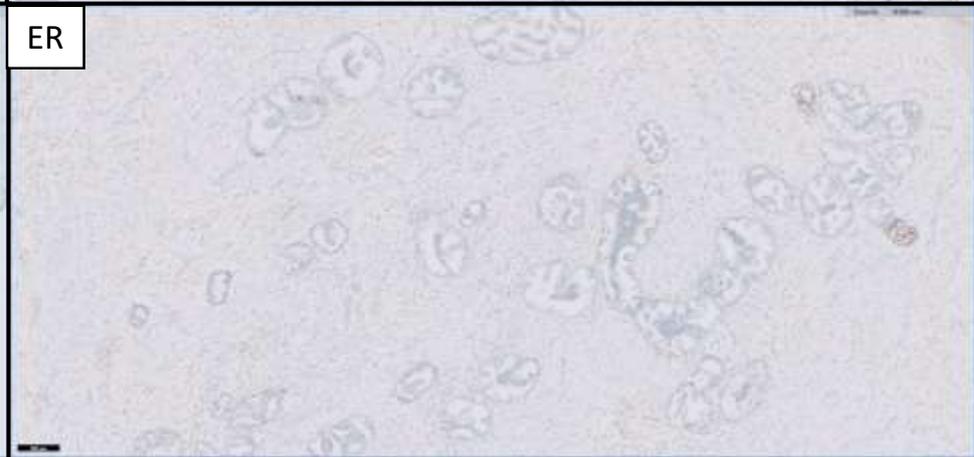
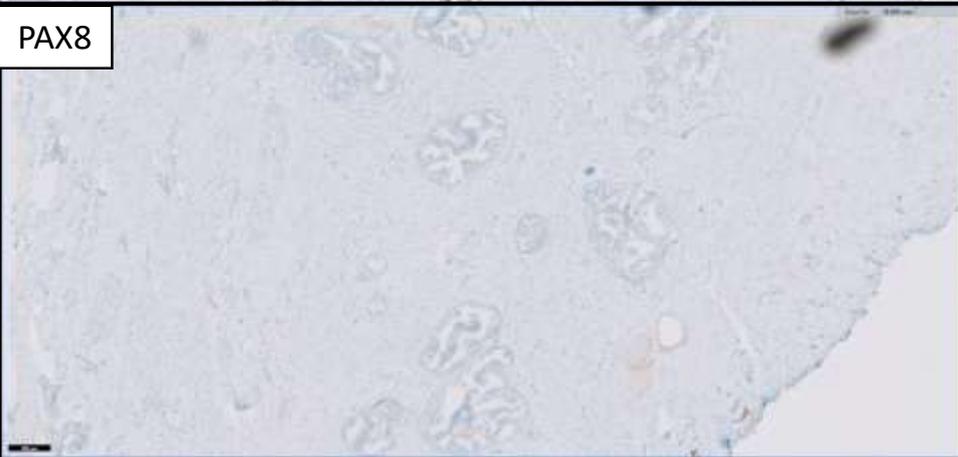
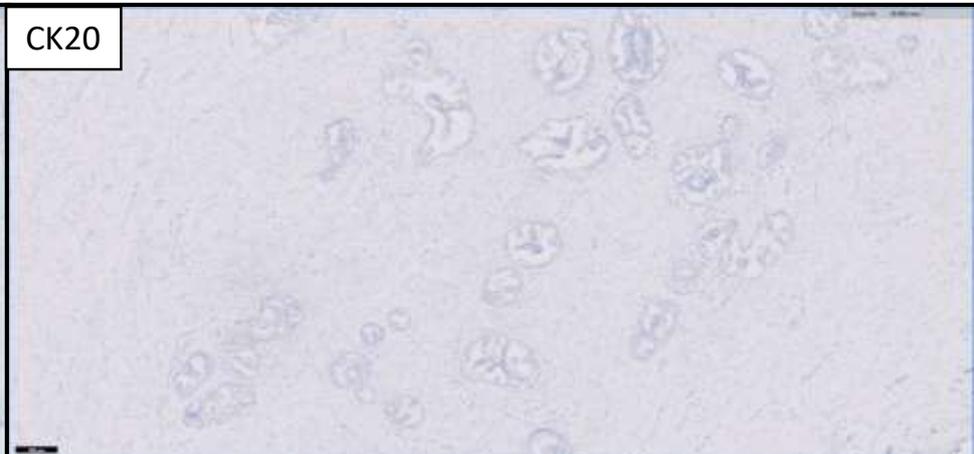
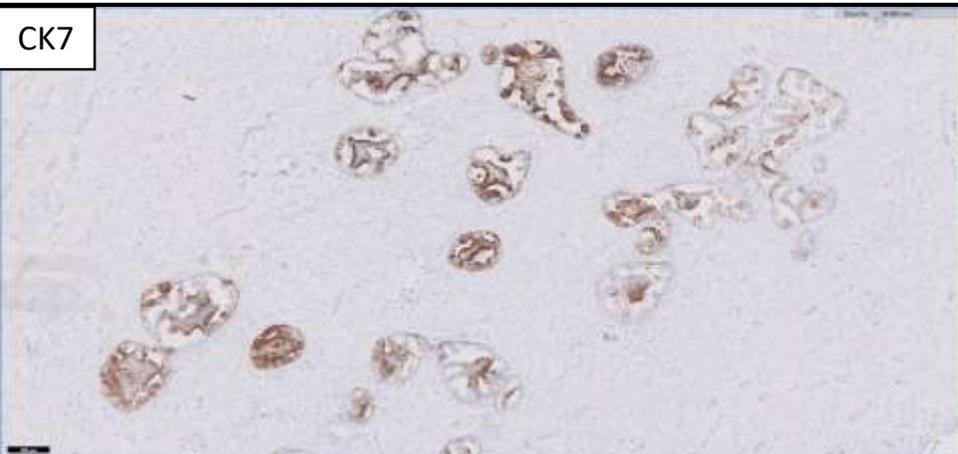
50  $\mu$ m

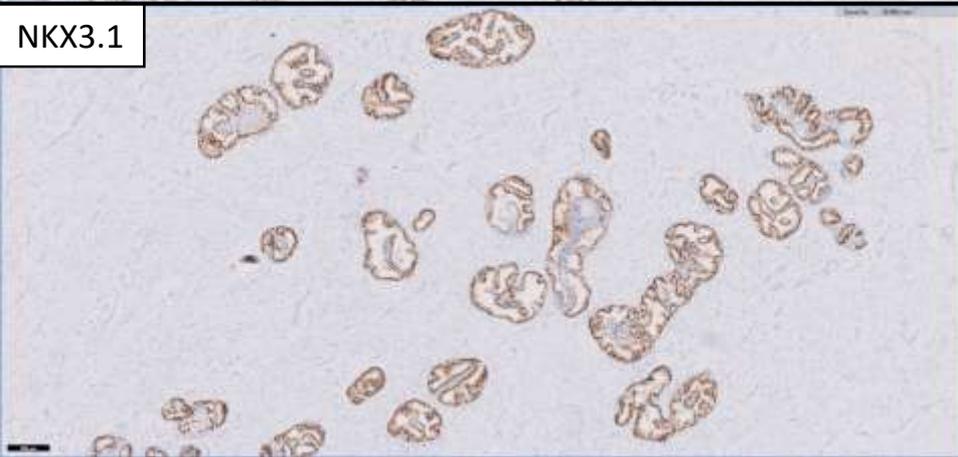
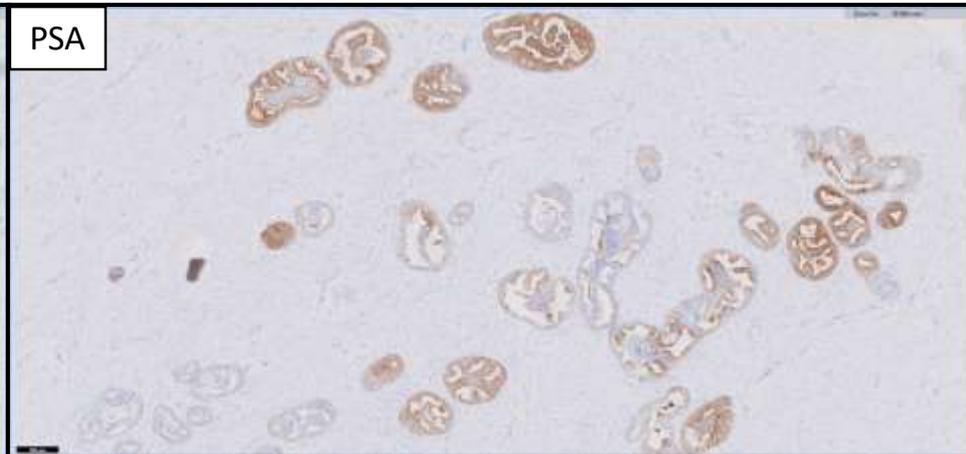
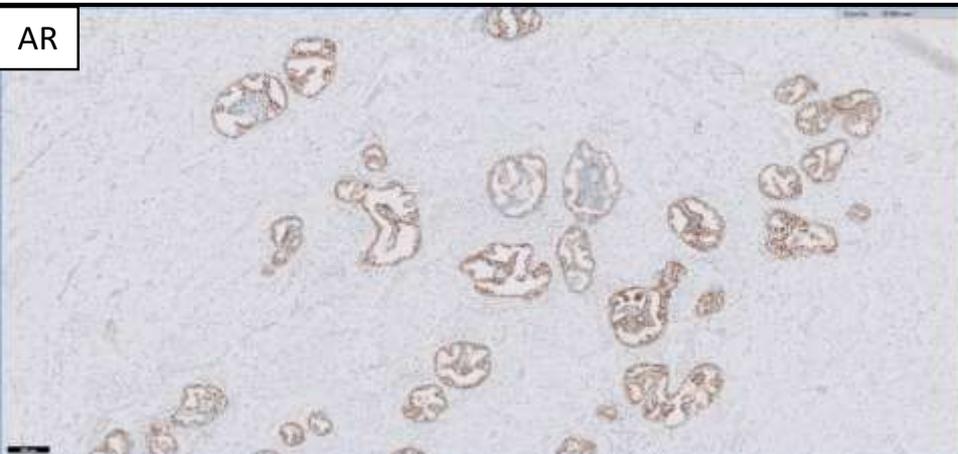


50 μm

# Differential diagnosis

- Carcinoma
  - Endometrioid adenocarcinoma
  - Endocervical adenocarcinoma
  - Adenoid basal carcinoma
- Squamous metaplasia within normal endocervical glands
- Mesonephric remnants
- Ectopic prostatic tissue





# Ectopic Prostatic Tissue in the Uterine Cervix and Vagina

## *Report of a Series With a Detailed Immunohistochemical Analysis*

*W. Glenn McCluggage, FRCPath,\* Raji Ganesan, MRCPath,† Lynn Hirschowitz, FRCPath,‡  
Keith Miller, FIBMS,§ and Terence P. Rollason, FRCPath†*

### **Possible explanations**

- Monoclonal teratoma -- A theoretical possibility.
- Prostatic metaplasia occurring within mesonephric remnants – No report shows association with mesonephric remnants and squamous metaplasia is not seen mesonephric remnants in cervix/vagina.
- **Prostatic metaplasia of endocervical glands – Prostatic metaplasia has been reported in surface epithelium and deep glands in vagina and cervix, particularly in the setting of excess androgen.**
- **Developmental anomaly; misplaced Skene's glands.**

Misplaced Skene's Glands: Glandular Elements in the Lower Female Genital Tract That Are Variably Immunoreactive With Prostate Markers and That Encompass Vaginal Tubulosquamous Polyp and Cervical Ectopic Prostatic Tissue

Paul Kelly, F.R.C.Path., Hilary A. McBride, F.I.B.M.S., Kathryn Kennedy, F.I.B.M.S., Lynette E. Connolly, F.I.B.M.S., and W.Glenn McCluggage, F.R.C.Path.

**Skene's glands**

Paired glands situated in the paraurethral tissues opening into the lower urethra and are considered to be the female equivalent of prostatic glands in the male.

Misplaced Skene's glands:

1. Ectopic prostatic tissue
2. Tubulosquamous polyp: Polypoid lesion in vagina, composed of squamous and glandular elements.

Both lesions are positive for NKX3.1, PSA and PSAP, confirming the Skene gland origin. Other IHC: AR, ER, CD10, AMACR also positive.

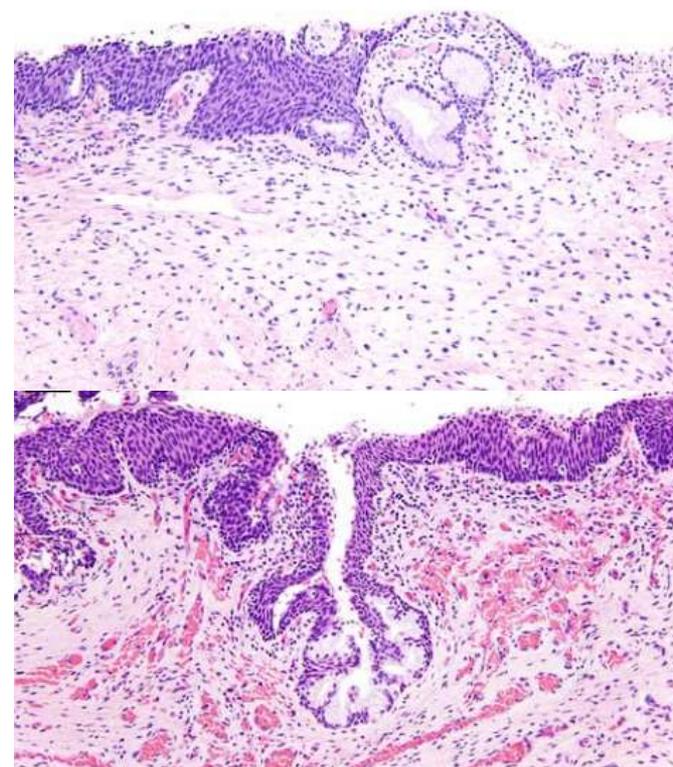
# Prostatic Metaplasia of the Vagina and Uterine Cervix

## An Androgen-associated Glandular Lesion of Surface Squamous Epithelium

William J. Anderson, MBChB,\*† David L. Kolin, MD, PhD,† Grace Neville, MB BCh,†  
David A. Diamond, MD,‡ Christopher P. Crum, MD,† Michelle S. Hirsch, MD, PhD,†  
and Sara O. Vargas, MD\*†

Case No.	Gland Location	Gland Distribution	# of Blocks Involved (Submitted)	Transitional Metaplasia	NKX3.1	PSA	AR	CK7	Additional Stains	
1	Vagina	SE	6 (6)	Yes	+	+	+	+	Negative: ER, GATA3, PAX8, CK20	
2	Vagina	SE	4 (5)	Yes	+	-	+	+		
3	Vagina	SE	1 (4)	Yes	+	+	+	+		
4	Vagina	SE	3 (3)	Yes	+	+	+	+		
5	Vagina	SE	6 (7)	Yes	+	+	+	+		
6	Vagina	SE	19 (29)	Yes	+	+	+	+		
7	Exocervix	SE	1 (2)	Yes	+	+	+	+	Negative: p63	
8	Vagina	SE+LP	1 (1)	No	+	+	+	+		
9	Vagina	SE+LP	1 (1)	No	+	+	+	+		
10	Vagina	SE+LP	1 (2)	No	+	-	+	+		
11	Vagina	SE+LP	3 (4)	No	+	+	+	+	Positive: CK20	
12	Vagina	SE+LP	1 (2)	Yes	+	-	+	-		
13	Vagina	SE	1 (1)	No	+	-	ND	ND	Negative: PAX8	
Total, n (%)					8/13 (62)	13/13 (100)	9/13 (69)	12/12 (100)	11/12 (92)	

- indicates negative; +, positive; LP, lamina propria; ND, not determined; SE, surface epithelium.



# Malignancy potential?

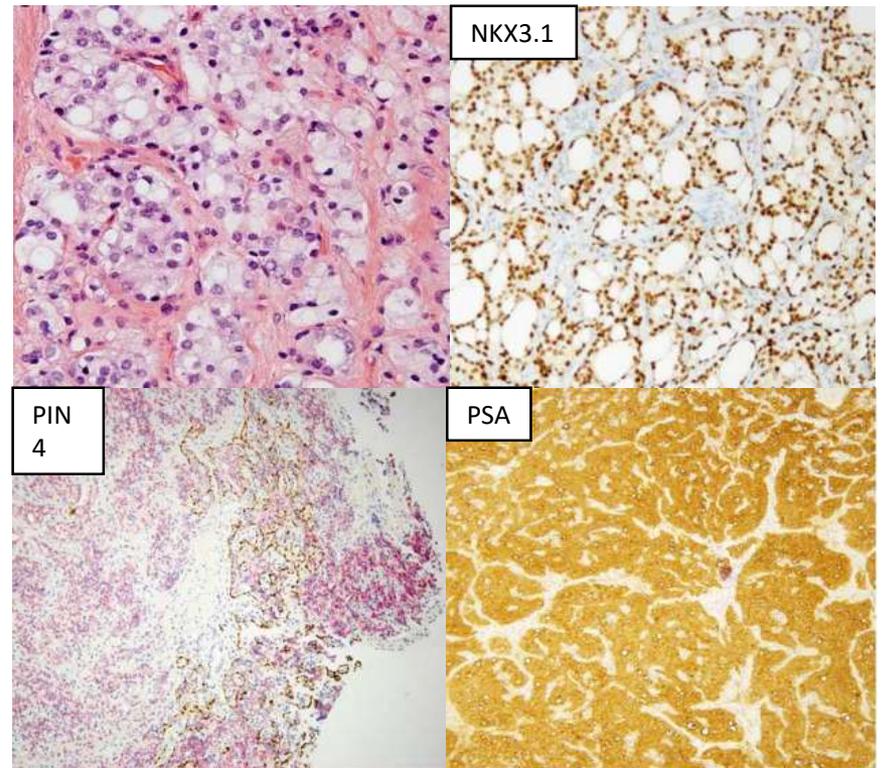
- Rare cases of adenocarcinomas arising from ectopic prostate tissue are reported in men.
- Rare cases of periurethral Skene gland adenocarcinomas are reported in women, resembling prostate adenocarcinoma.
- **No reports yet to show prostatic adenocarcinoma arising from ectopic prostate tissue in women.**

# Skene's Glands Adenocarcinoma

## A Series of 4 Cases

Aline C. Tregnago, MD\* and Jonathan I. Epstein, MD\*†

References	Age (y)	First Symptoms	Size (cm)	Site	Serum PSA	IHC
Svanholm et al <sup>3</sup>	72	Polypoid tumor	1.0	Urethra	NA	PSA+, PSAP+
Zaviacic et al <sup>1</sup>	70	Flat tumor	1.5	Anterior vaginal wall	NA	PSA+, PSAP+
Dodson et al <sup>5</sup>	70	Flat tumor	2.0	Adjacent to the urethra	5.9	PSA+, PSAP+
Sloboda et al <sup>4</sup>	46	Stress incontinence and urethritis	3.5	Paraurethral	NA	PSA+, PSAP+
Murphy et al <sup>6</sup>	NA	NA	NA	NA	NA	PSA+
Pongtippan et al <sup>8</sup>	88	Gross hematuria	3.0	Periurethral	1.3	PSA+
Korytko et al <sup>7</sup>	71	Painless hematuria, urge incontinence	3.0	Bladder neck	54.5	PSA+, PSAP+
Present report	63	NA	1.5	Periurethral	NA	PSA+, PSAP+, NKX3.1+, PIN4
Present report	87	Periurethral nodule	2.0	Periurethral	0.8	PSA+, PSAP+, NKX3.1+, PIN4
Present report	87	Bleeding urethral polyp	1.0	Periurethral	NA	PSA+, PSAP+, NKX3.1+, PIN4
Present report	61	Urethral polyp	1.5	Periurethral	4.9	PSA+, PSAP+, NKX3.1+, PIN4



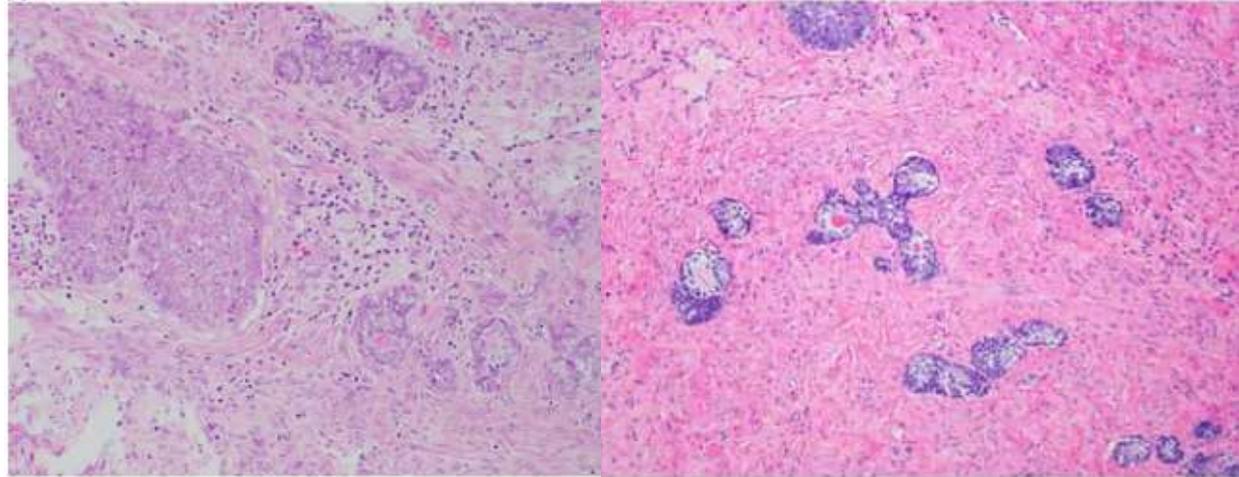
## Skene's Gland Derivatives in the Female Genital Tract and Cervical Adenoid Basal Carcinoma are Consistently Positive With Prostatic Marker NKX3.1

Rand Hawari, F.R.C.Path., Larissa Fernandes, F.I.B.M.S., Kay J. Park, M.D.,  
and W. Glenn McCluggage, F.R.C.Path.

**TABLE 2.** *Immunohistochemical results*

Case	Diagnosis	NKX3.1	PSA	PSAP
1	Adenoid basal carcinoma and ectopic prostatic tube	Diffuse	NP	NP
2	Adenoid basal carcinoma	Diffuse	Negative	Focal
3	Adenoid basal carcinoma	Diffuse	Negative	Focal
4	Adenoid basal carcinoma	Diffuse	Negative	Focal
5	Adenoid basal carcinoma	Diffuse	Negative	Negative
6	Adenoid basal carcinoma	Diffuse	Negative	Negative
7	Ectopic prostatic tissue	Diffuse	Focal	Focal
8	Ectopic prostatic tissue	Diffuse	Negative	Negative
9	Ectopic prostatic tissue	Diffuse	Focal	Focal
10	Ectopic prostatic tissue	Diffuse	Negative	NP
11	Ectopic prostatic tissue	Diffuse	Negative	NP
12	Ectopic prostatic tissue	Diffuse	NP	NP
13	Ectopic prostatic tissue	Diffuse	Focal	NP
14	Ectopic prostatic tissue	Diffuse	Negative	NP
15	Ectopic prostatic tissue	Diffuse	Negative	NP
16	Ectopic prostatic tissue	Diffuse	Focal	Focal
17	Tubulosquamous polyp	Diffuse	Negative	Diffuse
18	Tubulosquamous polyp	Diffuse	Negative	Focal
19	Tubulosquamous polyp	Diffuse	Negative	NP

NP indicates not performed; PSA, prostatic-specific antigen; PSAP, prostatic acid phosphatase.



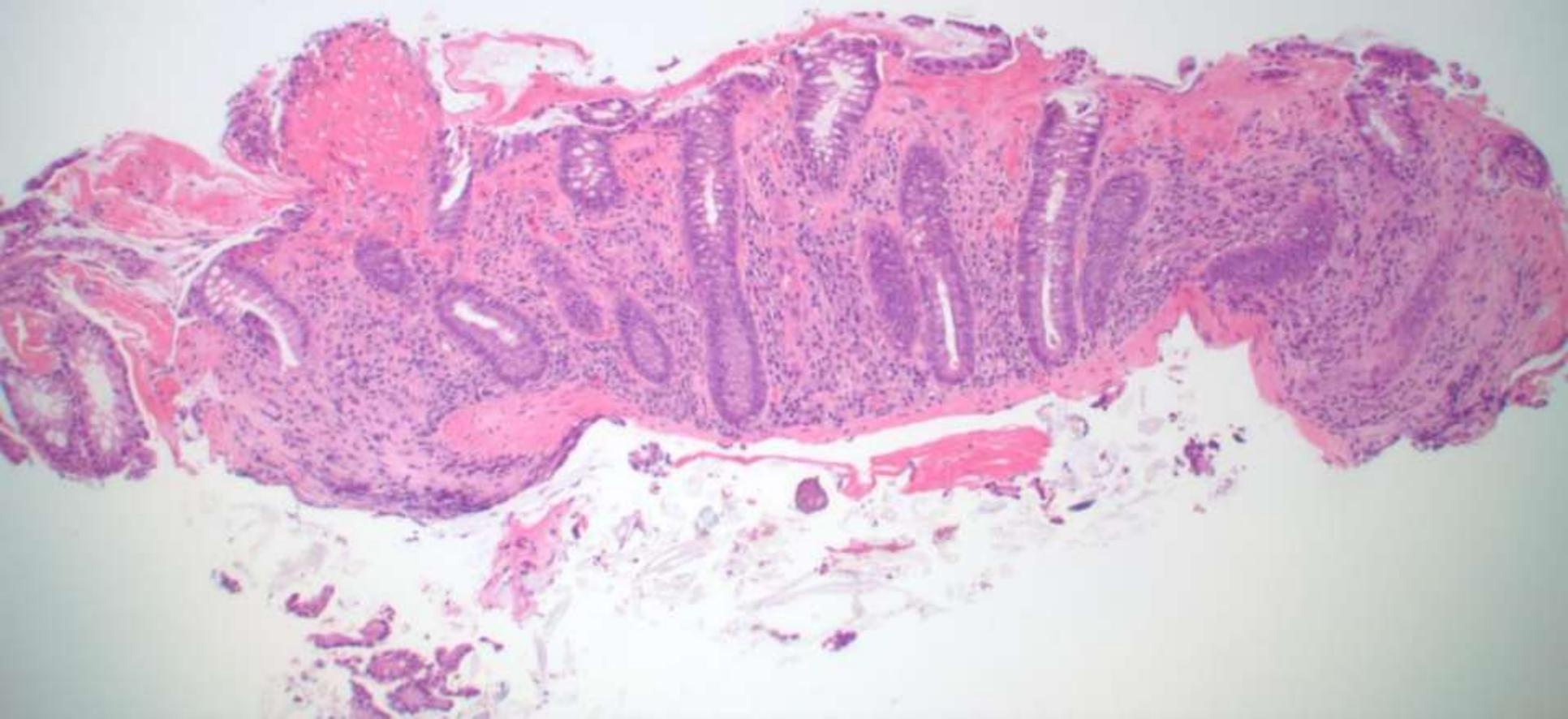
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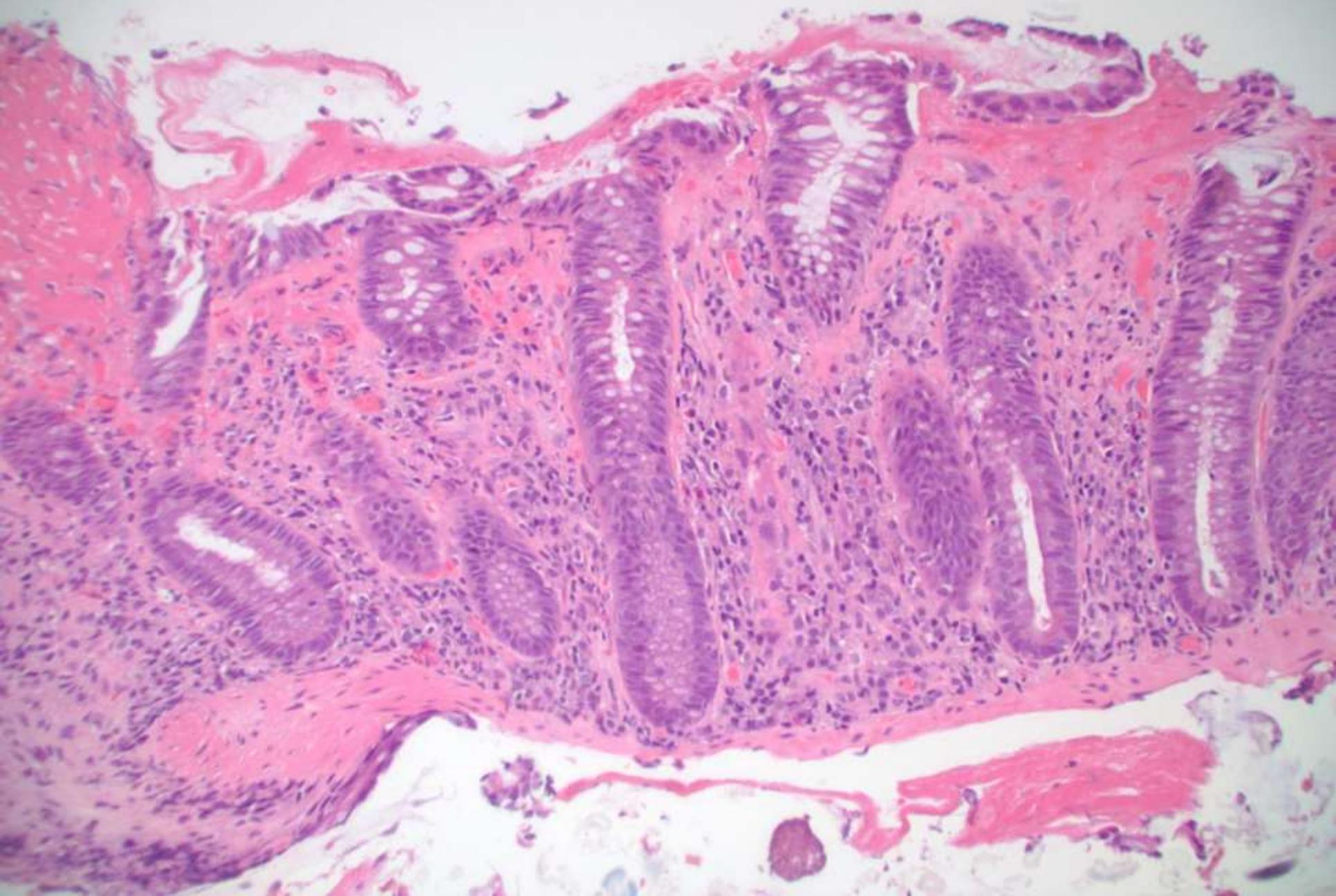
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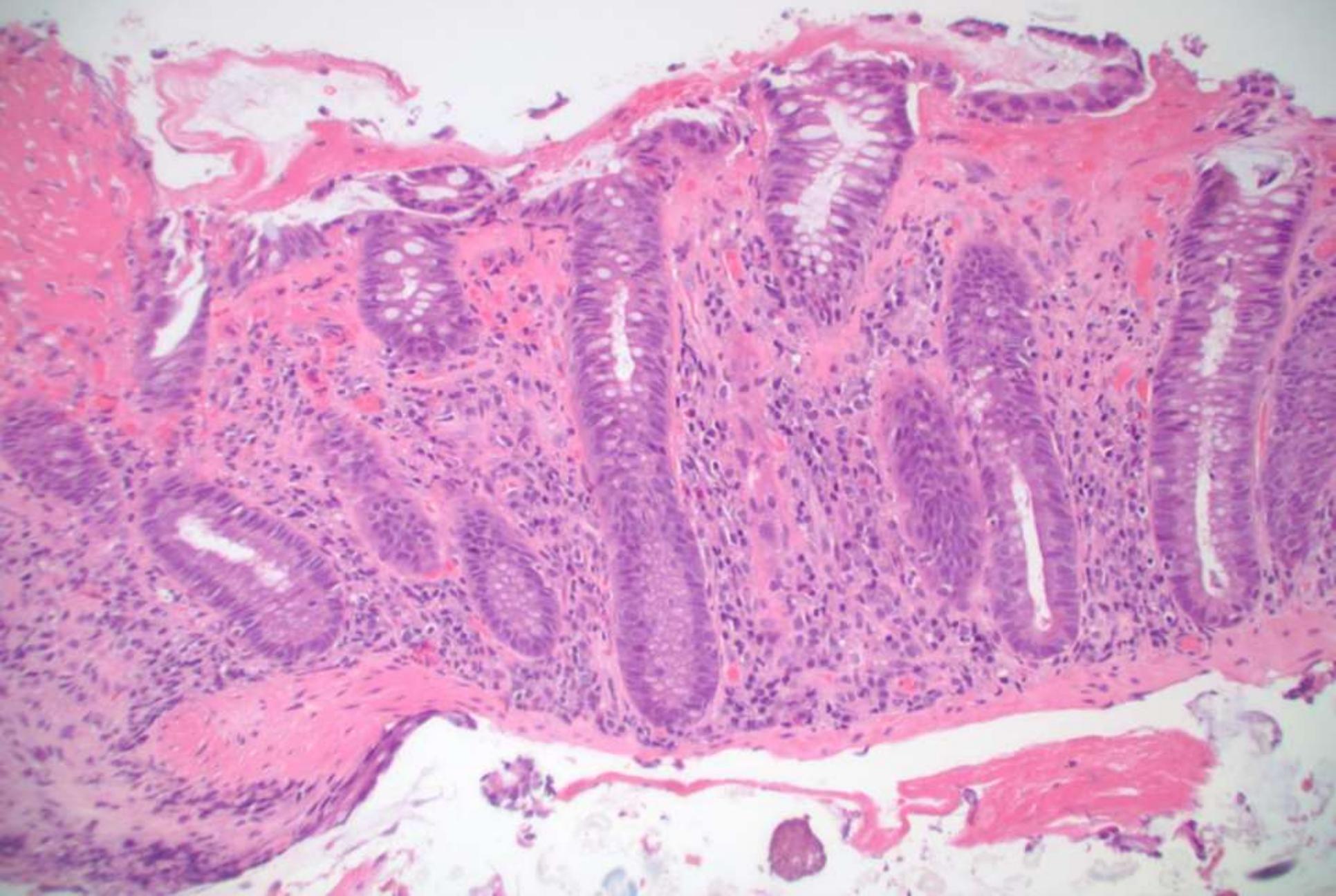
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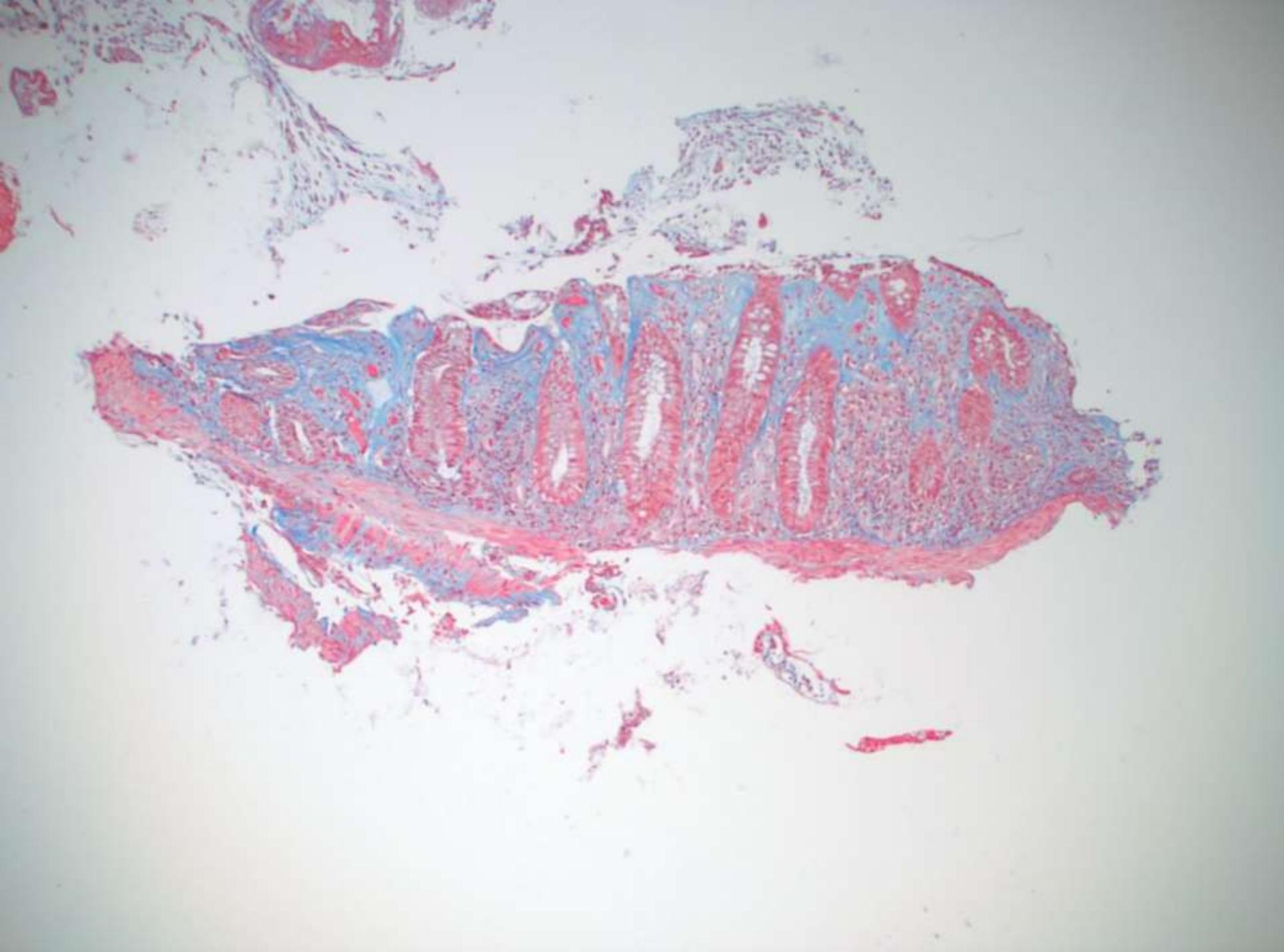
**Natalie Patel; El Camino Hospital**

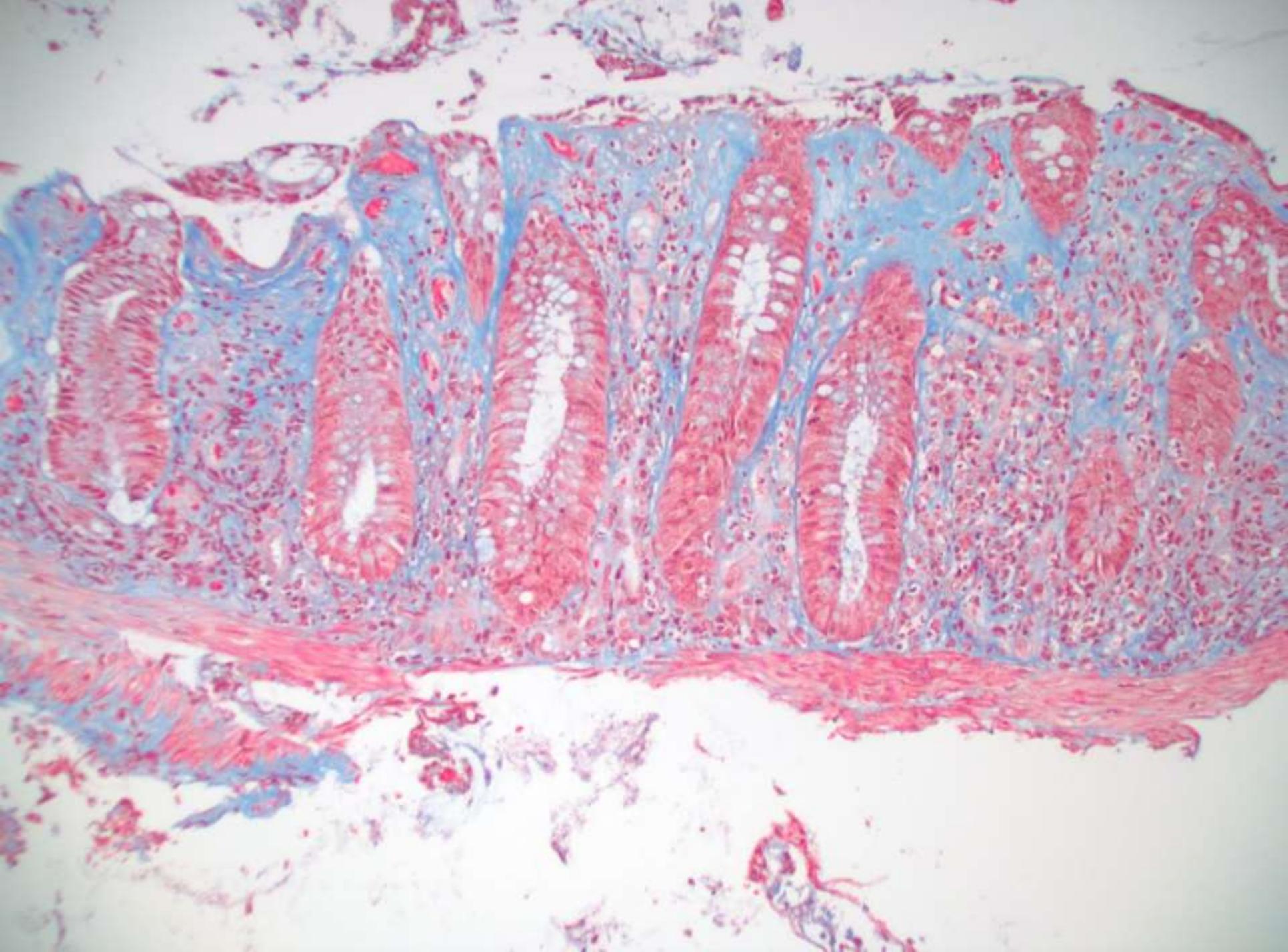
61-year-old F with diarrhea. Biopsies performed.











# Clinical findings



C.Difficile toxin negative X 3  
Stool cultures negative  
Stool biofire negative  
No medication history

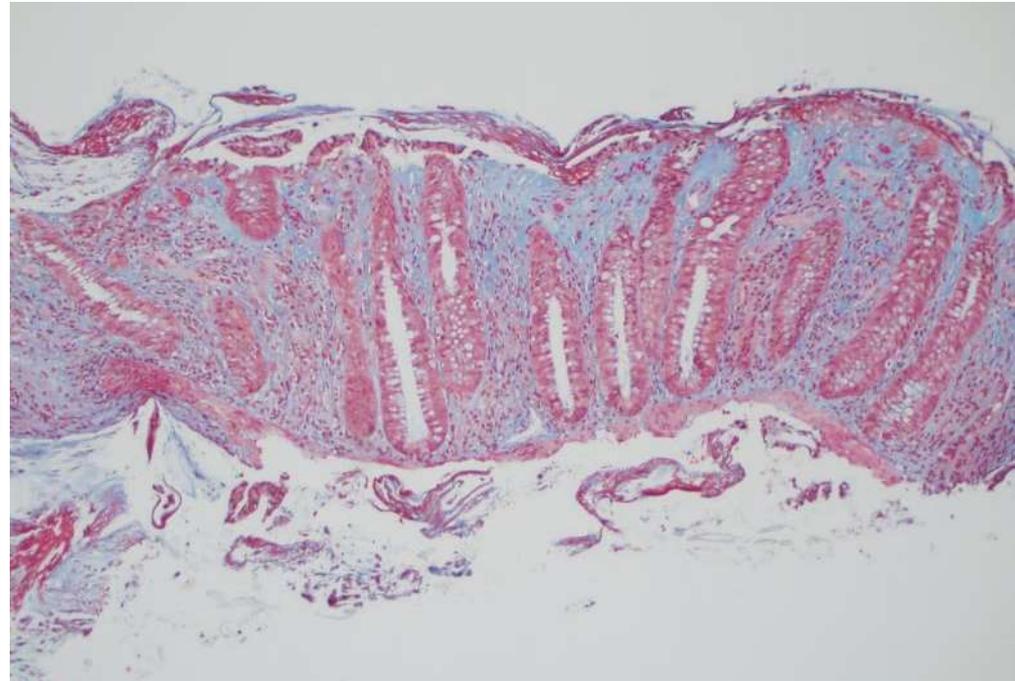
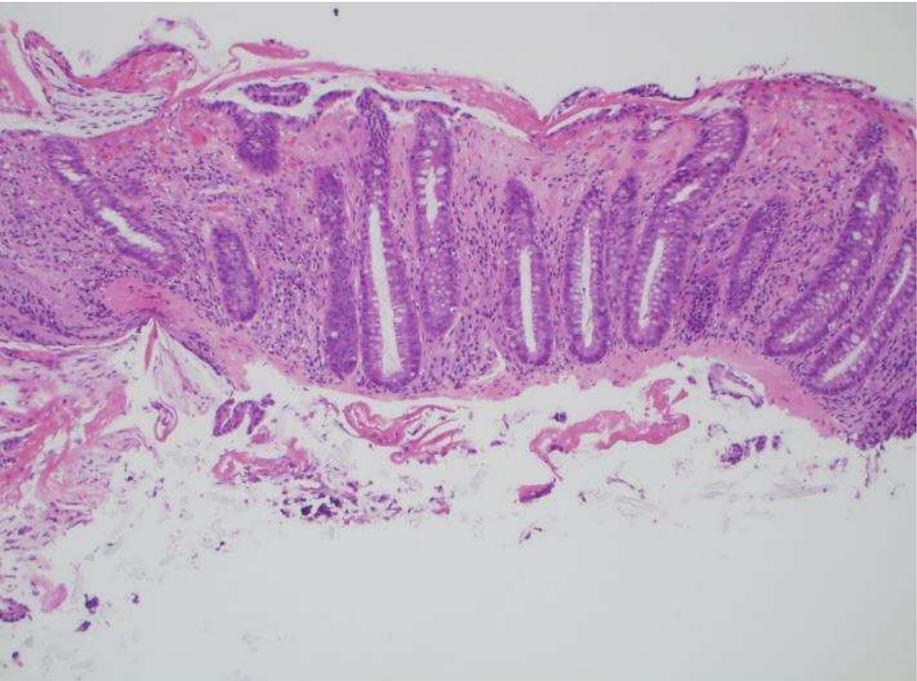


1 month of watery diarrhea

# Differential diagnosis - Pseudomembranous colitis

- C. difficile
- Other toxin induced infectious etiology (E. coli O157:H7)
- Ischemia
- NSAIDs
- Collagenous colitis





# Collagenous colitis

- 1<sup>st</sup> described in 1976 by Clas Lindstrom
- Typically normal endoscopy
- Thickened subepithelial collagen > 10 microns
- Intact crypt architecture
- Lymphocytosis
- +/- neutrophils
- Entrapped RBCs/capillaries

# Pseudomembranous collagenous colitis

- Variant form of collagenous colitis
- Requires exclusion of other etiologies
- May support possible toxic and/or ischemic mechanism for collagenous colitis

# Pseudomembranous Collagenous Colitis

*Shan Yuan, MD, Victoria Reyes, MD, and Mary P. Bronner, MD*

**TABLE 1.** Pseudomembranous Collagenous Colitis: Clinical Characteristics

Patient No.	Age (yr) (at Diagnosis)/Gender	Duration of Diarrhea	Endoscopic Findings	Endoscopic Diagnosis	<i>C. difficile</i> / <i>E. coli</i> O157:H7	Ischemia	Estrogen/NSAID Use
1*	31/F	Unknown	NA	Proctitis/ASLC	+/ND	Excluded	No/No
2	67/F	Chronic	TC linear ulcers	Crohn's	ND/ND	Excluded	NA
3*†	56/F	7 weeks	Normal	NA	-/-	Excluded	No/No
4	67/F	6 weeks	Ulcers in TI and RC	Crohn's	ND/ND	Excluded	NA
5*†	64/F	8 weeks	Inflamed rectum	Ulcerative colitis	-/ND	Excluded	No/No
6†	54/F	Unknown	TI and cecum ulcers	Crohn's	-/ND	Excluded	No/Yes
7	67/F	6 years	NA	NA	NA/NA	Excluded	NA
8	49/F	Months	RC ulcers	NA	ND/ND	Excluded	NA
9*†	61/F	8 weeks	Erythema and granularity	Crohn's	-/-	Excluded	Yes/Yes
10†	81/F	2 weeks	RC ulcer and erythema	Crohn's	-/-	Excluded	No/No

NA, not available; TC, transverse colon; TI, terminal ileum; RC, right colon; ND, not done; ASLC, acute self-limited colitis.

\*No pathogenic organisms identified in stool culture.

†Stool examination negative for ova and parasites.

# Follow-up

- Patient started on Budesonide with improvement in symptoms
- Stool biofire is negative
- Remember pseudomembranes can be seen in collagenous colitis!

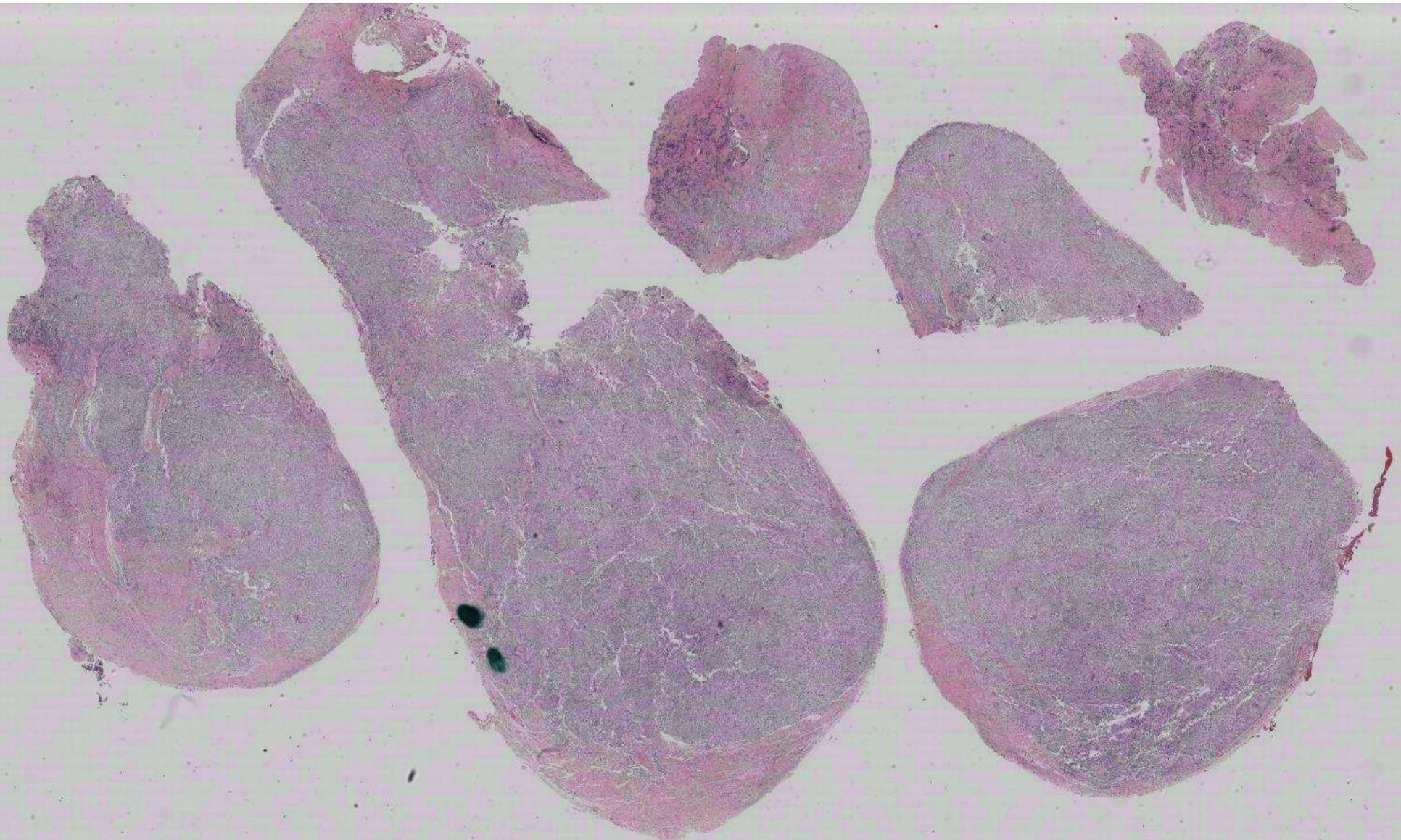
# References

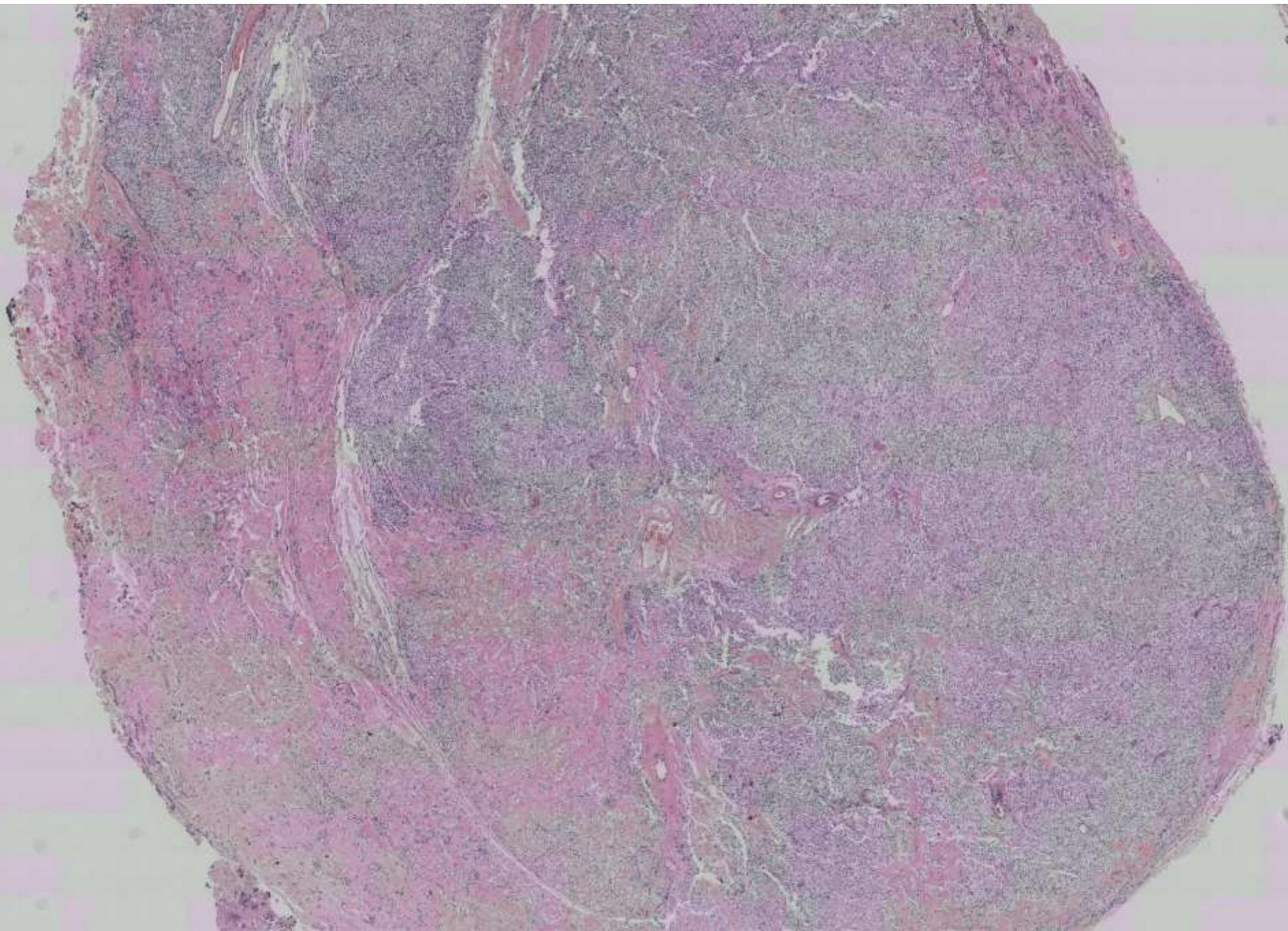
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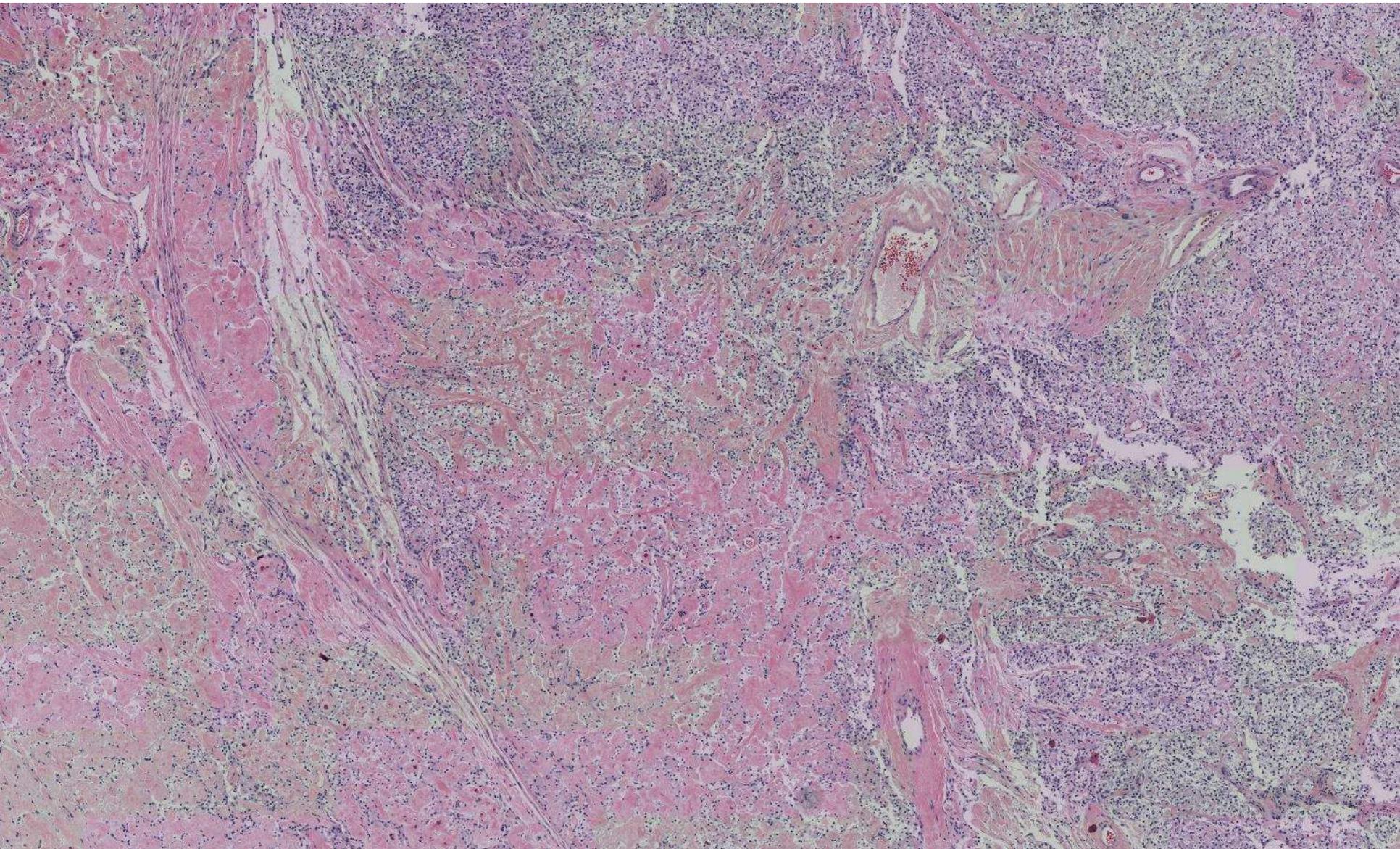
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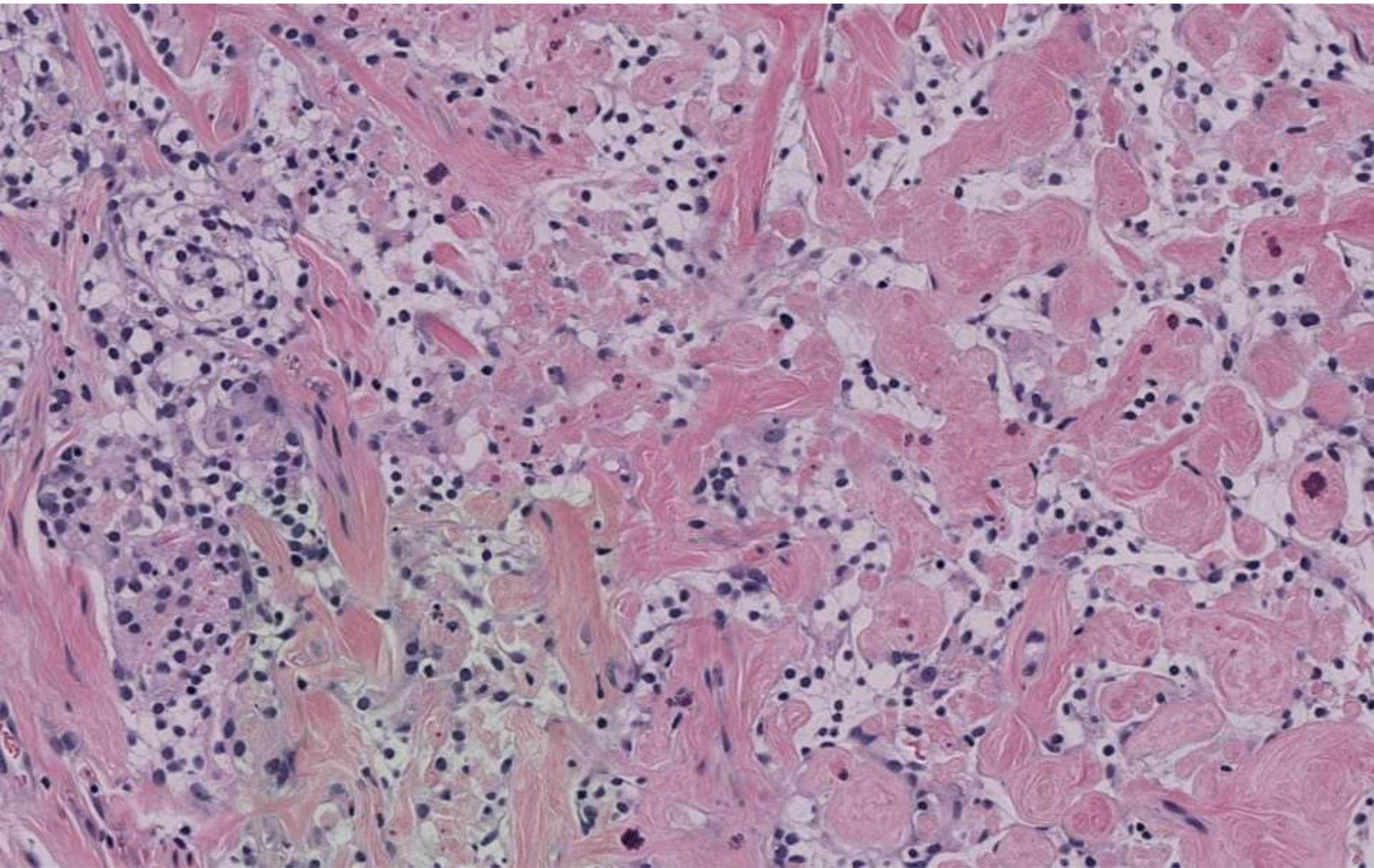
**Keith Duncan; Mills-Peninsula**

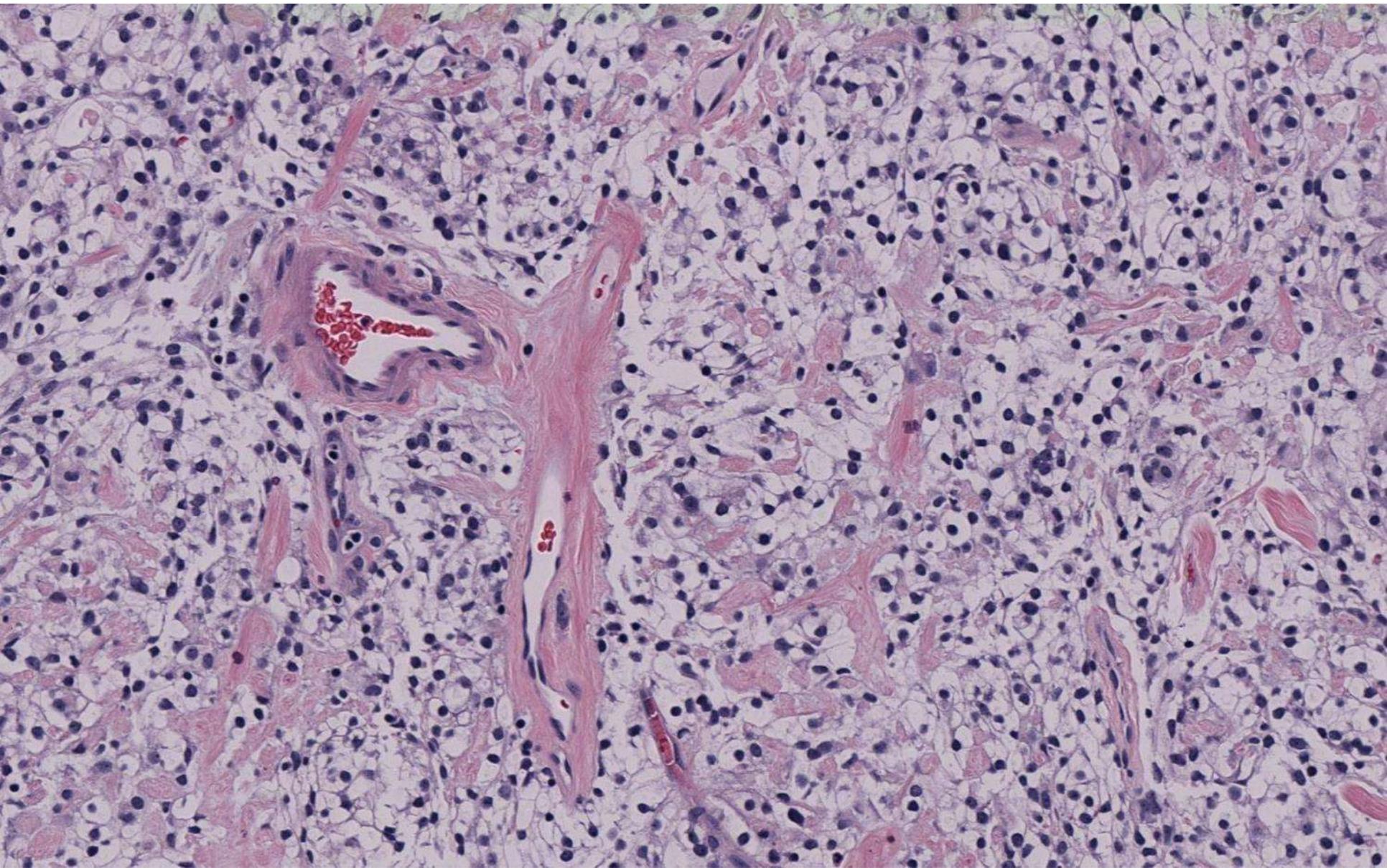
41-year-old M with leg weakness. MRI showed L4/L5  
lesion thought to be intradural schwannoma.

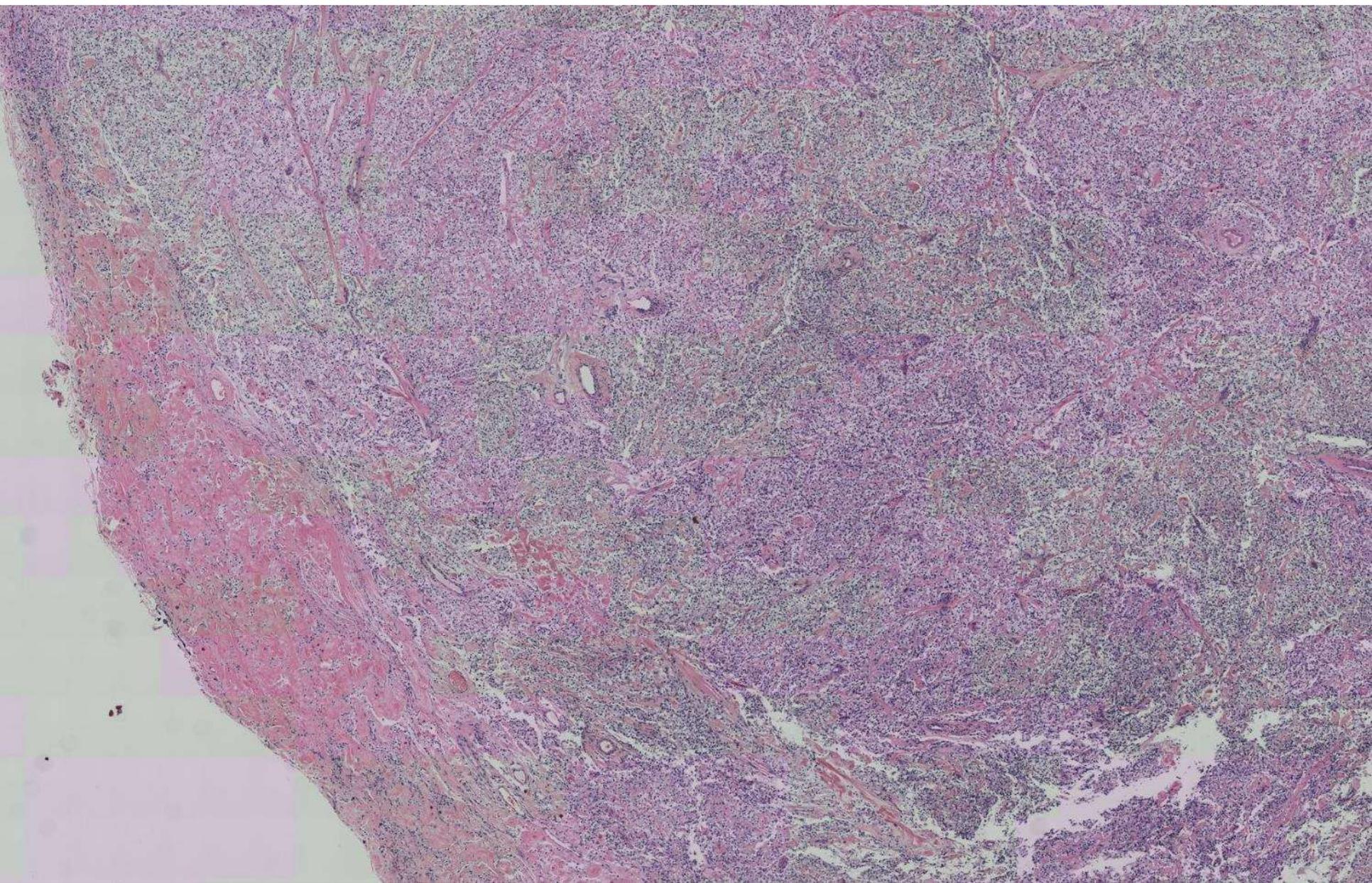


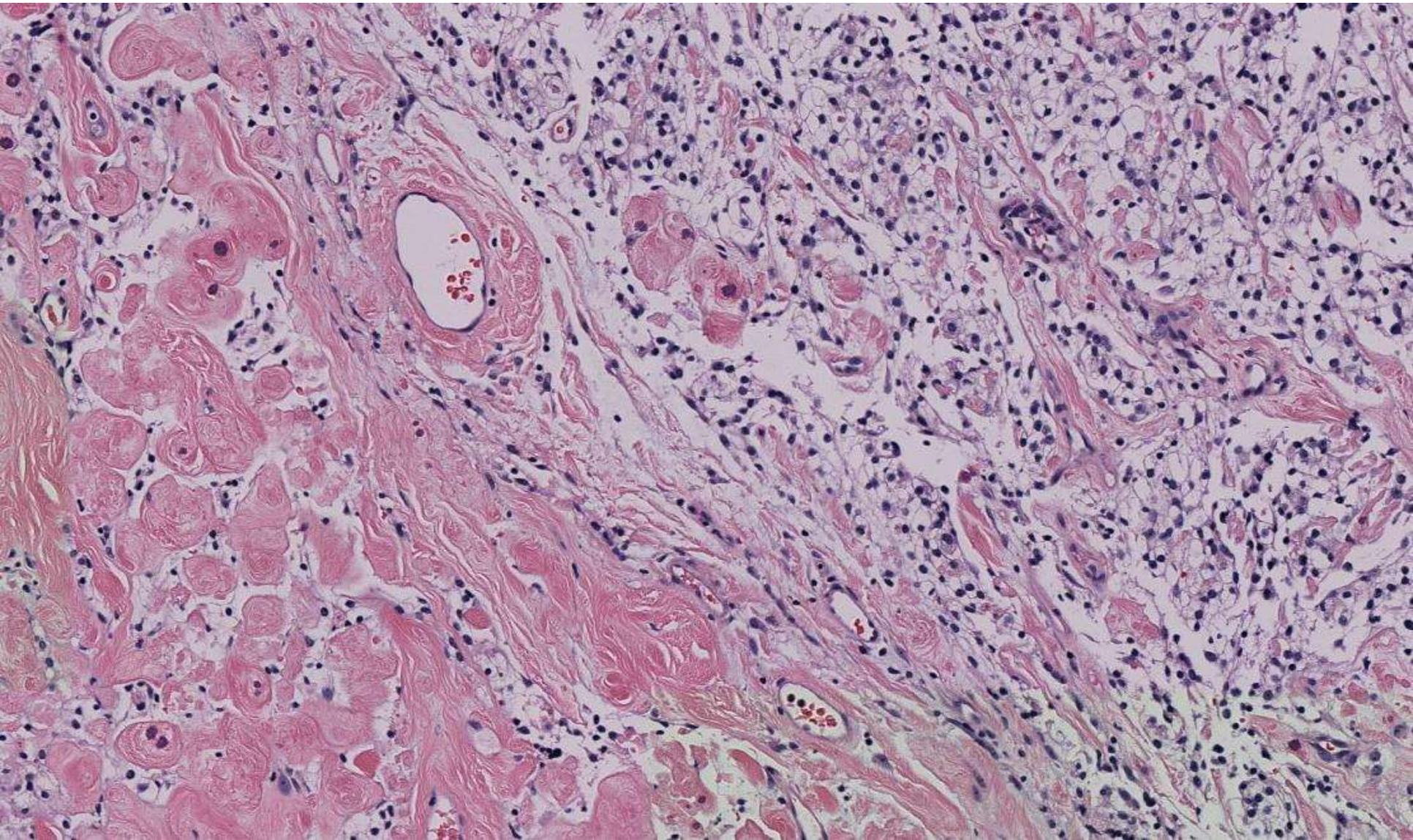


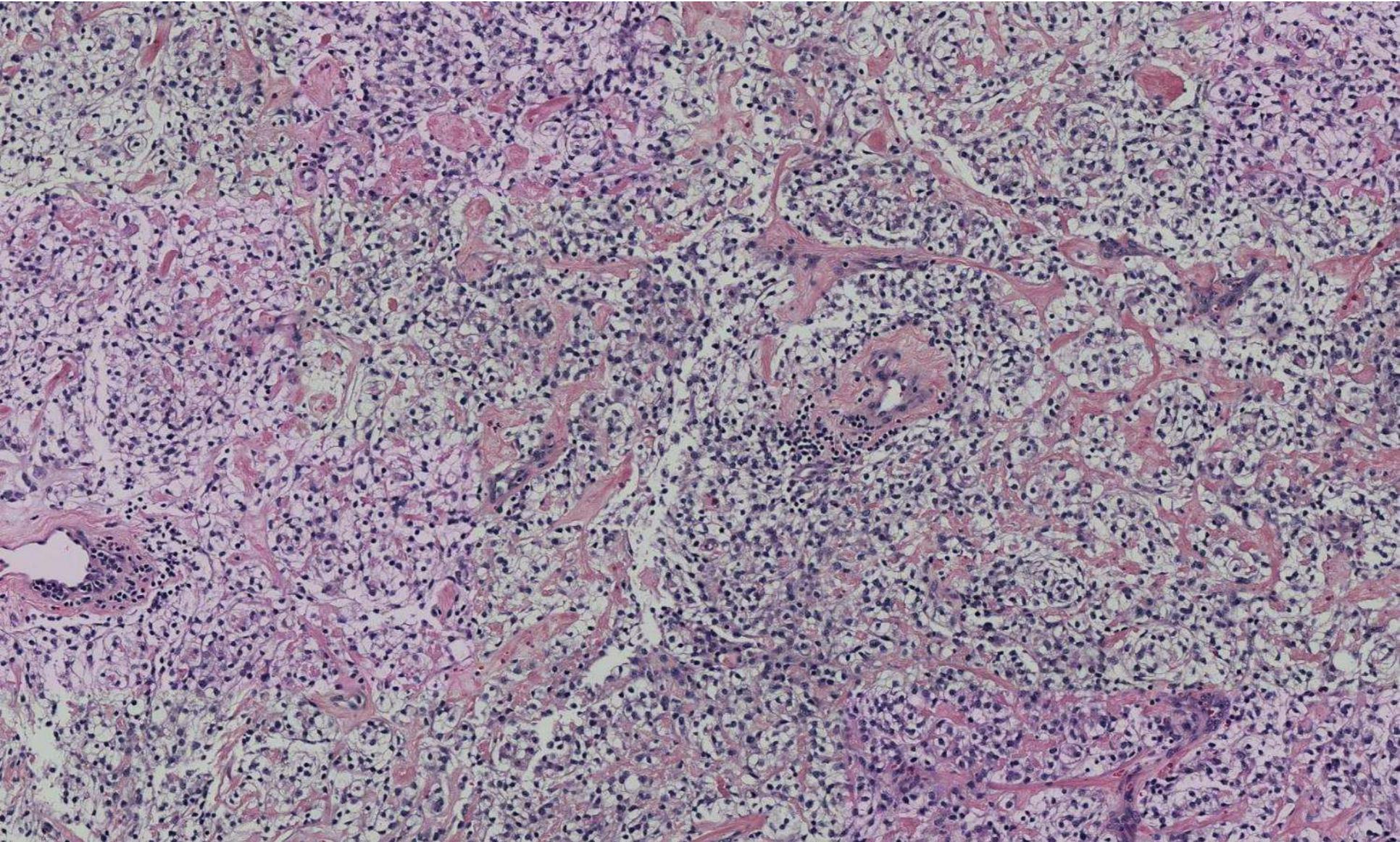


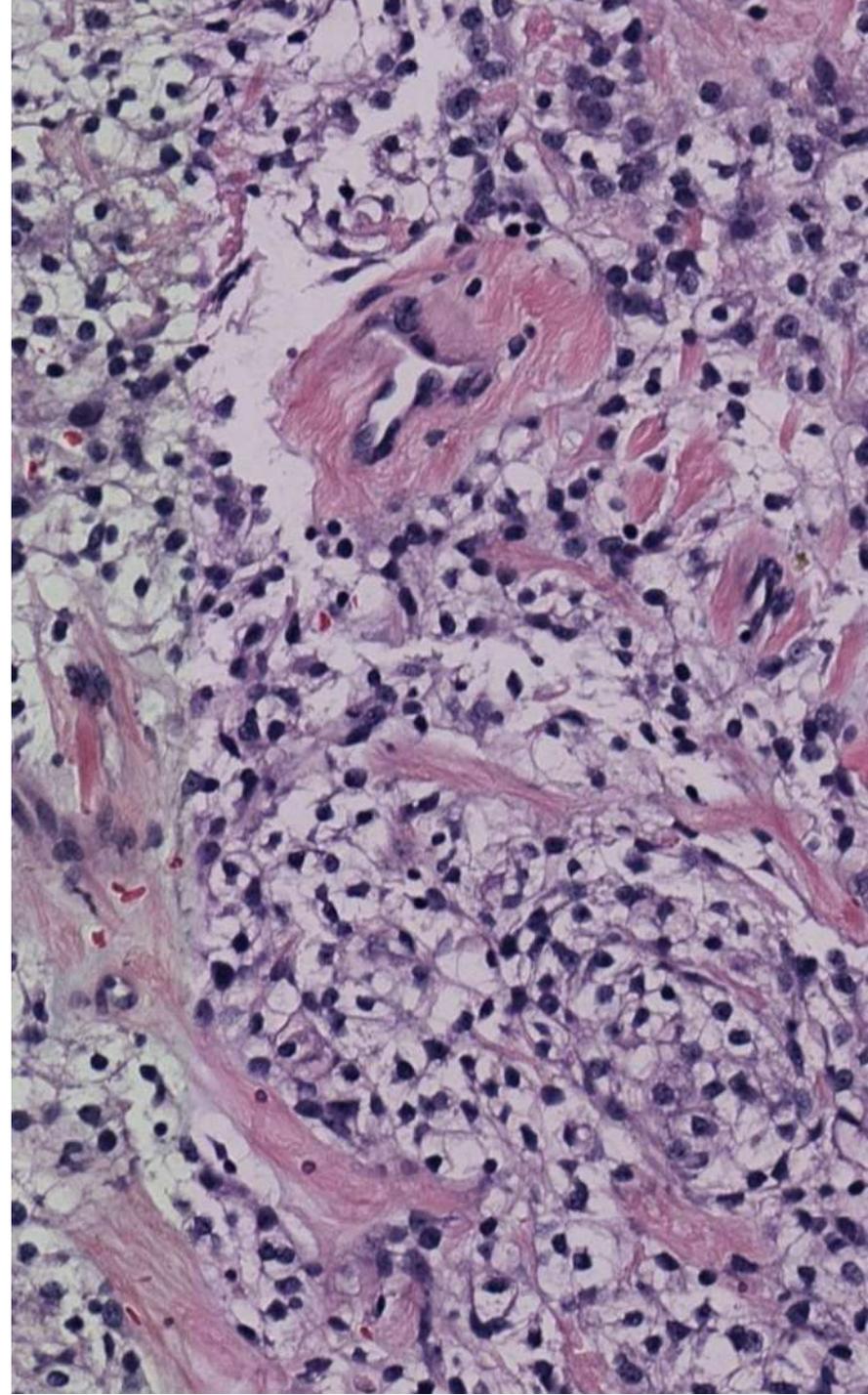
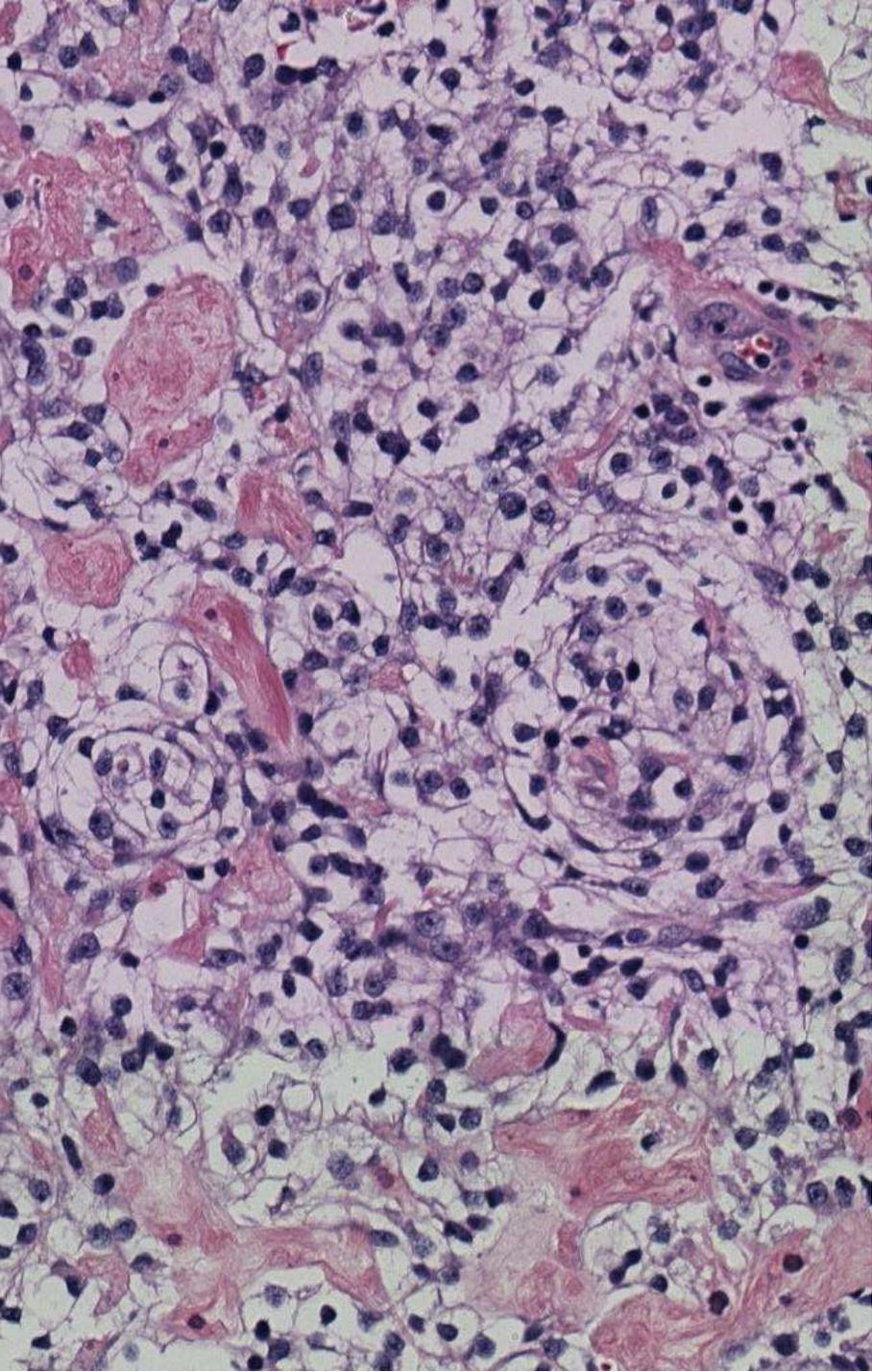


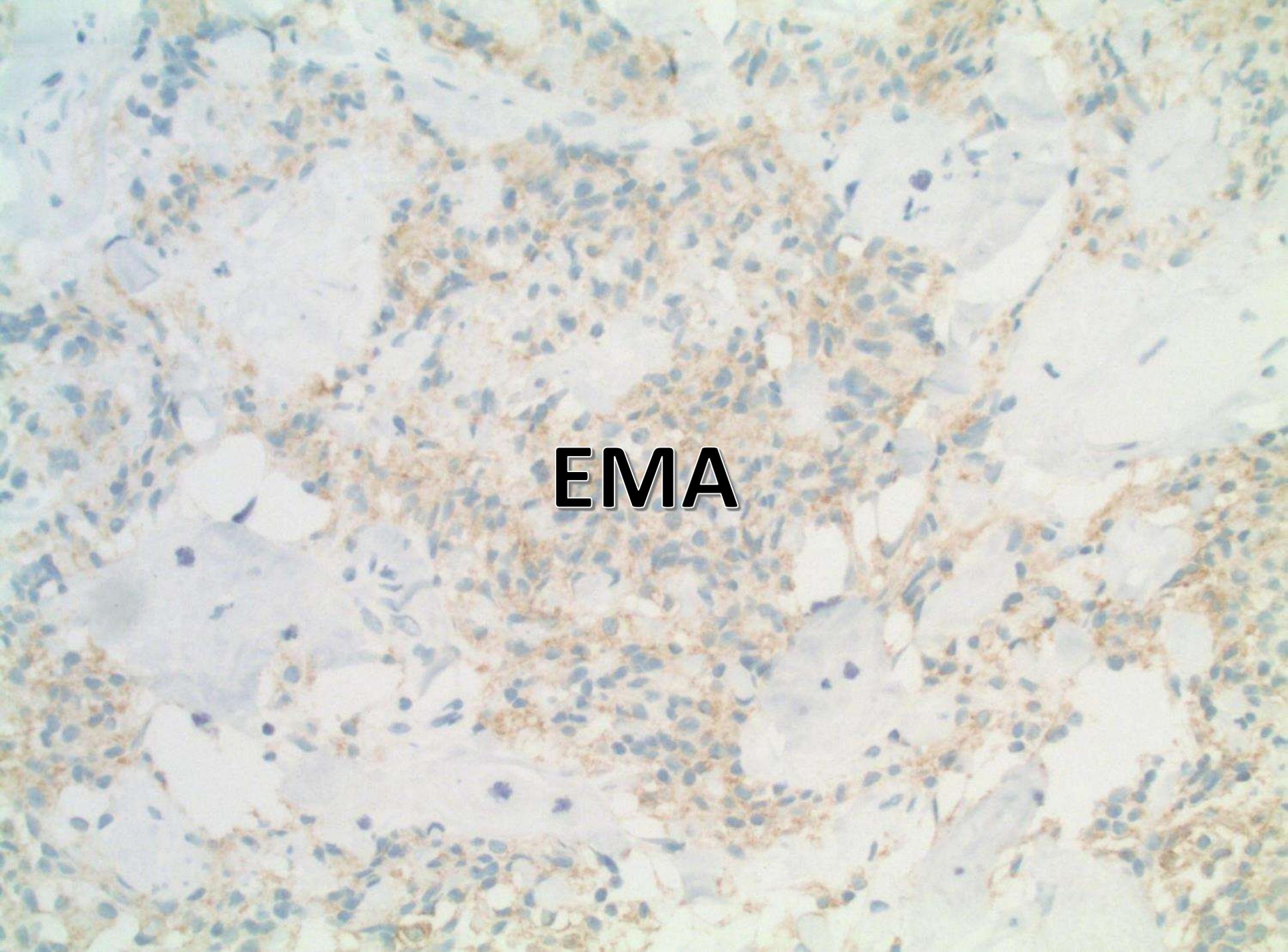




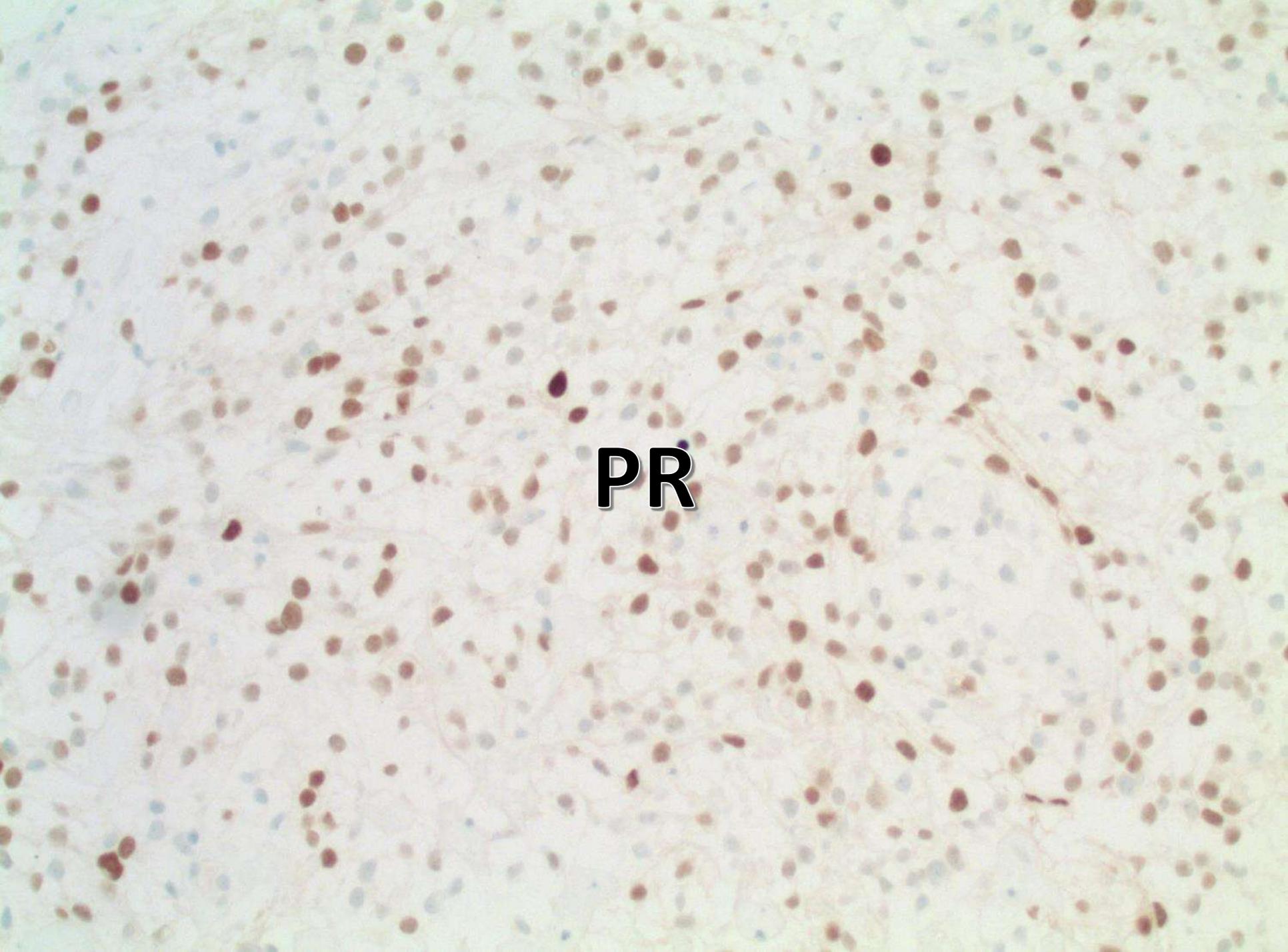






A histological slide showing a tissue section stained with hematoxylin and eosin (H&E). The tissue is densely cellular, with numerous small, dark blue nuclei (hematoxylin) and a pinkish, granular cytoplasm and extracellular matrix (eosin). The overall appearance is that of a highly cellular, possibly neoplastic, tissue. The text "EMA" is overlaid in the center of the image.

**EMA**

A histological slide showing a dense population of cells. The cells are stained with hematoxylin and eosin (H&E). The nuclei are stained blue, and the cytoplasm and extracellular matrix are stained pink. There are numerous small, dark brown spots scattered throughout the field, which are likely melanin pigment or hemosiderin deposits. The text 'PR' is overlaid in the center of the image.

**PR**

# SO BAY CASE 21-0306

## CLEAR CELL MENINGIOMA

- Rare variant, 0.2 - 0.8% of all meningiomas
- WHO grade II due to aggressiveness
- 20 - 60% chance of recurrence even with gross total resection
- More common in younger patients (mean age 29 years)
- Predilection for cauda equina and cerebellopontine areas

### **Radiology:**

Indistinguishable from classic meningioma

- Dural based, homogenously enhancing

# SO BAY CASE 21-0306

## CLEAR CELL MENINGIOMA

### **Microscopic description**

- Patternless arrangement of clear cells with sometimes distinct cell borders
- Prominent perivascular and interstitial collagen
- Little to no mitotic activity
- May not display any characteristic meningioma features (whorls, psammoma bodies, intranuclear inclusions)

### **Positive stains**

- [PAS](#), [EMA](#), [PR](#) (majority), [vimentin](#)

### **Negative stains**

- [Cytokeratins](#), [GFAP](#), [inhibin](#)

# SO BAY CASE 21-0306

## CLEAR CELL MENINGIOMA

### Differential diagnosis

- Clear cell ependymoma: GFAP +
- Germinoma / **seminoma**: PLAP+, OCT3 / 4+, cKIT+
- Hemangioblastoma: inhibin+, NSE +
- Metastatic renal cell carcinoma:  
keratin+
- Oligodendroglioma: GFAP +
- Schwannoma: S-100+

# SO BAY CASE 21-0306

## CLEAR CELL MENINGIOMA

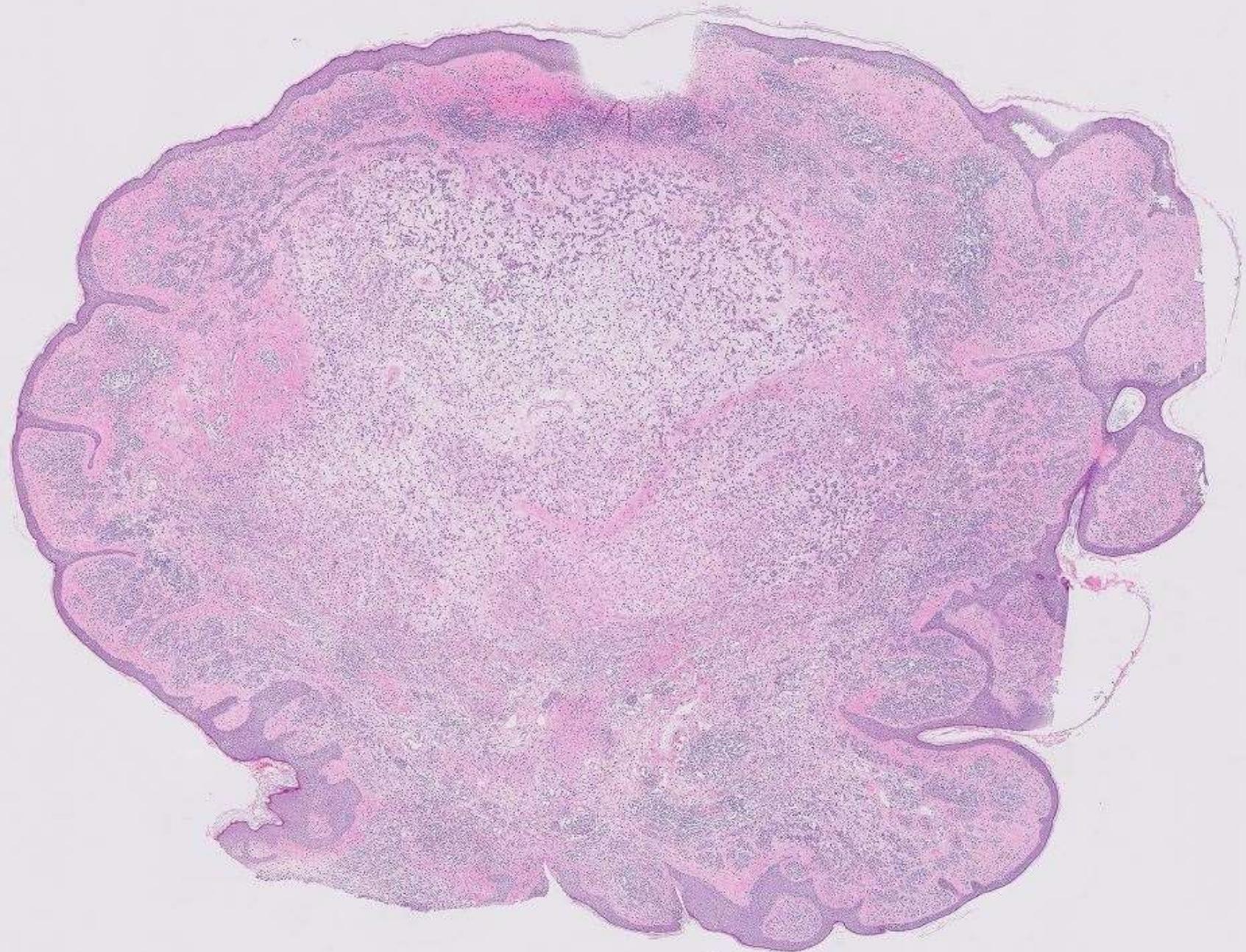
### **Treatment**

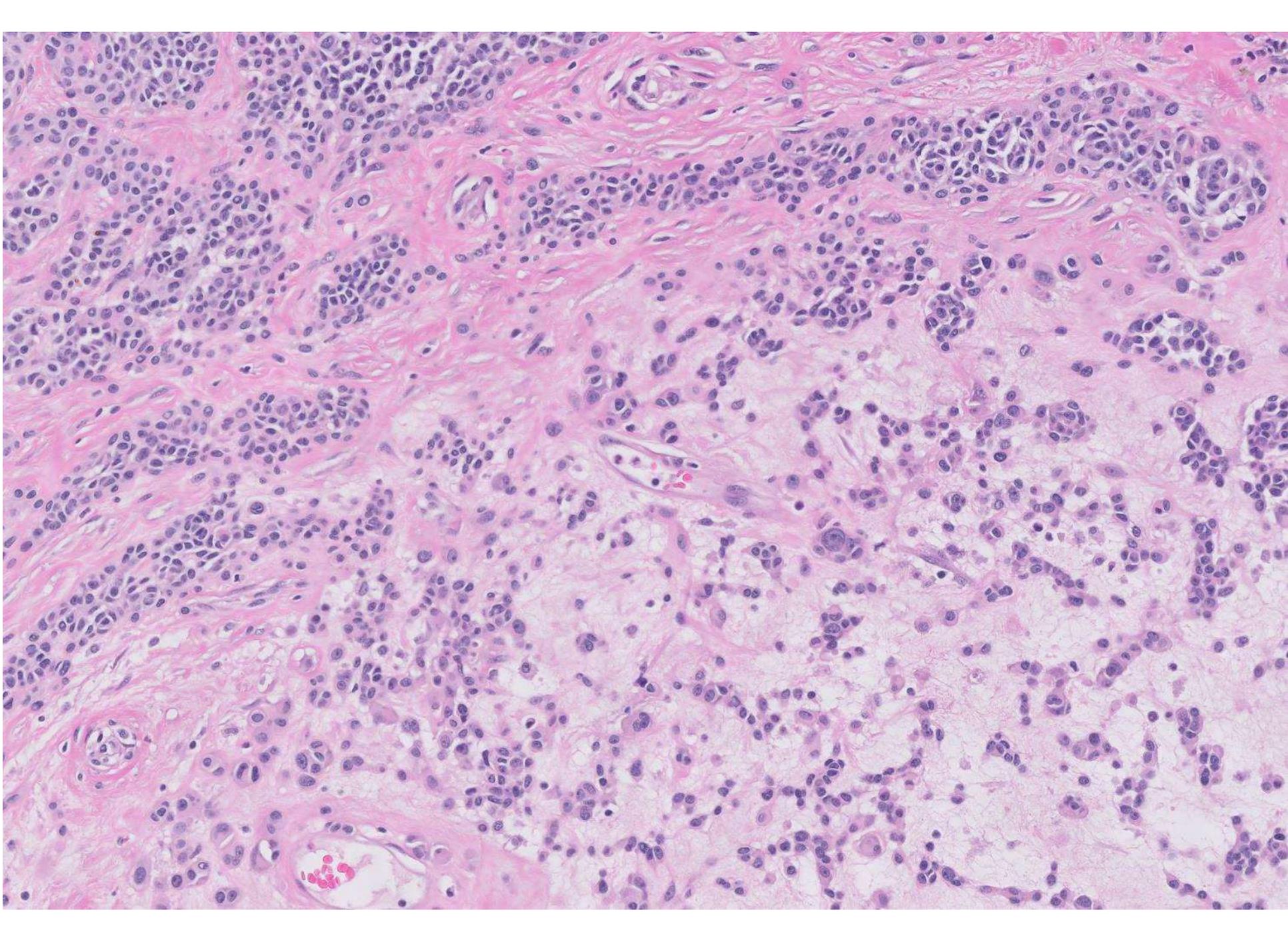
- Ideally gross total resection followed by postsurgical radiation
  - FOLLOW UP: s/p resection and then Cyberknife using 3 fractions
- Imaging studies 11/20:  
MRI indicates evolving post-operative changes with residual enhancing meningioma in right L4-L5 neuroforamina, with less avid solid enhancement

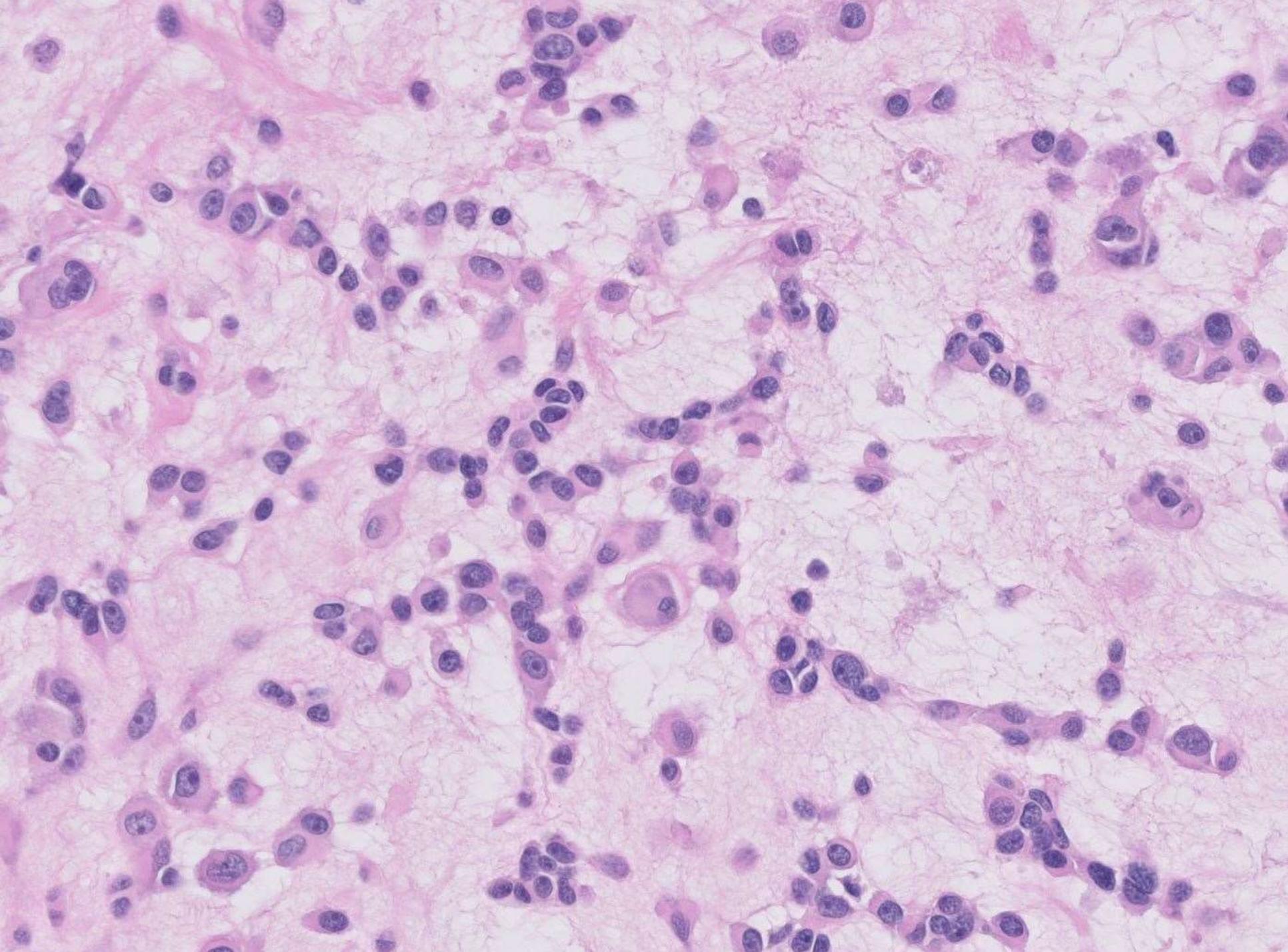
21-0307

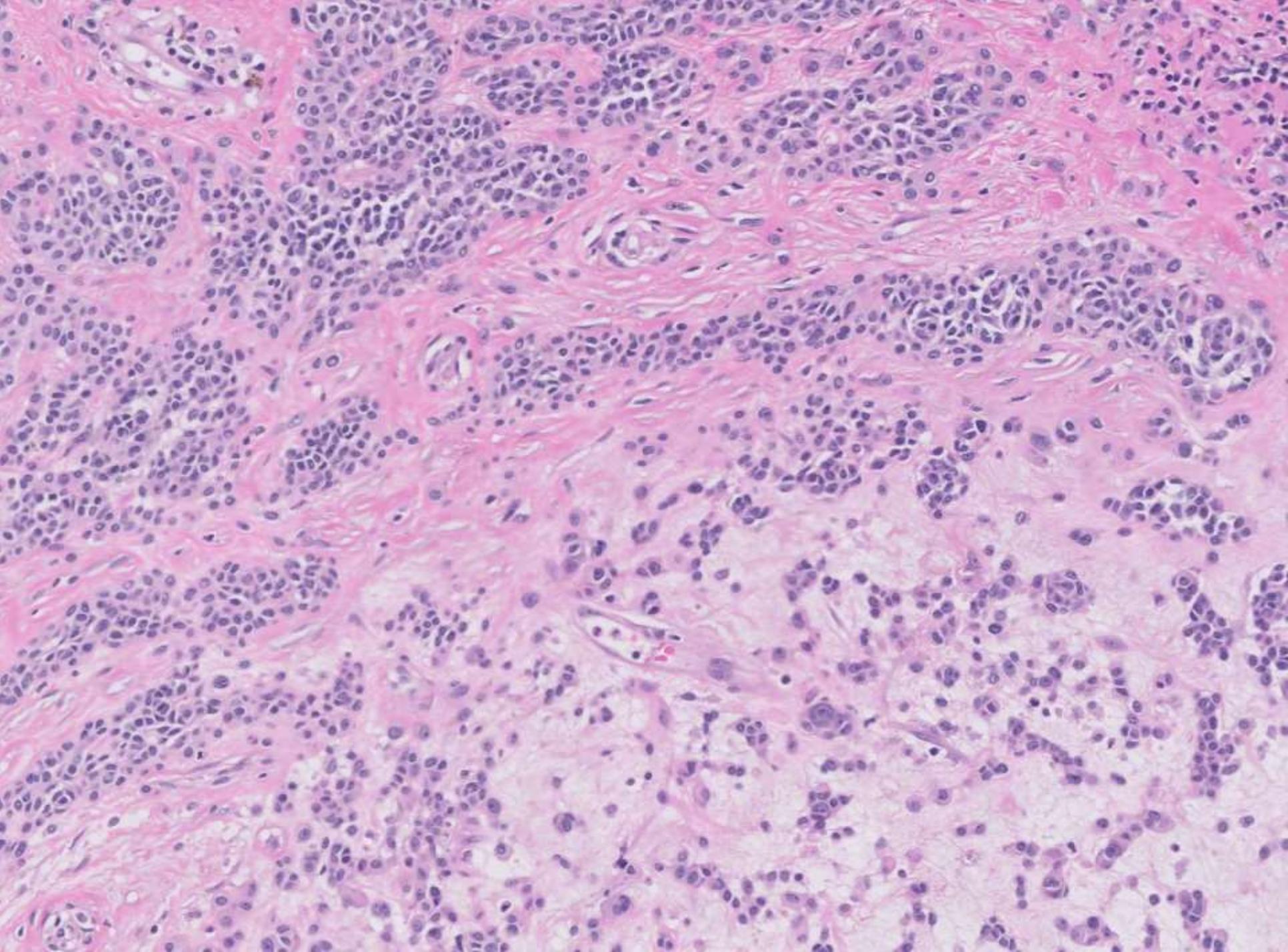
**Eman Bahrani/Kerri Rieger; Stanford**

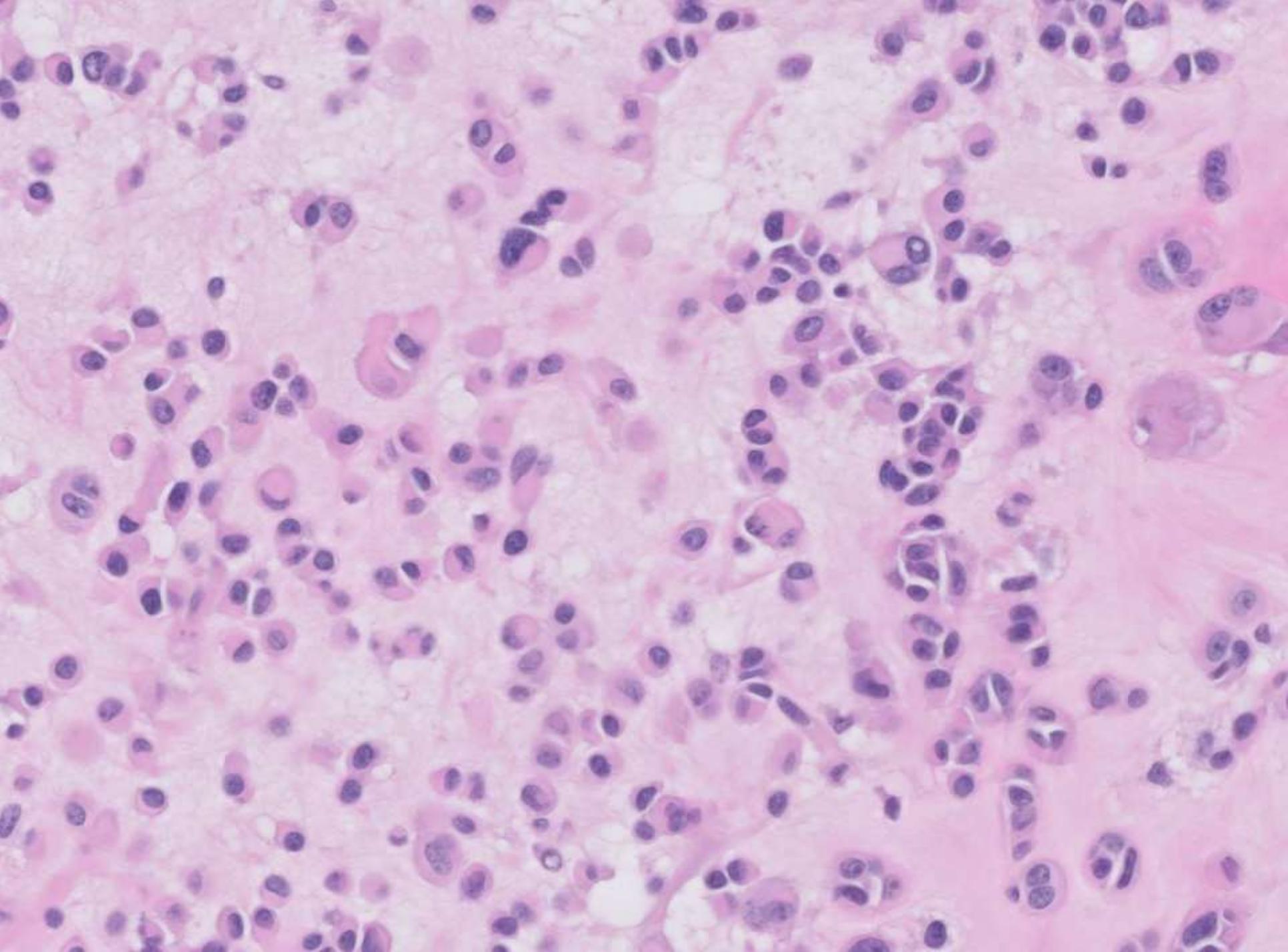
65-year-old F with 6x9mm near skin-colored papular  
nevus on central chest, itching, and changing.

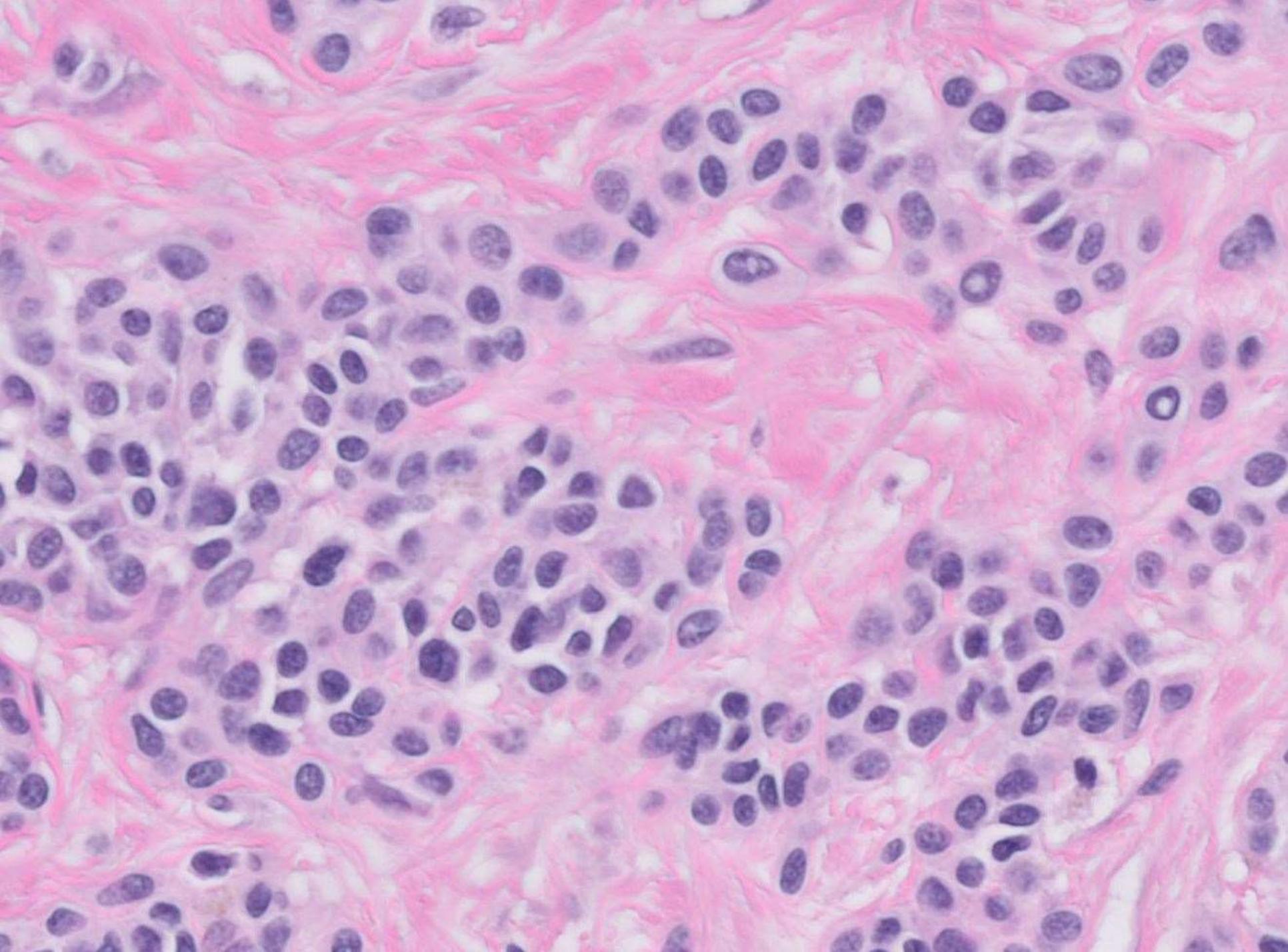


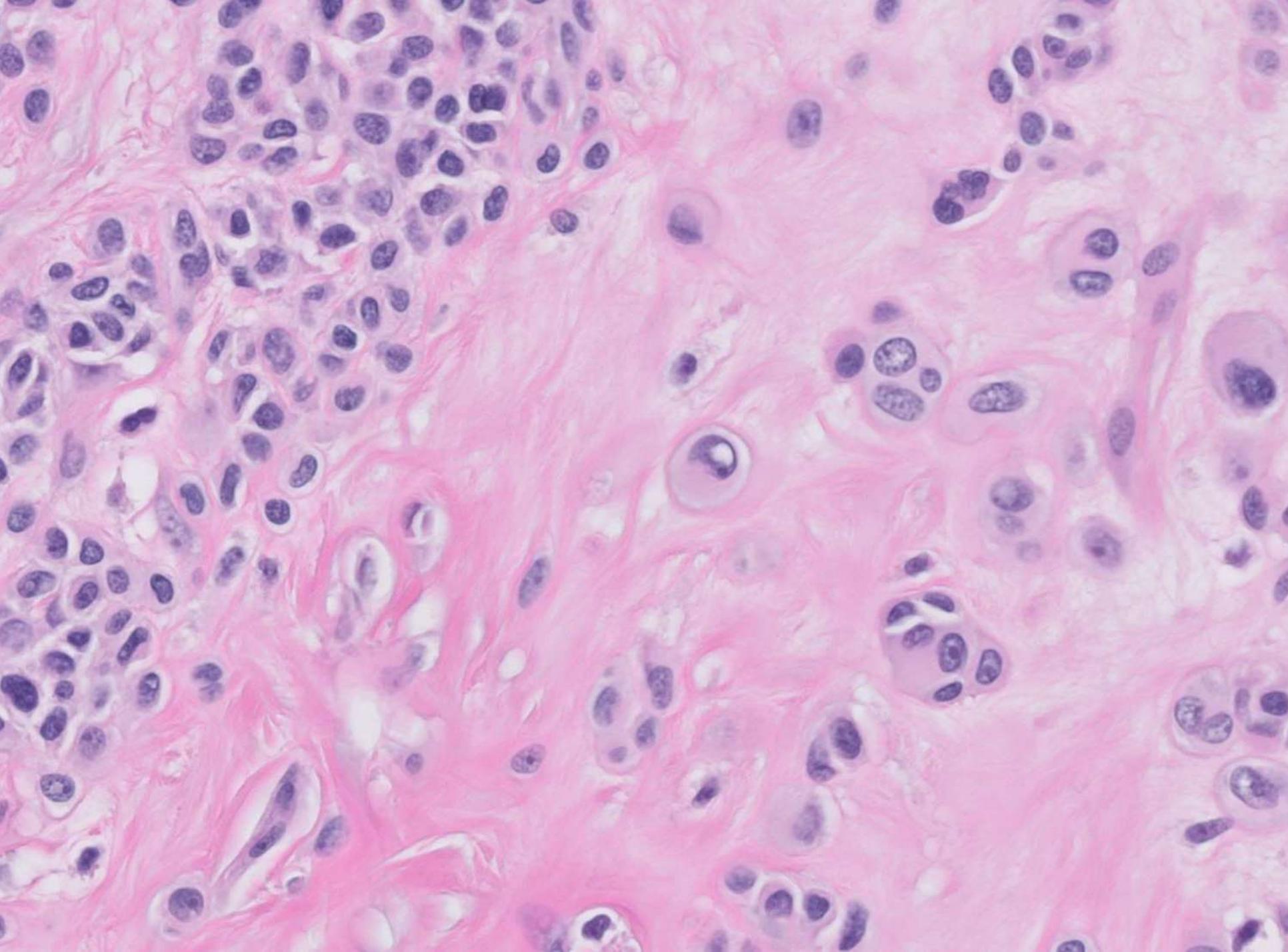




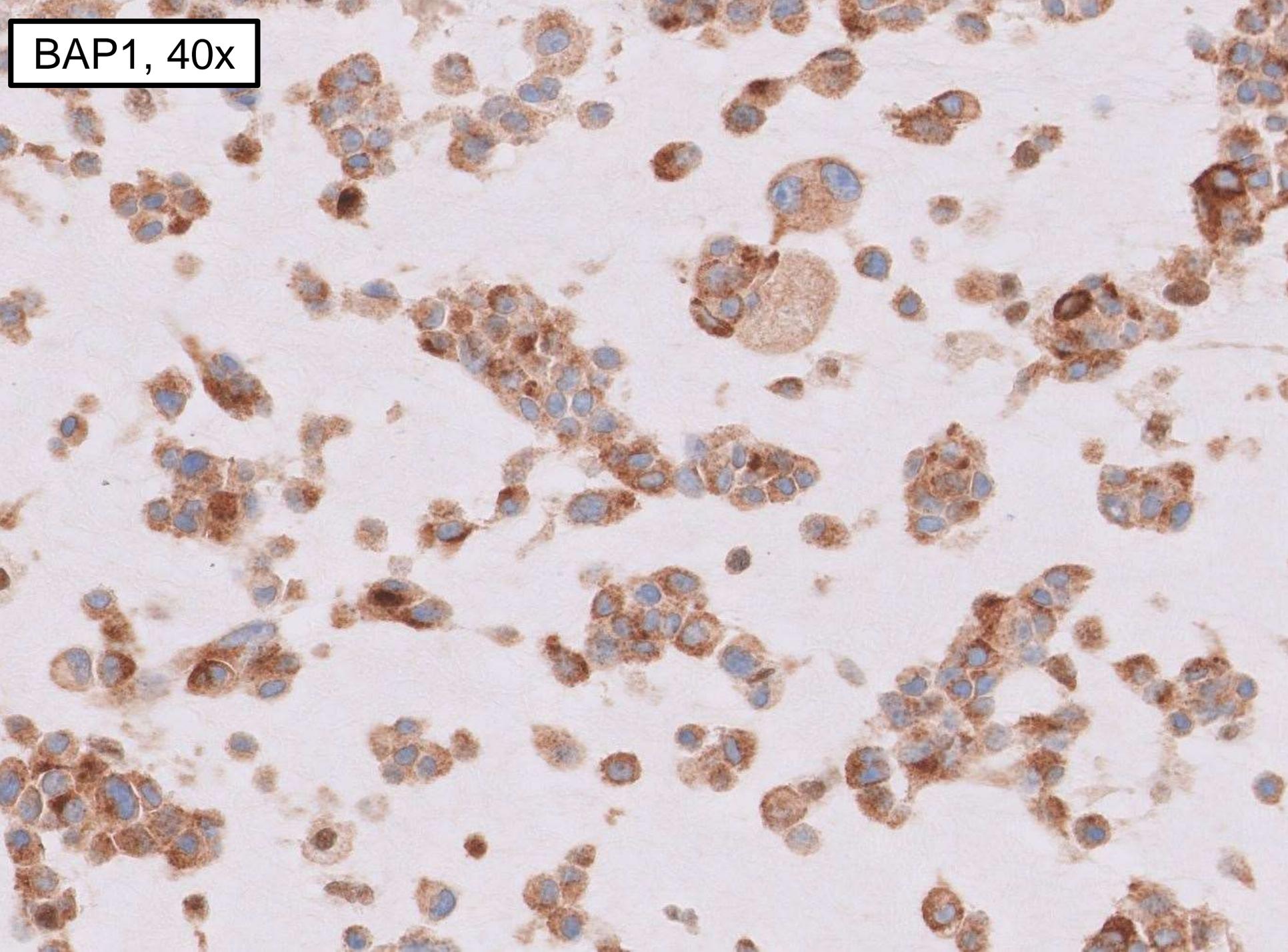




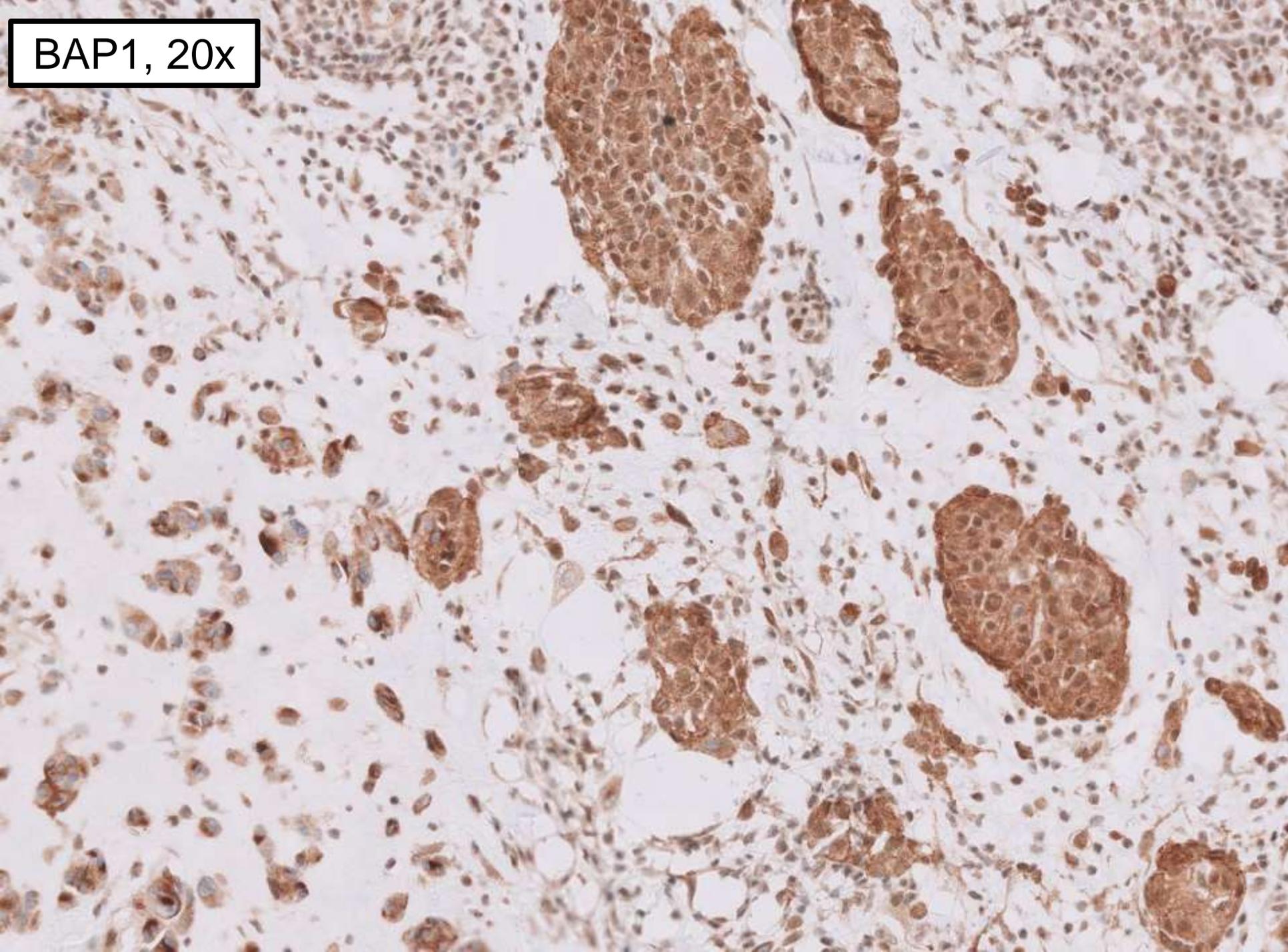




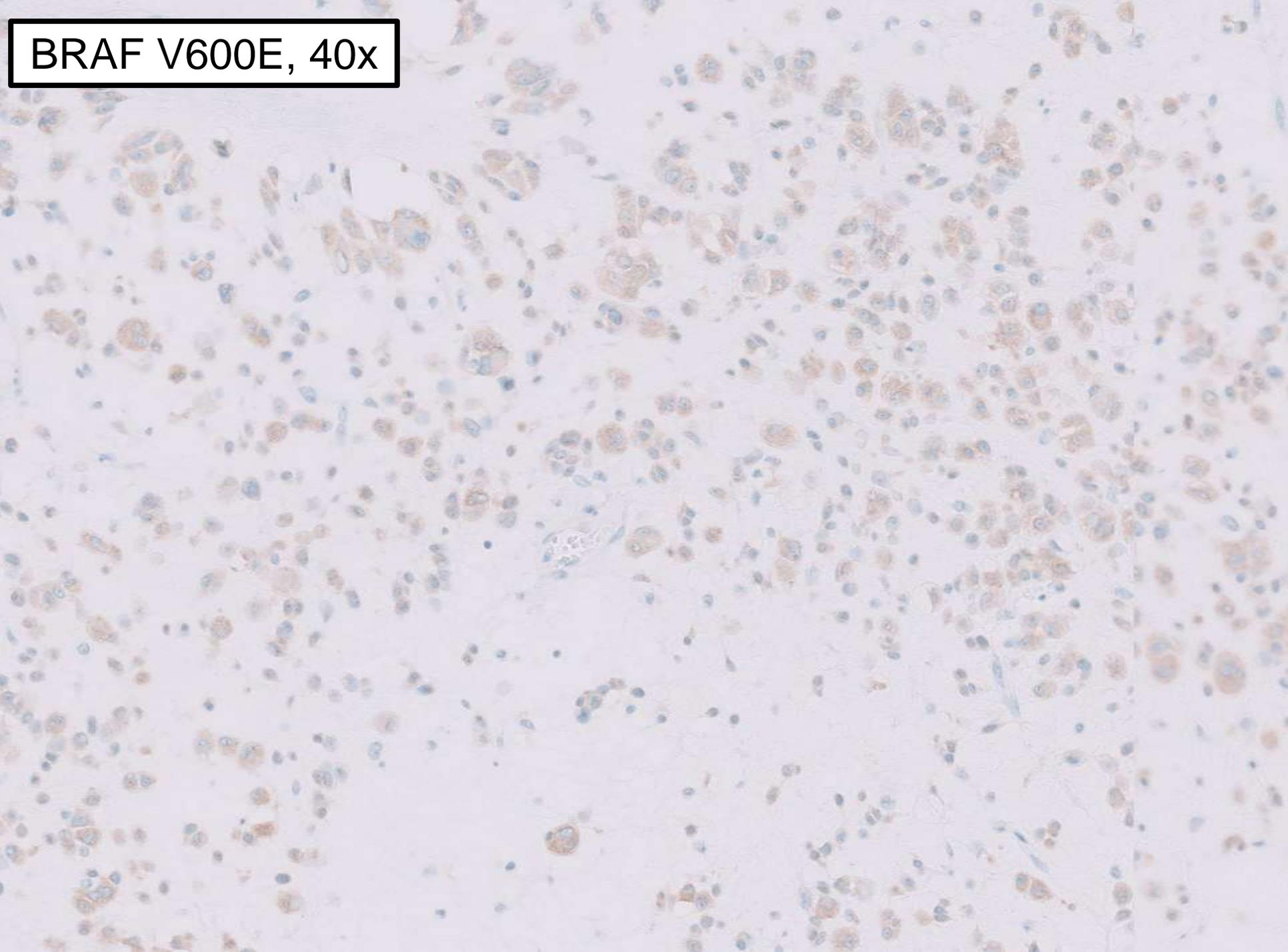
BAP1, 40x



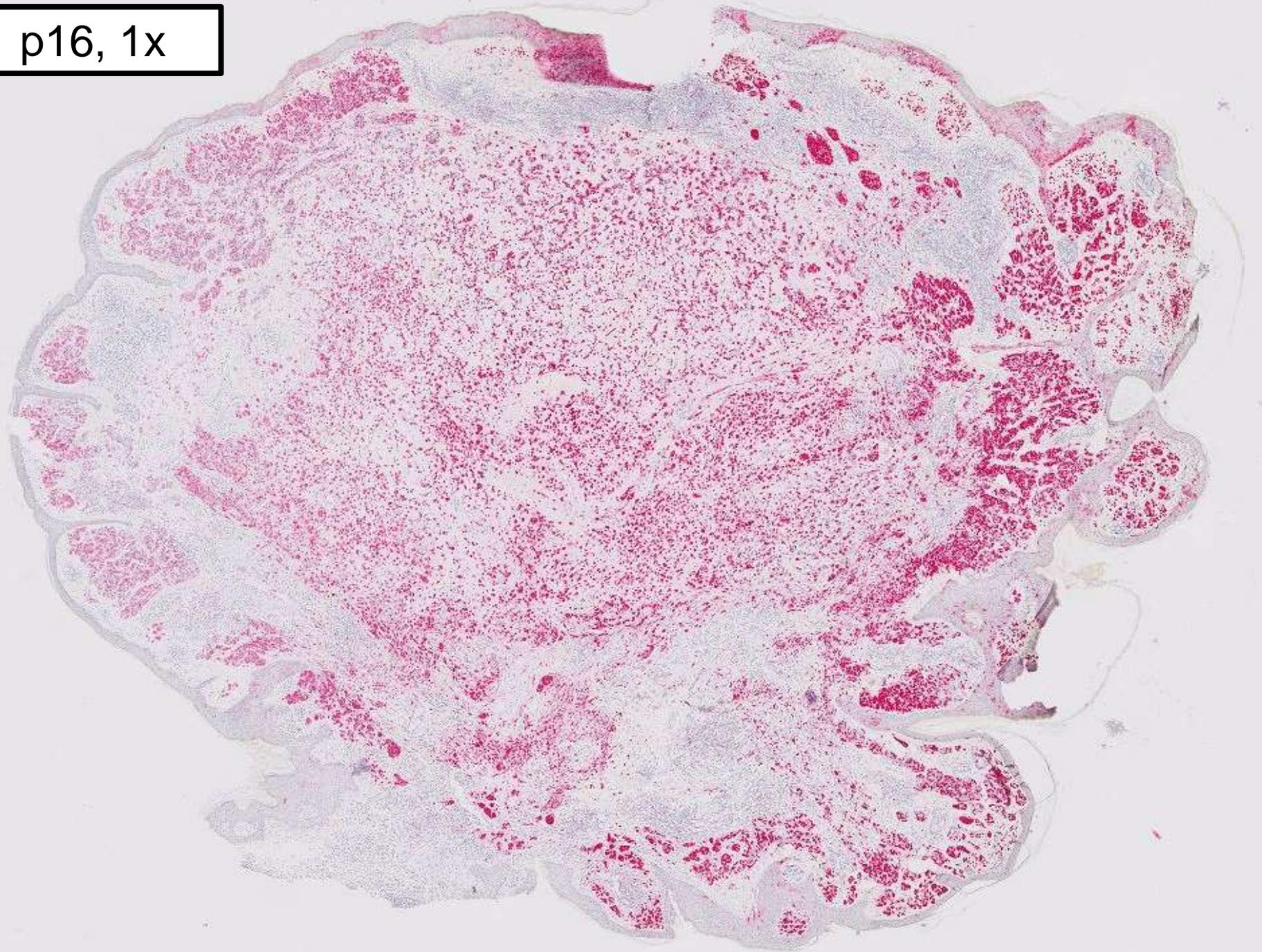
BAP1, 20x



BRAF V600E, 40x



p16, 1x



# Cutaneous BRCA1-associated protein (BAP1)-inactivated melanocytic tumor (BIMT)

- First described in 2011, Wiesner et al., *Nature Genetics*
- Pedunculated or sessile, skin-colored or orange-brown papule



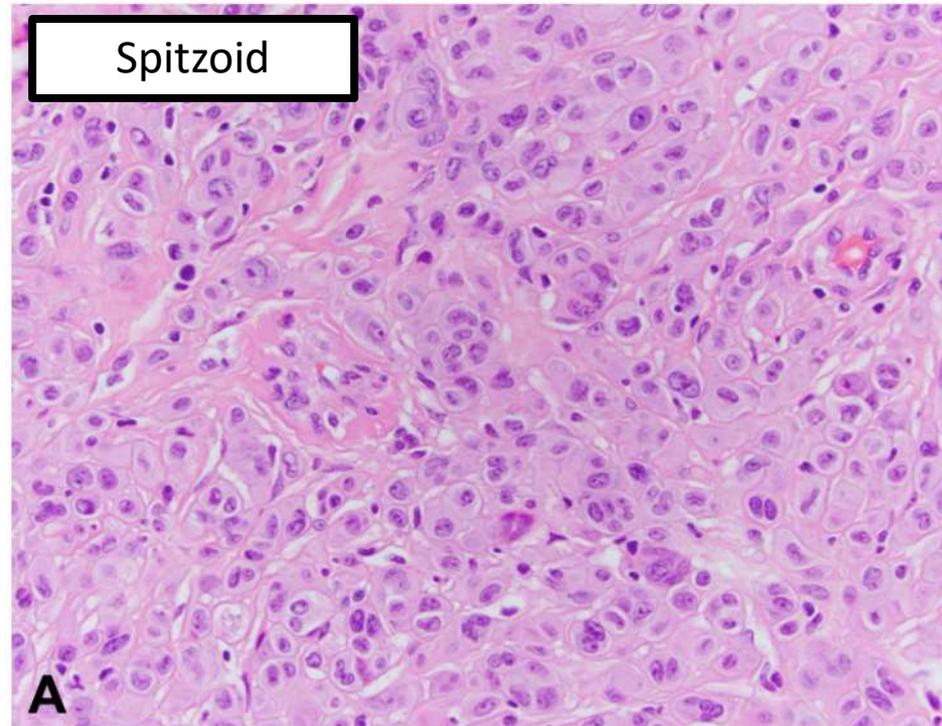
Wysozan et al., 2019

Zhang et al., 2019

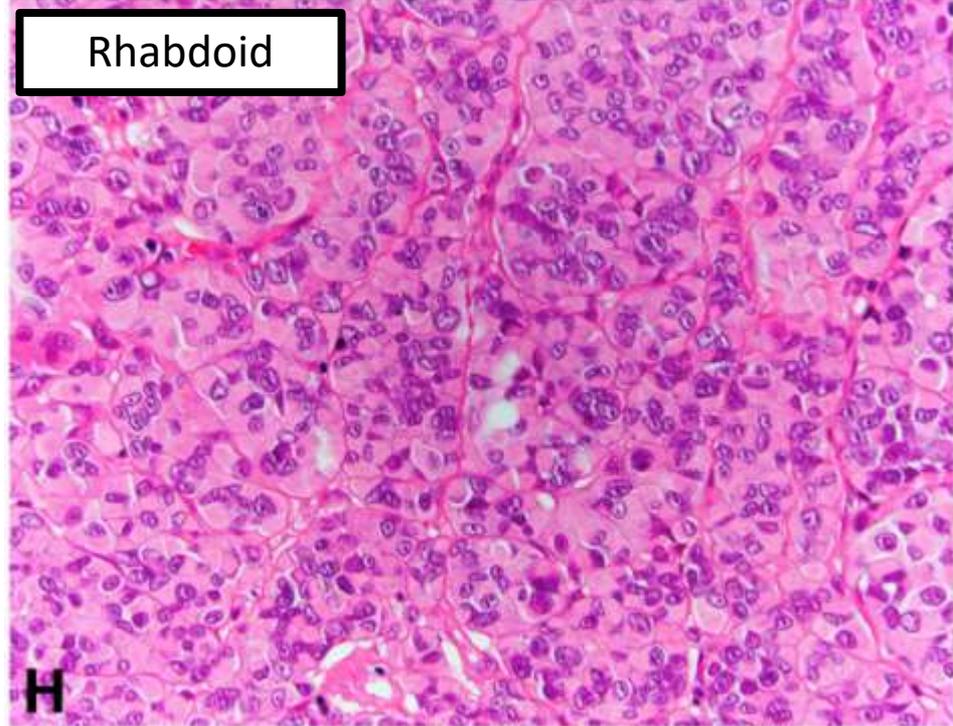
# Cutaneous BRCA1-associated protein (BAP1)-inactivated melanocytic tumor (BIMT)

- Histopathology
  - Dome-shaped, predominantly intradermal melanocytic tumor
  - Either monophasic and sheet-like, or biphasic melanocytic population (with background small nevoid cells)
  - Epithelioid, spitzoid, or rhabdoid melanocytes
  - Presence of junctional component may be associated with germline mutation
  - Haphazard maturation, low mitotic activity

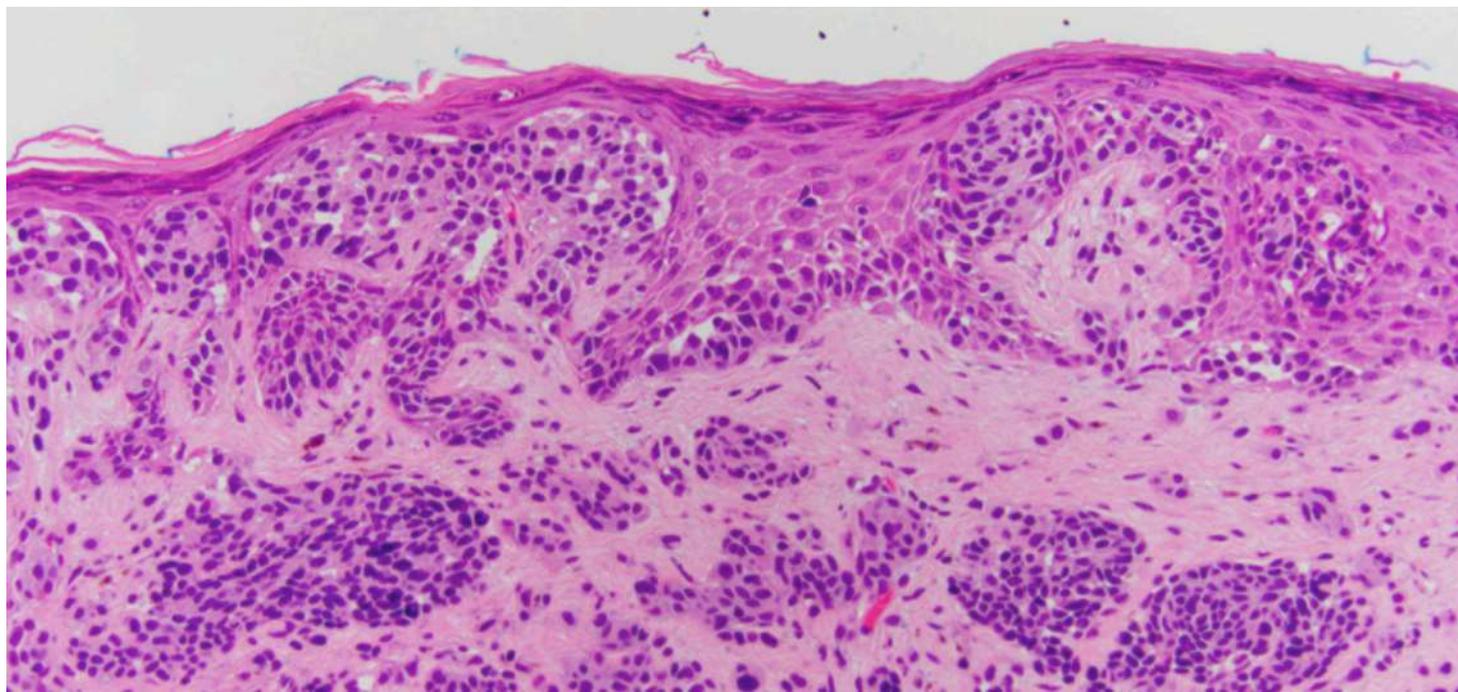
Spitzoid



Rhabdoid



Junctional  
component



# Previous Terminology

- Wiesner's nevus
- BAPoma
- Nevoid melanoma-like melanocytic proliferation
- Melanocytic *BAP1*-mutated atypical intradermal tumor
- *BAP1*-negative atypical Spitz tumor
- *BAP1*-inactivated Spitzoid nevus

# 2018 WHO Classification

## Low UV Radiation Exposure/CSD

Pathway	I			
Endpoint of pathway	Low-CSD melanoma/SSM			
Benign neoplasms (nevi)	Nevus			
Intermediate/low-grade dysplasias and melanocytomas	Low-grade dysplasia	BIN	DPN	
Intermediate/high-grade dysplasias and melanocytomas	High-grade dysplasia/MIS	<i>BAP1</i> -inactivated melanocytoma/MELTUMP	Deep penetrating melanocytoma/MELTUMP	PEM/MELTUMP
Malignant neoplasms	Low-CSD melanoma/SSM (VGP)	Melanoma in BIN (rare)	Melanoma in DPN (rare)	Melanoma in PEM (rare)
Common mutations	<b><i>BRAF</i> p.V600E<sup>b</sup></b> or <b><i>NRAS</i><sup>b</sup></b>  <i>TERT</i> <sup>d</sup> ; <i>CDKN2A</i> <sup>a</sup> ; <i>TP53</i> <sup>a</sup> ; <i>PTEN</i> <sup>a</sup>	<b><i>BRAF</i><sup>b</sup> or <i>NRAS</i><sup>b</sup></b> + <b><i>BAP1</i><sup>a</sup></b>	<b><i>BRAF</i><sup>b</sup>; <i>MAP2K1</i><sup>b</sup>;</b> or <b><i>NRAS</i><sup>b</sup> + <i>CTNNB1</i><sup>b</sup></b> or <b><i>APC</i><sup>a</sup></b>	<b><i>BRAF</i><sup>b</sup> + <i>PRKAR1A</i><sup>a</sup></b> or <b><i>PRKCA</i><sup>c</sup></b>

BIN: *BAP1*-inactivated nevus

# Clinical Implications

- Most BIMTs are sporadic
- Germline *BAP1* 3p21.1 mutation associated with tumor predisposition syndrome
  - Uveal melanoma
  - Mesothelioma
  - Cutaneous melanoma
  - Renal cell carcinoma
  - Nonmelanoma skin cancer
  - Multiple BIMTs
  - Other possibly associated tumors

# Clinical Implications

- BIMTs have highest penetrance and earliest average age of presentation of tumors in *BAP1* tumor predisposition syndrome
- If the patient has personal or family history of uveal melanoma, cutaneous melanoma, renal cell carcinoma, mesothelioma, or multiple *BAP1* melanocytic neoplasms, then a workup for a germline mutation in *BAP1* should be considered
- Identification could lead to life-saving screening

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