Disclosures
December 5, 2016

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

Presenters:

Peyman Samghabadi, MD
Hannes Vogel, MD
Jarish Cohen, MD
Karuna Garg, MD
Sarah Umetsu, MD
Nhu Thuy Can, MD
Poonam Vohra, MD
Greg Charville, MD, PhD
John Higgins, MD
Harris Goodman, MD
Ankur Sangoi, MD
Allison Zemek, MD
Sunny Kao, MD

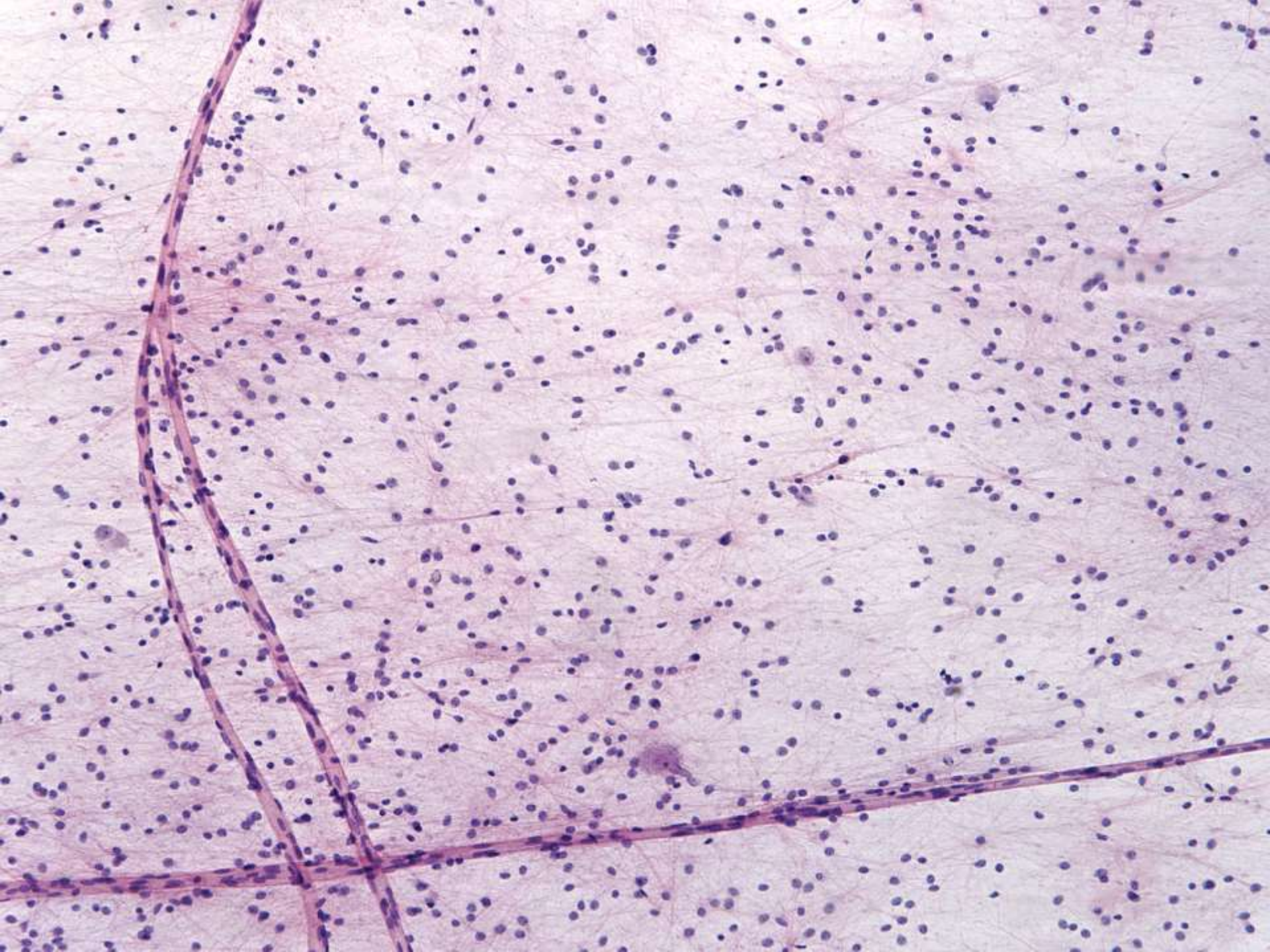
Activity Planners/Moderator:

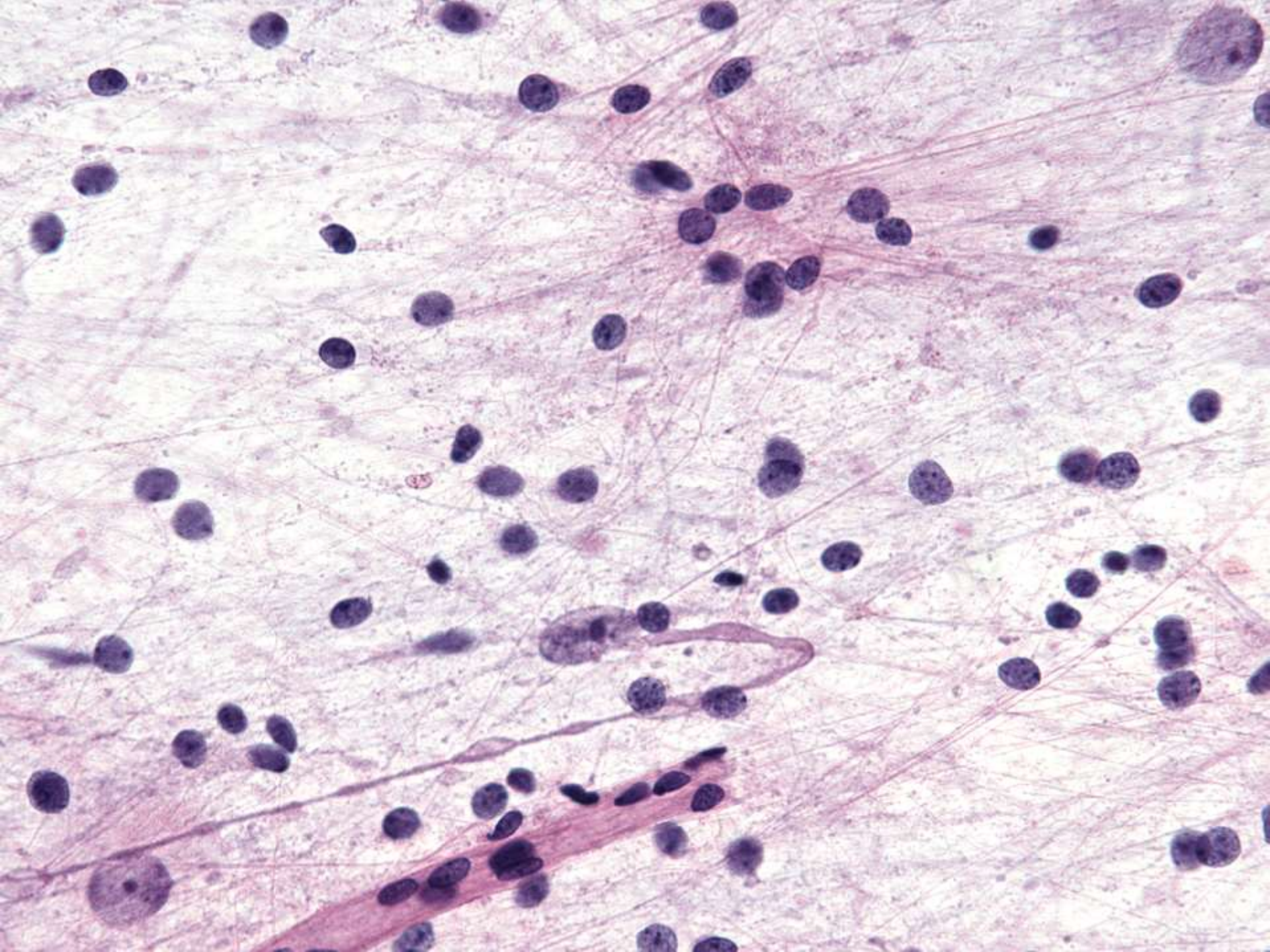
Kristin Jensen, MD
Ankur Sangoi, MD

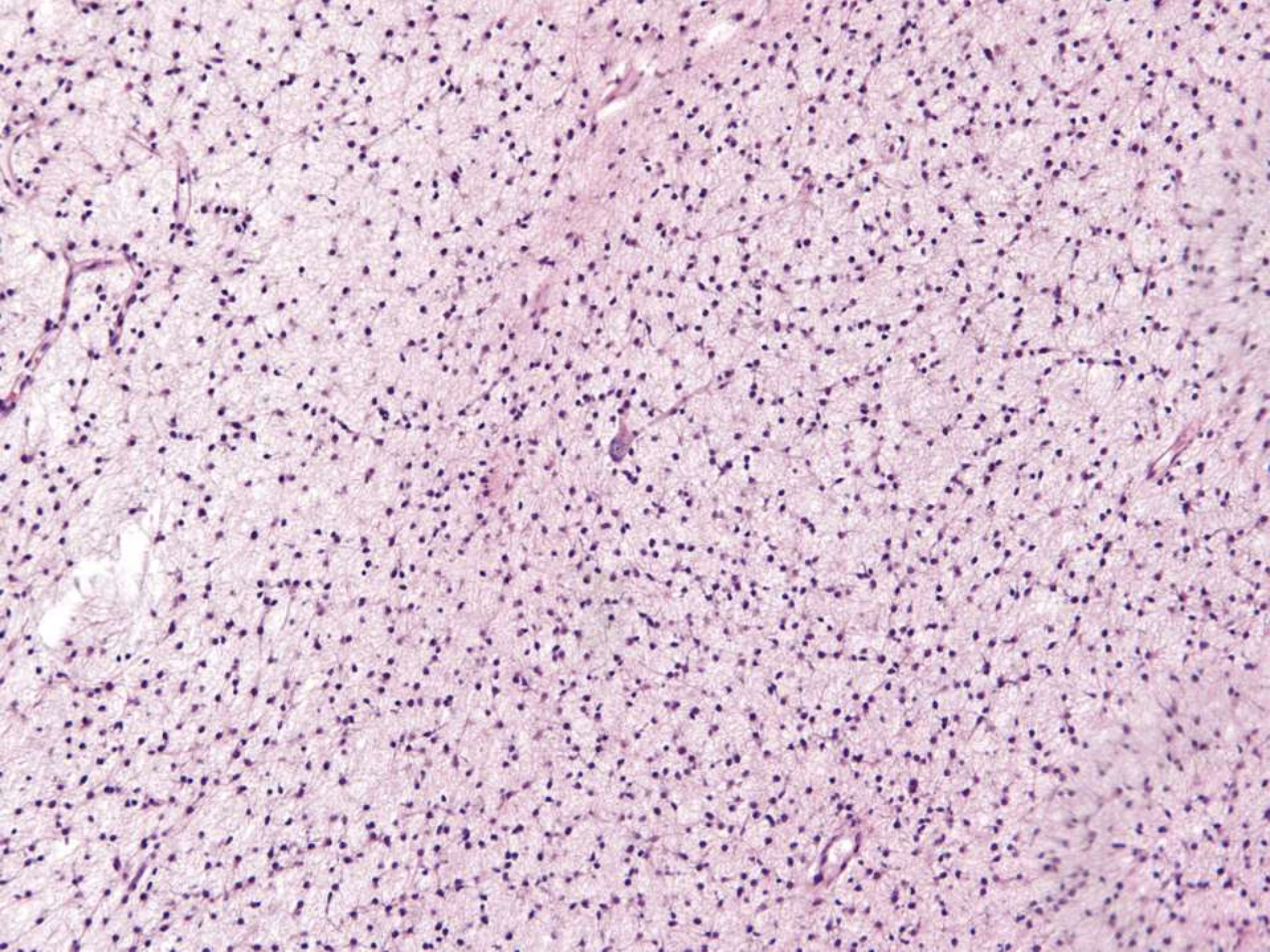
SB 6111

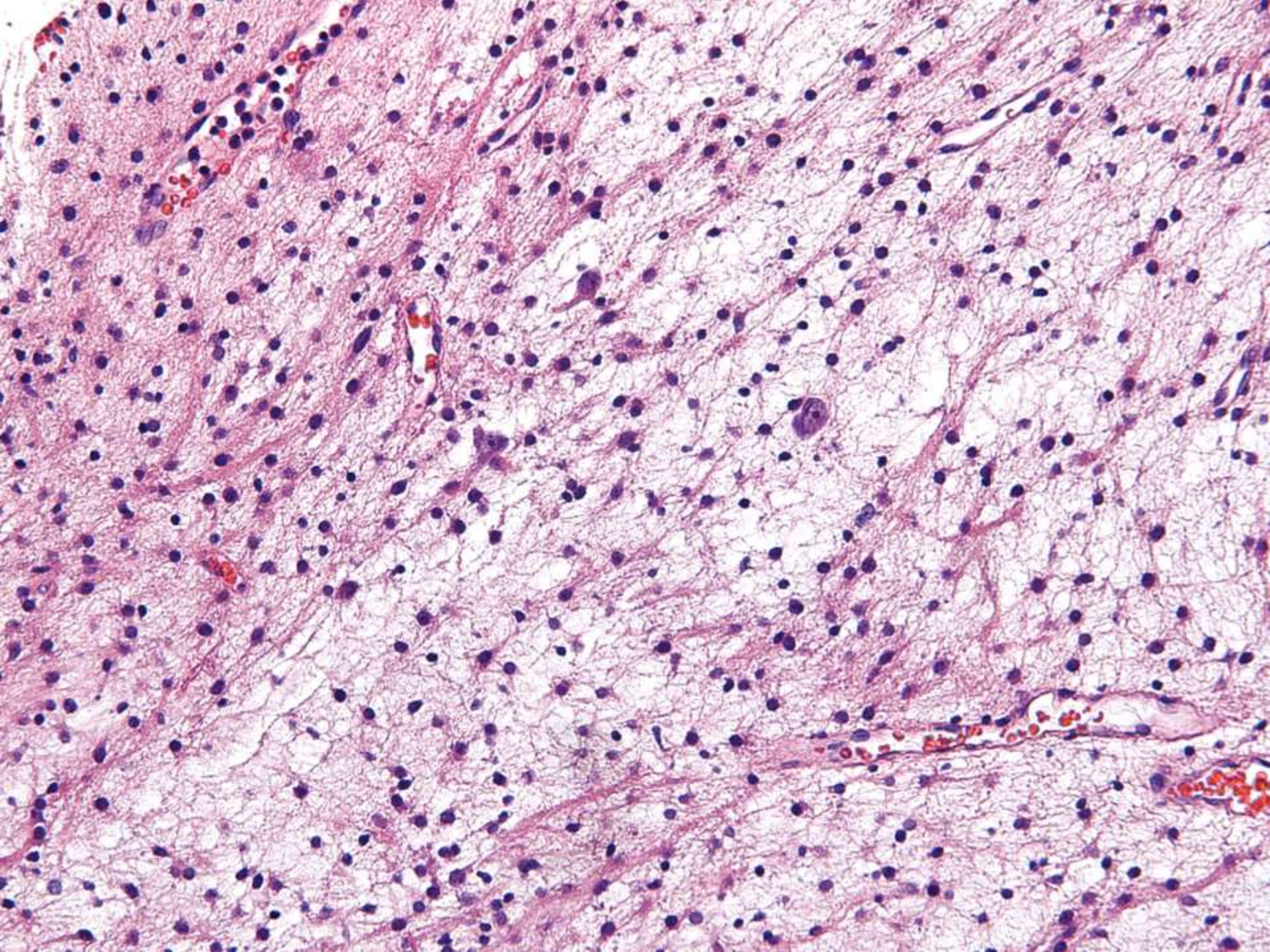
Peyman Samghabadi/Hannes Vogel; Stanford

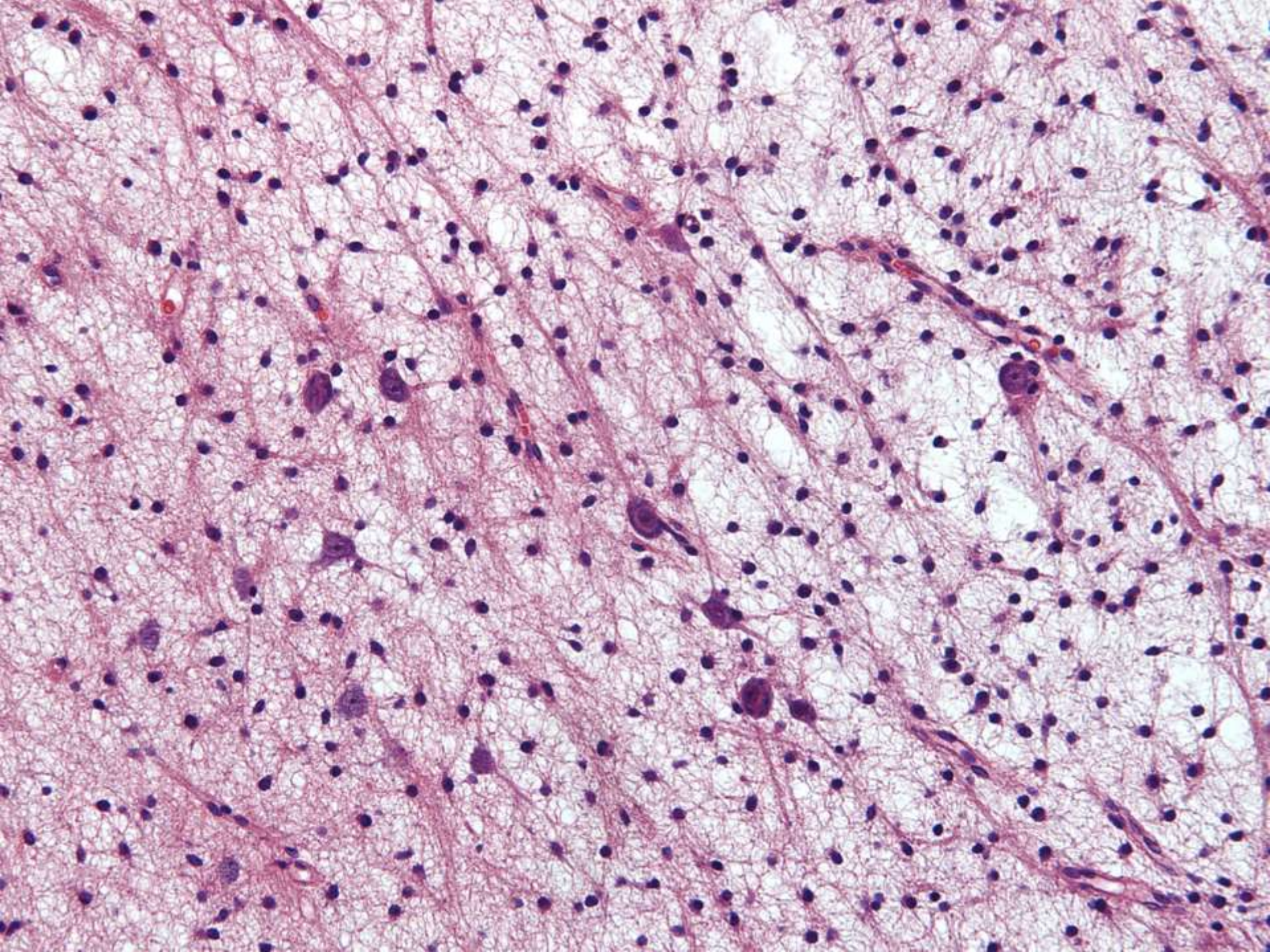
9-year-ld female with a history of medically refractory epilepsy emanating from the right cerebral hemisphere. MRI shows a lesion which expands the right sylvian fissure, measuring ~2.4 cm. The mass shows no associated enhancement. An incidental pineal cyst measures 9 mm, previously 7 mm.

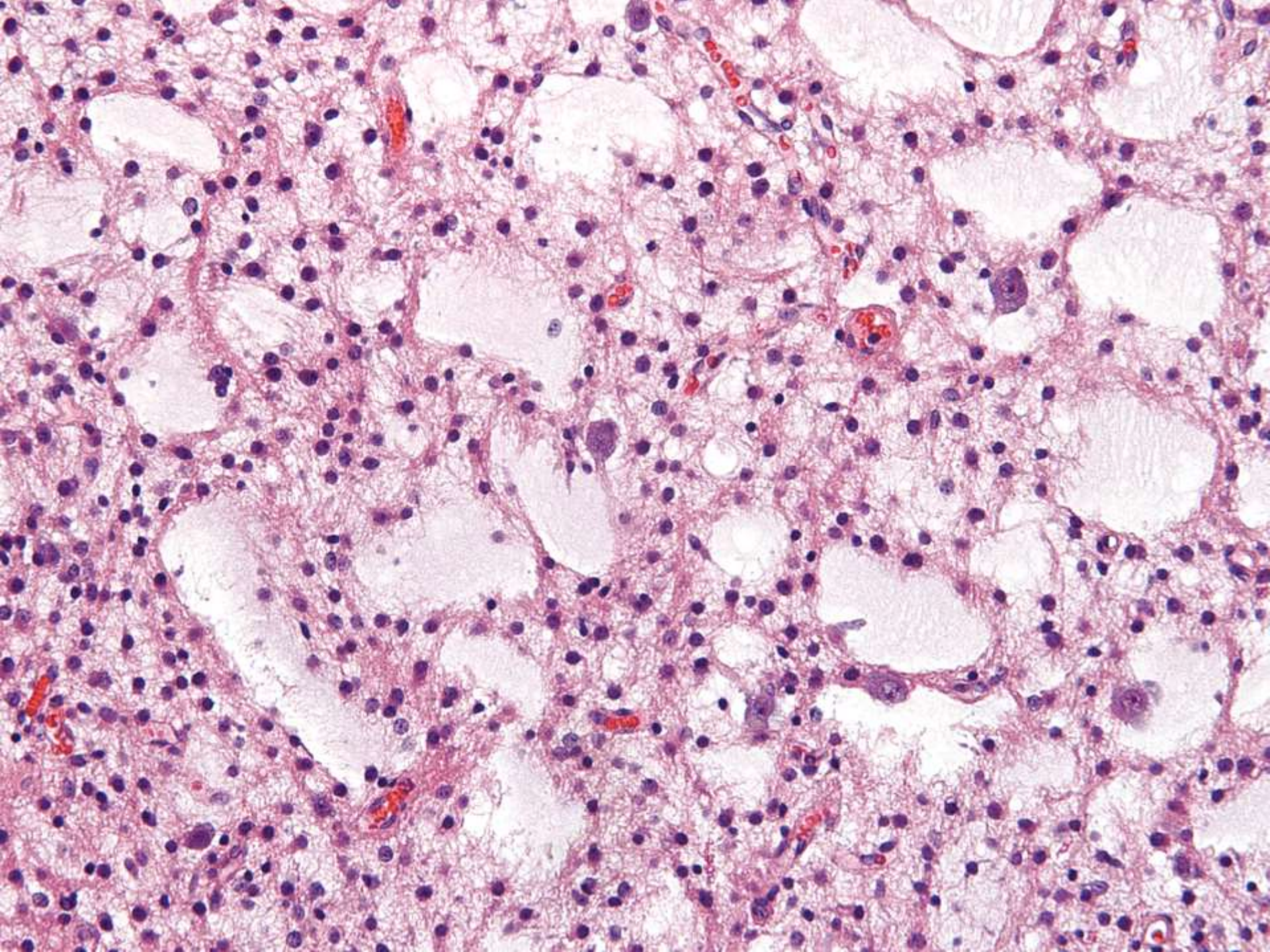






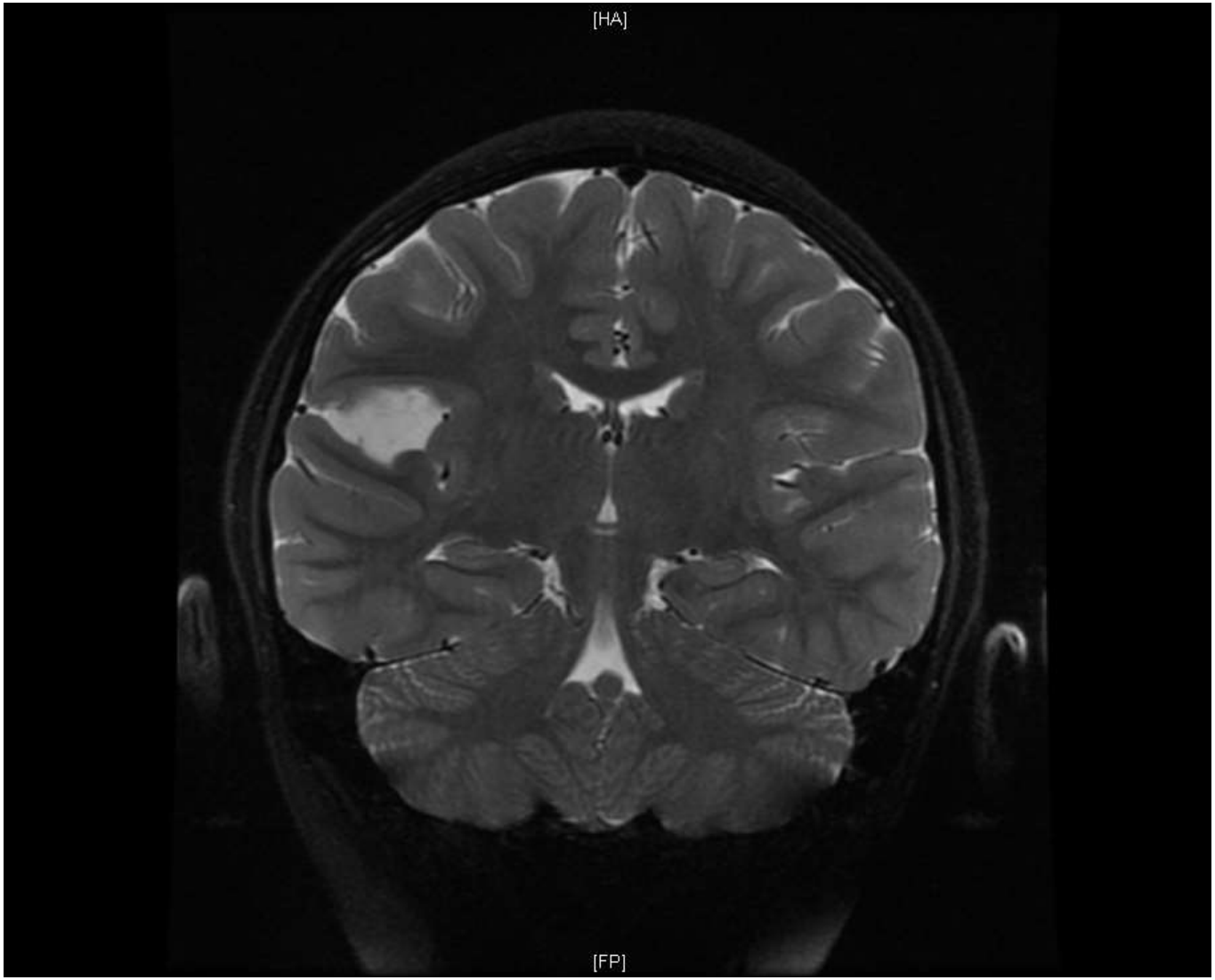




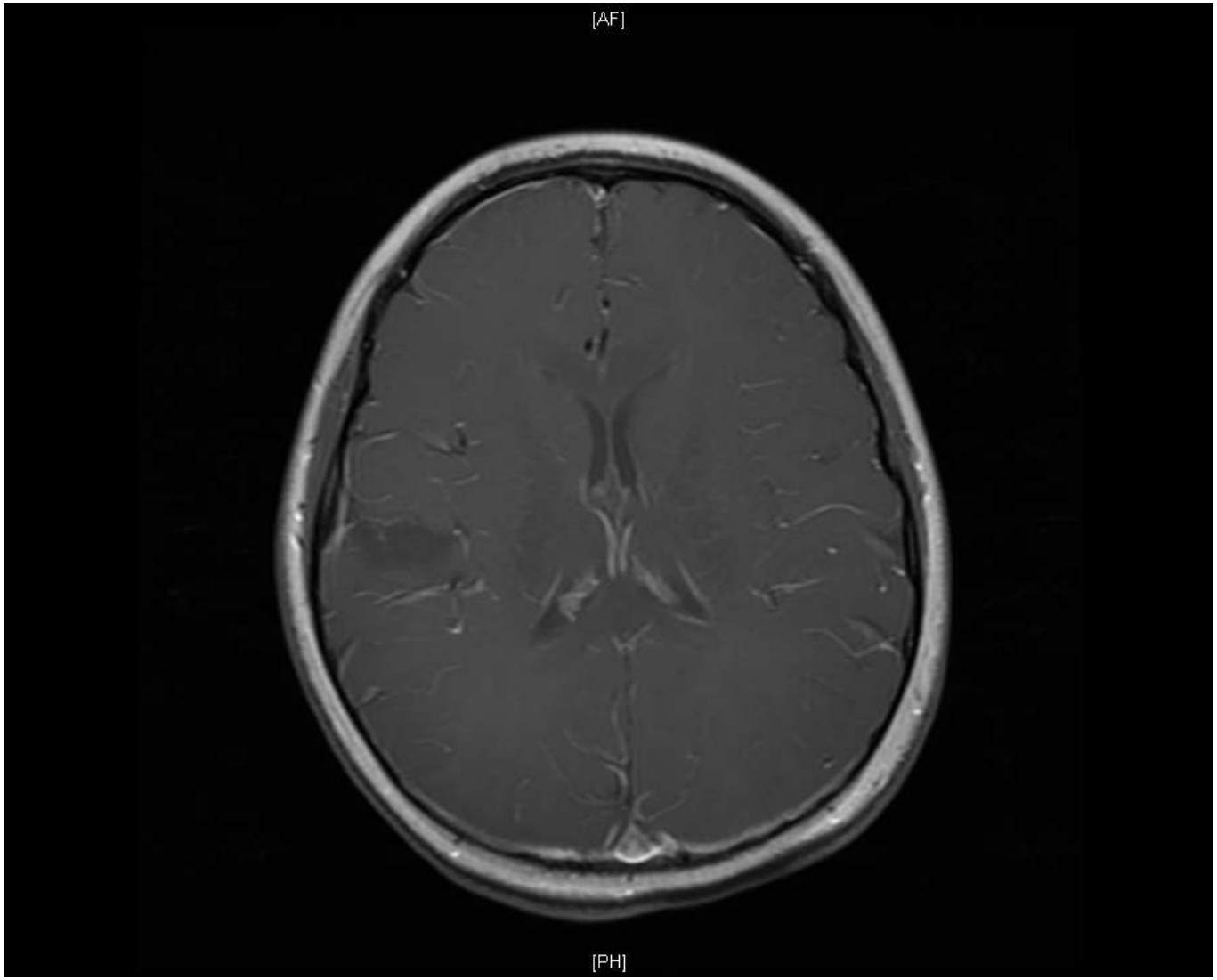


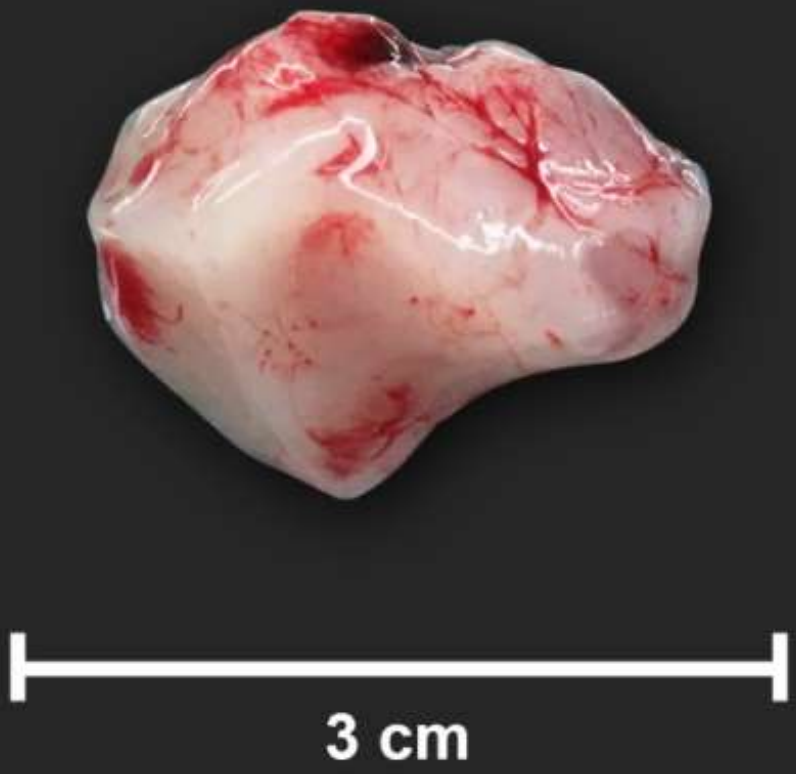
DIAGNOSIS

T2 Pre Contrast Coronal

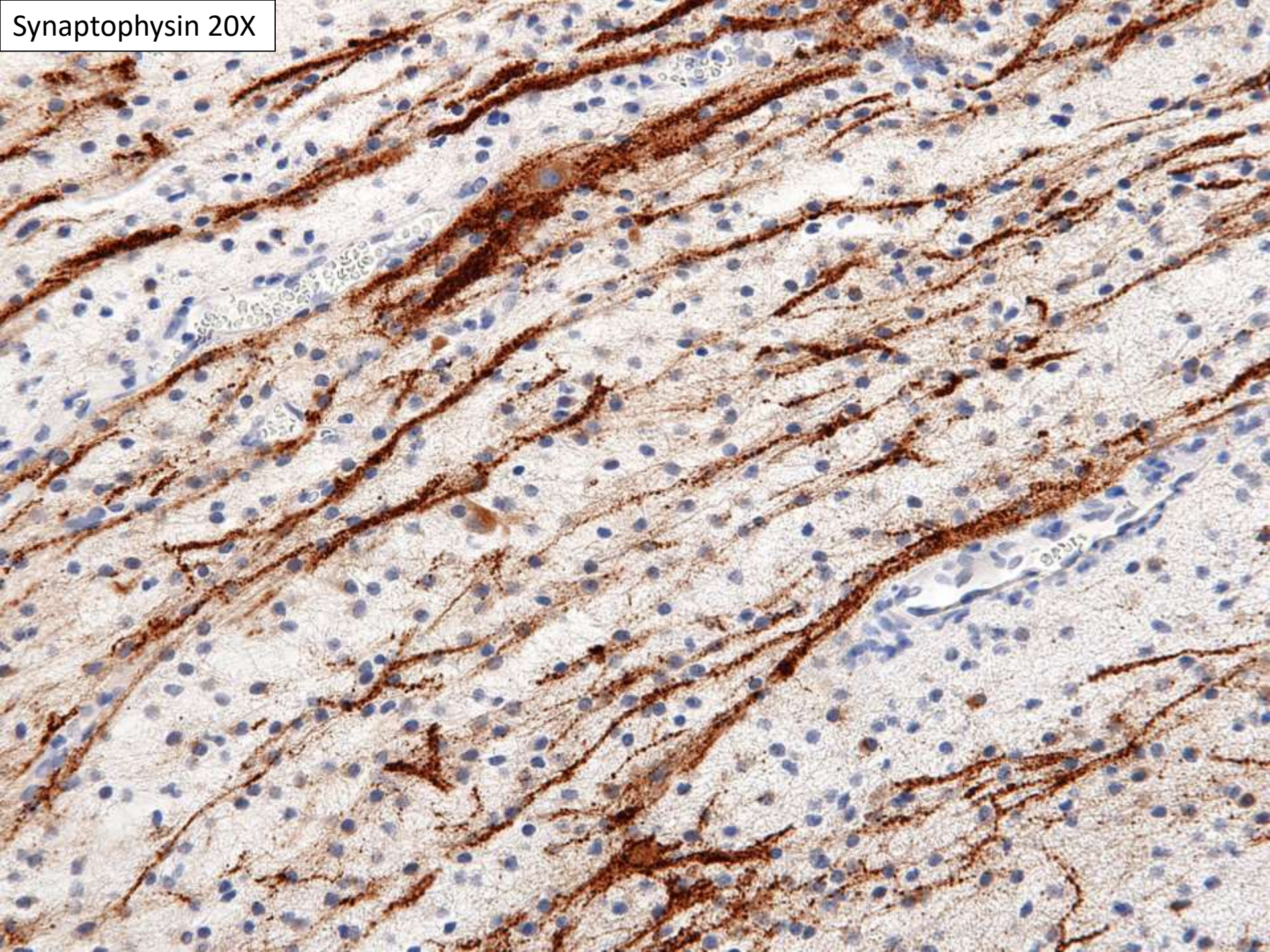


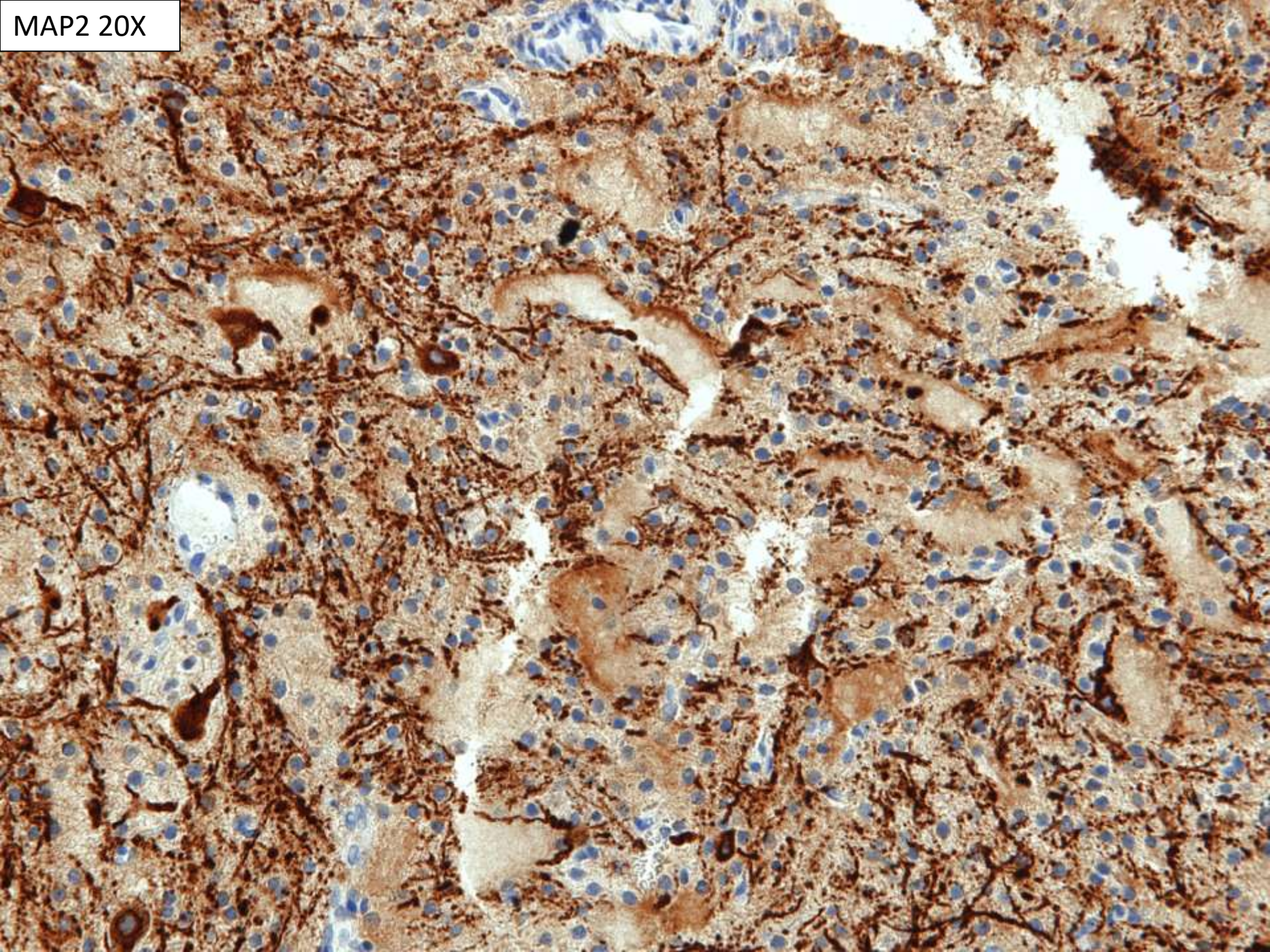
T1 Post Contrast Axial

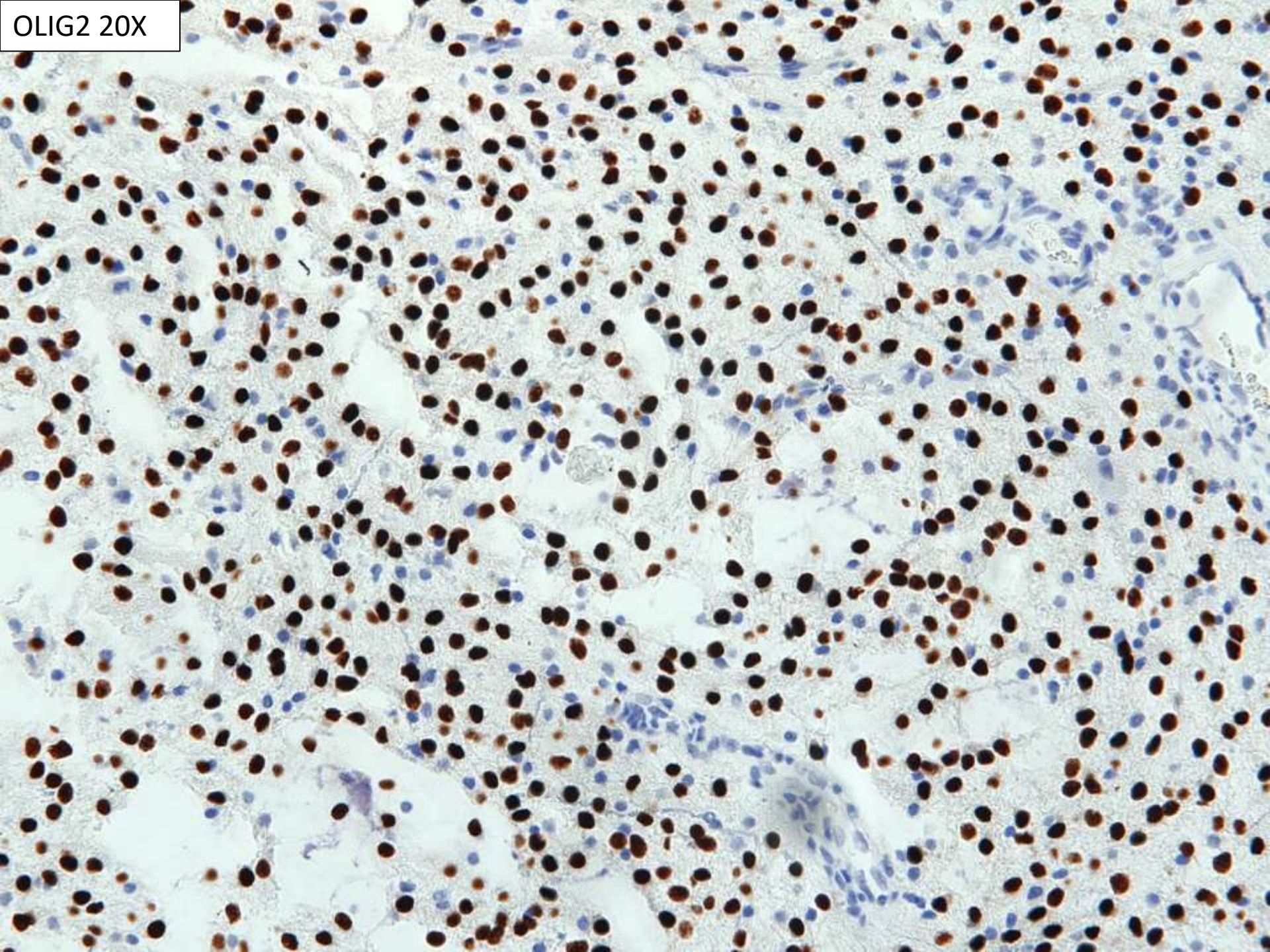


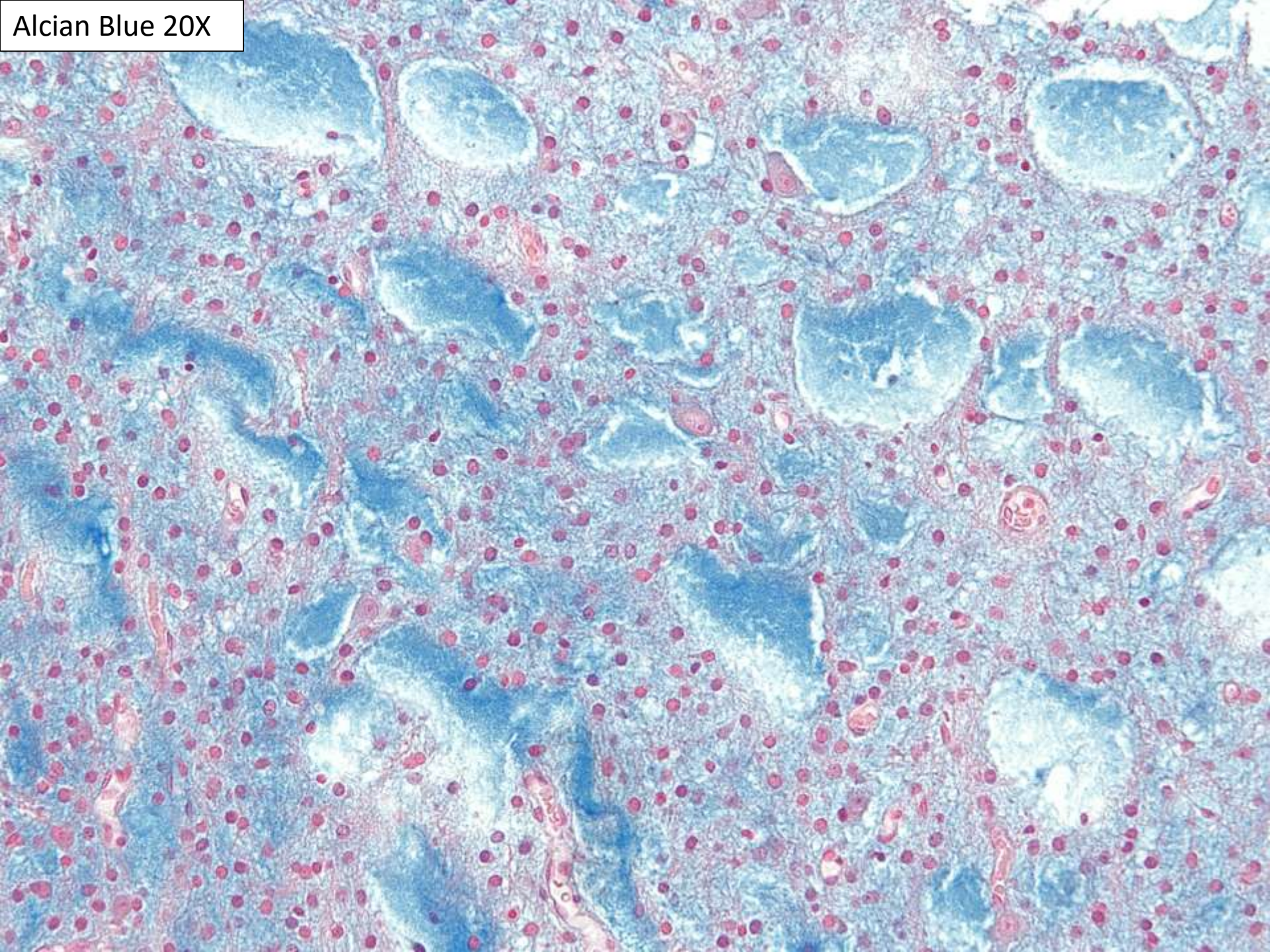

3 cm


6 cm


Synaptophysin 20X


MAP2 20X


OLIG2 20X


Alcian Blue 20X

DIAGNOSIS

DYSEMBRYOPLASTIC NEUROEPITHELIAL TUMOR, WHO GRADE I

Differential Diagnosis

- DNET
- Ganglioglioma
- Angiocentric Glioma
- PXA
- Oligodendroglioma

DNET

- Associated with early onset epilepsy, tumor of children/young adults
- Usually temporal, cortically based, nodular, T2 hyperintense and T1 iso/hypointense, can enhance
- Glioneuronal tumor with columns lined by oligodendrocyte-like cells; pools of mucin with “floating neurons”
  - Simple vs Complex (Non-specific/Diffuse)

Molecular Findings

Acta Neuropathol (2016) 131:847–863
DOI 10.1007/s00401-016-1549-x

ORIGINAL PAPER

Germline and somatic FGFR1 abnormalities in dysembryoplastic neuroepithelial tumors

Barbara Rivera[1,2] · Tenzin Gayden[2] · Jian Carrot-Zhang[2,3] · Javad Nadaf[2,3] · Talia Boshari[4] · Damien Faury[2] · Michele Zeinieh[2] · Romeo Blanc[5] · David L. Burk[6] · Somayyeh Fahiminiya[2,3] · Eric Bareke[2,3] · Ulrich Schüller[7] · Camelia M. Monoranu[8] · Ronald Sträter[9] · Kornelius Kerl[9] · Thomas Niederstadt[10] · Gerhard Kurlemann[11] · Benjamin Ellezam[12] · Zuzanna Michalak[13,14] · Maria Thom[13,14] · Paul J. Lockhart[15,16] · Richard J. Leventer[15,17,18] · Milou Ohm[19] · Duncan MacGregor[20] · David Jones[21,22] · Jason Karamchandani[23] · Celia M. T. Greenwood[2,24] · Albert M. Berghuis[6] · Susanne Bens[25] · Reiner Siebert[25] · Magdalena Zakrzewska[26] · Pawel P. Liberski[26] · Krzysztof Zakrzewski[27] · Sanjay M. Sisodiya[14,28] · Werner Paulus[29] · Steffen Albrecht[30] · Martin Hasselblatt[29] · Nada Jabado[2,31] · William D. Foulkes[1,2,4,32] · Jacek Majewski[2,3]

Received: 20 January 2016 / Revised: 16 February 2016 / Accepted: 16 February 2016 / Published onlin

Acta Neuropathol (2016) 131:833–845
DOI 10.1007/s00401-016-1539-z

ORIGINAL PAPER

Genetic alterations in uncommon low-grade neuroepithelial tumors: *BRAF*, *FGFR1*, and *MYB* mutations occur at high frequency and align with morphology

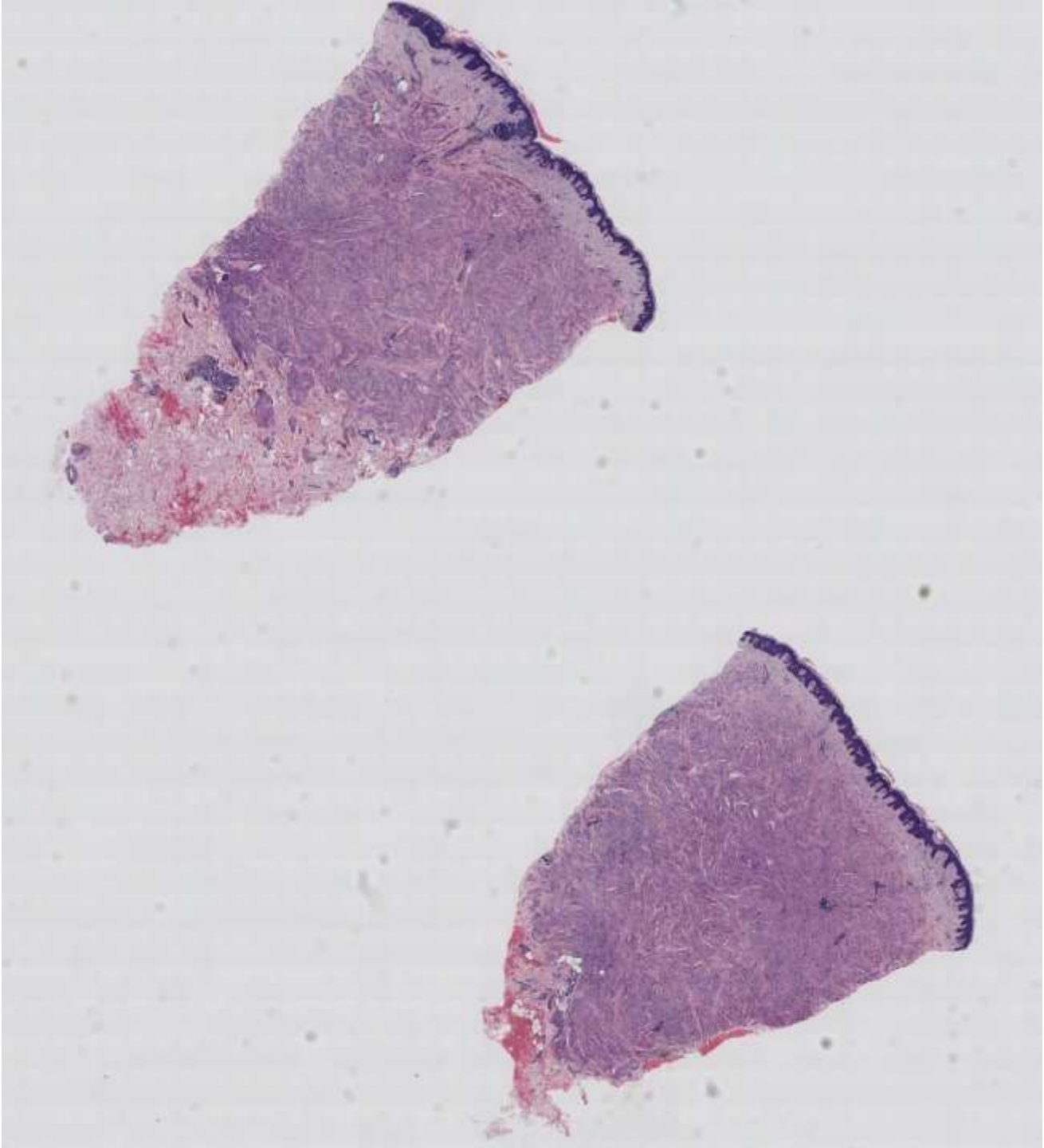
Ibrahim Qaddoumi[1] · Wilda Orisme[2] · Ji Wen[2] · Teresa Santiago[2] · Kirti Gupta[2] · James D. Dalton[2] · Bo Tang[2] · Kelly Haupfear[2] · Chandanamali Punchihewa[2] · John Easton[3] · Heather Mulder[3] · Kristy Boggs[3] · Ying Shao[3] · Michael Rusch[3] · Jared Becksfort[3] · Pankaj Gupta[3] · Shuoguo Wang[3] · Ryan P. Lee[2] · Daniel Brat[4] · V. Peter Collins[5] · Sonika Dahiya[6] · David George[7] · William Konomos[8] · Kathreena M. Kurian[9] · Kathryn McFadden[10] · Luciano Neder Serafini[11] · Hilary Nickols[12] · Arie Perry[13] · Sheila Shurtleff[2] · Amar Gajjar[1] · Fredrick A. Boop[14] · Paul D. Klimo Jr.[14] · Elaine R. Mardis[6] · Richard K. Wilson[6] · Suzanne J. Baker[15] · Jinghui Zhang[3] · Gang Wu[3] · James R. Downing[2] · Ruth G. Tatevossian[2] · David W. Ellison[2]

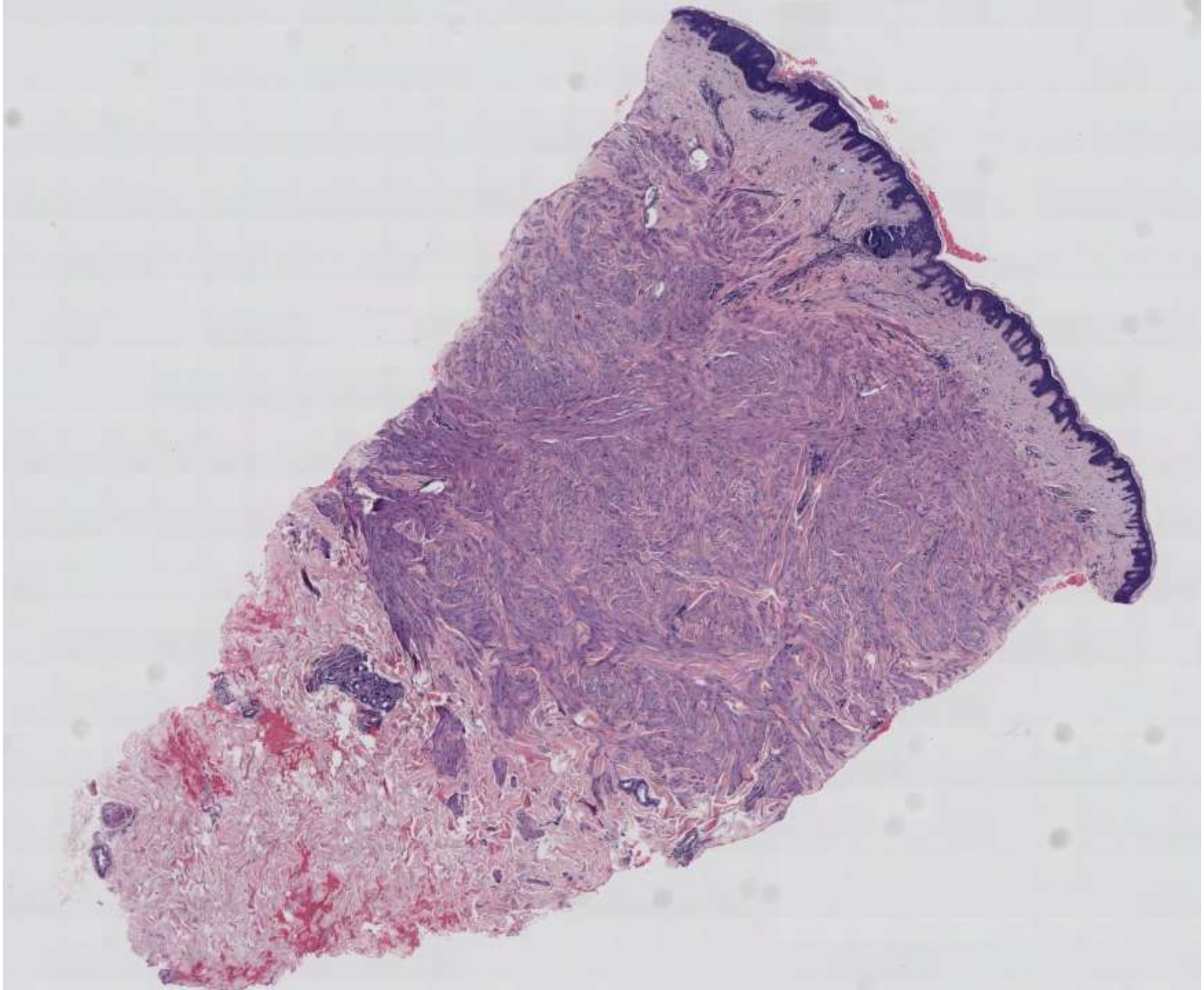
Received: 25 December 2015 / Revised: 16 January 2016 / Accepted: 17 January 2016 / Published online: 25 January 2016

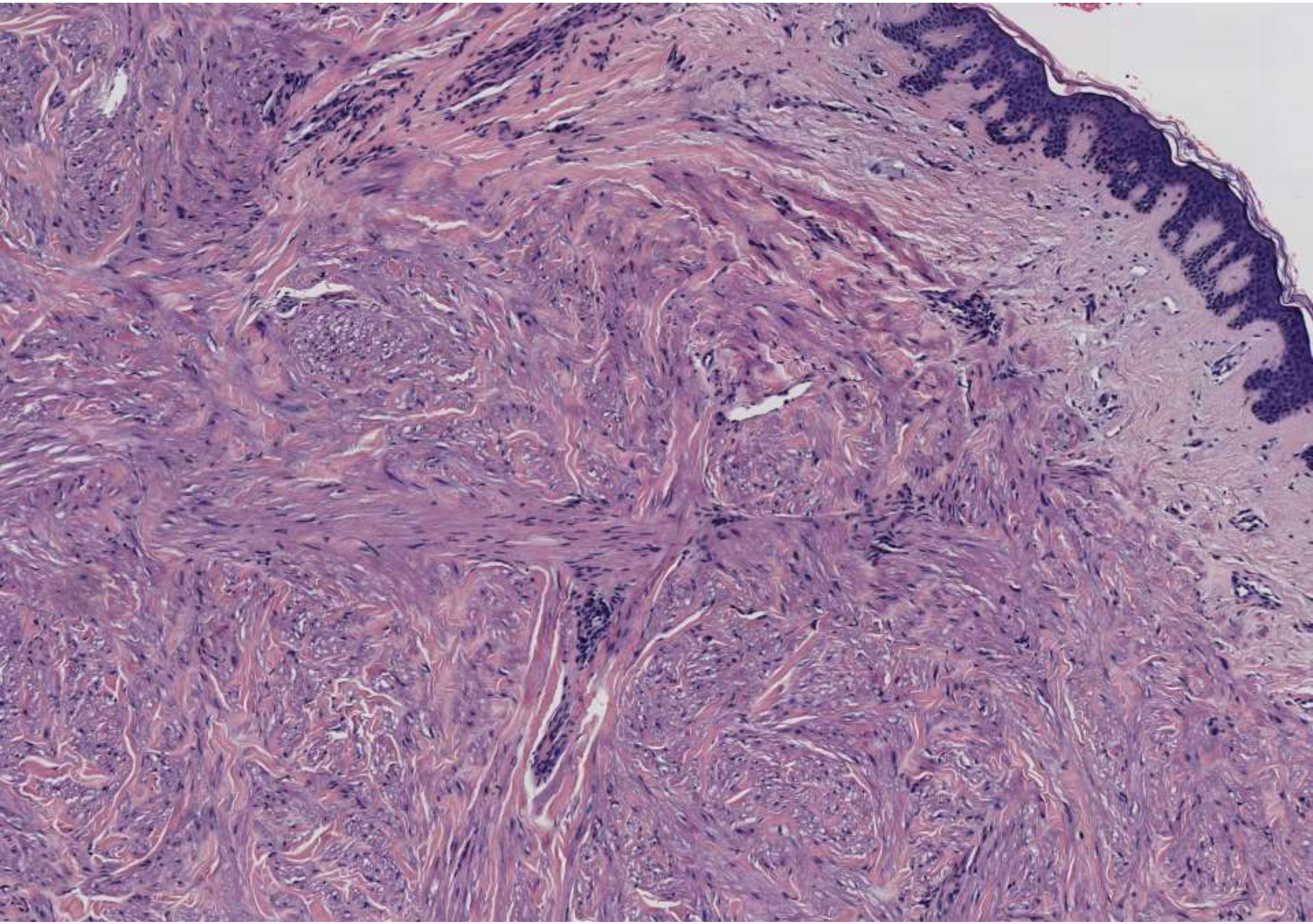
SB 6112
[scanned slide available]

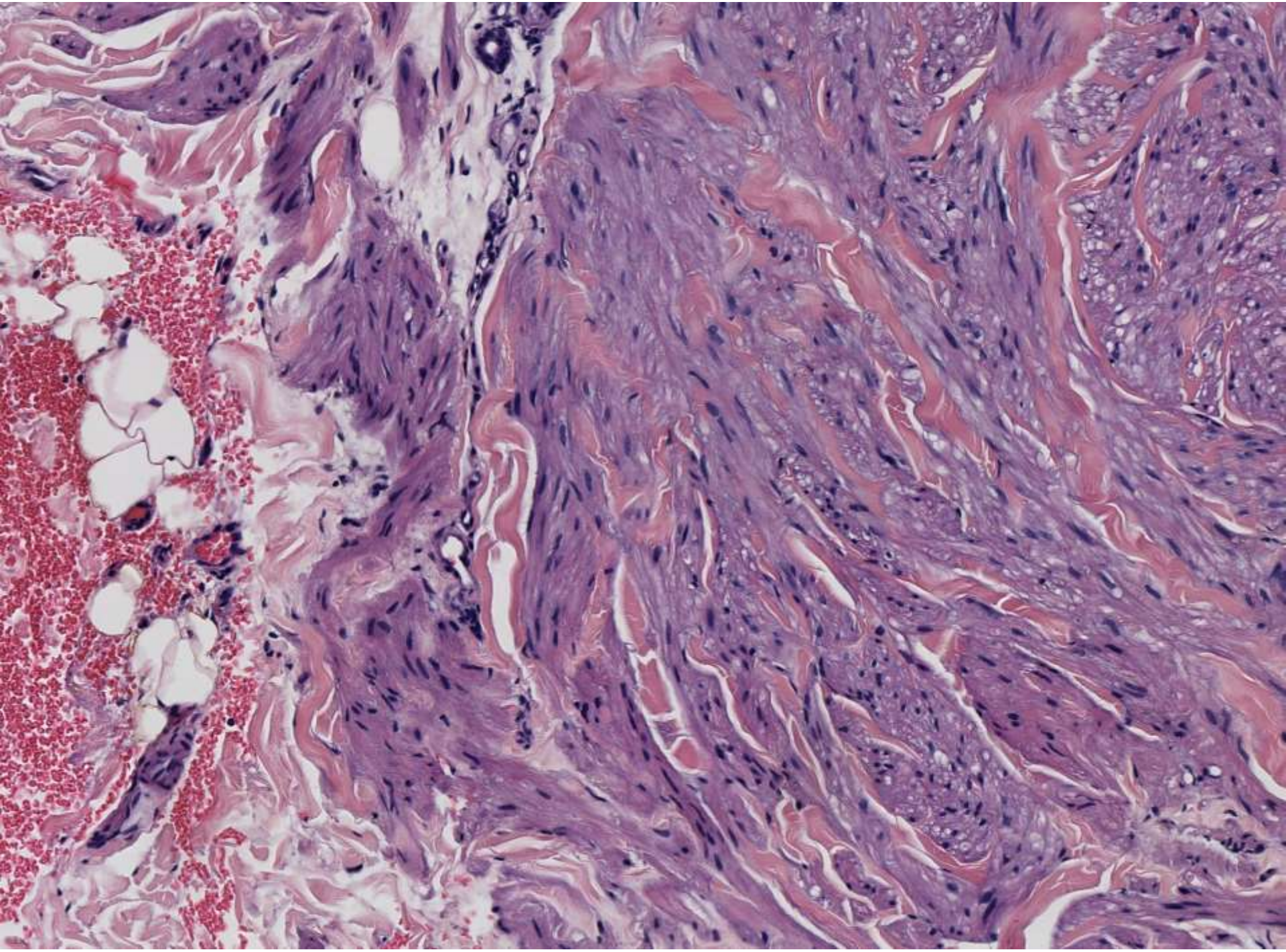
Jarish Cohen/Karuna Garg; UCSF

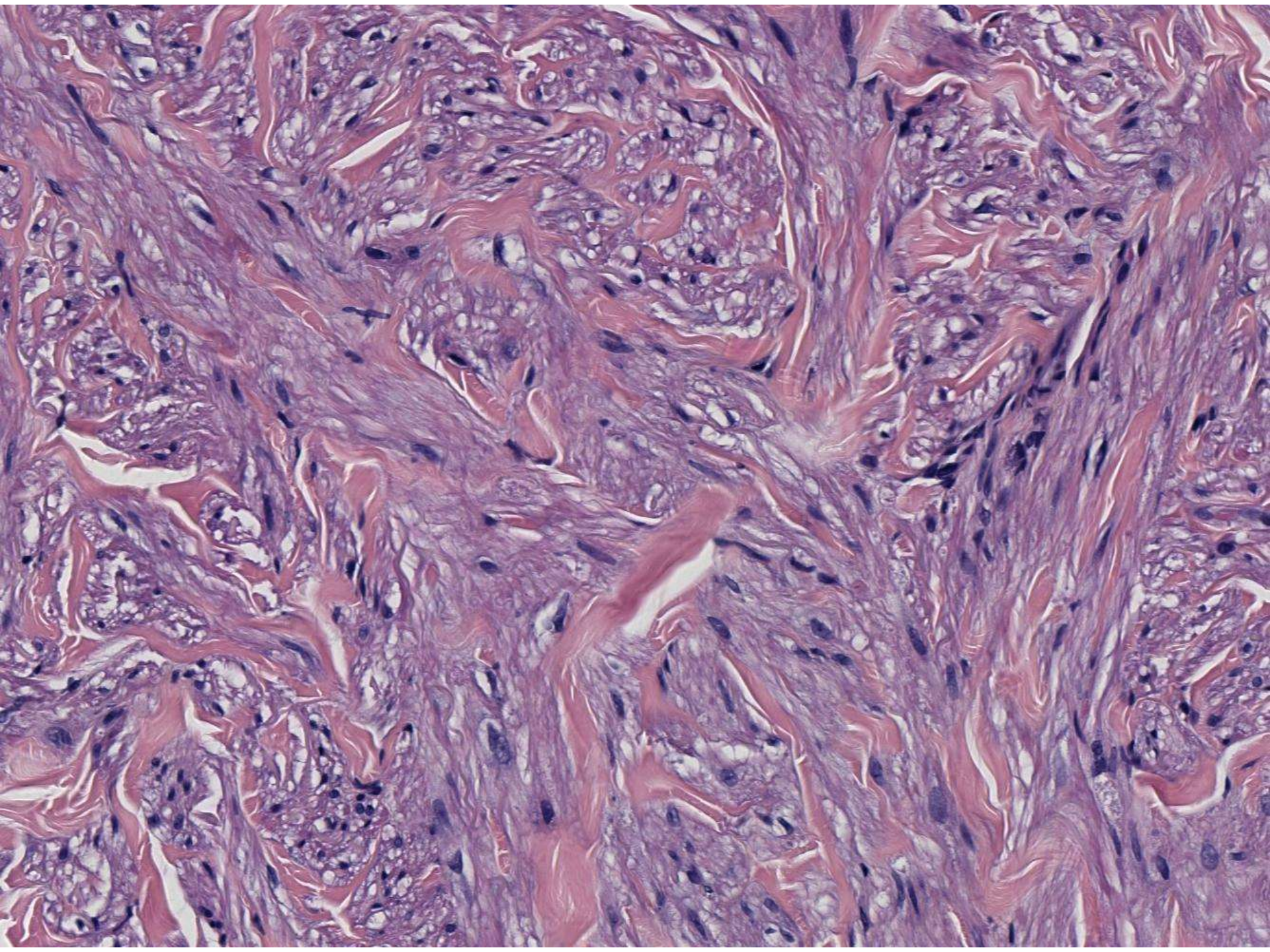
66-year-old woman with left flank skin nodules.

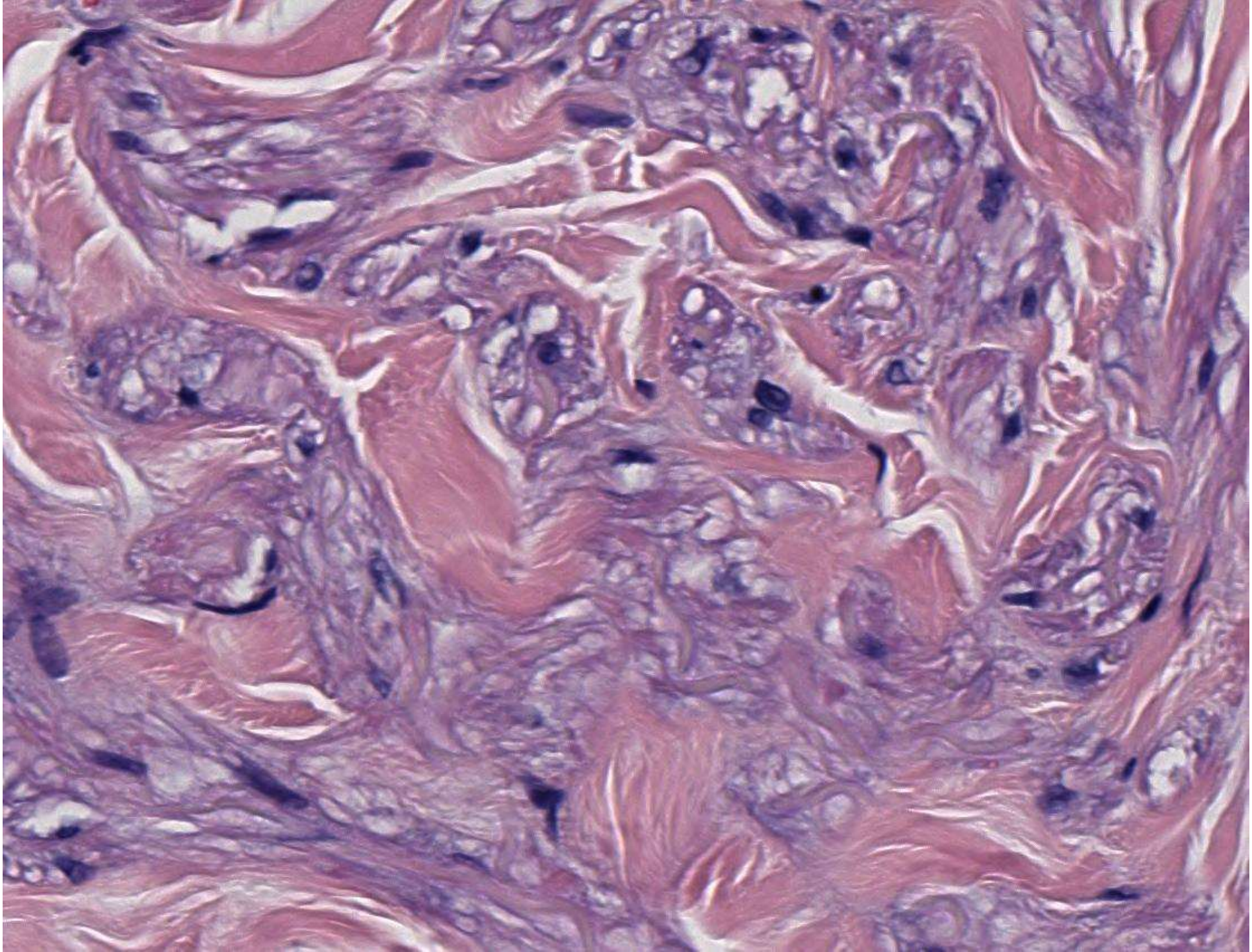


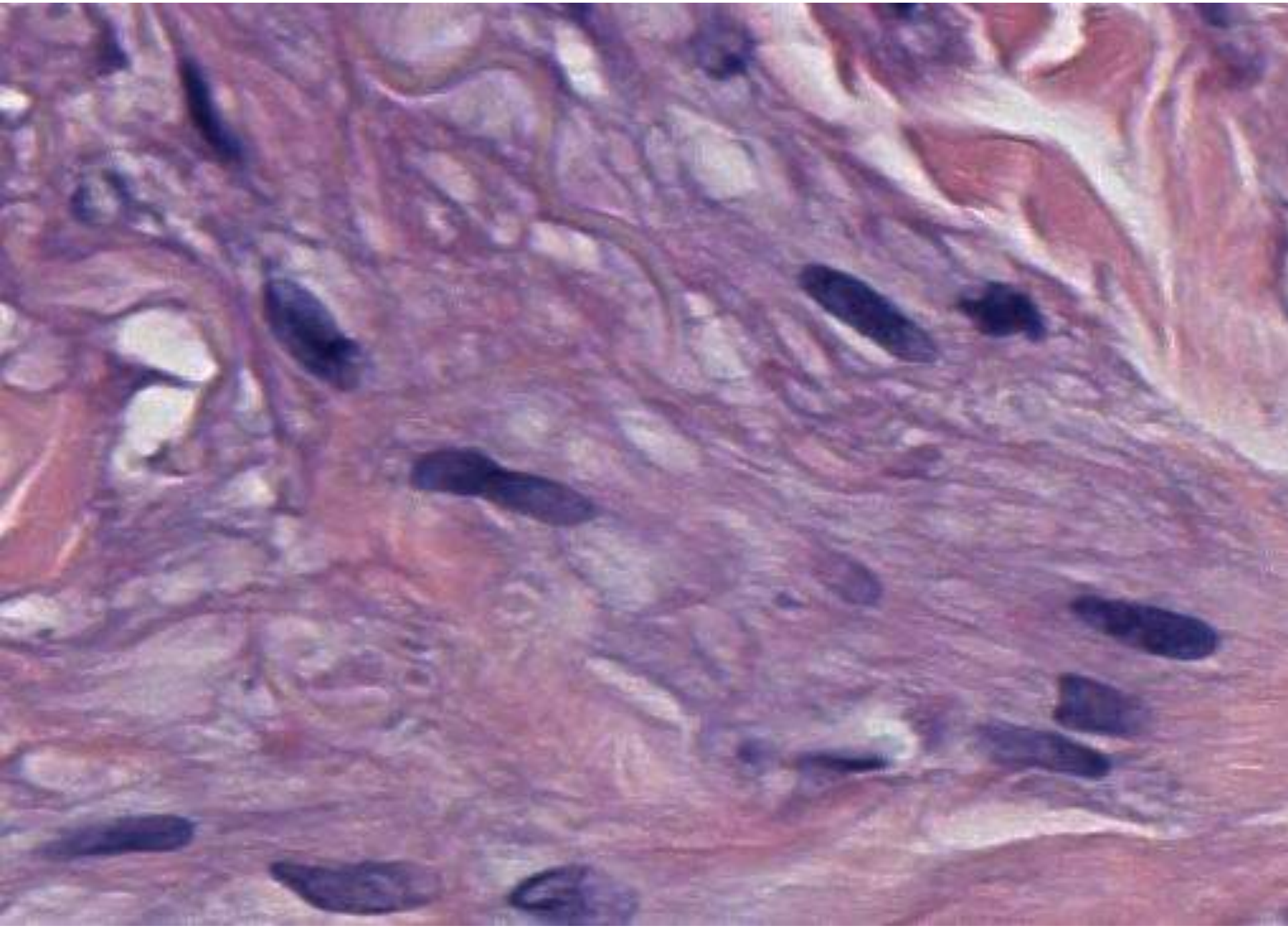




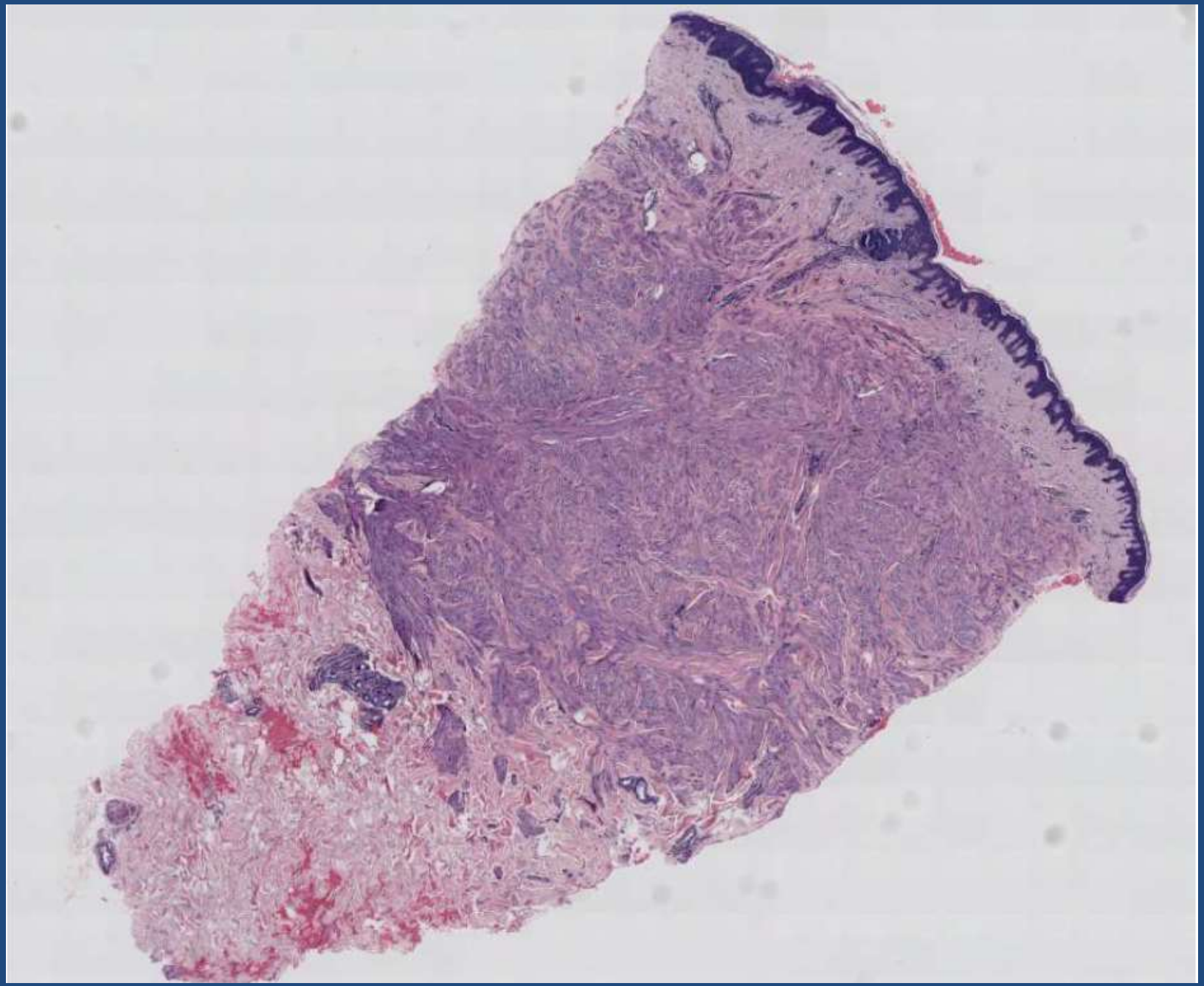


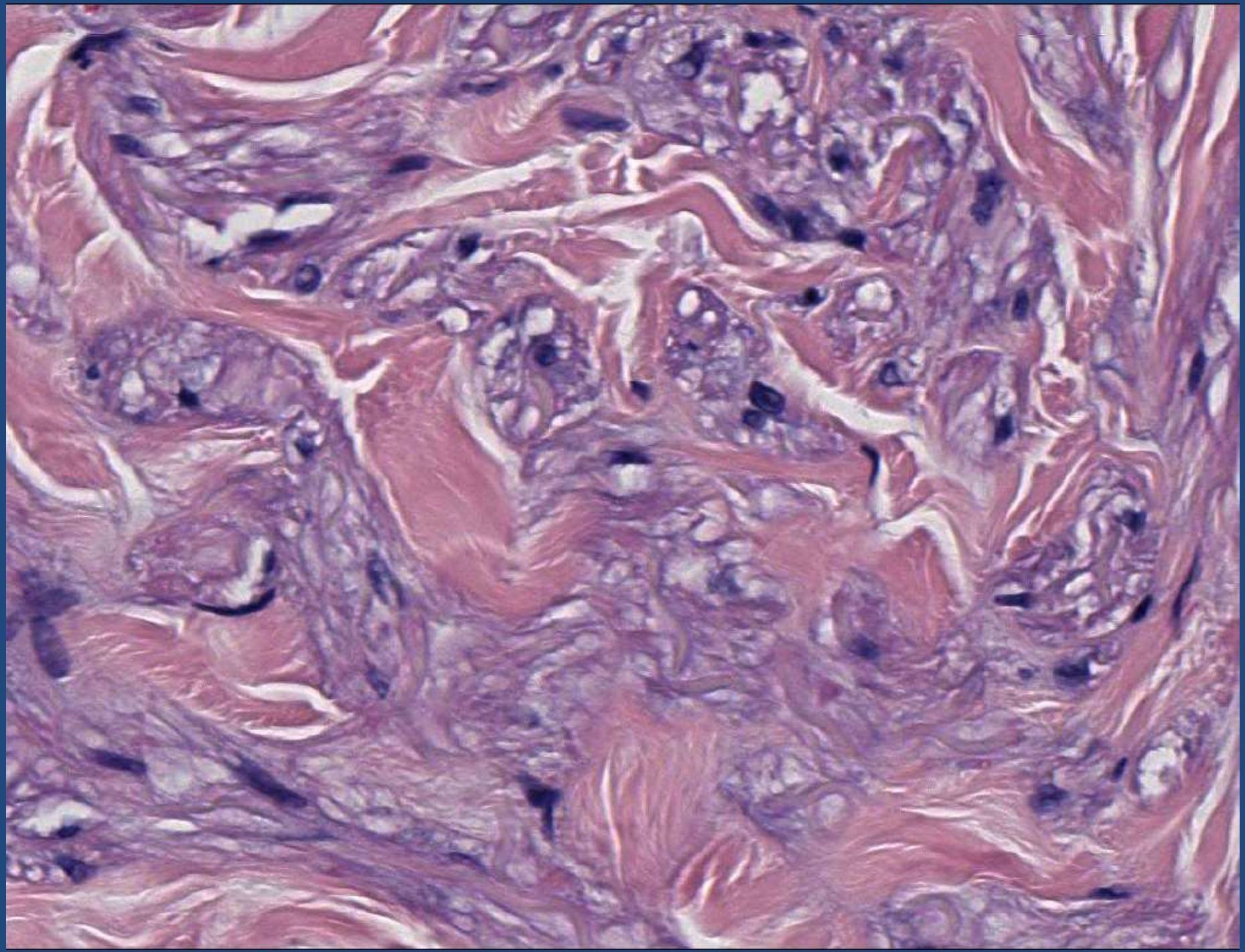






DIAGNOSIS

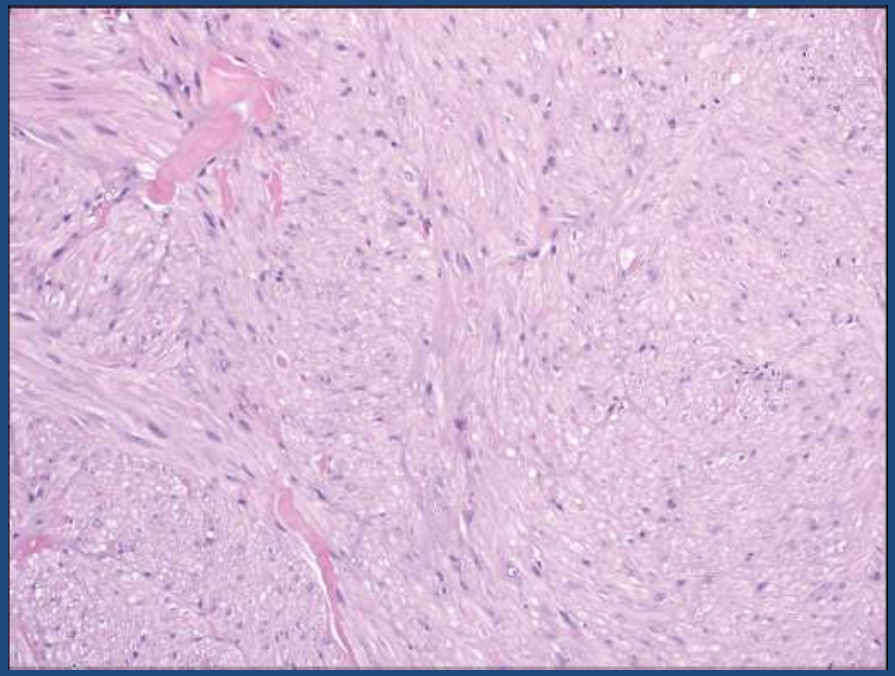




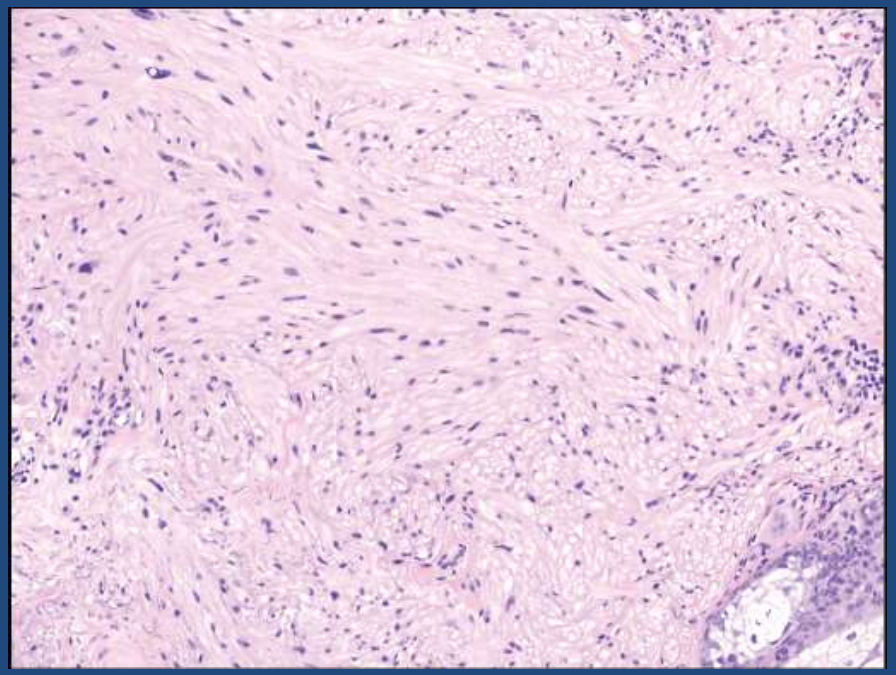
Immunohistochemistry for 2-Succinocysteine (2SC) and Fumarate Hydratase (FH) in Cutaneous Leiomyomas May Aid in Identification of Patients With HLRCC (Hereditary Leiomyomatosis and Renal Cell Carcinoma Syndrome)

Benjamin Buelow, MD, PhD, Jarish Cohen, MD, PhD,* Zoltan Nagymanyoki, MD, PhD,* Norma Frizzell, PhD,† Nancy M. Joseph, MD, PhD,* Timothy McCalmont, MD,‡ and Karuna Garg, MD**

Multiple cutaneous leiomyomas

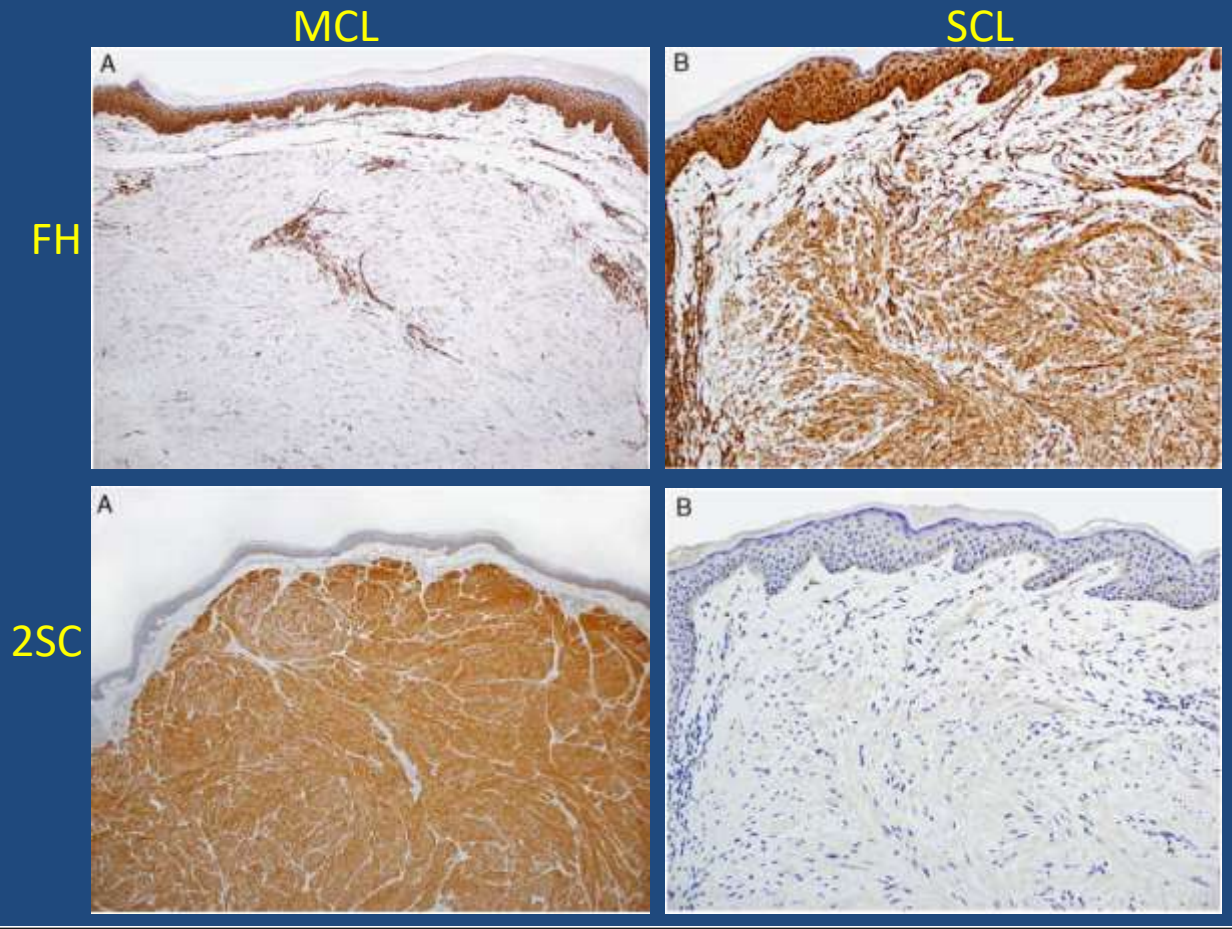


Single cutaneous leiomyoma



(*Am J Surg Pathol* 2016;40:982–988)

MCLs show loss of FH and gain of 2SC staining

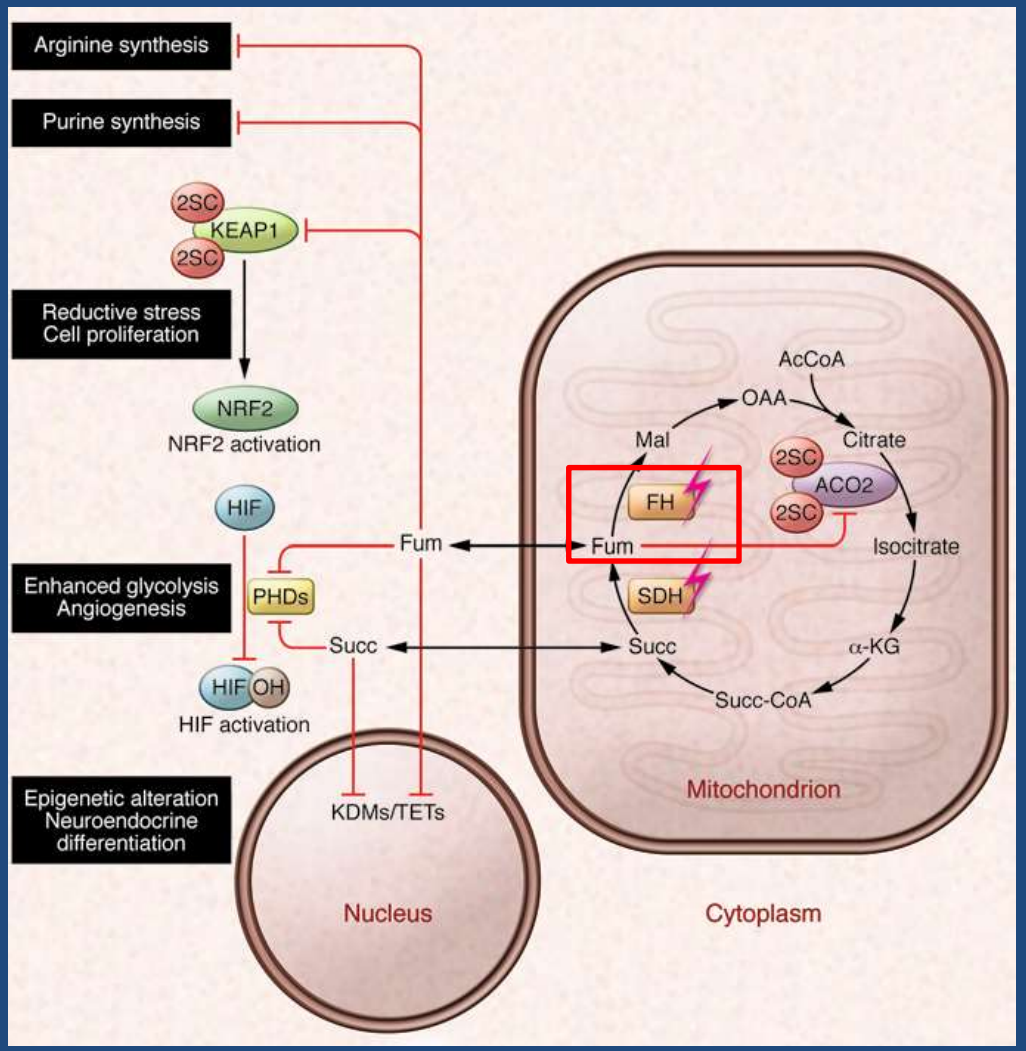


	Avg. age (std. error)	2SC positive	FH negative
MCL (40)	51 years (6.7)	37/40 (92.5%)	28/40 (70%)
SCL (25)	58.6 years (5.2)	2/25 (8%)	1/25 (4%)

(*Am J Surg Pathol* 2016;40:982–988)

HLRCC: Fumarate hydratase mutation

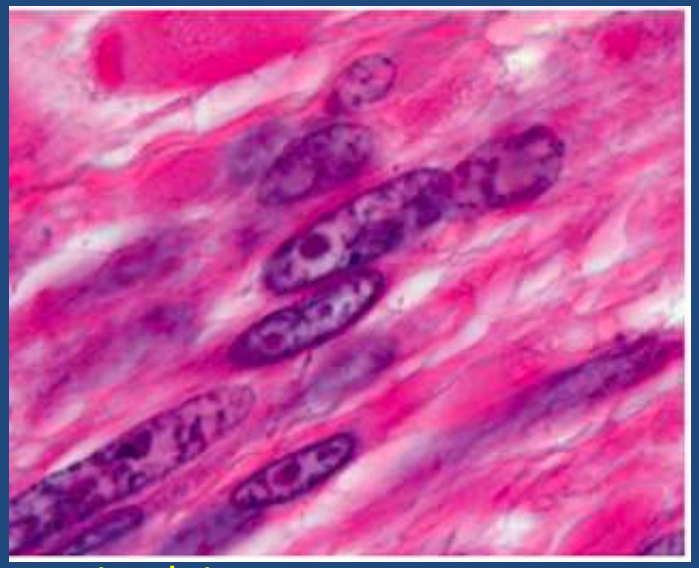
- Chromosome 1
- Kreb's cycle enzyme
- Majority of mutations are missense
- Increased fumarate results in metabolic dysregulation
  - Pseudohypoxia
  - Succination resulting in 2-succinyl-cysteine accumulation
  - Reductive stress and cellular proliferation



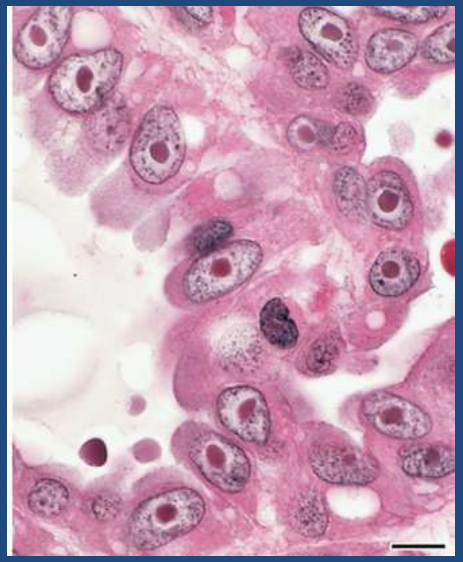
Yang M et al. J Clin Invest. 2013; 123(9):3652

Hereditary Leiomyomatosis and Renal Cell Carcinoma Syndrome (HLRCC)

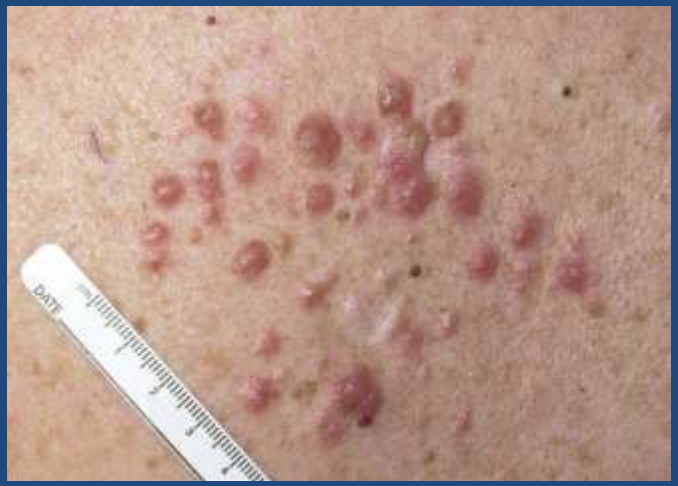
- Reed's syndrome
- Multiple cutaneous and uterine leiomyomas
- 20-30% develop an aggressive form of RCC



Uterine leiomyoma



RCC



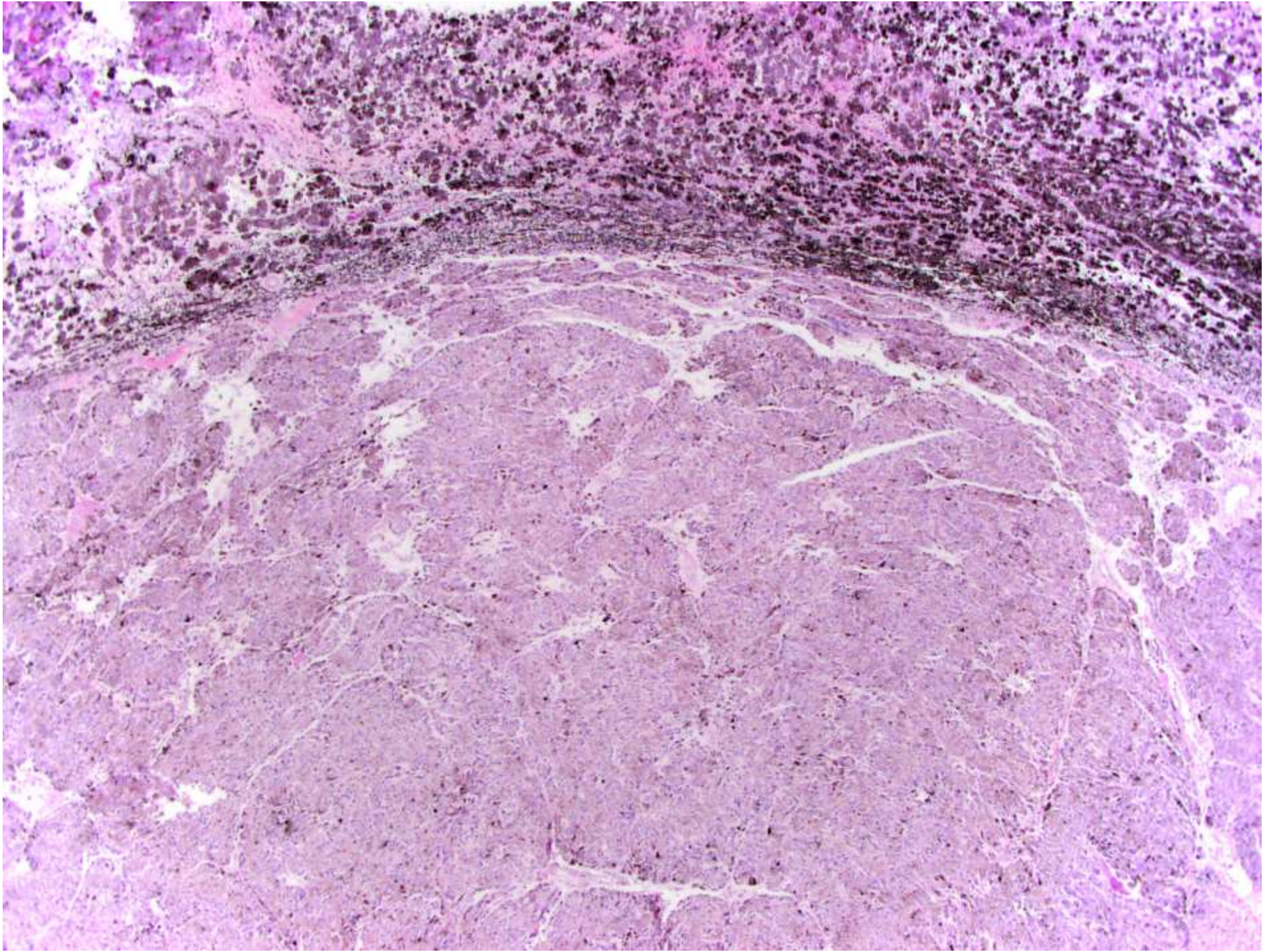
Cutaneous leiomyomas

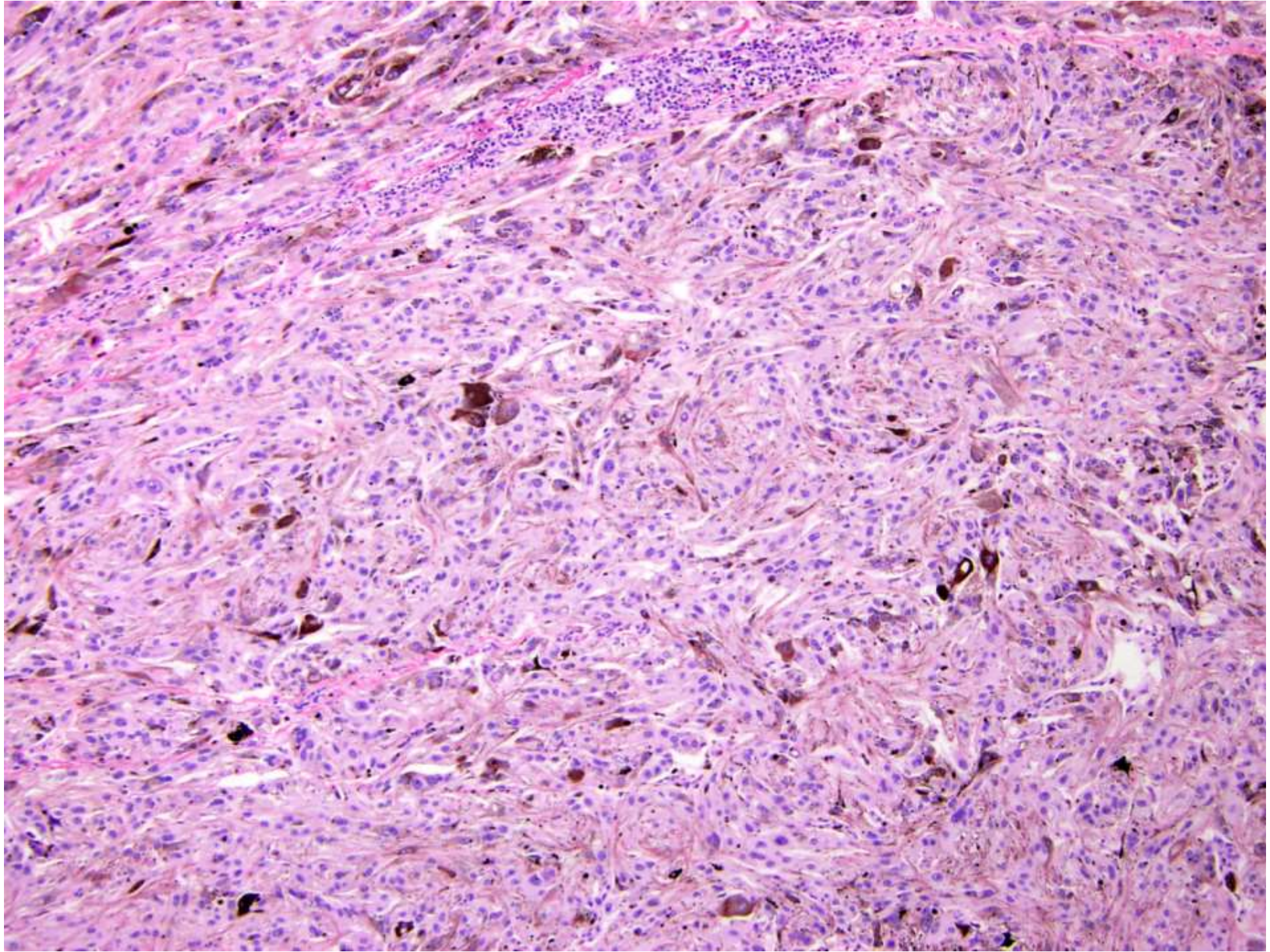
Grubb RL et al. J Urol. 2007. 177(6):2074
Sanz-Ortega J et al. Am J Surg Pathol. 2013. 37:74

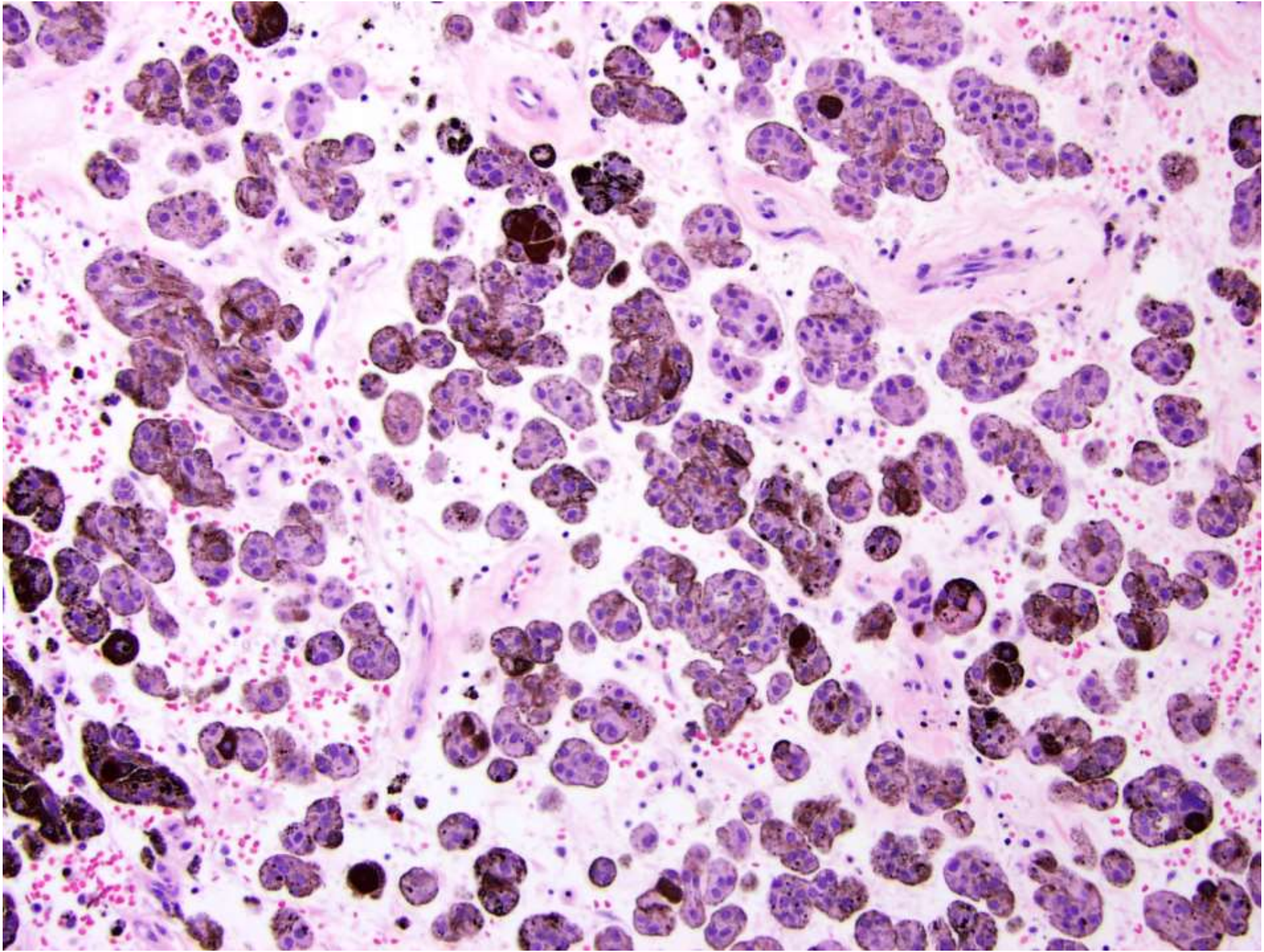
SB 6113

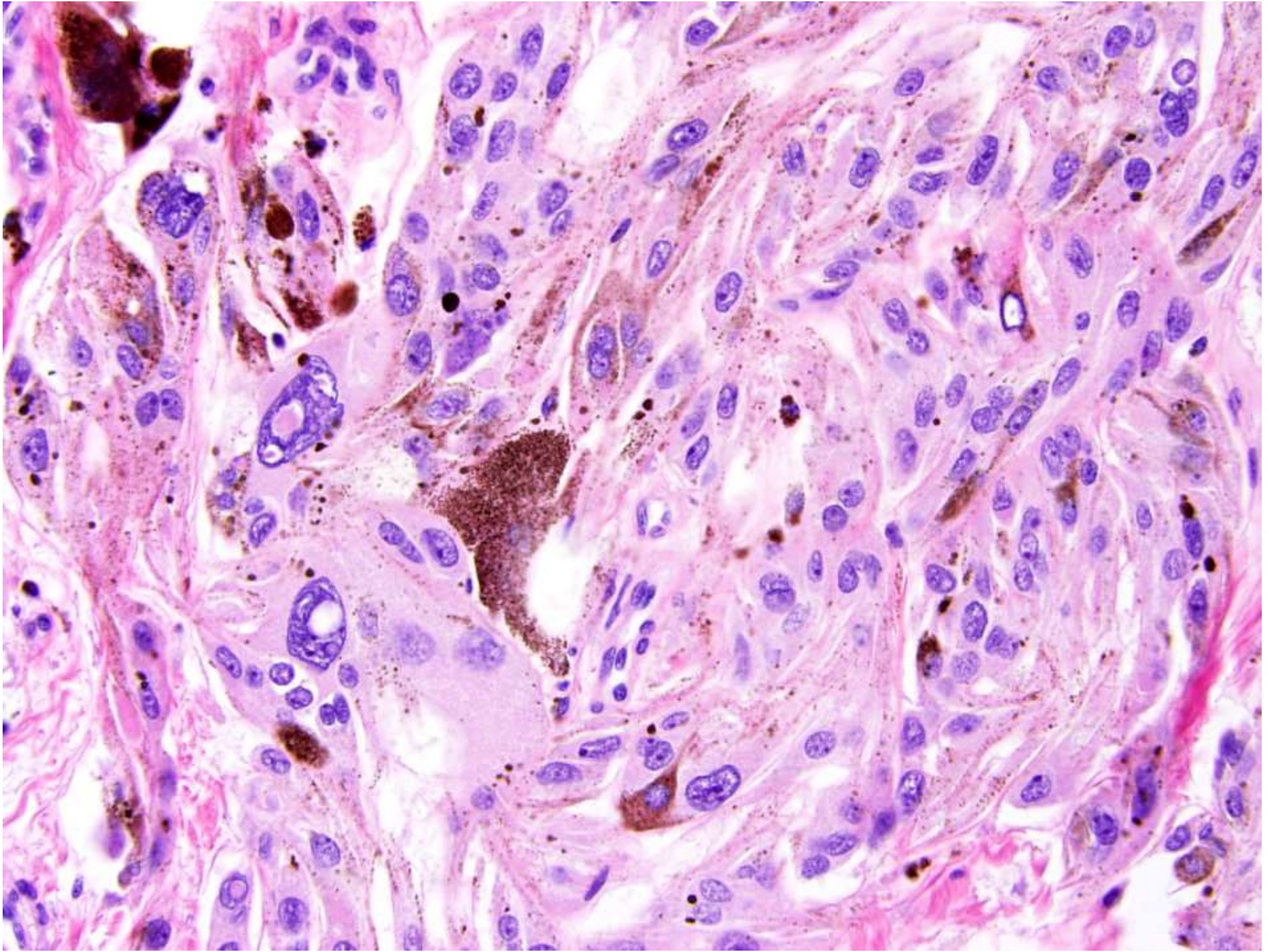
Jarish Cohen/Sarah Umetsu ; UCSF

35-year-old man with rhonchi and 9cm right lung posterior mediastinal mass.





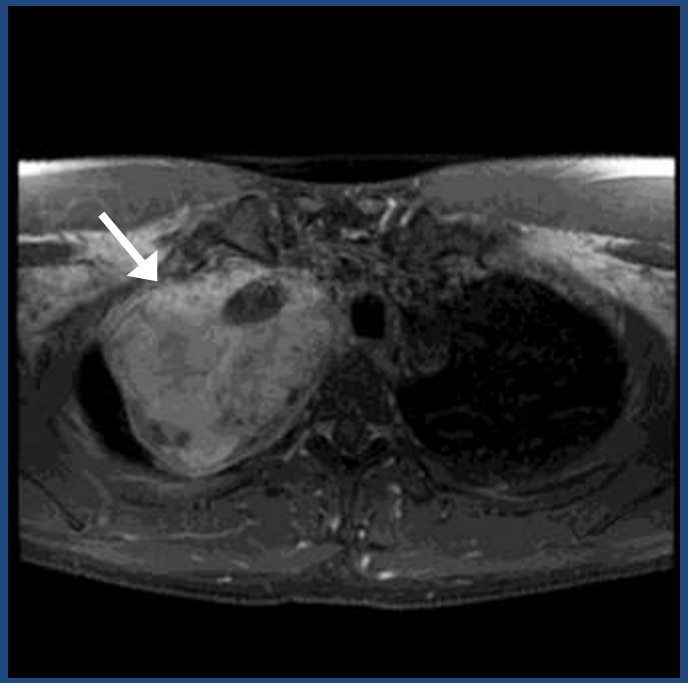


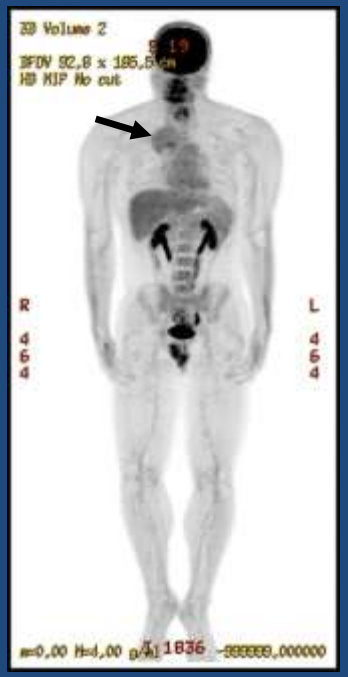


DIAGNOSIS

History

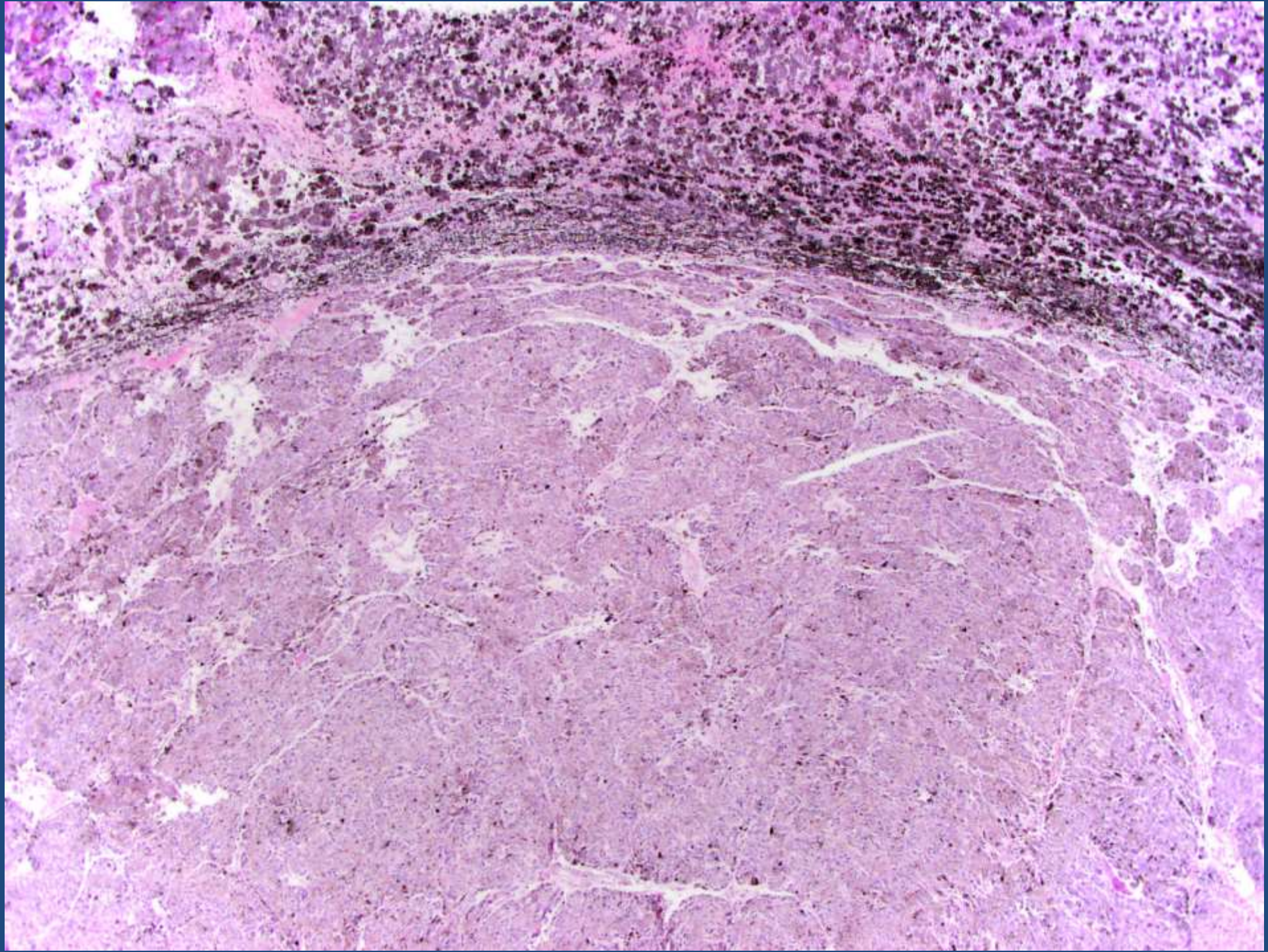
- 35 yo otherwise healthy male who presented to PCP w/ rhonchi
- Imaging showed a 9 cm right lung hilar mass

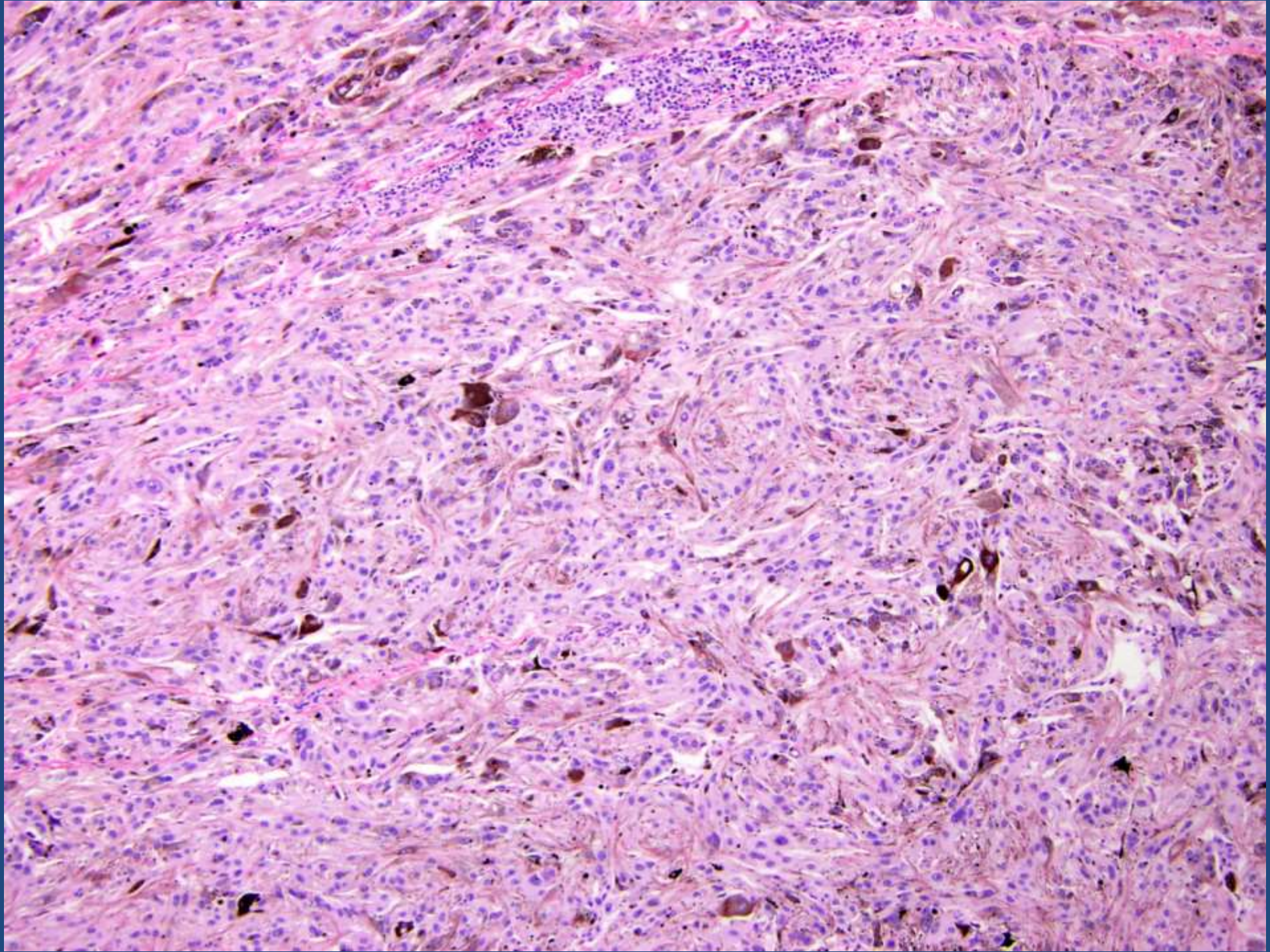


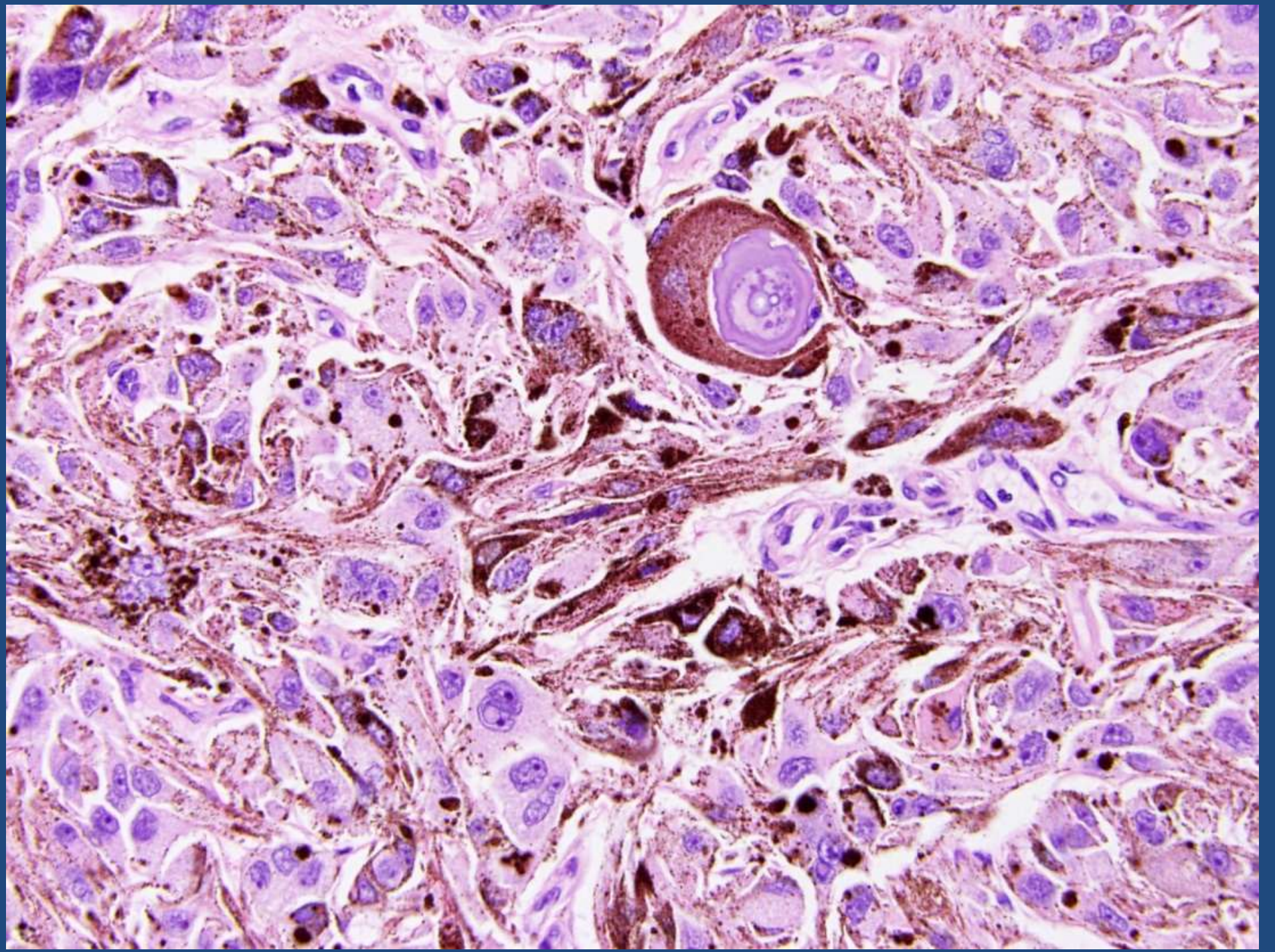


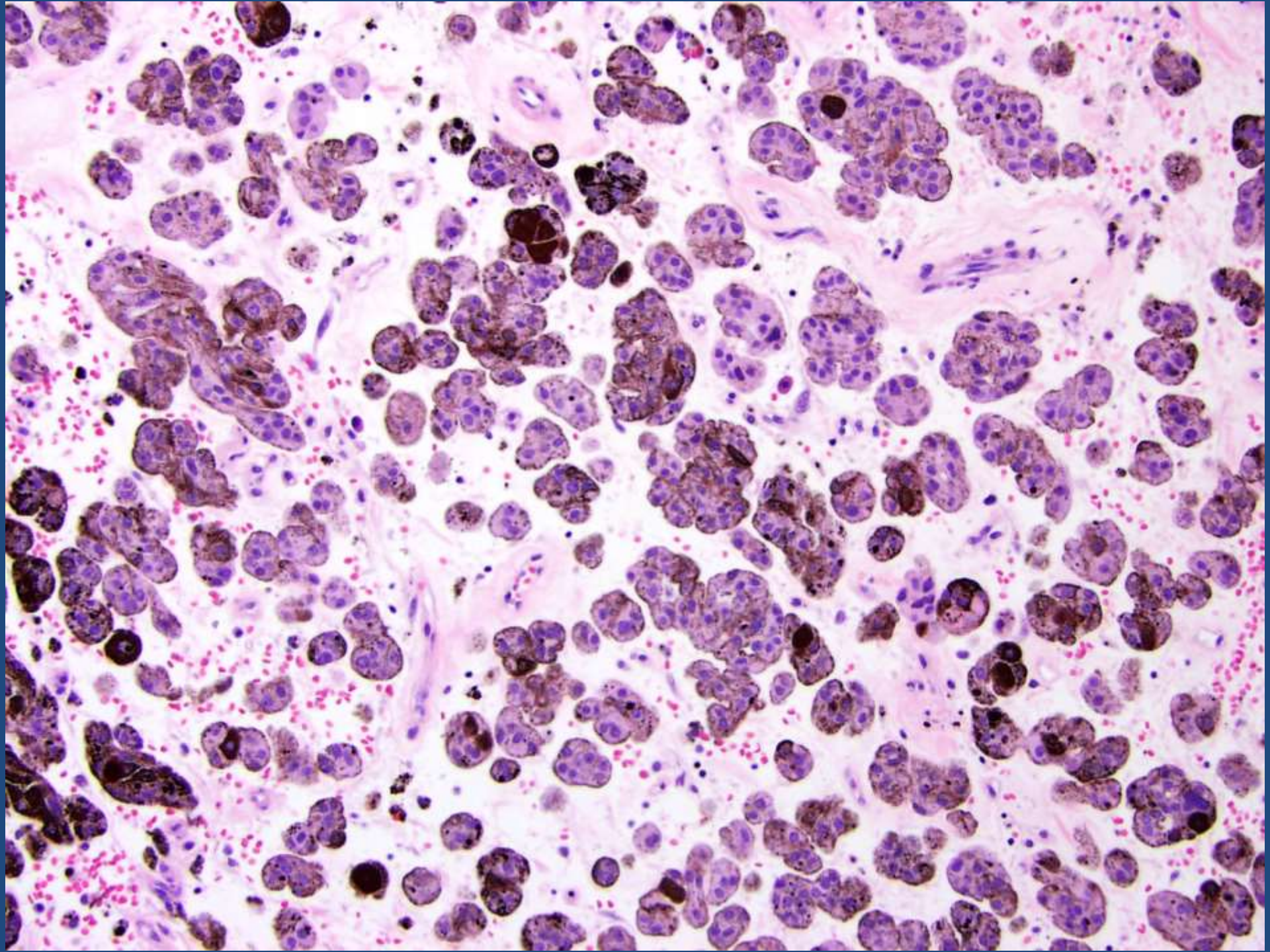
History

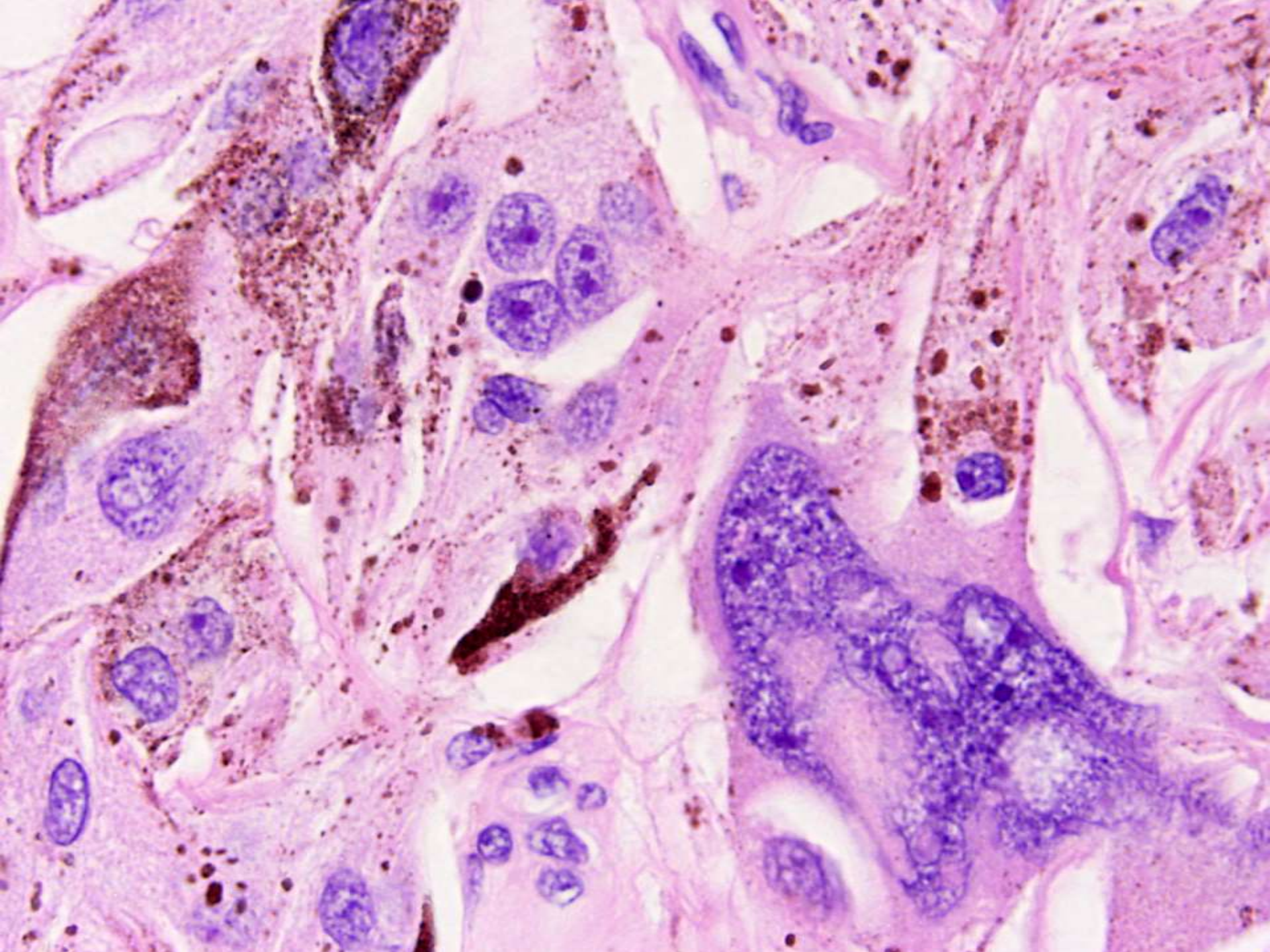
- FNA and core needle biopsy: Malignant melanoma.
- No suspicious lesions on full body skin exam.
- Patient started on ipilimumab (anti-CTLA4) and nivolumab (anti-PD1).
  - Developed painless jaundice, fever, abnormal LFTs
- Liver biopsy: Active hepatitis with duct damage and cholestasis.
- UCSF 500 cancer gene panel testing of FNA/core biopsy material: *PRKAR1A* p.A7fs hemizygous mutation, focal loss on 17q.
- Underwent resection of the mass
  - Surgeon noted that it seemed to be attached to a nerve in the posterior mediastinum

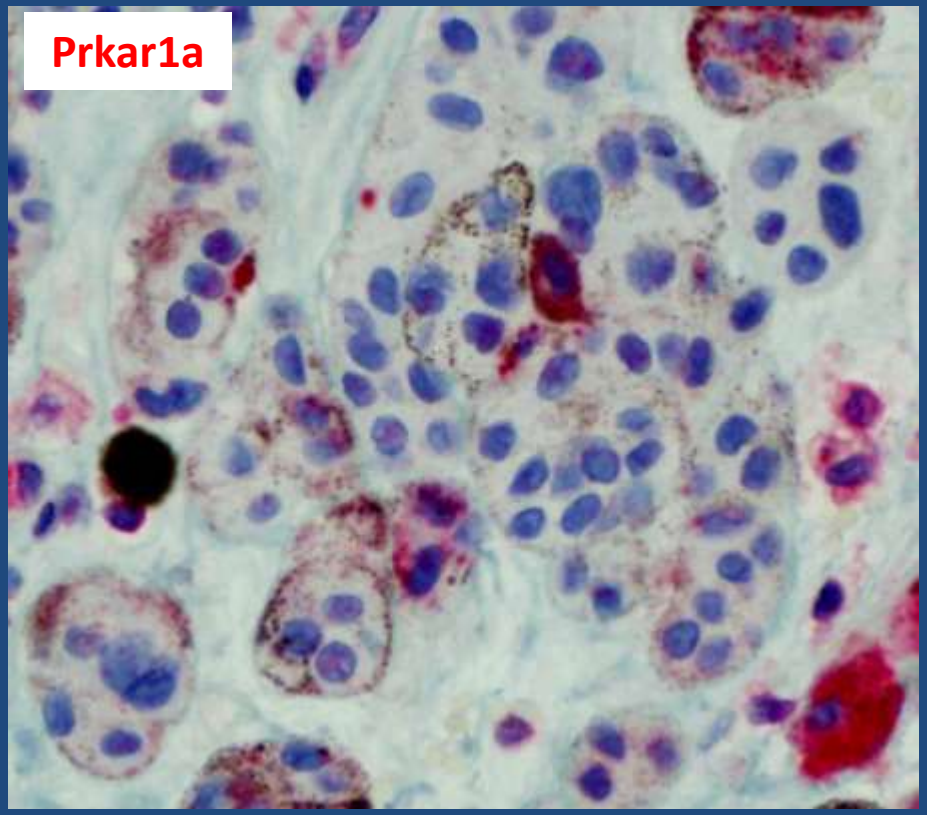


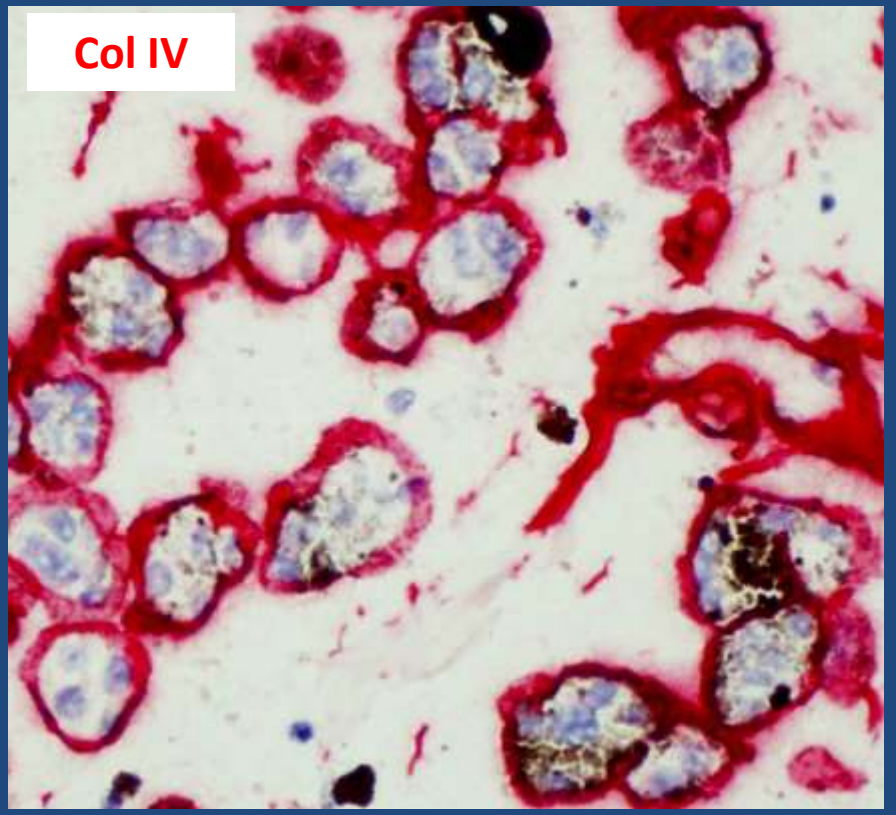









Prkar1a


Col IV

Immunohistochemistry

Marker	Result
HMB45	Positive
MelanA	Positive
Sox10	Positive
S100	Positive
BAP1	Positive (intact nuclear staining)
Collagen IV	Strong Positive
Prkar1a	Negative (loss of cytoplasmic staining)
Ki-67	low

Differential diagnosis

- Malignant melanoma
- Melanotic schwannoma
- Melanocytoma

Features favoring melanotic schwannoma over melanoma

- Paravertebral location
- Predominantly spindled morphology
- Heavy melanin pigmentation
- Psammoma bodies
- Striking nuclear pleomorphism with relatively low mitotic rate
- Loss of Prkar1a

Melanotic schwannoma

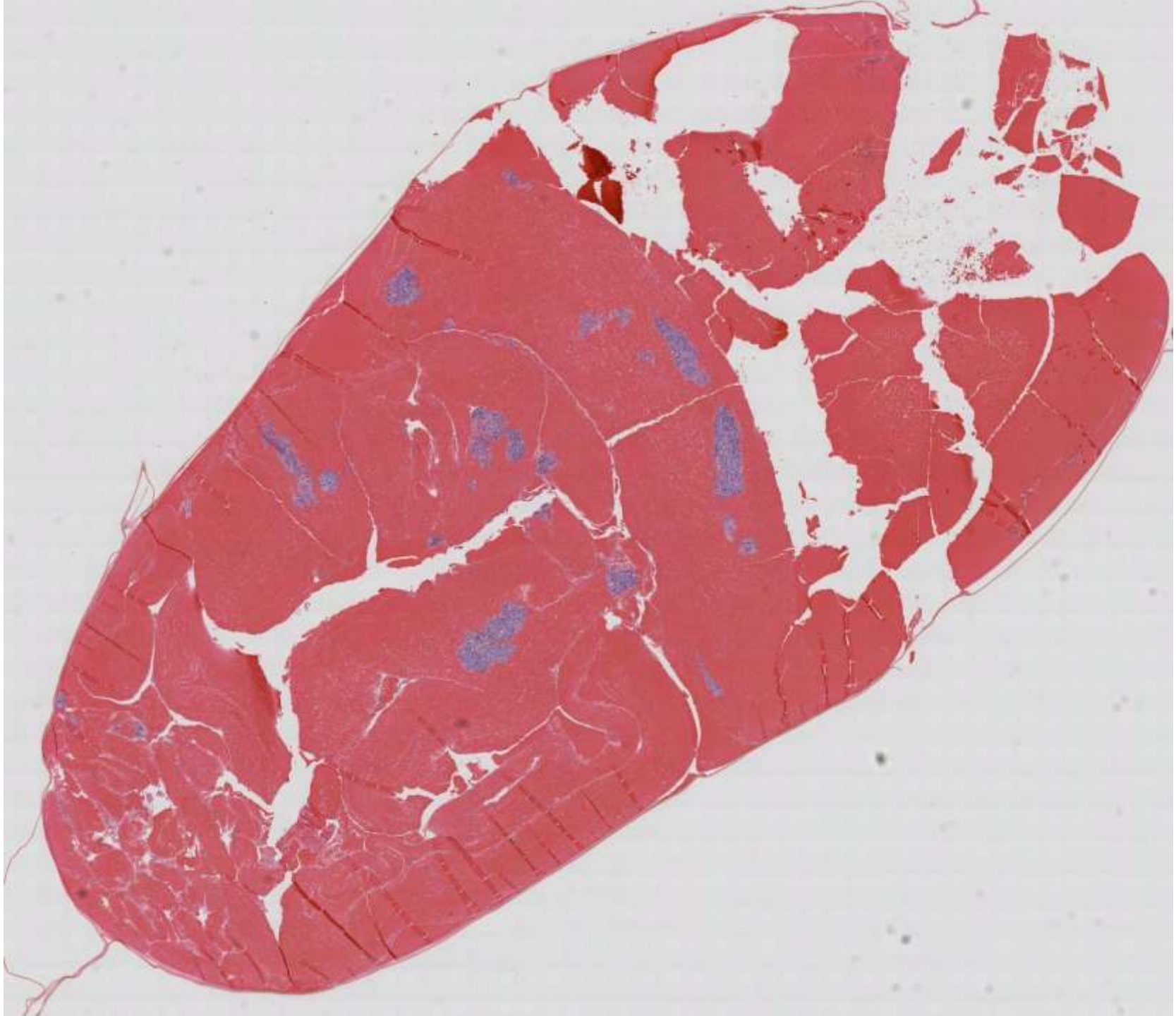
- Rare tumor of neural crest origin
- Paravertebral nerve roots, mediastinum, sacrum
- Associated with Carney complex (defects in *PRKAR1A*)
- 33% of cases show loss of cytoplasmic Prkar1a expression by IHC
- Low proliferation rate: 92% of cases with Ki-67 <5%
- 15-45% of cases with distant metastases
- Proposal for reclassification as “malignant melanotic schwannian tumor”

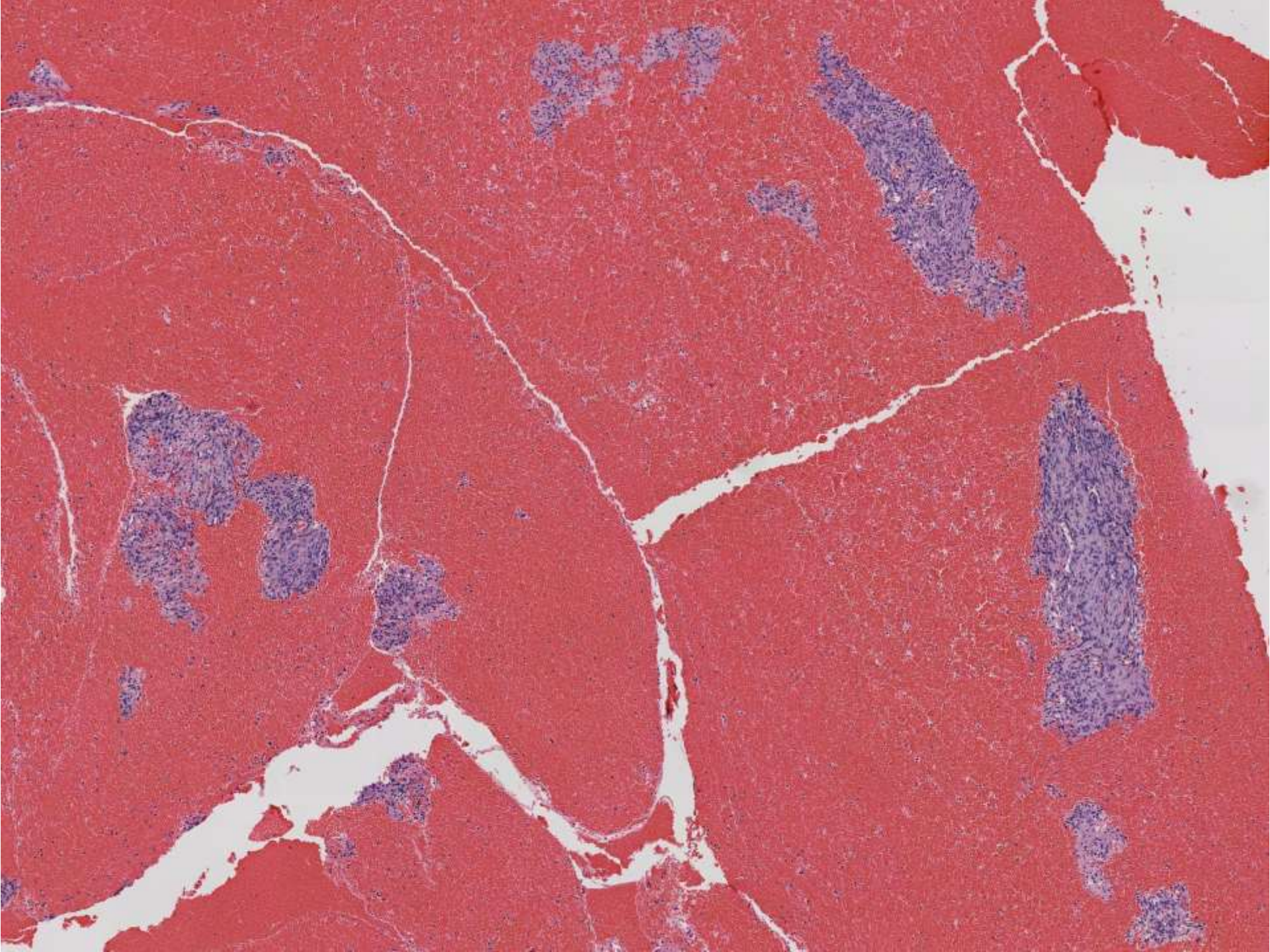
Folpe A. AJSP. 2014; 38:94

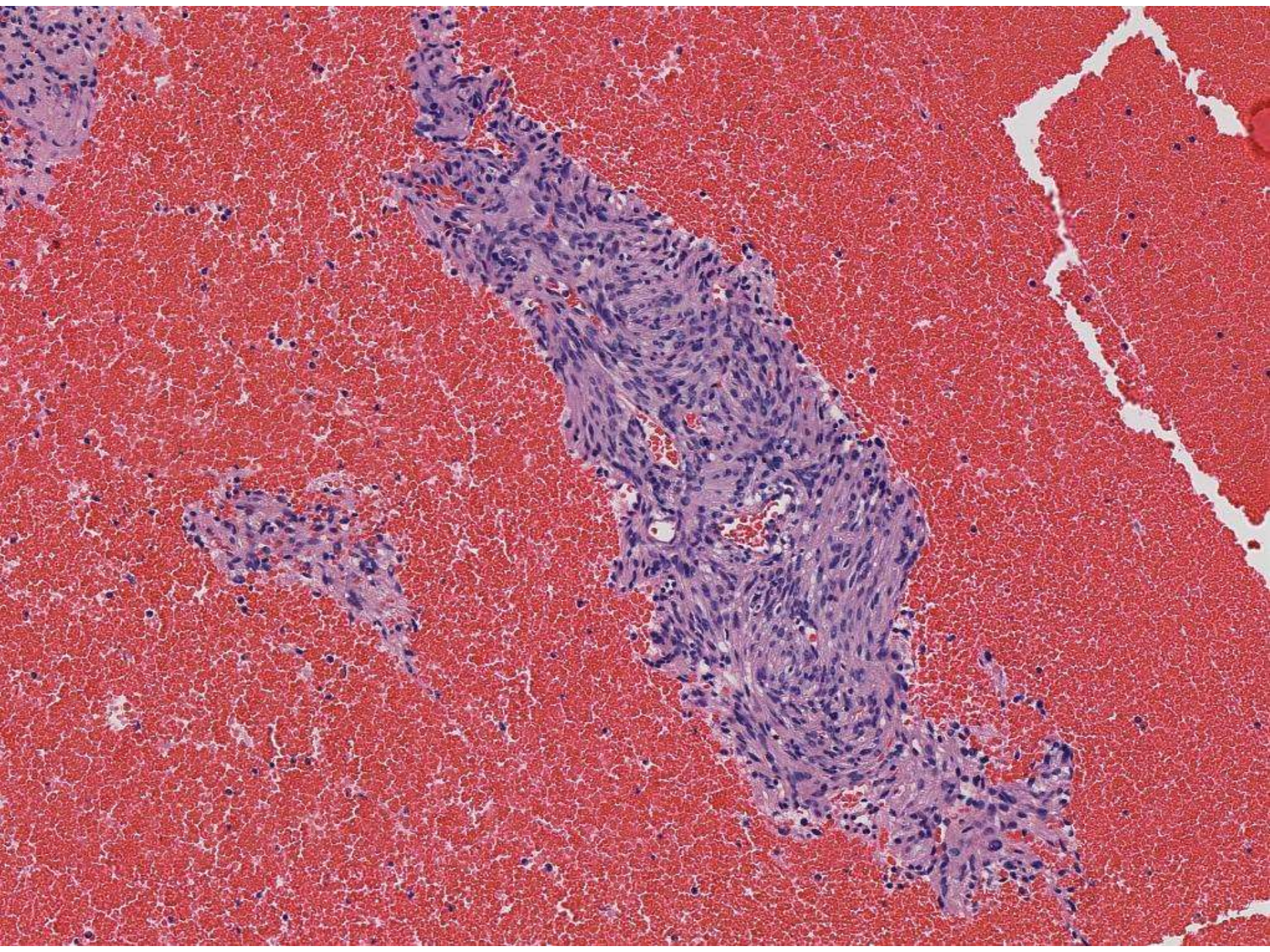
SB 6114(scanned slide available)

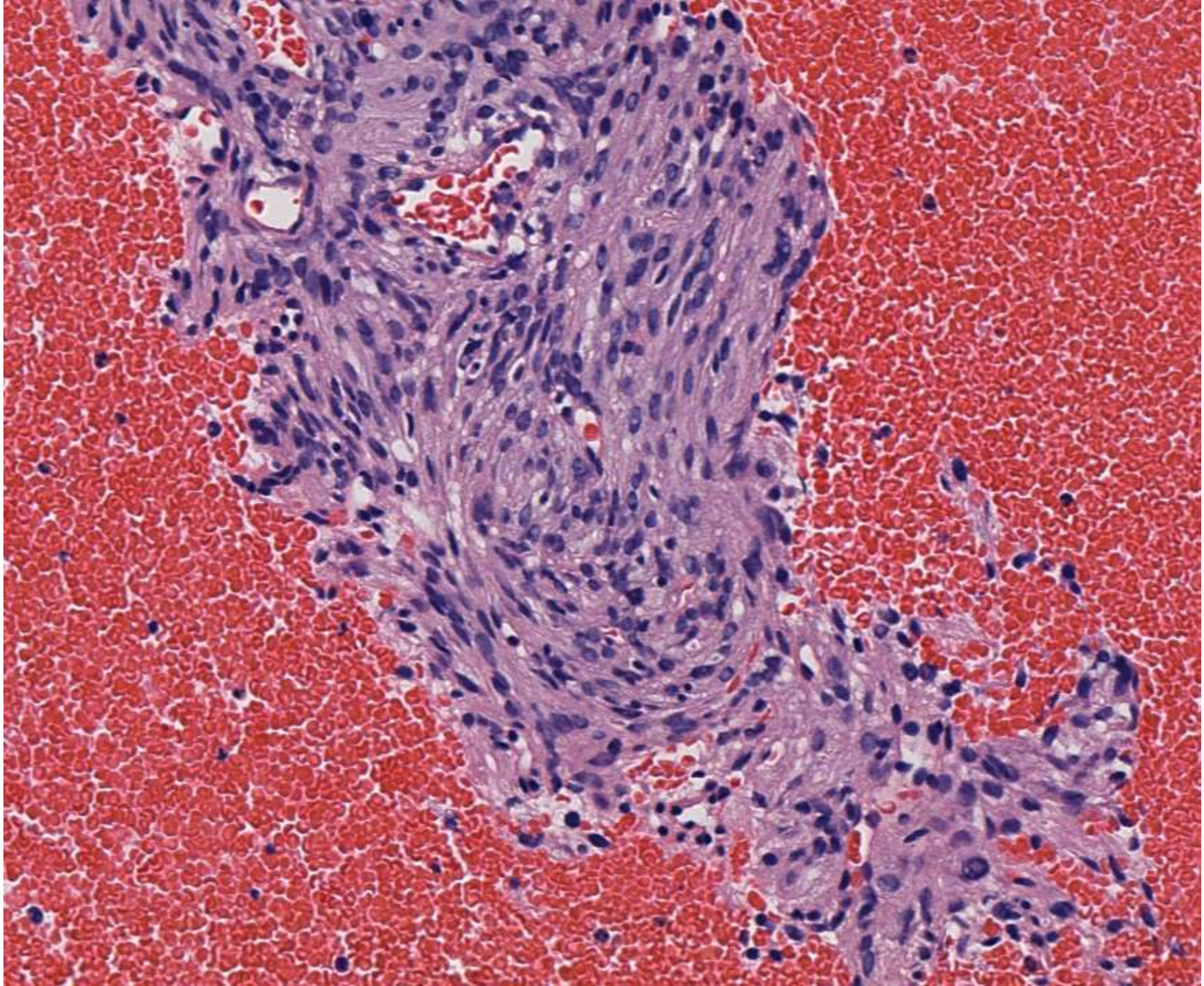
Nhu Thuy Can/Poonam Vohra; UCSF

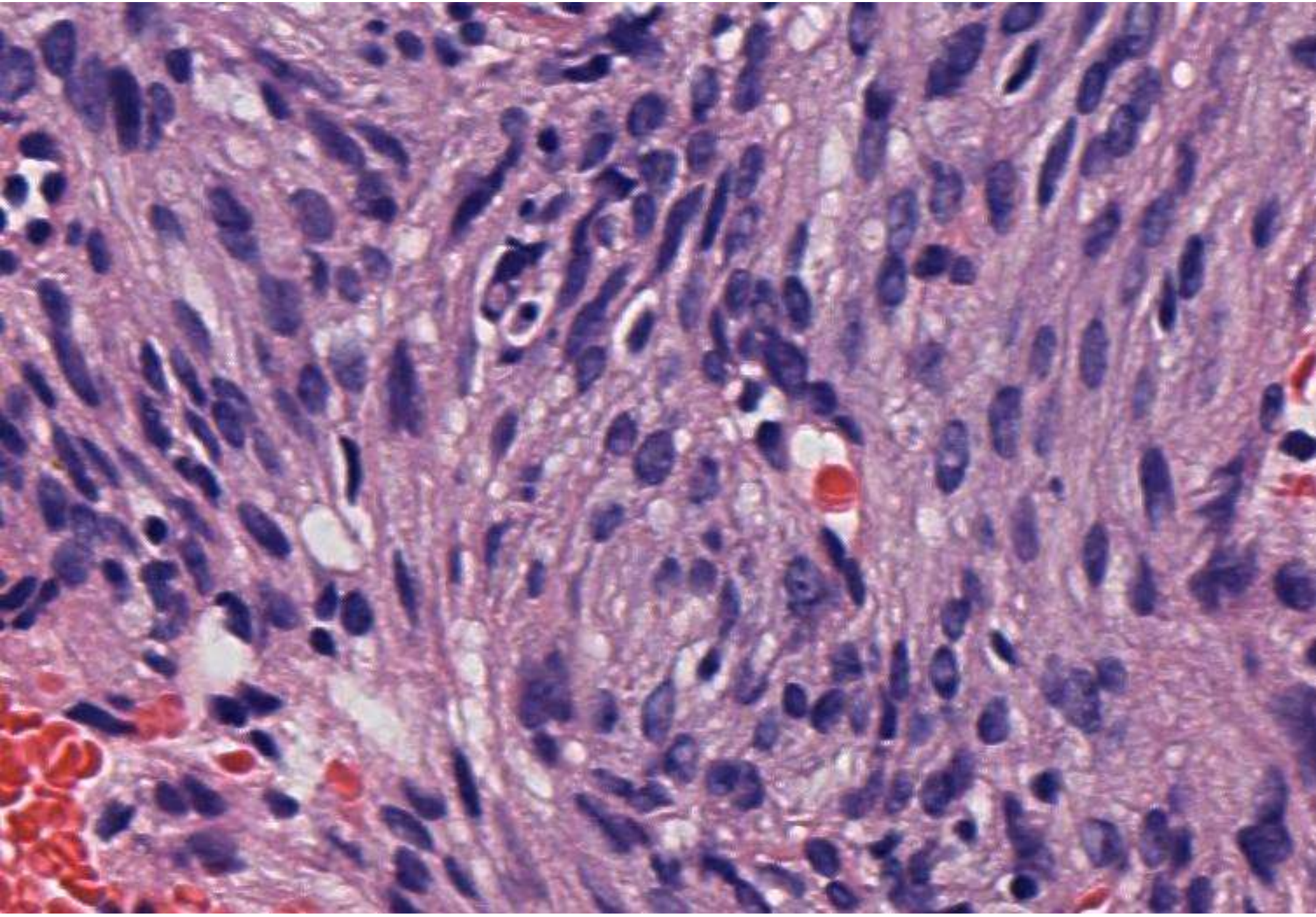
69-year-old man with history of brain mass who presents 2 years status post subtotal resection and radiation with right frontal lobe abscess and CT abdomen/pelvis with innumerable hypervascular masses in liver.



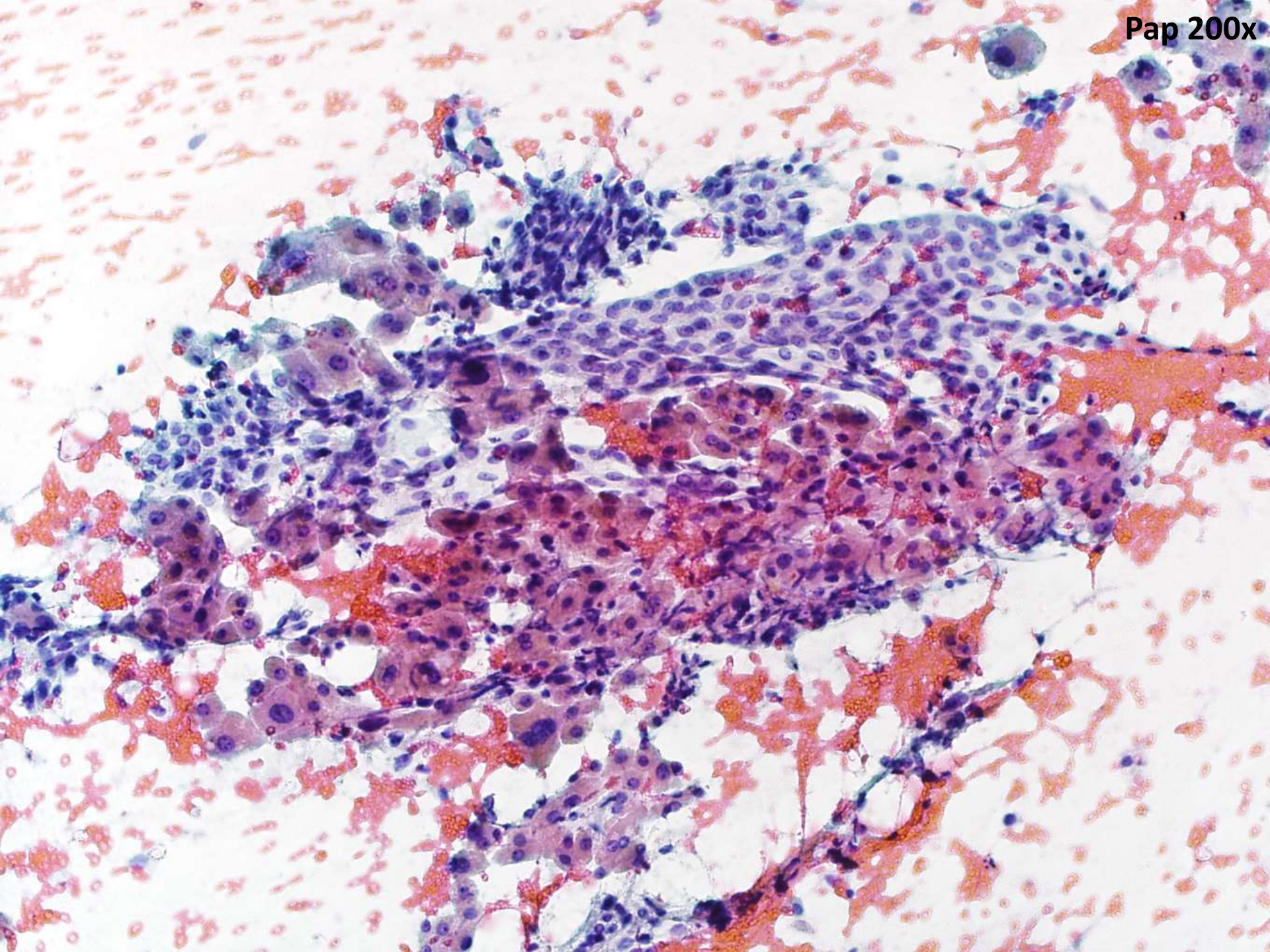


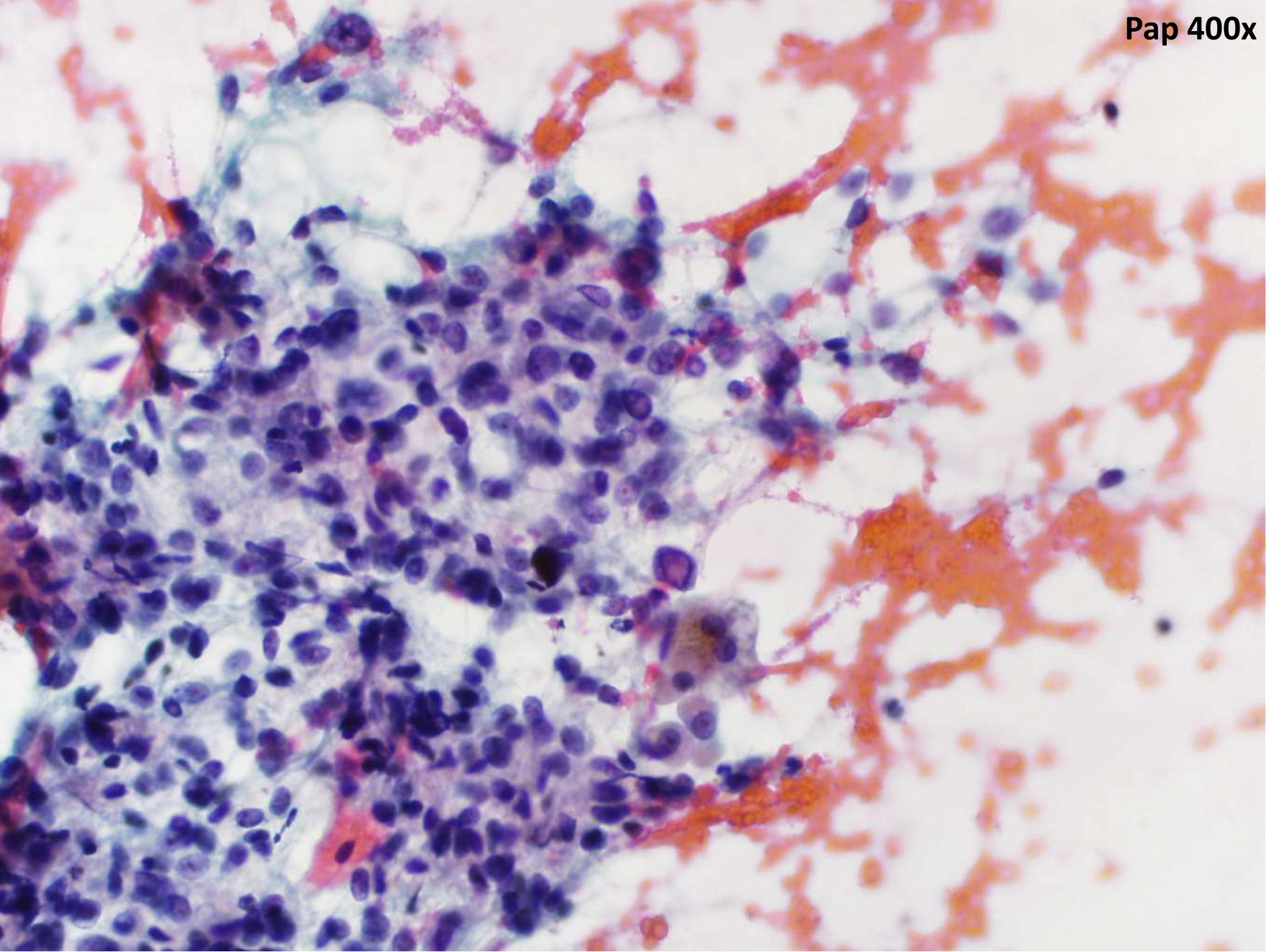


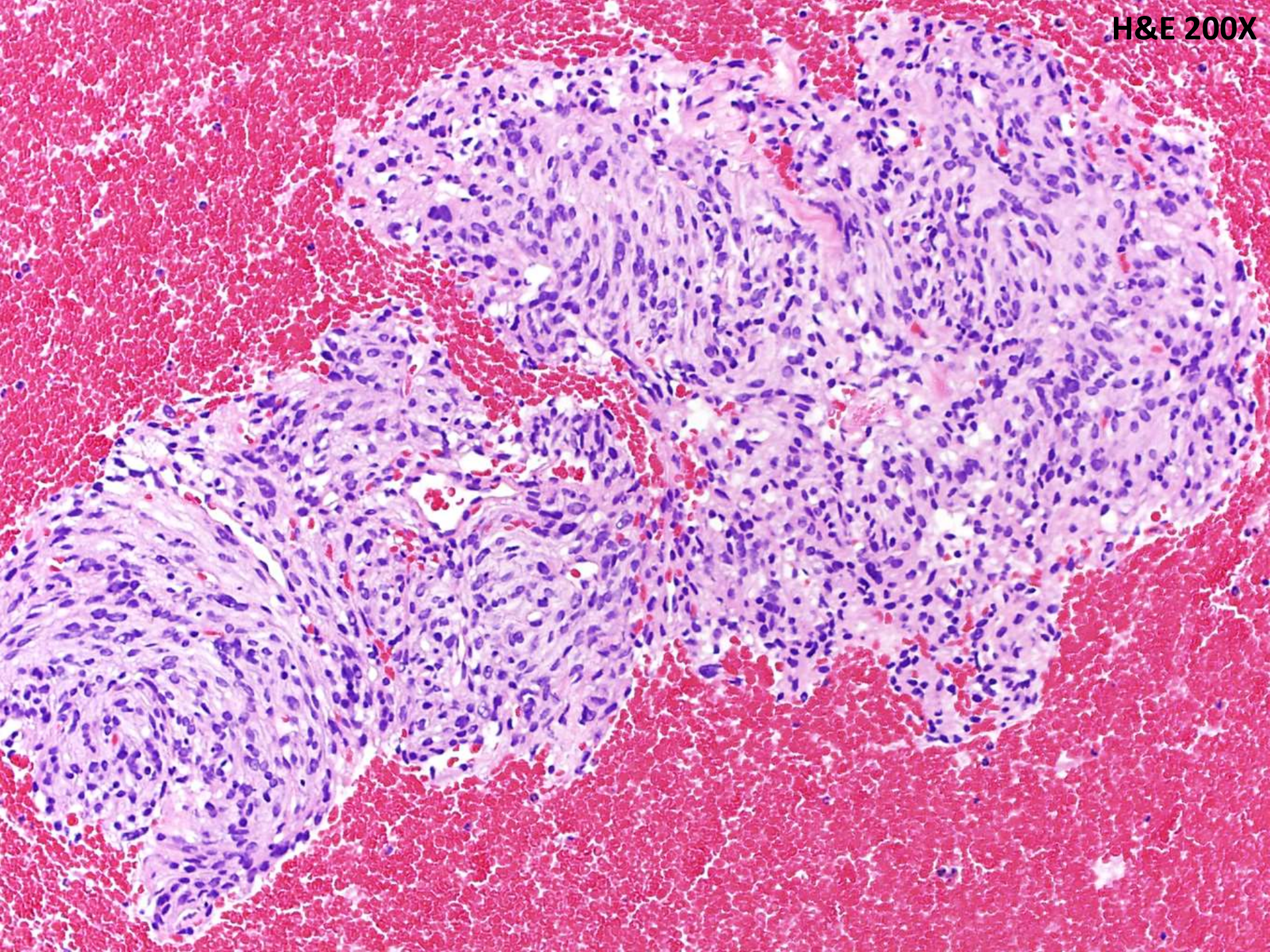


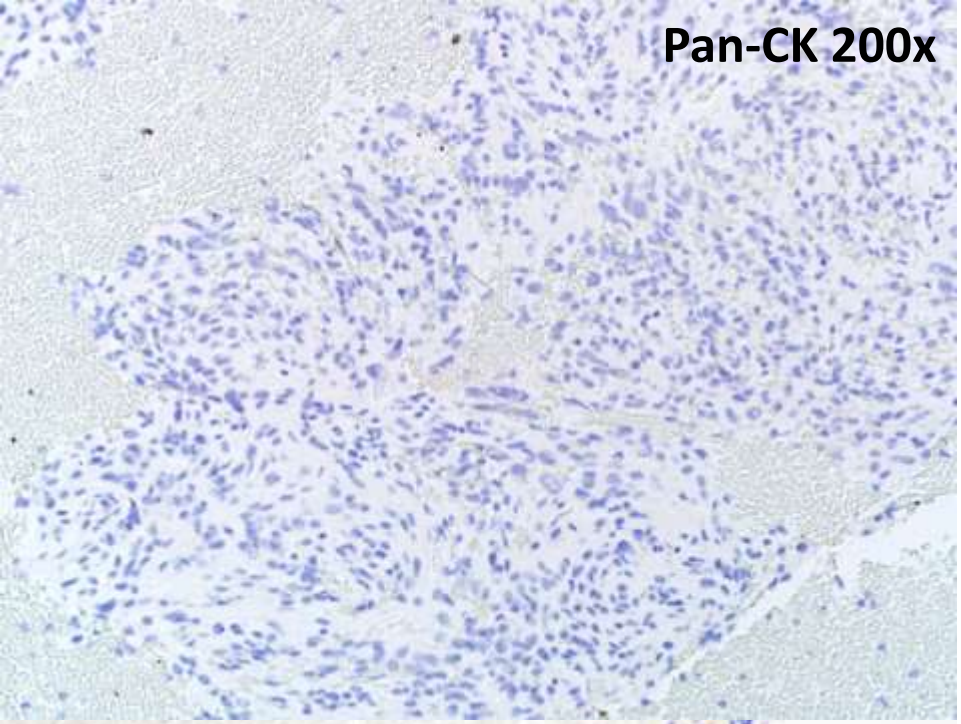


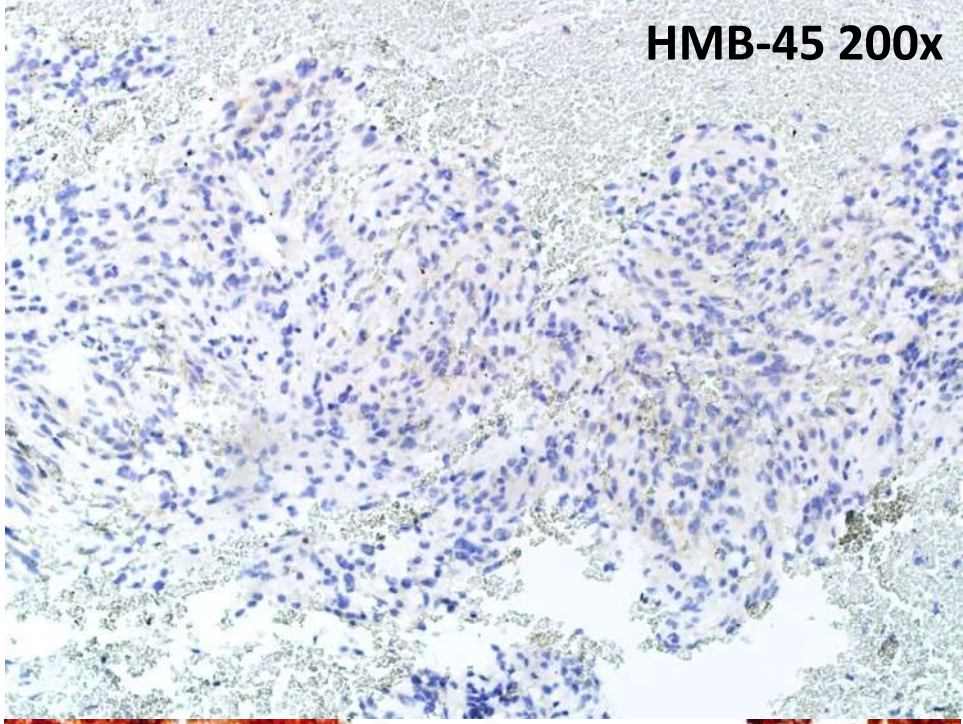
DIAGNOSIS

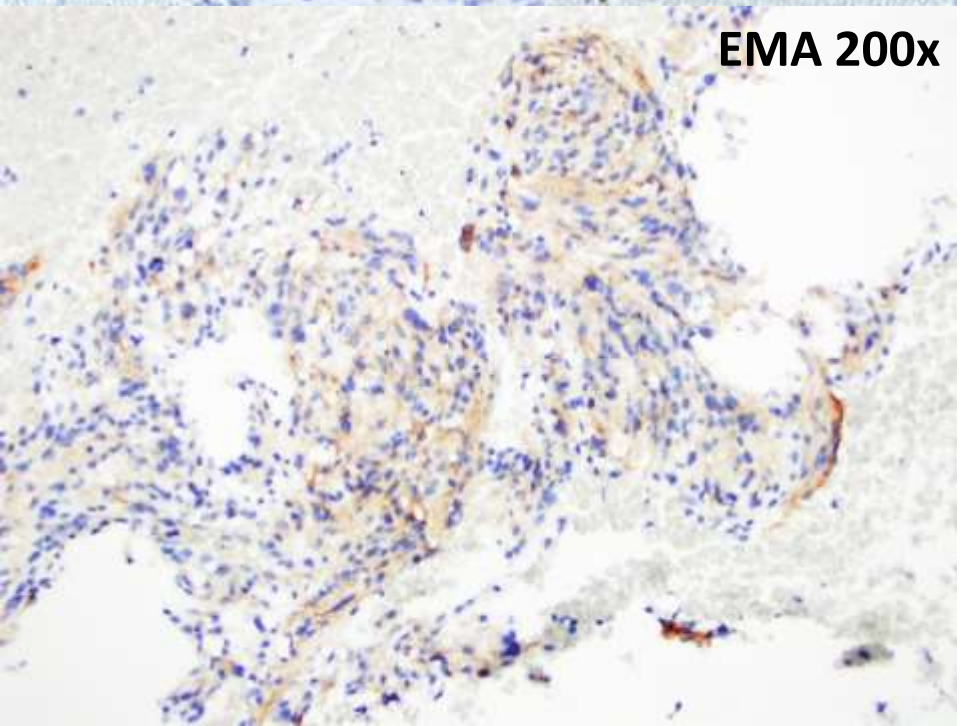

Pap 200x

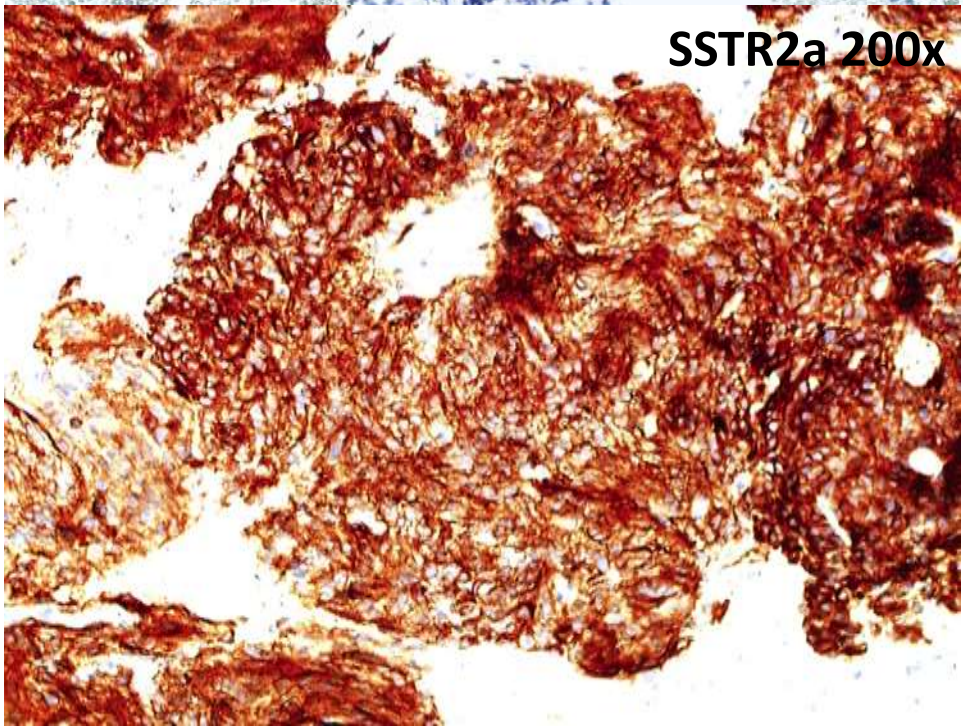

Pap 400x


H&E 200X


Pan-CK 200x


HMB-45 200x


EMA 200x


SSTR2a 200x

Diagnosis: Metastatic meningioma

Review: Meningioma Grading

- **Grade I:**
  - **Meningothelial**
  - **Fibrous (fibroblastic)**
  - **Microcystic**
  - **Transitional**
  - **Psammomatous**
  - **Angiomatous (includes hemangioblastic, angioblastic)**
  - **Secretory subtypes**
  - **Metaplastic**
  - **Lymphoplasmacyte-rich**
- **Grade II:**
  - **Clear cell and chordoid subtypes, or atypical by criteria**
- **Grade III:**
  - **Rhabdoid and papillary subtypes, or anaplastic by criteria**

Review: Meningioma Grading

Atypical, grade II

- 4-19 mitotic figures/10 HPF

OR

- Brain invasion

OR

- Three of these histologic features:
  - Increased cellularity
  - Small cells with high N/C ratio
  - Large and prominent nucleoli
  - Patternless or sheetlike growth
  - Foci of geographic necrosis

Anaplastic, grade III

- 20 or more mitotic figures/10 HPF

OR

- Frank sarcomatous or carcinomatous histology

Metastatic meningioma

- **Extracranial metastases of grade I meningioma are rare and occur in 0.1% of cases**
  - **1.3% atypical meningiomas (grade II) have extracranial metastases**

Table 2 Subtype of metastasised meningiomas in the present analysis

Subtype	*n*	%
Anaplastic	36	31.3
Atypical	22	19.1
Meningothelial	9	7.8
Transitional	8	7.0
Fibroblastic	6	5.2
Papillar	4	3.5
Rhabdoid	3	2.6
Psammomatous	2	1.7
Not reported	25	21.7
Total	115	100

Table 3 Localisation and frequency of distant metastases in meningiomas

Localisation	Metastases (*n*)	Frequency (%)
Lung	61	37.2
Bone	27	16.5
Intraspinal	25	15.2
Liver	15	9.2
Pleura	9	5.5
Cervical lymph nodes	8	4.9
Cervical soft tissue	4	2.4
Cutis and subcutis	3	1.8
Kidney	3	1.8
Muscle	3	1.8
Parotid gland	2	1.2
Adrenal gland	1	0.6
Thyroid gland	1	0.6
Spleen	1	0.6
Perirenal tissue	1	0.6
Total	164	100

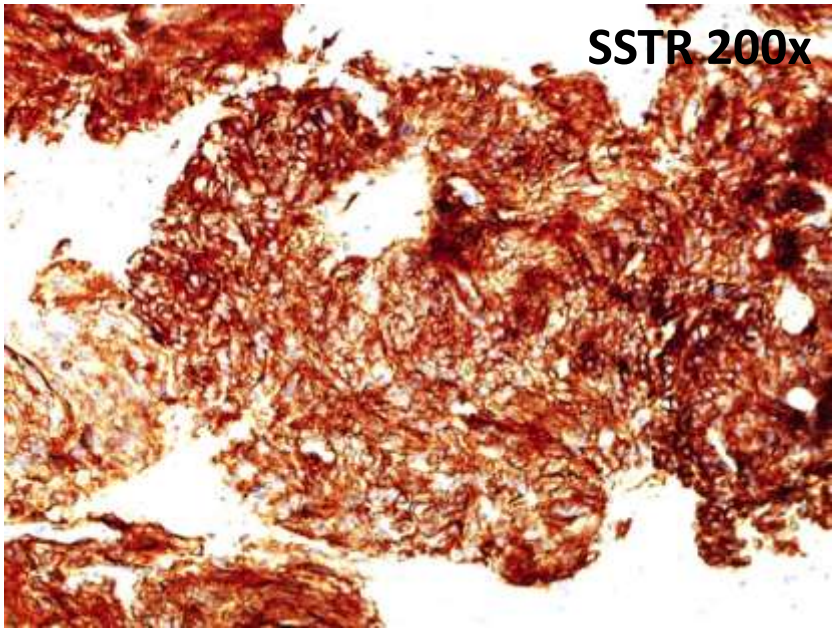
Surov A, Gottschling S and Bolz J. Distant metastases in meningioma: An underestimated problem. J Neurooncol. 2013;112:323-7.

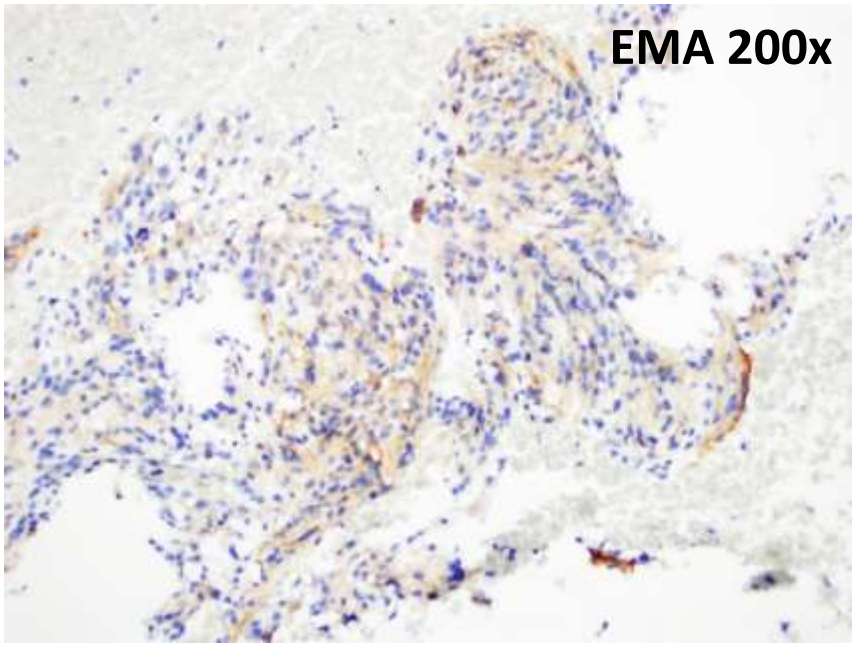
Metastatic Meningioma

- **Other risk factors:**
  - **Previous craniotomy**
  - **Venous sinus invasion**
  - **Local recurrences**
  - **Papillary morphology**
- **Can precede/coincide with diagnosis of intracranial meningioma**

Metastatic meningioma

- **EMA can be negative in atypical/anaplastic (grade II/III) meningiomas**
  - **Somatostatin receptor 2a (SSTR2a) is a highly sensitive and specific marker for meningioma, particularly helpful in high-grade meningiomas**





Take home points

- **Extracranial metastases can be seen in grade I meningioma, but are more common with grade II/III meningiomas**
- **Most common location for extracranial metastases of meningioma is lung, but can also be seen in bone and liver**
- **EMA can be negative in atypical/anaplastic meningiomas; somatostatin receptor 2a can be helpful in these cases**

References

Andric M et al. Atypical meningiomas – A case series. Clin Neurol and Neurosurg. 2012;114:699-702

Drummond KJ et al. Metastatic atypical meningioma: Case report and review of the literature. J Clin Neurosci. 2000;7(1):69-72

Frydrychowicz C et al. Two cases of atypical meningioma with pulmonary metastases: A comparative cytogenetic analysis of chromosomes 1p and 22 and a review of the literature. Neuropathol 2016;35:175-83.

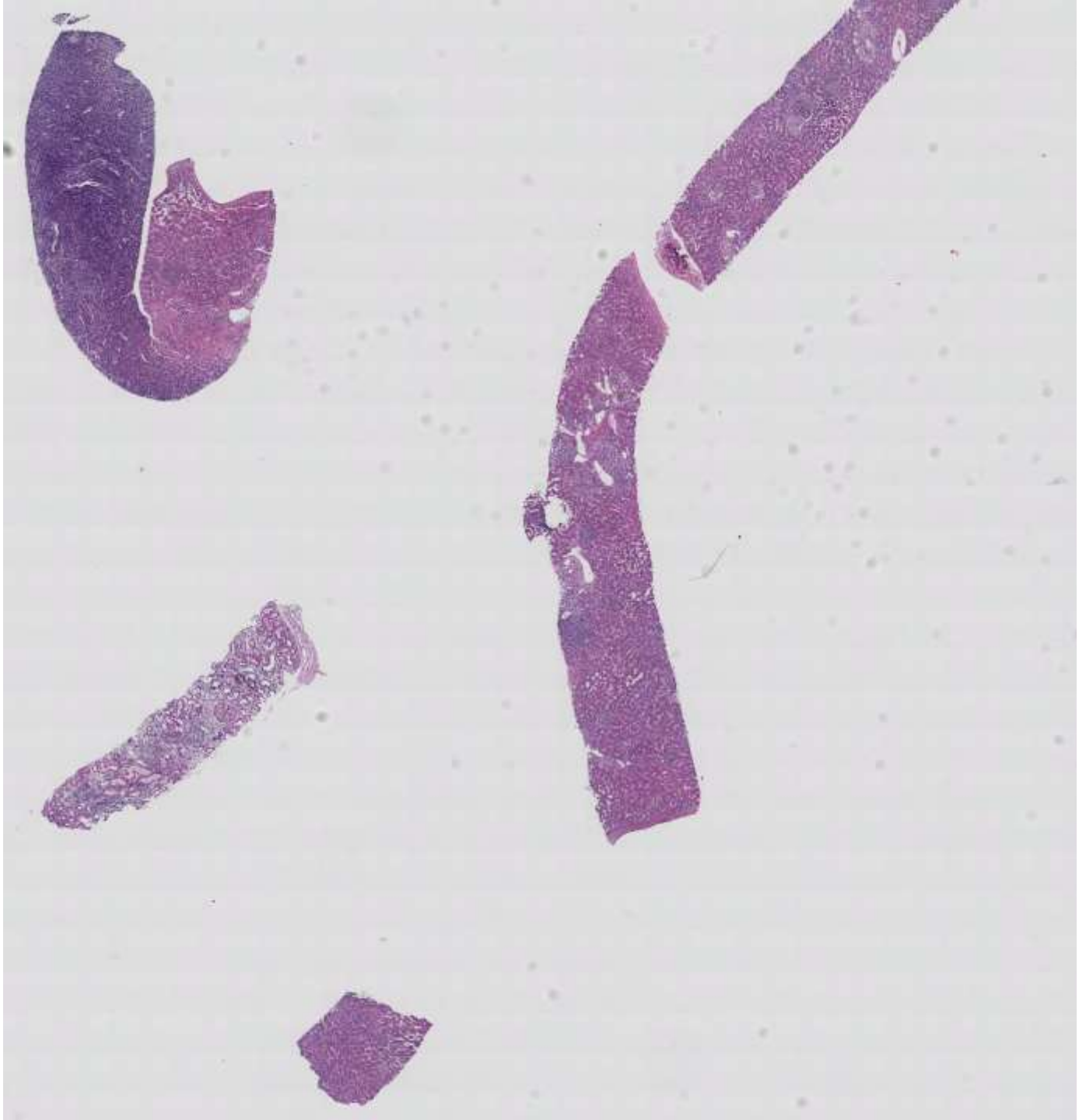
Menke JR et al. Somatostatin receptor 2a is a more sensitive diagnostic marker of meningioma than epithelial membrane antigen. Acta Neuropathol. 2015;130:441-3.

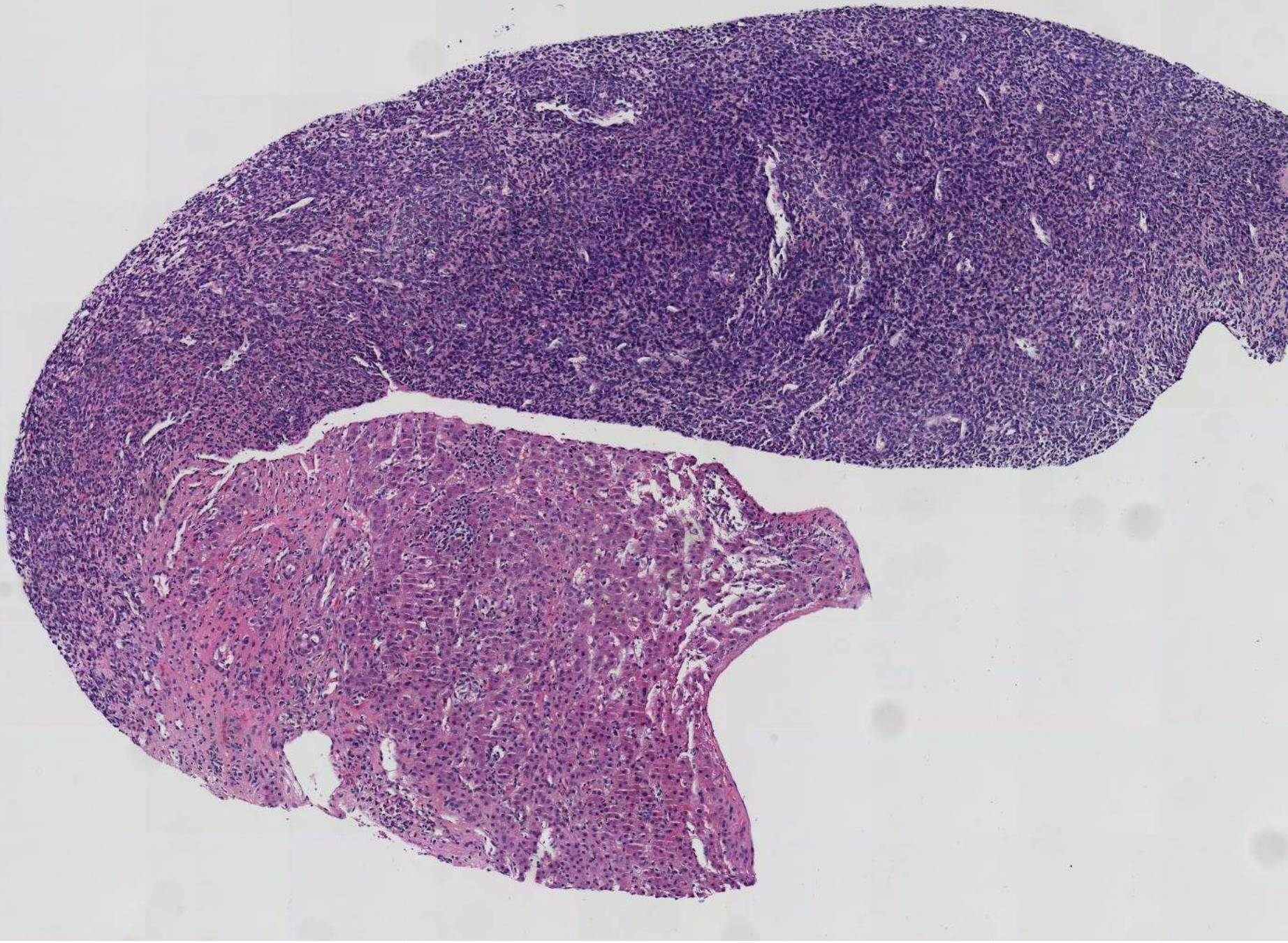
Surov A, Gottschling S and Bolz J. Distant metastases in meningioma: An underestimated problem. J Neurooncol. 2013;112:323-7.

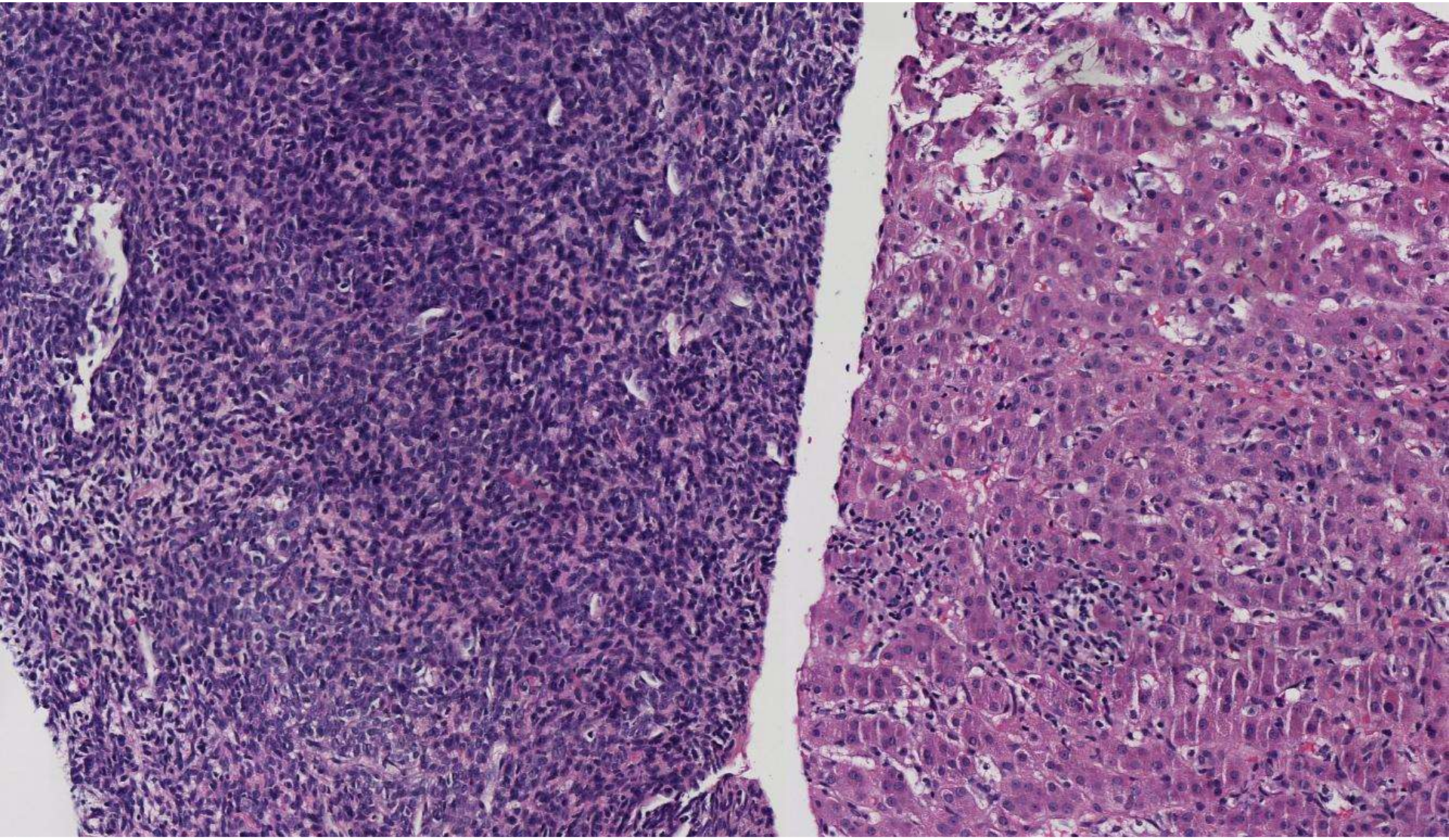
SB 6115 (scanned slide available)

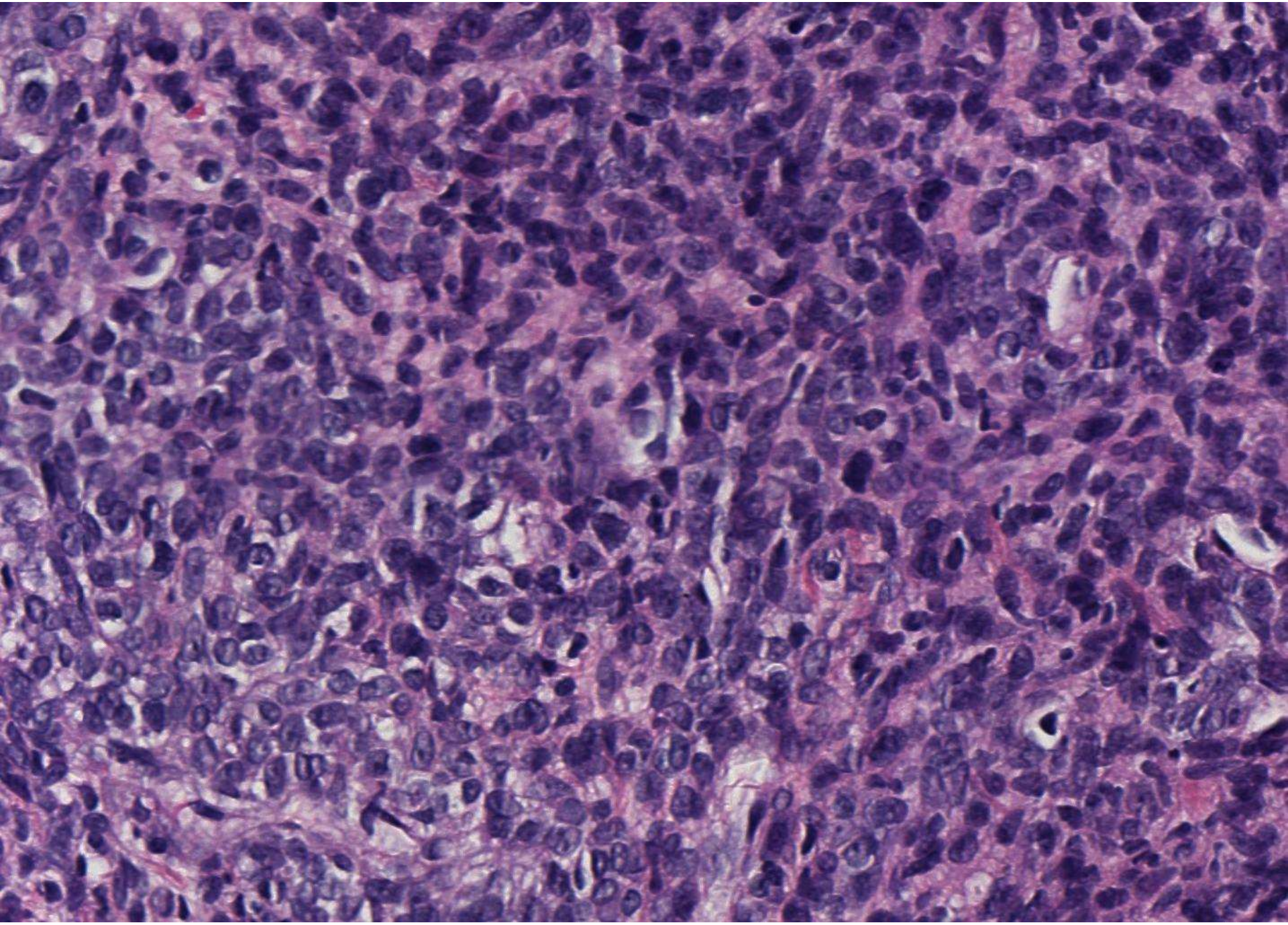
Nhu Thuy Can/Poonam Vohra; UCSF

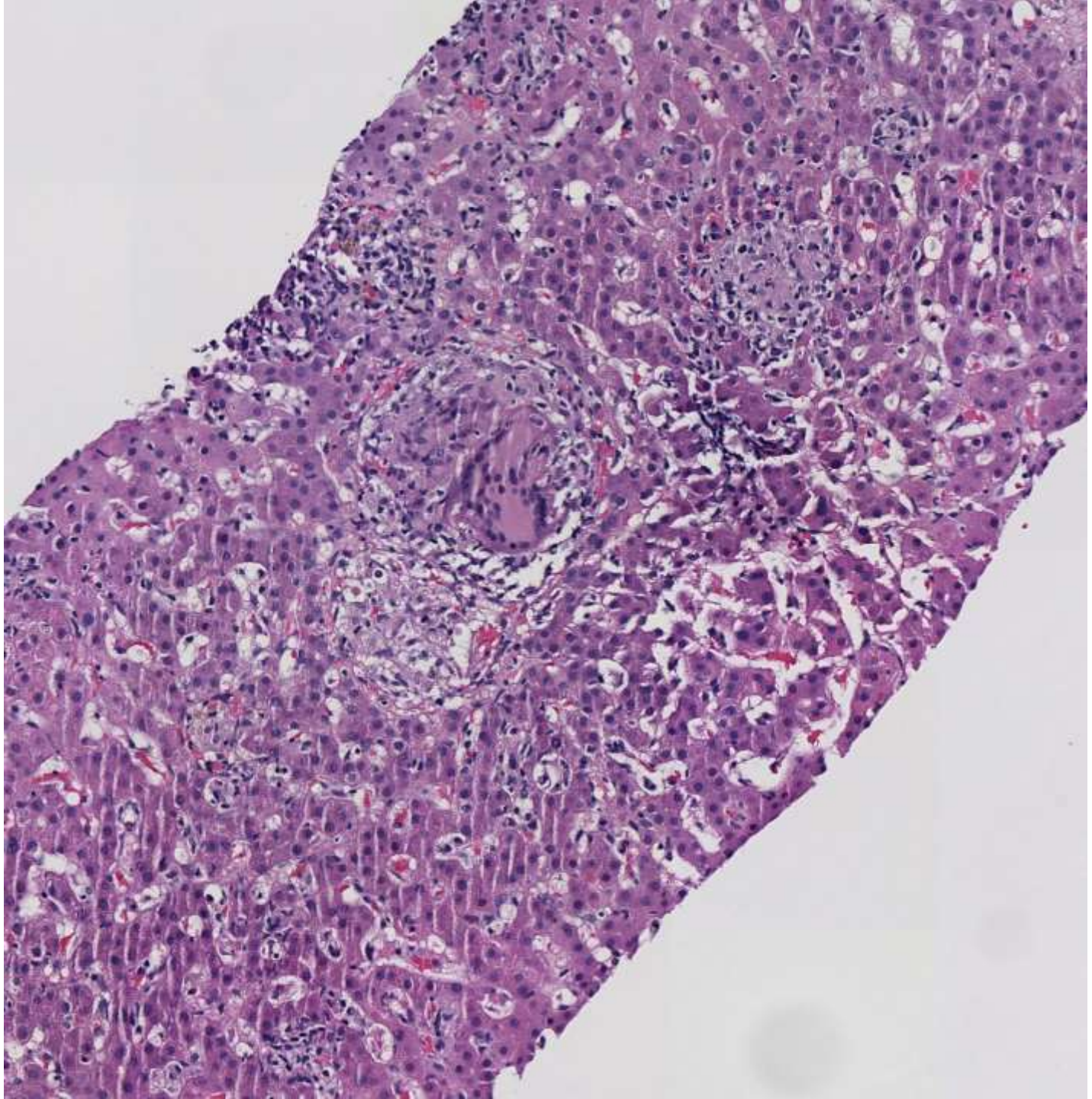
32-year-old man with history of HIV/AIDS (CD4=52) and MAC bacteremia with GI involvement. He presents with worsening abdominal pain, inability to gain weight, and abnormal liver function tests (ALT 88, AST 77, Alk pho 747). Abdominal CT scan demonstrates enlarged retroperitoneal and mesenteric lymph nodes with central necrosis as well as a rim-enhancing liver lesion compatible with MAC infection.

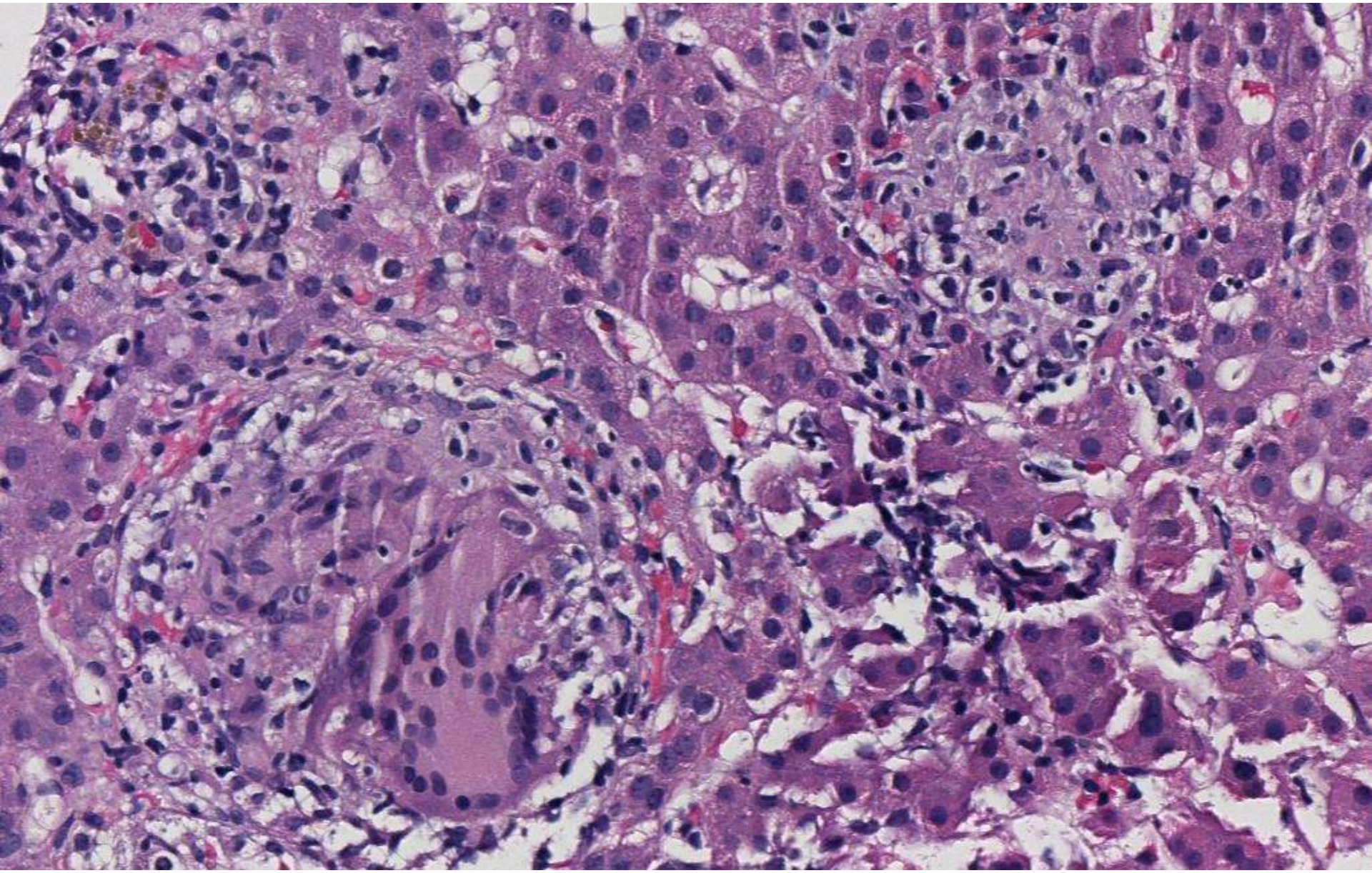


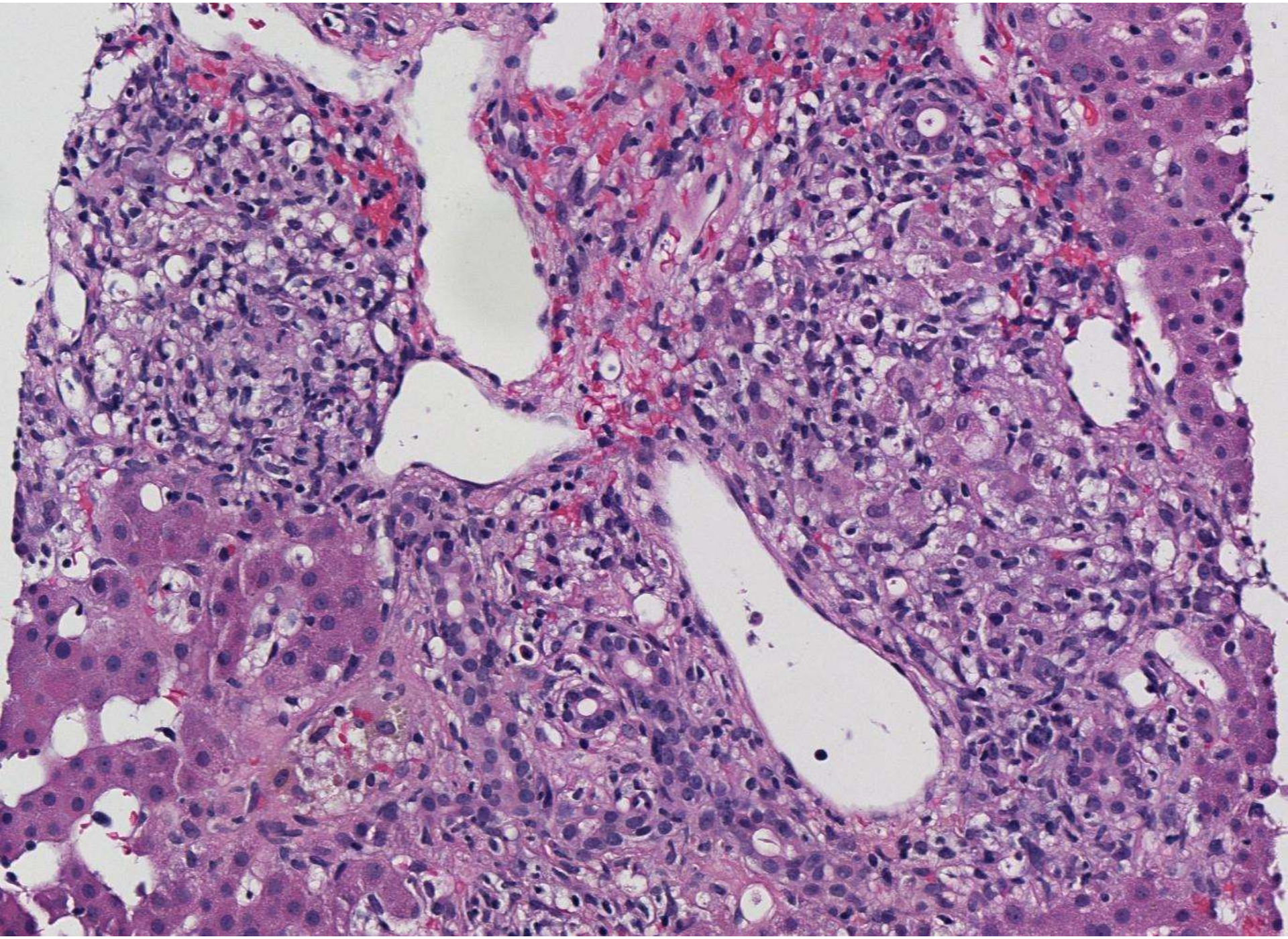




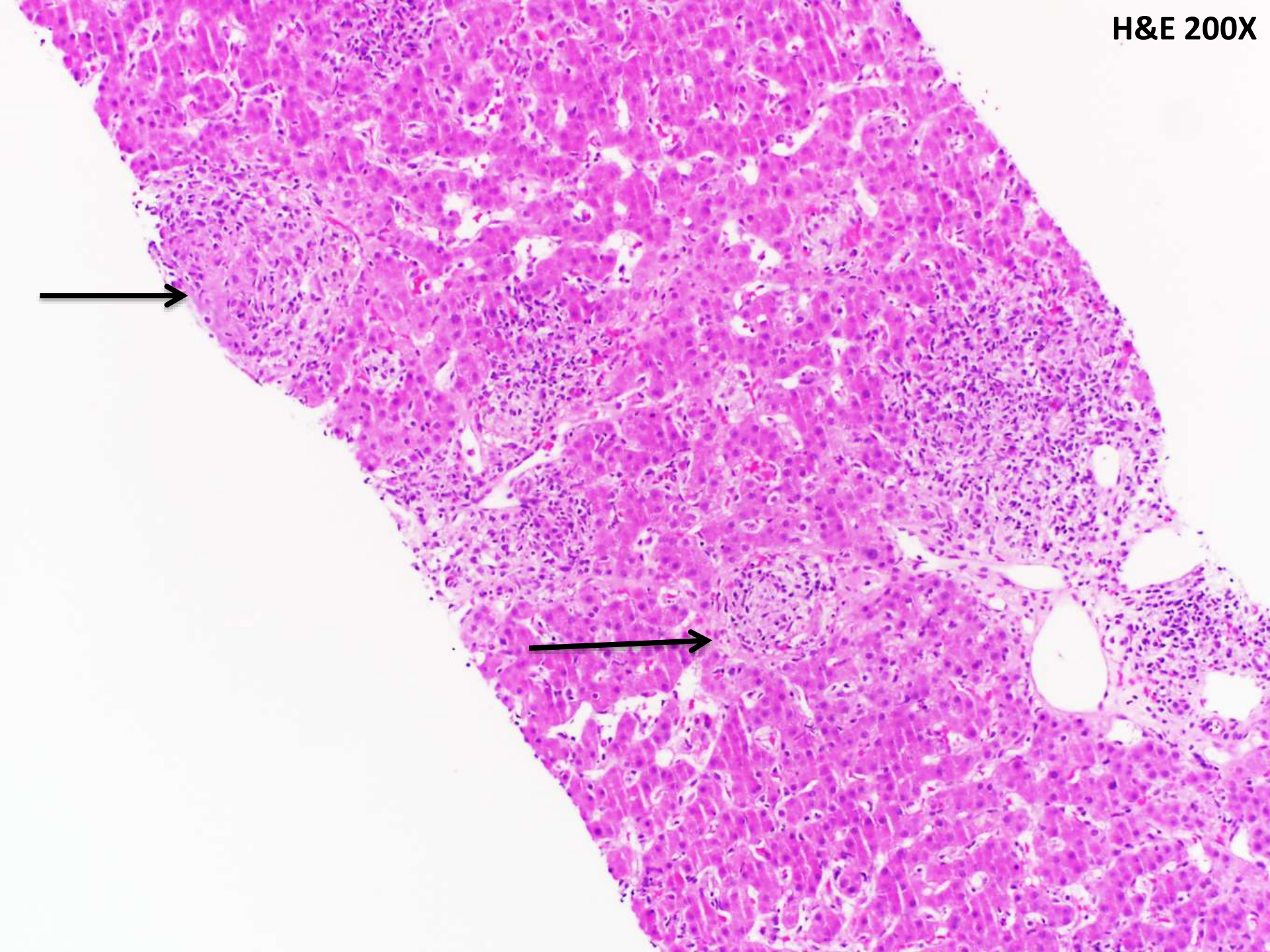


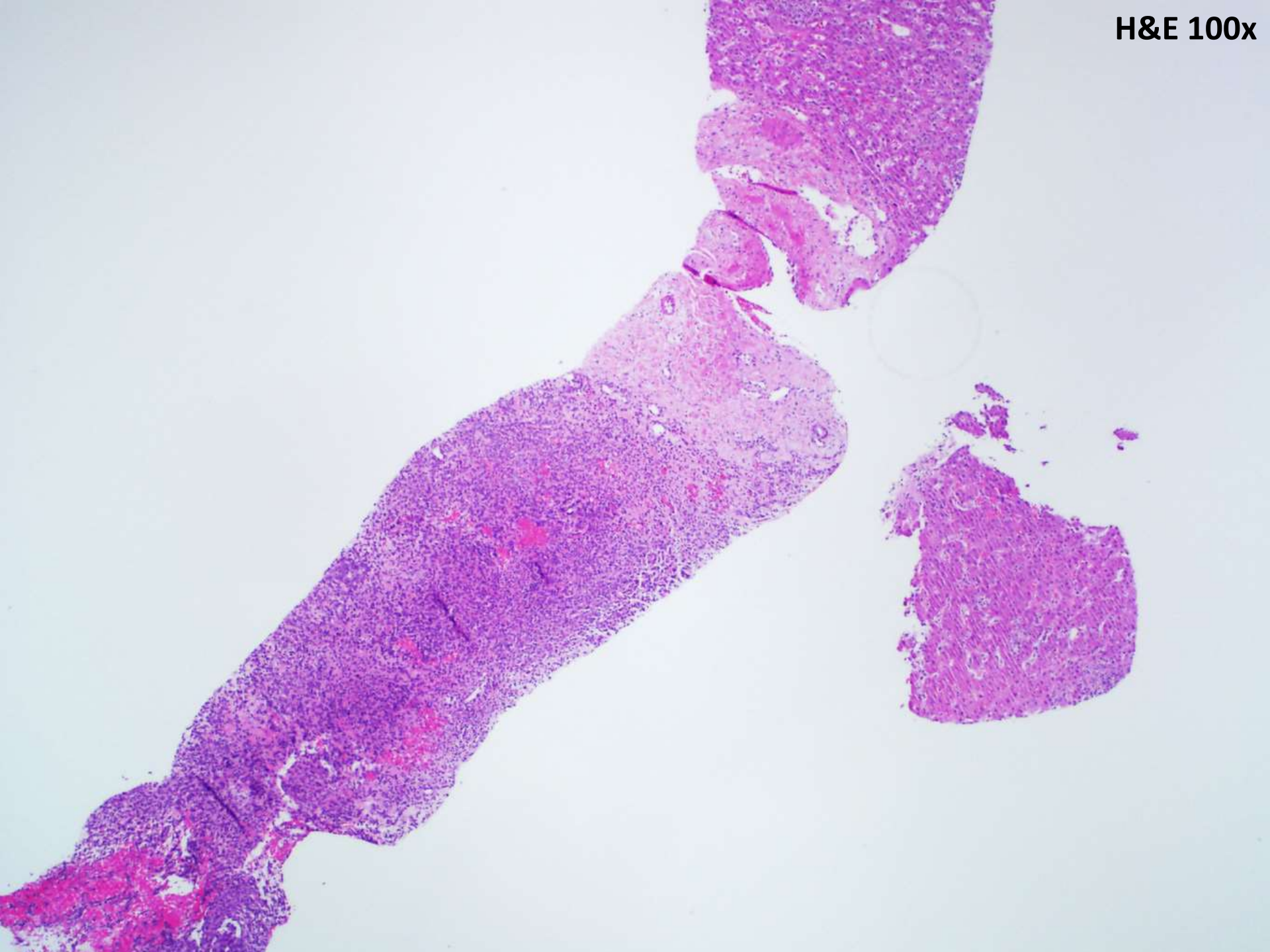


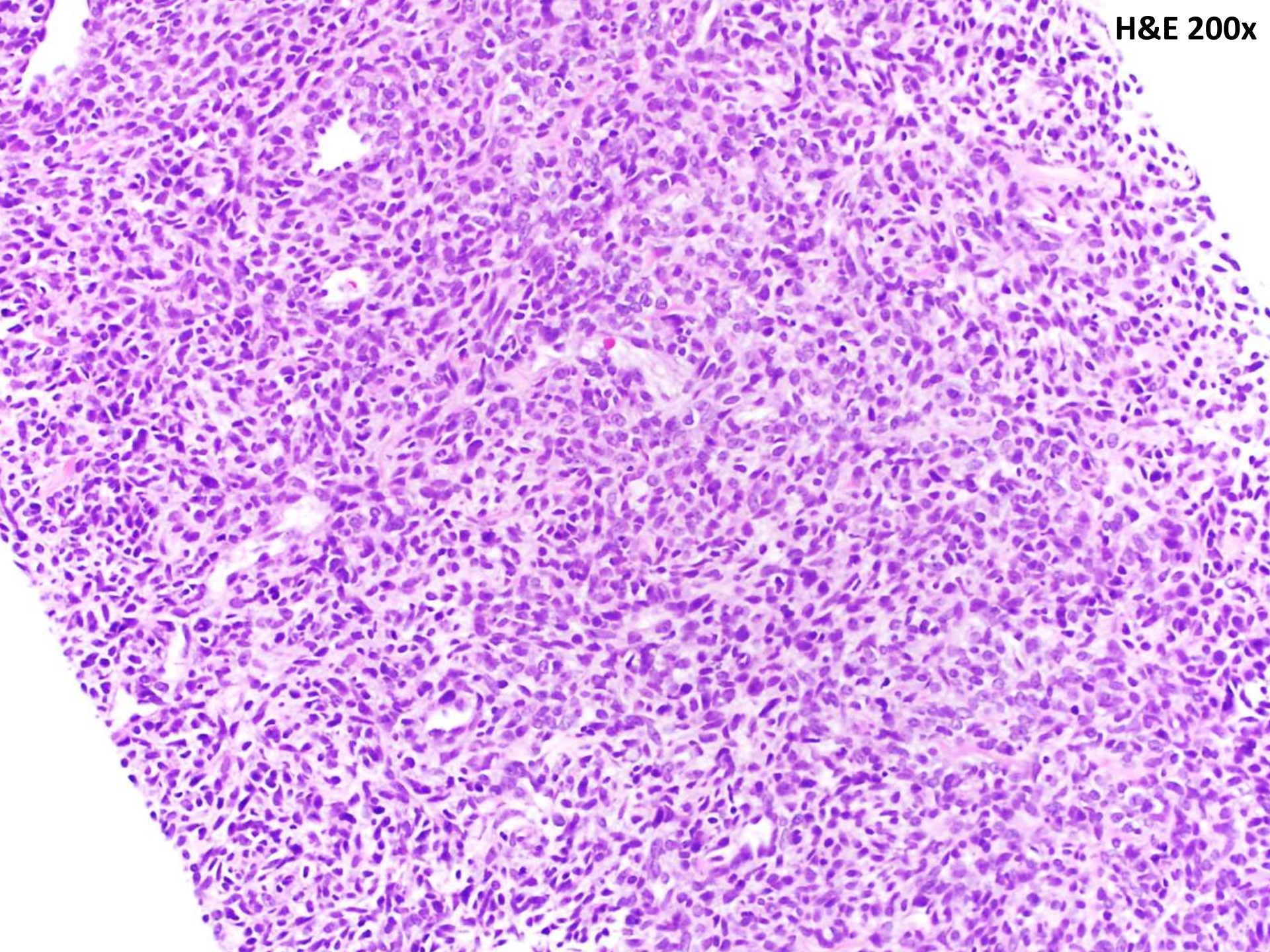




DIAGNOSIS


H&E 200X


H&E 100x

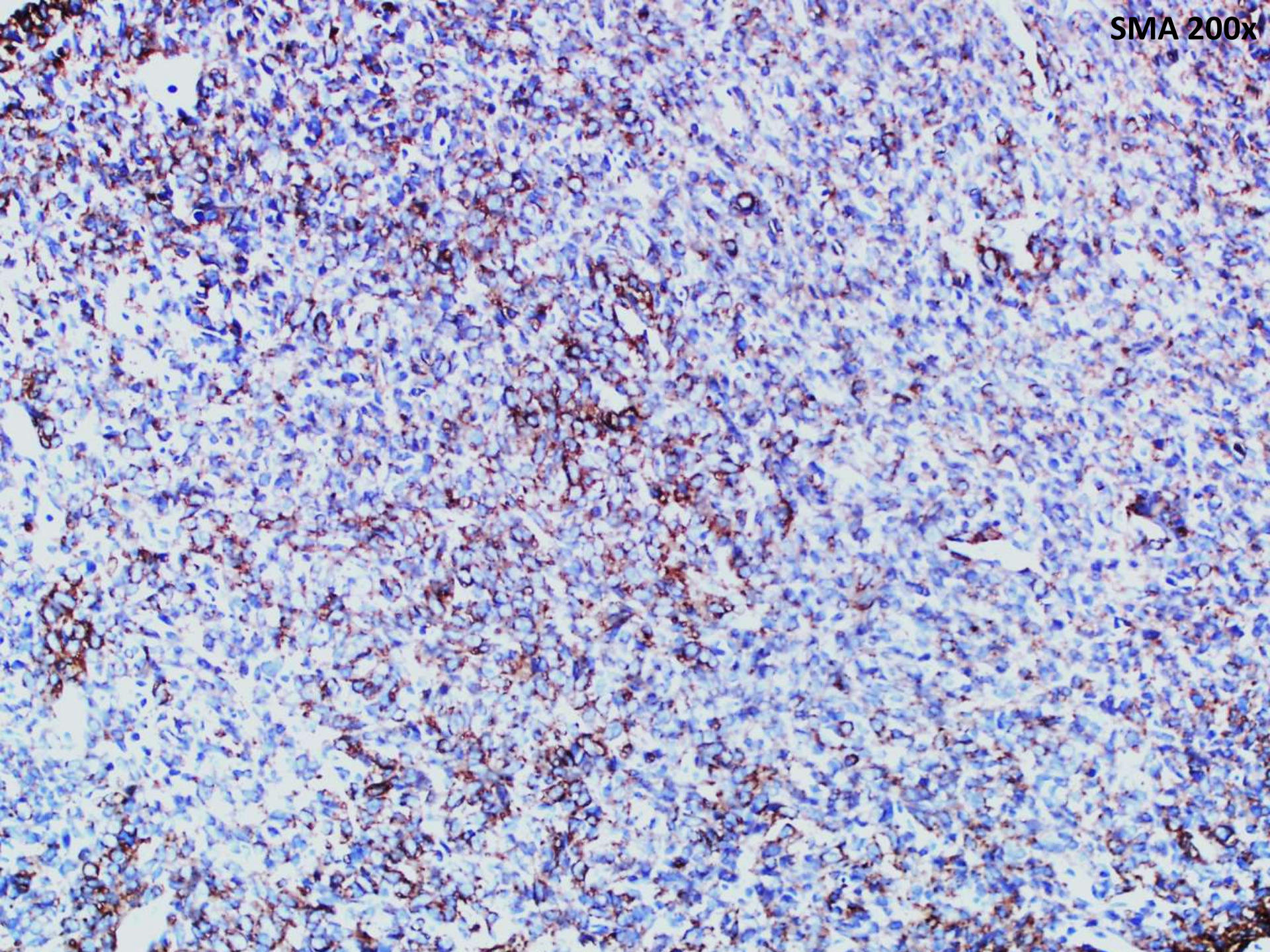

H&E 200x

Differential

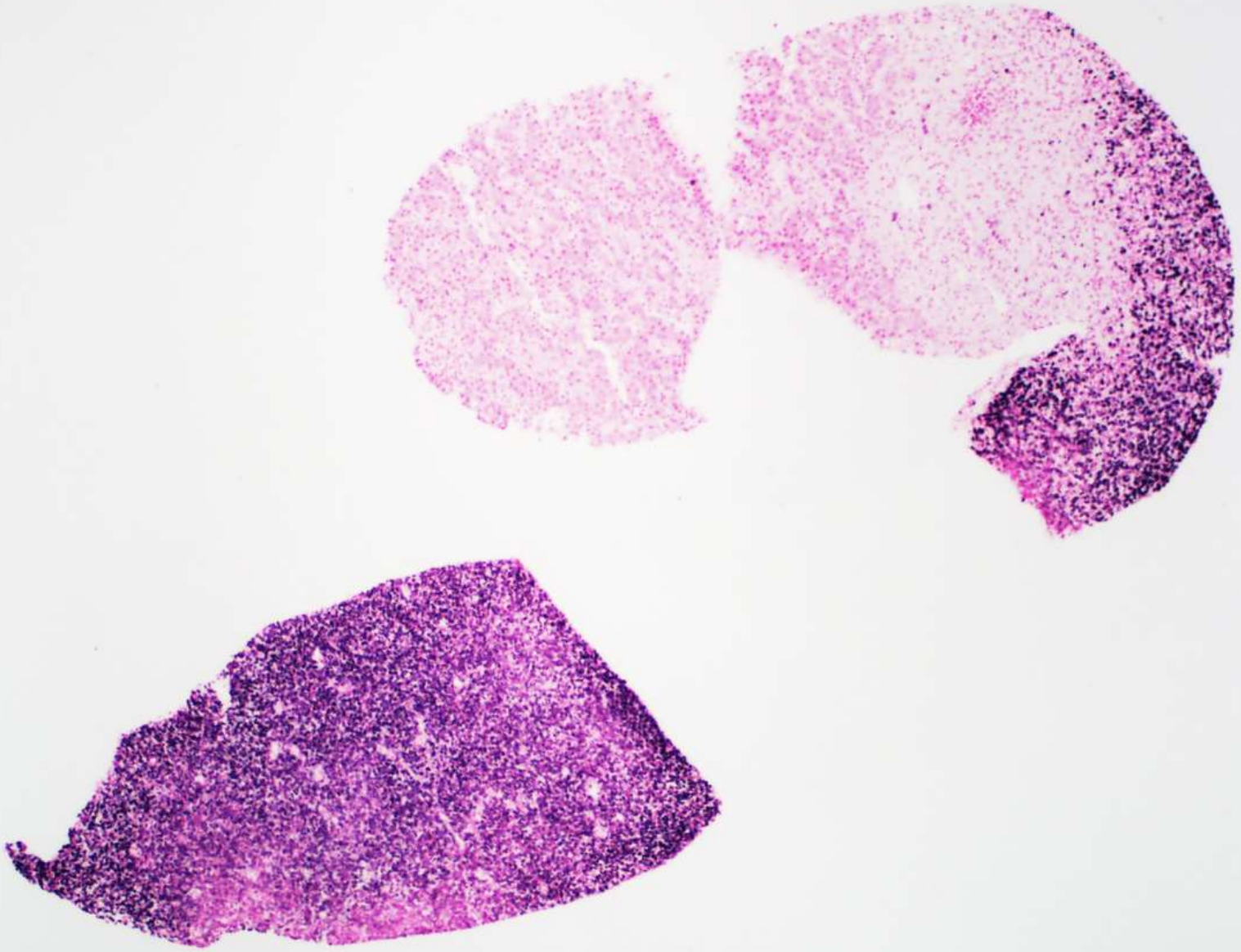
- Kaposi sarcoma
- Mycobacterial spindle cell pseudotumor
- EBV-associated smooth muscle tumor
- Angiomyolipoma
- Solitary fibrous tumor
- Follicular dendritic cell tumor
- Myofibroblastoma
- Metastatic gastrointestinal stromal tumor

Negative Stains

- HHV-8
- CD31
- CD34
- Desmin
- CD117
- DOG1
- CD68
- CD45
- CD3
- CD20
- CD21
- CD23
- Caldesmon
- HMB45
- Pancytokeratin
- AFB
- GMS
- Warthin-Starry


SMA 200x

EBV ISH 40x



Diagnosis

1. **Spindle cell lesion consistent with EBV-associated smooth muscle tumor**
2. **Liver parenchyma with granulomatous inflammation**

EBV-associated smooth muscle tumor

- First described in post-transplant setting in 1970 by Pritzker et al
  - Now known to also occur in association with HIV/AIDS and congenital immune deficiency
  - 2nd most common type of neoplasm arising in children with AIDS
- Pathogenesis unclear
  - Latent EBV infection, similar to PTLD
  - Possibly originates from smooth muscle in vessel walls

EBV-associated smooth muscle tumor

- **Liver, GI tract, and lung are most common locations, but can occur anywhere and be multifocal and/or multicentric**
- **A few studies have shown that multiple tumors in a single patient are non-clonal, likely representing separate primaries rather than metastases**

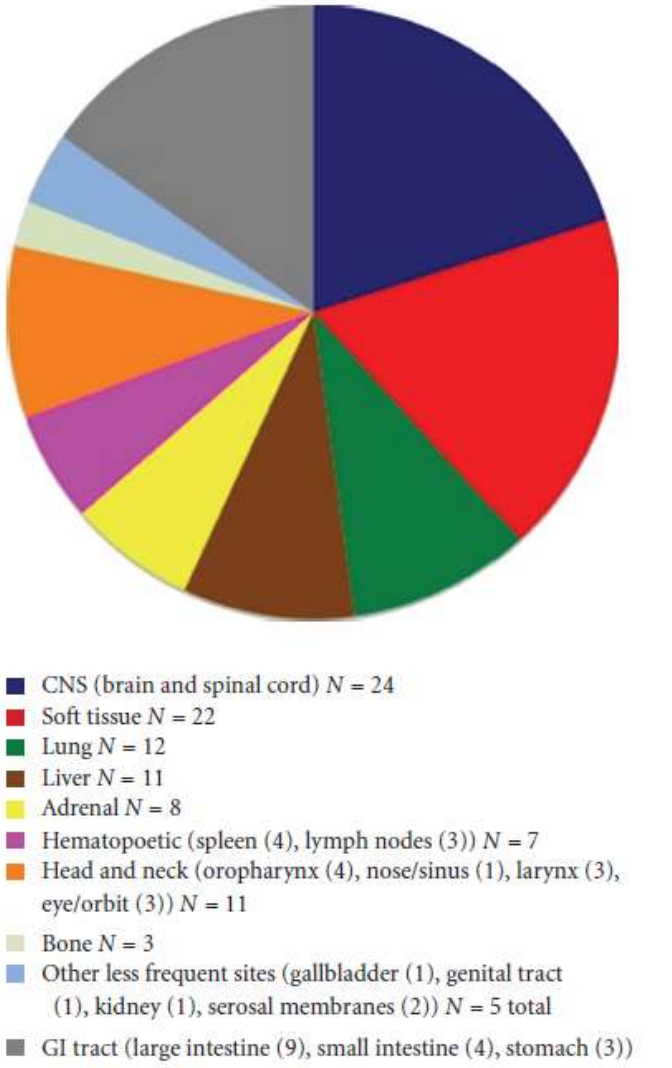
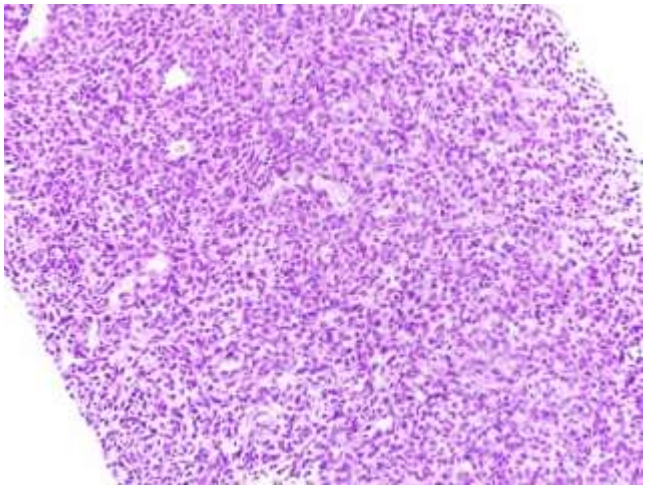


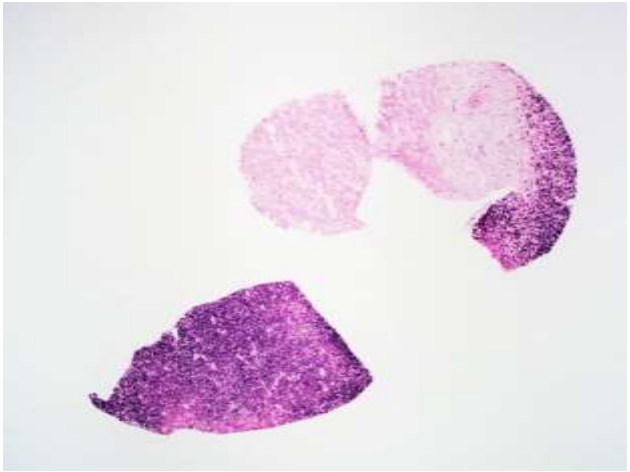
FIGURE 1: Anatomic location of SMT in HIV-infected patients.

Purgina et al. Pathol Res Int. 2011.

EBV-associated smooth muscle tumor

- **Histology**
  - **Interlacing fascicles of spindle cells with eosinophilic cytoplasm**
  - **Elongated, blunt-ended nuclei with finely stippled chromatin**
  - **Low mitotic count (<1/10 HPF) and little to no necrosis**
  - **Lack significant nuclear pleomorphism**
  - **Can have prominent intratumoral lymphocytes**
  - **Can have primitive round cell areas without myogenic differentiation**
  - **Typically positive for SMA and desmin negative, but EBV ISH is most helpful**





EBV-associated smooth muscle tumor

- **Originally divided into EBV-associated leiomyomas vs. leiomyosarcomas, but uncertain malignant potential**
  - **Typically indolent, but can be unpredictable**
  - **Behavior does not correlate with histologic grade**
  - **Mitotic rate does not seem to distinguish cases with malignant outcome**

Treatment

- Surgical resection
- Decreasing immunosuppressive therapy
- Antiretroviral therapy
- Anti-EBV antiviral therapy

Take home points

- **EBV-associated smooth muscle tumors are seen in immunocompromised patients**
- **Tumors can be multifocal/multicentric, but this is not thought to represent metastasis**
- **Uncertain malignant potential; histologic features are not predictive of behavior**
- **Consistently positive for SMA and EBV ISH**

References

Cheuk W et al. Epstein-Barr virus-associated smooth muscle tumor: A distinctive mesenchymal tumor of immunocompromised individuals. Pathology. 2002;34(3):245-9.

Dekate J and Chetty R. Epstein-Barr virus-associated smooth muscle tumor. Arch Pathol Lab Med. 2016;140:718-22.

Deyrup et al. Epstein-Barr virus-associated smooth muscle tumors are distinctive mesenchymal tumors reflecting multiple infection events: A clinicopathologic and molecular analysis of 29 tumors from 19 patients. Am J Surg Pathol. 2006;30(1):75-82

Dalal KM et al. EBV-associated smooth muscle neoplasm: Solid tumors arising in the presence of immunosuppression and autoimmune diseases. 2008.

Hussein K et al. Clinicopathological characteristics of different types of immunodeficiency-associated smooth muscle tumours. European J of Cancer. 2014;50:2417-24.

Jossen J et al. Epstein-Barr virus-associated smooth muscle tumors in children following solid organ transplantation: A review. Pediatric Transplantation. 2015;19:235-43.

Miettinen M. Smooth muscle tumors of soft tissue and non-uterine viscera: Biology and prognosis. 2014;27:S17-29.

Purgina B et al. AIDS-related EBV-associated smooth muscle tumors: A review of 64 published cases. Pathology Research International. 2011.

Raheja A et al. Epstein-Barr virus-associated smooth muscle tumor of the cavernous sinus: A delayed complication of allogenic peripheral blood stem cell transplantation: Case report. J Neurosurg. 2016;24:1-5.

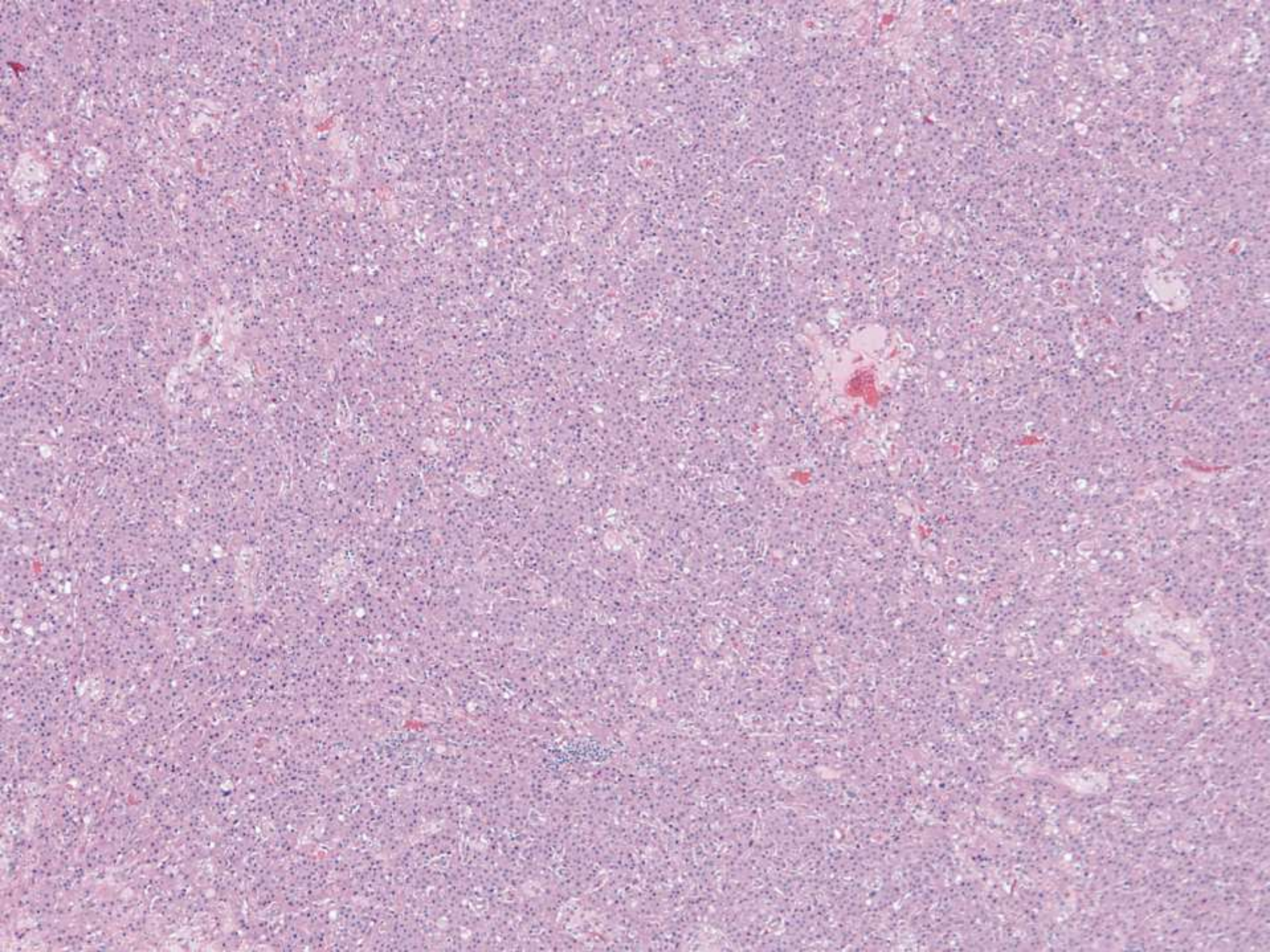
Salamanca J and Suarez Massa D. EBV-associated hepatic smooth muscle tumor after lung transplantation: Report of a case and review of the literature. J Hear t Lung Transplant. 2009;28:1217-20.

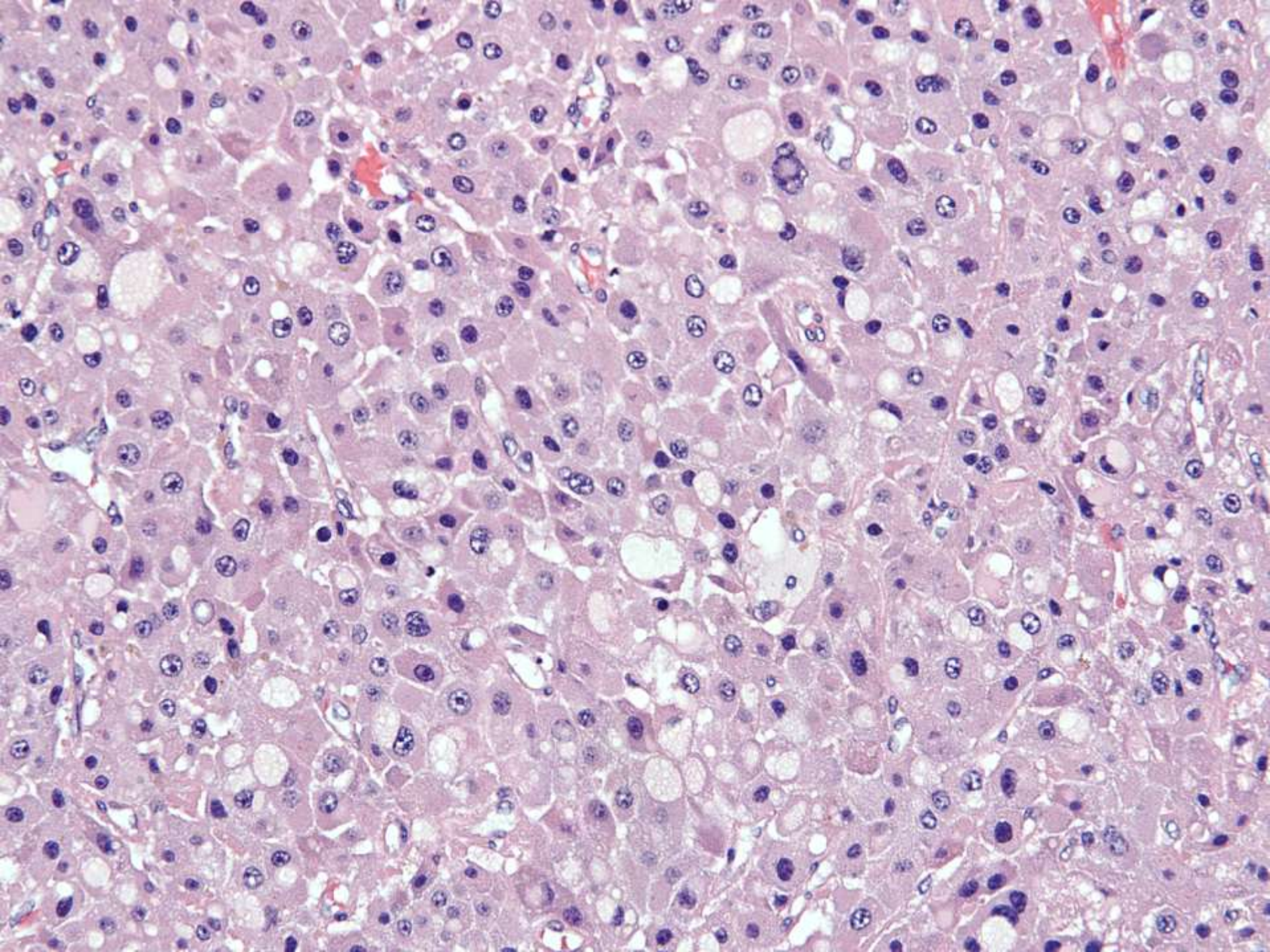
Thong JF and Chuah KL. EBV-associated smooth muscle tumour presenting as a parapharyngeal mass – A rare presentation. Auris Nasus Larynx. 2009; 35:120-22.

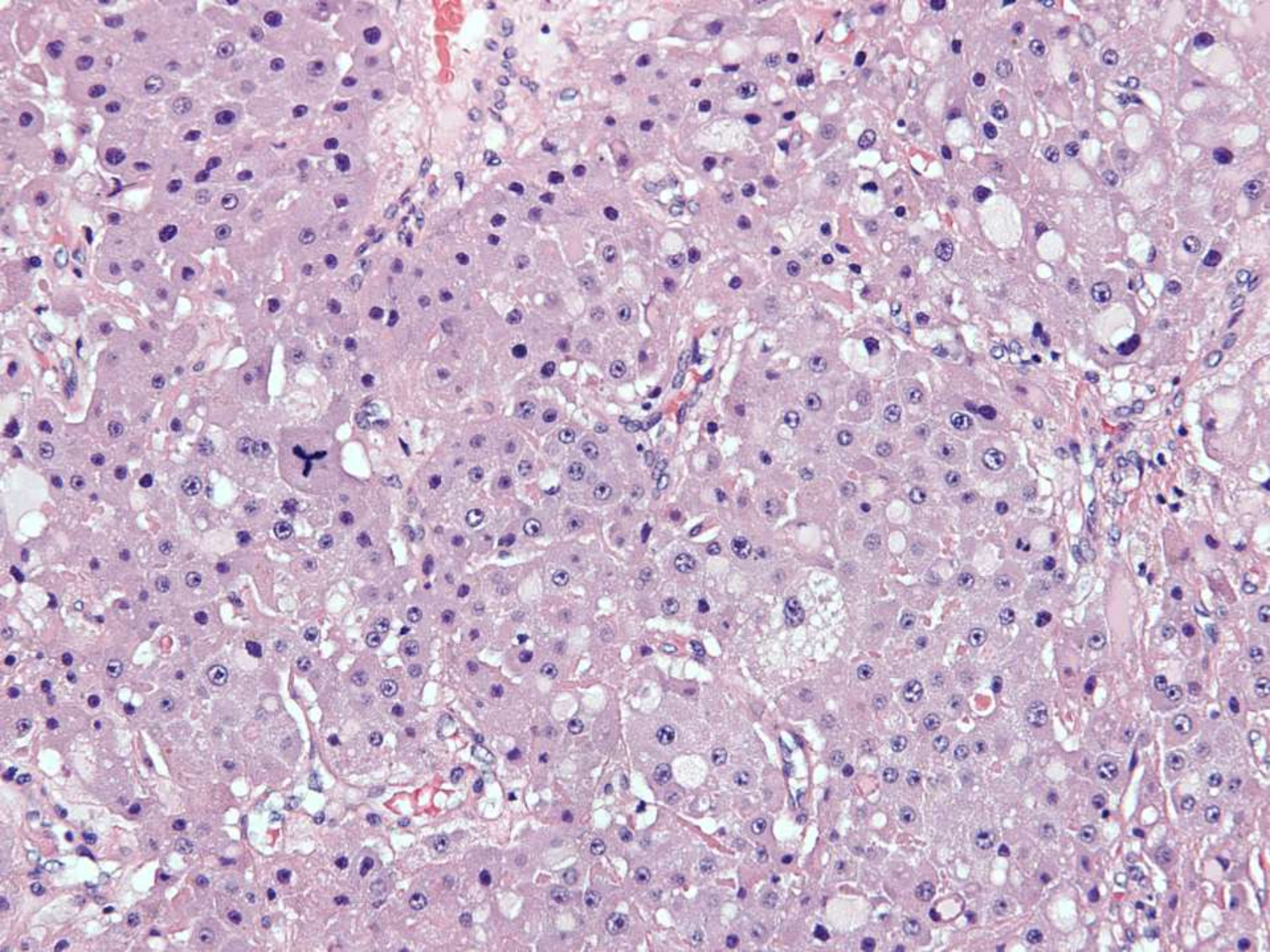
SB 6116

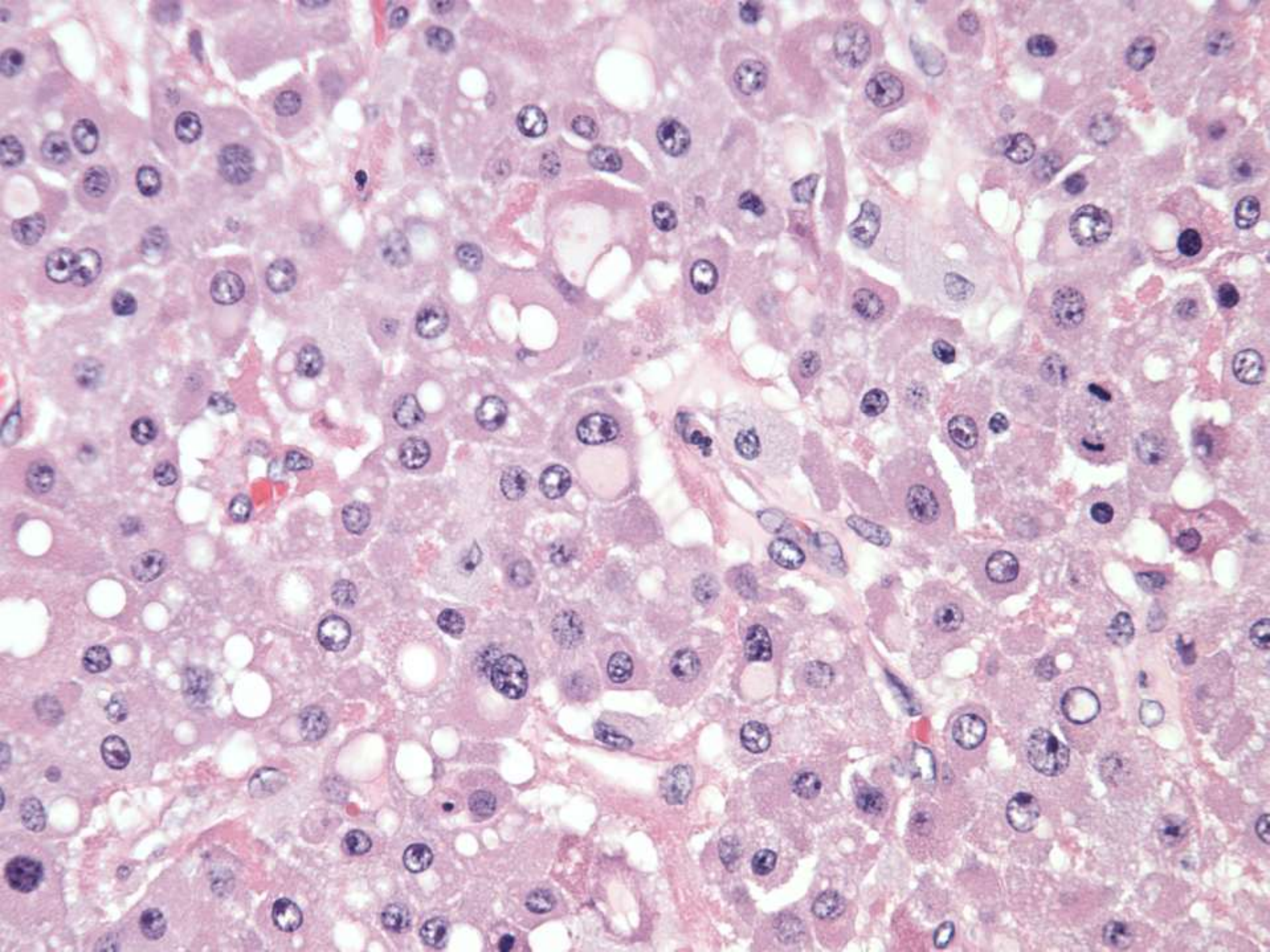
Greg Charville/John Higgins; Stanford

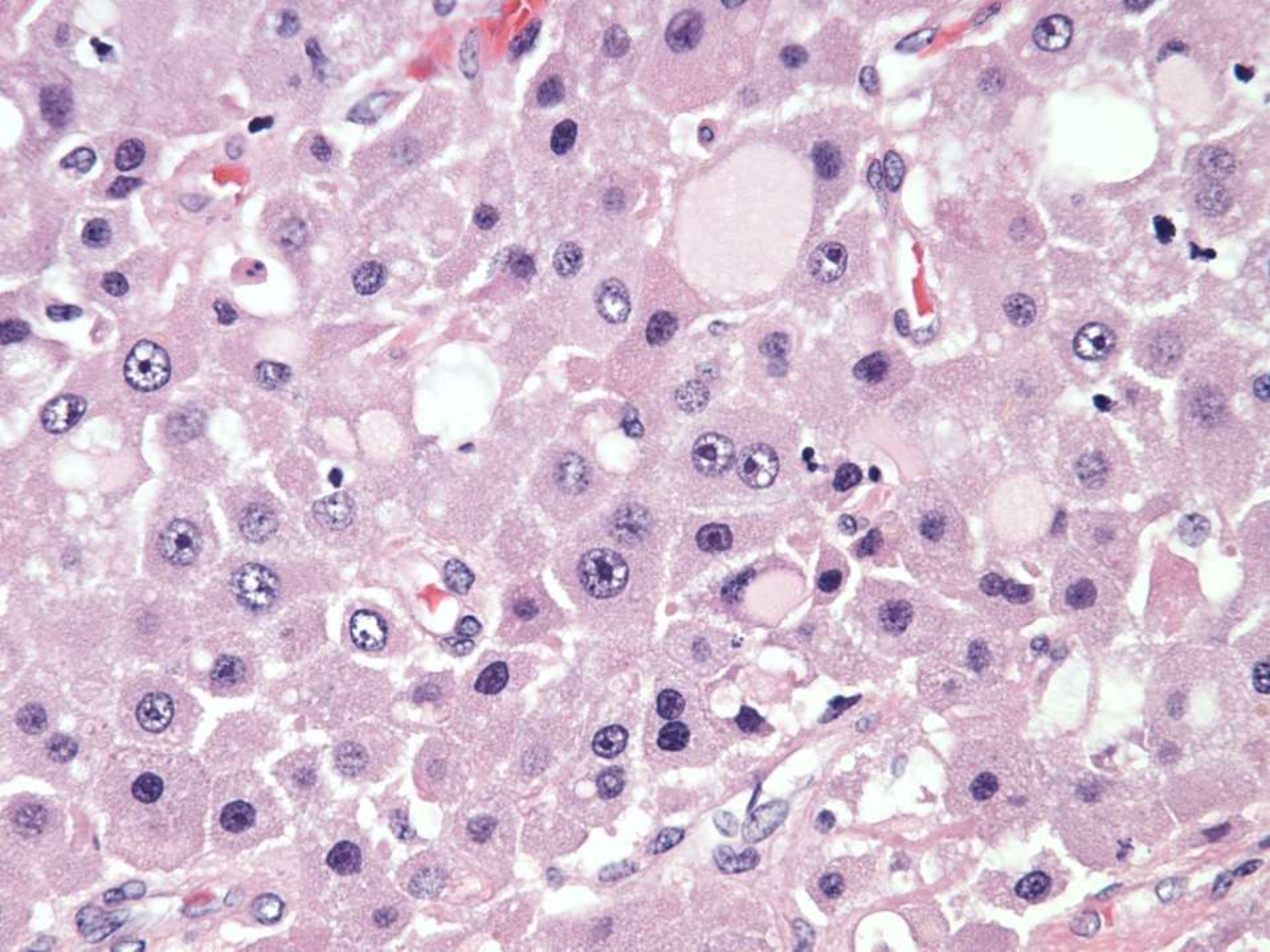
11-year-old male with 9cm liver mass.



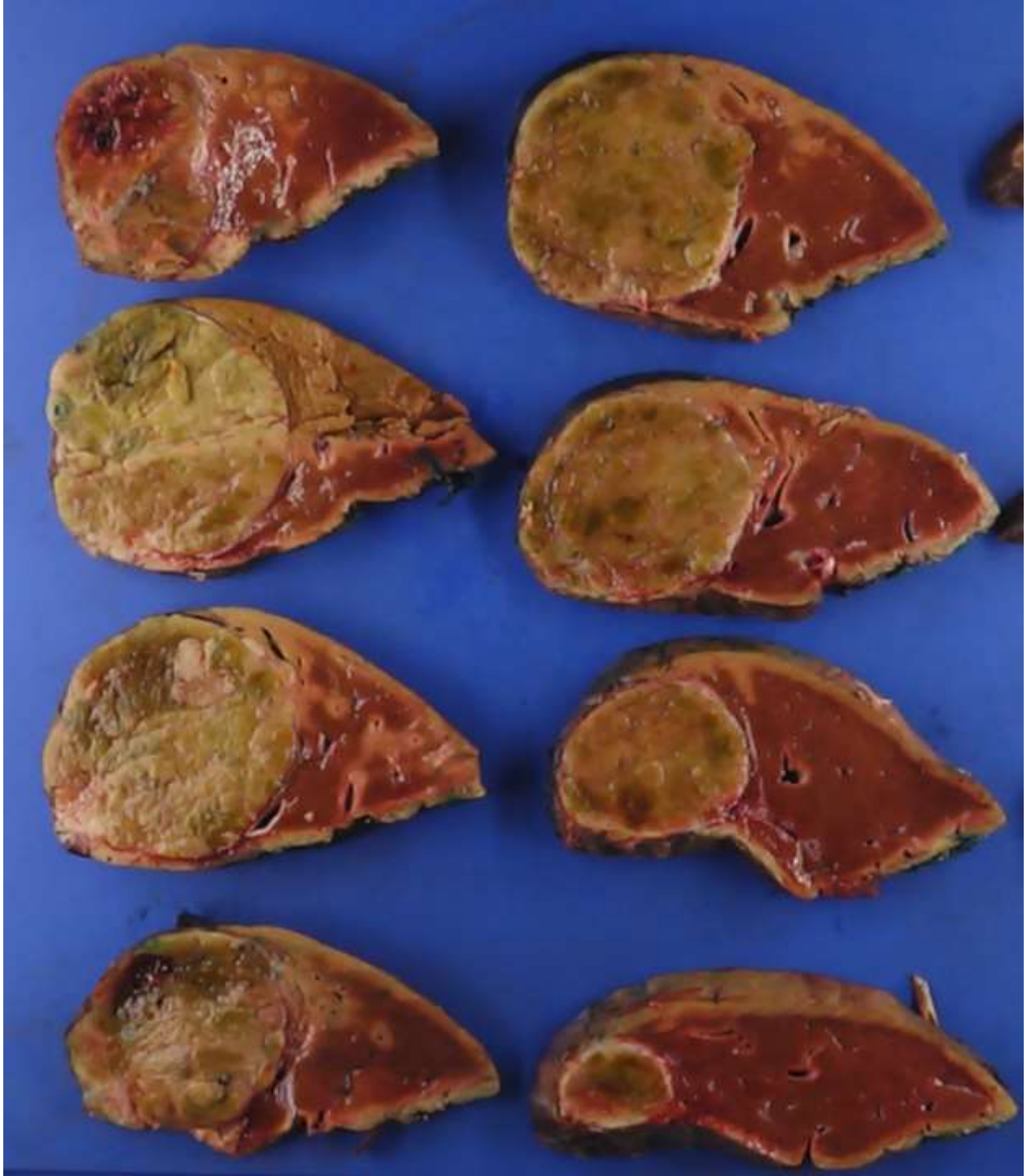


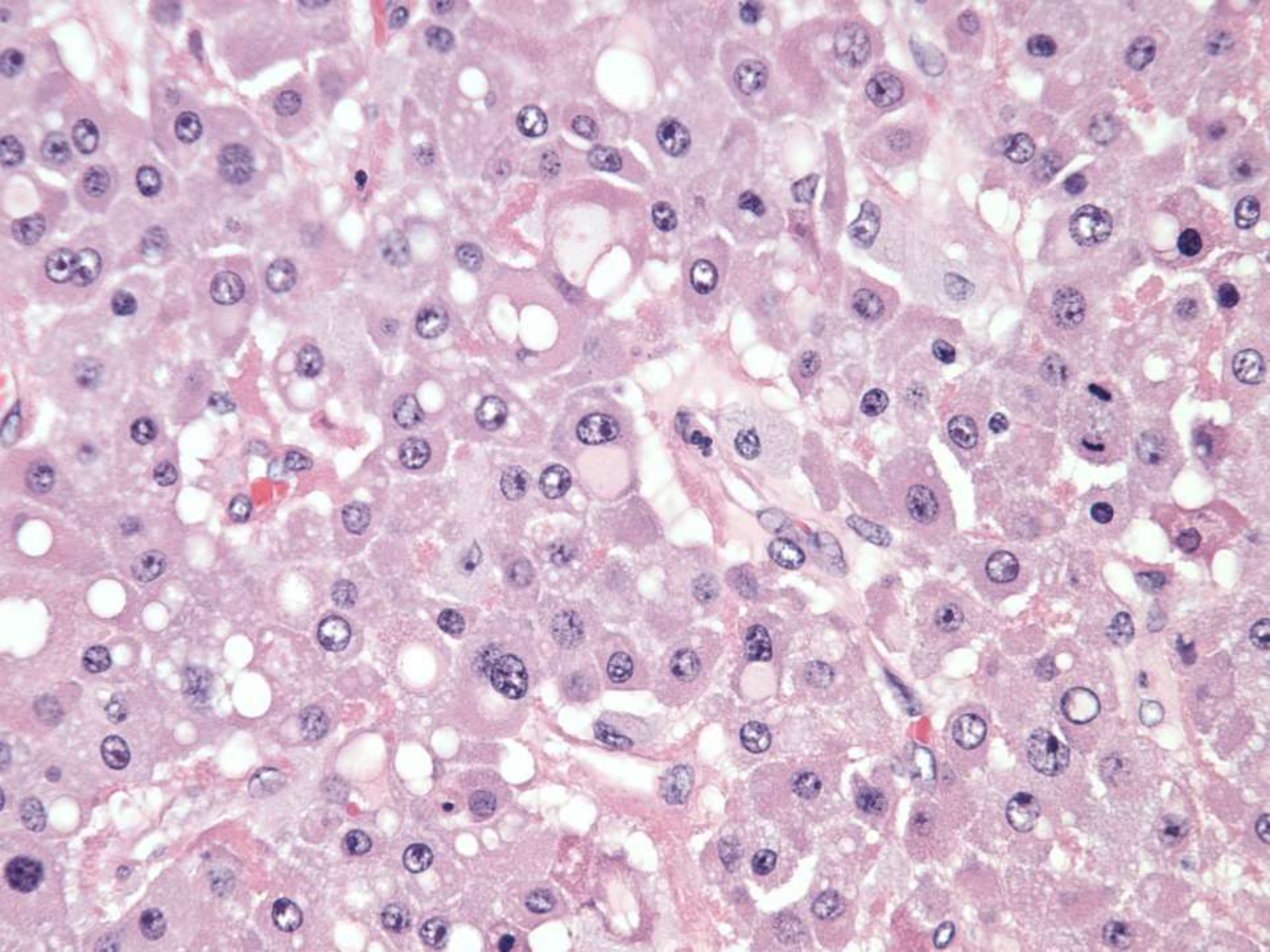






DIAGNOSIS





Pediatric liver tumors – differential diagnosis

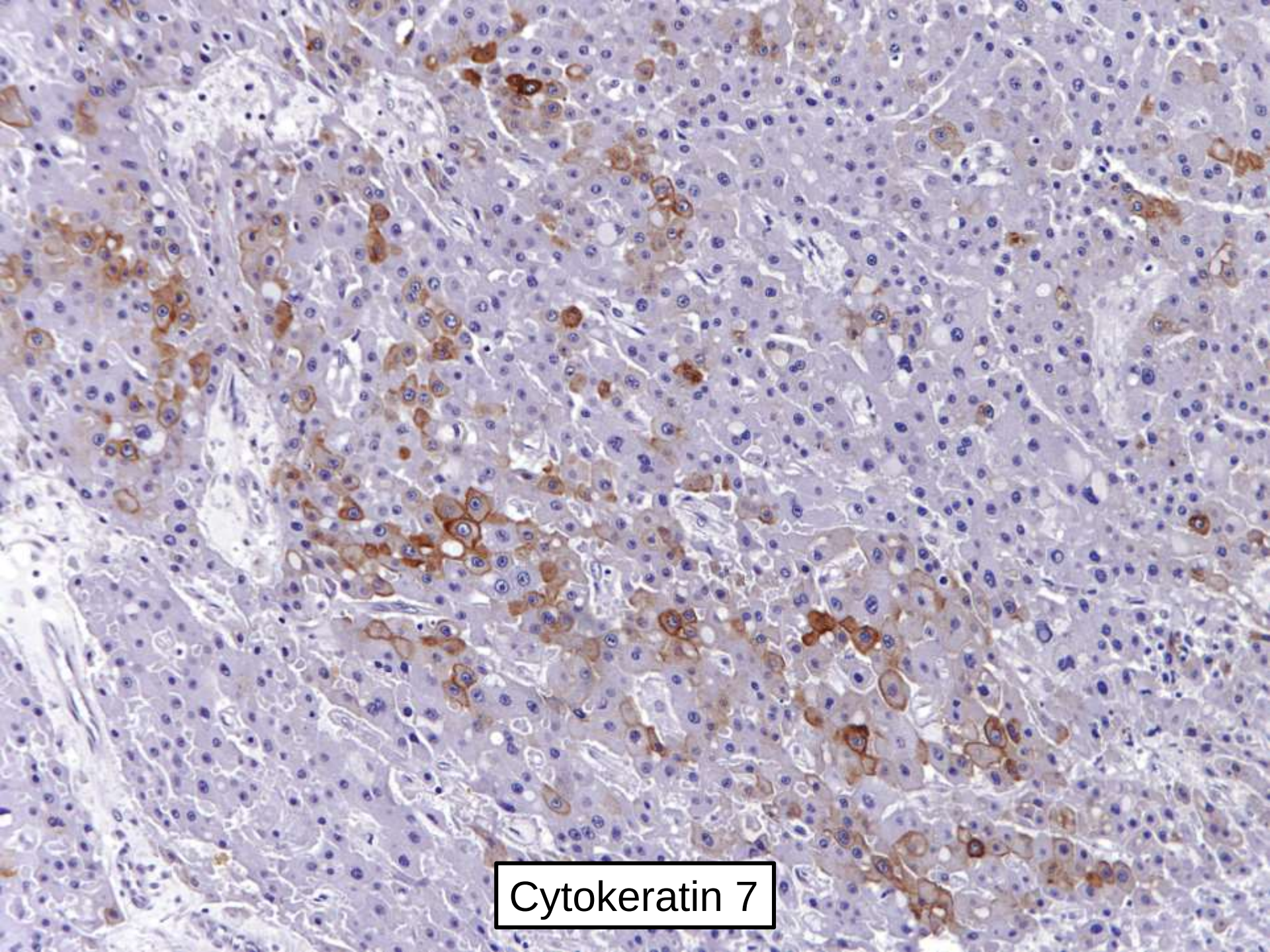
- Hepatocellular carcinoma
- Fibrolamellar variant of HCC

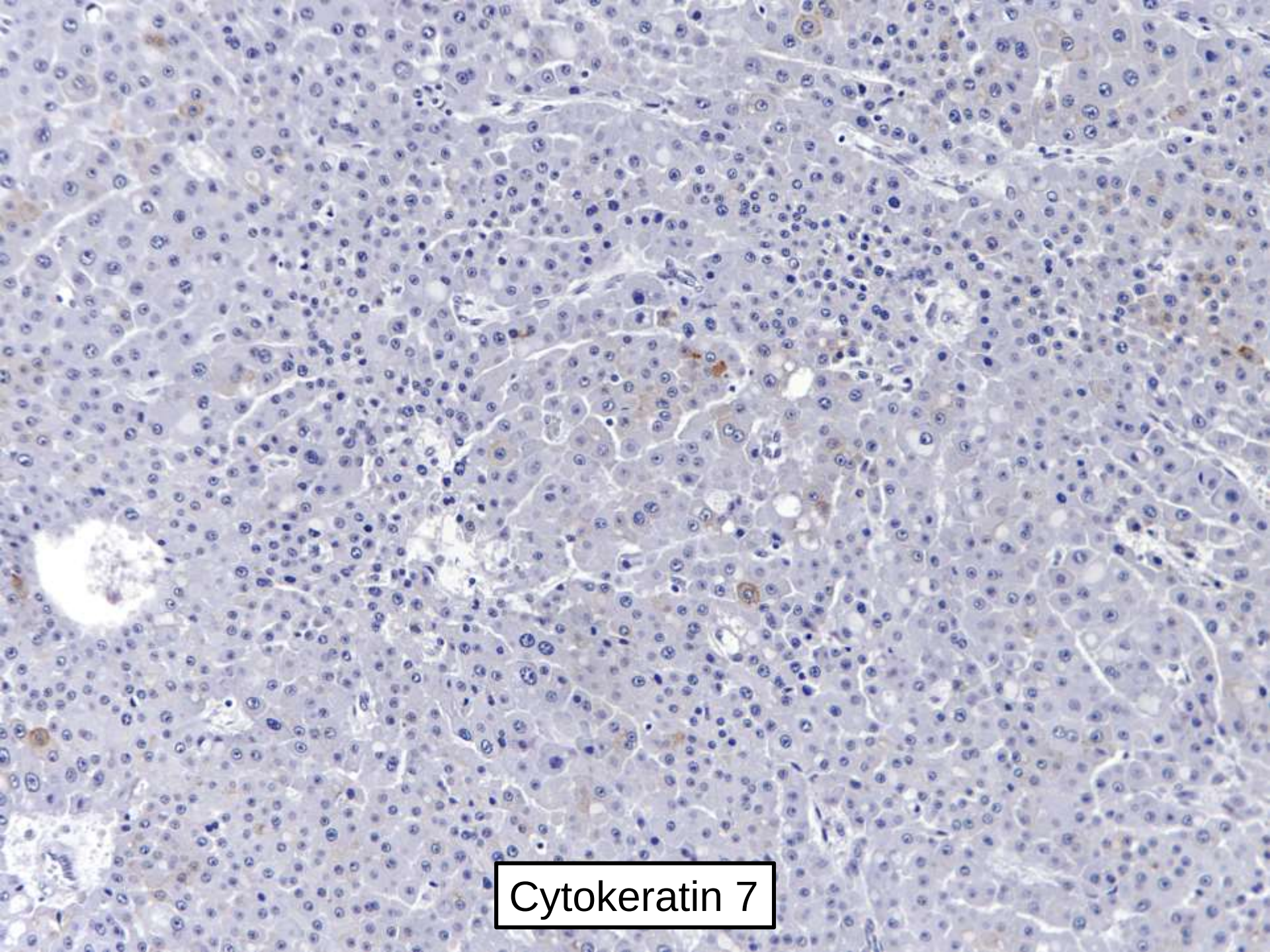
- Hepatocellular adenoma
- Focal nodular hyperplasia
- Hepatoblastoma
- Metastatic disease

Table 1 Clinicopathologic characteristic of fibrolamellar hepatocellular carcinoma in comparison to conventional hepatocellular carcinoma

Characteristic	FL-HCC	HCC	Comments
Age at presentation	Young	Older	
Sex predilection	No	4–8 times more often in men	
Distinct geographic distribution	No	Yes	HCC is more often seen in Africa and Asia
Distribution of lesions	Mostly solitary	Mostly multiple	
Growth pattern	Indolent	Aggressive	
Stage at diagnosis	Mostly advanced	Mostly advanced	Despite the advanced stage at diagnosis, prognosis is in favor of FL-HCC patients
Chronic viral infection	Absent	Present	
Liver cirrhosis	Absent	Present	Occasionally, underlying liver disease may be present in patients with FL-HCC. If present, incidental and not causative for FL-HCC
α-fetoprotein	Within normal range	Mostly elevated	
Liver resection	Treatment of choice	Not standard	Limited indication in HCC due to cirrhosis
Liver transplantation	Not standard	Curative treatment	If requirements for LT are fulfilled
Prognosis	Favorable	Mostly dismal	No difference in non-cirrhotic patients

Kassahun, *World Journal of Surgical Oncology*, 2016.


Cytokeratin 7


Cytokeratin 7

Primary Liver Carcinoma Arising in People Younger Than 30 Years

Walter M. Klein, MD,[1] Ernesto P. Molmenti, MD,[2] Paul M. Colombani, MD,[2] Davinder S. Grover,[2] Kathleen B. Schwarz, MD,[3] John Boitnott, MD,[1] and Michael S. Torbenson, MD[1]

Am J Clin Pathol 2005;124:512-518

- 7 of 9 pediatric conventional HCCs were CK7 positive
- Adult conventional HCCs showed less CK7 positivity (37%)

Detection of a Recurrent *DNAJB1-PRKACA* Chimeric Transcript in Fibrolamellar Hepatocellular Carcoma

Joshua N. Honeyman,[1,2]* Elana P. Simon,[1,3]* Nicolas Robine,[4]* Rachel Chiaroni-Clarke,[1] David G. Darcy,[1,2] Irene Isabel P. Lim,[1,2] Caroline E. Gleason,[1] Jennifer M. Murphy,[1,2] Brad R. Rosenberg,[5] Lydia Teegan,[1] Constantin N. Takacs,[1] Sergio Botero,[1] Rachel Belote,[1] Soren Germer,[4] Anne-Katrin Emde,[4] Vladimir Vacic,[4] Umesh Bhanot,[6] Michael P. LaQuaglia,[2] Sanford M. Simon[1]†

28 FEBRUARY 2014 VOL 343 SCIENCE

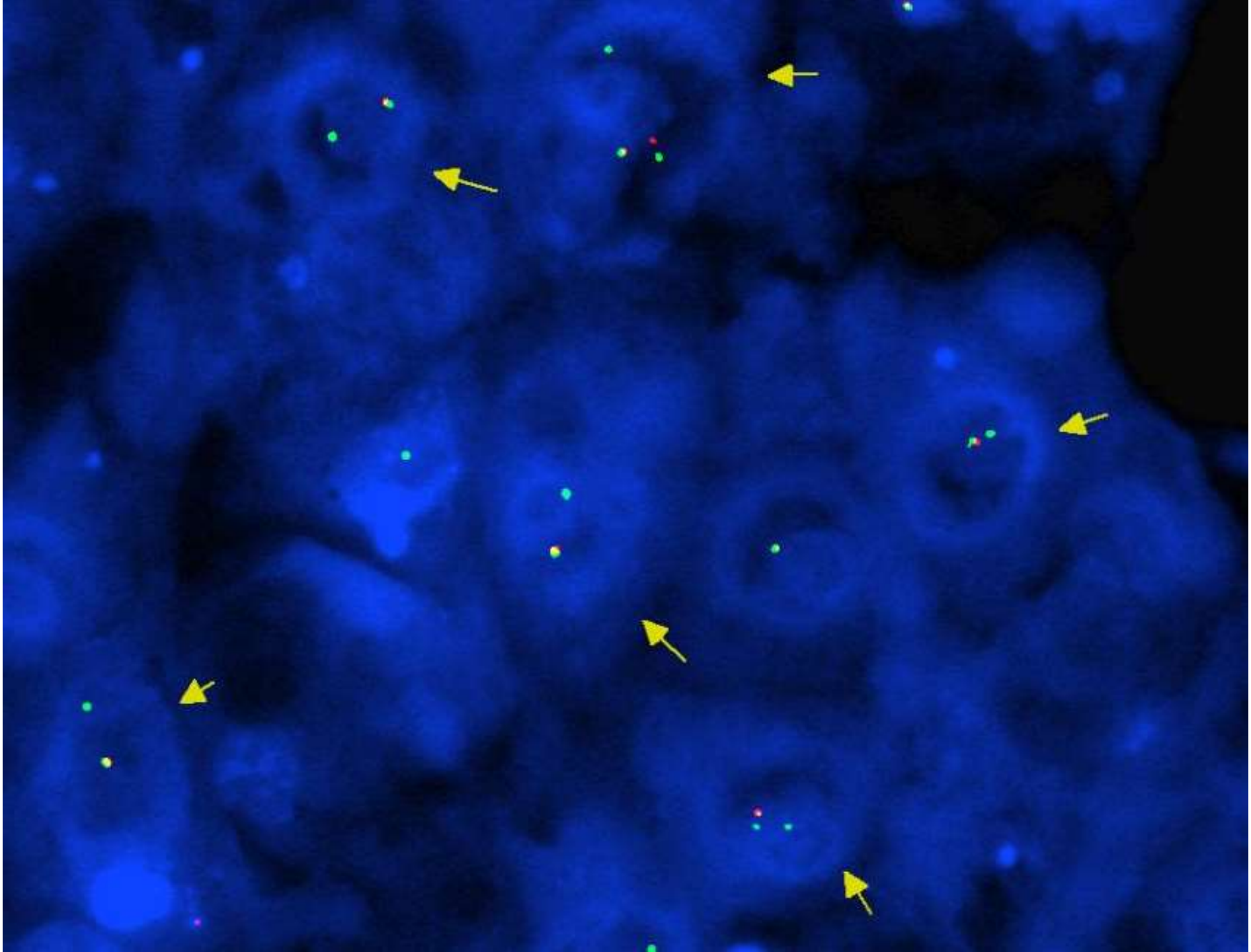
- Fusion protein present in fibrolamellar HCC (15/15 cases) but not in adjacent normal liver

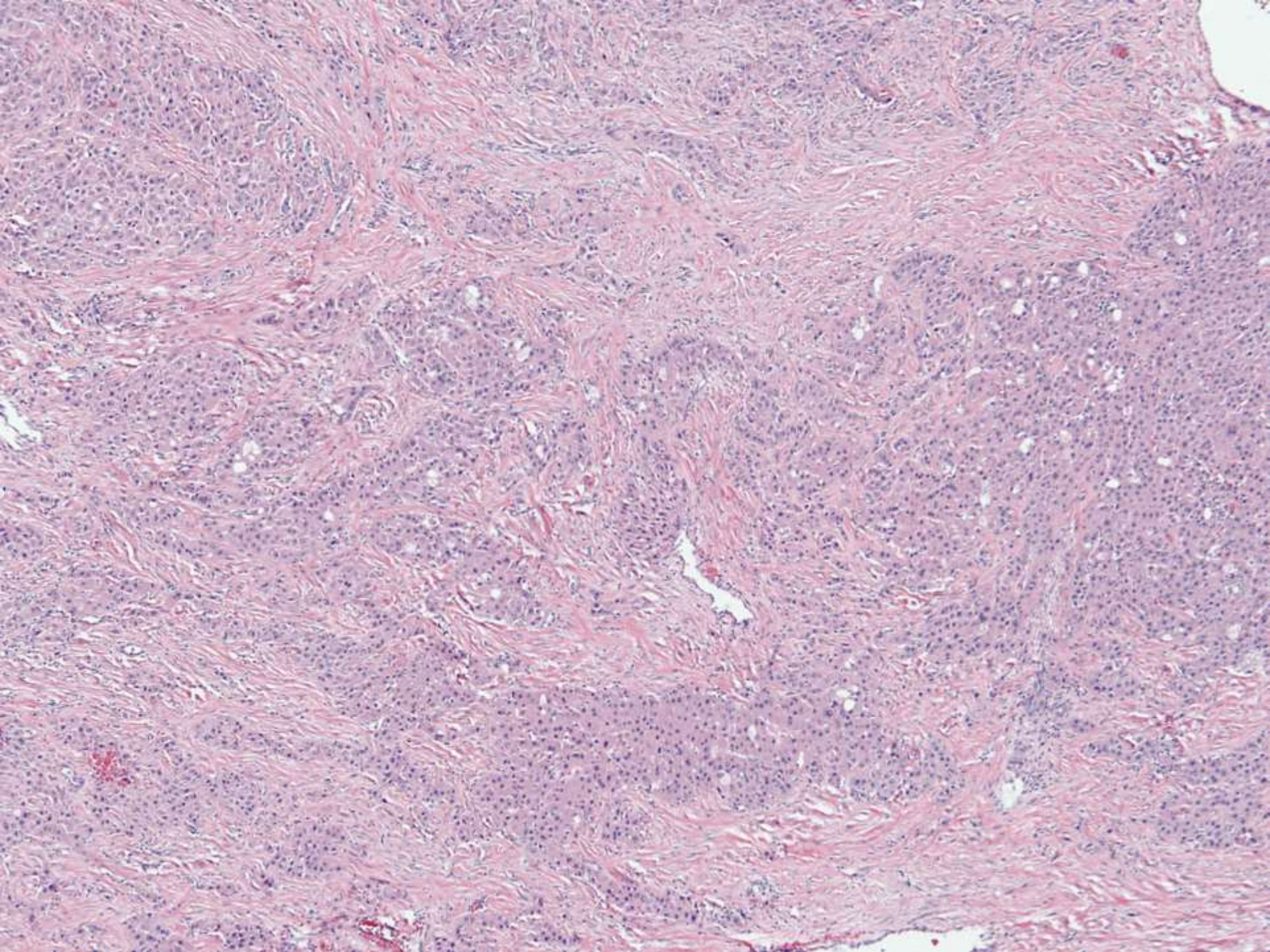
DNAJB1-PRKACA is specific for fibrolamellar carcinoma

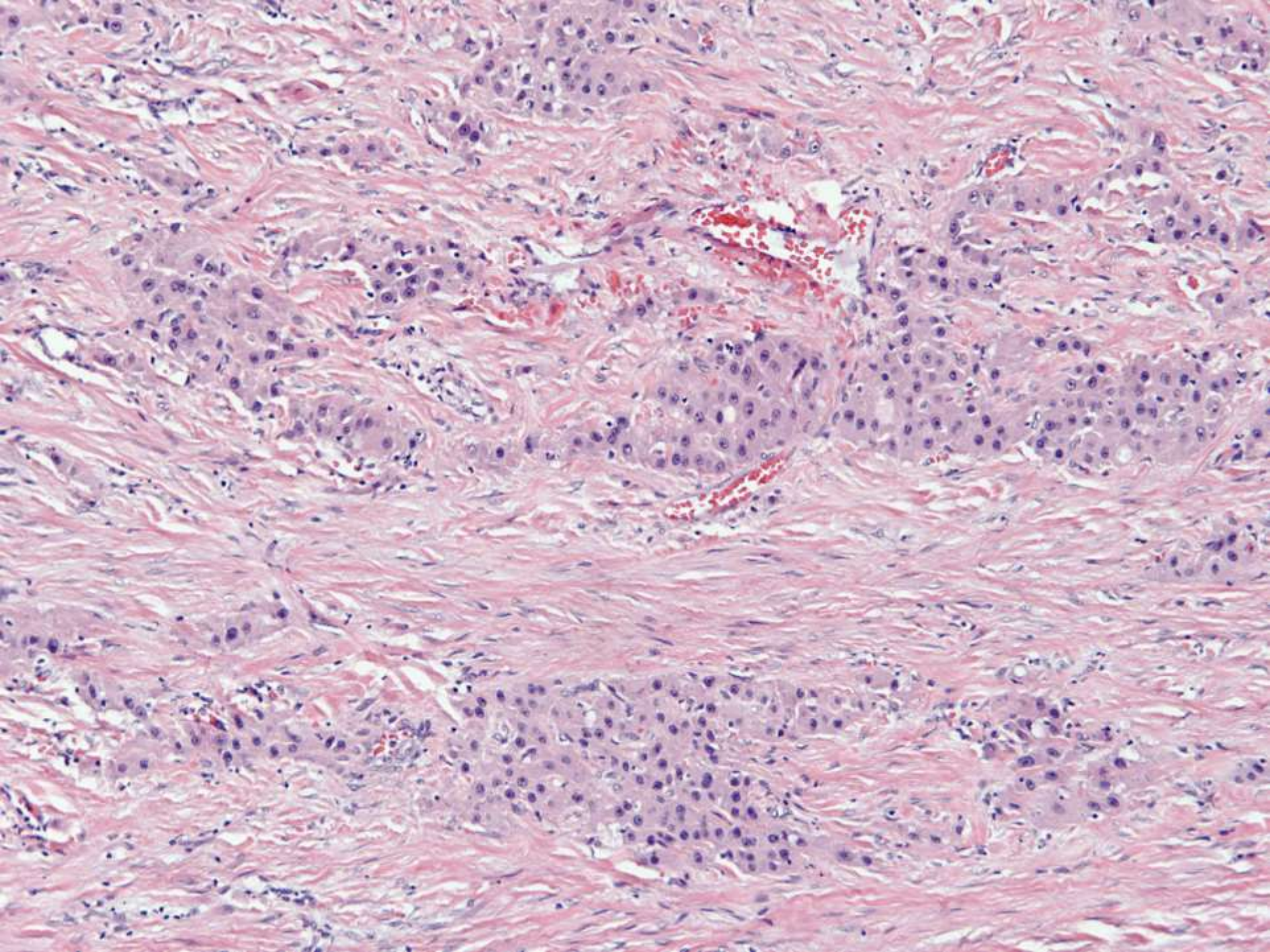
Rondell P Graham[1], Long Jin[1], Darlene L Knutson[2], Sara M Kloft-Nelson[2], Patricia T Greipp[2], Nina Waldburger[3], Stephanie Roessler[3], Thomas Longerich[3], Lewis R Roberts[4], Andre M Oliveira[1], Kevin C Halling[1], Peter Schirmacher[3] and Michael S Torbenson[1]

MODERN PATHOLOGY (2015) 28, 822–829

- 26 fibrolamellar HCCs
  - 24/26 successfully analyzed, all 24 fusion positive
- Fusion not identified in other liver tumors: conventional HCC, cholangioca., hepatic adenoma, or hepatoblastoma







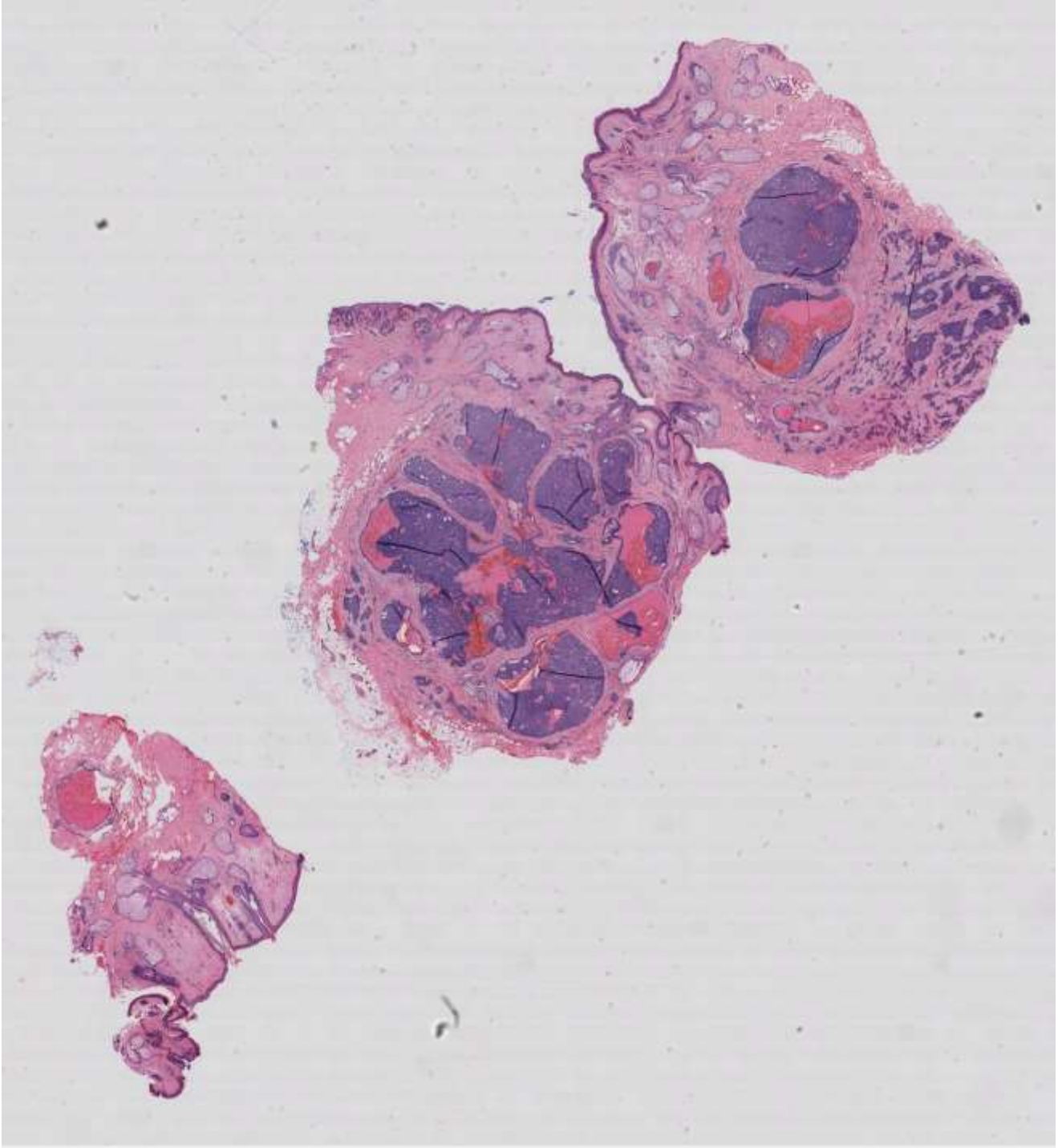
Fibrolamellar HCC – take home points

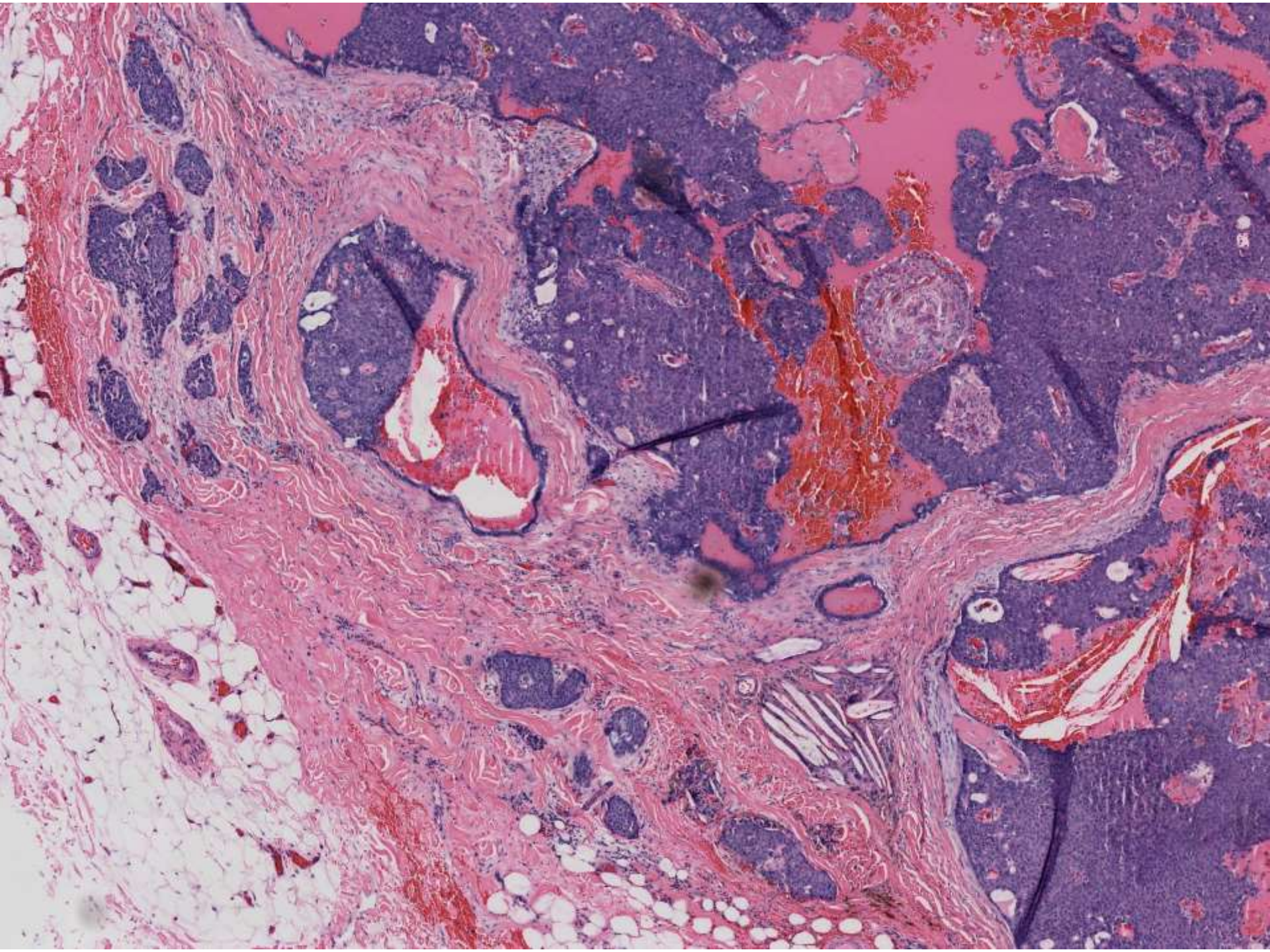
- ~8% of all liver tumors, classically occurring in young patients without underlying liver disease
- May require a search for “typical” morphologic features
- CK7 is not entirely specific for fibrolamellar HCC, especially in children and young adults
- Detection of a newly identified fusion transcript may be helpful in ambiguous cases

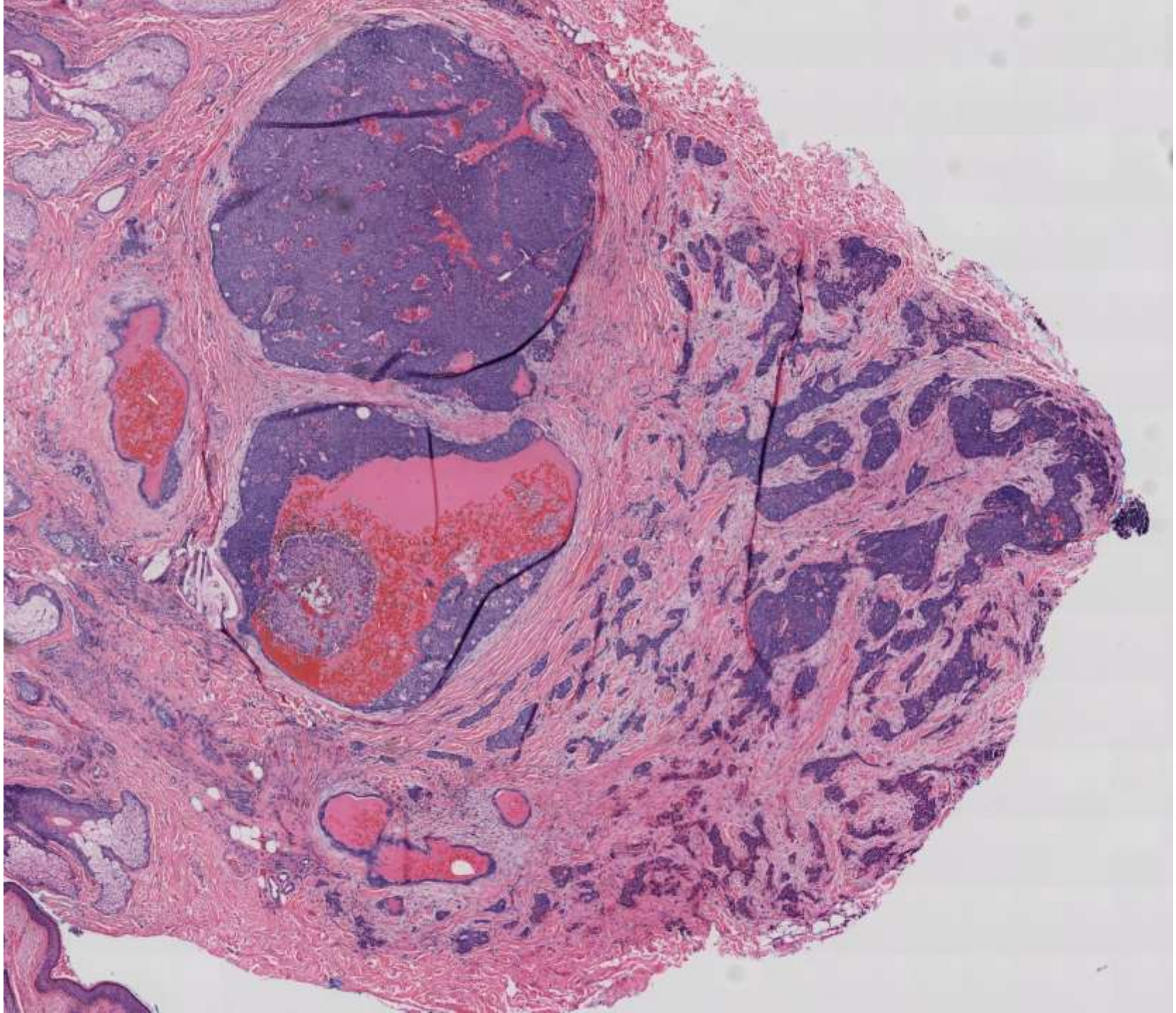
SB 6117
[scanned slide available]

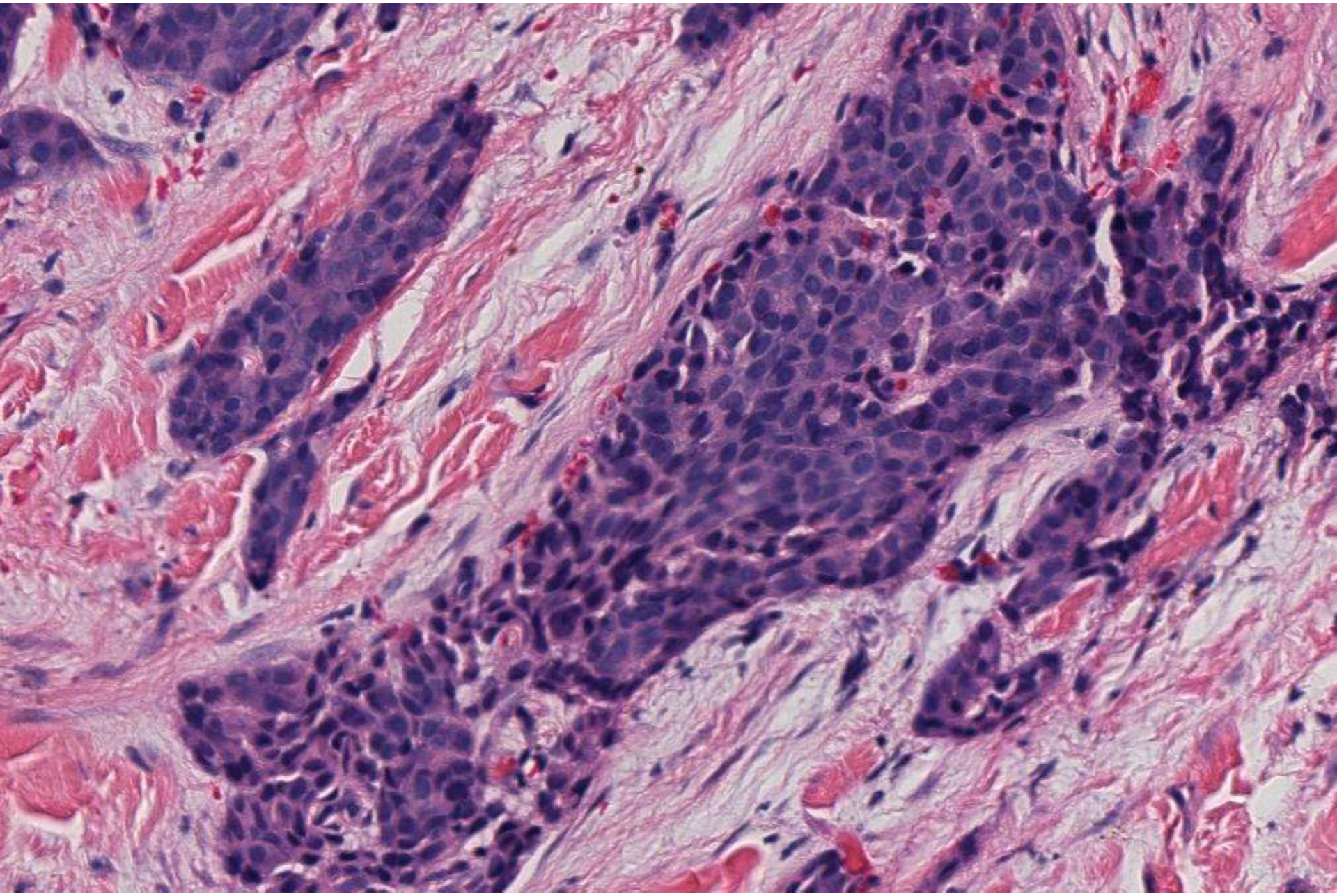
Harris Goodman; Saint Frances Hospital

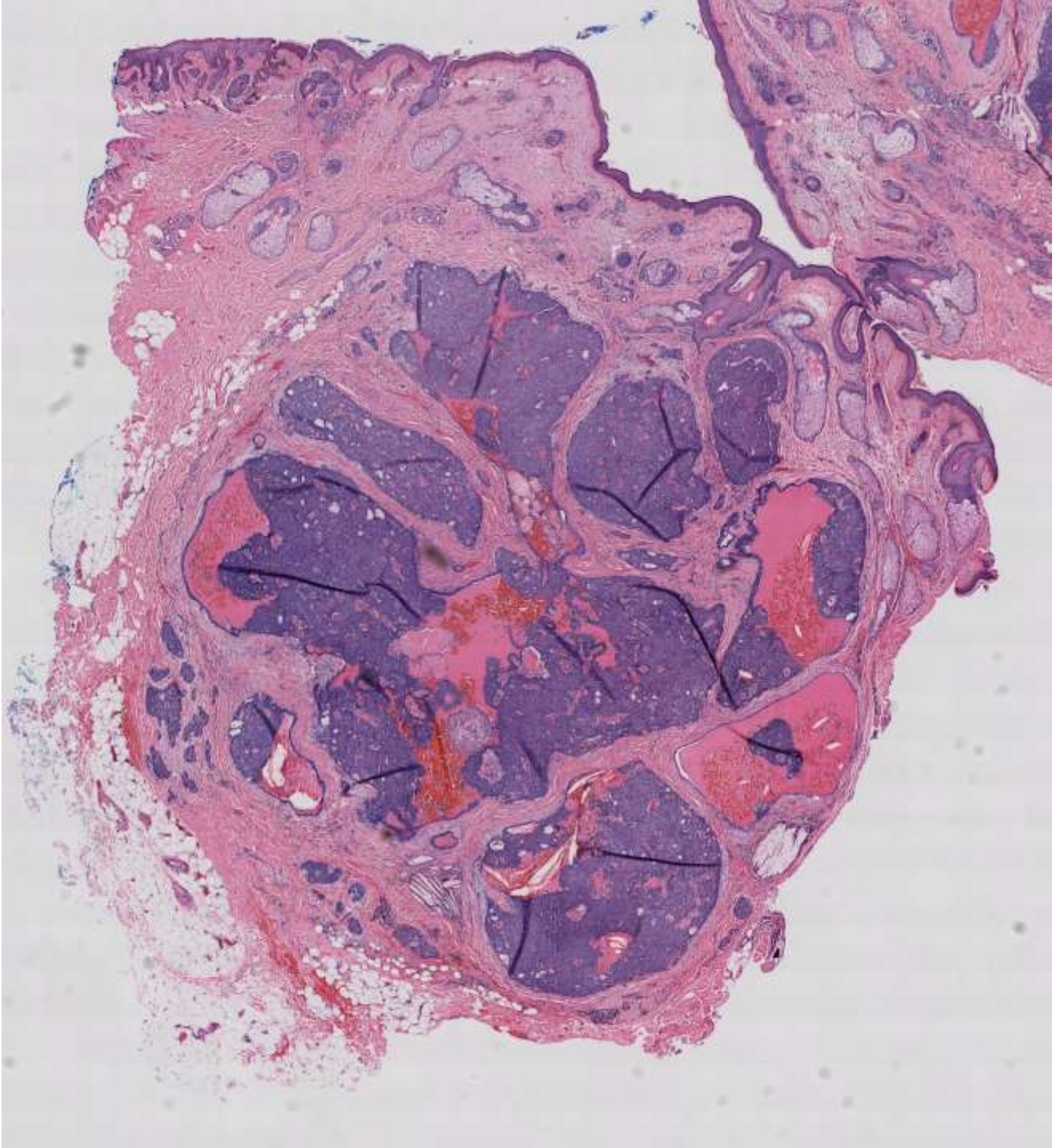
76-year-old female with a sebaceous cyst of right cheek.

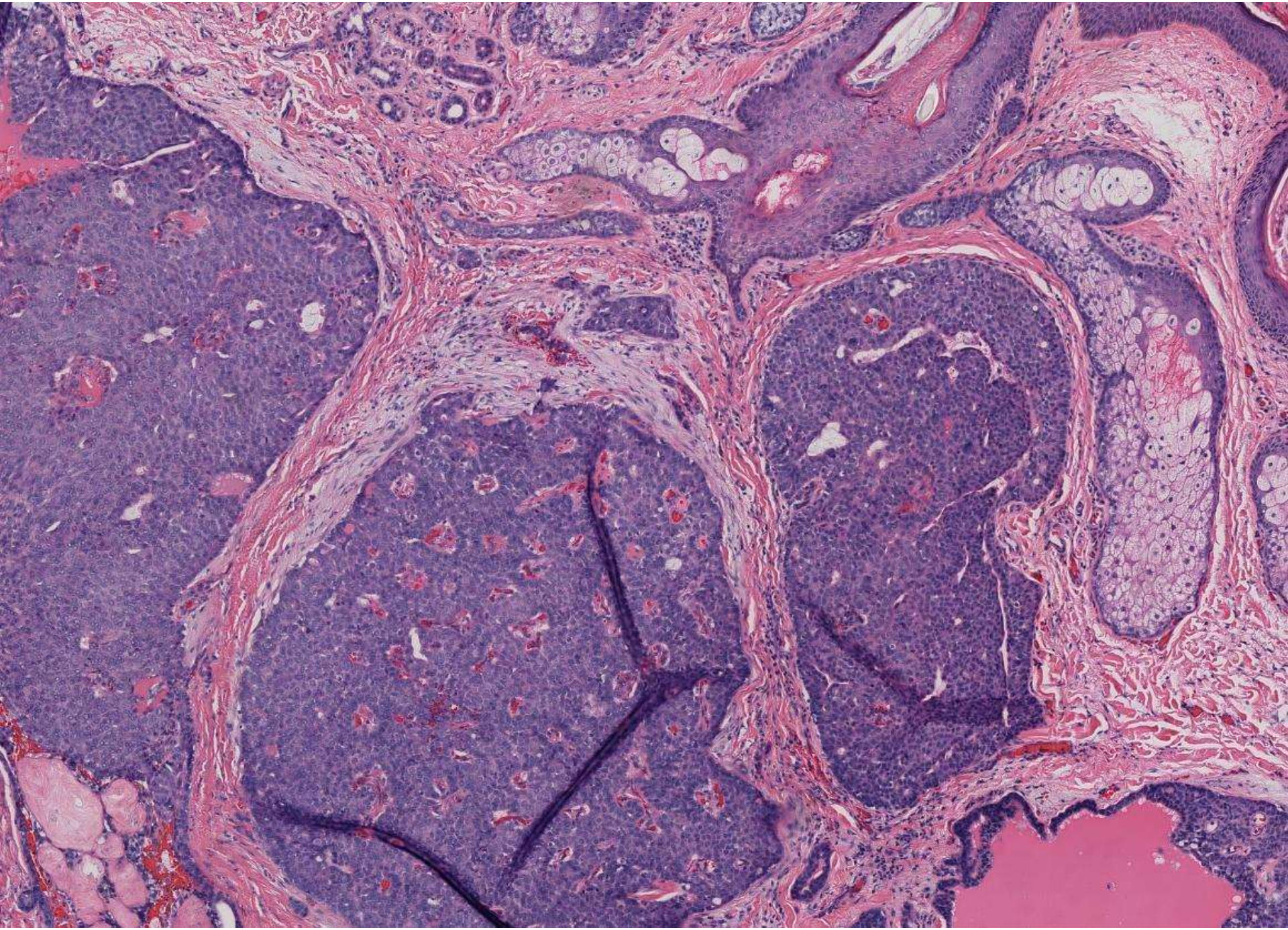


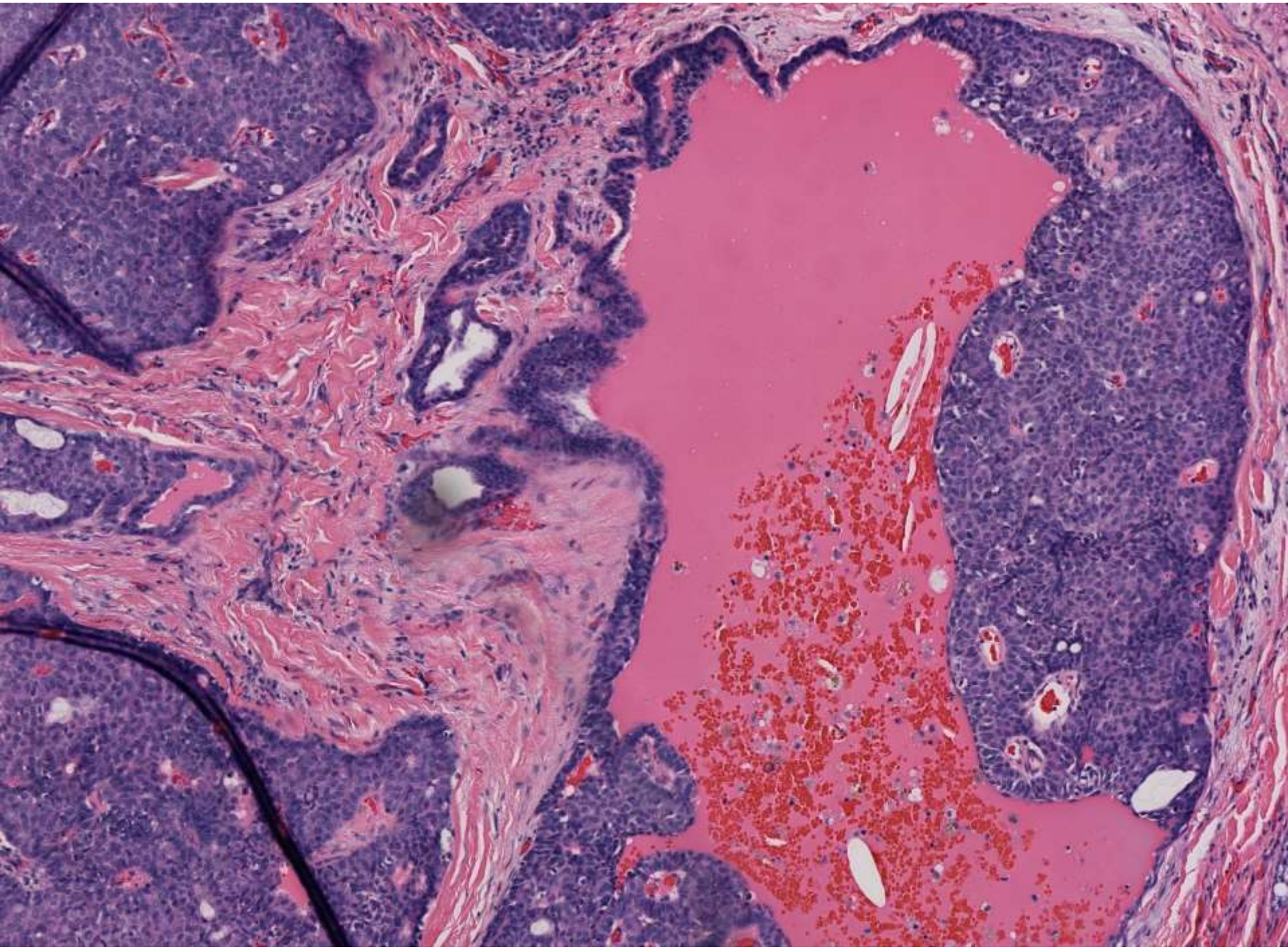


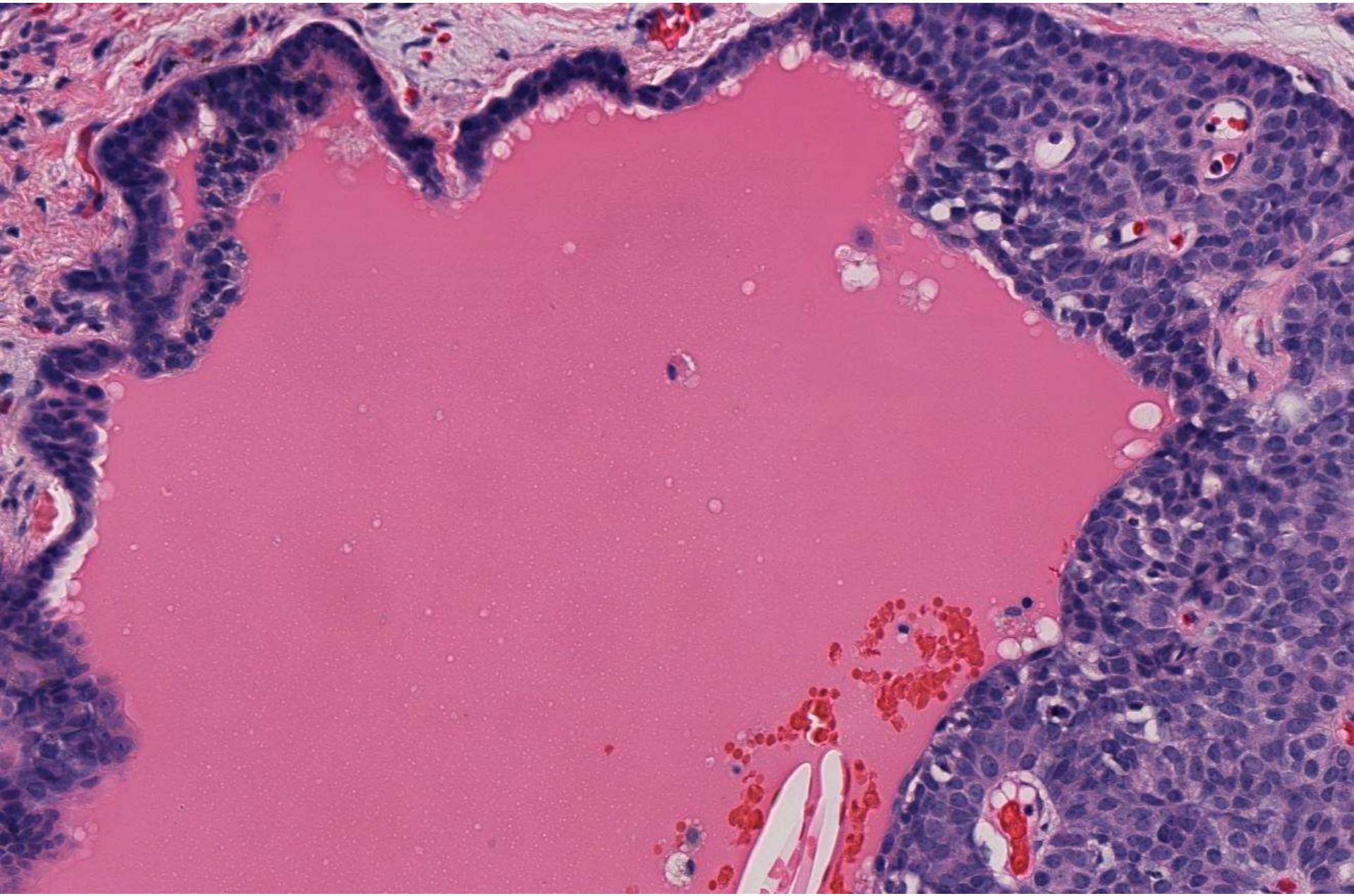


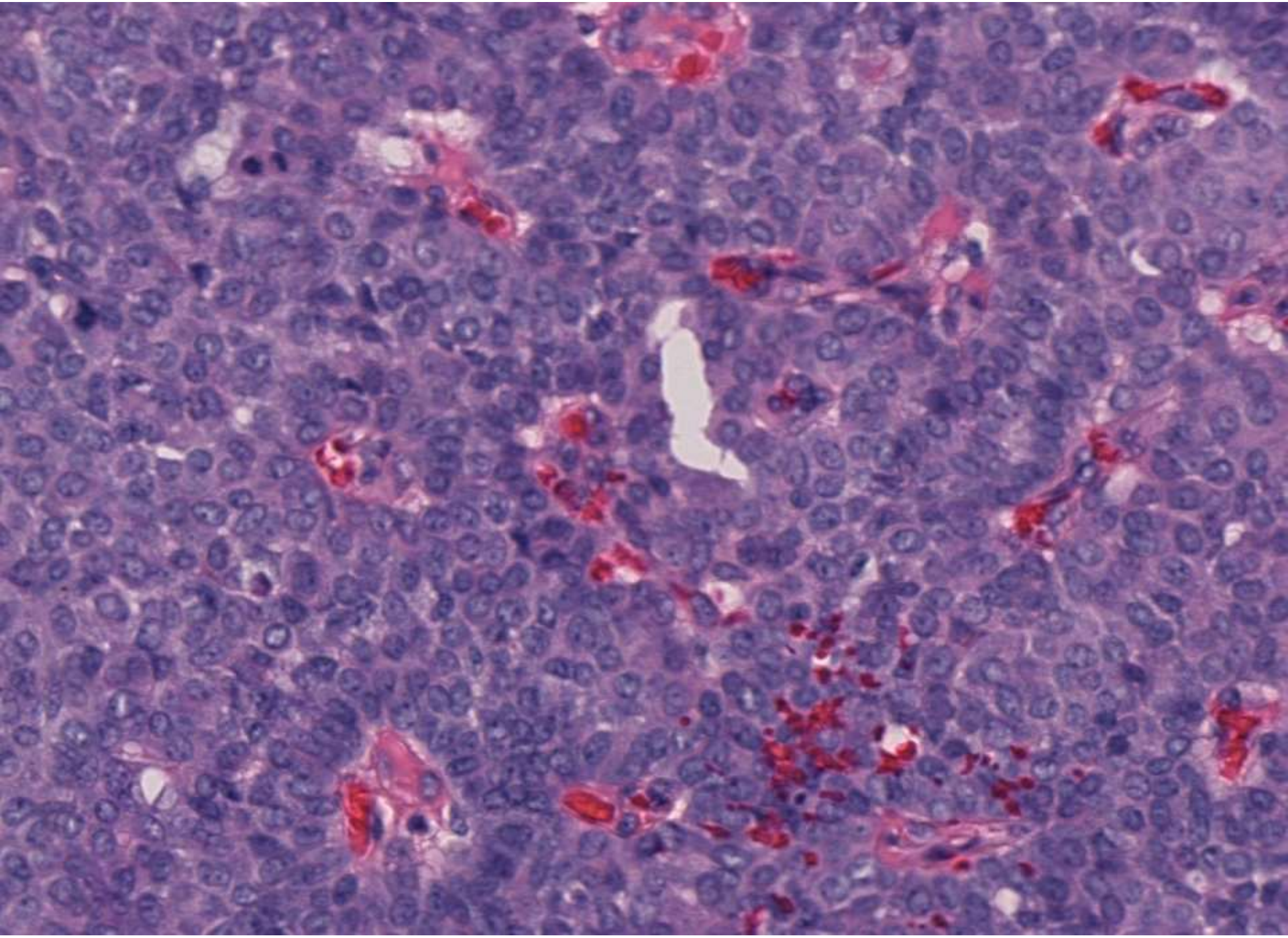


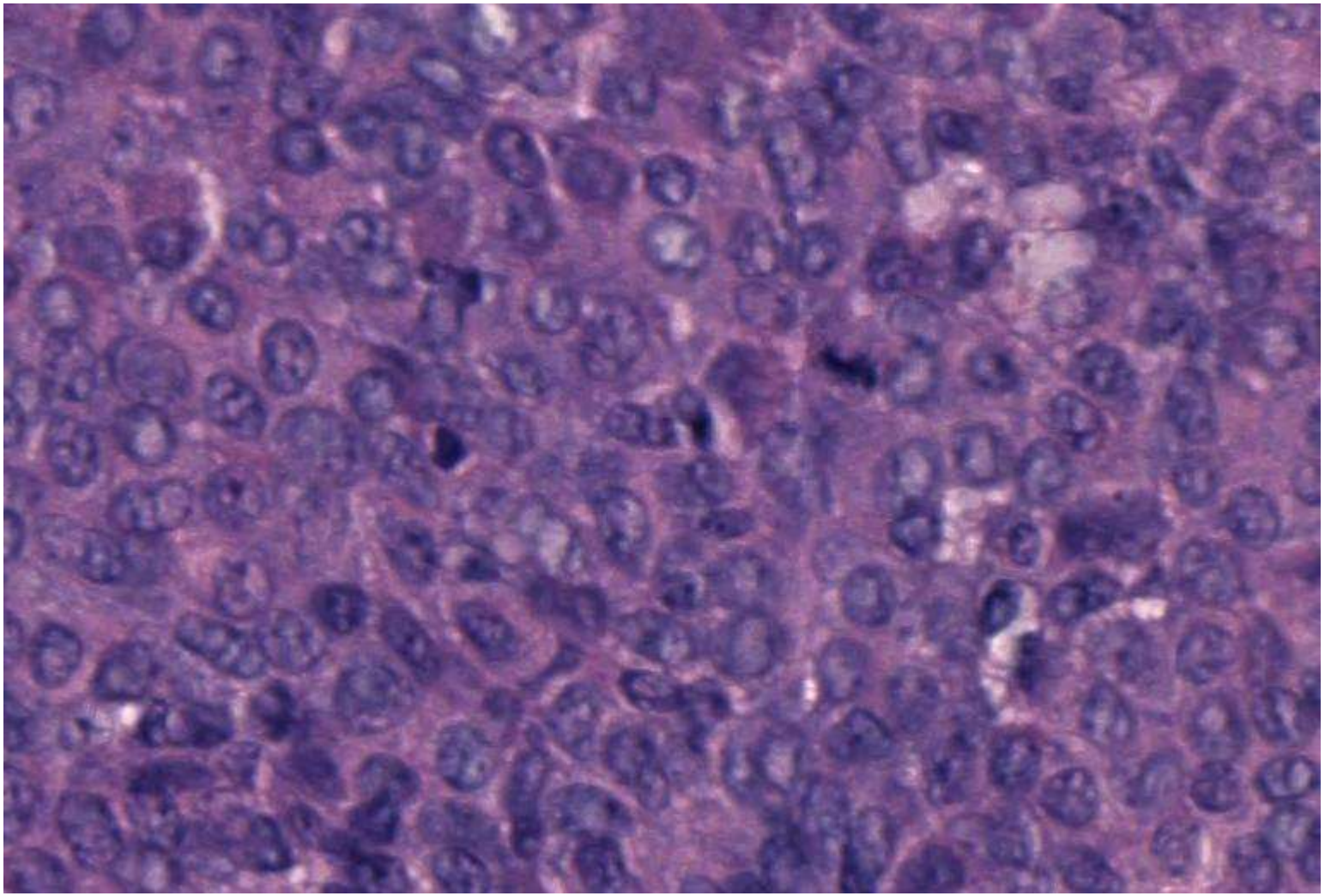












DIAGNOSIS

DESMOPLASTIC APOCRINE ADENOCARCINOMA EX APOCRINE ADENOMA

Apocrine glands

-- Axilla
-- Groin
-- Anogenital Region
-- Umbilicus
-- Eyelid (Moll's Glands)
-- Areola
-- External Auditory Meatus

Primary Cutaneous Apocrine Gland Carcinoma

-- Extremely rare (about 50 cases reported)
-- Fifth to seventh decade of life
-- Most involve axilla
-- May be associated with benign lesions (such as apocrine adenoma and apocrine hyperplasia)
-- May be indolent and slow growing, but can be aggressive with metastases
-- DDx: metastatic breast carcinoma
-- Treatment of choice: wide local excision

J Clin Pathol. 2007 Feb; 60(2): 145–159.

Published online 2006 Aug 1. doi: 10.1136/jcp.2006.041608

PMCID: PMC1860616

Skin adnexal neoplasms—part 2: An approach to tumours of cutaneous sweat glands

Nidal A Obaidat, Khaled O Alsaad, and Danny Ghazarian

PMC full text: J Clin Pathol. 2007 Feb; 60(2): 145–159.
Published online 2006 Aug 1. doi: 10.1136/jcp.2006.041608

Table 2 Cutaneous sweat gland lesions and their synonyms

Lesion	Synonyms
Hidrocystoma	Apocrine/eccrine hidrocystoma, cystadenoma
Syringofibroadenoma	Acrosyringeal adenomatosis, acrosyringeal nevus
Poroma	Hidroacanthoma simplex (intraepidermal poroma), eccrine poroma, and dermal duct tumour
Hidradenoma	Nodular hidradenoma, solid-cystic hidradenoma, clear cell hidradenoma, clear cell acrospiroma, eccrine acrospiroma
Cylindroma (multiple)	Turban tumour
Tubulopapillary hidradenoma	Papillary eccrine adenoma, tubular apocrine adenoma, papillary apocrine fibroadenoma
SCAP	Papillary syringadenoma
Hidradenoma papilliferum	Papillary hidradenoma
Chondroid syringoma	Mixed tumour of the skin
Digital papillary adenocarcinoma	Aggressive digital papillary tumour, aggressive digital papillary adenoma/carcinoma, aggressive digital papillary adenoma
Sweat gland ductal carcinoma	Syringoid eccrine carcinoma, eccrine ductal carcinoma
Porocarcinoma	Malignant "eccrine" poroma
Microcystic adnexal carcinoma	Sclerosing sweat duct carcinoma
Hidradenocarcinoma	Malignant nodular/clear cell hidradenoma, malignant acrospiroma, malignant clear cell acrospiroma, clear cell eccrine carcinoma, primary mucoepidermoid cutaneous carcinoma
Apocrine carcinoma	Tubular apocrine carcinoma, malignant hidradenoma papilliferum

SCAP, syringocystadenoma papilliferum.

PMC full text: J Clin Pathol. 2007 Feb; 60(2): 145–159.
Published online 2006 Aug 1. doi: 10.1136/jcp.2006.041608

Table 1 Classification of cutaneous sweat gland adnexal lesions according to the current concept of the predominant "accepted" origin

Origin	Benign	Malignant
Eccrine and apocrine (mixed origin)	Hidrocystoma	Malignant mixed tumour of the skin (has eccrine/apocrine and mesenchymal components)
	Apocrine/eccrine nevus	
	Tubulopapillary hidradenoma (including papillary eccrine adenoma and tubular apocrine adenoma)	
	Chondroid syringoma	
Eccrine	Poroma	Porocarcinoma
	Hidradenoma	Hidradenocarcinoma
	Spiradenoma	Spiradenocarcinoma
	Cylindroma	Malignant cylindroma
	Syringometaplasia	Syringoid carcinoma
	Syringoma	Microcystic adnexal carcinoma
	Syringofibroadenoma	Mucinous carcinoma
		Adenoid cystic carcinoma
		Aggressive digital papillary adenocarcinoma
Apocrine	SCAP	Syringocystadenocarcinoma
	Hidradenoma papilliferum	Apocrine carcinoma
		Extramammary Paget's disease
Composite/mixed cutaneous adnexal tumours		

SCAP, syringocystadenoma papilliferum.

Take-home messages:

1. Many sweat gland tumors have both eccrine and apocrine origins

Take-home messages:

2. A malignant counterpart to most benign lesions has been described. Features that suggest malignancy include asymmetry of the lesion, jagged/infiltrative borders, irregular arrangement of neoplastic cells, nuclear atypia and increased mitotic activity.

Take-home messages:

3. Differentiating primary cutaneous sweat gland carcinomas from metastatic carcinoma may be difficult; clinical history is very important

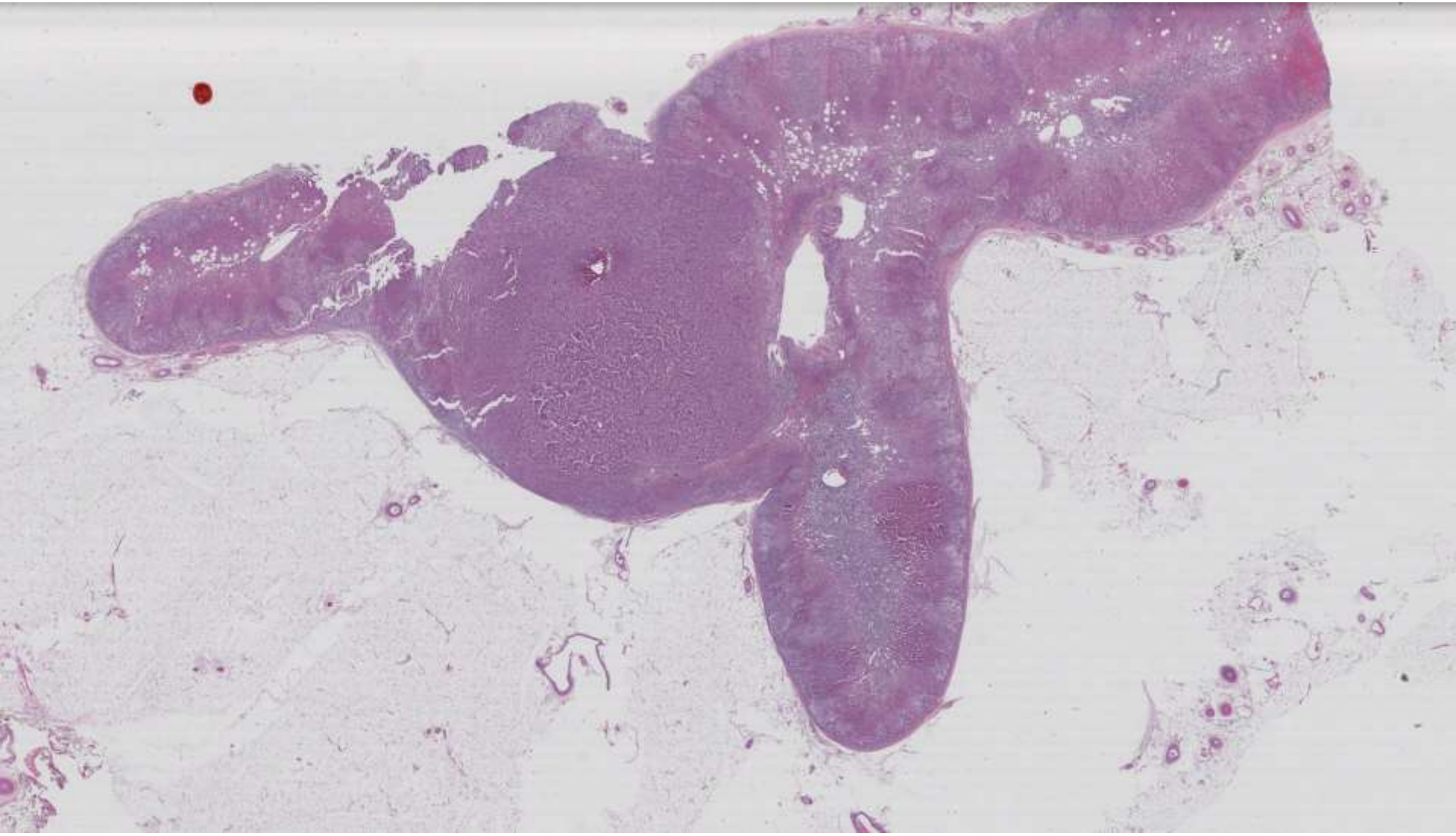
Take-home messages:

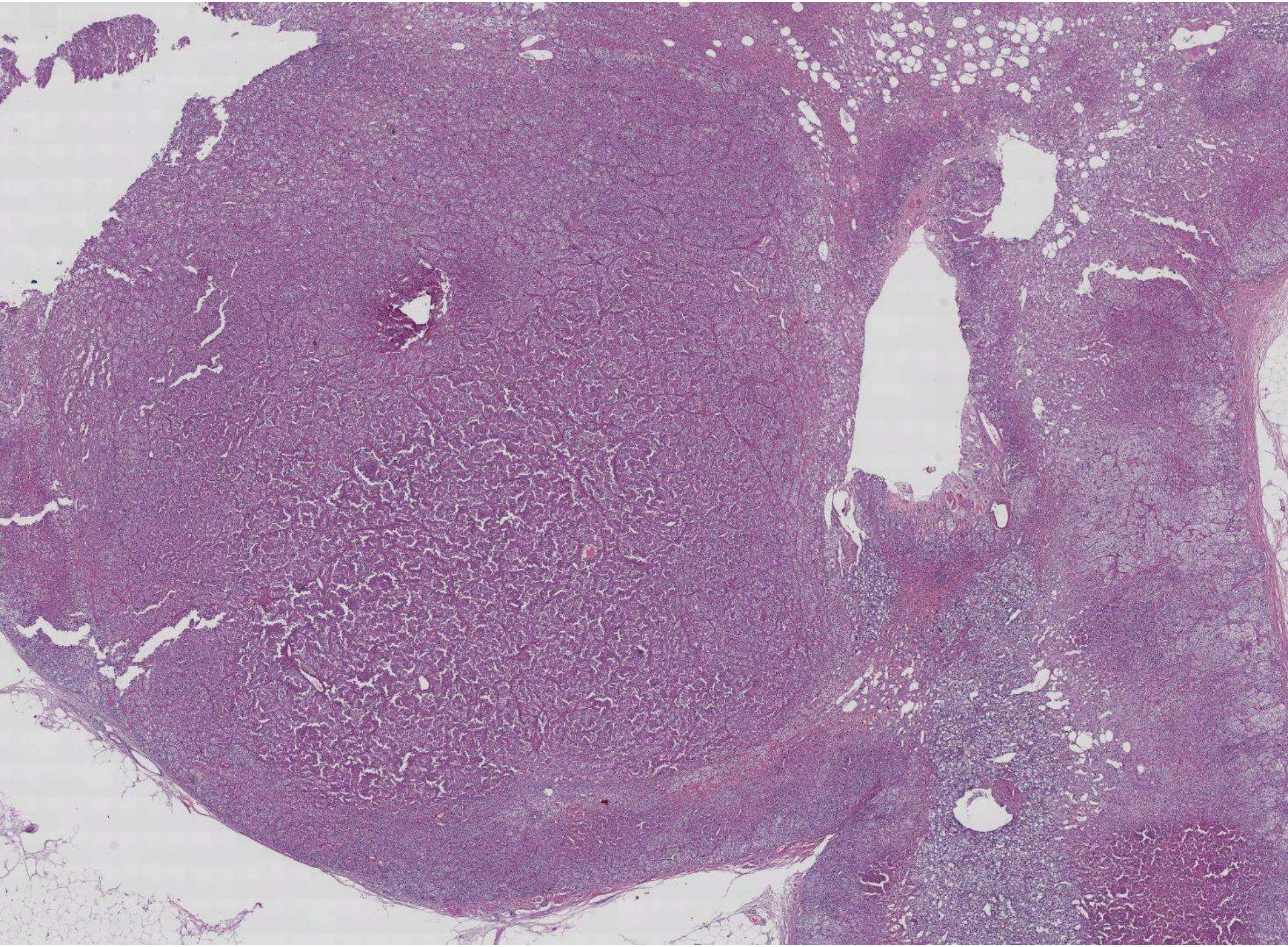
4. Composite/mixed adnexal tumors may display a varied composition, with a mixture of eccrine, apocrine, sebaceous and pilar differentiation.

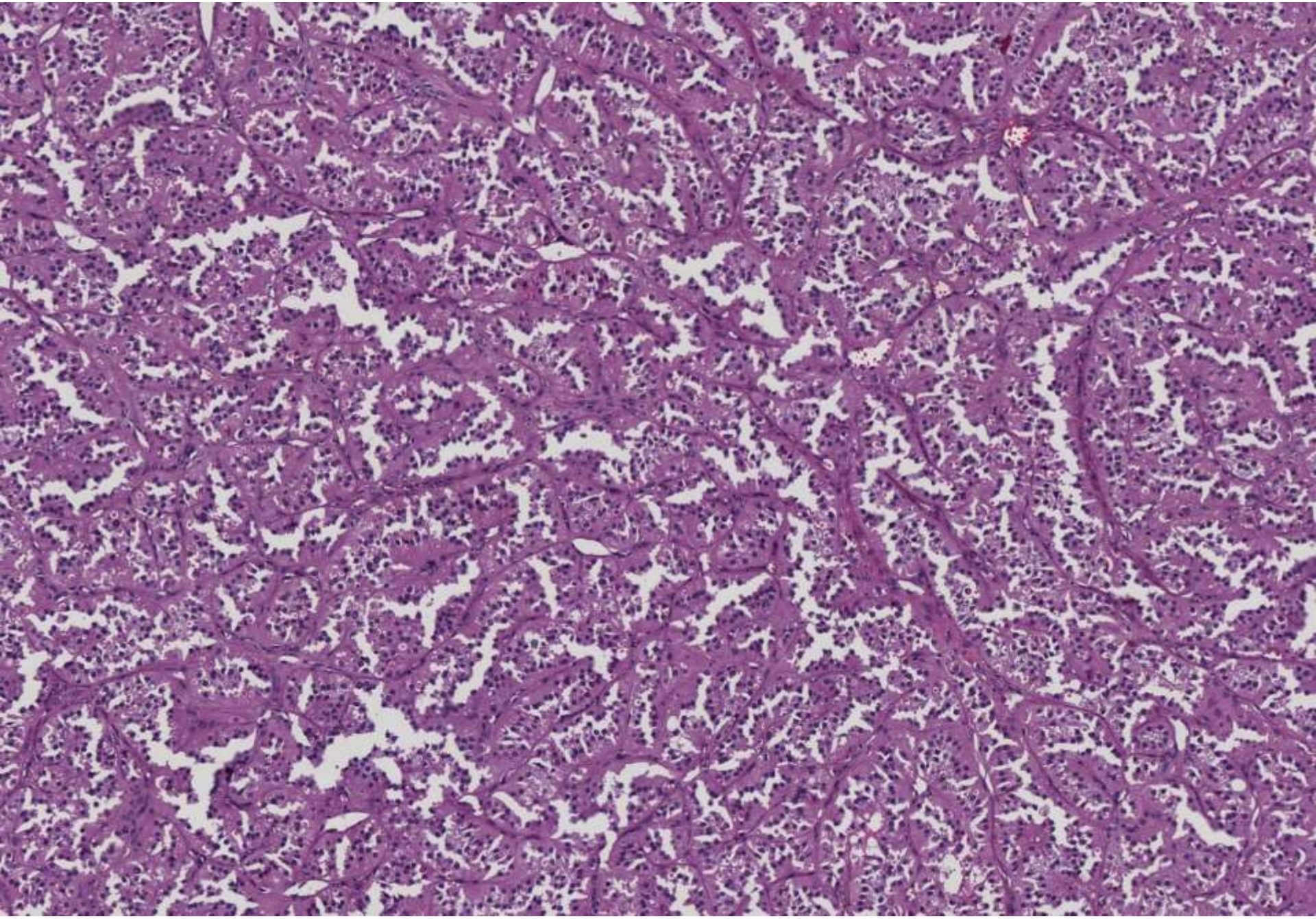
SB 6118
[scanned slide available]

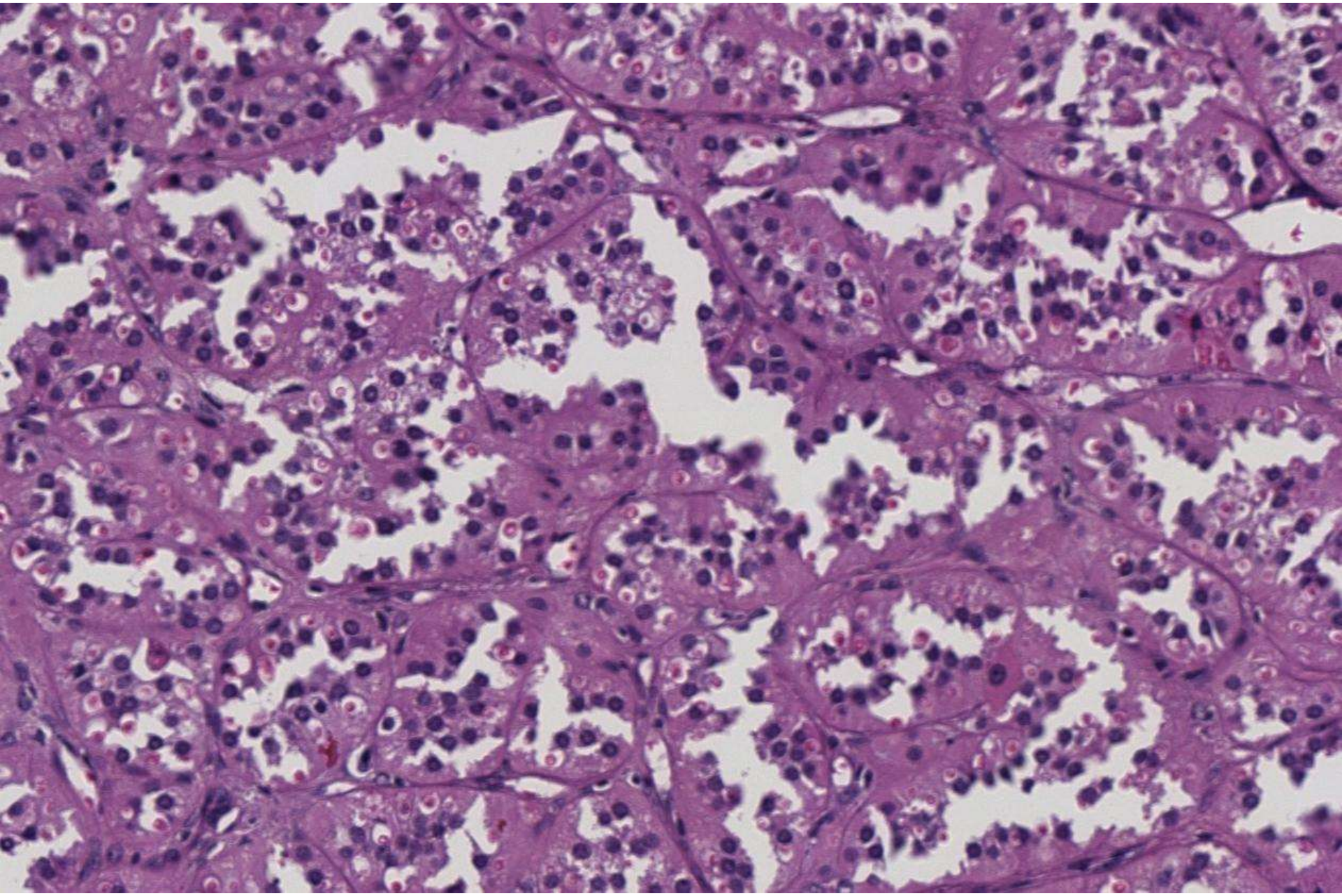
Ankur Sangoi; El Camino Hospital

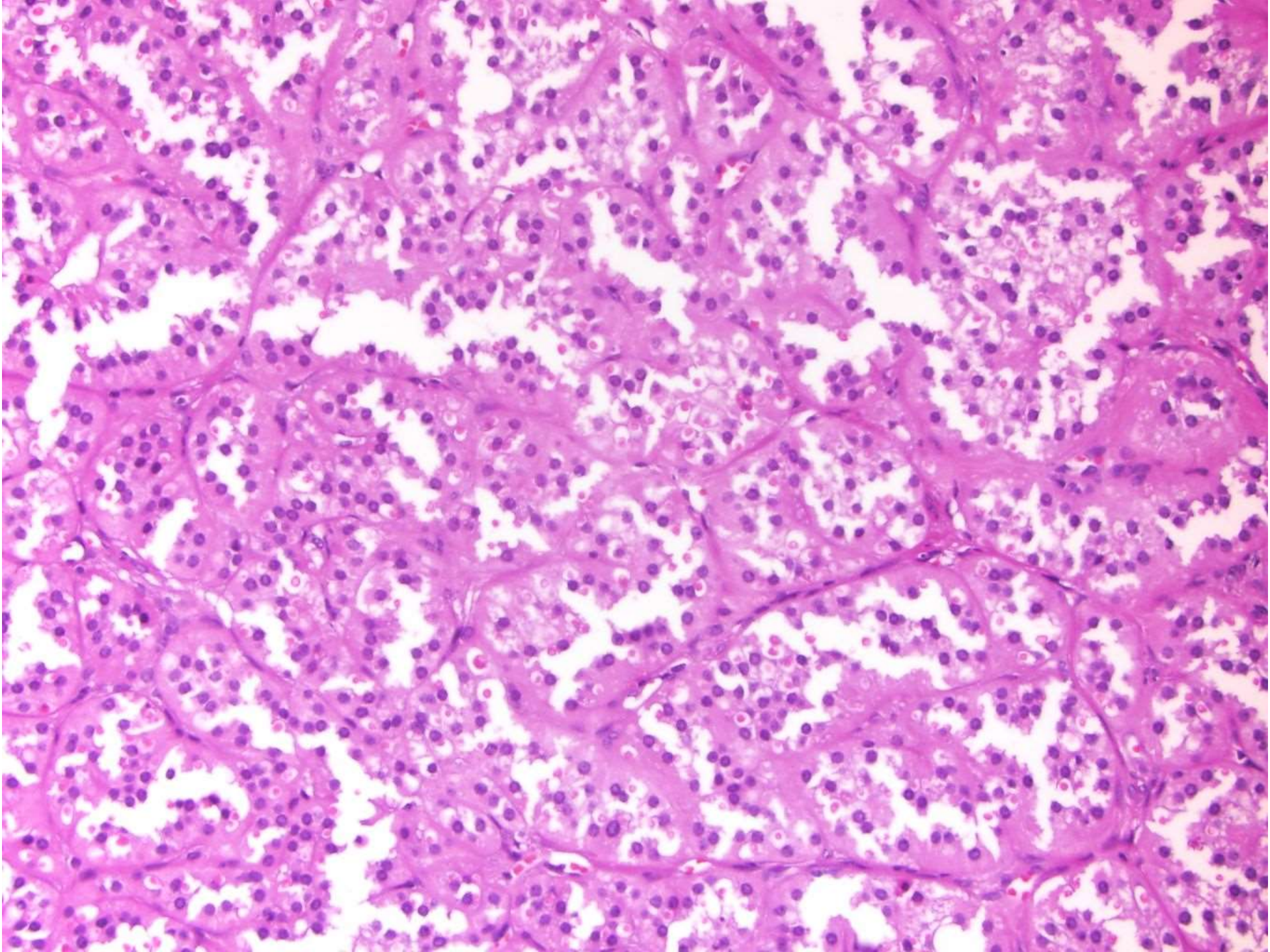
46-year-old male with left adrenal tumor.

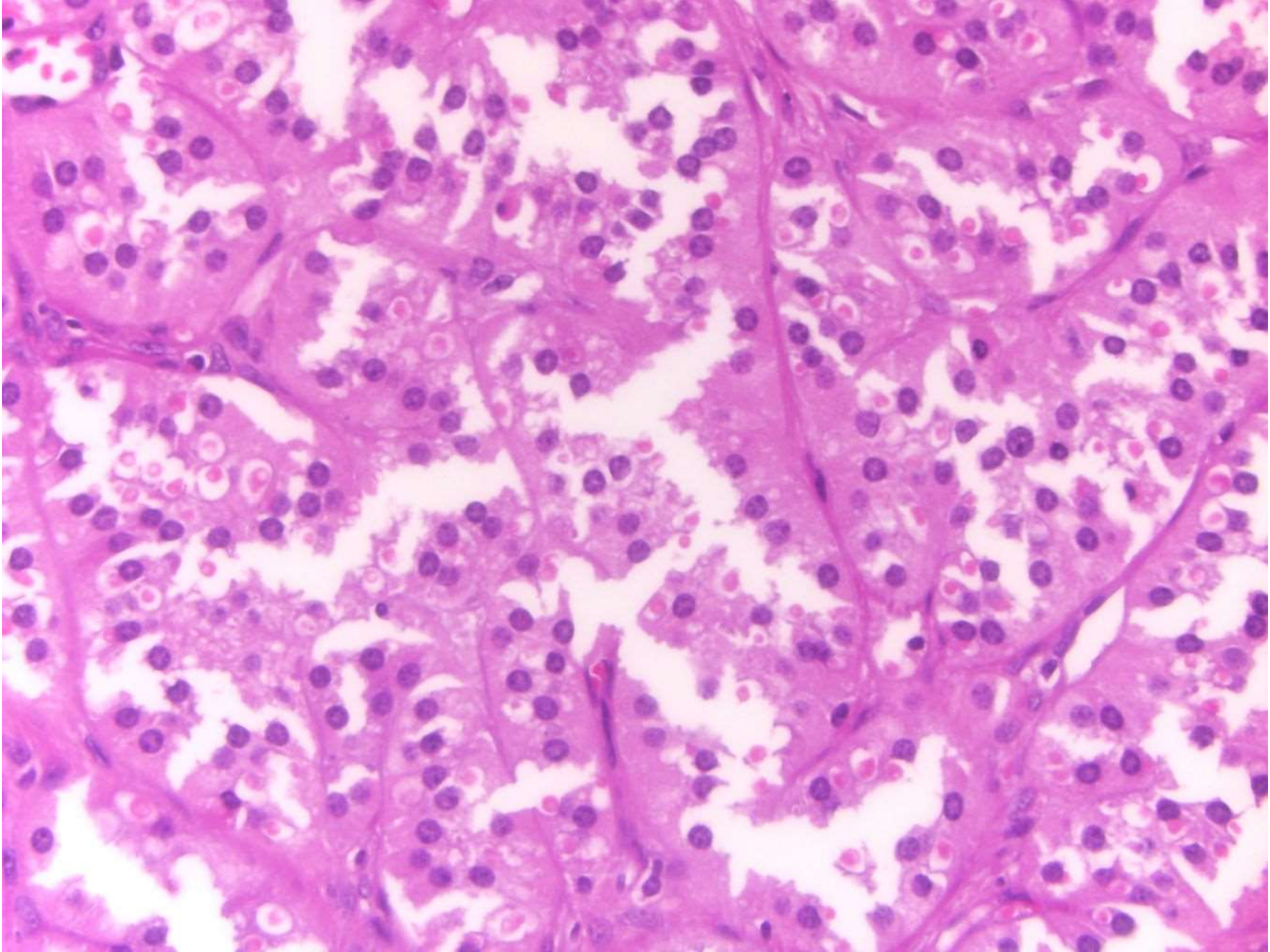


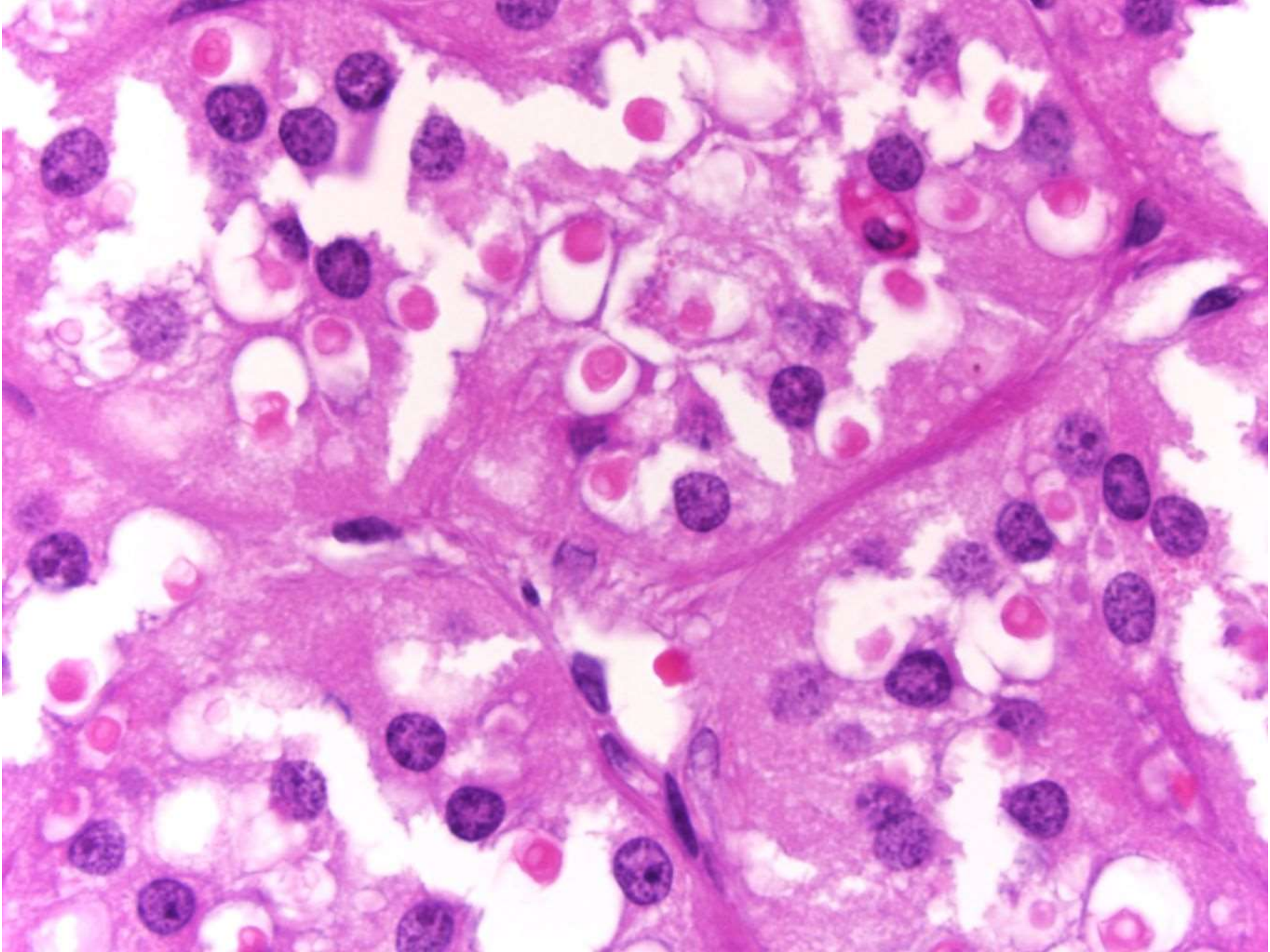












DIAGNOSIS

What Rx did this patient receive?

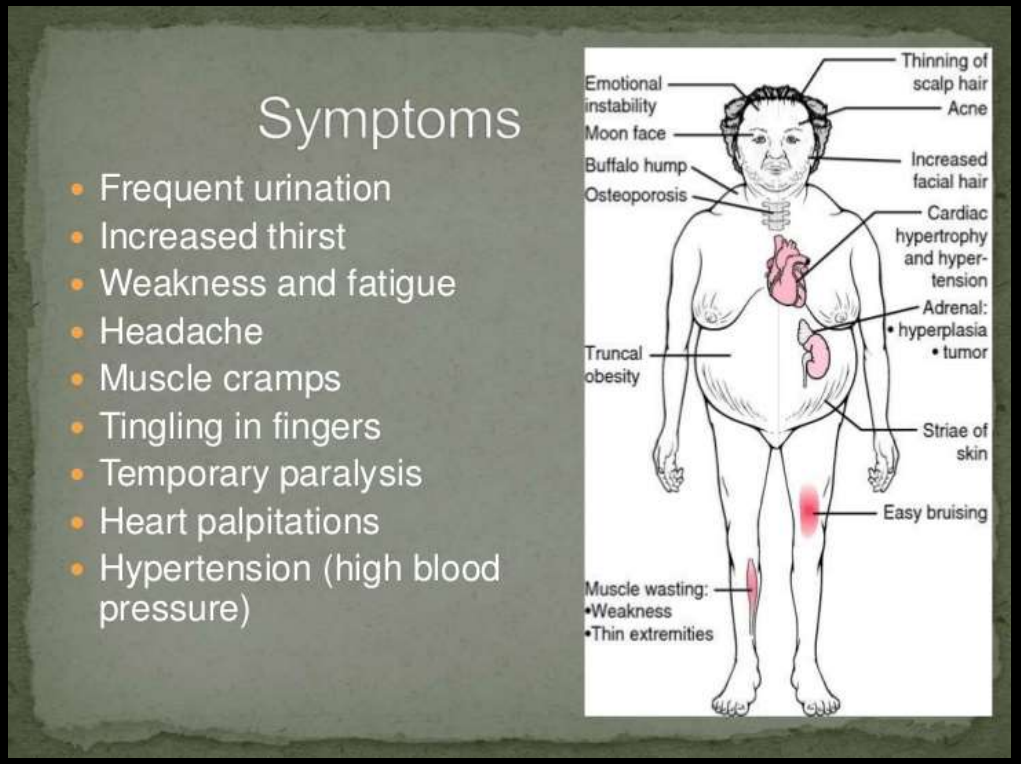
DIAGNOSIS:

- **Adrenal cortical adenoma**
  - With spironolactone bodies
    - Consistent with Conn's syndrome

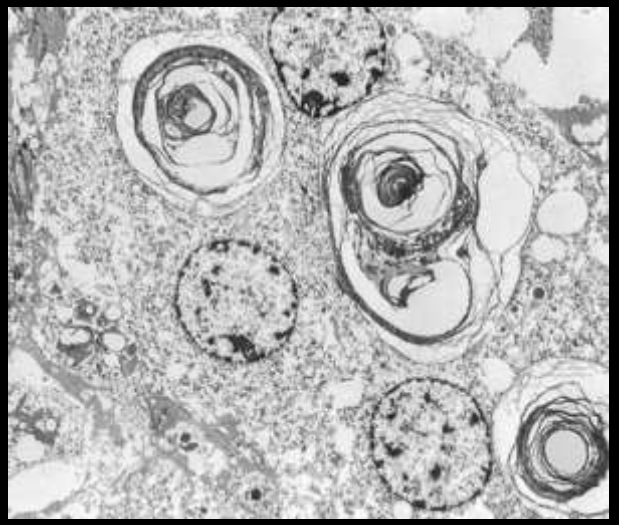
Spironolactone

- Aldosterone antagonist
- Used in treatment of Conn's syndrome

- Also used to treat HTN and adult acne



Spironolactone bodies



- Seen in patients Rx with spironolactone
- Concentric cytoplasmic bodies in lesional zona glomerulosa cells
- Stain + with anti-aldosterone antibody

Patel et al. Diagnostic Pathology 2014, 9:147
http://www.diagnosticpathology.org/content/9/1/147

DIAGNOSTIC PATHOLOGY

RESEARCH Open Access

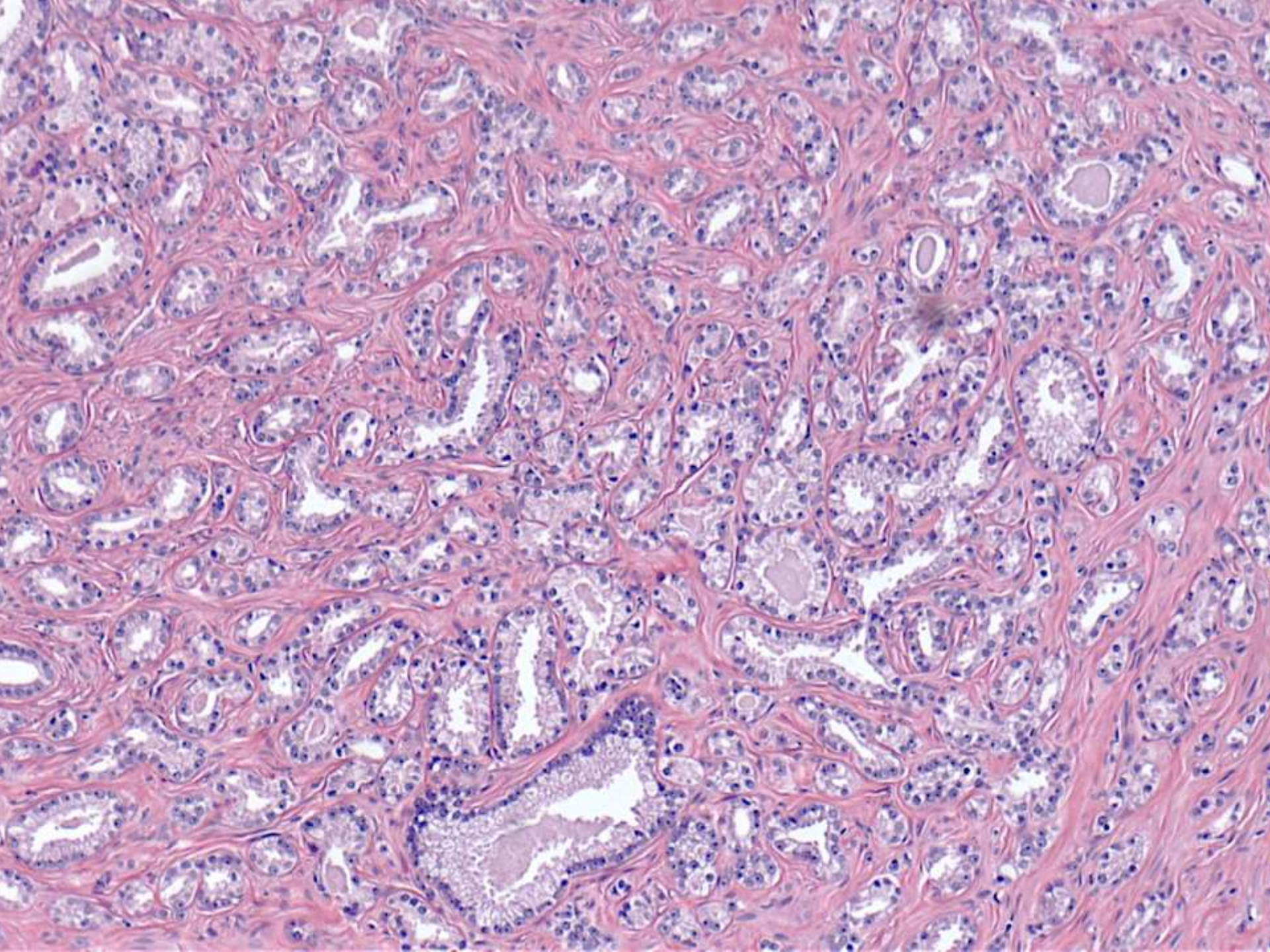
Adrenal gland inclusions in patients treated with aldosterone antagonists (Spironolactone/ Eplerenone): incidence, morphology, and ultrastructural findings

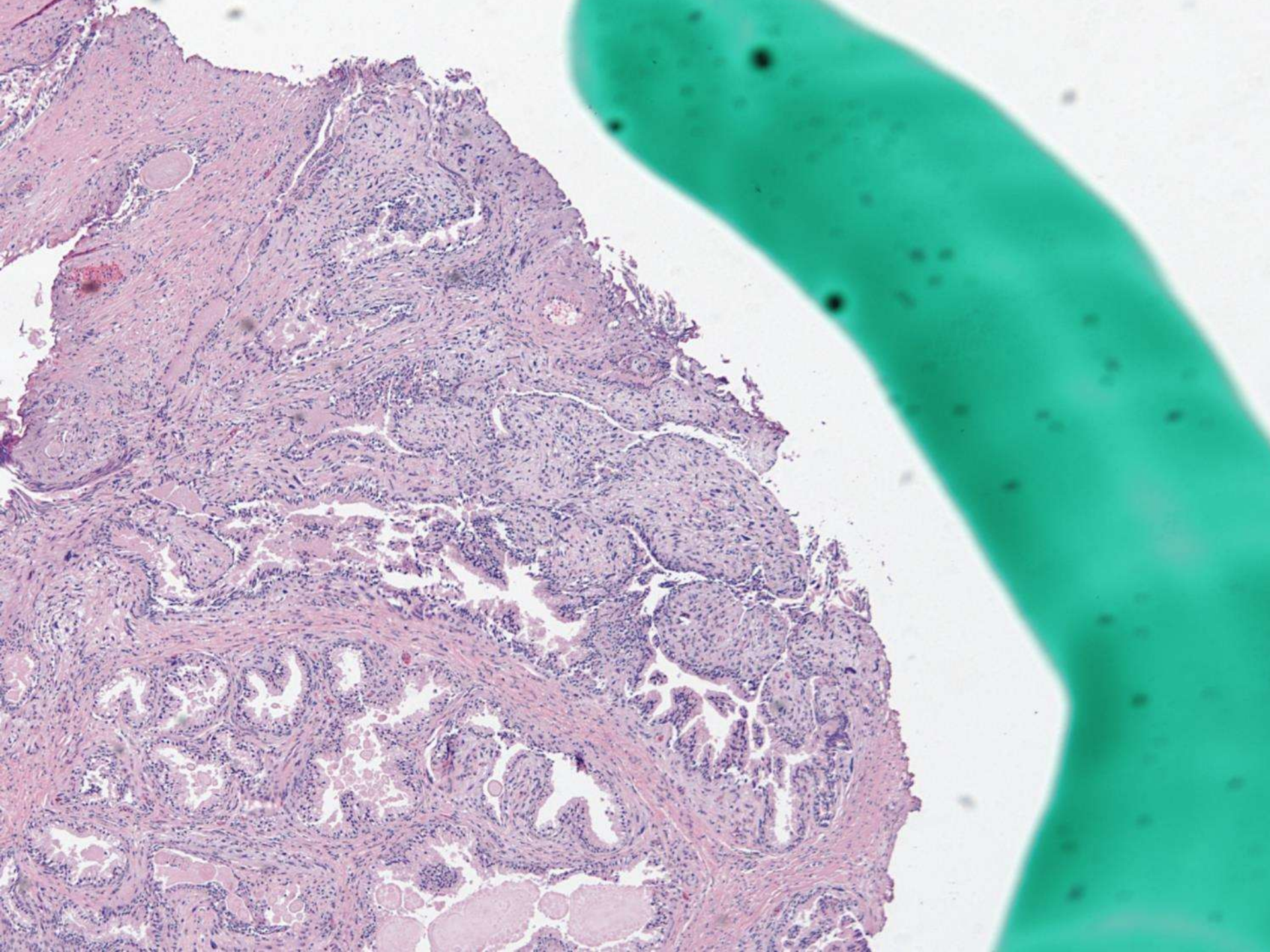
- **Bodies detected in only 33% of treated primary hyperaldosteronism patients (vs 74-100% previous literature)**
- **50% of patients Rx with spironolactone had inclusions vs 0% Rx with novel agent eplerenone only**
- **# of bodies seen peaks at 4-6 weeks after spironolactone Rx**
- **Mixed data on whether long-term Rx results in eventual absence of inclusion detection**

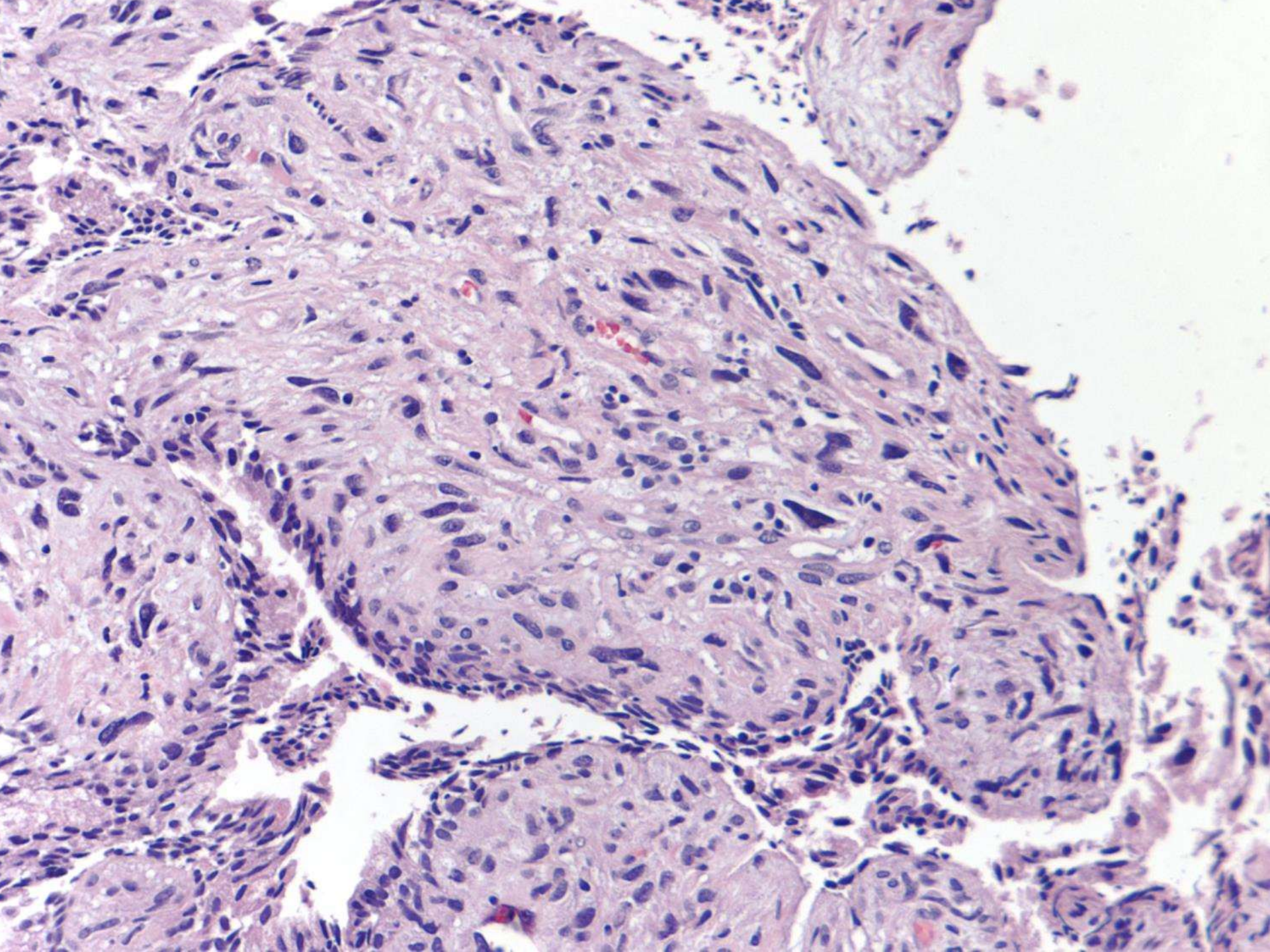
SB 6119

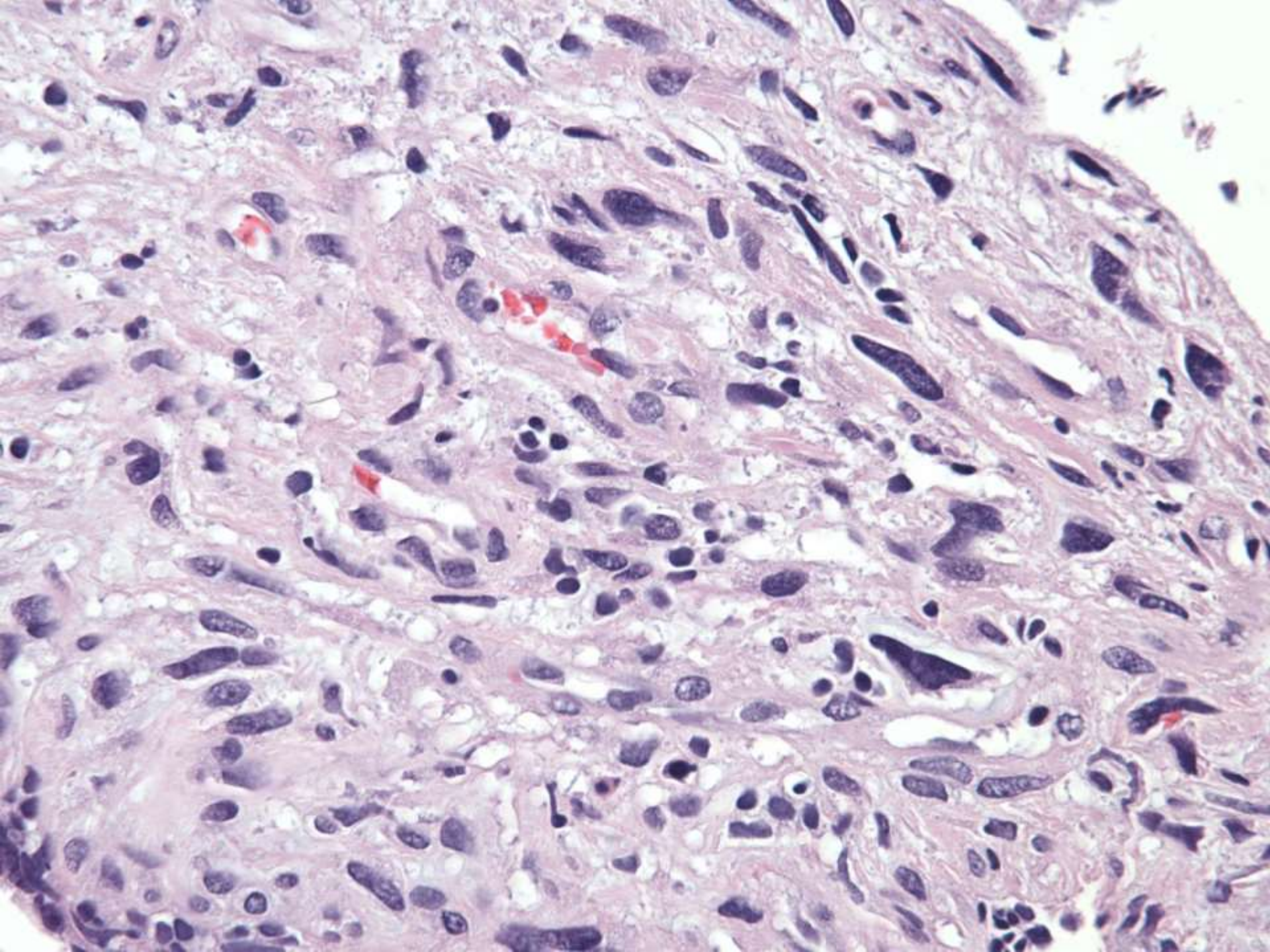
Allison Zemek/Sunny Kao; Stanford

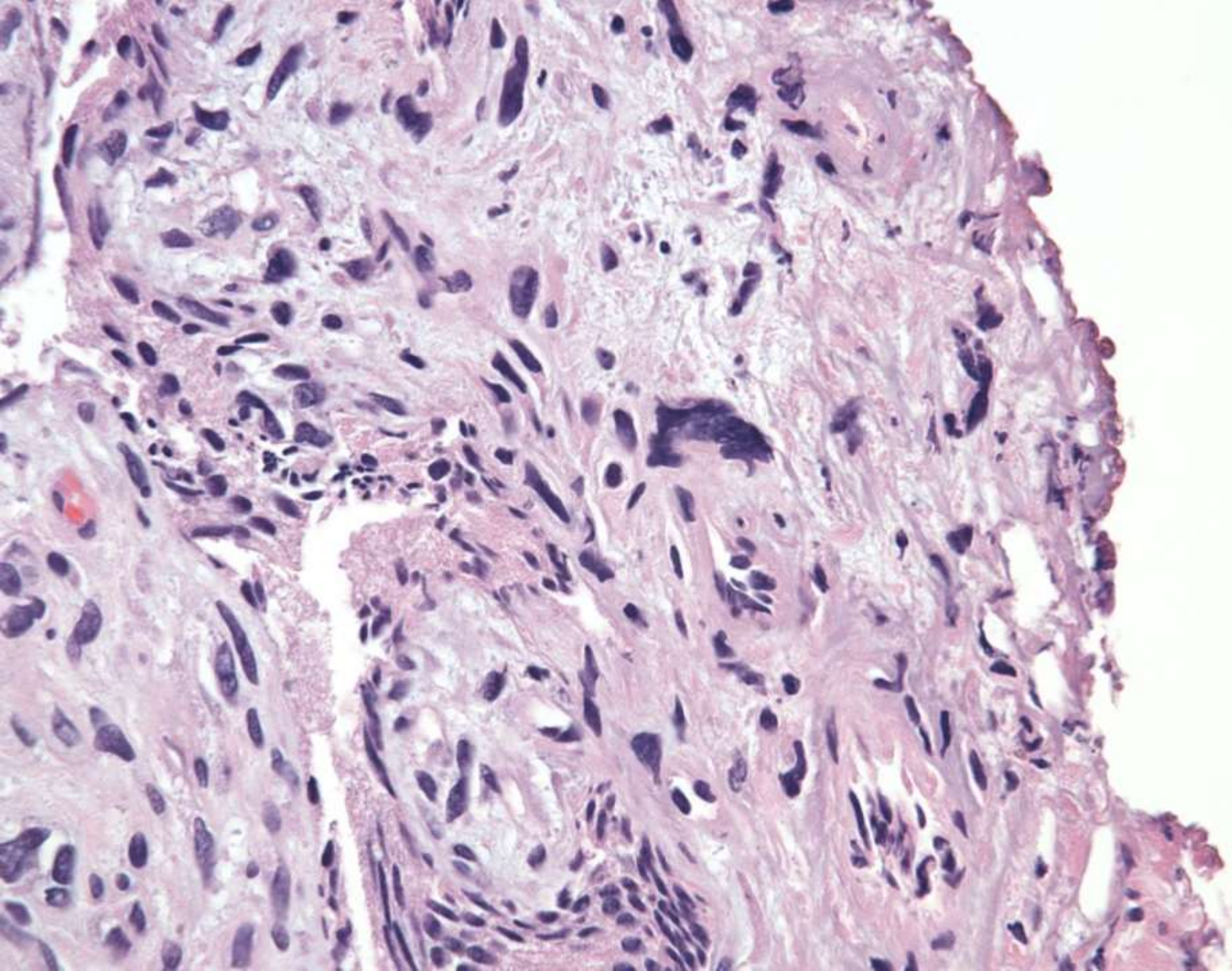
74-year-old male with BPH and lower urinary tract symptoms, TURP performed.



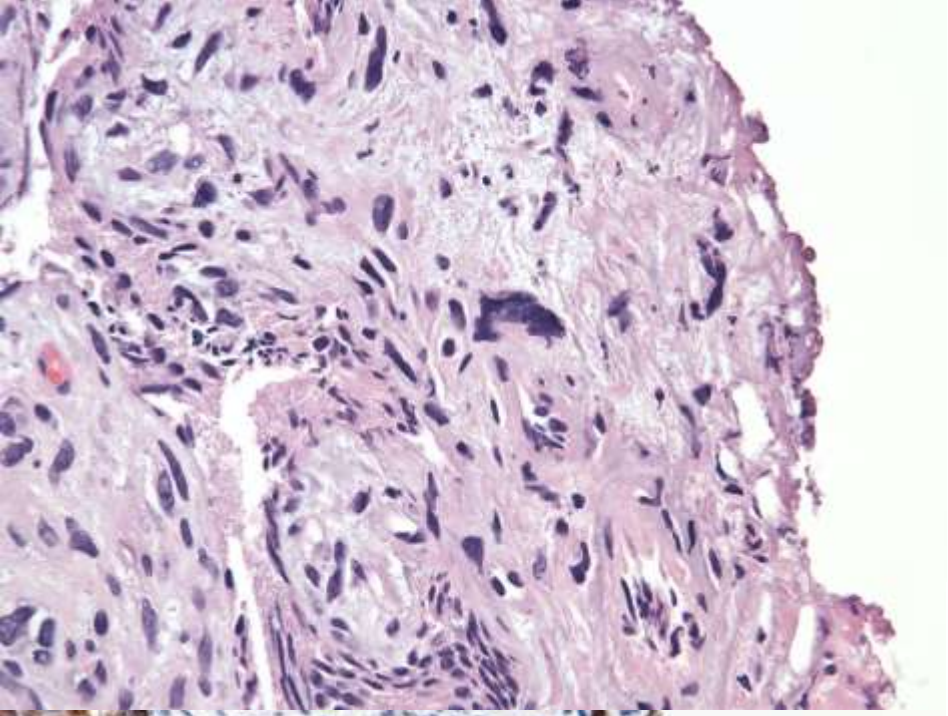


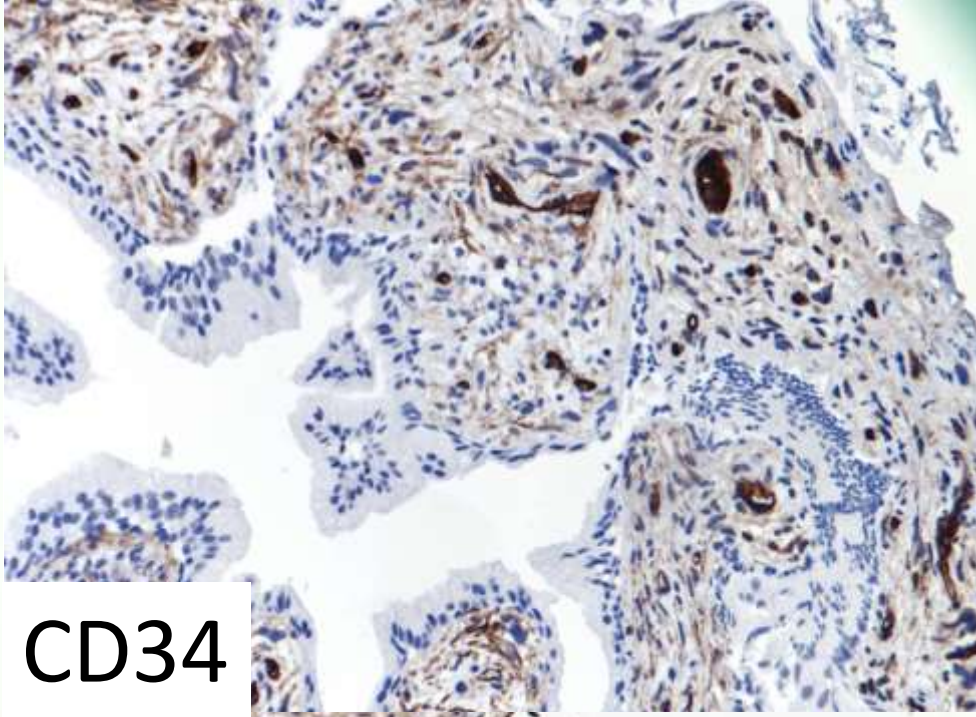




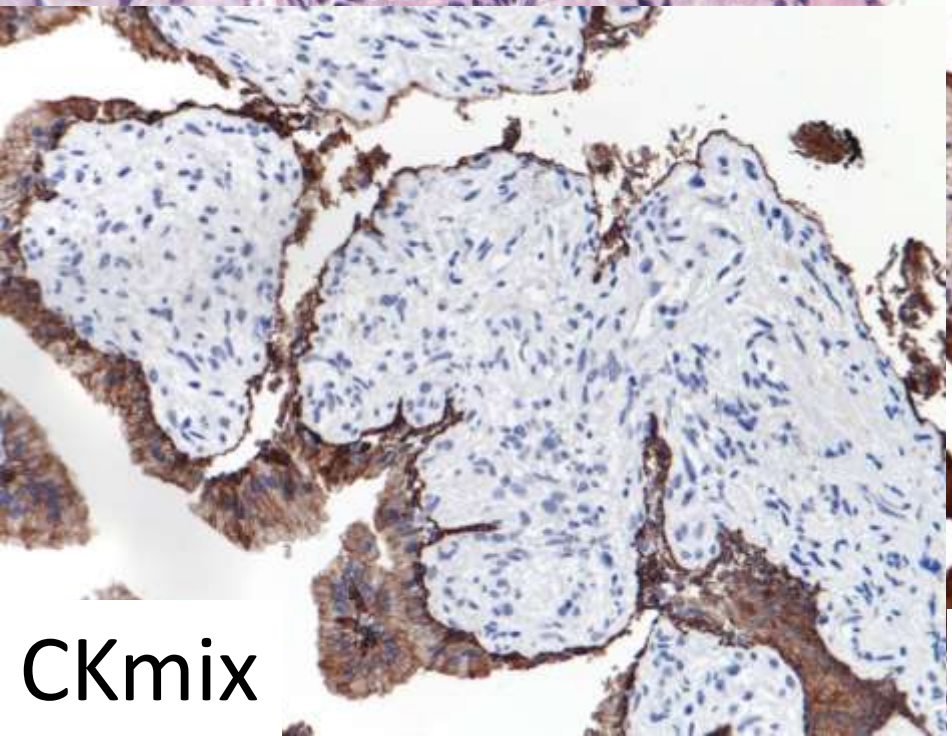


DIAGNOSIS

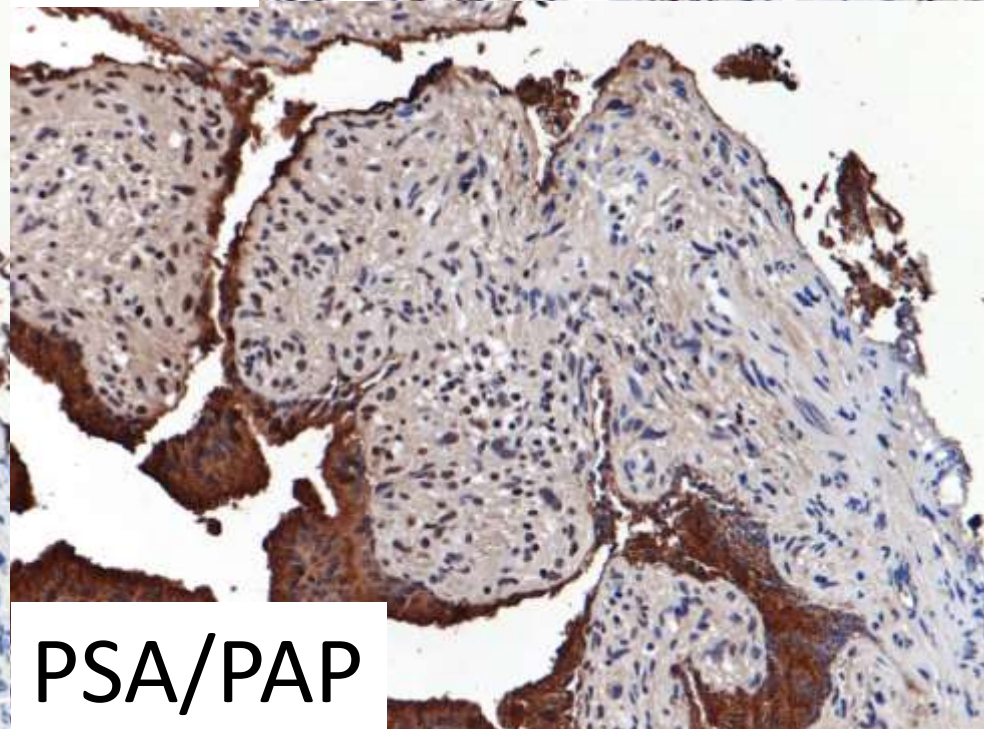




CD34



CKmix



PSA/PAP

Stromal Tumor of Uncertain Malignant Potential

Clinical features:

- Clinically heterogeneous, >60 yo
- Usually indolent
- Typically confined to prostate
- Can present as mass lesion

Pathogenesis:

- Most thought to have a benign clinical course
- Rare cases believed to progress to stromal sarcoma*

Stromal Tumor of Uncertain Malignant Potential

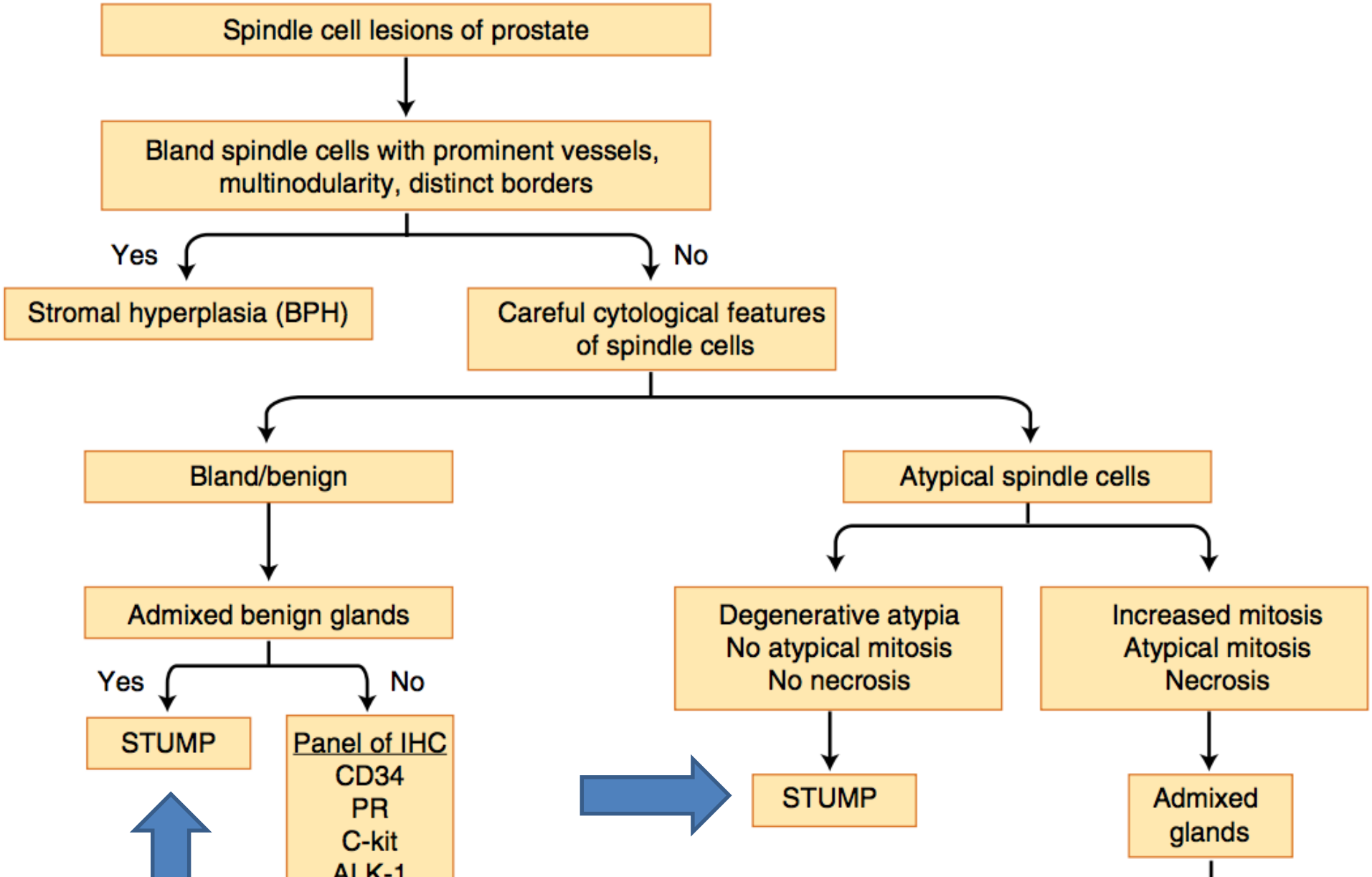
Histopathologic features:

- Mitosis and necrosis generally absent
- Five patterns:
  - Degenerative atypia (>50%)
  - Myxoid pattern
  - Phyllodes-type growth
  - Hypercellular stroma (subtle)
  - Epithelioid stroma (subtle)

Immunohistochemical features:

+ for CD34, PR, vimentin, desmin, SMA

STUMP: a broad category



Other spindle cell lesions

	CD34	PR	ER	CD117	ALK	SMA	Desm	Myog
STUMP	+	+	±	-	-	±	±	-
Stromal sarcoma	+	+	±	-	-	-	-	-
IMT	-	-	-	±	+	+	+	-
SFT	+	±	-	-	-	-	-	-
GIST	+	-	-	+	-	±	±	-
Leiomyosarcoma	-	±	±	-	-	+	+	-
Rhabdomyo-sarcoma	-	-	-	-	-	+	+	+

Stromal Tumor of Uncertain Malignant Potential

Treatment:

- Radical prostatectomy with negative surgical margins
- If older patients, close observation

Prognosis:

- Surgery thought to be curative

Follow up:

- Additional imaging (MRI)

References

1. Rare Genitourinary Tumors. Lance Pagliaro. Springer 2016.

2. Prostate Biopsy Interpretation: An Illustrated Guide. Rajal Shah, Ming Zhou. Springer 2016.

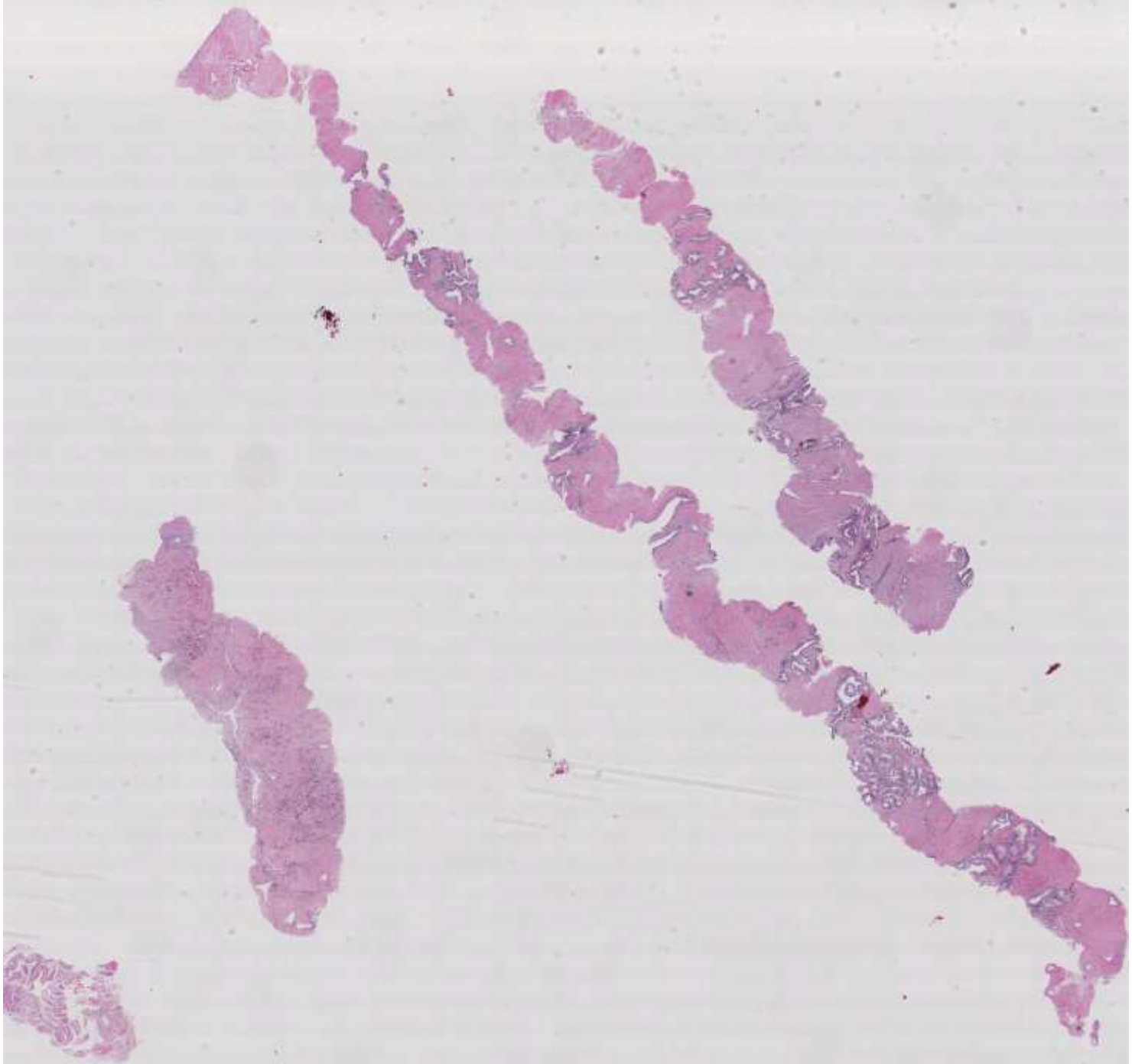
3. Specialized Stromal Tumors of the Prostate: A Clinicopathologic Study of 50 Cases Mehsati Herawi, MD, PhD* and Jonathan I. Epstein, MD* Am J Surg Pathol 2006;30:694–704

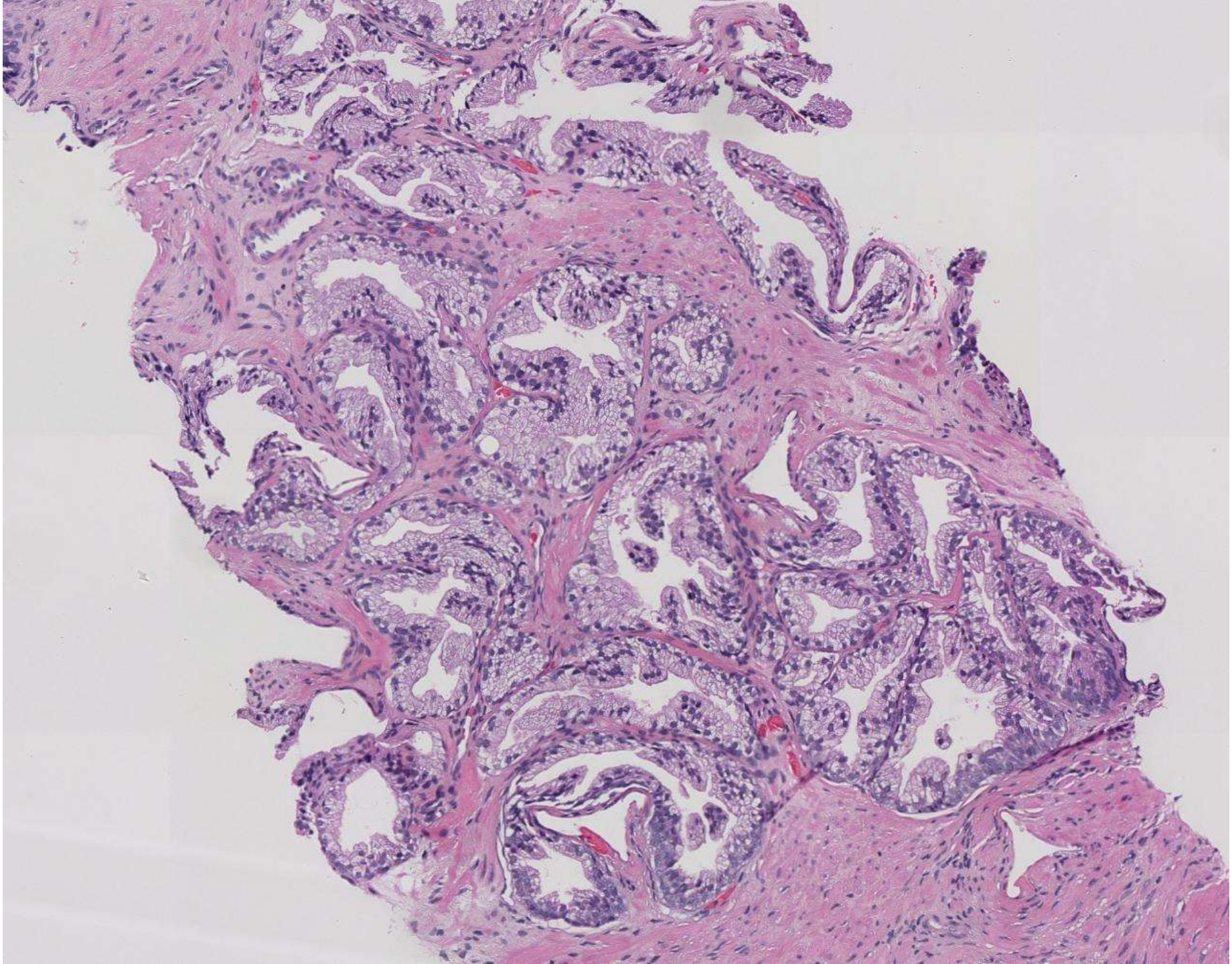
4. Non-epithelial neoplasms of the prostate. Paner et al. Histopathology 2012; 60:166-186

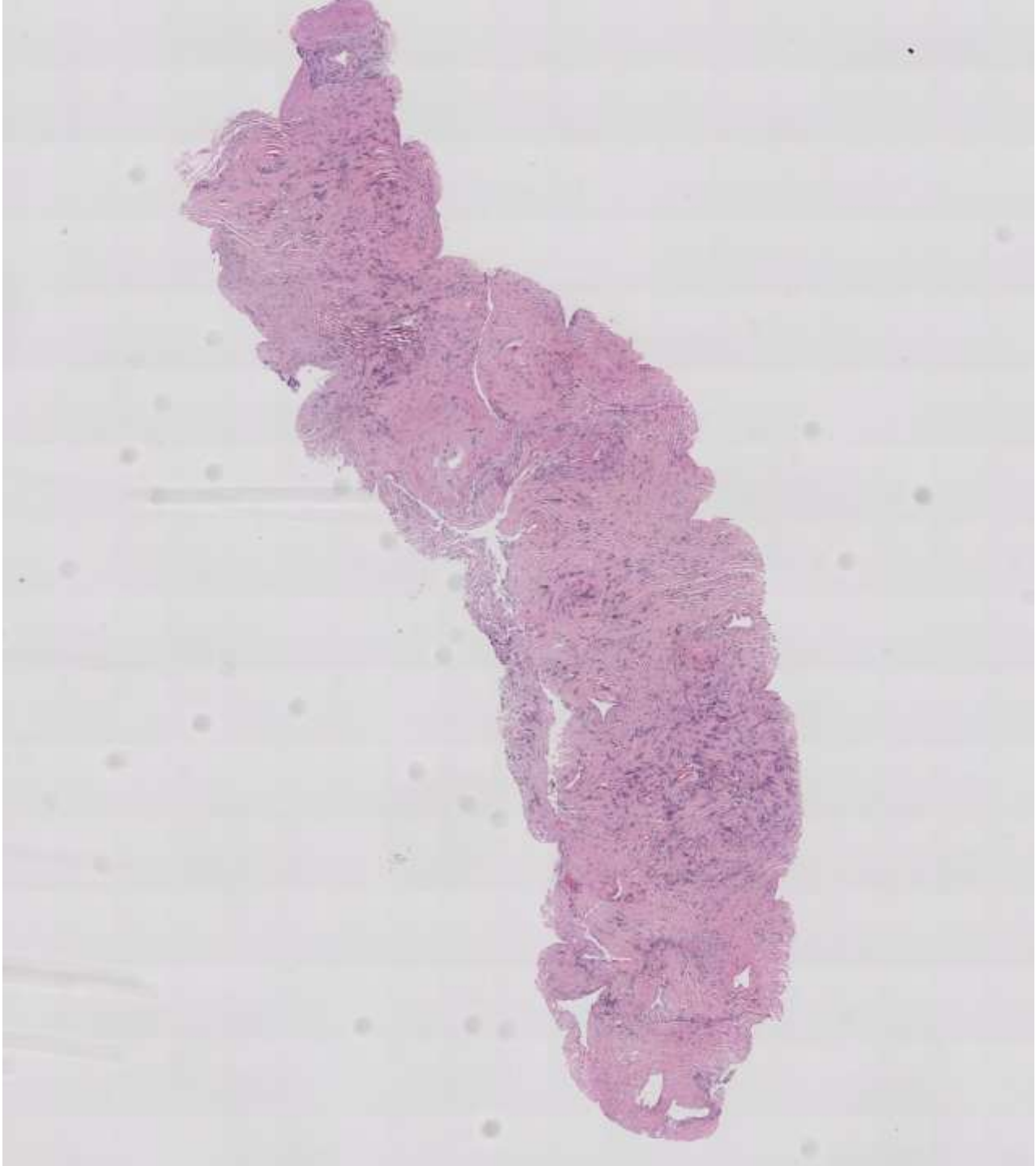
SB 6120
[scanned slide available]

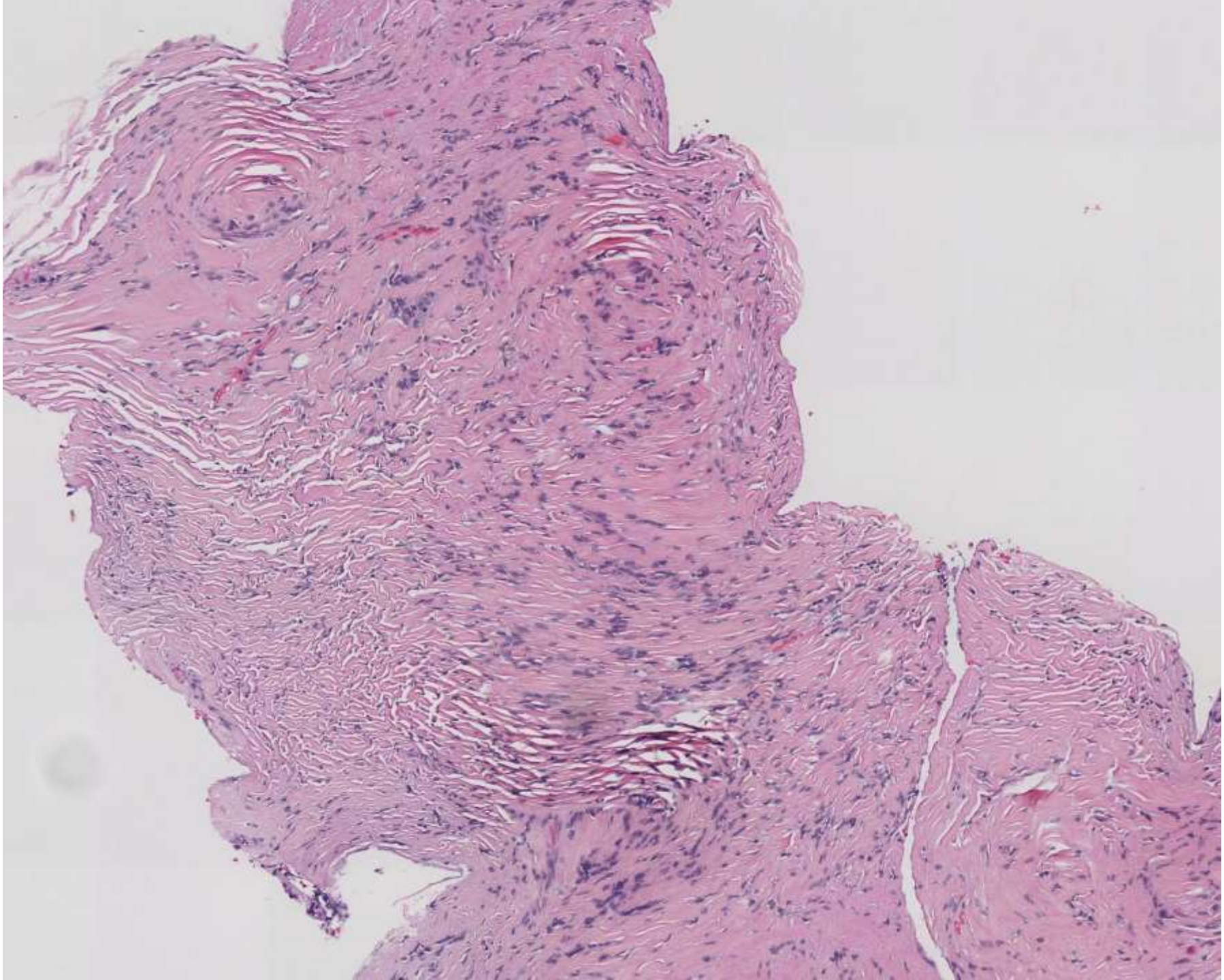
Ankur Sangoi; El Camino Hospital

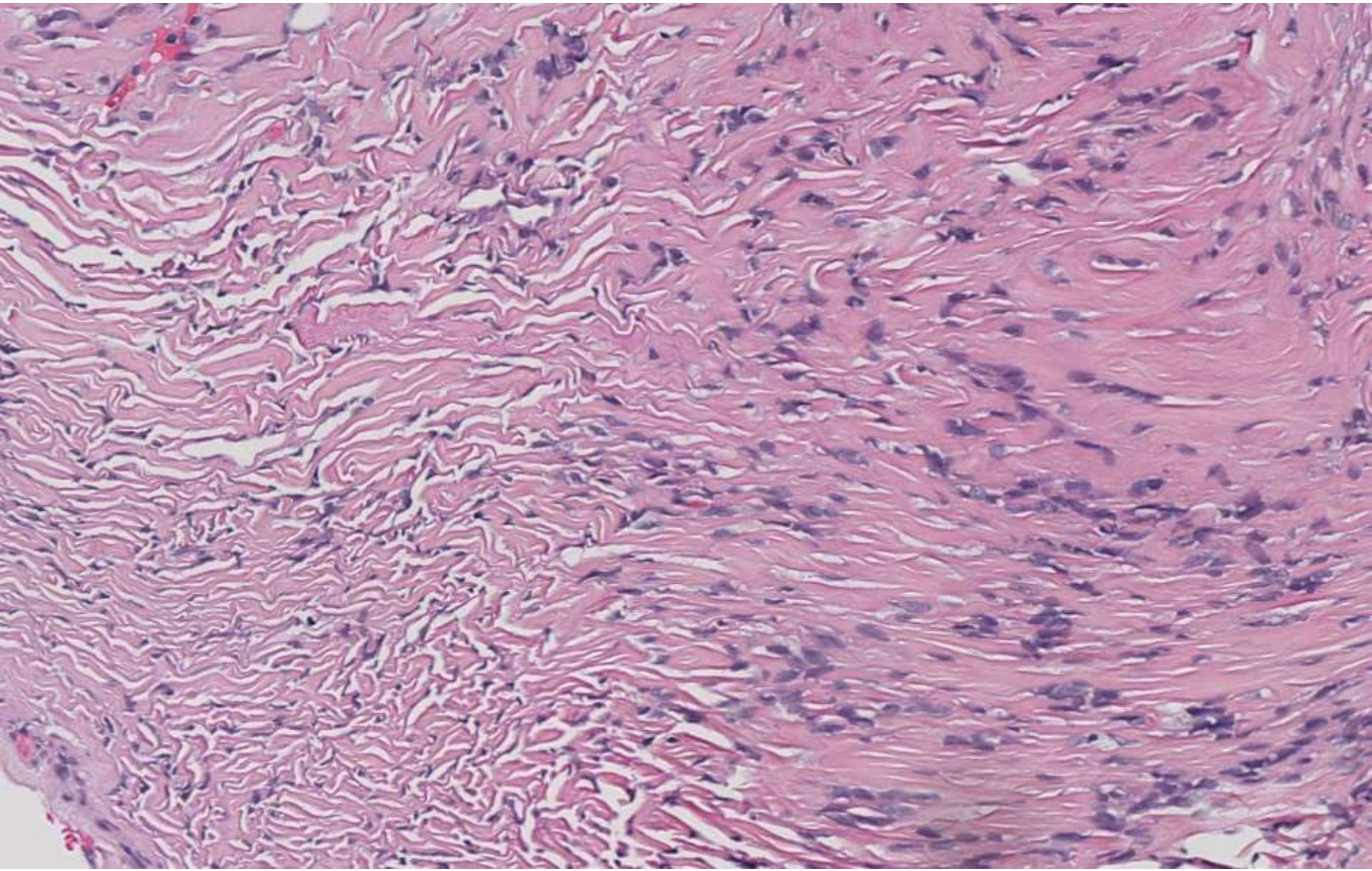
40-year-old male with PSA 0.3 and nodular prostate, biopsy performed.

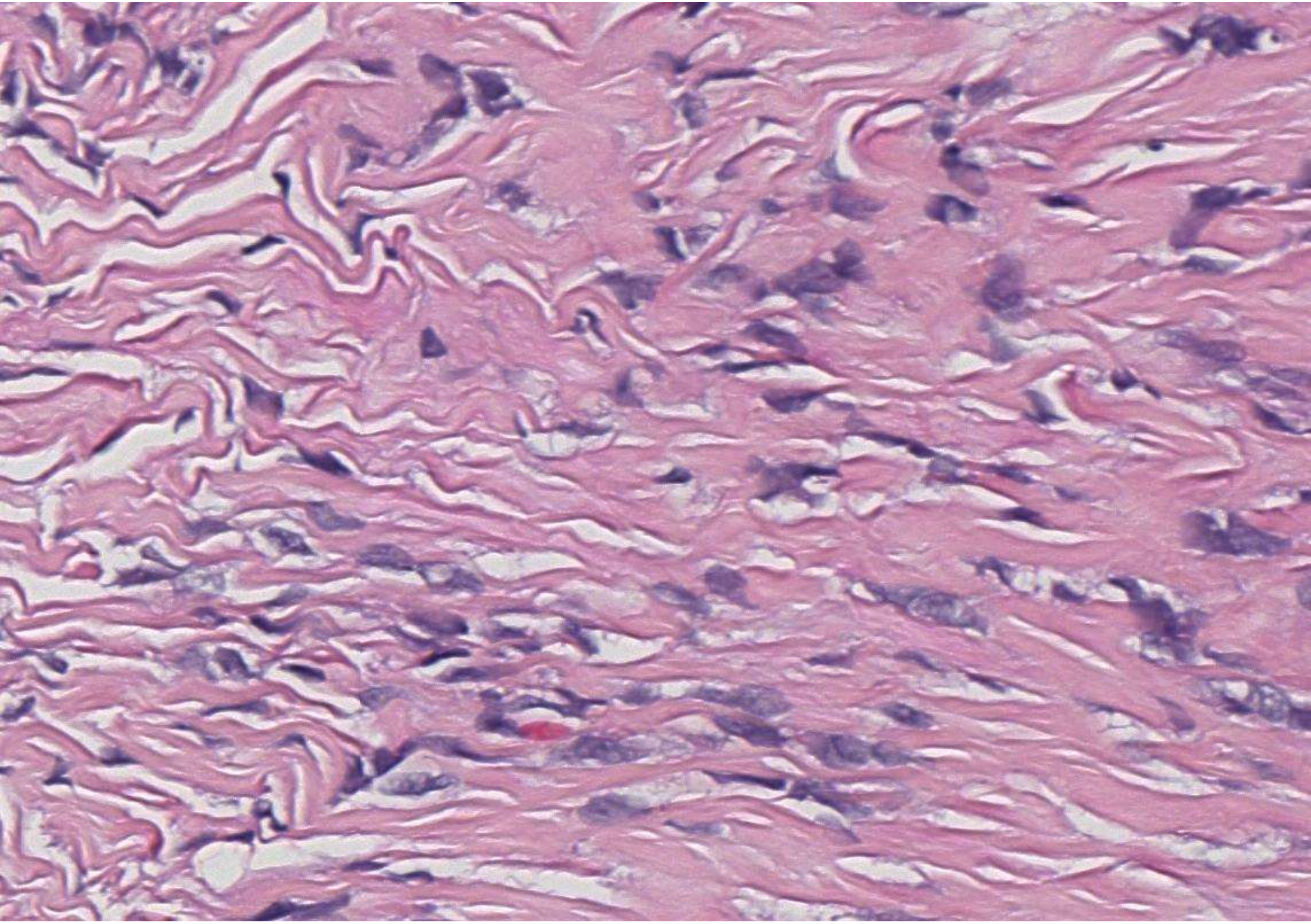


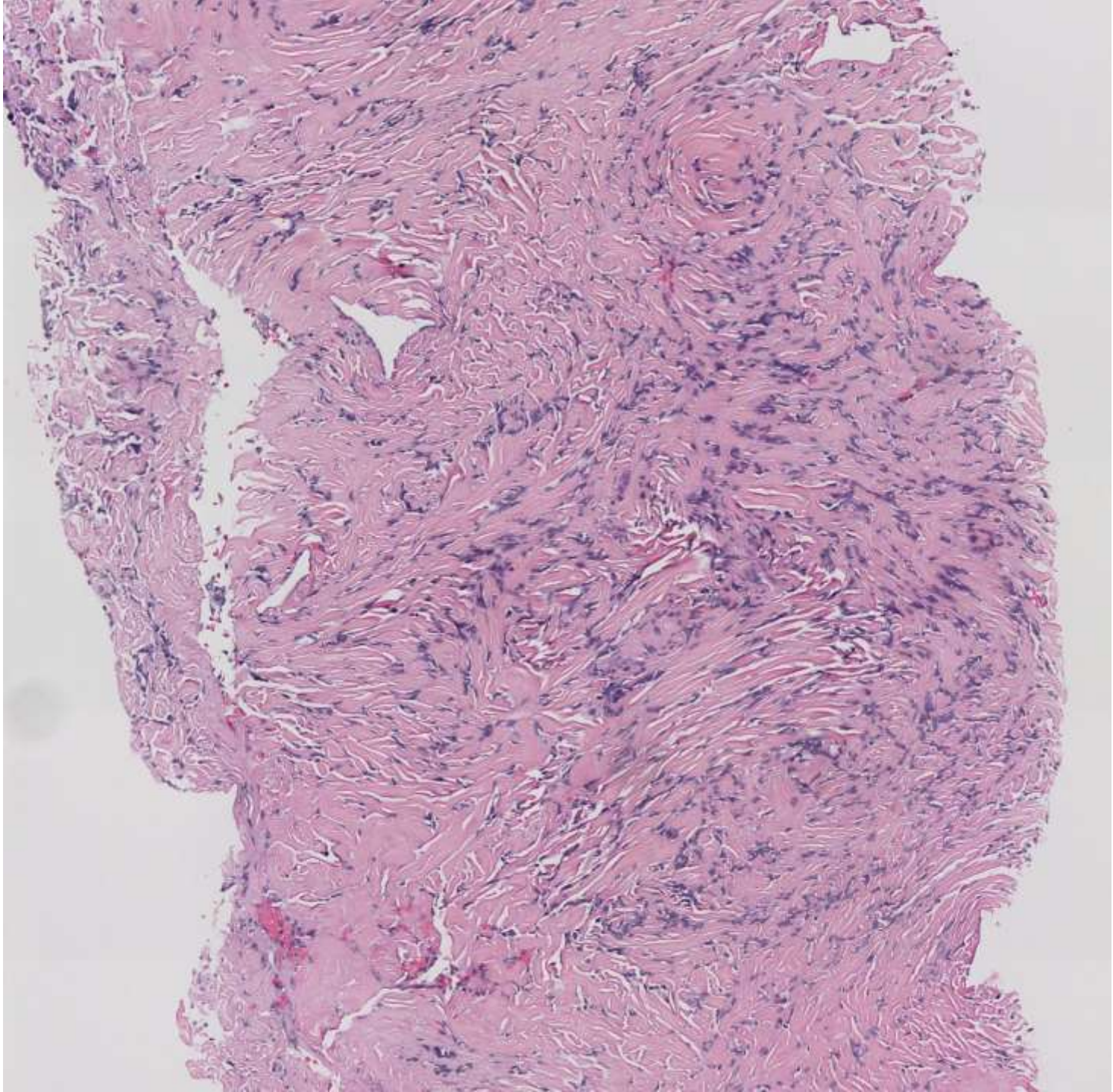


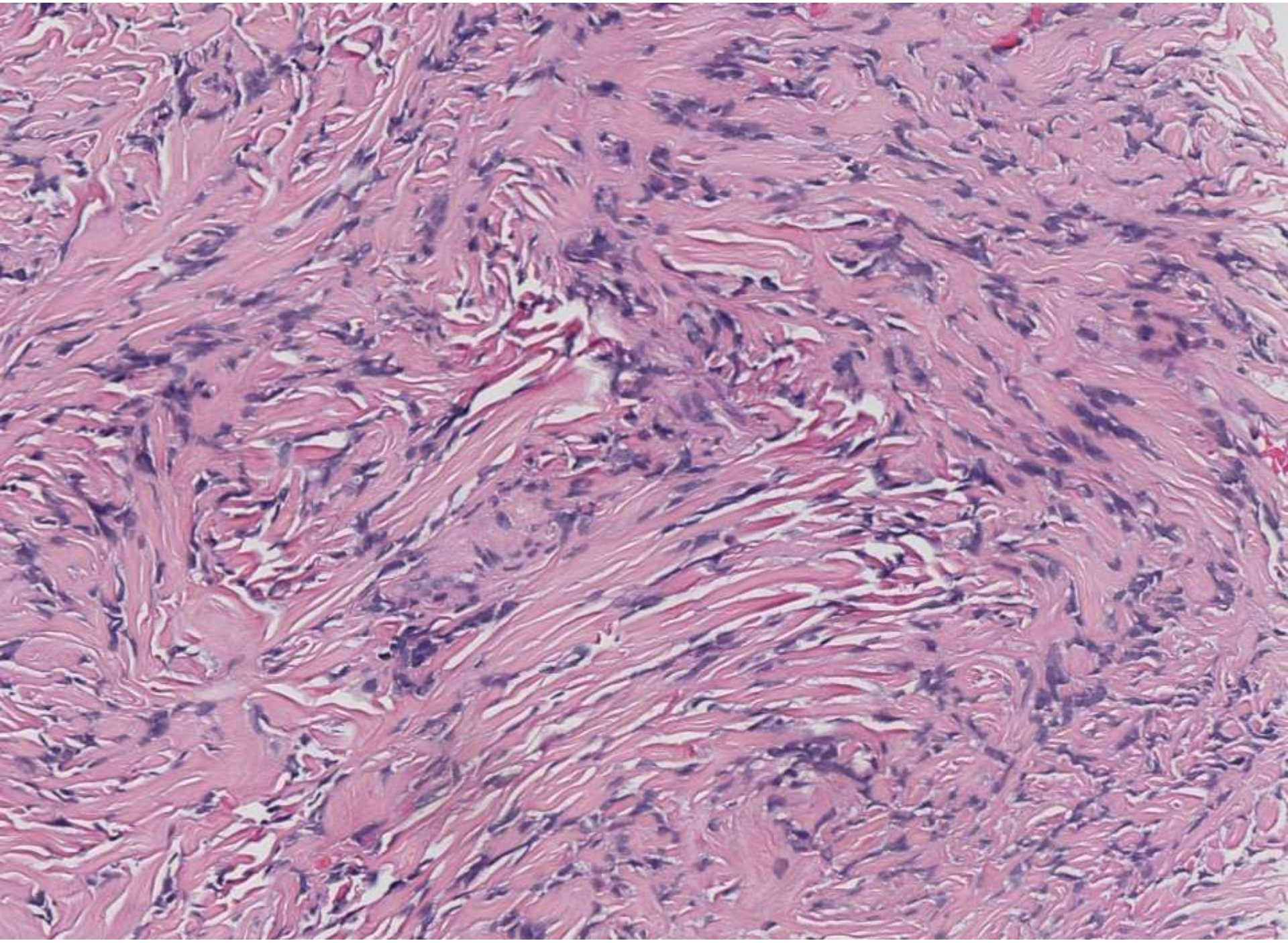










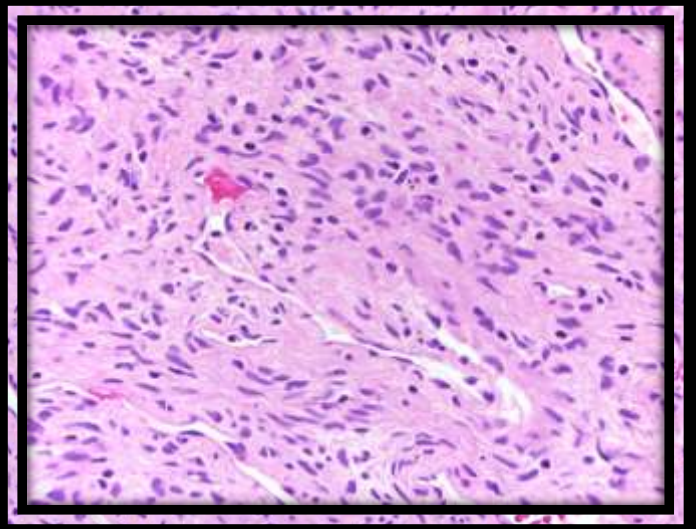


DIAGNOSIS

2010 DDx

- **BPH nodule**
- **Prostatic stromal sarcoma**
- **Prostatic stromal tumor of uncertain malignant potential (STUMP)**
- **Neural tumor**
  - Neurofibroma vs schwannoma
- **Solitary fibrous tumor (SFT)**
- **Inflammatory myofibroblastic tumor (IMT)**
- **Leiomyoma**
- **Gastrointestinal stromal tumor (GIST)**

BPH nodule



IHC (2010)

- CD34: positive (strong)
- PR: positive (moderate)
- BCL2: positive (moderate)
- Desmin: positive (moderate)
- CD117: negative
- Pankeratin: negative
- S100: negative
- p63: negative
- CK5: negative

2010 DIAGNOSIS

- **Prostate, left mid and base, bx:**
  - Prostatic stromal proliferation of uncertain malignant potential (PSPUMP)

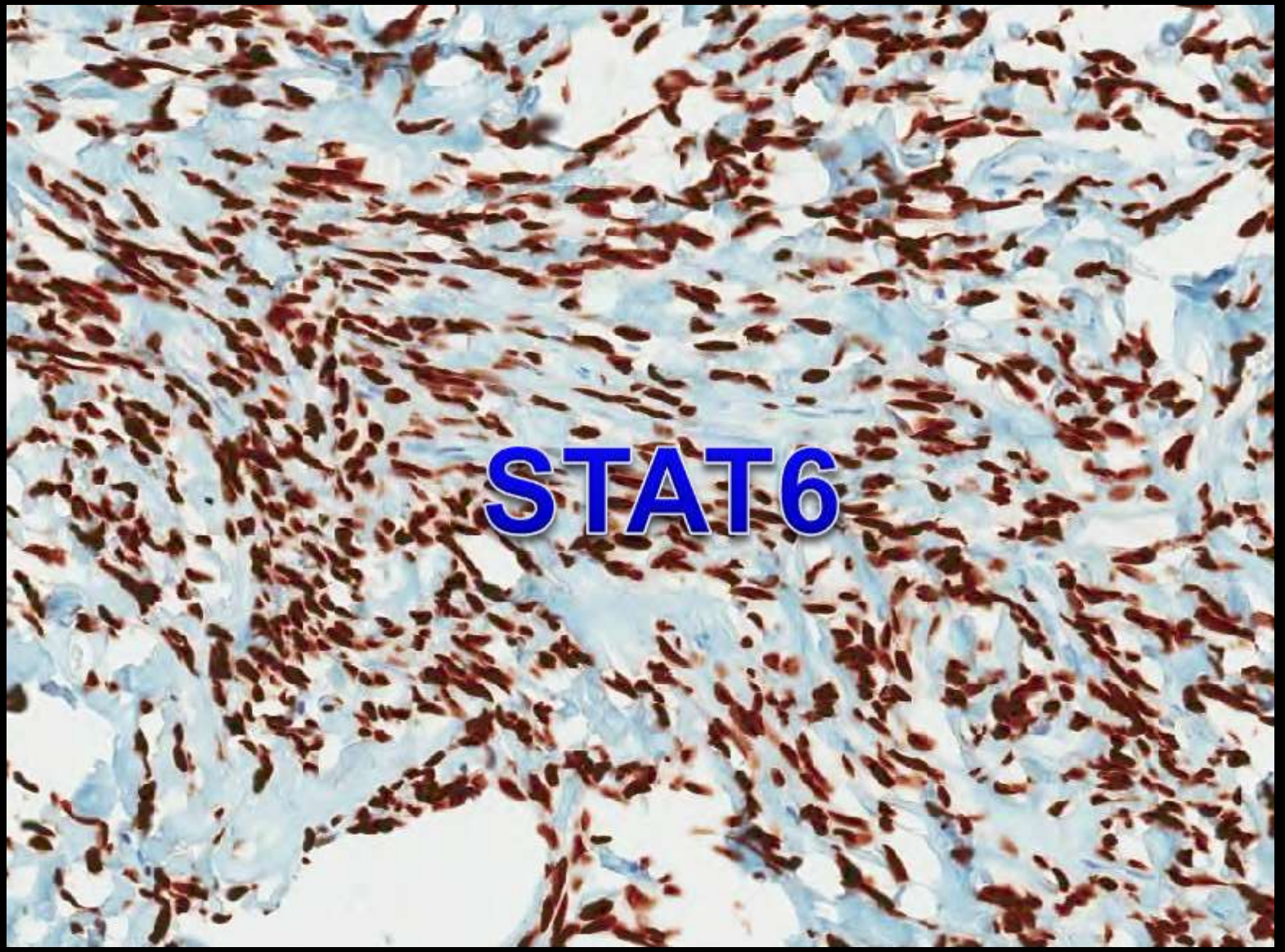
- **Prostate, right mid and base, bx:**
  - Benign prostatic glands and stroma

2010 DIAGNOSIS

- **Prostate, TUR:**
  - Prostatic stromal proliferation of uncertain malignant potential (PSPUMP)

2014 DIAGNOSIS

- **Prostate, TUR:**


STAT6

2014 DIAGNOSIS

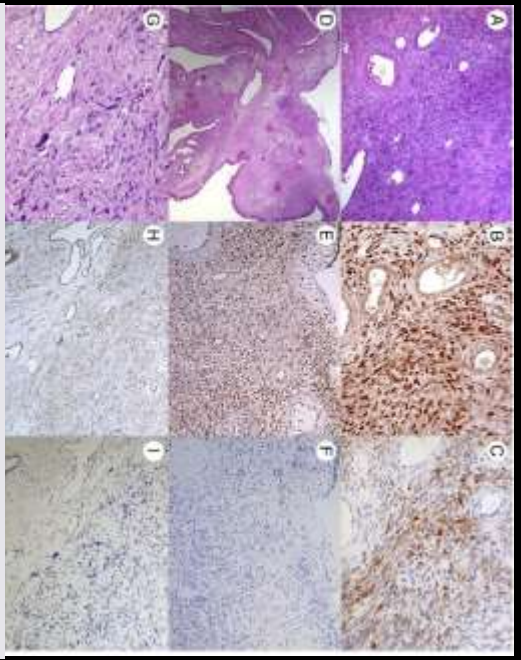
- **Prostate, TUR:**
  - Consistent with solitary fibrous tumor

The utility of STAT6 and ALDH1 expression in the differential diagnosis of solitary fibrous tumor versus prostate-specific stromal neoplasms☆,☆☆,★

Human Pathology (2016) **54**, 184–188

Table 1 Staining properties of SFT, STUMP, and PSS

	SFT (%)	STUMP (%)	Stromal sarcoma (n)
STAT6 (+)	10/11 [a] (91)	4/16 (25)	0/4 (0)
ALDH1 (+)	10/12 (83.3)	3/15 [b] (20)	2 (50)
STAT6 (+) ALDH1 (−)	0 (0)	4/15 [b] (27)	0 (0)
STAT6 (−) ALDH1 (+)	0 (0)	3/15 [b] (20)	2 (50)
STAT6 (+) ALDH1 (+)	10/11 [a] (91)	0 (0)	0 (0)
STAT6 (−) ALDH1 (−)	1/11 [a] (9)	8/15 [b] (53)	2 (50)

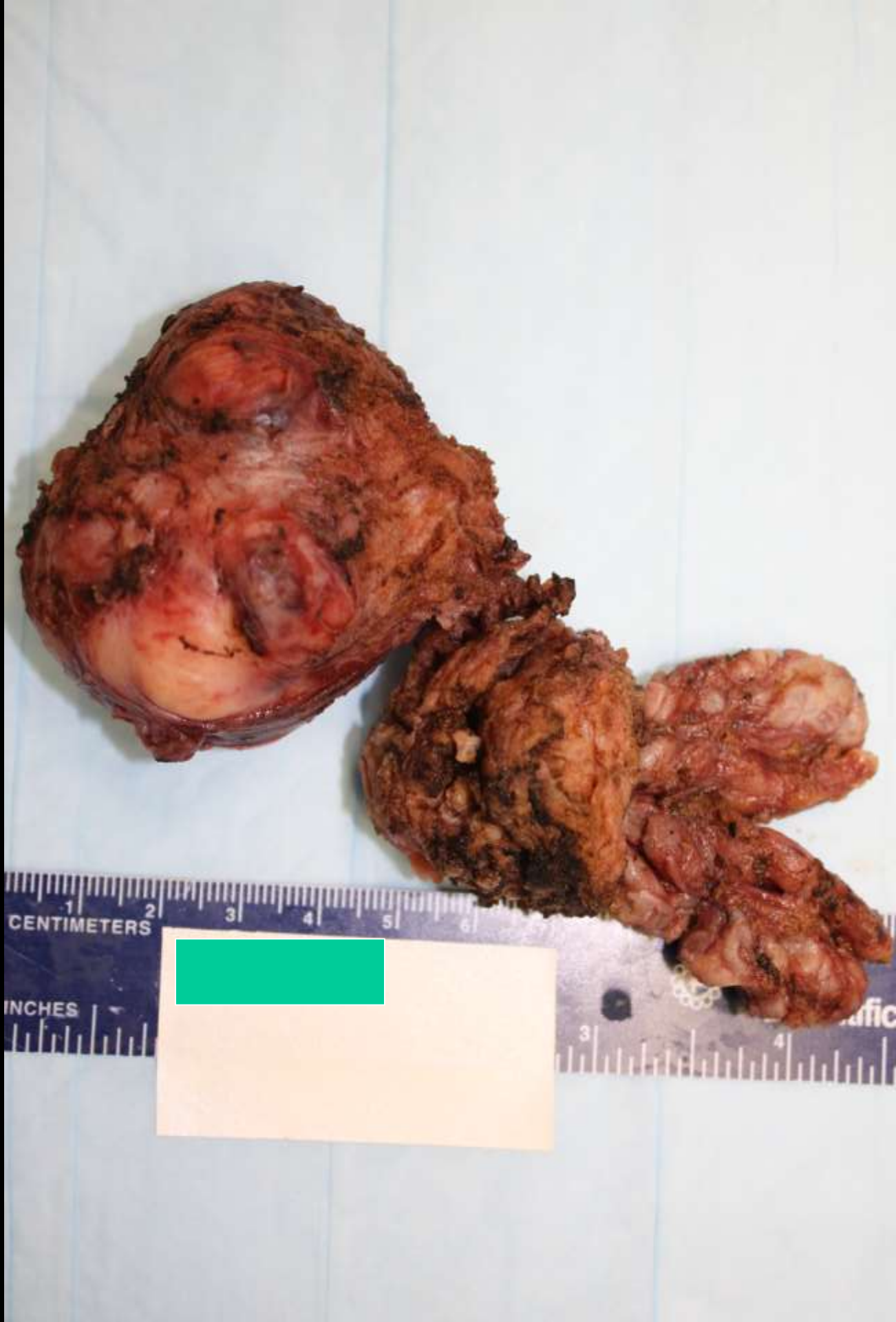


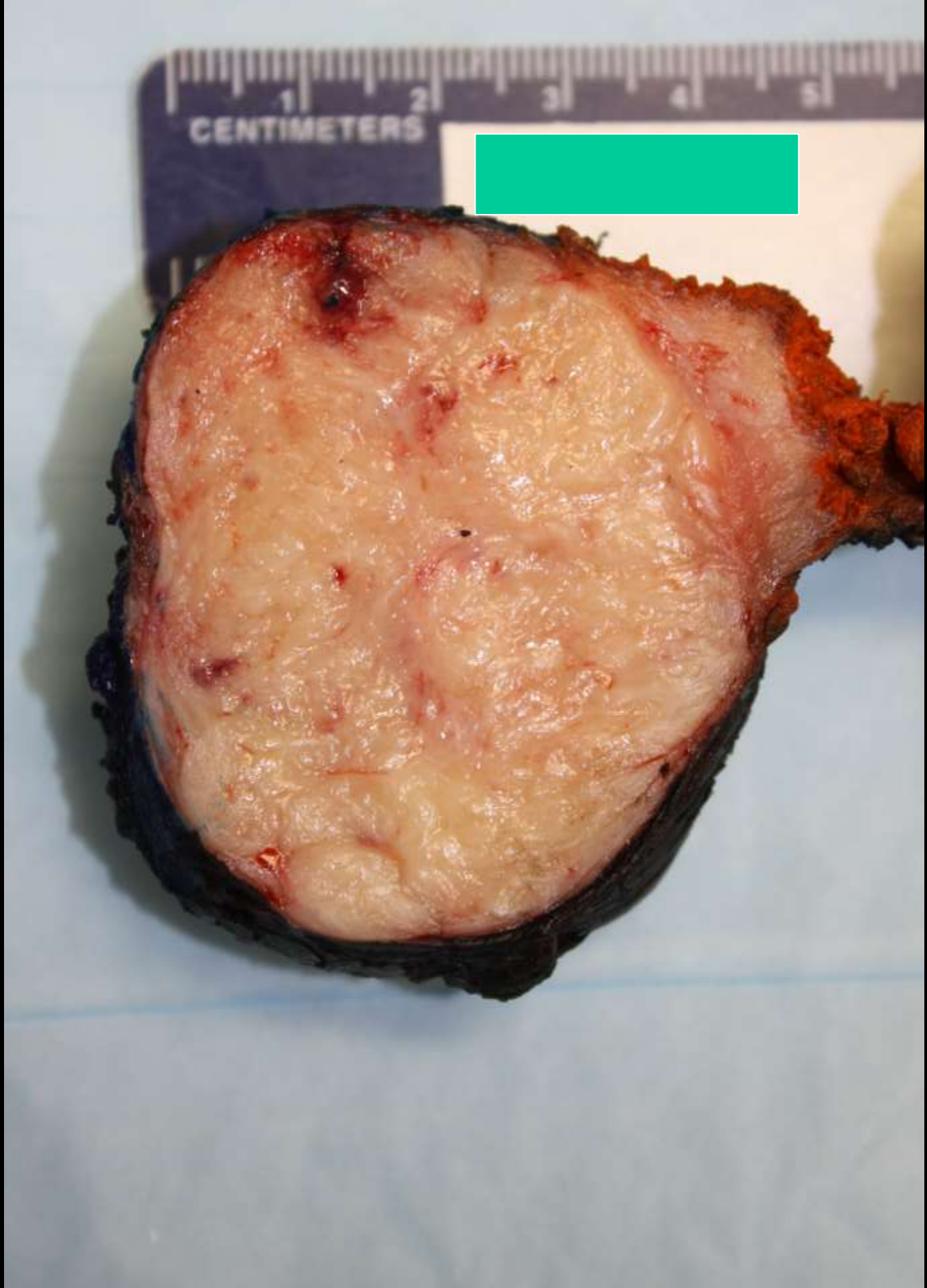
2014 DIAGNOSIS

- **Prostate, simple prostatectomy:**
  - Solitary fibrous tumor
    - 5.5cm, low mitotic rate

    →"Low risk"

Demicco EG et al. Solitary fibrous tumor: a clinicopathological study of 110 cases and proposed risk assessment model. Mod Pathol. 2012 Sep;25(9):1298-306.


CENTIMETERS
INCHES


CENTIMETERS
1
2
3
4
5