Disclosures
September 12, 2016

Dr. Keith Duncan has disclosed that he receives an hourly fee for slide review from Abbvie Biotherapeutics and Oxford Biotherapeutics. The planners have determined that this financial relationship is not relevant to the case being presented and does not present a conflict of interest.

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

Presenters:

David Bingham, MD
Mahendra Ranchod, MD
Nabeen Nayak, MD
Sunny Kao, MD
Alana Shain, MD
Teri Longacre, MD
Sarah Cherny, MD
Peyman Samghabadi, MD
Edward Plowey, MD
Hannes Vogel, MD
Greg Charville, MD, PhD
Brock Martin, MD
Richard Sibley, MD
Adam Gomez, MD

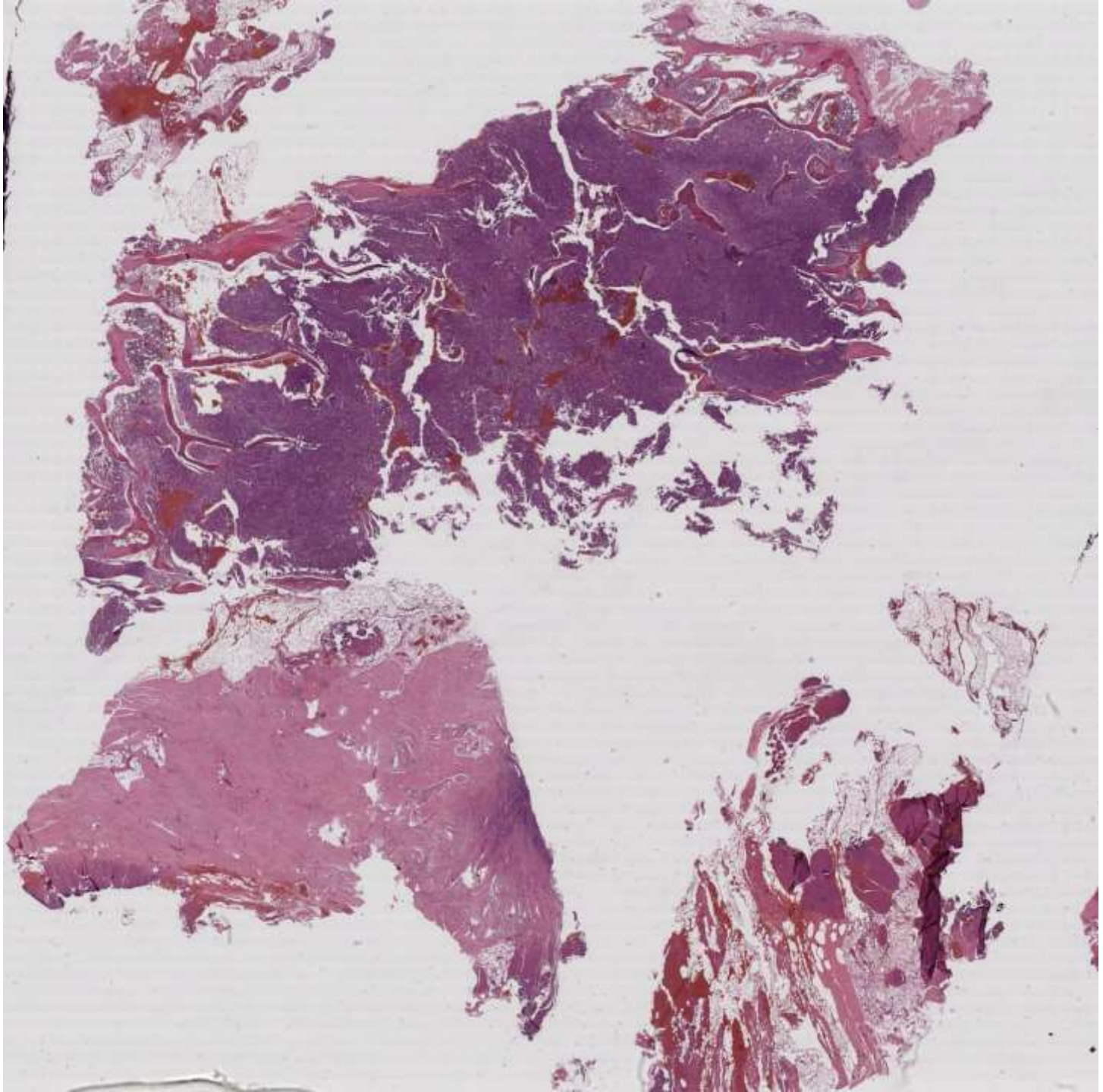
Activity Planners:

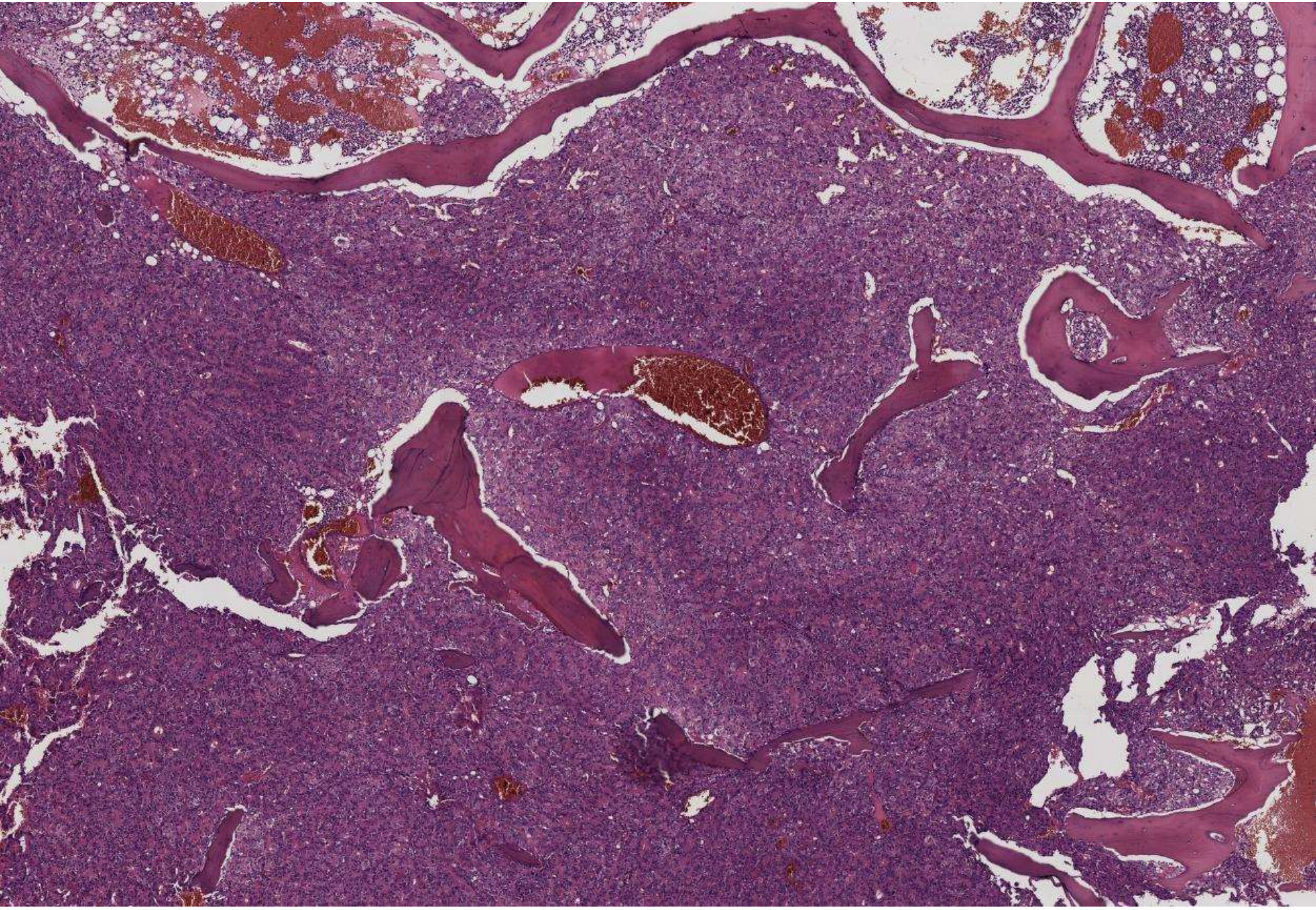
Kristin Jensen, MD
Ankur Sangoi, MD

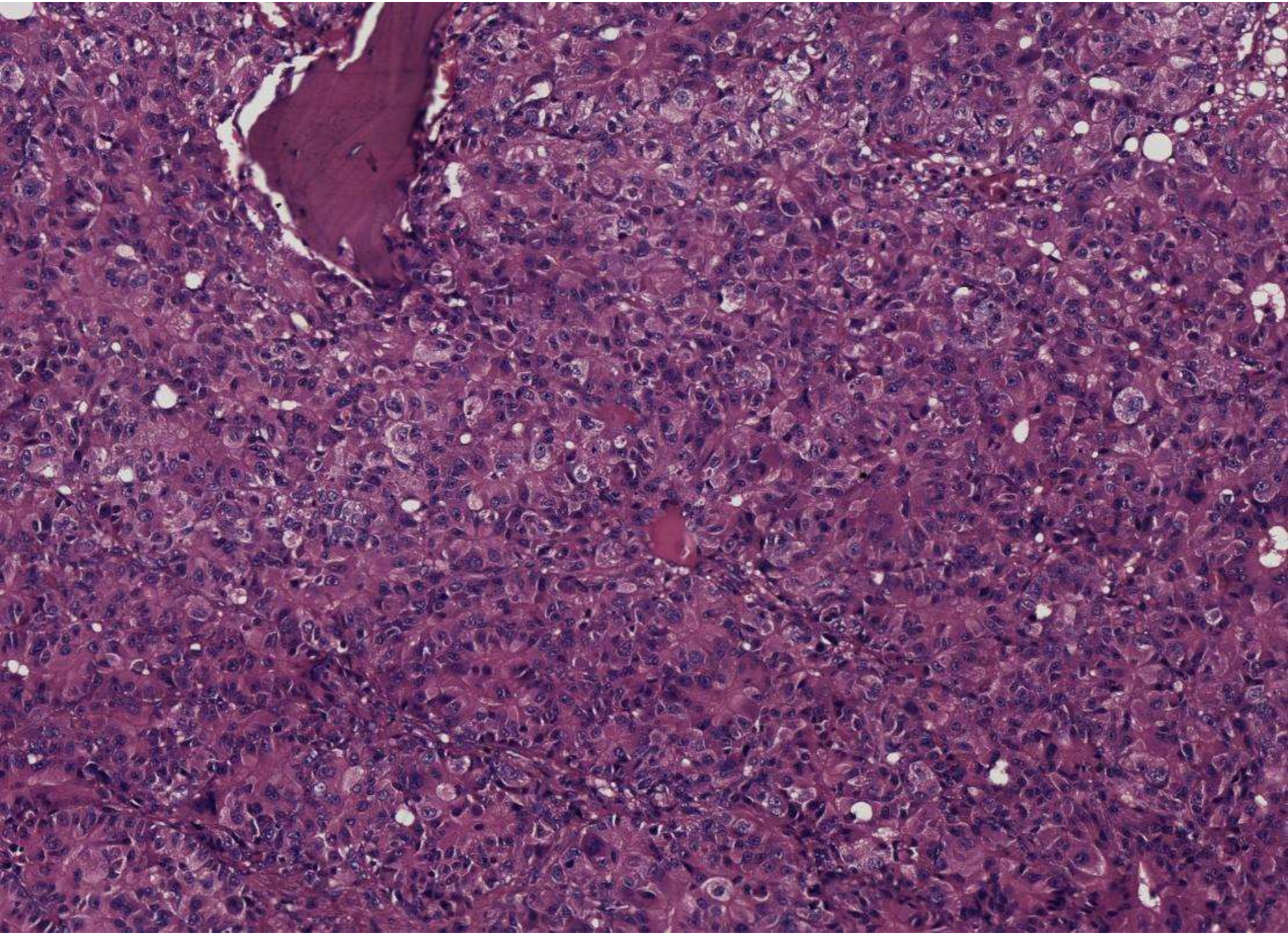
SB 6081

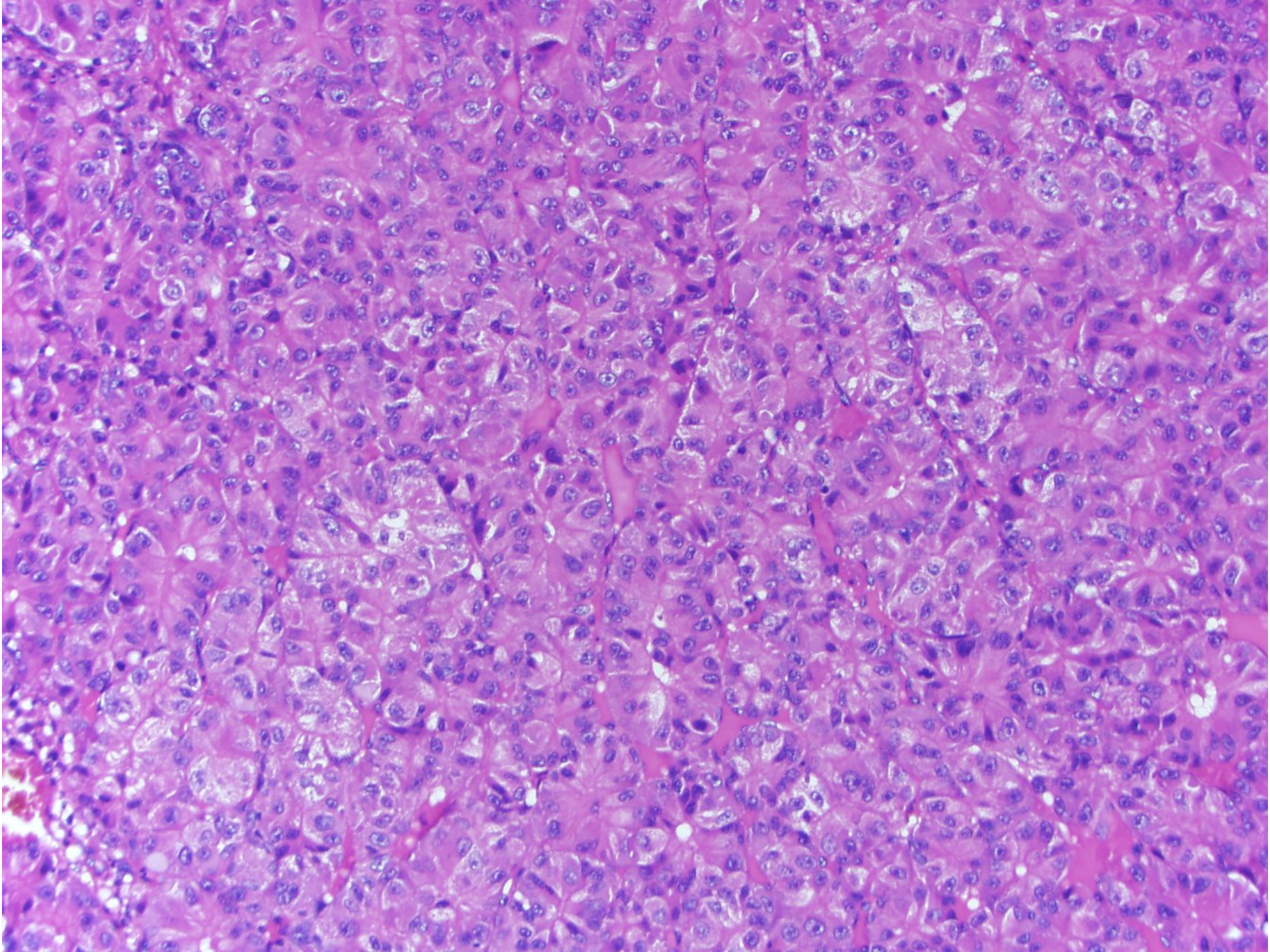
Nabeen Nayak; Sir Ganga Ram Hospital, New Dehli

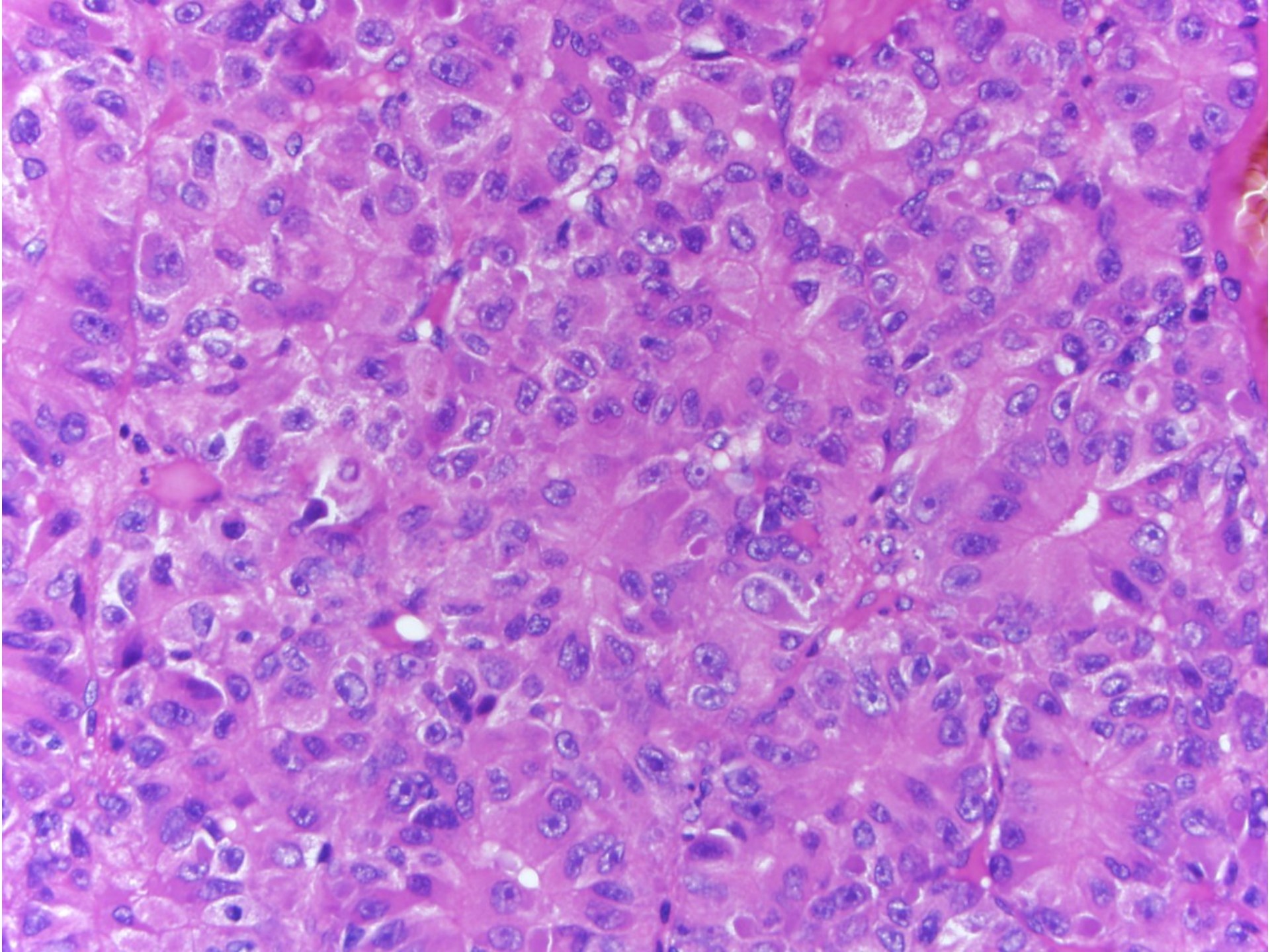
55-yr-old male had paraplegia with destructive lesions in D1, D2 & D3 spines extending to soft tissues.

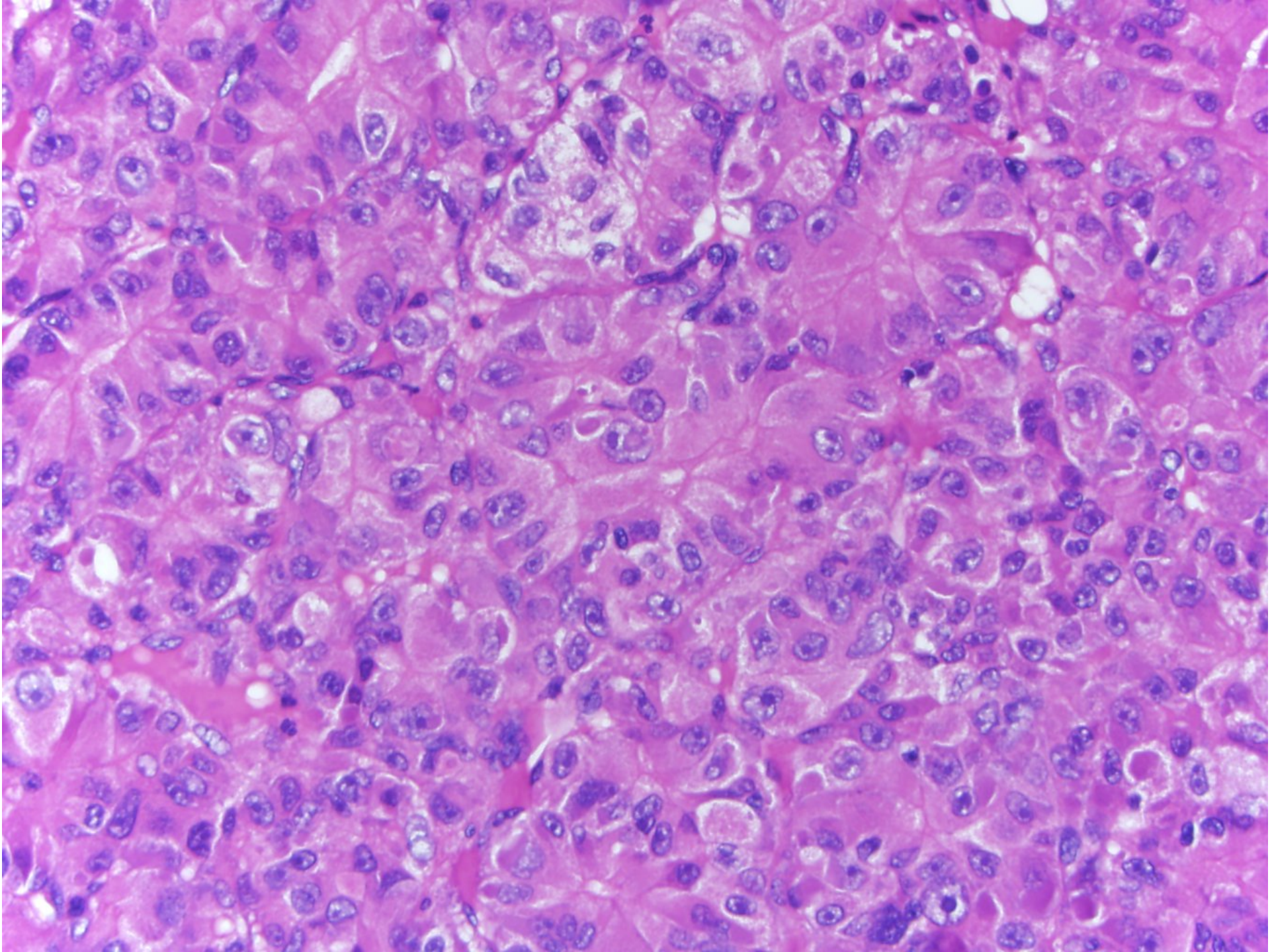




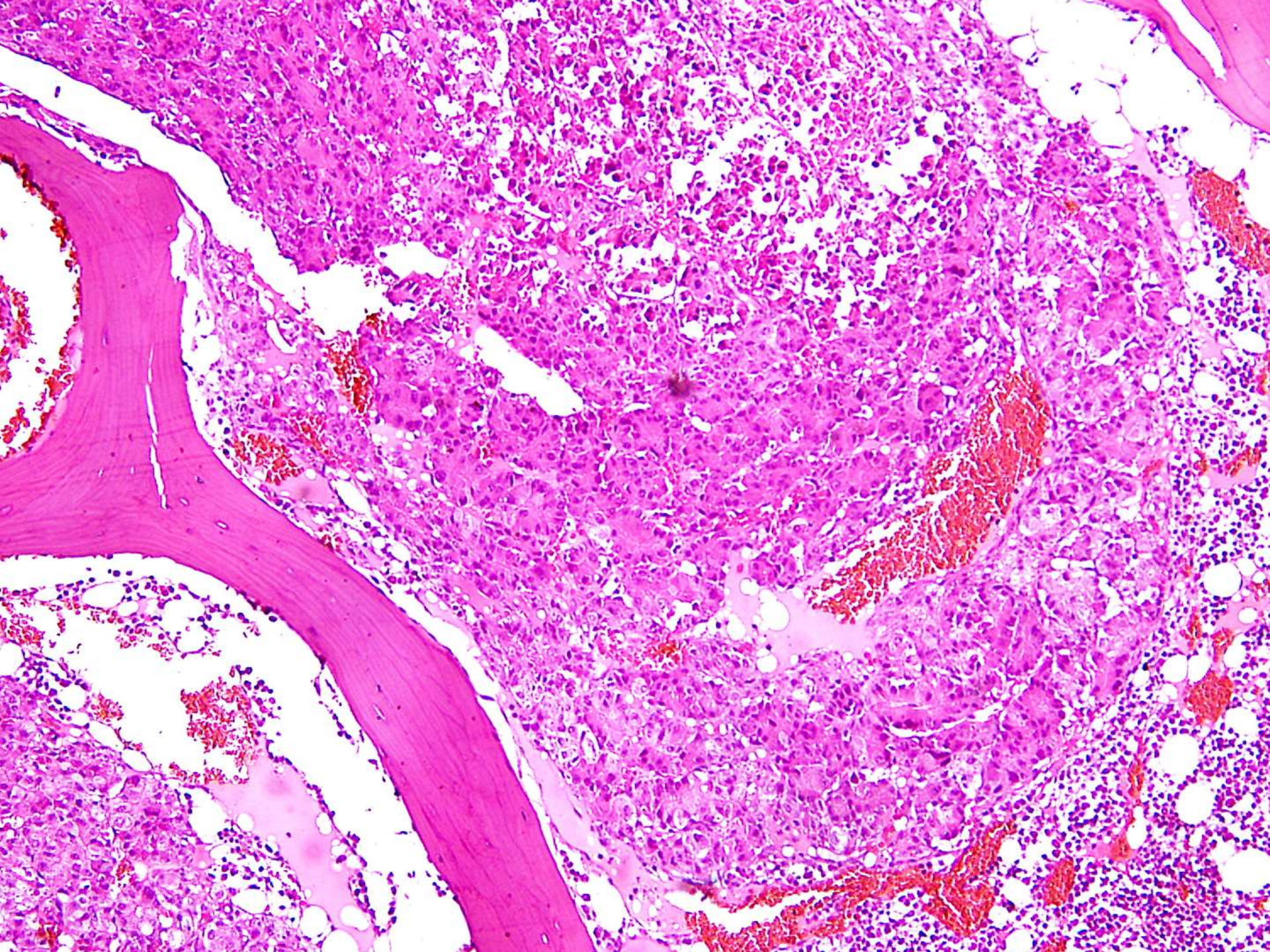


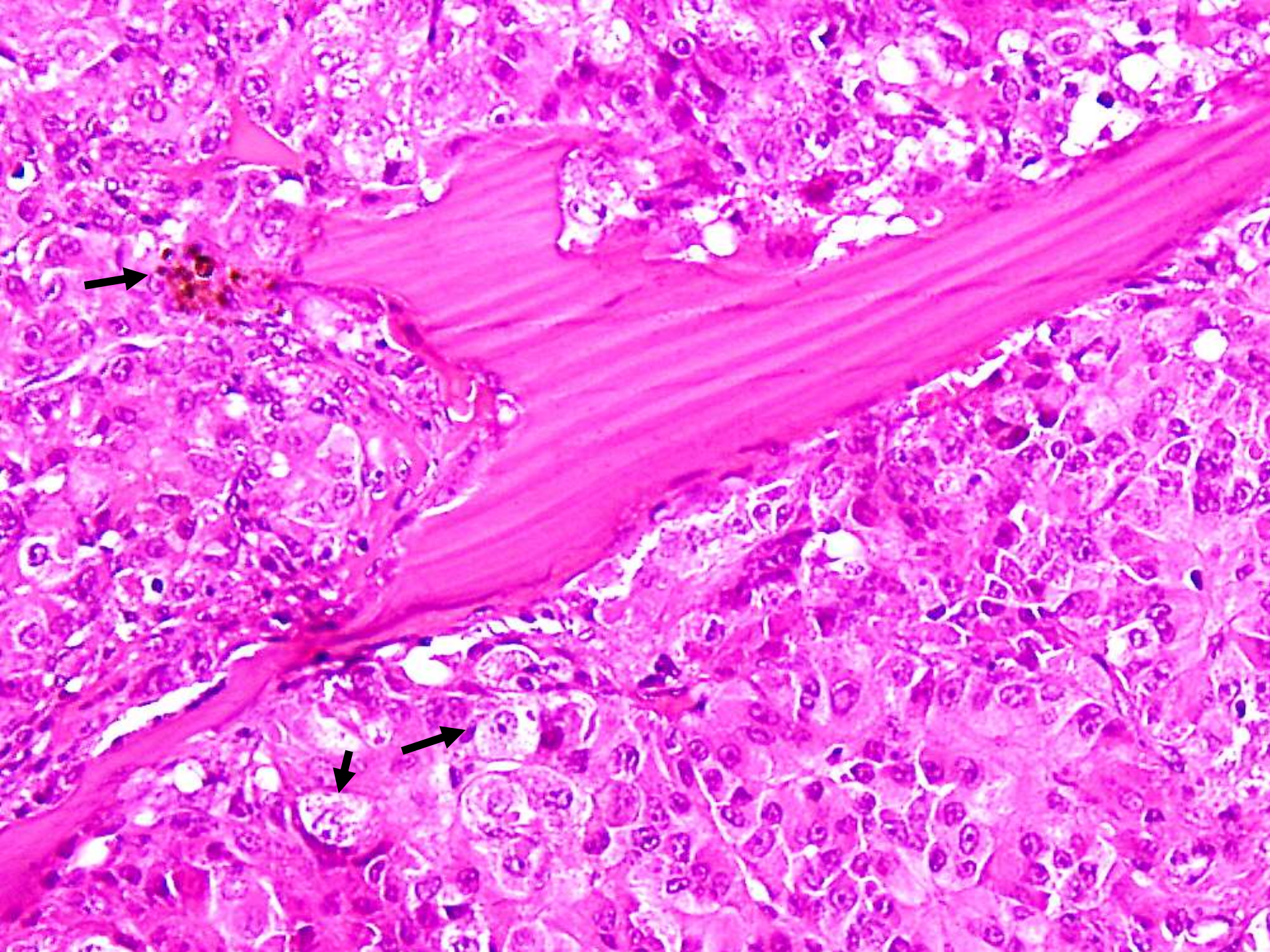


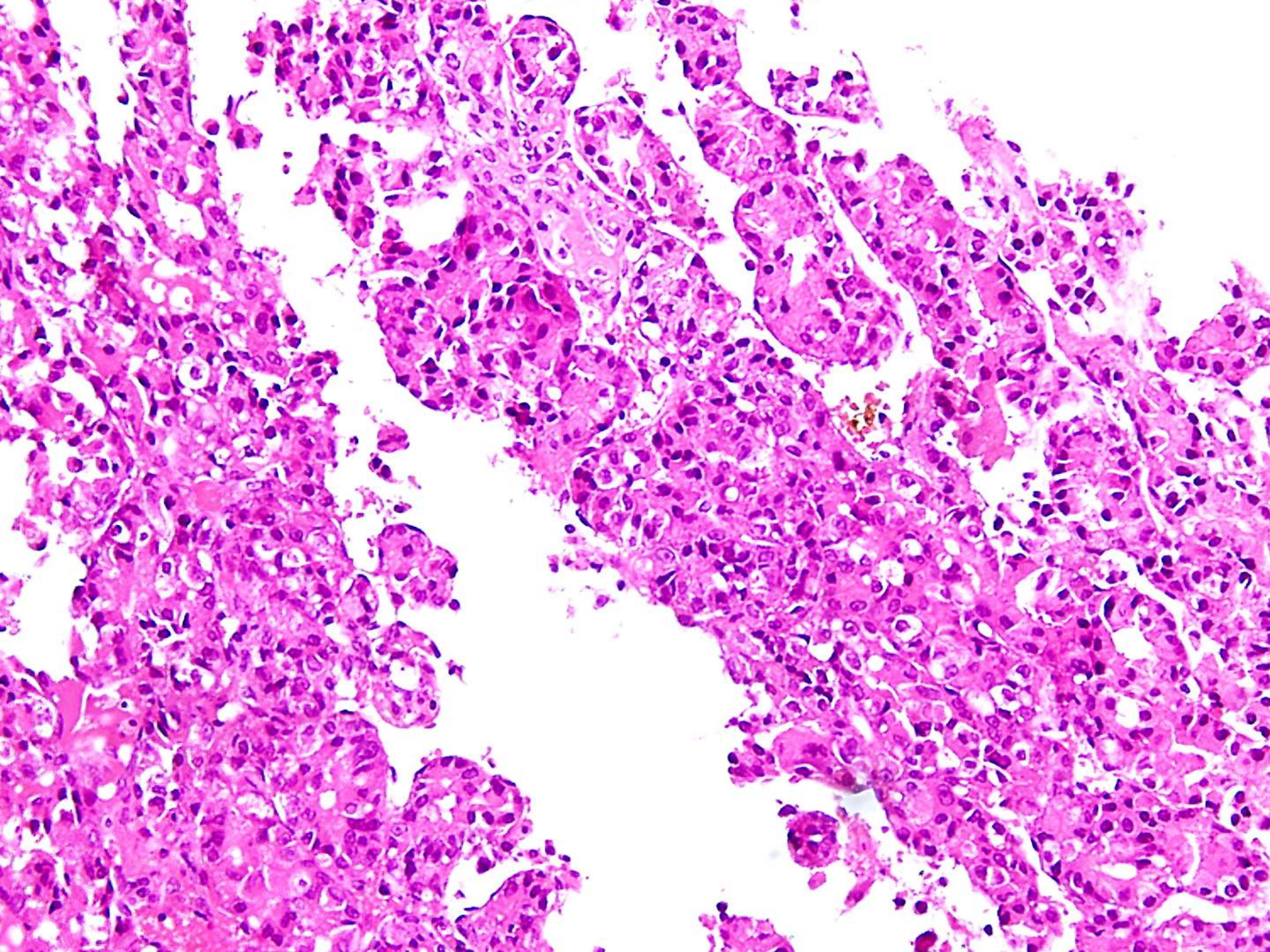


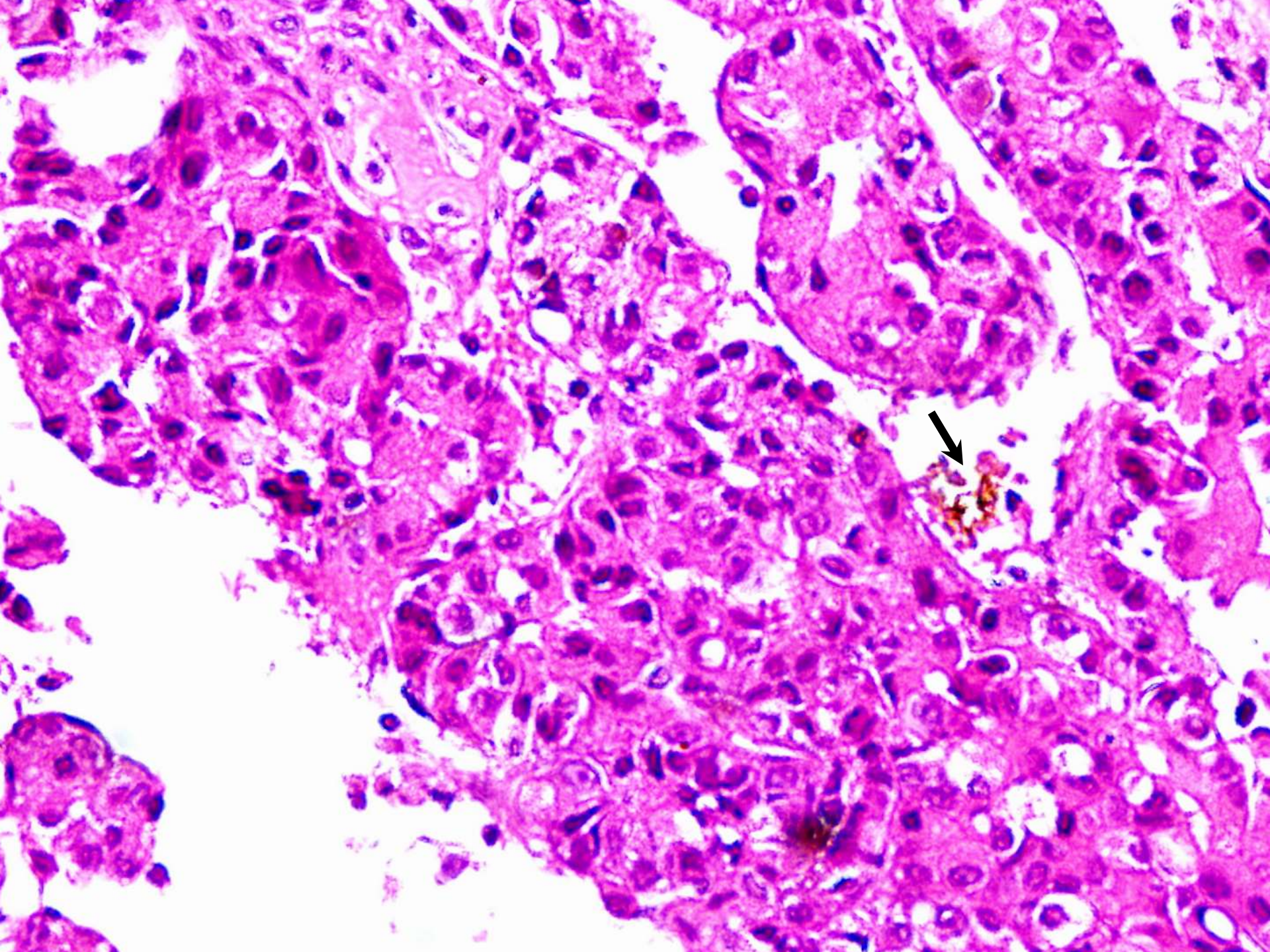


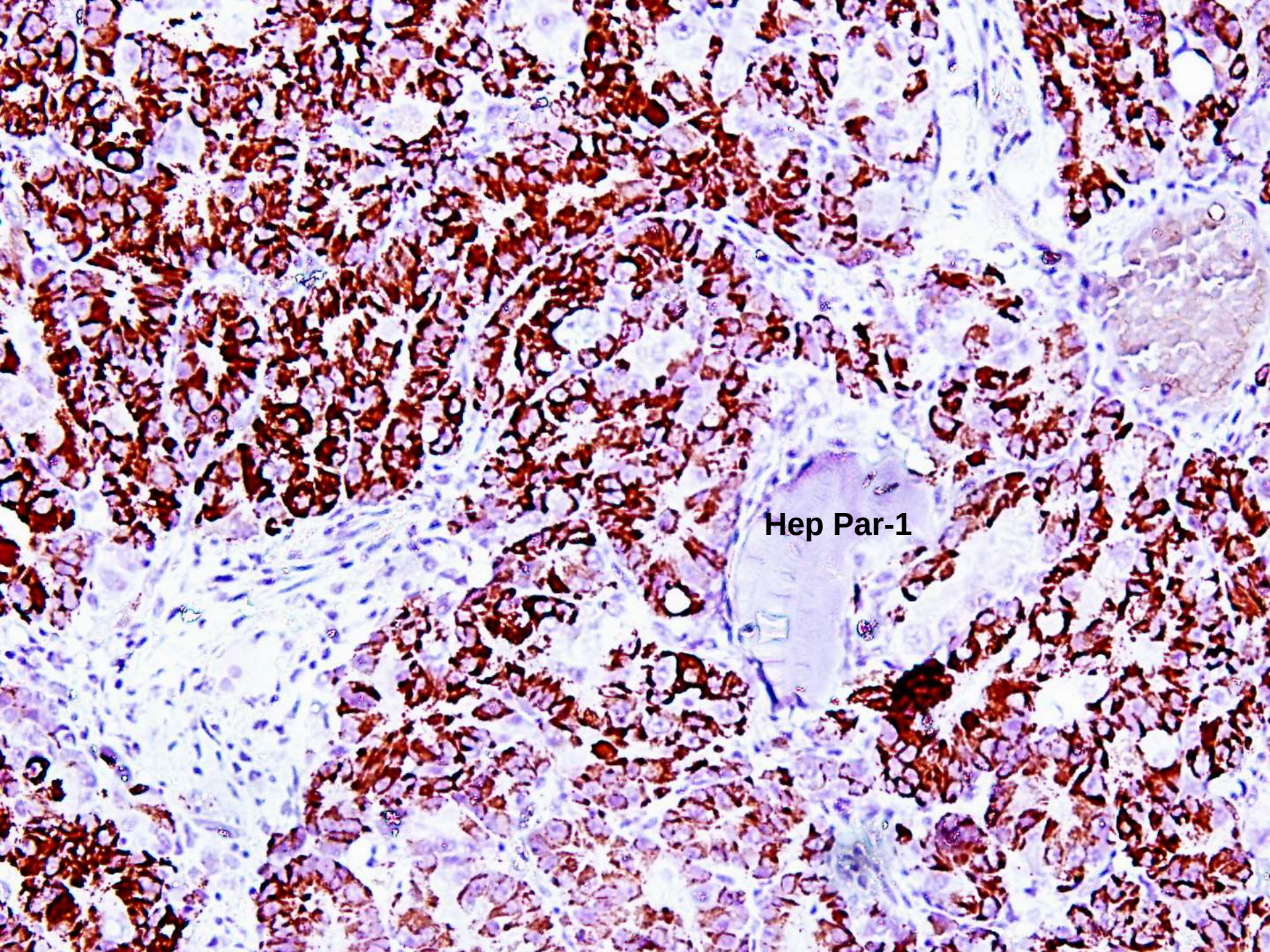
DIAGNOSIS?

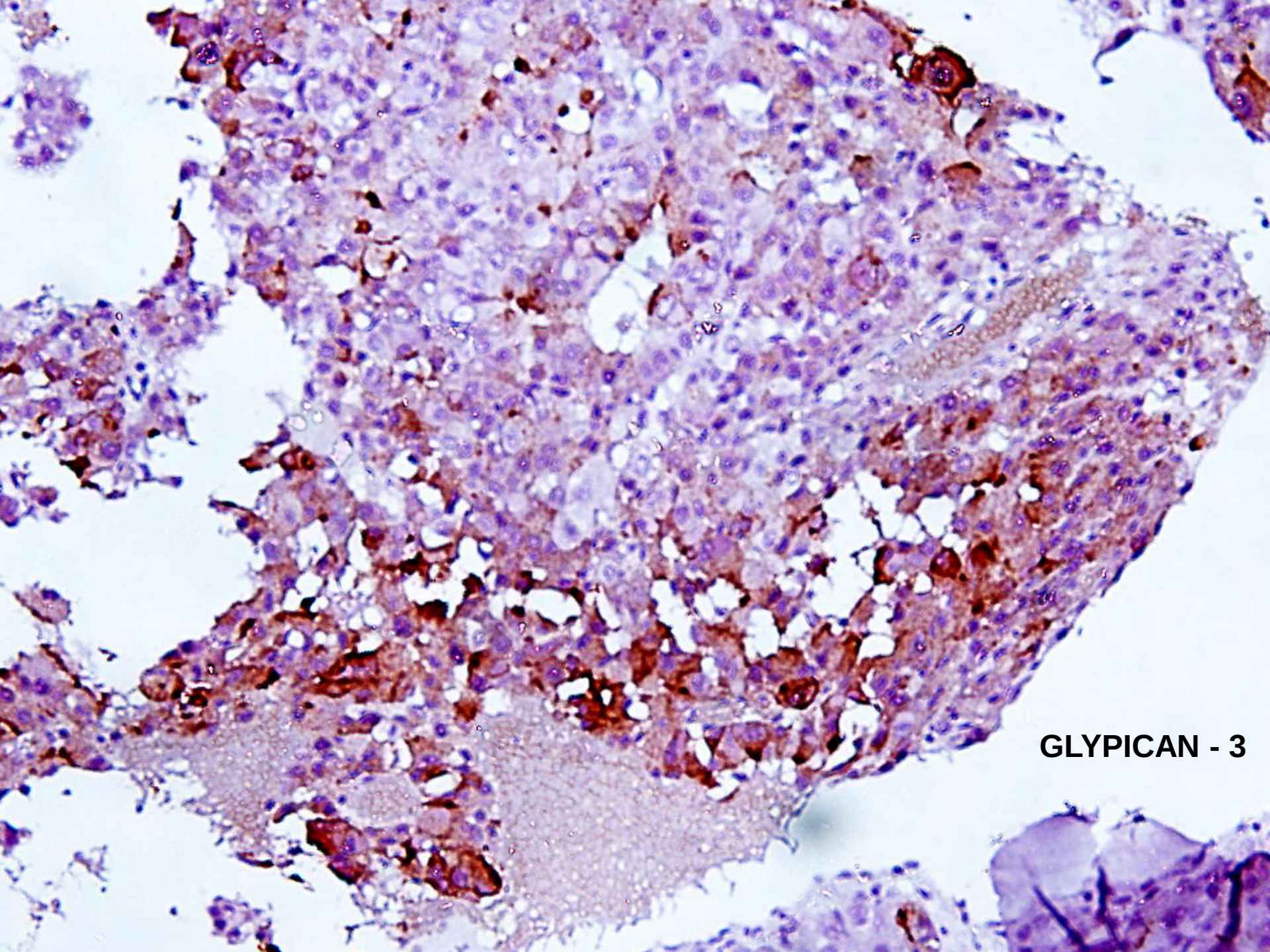









Hep Par-1


GLYPICAN - 3

Diagnosis: Metastatic Hepatocellular Carcinoma, D1- D3

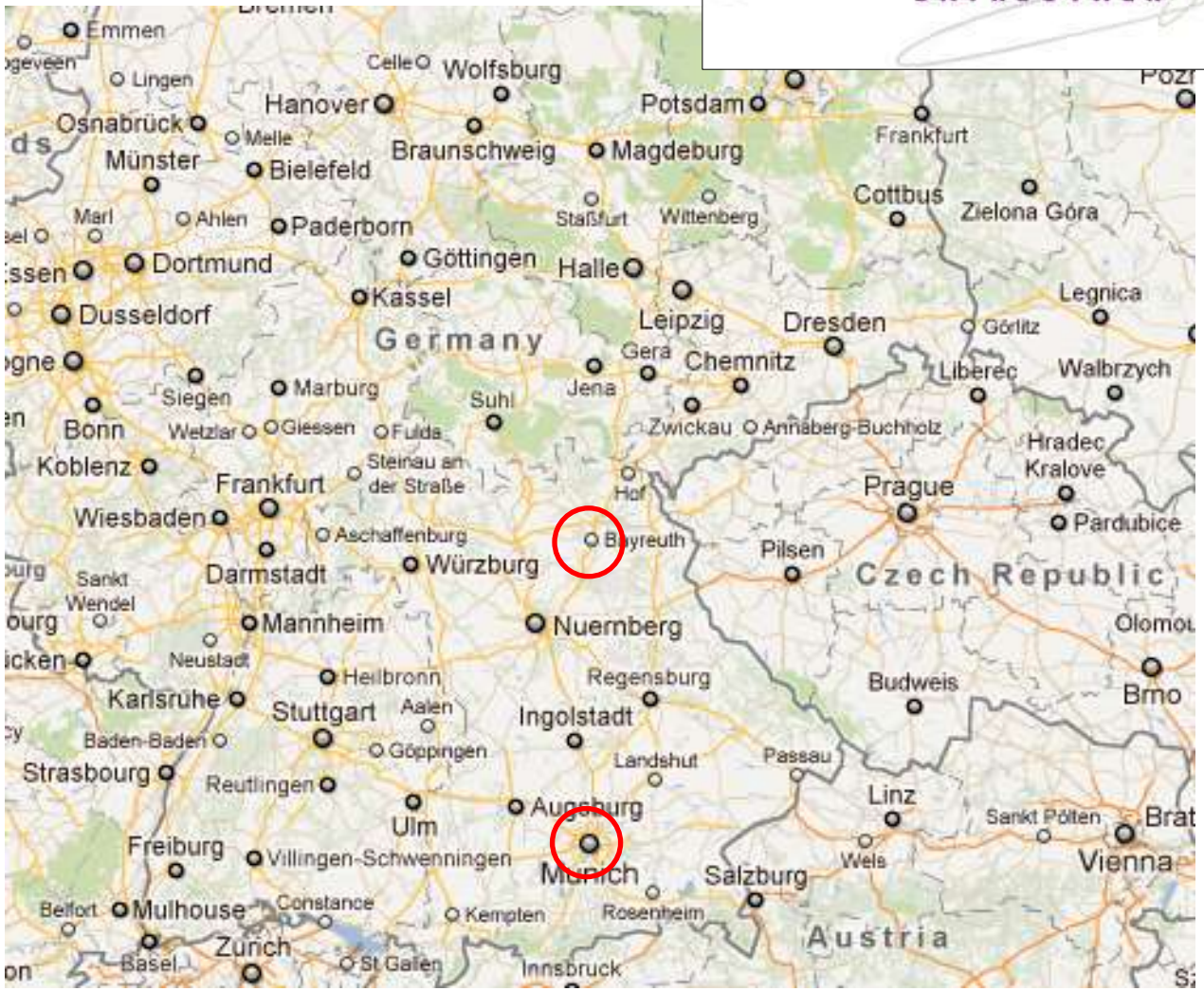
This patient was referred by his primary physician to our Neurosurgeon for biopsy of the dorsal vertebral lesion with a clinical diagnosis of Tuberculosis / Tumor of spine. The lungs were clear and no other clinical data were available to us at that time.

On further detailed examination and tests the patient was found to have HCV-related liver cirrhosis with a 6.5 cm tumor in the upper part of the right lobe.

Extra-hepatic metastasis of HCC is mostly seen in Grade IV tumors. Common sites of these metastasis are: Lungs, abdominal lymph nodes, bones and adrenals in that order of frequency. Other sites are extremely rare **(Int J Clin Exp Pathol. 2013;6:816-820)**

Richard Wagner

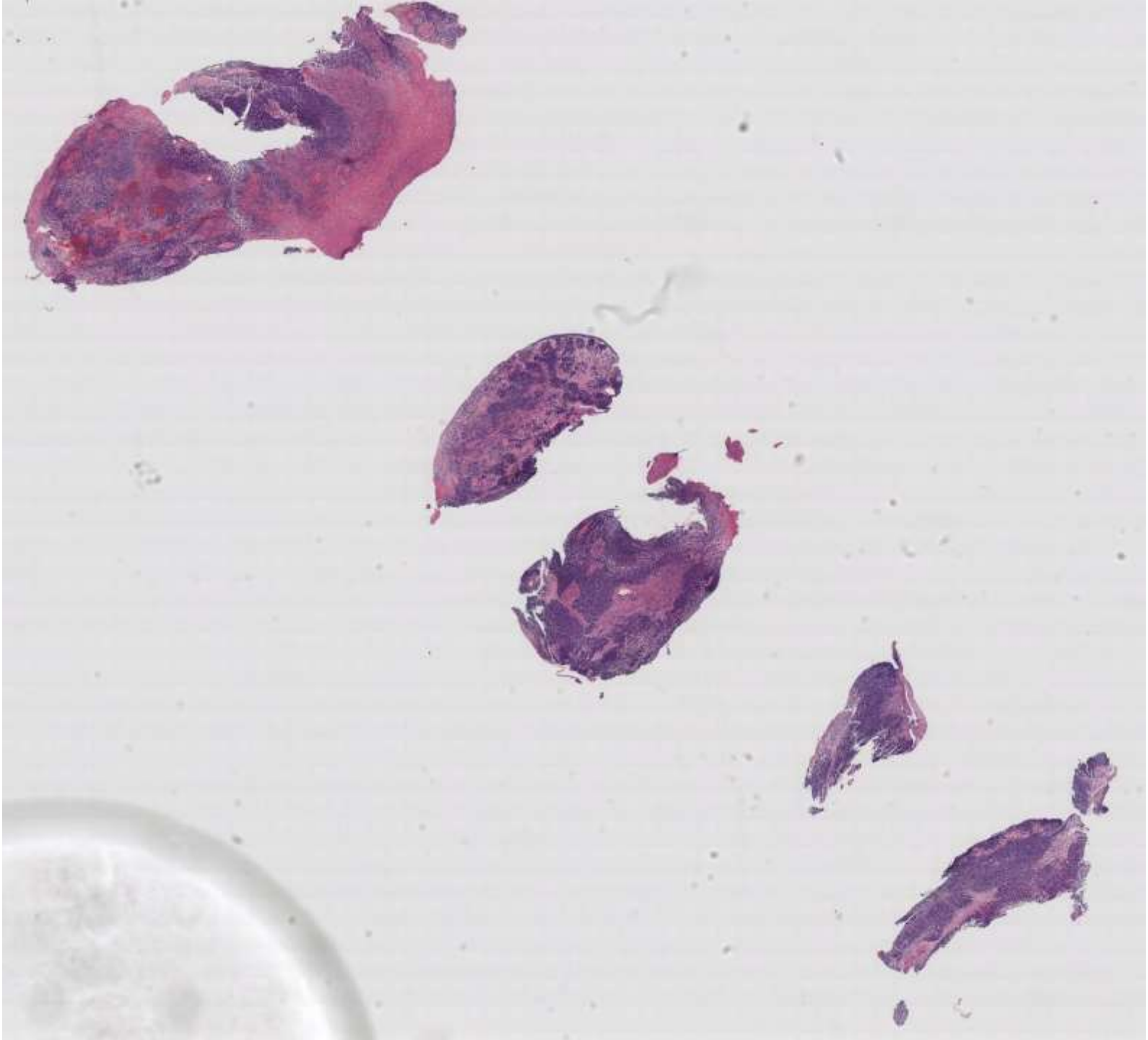
BAYREUTHER FESTSPIELE

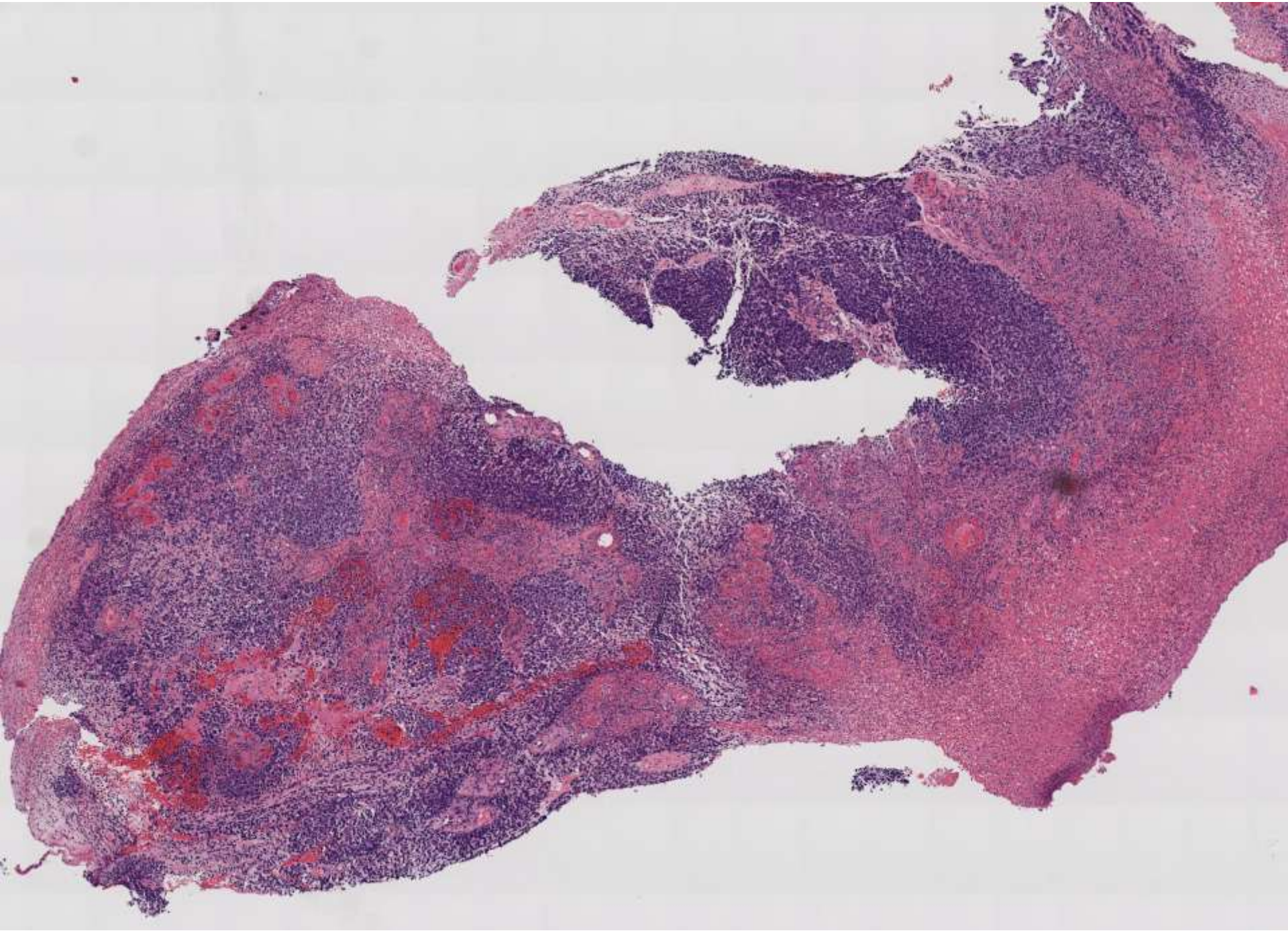


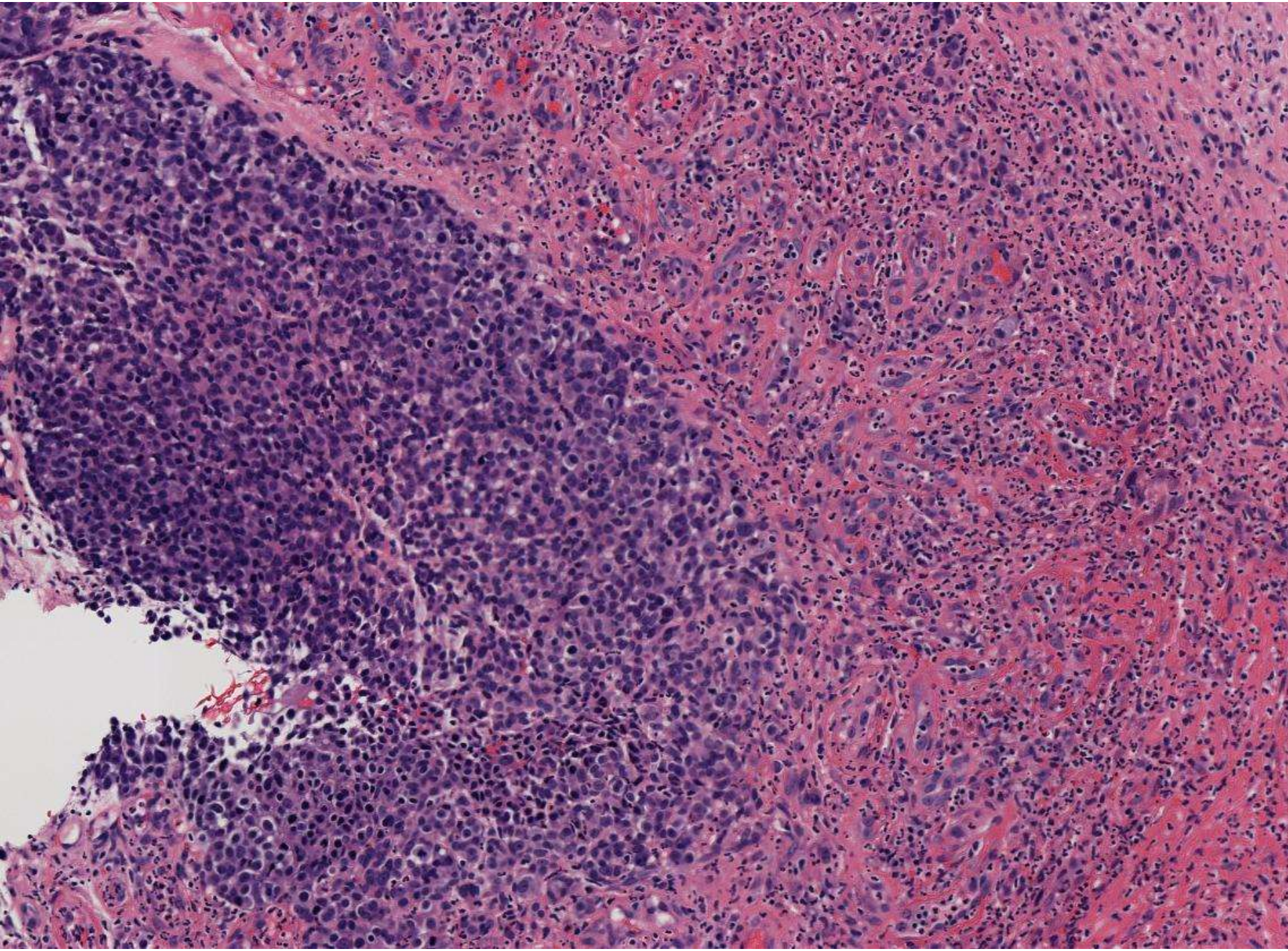
SB 6082

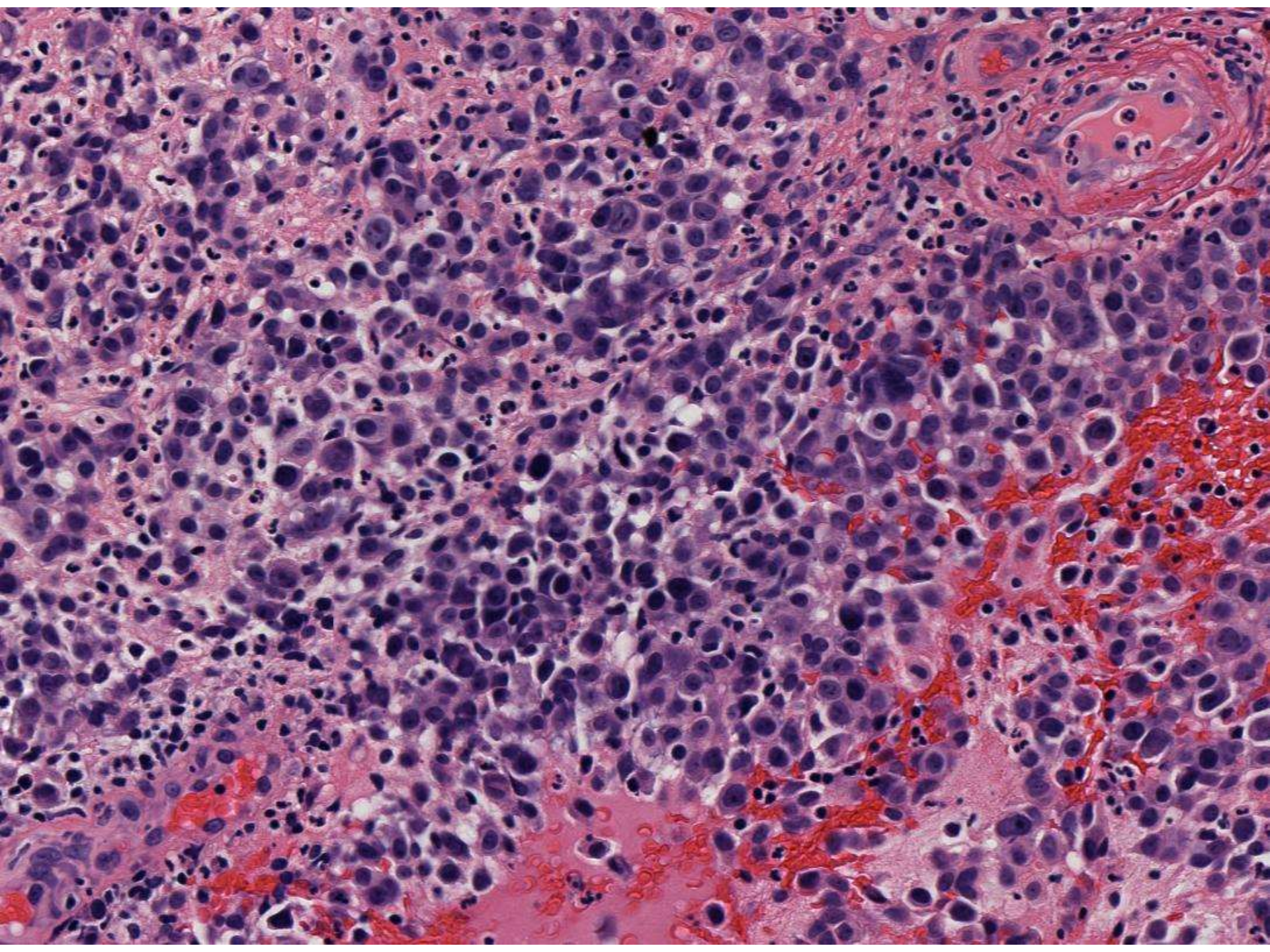
Keith Duncan; Mills-Peninsula Hospital

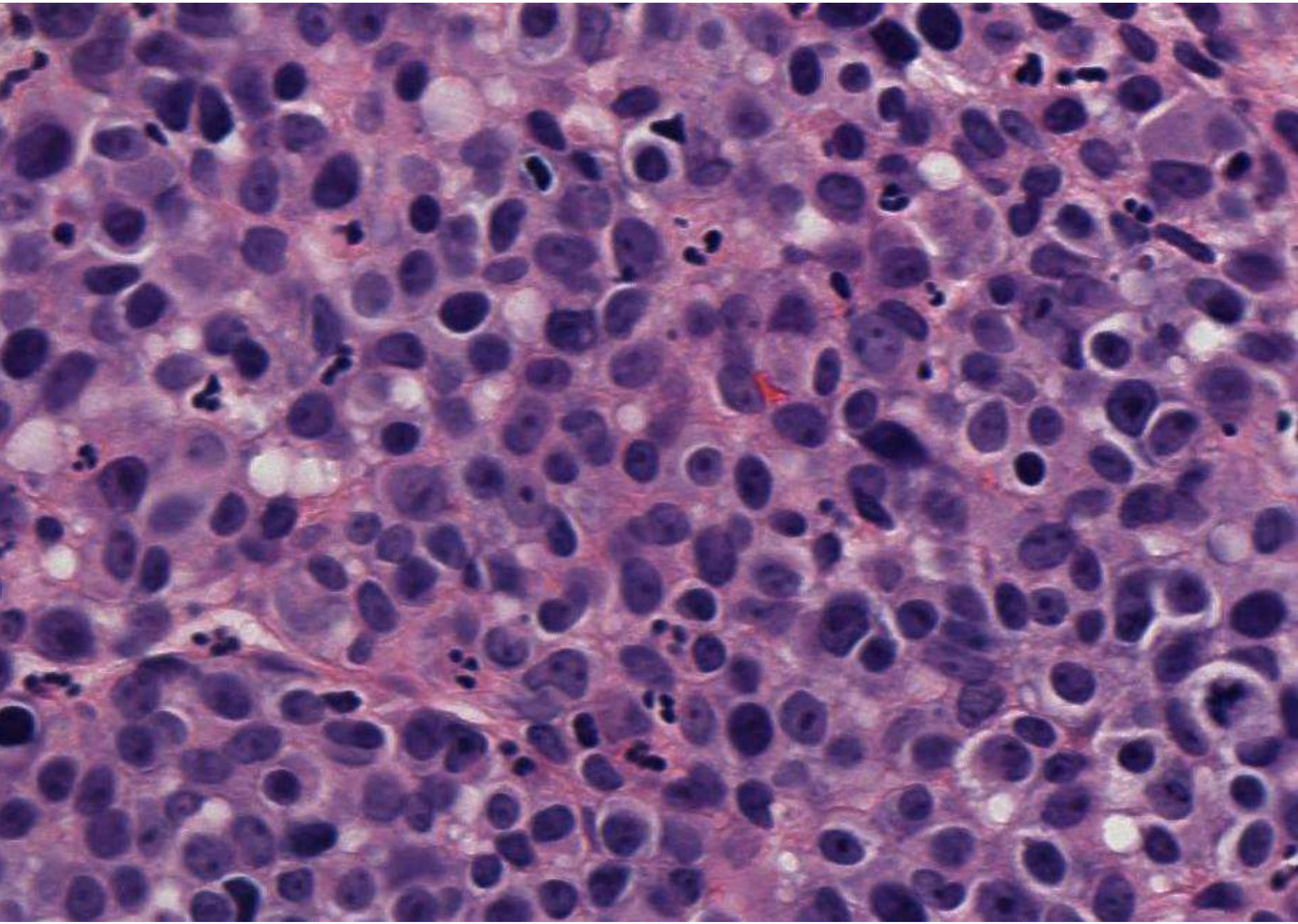
69-year-old female with exophytic large nasal mass.











DIAGNOSIS?

MELANOMA NASOPHARYNGEAL CAVITY

1% of all melanomas occur in this region, usually in nasal cavity
Frequently misclassified
Mean age 64 years, range 13-93 years, no gender preference
Established risk factors for cutaneous melanoma of sun damage, family history and atypical nevi do not apply to this region
Difficult to diagnose if no intraepithelial component and no pigment
Poor prognosis, usually recurs; median survival 3 years; 5 year survival is 35%

MELANOMA
NASOPHARYNGEAL CAVITY

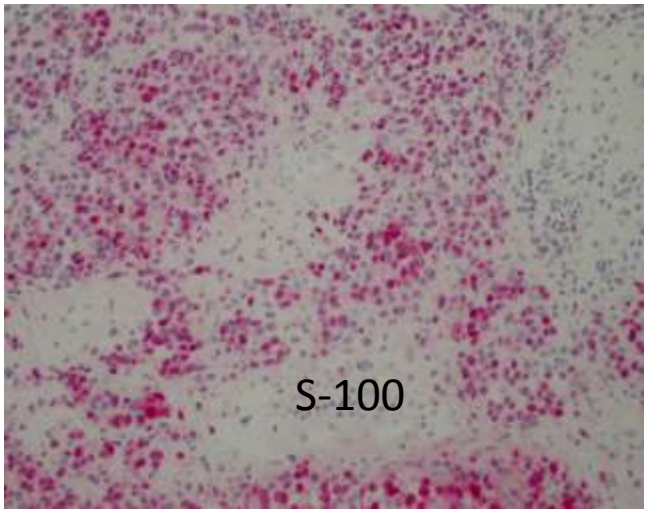
Small uniform cells, 70% with pigment
1/3 have junctional component
Often nesting growth pattern
Other patterns are small blue cell, spindle cell, epithelioid, pleomorphic
Frequent vascular and deep tissue invasion
May have minimal pleomorphism, prominent spindle cells

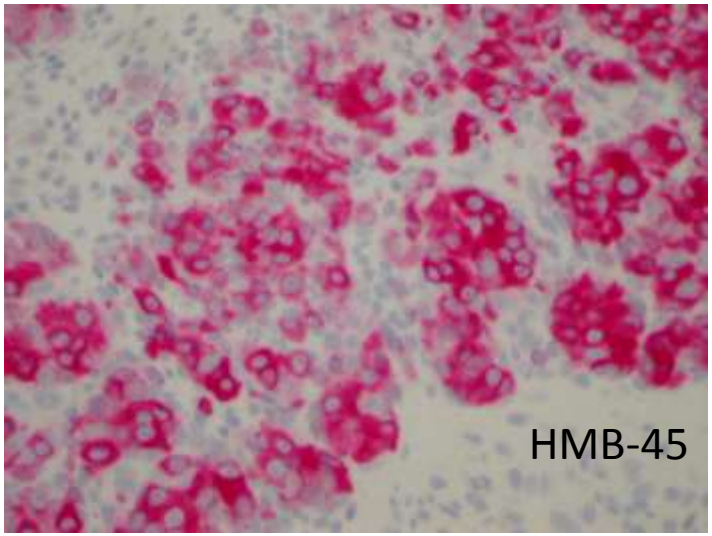
MELANOMA
NASOPHARYNGEAL CAVITY

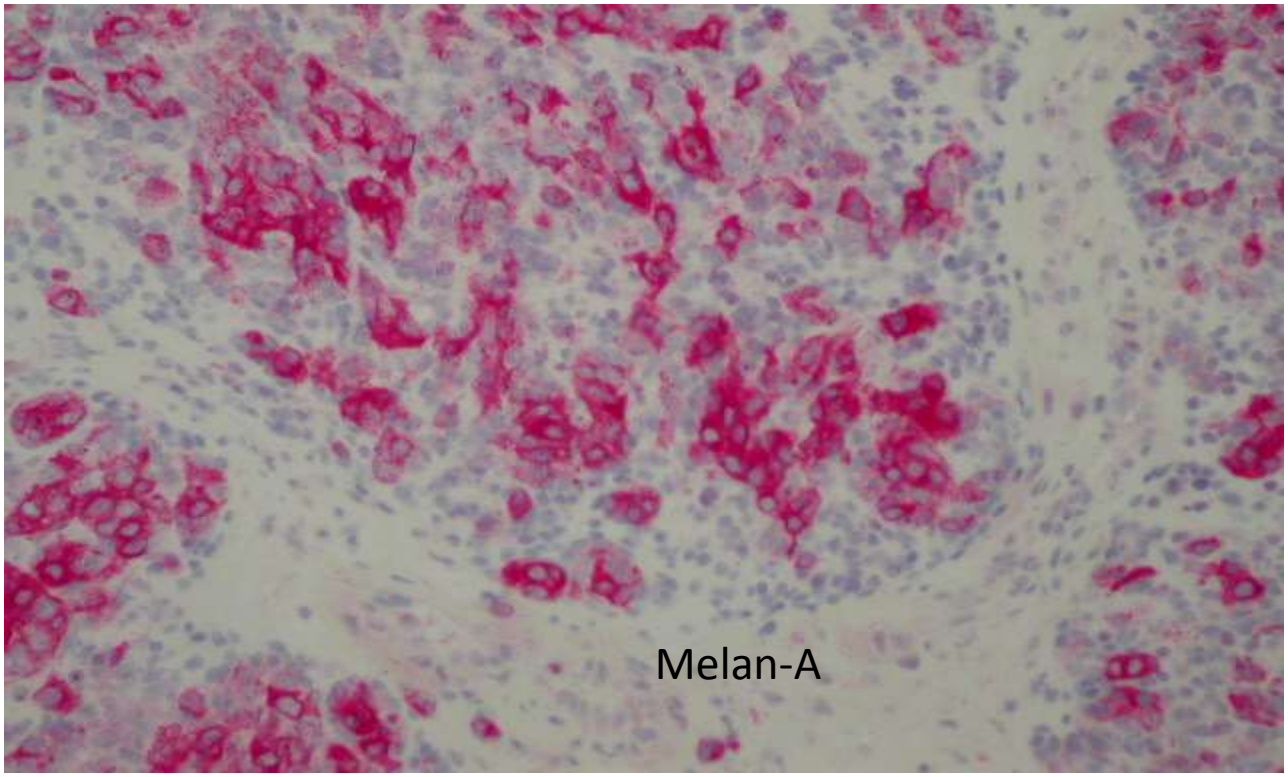
Positive stains
S100 (95%), HMB45 (98%), MelanA/Mart1 (100%), tyrosinase (100%), Vimentin

Negative stains
EMA, CD3, CD4, CD8, CD56

Differential diagnosis
Olfactory neuroblastoma: S100+, but not diffuse and strong; HMB45 negative


S-100


HMB-45


Melan-A

Am J Surg Pathol. 2003 May;27(5):594-611.

Sinonasal tract and nasopharyngeal melanomas: a clinicopathologic study of 115 cases with a proposed staging system.

Thompson LD[1], Wieneke JA, Miettinen M.

Primary sinonasal tract mucosal malignant melanomas are uncommon tumors that are frequently misclassified, resulting in inappropriate clinical management. A total of 115 cases of sinonasal tract mucosal malignant melanoma included 59 females and 56 males, 13-93 years of age (mean 64.3 years). Patients presented most frequently with epistaxis (n = 52), mass (n = 42), and/or nasal obstruction (n = 34) present for a mean of 8.2 months. The majority of tumors involved the nasal cavity (n = 34), septum alone, or a combination of the nasal cavity and sinuses (n = 39) with a mean size of 2.4 cm.

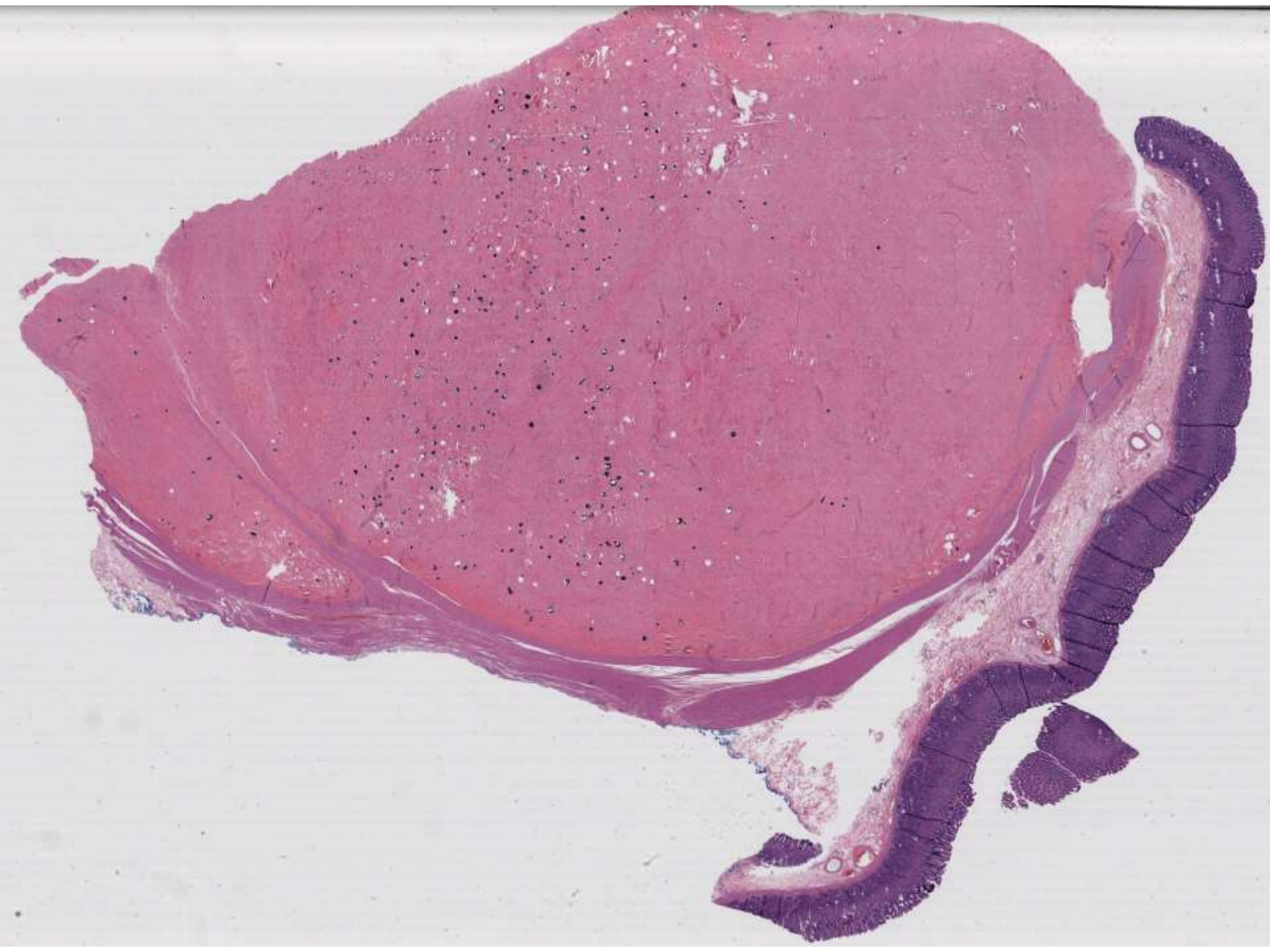
Histologically, the tumors were composed of a variety of cell types (epithelioid, spindled, undifferentiated), frequently arranged in a peritheliomatous distribution (n = 39). Immunohistochemical studies confirmed the diagnosis of sinonasal tract mucosal malignant melanomas with positive reactions for S-100 protein, tyrosinase, HMB-45, and melan A.

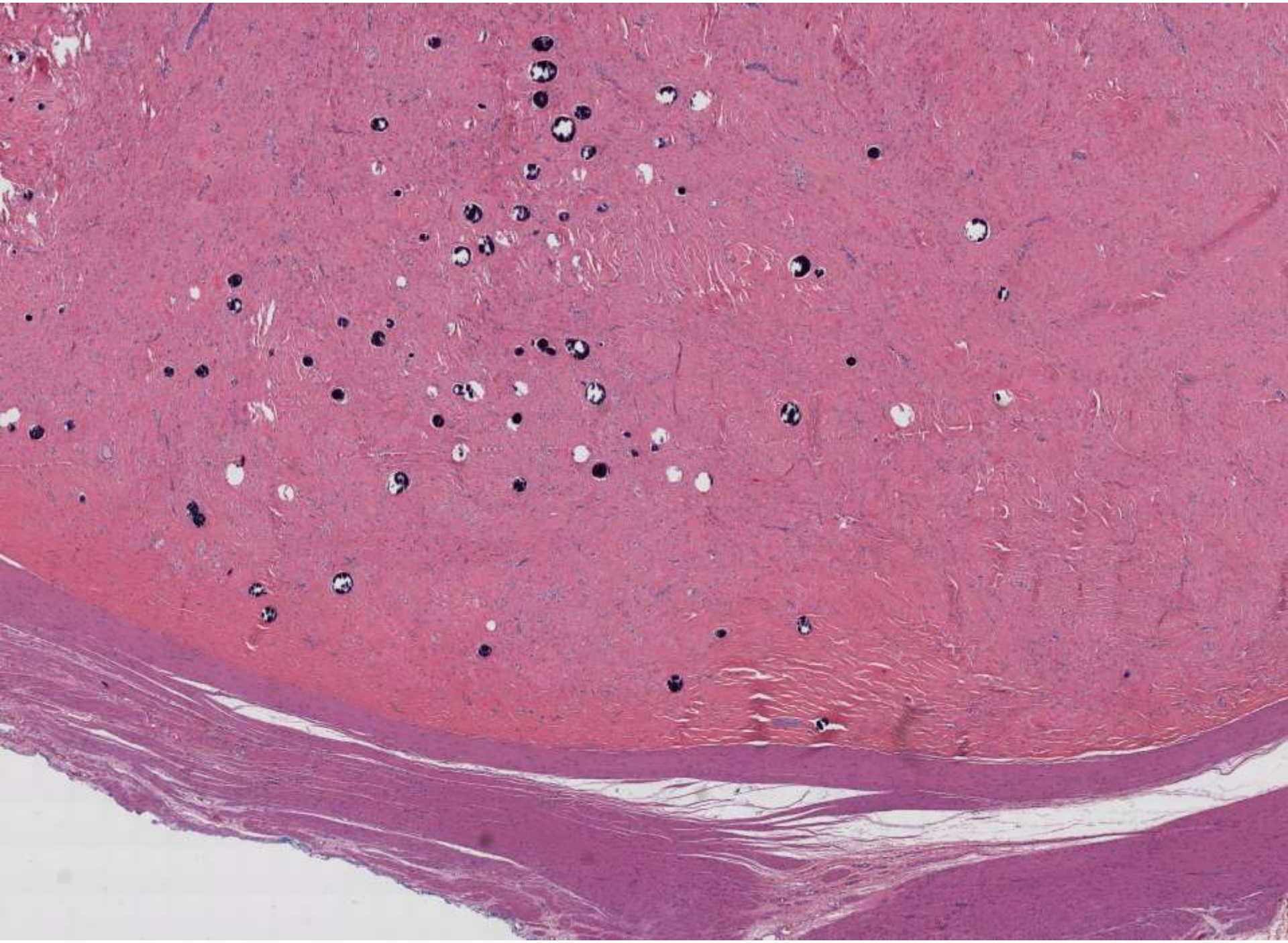
Sinonasal tract mucosal malignant melanomas need to be considered in the differential diagnosis of most sinonasal malignancies, particularly carcinoma, lymphoma, sarcoma, and olfactory neuroblastoma

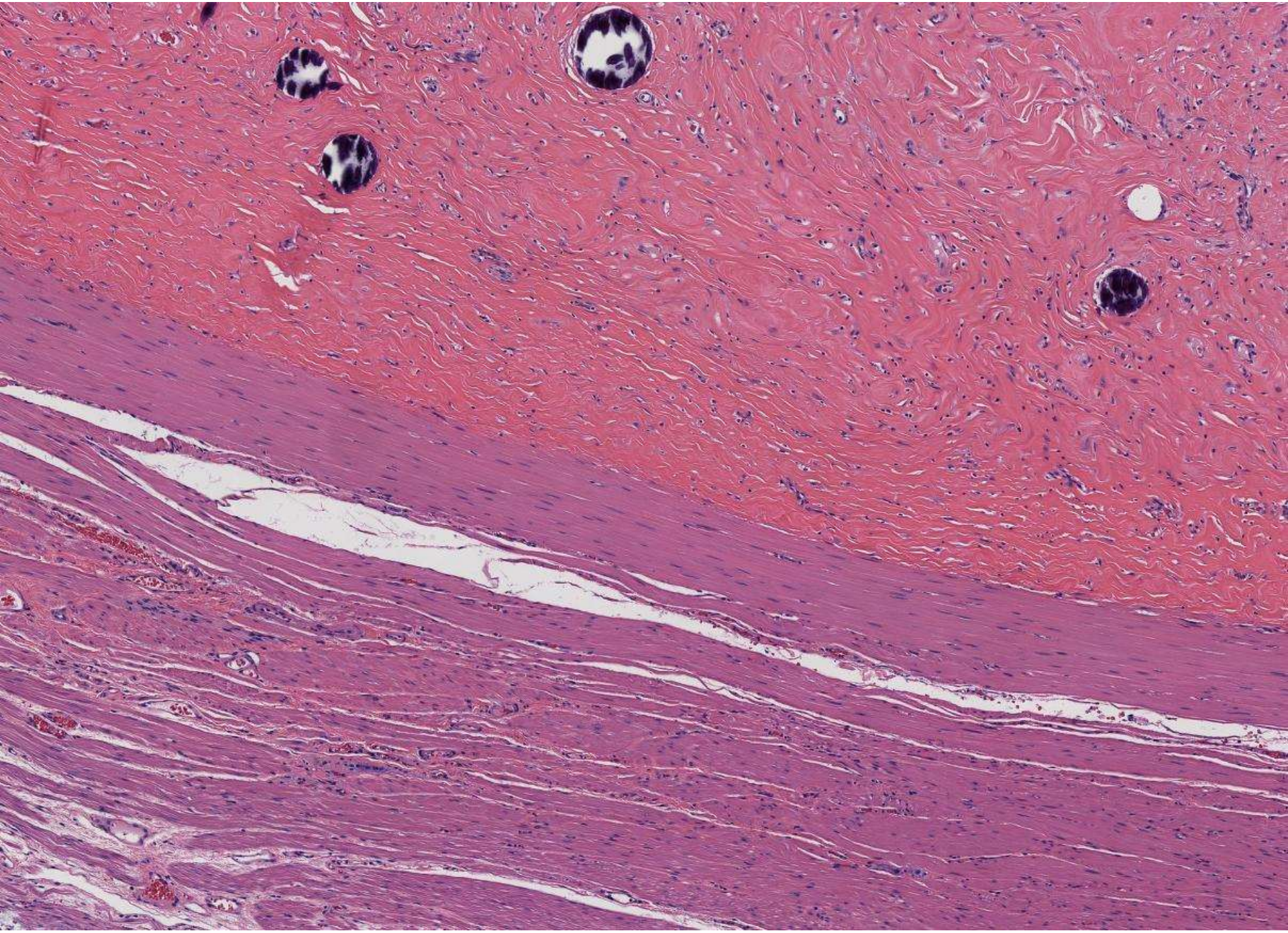
SB 6083

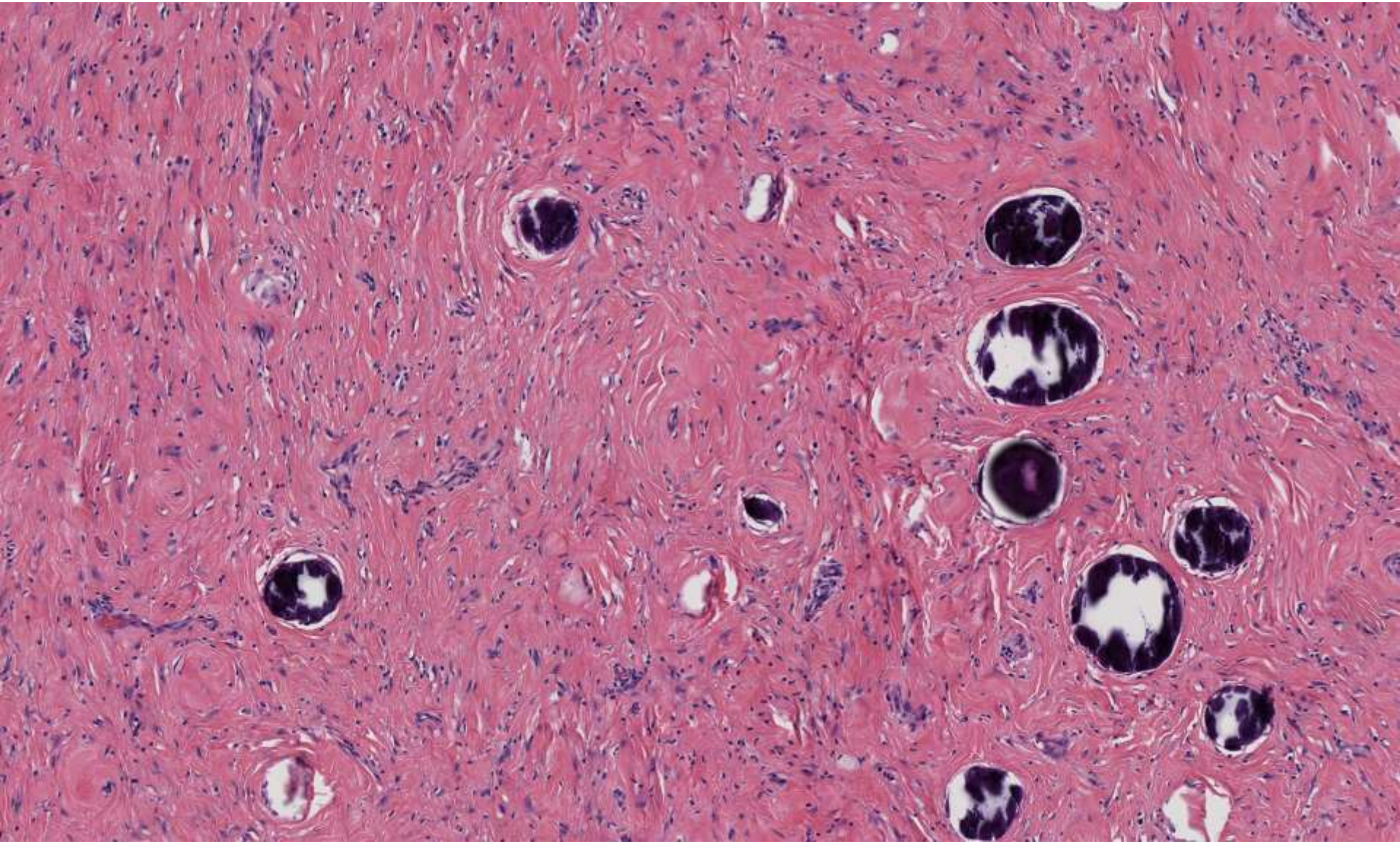
Mahendra Ranchod; Good Samaritan Hospital

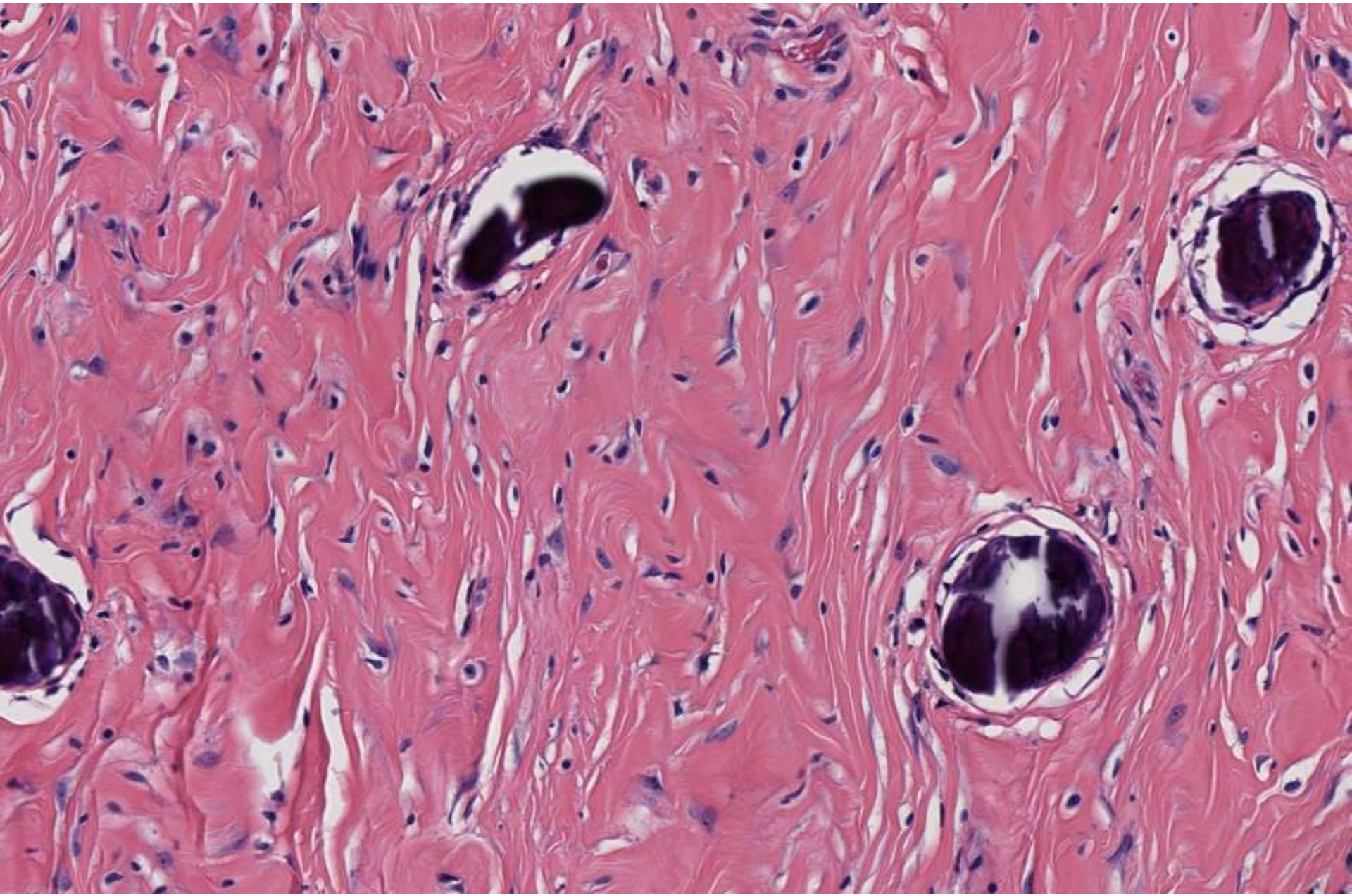
36-year-old female had partial gastrectomy for 6cm tumor.

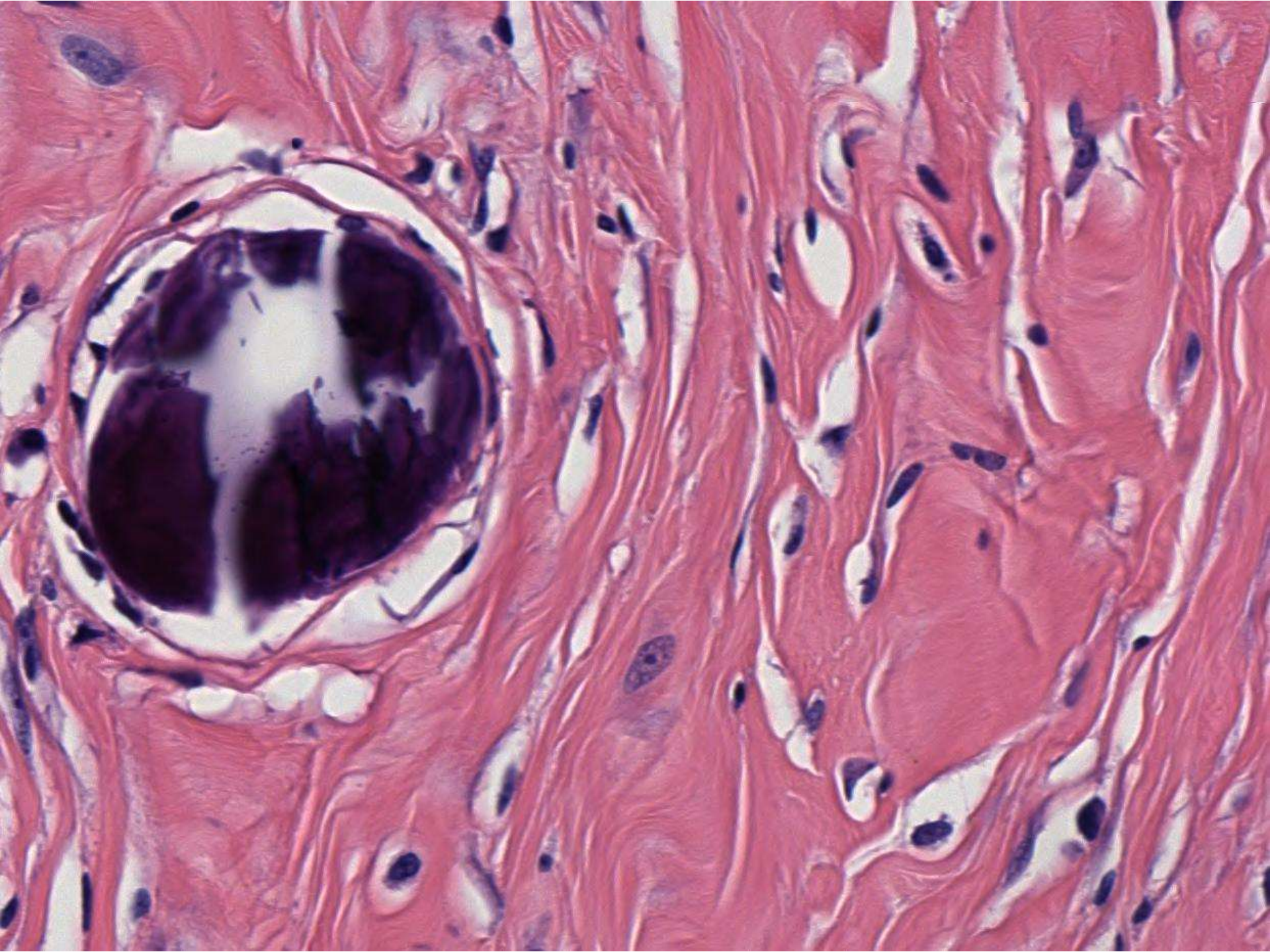












DIAGNOSIS?

Calcifying Fibrous Tumor of Stomach

- **Benign circumscribed mass**
- **1- 5cm, usually <3cm**
- **Often found incidentally**
- **Paucicellular**
- **Fibroblasts with abundant collagen**
- **Scattered calcification**
- **Foci of chronic inflammation**

Calcifying Fibrous Tumor of Stomach
IHC

- **Vimentin** +
- **Factor XIIIa** +
- **CD117** -
- **CD34** - or focal +
- **Desmin** -
- **Alk-1** -
- **S100** -
- **KIT mutations** -

Calcifying Fibrous Tumor of Stomach

- **Is this a specific entity or the late stage of some other neoplasm?**
  - **GIST**
  - **Leiomyoma**
  - **Schwannoma**
  - **Inflammatory fibroid polyp**
  - **Inflammatory myofibroblastic tumor**
  - **Nodular fibrous pseudotumor**
  - **Plexiform fibromyxoma**

A

C.C.

Good Samaritan Hosp.
San Jose, CA

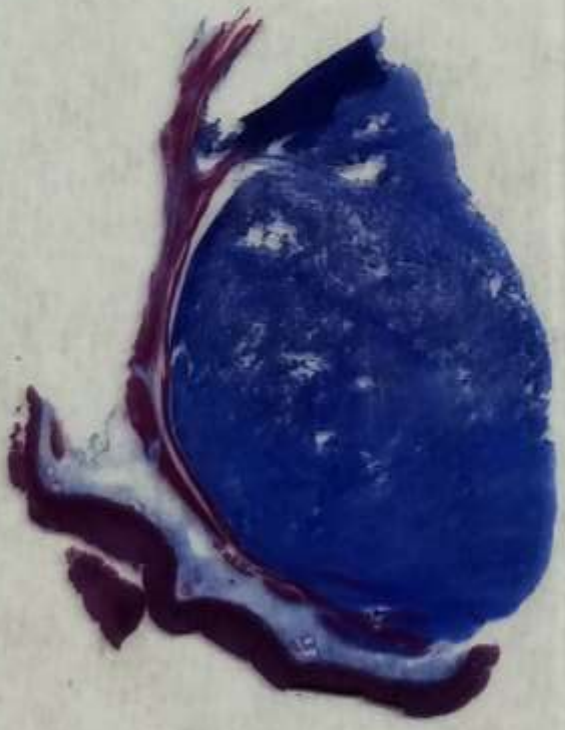
Starfrost

A Trichrome

.C.

Good Samaritan Hosp.
San Jose, CA

Starfrost

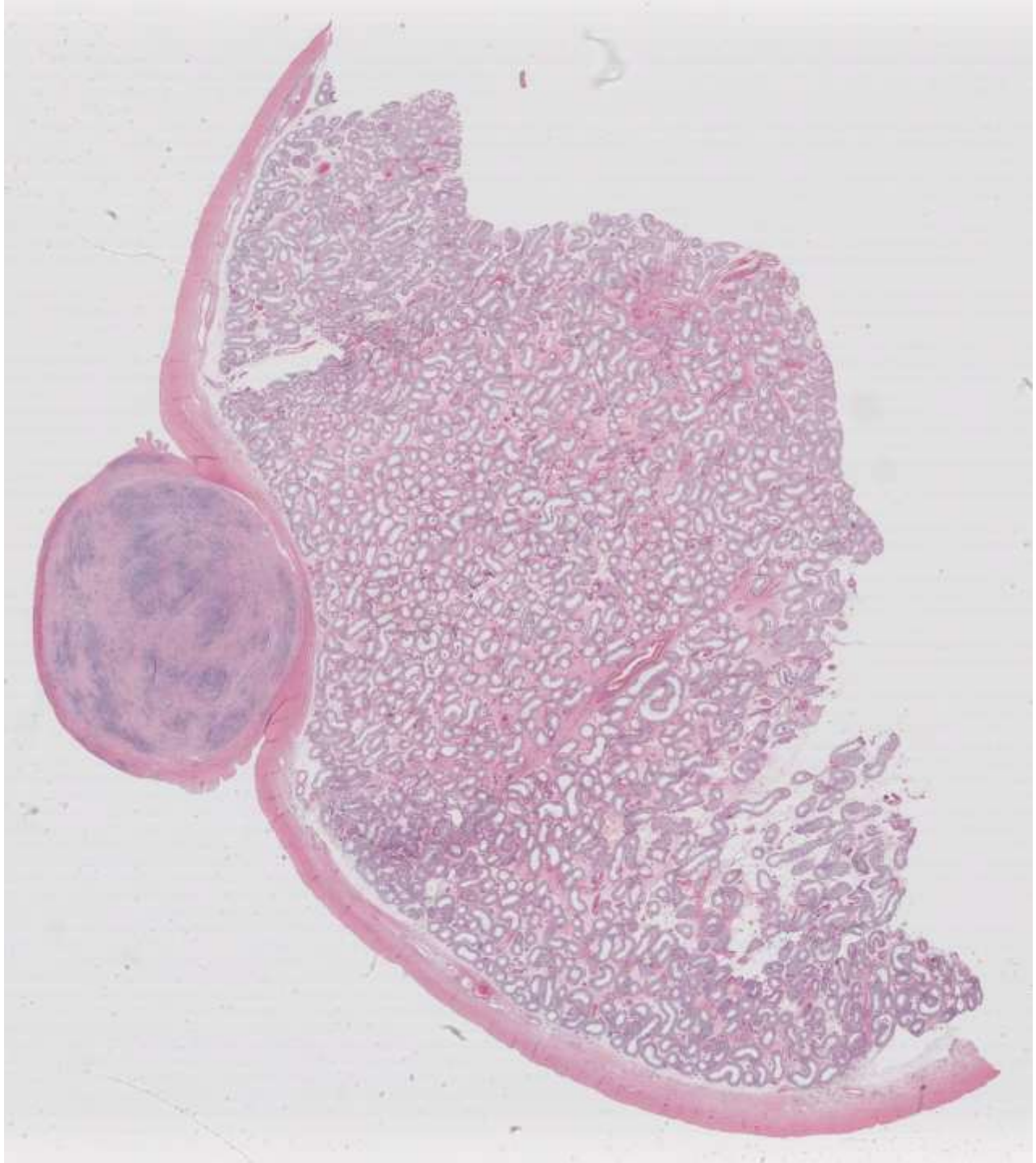


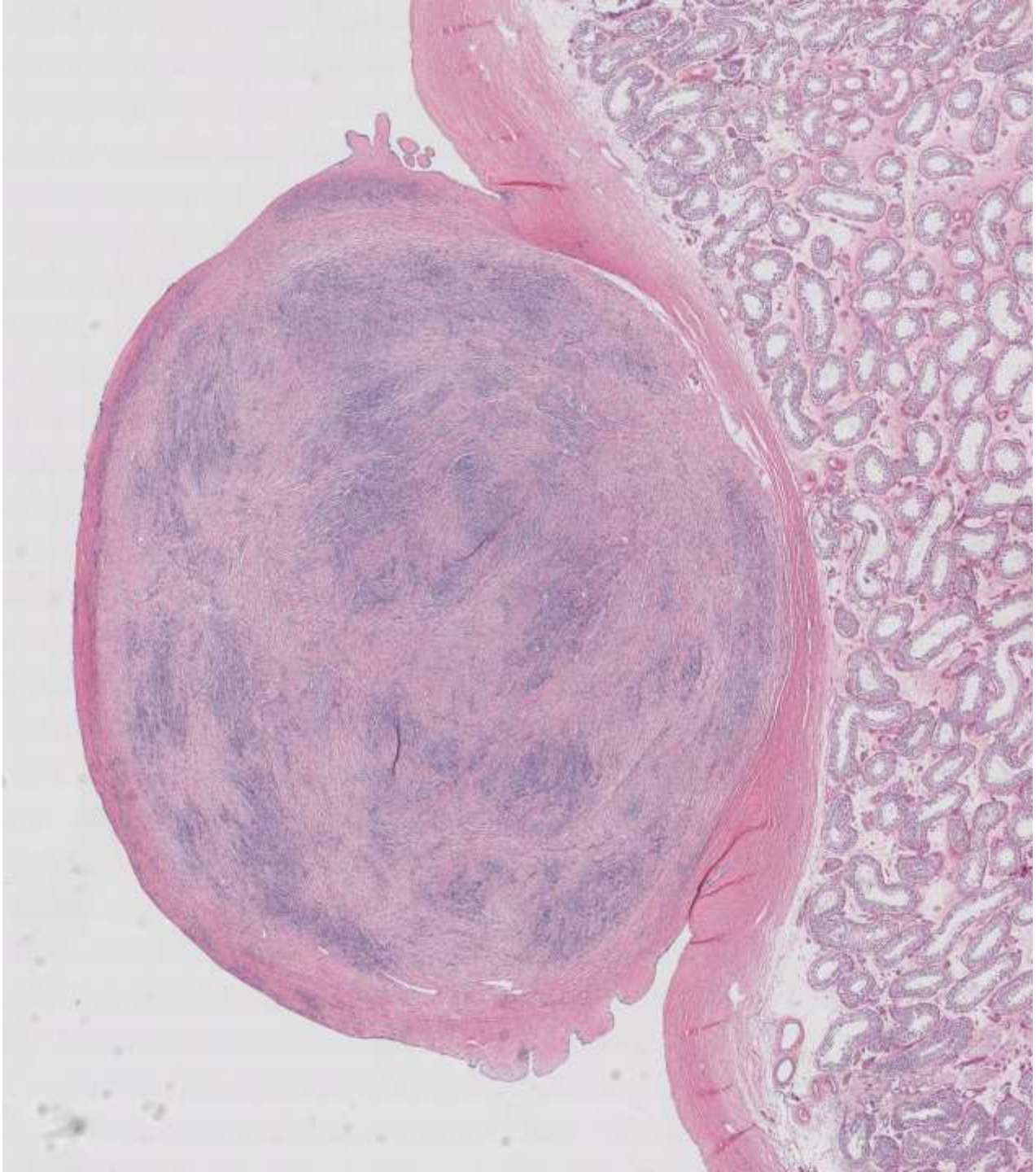

Richard Wagners Russ

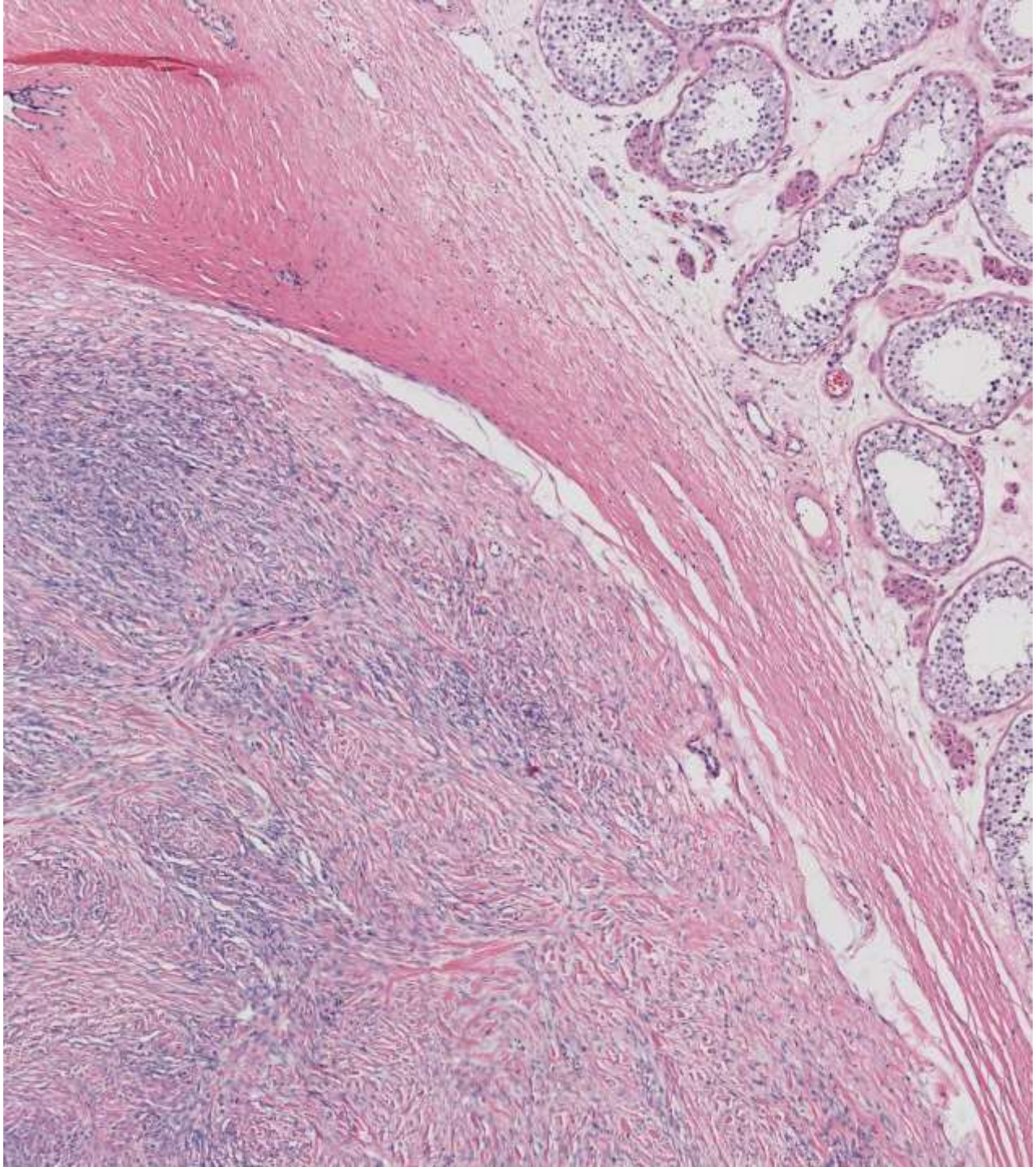
SB 6084

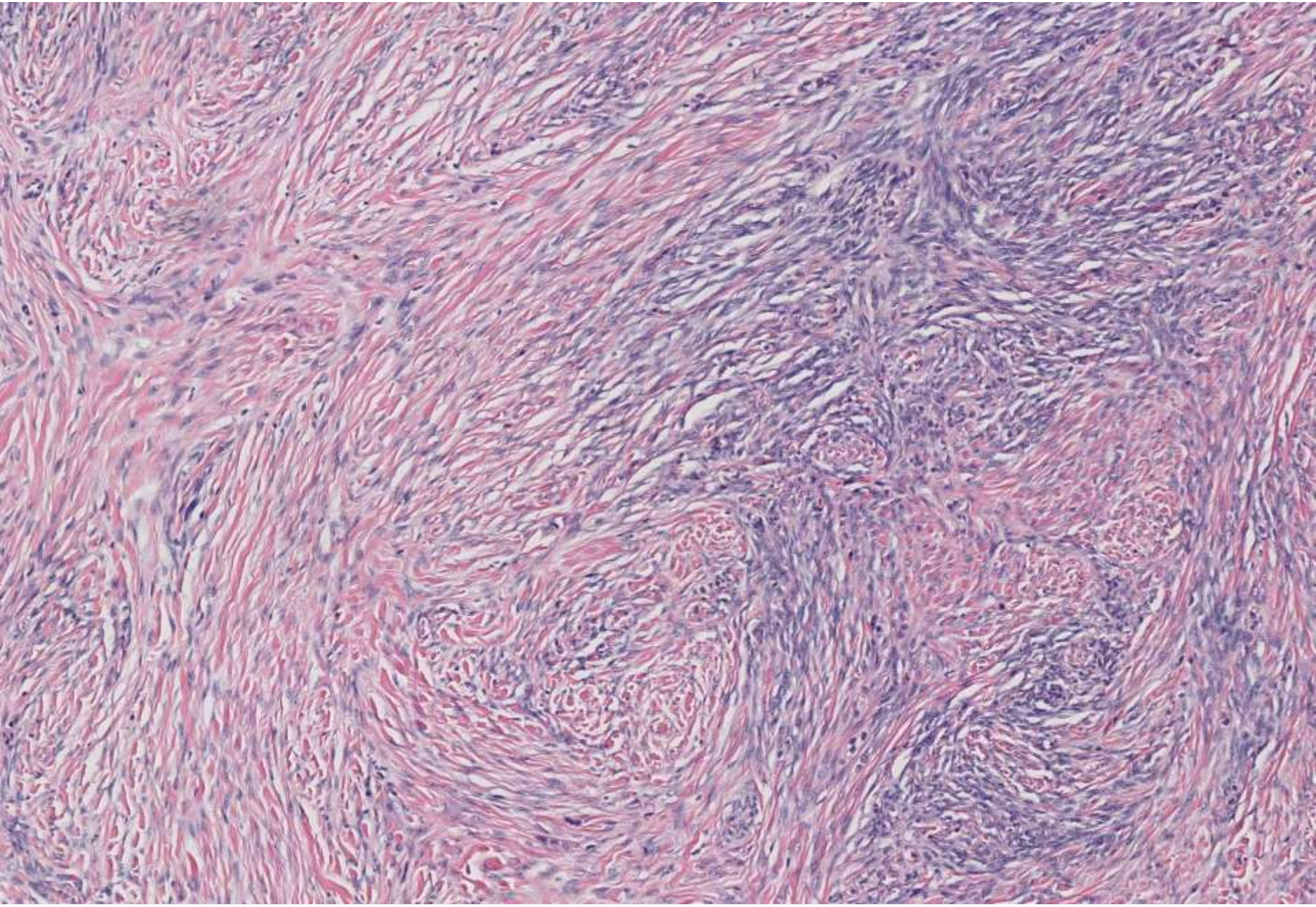
Sunny Kao; Stanford

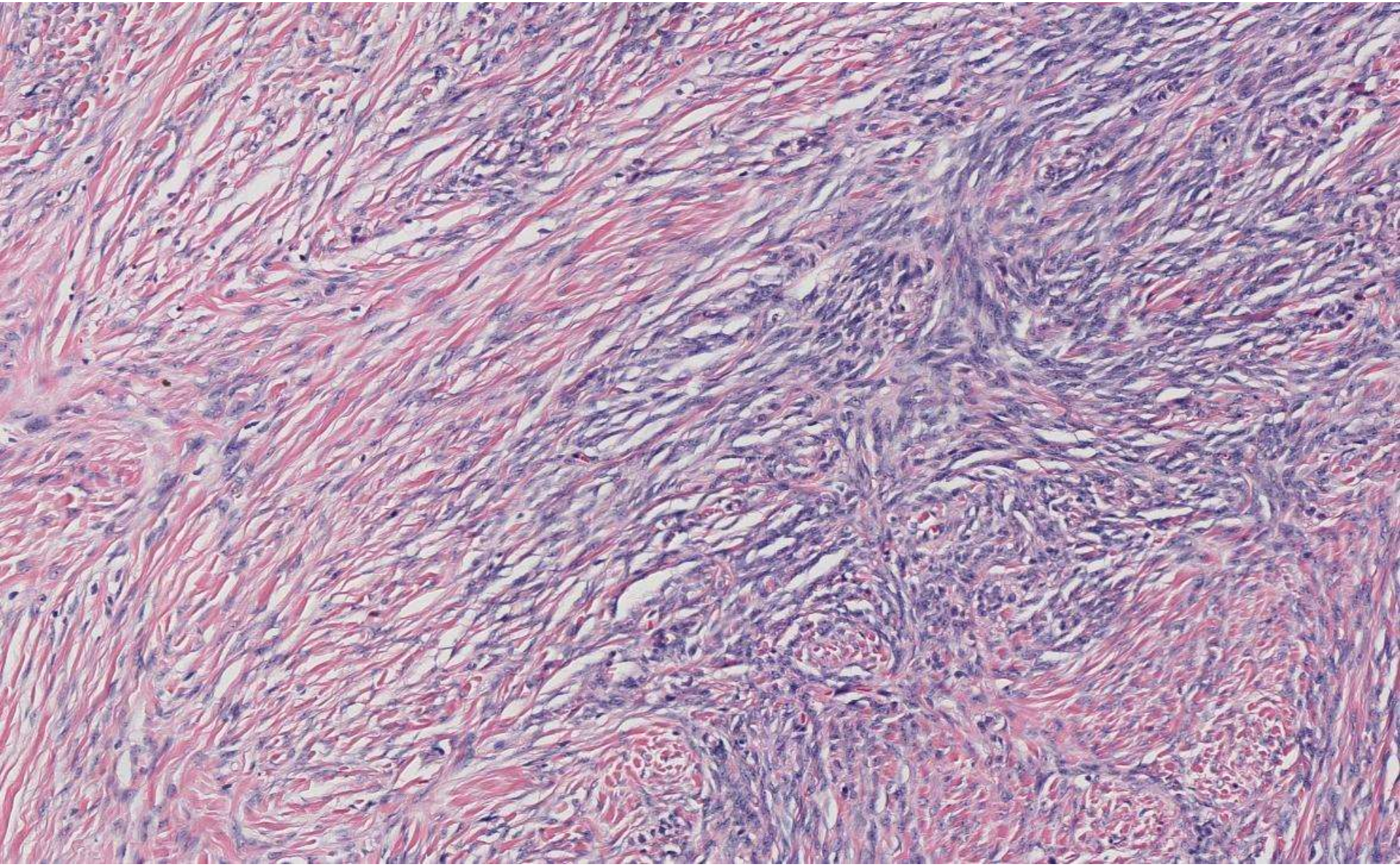
44-year-old male with left testicular tumor.

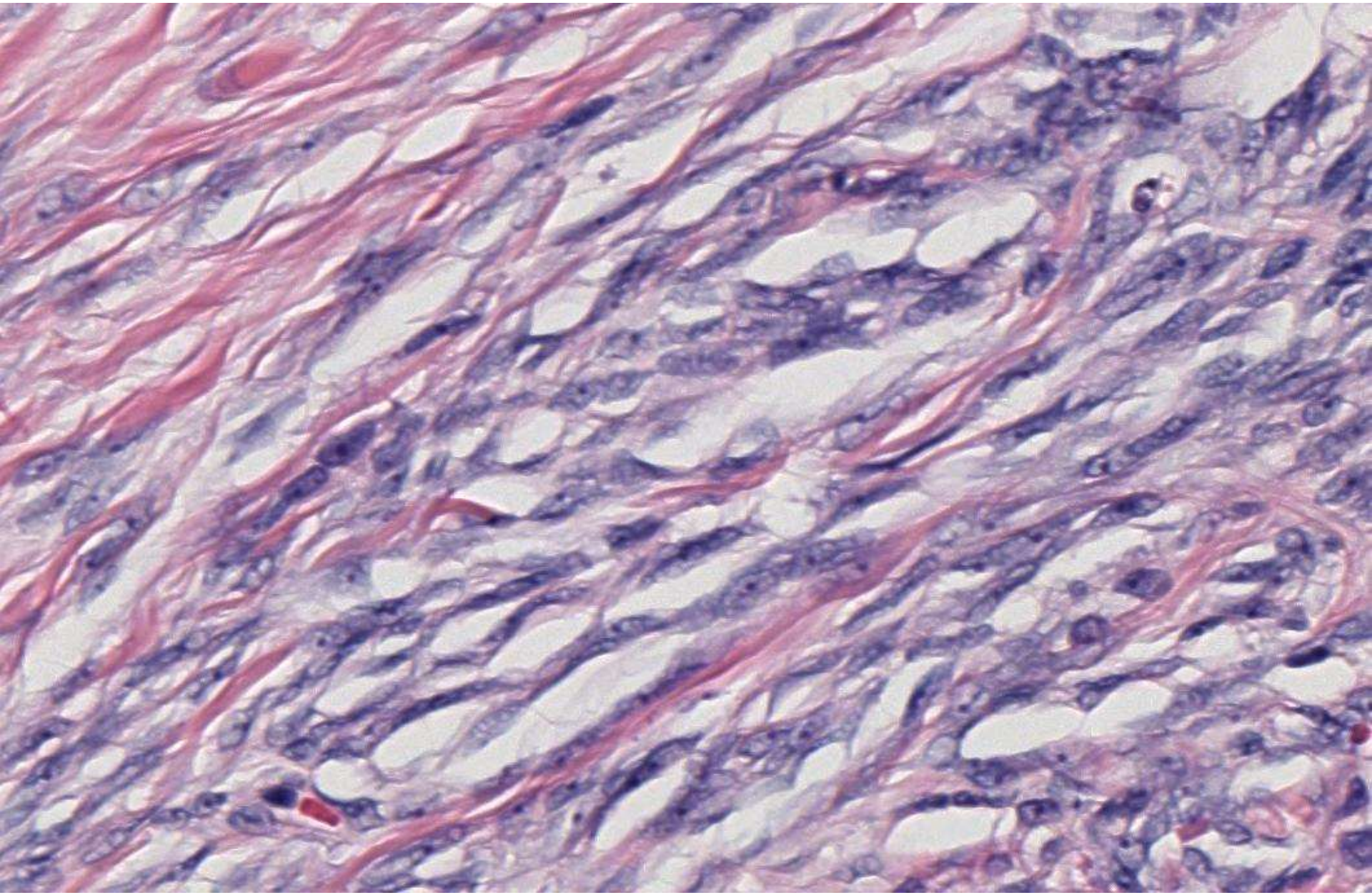












DIAGNOSIS?

Differential Diagnosis

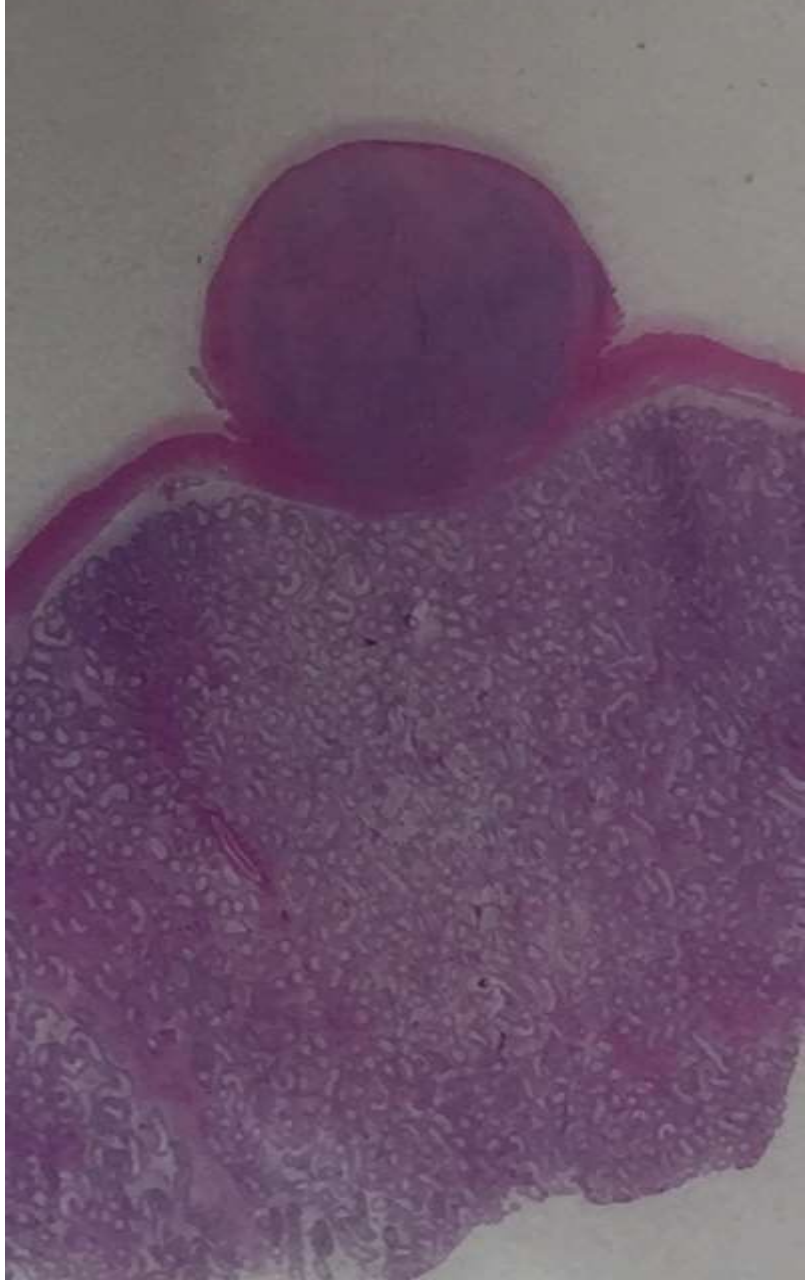
- Fibroma of tunica albuginea
- Fibroma of soft tissue type
- Angiomyofibroblastoma-like tumor (cellular angiofibroma)
- Fibrous pseudotumor
- Proliferative funiculitis (inflammatory myofibroblastic tumor)
- Solitary fibrous tumor
- Desmoplastic mesothelioma
- Leiomyoma

Staining results

- Smooth muscle actin ++
- Caldesmon –
- S100 –
- SF-1 –
- WT-1 –
- STAT6 –

Fibroma of tunica albuginea

- Wide age range; 2nd to 8th decade
- Circumscribed, white, whorled nodules that may be pedunculated
- Variably cellular (mild to moderate) bland spindled/stellate cells
- Lack the association with a hydrocele, trauma, or inflammation that is often present in non-neoplastic proliferations
- Benign



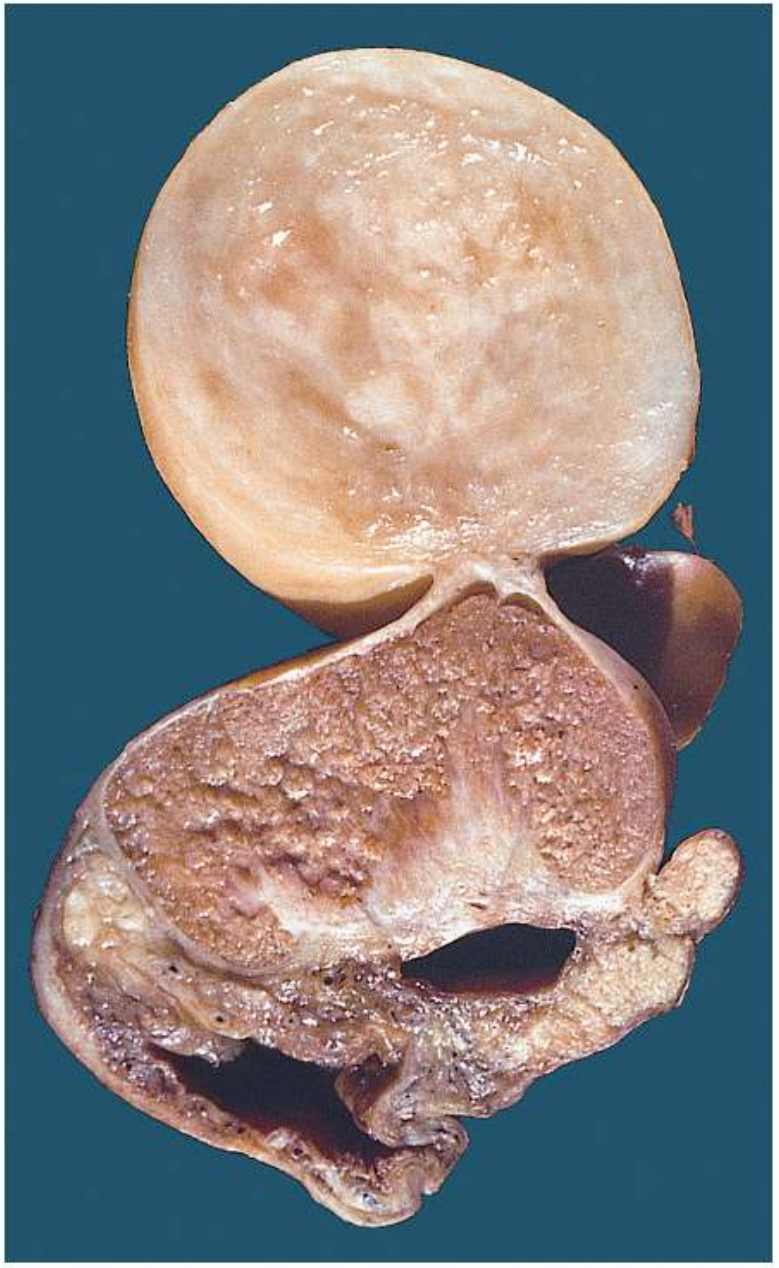


Figure 7-70

FIBROMA OF TUNICA ALBUGINEA

Key Learning Points

- **DDX for fibromatous (para)testicular lesions**

- **Features of fibroma of tunica albuginea**

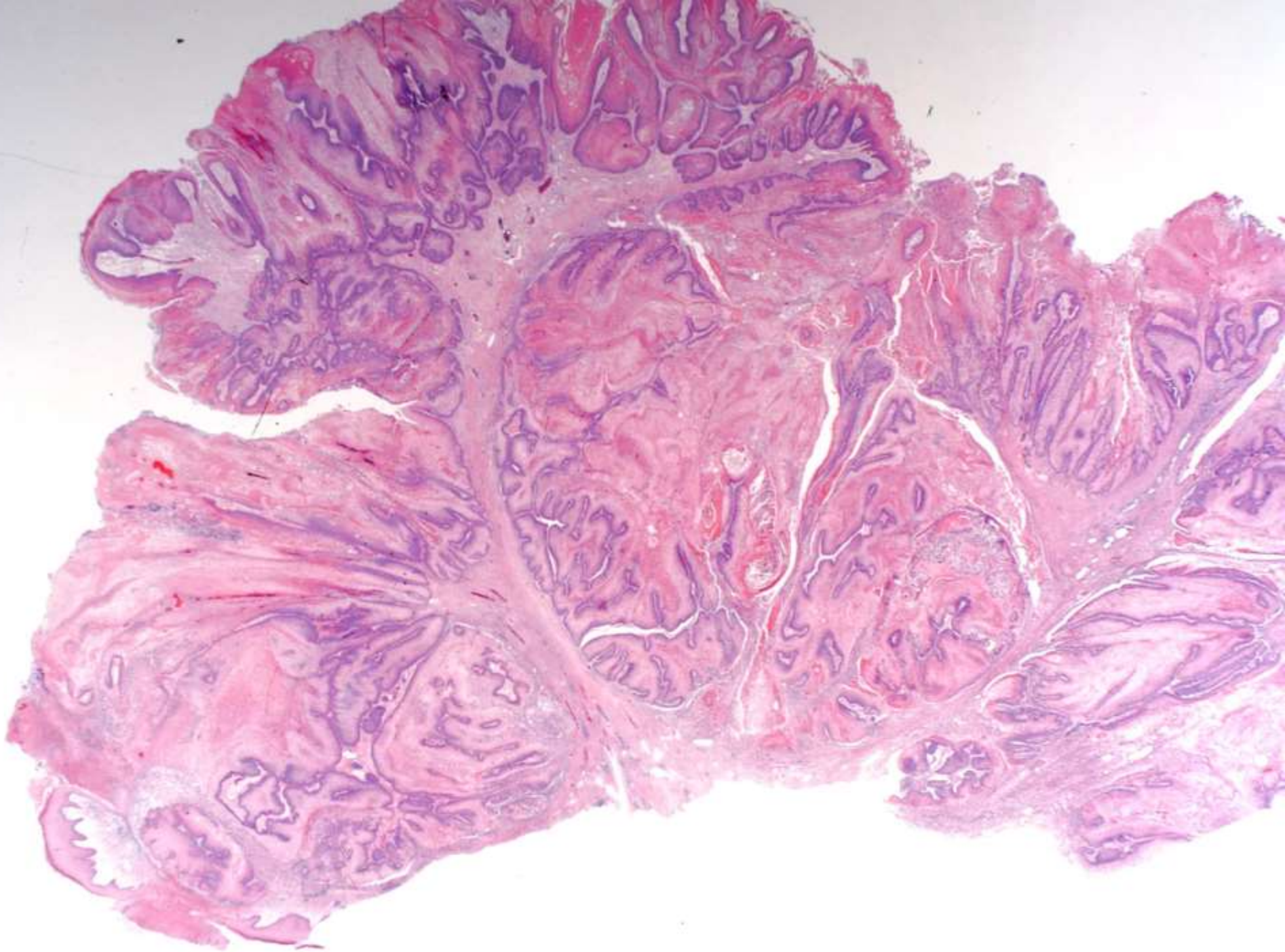
References

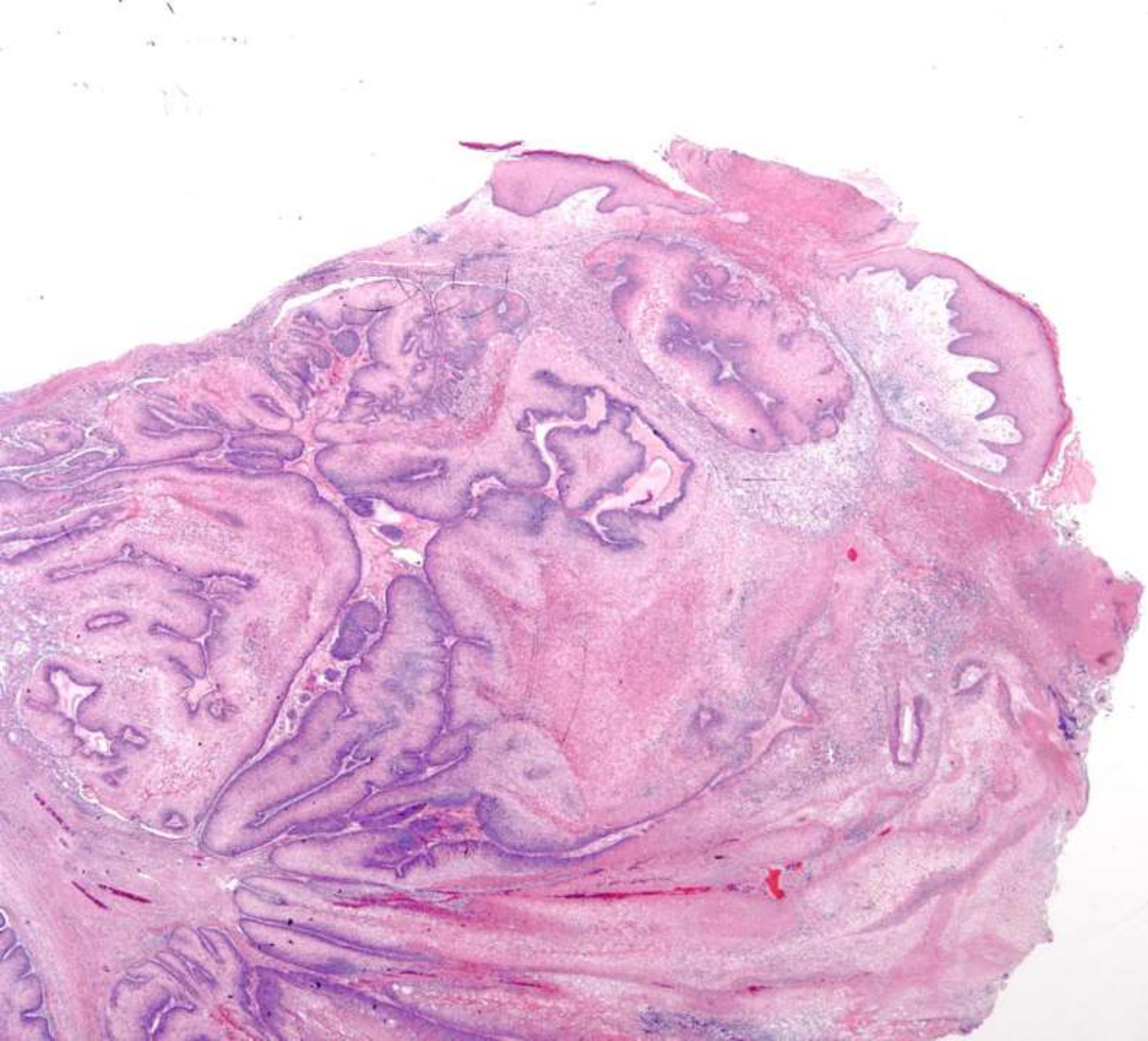
- **Ulbright and Young.** AFIP Atlas of Tumor Pathology. Series 4. Tumors of the Testis and Adjacent Structure.

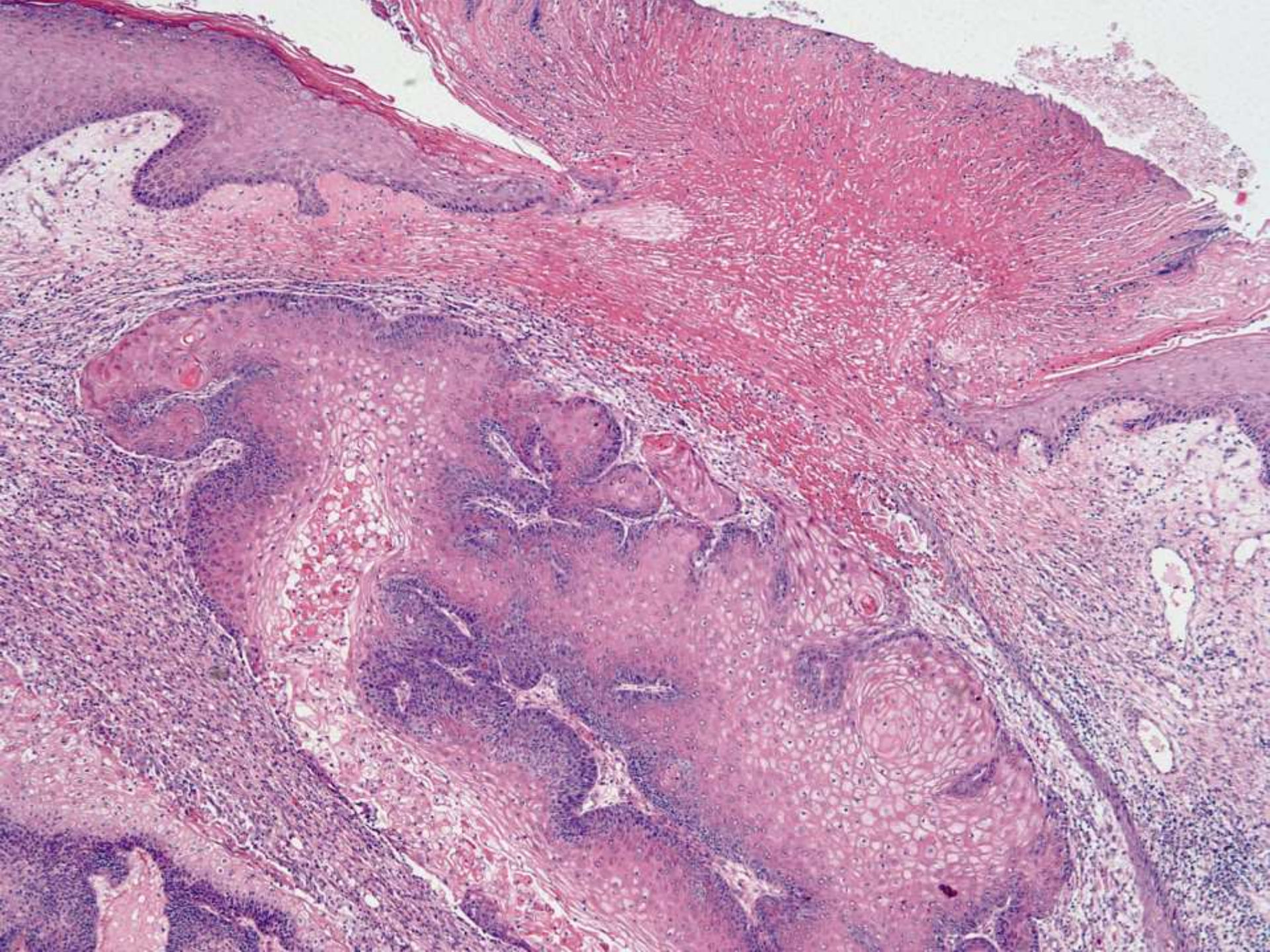
SB 6085

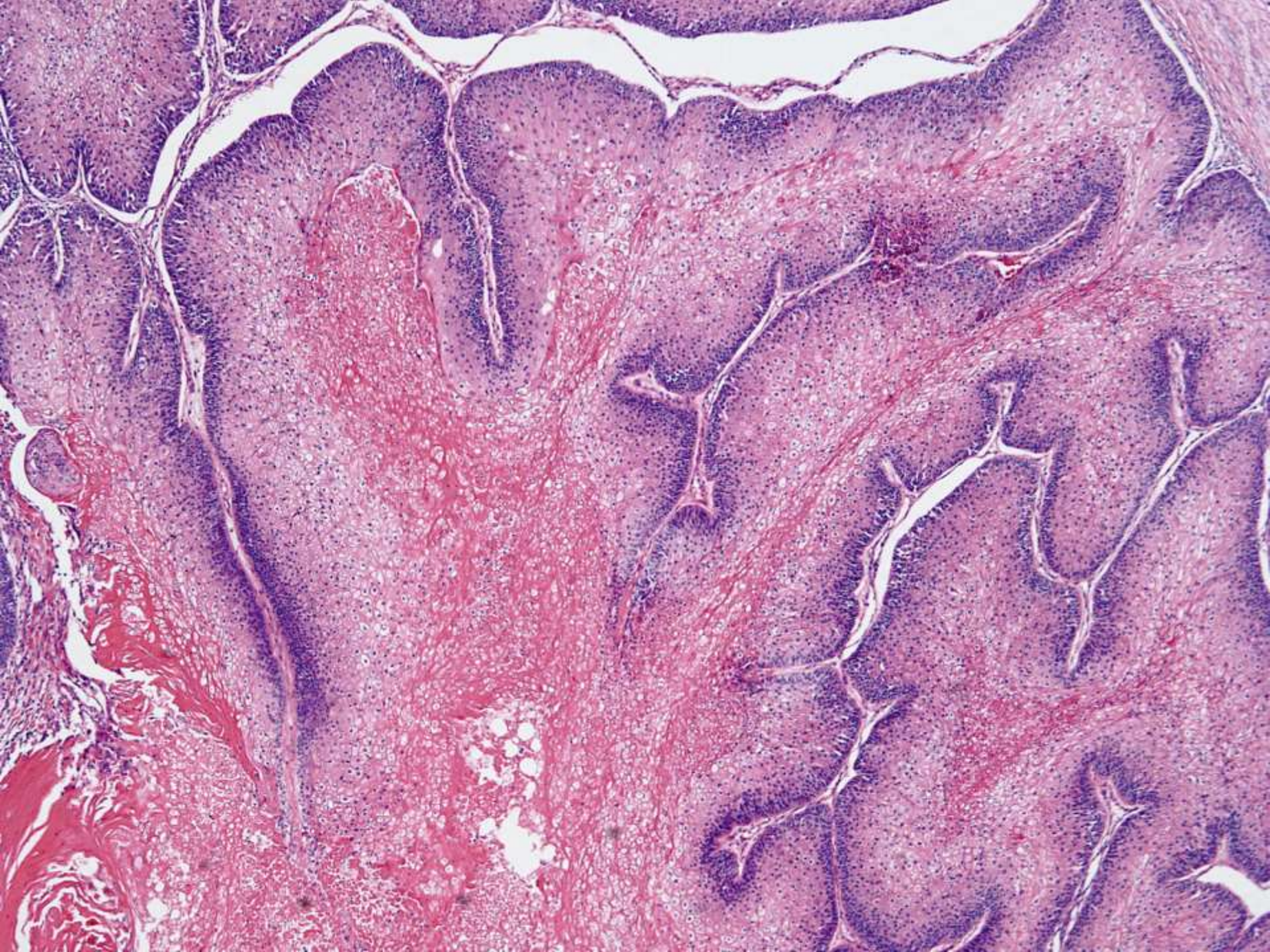
Alana Shain/Teri Longacre; Stanford

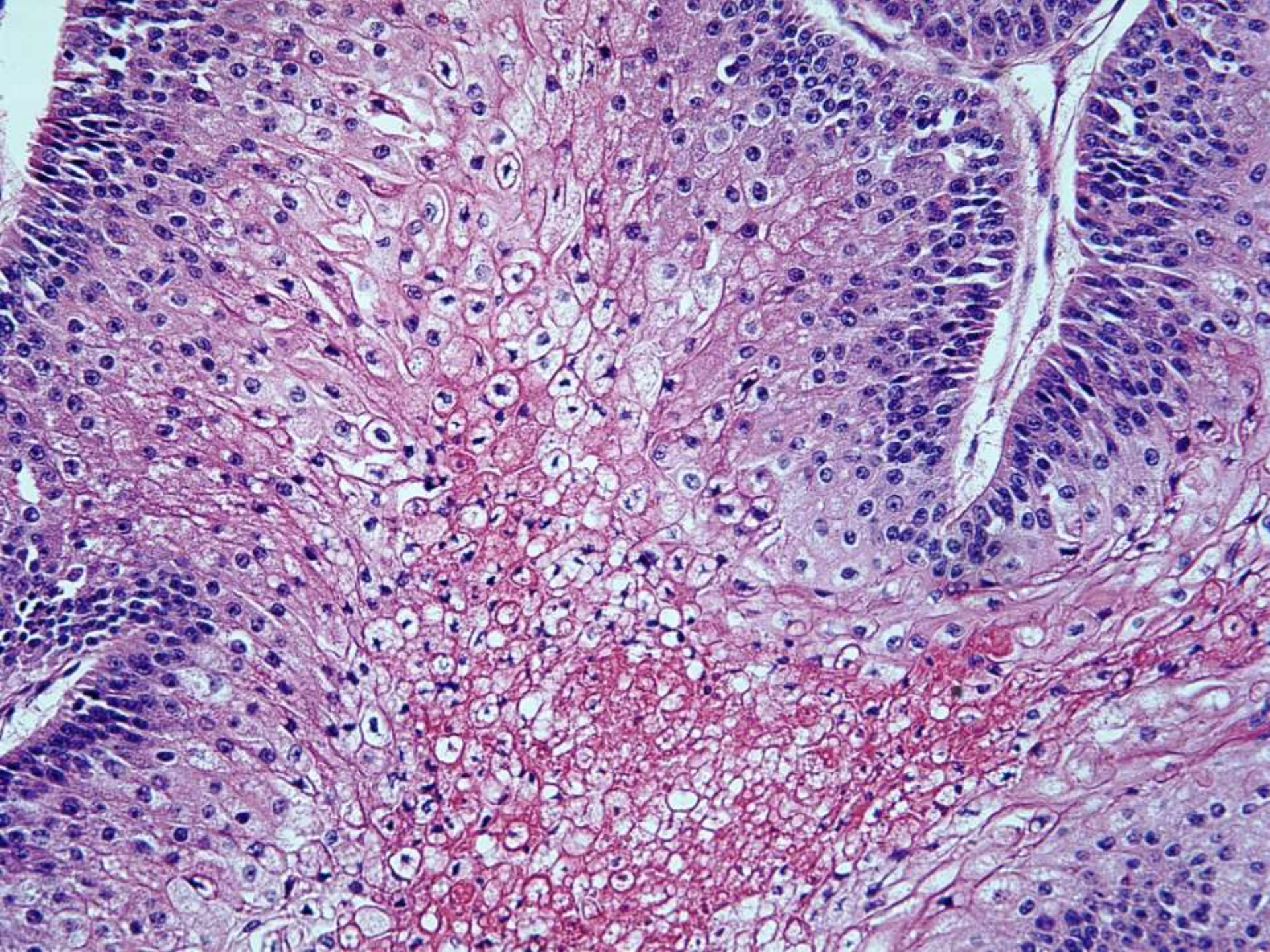
53-year-old male with fungal mass arising from skin of left hip.

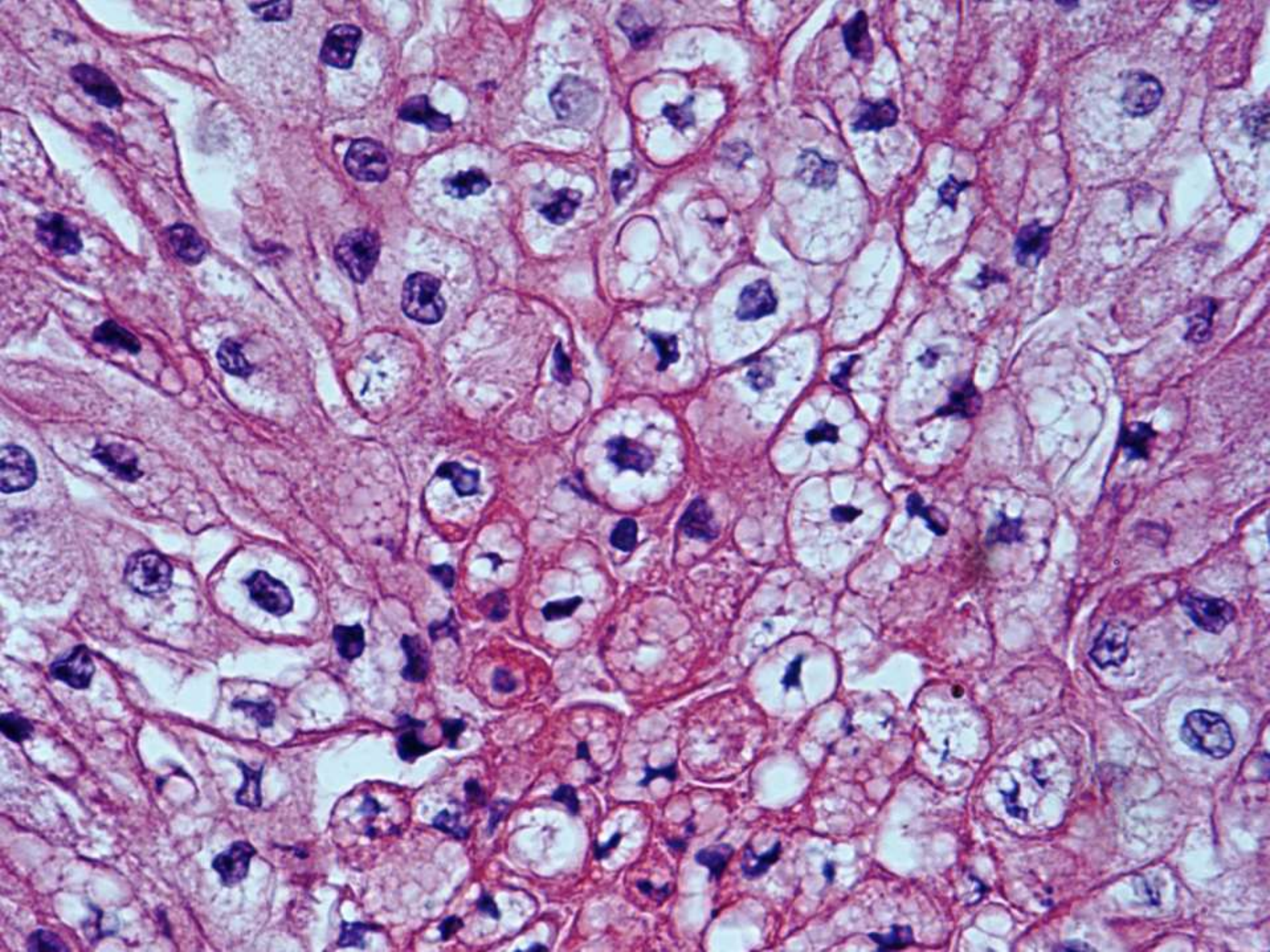












DIAGNOSIS?

SB 6085
53 year old male with fungating left hip mass

Alana Shain, MD/Teri Longacre, MD (Stanford Health Care)

Case contributed by Dr. Deepak Mohan

(San Joaquin General Hospital)

Differential Diagnosis

Benign

- Sebaceous adenoma

Malignant

- Basal cell carcinoma with sebaceous differentiation
- Squamous cell carcinoma
- Sebaceous carcinoma
- Other neoplasms with clear cells
  - Dermal adnexal tumors, melanoma, metastasis (RCC), etc.

Sebaceous Carcinoma

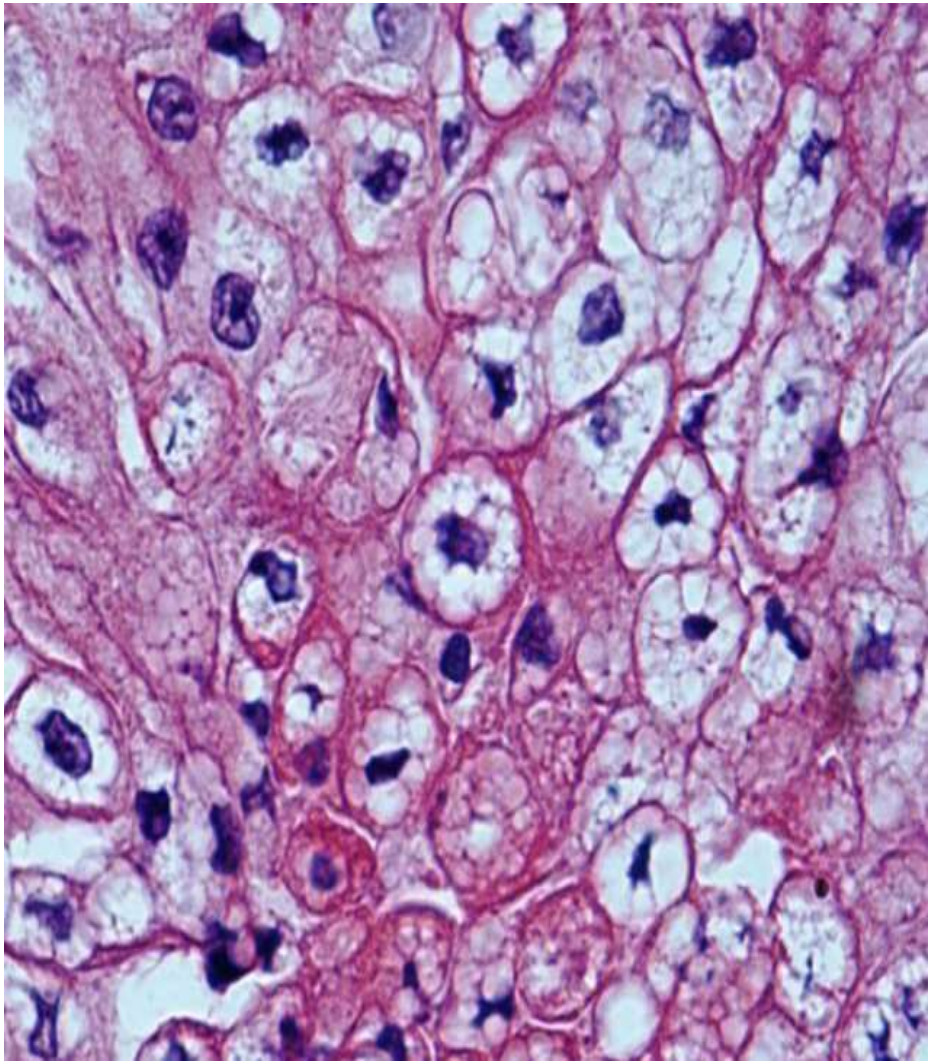
- **Ocular**: more common, females, 1% of eyelid tumors.
  - 1/3 nodal metastases
  - 20% 5 year mortality

- **Extra-ocular**: yellow-tan firm nodules, ulcerated, 1-4 cm+
  - 20% of all sebaceous carcinomas
  - Muir-Torre, organoid nevi (nevus sebaceus), organ transplant recipients

- **Wide local excision**

Sebaceous Carcinoma

- Sebaceous differentiation
- Deep or infiltrative growth, lobular architecture
- Cytologic atypia (large nuclei, nucleoli)
- Mitotic figures
- Necrosis: Focal or comedo-like
- Ulceration
- Abundant lipid



Ancillary Studies

- **IHC testing for loss of mismatch repair protein expression**
- Diagnosis predominantly on H&E, but some stains can help differentiate poorly differentiated sebaceous carcinoma vs BCC and SCC

	Sebaceous Ca	BCC	SCC
EMA	+	-	+
AR	+	+	-
BerEP4	+/-	+	-
Adipophilin (membranous vesicular)	+		- /+
Factor XIIIa* (nuclear)	+		- (2/26+)

***clone AC-1A1 mouse monoclonal**

Clark et al. J Cutan Pathol 2016

Plaza et al. The American Journal of Dermatopathology 2015

Muir-Torre Syndrome

- Autosomal dominant, 90% *MSH2* germline mutations
- Phenotypic variant of Lynch syndrome (HNPCC)

- Sebaceous neoplasms
- Keratoacanthomas
- Visceral malignancy (usually GI)

References

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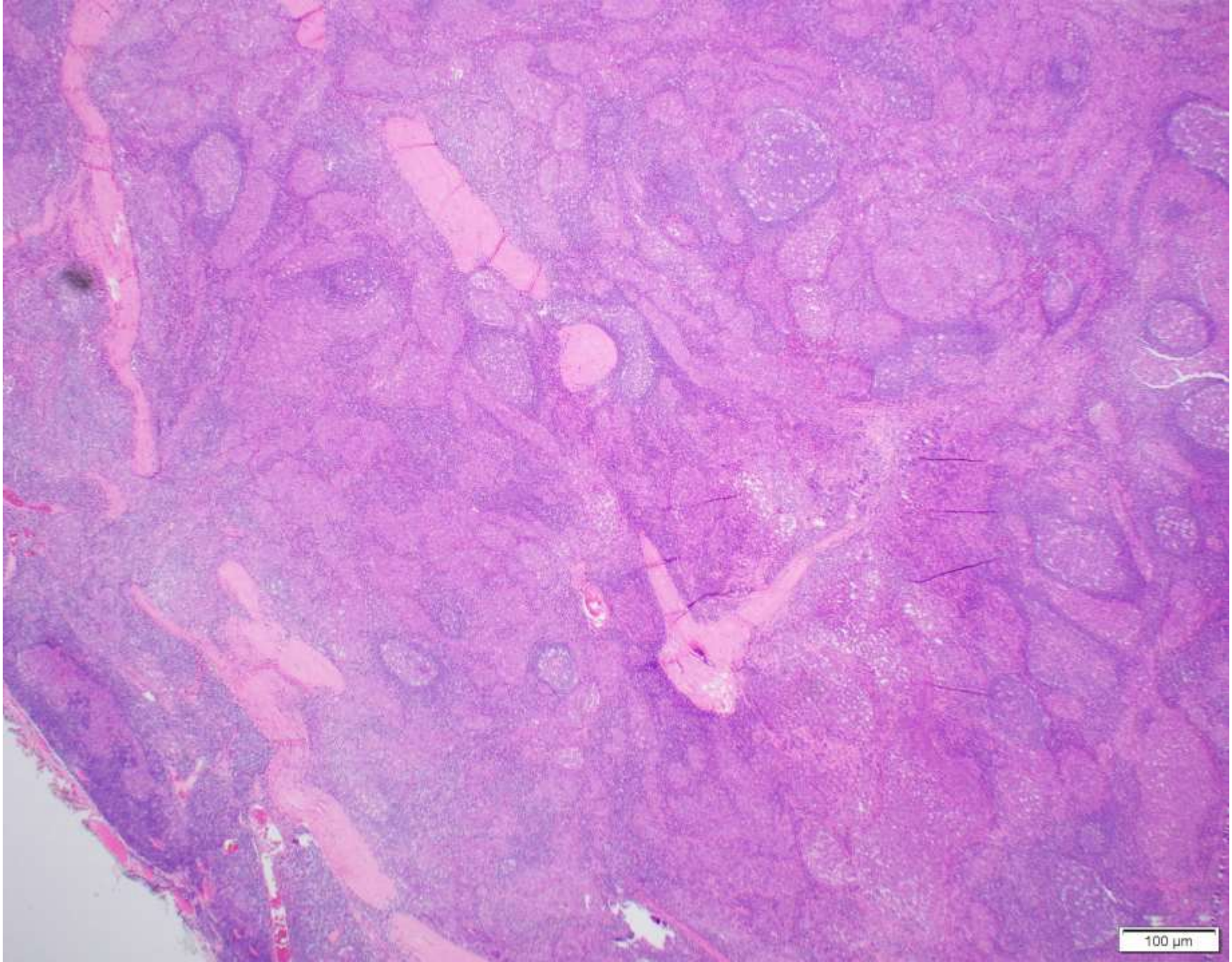
SB 6086

Sarah Cherny; Kaiser San Francisco

52-year-old female with 3.9cm parotid mass.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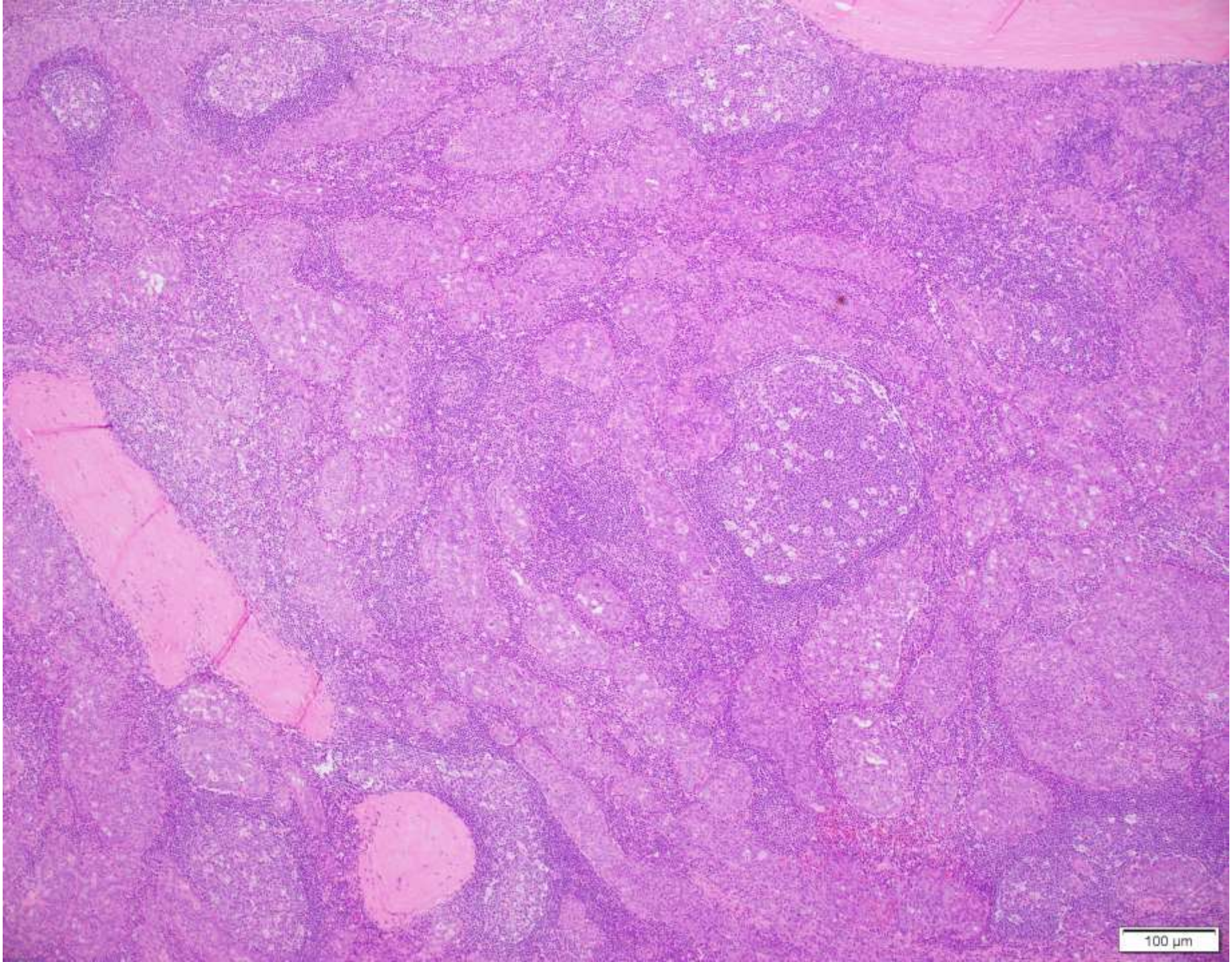
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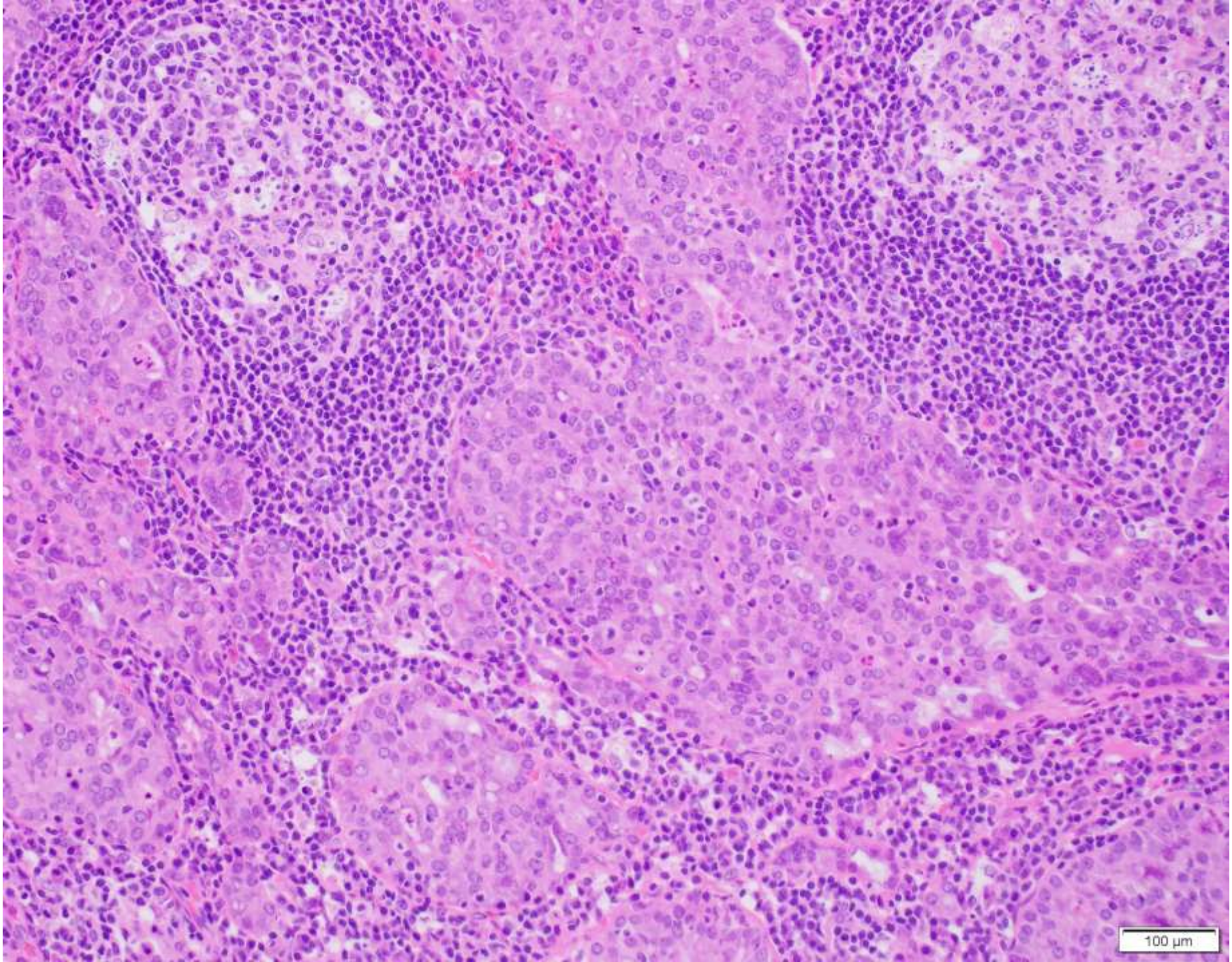
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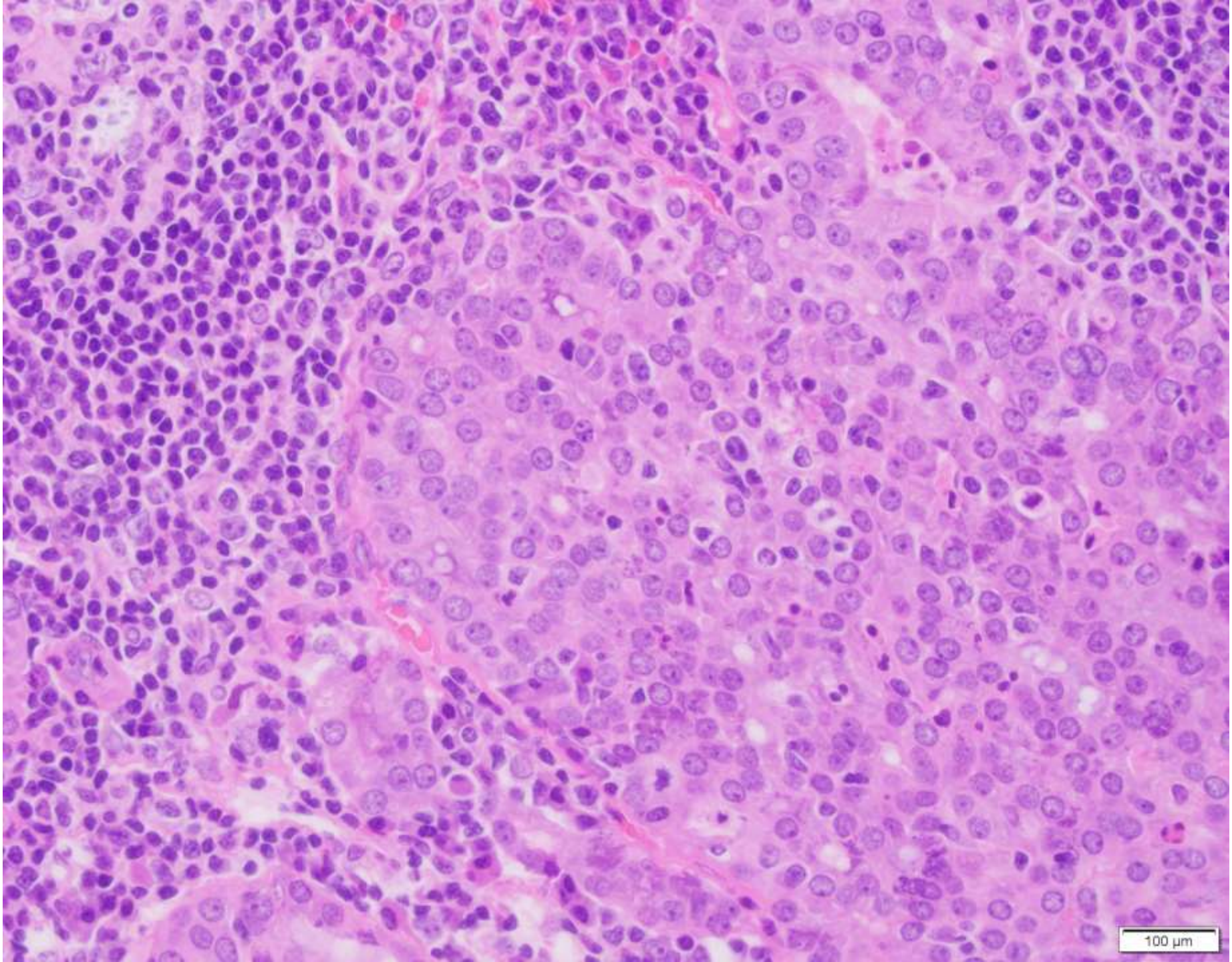
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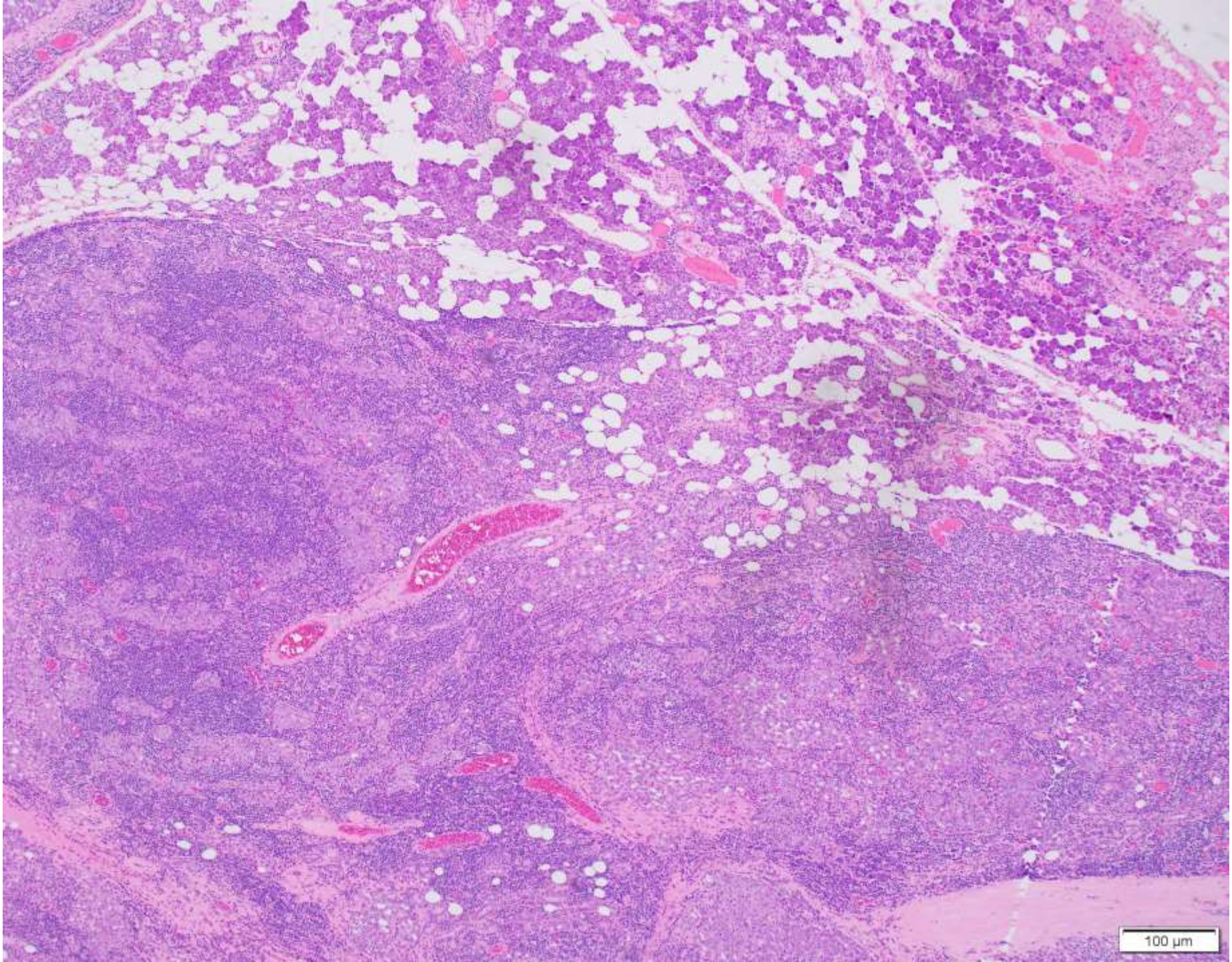
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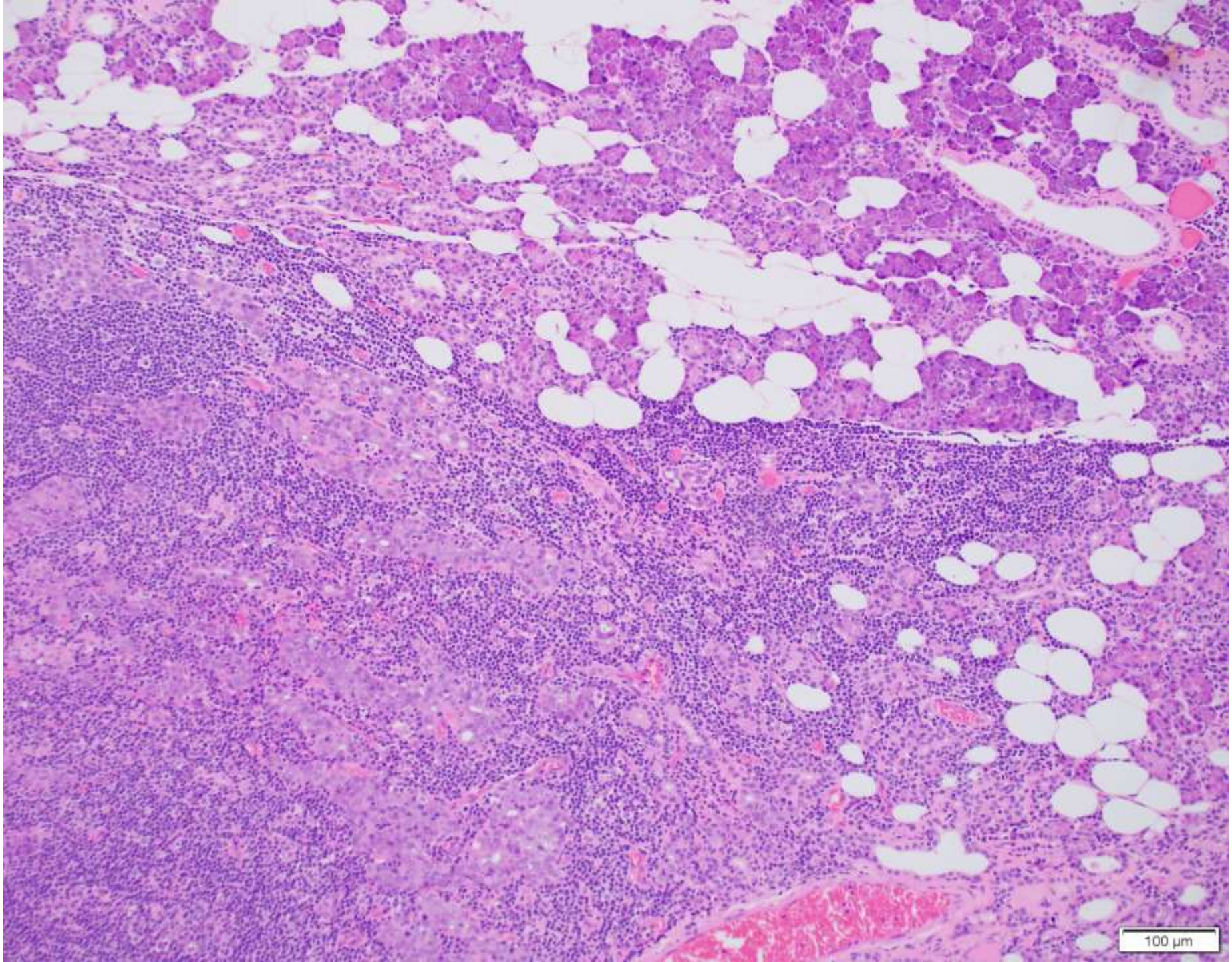
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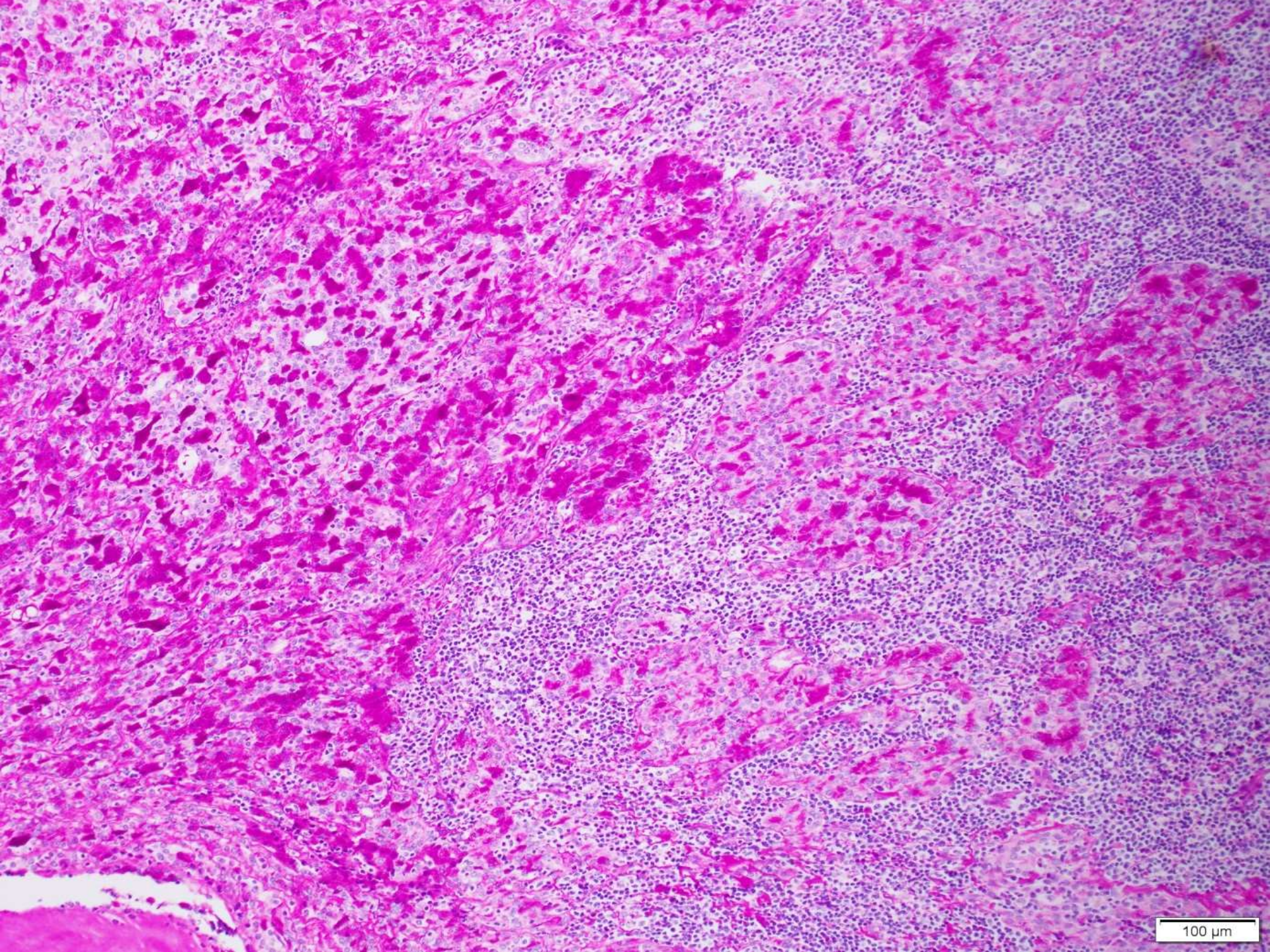
DIAGNOSIS?

- Ddx:
  - Acinic cell carcinoma
    - involving an intraparotid node??
  - Oncocytoma or other oncocytic salivary gland neoplasm
    - Involving an intraparotid node??
  - Warthin's tumor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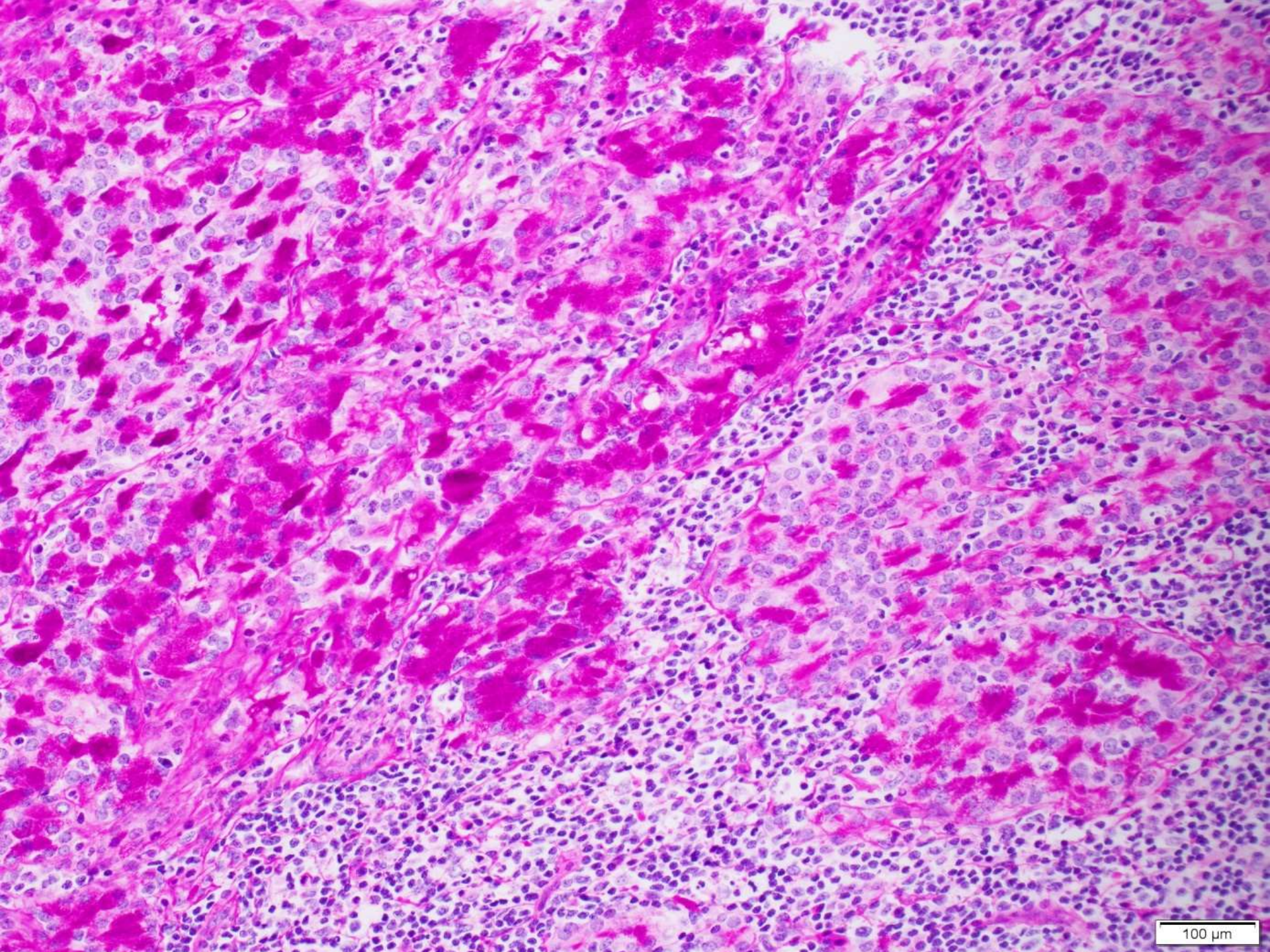
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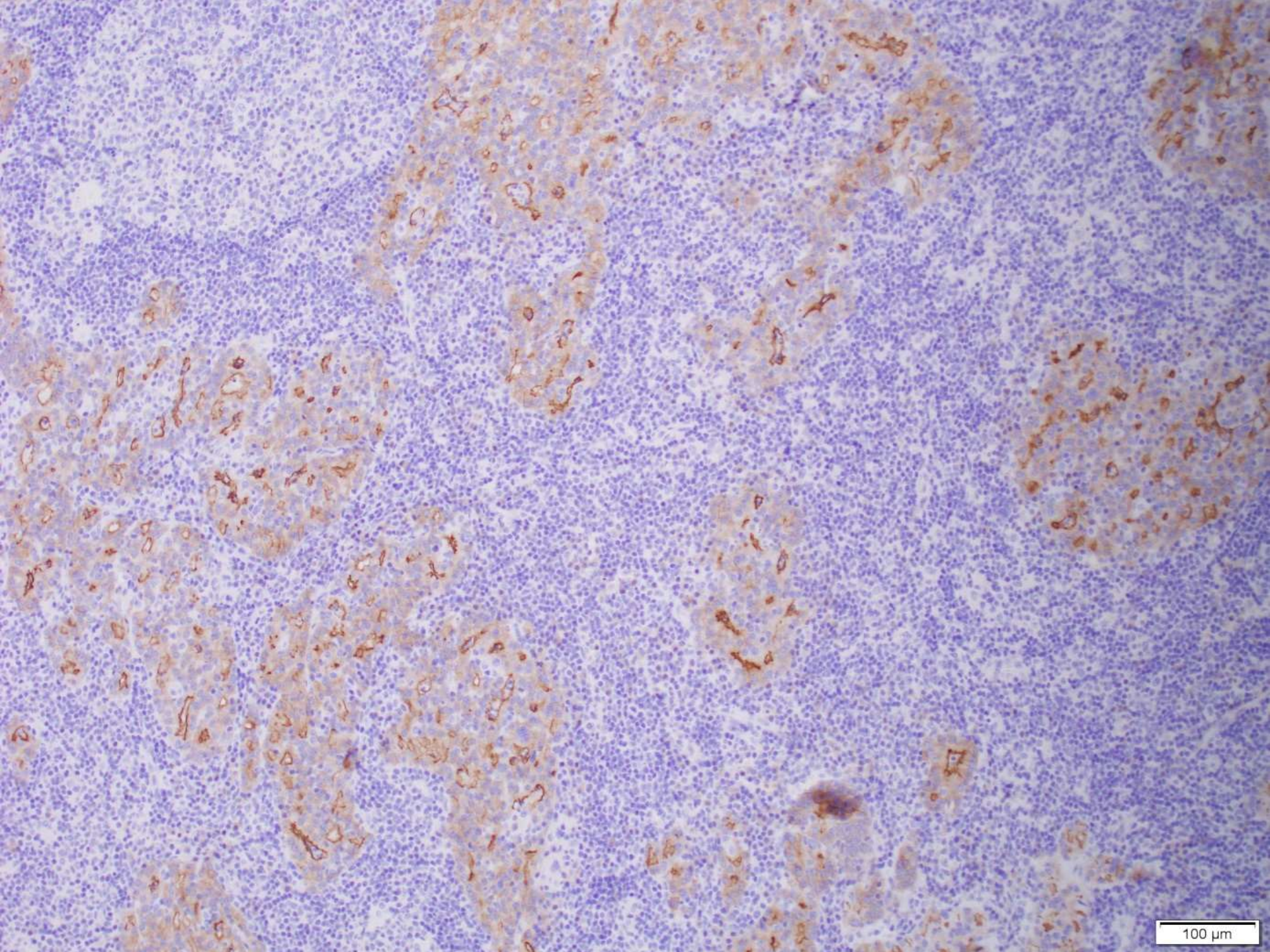
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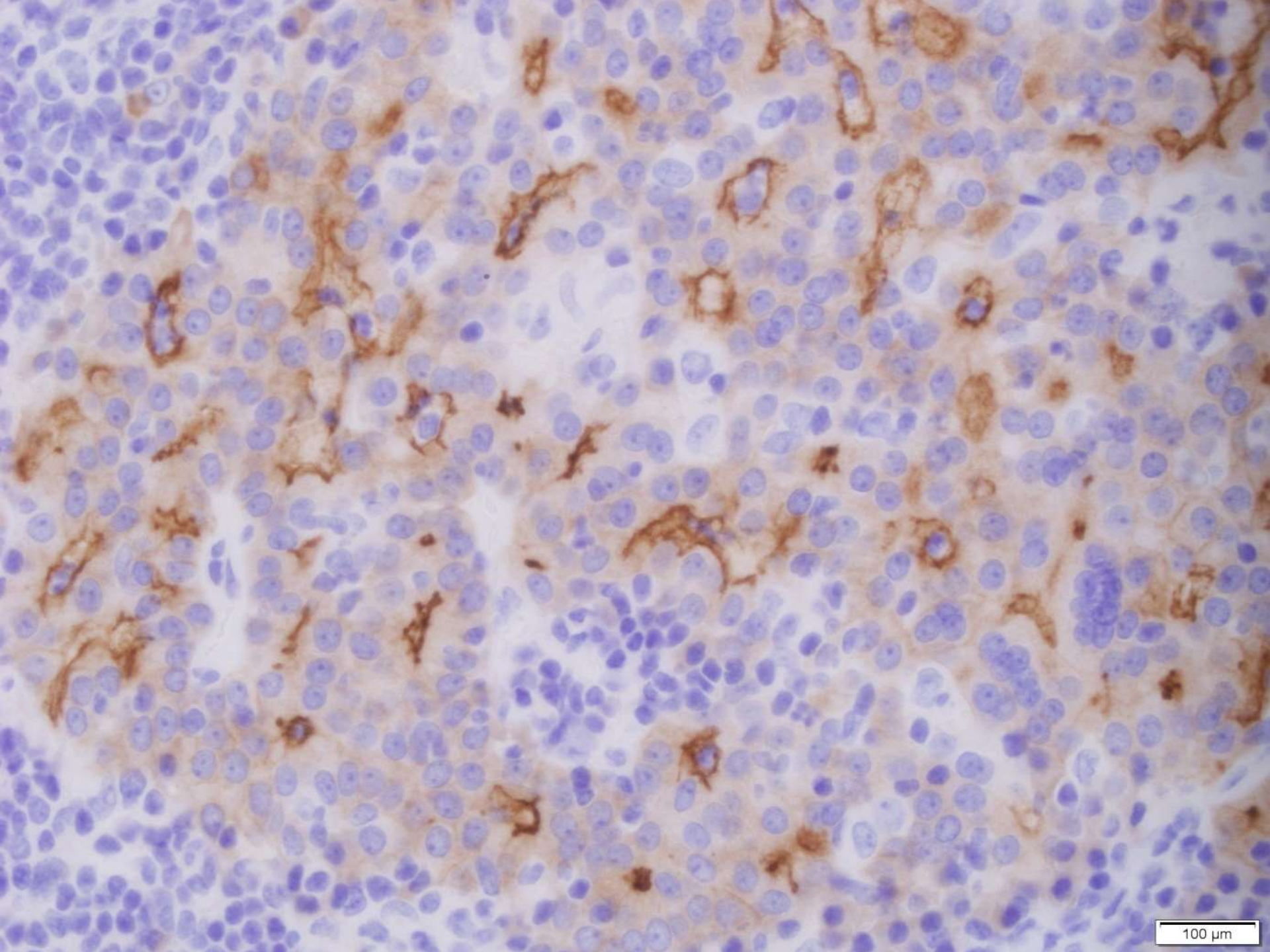
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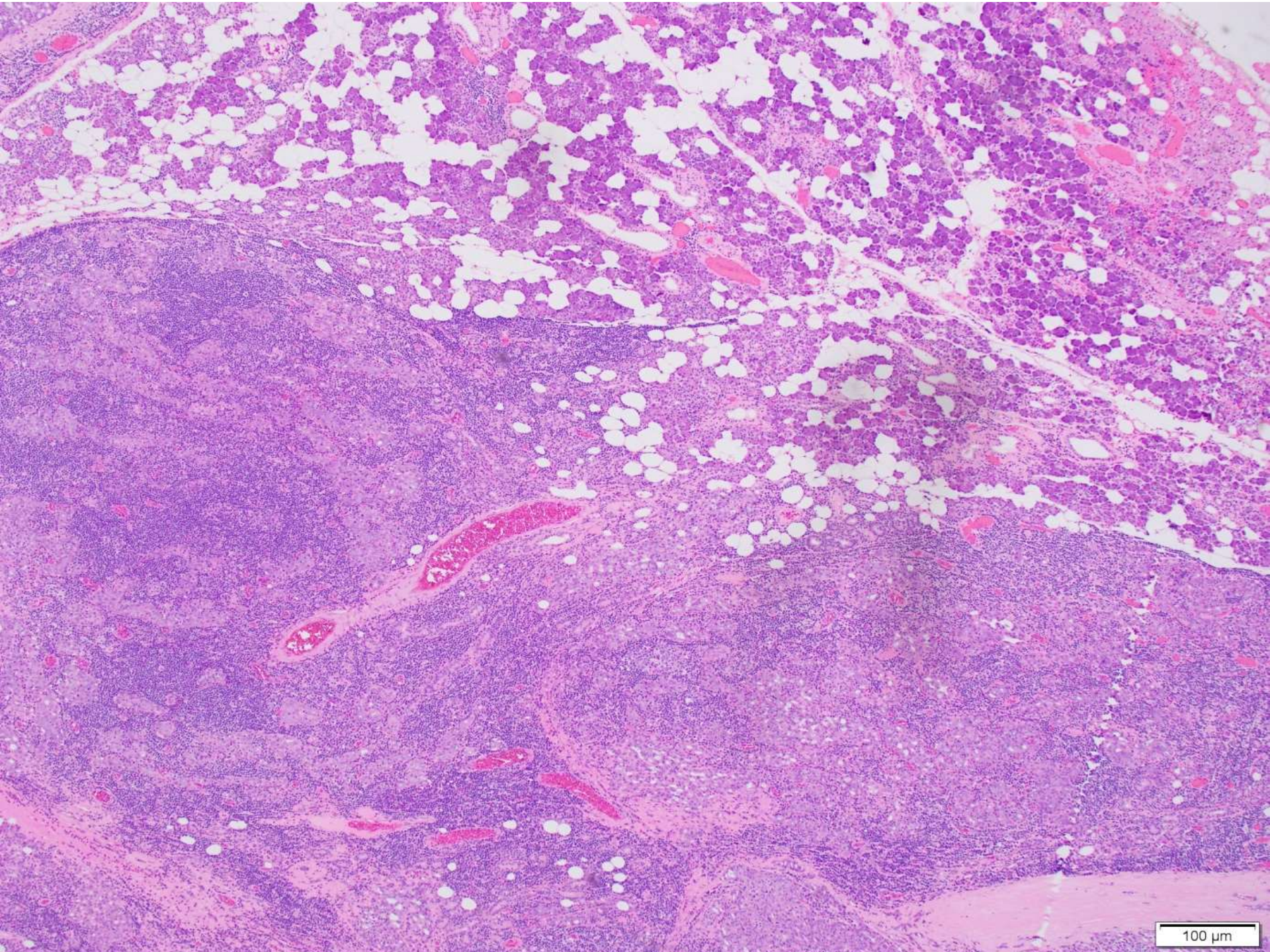
MODERN PATHOLOGY (2012) 25, 919–929

DOG1: a novel marker of salivary acinar and intercalated duct differentiation

Jacinthe Chênevert[1], Umamaheswar Duvvuri[2], Simion Chiosea[1], Sanja Dacic[1], Kathleen Cieply[1], Jean Kim[2], Daniel Shiwarski[2] and Raja R Seethala[1,2]

[1]*Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA and*
[2]*Department of Otolaryngology, University of Pittsburgh Medical Center, Pittsburgh, PA, USA*

Anoctamin-1 (ANO1) (DOG1, TMEM16a) is a calcium-activated chloride channel initially described in gastrointestinal stromal tumors, but now known to be expressed in a variety of normal and tumor tissues including salivary tissue in murine models. We herein perform a comprehensive survey of DOG1 expression in 156 cases containing non-neoplastic human salivary tissues and tumors. *ANO1* mRNA levels were significantly higher (8-fold increase, $P<0.0001$) in normal parotid tissue ($n=6$) as compared with squamous mucosa ($n=15$). By immunohistochemistry, DOG1 showed a diffuse moderate (2+) apical membranous staining pattern in normal serous acini, 1+ apical membranous pattern in mucous acini, and variable 1–2+ apical staining of distal intercalated ducts. Myoepithelial cells, striated and excretory ducts were invariably negative. All acinic cell carcinomas ($n=28$) were DOG1 positive demonstrating a complex mixture of intense (3+) apical membranous, cytoplasmic and complete membranous staining. Most ductal tumor types were negative or only showed a subset of positive cases. Within the biphasic tumor category, adenoid cystic carcinomas (18/24 cases) and epithelial–myoepithelial carcinomas (8/15 cases) were frequently positive, often showing a distinctive combined apical ductal and membranous/cytoplasmic myoepithelial staining profile. Thus, DOG1 staining is a marker of salivary acinar and to a lesser extent intercalated duct differentiation. Strong staining can be used to support the diagnosis of acinic cell carcinoma. DOG1 may also be a marker of a 'transformed' myoepithelial phenotype in a subset of biphasic salivary gland malignancies.
Modern Pathology (2012) **25,** 919–929; doi:10.1038/modpathol.2012.57; published online 30 March 2012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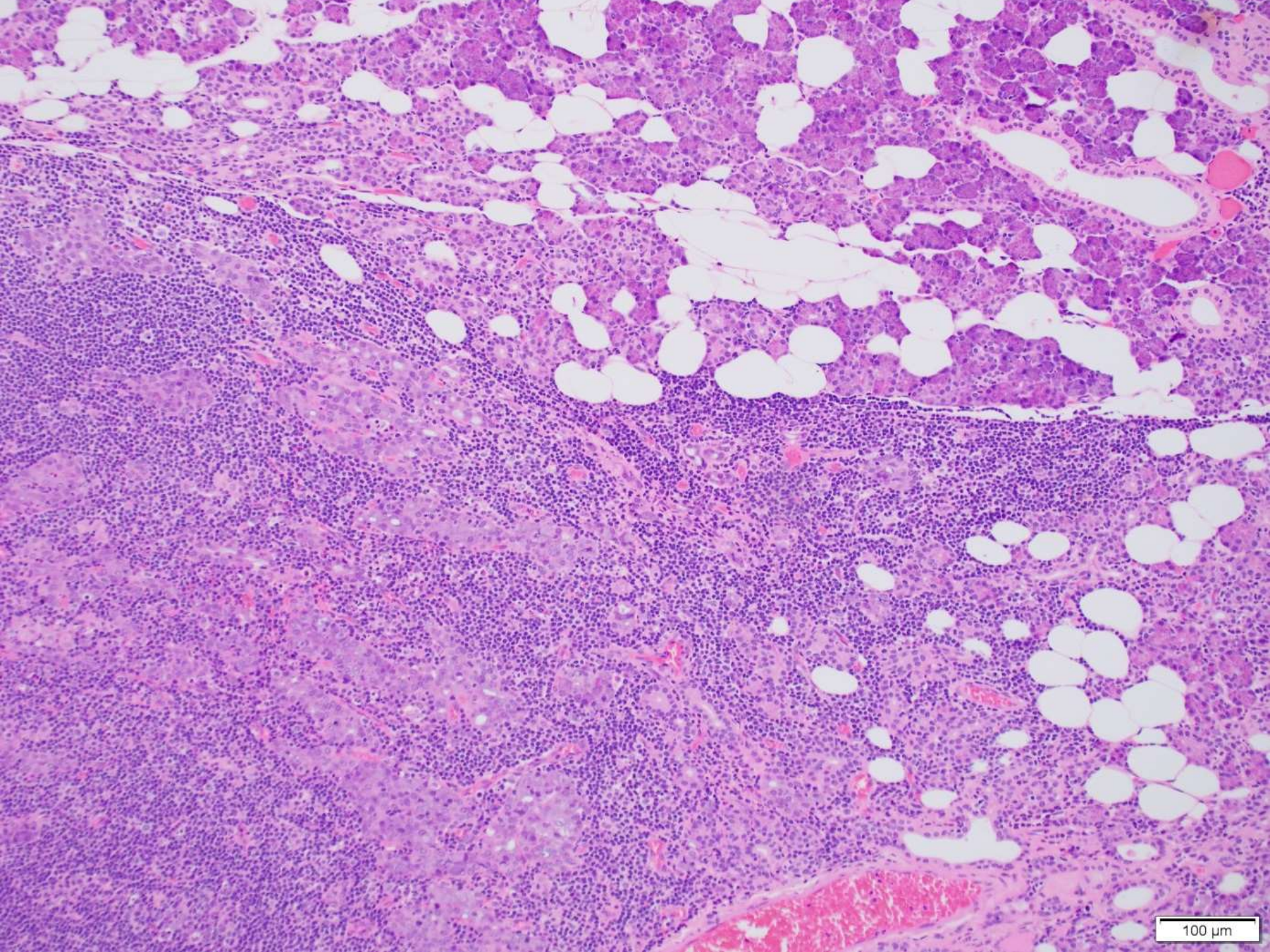
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- Diagnosis:
- Acinic Cell Carcinoma
  - With dense associated lymphoid infiltrate

Acinic Cell Carcinoma: Epidemiology

- Broad age range, from young children to elderly adults
  - Most patients between 2nd to 7th decades
- Slightly female predominance
- No predilection for any ethnic group

Acinic Cell Carcinoma: Clinical Features

- ~80% occur in parotid gland
  - Slowly enlarging mass
  - ~1/3 of patients report pain
  - 5-10% patients develop facial paralysis
- Usually 1-3 cm, circumscribed
  - Some are ill-defined and/or multinodular

Acinic Cell Carcinoma: Histopathology

- Low grade carcinomas with serous acinar cell differentiation
  - Variety of growth patterns and cell types
    - Cell types: acinic cell, intercalated ductal cell, clear cell, non-specific glandular cell, vacuolated cell
    - Growth patterns: solid, microcystic, papillary-cystic, follicular
    - Patient outcome not consistently correlated with cell type or growth pattern
- PASd highlights cytoplasmic granules within acinic cells
  - May be patchy
- DOG-1: demonstrates canalicular pattern
  - Not specific for Acinic Cell Carcinoma

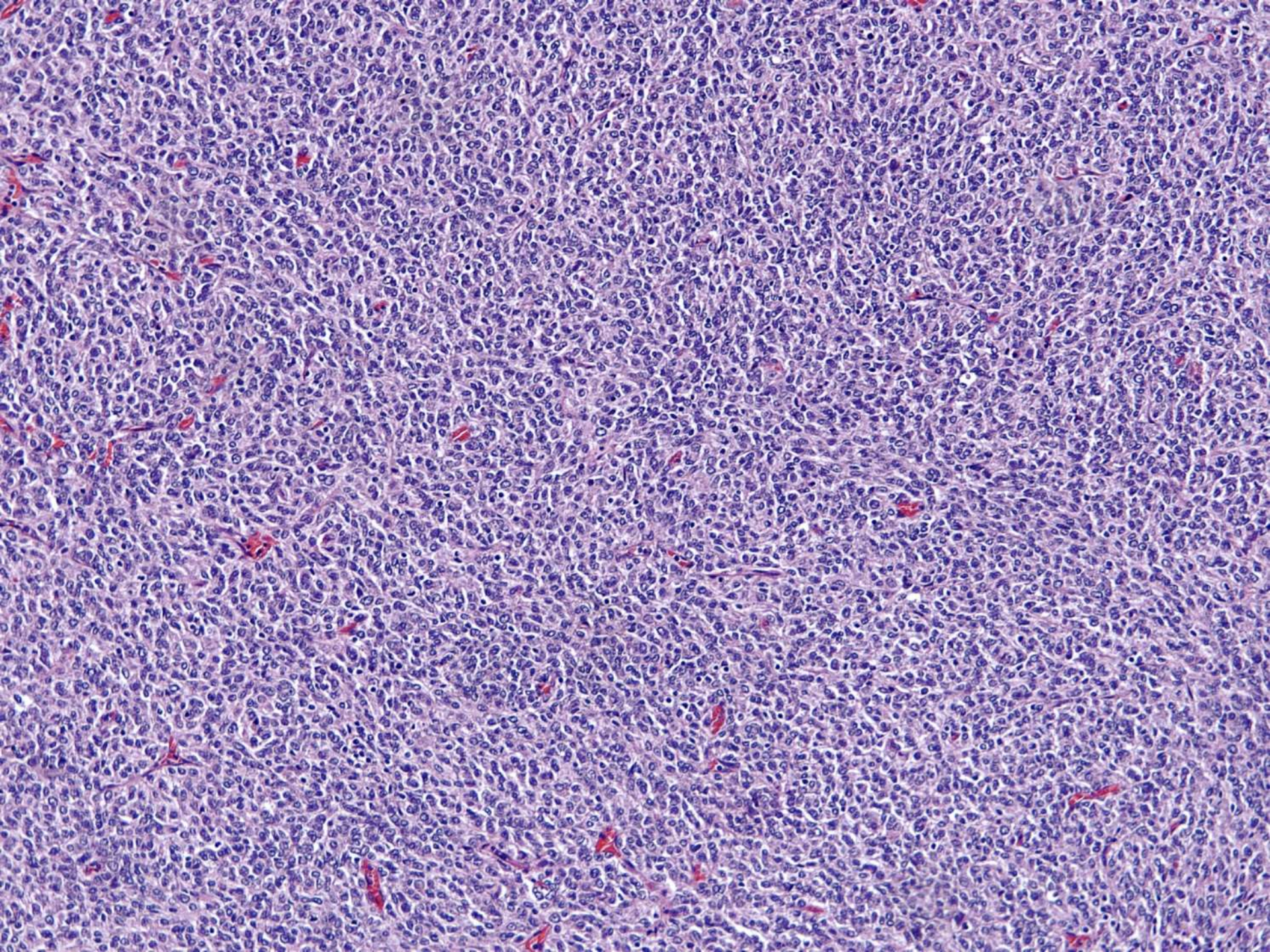
Acinic Cell Carcinoma: Histopathology

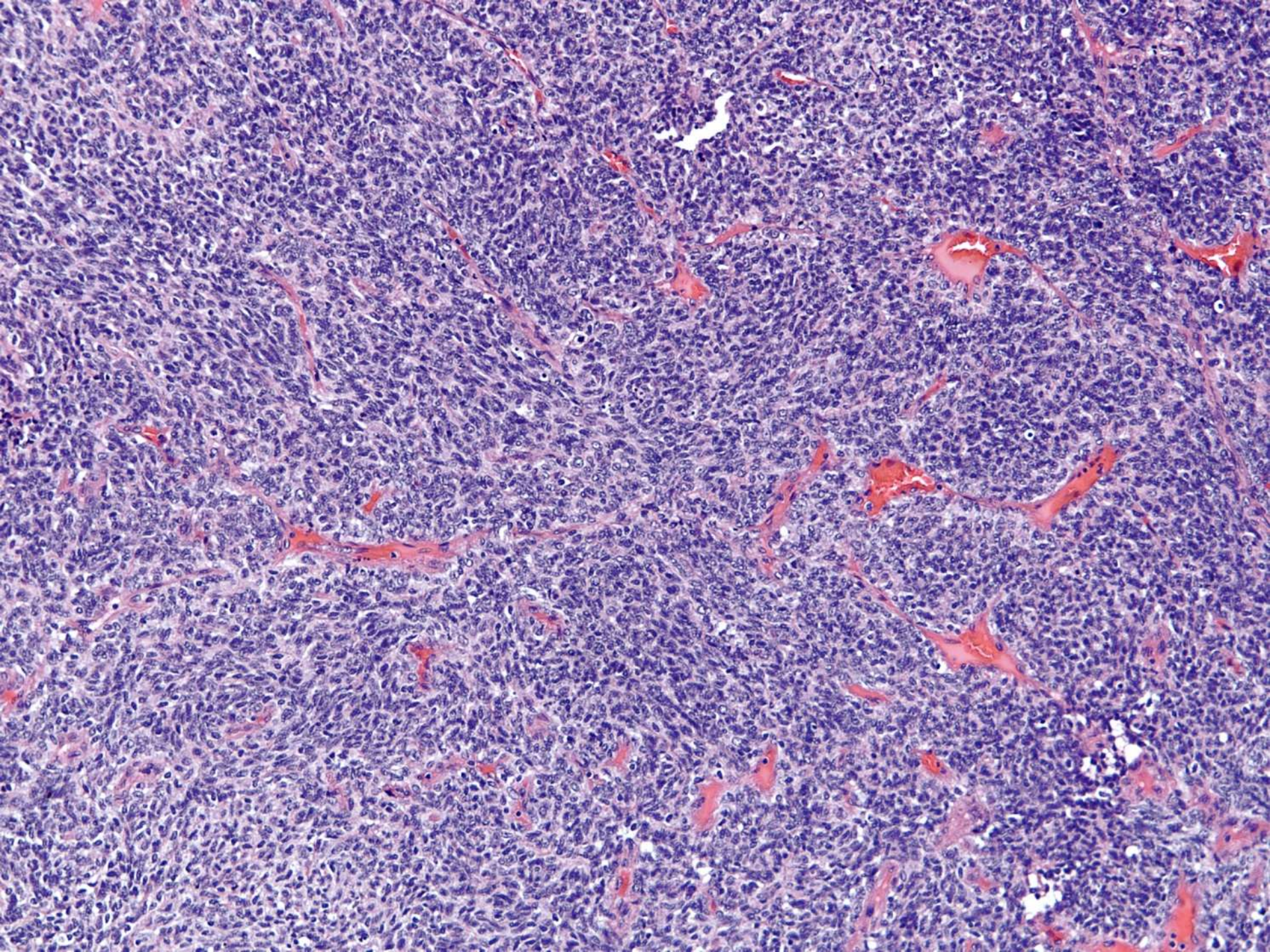
- A prominent lymphoid infiltrate with germinal center formation is associated with many acinic cell carcinoma
  - Tumor Associated Lymphoid Proliferation (“TALP”)
  - Represents immune reaction to tumor
- No prognostic significance
  - But misinterpretation can lead to inappropriate tumor staging -> potential for overly aggressive patient management

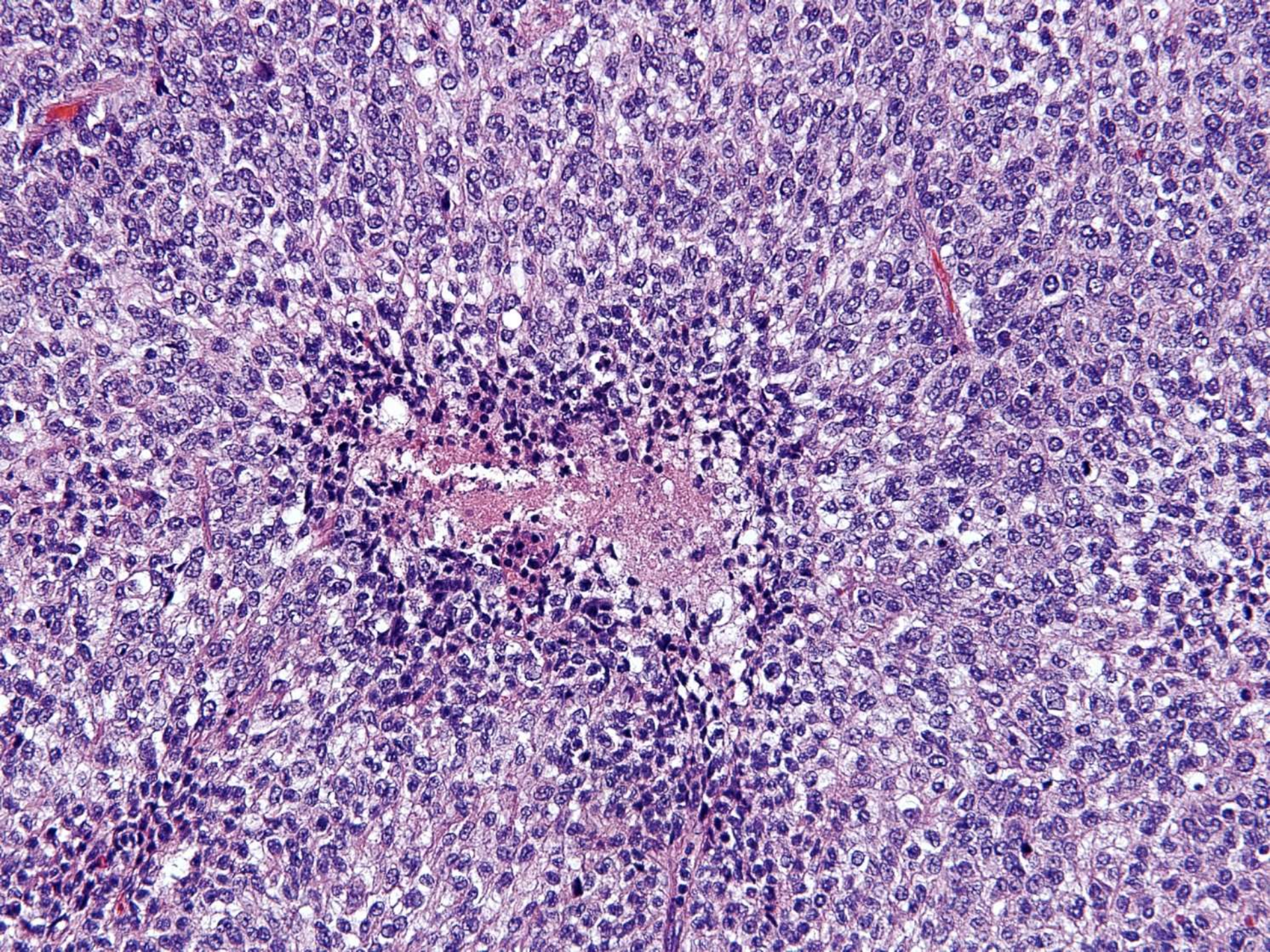
SB 6087

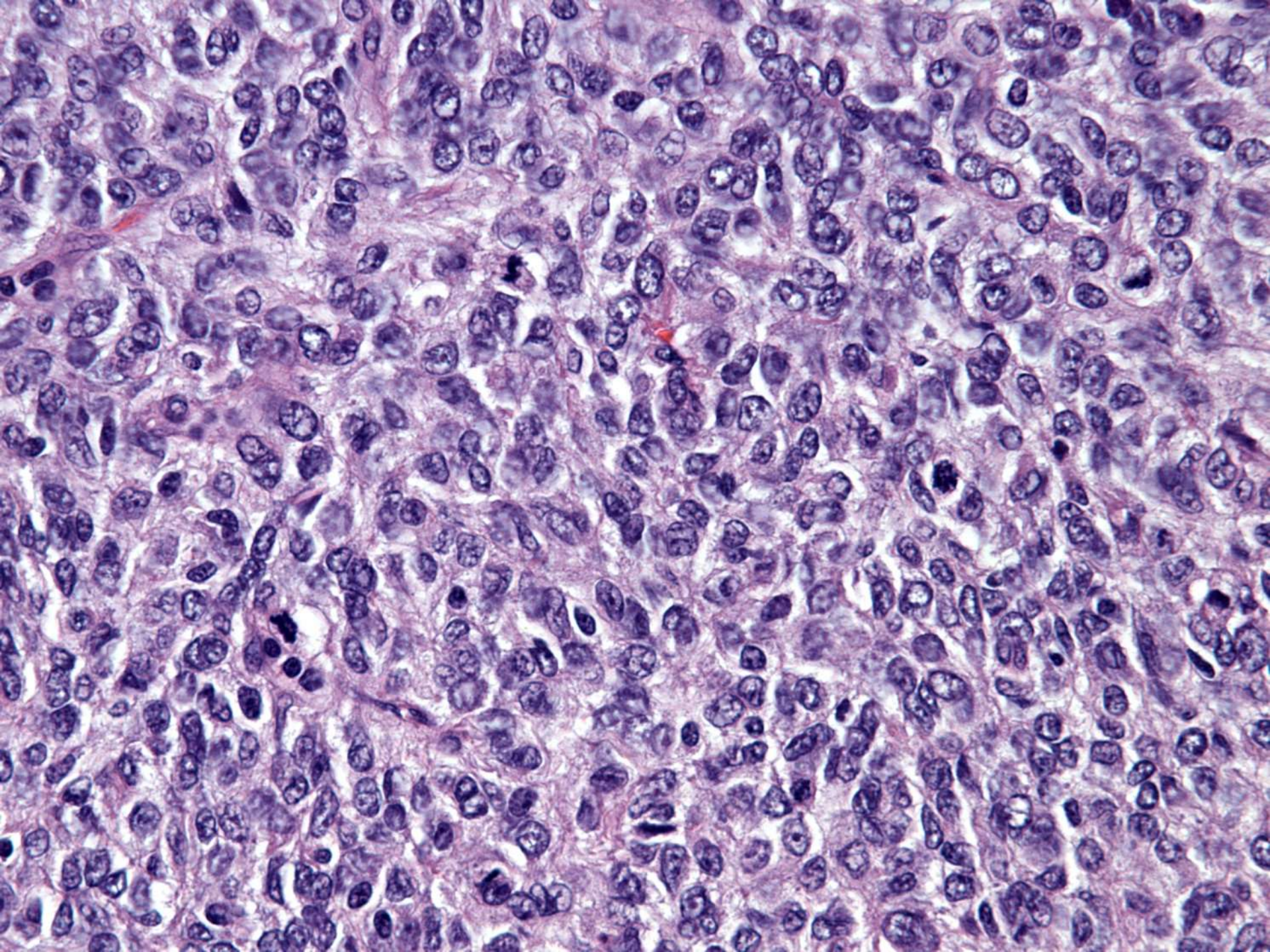
Peyman Samghabadi/Edward Plowey/Hannes Vogel; Stanford

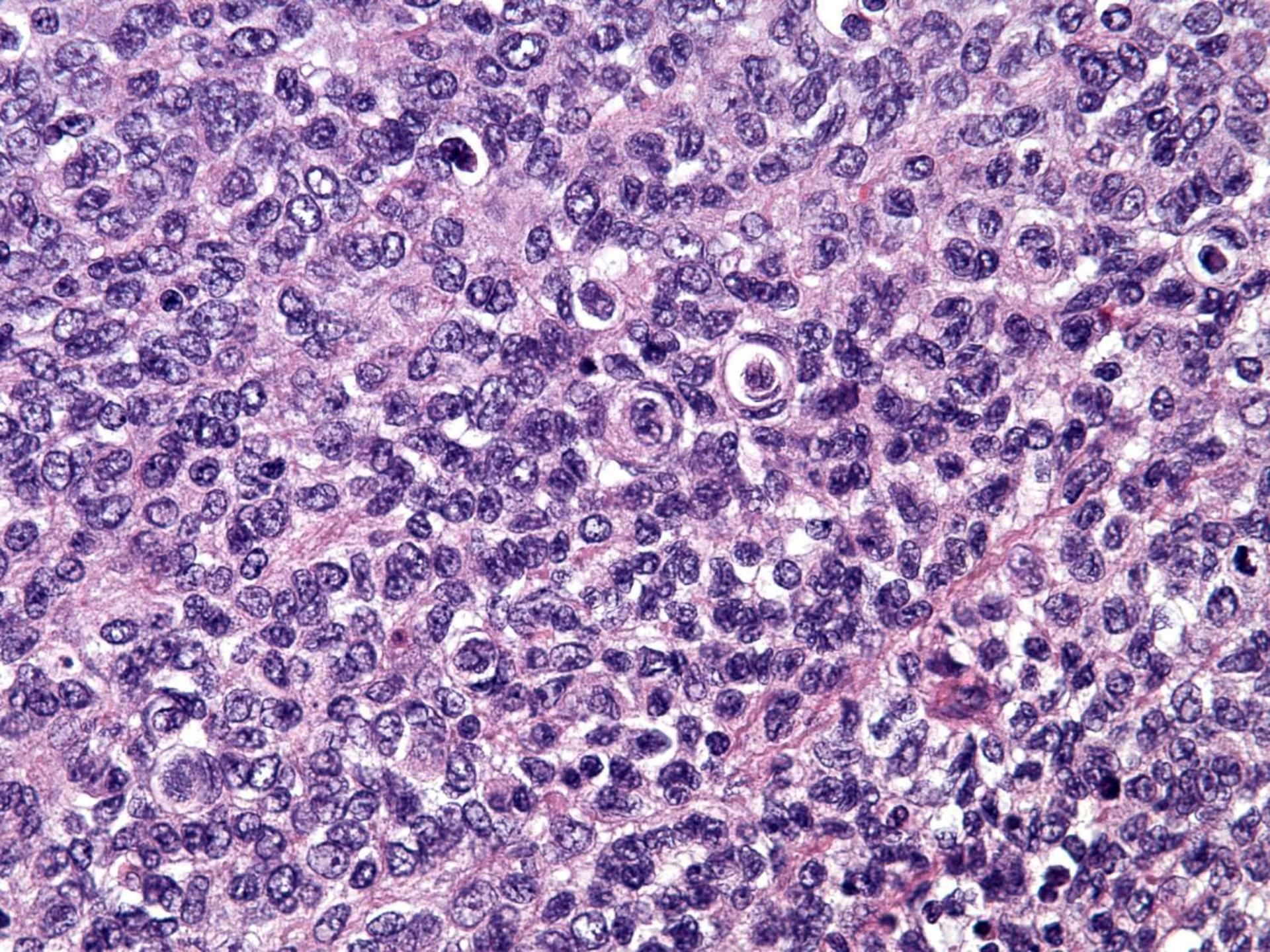
104-year-old male with 5cm right parietal mass.





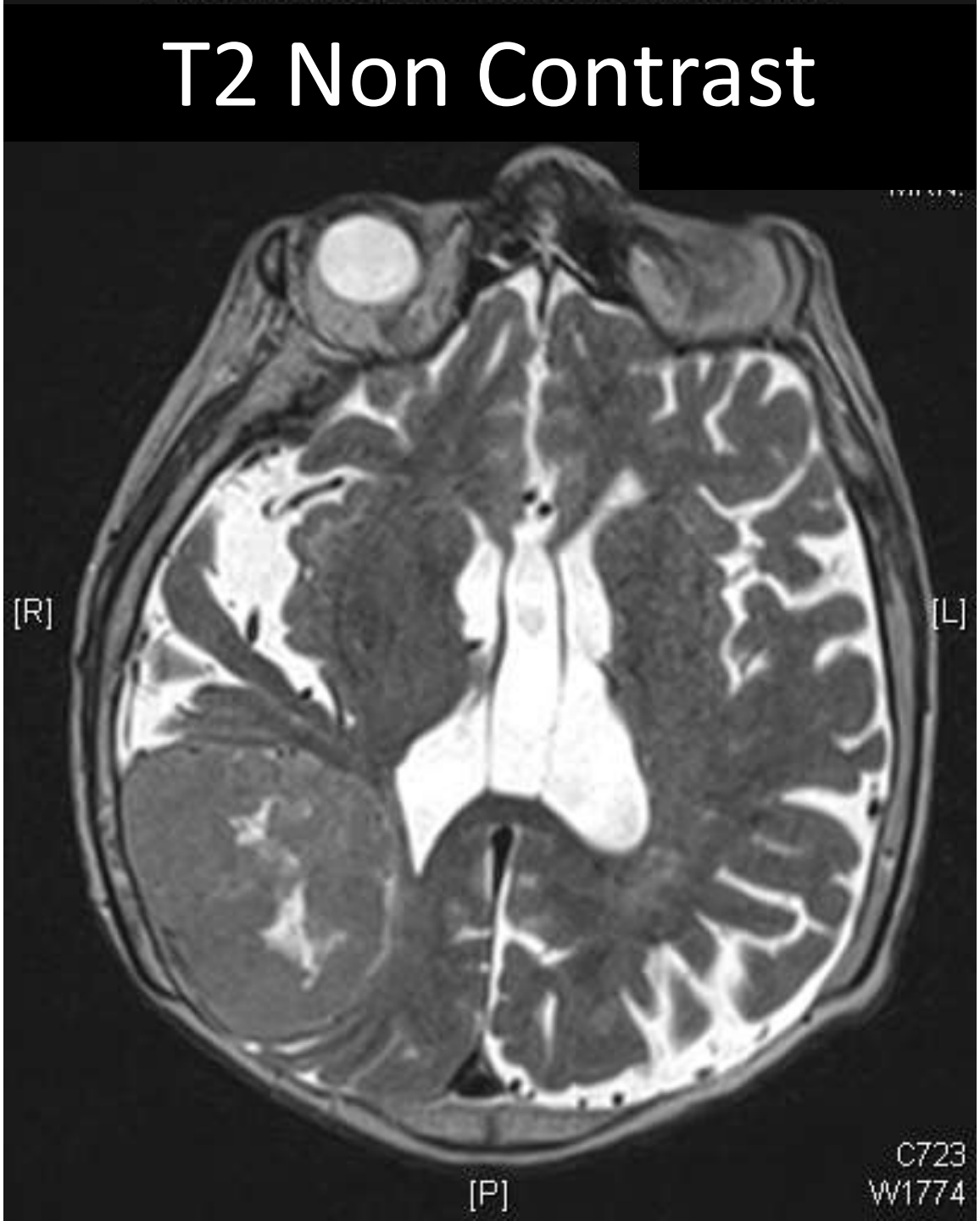






DIAGNOSIS?

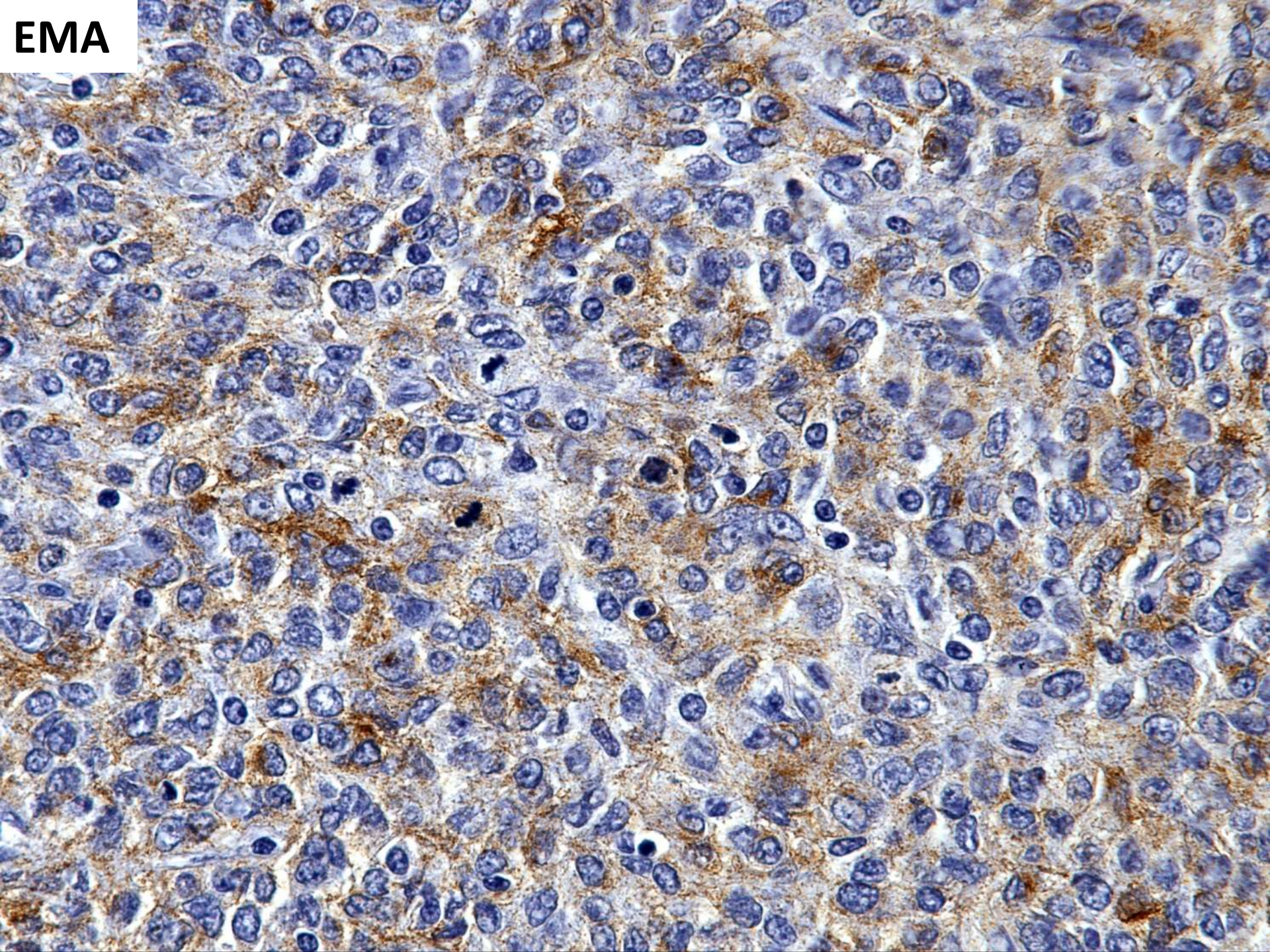
T2 Non Contrast



Immunohistochemistry

Negative Studies:

- Cam 5.2
- Pancytokeratin
- GFAP
- STAT6
- Synaptophysin
- Chromogranin
- P53
- HMB45
- MiTF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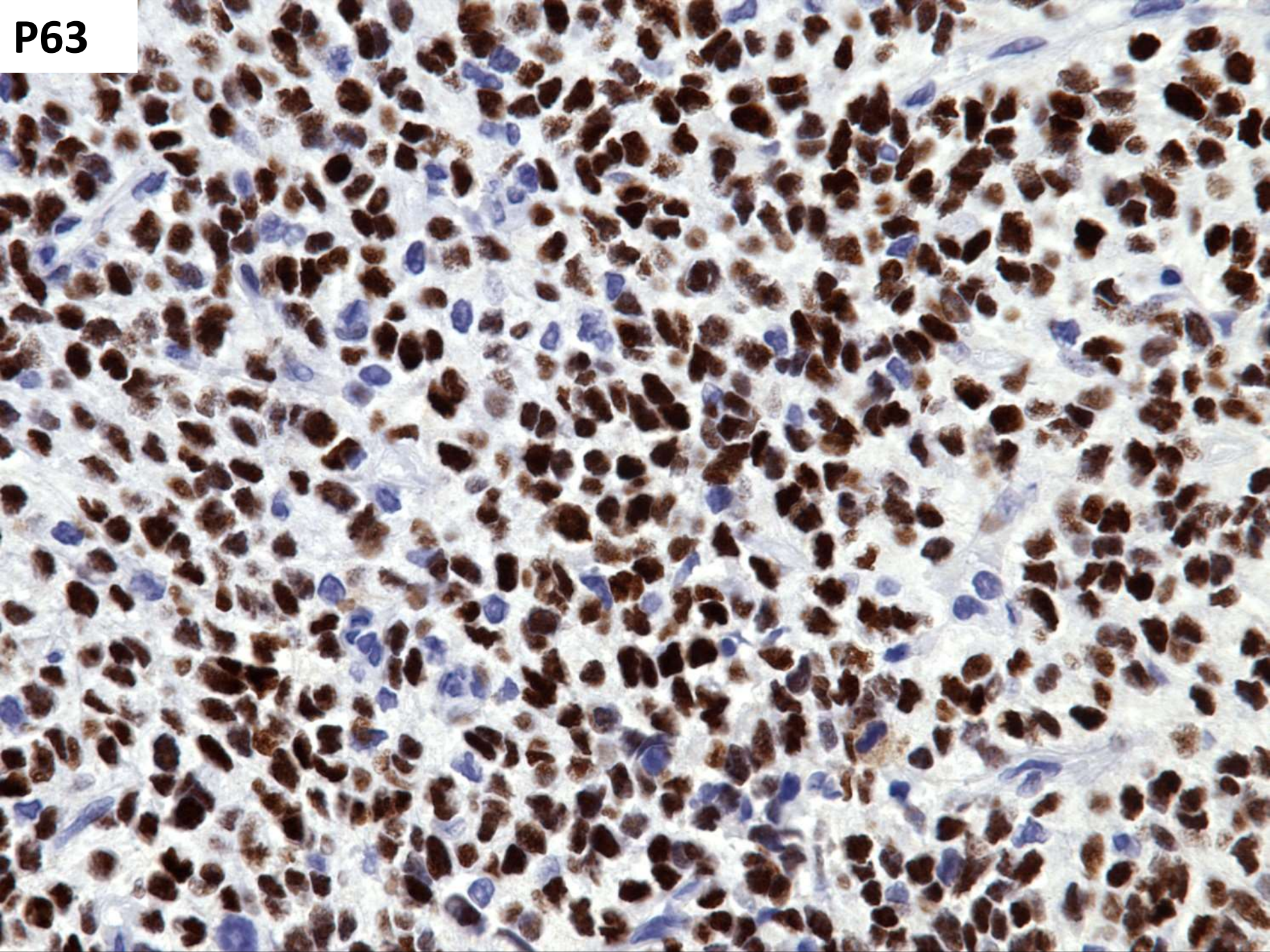
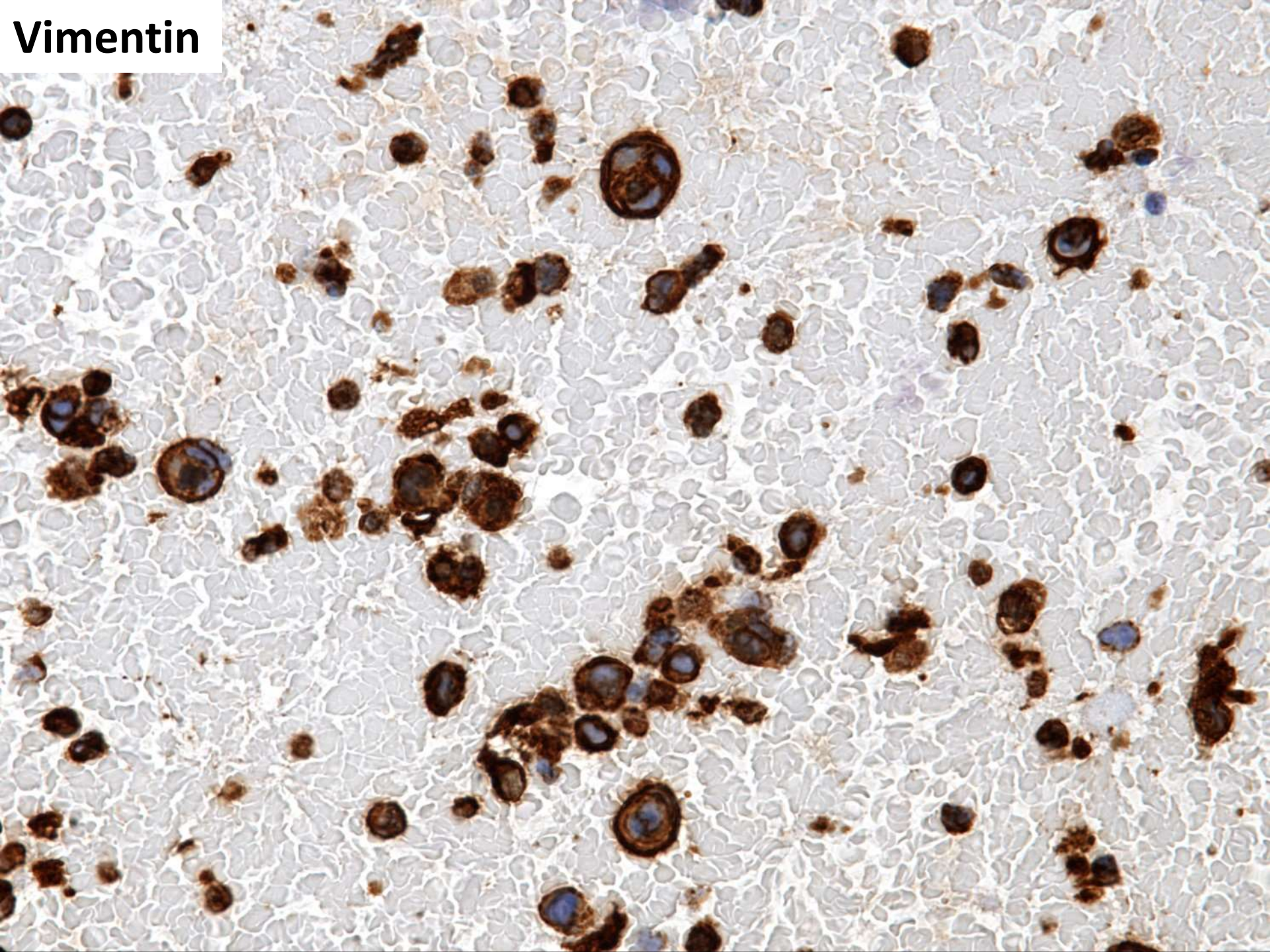
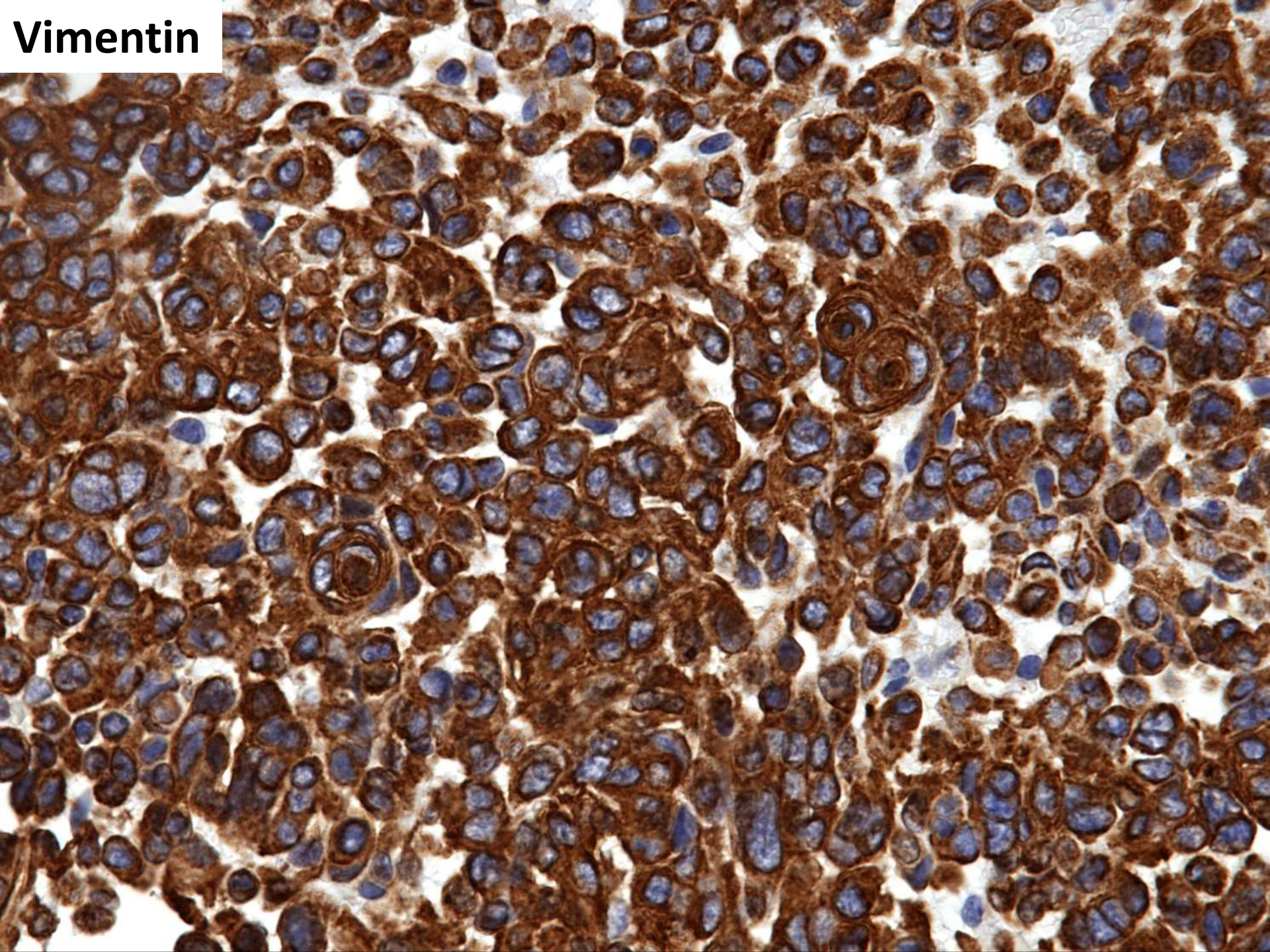

P63


Vimentin


Vimentin

DIAGNOSIS

ANAPLASTIC MENINGIOMA, WHO GRADE III

Meningioma

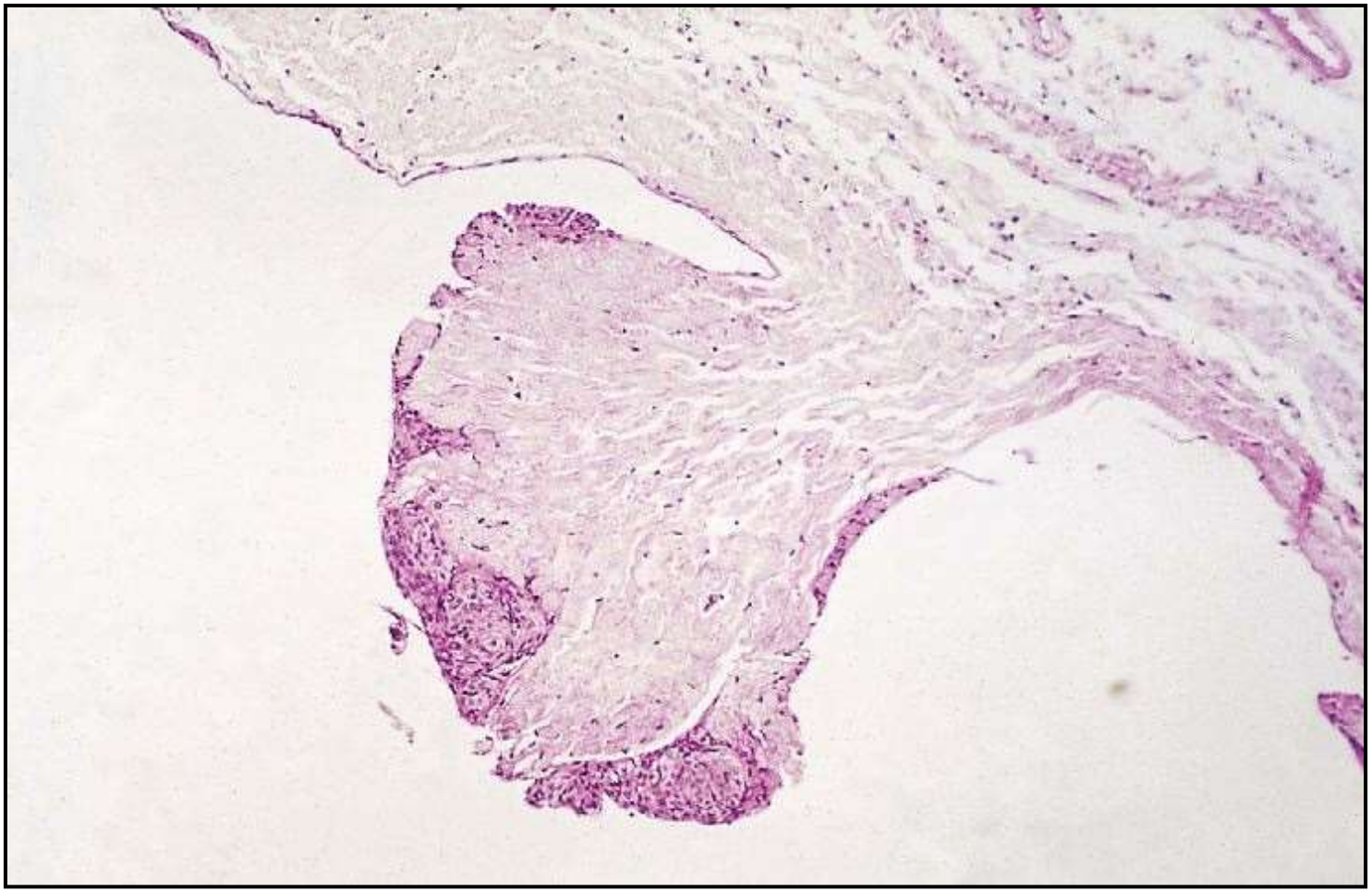


Table 2. World Health Organization (WHO) Grading of Meningiomas

WHO Grade I
Benign meningioma Histologic variant other than clear cell, chordoid, papillary, and rhabdoid Lacks criteria of grades II and III meningiomas
WHO Grade II
Atypical meningioma Mitotic index ≥4 per 10 high-power fields *or* At least 3 of 5 parameters: Sheeting architecture (loss of whorling and/or fascicles) Small cell formation (high N/C ratio) Macronucleoli Hypercellularity Spontaneous necrosis (i.e., not induced by embolization or radiation) *or* Brain invasion *or* Clear cell meningioma *or* Chordoid meningioma
WHO Grade III
Anaplastic (malignant) meningioma Mitotic index ≥20 per 10 high-power fields *or* Frank anaplasia (sarcoma, carcinoma, or melanoma-like histology) *or* Papillary meningioma *or* Rhabdoid meningioma

* N/C indicates nuclear/cytoplasmic.

Meningioma

- Immunophenotype
  - EMA (most, variable)
  - SSTR2A (almost all, even WHO III)
  - Vimentin (all)
  - S100 (variable; *fibrous*)
  - PR (inversely associated with grade)

Meningioma

International Journal of Surgical Pathology
Volume 16 Number 1
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Correlation of p63 Immunoreactivity With Tumor Grade in Meningiomas

Elisabeth J. Rushing, MD, Cara Olsen, MS, and Yan-Gao Man, MD, PhD

Predicting tumor behavior in meningiomas based on morphologic features alone remains difficult. The present study was undertaken to assess the correlation between p63 expression and histological grade of meningiomas. A total of 37 archival intracranial meningiomas were classified into 20 grade I, 13 grade II, and 4 grade III meningiomas. Using immunohistochemical methods, staining was scored based on nuclear and/or cytoplasmic distribution as follows: 0, no staining; 1, 50% or less of the cells; 2, more than 50% of the cells. Of grade I meningiomas, 95% (19/20) lacked nuclear p63 expression and none exhibited cytoplasmic staining. Overall, 92% of grade II tumors showed nuclear expression and 31% (4/13) showed cytoplasmic expression. Grade III tumors showed an overall nuclear expression of 75% (3/4) with all exhibiting cytoplasmic staining. Our results indicate a good correlation exists between histological grade and p63 protein expression, suggesting that p63 expression might be correlated with the clinical outcome.

Keywords: brain; immunohistochemistry; meningioma; pathology; p63

The separation of benign from aggressive meningiomas continues to pose challenges. Numerous studies have attempted to establish reliable clinical and pathological prognostic markers to identify p62[5] and claudin.[4] Karja and Alafuzoff found that p62, a cytosolic conserved protein that binds noncovalently to ubiquitin, is only expressed in benign meningiomas.[6] Claudin-1, a tight junction-associated

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20(4) 349-354

DOI: 10.1177/1066896911434649
http://ijp.sagepub.com
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Correlation of p63 Protein Expression With Histological Grade of Meningiomas: An Immunohistochemical Study

Suchi Mittal, MBBS[1], Deepali Jain, MD, DNB[1], Subimal Roy, MD, PhD[1], and Veer Singh Mehta, Mch[2]

Abstract

Prediction of tumor behavior in meningiomas based on morphological features alone remains difficult. Several immunohistochemical biomarkers have been proposed to assist conventional methods. However, no single immunohistochemical marker can unequivocally discriminate between benign and aggressive meningiomas. There is only 1 study available in the literature that correlates p63 expression with overall histological grade of the meningioma. The present study is undertaken to assess the correlation between p63 expression and histological grade of meningiomas. For this purpose, the authors studied and analyzed the immunohistochemical expression of p63 in 85 cases of meningioma, including WHO grade I (63), grade II (11), and grade III (11) cases. Correlation between histological grade and nuclear immunoreactivity to p63 antibody was performed. Furthermore, expression of p63 protein was correlated with short clinical follow-up and Ki-67 proliferation index. Among 85 patients analyzed, there were 61 women (71.7 %) and 24 men (28.2%) between 7 and 75 years old. Expression of p63 protein was found in 34.9% of grade I cases, but in grade II and III, 63.6% of cases each were immunoreactive. Correlation between histological grade and p63 immunoreactivity was significant ($P = .02$). p63-positive grade I meningiomas did not show elevated Ki-67 index. The present study contradicts earlier reports because there are a considerable number of grade I meningiomas that express p63. Although p63 expression is significantly associated with higher histological grade of meningiomas, it may not be considered as a sole biomarker to assess aggressive behavior of the tumor.

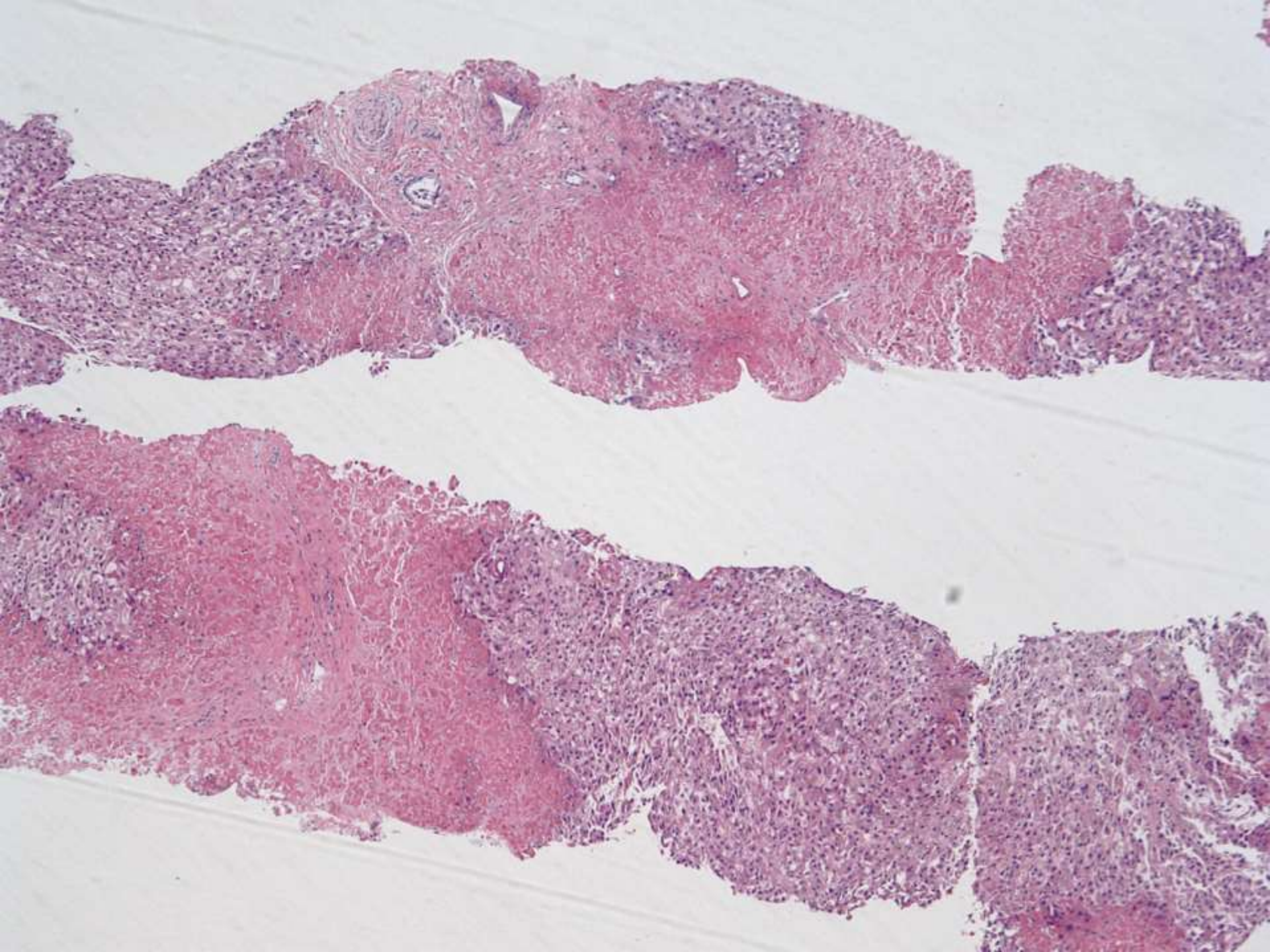
Molecular Genetics

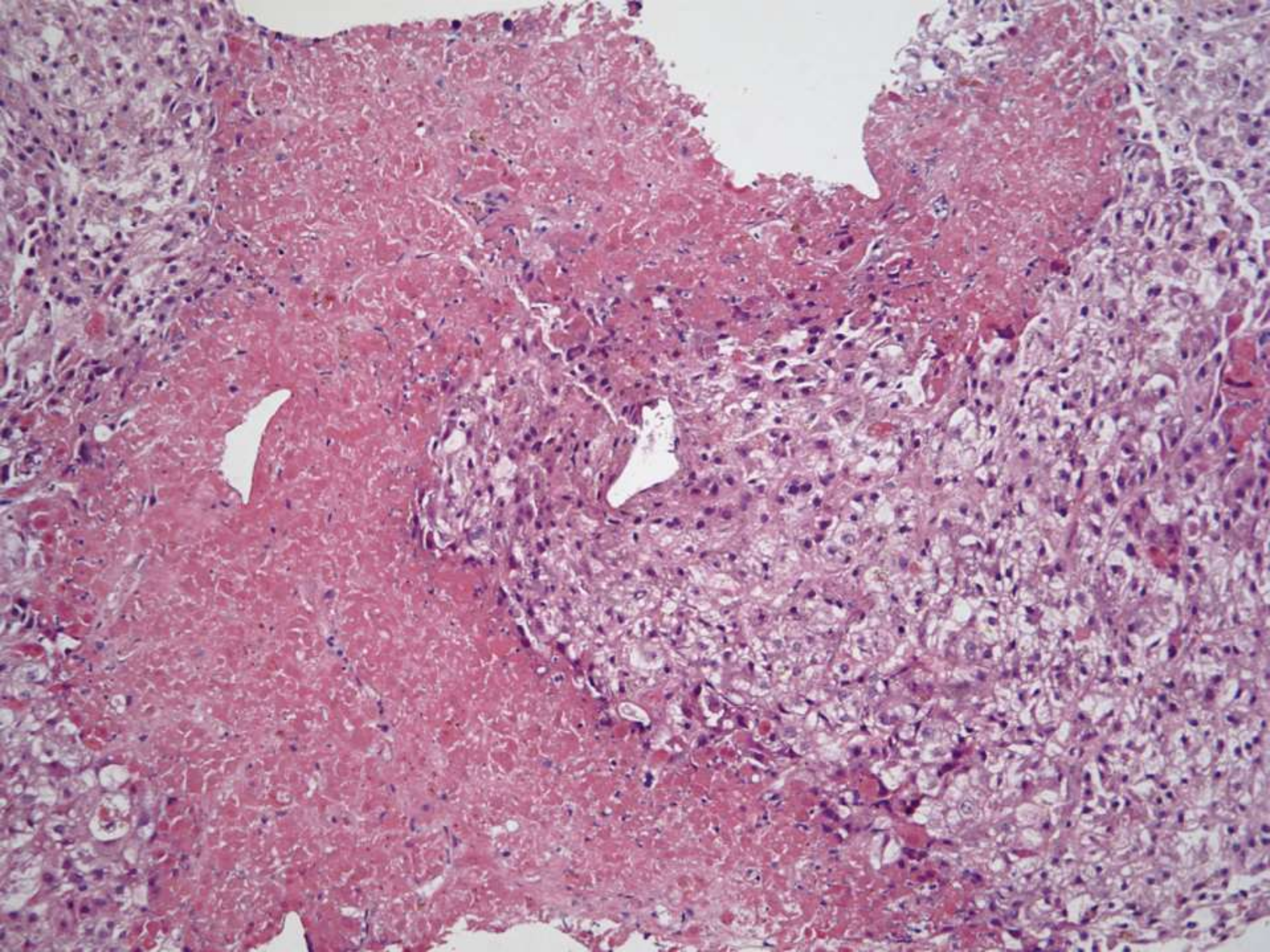
WHO Grade	I	II	III
Chromosomal abnormalities	22q loss (50-60%) 9p losses (5%)	1p loss 6q loss 9p losses (18%) 10 loss 14q loss 18q loss 1q, 9q, 12q, 15q, 17q, 20q gains	1p loss 6q loss 9p losses (38%) 9p21 (p16/p15 CDKN2A/B, p14 ARF) loss 10 loss 14q loss 17q23 amplification 18q loss
Gene expression	NF2 mutations (50%–60%) **TRAF7** **KLF4** **AKT1** **SMO** EGFR activation PDGFRB activation	Telomerase/hTERT activation Notch/Wnt, IGF, VEGF activation Phosphorylated AKT increase SUFU alterations at 10q24	NDRG2 hypermethylation Phosphorylated AKT increase SUFU alterations at 10q24
Protein expression	PR gain YAP overexpression and nuclear localization Merlin loss (50%) 4.1B (DAL-1) loss (50%) TSLC-1 loss (30-85%)	PR loss TSLC1 loss	PR loss TSLC1 loss

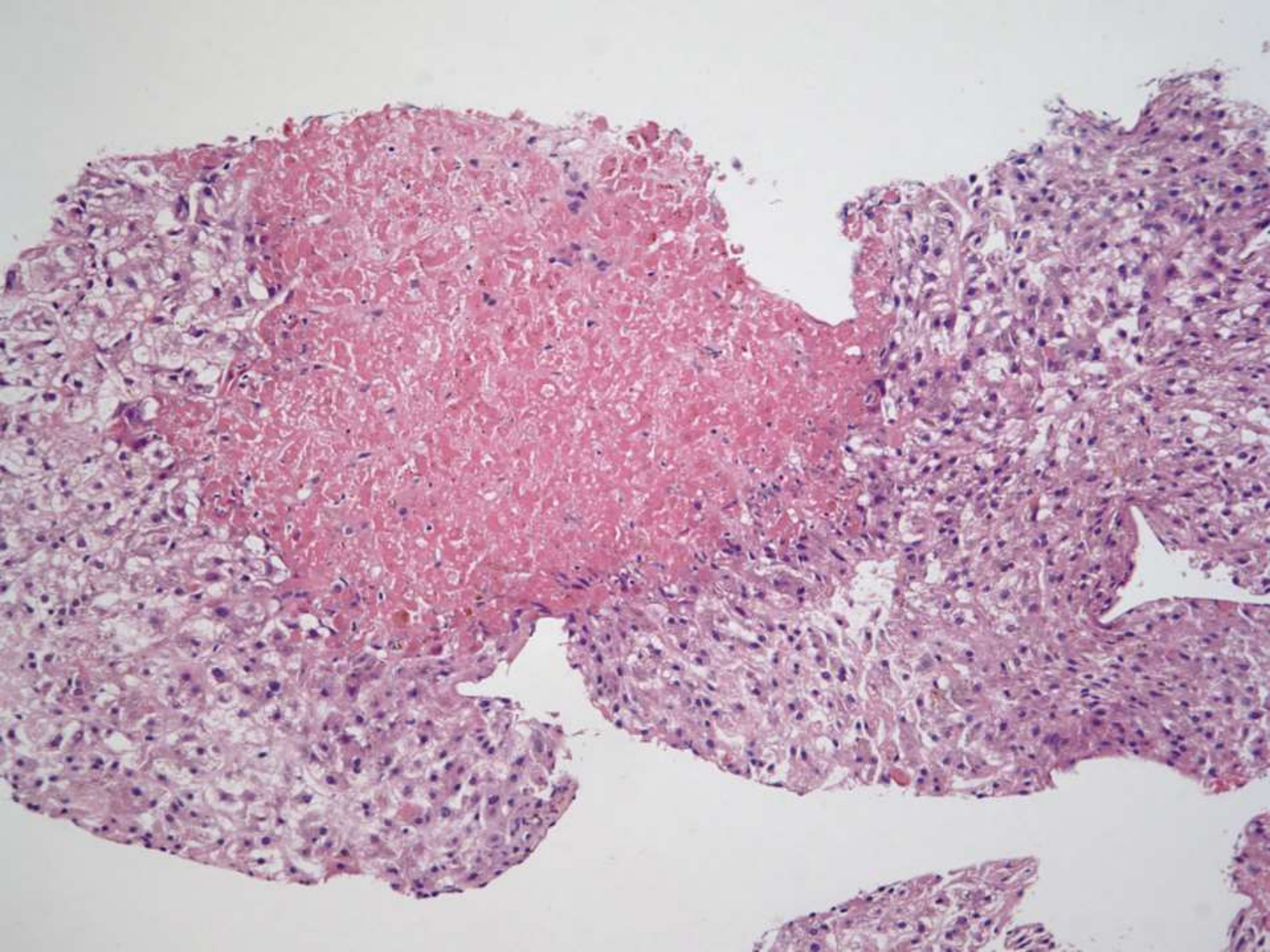
SB 6088

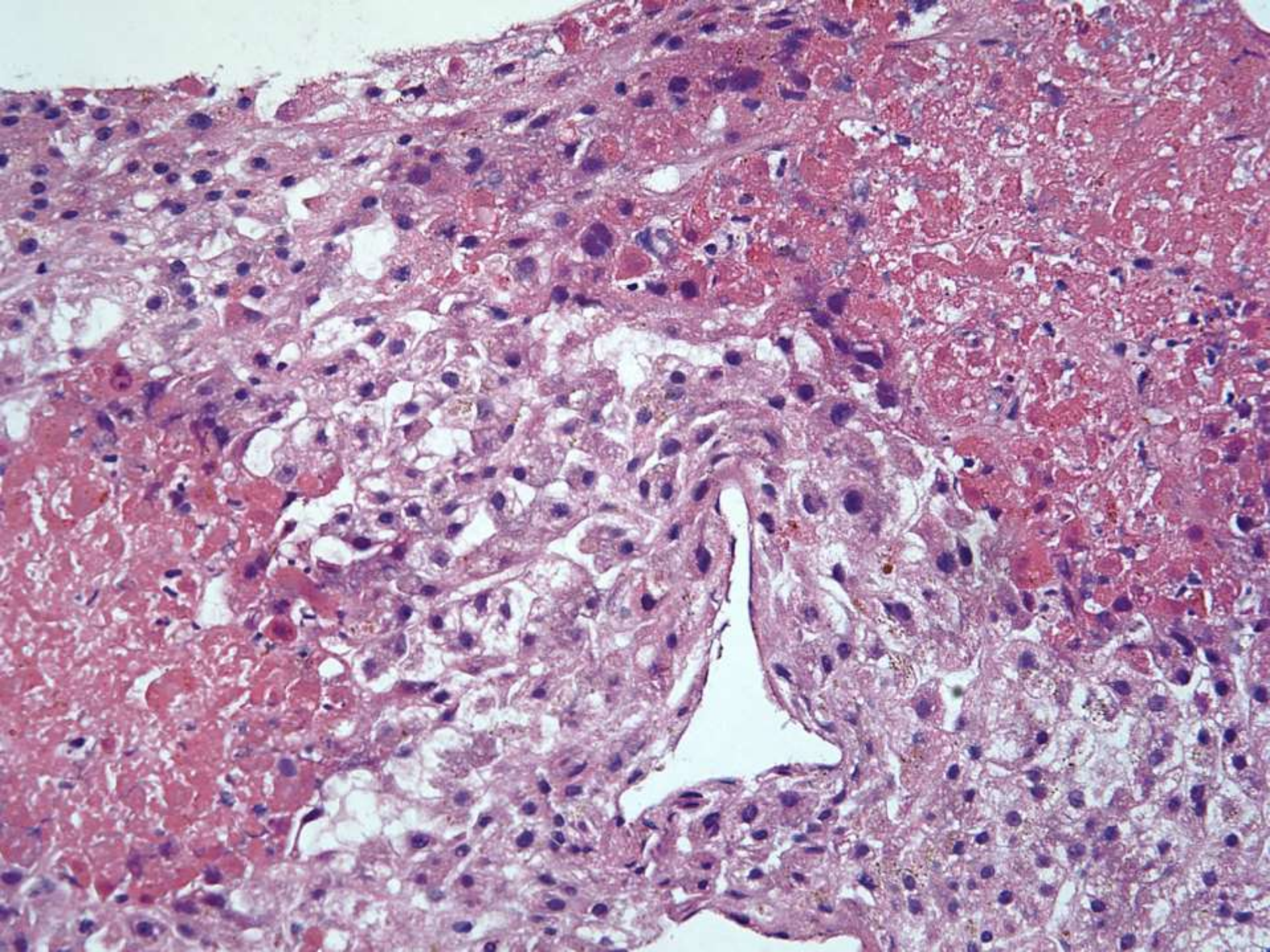
Greg Charville/Brock Martin/Richard Sibley; Stanford

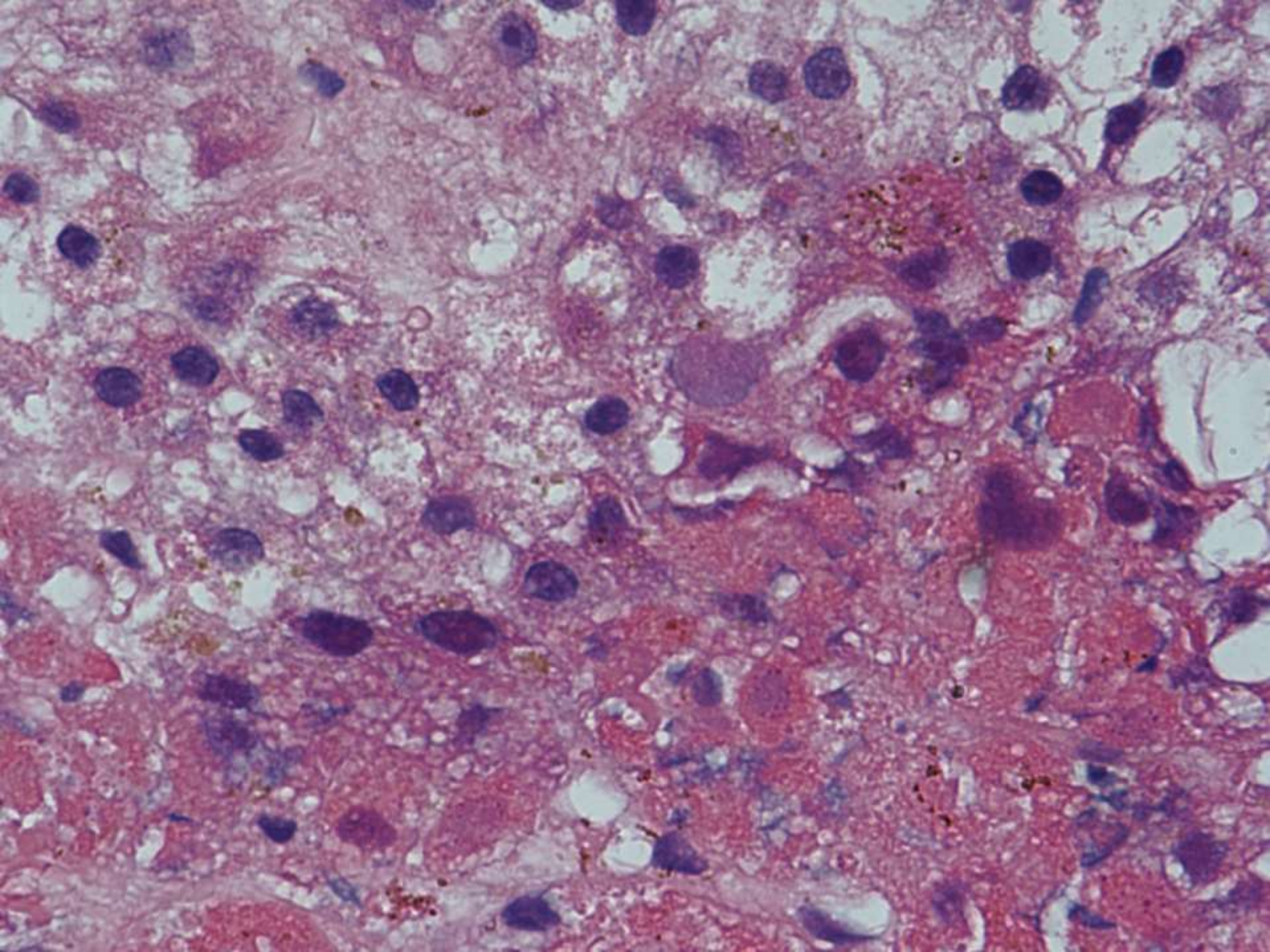
1-year-old boy with history of acute lymphocytic leukemia, now presenting with increased serum transaminases and concern for hemophagocytic lymphohistiocytosis.

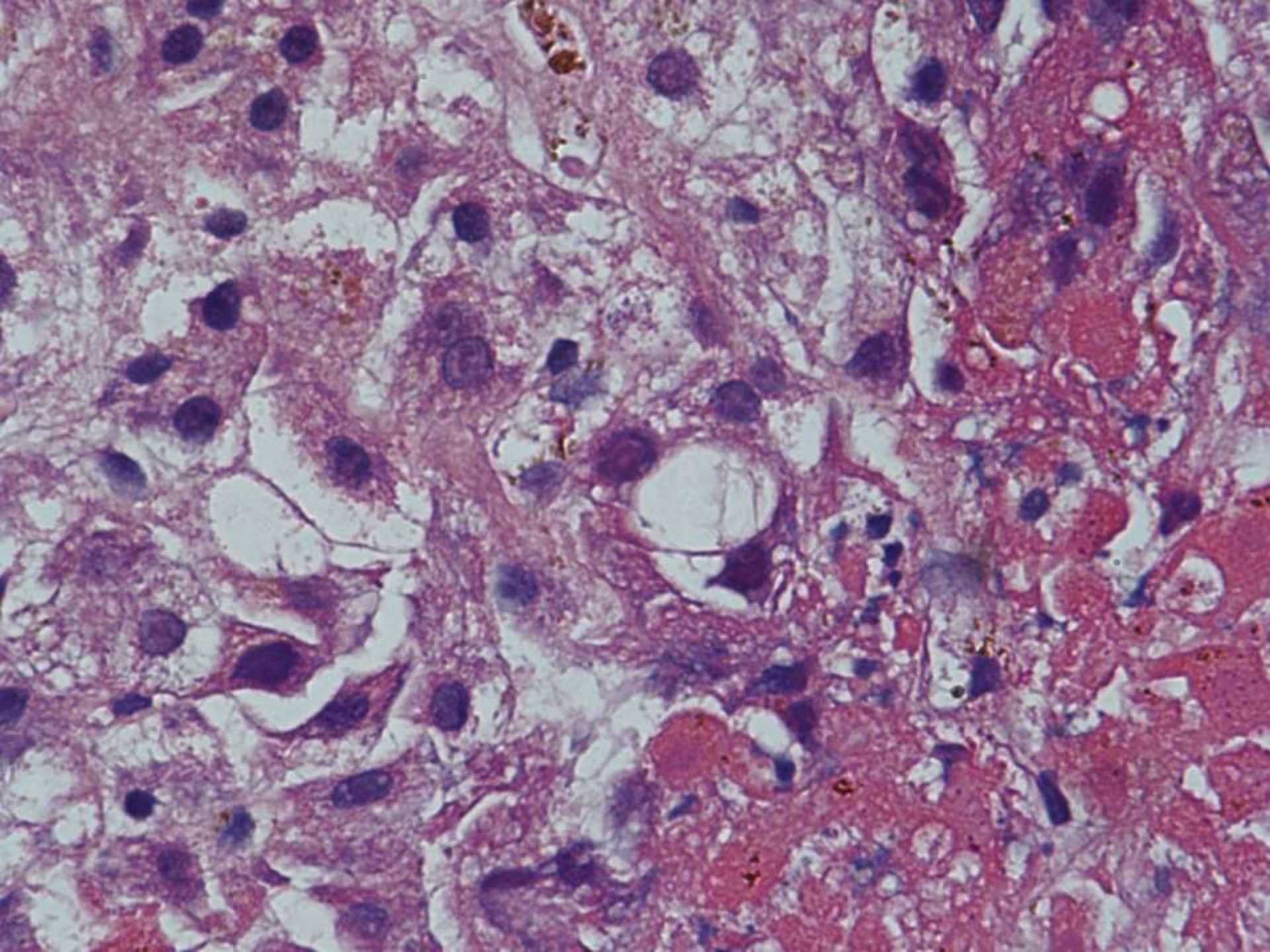








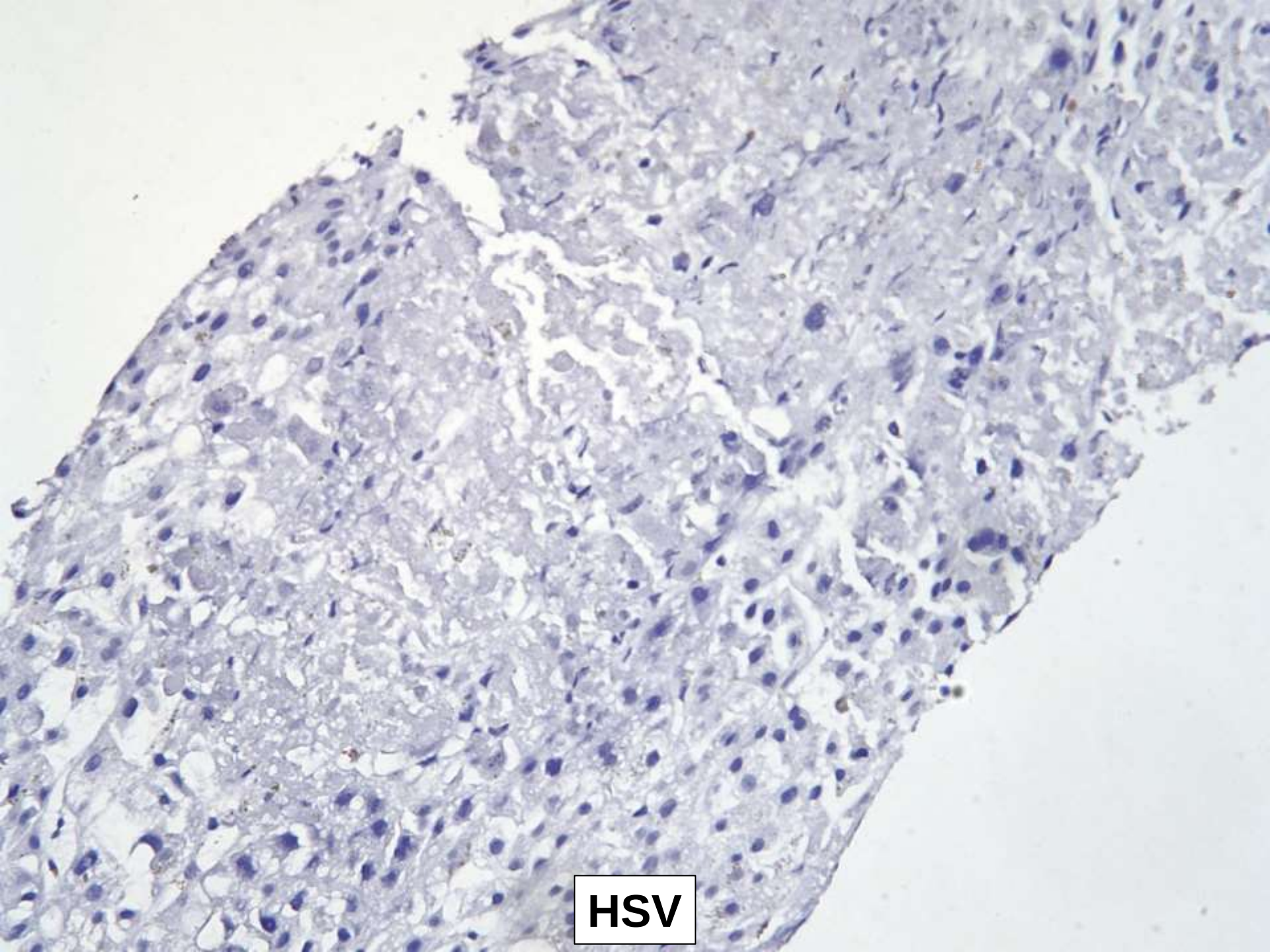


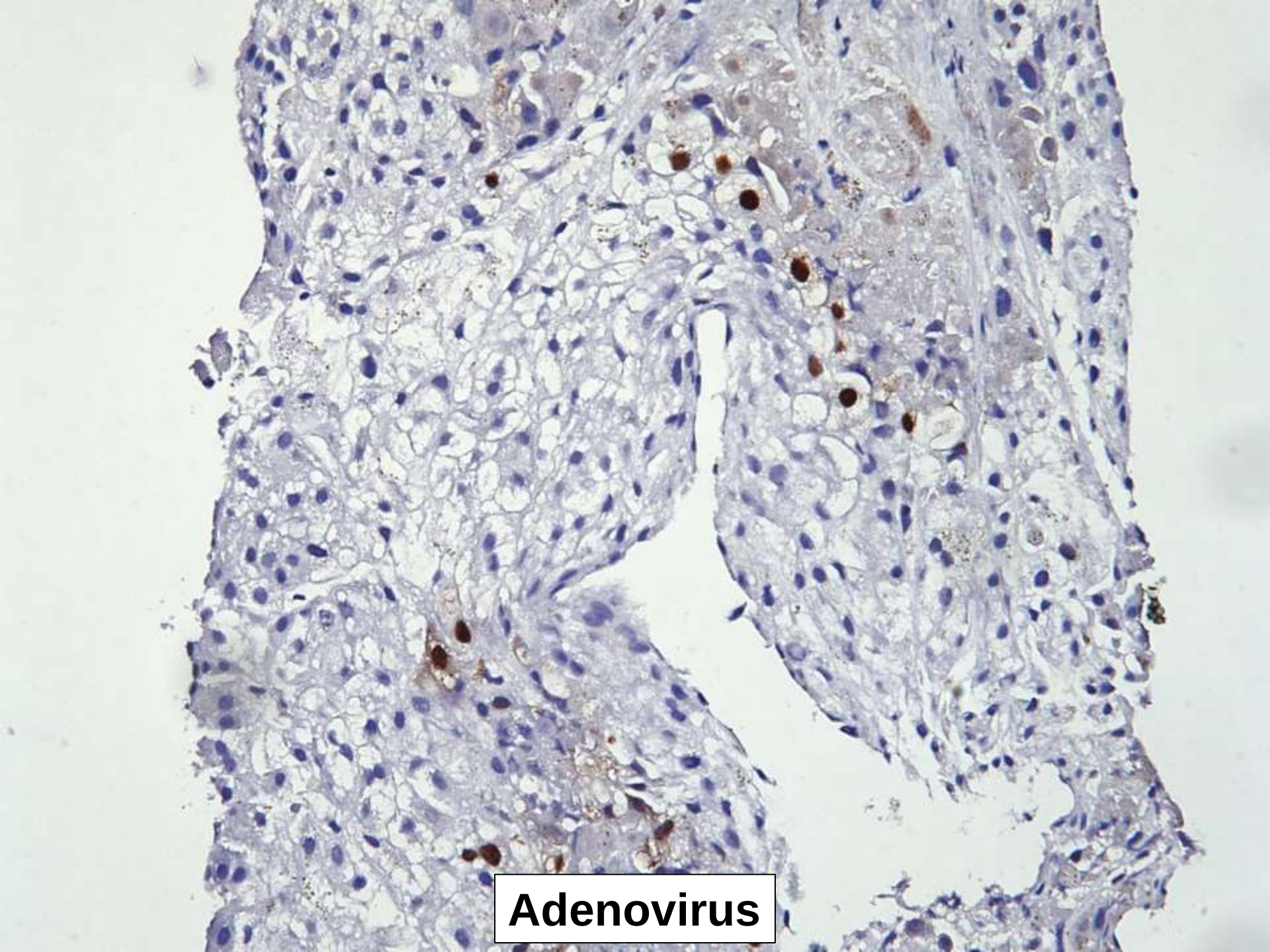


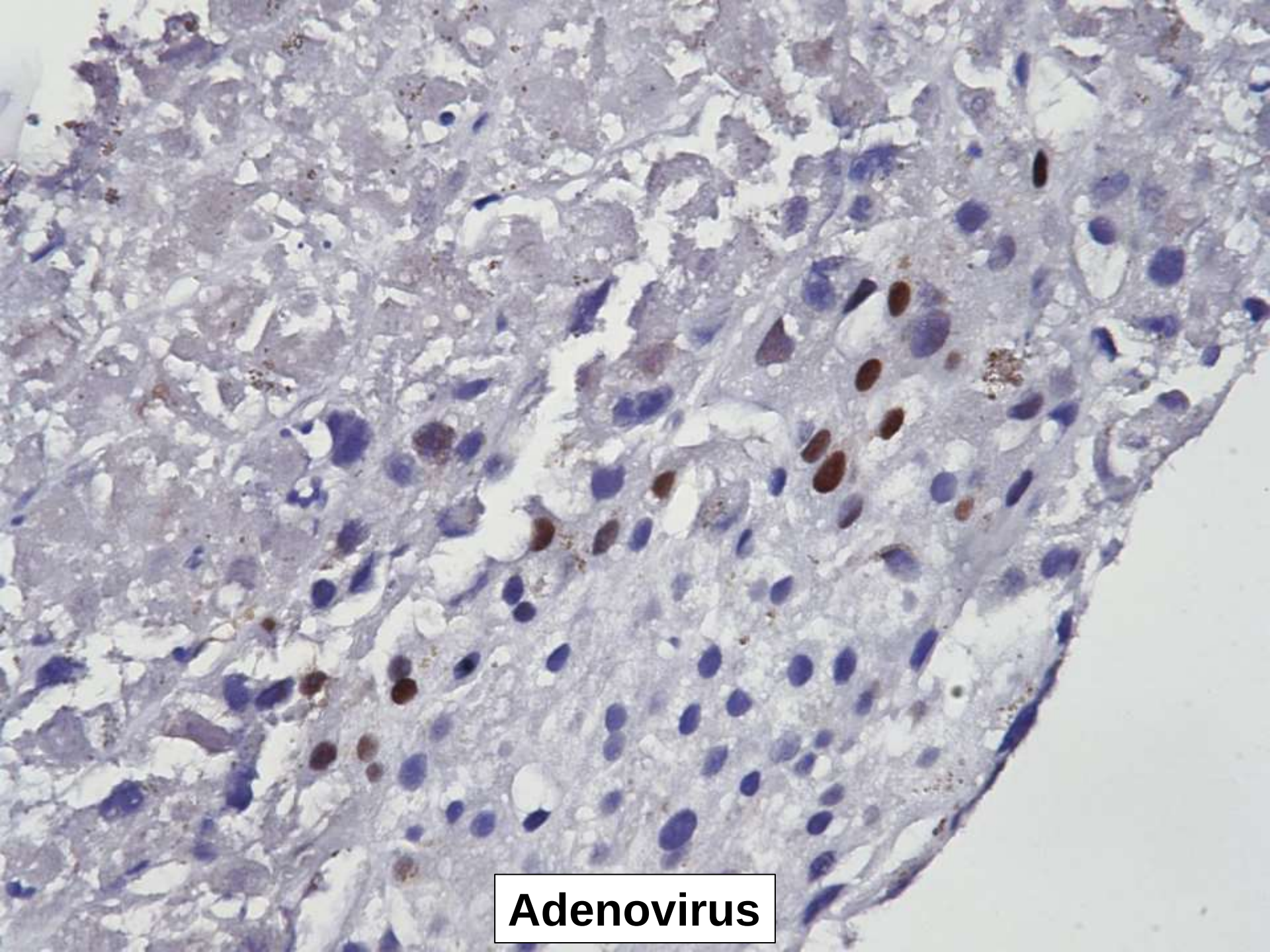
DIAGNOSIS?

Submassive hepatic necrosis – differential diagnosis

- Non-hepatotropic viral hepatitis: HSV, VZV, AdenoV
- Ischemic necrosis: shock, acute Budd-Chiari syndrome
- Drug/toxin-induced injury: Acetaminophen


HSV


Adenovirus


Adenovirus

AdenoV hepatitis – demographics

Table 1 Characteristics of 89 patients with HAdV hepatitis

Characteristic	Number of patients (%)
Age	
Pediatric (0–17)	57 (64)
Adult (18 and older)	32 (36)
Gender	
Male	32 (53)
Female	28 (47)
Underlying condition	
Liver transplant	43 (48)
Bone marrow transplant	19 (21)
Chemotherapy	11 (12)
SCID	5 (6)
HIV infection	4 (4)
Renal transplant	2 (2)
Heart transplant	2 (2)
Neonates (no known comorbidity)	2 (2)
CLL	1 (1)

Ronan et al, Infection, 2014.

AdenoV hepatitis – clinicopathologic features

Table 2 Clinical manifestations, imaging findings, histopathology and outcomes of patients with HAdV hepatitis

	Number of patients (%)
Presenting symptoms ($N = 74$)	
Fever	68 (92)
Lethargy/malaise	15 (20)
Diarrhea	9 (12)
Jaundice	7 (10)
CT imaging findings ($N = 9$)	
Multiple hypodense lesions	7 (78)
Single hypodense lesion	1 (11)
Normal	1 (11)
Liver histopathology ($N = 64$)	
Necrosis	60 (94)
Intranuclear inclusions	46 (72)
Smudge cells	13 (21)
Method of adenovirus detection in the liver ($N = 89$)	
Culture	58 (65)
Immunohistochemistry	53 (60)
Electron microscopy	48 (54)
Polymerase chain reaction	5 (6)
In-situ hybridization	4 (5)
Outcome ($N = 89$)	
Survival	24 (27)
Death	65 (73)

Ronan et al, Infection, 2014.

AdenoV hepatitis – treatment strategies

Table 3 Management-based outcomes of patients with HAdV hepatitis. ($N = 47$)

Treatment	Number of cases	Survival
Reduced immunosuppression	25	14 (59 %)
Reduced immunosuppression + antiviral	1 cidofovir	1
	1 ribavirin	1
Liver re-transplantation	12	6 (50 %)
Cidofovir + IVIG	2	2
IVIG alone	4	0
Cidofovir alone	2	0

Ronan et al, Infection, 2014.

Our case: clinical follow-up

August 2014: Diagnosed with B-ALL, on chemotherapy

June 2015: Admitted for continued chemotherapy, developed neutropenic fever, worsening hepatosplenomegaly

July 2015: Severe transaminitis, adenoviremia detected

6 July 2015: Cidofovir started

17 July 2015:Transfer to LPCH: AST 3940, ALT 966, cidofovir redosed

20 July 2015: Liver biopsy

21 July 2015: Evaluated for liver transplant, felt to be clinically unstable

29 July 2015: Patient died

AdenoV hepatitis – take home points

- Disease of the immunocompromised and young
- Necrosis (with no particular zonal distribution) and intranuclear viral inclusions are key histologic features
- Available treatments include reduced immunosuppression and intravenous antiviral medications
- However, death due to fulminant hepatic failure is the most common outcome in reported cases (73%)

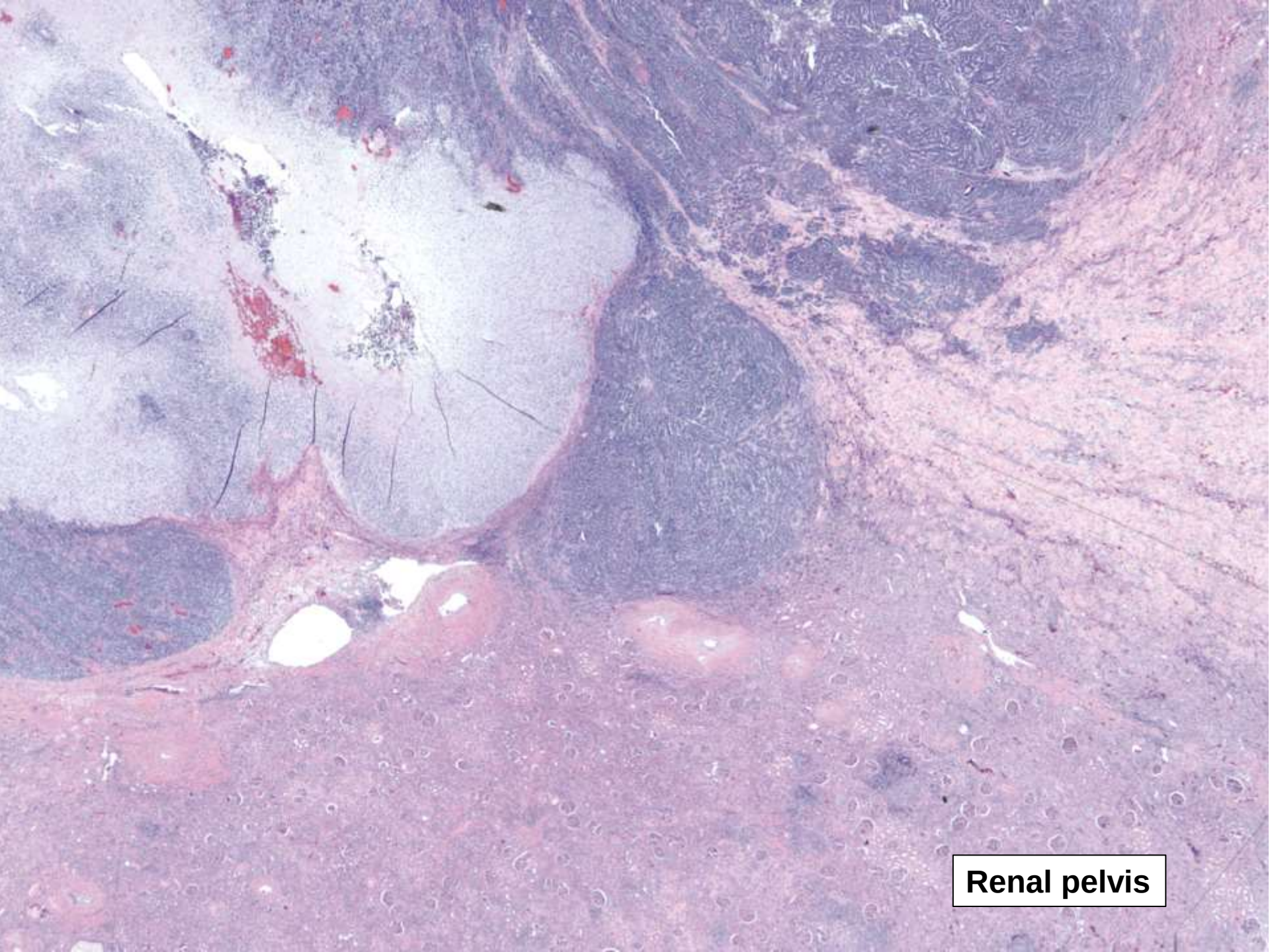
"…For a pilgrimage is what it is. The devotees come from the very ends of the earth to worship their prophet in his own Kaaba in his own Mecca".

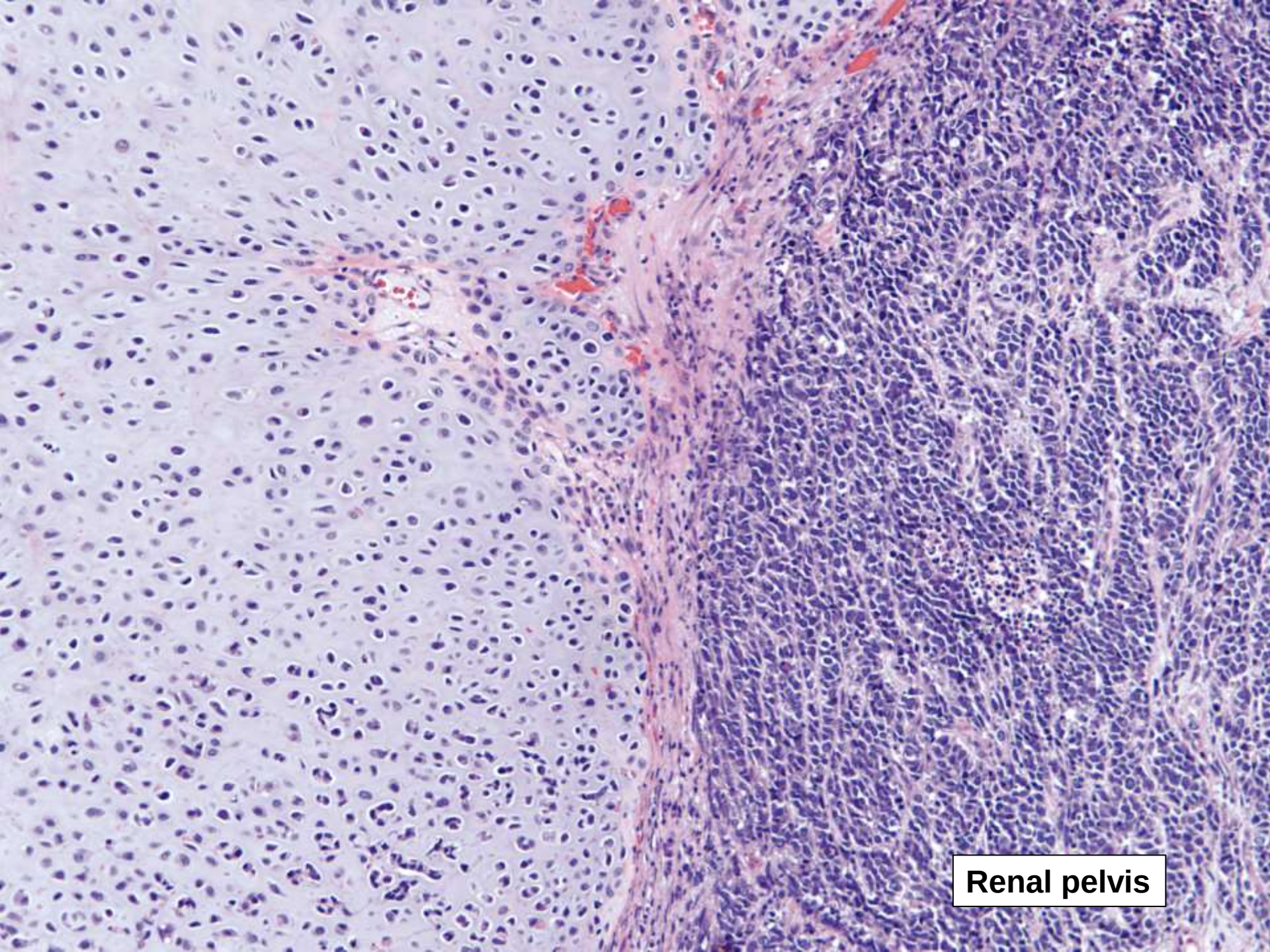
"Wagner's music is better than it sounds."
- *Mark Twain's Autobiography*

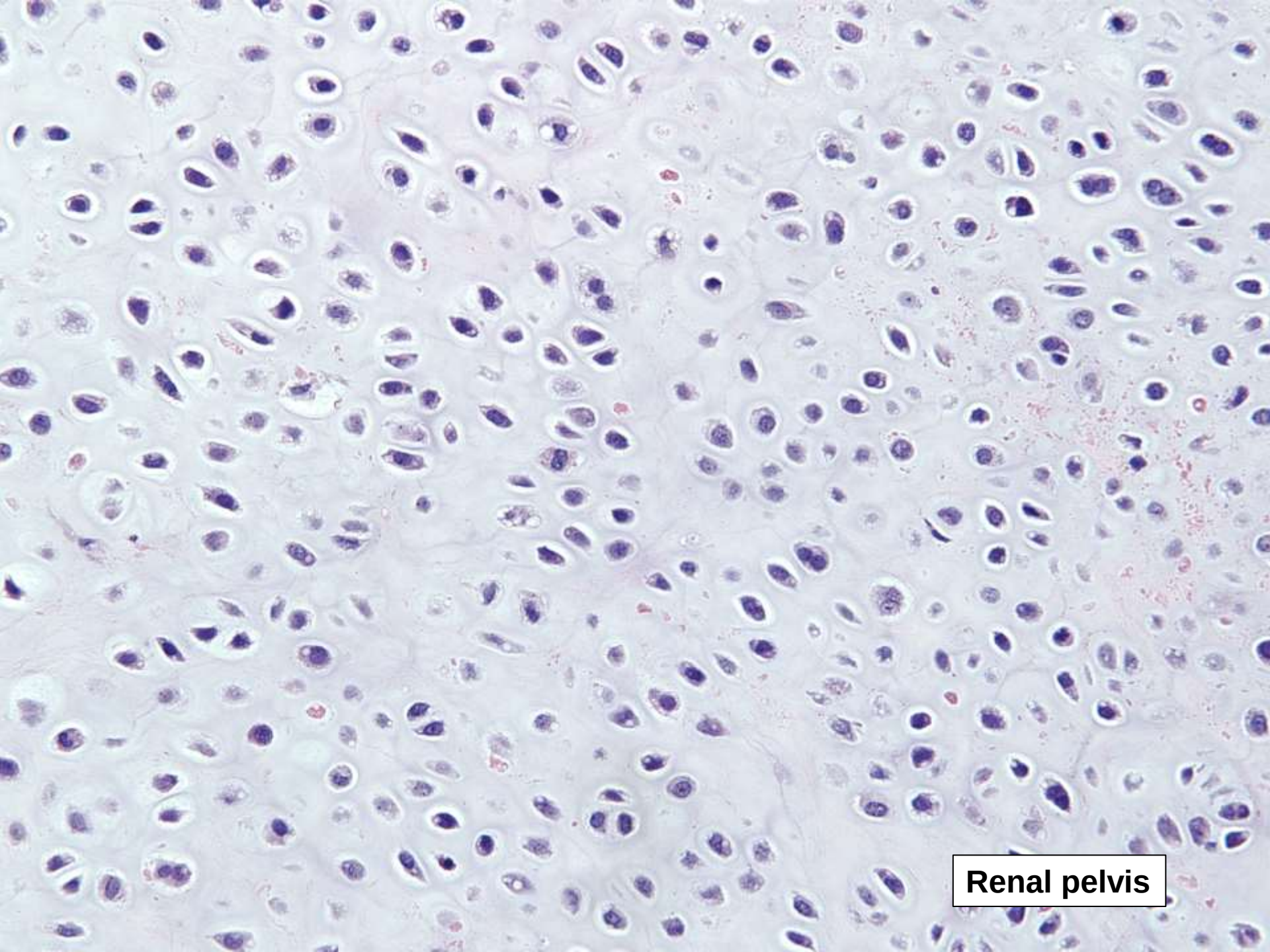
SB 6089

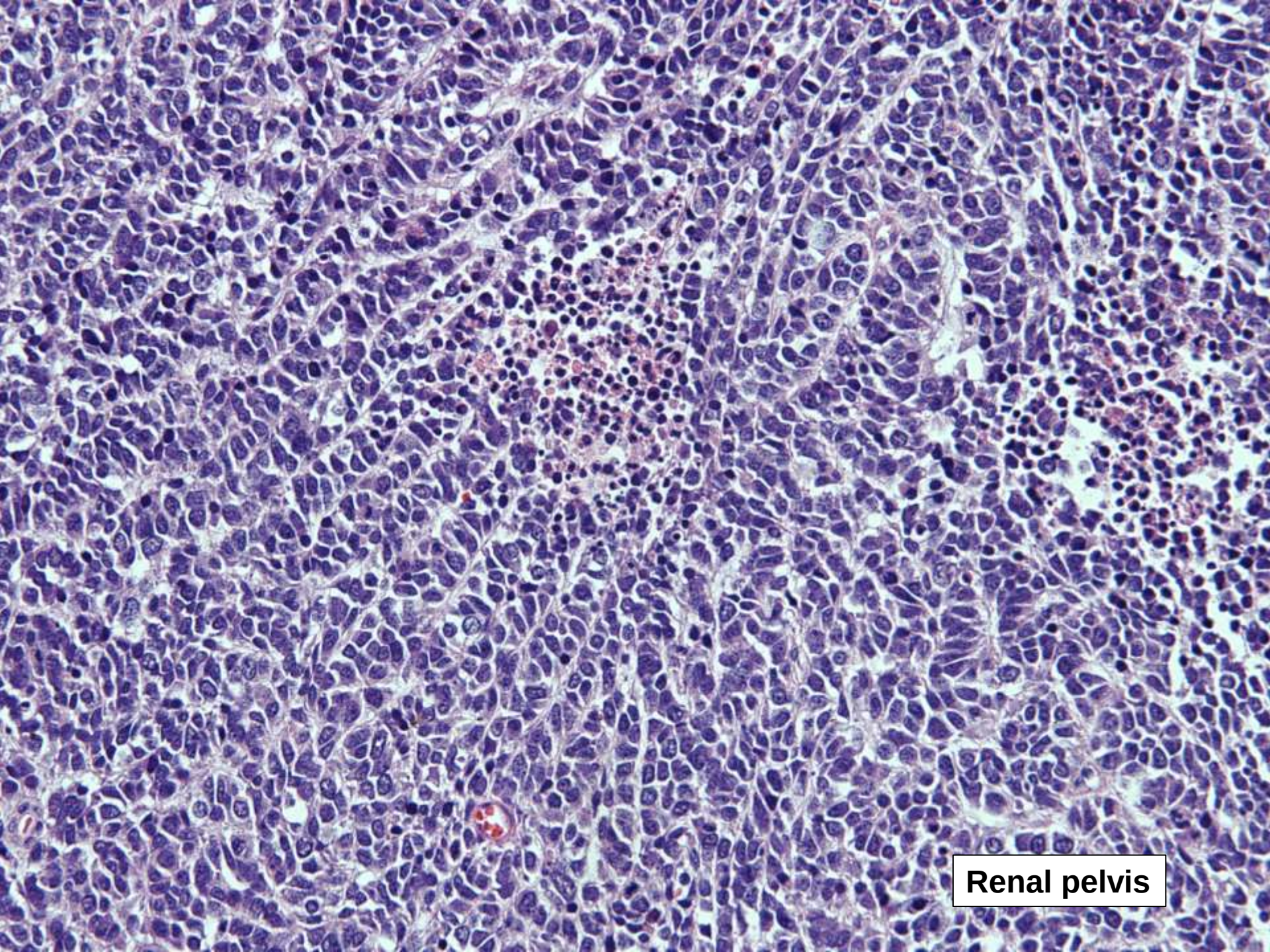
Greg Charville/Sunny Kao; Stanford

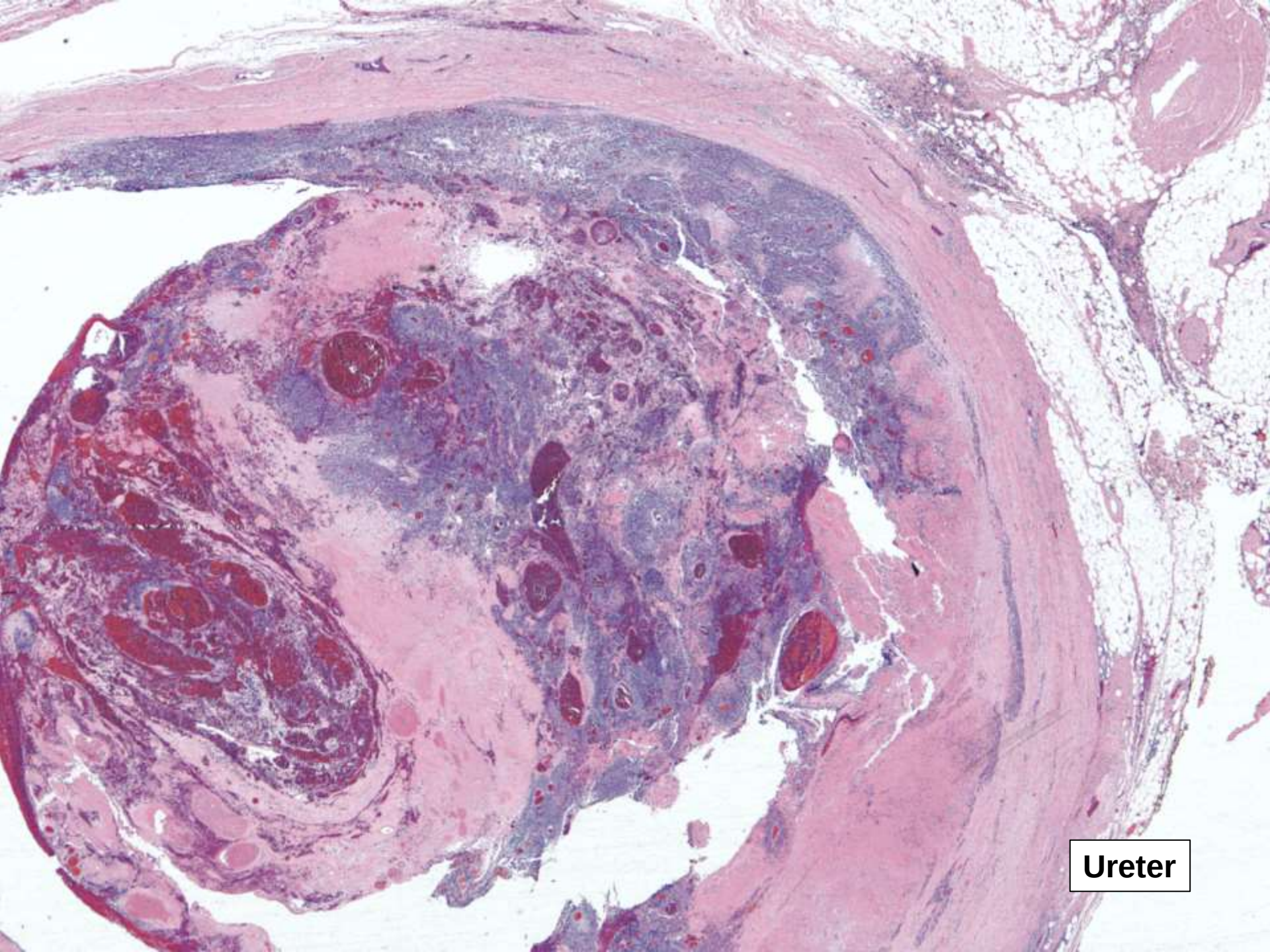
73-year-old female with hematuria and hydronephrosis with renal and ureteral masses.


Renal pelvis


Renal pelvis


Renal pelvis


Renal pelvis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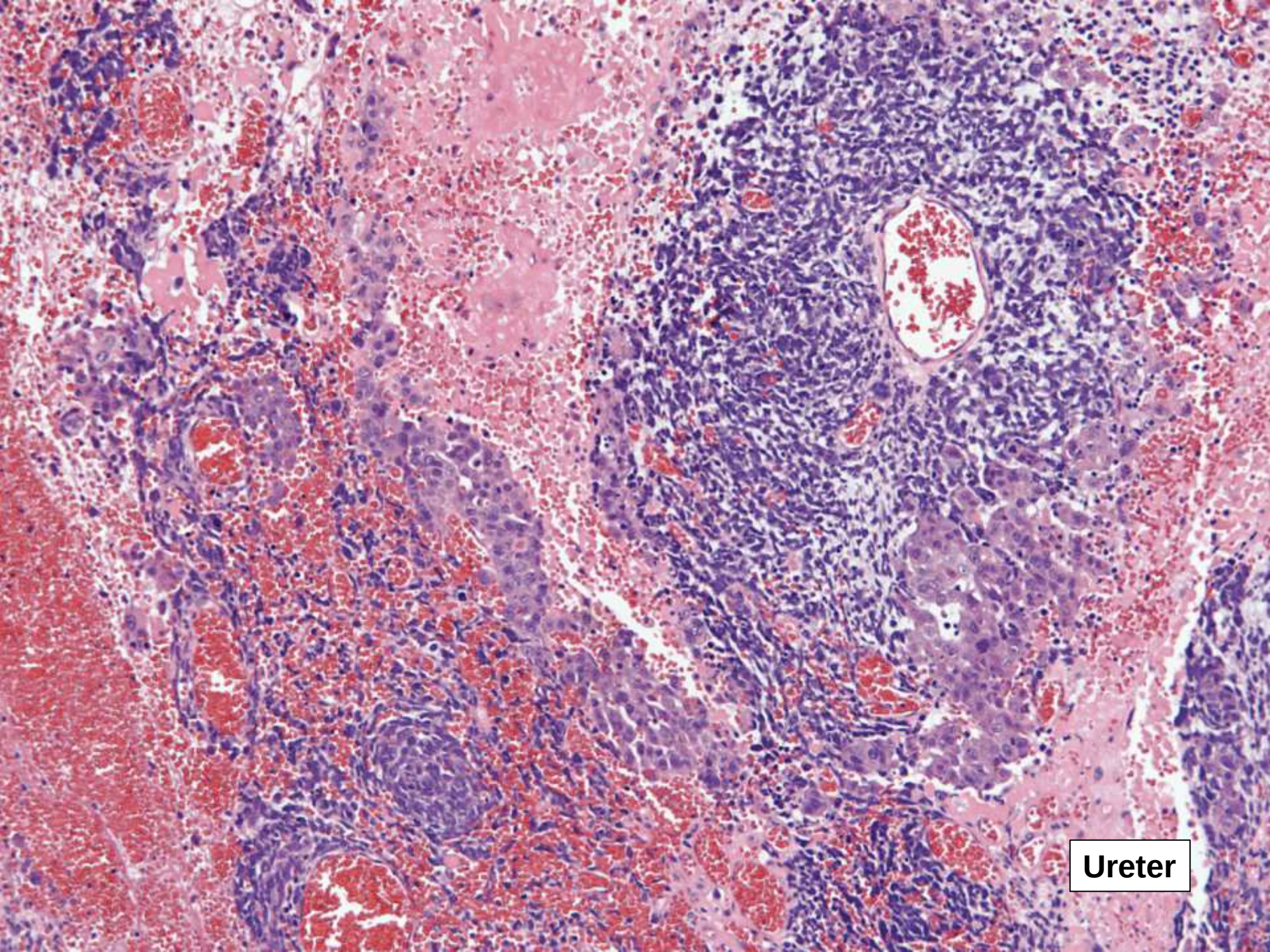
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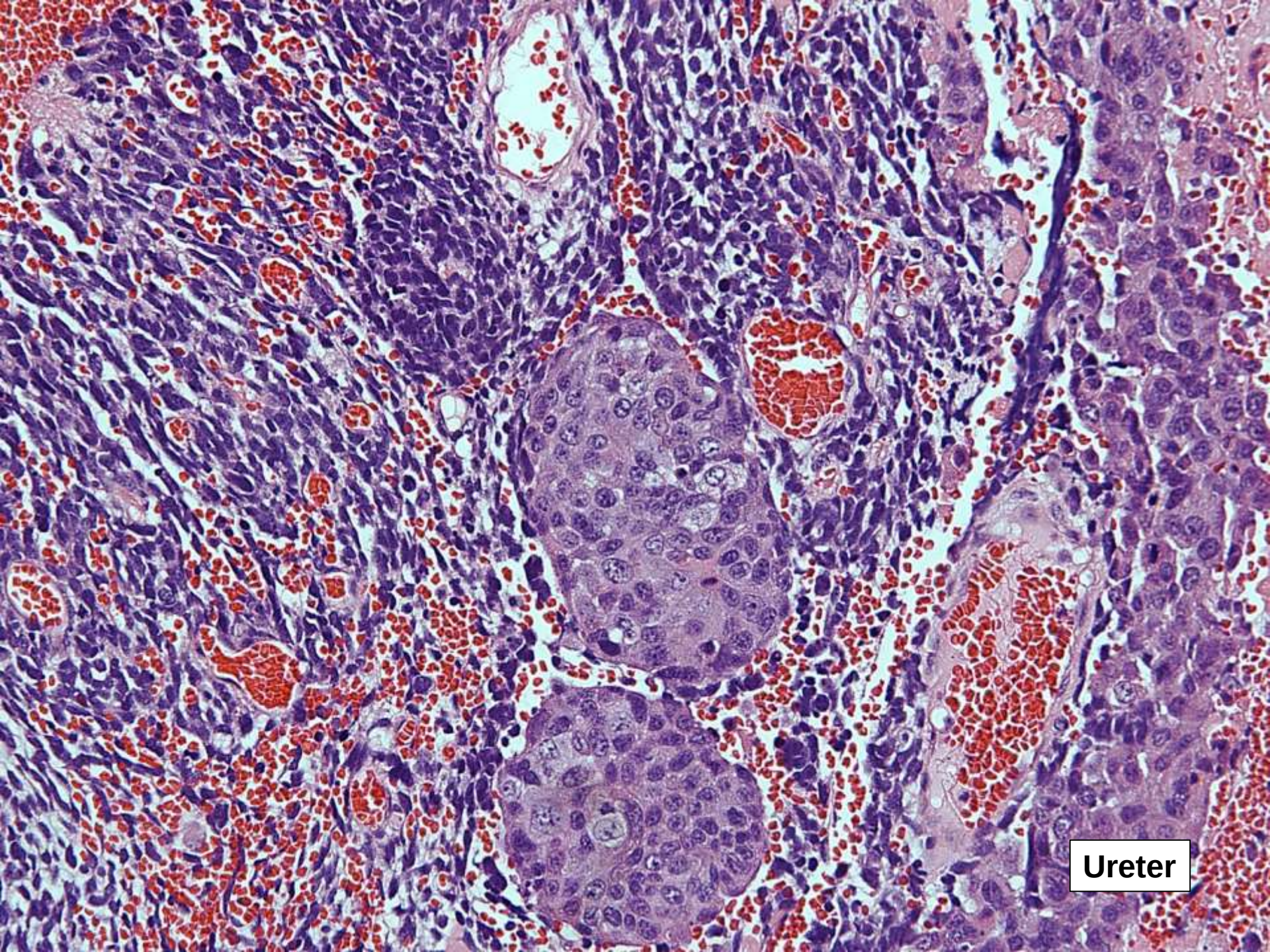
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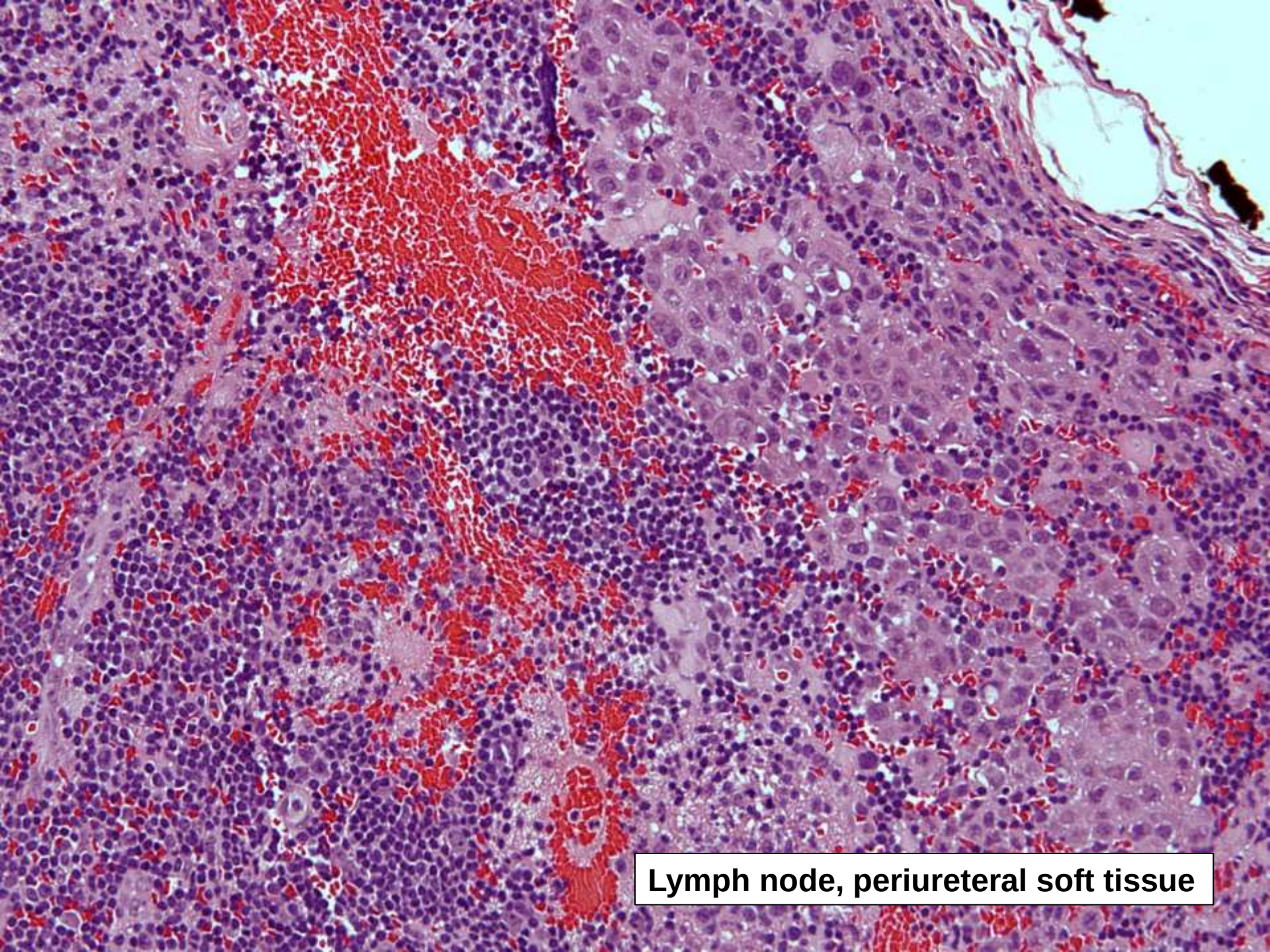
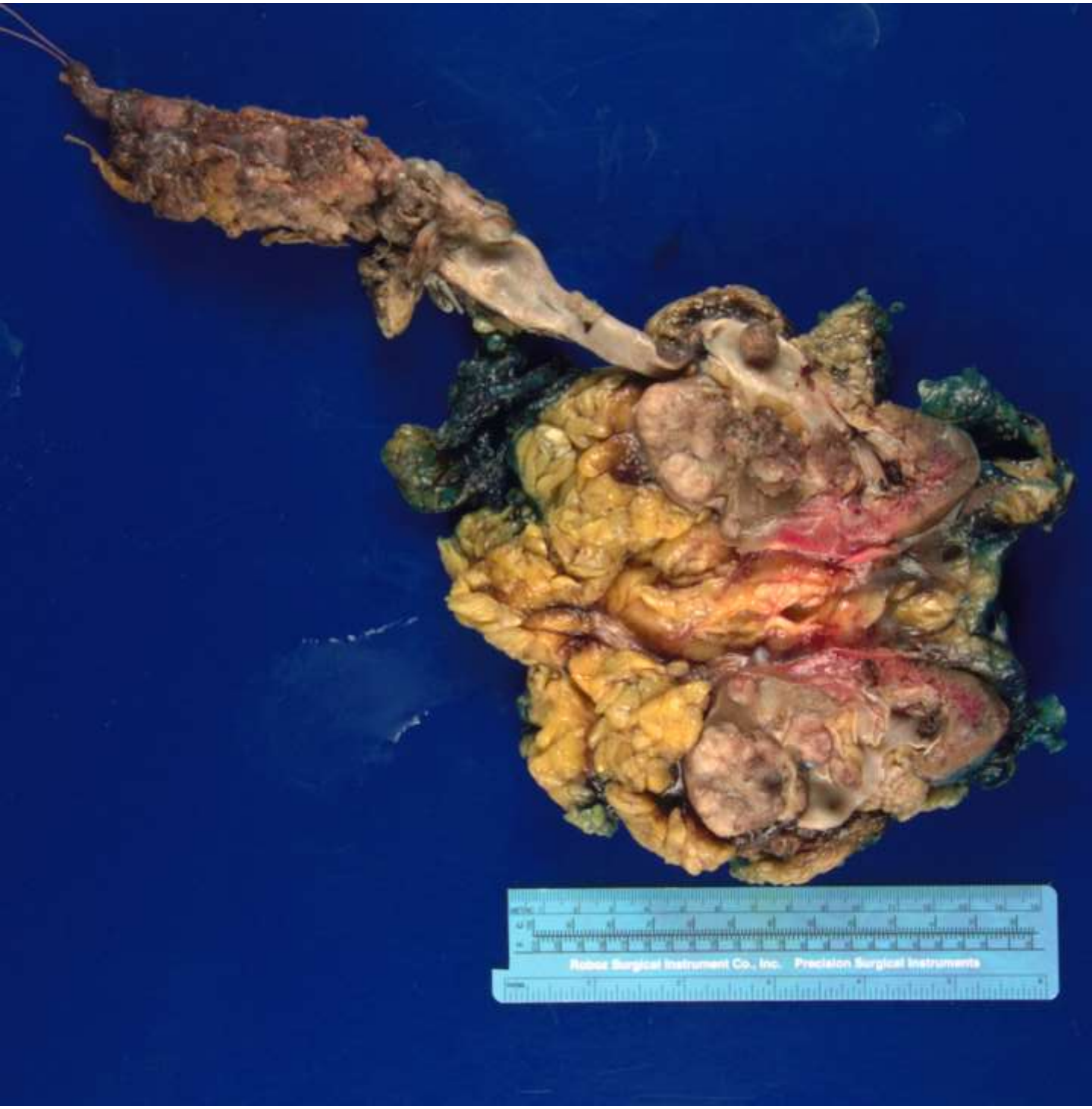
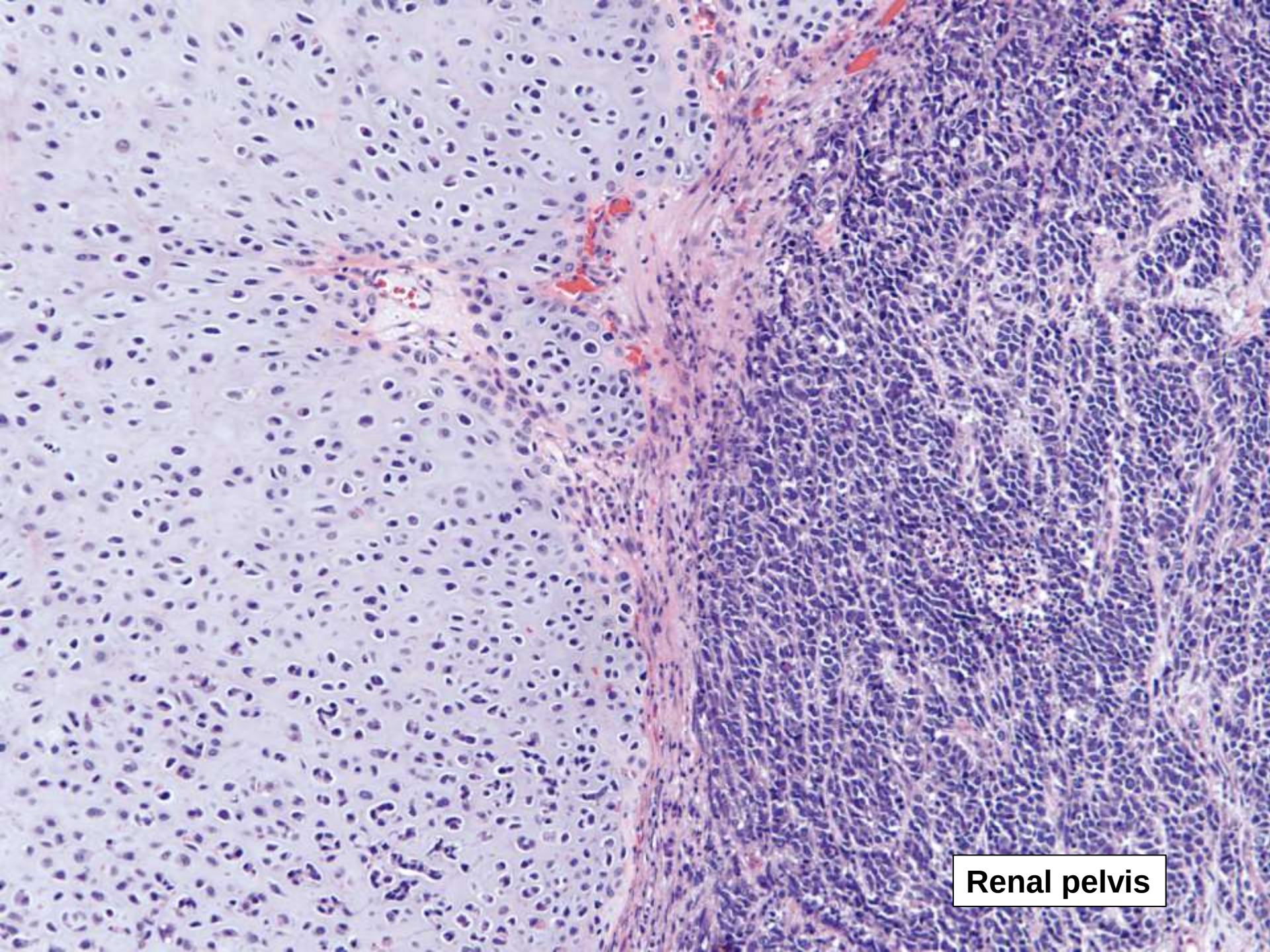
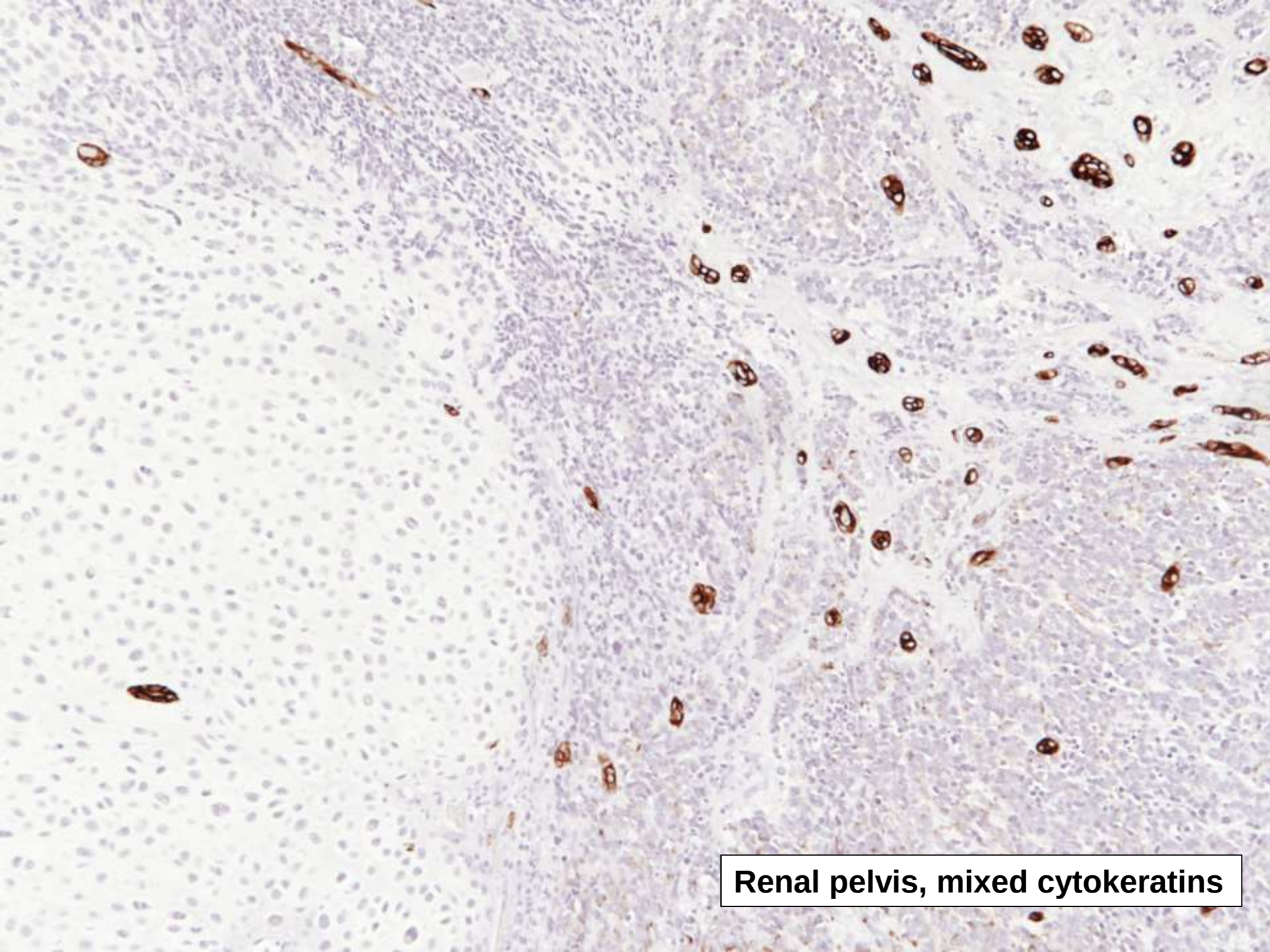
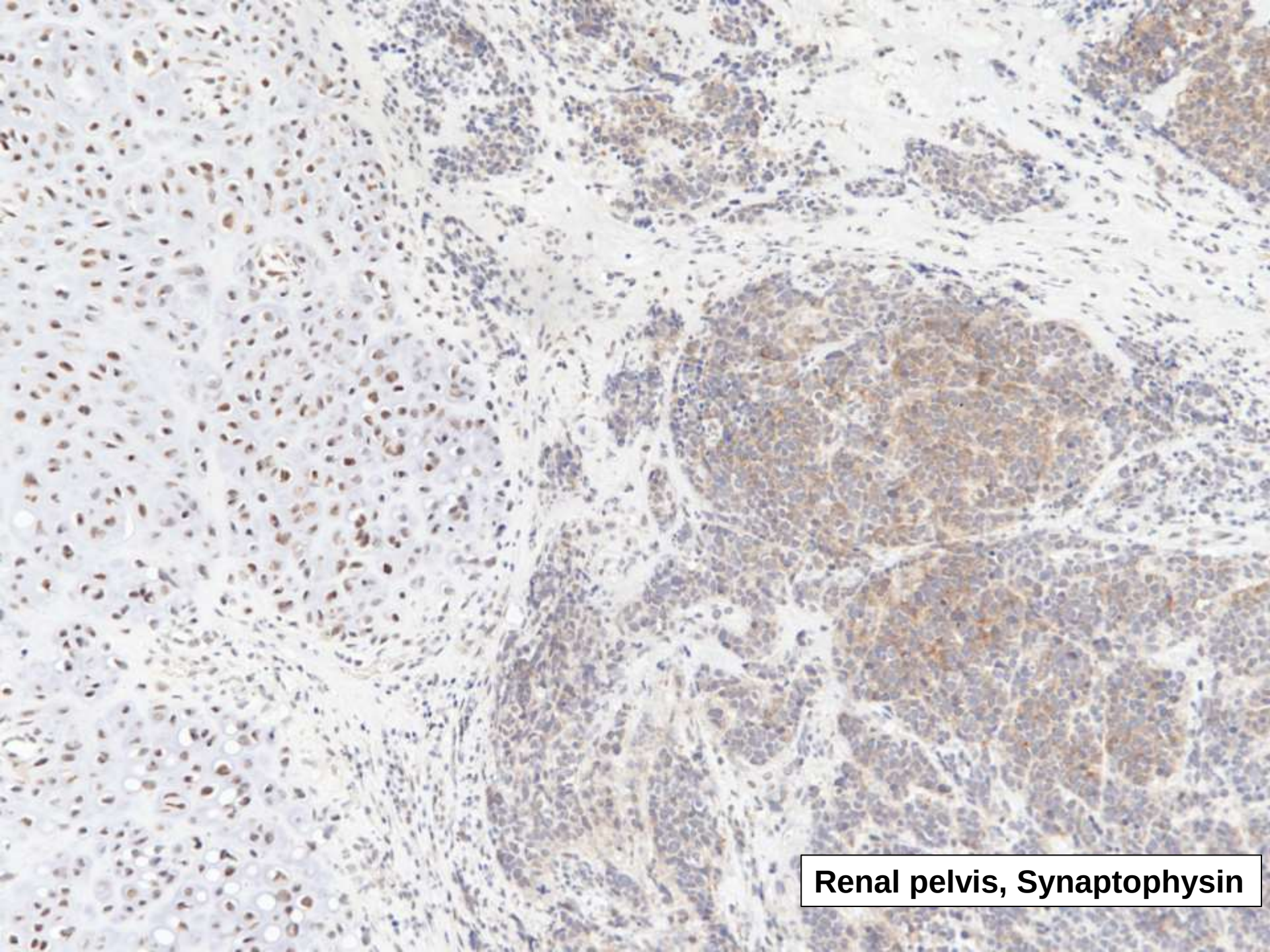

Lymph node, periureteral soft tissue

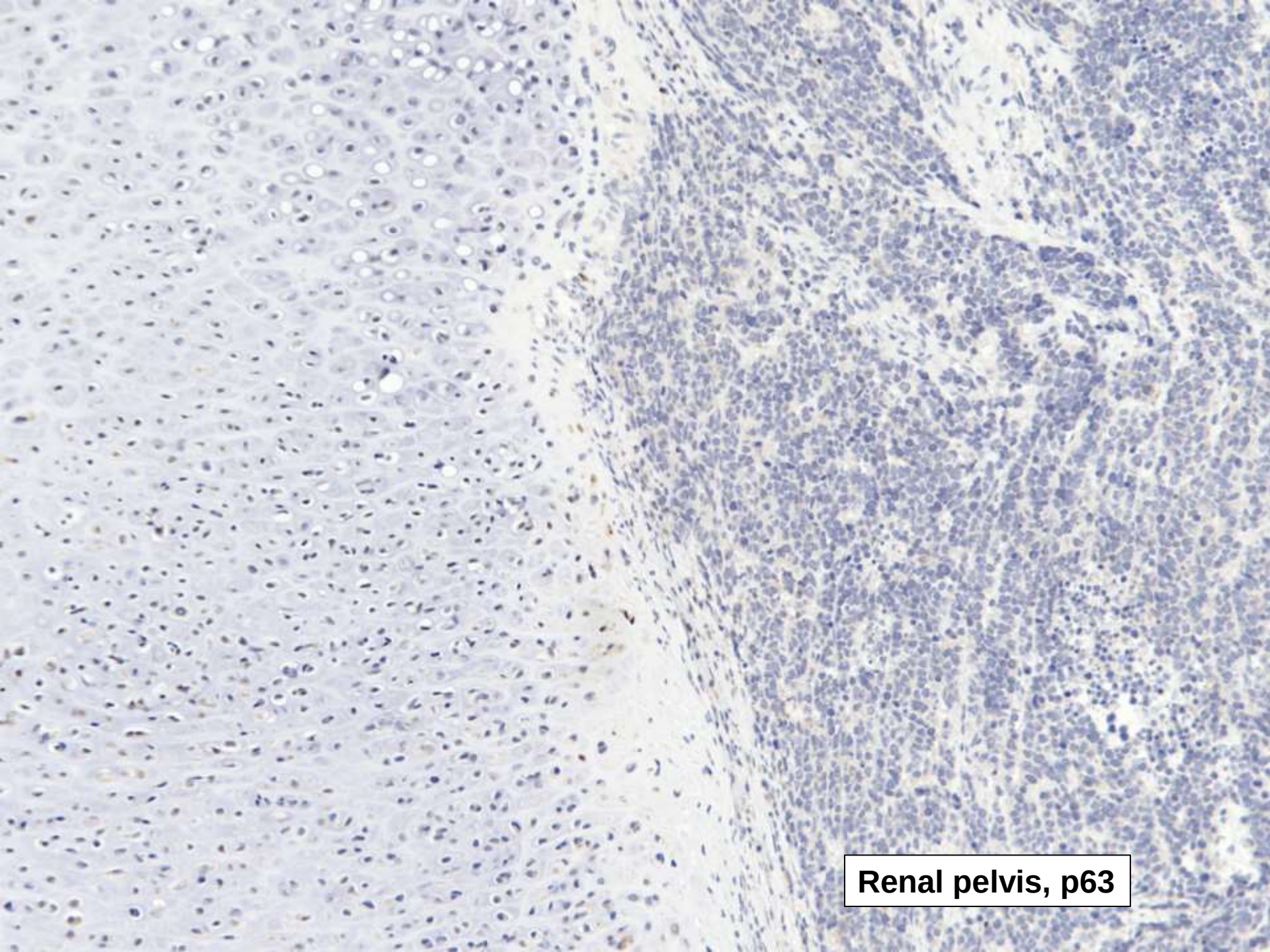
DIAGNOSIS?

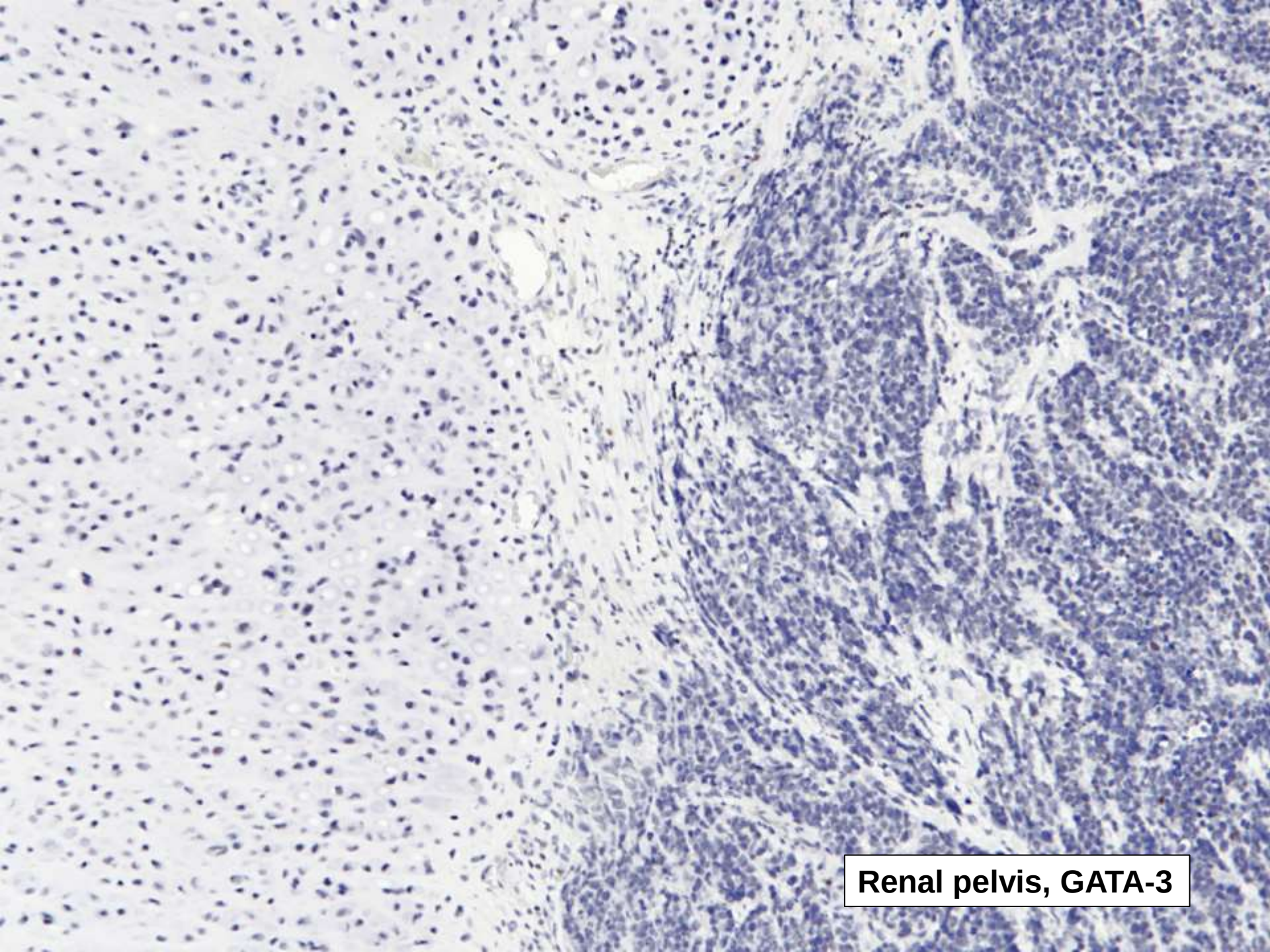

Robot Surgical Instrument Co., Inc. Precision Surgical Instruments

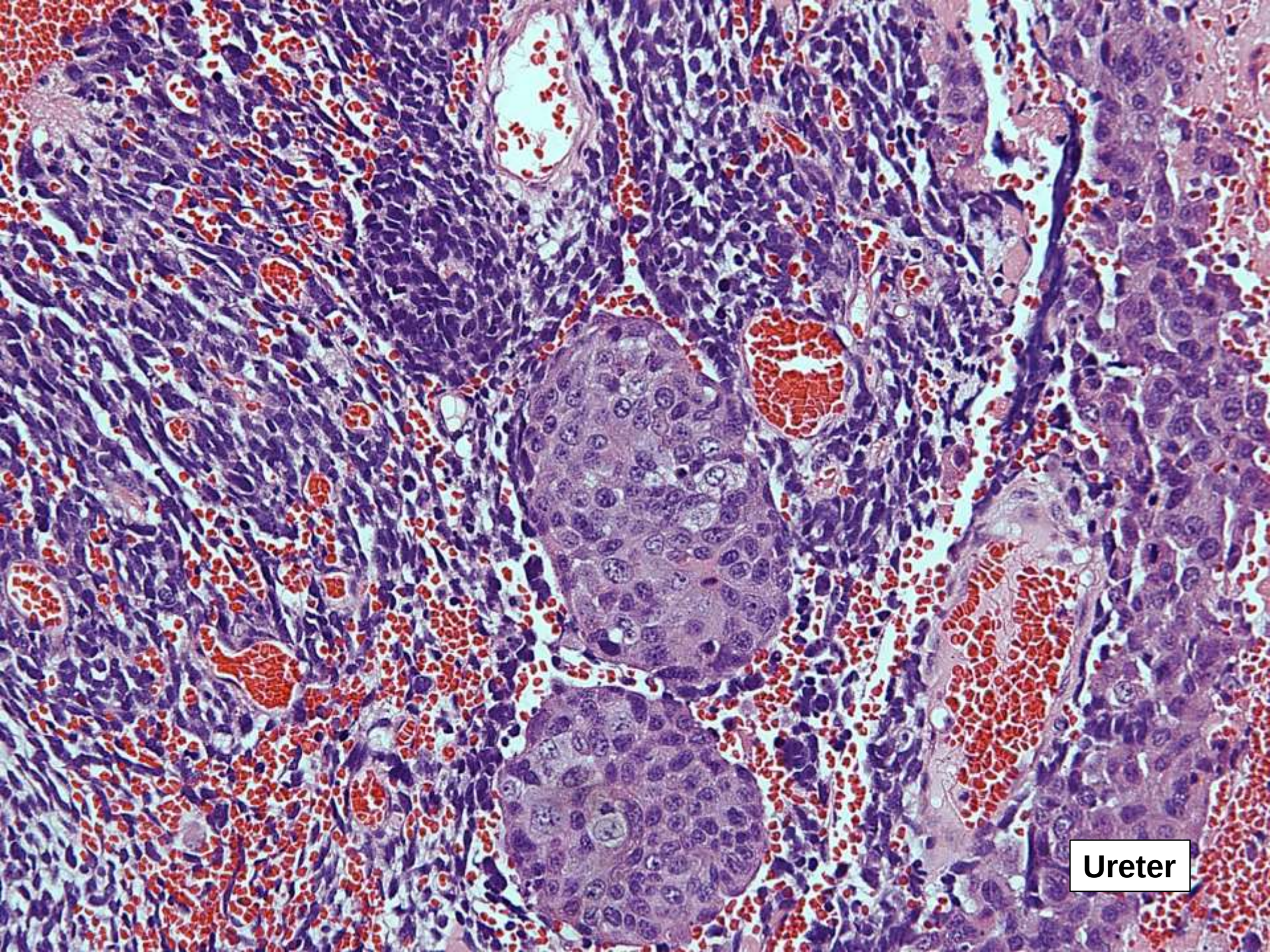

Renal pelvis

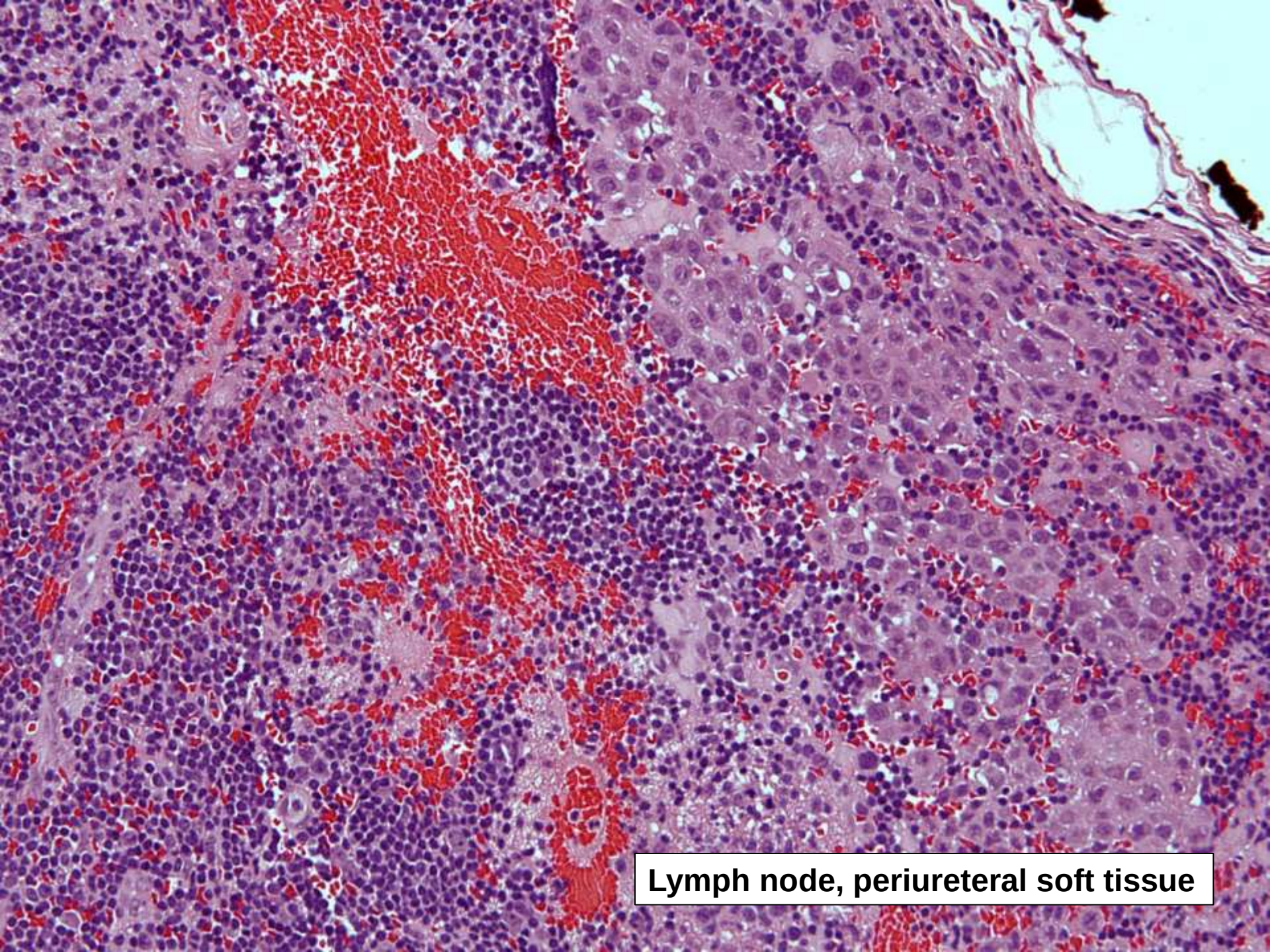

Renal pelvis, mixed cytokeratins


Renal pelvis, Synaptophysin


Renal pelvis, p63


Renal pelvis, GATA-3


Ureter


Lymph node, periureteral soft tissue

Sarcomatous tumor of the renal pelvis: differential diagnosis

- Sarcomatoid renal cell carcinoma secondarily involving the renal pelvis
- Variety of sarcomas which can rarely arise in the renal pelvis as a primary site or as a site of metastasis
- Metaplasia in a pure urothelial carcinoma
- Urothelial carcinoma with pseudosarcomatous stromal reaction
- **Sarcomatoid variant of urothelial cell carcinoma**

Sarcomatoid variant of urothelial carcinoma

- Biphasic malignant neoplasm with evidence of carcinomatous and sarcomatous differentiation
- Rare entity: Rink *et al*. found 2.4% (39/1648) of upper tract urothelial carcinomas were sarcomatoid

UC Histology	No. Pts (%)
Pure	1,250 (75.8)
Variant differentiation:	398 (24.2)
Squamous cell	163 (9.9)
Glandular	66 (4.0)
Sarcomatoid	39 (2.4)
Micropapillary	31 (1.9)
Small cell	32 (1.9)
Plasmacytoid	3 (0.2)
Multiple	64 (3.9)

Rink et al, J Urol, 2007.

Sarcomatoid urothelial carcinoma – histology

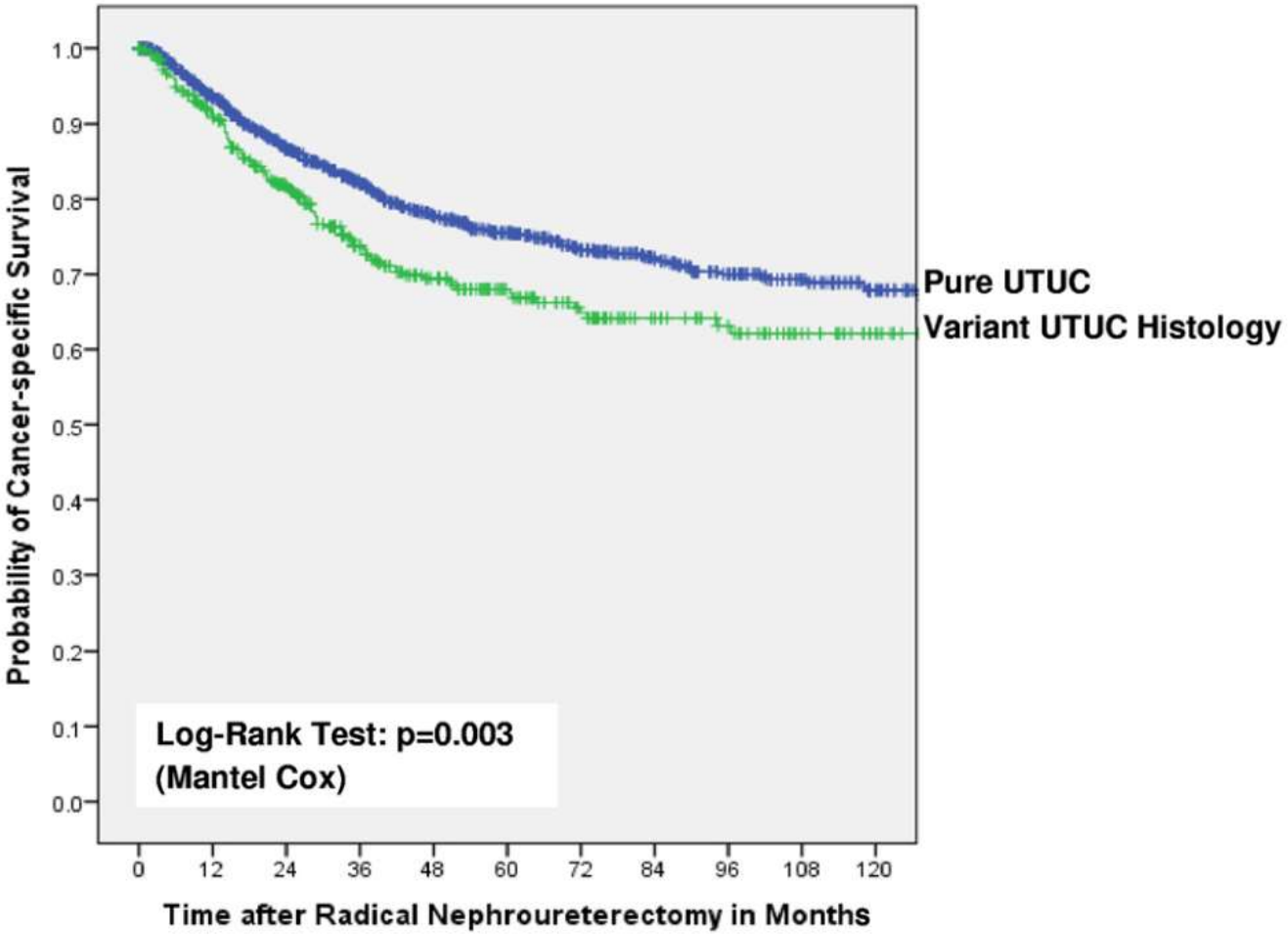
- "Conventional" urothelial carcinoma, sarcomatous areas, and transitions between the two
- Carcinoma is invariably high-grade, may be present as carcinoma in situ
- Heterologous components may consist of osteosarcoma, leiomyosarcoma, chondrosarcoma, rhabdomyosarcoma, or liposarcoma (in order of decreasing frequency)
- Compared to "pure" conventional UC, more commonly associated with: (1) advanced tumor stage, (2) tumor multifocality, (3) sessile tumor architecture, (4) tumor necrosis, (5) lymphovascular invasion, and (6) lymph node metastasis

Rink et al, J Urol, 2007.

Amin, Mod Path, 2009.

Variant UC histology – clinical outcomes

- Variant histology is associated with disease recurrence and cancer-specific mortality in univariable analyses of upper tract UC



Rink et al, J Urol, 2007.

Our case: clinical follow-up

November 2015: Nephroureterectomy, stage pT3 pN1, positive periureteral soft tissue margins

December 2015: Postoperative staging PET-CT with hypermetabolic right iliac lymph nodes

February 2016: First of two treatments with dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin (ddMVAC)

March 2016: Hospitalization for neutropenic fever/pneumonia

April 2016: PET-CT shows treatment response with no active disease

September 2016: Plan for follow-up surveillance imaging

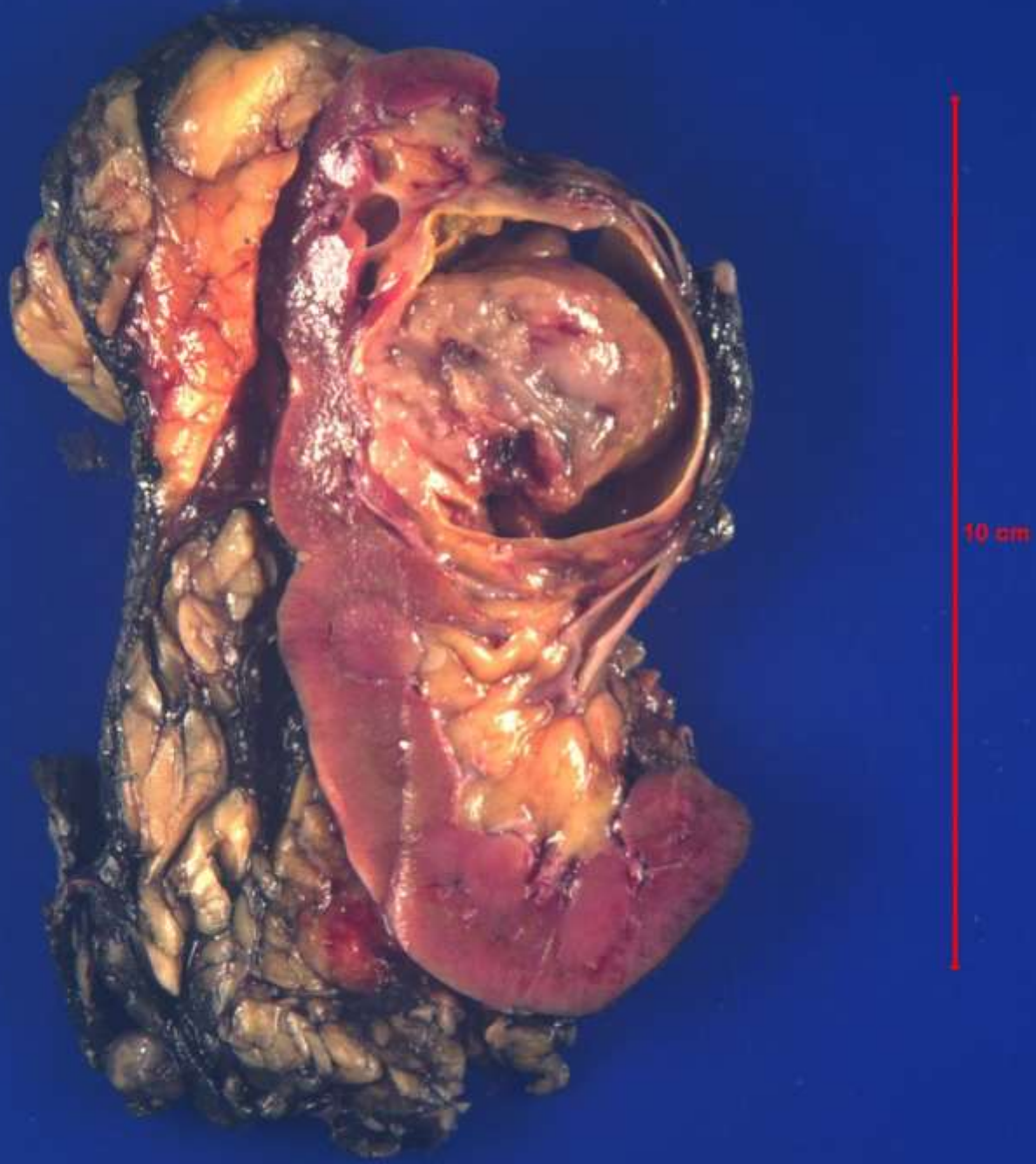
Sarcomatoid urothelial carcinoma – take home points

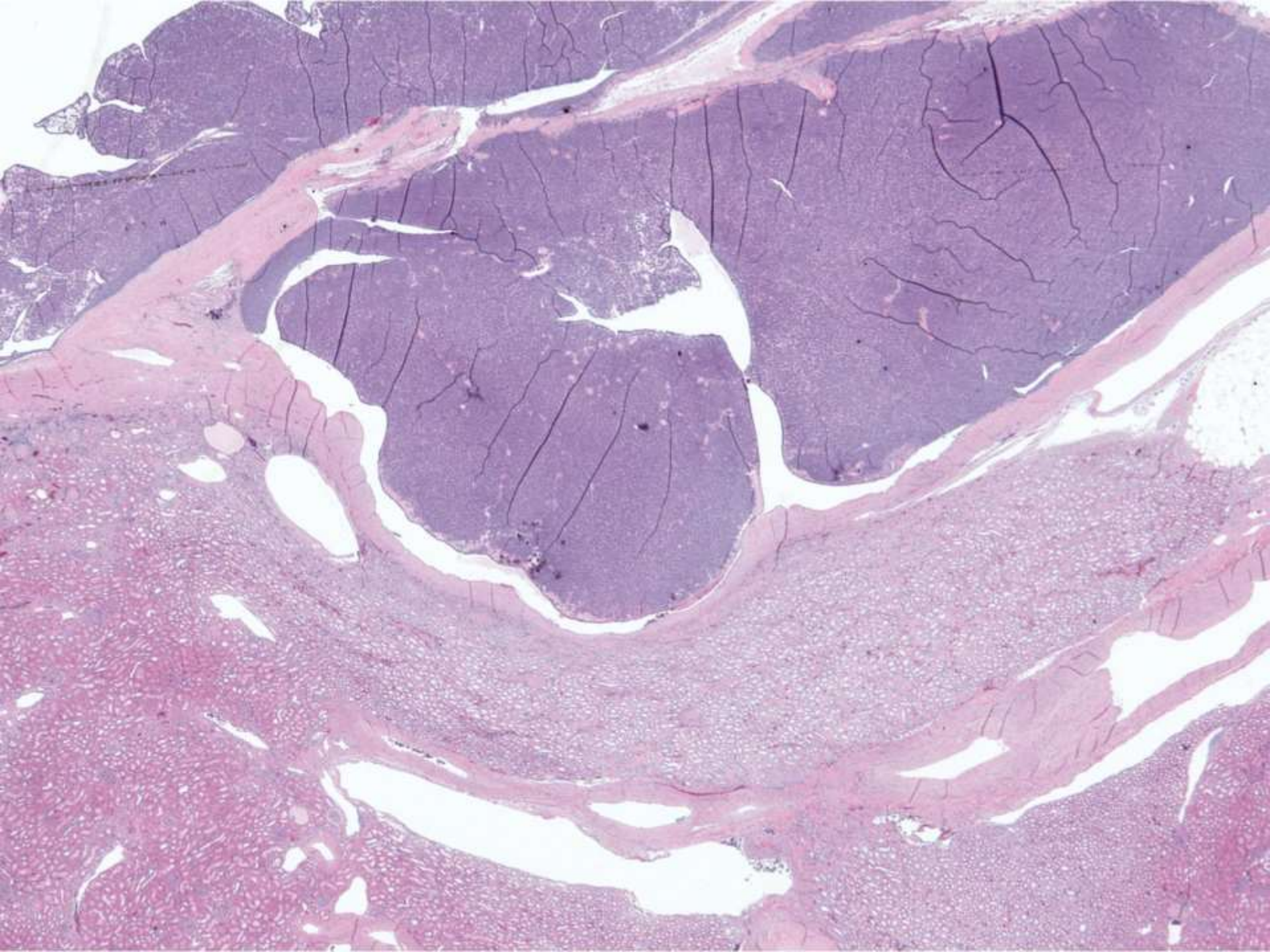
- Variant histology in the urothelial tract warrants exhaustive sampling to exclude a biphasic malignancy
- Histologic appearance of sarcomatoid UC is variable and capable of mimicking a number of entities
- X-chromosome inactivation and loss of heterozygosity studies suggest a monoclonal origin with clonal divergence
- Sarcomatoid UC of the upper tract has a worse prognosis than “pure” conventional UC, as in the bladder

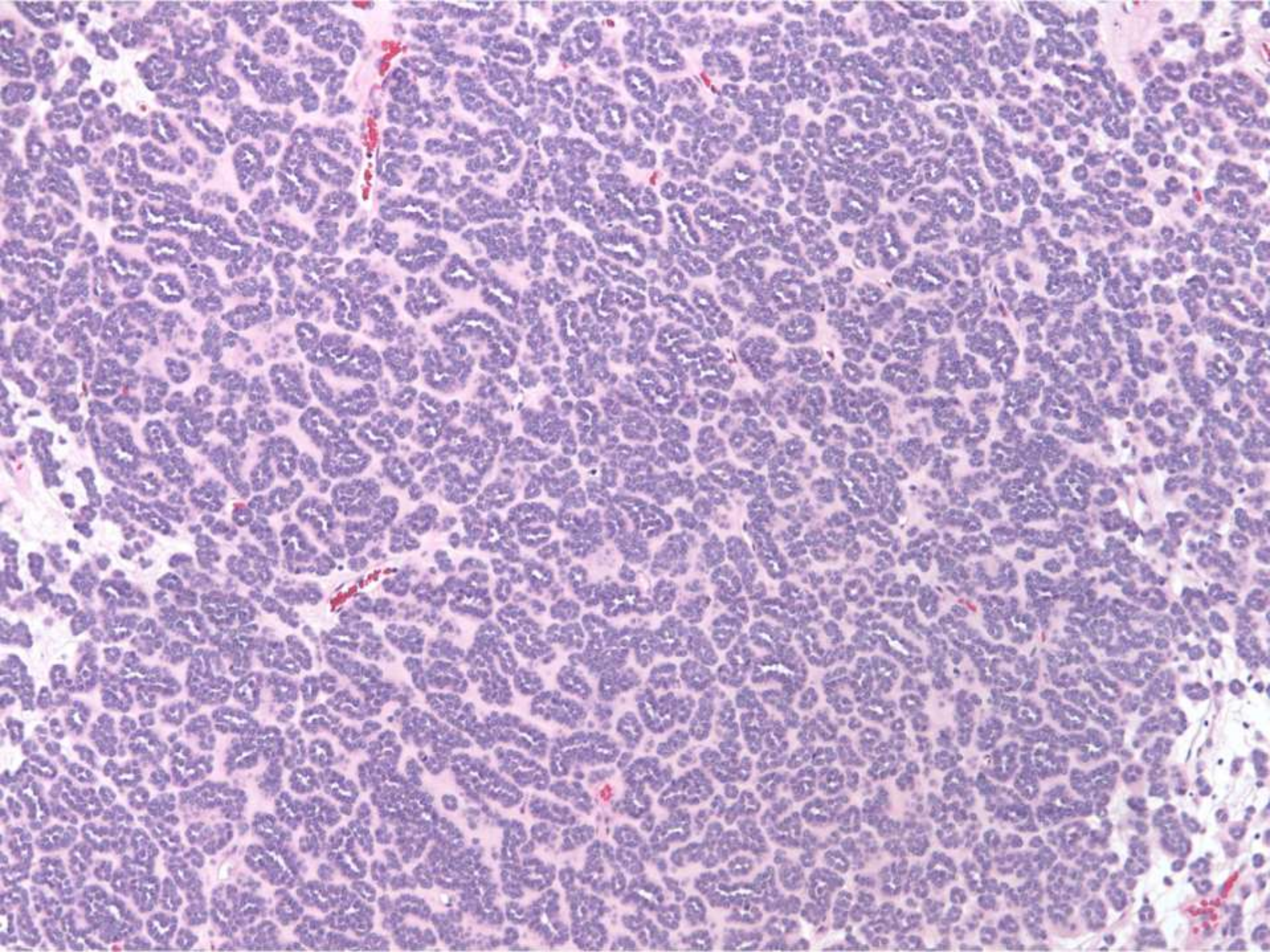
SB 6090

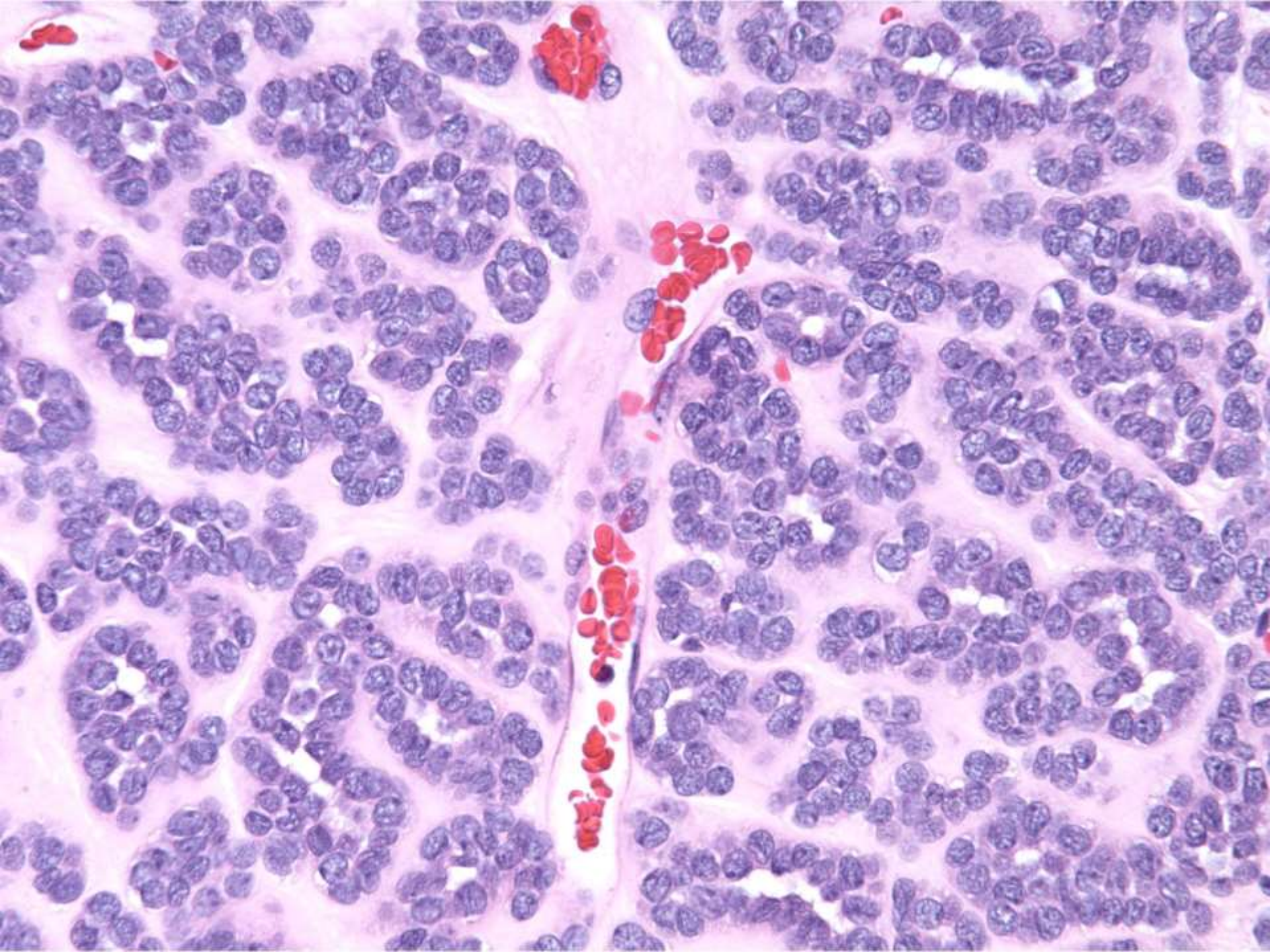
Adam Gomez/Richard Sibley; Stanford

61-year-old female with right cystic renal mass.

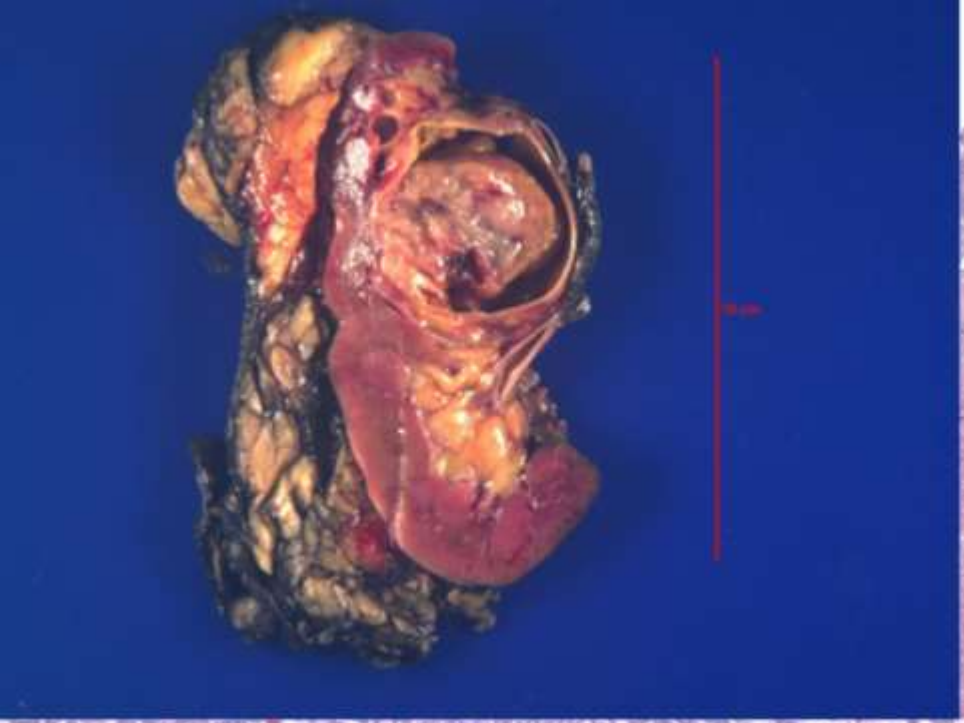

10 cm

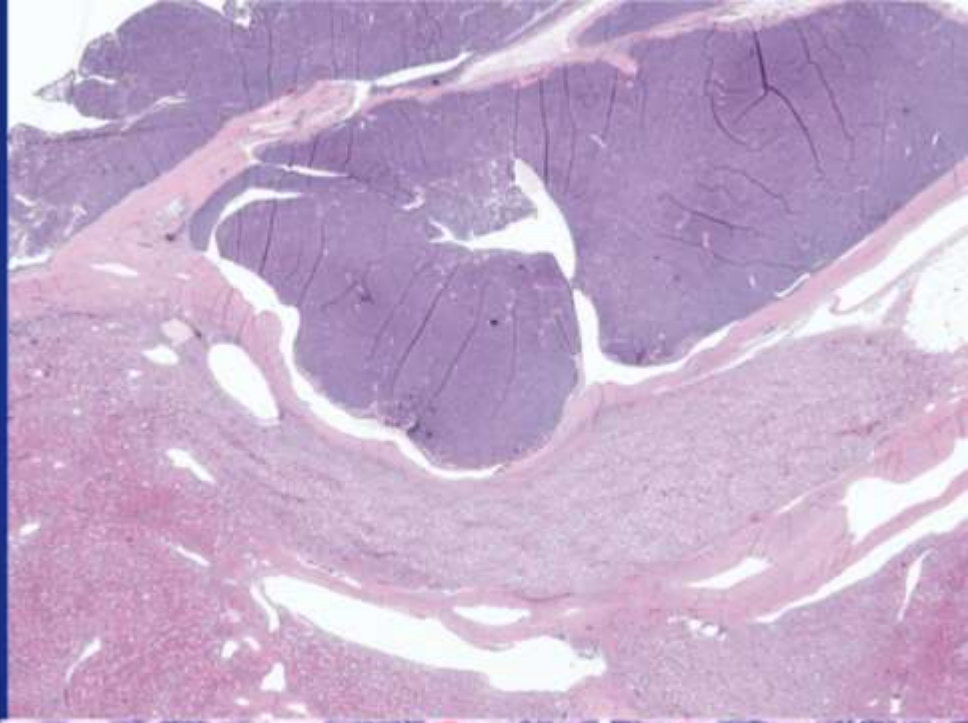


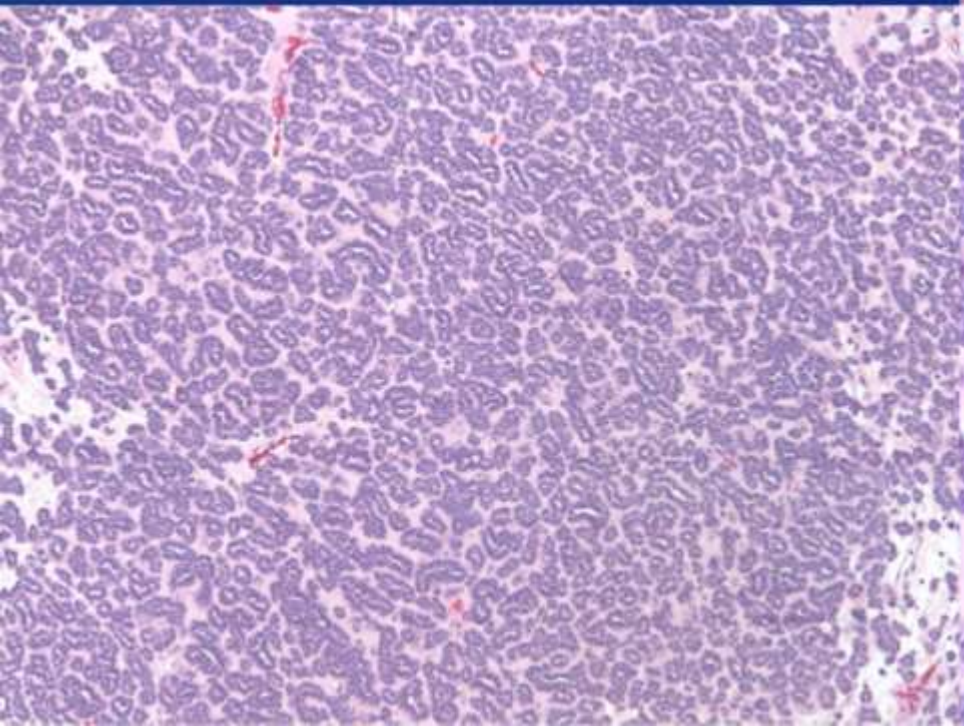


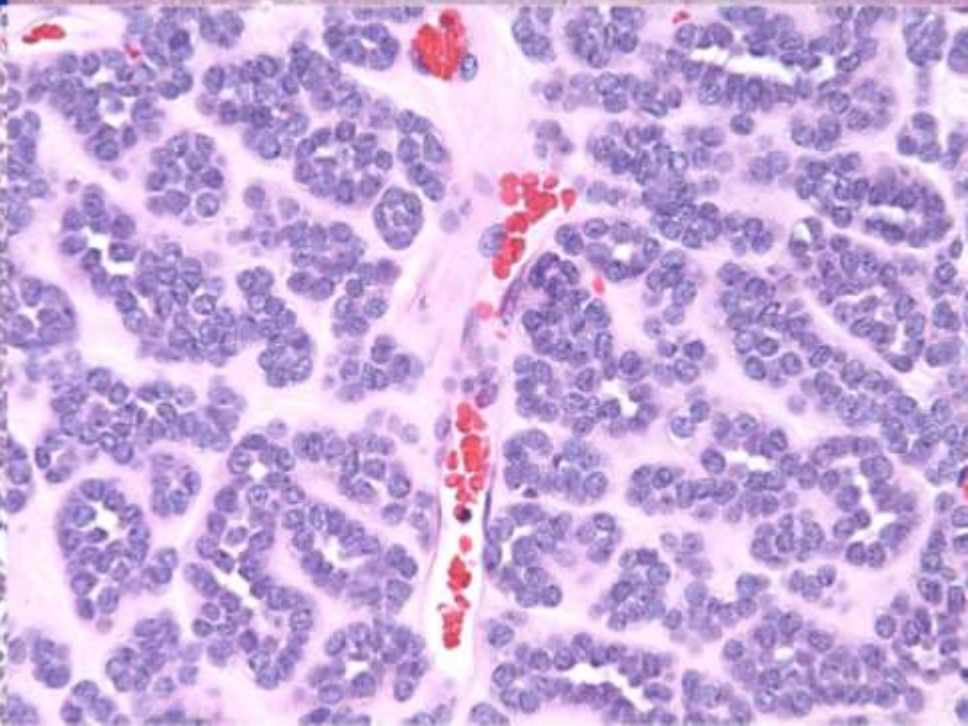


DIAGNOSIS?









Differential Diagnosis

- Papillary renal cell carcinoma
- Metanephric adenoma
- Epithelial-predominant nephroblastoma/Wilms tumor

Differential Diagnosis

Feature	PRCC	Metanephric Adenoma
Age, mean (range)	55 yr (30-80)	49 yr (3-79)
Size, mean (range)	**4.1 cm** (0.9-10.0)	**2.9 cm** (1.2-7.5)
Pseudocapsule	**87%**	10%
Branching fronds	0%	**81%**
Psammoma bodies	30%	**100%**
Multifocality	22%	0%
Papillary hyperplasia/adenoma	30%	0%
"Spillover"	*39%*	*29%*
Fibrous bands	*56%*	*67%*
Glomeruloid bodies	*43%*	*33%*

Padilha, et al. Metanephric adenoma and solid variant of papillary renal cell carcinoma: common and distinctive features. Histopathology 2013, 62, 941–953. DOI: 10.1111/his.12106.

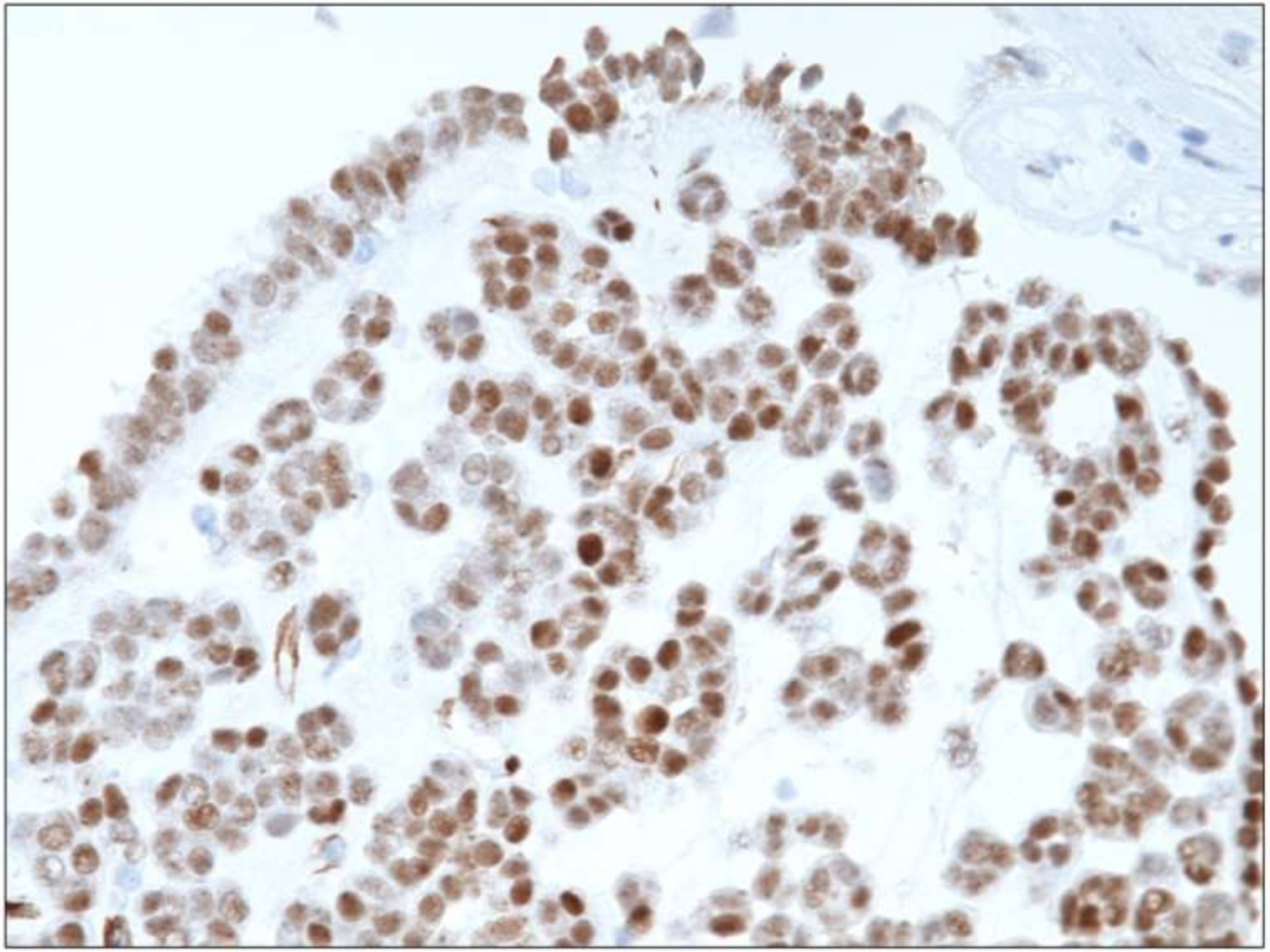
Differential Diagnosis

Immunohistochemistry	PRCC	Metanephric Adenoma
CD57	70%	100%
WT1	0%	**95%**
CK7	100%	57%
EMA	100%	0%
AMACR	100%	5%
S100	22%	100%
BRAF V600E	1 case with known BRAF V600E mutation	**76%**

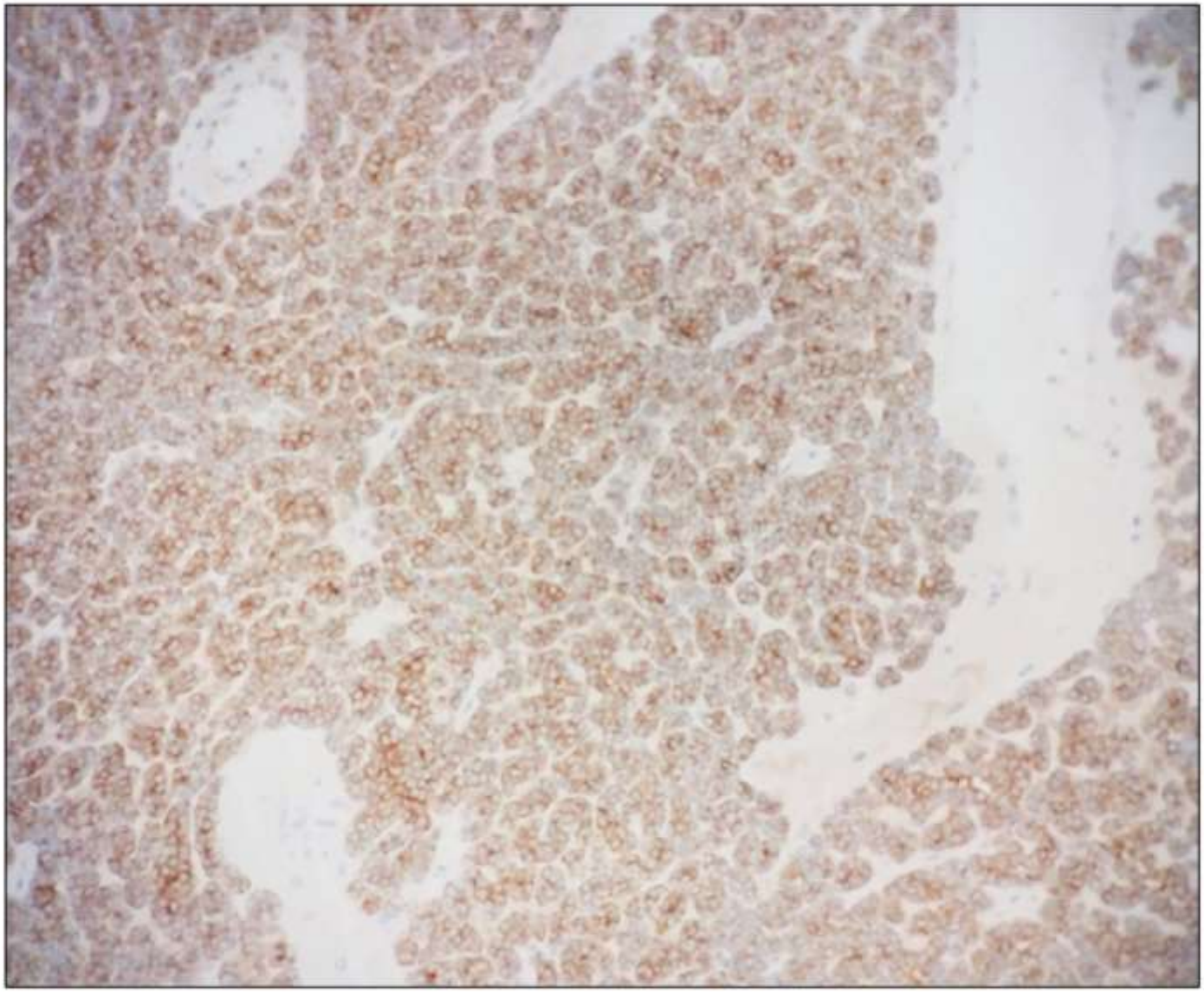
Pinto, et al. Immunohistochemical staining for BRAF V600E supports the diagnosis of metanephric adenoma. Histopathology. 2015 May;66(6):901-4. doi: 10.1111/his.12509. Epub 2015 Jan 23.

Udager, et al. Molecular and immunohistochemical characterization reveals novel BRAF mutations in metanephric adenoma. Am J Surg Pathol. 2015 Apr;39(4):549-57. doi: 10.1097/PAS.0000000000000377.

Padilha, et al. Metanephric adenoma and solid variant of papillary renal cell carcinoma: common and distinctive features. Histopathology 2013, 62, 941–953. DOI: 10.1111/his.12106.



WT1



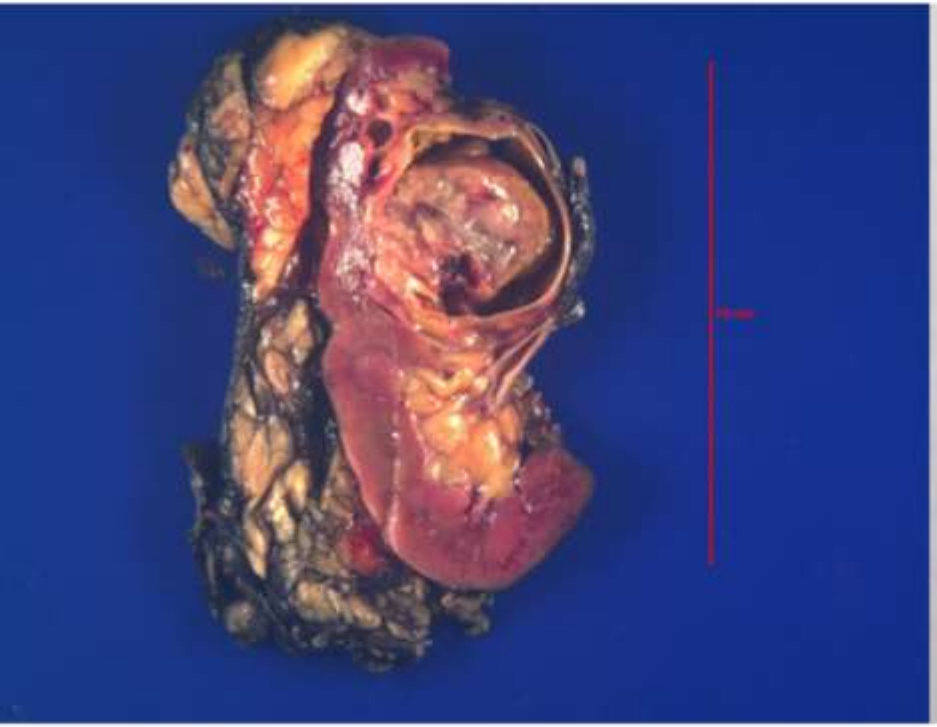
BRAFV600E

Metanephric Adenoma

- Considered to constitute maturation of nephroblastoma/Wilms tumor
  - Lacks gains of chromosome 7 and 17 and loss of Y seen in PRCC and common in Wilms tumor
- Associated with polycythemia (10%)
- Metastatic spread not reported

- Spectrum of metanephric tumors:
  - Metanephric adenoma
  - Metanephric adenofibroma
  - Metanephric stromal tumor

Metanephric Adenoma



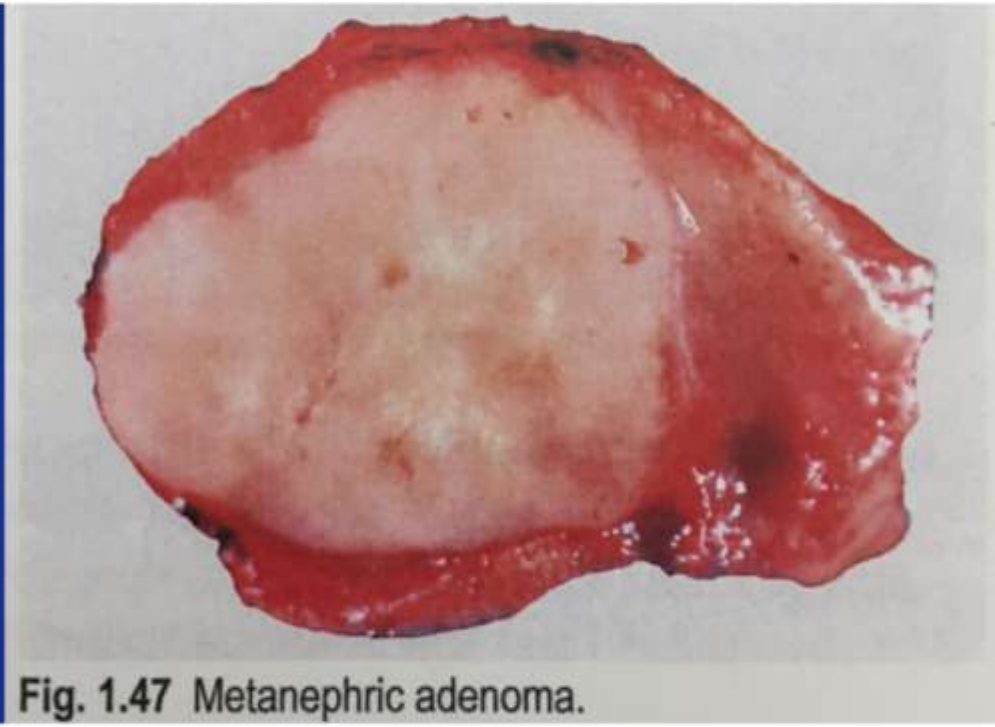


Fig. 1.47 Metanephric adenoma.

- Gross: usually solid, tan-grey, soft or firm
- Larger tumors: hemorrhage, focal necrosis
  - Cystic degeneration in 10%

WHO Classification of Tumours of the Urinary System and Male Genital Organs. Fourth edition.

References

- WHO Classification of Tumours of the Urinary System and Male Genital Organs. Fourth edition.

- Pinto, et al. Immunohistochemical staining for BRAF V600E supports the diagnosis of metanephric adenoma. Histopathology. 2015 May;66(6):901-4. doi: 10.1111/his.12509. Epub 2015 Jan 23.

- Udager, et al. Molecular and immunohistochemical characterization reveals novel BRAF mutations in metanephric adenoma. Am J Surg Pathol. 2015 Apr;39(4):549-57. doi: 10.1097/PAS.0000000000000377.

- Padilha, et al. Metanephric adenoma and solid variant of papillary renal cell carcinoma: common and distinctive features. Histopathology 2013, 62, 941–953. DOI: 10.1111/his.12106.