2017 Annual Meeting | September 14-17 | Deerhurst Skyline Resort | Huntsville, Ontario

DIAGNOSTIC SLIDE SEMINAR: PART 2 NEPHRECTOMY/PARTIAL NEPHRECTOMY CASES

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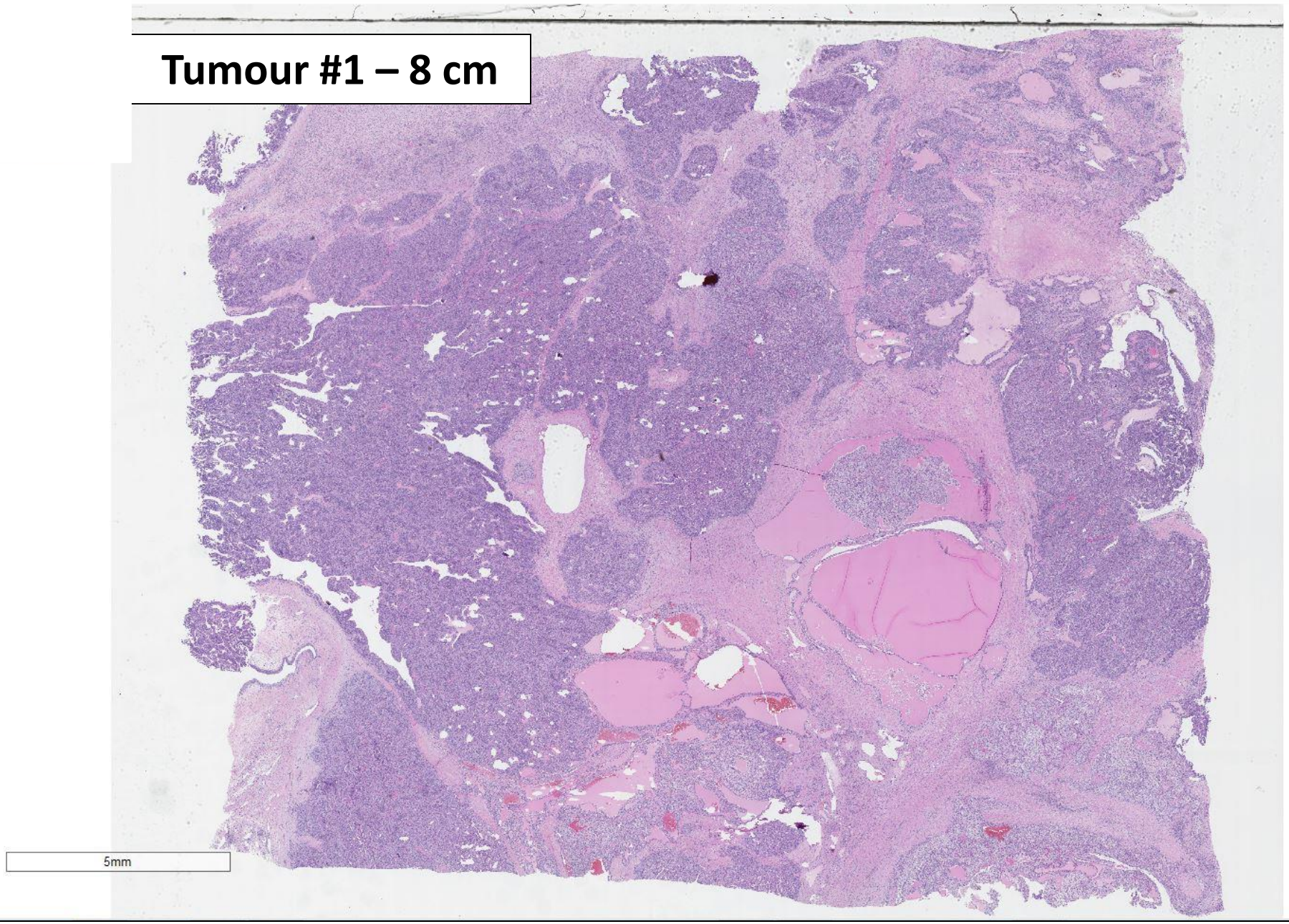
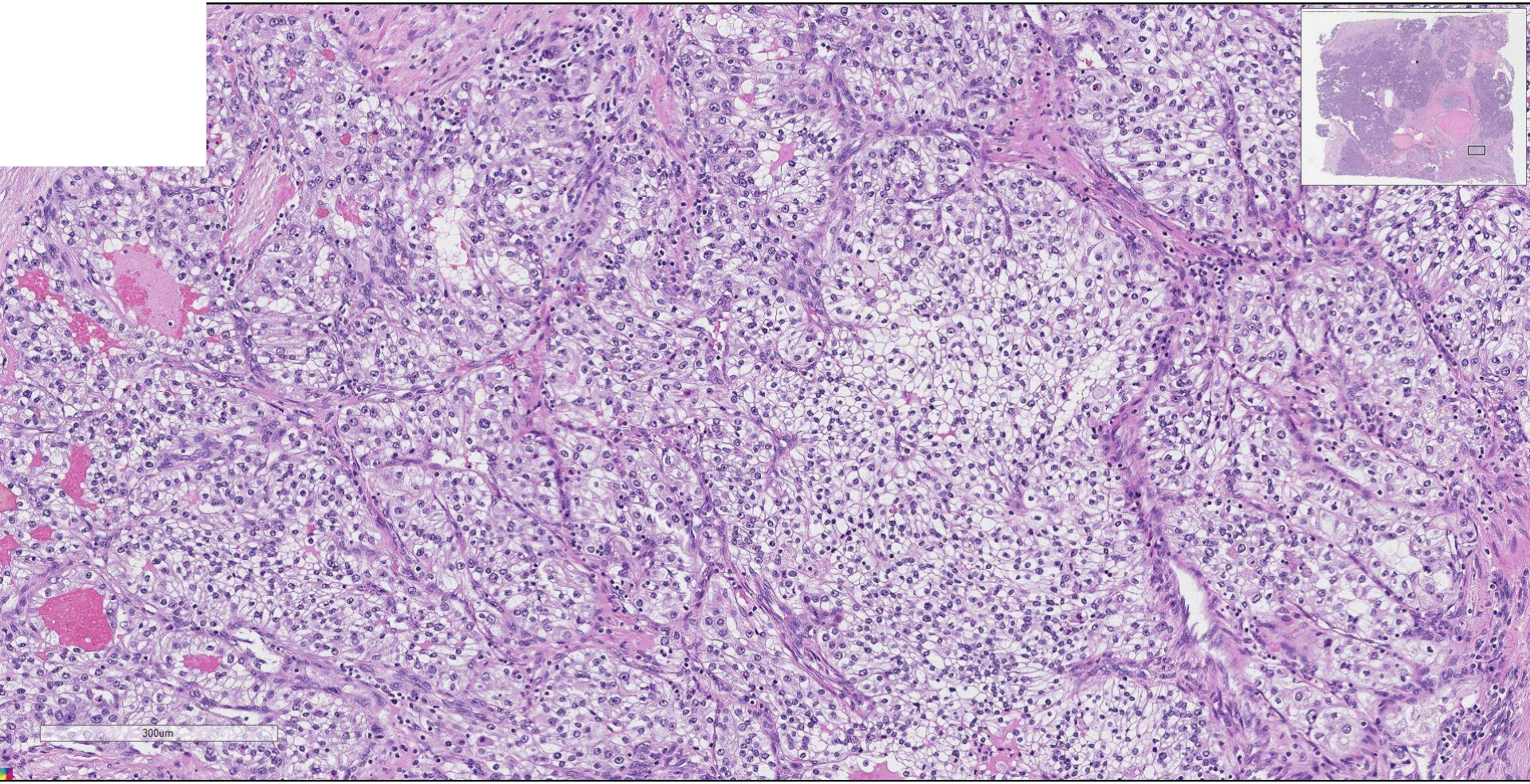
Consultant in Genitourinary Pathology
University Health Network, Toronto, ON

Case 1

45 year-old male, weight loss, flank pain, multiple bilateral renal masses, left radical nephrectomy

Tumour #1 – 8 cm

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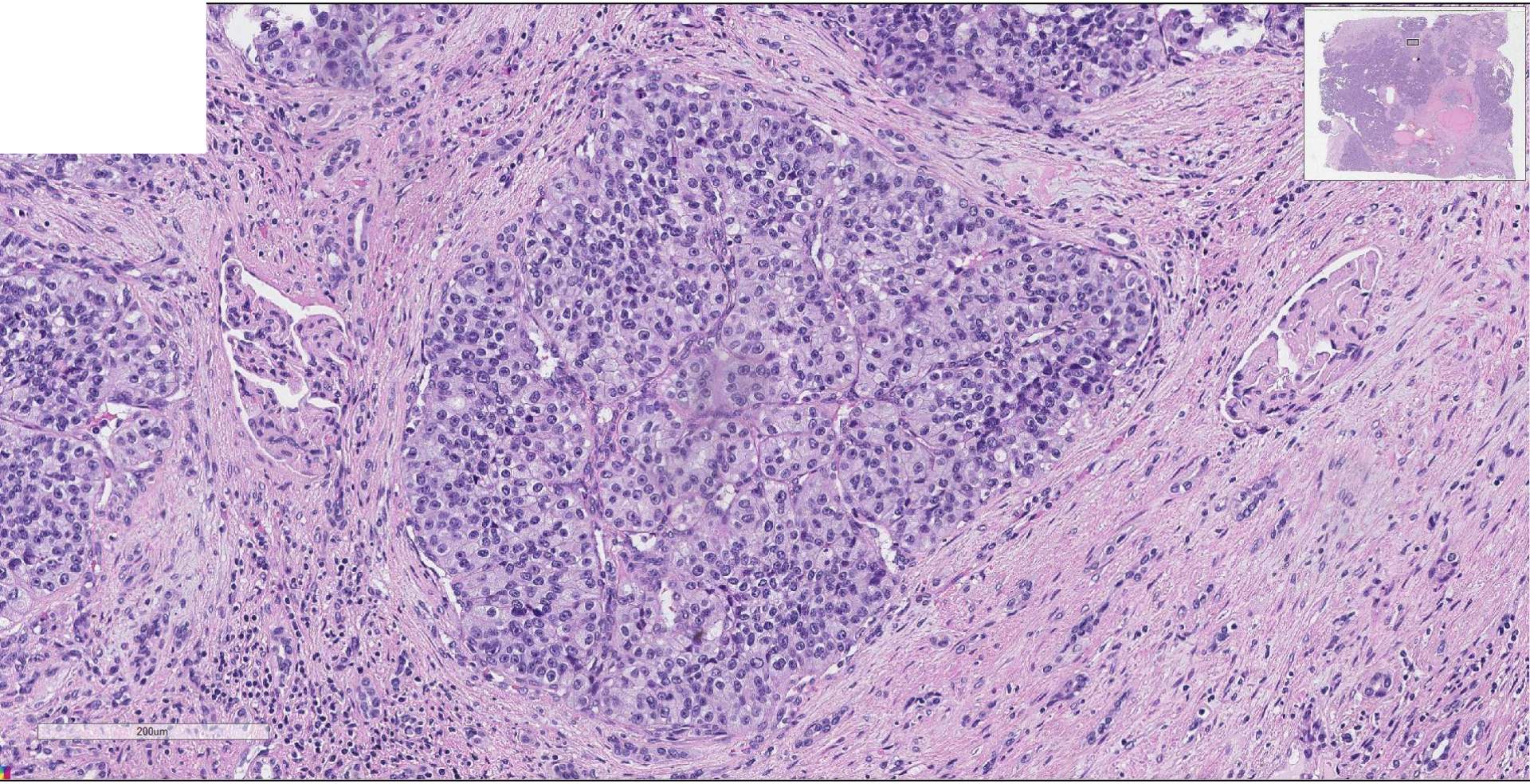
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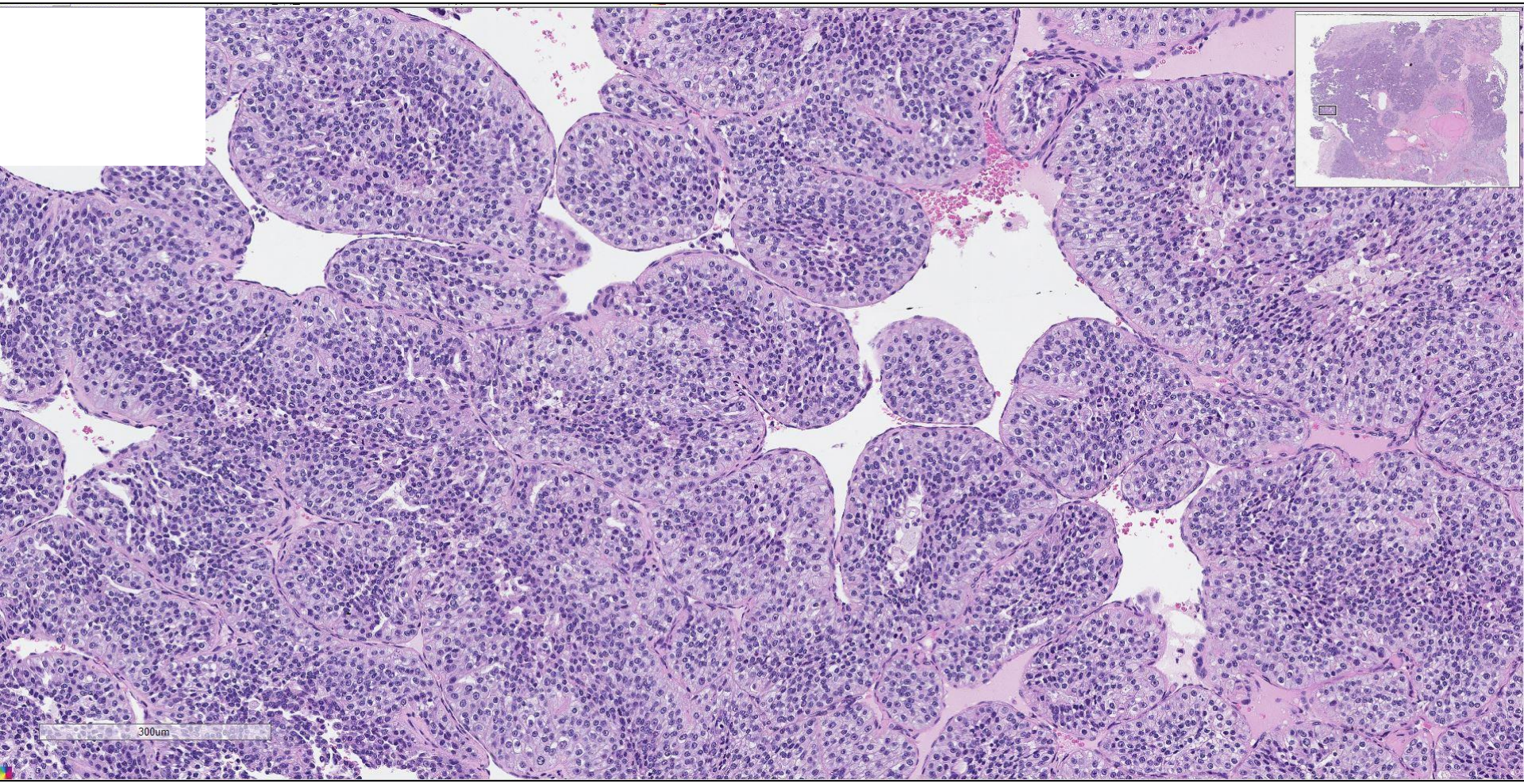
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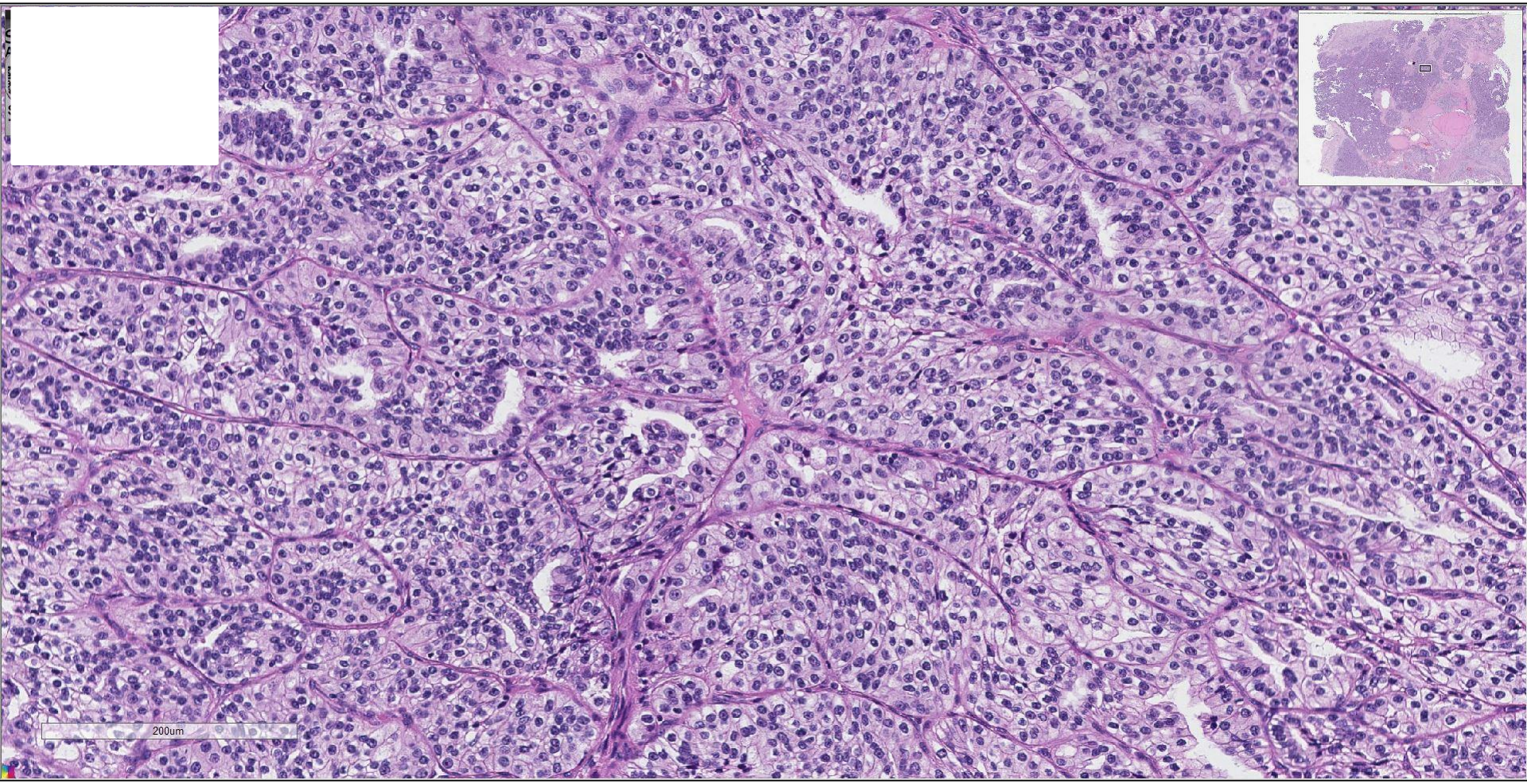
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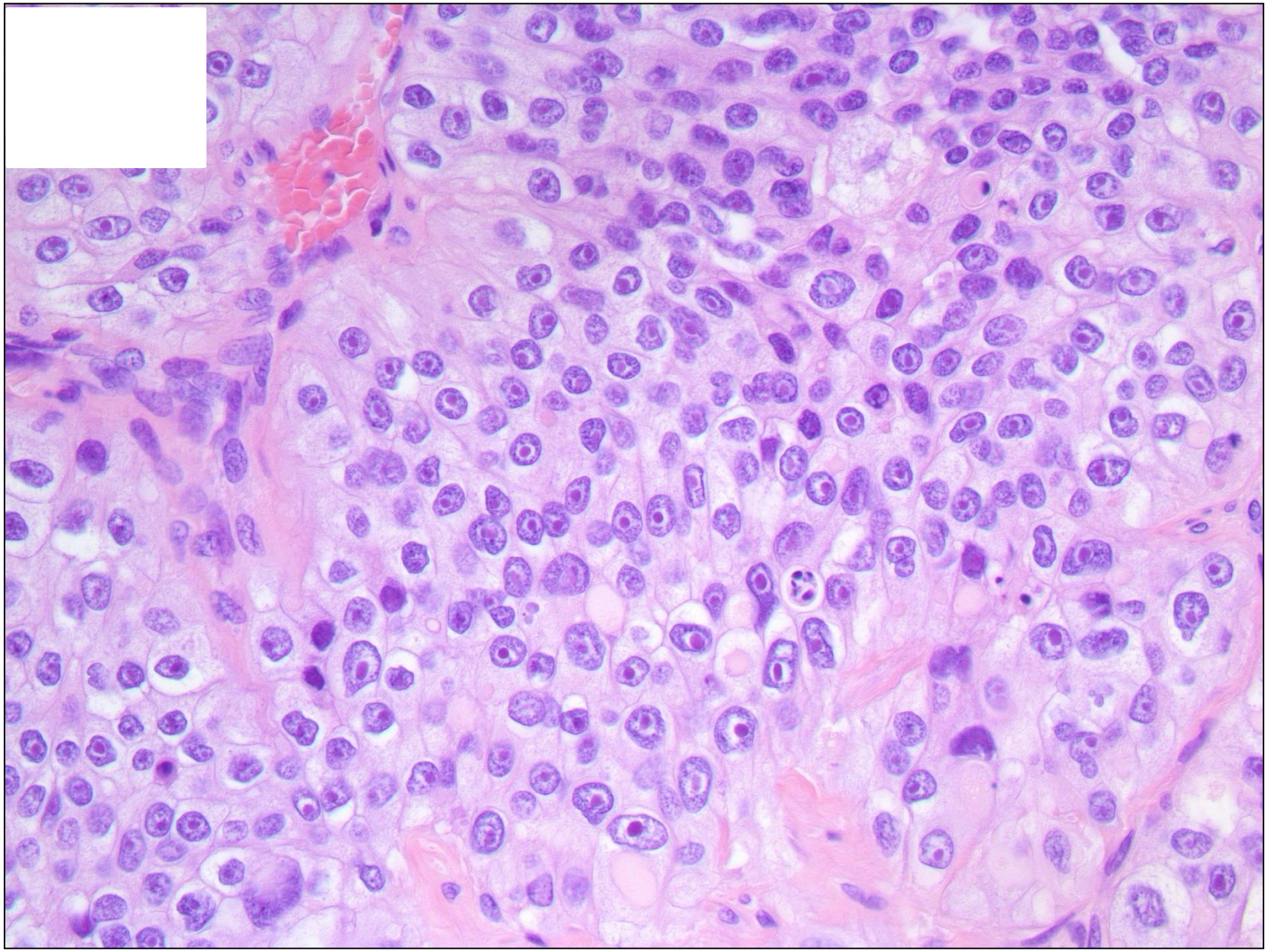
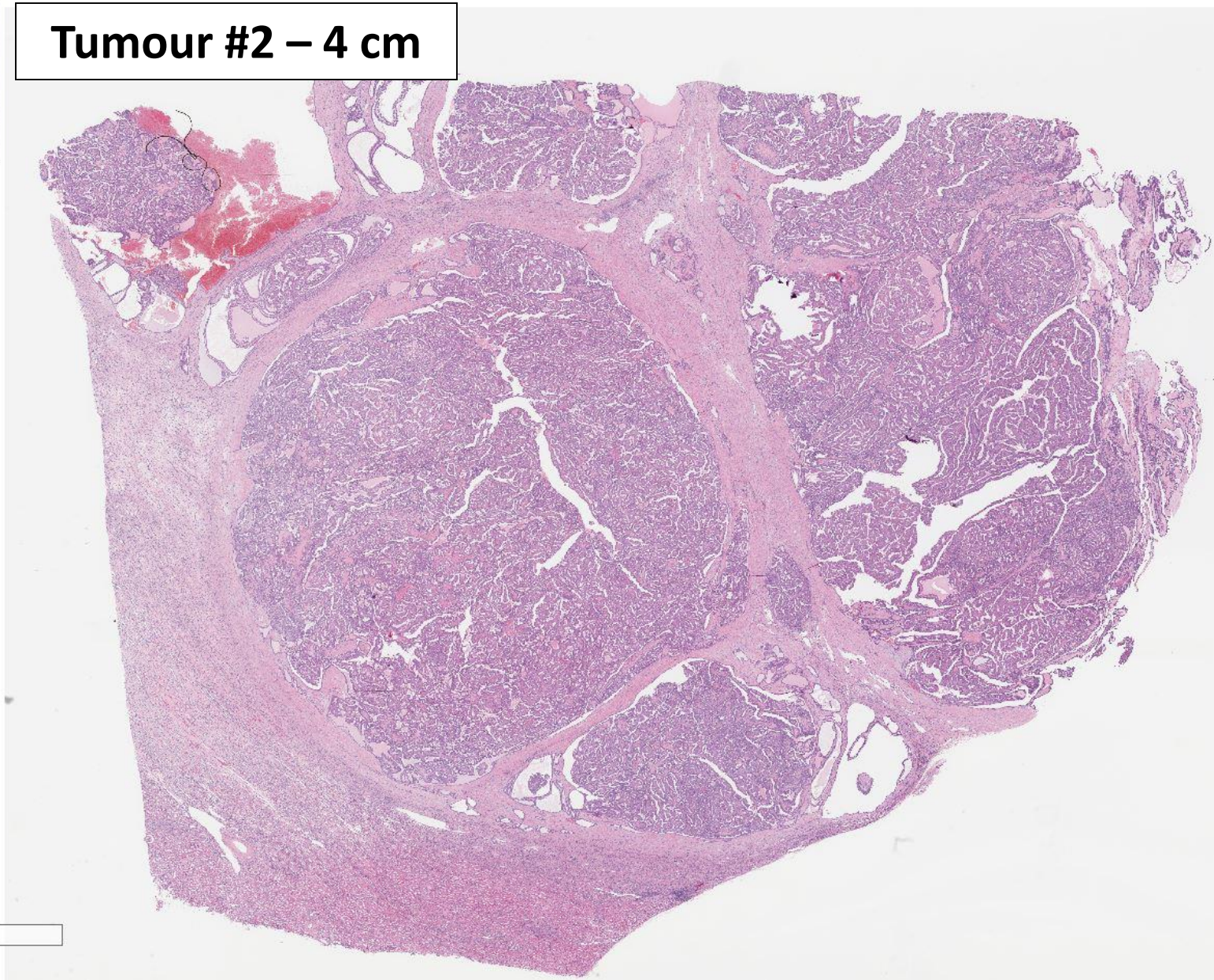
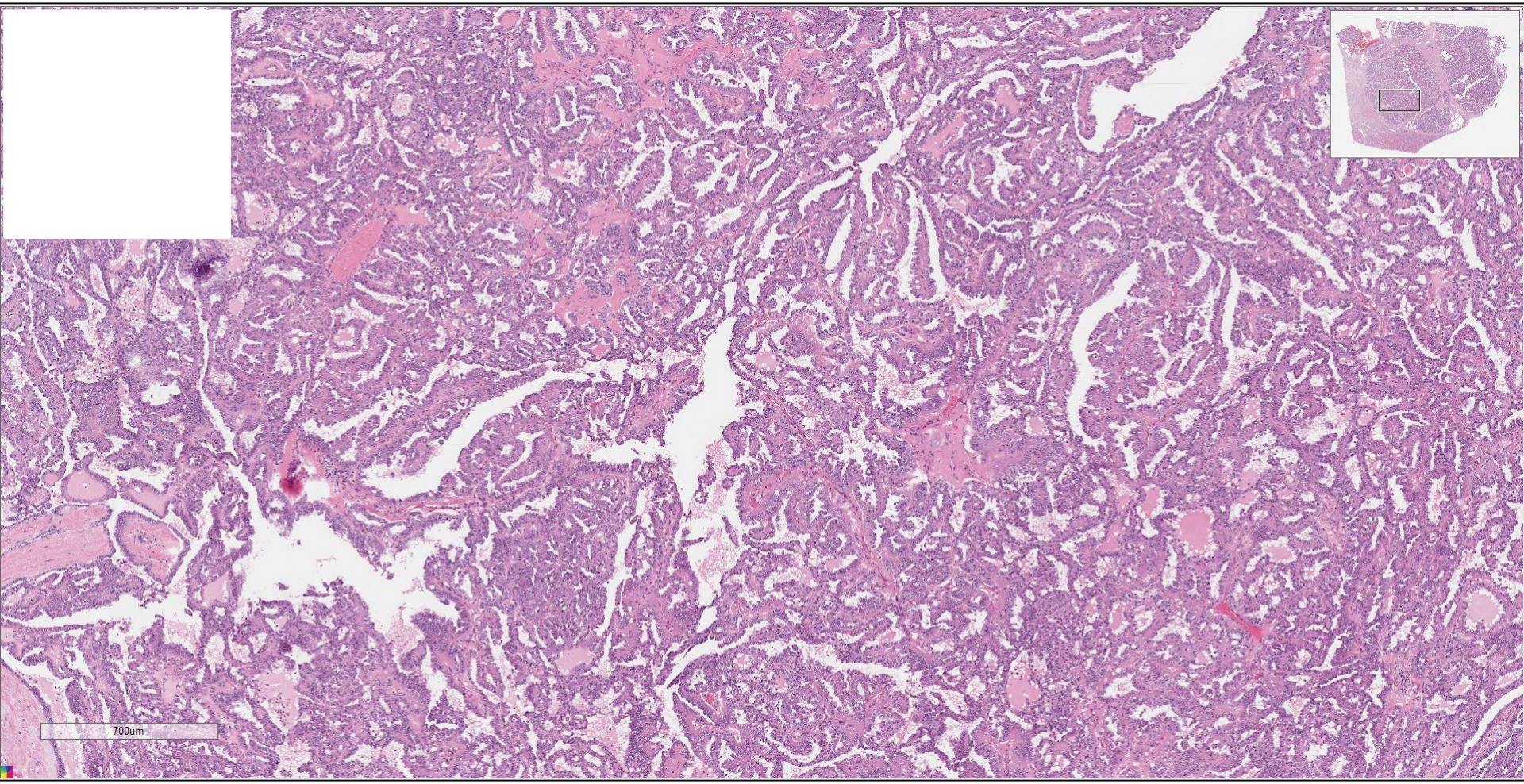
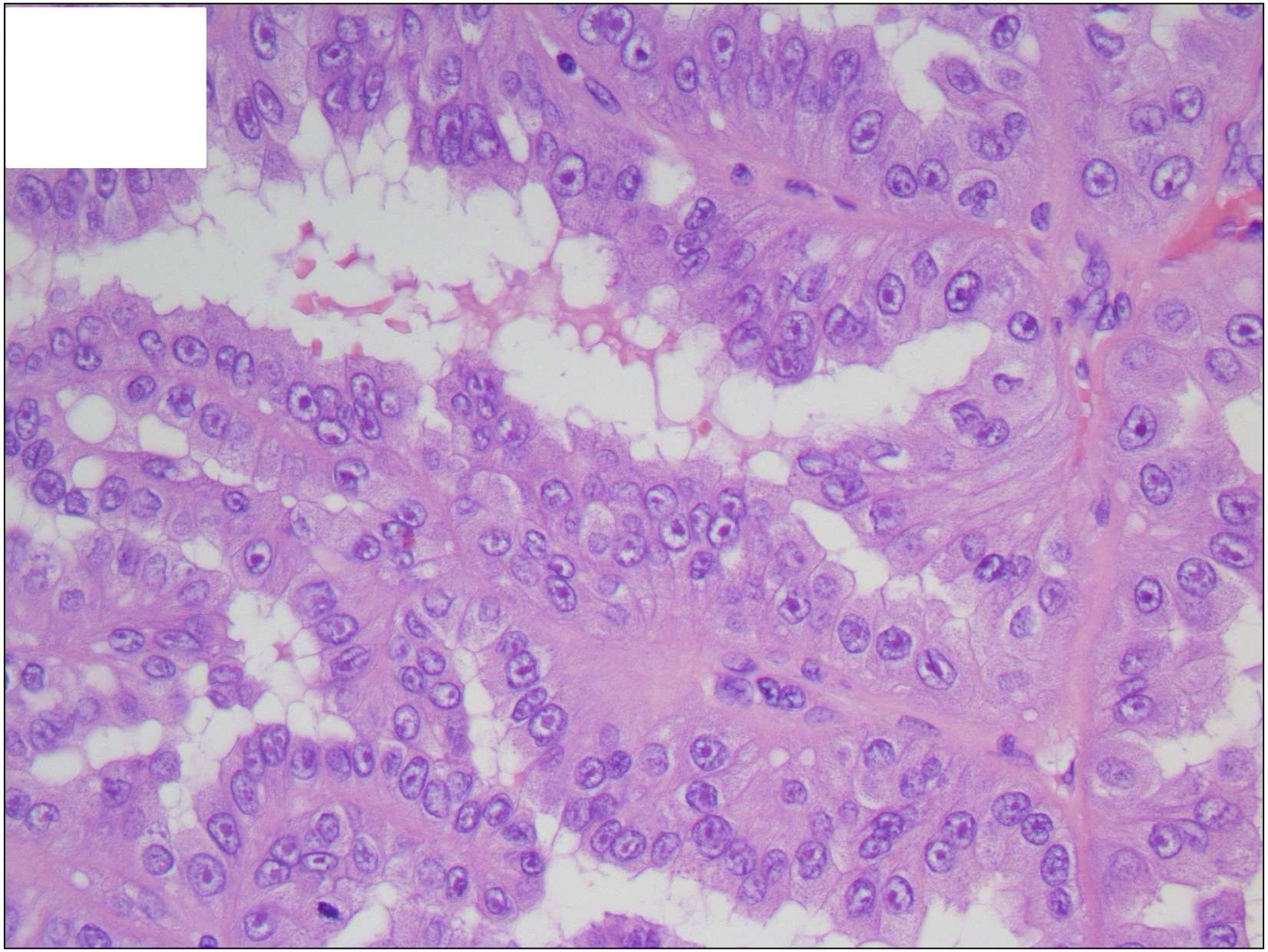


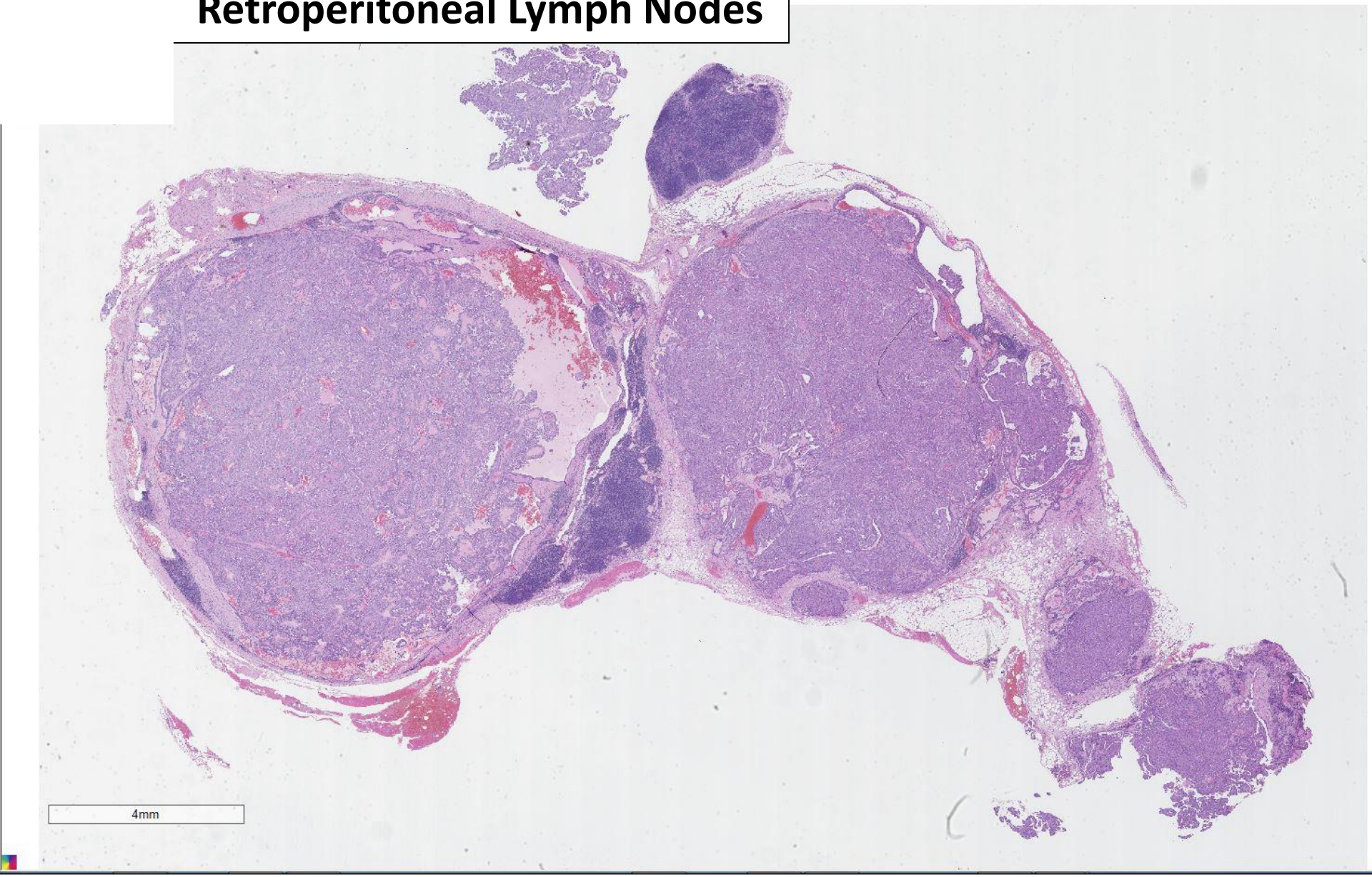
Tumour #2 – 4 cm

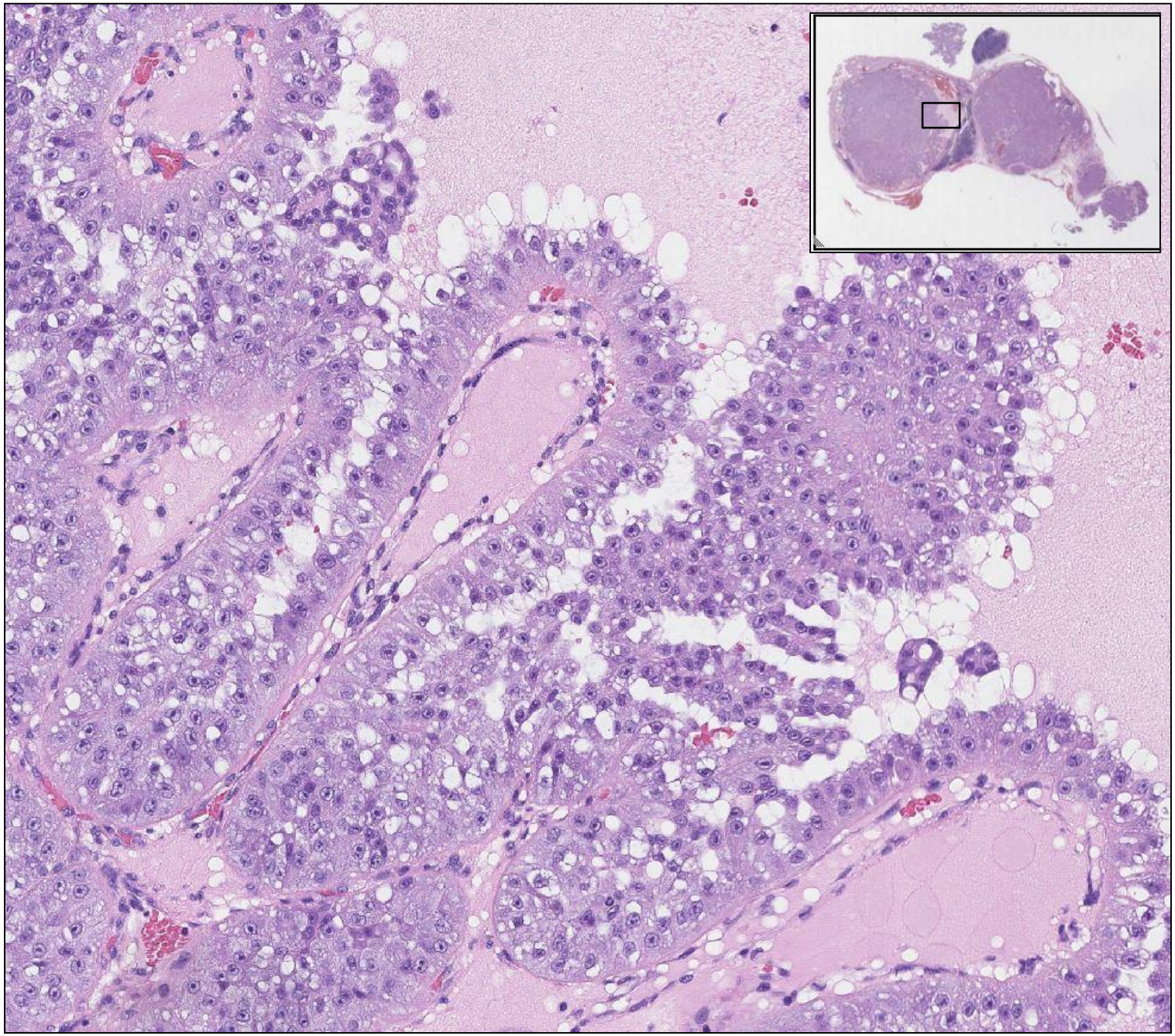



700um



Retroperitoneal Lymph Nodes





Immunohistochemistry

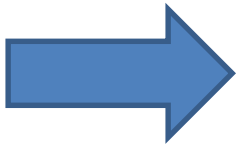
Positive

- AE1/AE3
- PAX8
- AMACR

Negative

- CK7 (completely negative)
- CD10
- HMWK (34βE12)

- *CAIX ?*
- *Fumarate hydratase?*
- *FH mutation?*
- *Other?*

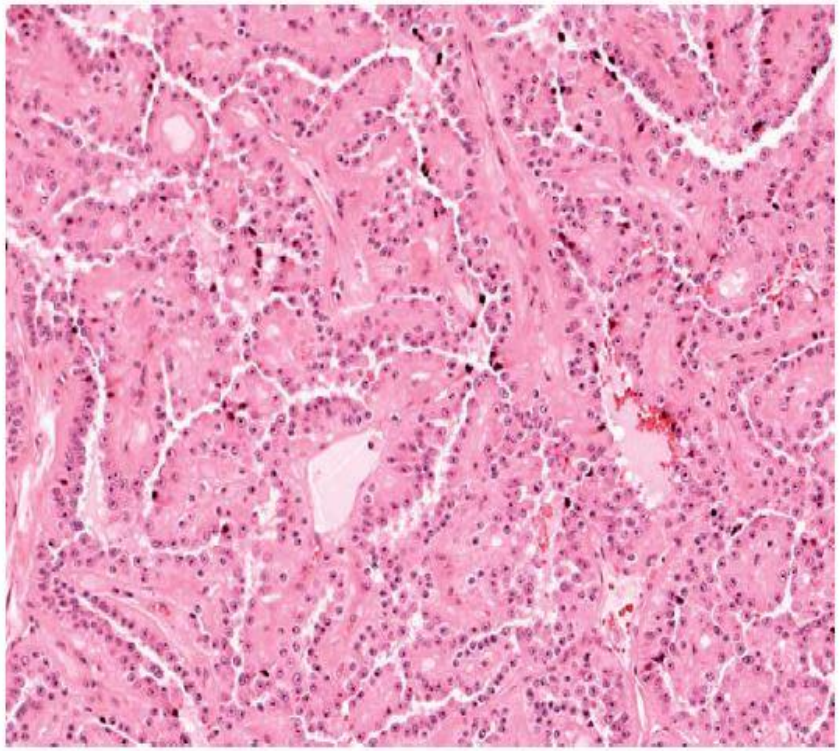


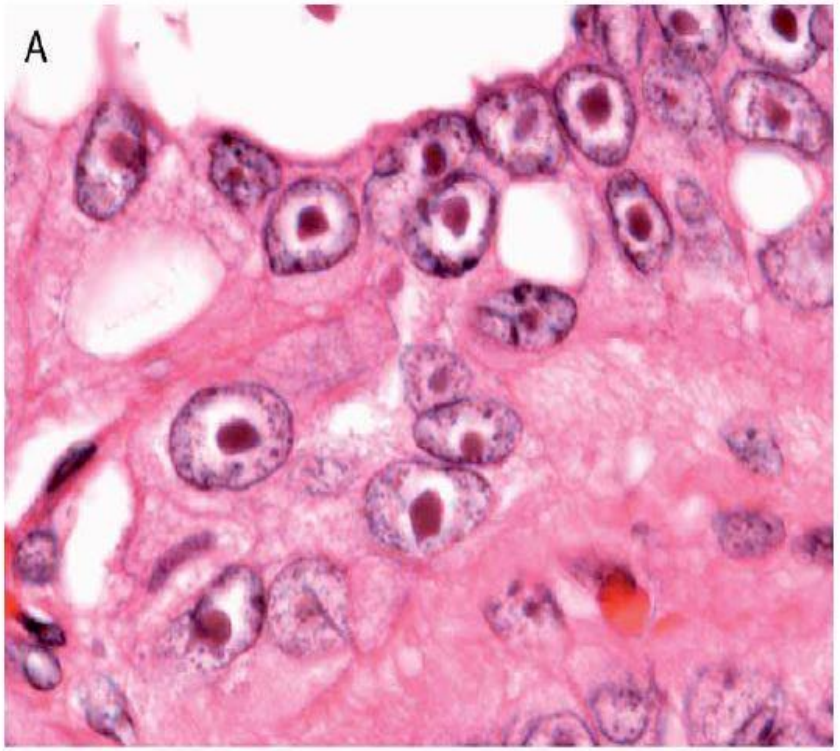
Case referred to NIH, Bethesda MD for molecular work-up

The Morphologic Spectrum of Kidney Tumors in Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC) Syndrome

Maria J. Merino, MD, Carlos Torres-Cabala, MD,* Peter Pinto, MD,†*
and William Marston Linehan, MD†

(*Am J Surg Pathol* 2007;31:1578–1585)





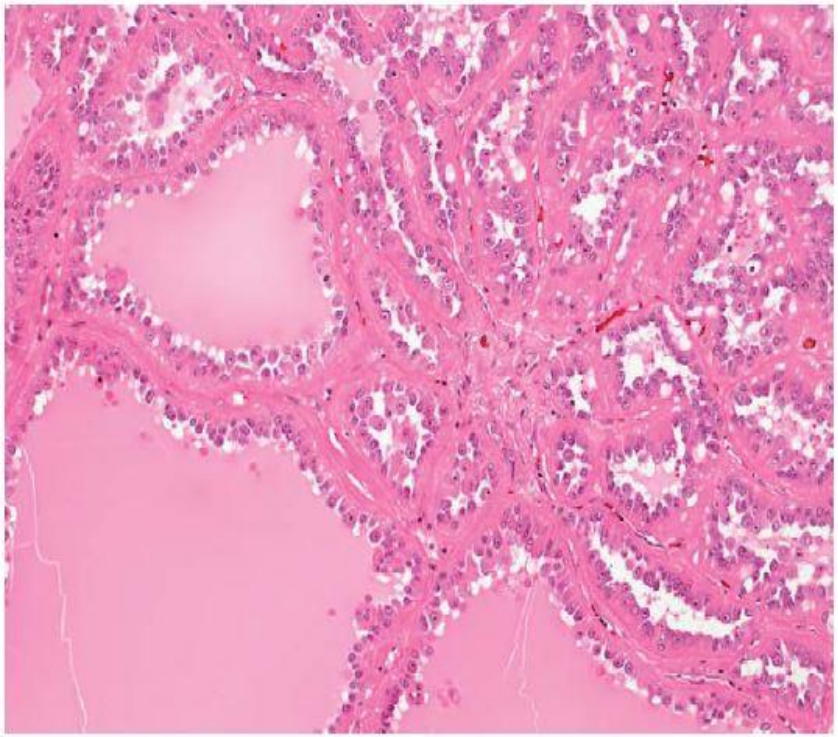


FIGURE 5. Oncocytic and cystic tumor. This case was diagnosed as an oncocytoma; however, the characteristic nuclear features of HLRCC were present (hematoxylin and eosin, 10×).

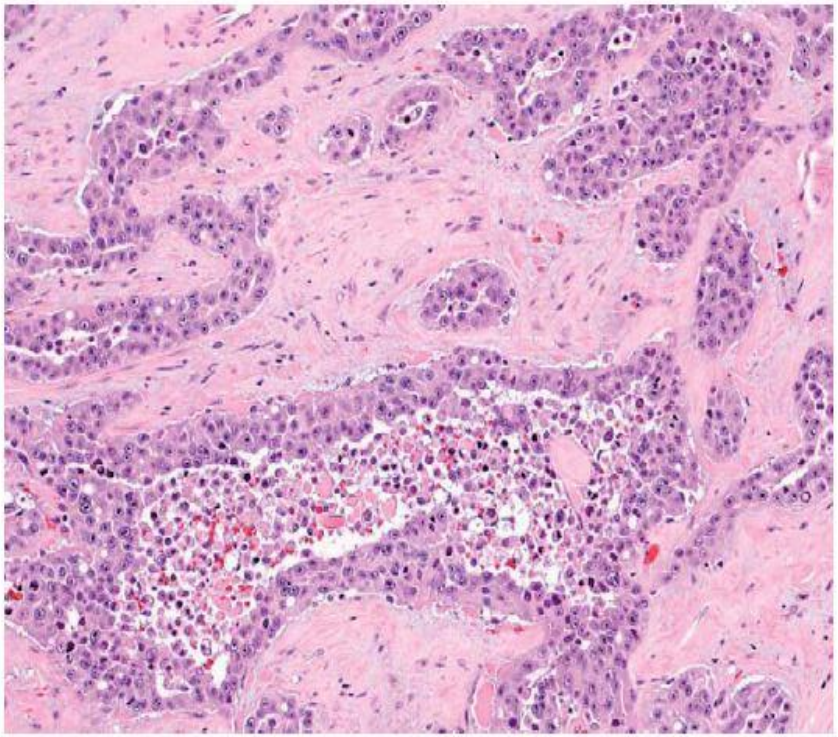


FIGURE 7. HLRCC tumor with desmoplastic reaction and a solid and tubular pattern (hematoxylin and eosin, 10×).

Broad morphologic spectrum

- can resemble oncocytoma!

TABLE 2. Architectural Patterns of HLRCC Kidney Tumors

	Papillary	Tubular	Tubulo-papillary	Solid	Mixed*	Total
No cystic component	15/40	0/40	0/40	0/40	4/40	19/40
With cystic areas†	8/40	2/40	5/40	1/40	0/40	16/40
Predominantly cystic†	2/40	0/40	3/40	0/40	0/40	5/40
Total	25/40	2/40	8/40	1/40	4/40	40/40
With desmoplastic reaction	0/40	0/40	1/40	1/40	0/40	2/40
With clear cells‡	3/40	0/40	1/40	1/40	0/40	5/40

*Any combination of the 4 main patterns.

†Defined as cystic component involving less than 50% ("with cystic areas") or more than 50% ("predominantly cystic") of the tumor.

‡Tumors showing focal clear cell change. One case (case 34) was originally classified as clear cell RCC.

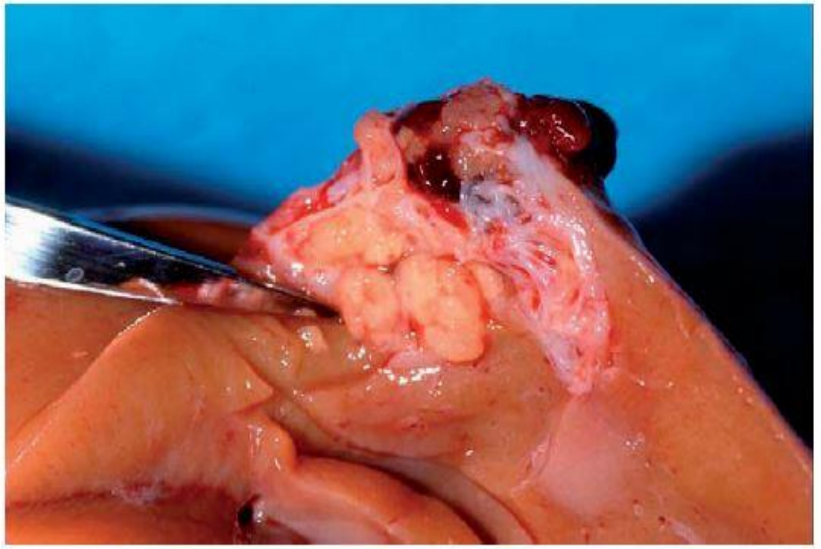


FIGURE 1. Gross photograph of a renal tumor with cystic and solid areas. Although the tumor was small in size, it had penetrated the capsule and there were metastases in adjacent lymph nodes.

High stage with metastases

- even if small in size

WHO classification of tumours of the kidney

Renal cell tumours	
Clear cell renal cell carcinoma	8310/3
Multilocular cystic renal neoplasm of low malignant potential	8316/1*
Papillary renal cell carcinoma	8260/3
Hereditary leiomyomatosis and renal cell carcinoma–associated renal cell carcinoma	8311/3*
Chromophobe renal cell carcinoma	8317/3
Collecting duct carcinoma	8319/3
Renal medullary carcinoma	8510/3*
MiT family translocation renal cell carcinomas	8311/3*
Succinate dehydrogenase–deficient renal carcinoma	8311/3
Mucinous tubular and spindle cell carcinoma	8480/3*
Tubulocystic renal cell carcinoma	8316/3*
Acquired cystic disease–associated renal cell carcinoma	8316/3
Clear cell papillary renal cell carcinoma	8323/1
Renal cell carcinoma, unclassified	8312/3
Papillary adenoma	8260/0
Oncocytoma	8290/0
Metanephric tumours	
Metanephric adenoma	8325/0
Metanephric adenofibroma	9013/0
Metanephric stromal tumour	8935/1
Nephroblastic and cystic tumours occurring mainly in children	
Nephrogenic rests	
Nephroblastoma	8960/3
Cystic partially differentiated nephroblastoma	8959/1
Paediatric cystic nephroma	8959/0
Mesenchymal tumours	
Mesenchymal tumours occurring mainly in children	
Clear cell sarcoma	8964/3
Rhabdoid tumour	8963/3
Congenital mesoblastic nephroma	8960/1
Ossifying renal tumour of infancy	8967/0
Mesenchymal tumours occurring mainly in adults	
Leiomyosarcoma	8890/3
Angiosarcoma	9120/3
Rhabdomyosarcoma	8900/3
Osteosarcoma	9180/3
Synovial sarcoma	9040/3
Ewing sarcoma	9364/3
Angiomyolipoma	8860/0
Epithelioid angiomyolipoma	8860/1*
Leiomyoma	8890/0
Haemangioma	9120/0
Lymphangioma	9170/0
Haemangioblastoma	9161/1
Juxtaglomerular cell tumour	8361/0
Renomedullary interstitial cell tumour	8966/0
Schwannoma	9560/0
Solitary fibrous tumour	8815/1
Mixed epithelial and stromal tumour family	
Cystic nephroma	8959/0
Mixed epithelial and stromal tumour	8959/0
Neuroendocrine tumours	
Well-differentiated neuroendocrine tumour	8240/3
Large cell neuroendocrine carcinoma	8013/3
Small cell neuroendocrine carcinoma	8041/3
Phaeochromocytoma	8700/0
Miscellaneous tumours	
Renal haematopoietic neoplasms	
Germ cell tumours	
Metastatic tumours	

The morphology codes are from the International Classification of Diseases for Oncology (ICD-O) [917A]. Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours. The classification is modified from the previous WHO classification [756A], taking into account changes in our understanding of these lesions.
*New code approved by the IARC/WHO Committee for ICD-O.

Fig. 1 – World Health Organization (WHO) classification of tumours of the kidney. Reproduced with permission from the WHO International Agency for Research on Cancer [1].
WHO = World Health Organization.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Comprehensive Molecular Characterization of Papillary Renal-Cell Carcinoma

The Cancer Genome Atlas Research Network*

N ENGL J MED 374;2 NEJM.ORG JANUARY 14, 2016

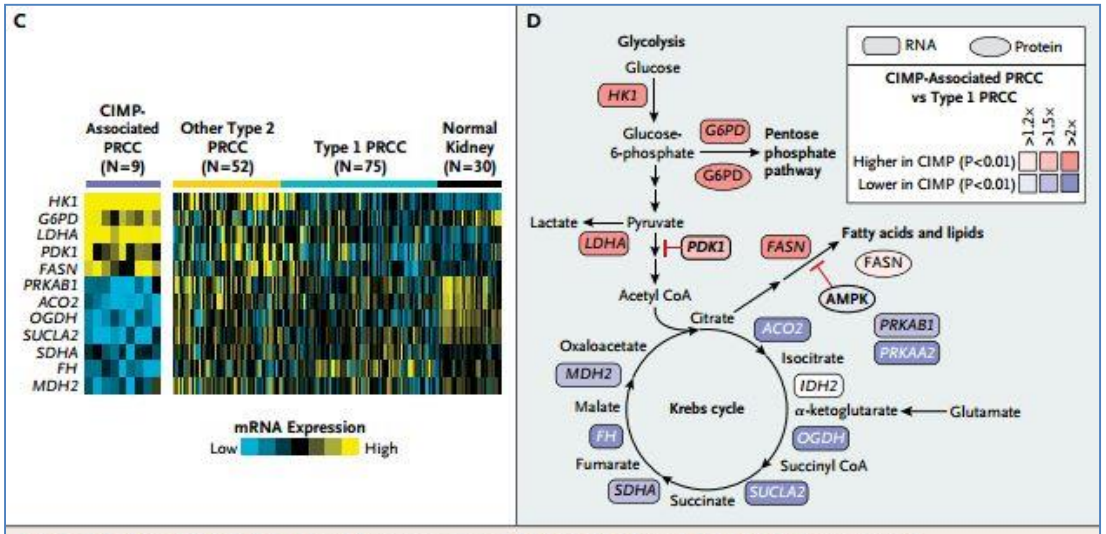


Figure 3. A Subgroup of Papillary Renal-Cell Carcinoma That Manifests a CpG Island Methylator Phenotype (CIMP).

As depicted in Panel A, molecular subtyping by means of a DNA methylation platform revealed three subtypes of papillary renal-cell carcinoma (PRCC), one of which showed widespread DNA hypermethylation patterns characteristic of CIMP-associated tumors (the other subtypes are identified as cluster 1 and cluster 2). Corresponding data tracks highlight molecular features associated with CIMP tumors (nine cases), including *CDKN2A* silencing, germline or somatic mutations of *FH*, type 2 histologic status, and expression of both cell-cycle–related genes[23] and hypoxia-related genes.[24] Panel B shows differences in patient age and overall survival among the three subtypes. Data on survival were not available for two patients in the cluster 2 group. Panel C shows differential messenger RNA (mRNA) expression patterns for key genes involved in metabolism among CIMP-associated PRCC, type 1 PRCC, non–CIMP-associated type 2 PRCC, and normal kidney. Panel D shows differential expression patterns of CIMP-associated tumors versus type 1 tumors in metabolism-related pathways, with a focus on gene-expression and protein-expression patterns previously associated with Warburg-like effects in kidney cancer.[21] P values were calculated with the use of a t-test.

Type 2 Papillary RCC with CpG Island Methylator Phenotype (CIMP)

- CDKN2A
- ***Somatic FH mutations***
- Cell cycle-related genes
- Hypoxia-related genes

- *Poor survival*

Case 2

32 year-old male, 4.0 cm left renal mass, partial nephrectomy

Renal Tumours with Oncocytic/Eosinophilic Cytoplasm

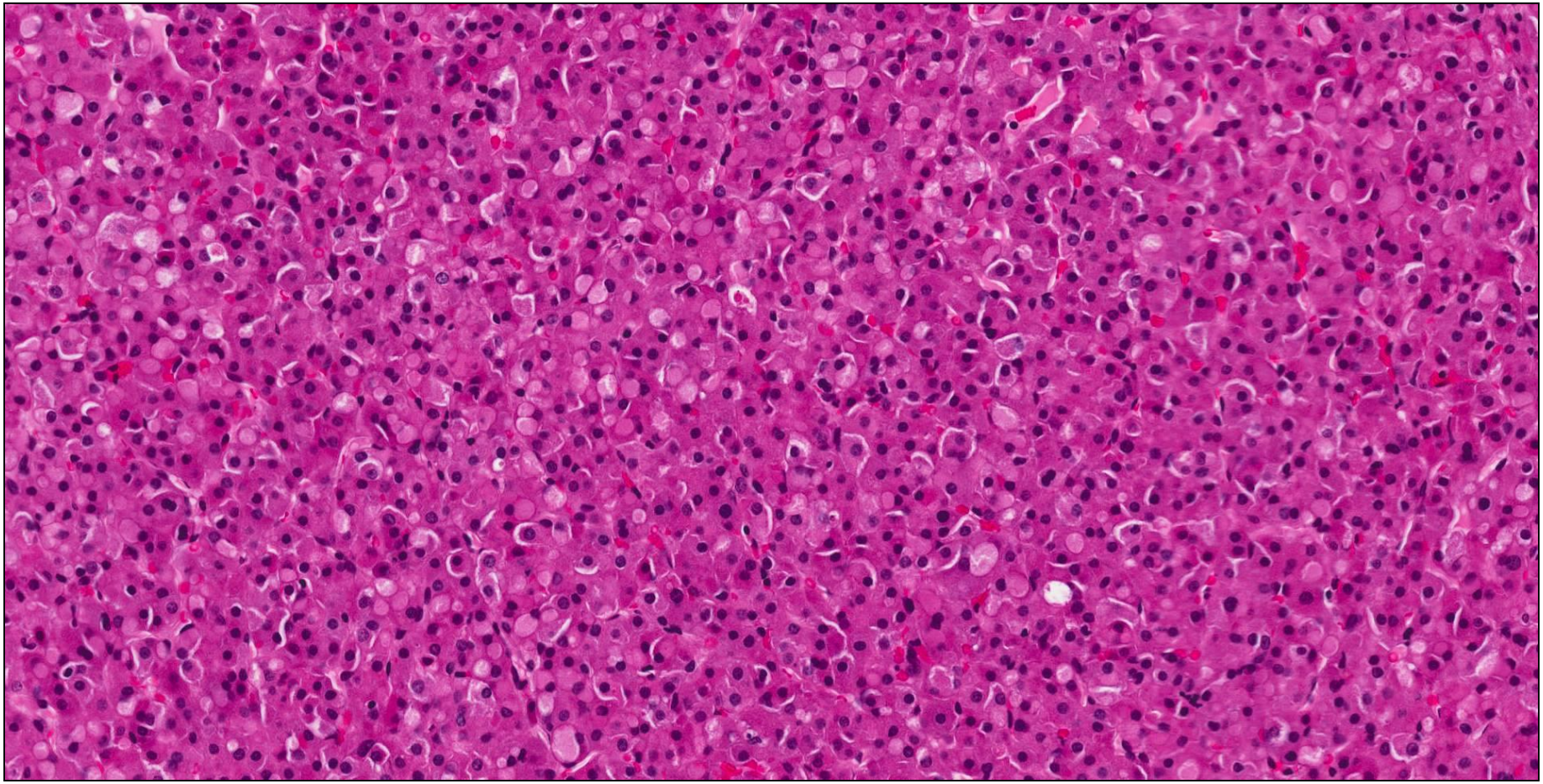
Table 2 – Tumours characterized by cells with oncocytic or eosinophilic cytoplasm.

Oncocytoma
Chromophobe renal cell carcinoma, eosinophilc variant
Hybrid oncocytic-chromophobe tumours
Clear cell renal cell carcinoma with eosinophilic cytoplasm (usually high grade)
Papillary renal cell carcinoma with oncocytic features
Papillary renal cell carcinoma, Type 2
Tubulocystic renal cell carcinoma
Follicular thyroid-like carcinoma
Acquired cystic kidney disease associated renal cell carcinoma
Renal tumours associated with SDH-B mutations
Epithelioid angiomyolipoma
MiTF family translocation renal cell carcinoma
Renal cell carcinoma of any histologic type with rhabdoid features

Usual Issue

Expanded Differential Diagnosis

SDH-Deficient Renal Cell Carcinoma



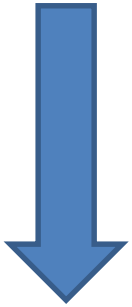
Immunohistochemistry

Positive

- PAX8
- CK7 (very rare, < 5%)
- AE1/AE3 (30% - most are weak positive/negative)

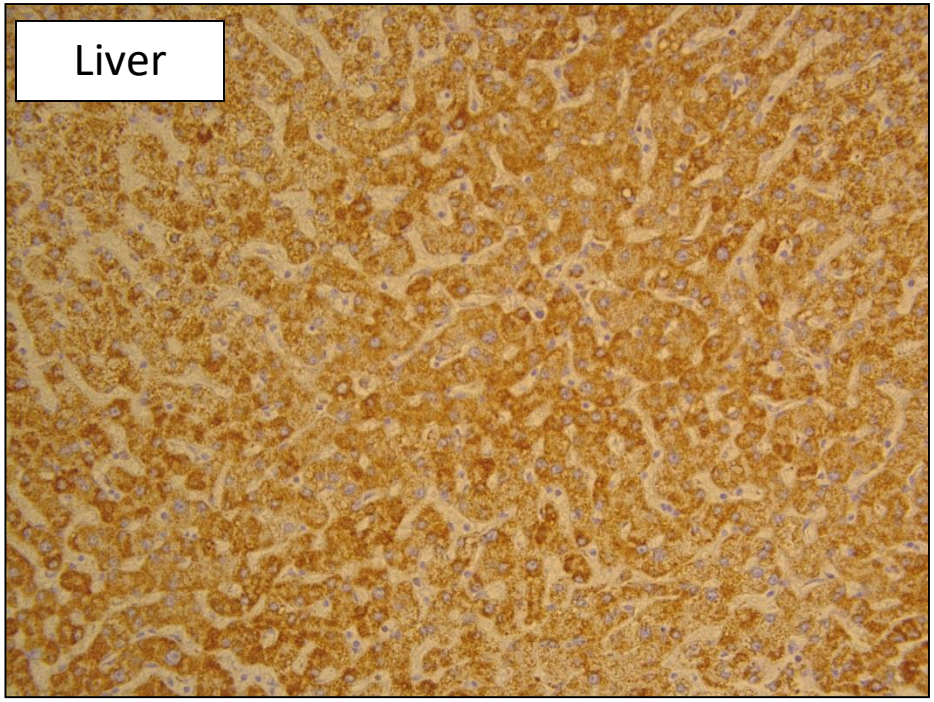
Negative

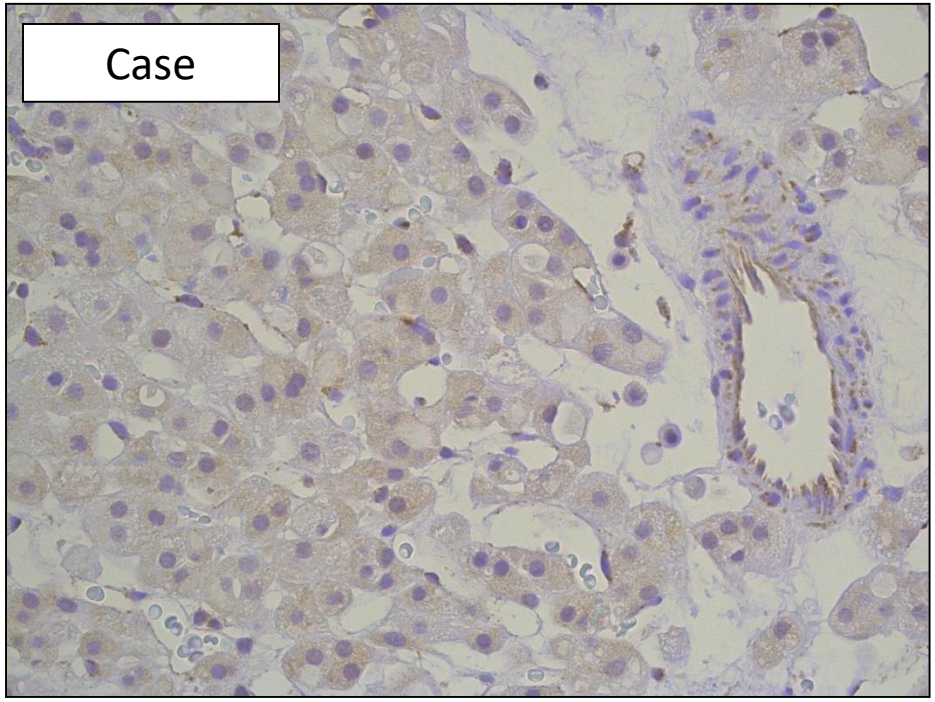
- CD117 (scattered mast cells are positive)
- SDH-B

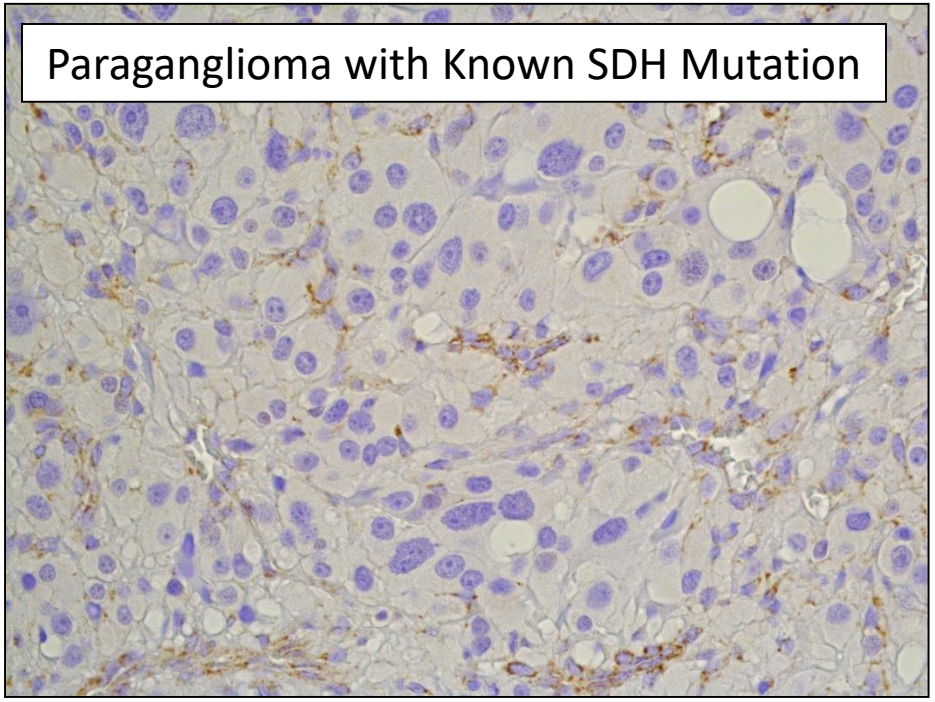


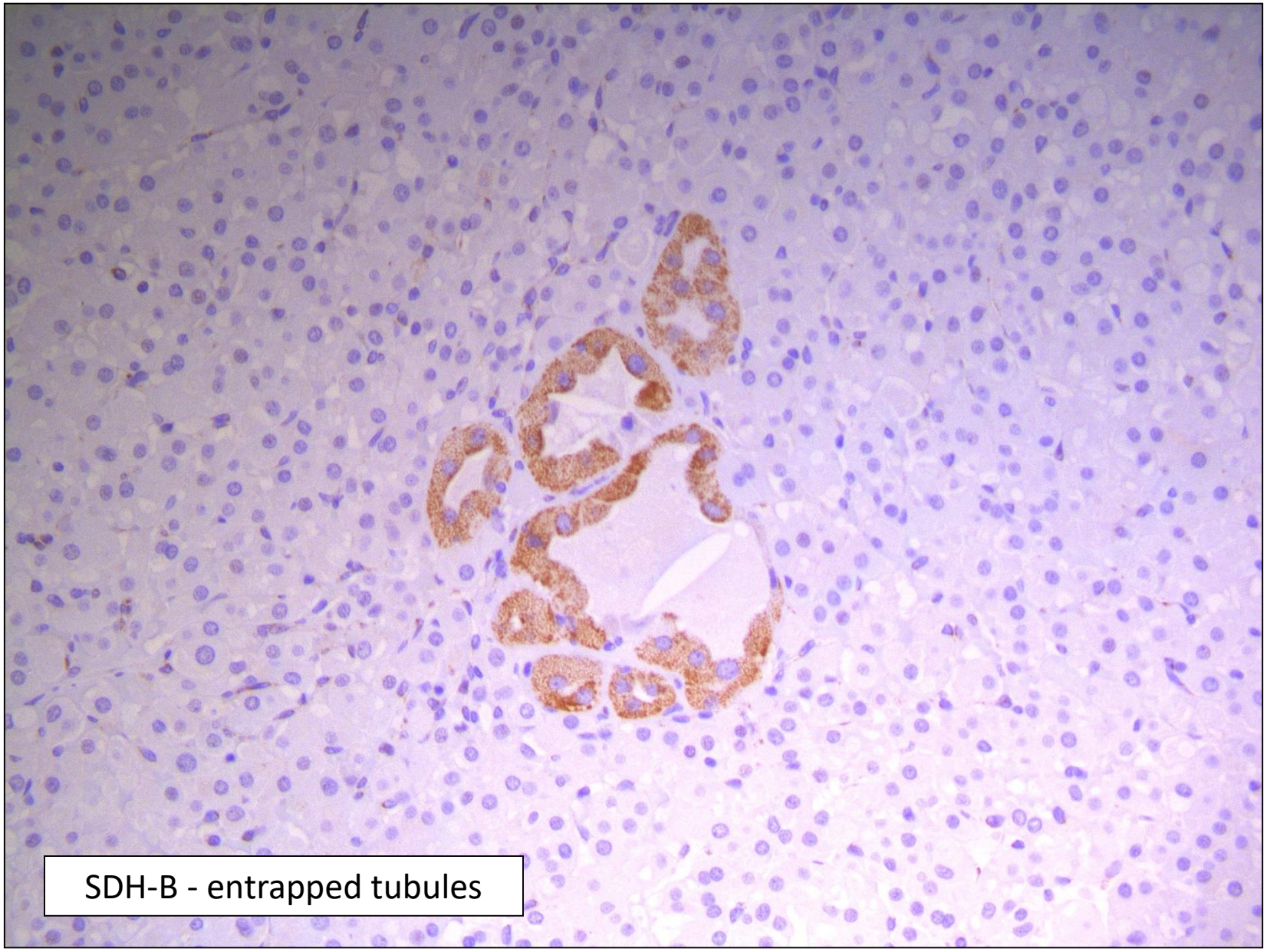
Refer for germline mutation testing for SDH-B, SDH-C, SDH-D or SDH-A

SDH-B Immunohistochemistry








SDH-B - entrapped tubules

The International Society of Urological Pathology (ISUP) Vancouver Classification of Renal Neoplasia

John R. Srigley, MD, Brett Delahunt, MD,† John N. Eble, MD,‡ Lars Egevad, MD, PhD,§ Jonathan I. Epstein, MD,‖ David Grignon, MD,‡ Ondrej Hes, MD, PhD,¶ Holger Moch, MD,# Rodolfo Montironi, MD,** Satish K. Tickoo, MD,†† Ming Zhou, MD, PhD,‡‡ Pedram Argani, MD,§§ and The ISUP Renal Tumor Panel*

(*Am J Surg Pathol* 2013;37:1469–1489)

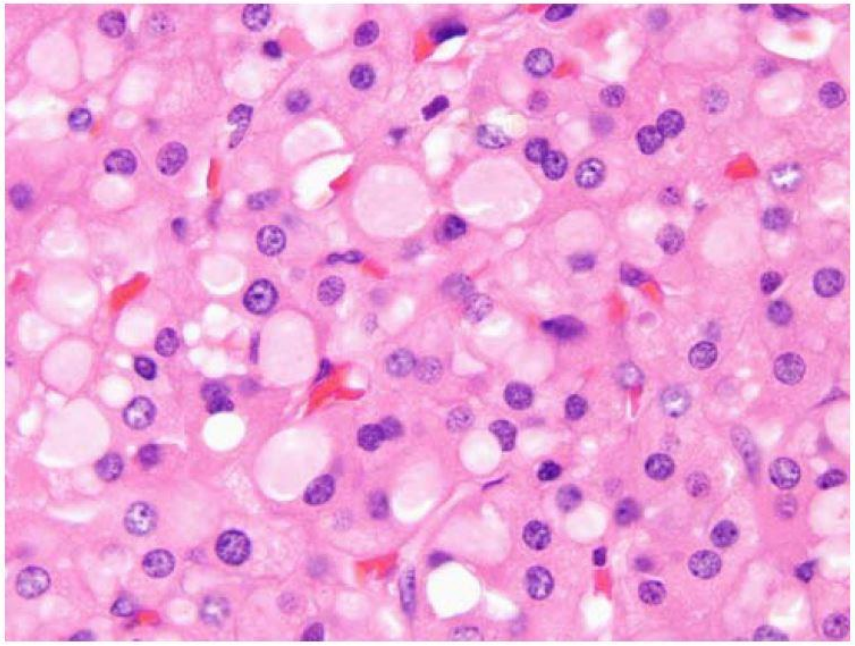


FIGURE 7. SDHB RCC. Note compact nests of eosinophilic polygonal cells with vacuolated cytoplasm. Distinctive pale eosinophilic cytoplasmic inclusions are present.

SDH-Deficient Renal Cell Carcinoma

- Most SDHB RCC follow an indolent course
- Rare cases with sarcomatoid change and/or metastases

- Other SDH-deficient neoplasms
  - paraganglioma/pheochromocytoma
  - GIST
  - pituitary adenoma

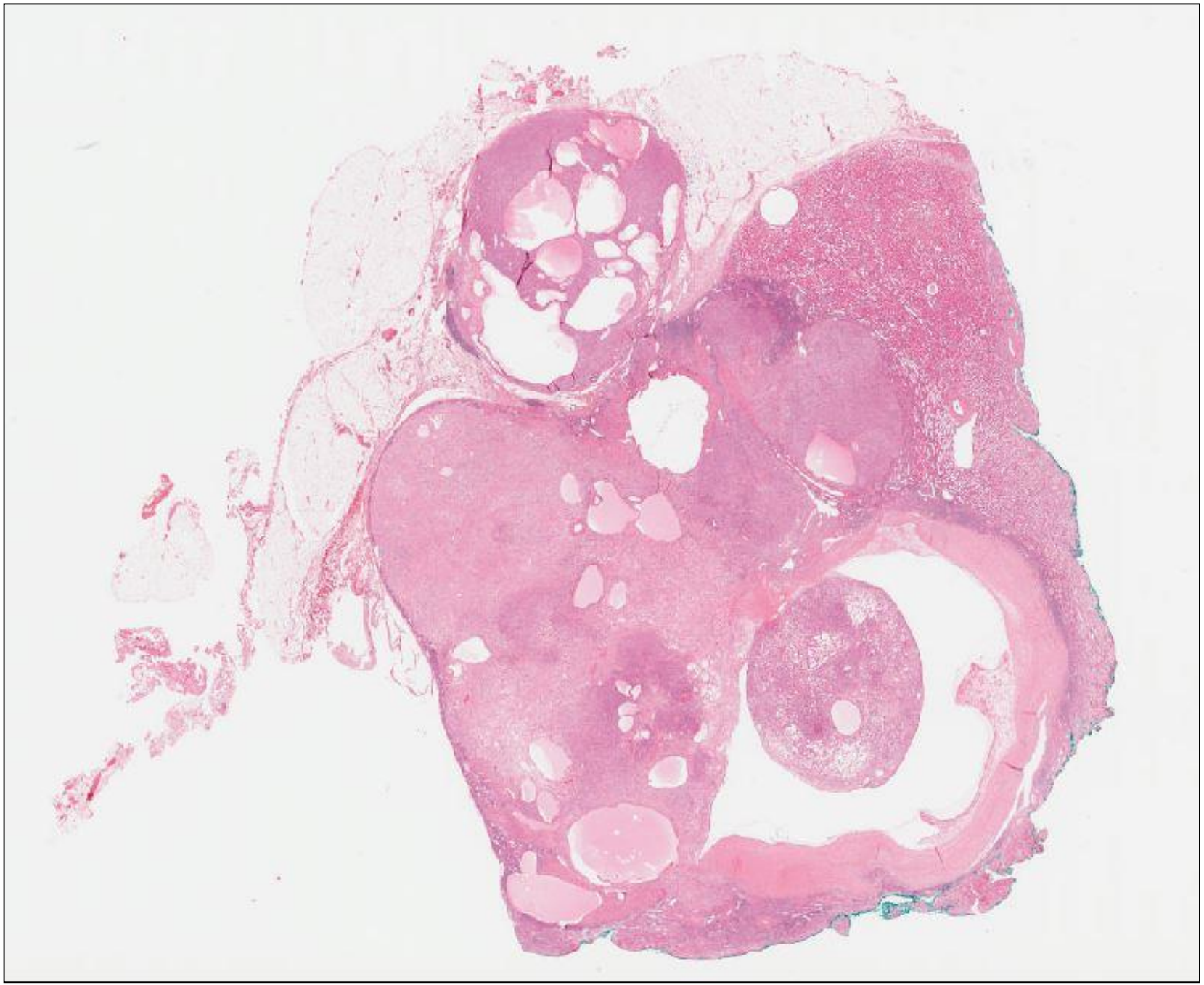
Case 3

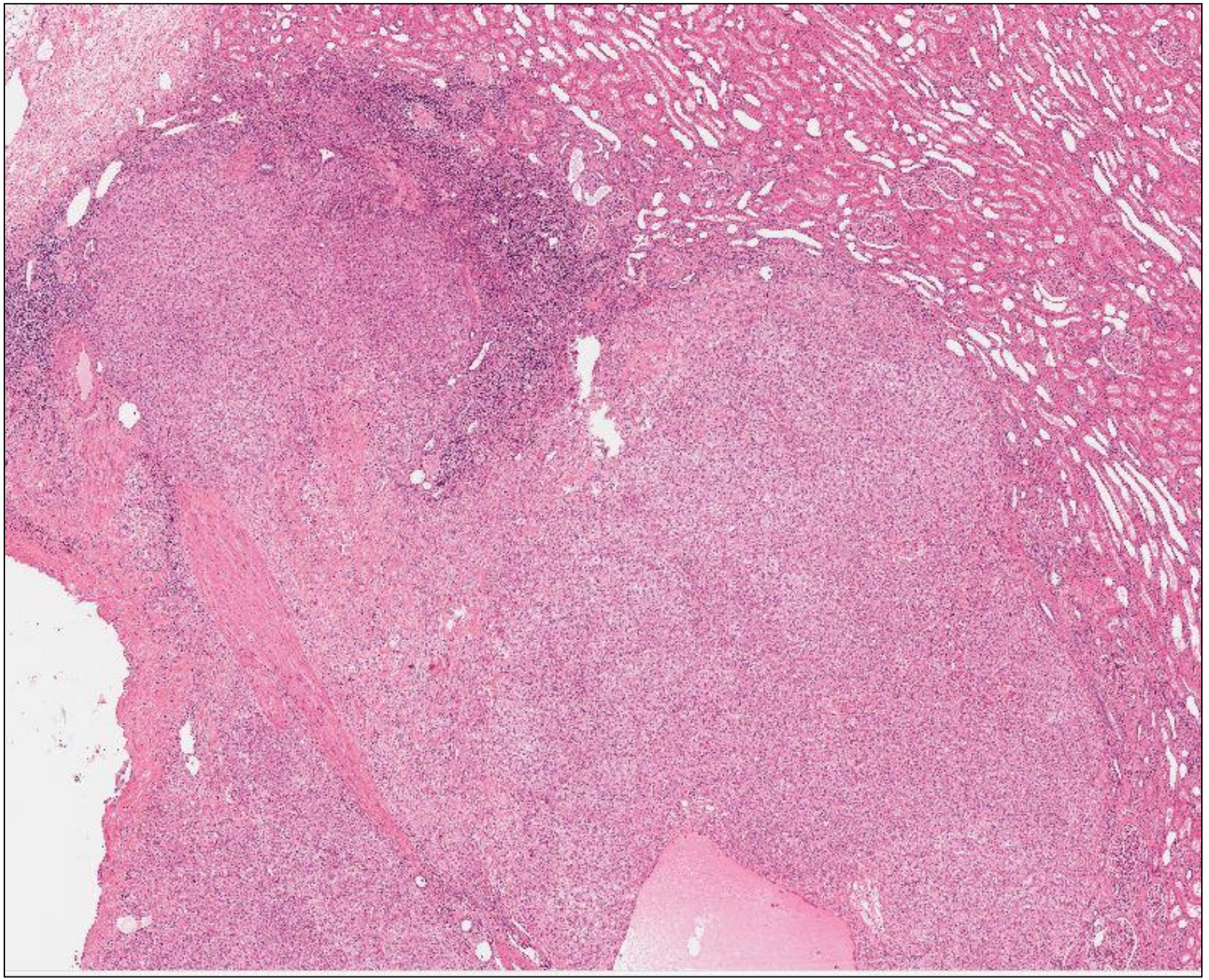
53 year-old female, 2.9 cm incidentally found right renal mass, partial nephrectomy

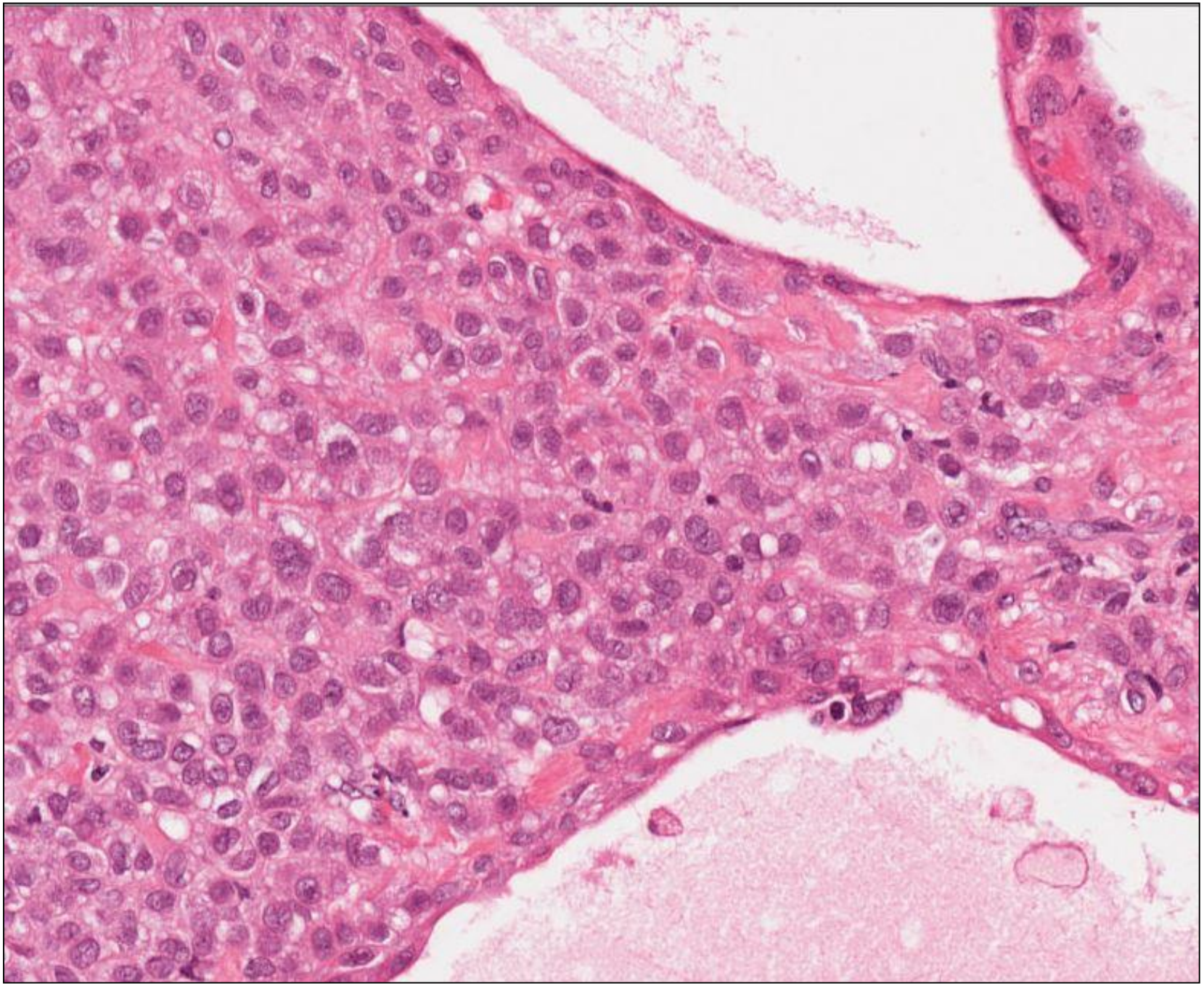
(*History of severe hypertension*)

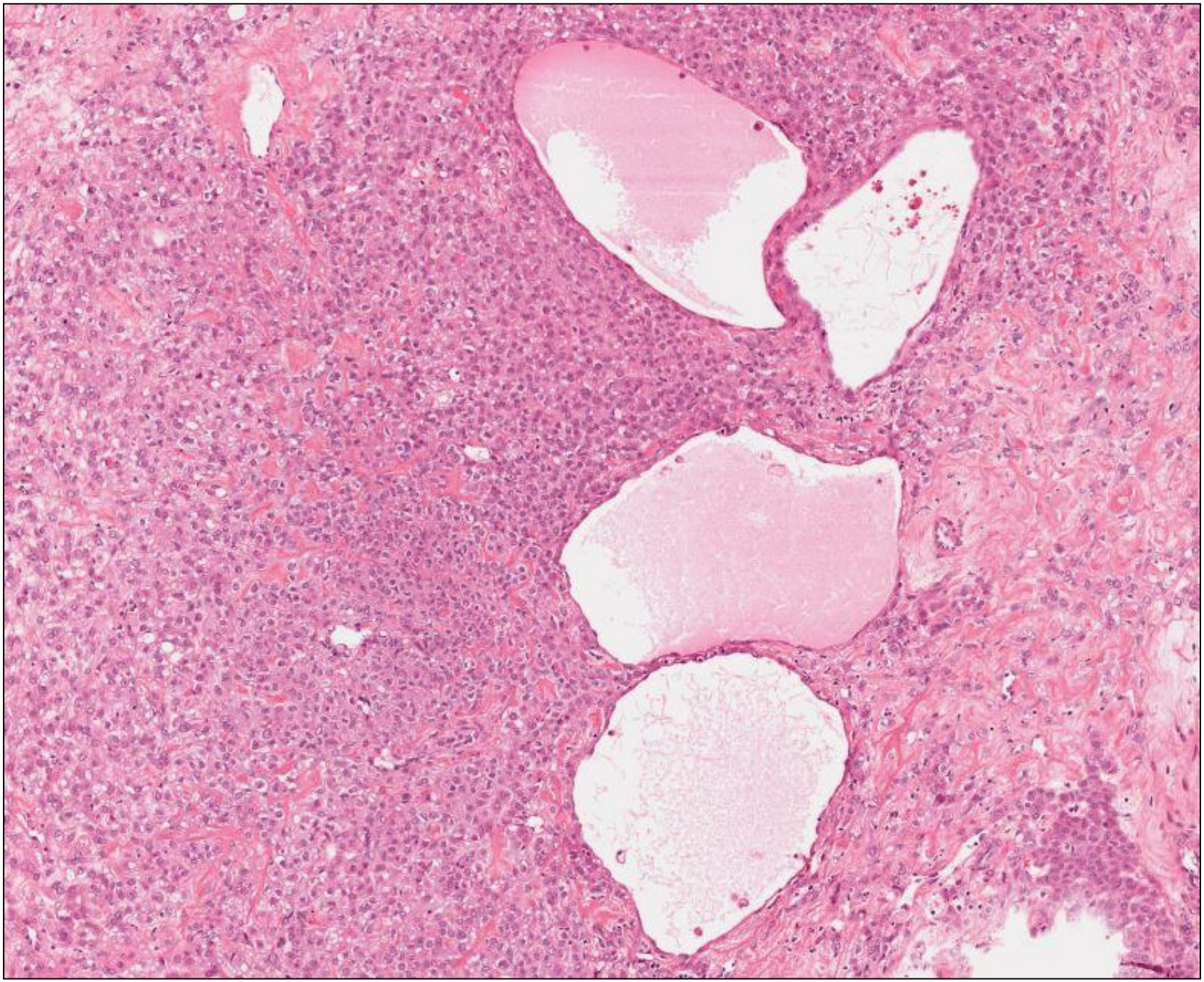
Gross Description

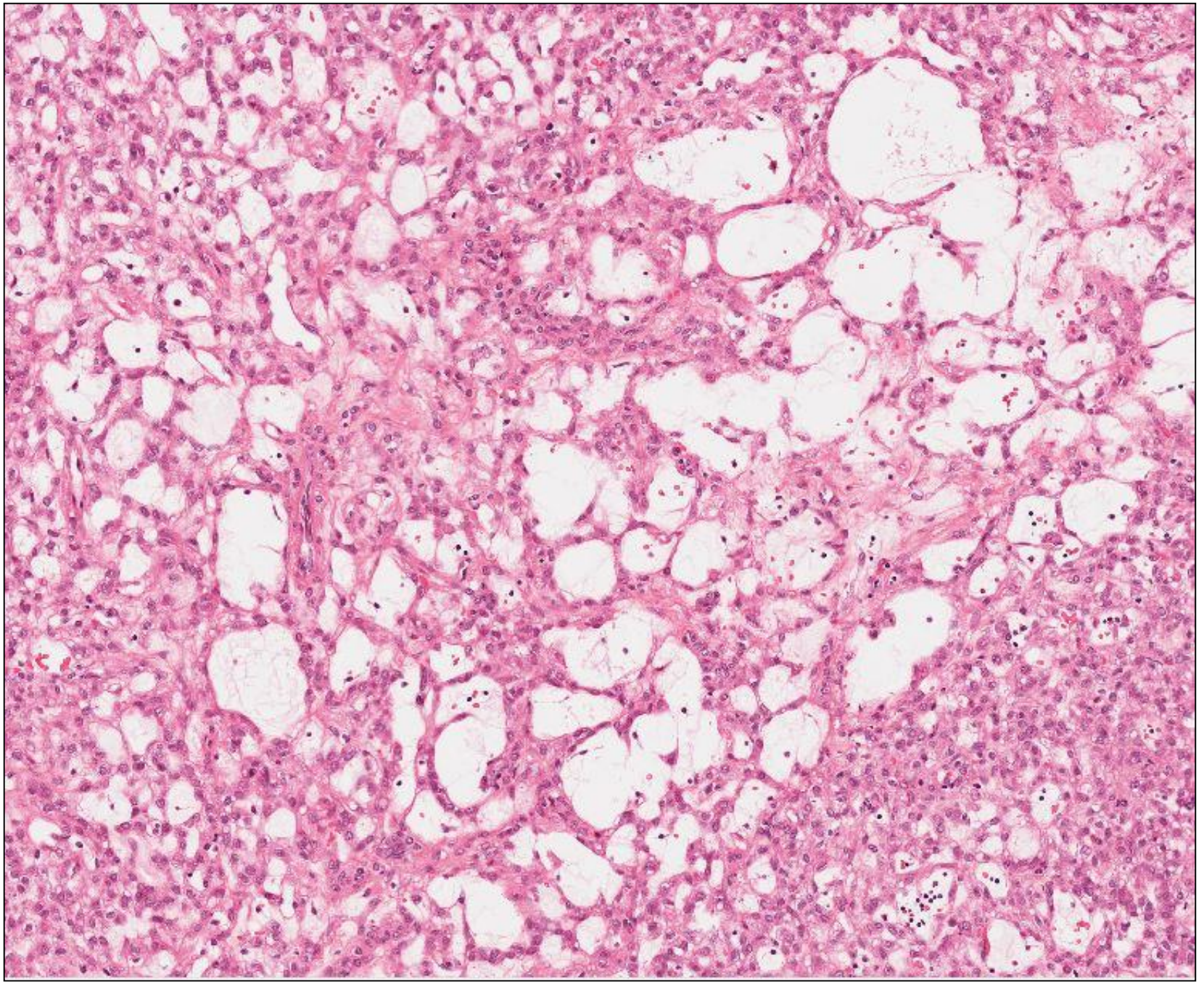
- Partial nephrectomy specimen including perinephric fat
- 2.9 cm well-defined, lobulated, pale-tan mass
- Solid and cystic areas with focal hemorrhage
  - cysts containing clear serous fluid
  - solid areas of variable consistency - firm and soft/edematous
- Tumour grossly confined to the kidney - focally exophytic forming a pushing border with perinephric fat

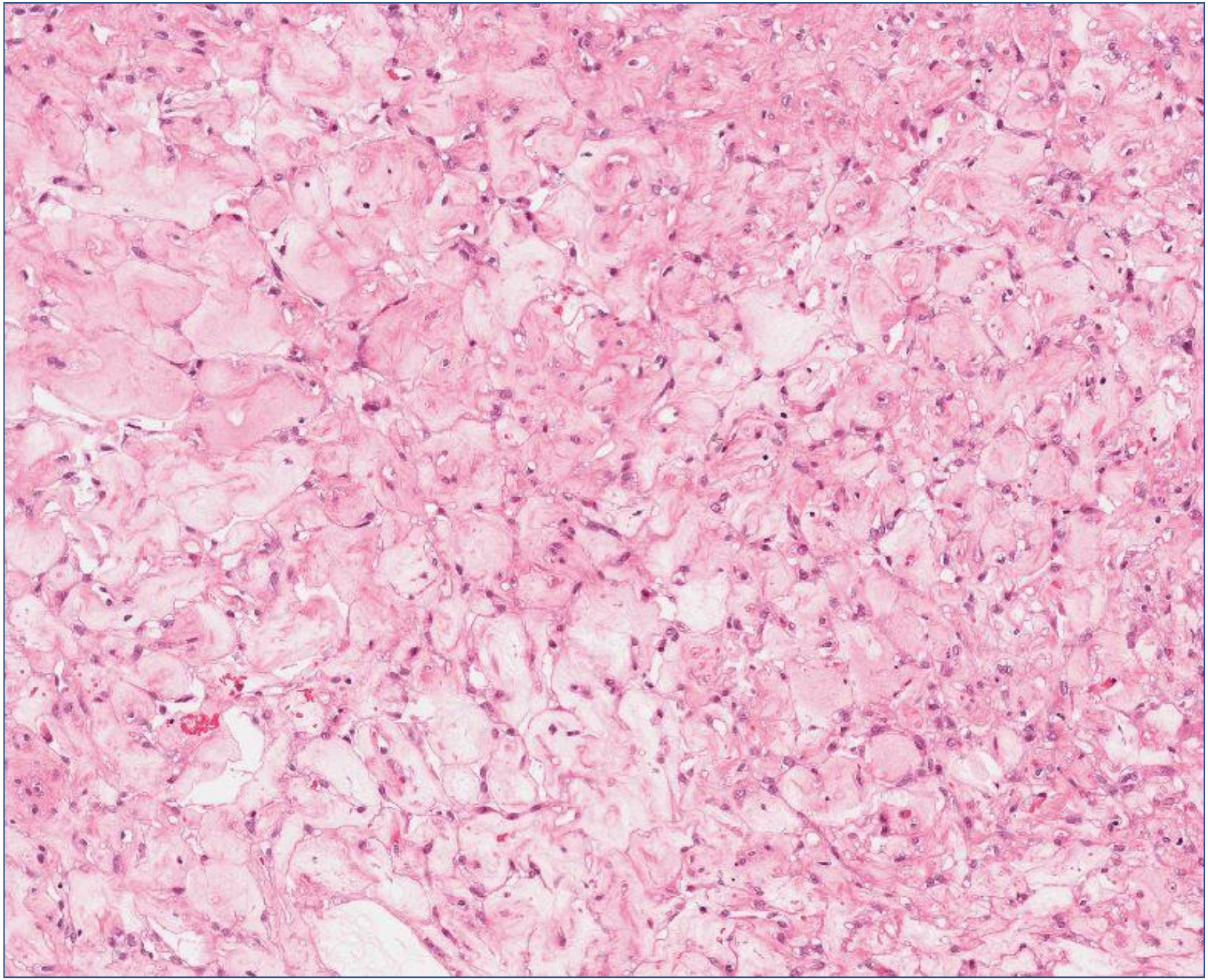


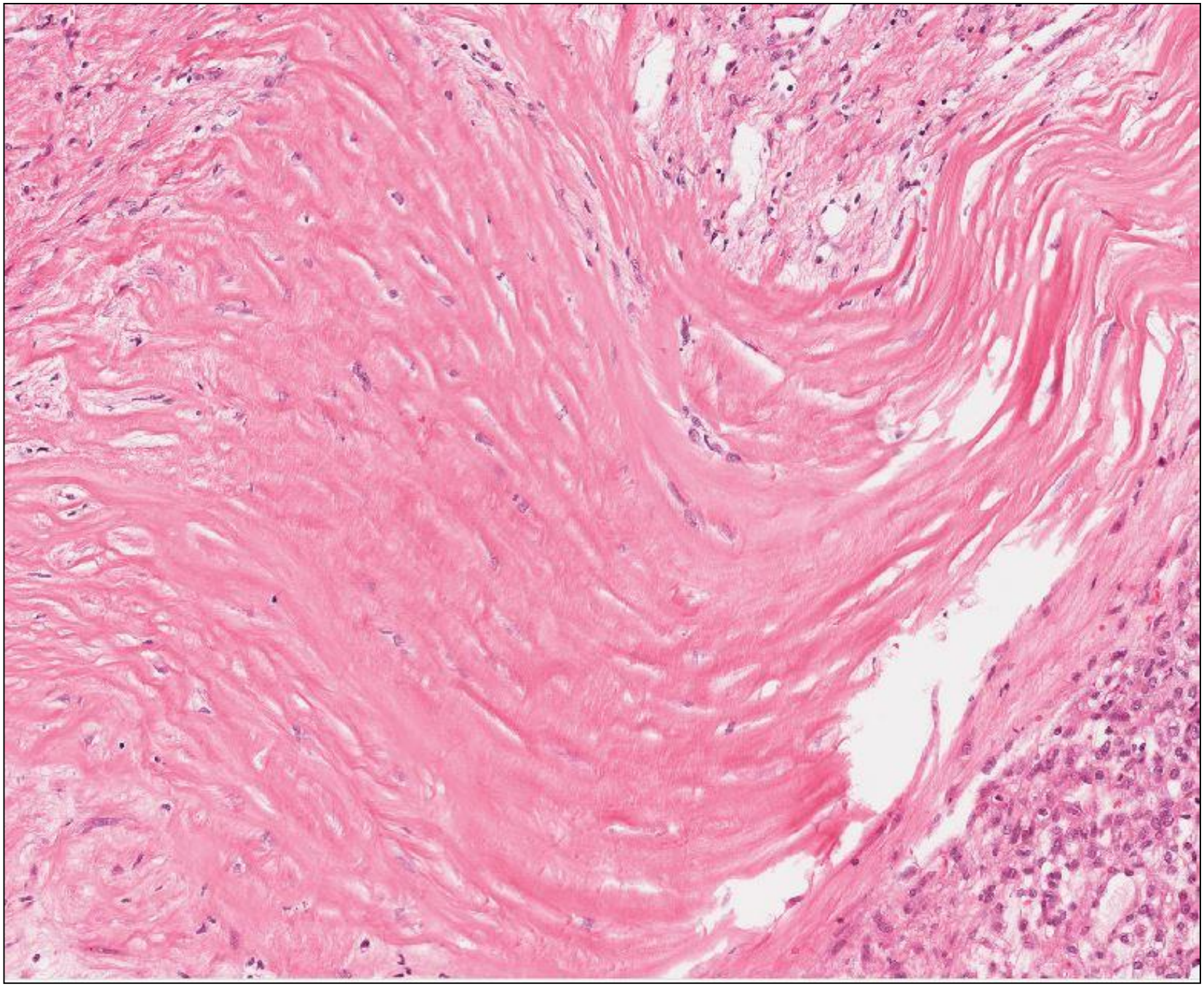


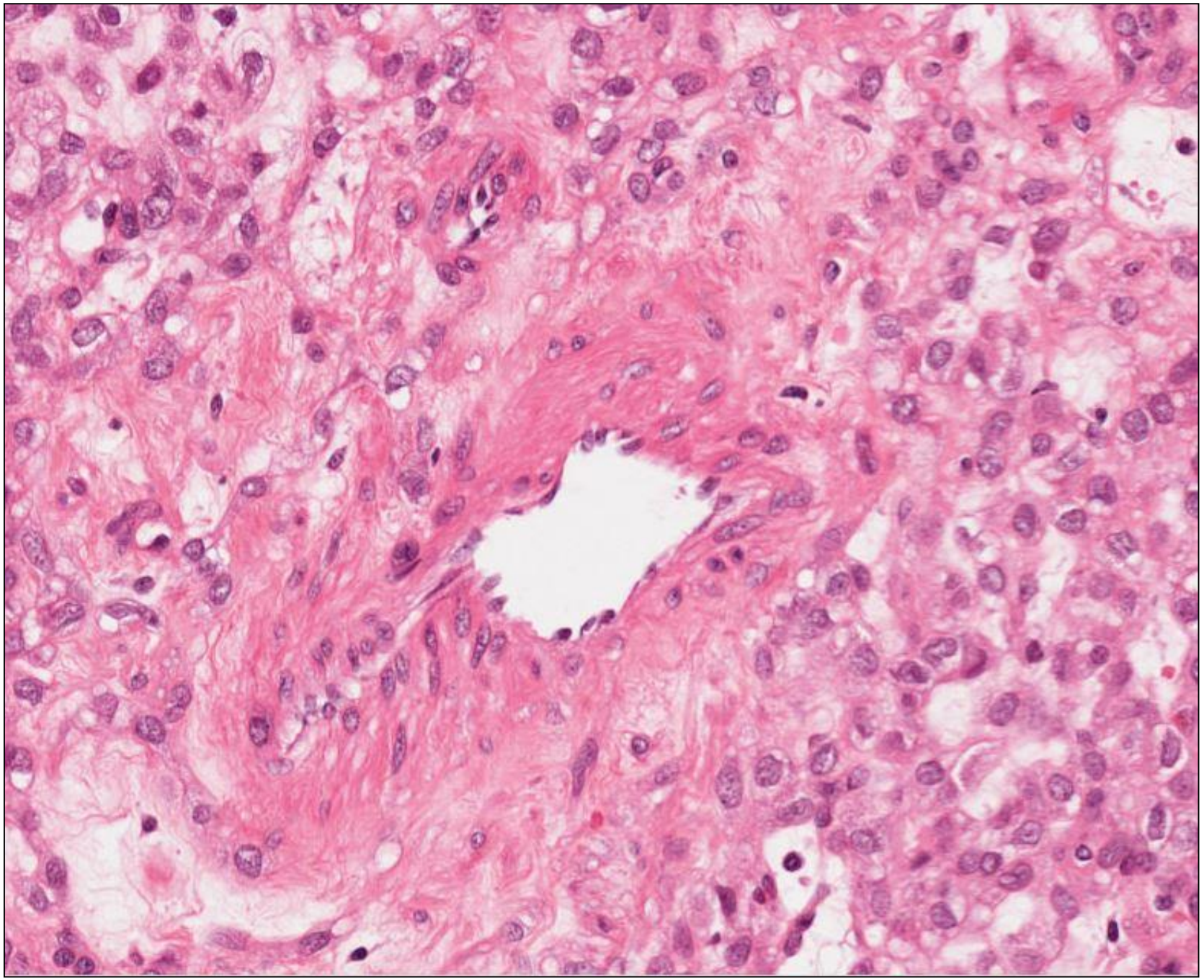


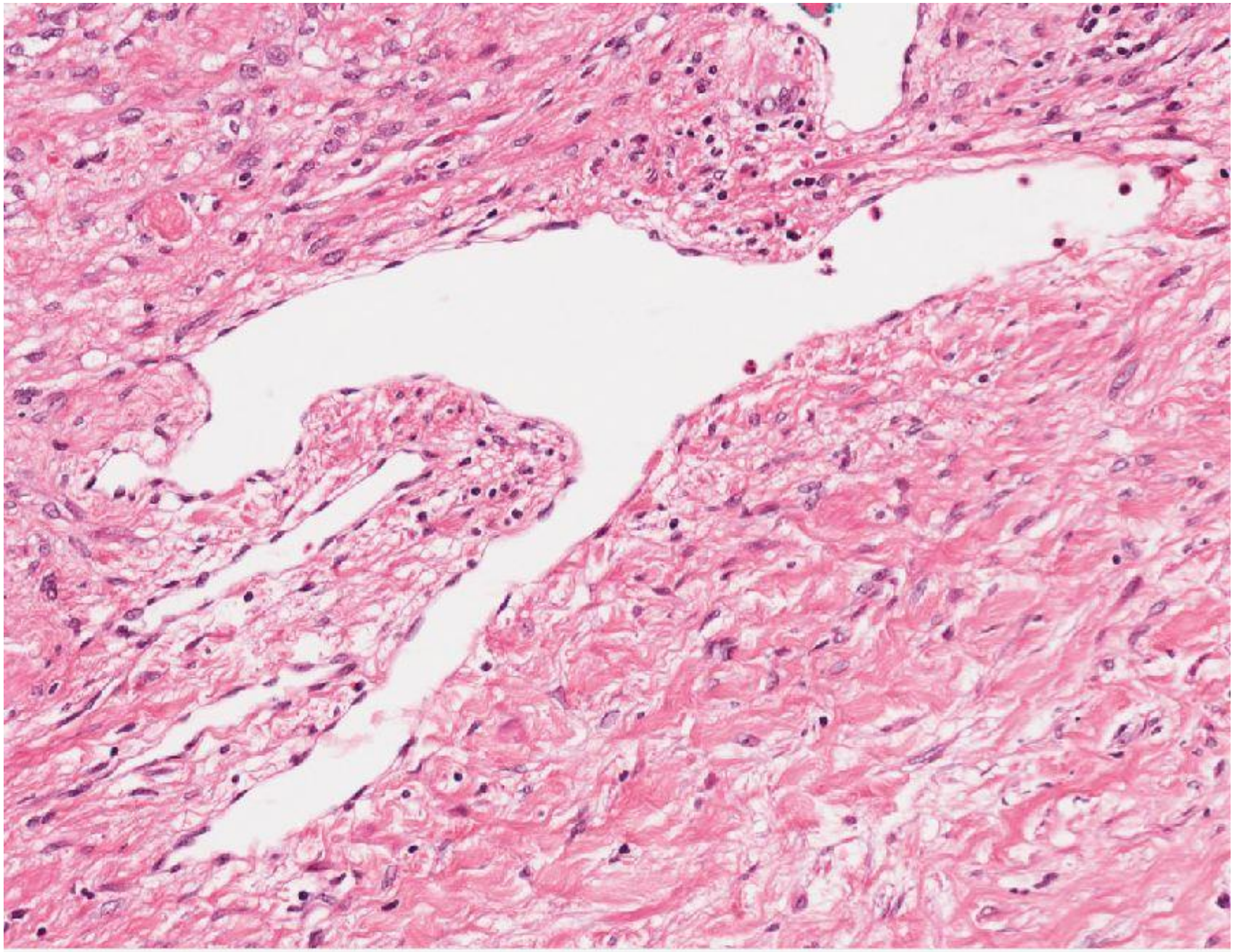












Summary of H&E Morphology

- Multinodular mass forming a well-demarcated border with the adjacent kidney
- Polygonal uniform cells with pale eosinophilic cytoplasm - no mitotic activity
- Solid growth, cystic and microcystic areas along with areas of densely hyalinized stroma
- Scattered branching epithelium-lined tubular structures
- Aggregates of blood vessels within the tumour
  - thick-walled
  - thin-walled and gaping/branching, focally staghorn in shape

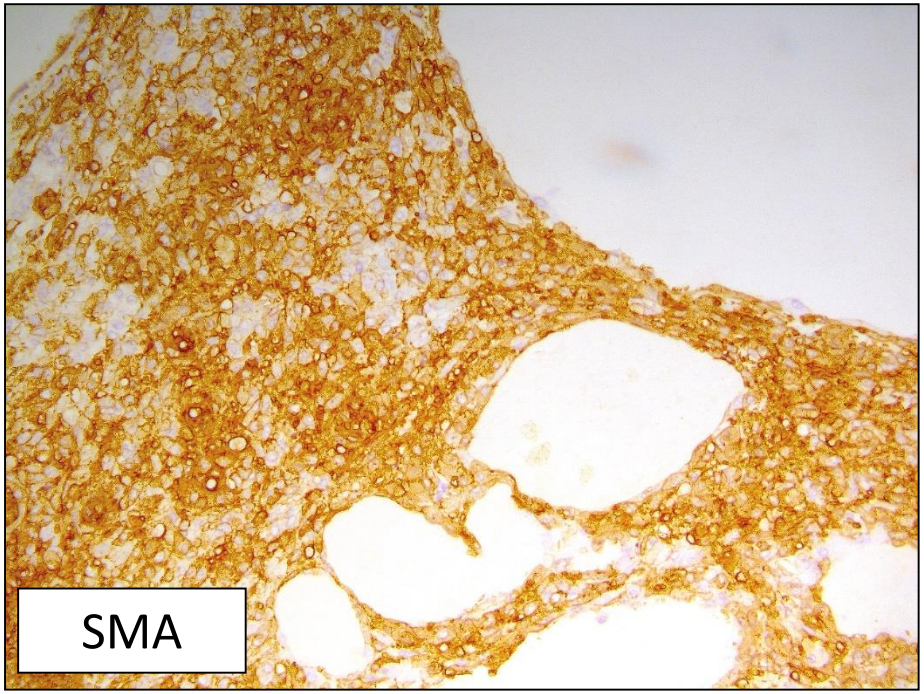
Immunohistochemistry

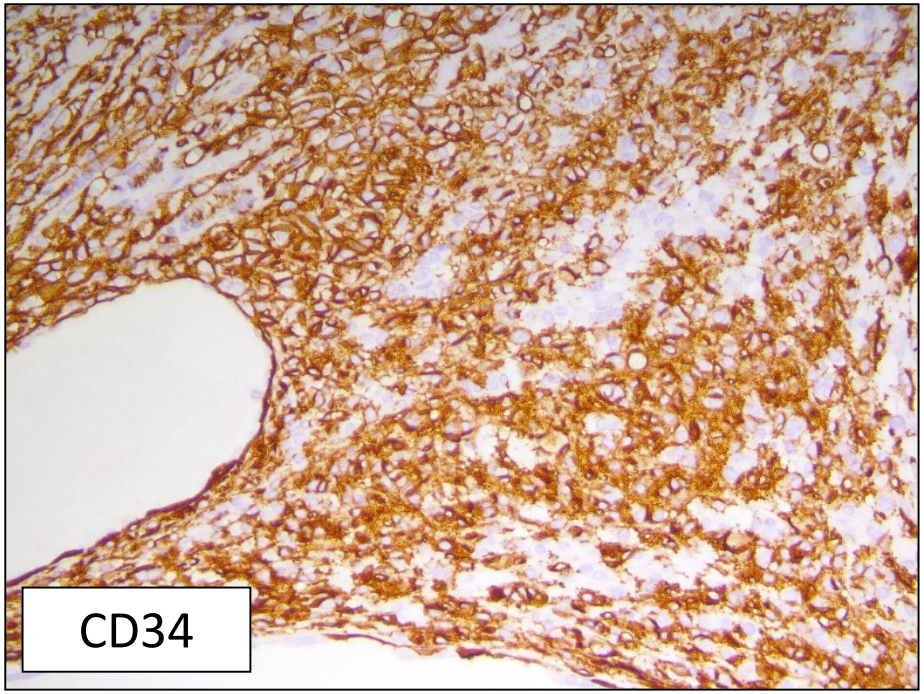
Positive

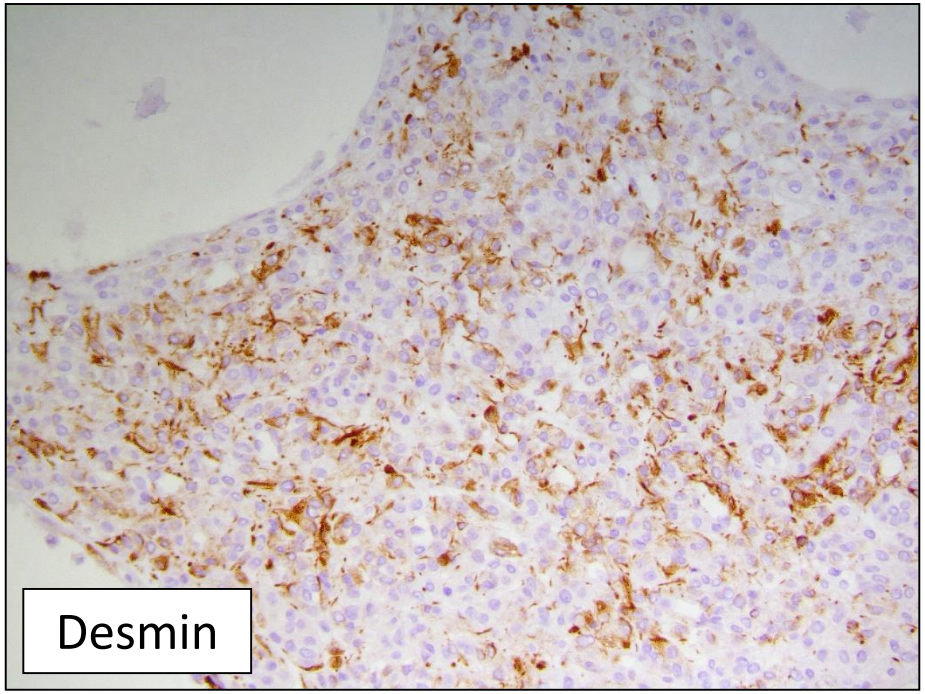
- SMA
- CD34
- Desmin (focal)
- CD117 (tumour and admixed mast cells)

Negative

- AE1/AE3
- HMB45
- Melan A
- MiTF
- CD31


SMA

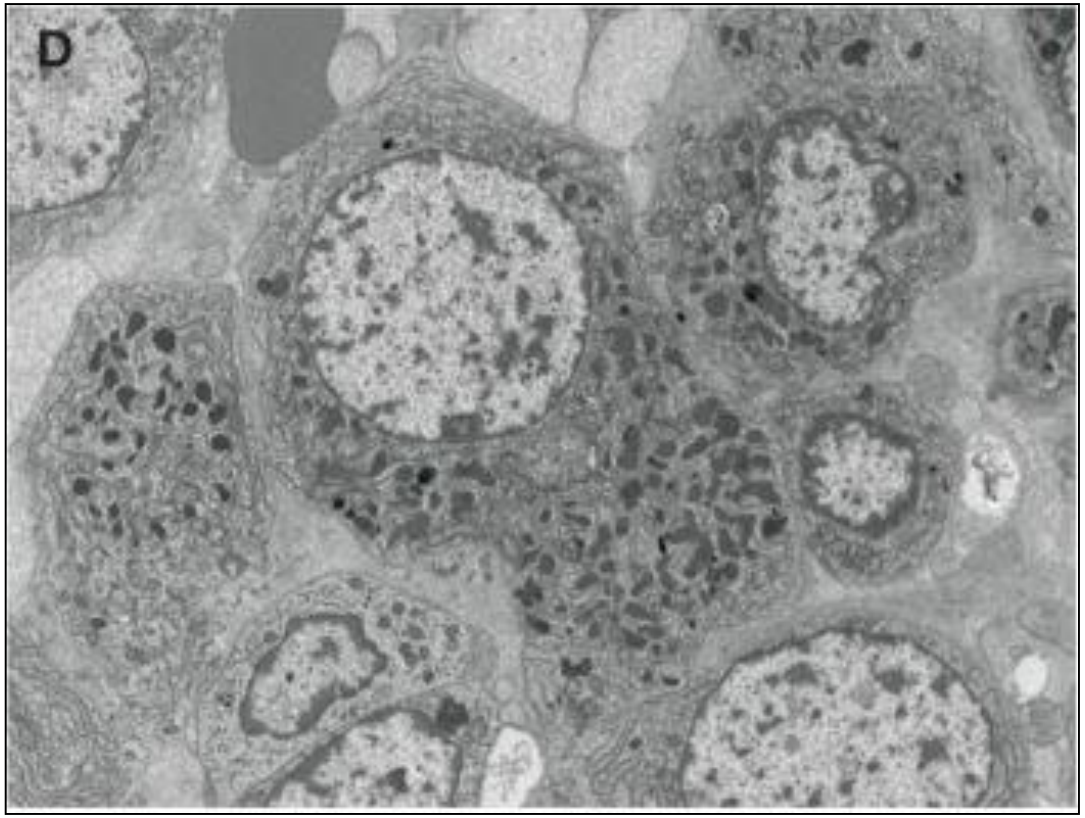

CD34


Desmin

Juxtaglomerular Cell Tumour

- Rare, benign tumour typically occurring in young adults (mean age 26.8 years) with a slight female predominance
- Usually associated with severe hypertension due to renin production by the tumour cells - rare cases are non-functioning (as in the present case)
- Characteristic H&E morphology and immunophenotype as illustrated by the present case
- Electron microscopy - tumour cells contain rhomboid renin protogranules (not performed in this case)

Electron Microscopy: Renin Protogranules/Crystals



frontiers in PEDIATRICS

CLINICAL CASE STUDY
published: 15 August 2014
doi: 10.3389/fped.2014.00089

Reninoma: an uncommon cause of renin-mediated hypertension

Peter Trnka[1,2], Luisa Orellana[2], Mark Walsh[3], Louis Pool[4] and Peter Borzi[1,5]*

Main Histologic Differential Diagnosis

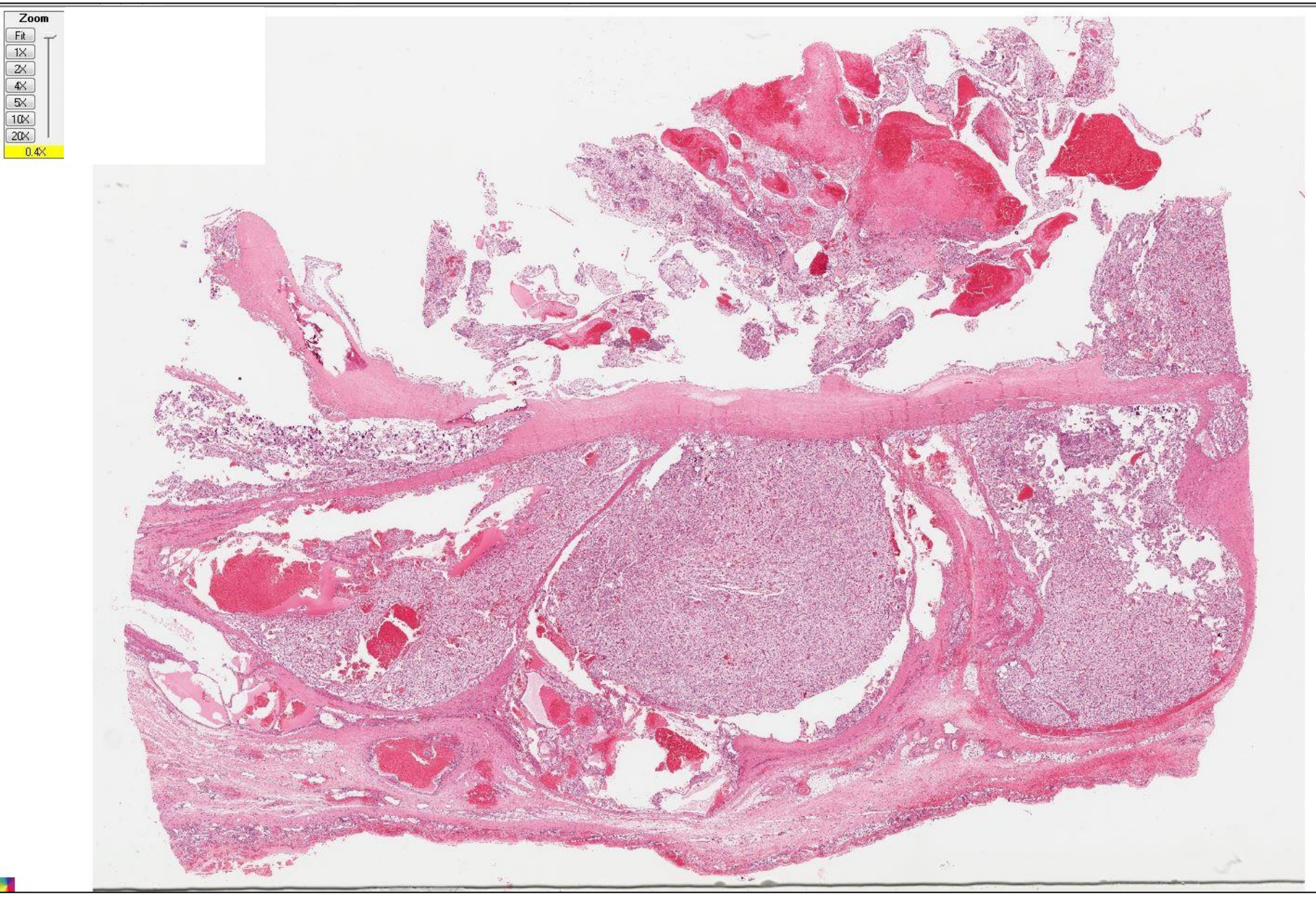
- Hemangiopericytoma
  - lack thick-walled blood vessels and polygonal cells with abundant cytoplasm
  - negative staining with actin
  - not associated with hypertension
- Glomus tumour
  - considerable morphologic and immunophenotypic overlap with juxtaglomerular cell tumour
  - no apparent endocrine function
- Epithelioid angiomyolipoma
  - admixed fat
  - positive staining for HMB45

References

- Martin SA et al. Juxtaglomerular cell tumor: a clinicopathologic study of four cases and review of the literature. Am J Clin Pathol, 116(6):854-856, 2001.
- Kim HJ et al. Juxtaglomerular cell tumor of kidney with CD34 and CD117 immunoreactivity: report of 5 cases. Arch Pathol Lab Med, 130(5):707-711, 2006.

Case 4

35 year-old female, 5.0 cm left renal mass, radical nephrectomy and right para-caval lymphadenectomy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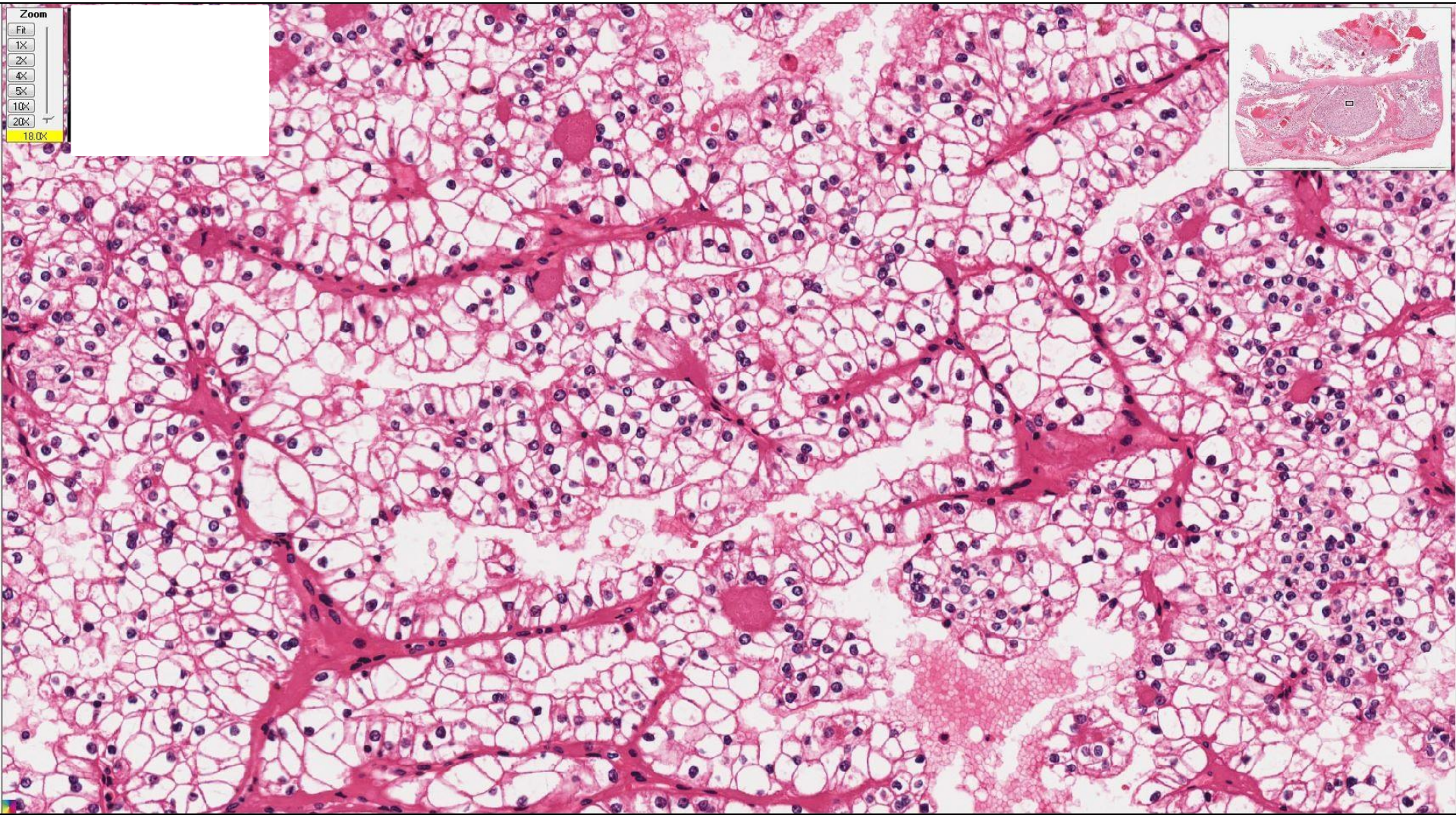
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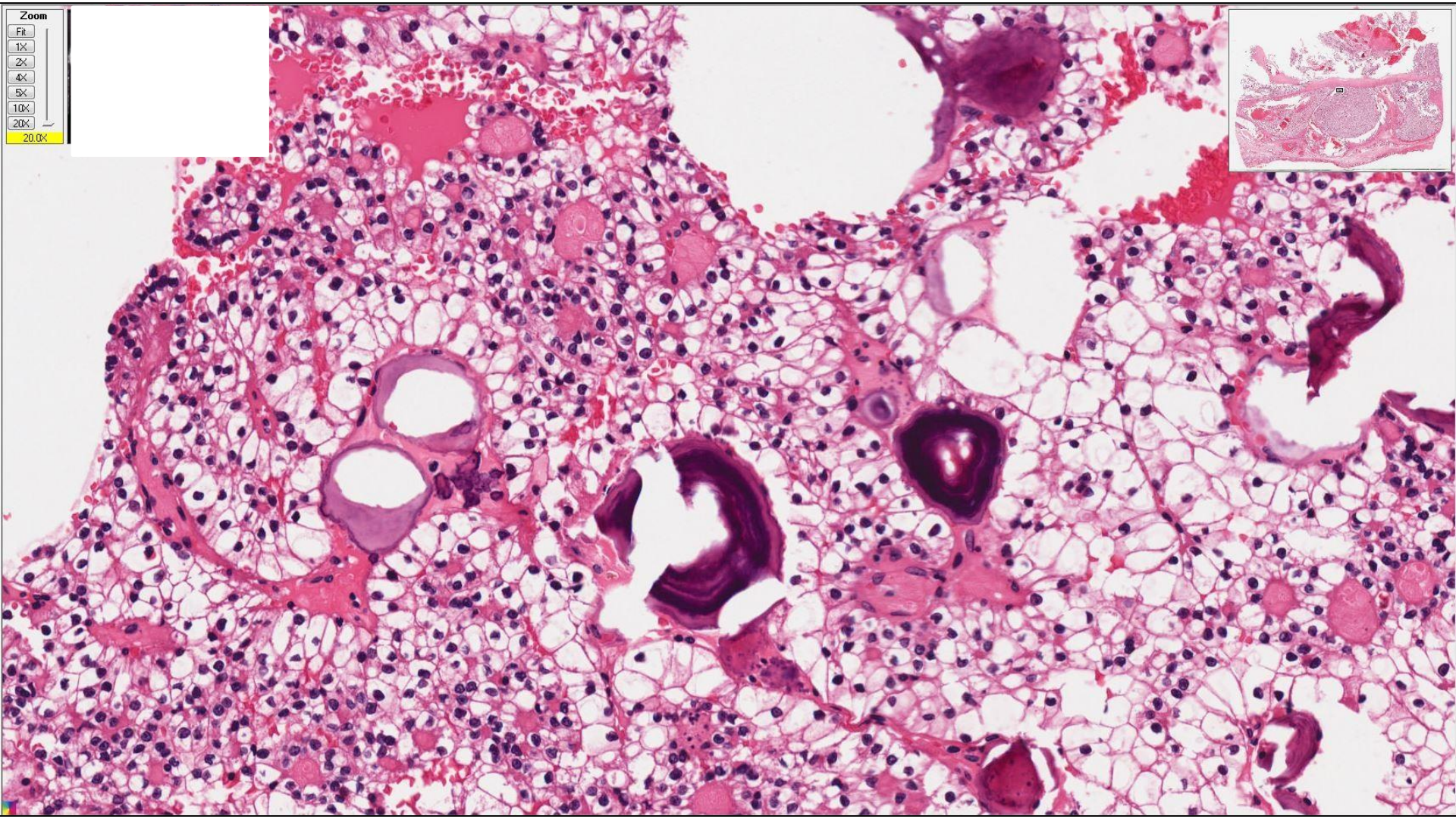
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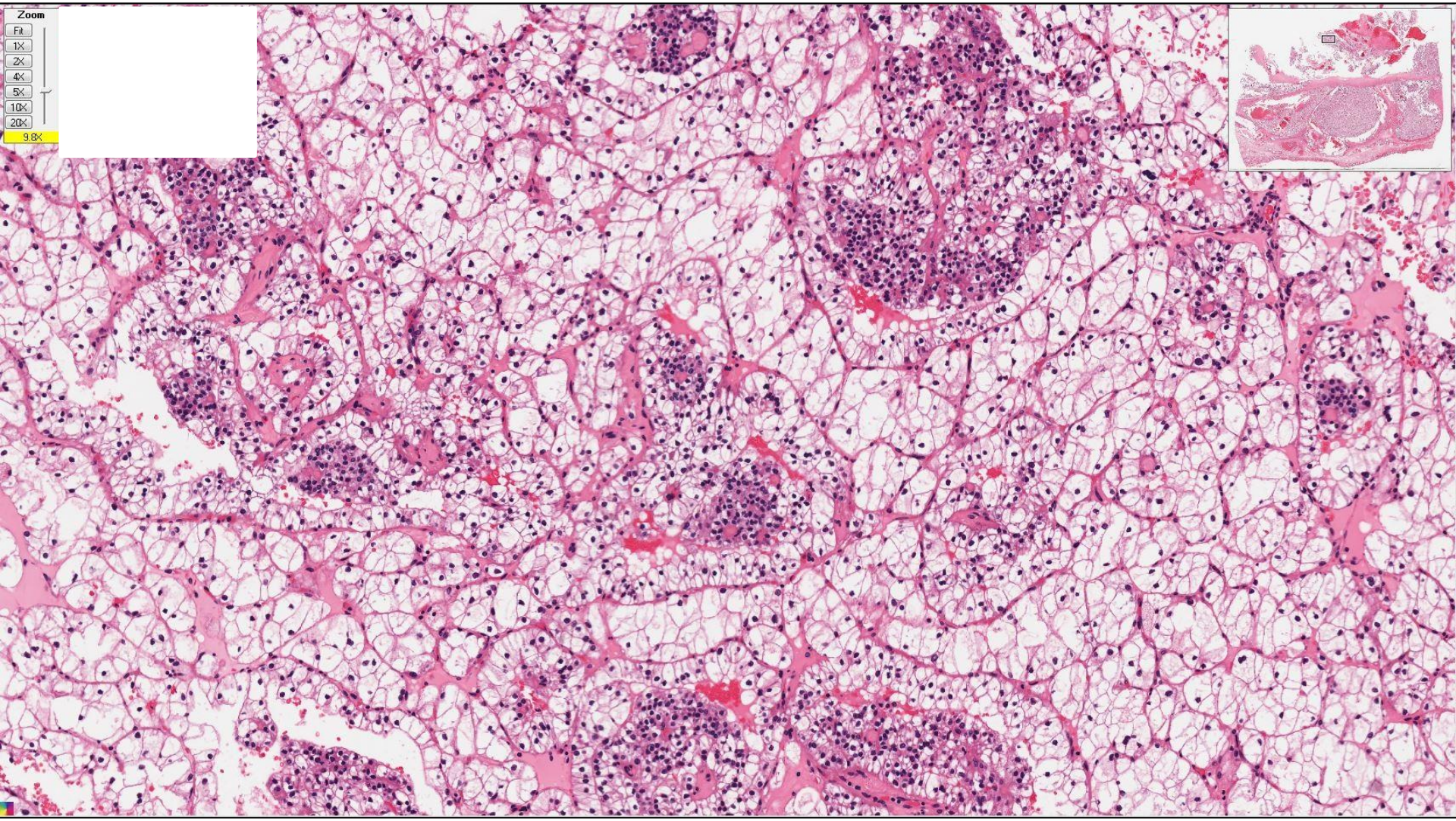
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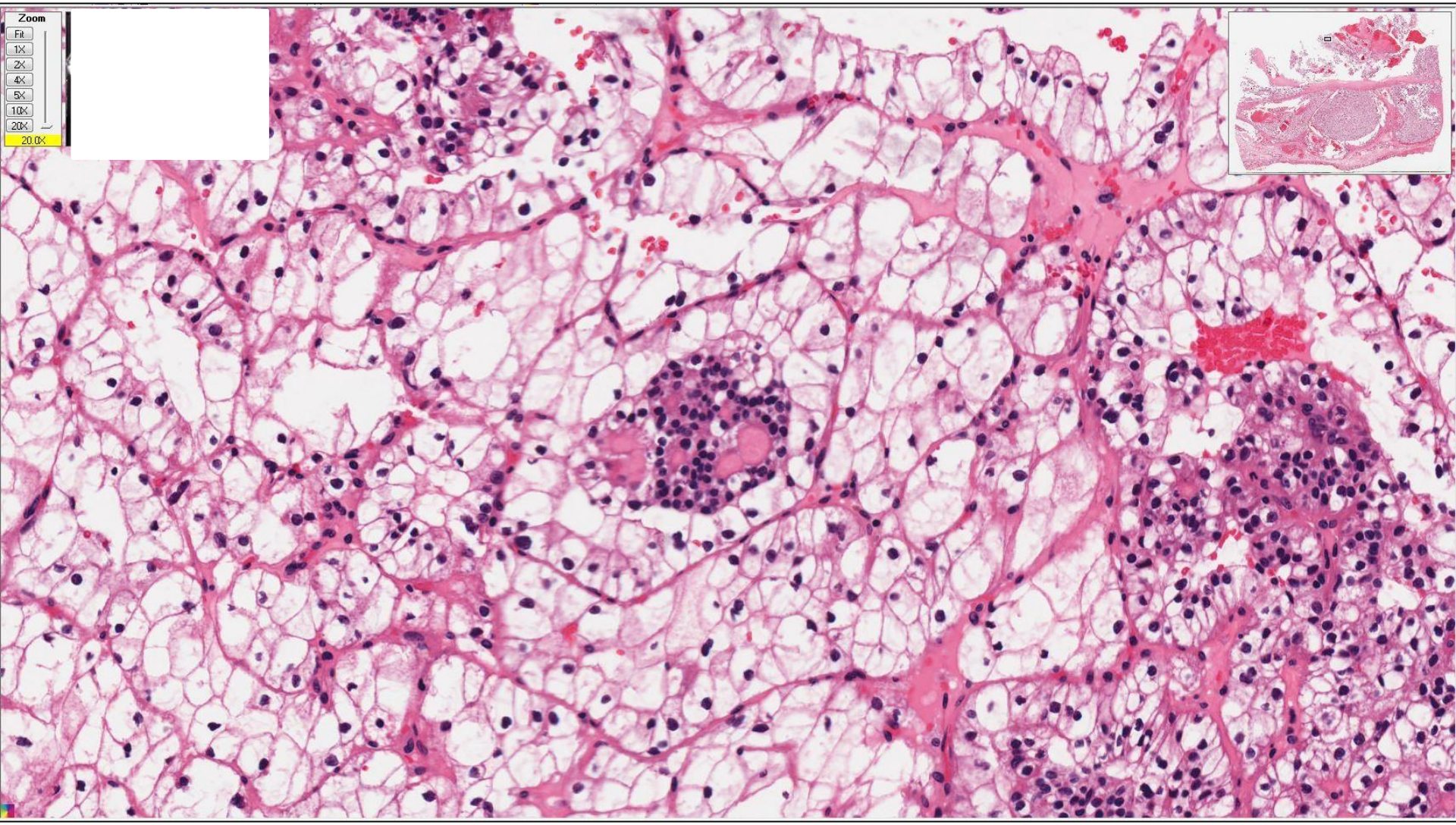
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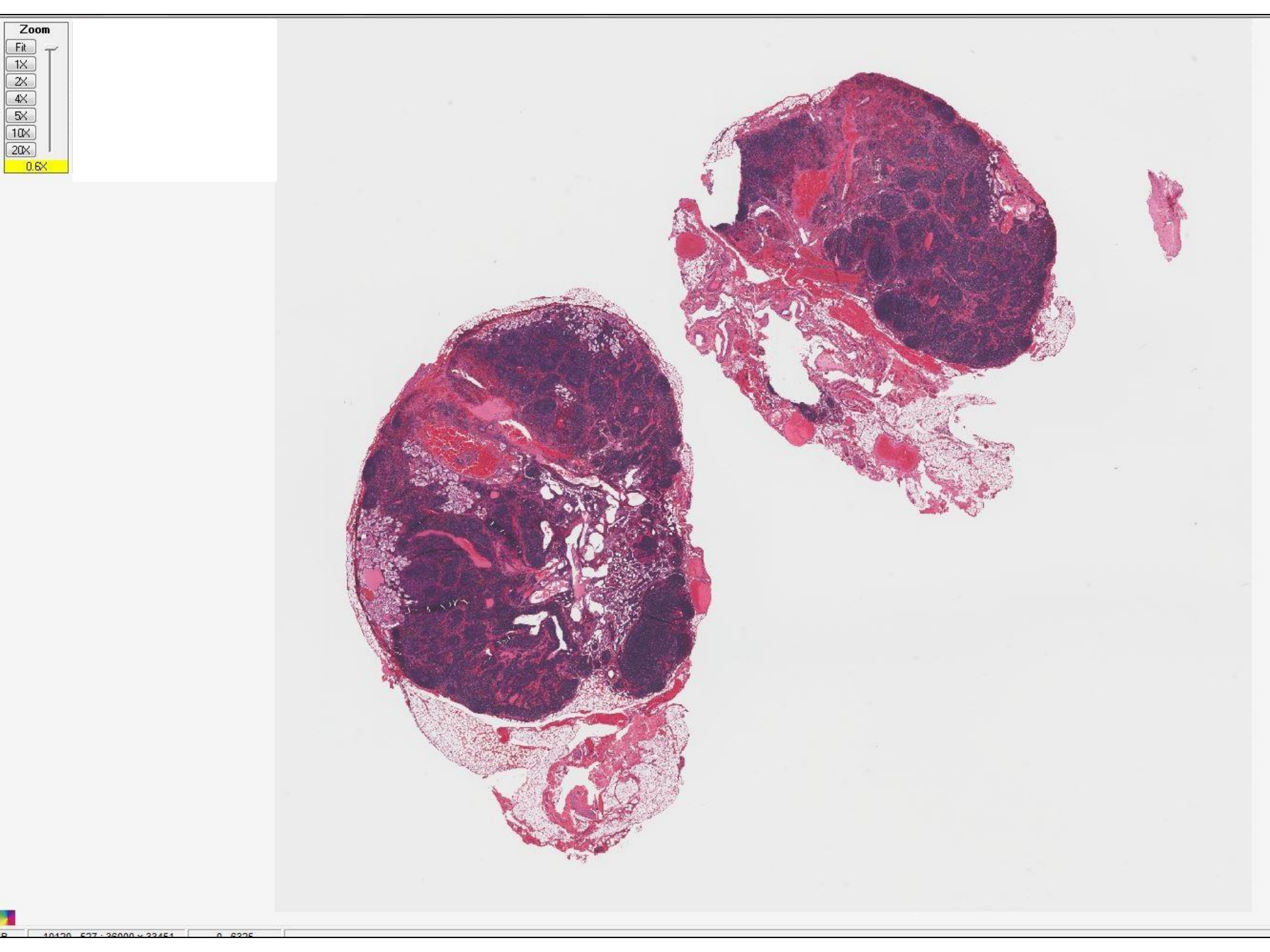
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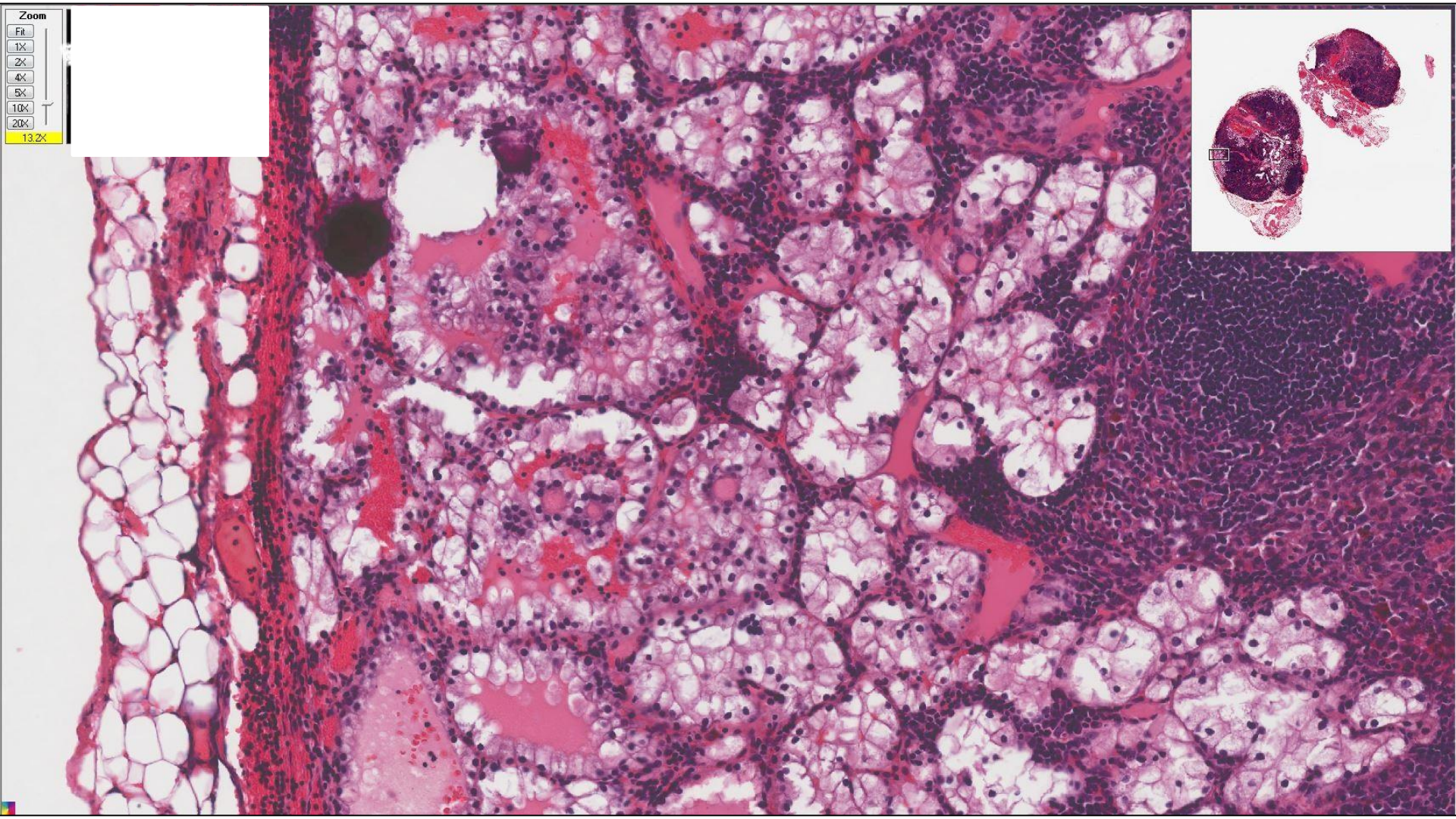
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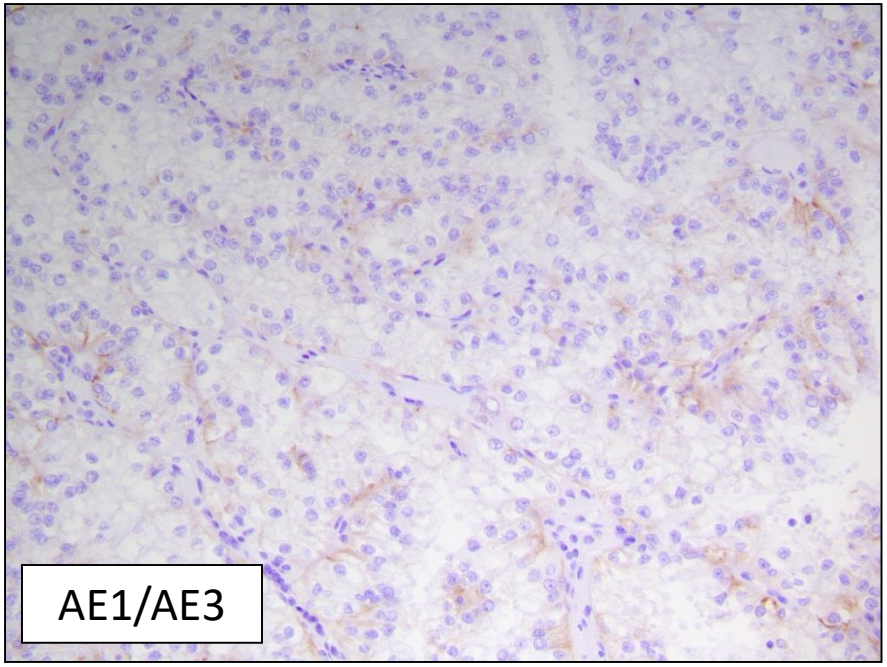
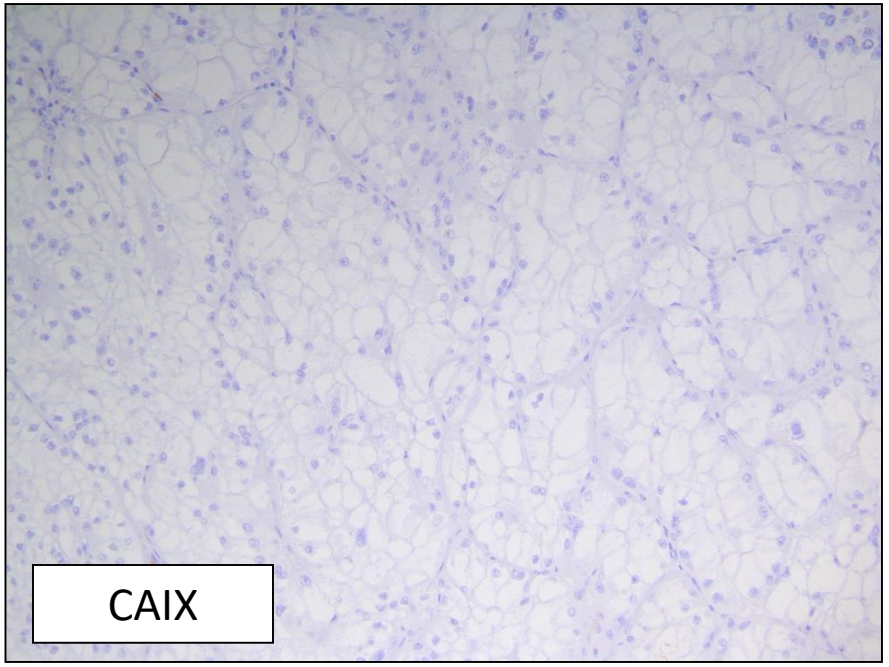
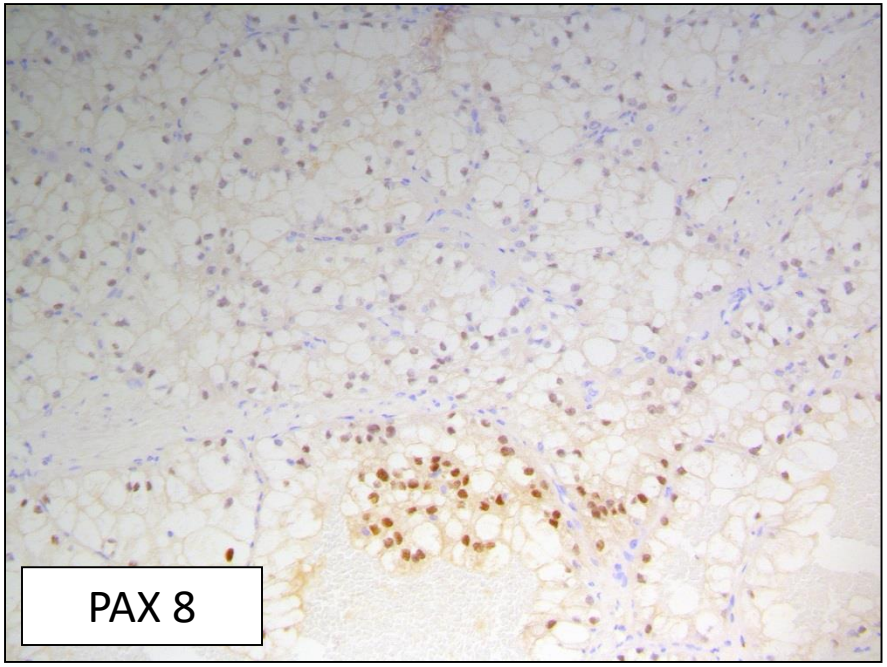
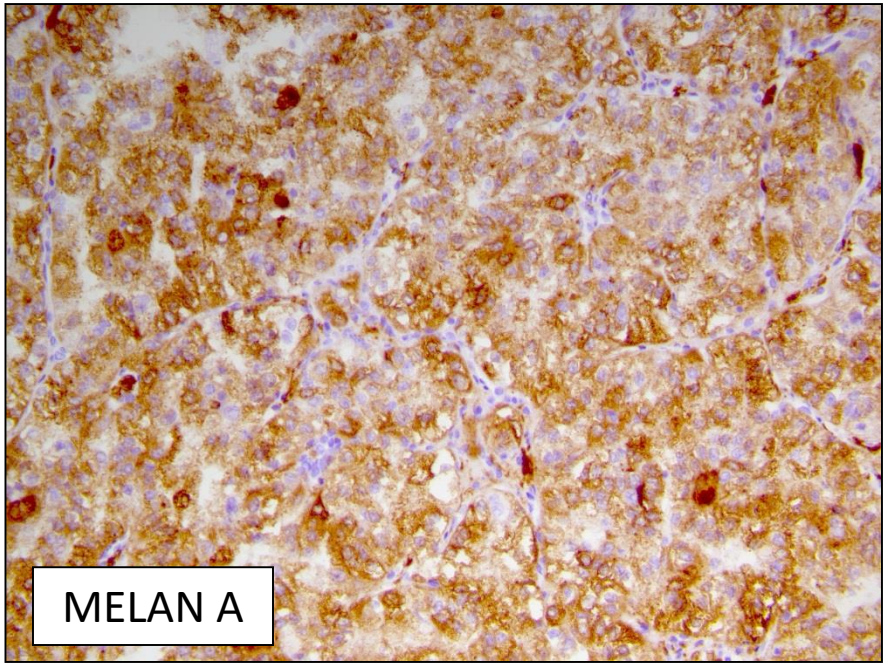
Differential Diagnosis

- Metastatic ovarian clear cell carcinoma
- Conventional clear cell RCC with foci of granular cell change
- Chromophobe RCC
- Epithelioid PEComa
- Xp11 translocation-associated RCC
- t(6;11) translocation-associated RCC


AE1/AE3


CAIX


PAX 8


MELAN A

MiTF Translocation Renal Neoplasms

- **Recognized by WHO only for last 10 years**

- **Outcomes highly variable**
  - overall survival similar to clear cell RCC
  - presentation with positive lymph nodes in children - good
  - presentation with distant metastases in adults - poor

- **Translocations involving MiT transcription factors (MiTF, TFEB, TFEC, TFE3)**
  - TFE3/Xp.11 RCC
  - TFEB/t(6;11) (MALAT1-TFEB) RCC
  - Melanocytic Xp11 translocation renal cancer
  - TFE3-associated PEComa

SEMINARS IN DIAGNOSTIC PATHOLOGY 32 (2015) 103–113

Available online at www.sciencedirect.com

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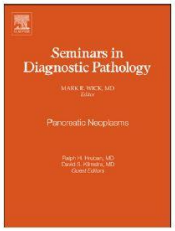


MiT family translocation renal cell carcinoma

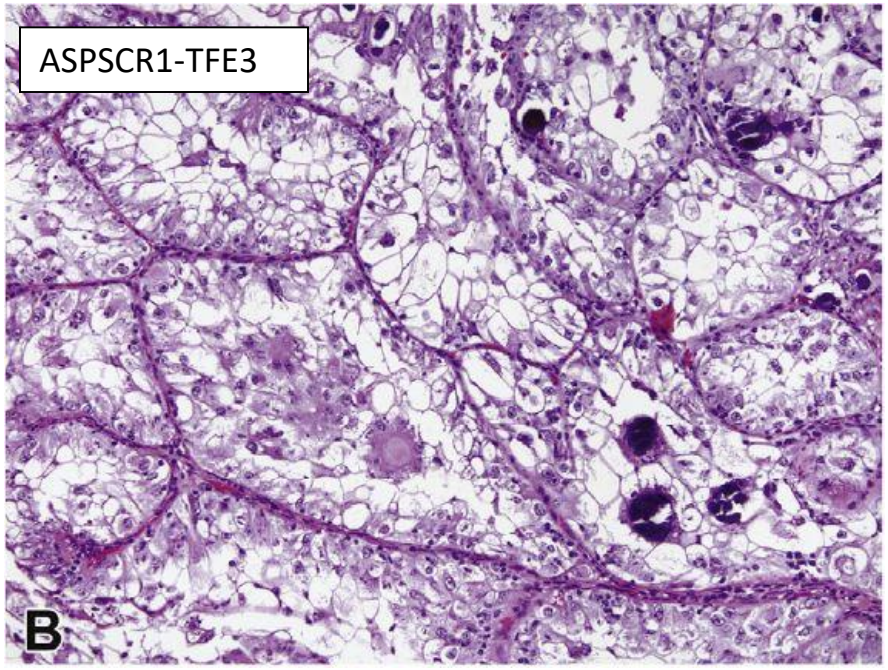
Pedram Argani, MD

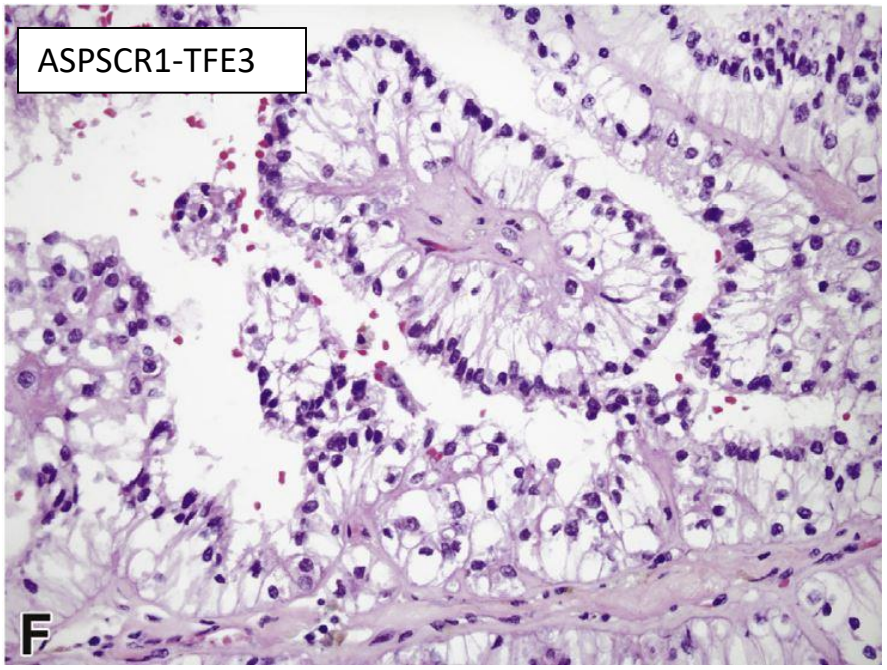
Department of Pathology, The Johns Hopkins University School of Medicine, The Johns Hopkins Hospital, 401 North Broadway, Weinberg 2242, Baltimore, Maryland 21231

Table 1 – Cancers with Xp11 translocation/*TFE3* gene fusions

Neoplasm	Fusion	Age range (years)	Translocation
ASPS	*ASPSCR1–TFE3*	1–71	der(17)(X;17)(p11.2q25)
RCC	*ASPSCR1–TFE3*	1–75	t(X;17)(p11.2;q25)
RCC	*PRCC–TFE3*	2–69	t(X;1)(p11.2;q21)
RCC	*SFPQ–TFE3*	3–68	t(X;1)(p11.2;q34)
RCC	*NonO–TFE3*	39	inv(X)(p11.2;q12)
RCC	*CLTC–TFE3*	14	t(X;17)(p11.2;q23)
RCC	*Unknown*	32	t(X;3)(p11.2;q23)
RCC	*Unknown*	77	t(X;10)(p11.2;q23)
Xp11 PEComa	*SFPQ–TFE3 and others*	9–55	t(X;1)(p11.2;q34) and others
Melanotic Xp11 Translocation Cancer	*SFPQ–TFE3 and likely others*	11–55	t(X;1)(p11.2;q34) and likely others
Subset of Epithelioid Hemangioendothelioma[57]	*YAP1–TFE3*	14–50	t(X;11)(p11.2;q13)

ASPS = alveolar soft part sarcoma.
RCC = renal cell carcinoma.
PEComa = perivascular epithelioid cell tumor.


ASPSCR1-TFE3
B


ASPSCR1-TFE3
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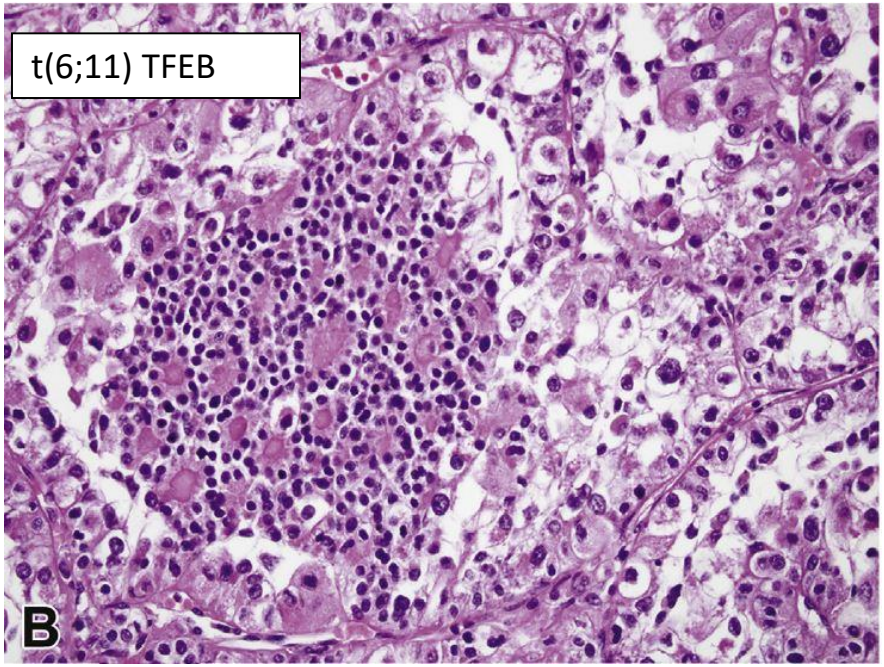
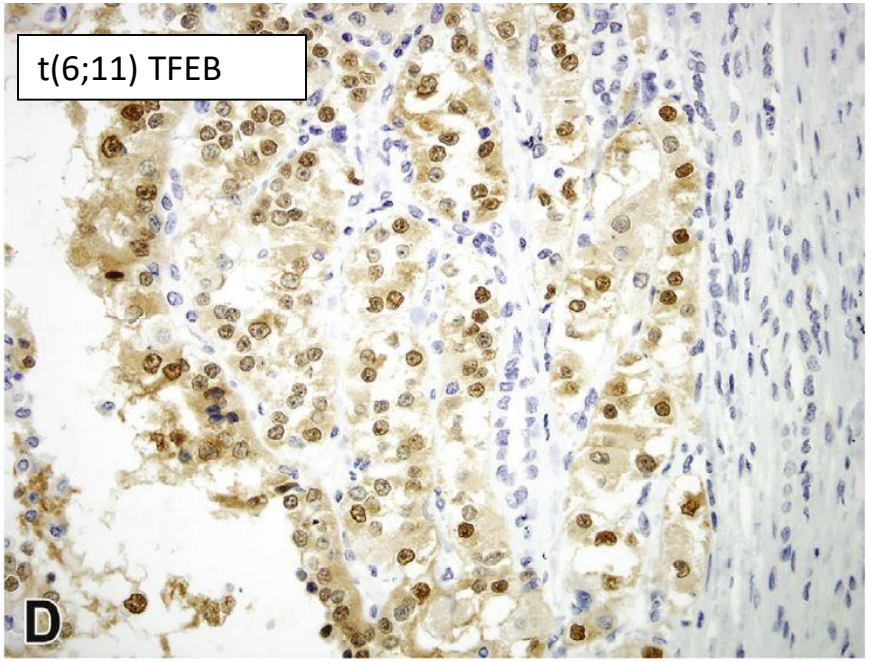

t(6;11) TFEB
B


t(6;11) TFEB
D

H&E Morphology and IHC Features That Sort Out The Differential

- well circumscribed solid and cystic
- predominantly clear cytoplasm with clusters of cells having granular eosinophilic cytoplasm
- distinctive second population of smaller cells with scant cytoplasm and entrapped eosinophilic hyaline basement membrane-like material
- weak AE1/AE3 positivity and strong expression of melanocytic markers, particularly MelanA and HMB45

Immunohistochemistry and FISH

Biomarker	Reaction
AE1/AE3	Focal Positive
CD117	Negative
CK7	Rare entrapped cells
AMACR	Diffuse, weak blush
MelanA	Diffuse, strong
HMB45	Strong, focal
PAX8	Diffuse, strong nuclear
TFE3 FISH	Negative for rearrangement
TFEB FISH	Rearrangement detected

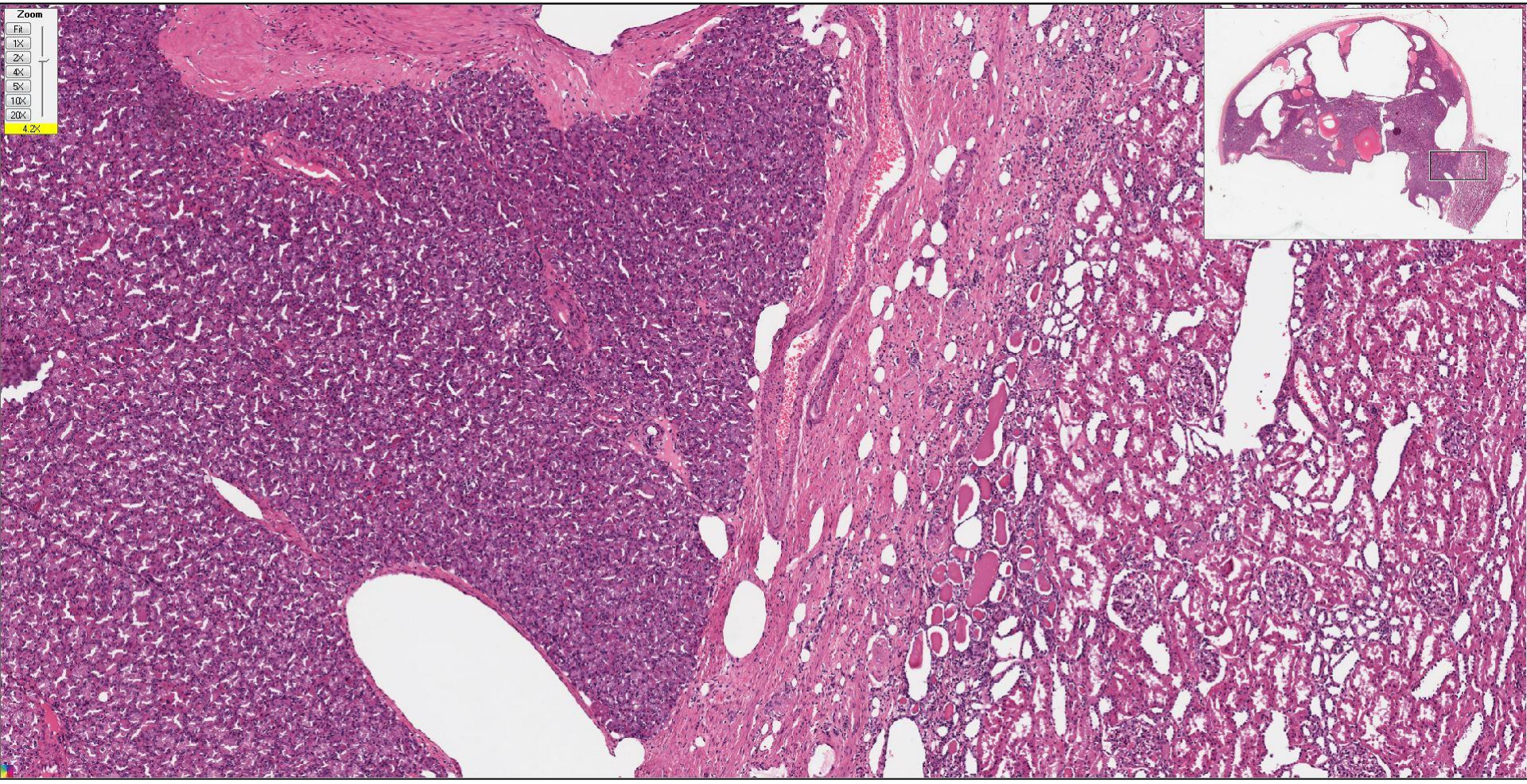
Dr. Steven Smith, VCU, ISUP COTM, May 2016

Diagnosis

- **T(6;11) TFEB translocation-associated RCC**
- less common than Xp11 carcinomas, with < 100 cases reported
- described over a wide age range (3-68y), typically young adults
- many reported cases follow a benign course - well characterized metastatic cases have been described suggesting a subset may be aggressive

Case 5

31 year-old female, 2.9 cm left renal mass, partial nephrectomy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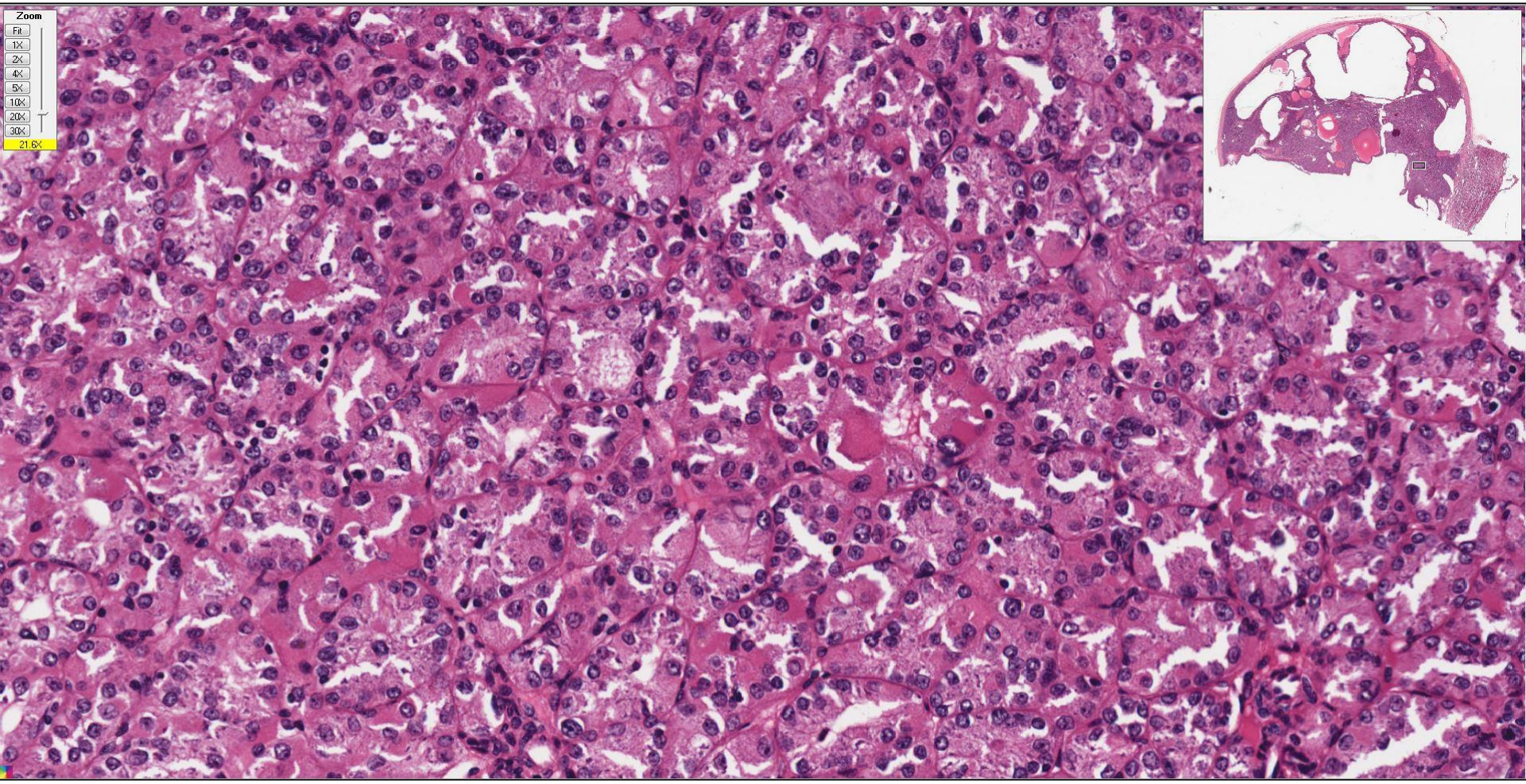
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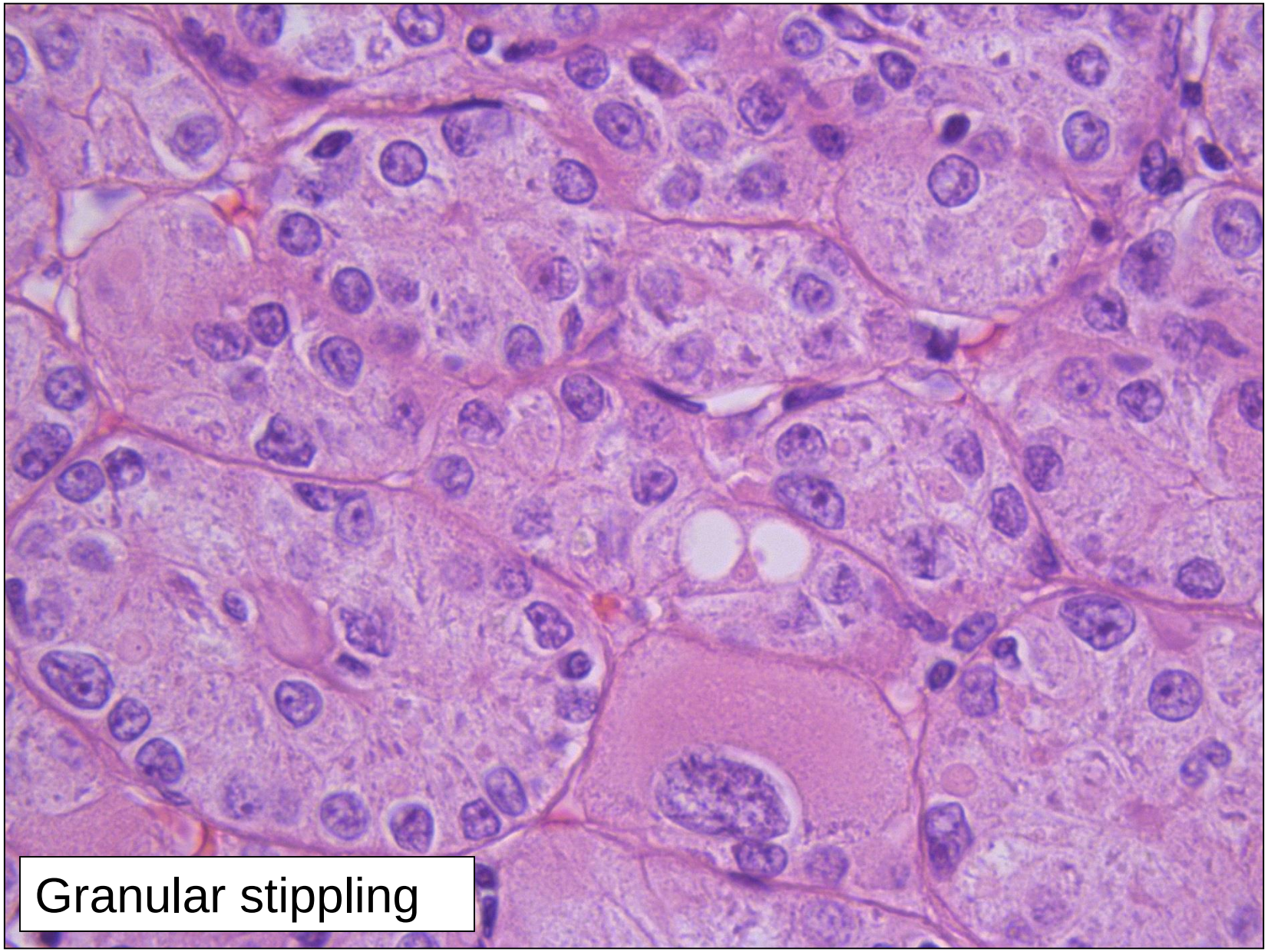
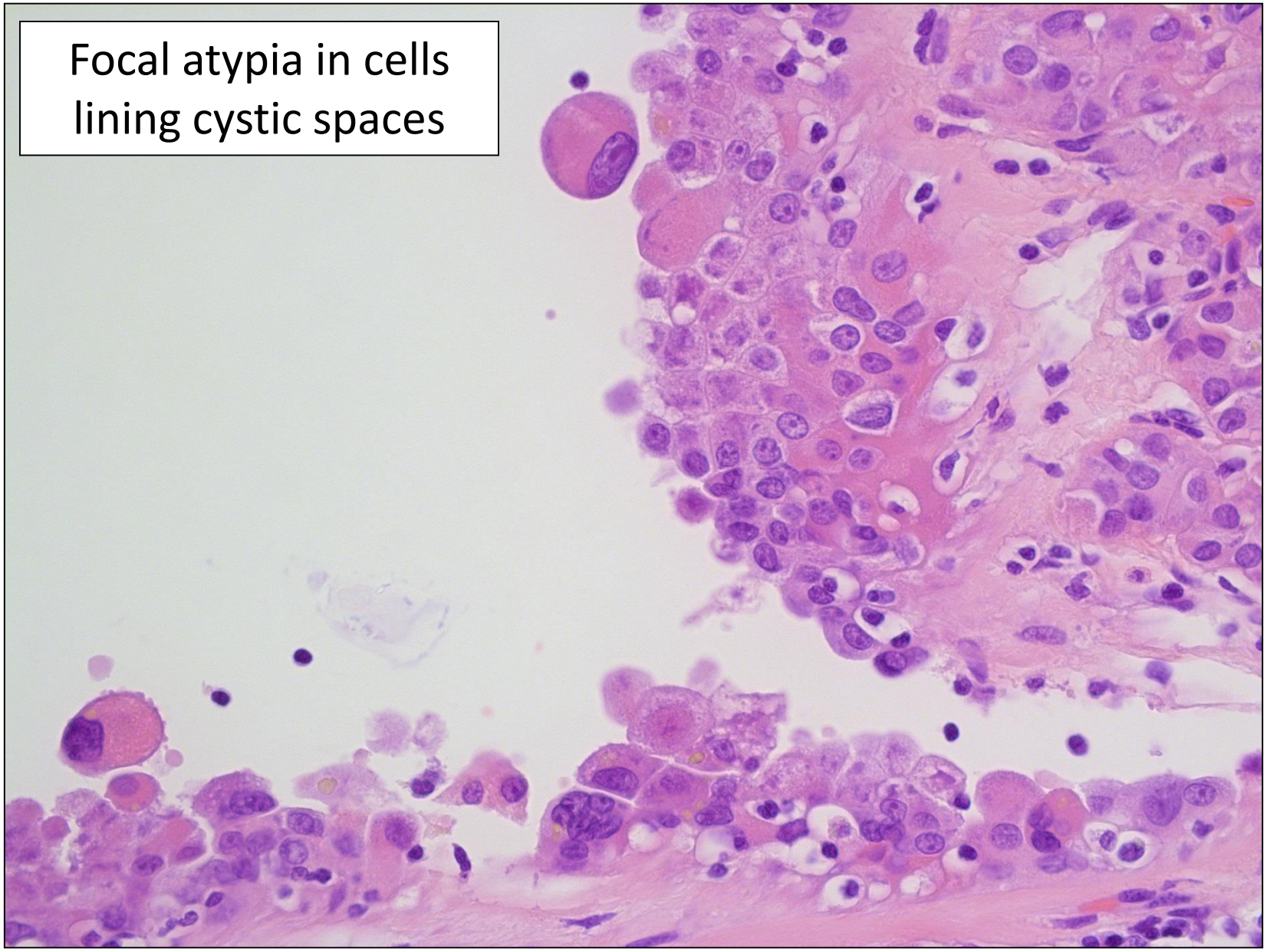
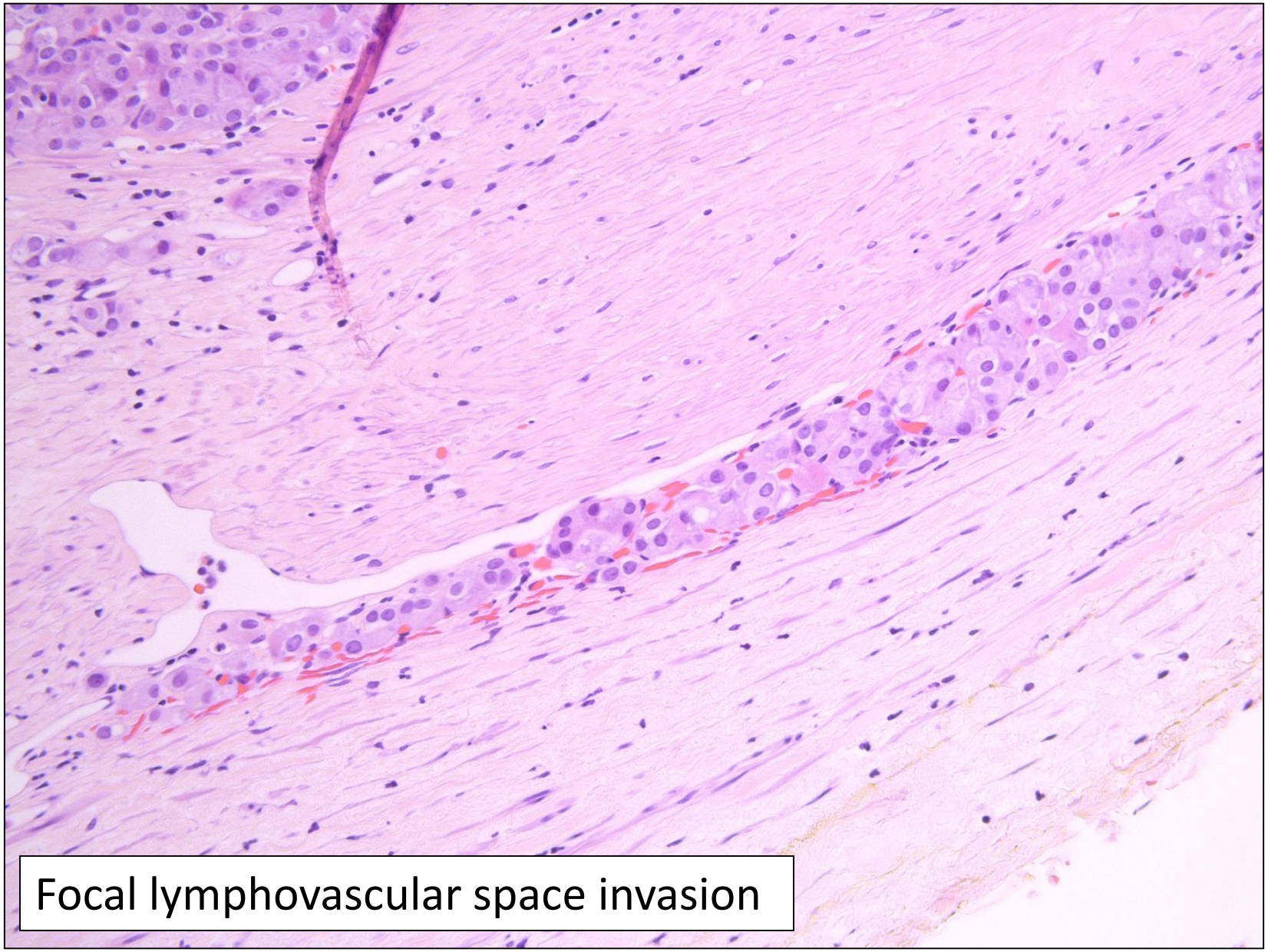

Granular stippling


Focal atypia in cells
lining cystic spaces


Focal lymphovascular space invasion

Immunohistochemistry

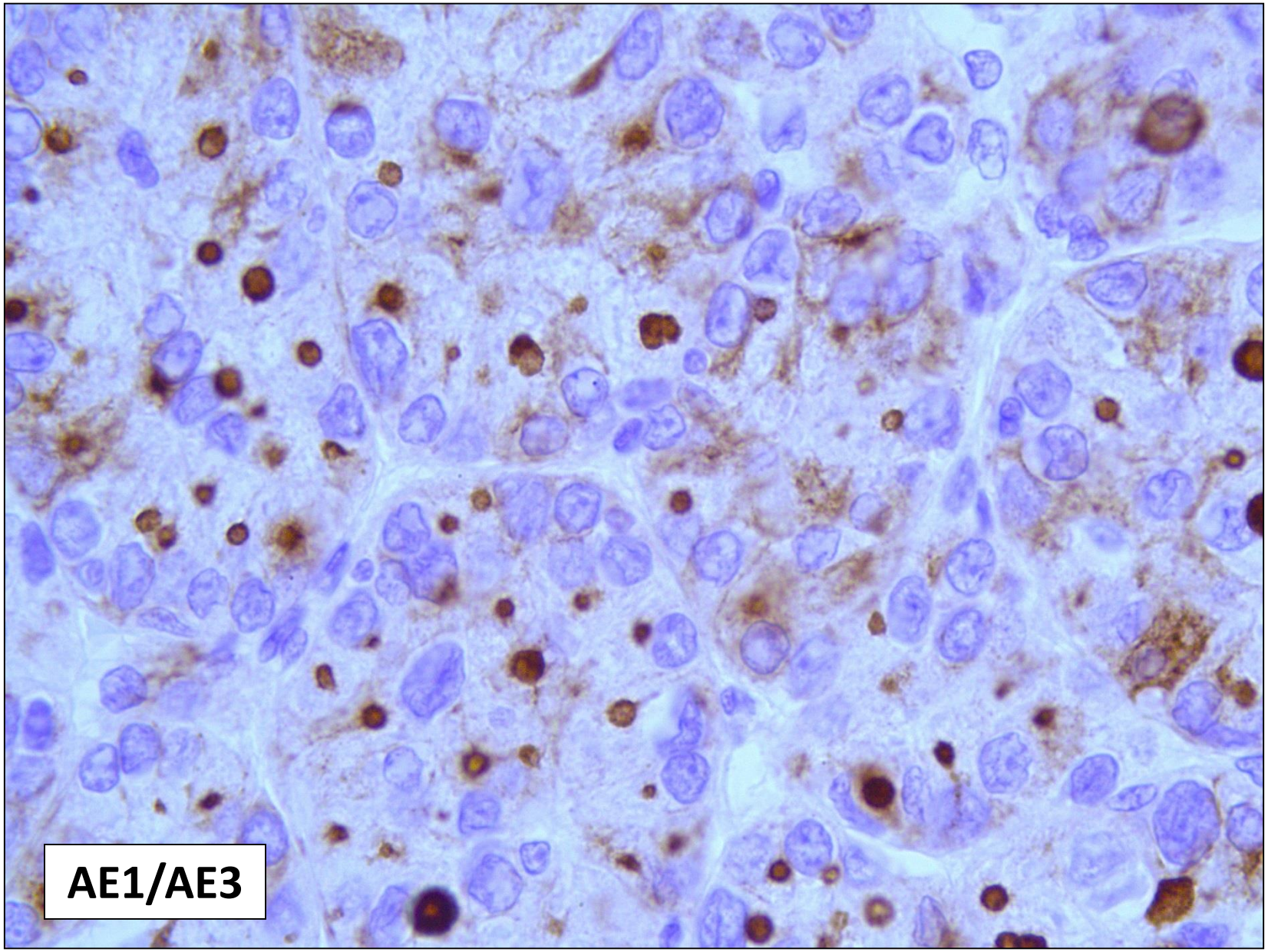
Positive

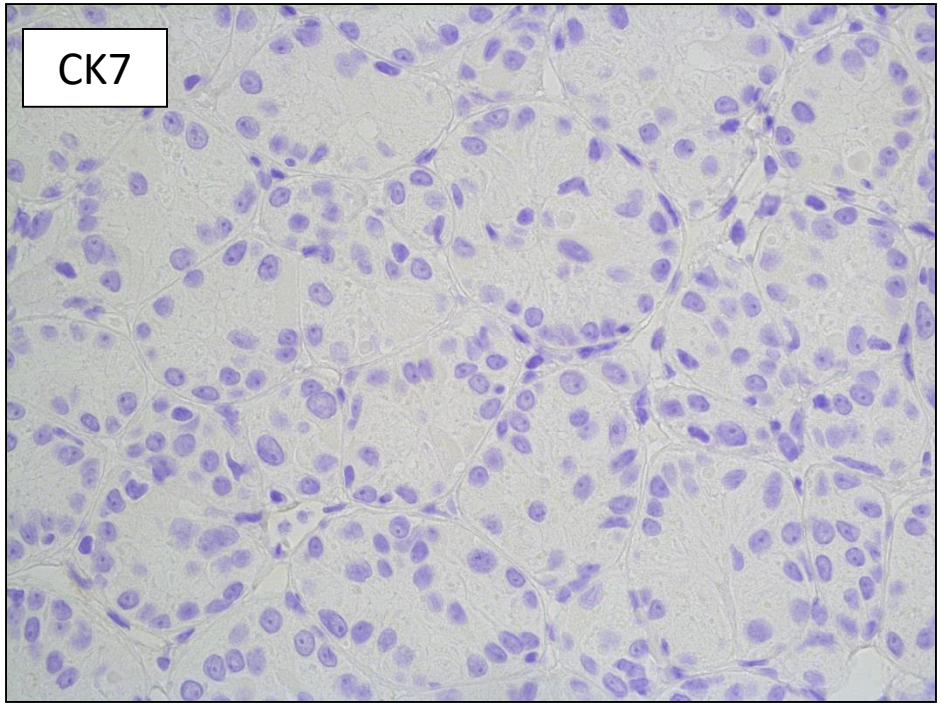
- PAX-8
- AE1/AE3*
- CAM 5.2*
- CK18*
- SDHB - intact expression
- MIB1 - < 1% of nuclei

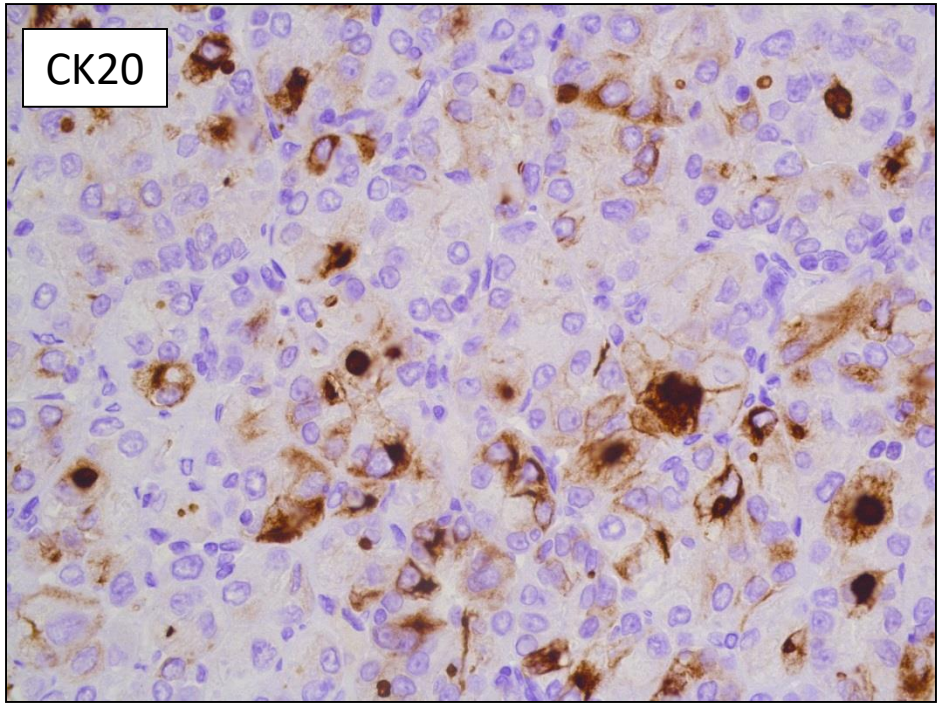
Negative

- CK7
- CD117
- Chromogranin
- Synaptophysin
- CAIX
- HMB45

* *Dot-like/chunk-like*


AE1/AE3





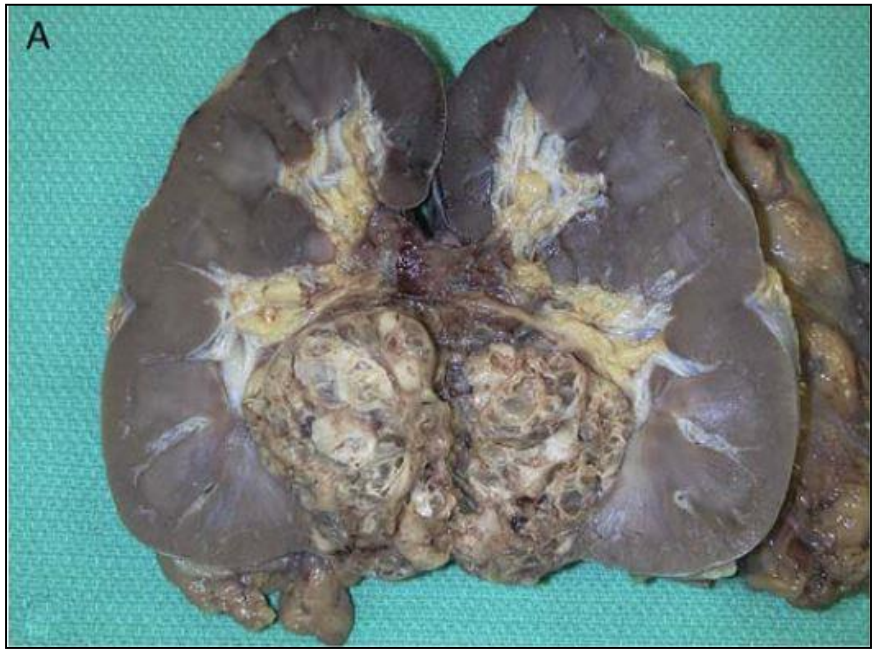
CK20 positivity is very rare in renal tumours

Eosinophilic, Solid, and Cystic Renal Cell Carcinoma

Clinicopathologic Study of 16 Unique, Sporadic Neoplasms Occurring in Women

Kiril Trpkov, MD, FRCPC, Ondrej Hes, MD, PhD,† Michael Bonert, MD,* Jose I. Lopez, MD, PhD,‡ Stephen M. Bonsib, MD,§ Gabriella Nesi, MD,‖ Eva Comperat, MD,¶ Mathilde Sibony, MD,# Daniel M. Berney, MD,** Petr Martinek, MSc,† Stela Bulimbasic, MD,†† Saul Suster, MD,‡‡ Ankur Sangoi, MD,§§ Asli Yilmaz, MD,* John P. Higgins, MD,‖‖ Ming Zhou, MD, PhD,¶¶ Anthony J. Gill, MD, PhD,## Christopher G. Przybycin, MD,*** Cristina Magi-Galluzzi, MD, PhD,*** and Jesse K. McKenney, MD****

(*Am J Surg Pathol* 2016;40:60–71)



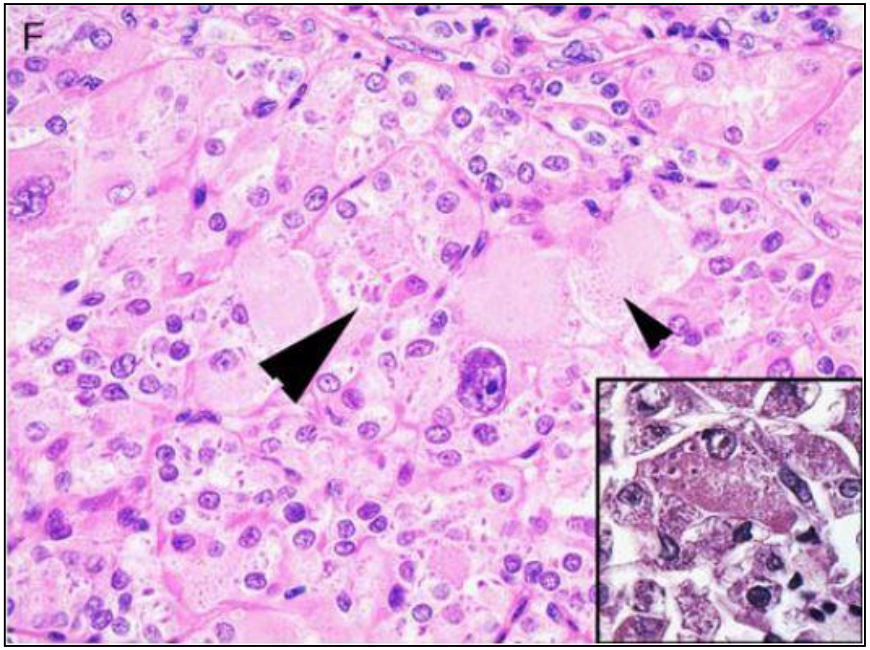


TABLE 2. Summary of the Key Features of ESC RCC

Clinical	Females, usually low stage, good prognosis
Gross	Solid and cystic or solid (minority), tan, single tumors
Light microscopy	Architecture: Solid and cystic. Hobnail arrangement of cells lining septa. Diffuse or tightly compact acinar or nested growth in solid foci. Capsule absent. Cytology: Eosinophilic, voluminous cytoplasm with granular stippling, round to oval nuclei, and prominent nucleoli. Scattered foamy histiocytes, lymphocytes, and multinucleated cells.
IHC	Positive: PAX8, $CK20^{+}/CK7^{-}$ phenotype most common, Vimentin, AMACR (+/–), CD10 (+/–) Negative: CA9, CD117, HMB45
Electron microscopy	Abundant rough endoplasmic reticulum
Molecular karyotype	LOH: 16p and Xq (3/3 cases); 11p (2/3 cases) CN gains: 1p, 7p-q, 10q, 13q, 16p-q (2/3 cases) CN losses: 19p, 19q, Xp, Xq (2/3 cases)
aCGH	Gain of Chr 16 (only 1 case analyzed)

CN indicates copy number.

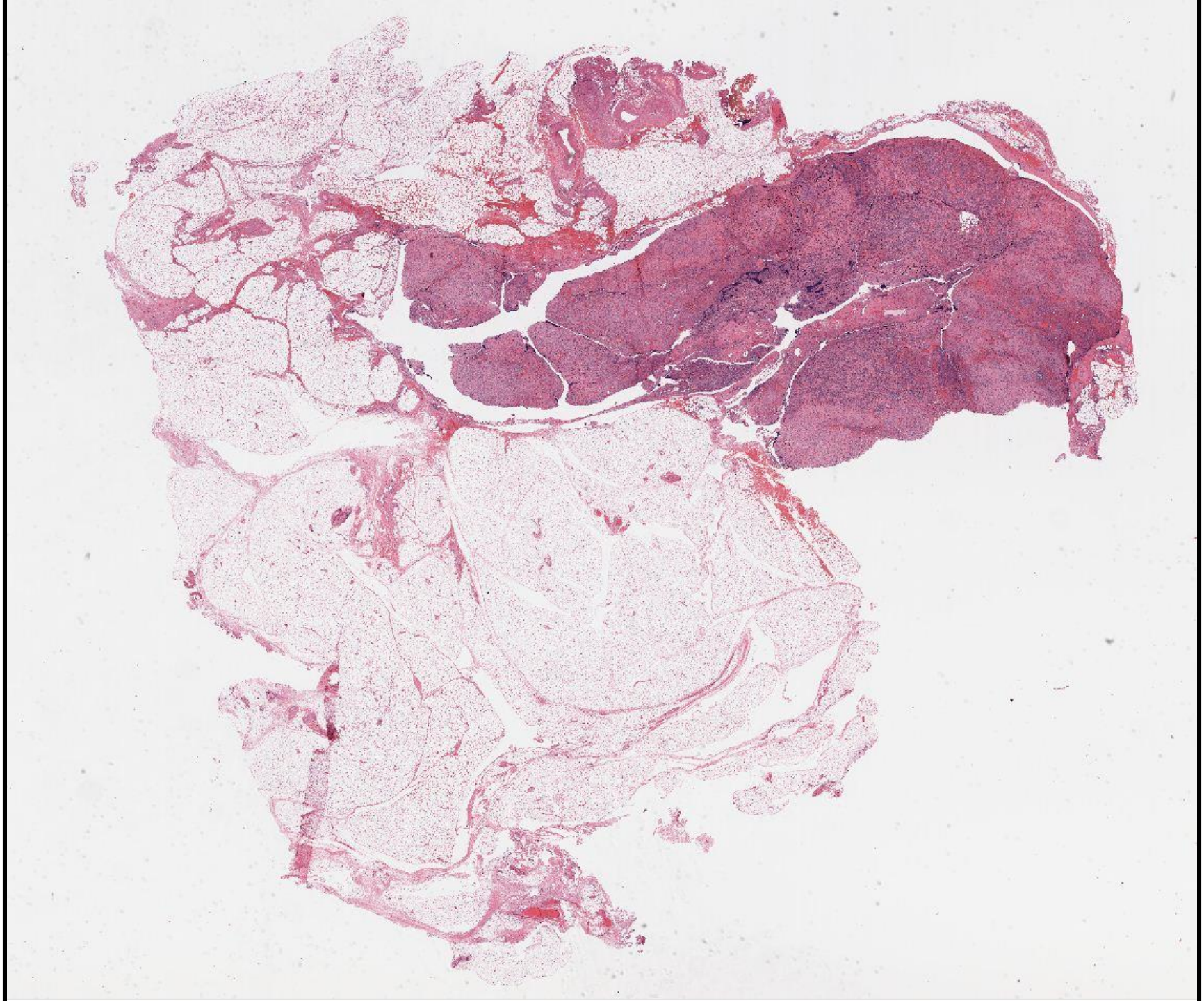
Association with tuberous sclerosis ???

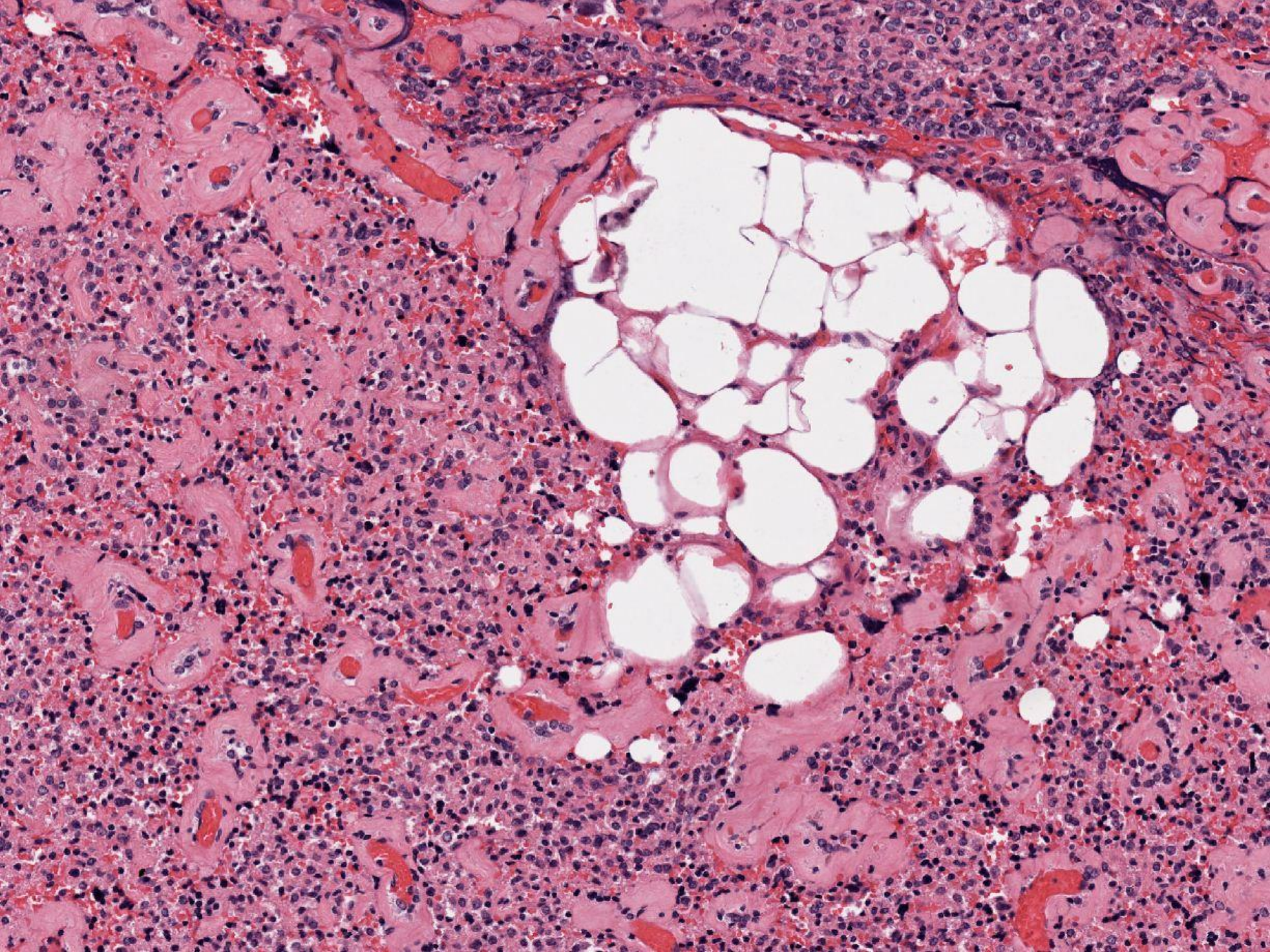
TABLE 3. Key Features and Immunostains Helpful in Distinguishing ESC RCC From Other Renal Tumors

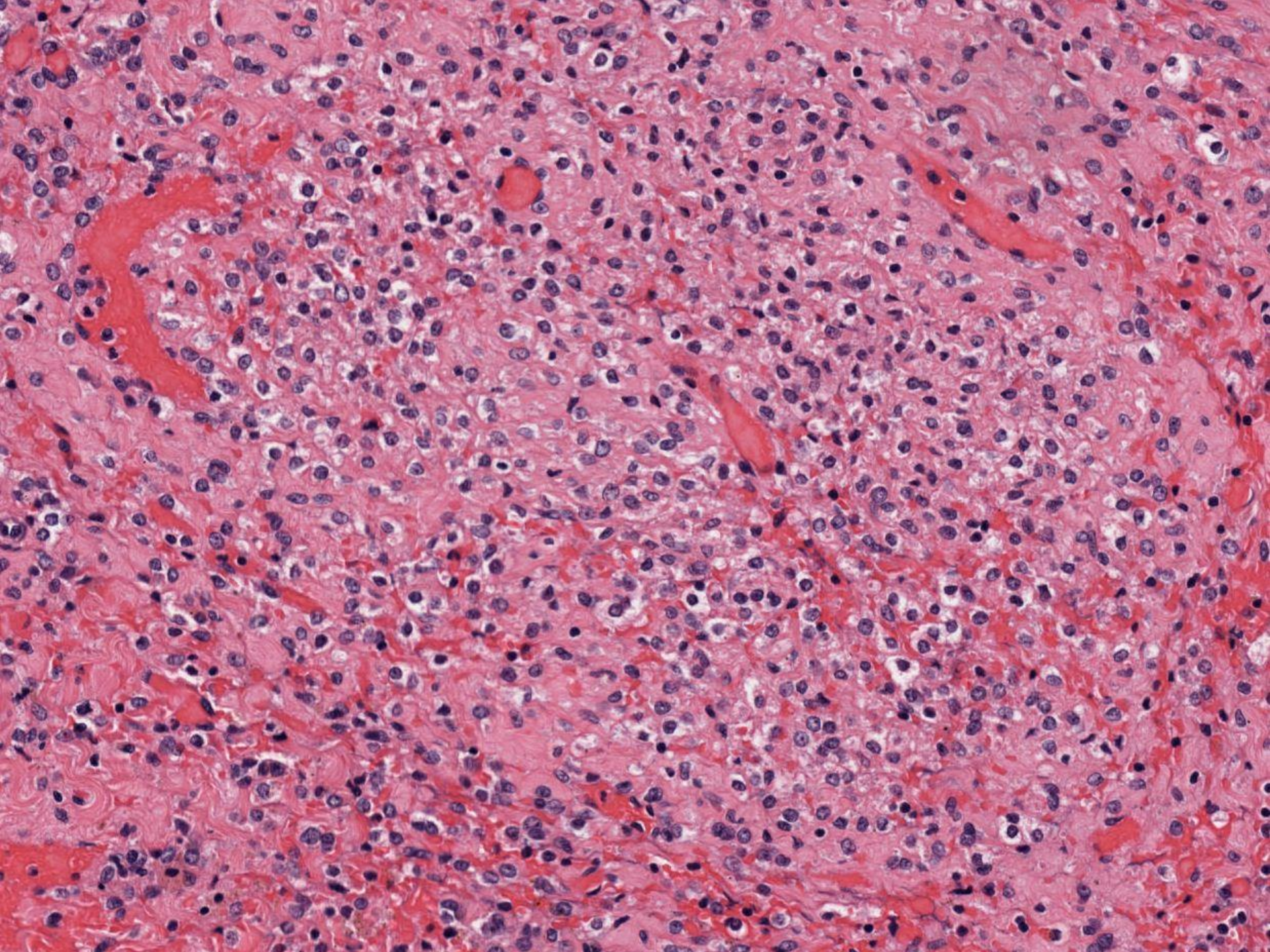
Diagnosis	Key Distinguishing Features	IHC
ESC RCC	Female individuals, solid and cystic growth, voluminous eosinophilic cytoplasm, granular cytoplasmic stippling, usually low stage	$CK20^+/CK7^-$, $CD117^-$, $PAX8^+$, $PanCK^+$, $HMB45^-$, $CA9^-$ (no membranous reactivity)
Chromophobe RCC, eosinophilic	Solid and uniform architecture, irregular nuclear membranes, perinuclear halos	$CD117^+$, $CK7^+$, $CK20^-$
Oncocytoma	Uniform cytology, lacks macrocysts	$CD117^+$, $CK7^{-/+}$, $CK20^-$
Epithelioid angiomyolipoma	Epithelioid cells that may be pleomorphic, lacks macrocysts	$PAX8^-$, $HMB45^+$, $PanCK^-$, $CK7^-$, $CK20^-$
Papillary RCC, oncocytic	Papillary formations (at least focal), uniform cytology	$CK7^+$, $CK20^-$
Clear cell RCC, eosinophilic morphology	Focal clear cell areas, delicate vasculature, may contain macrocysts	$CA9^+$, $CK20^-$
MiT translocation RCC	Large cells with clear (or eosinophilic) morphology, focal papillary and nested growth, lack cysts (usually)	$TFE3^+$, $TFEB^+$, $HMB45^+$, $PanCK^-$
SDH-deficient RCC	Lacks macrocysts, uniform low-grade oncocytic cells with flocculent to densely eosinophilic cytoplasmic vacuoles	$CD117^-$, $SDHB^-$, $SDHA^+$, $CK20^-$

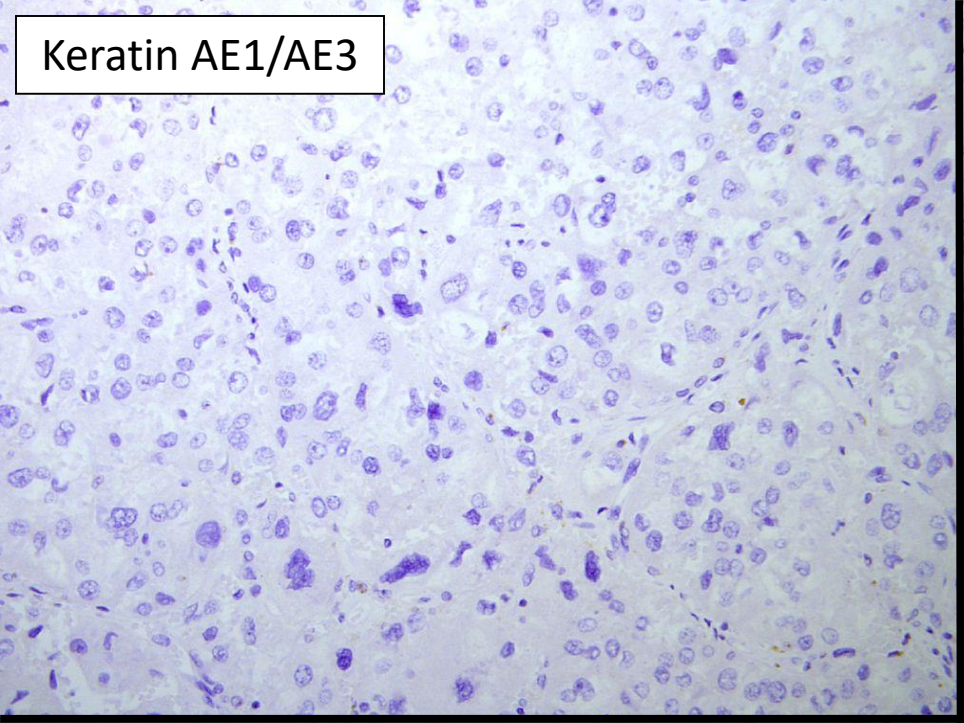
Case 6

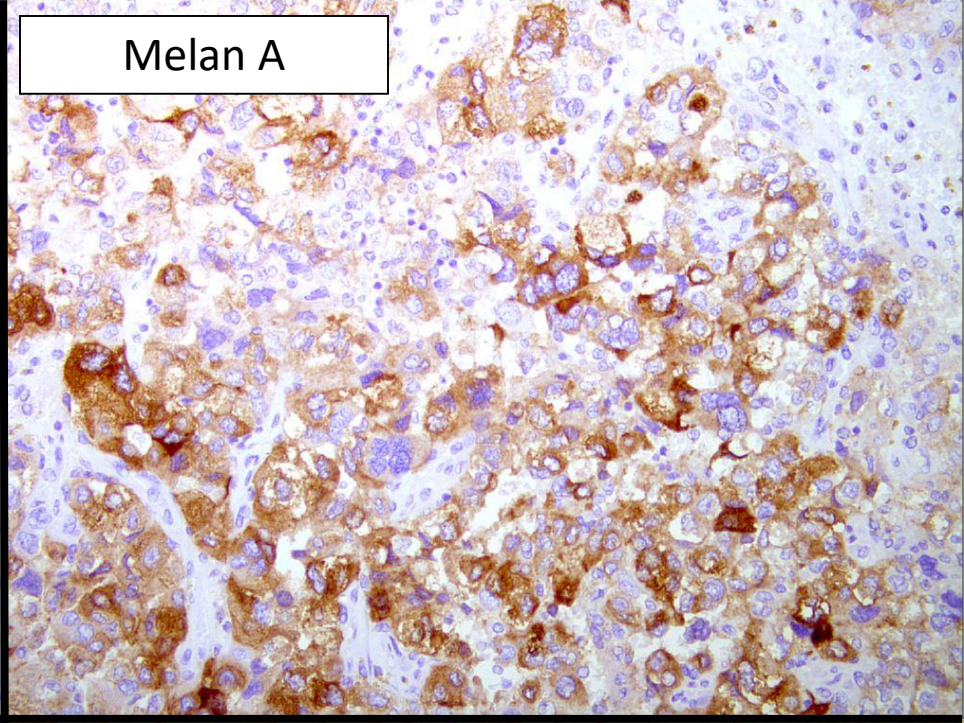
39 year-old male, bilateral renal masses 5.0 cm left renal mass, partial nephrectomy - previous right nephrectomy for “RCC of unknown histological subtype”

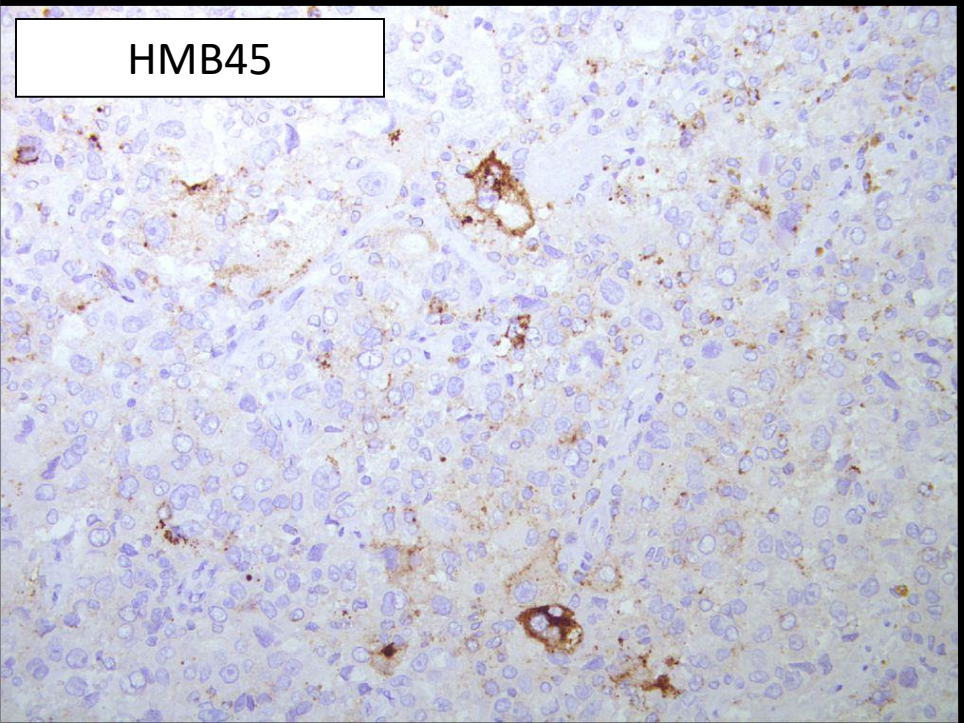


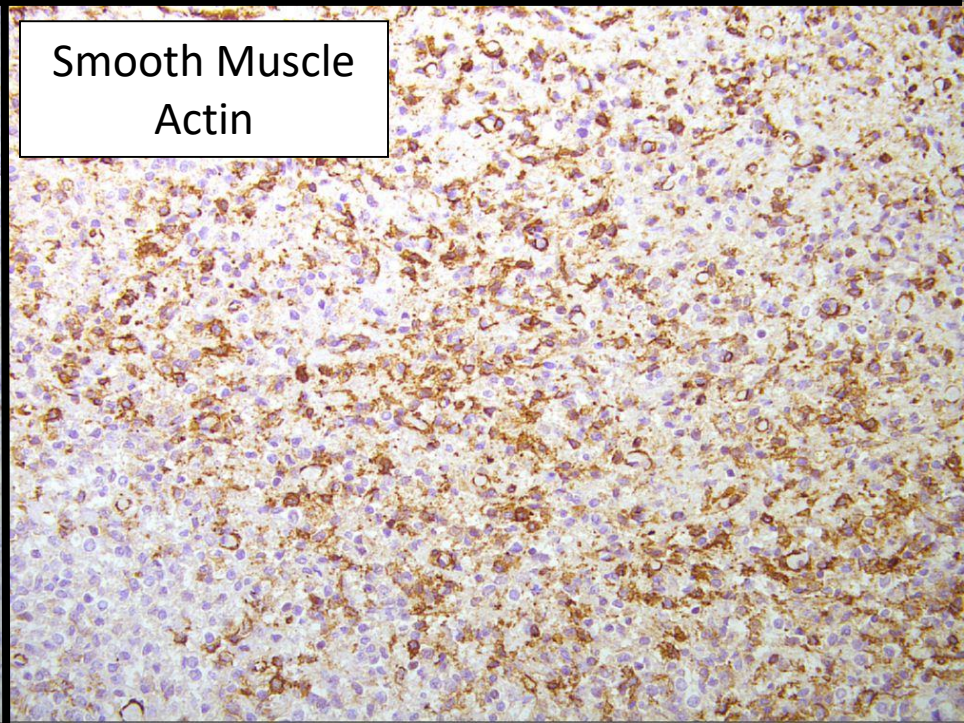


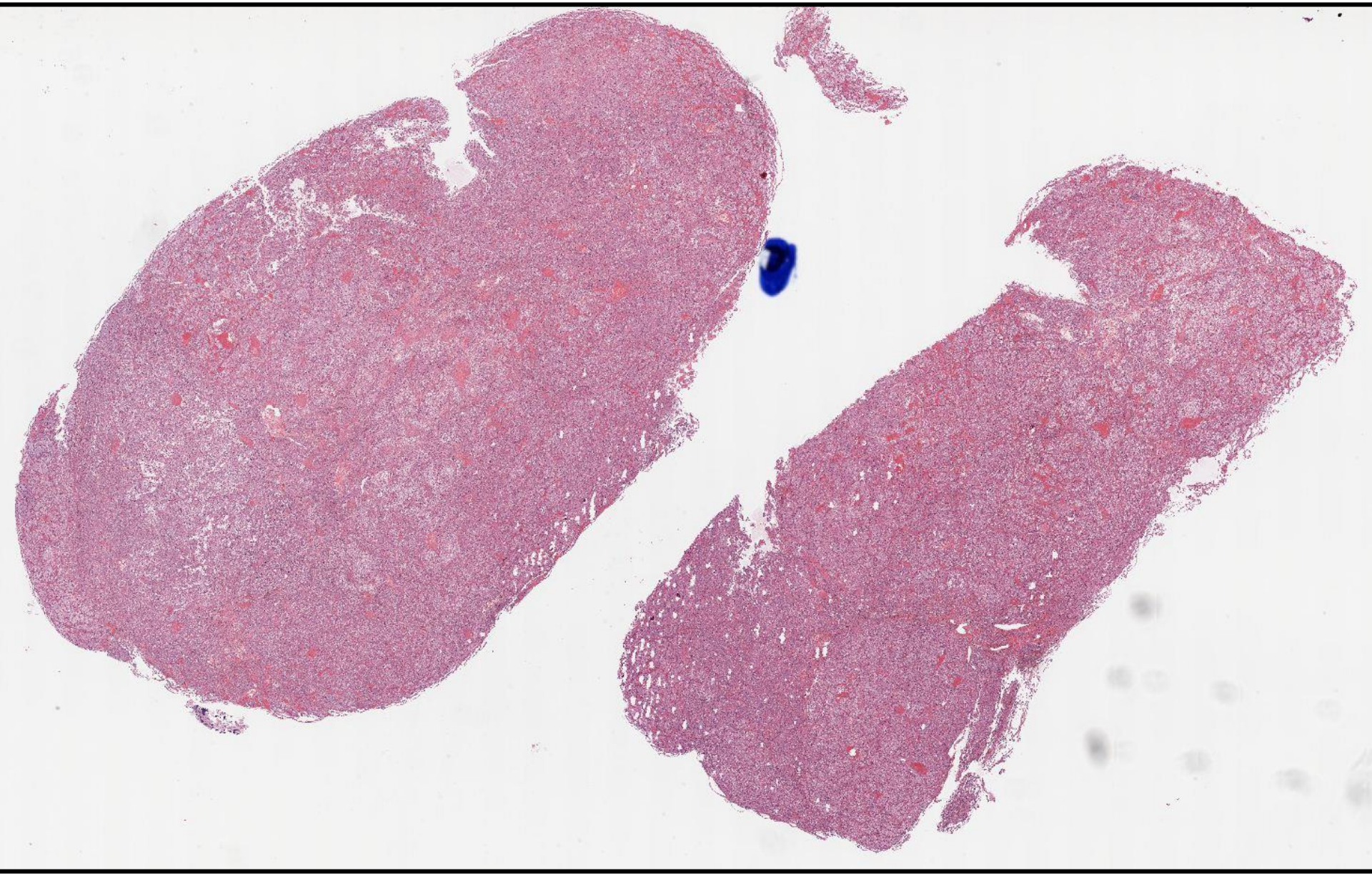


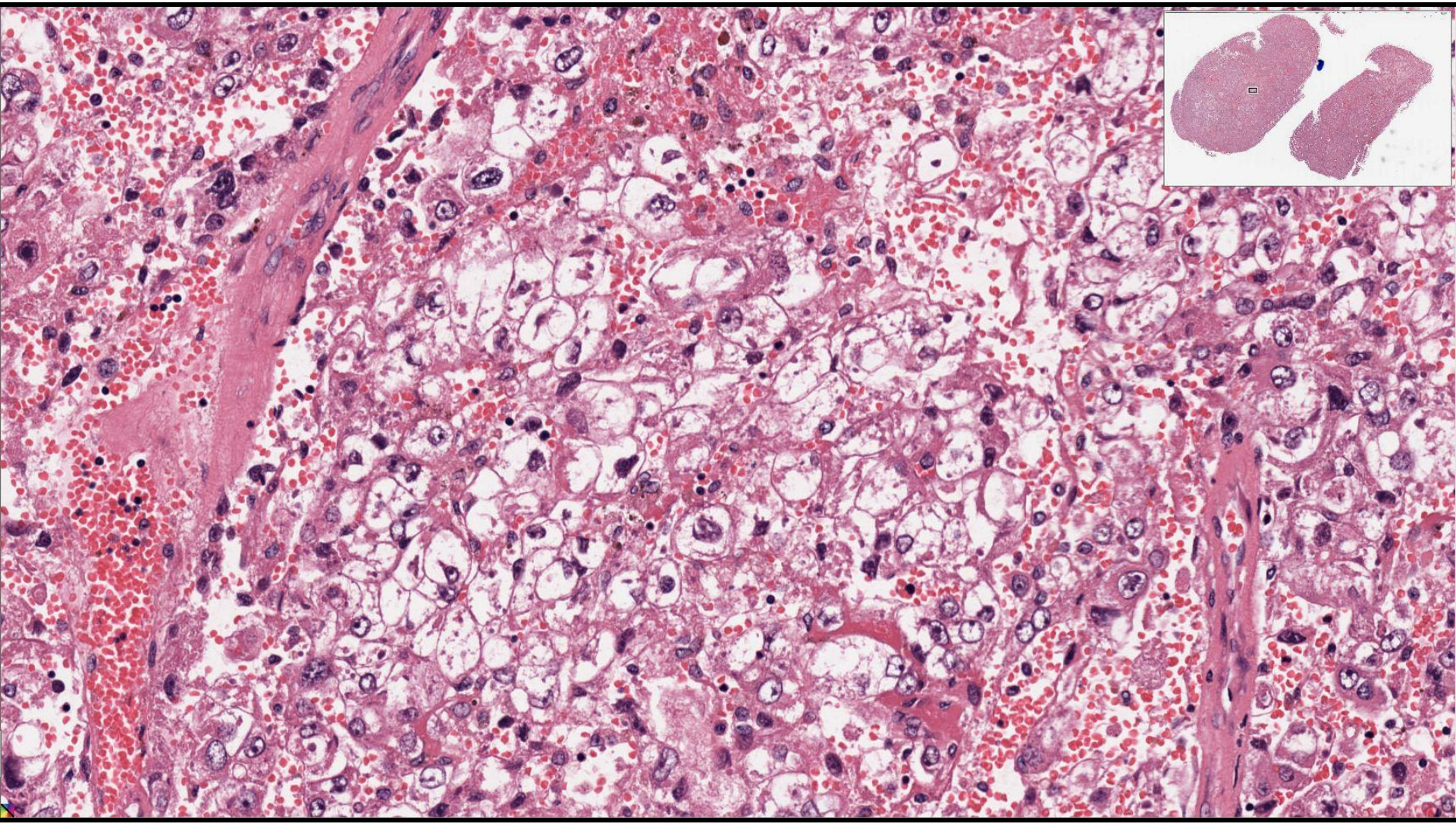

Keratin AE1/AE3


Melan A

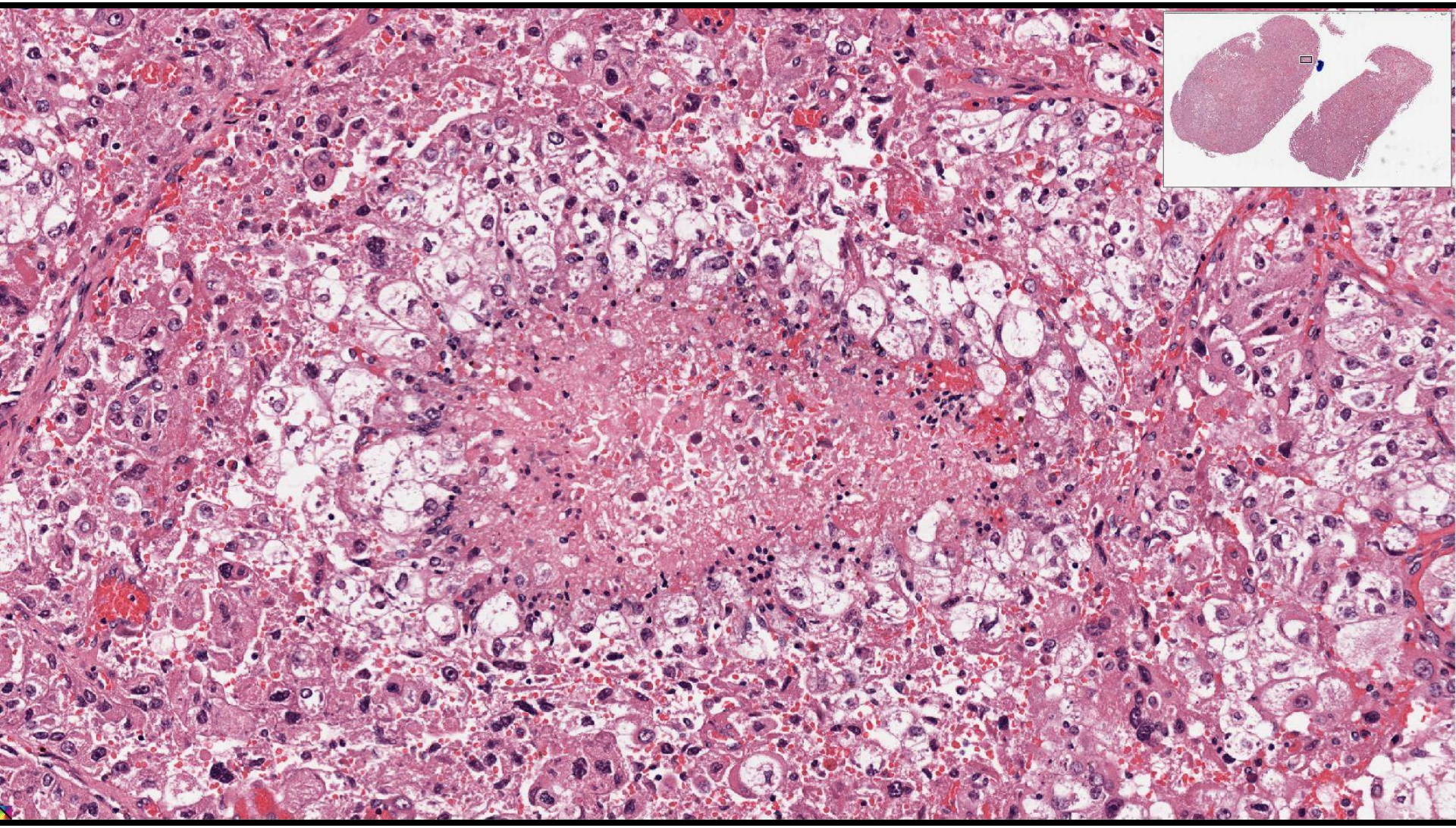

HMB45


Smooth Muscle Actin





Cytologic Atypia



Focal Necrosis

Atypical Epithelioid Angiomyolipoma

- typically follow benign course
- diagnostic confusion with:
  - clear cell RCC ± sarcomatoid features in TSC
  - Delgado *et al*, Cancer, **1998**
- rare malignant transformation - *sarcoma ex AML*
- metastases and death within 1 year
  - Pea *et al*, Am J Surg Pathol, **1998**

(*Am J Surg Pathol* 2010;34:715–722)

Renal Epithelioid Angiomyolipoma With Atypia: A Series of 40 Cases With Emphasis on Clinicopathologic Prognostic Indicators of Malignancy

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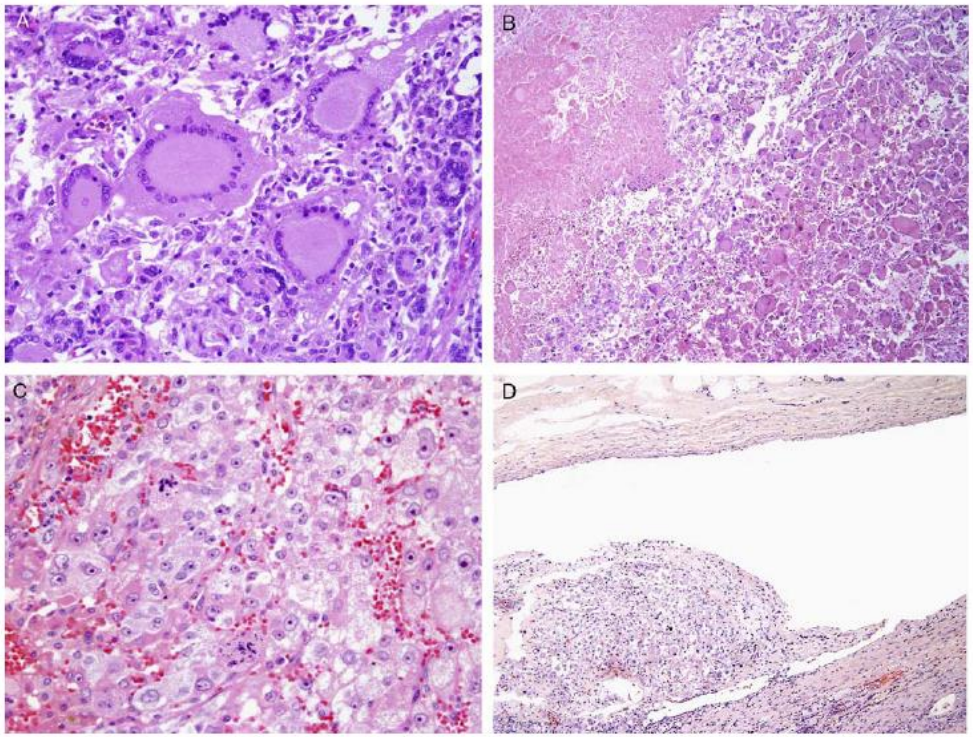

FIGURE 2. A, Neoplastic multinucleated giant cells with nuclei arranged peripherally in a ring-like fashion tracing the cell contour were seen in about half of cases of epithelioid AML with atypia. B, Coagulative necrosis in an epithelioid AML with severe atypia. C, Epithelioid AML with severe atypia showing atypical mitotic figures. D, Renal vein invasion was seen in a minority of cases.

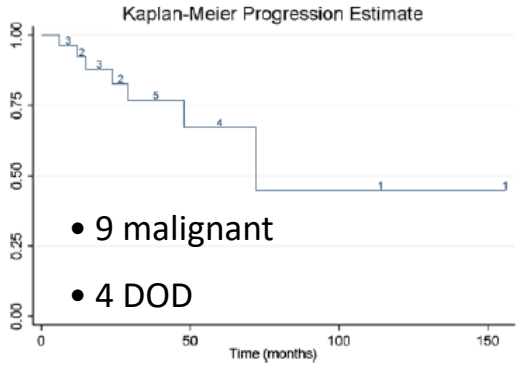

FIGURE 3. Kaplan-Meier progression estimate for epithelioid AML with atypia showing 2, 3, and 5 year estimated progression-free probabilities of 83%, 77%, and 67%, respectively.

TABLE 4. Pathologic Features Predictive of Malignancy in Epithelioid AML With Atypia

1. ≥ 70% atypical epithelioid cells
2. ≥ 2 mitotic figures per 10 hpf
3. Atypical mitotic figures
4. Necrosis

Three or more of the above features predicts increased risk of clinically malignant behavior.

Renal Angiomyolipoma

Clinicopathologic Study of 194 Cases With Emphasis on the Epithelioid Histology and Tuberous Sclerosis Association

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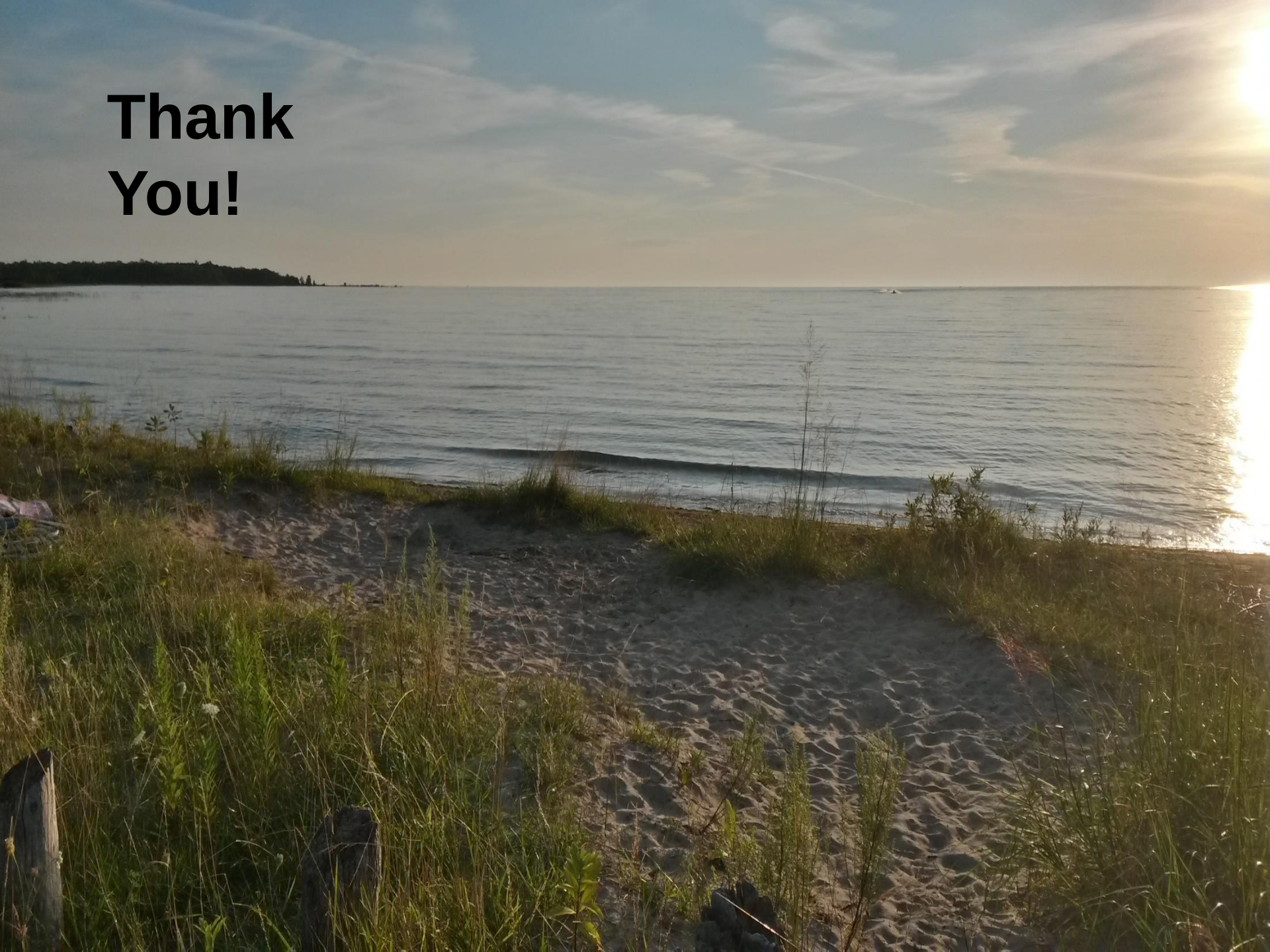
(*Am J Surg Pathol* 2009;33:289–297)

TABLE 1. Clinical Features of Epithelioid and Nonepithelioid Renal Angiomyolipomas

	Epithelioid AML (n = 15)	Nonepithelioid AML (n = 179)	*P*
Mean age at surgery (y)	38.6	52.3	0.000
Male/female	1:6.5	1:4	NS
Clinical presentation			0.007
Non-TSC	11 (73.3%)	167 (93.3%)	
TSC	4 (26.7%)	12 (6.7%)	
Size (cm, range)	8.6 (1-30)	5.6 (0.2-35)	0.021
Follow-up available	15/15 (100%)	137/179 (76.5%)	0.034
Follow-up duration			NS
Mean	5.1	3.0	
Range	0.1-19.9	0.1-23.7	
Recurrence/ metastasis	0	0	NS

TABLE 3. Clinicopathologic Features of Renal Angiomyolipomas in Patients With and Without Tuberous Sclerosis Complex

	Associated With TSC (n = 16)	Not Associated With TSC (n = 178)	*P*
Mean age	31.5	53.0	< 0.001
Male to female ratio	1:1.3	1:3.5	NS
Mean size (cm) and range	12.9 (2.5-35)	5.3 (0.2-28)	< 0.001
Epithelioid AML	4 (25.0%)	11 (6.2%)	0.007
Epithelial cyst	7 (43.5%)	6 (3.4%)	< 0.001
Microscopic AML foci			< 0.001
Present	10 (62.5%)	11 (6.2%)	
Mean number	26.2	5.3	
Range	7-50	1-12	


Thank
You!