

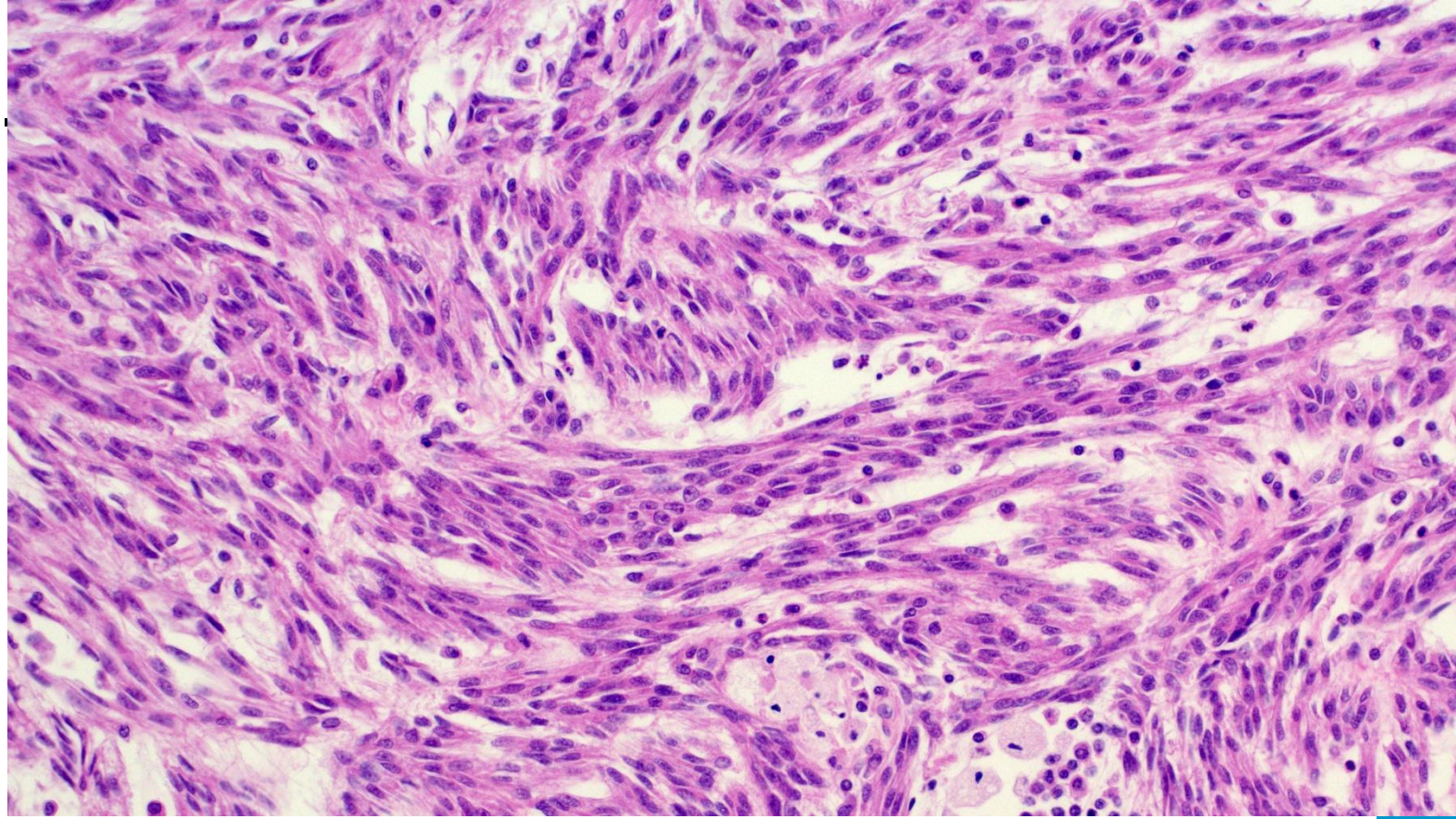
Mesenchymal GU Lesions: An overview

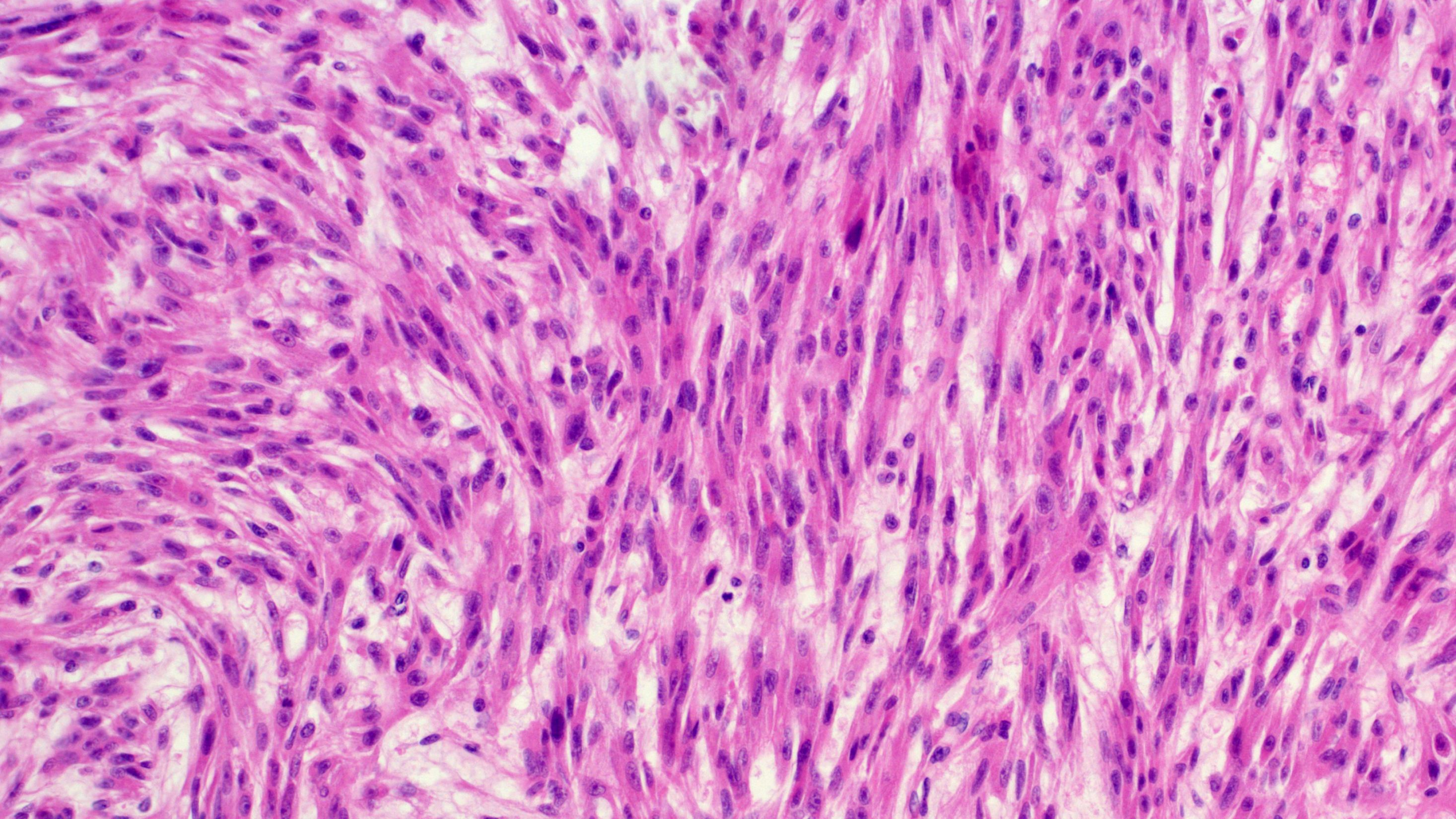
Abbas Agaimy, MD
Institut für Pathologie
Universität Erlangen, Germany
Abbas.agaimy@uk-erlangen.de



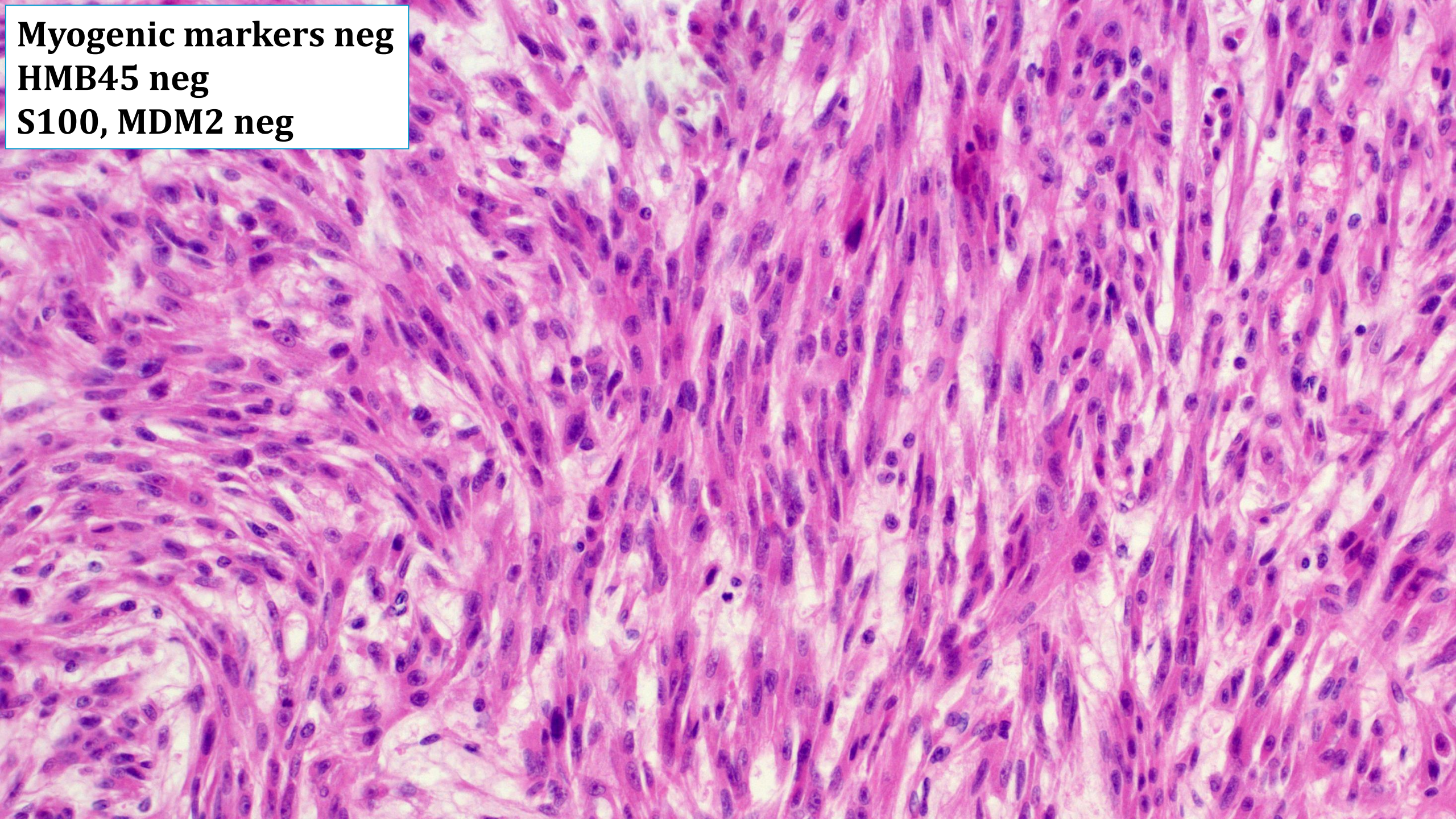
Mesenchymal GU Lesions: teaching case

- 58 yo female with large cortical kidney mass, confined to the kidney.
- Radical NE.
- Monomorphic spindle cells.
- Compact fascicles.
- Low mitotic activity.

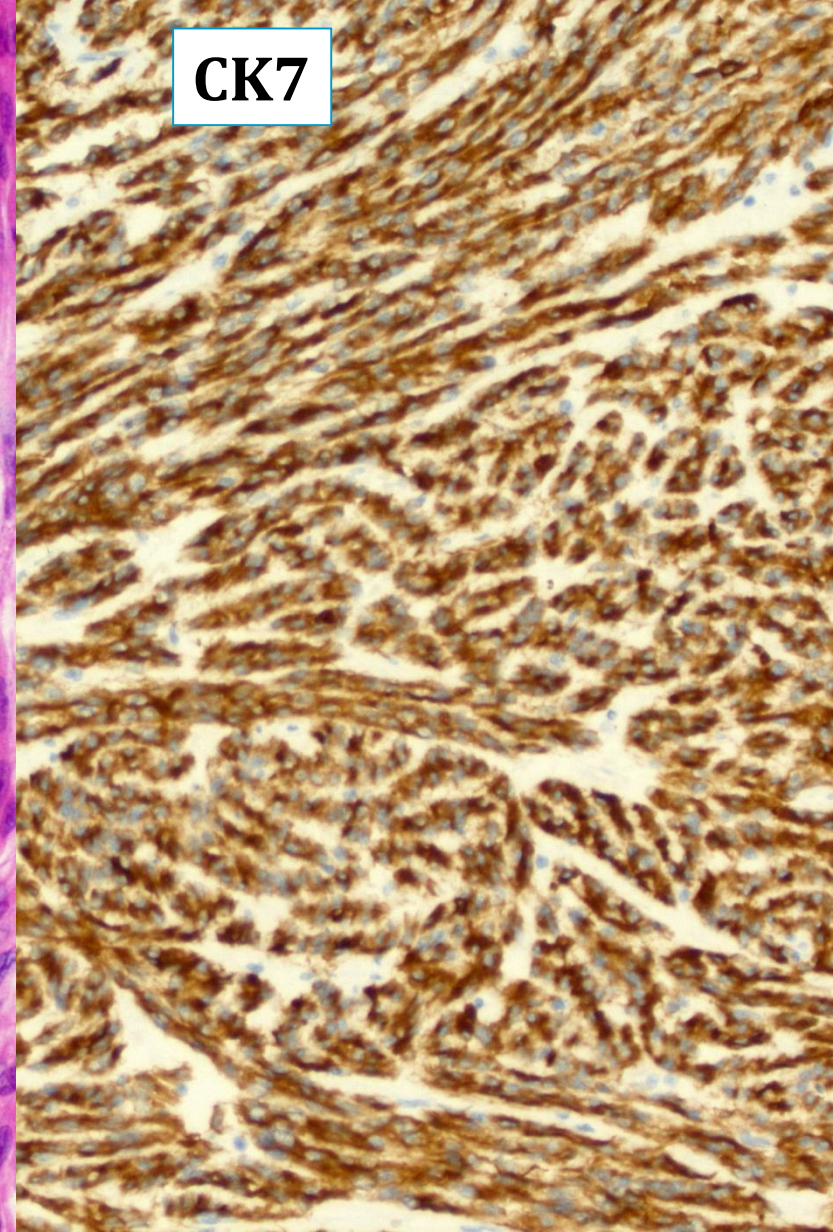
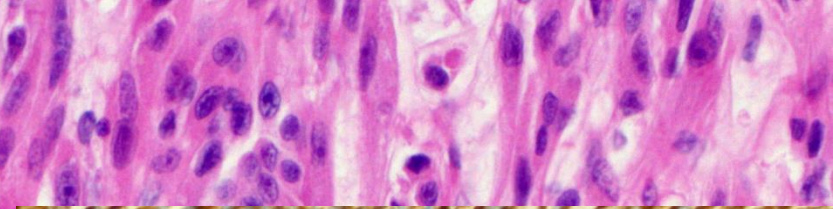
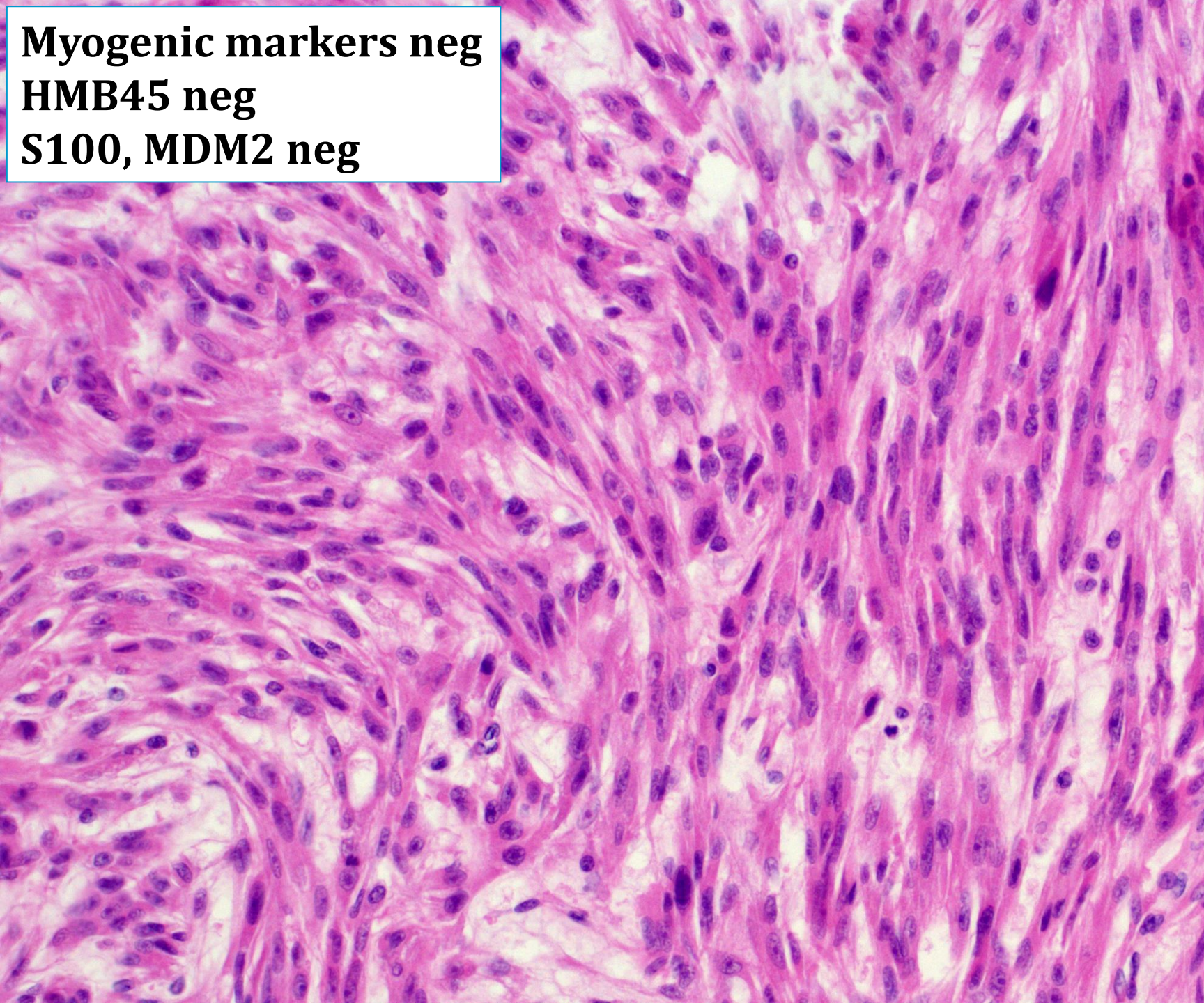




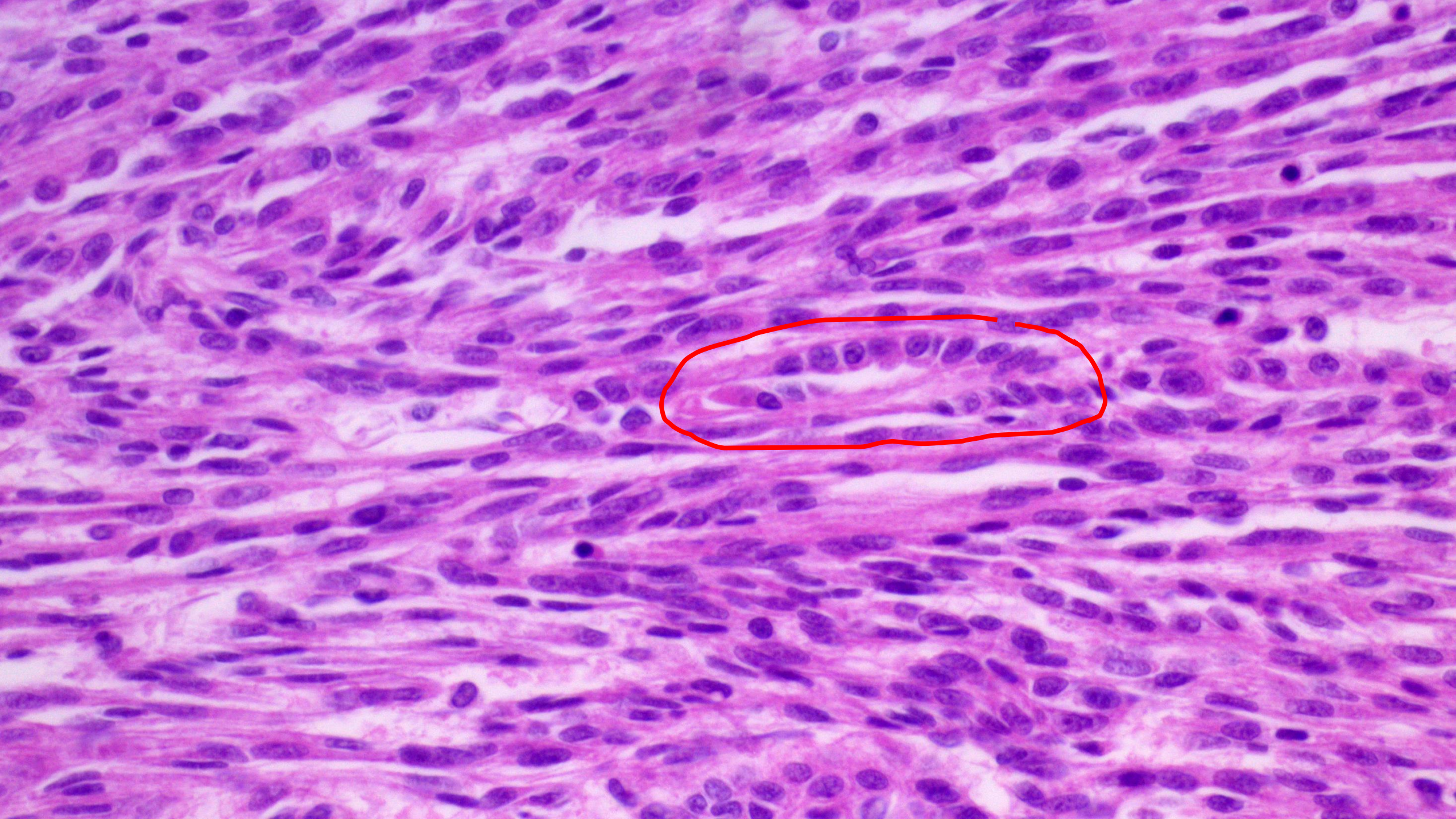
Myogenic markers neg
HMB45 neg
S100, MDM2 neg



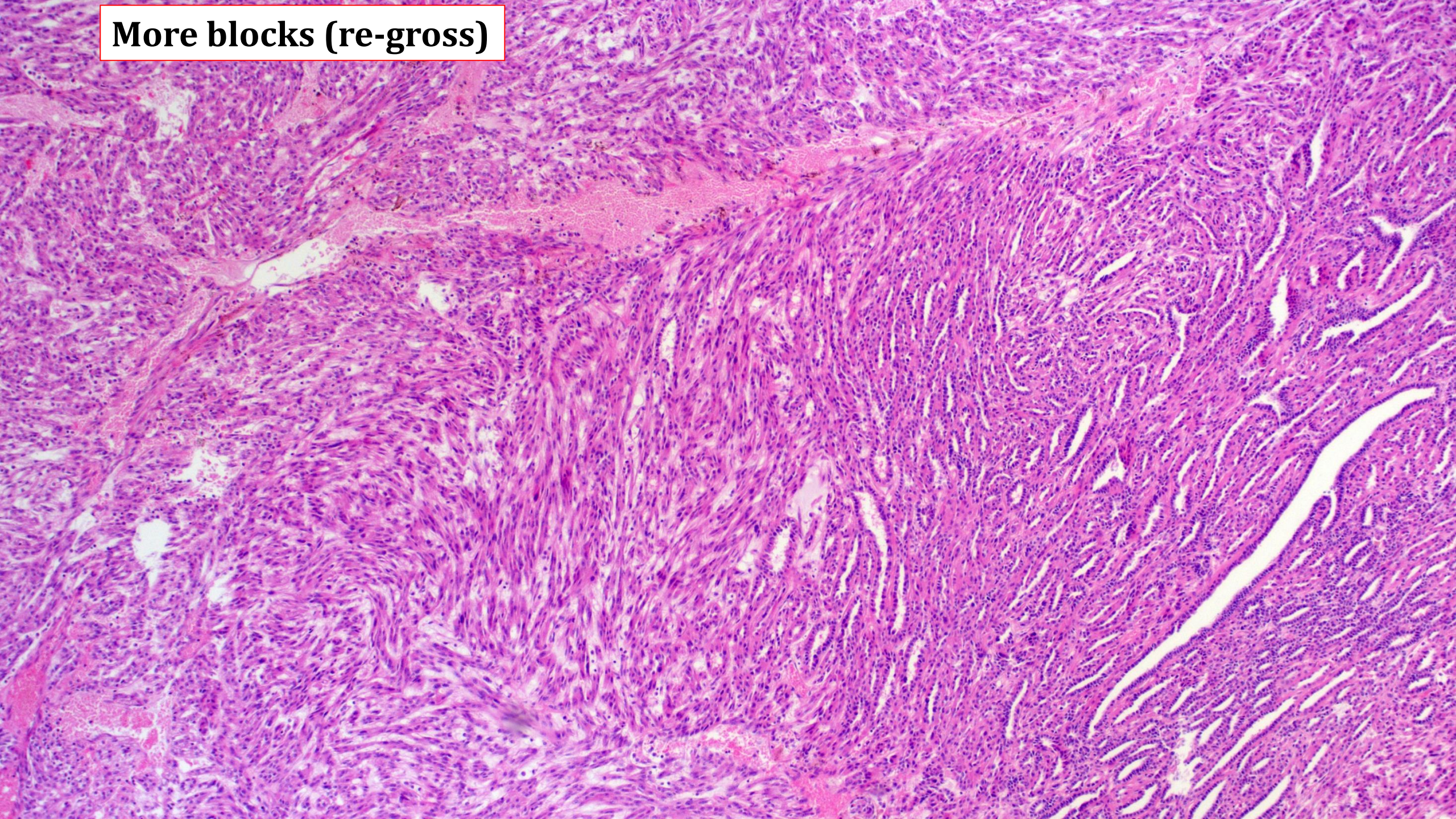
Myogenic markers neg
HMB45 neg
S100, MDM2 neg



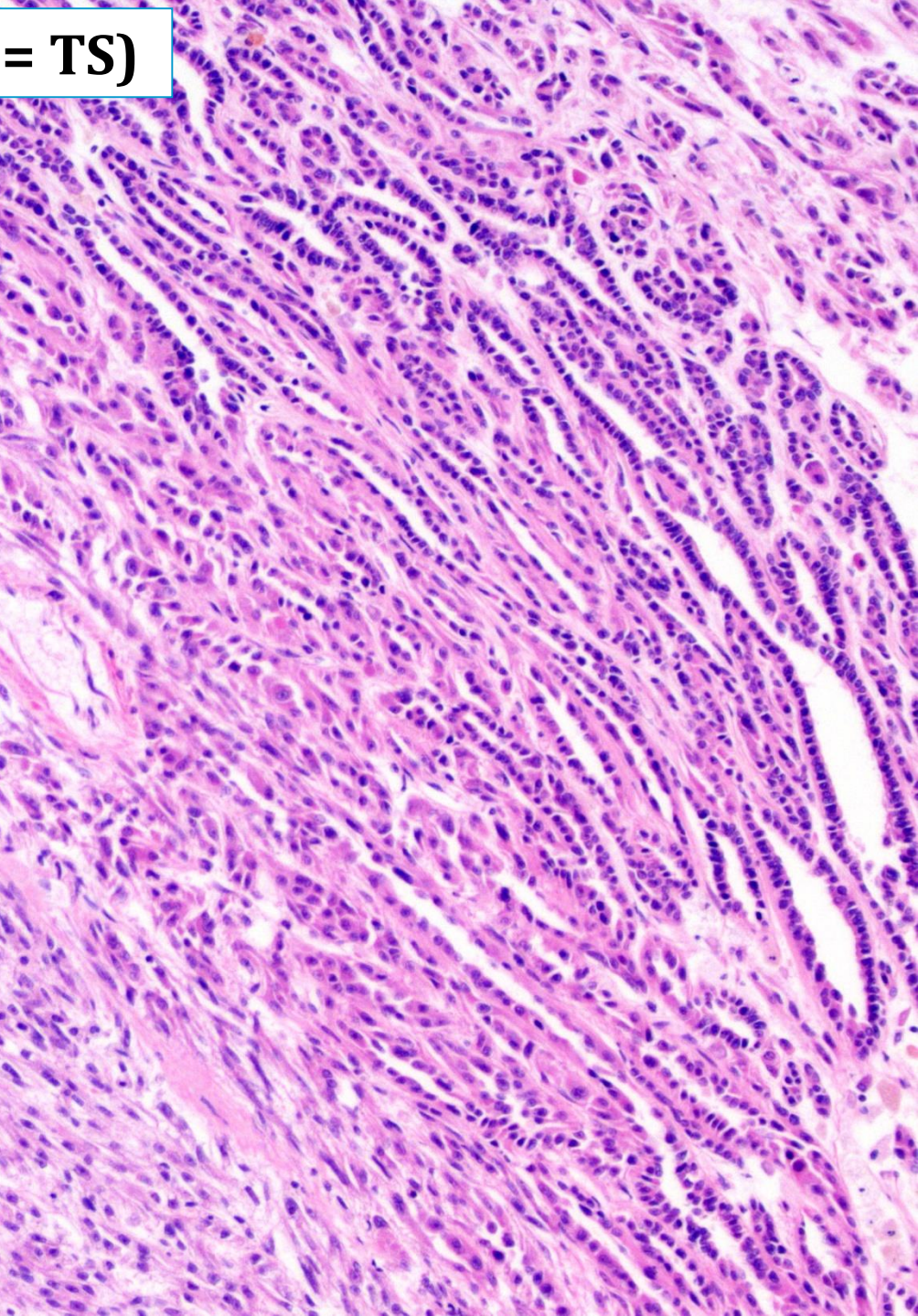
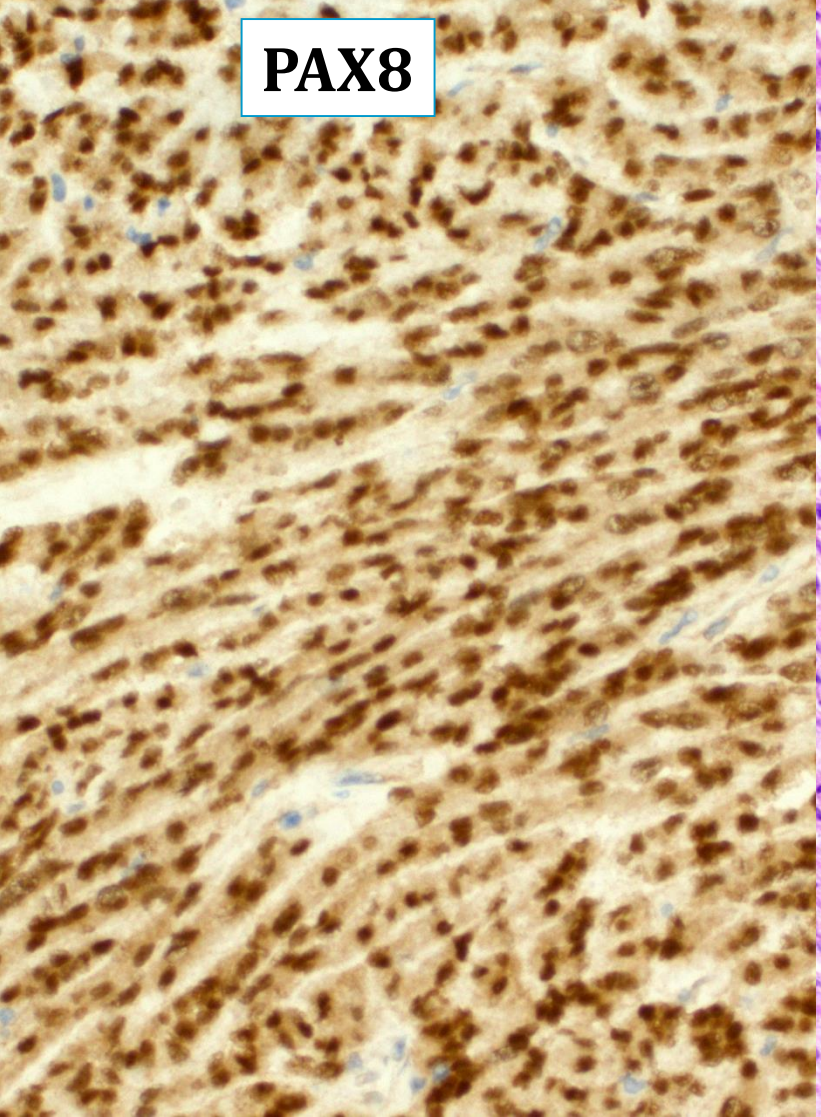
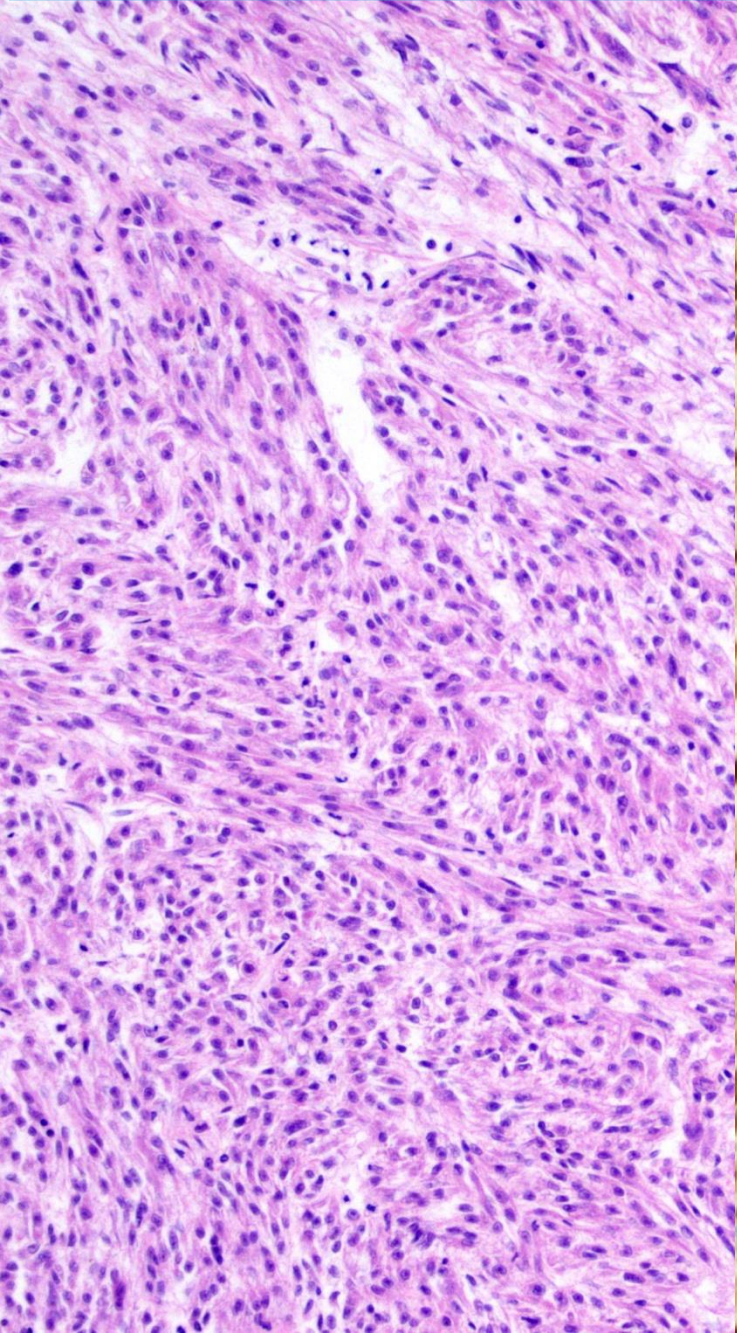
CK7



More blocks (re-gross)



Mucinous-tubular-spindle cell RCC (here the MTS-M = TS)



Mesenchymal GU Lesions:

Before considering genuine mesenchymal lesions, beware of the spindle cell change in common RCC types

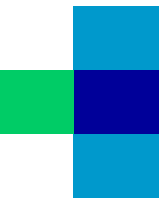
- Mucinous-tubular –spindle cell RCC is the prototype of this group.
- Uncommon: bland spindle cell change in ccRCC (low-grade).
- Sarcomatoid RCC (high-grade morphology).

Pankeratin & PAX8 most helpful



Mesenchymal GU Lesions: benign, intermediate & aggressive biology

- Uncommon but diverse.
- Problem might be just to find a good name.
- Uncertainty might lead to overtreatment.
- Mostly homogeneous = Biopsy usually representative.
- Imaging much helpful (size, fat? medullary vs. cortical, renal vs. perirenal, prostatic vs. paraprostatic, etc.).
- Age & exact site most important.



Mesenchymal GU Lesions: distinctive anatomic, & clinical profiles

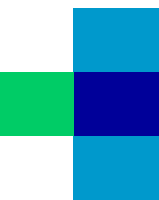
10.0: Mesenchymal tumours

- 10.0.0.1: Mesenchymal tumours: Introduction
- 10.0.1: Fibroblastic and myofibroblastic tumours
 - 10.0.1.1: The angiofibroma family of tumours → Paratestis/ spermatic cord/ inguinal
 - 10.0.1.2: Solitary fibrous tumour → ubiquitous
 - 10.0.1.3: Inflammatory myofibroblastic tumour → Almost bladder only
- 10.0.2: Vascular tumours
 - 10.0.2.1: Haemangioma → Most kidney, rare bladder
 - 10.0.2.3: Angiosarcoma → Almost bladder only
- 10.0.3: Pericytic (perivascular) tumours
 - 10.0.3.1: Glomus tumour
 - 10.0.3.2: Myointimoma → penis
 - 10.0.3.4: Myopericytoma
 - 10.0.3.3: Extrarenal PEComa
- 10.0.4: Smooth muscle tumours
 - 10.0.4.1: Leiomyoma
 - 10.0.4.2: Leiomyosarcoma → Most kidney, rare bladder
- 10.0.5: Skeletal muscle tumours
 - 10.0.5.1: Rhabdomyosarcoma → Bladder, rare prostate, children
- 10.0.6: Tumours of uncertain differentiation
 - 10.0.6.1: Synovial sarcoma → kidney
 - 10.0.6.2: Extrarenal rhabdoid tumour
 - 10.0.6.3: Desmoplastic small round cell tumour → Paratestis/ rarely kidney

WHO 2022

Mesenchymal Renal Lesions: benign & intermediate biology

- Angiomyolipoma & PEComas.
- **Hemangiomas (anastomosing variant).**
- **Inflammatory pseudotumors.**
- Renomedullary fibromas.
- Metanephric stromal tumors.
- Juxtaglomerular cell tumors.
- Perivascular myoid (glomus, myopericytoma, etc.).



Mesenchymal kidney lesions: Anastomosing hemangioma

- Renal vascular tumors are rare.
- To date <300 hemangioma & <50 angiosarcomas reported.
- Most are incidental but may present macrohematuria.
- Rarely associated with systemic disorders (Klippel-Trenaunay & Sturge-Weber Syndrome).
- **9% of ESRD kidneys contain hemangiomas.**

Mesenchymal kidney lesions:

Anastomosing hemangioma

- 30% associated with ESRD.
- Main hemangioma type in GU.
- Variable architecture (often mistaken for angiosarcoma).
- Reminiscent of splenic sinusoids.
- Benign, no recurrences.
- IHC +: CD31, CD34, FVIII, ERG. FLI-1.
- Neg.: D2-40, HHV8, GLUT-1.
- Most reveal GNA11, GNA14 or GNAQ mutations.

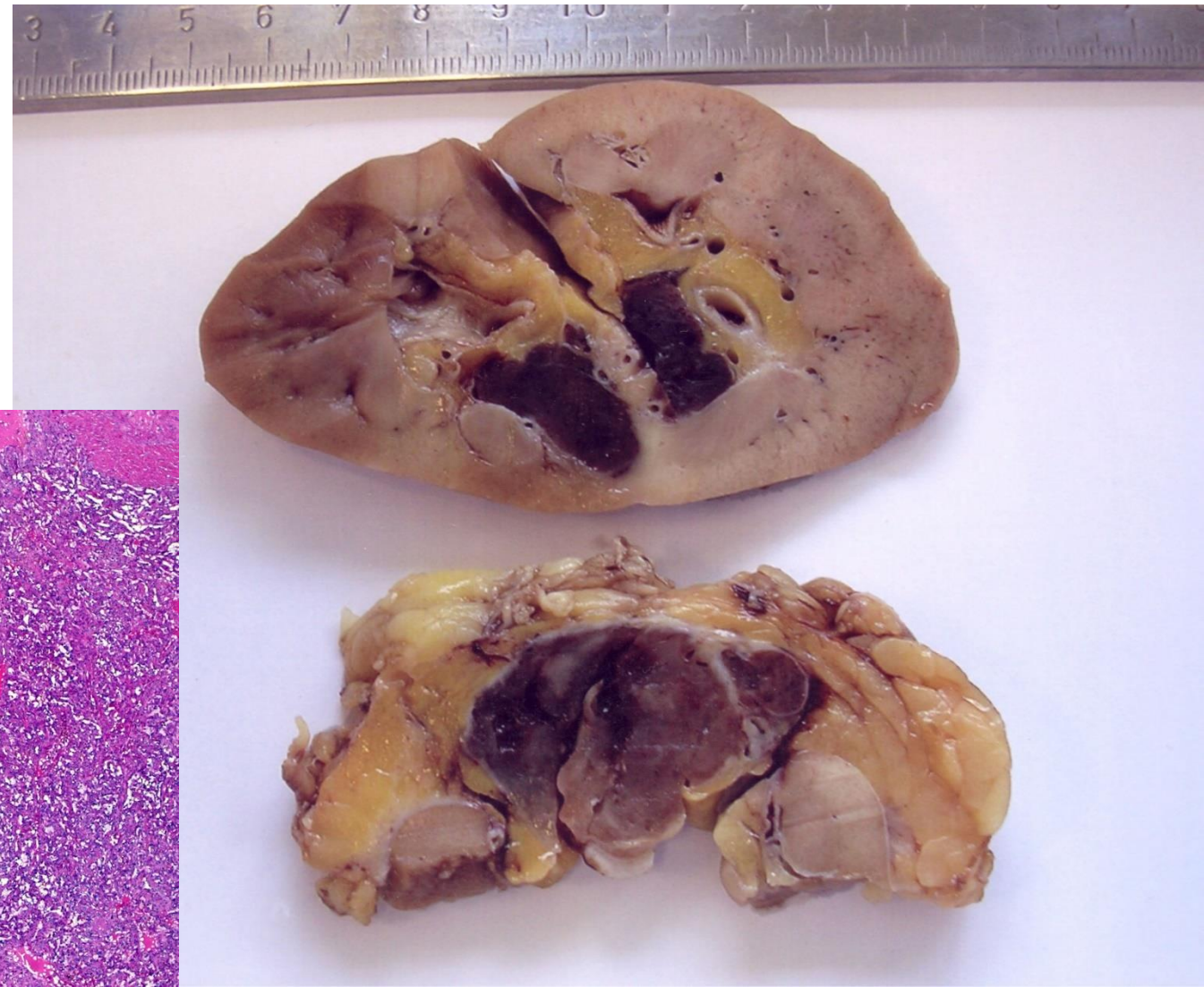
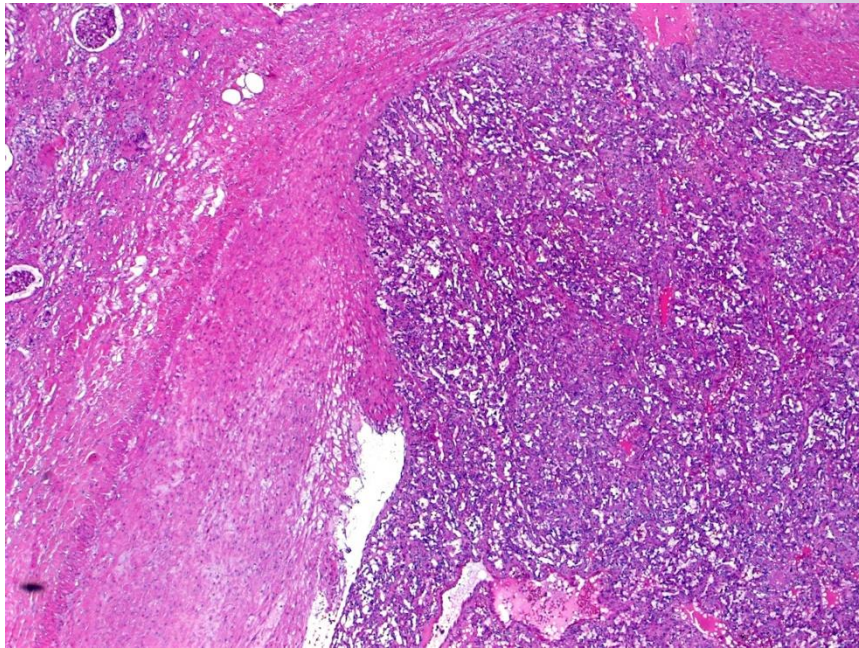


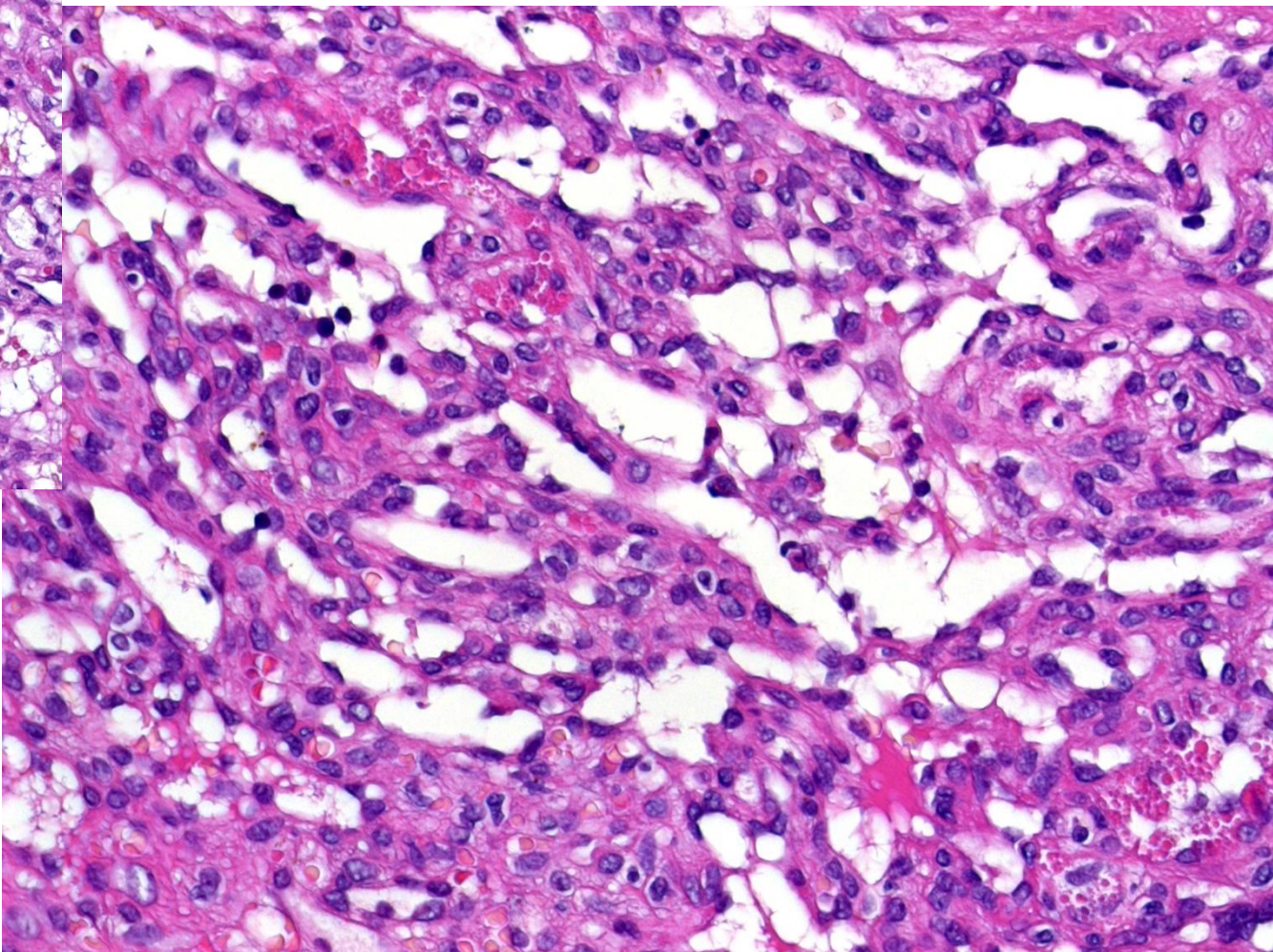
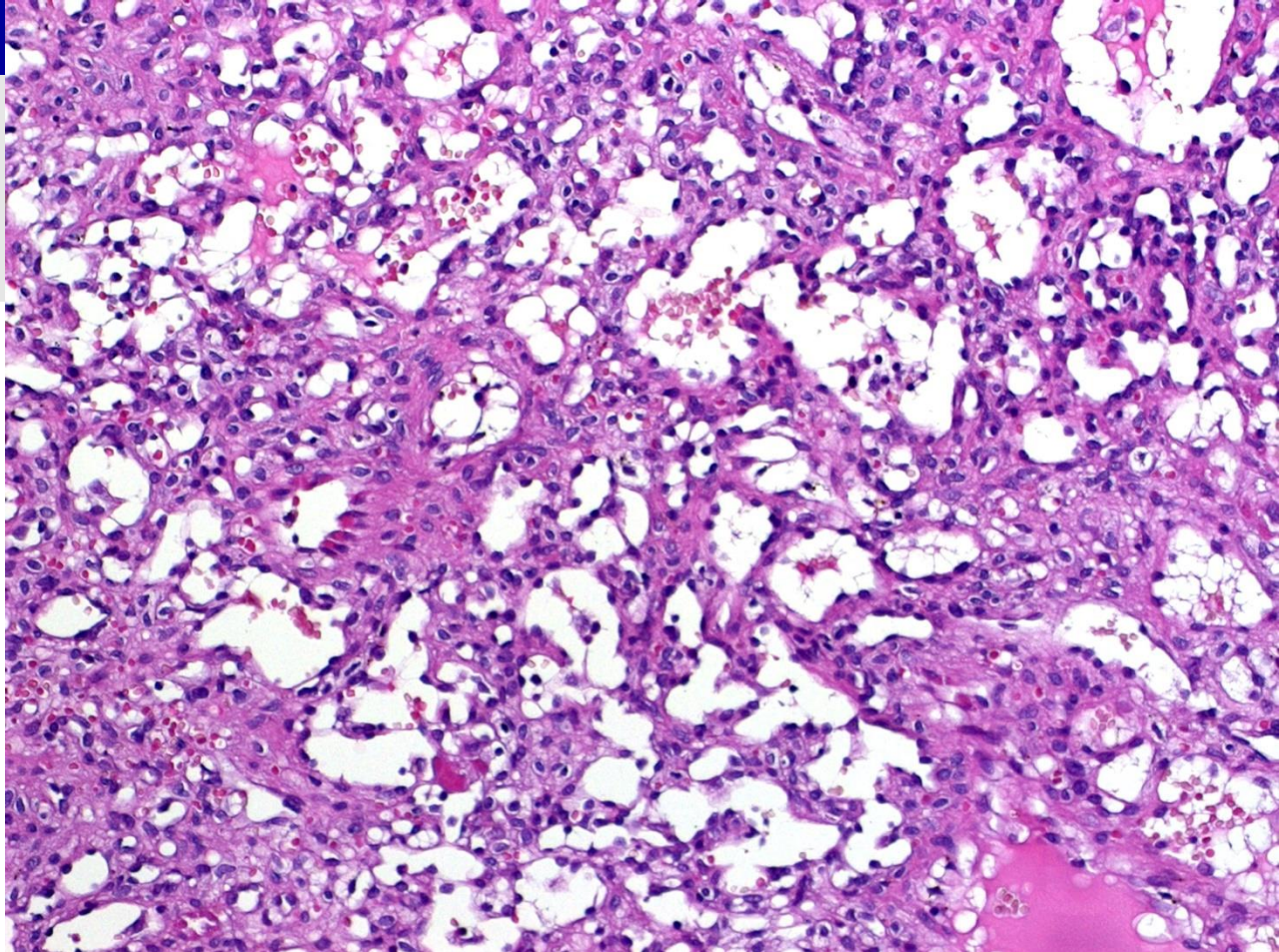
Mesenchymal kidney lesions: Anastomosing hemangioma

Frequently medullary/ perihilar.

May involve perirenal tissue.

Rarely intravascular.



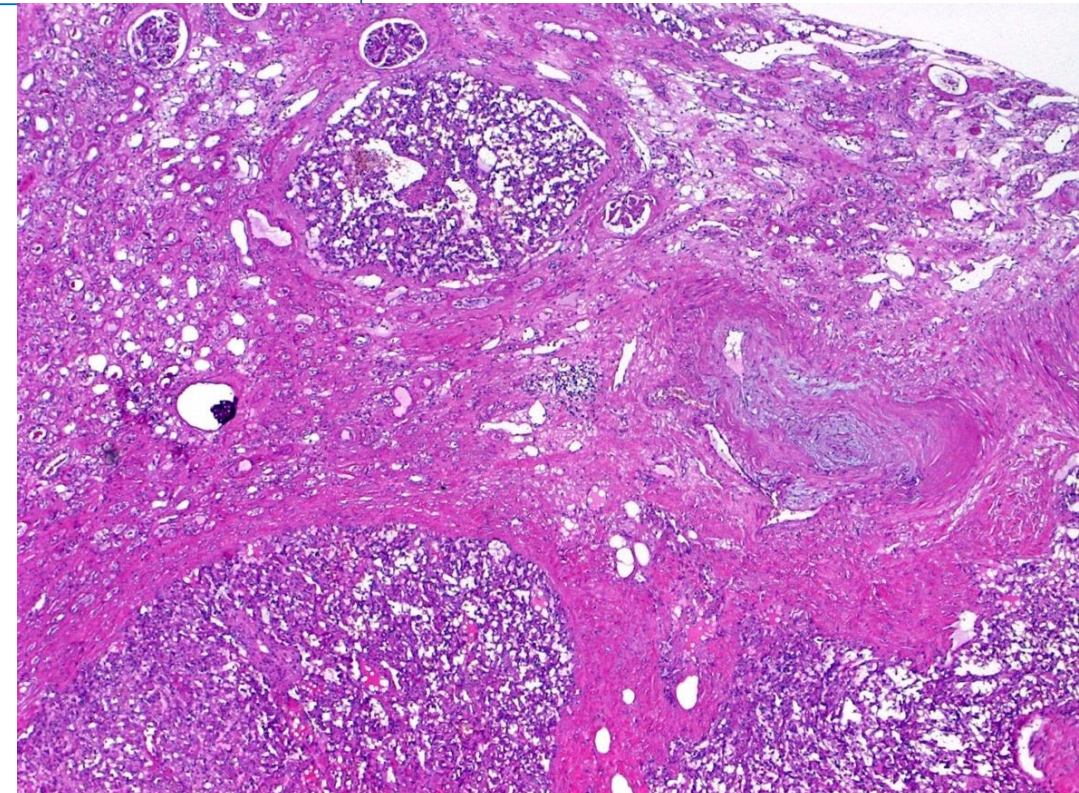


Benign mesenchymal tumours and tumour-like lesions in end-stage renal disease

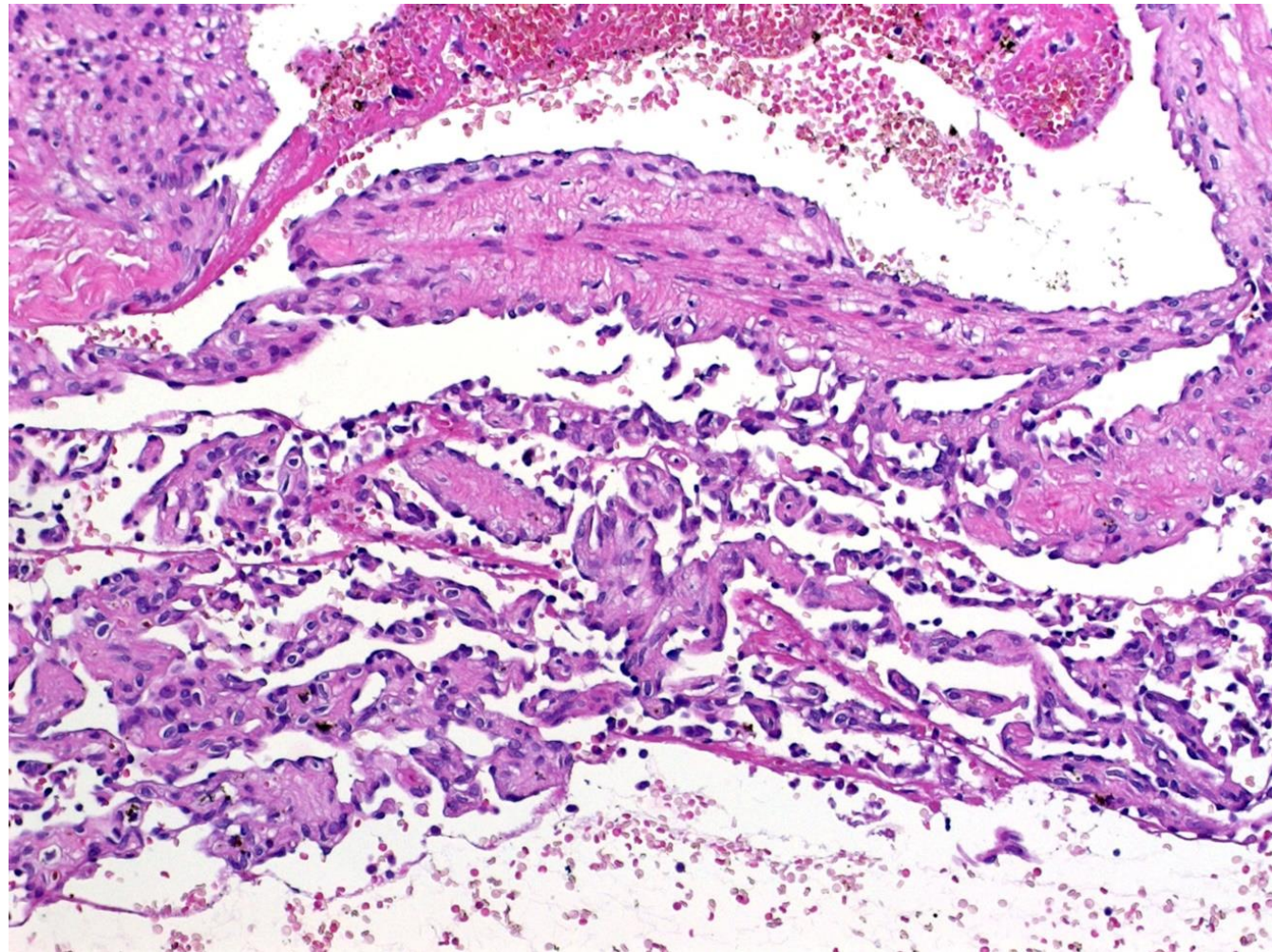
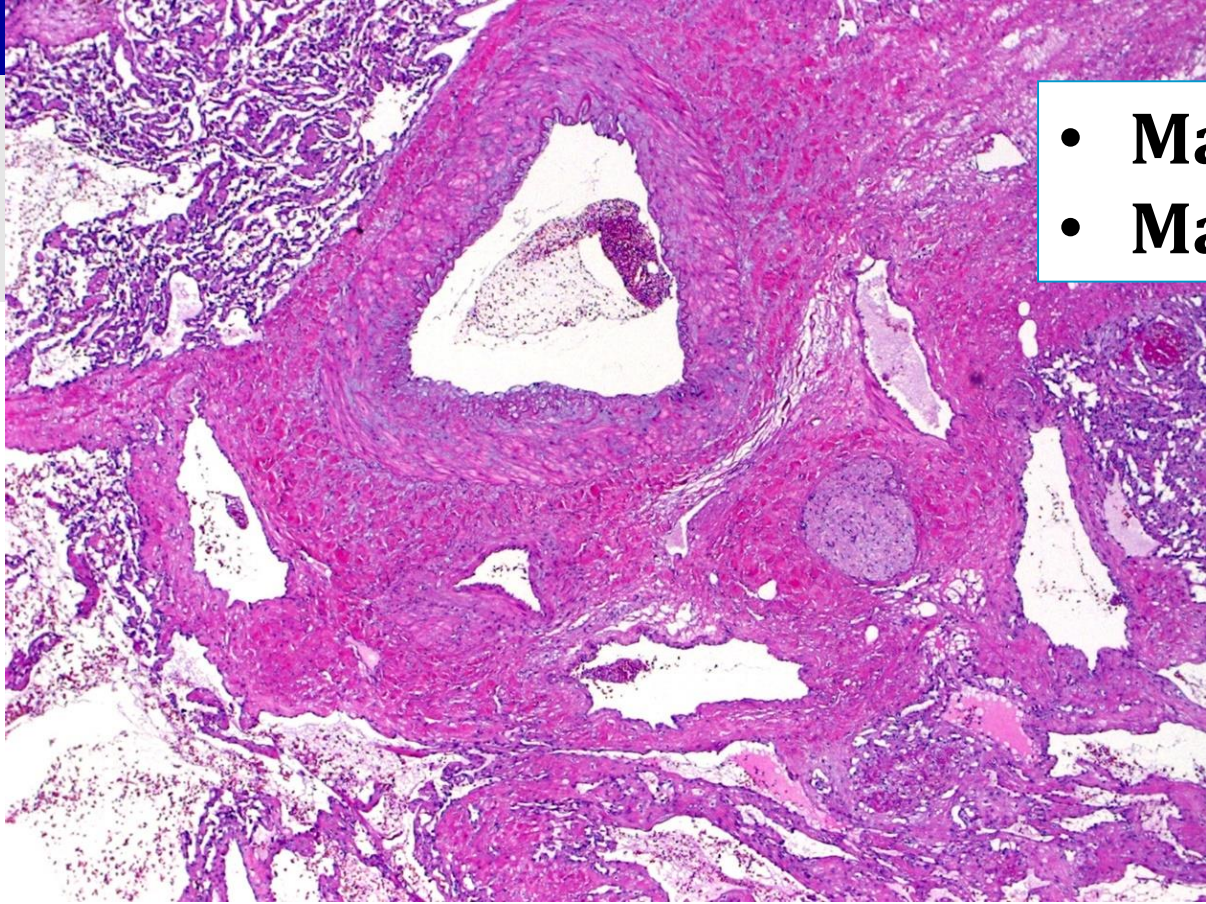
Maike Büttner,¹ Verena Kufer,¹ Kathrin Brunner,² Arndt Hartmann,² Kerstin Amann¹ & Abbas Agaimy²

¹*Institute of Pathology, and* ²*Department of Nephropathology, University Hospital of Erlangen, Erlangen, Germany*

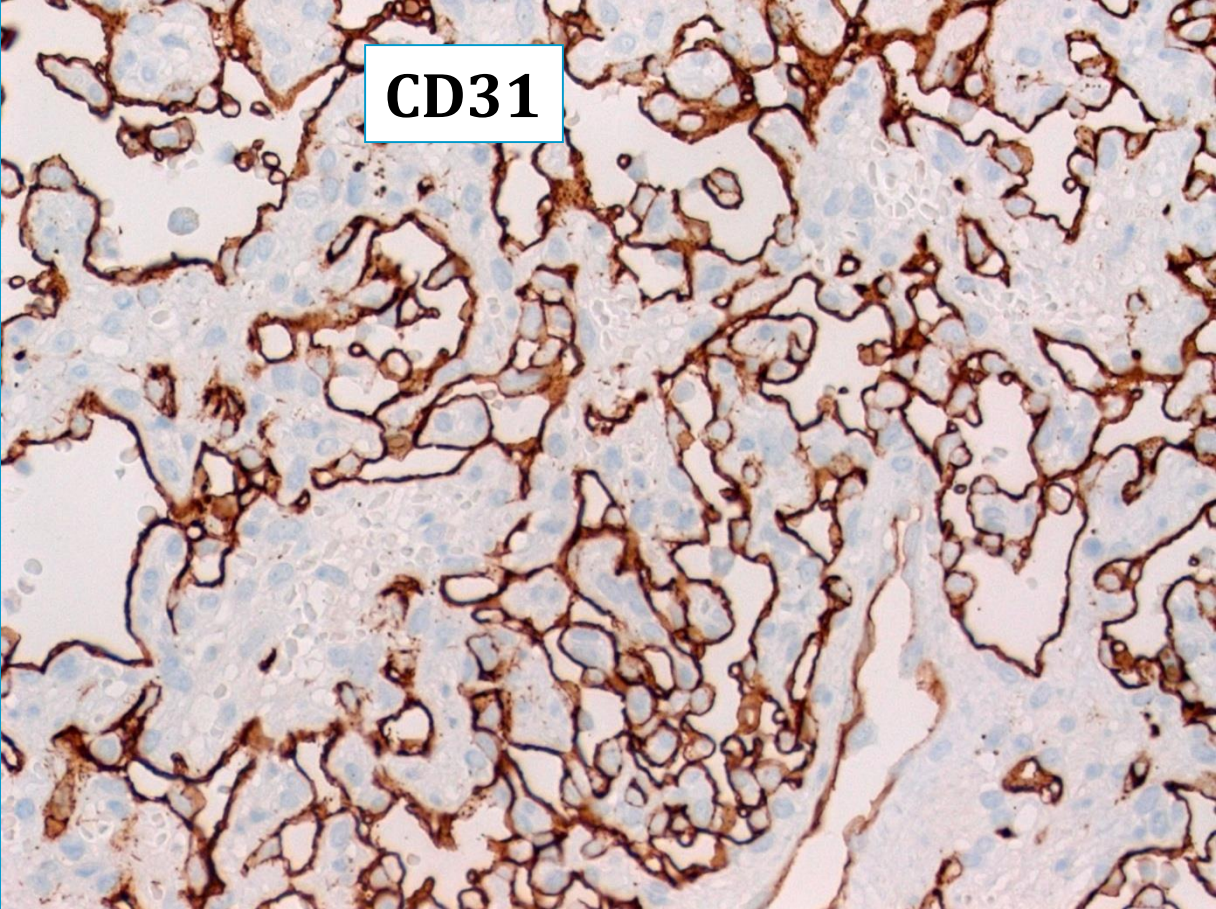
**Multiple lesions in ESRD
May mimic invasion**



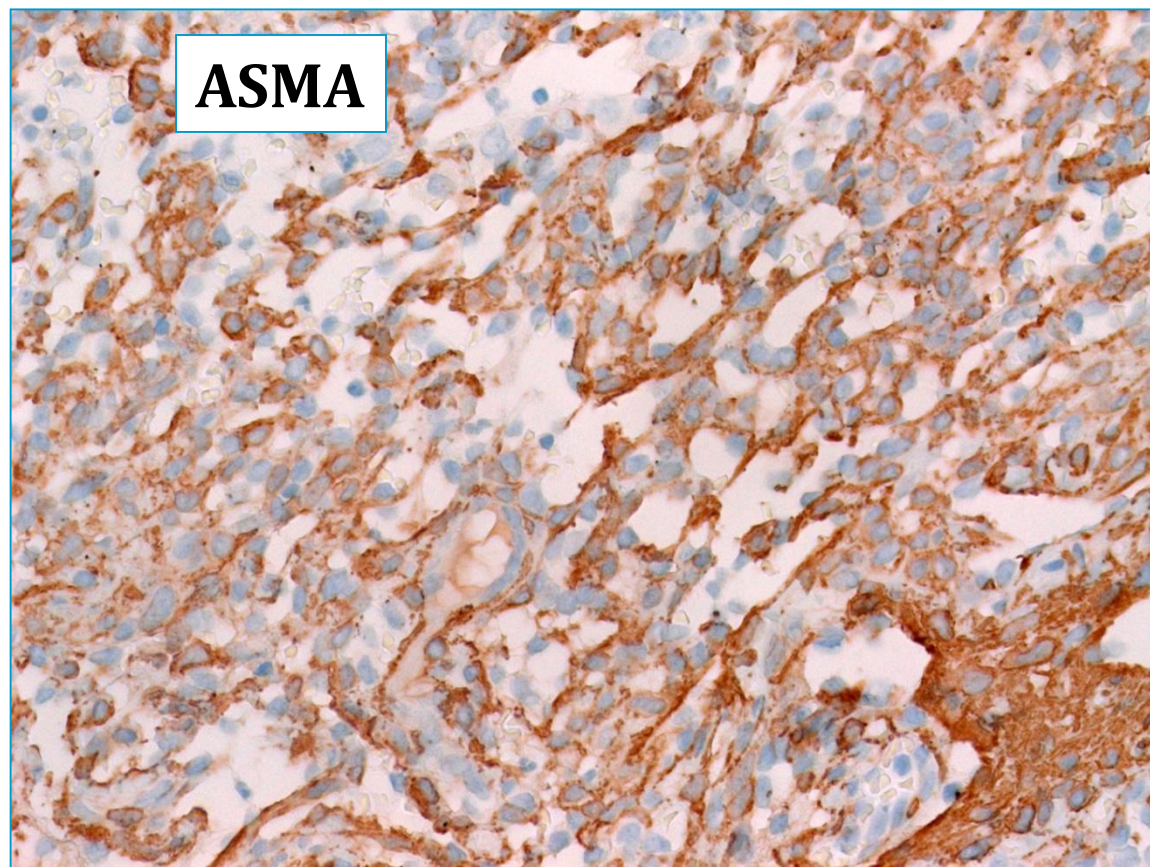
- May be associated with hilar veins
- May show endovascular growth



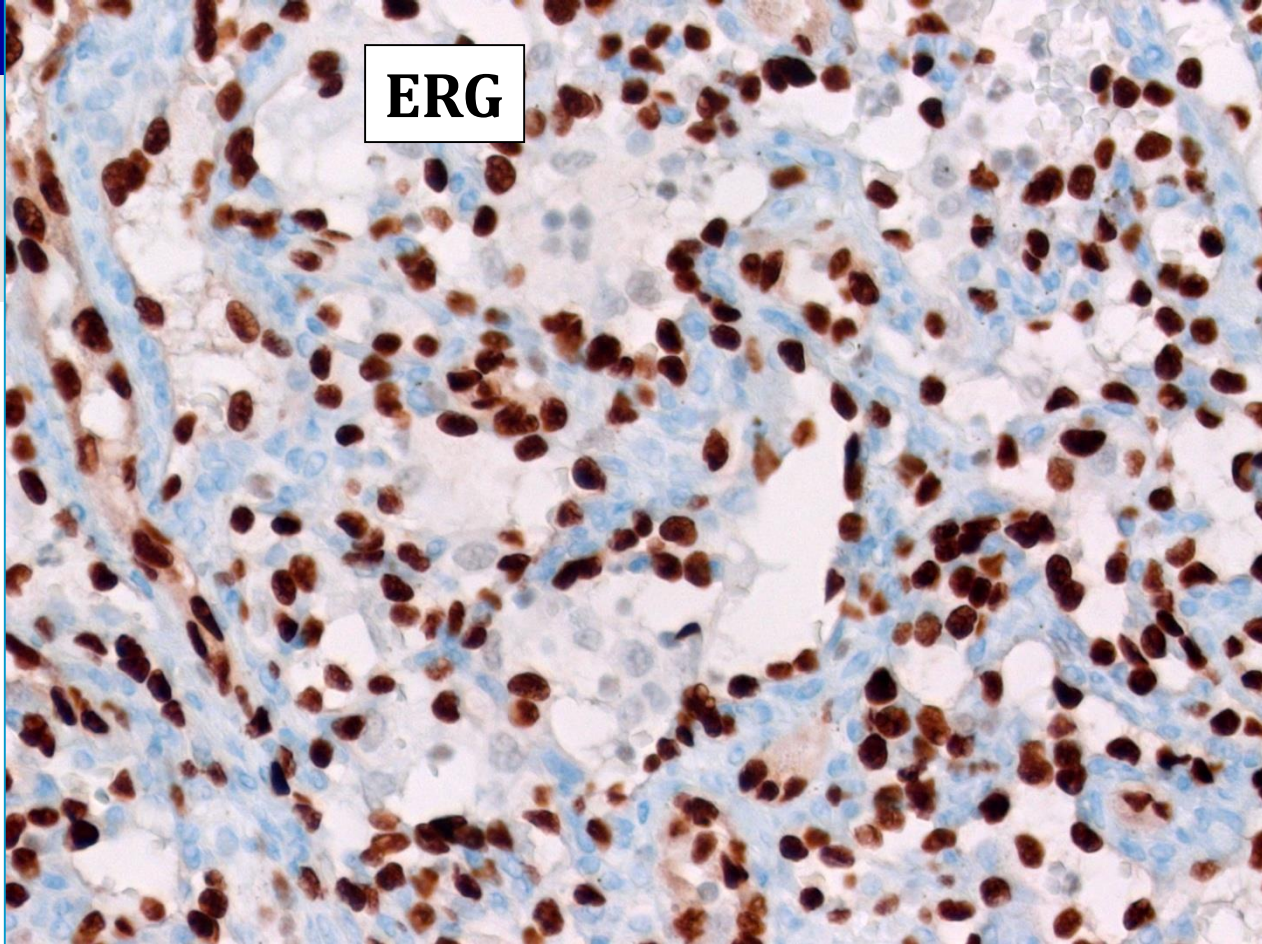
CD31



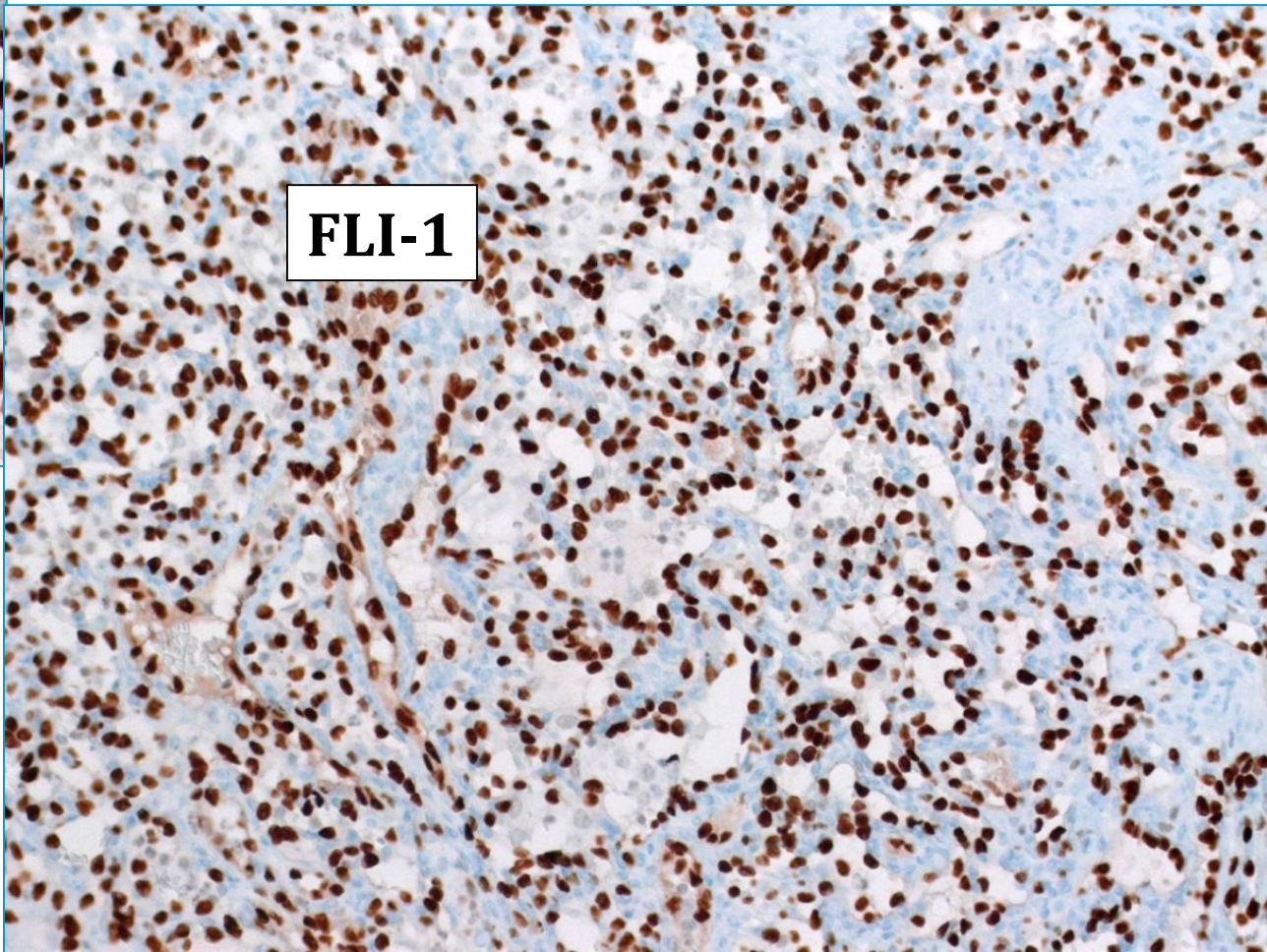
ASMA



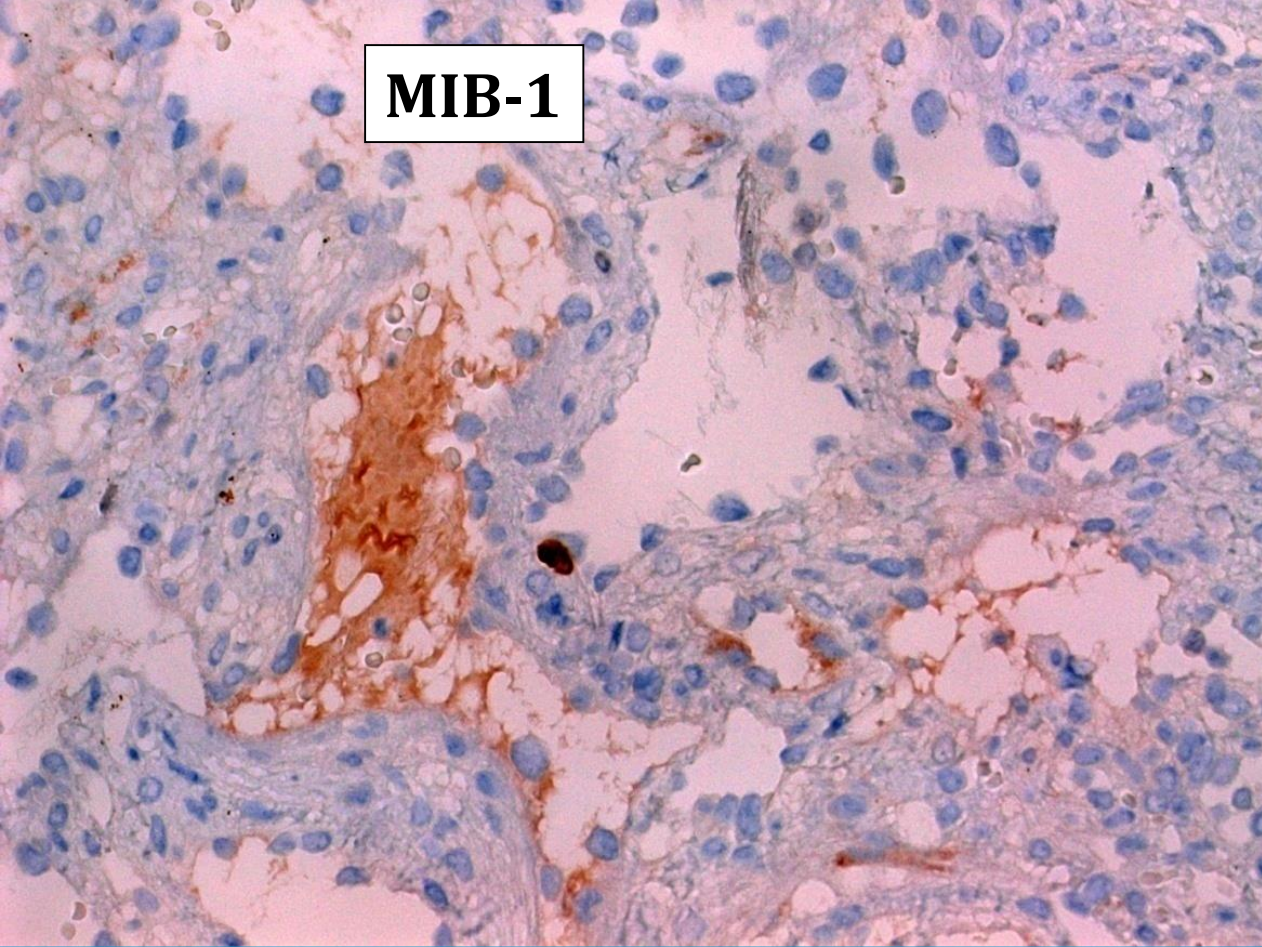
ERG



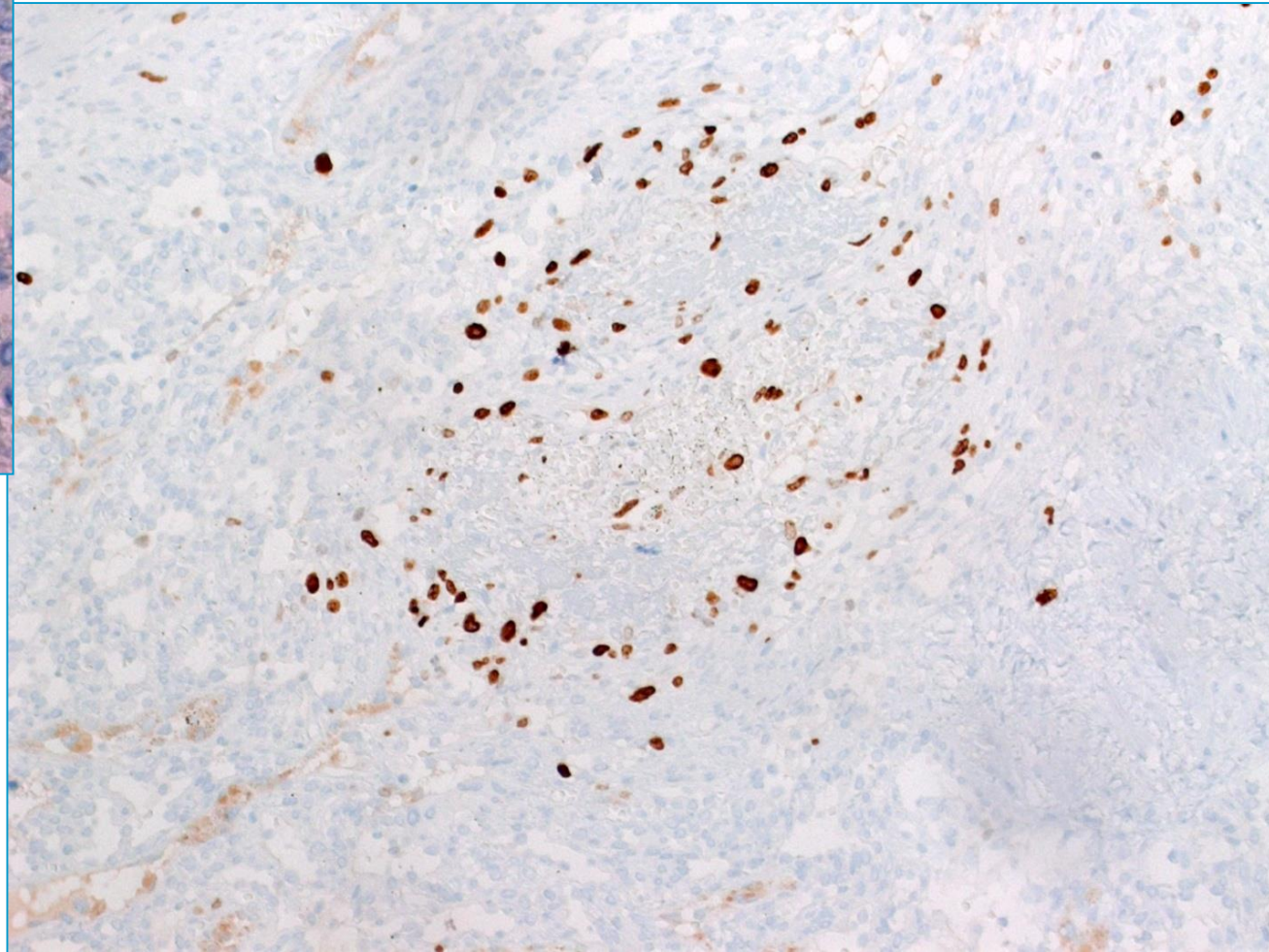
FLI-1

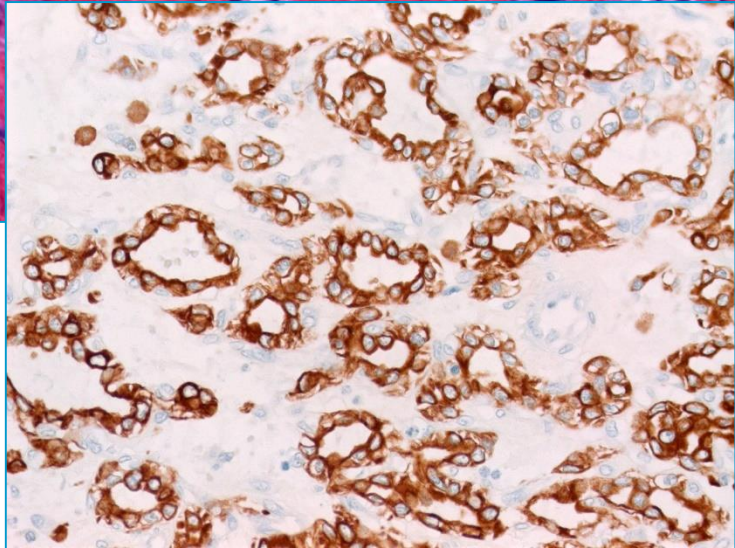
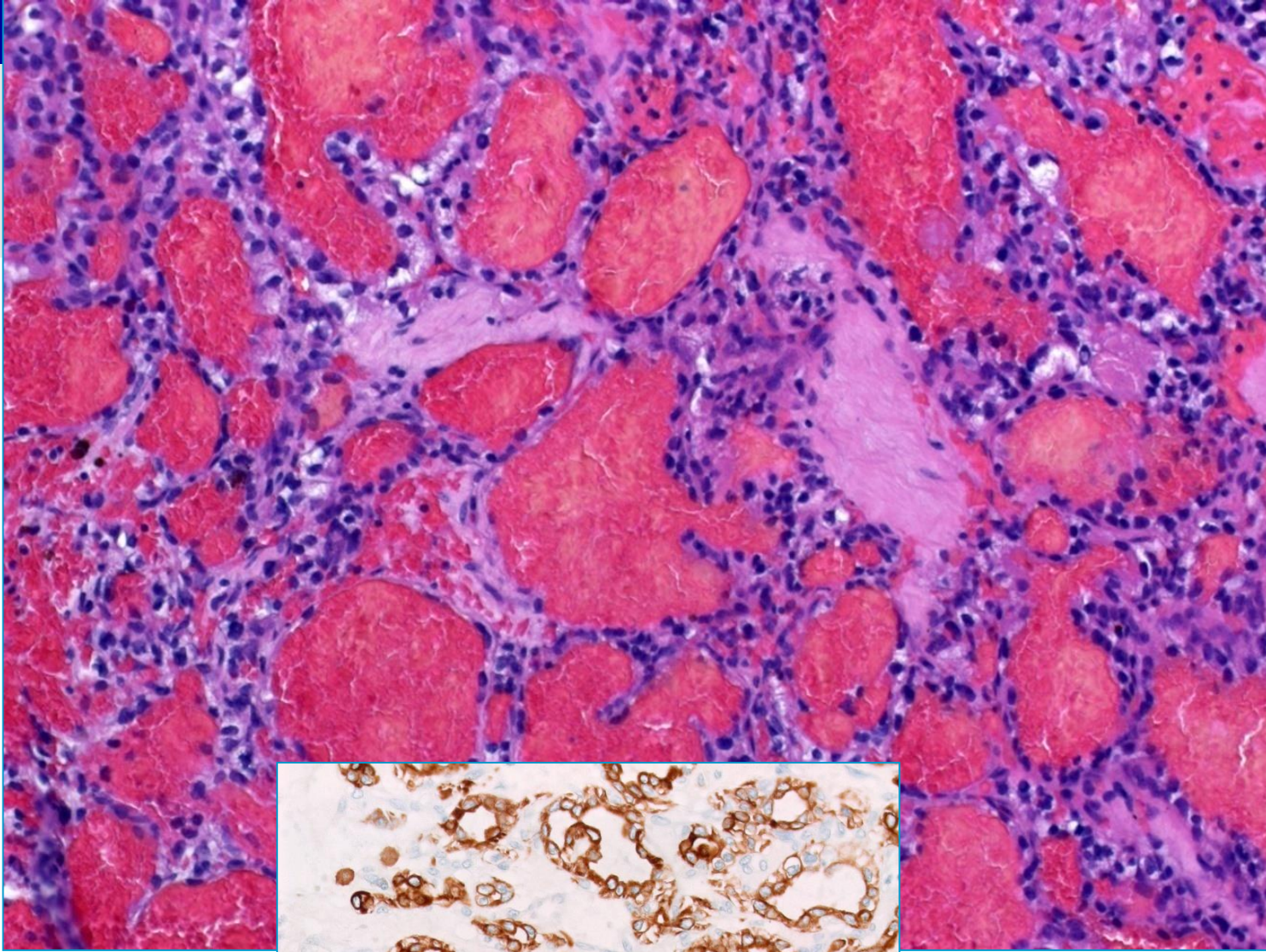


MIB-1



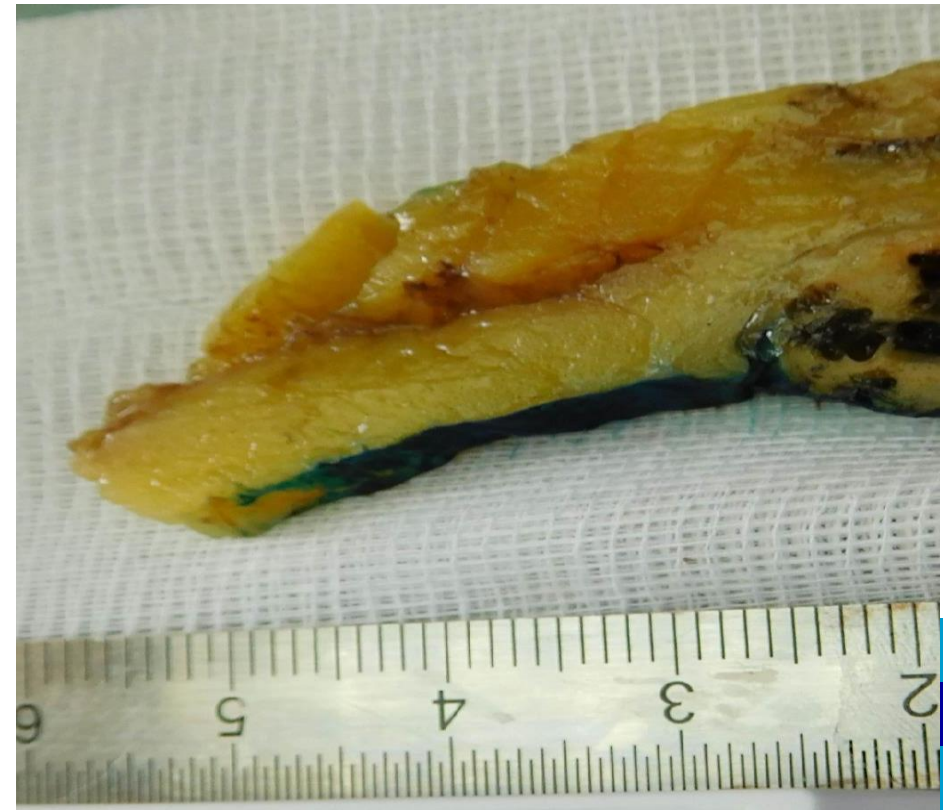
Focal ischemic necrosis shows high proliferation



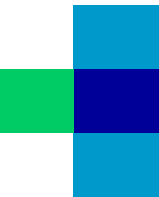
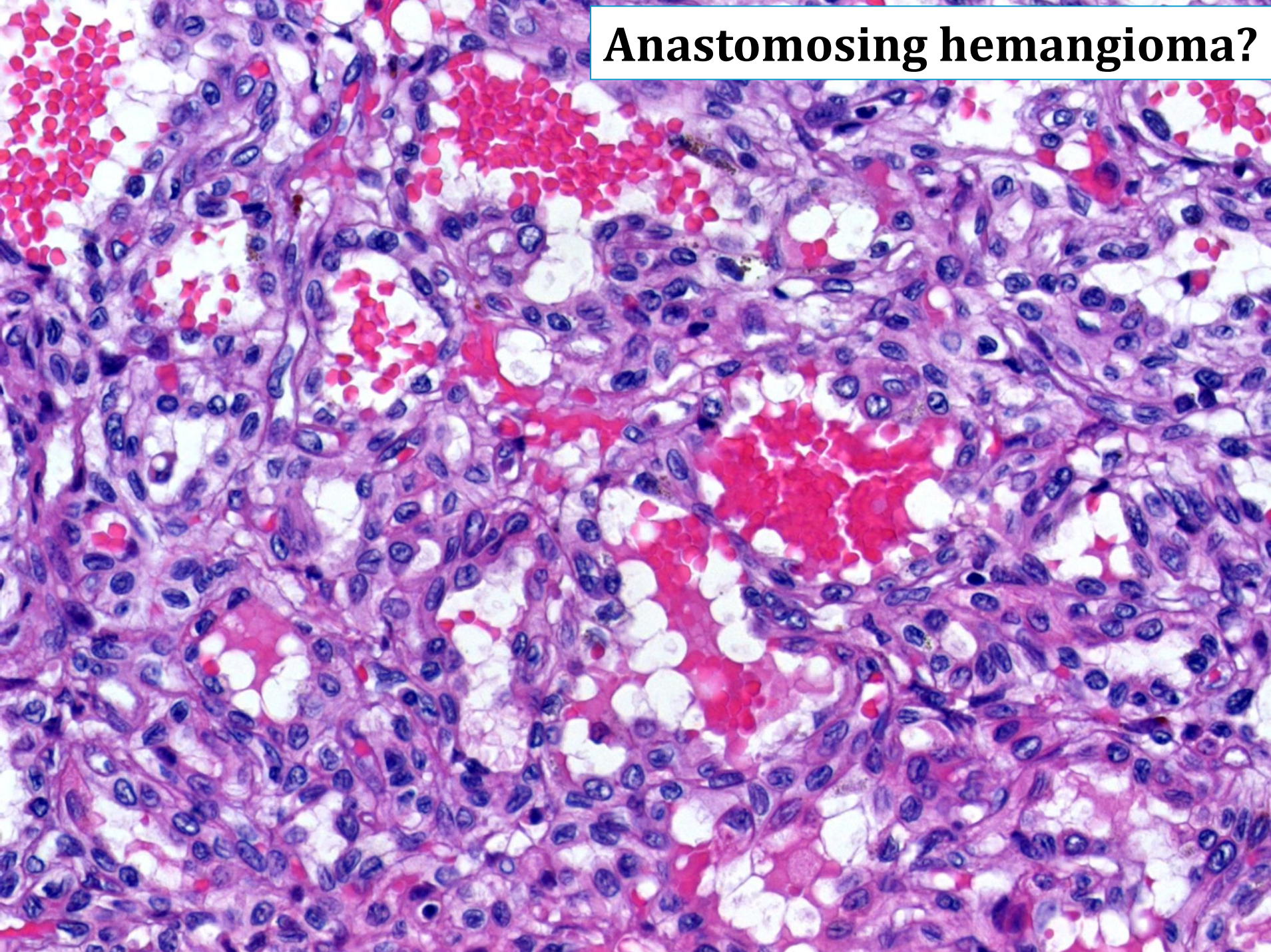


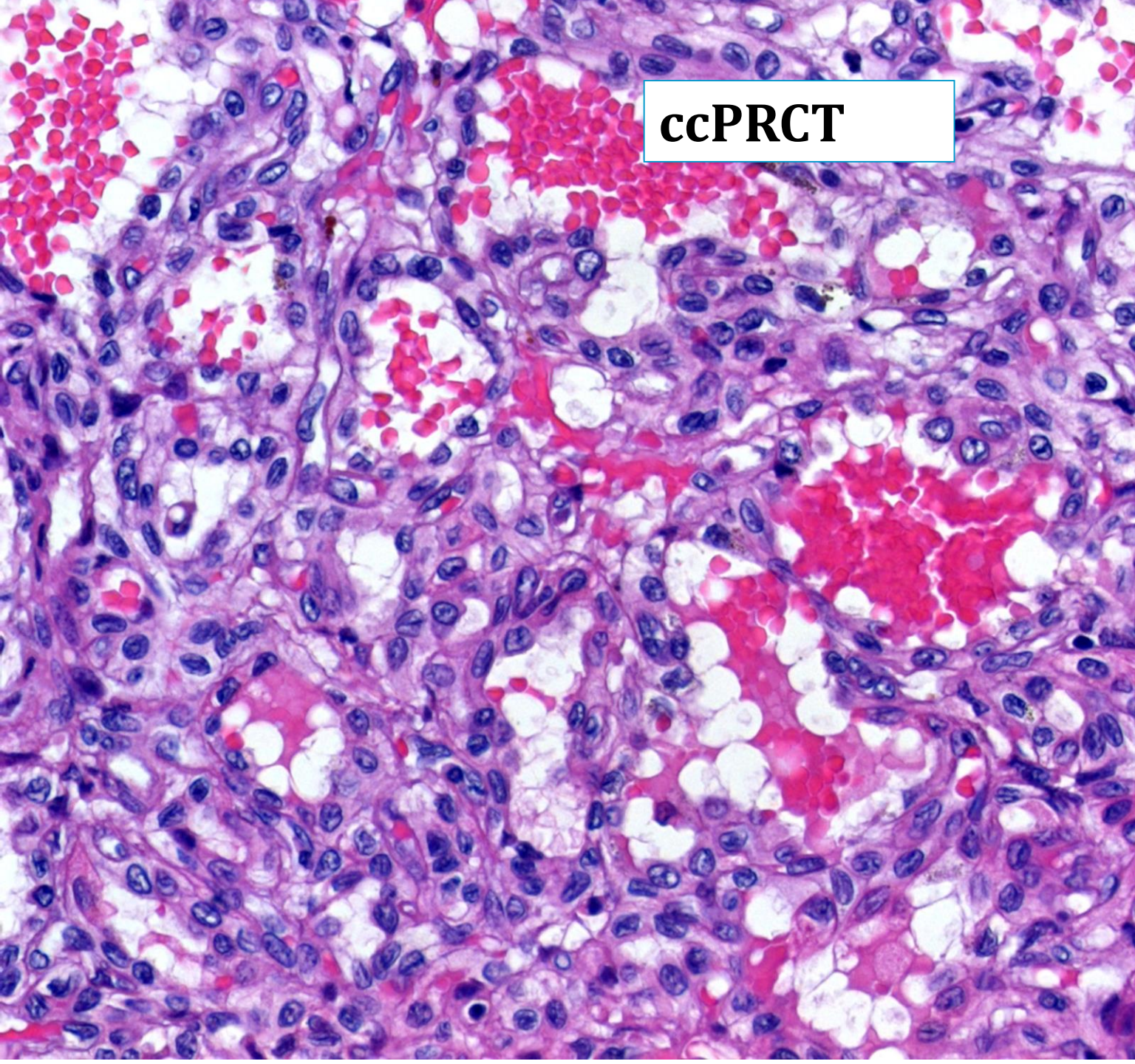
DDx: pseudoangiomas:

- ccRCC
- ccPRCC
- Angiect. oncocytoma
- Juxtaglomerular tumor

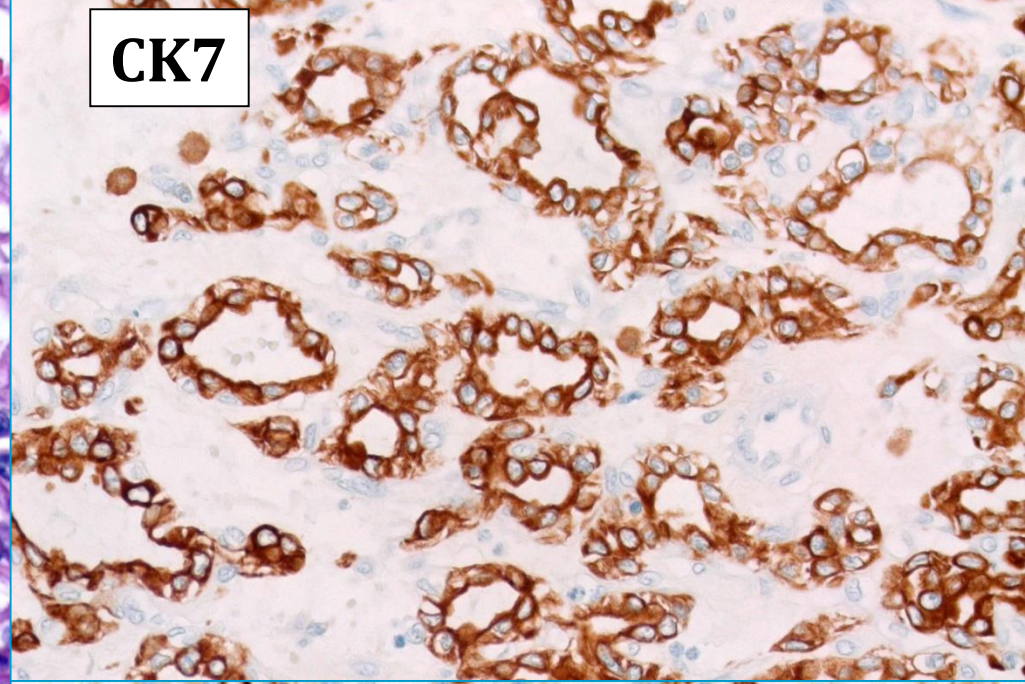


Anastomosing hemangioma?

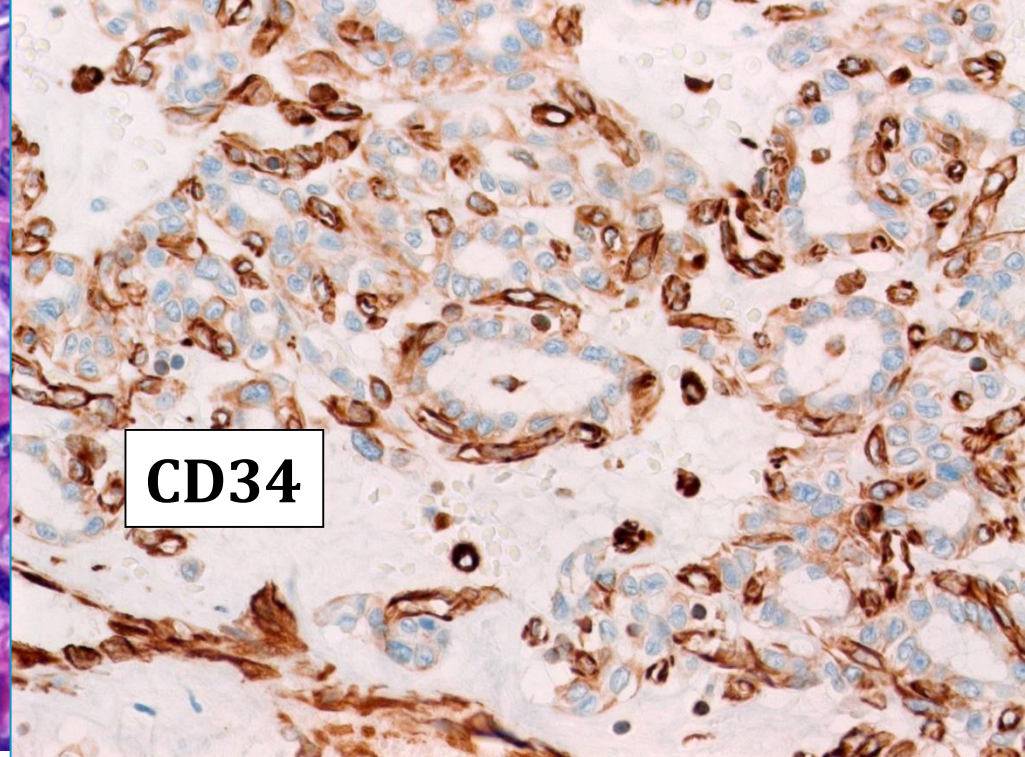




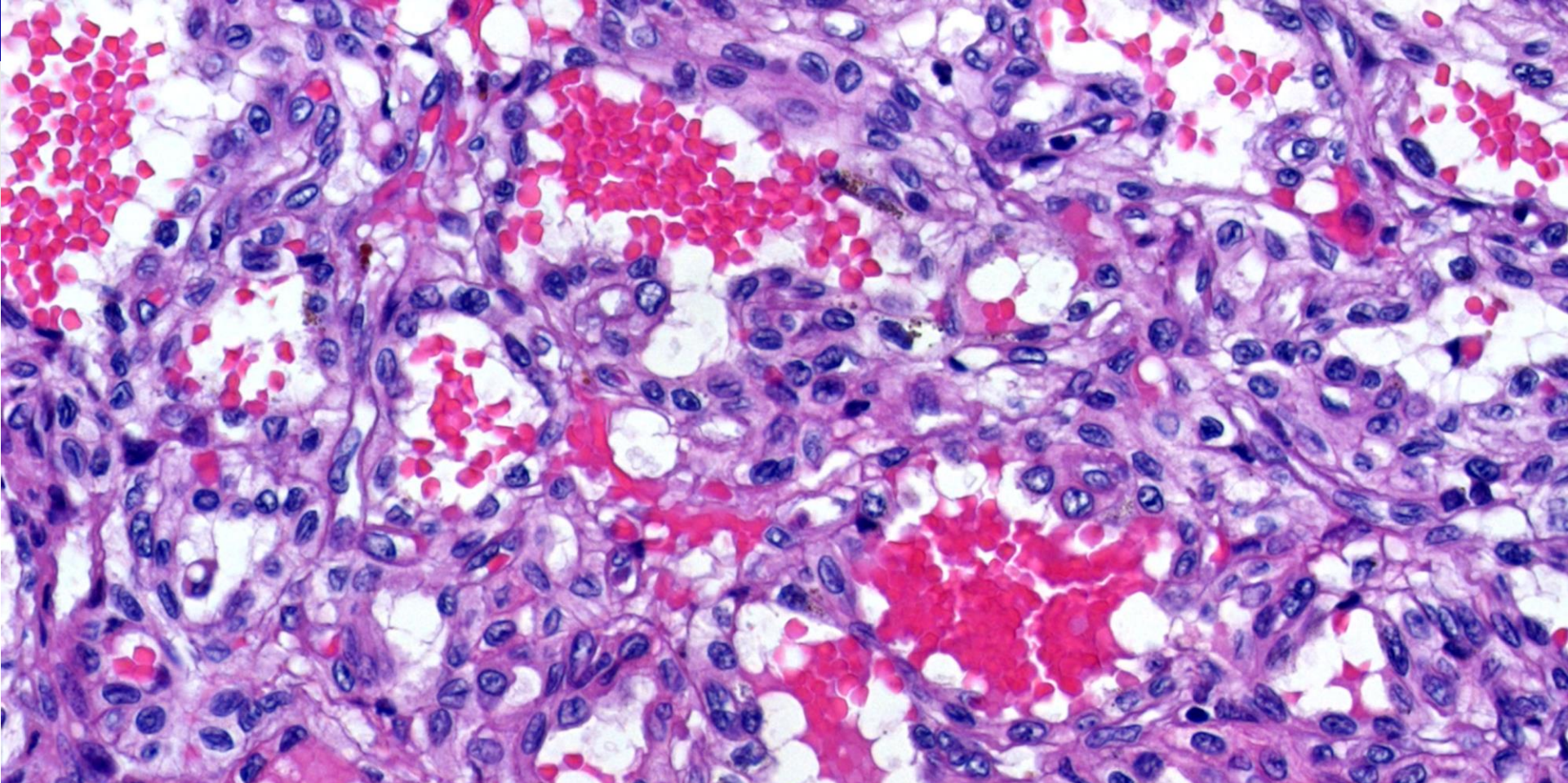
ccPRCT



CK7



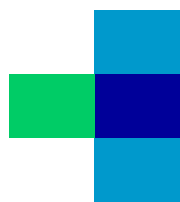
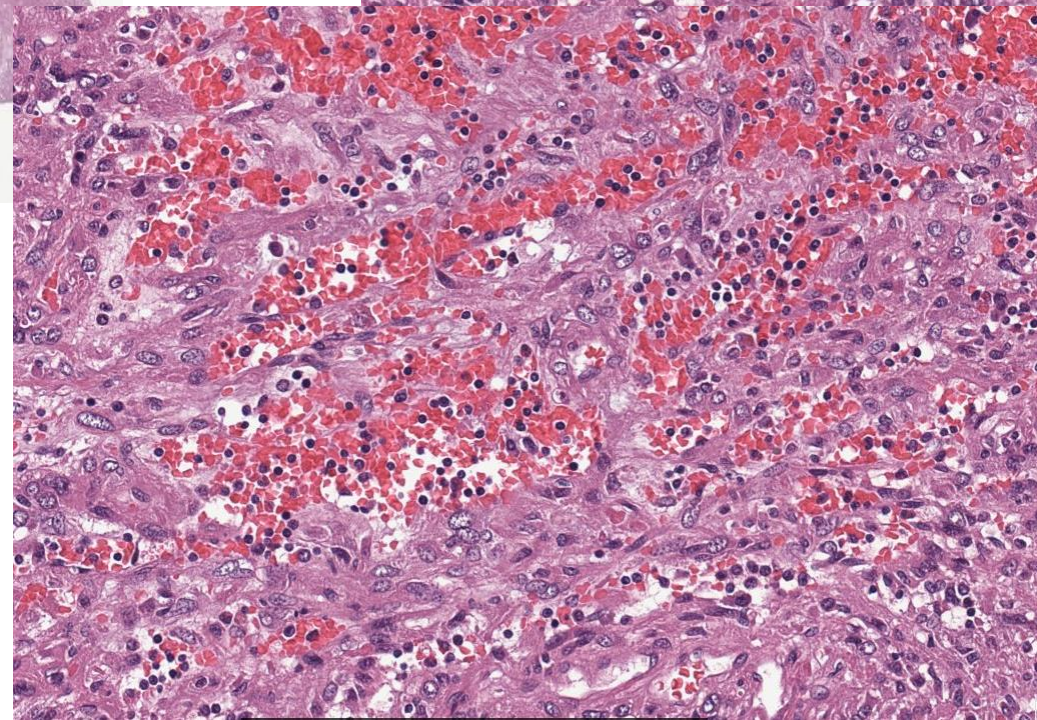
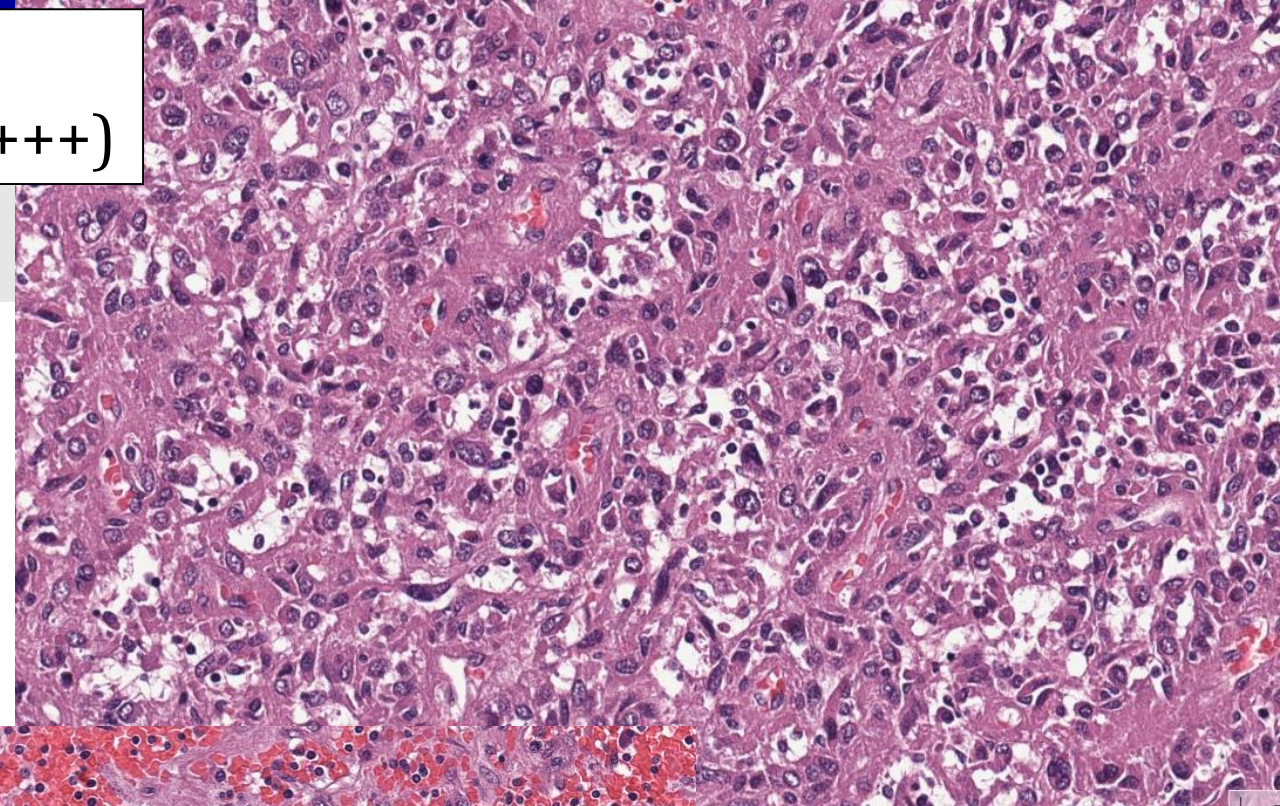
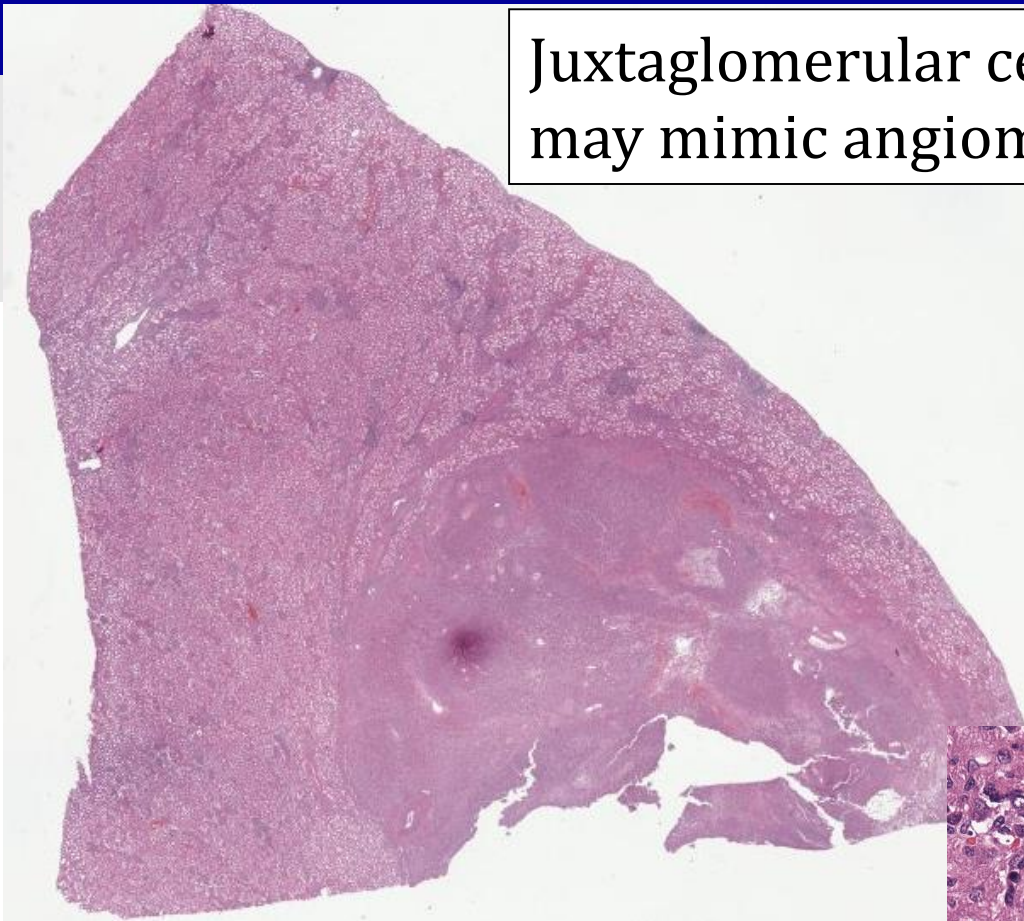
CD34

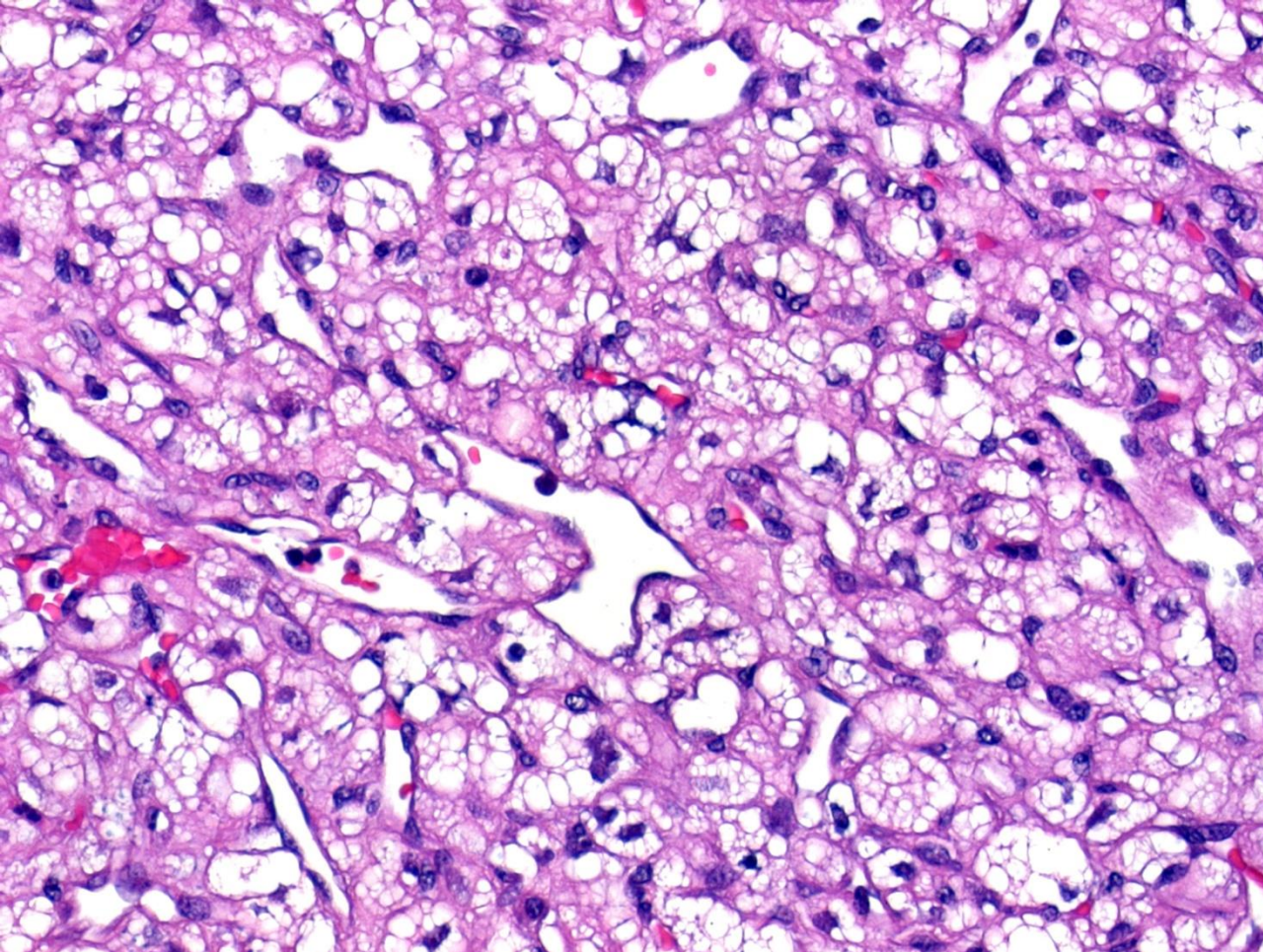


Benign Renal Angiomyoadenomatous Tumor: A Previously Unreported Renal Tumor

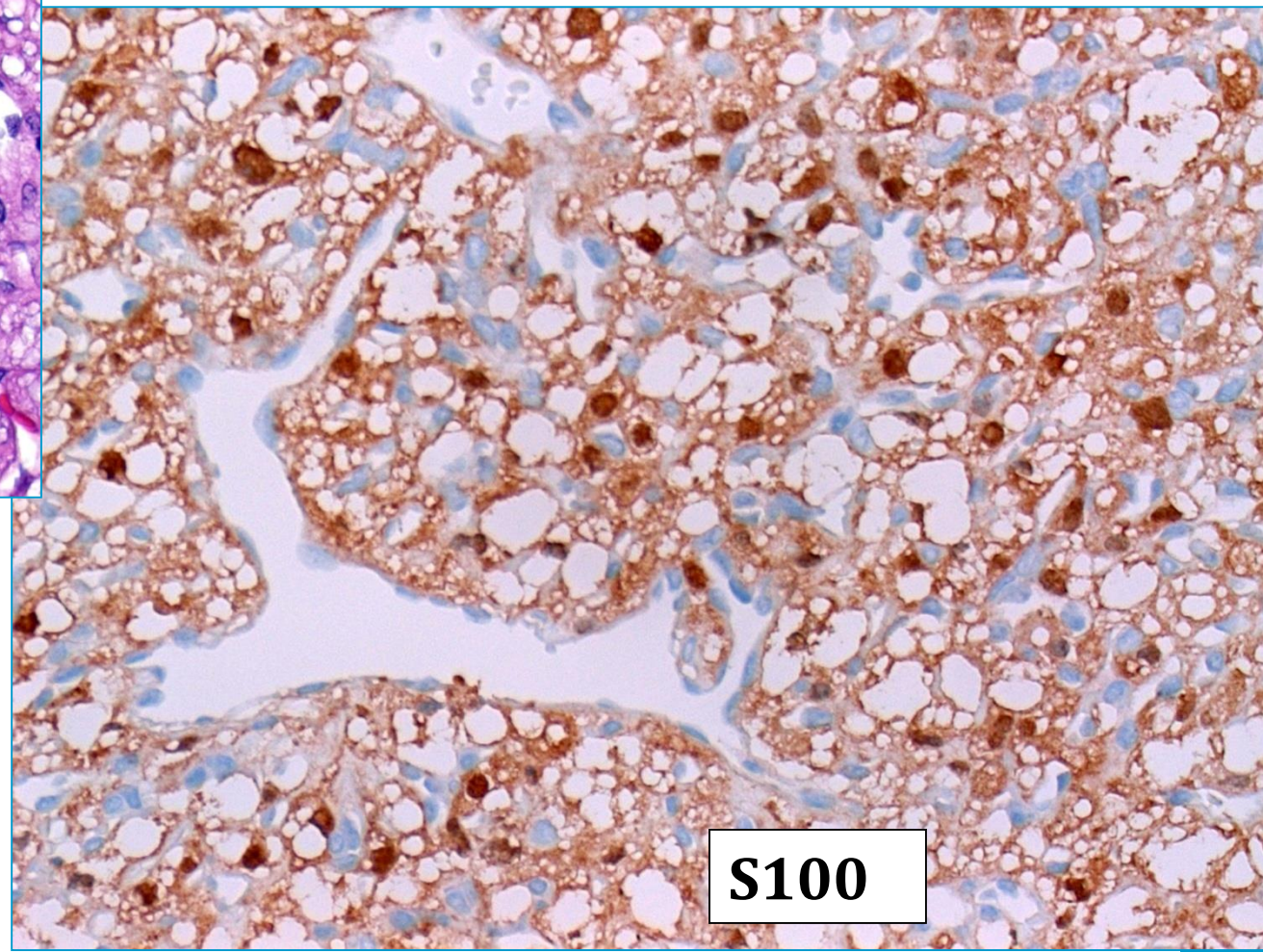
*Michal Michal, MD, Ondrej Hes, MD, and Frantisek Havlicek, MD
Ann Diagn Pathol 4: 311-315, 2000.*

Juxtaglomerular cell tumor
may mimic angioma (CD34+++)



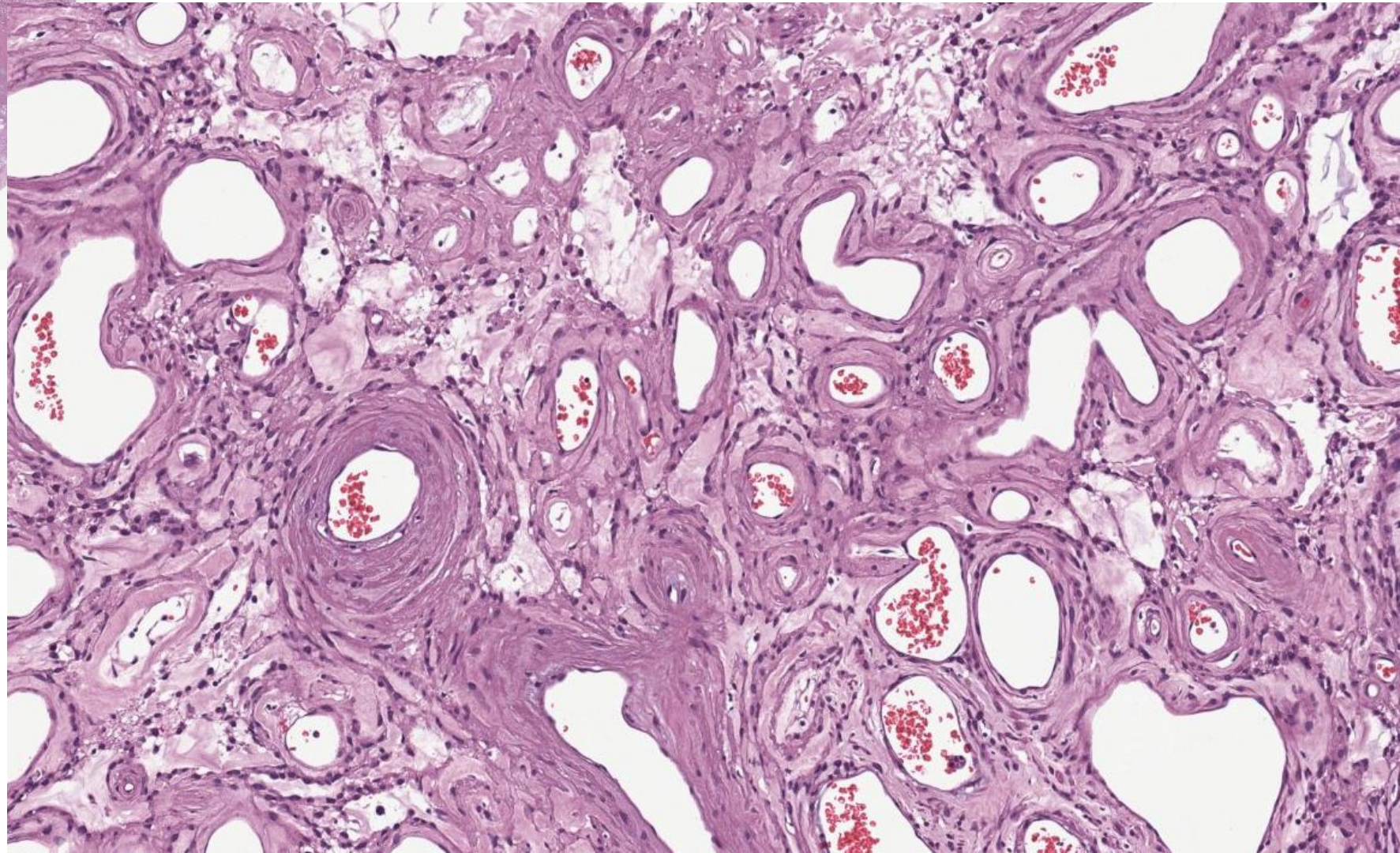
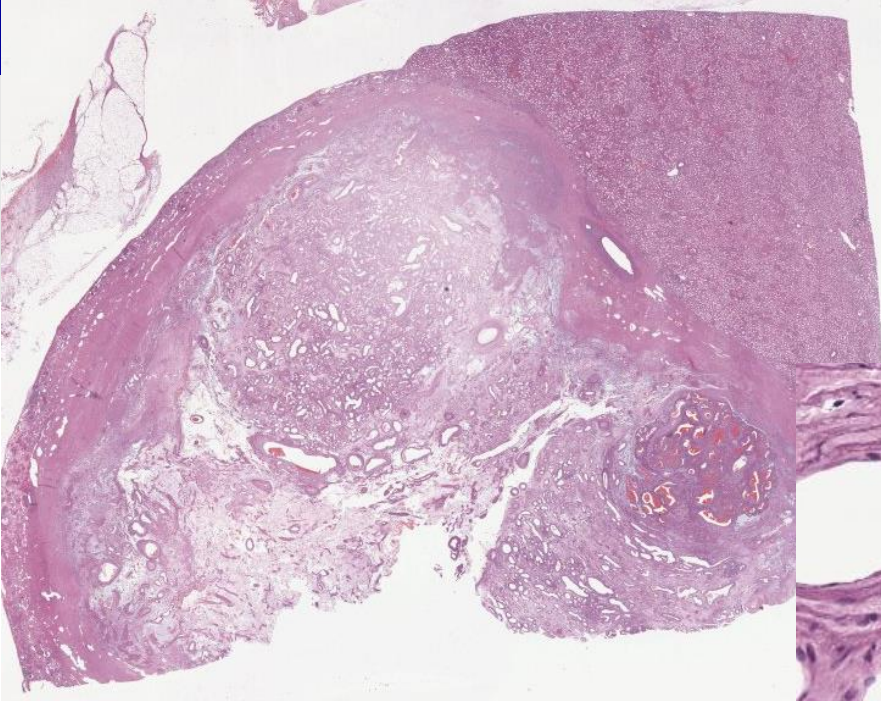


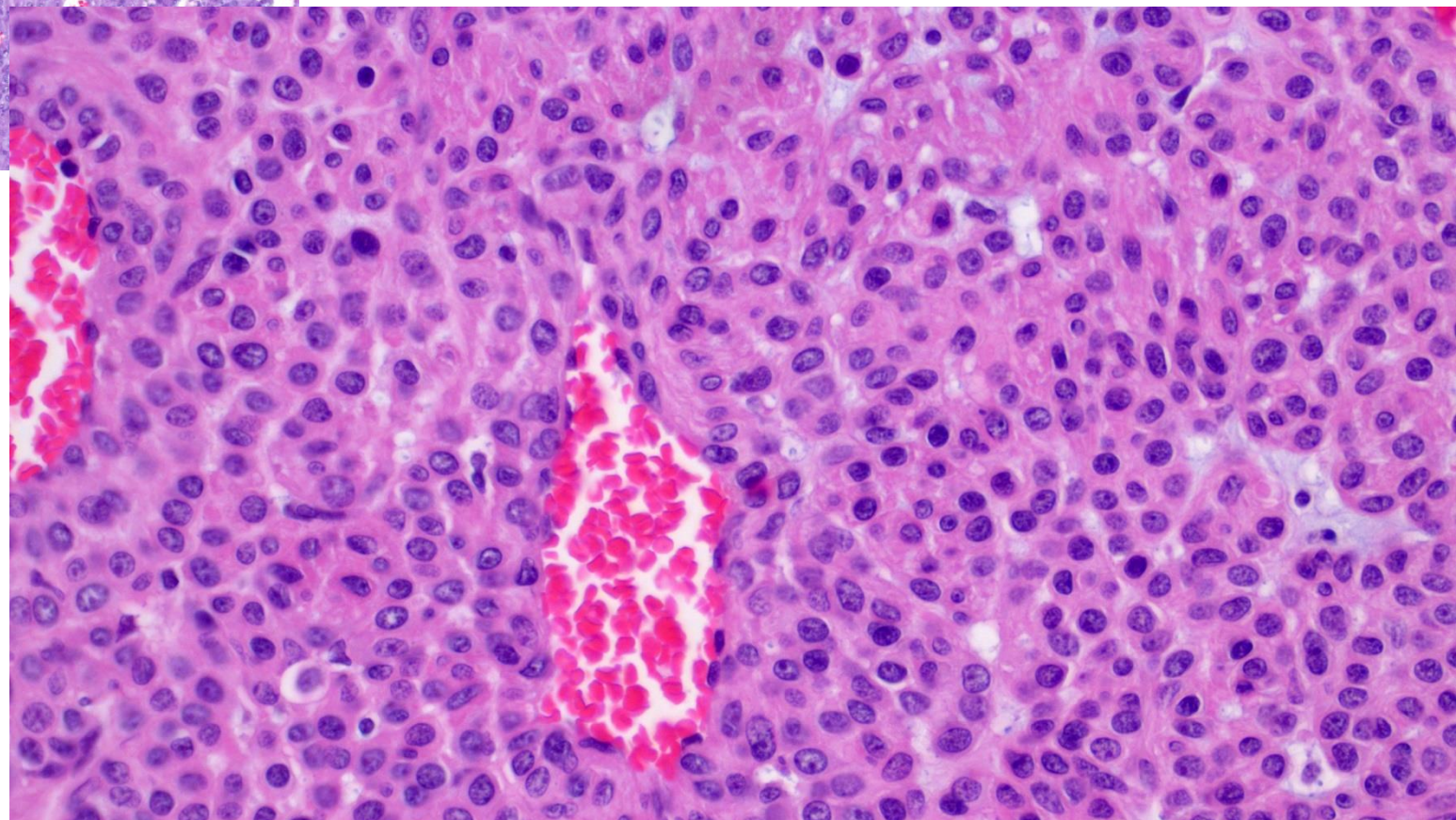
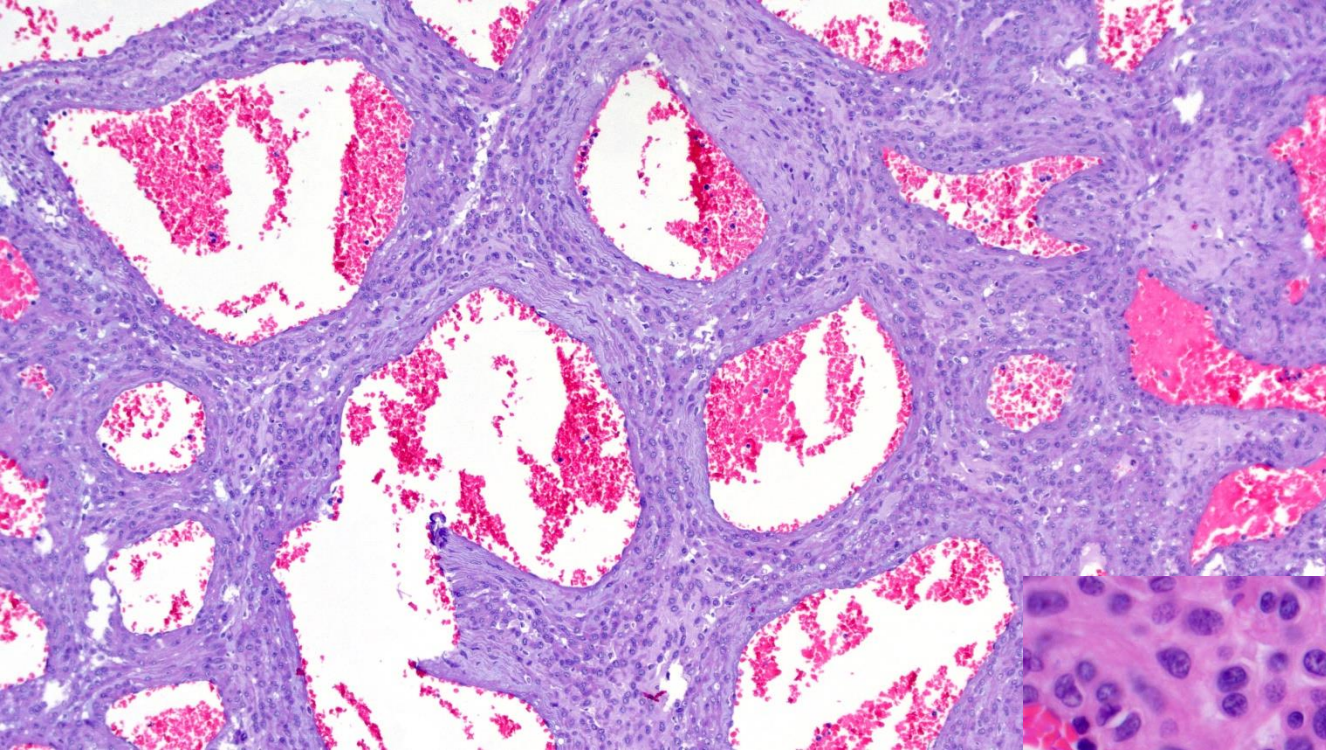
DDx:
capillary hemangioblastoma



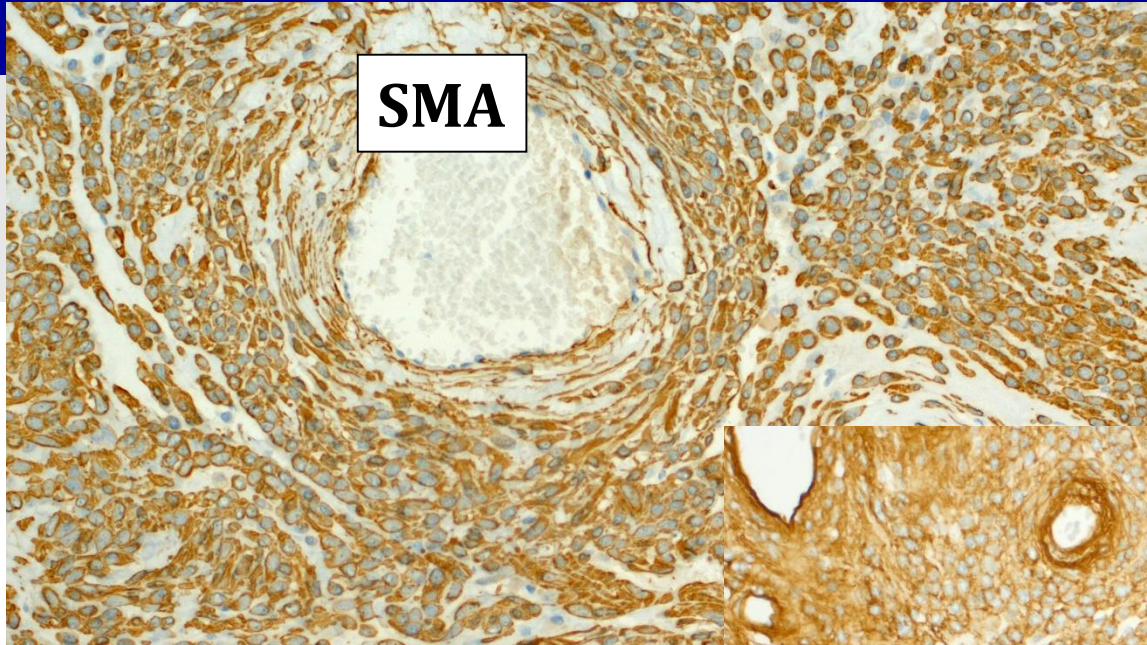
S100

Venous hemangioma?



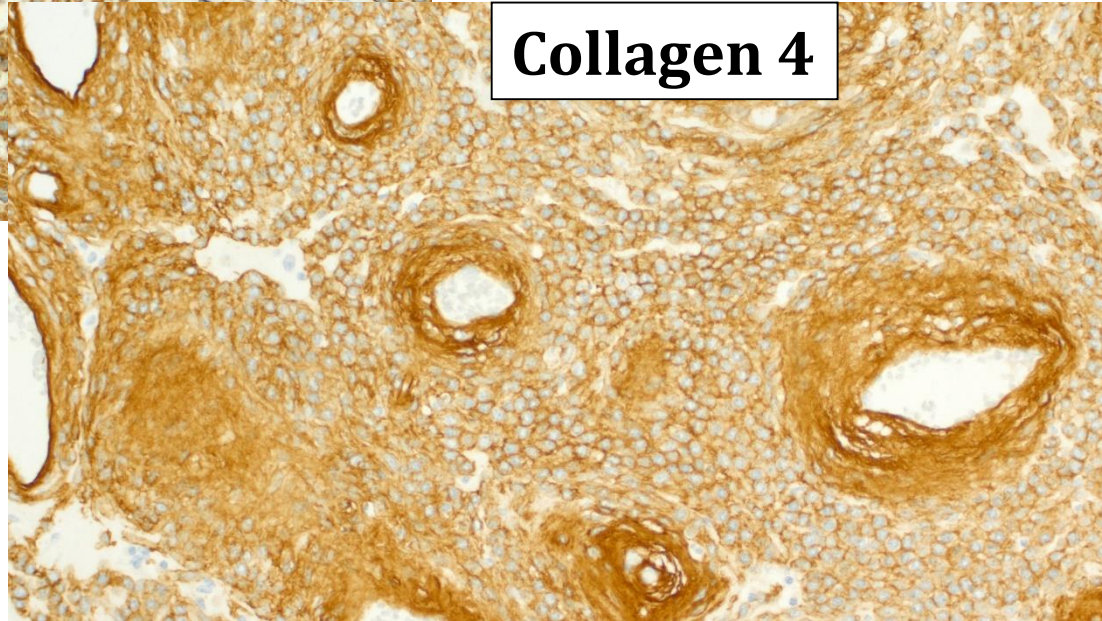


SMA

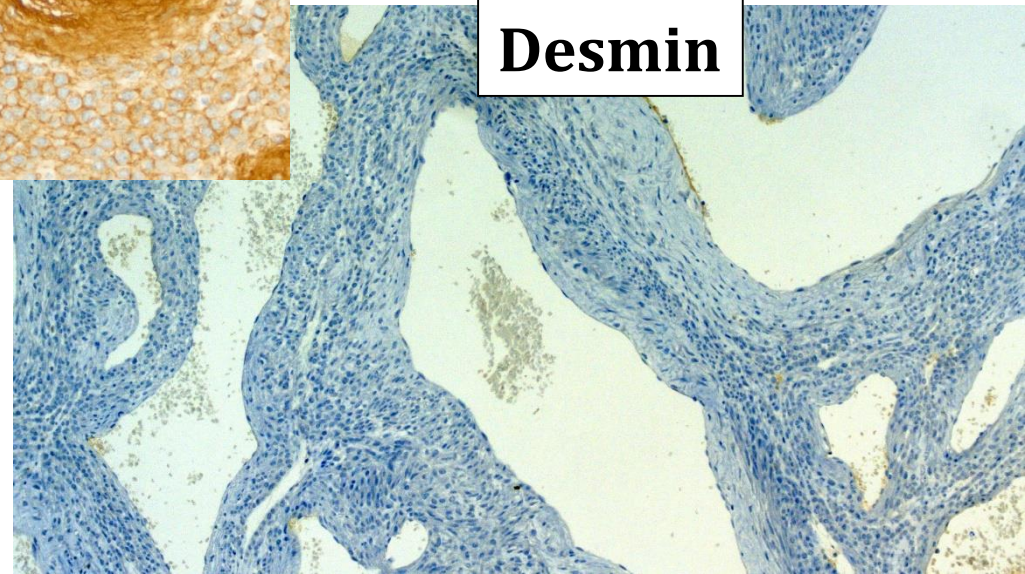


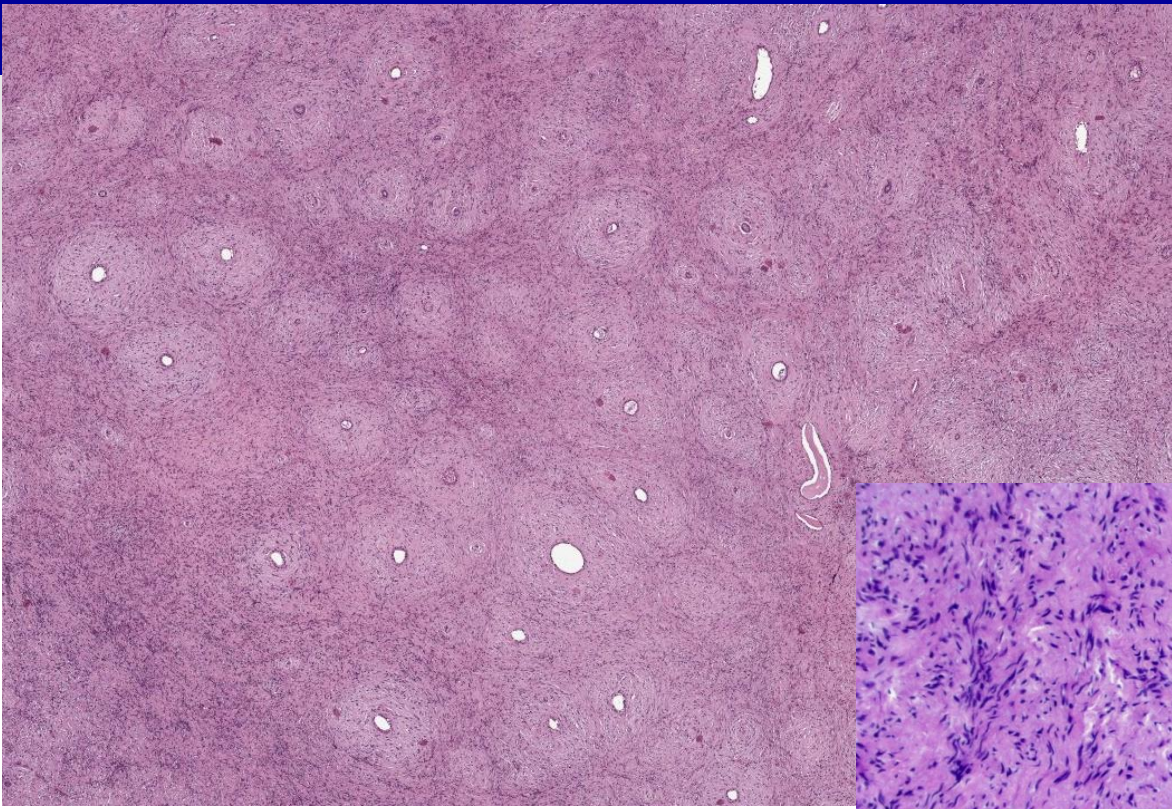
**Glomus tumor/
glomangiomyoma**

Collagen 4



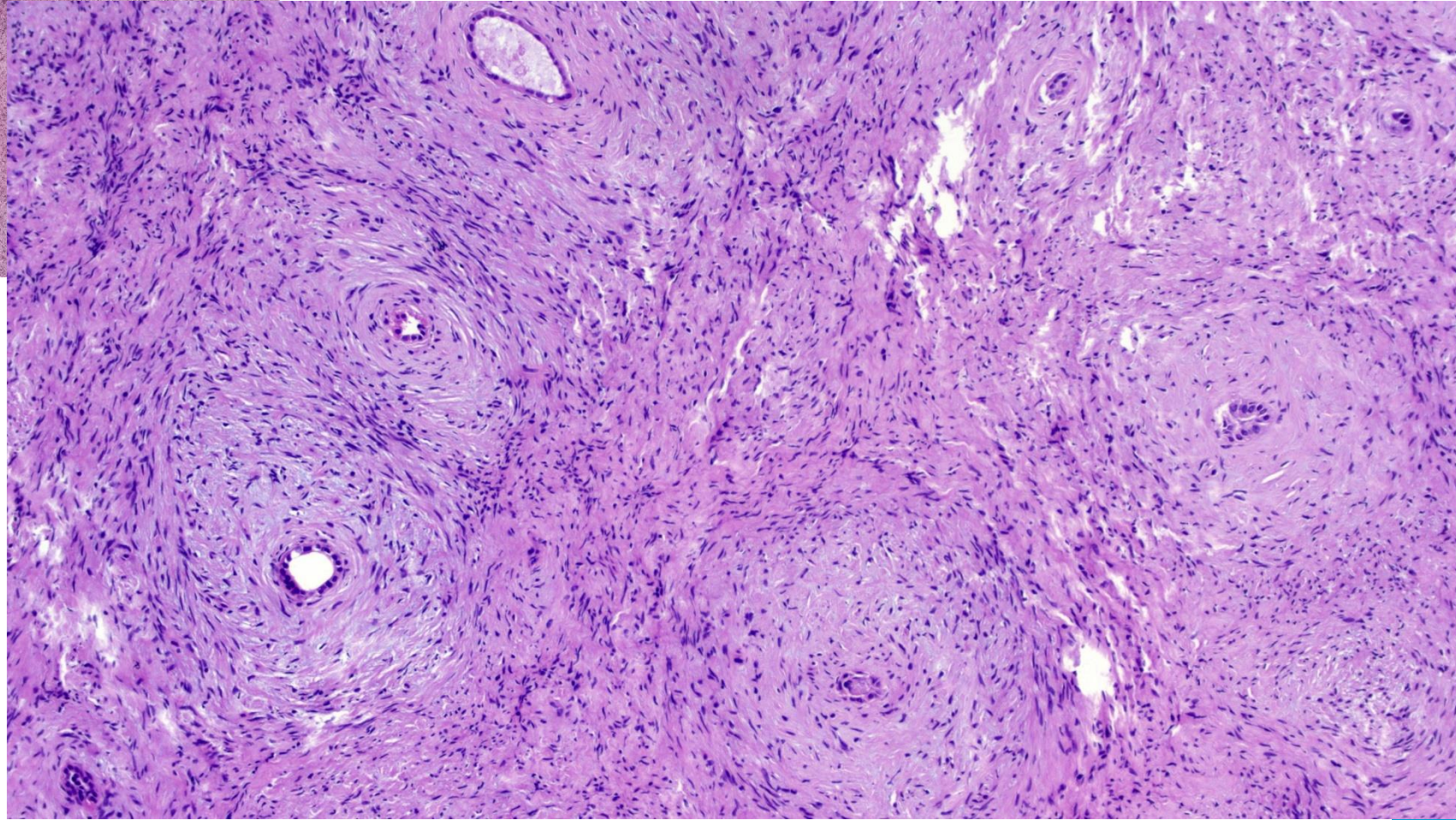
Desmin



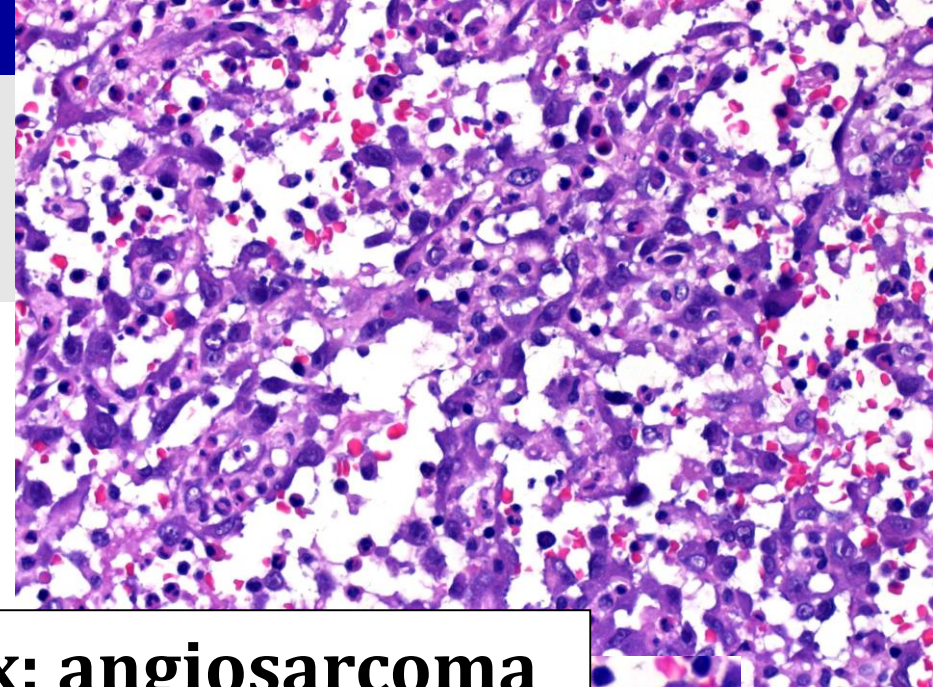
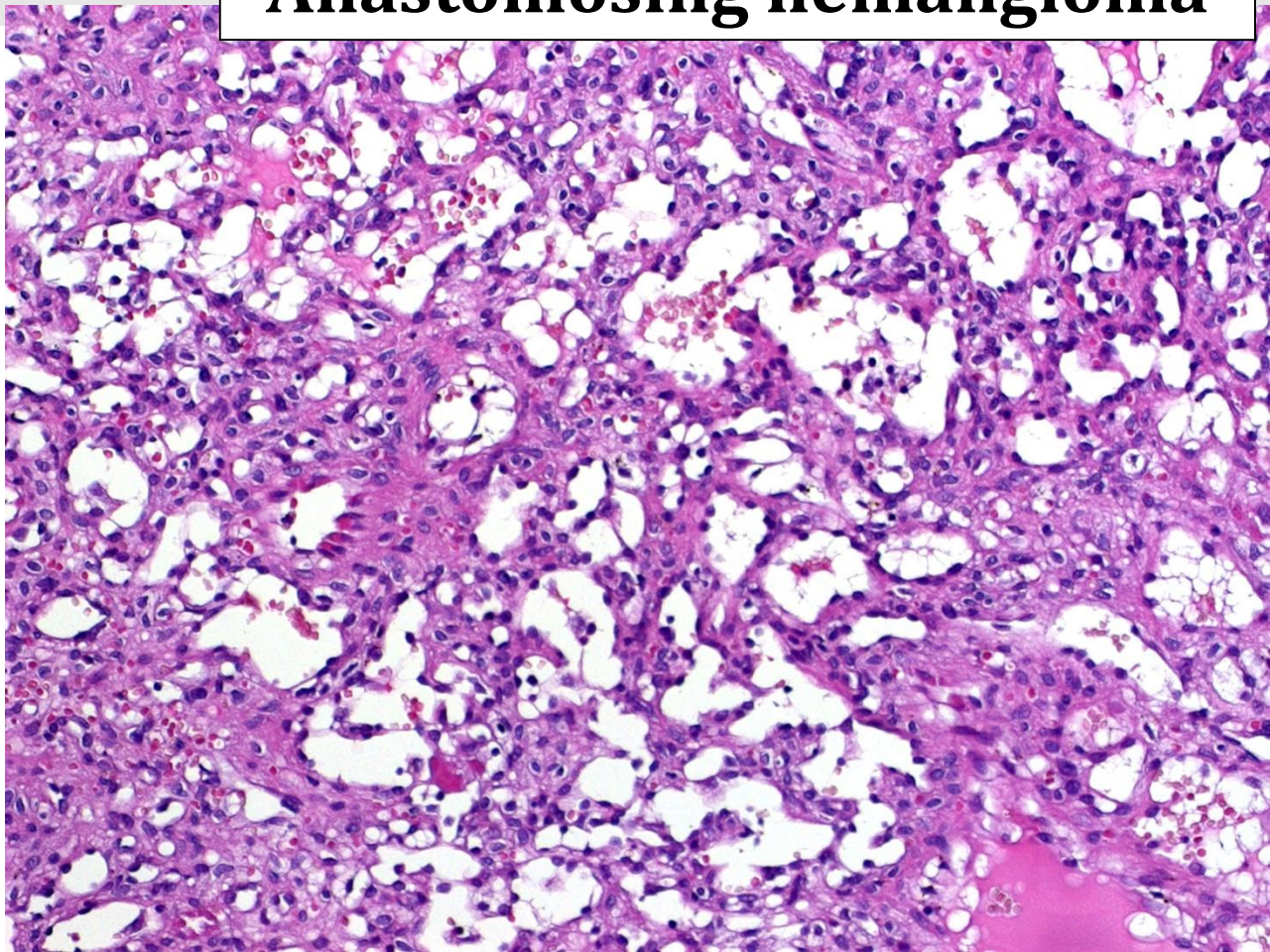


DDx: metanephric stromal tumor

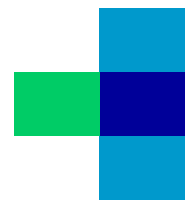
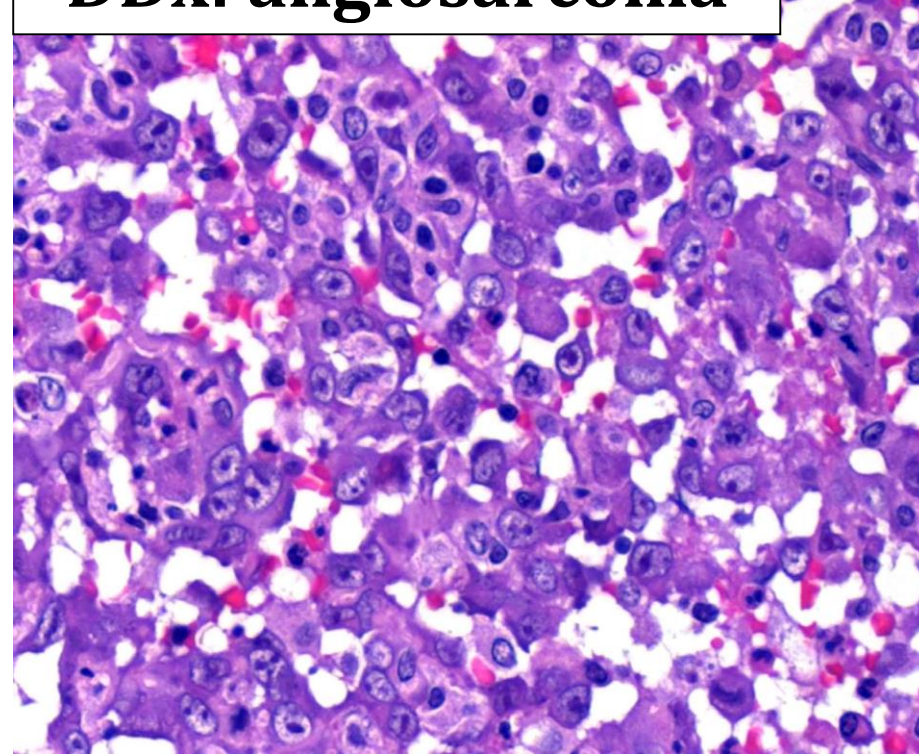
Tubules within myopericytoma-like concentric whorls are diagnostic



Anastomosing hemangioma



DDx: angiosarcoma



TaHoMe vascular lesions of kidney

In any candidate vascular kidney tumor:

True vascular? Nothing between vessels??? CK?

In any potential renal angiosarcoma:

Possibly anastomosing hemangioma!!!



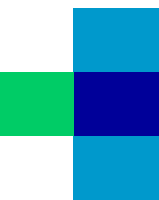
Inflammatory pseudotumors of the kidney

Tumefactive fibroinflammation (diverse etiology)

- Xanthogranulomatous pyelonephritis.
- **IgG4-related disease/pseudotumors.**
- **Malakoplakia.**
- Inflammatory myofibroblastic tumors (vanishingly rare).
- Inflammatory pseudotumor NST.
- **Perinephric myxoid inflammatory pseudotumor.**

DDx: inflammatory paucicellular sarcomatoid RCC

DDx: inflammatory well diff liposarcoma



Perinephric myxoid pseudotumor of fat

- Recently described paucicellular myxoid lesion.
- Mainly within perinephric fat.
- Plasma cell-dominanted chronic inflammation.
- Secondary bleeding and vasculopathies may be seen.
- No atypia, no sclerosis, no angiitis.
- IHC: not contributory (MDM2/CDK4/IgG4-neg).



Perinephric myxoid pseudotumor of fat

- First described by Folpe et al in 2019.
- M: F = 10: 1
- Age: 43 – 84 y (median: 63.5).
- Tumor size: 2 - 28 cm (median: 9.3 cm)
- Benign but frequent cause of NE.
- Associated with other kidney diseases (ESRD, RCC, etc.).

Human Pathology (2019) 87, 37–43



ELSEVIER

Original contribution

Perinephric myxoid pseudotumor of fat: a distinctive pseudoneoplasm most often associated with non-neoplastic renal disease[☆]

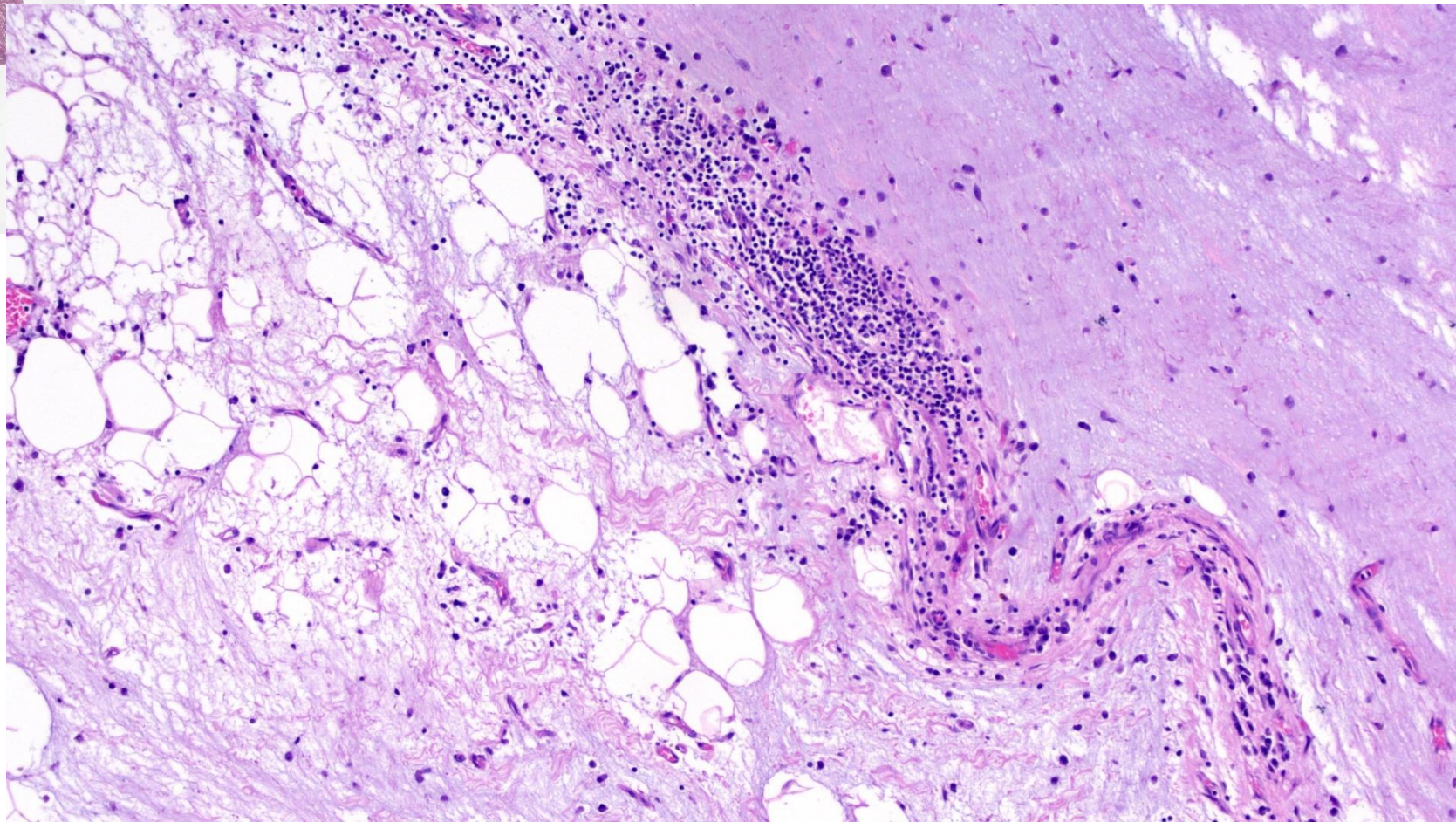
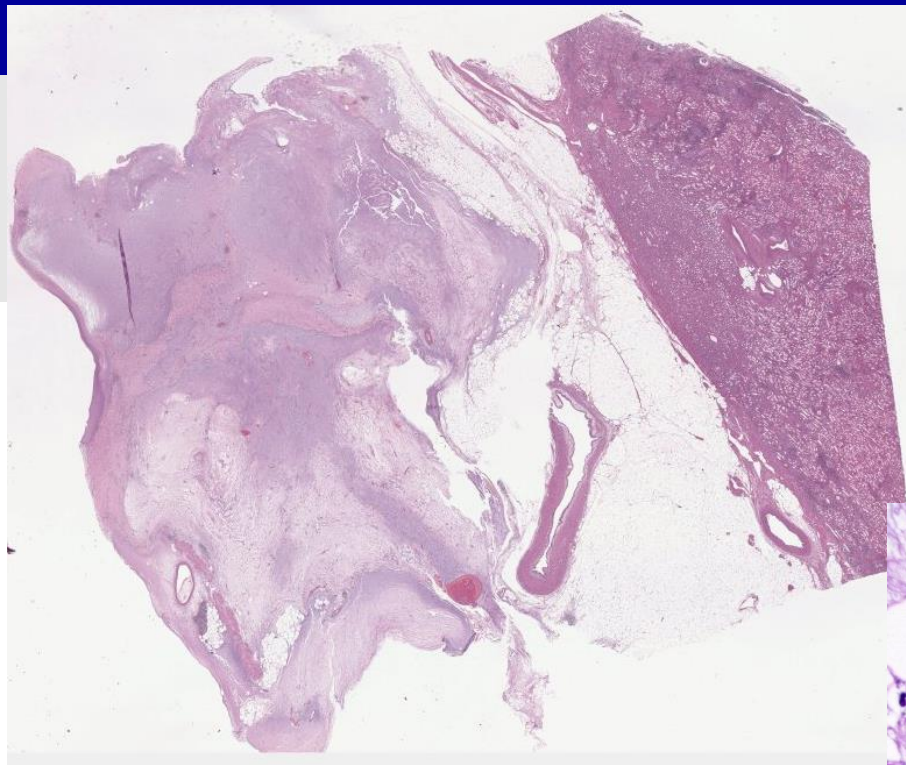
Nooshin K. Dashti MD, Karen J. Fritchie MD, Andrew L. Folpe MD*

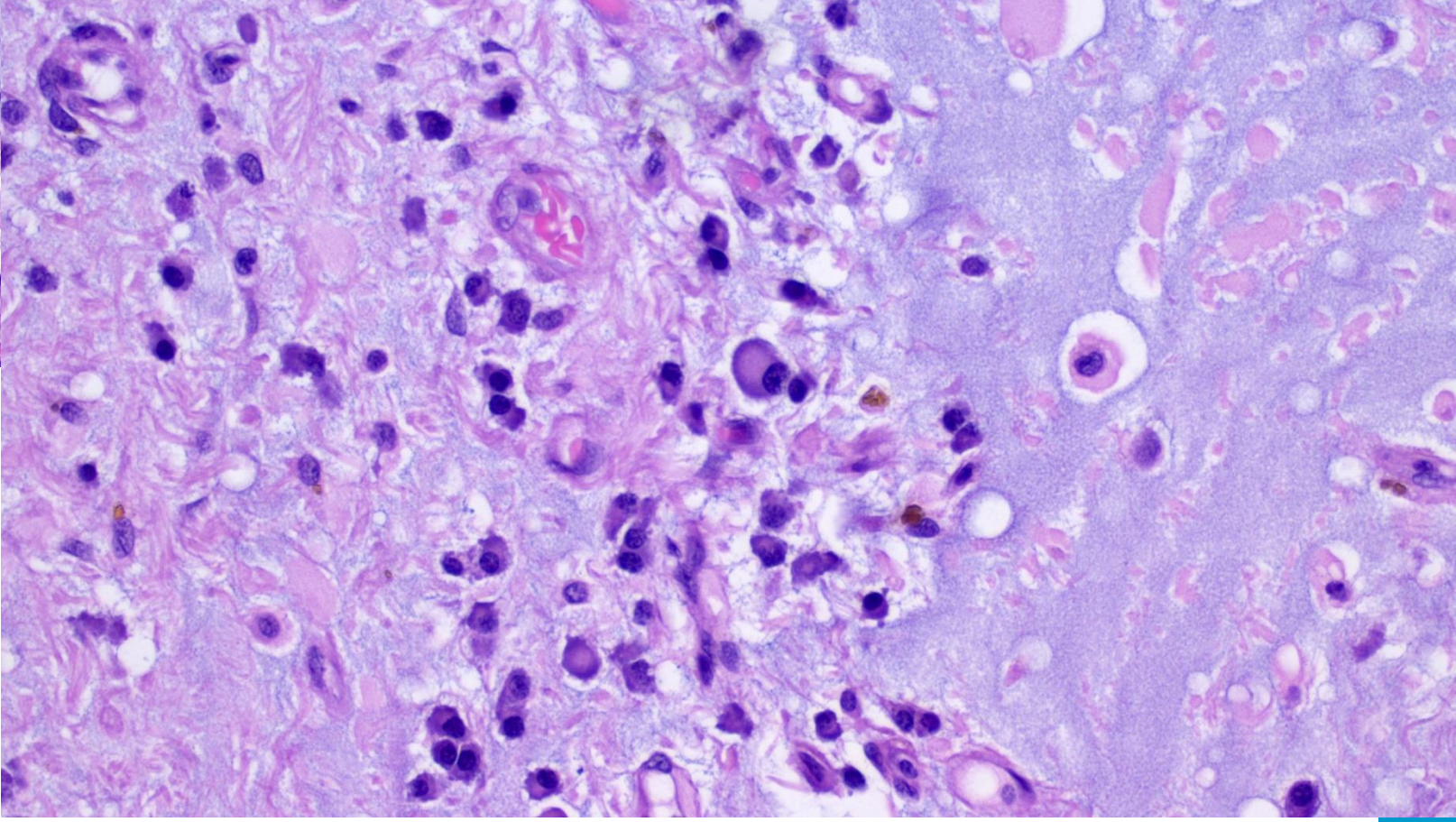
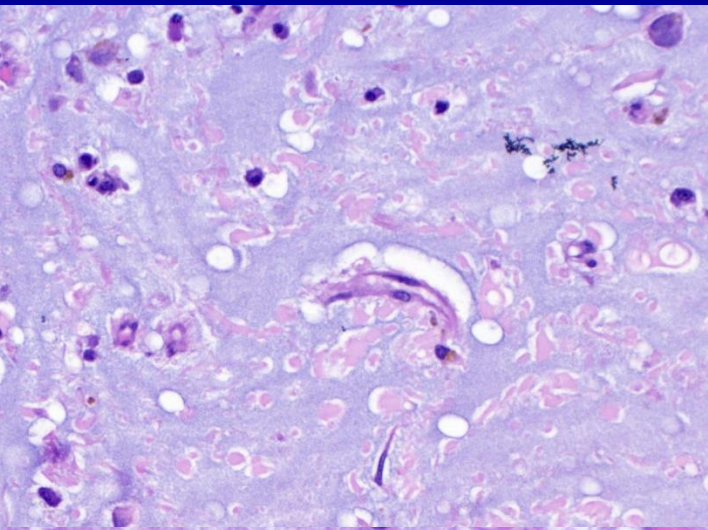
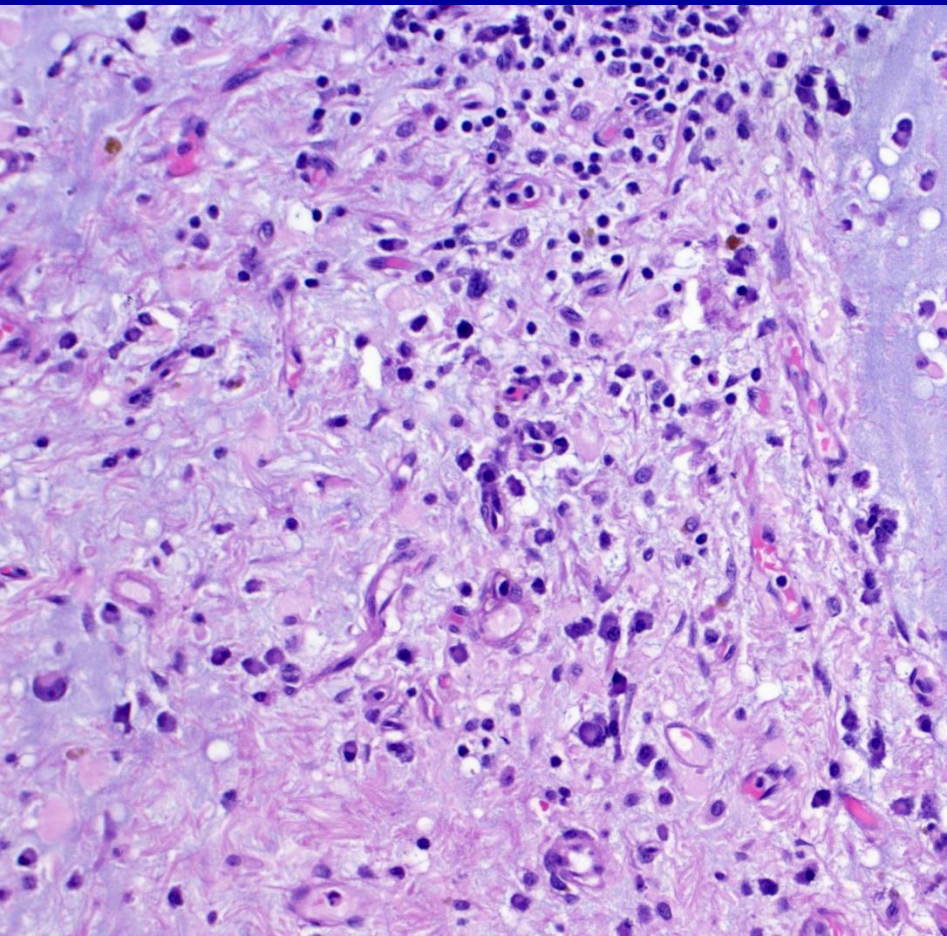
Human
PATHOLOGY

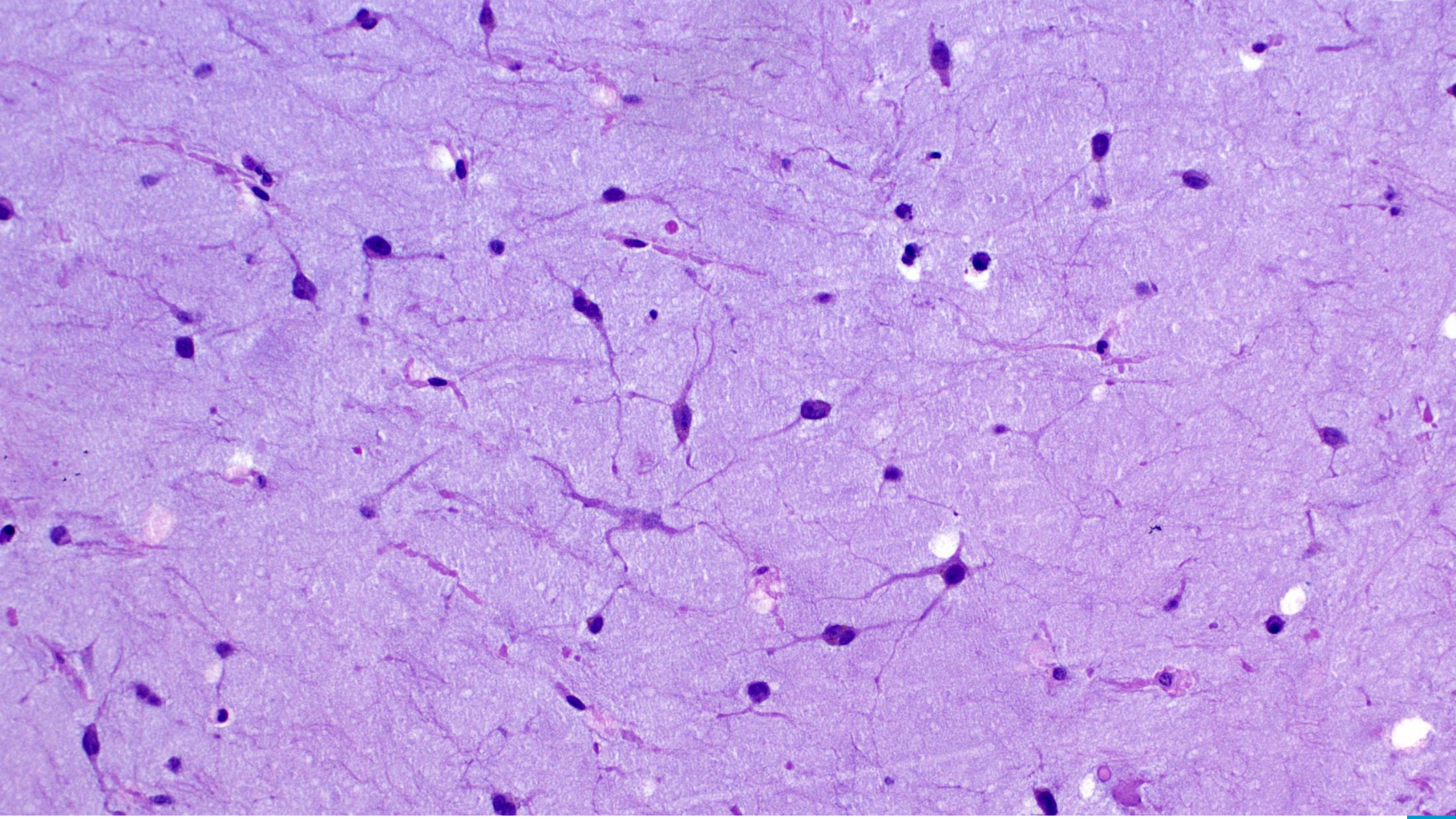
www.elsevier.com/locate/humpath

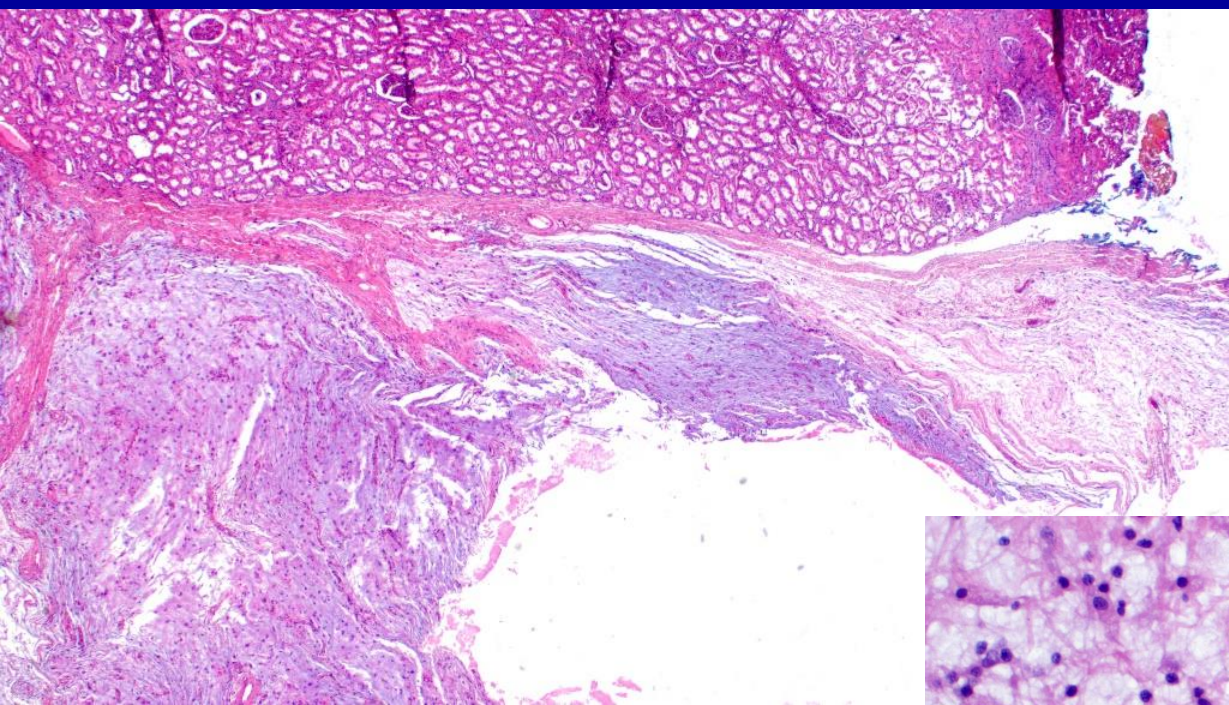




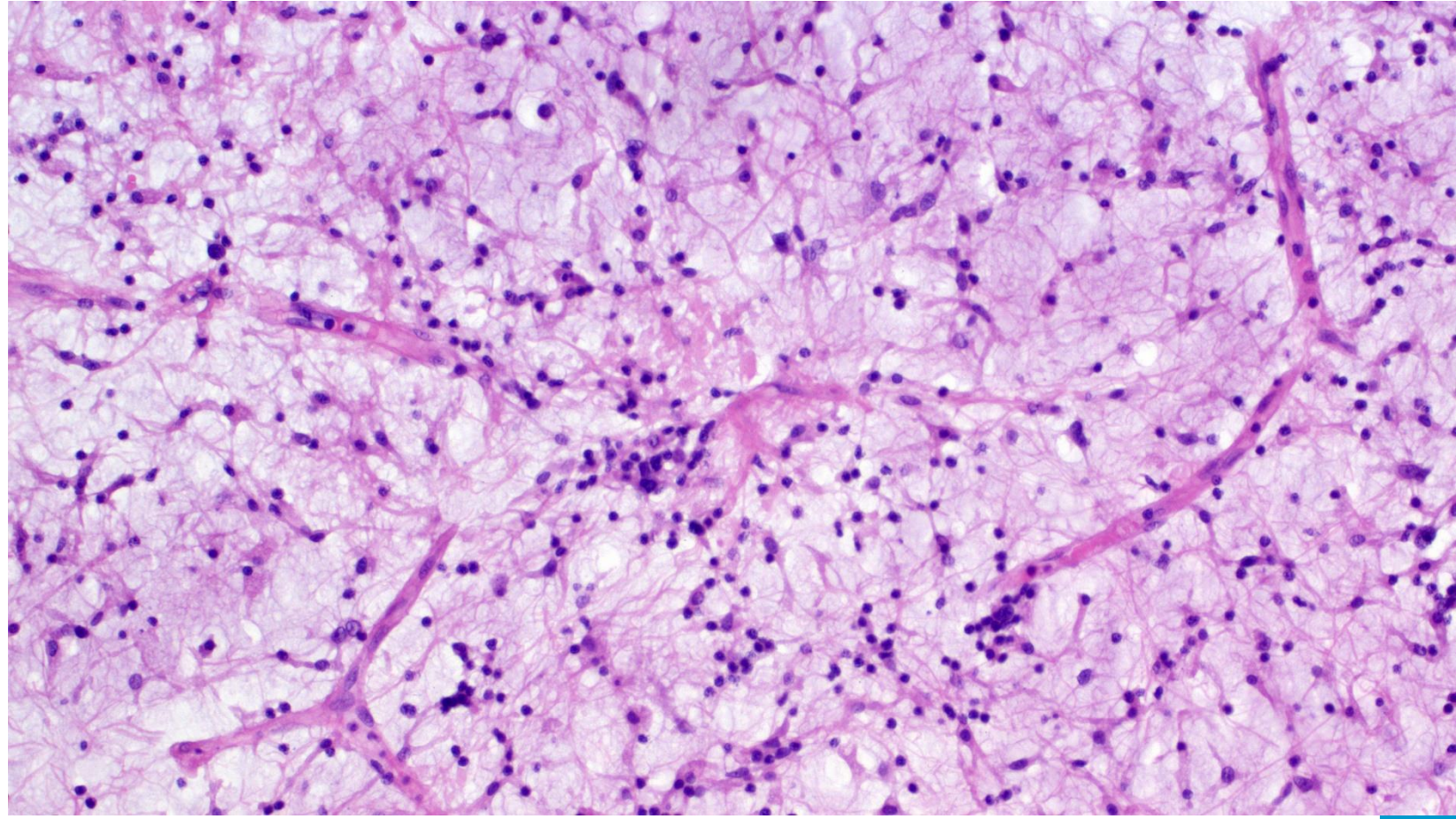


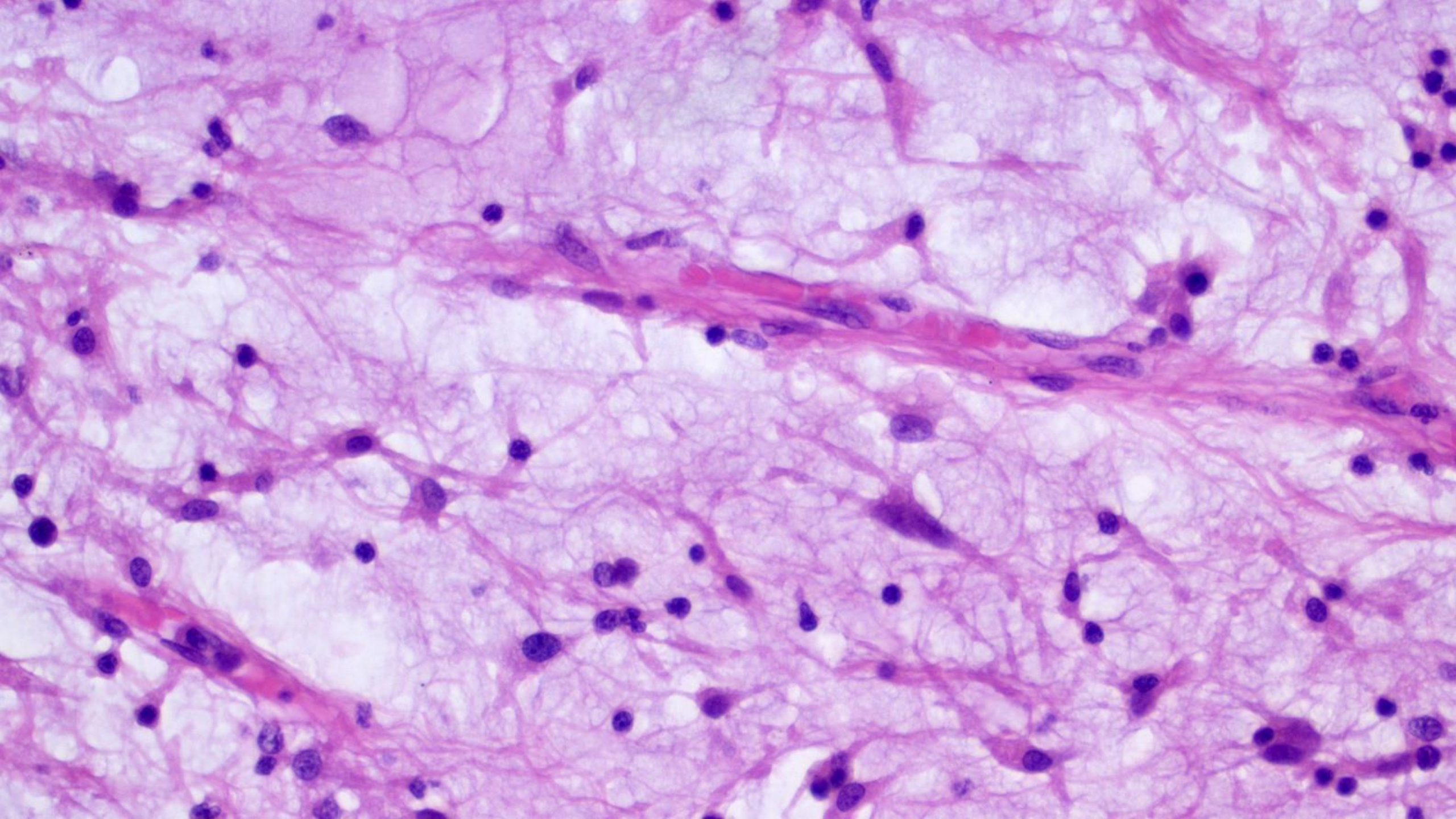




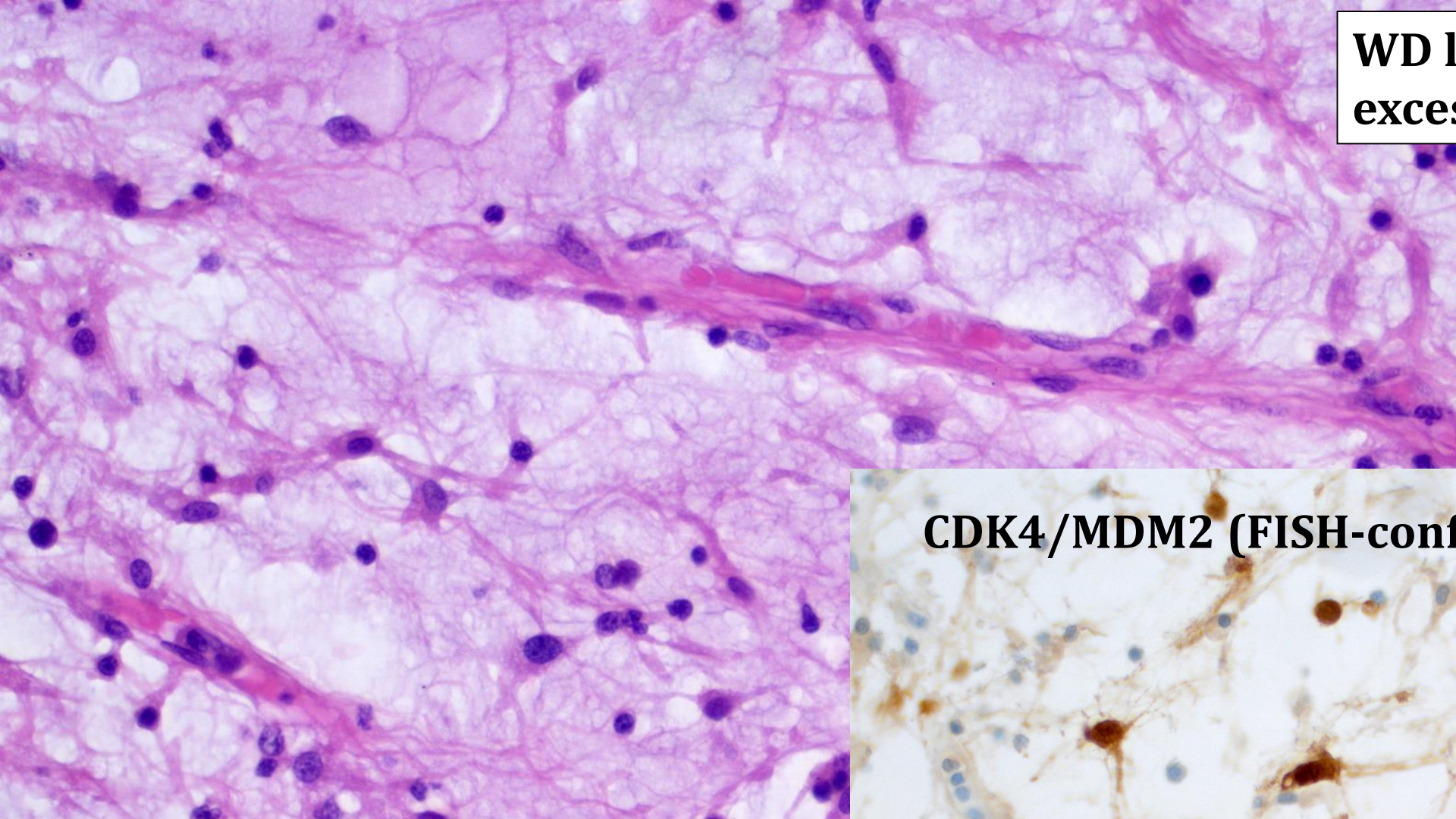


**65 yo male, submitted with
diagnosis of „perinephric myxoid
pseudotumor“**

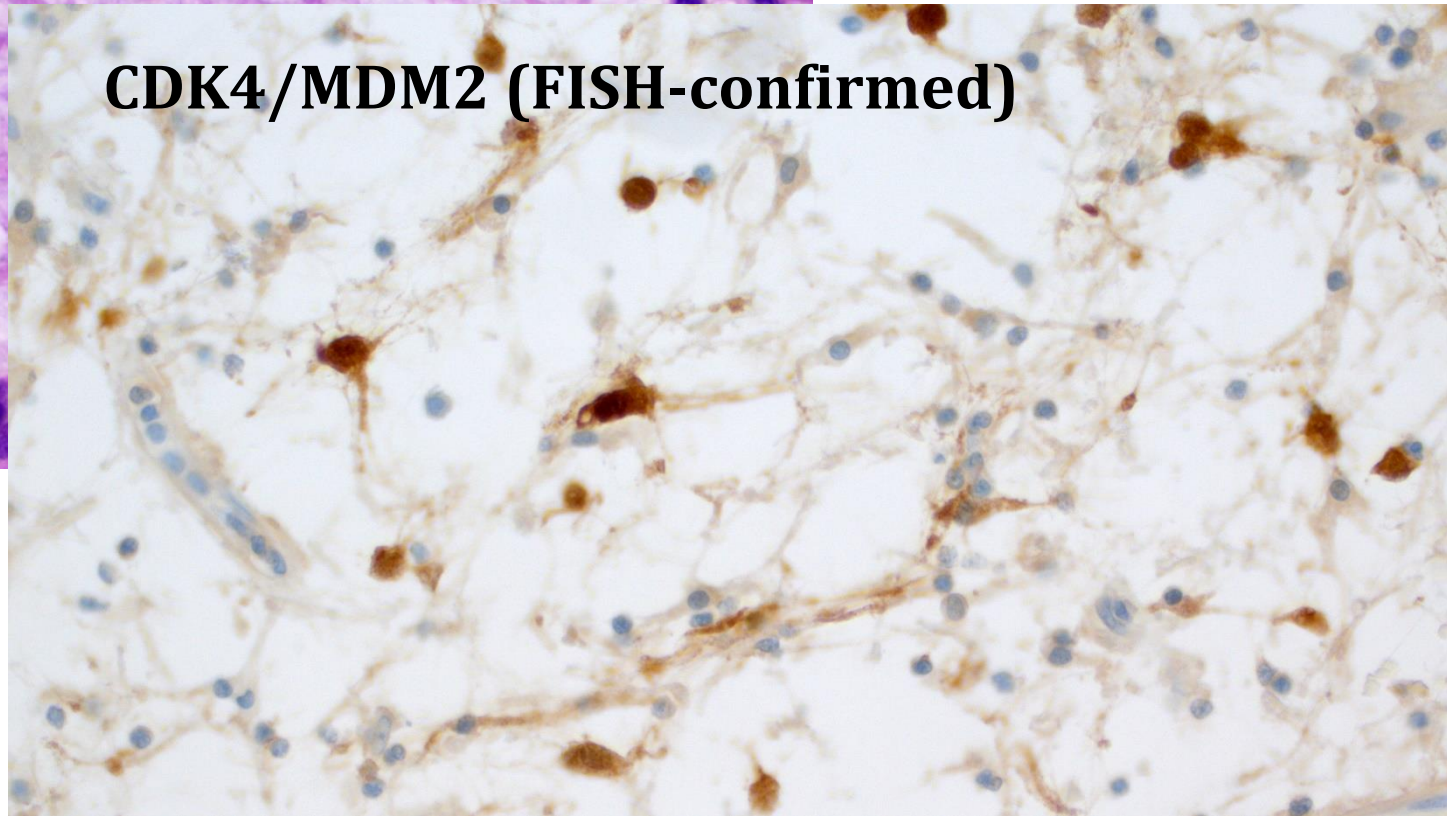




**WD liposarcoma with
excessive myxoid change**



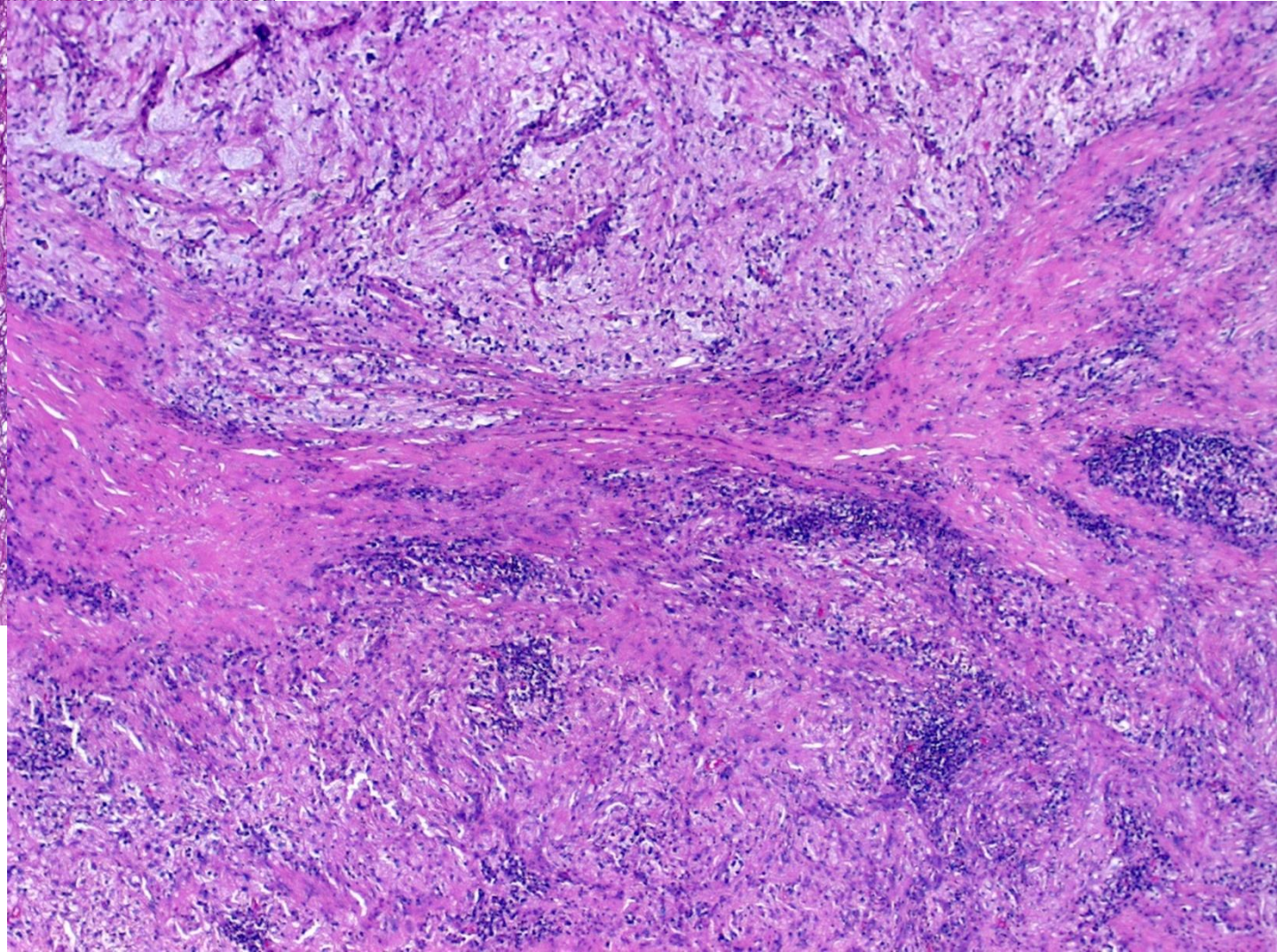
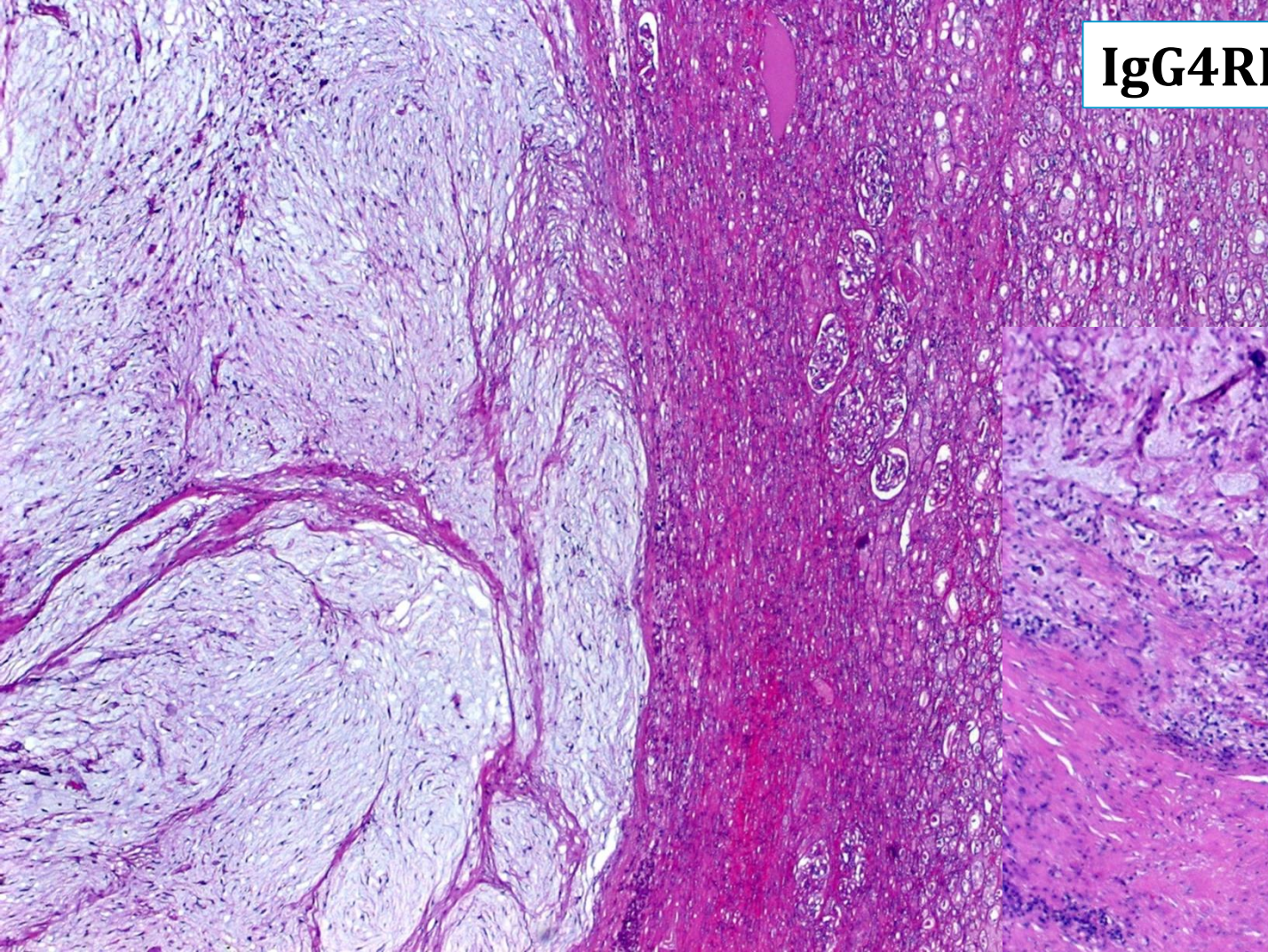
CDK4/MDM2 (FISH-confirmed)



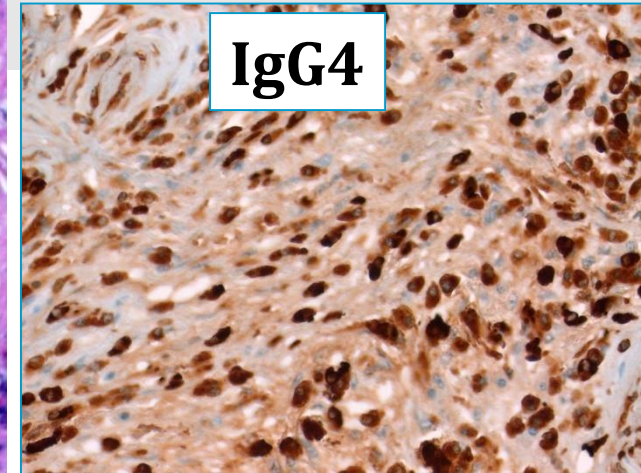
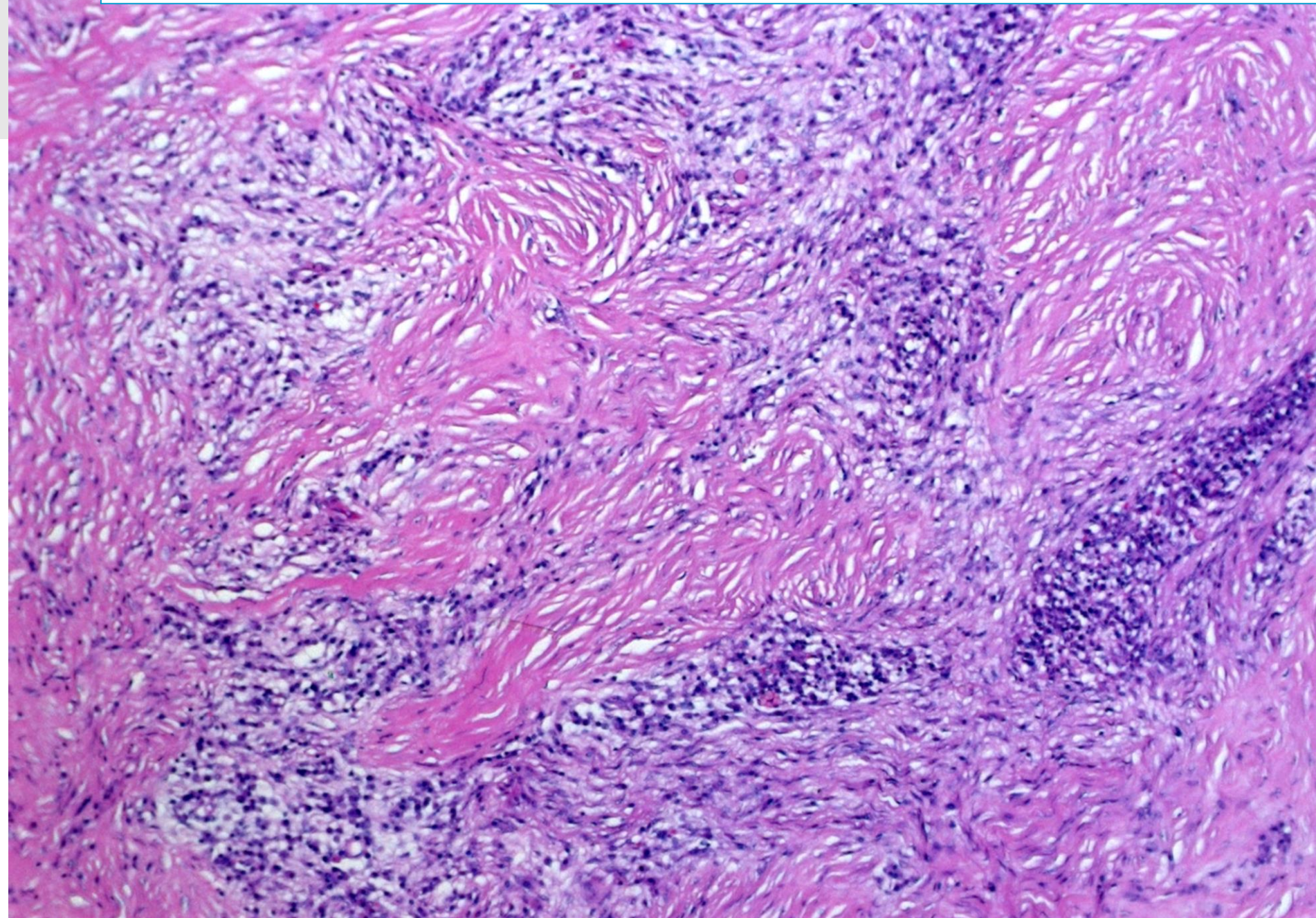
IgG4-related kidney disease may present as mass lesion and display myxoid features



IgG4RD + perinephric myxoid pseudotumor



IgG4-RSD: Typical storiform fibrosis & basket weave collagen pattern



IgG4

IgG4: IgG = 1: 1



IgG

IgG4-related disease

Check previous reports

Contact clinicians

Additional manifestations?

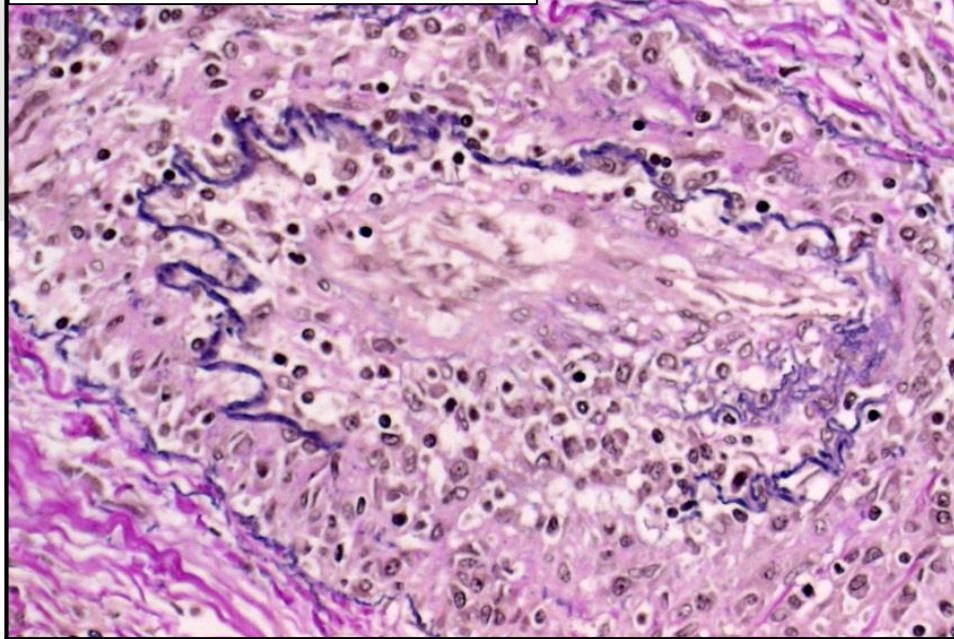
IgG4 serology?

Table 2. Names of previously recognized conditions that comprise or may comprise parts of the IgG4-related disease spectrum

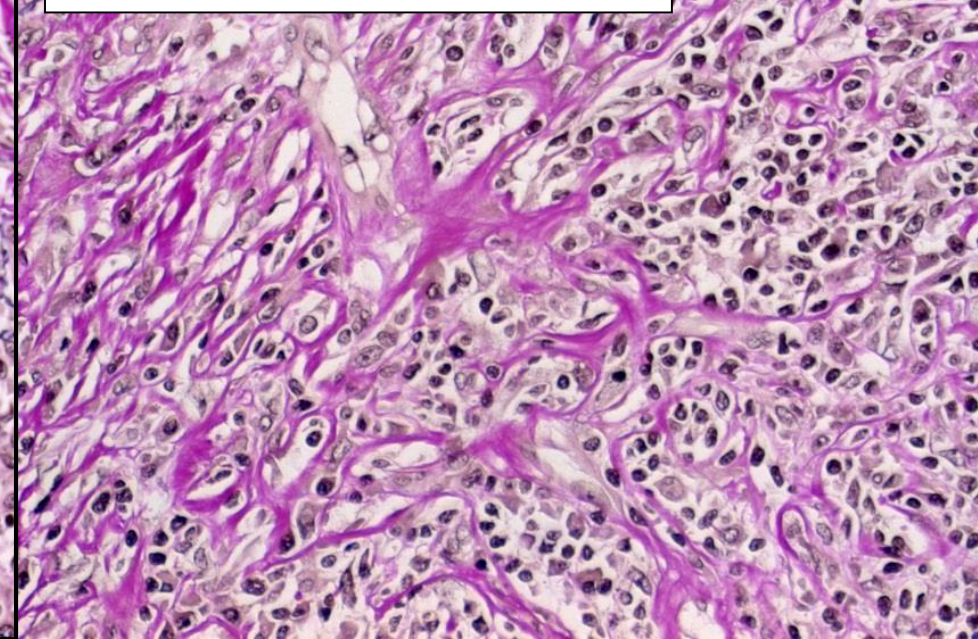
Mikulicz disease
Küttner tumor
Riedel thyroiditis
Eosinophilic angiocentric fibrosis
Multifocal fibrosclerosis
Lymphoplasmacytic sclerosing pancreatitis/
autoimmune pancreatitis
Inflammatory pseudotumor
Fibrosing mediastinitis
Sclerosing mesenteritis
Retroperitoneal fibrosis (Ormond disease)
Periaortitis/periarteritis
Inflammatory aortic aneurysm
Cutaneous pseudolymphoma
Idiopathic hypertrophic pachymeningitis
Idiopathic tubulointerstitial nephritis
Idiopathic hypocomplementemic tubulointerstitial nephritis
with extensive tubulointerstitial deposits
Idiopathic cervical fibrosis



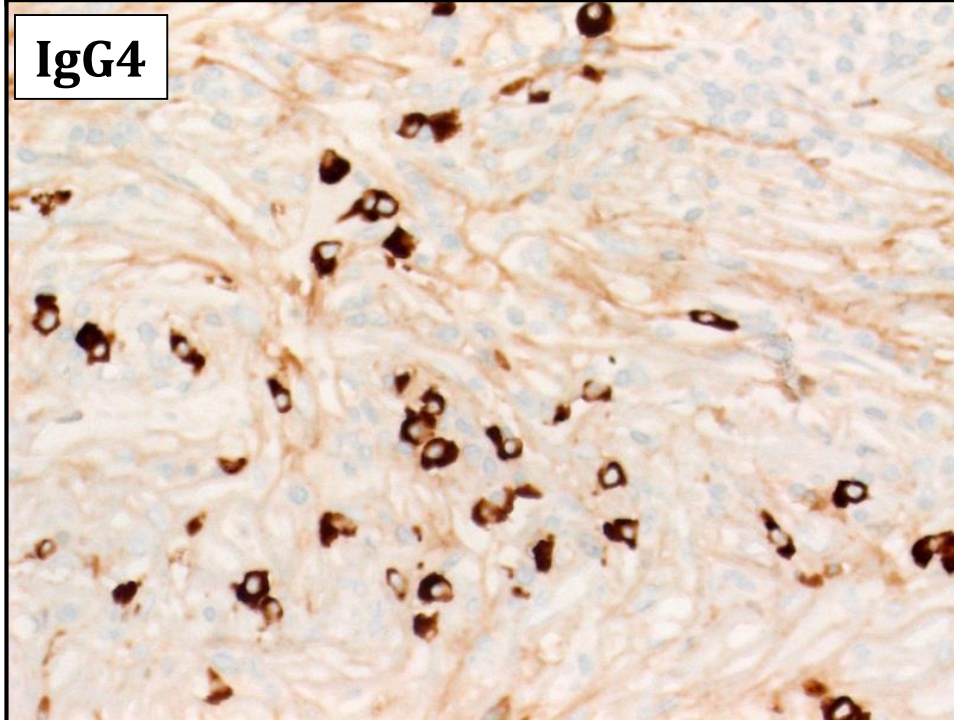
Obliterative angiitis



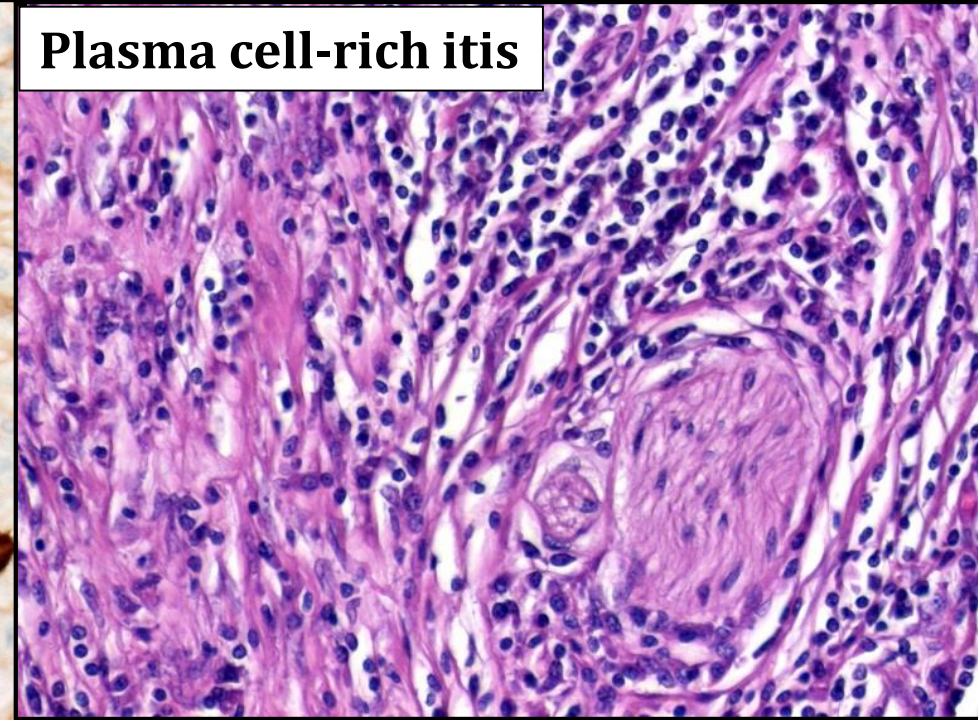
Storiform fibrosclerosis



IgG4

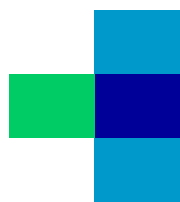
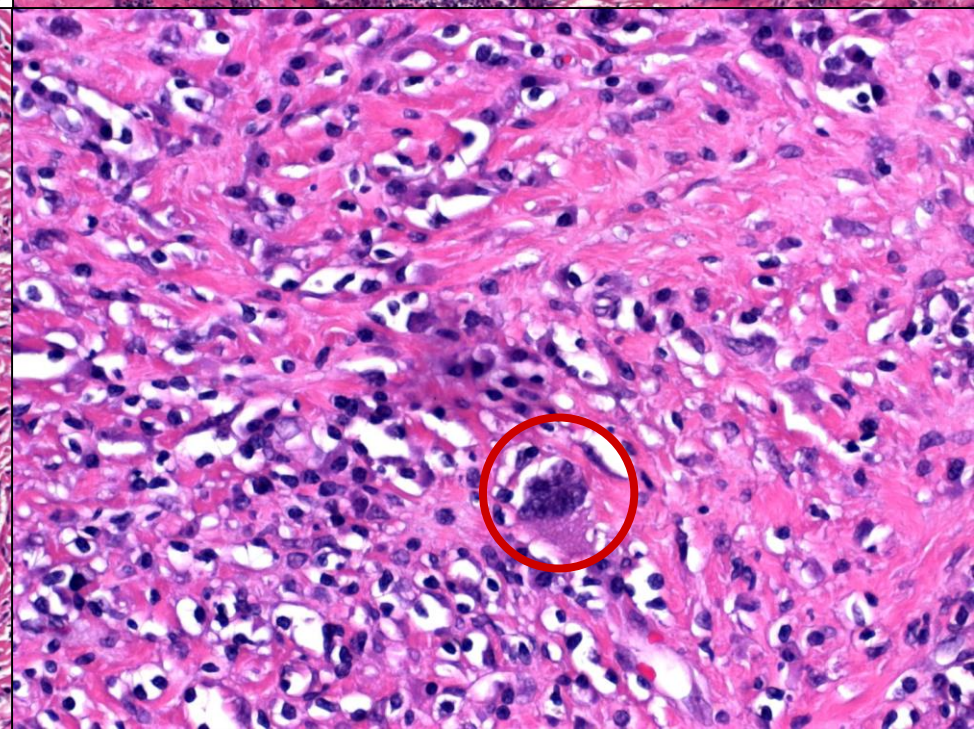
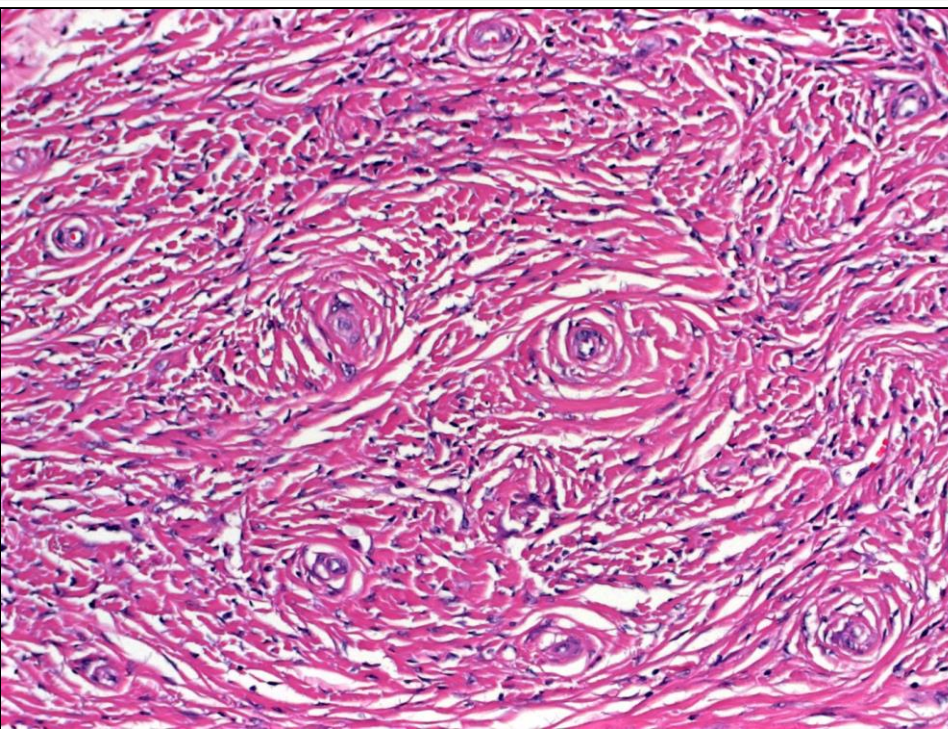
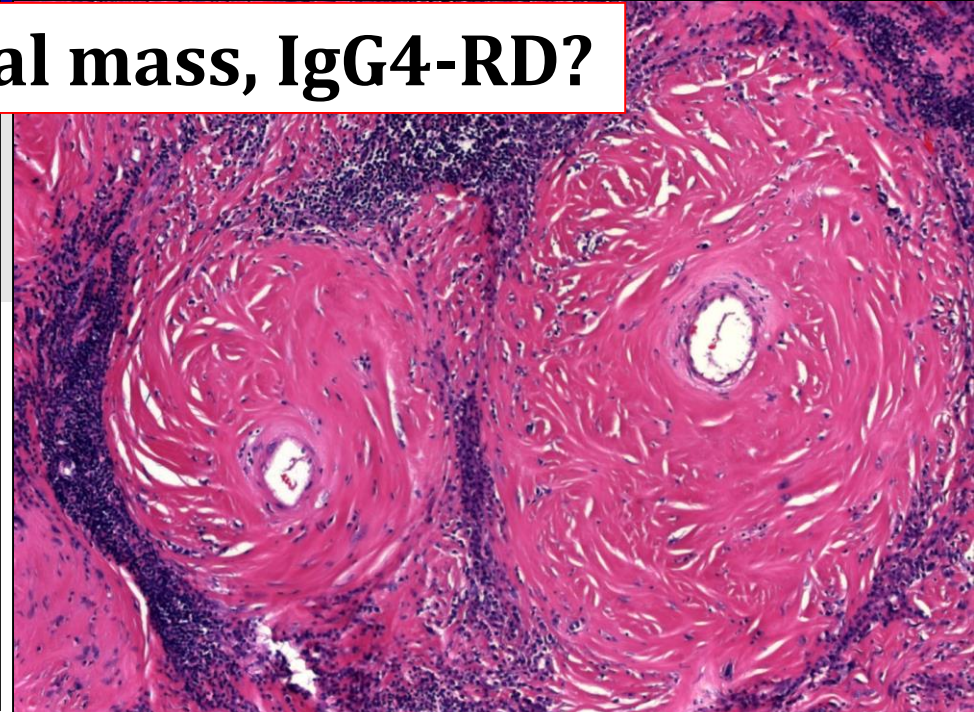


Plasma cell-rich itis

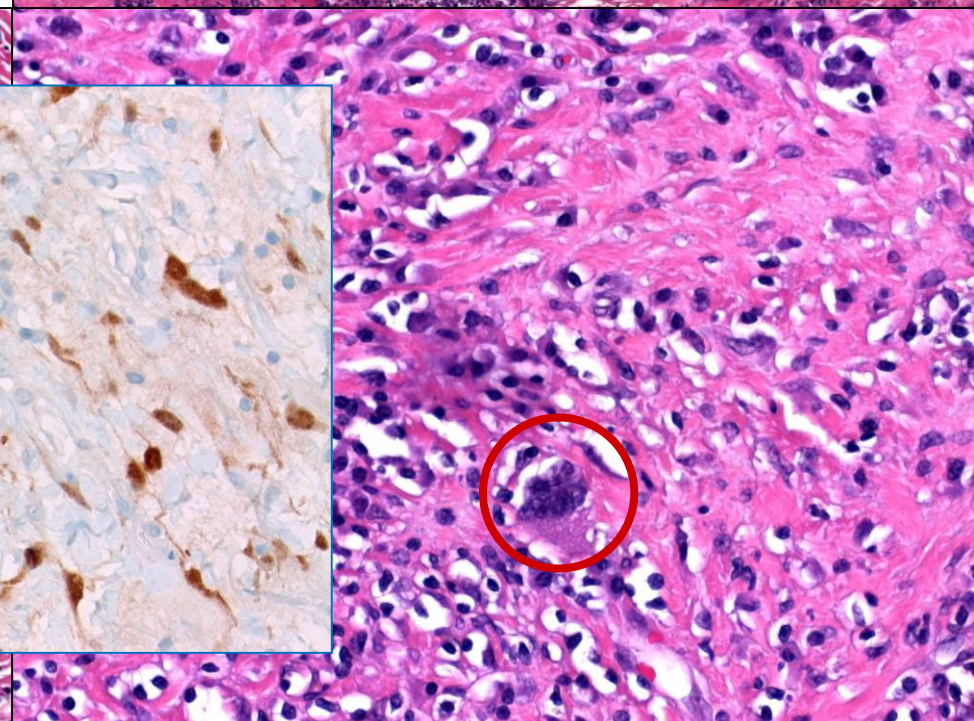
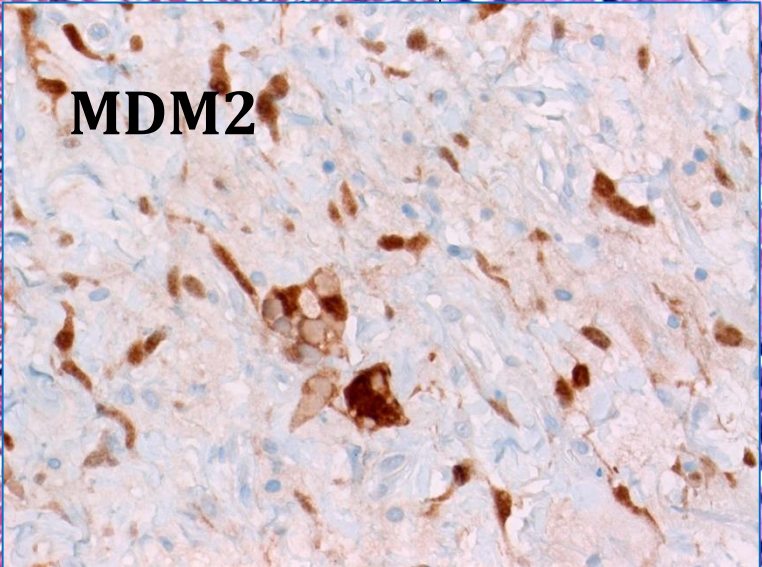
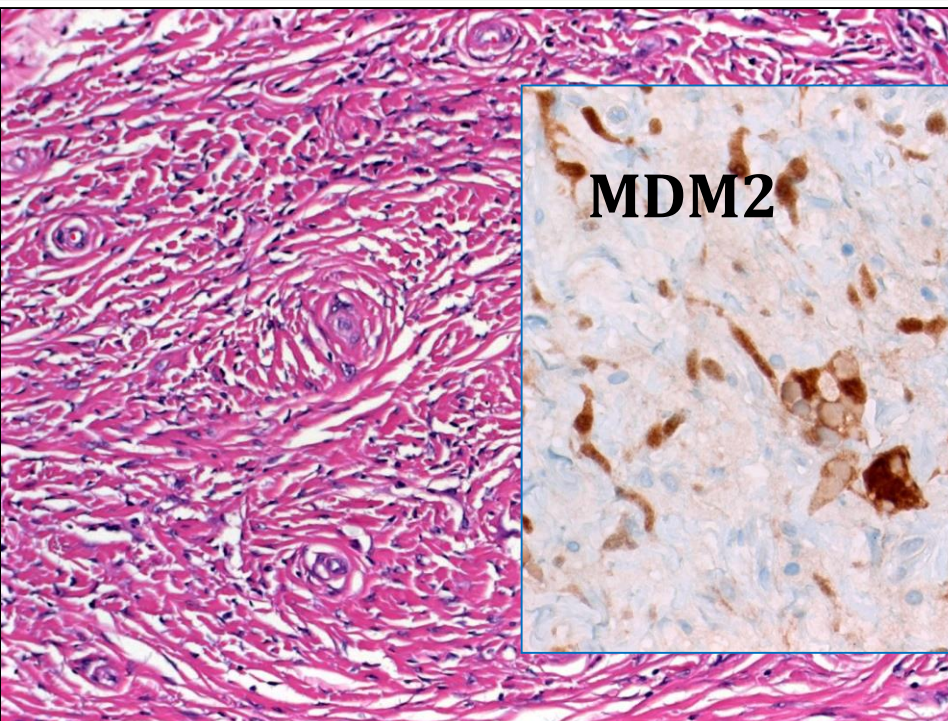
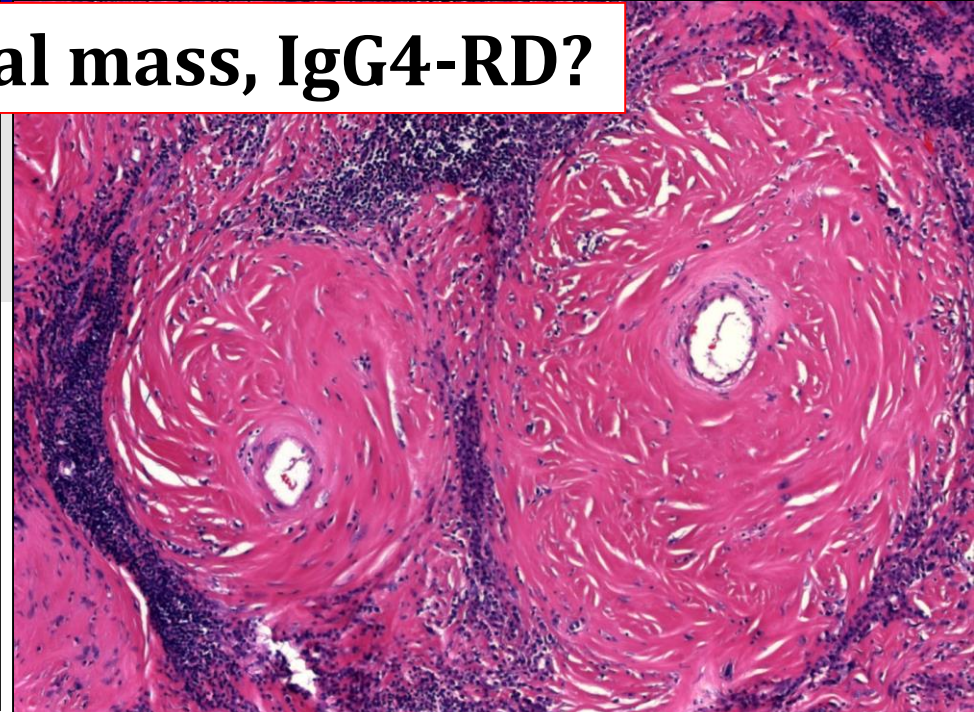


**The 4
cardinal features
of IgG4-RSD**

Huge perihilar renal mass, IgG4-RD?



Huge perihilar renal mass, IgG4-RD?



um



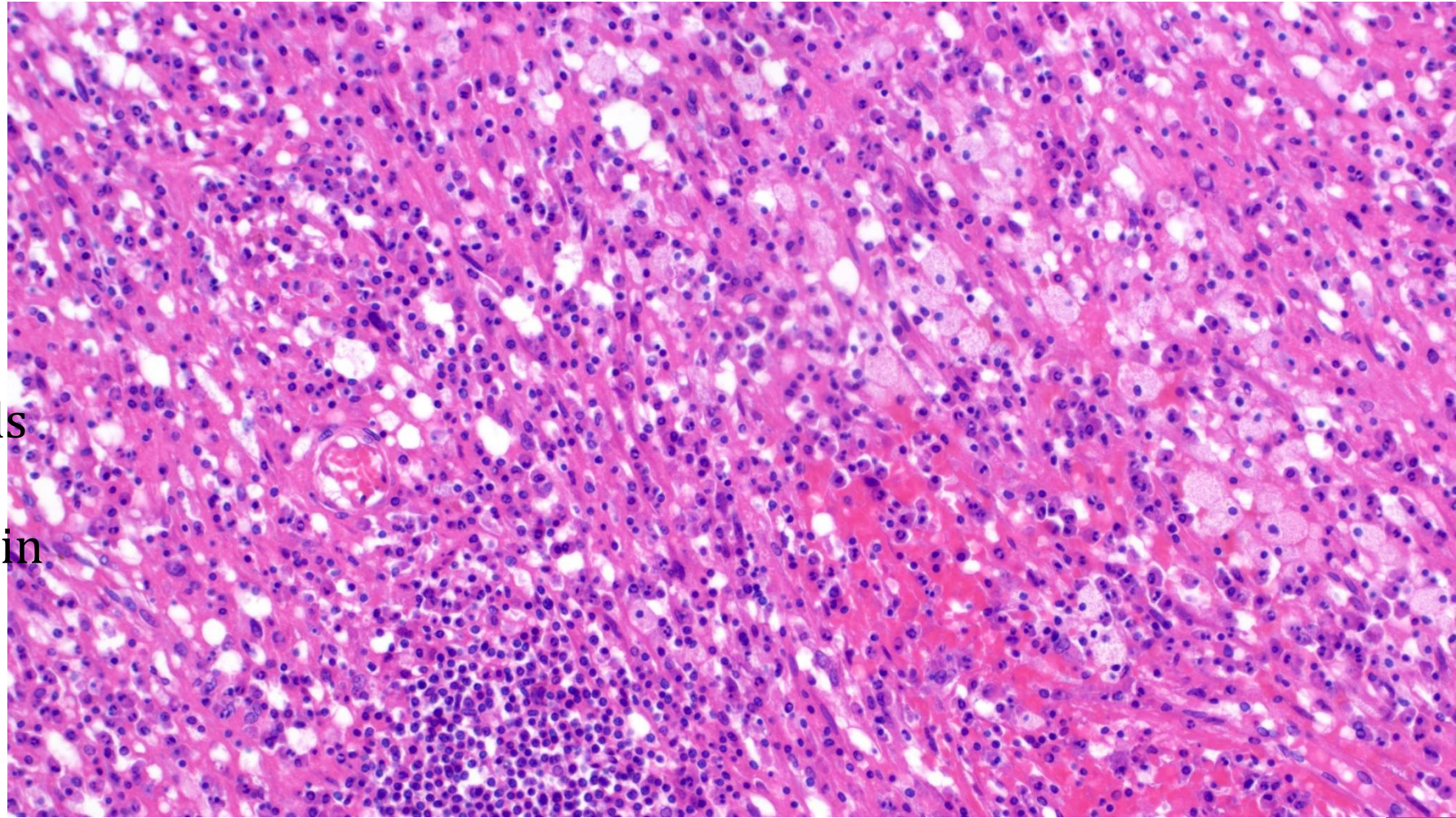
Xanthogranulomatous nephritis

Geographic or nidus-like necrosis.

Histiocytic palisades at periphery of necrosis.

Predominance of foamy cells

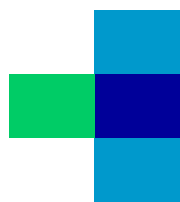
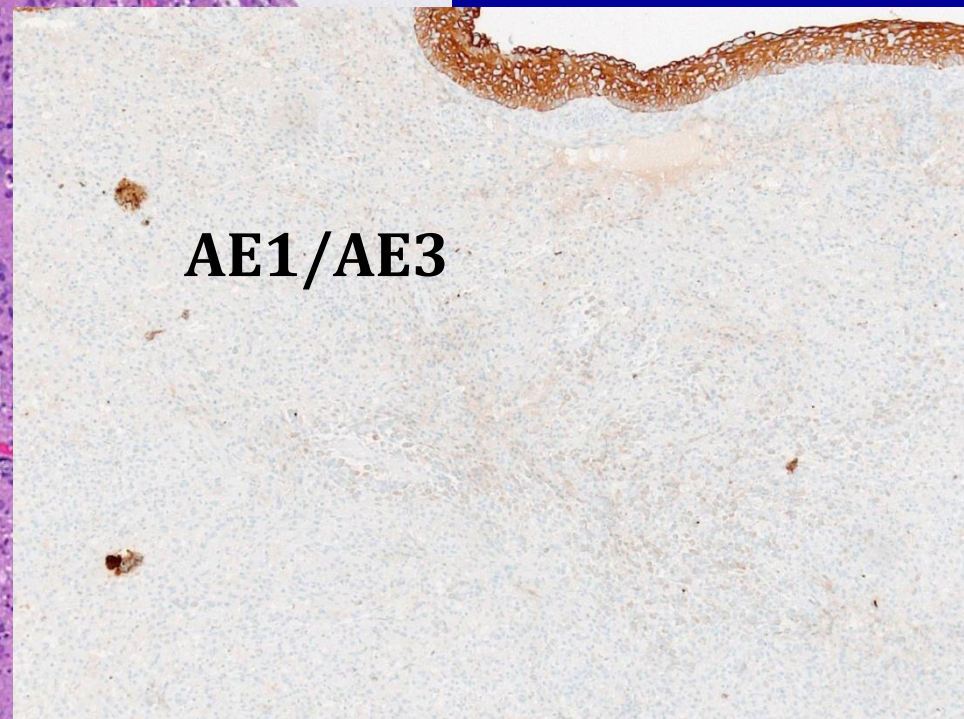
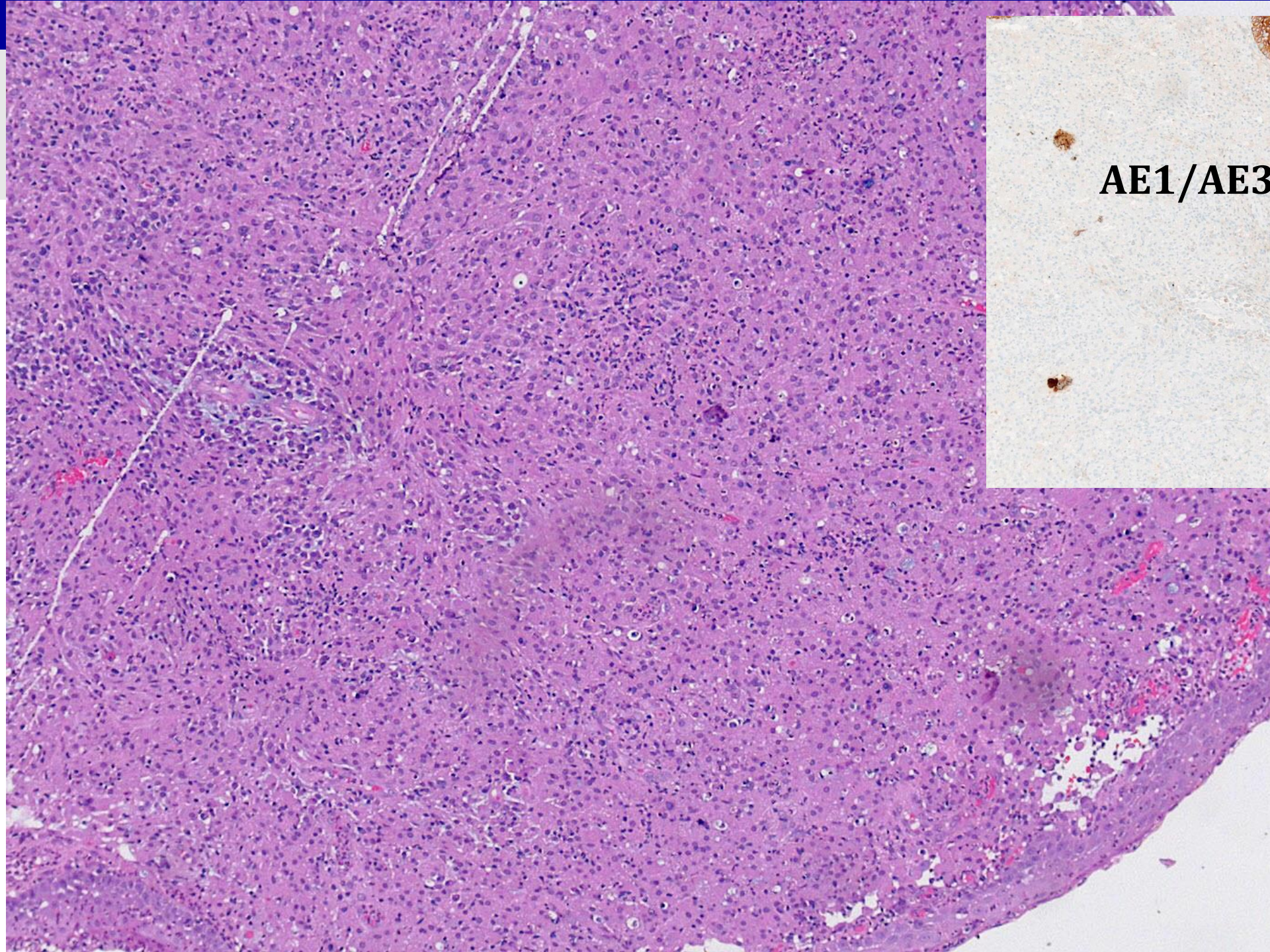
Remnants of secretion within necrotic centers.

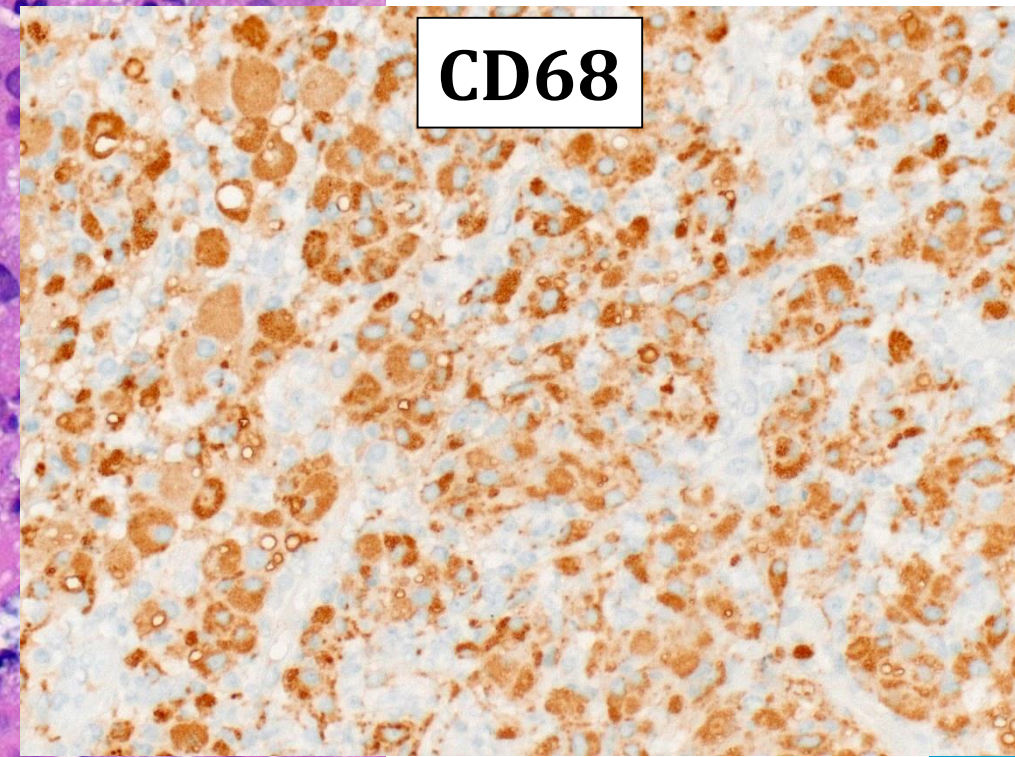
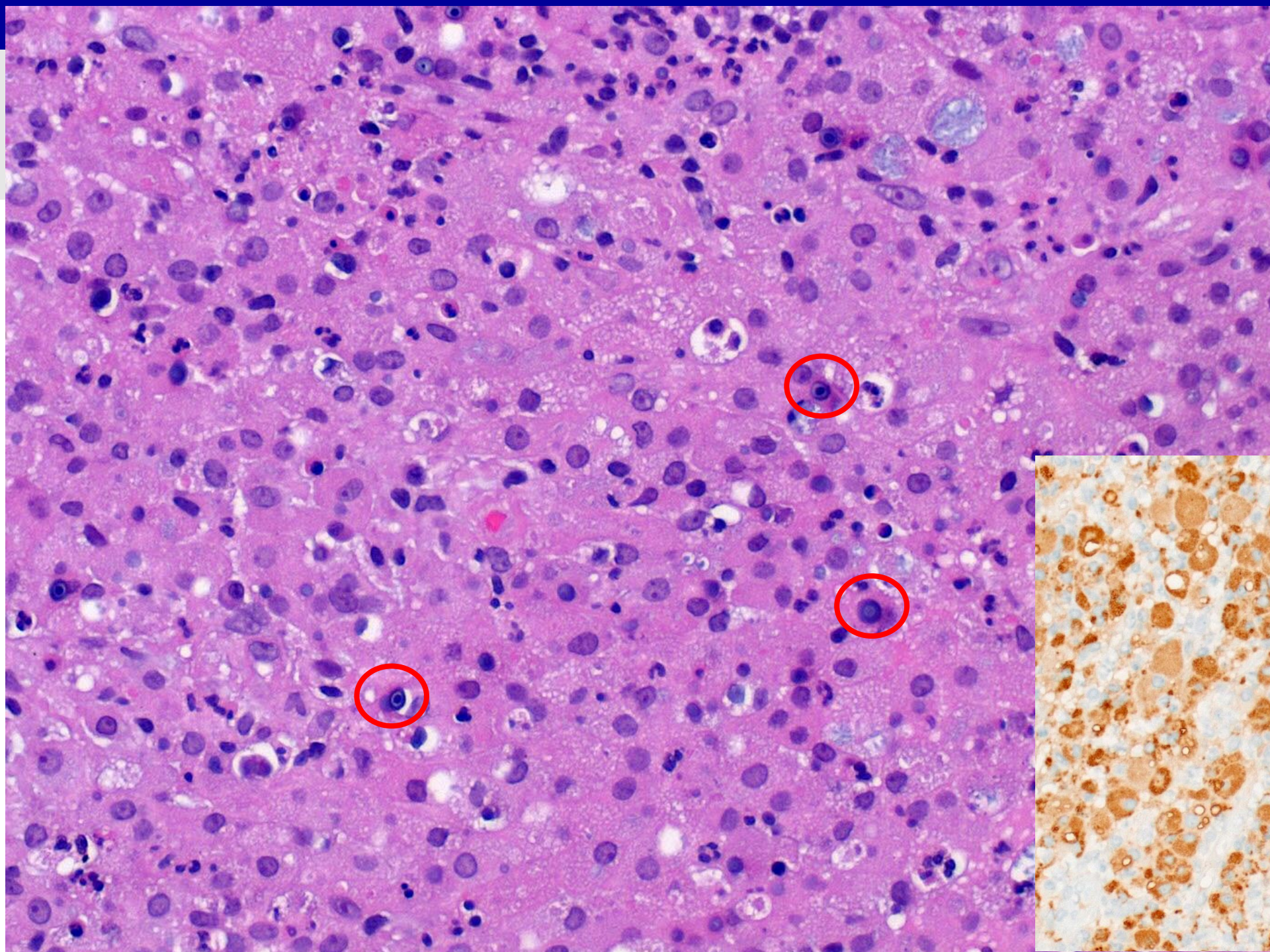


Malakoplakia

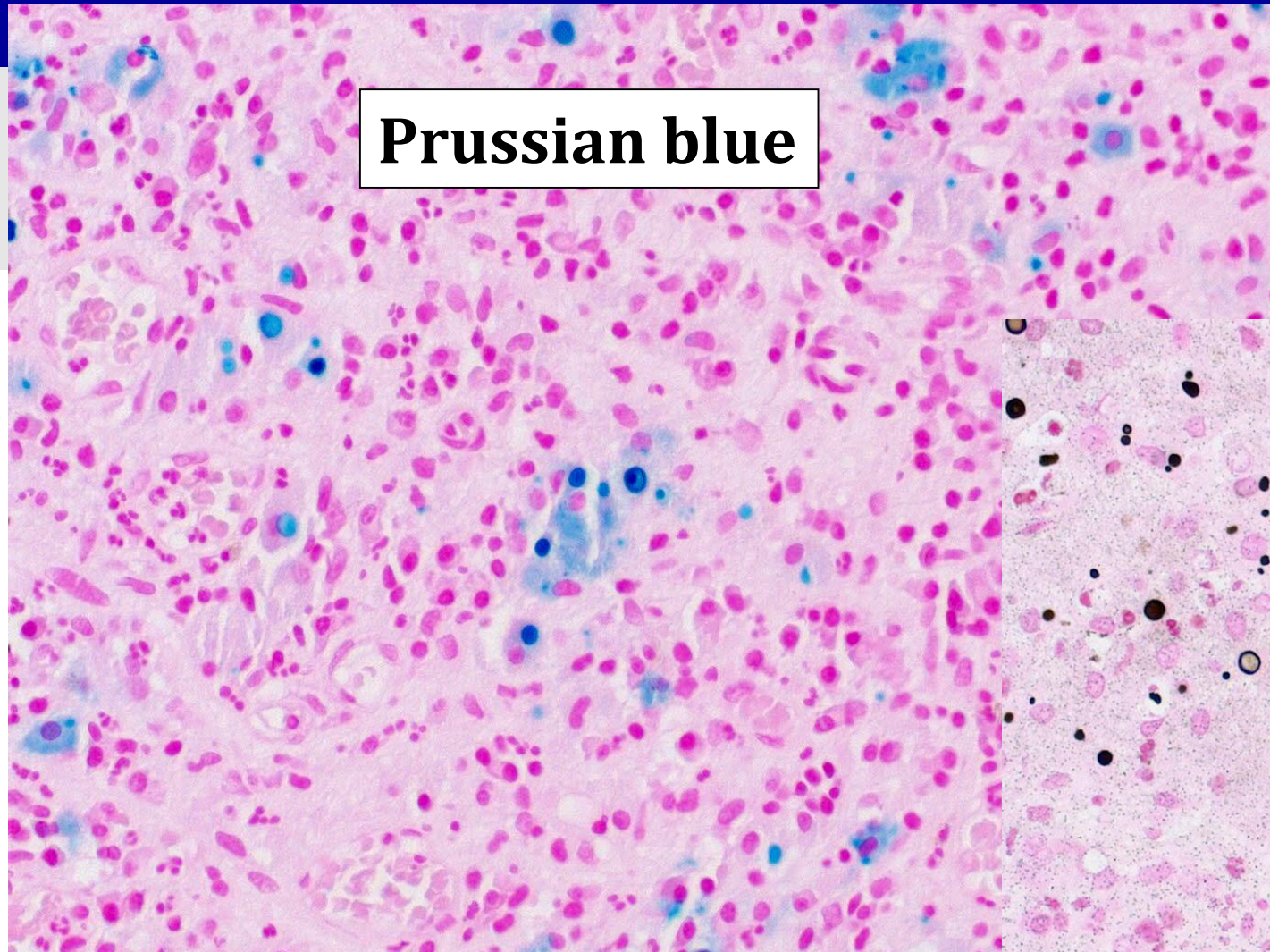
- Rare tumor-like mass-forming itis.
 - **Mainly kidney & bladder.**
 - Etiology elusive.
 - Characteristic histology:
 - Pinkish CD68+ histiocytes (von Hanseman cells).
 - Michaelis-Gutmann bodies (PB+, von Kossa+).
- DDx: xanthogranulomatous PN.



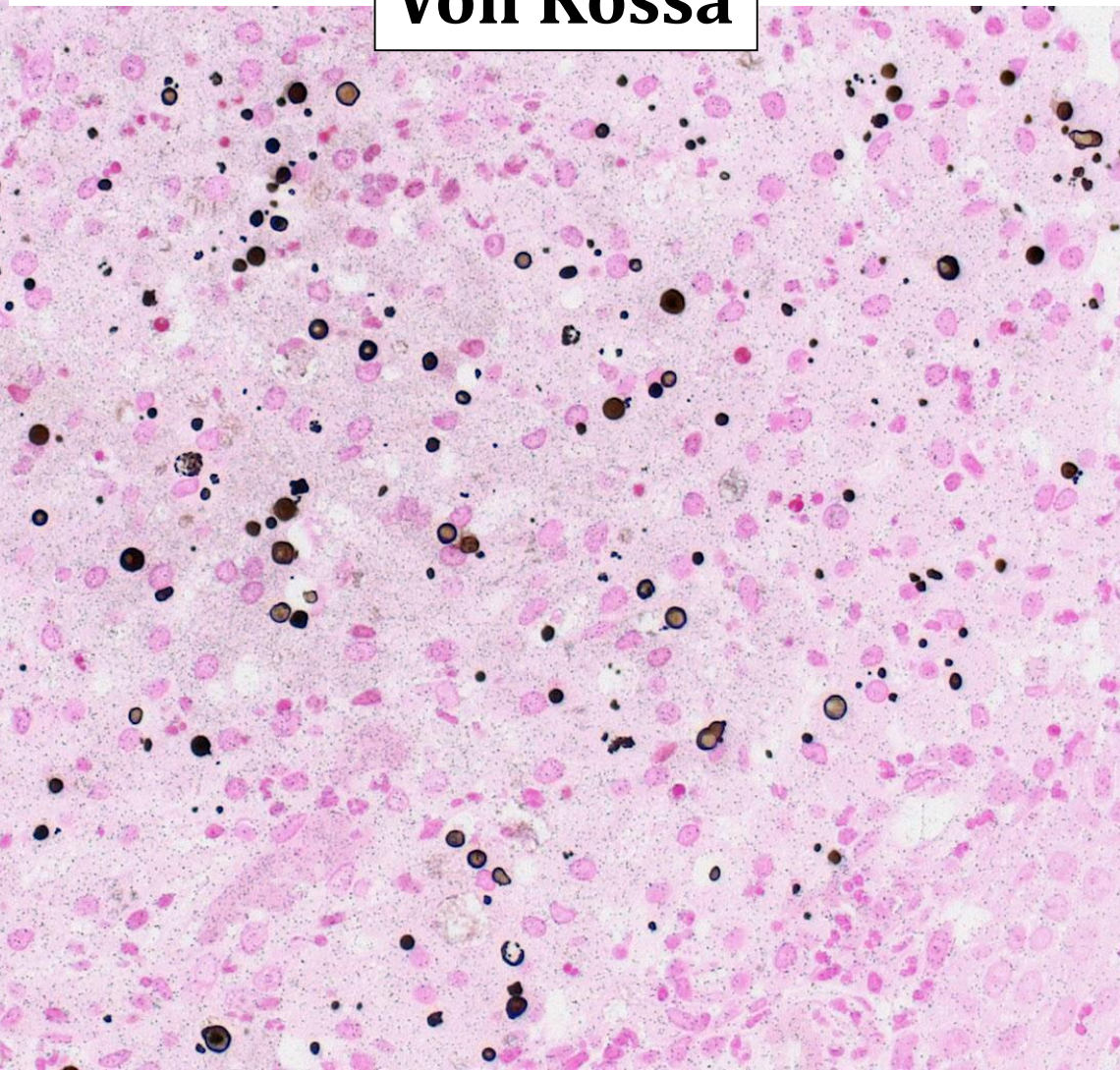




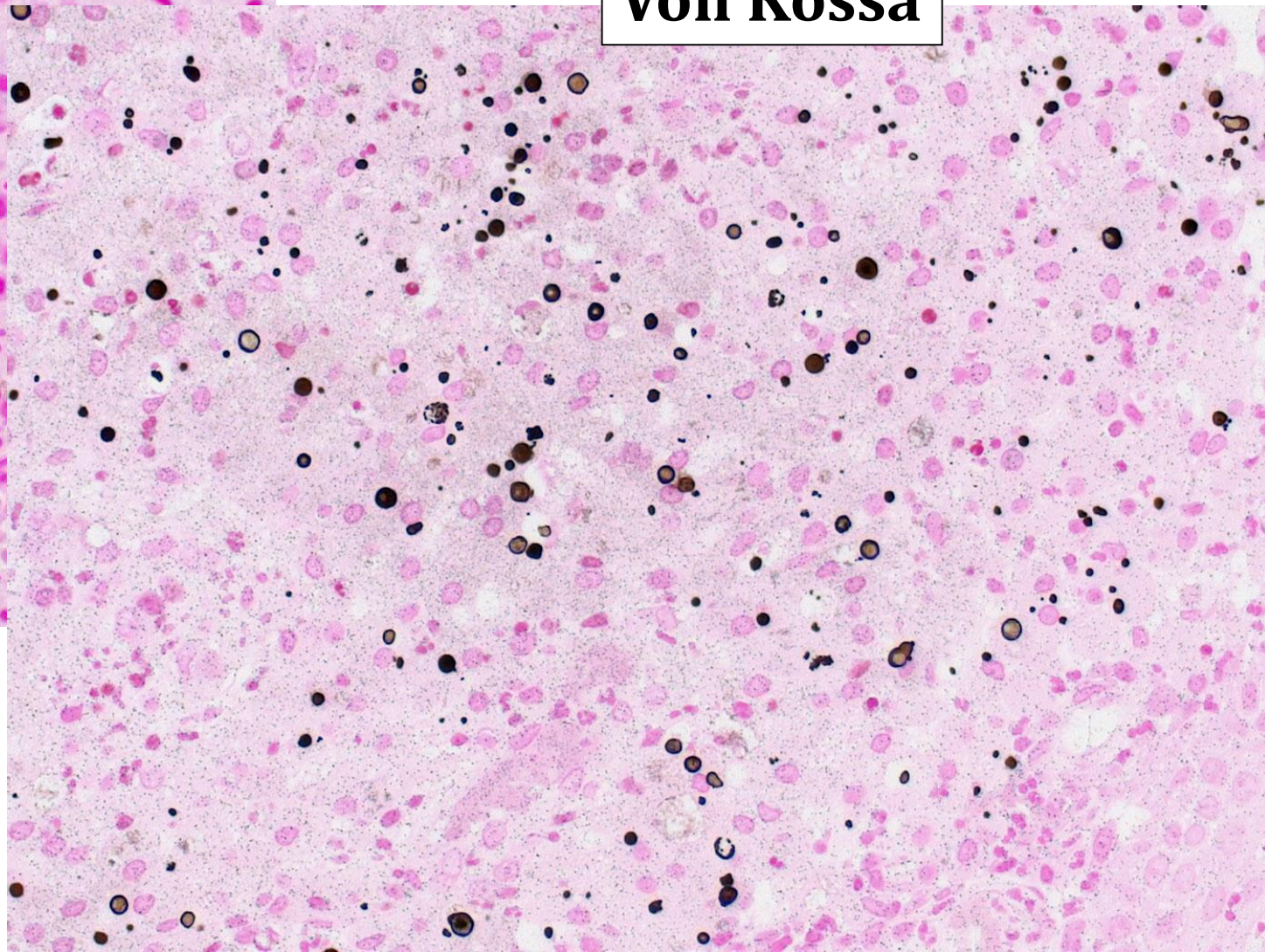
Prussian blue



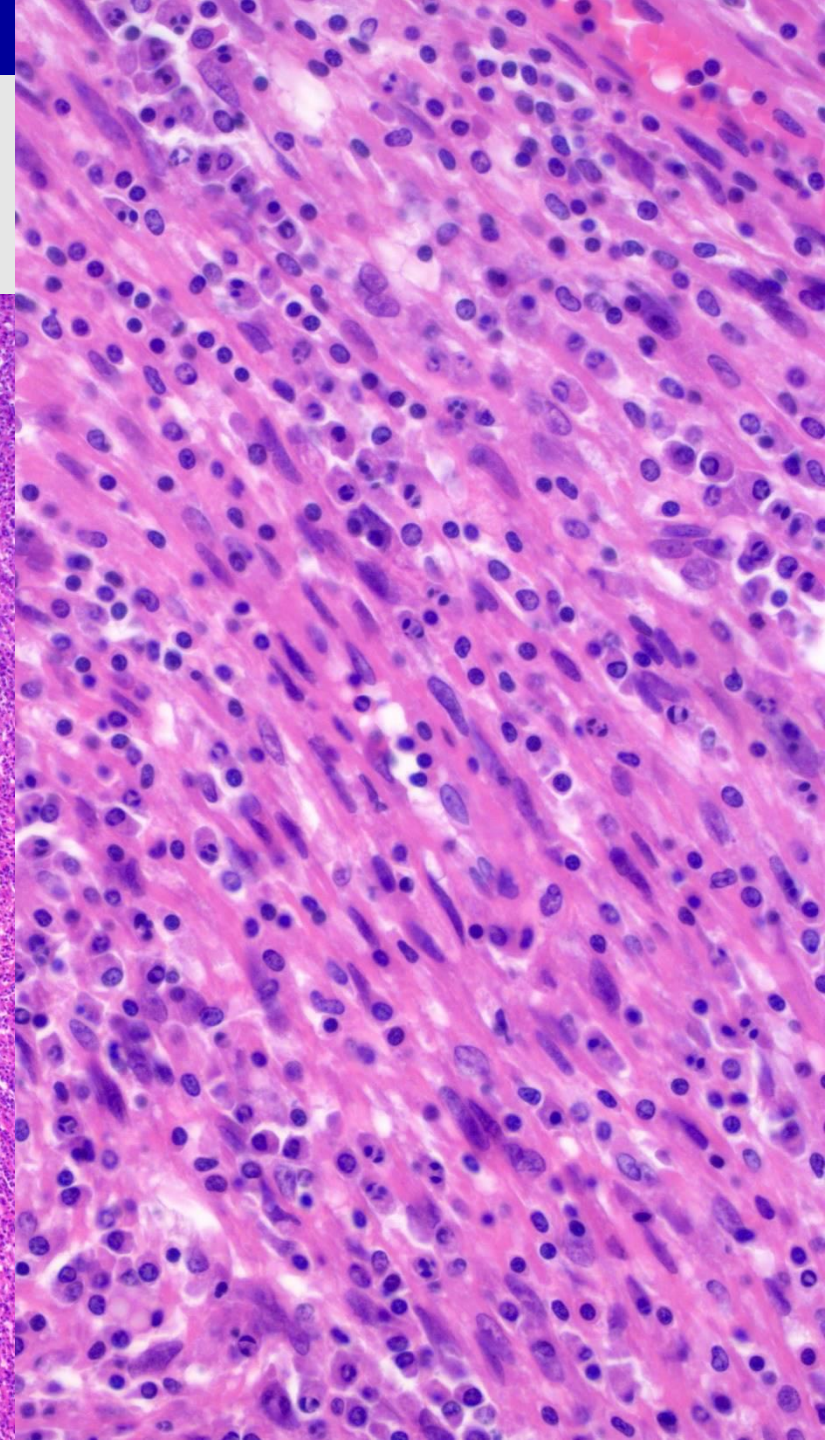
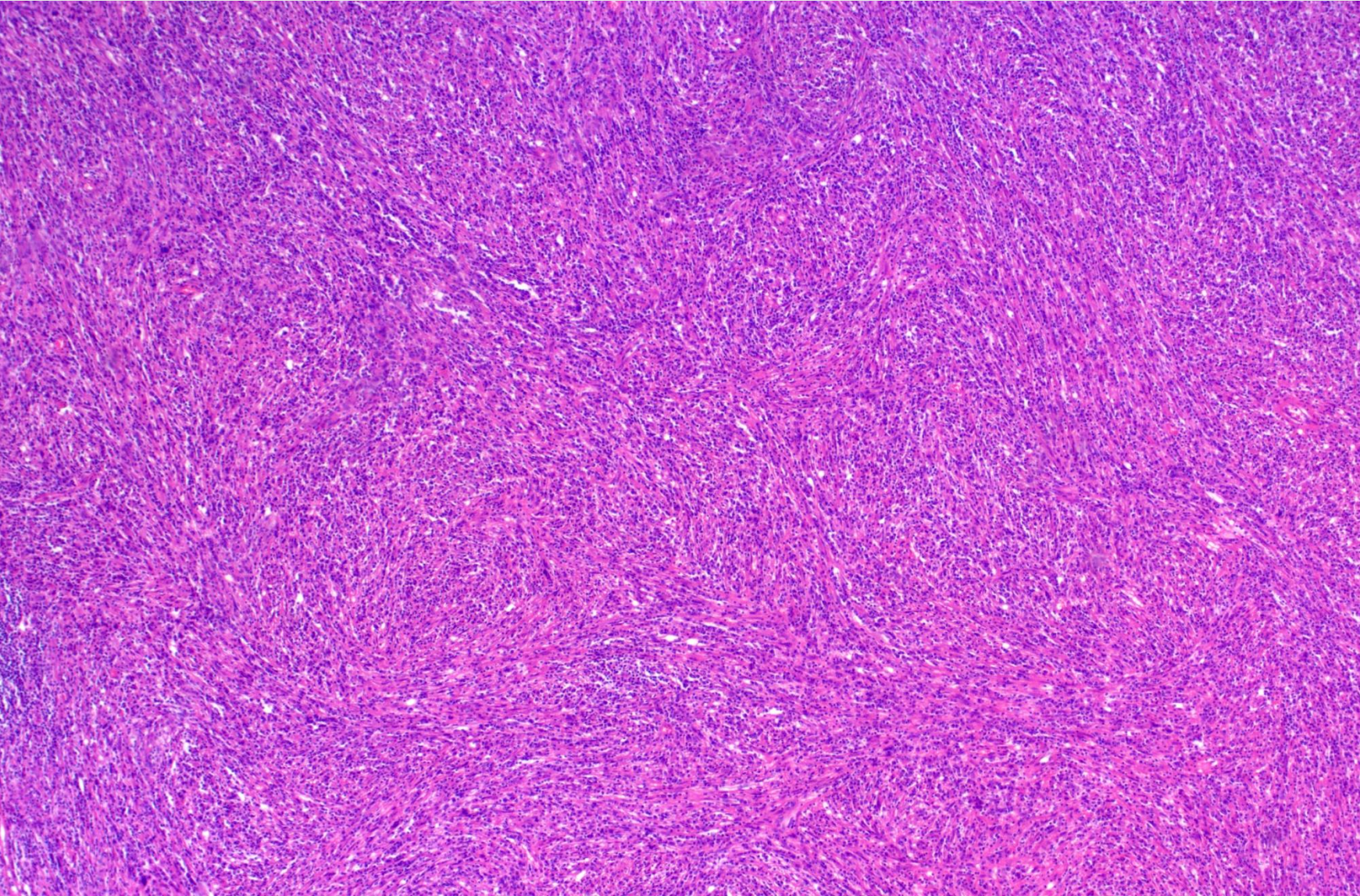
Michaelis-Gutmann bodies



Von Kossa



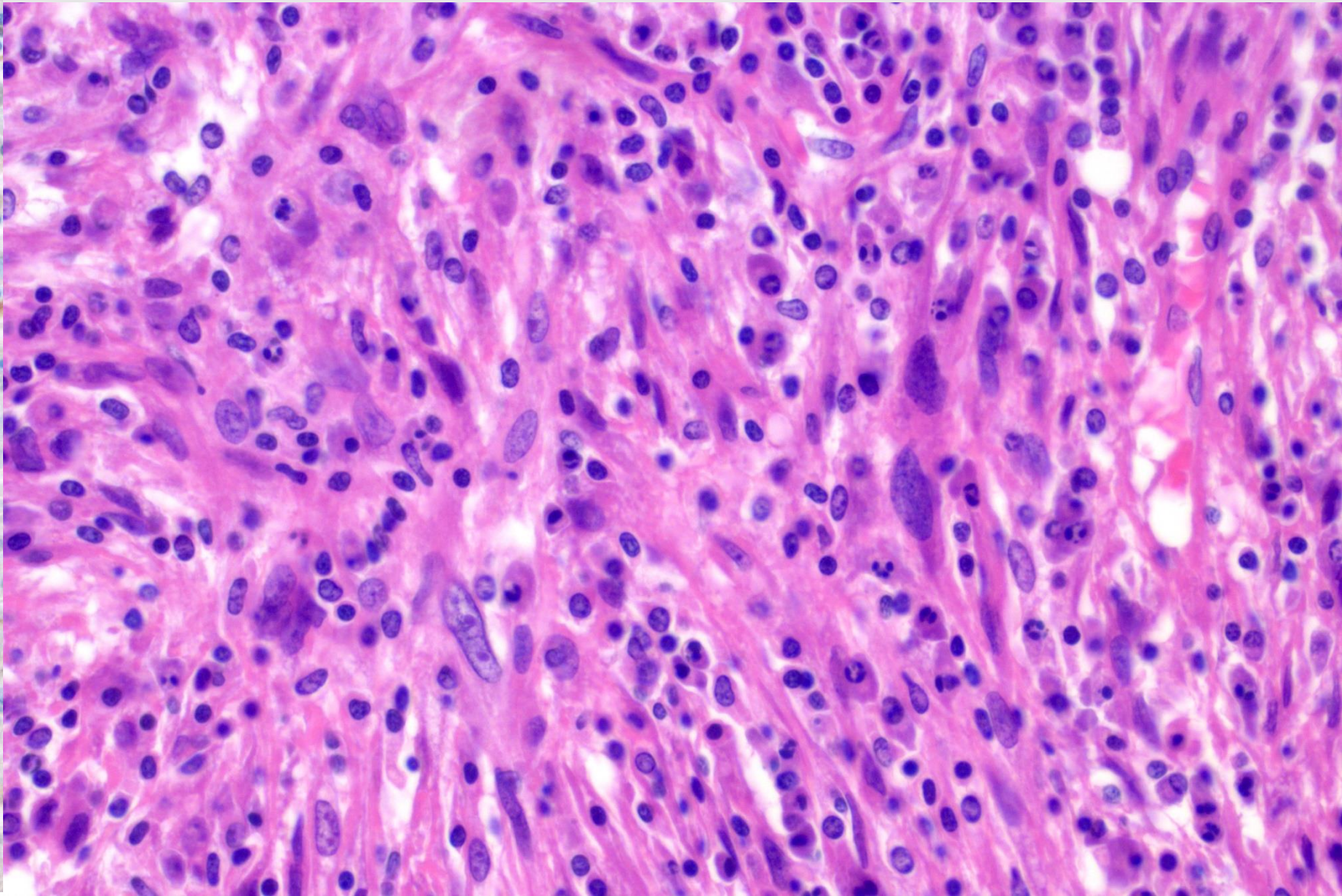
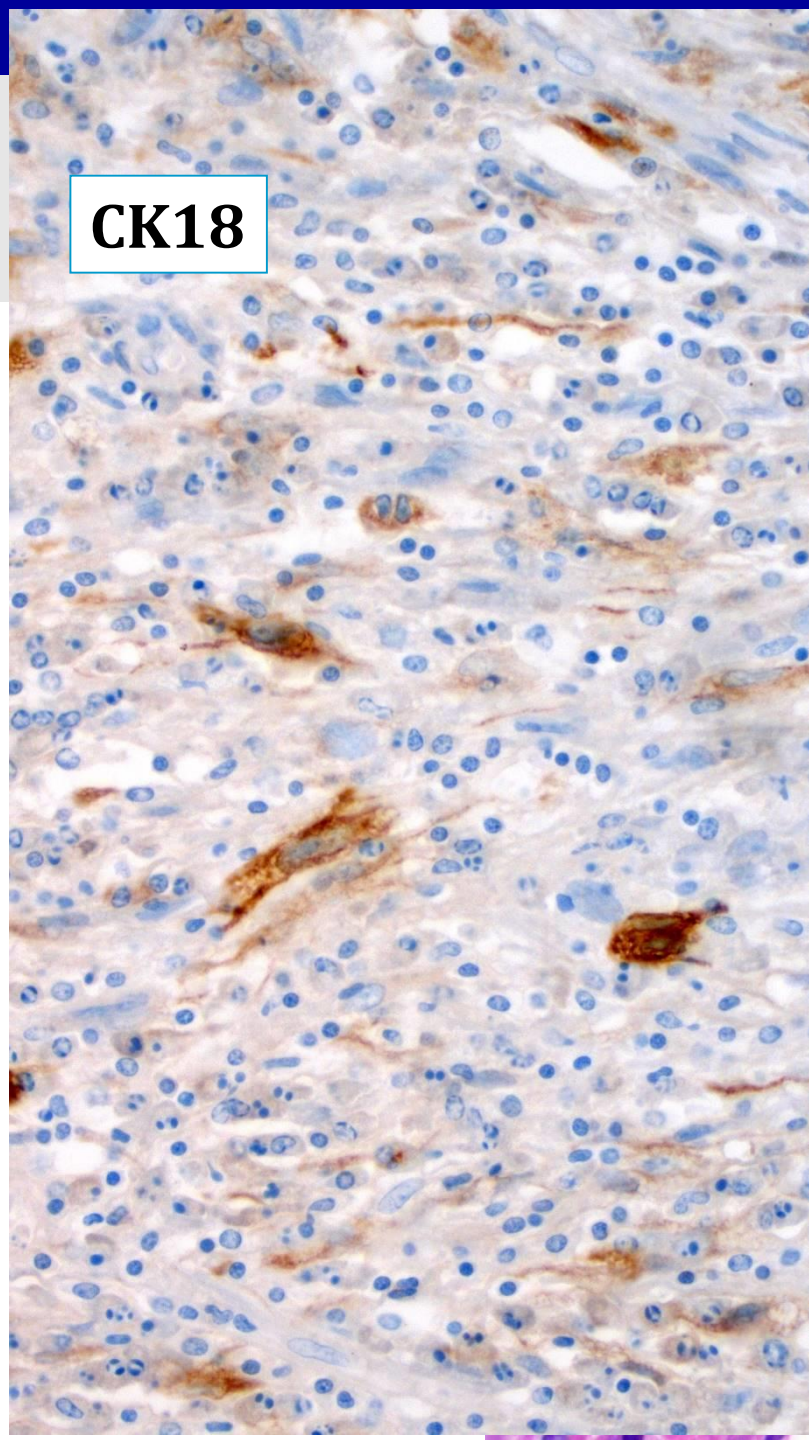
18 yo male of African origin, huge renal mass



IMT-like but ALK-

IMT-like sarcomatoid RCC???

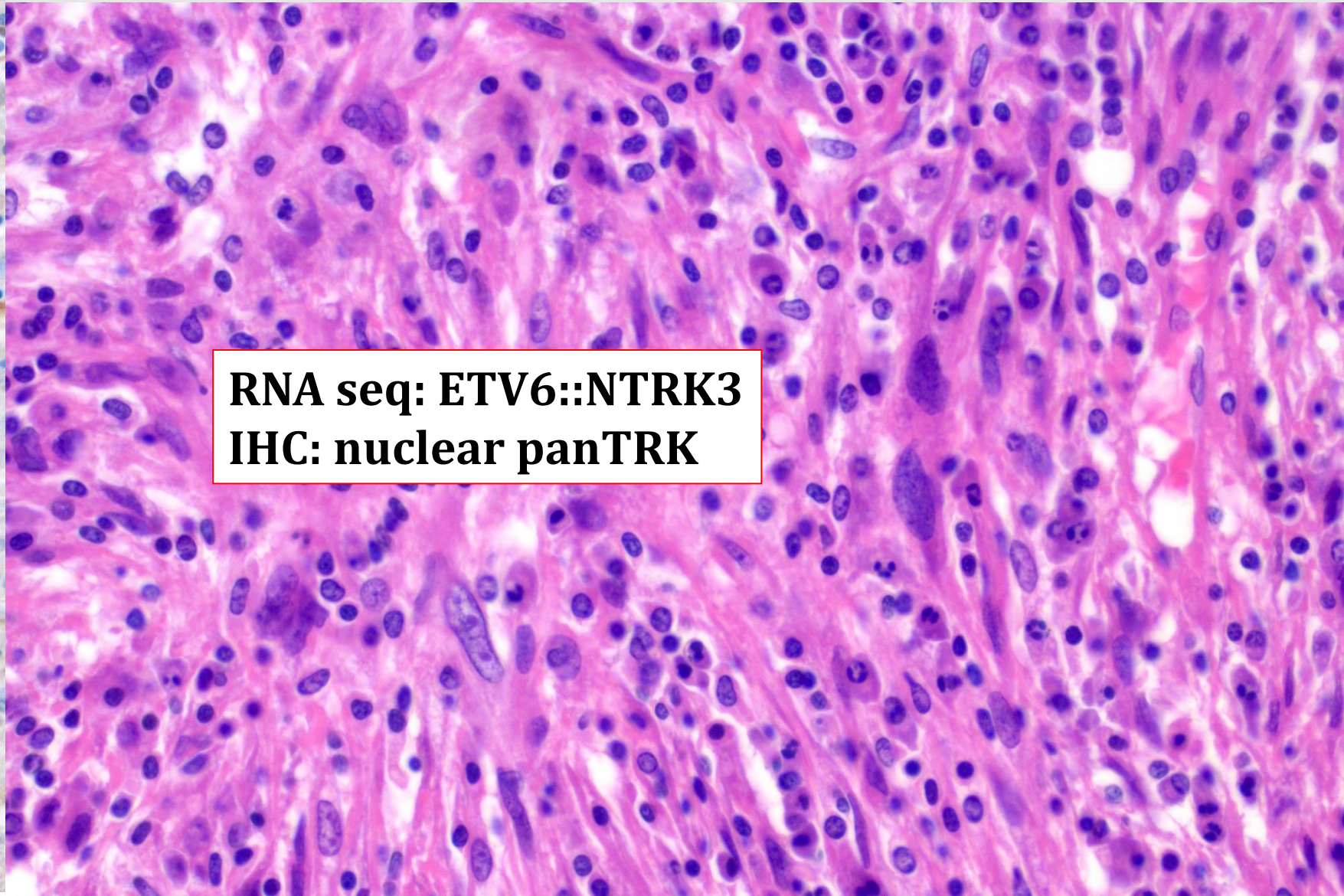
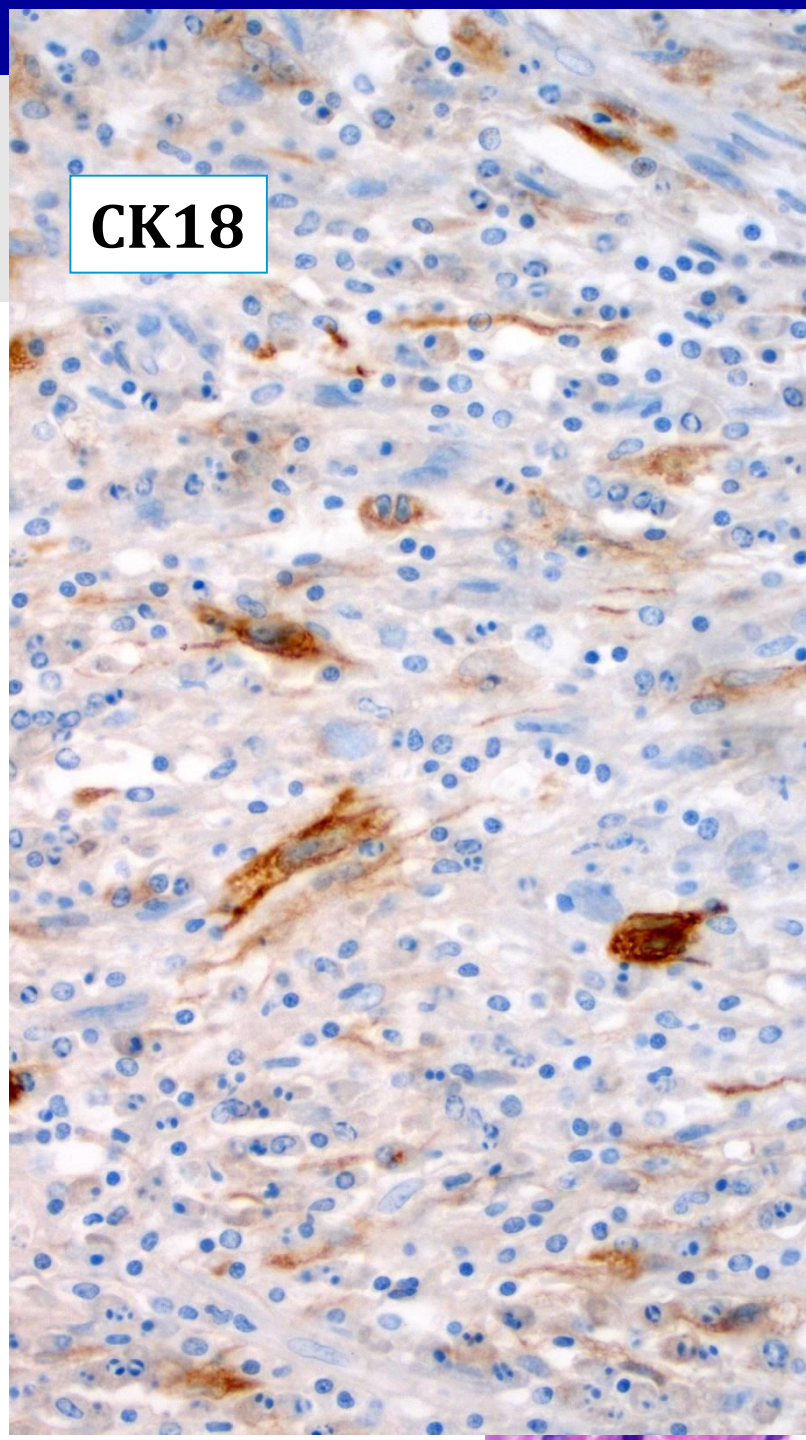
CK18



IMT-like but ALK-

IMT-like sarcomatoid RCC???

CK18



**RNA seq: ETV6::NTRK3
IHC: nuclear panTRK**

Intrarenal sarcoma/sarcomatoid neoplasms and how to approach them

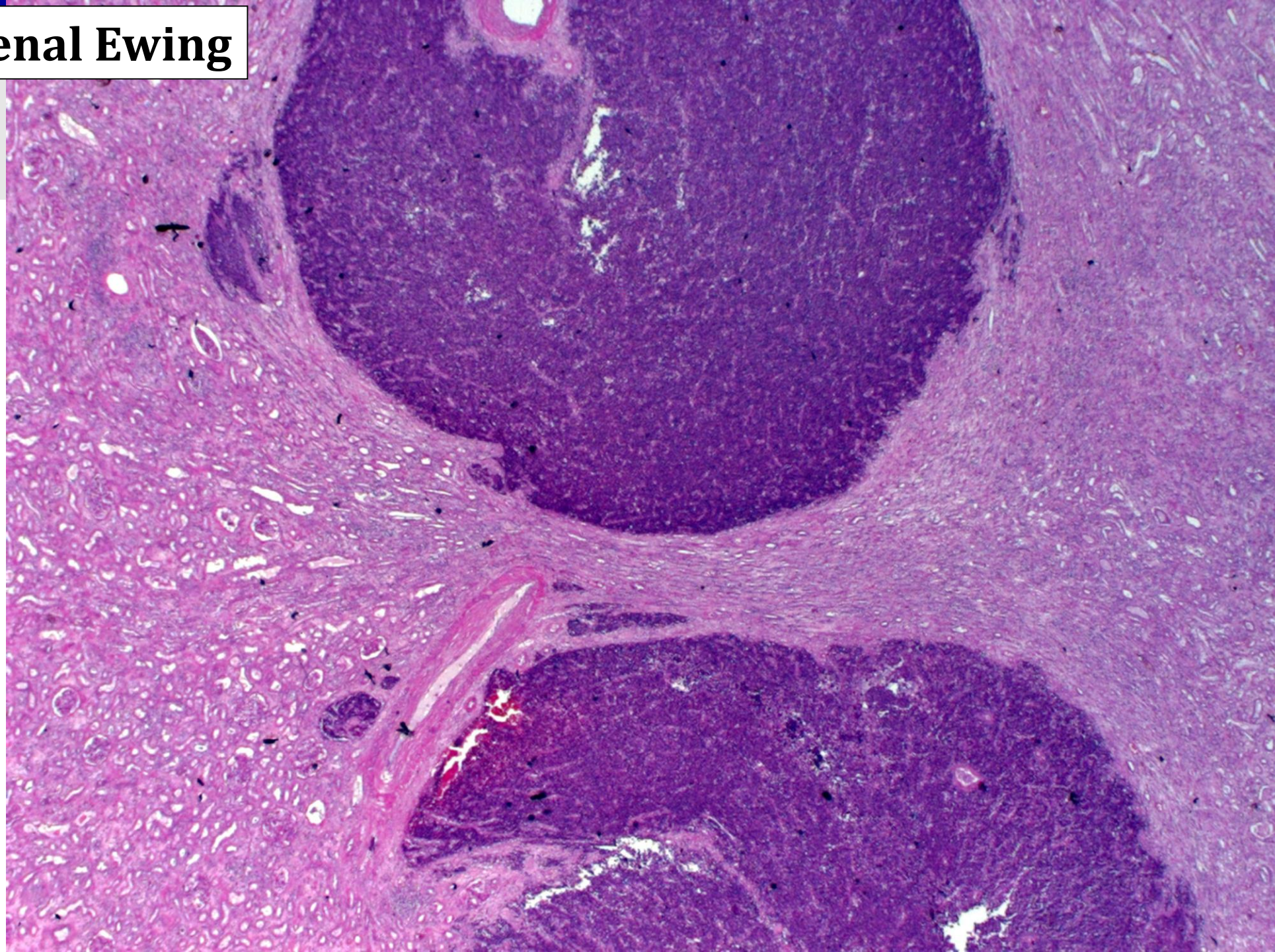
- **Primry sarcomas:**
- Monomorphic sarcomas: fusion-driven (Ewing, synovial, SEF, etc.).
- Occasionally pleomorphic with specific phenotype: angiosarcoma, LMS).
- **Undifferentiated pleomorphic (UPS) or mixed-pattern sarcomas:**
 - Sarcomatoid carcinoma with/ without heterologous elements
 - Secondary sarcomas (perirenal retroperitoneal, mets).
 - Otherwise almost non-existent as true renal primary.

Primary renal Ewing sarcoma

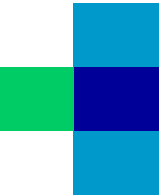
- Described in 1975 (Seemayer et al).
- <300 cases reported (many als PNET).
- **Median age: 30 y (4–46).**
- **M > F (1,5: 1).**
- **Poor prognosis (median survival 26 mo).**

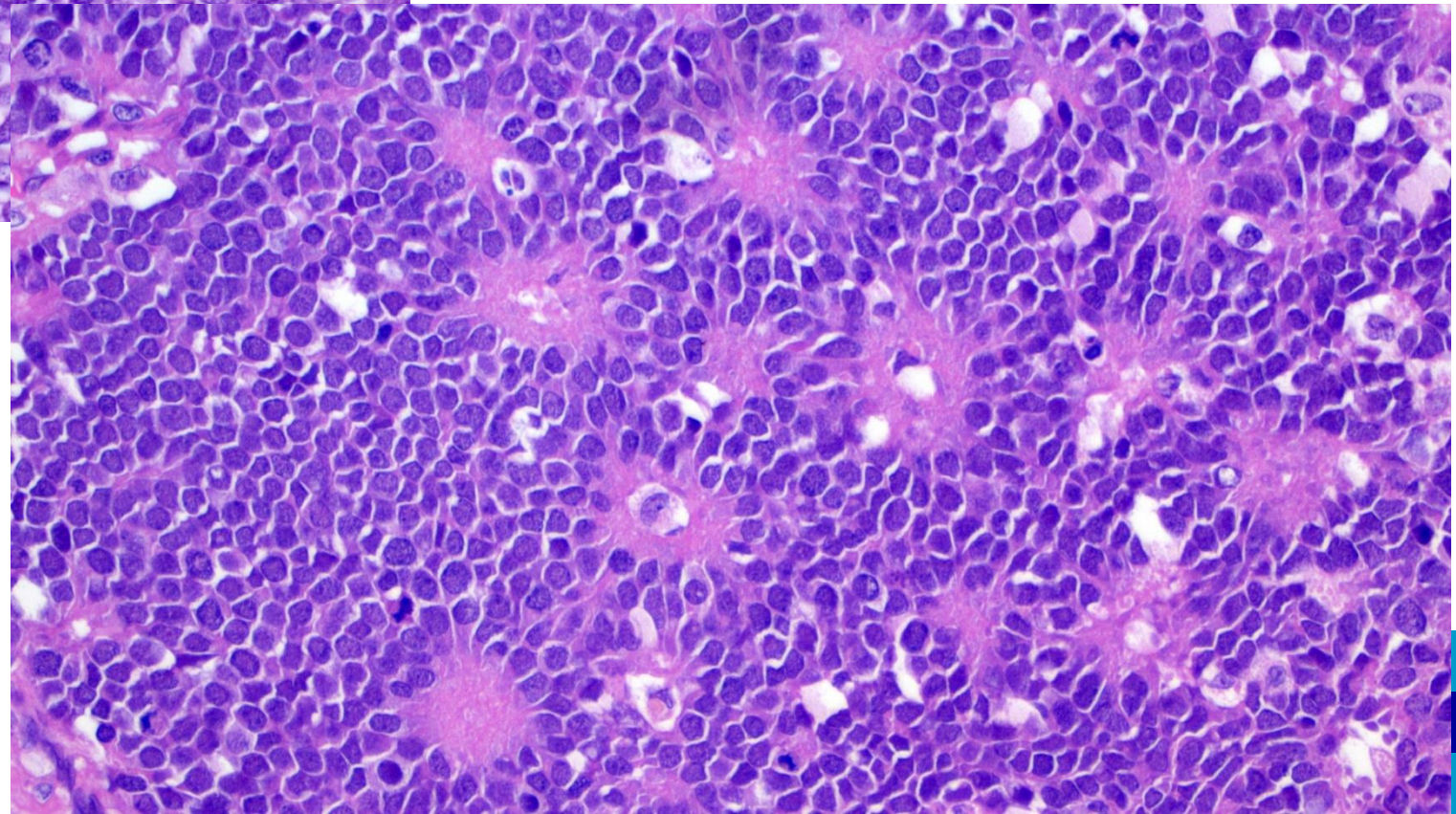
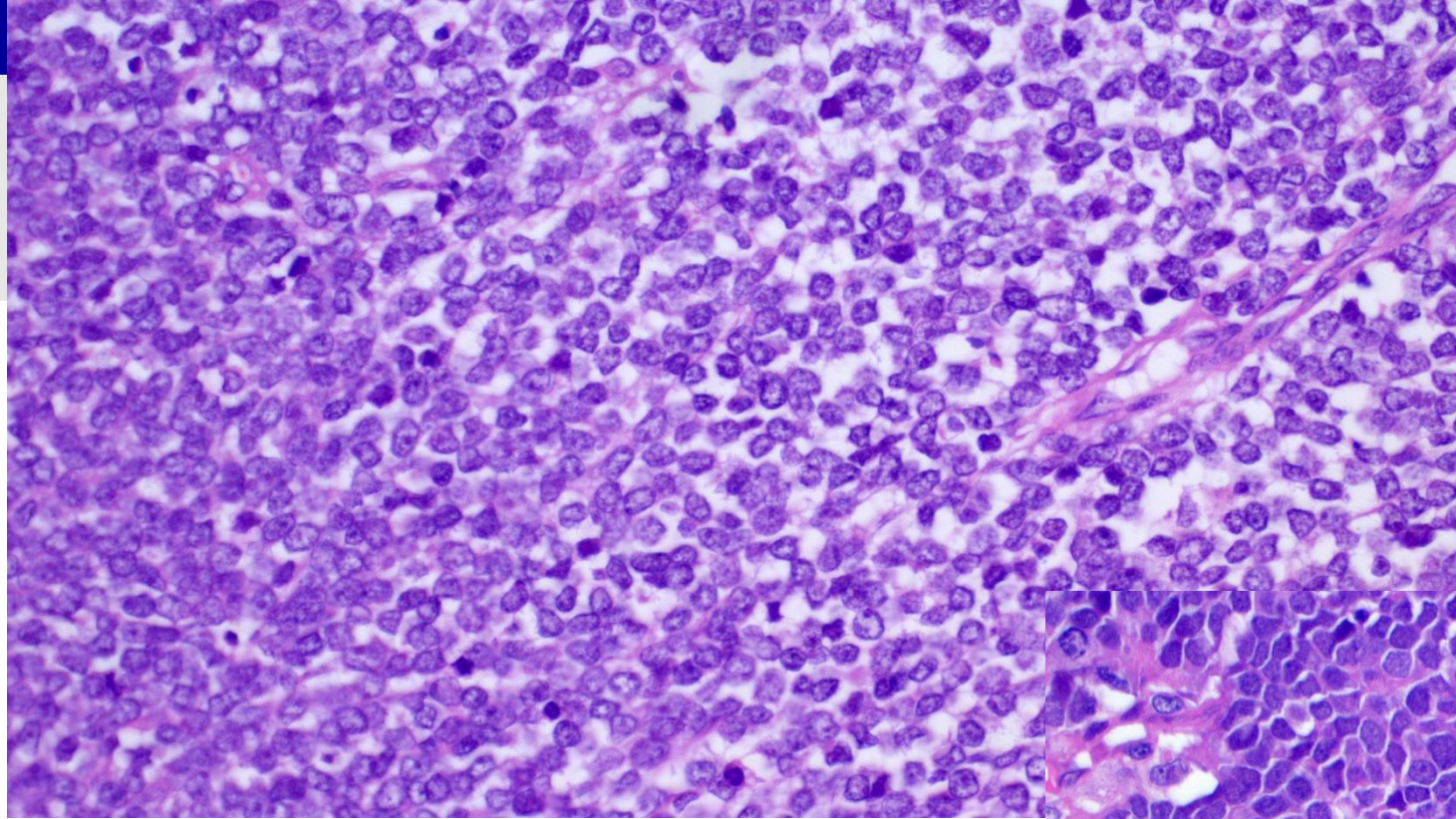


renal Ewing

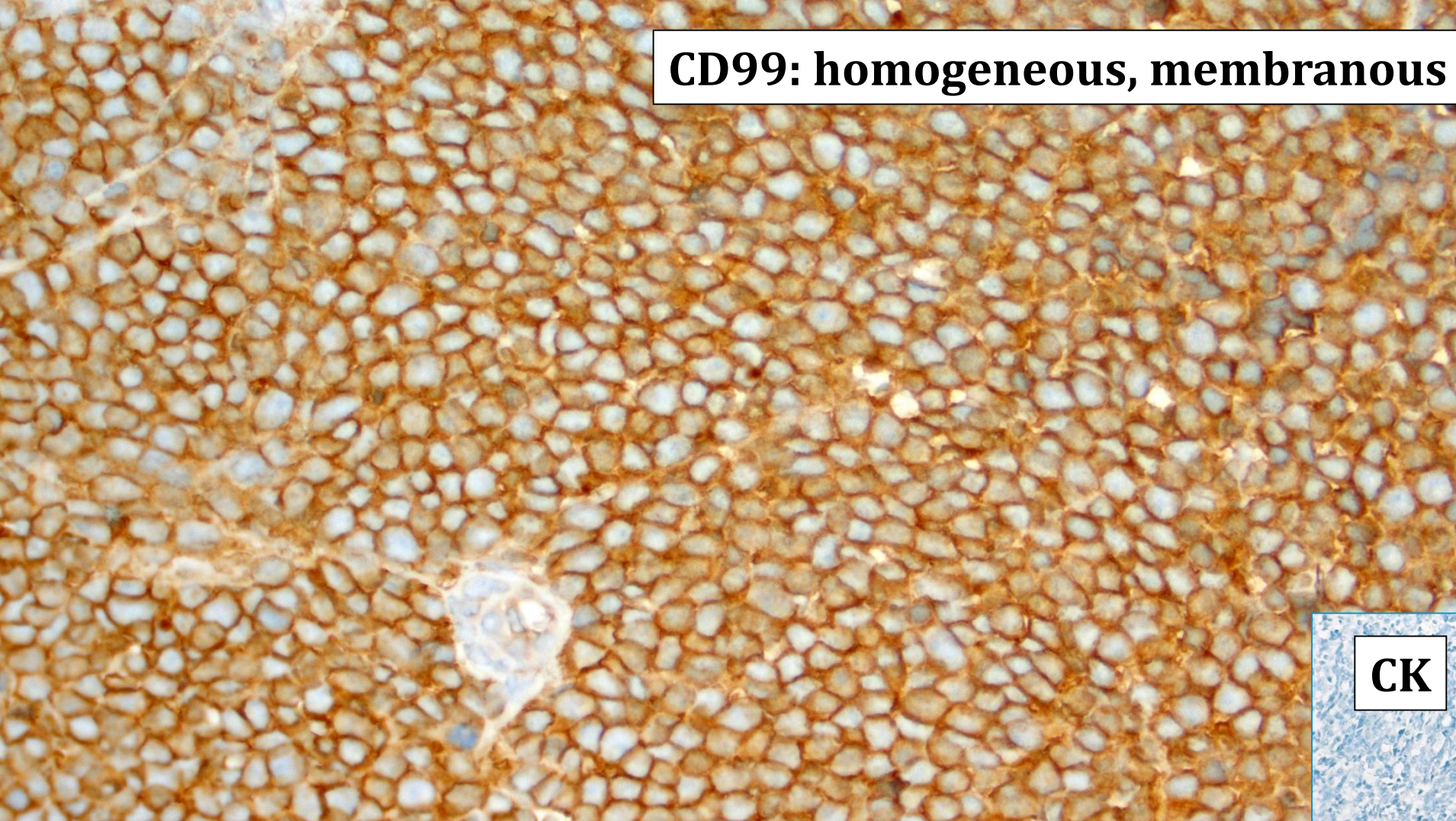


um

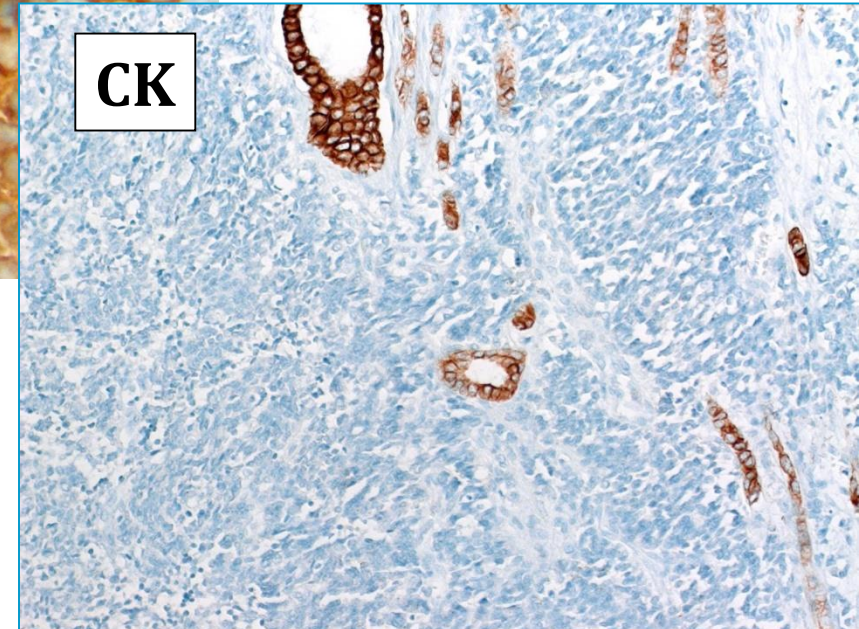




CD99: homogeneous, membranous



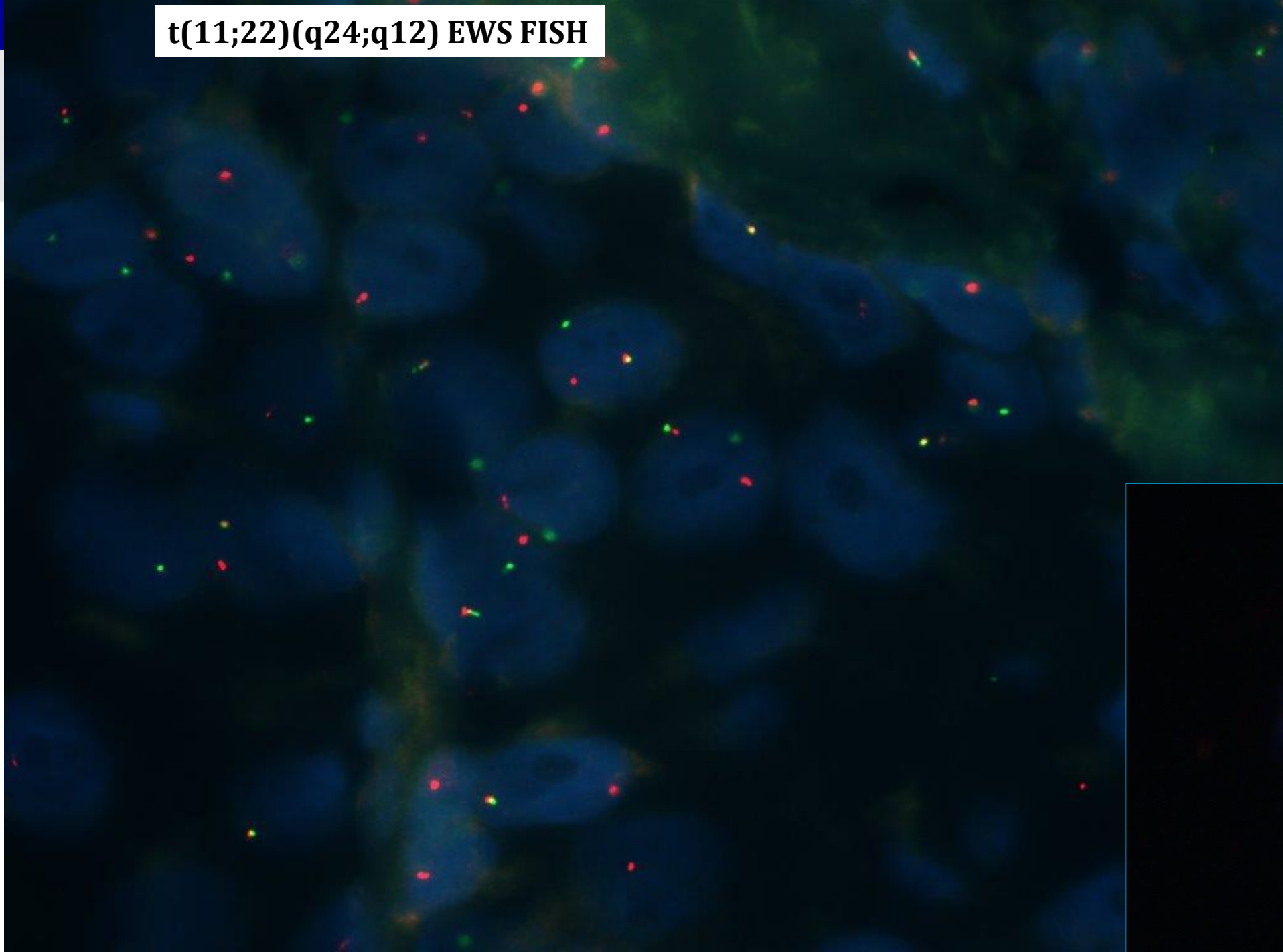
CK

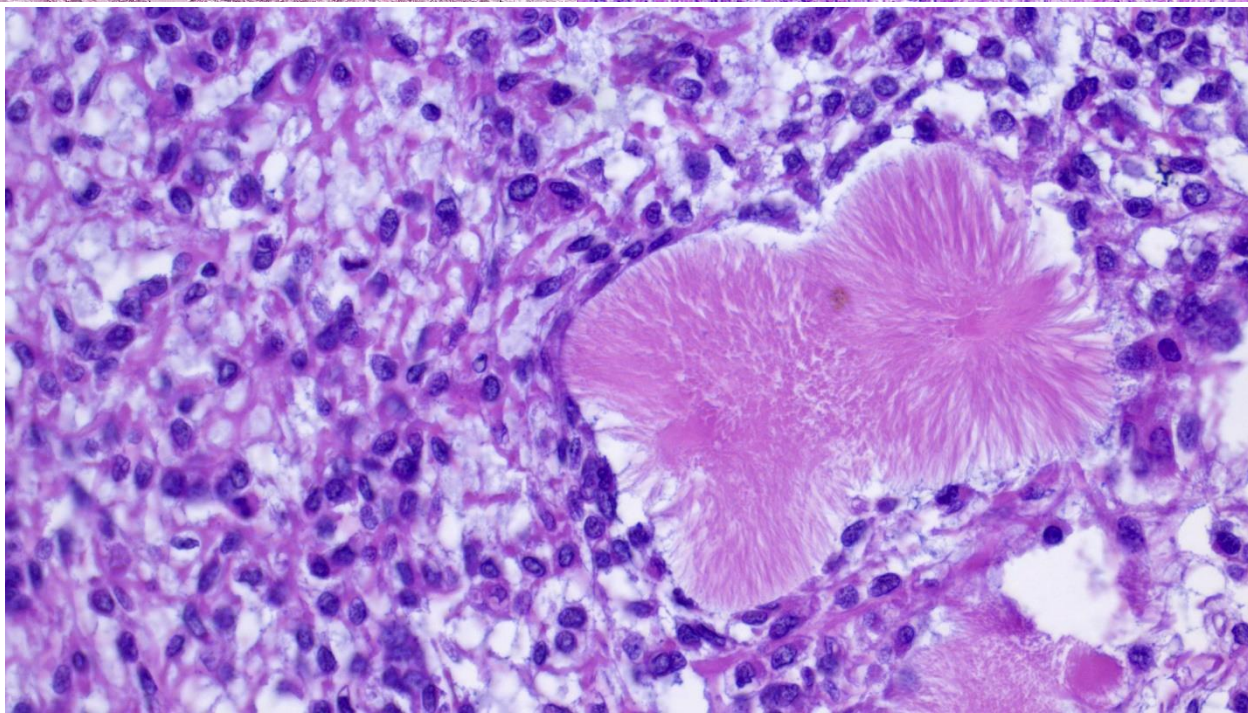
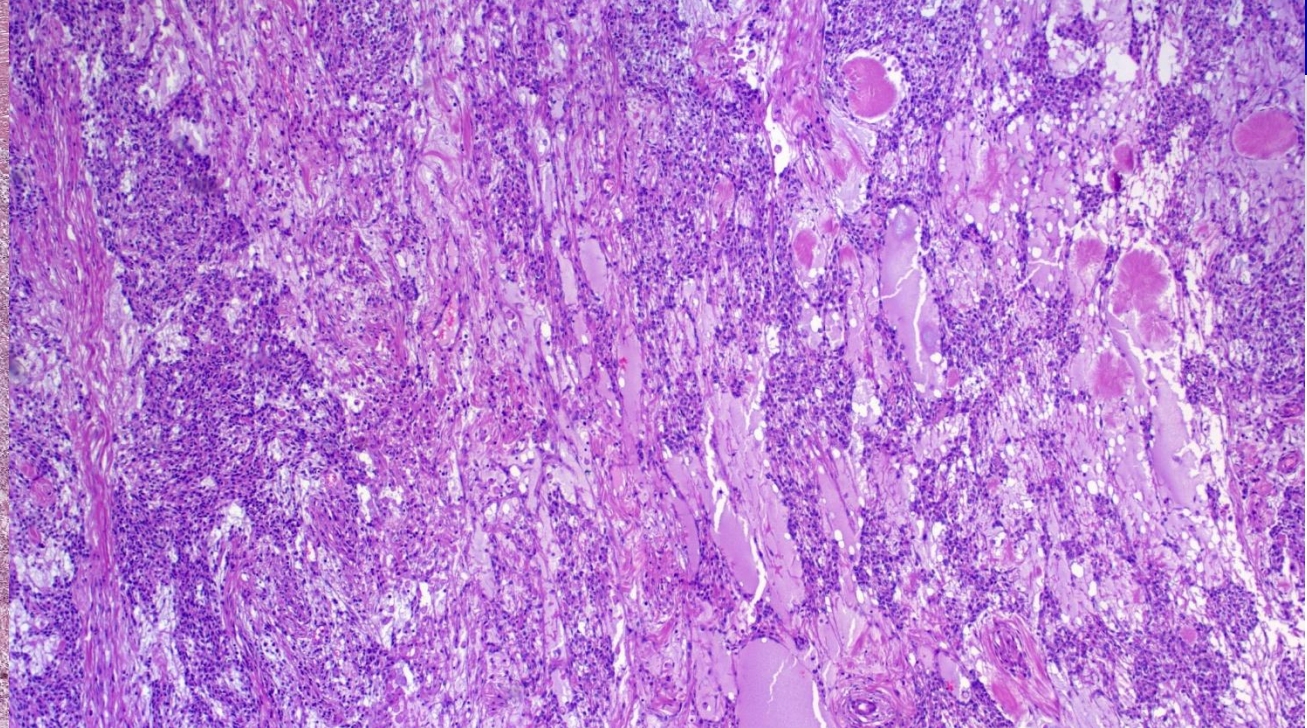
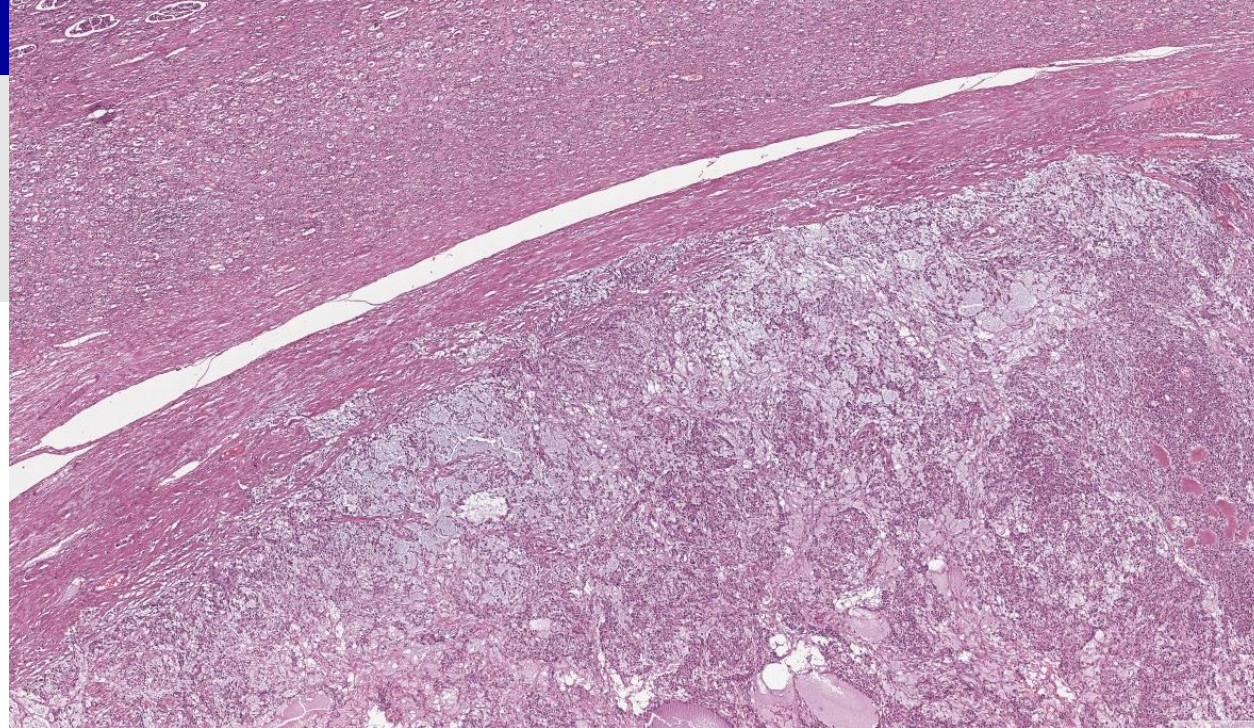


Primary renal Ewing sarcoma: DDX

- Blastemal Wilms (CD57, WT1, etc.).
- Neuroblastoma (NF, S100, NSE, Synapto, etc.).
- Hamatological: ALL, Chloroma, NHL (CD45, CD34, etc.)
- Malignant rhabdoid tumor (CK, INI1, SMARCA4).
- Solid alveolar RMS (Desmin, Myogenin).
- Small cell synovial sarcoma (SS18).
- DSRCT (CK, Desmin, WT1), NUT carcinoma (p40, CK, NUT).

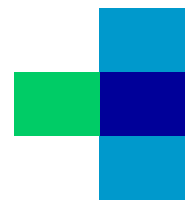
t(11;22)(q24;q12) EWS FISH





EWSR1 FISH pos

Ewing?????

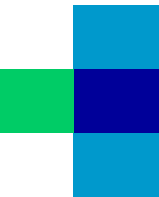


CD34

Targeted RNA Seq (TruSight Panel, Illumina): EWSR1-CREM Fusion

EMA

MUC4



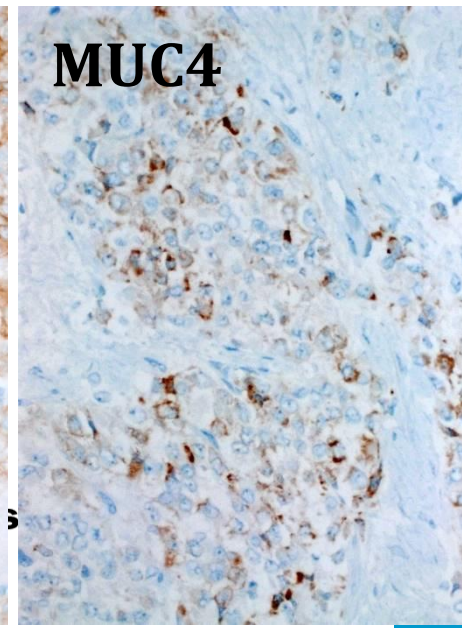
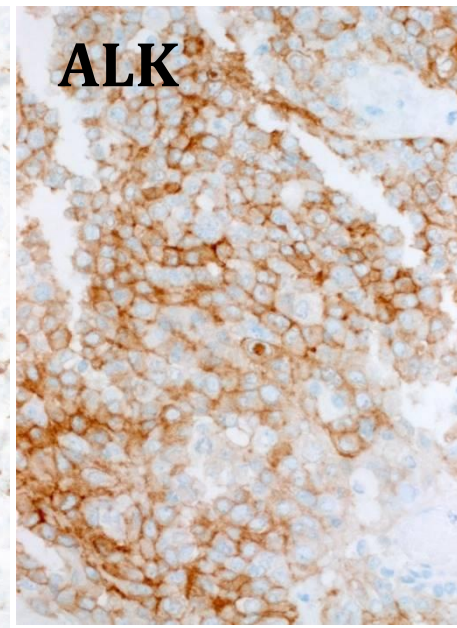
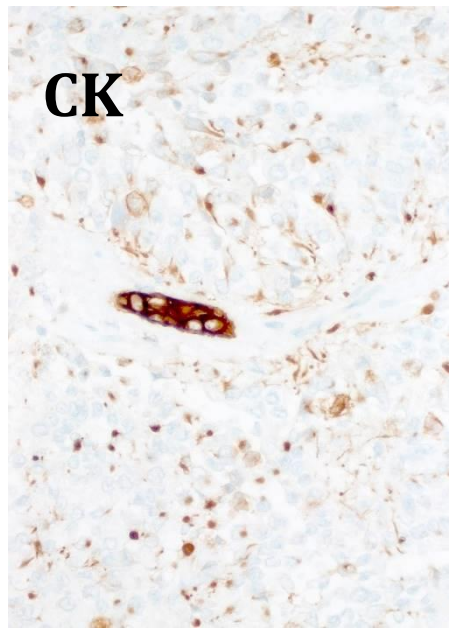
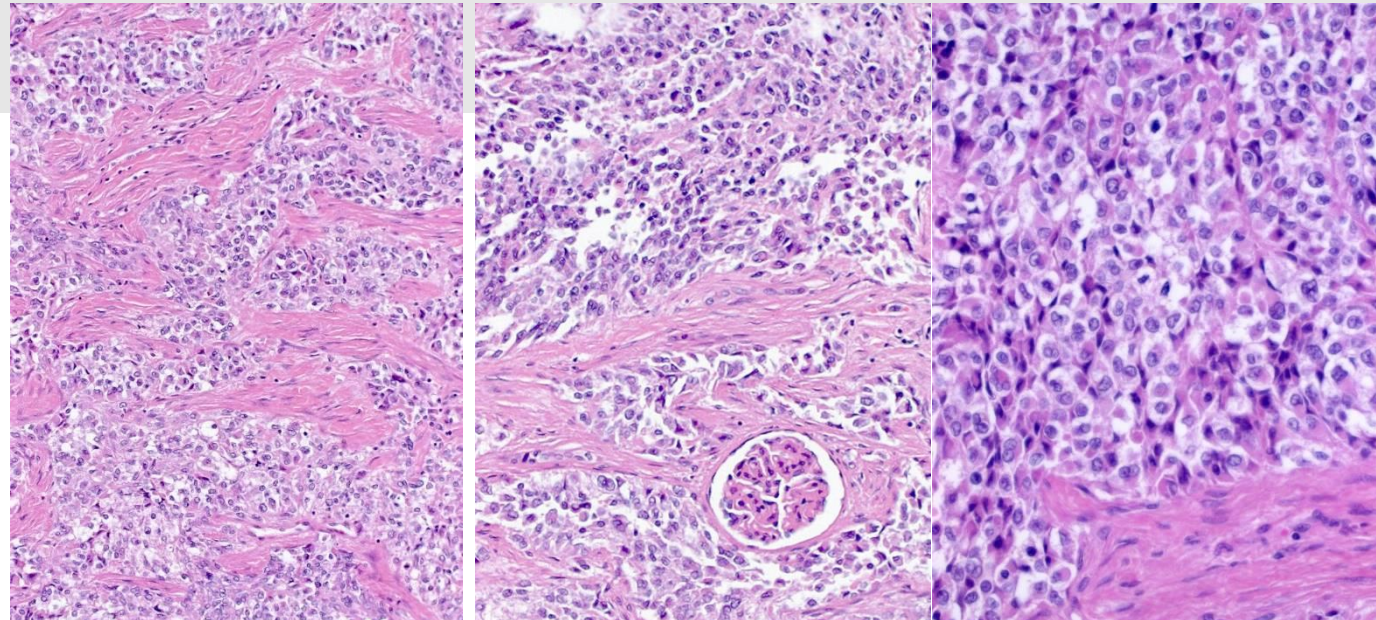


Intra-abdominal *EWSR1/FUS-CREM*-rearranged malignant epithelioid neoplasms: two cases of an emerging aggressive entity with emphasis on misleading immunophenotype

Abbas Agaimy^{1,2} · Robert Stoehr^{1,2} · Mike Otto³ · Jan Hinrich Bräsen⁴ · Nicole Pfarr⁵ · Björn Konukiewitz⁵ · Atsuko Kasajima⁵ · Arndt Hartmann^{1,2} · Günter Klöppel⁵

Beware of „non-ALK“ ALK!

ALK without PAX8 clue.



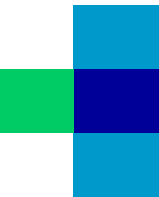
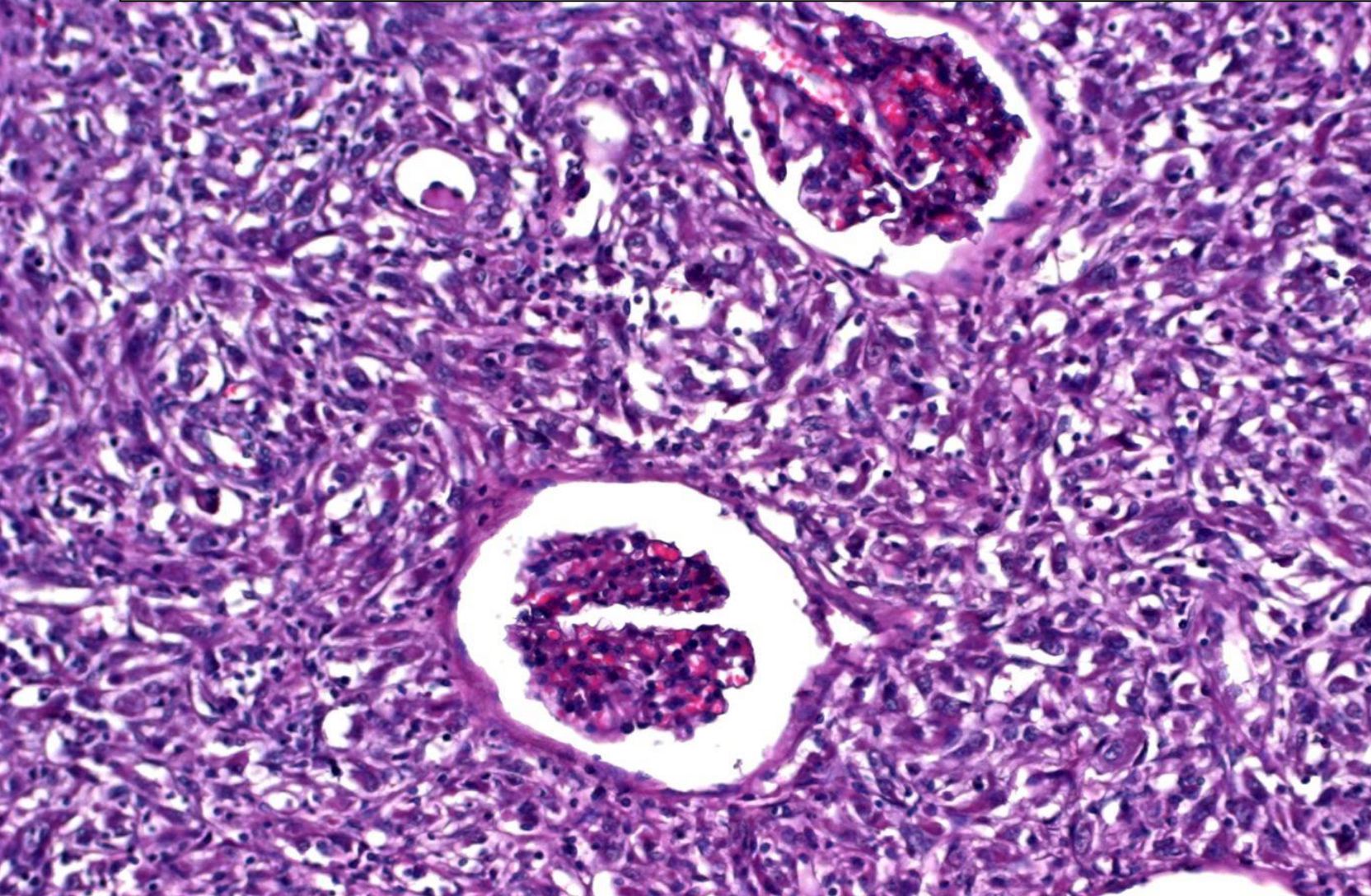
Spectrum EWSR1-rearranged primary renal neoplasms with round cell & epithelioid Morphology (Agaimy et al., unpublished)

EWSR1 not equals Ewing

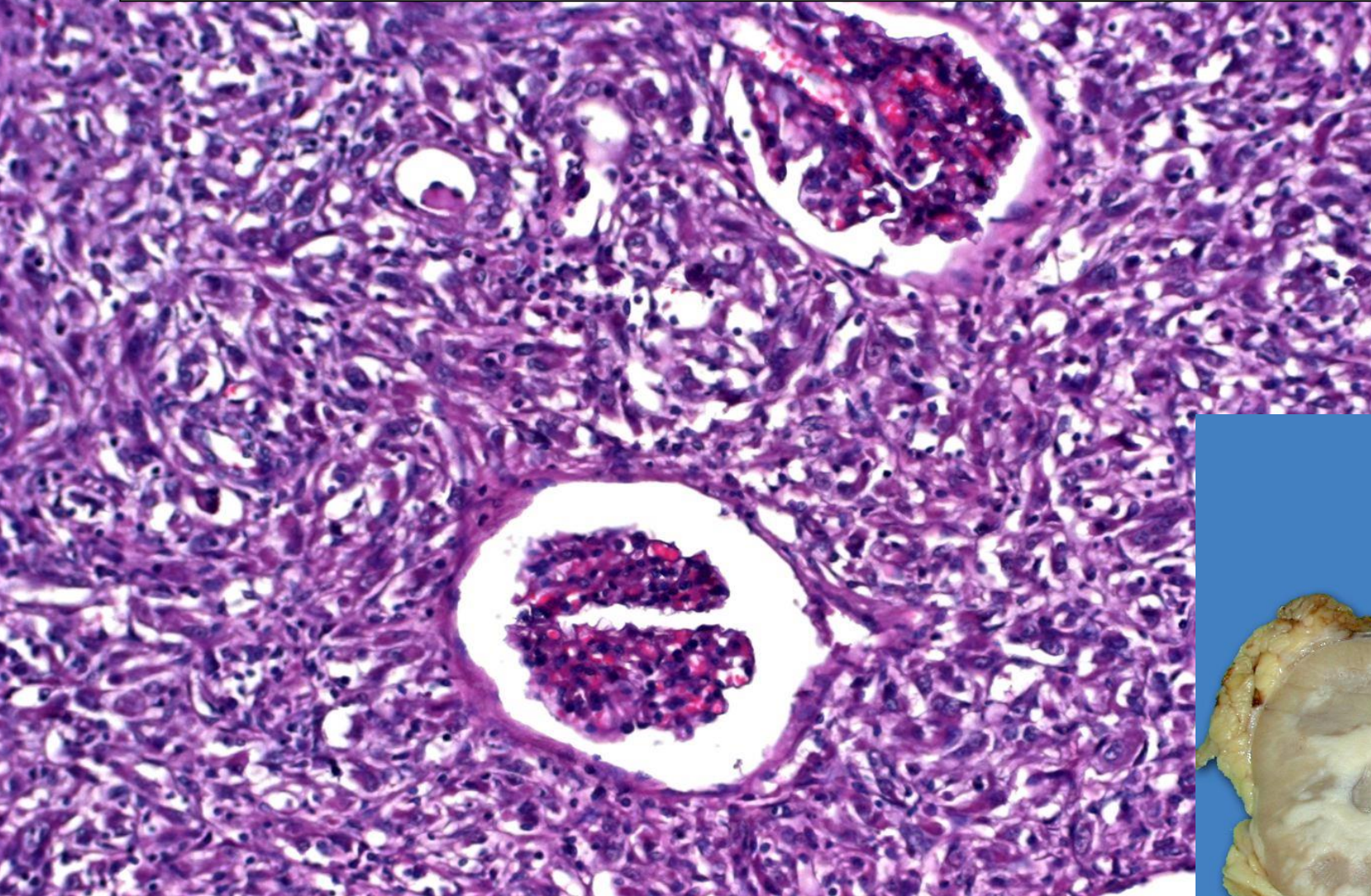
Age, morphology

No	Age/sex	Size cm	Diagnosis	Gene fusion
1	28/M	NA	Ewing sarcoma	EWSR1::FLI1
2	66/M	17	Ewing sarcoma	EWSR1::FLI1
3	61/M	NA	Ewing sarcoma	EWSR1::FLI1
4	46/M	NA	Ewing sarcoma	EWSR1::FLI1
5	22/F	NA	Ewing sarcoma	EWSR1::FLI1
6	38/M	NA	Ewing sarcoma	EWSR1::FLI1
7	26/M	NA	Ewing sarcoma	EWSR1::FLI1
8	15/M	16	Ewing sarcoma	EWSR1::FLI1
9	21/M	13	Ewing sarcoma	EWSR1::FLI1
10	09/F	17	Ewing sarcoma	EWSR1::FLI1
11	36/F	14	Ewing sarcoma	EWSR1::FLI1
12	16/F	NA	Ewing sarcoma	EWSR1::FLI1
13	29/F	12	Ewing sarcoma	EWSR1::FLI1
14	13/F	6	Ewing sarcoma	EWSR1::FLI1
15	23/F	22	SEF	EWSR1::CREB3L1
16	42/M	4.2	SEF	EWSR1::CREB3L1
17	55/M	NA	Unclassified sarcoma	EWSR1::CREM
18	34/F	7.5	Unclassified sarcoma	EWSR1::CREM
19	50/F	NA	DSRCT	EWSR1::WT1
20	76/F	NA	Unclassified sarcoma	EWSR1::PATZ1
21	54/F	3	Unclassified sarcoma	EWSR1::POU5F1P3

Intrarenal UPS = sarcomatoid ca until proven otherwise



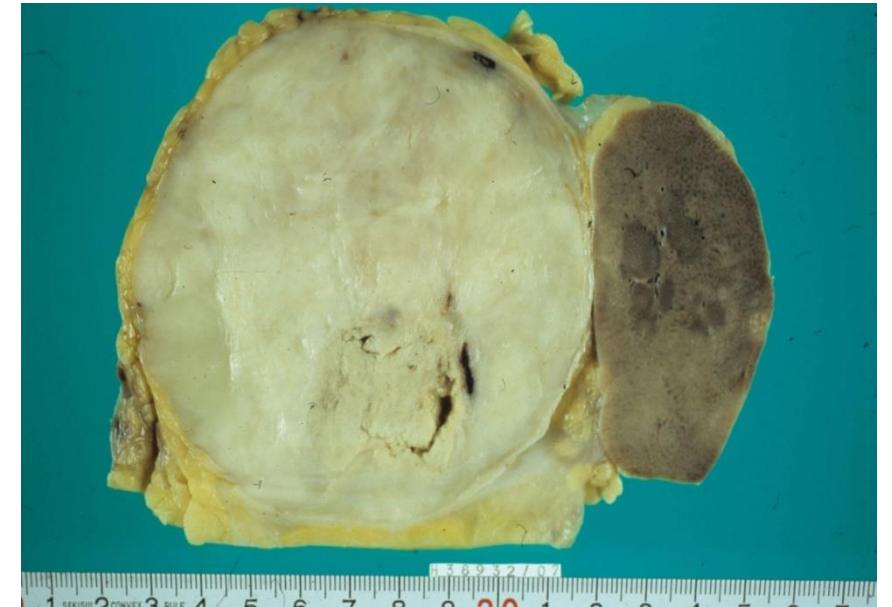
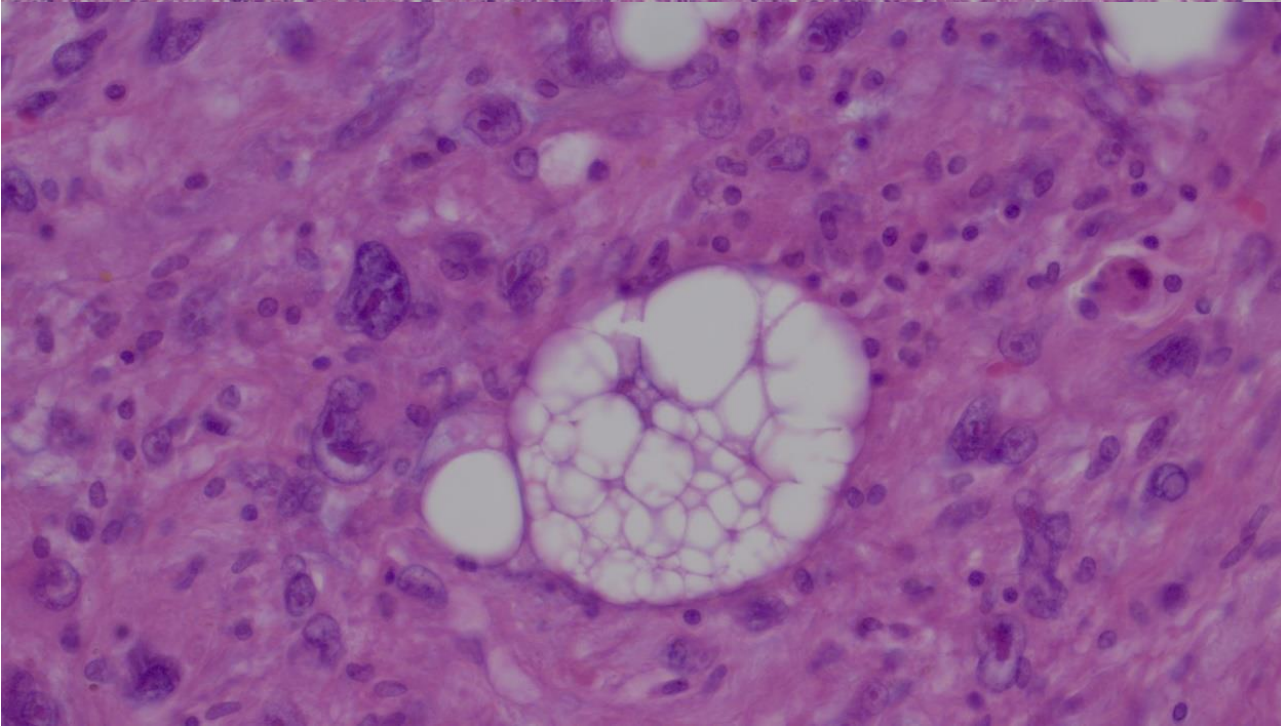
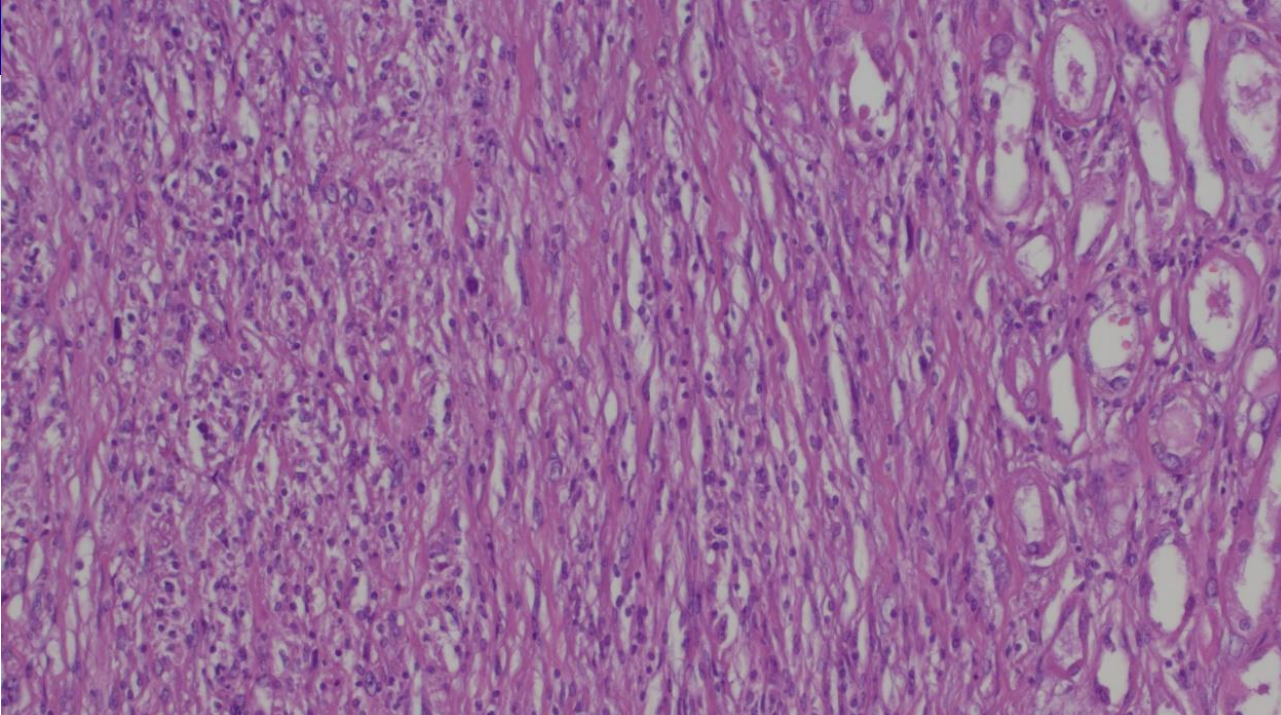
Intrarenal UPS = sarcomatoid ca until proven otherwise



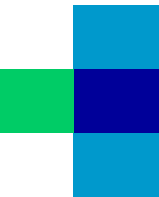
Regrossing is best marker

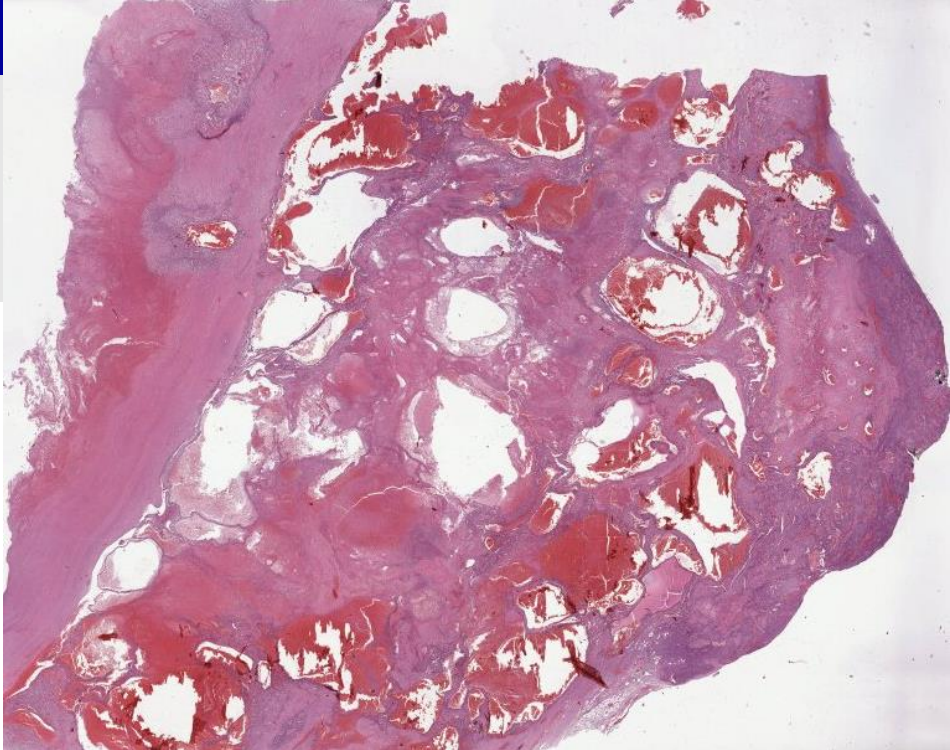


UPS: verify imaging

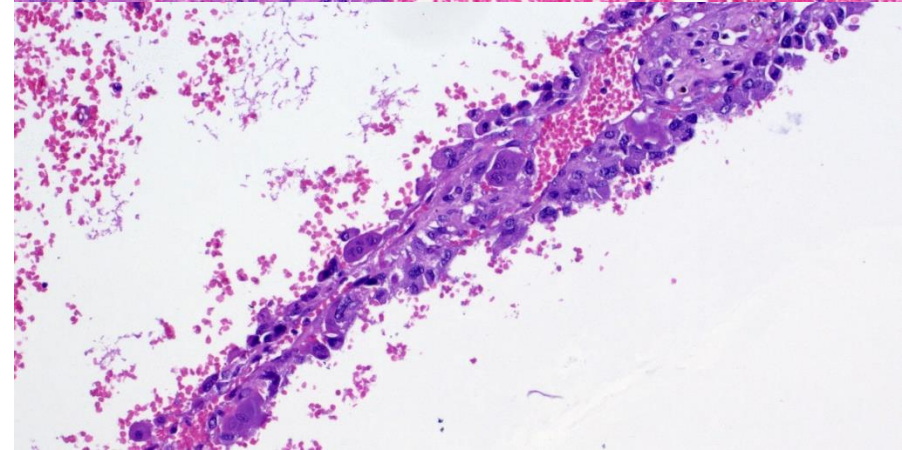
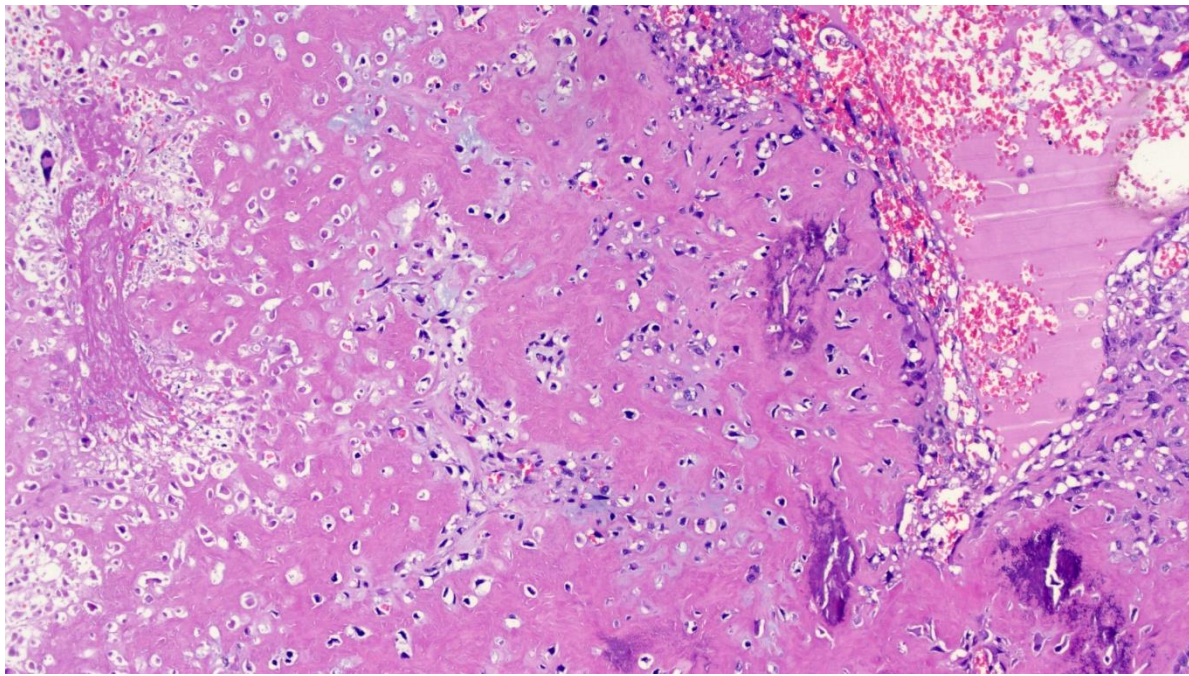
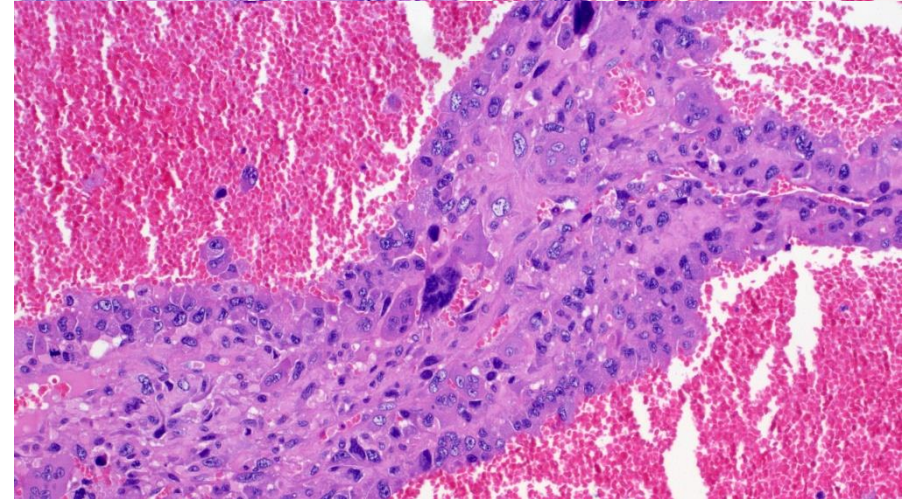
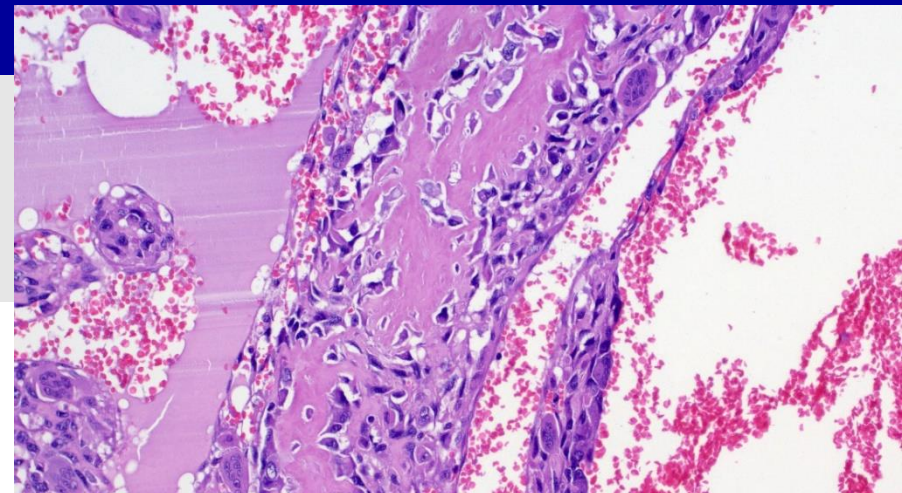


pararenals dediff LS

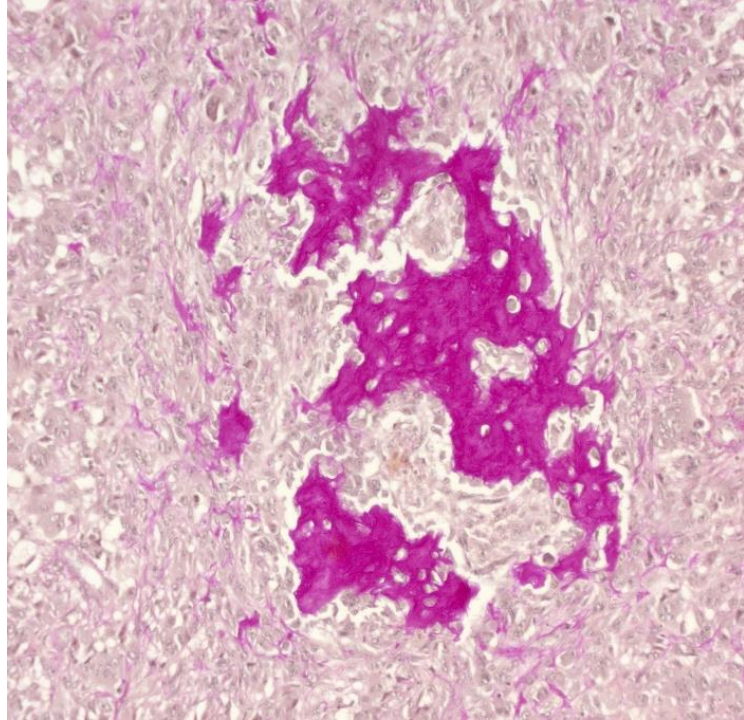
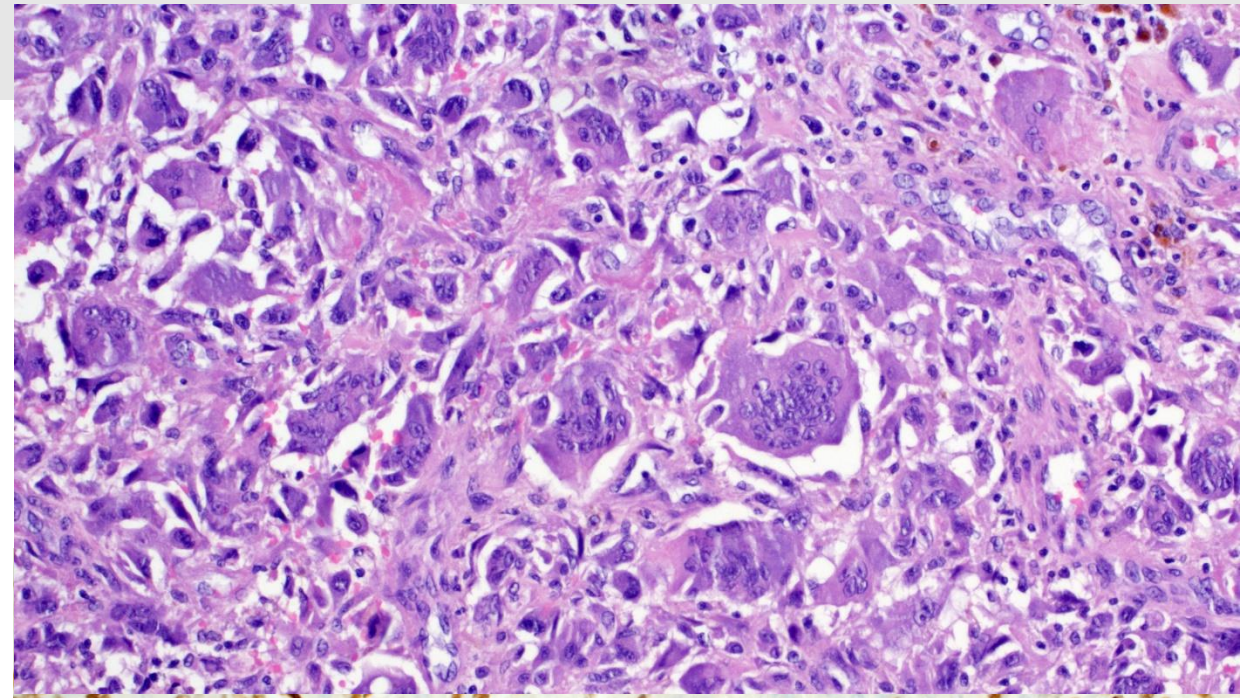
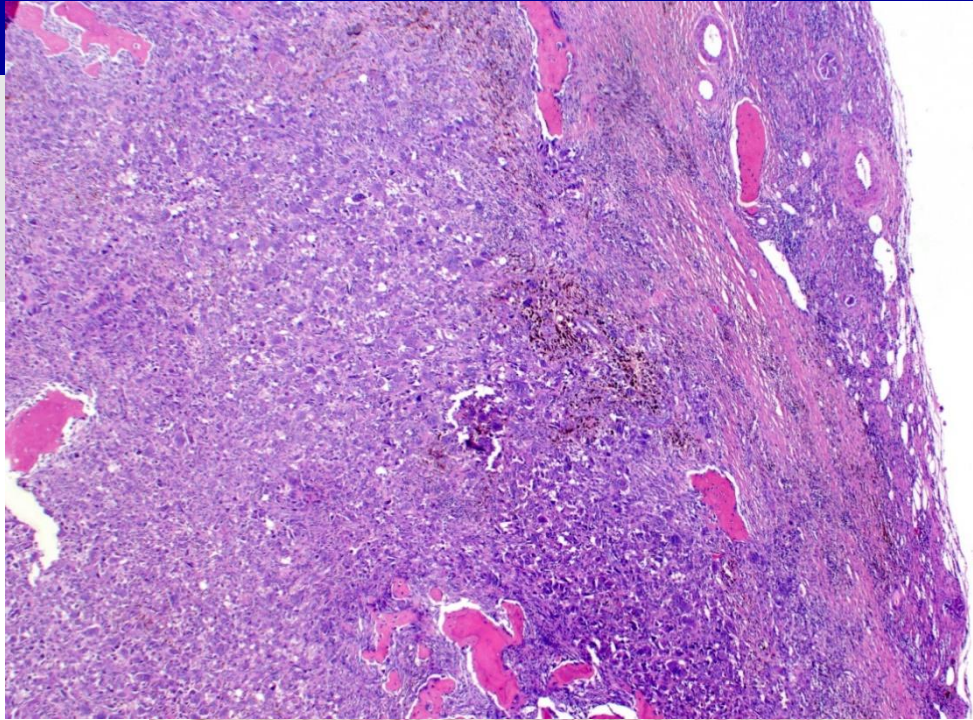




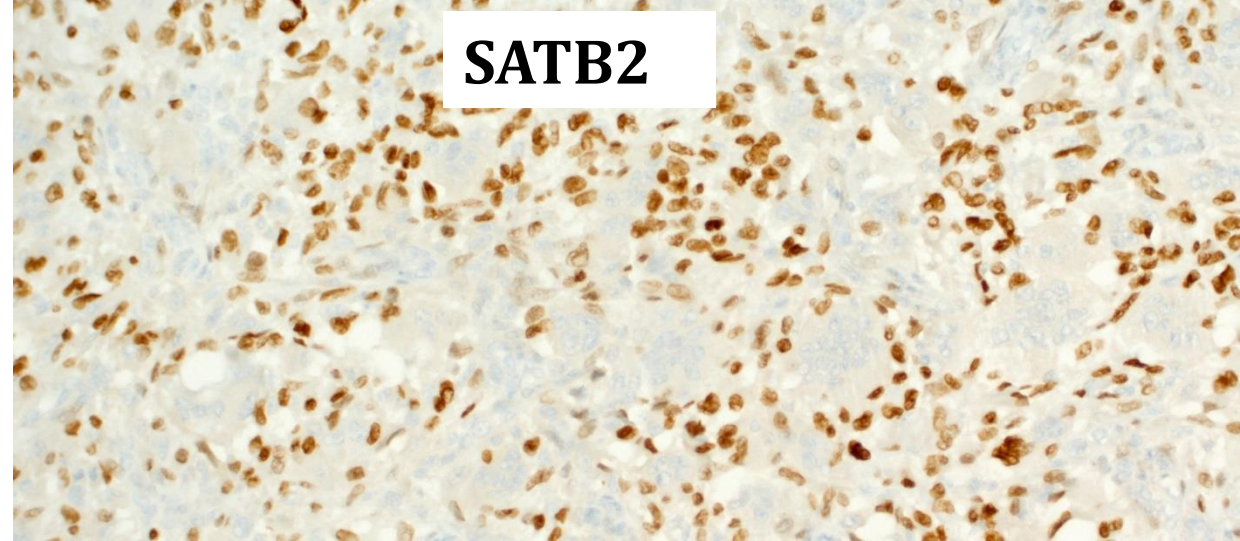
78 yo male,
Huge intrarenal mass



Undiff with osteoclastic giant cells and/ or bone forming = sarcomatoid ca



SATB2



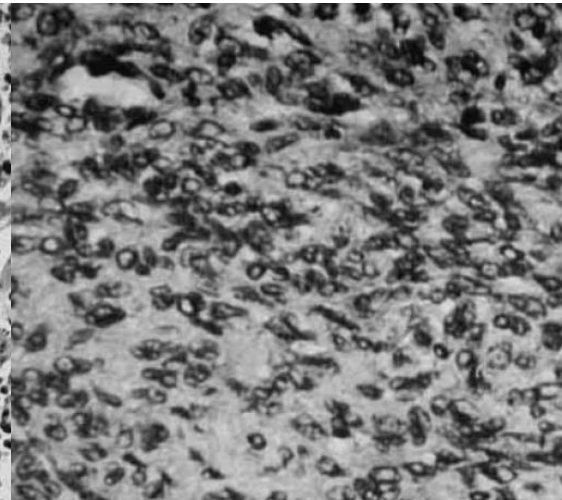
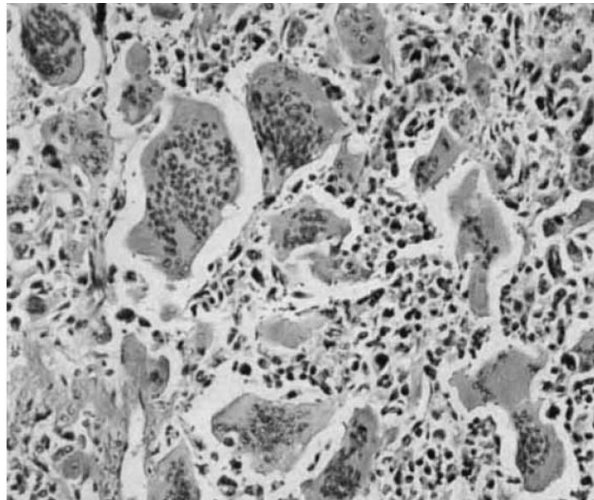
CARCINOMA OF PANCREAS SIMULATING GIANT CELL TUMOR OF BONE

Electron-microscopic Evidence of Its Acinar Cell Origin

JUAN ROSAI, MD*

Cancer. 1968 Aug;22(2):333-44

Two cases of a previously undescribed tumor were studied. The lesion is a primary pancreatic neoplasm, which by light microscopy has an appearance indistinguishable from that of a giant cell tumor of bone. Electron microscopy was done in one of the two cases. Both giant and "stromal" cells have abundant granular endoplasmic reticulum containing intracisternal granules of proteic nature similar to those described in pancreatic acinar cells. Microvilli are present in the giant cells, and numerous desmosomes are found between the "stromal" cells. These features are strongly suggestive that epithelial—and specifically acinar—elements are the cells of origin of the tumor.



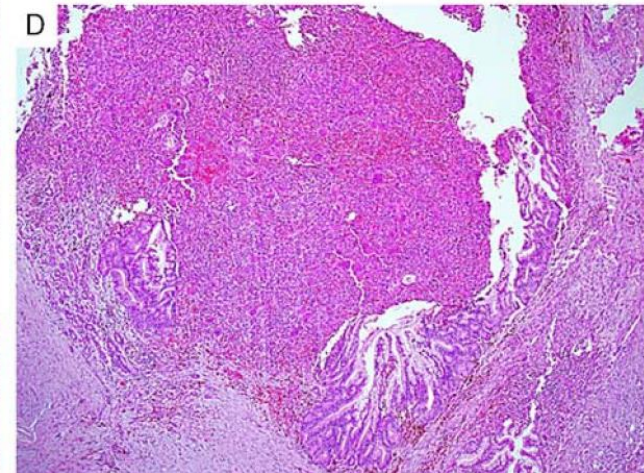
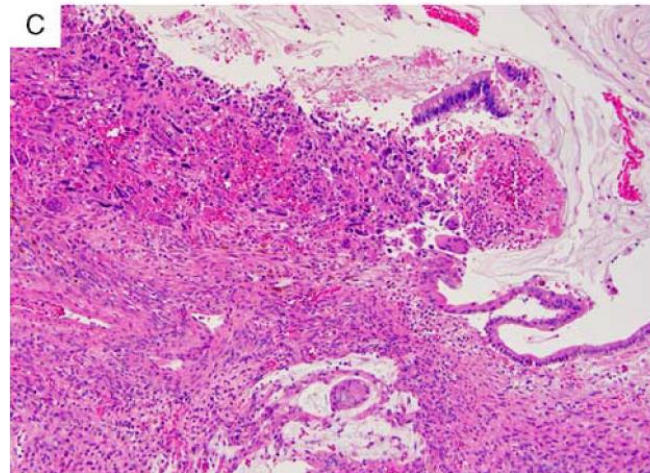
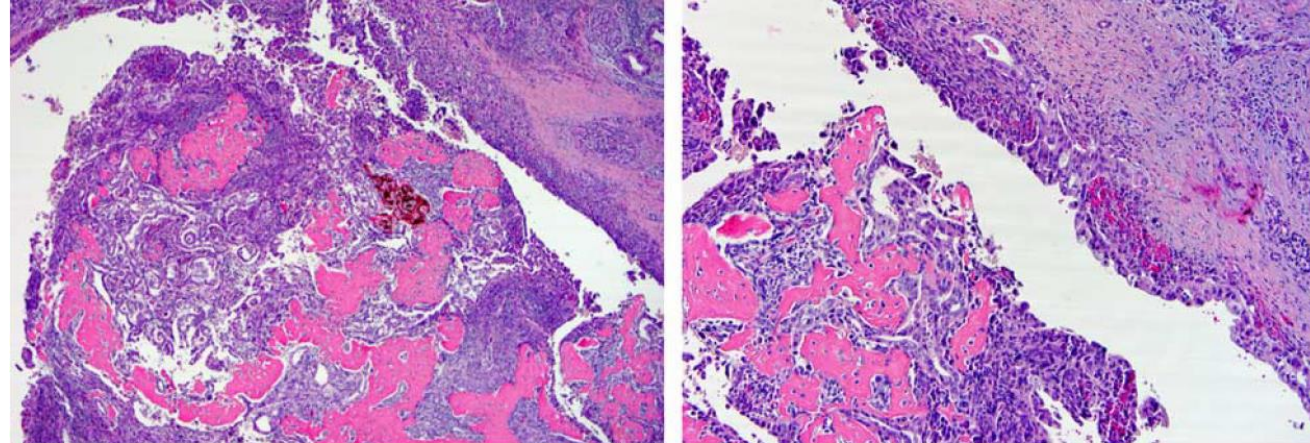
um



Undifferentiated Carcinoma With Osteoclastic Giant Cells of the Pancreas

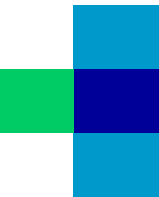
Clinicopathologic Analysis of 38 Cases Highlights a More Protracted Clinical Course Than Currently Appreciated

Takashi Muraki, MD, PhD, Michelle D. Reid, MD,* Olca Basturk, MD,† Kee-Taek Jang, MD,‡
Gabriela Bedolla, MD,* Pelin Bagci, MD,§ Pardeep Mittal, MD,|| Bahar Memis, MD,*
Nora Katabi, MD,† Sudeshna Bandyopadhyay, MD,¶|| Juan M. Sarmiento, MD,#
Alyssa Krasinskas, MD,* David S. Klimstra, MD,† and Volkan Adsay, MD**



TaHoMe

- ❖ Bladder sarcomatoid ca: sure not IMT? CK+++ means IMT and not UC.
- ❖ Renal angiosarcoma: sure not anastomosing hemangioma?
- ❖ Renal angioma: think of pseudovascular RCC (CK), juxtaglomerular Tumor!
- ❖ Undiff pleomorphic sarcoma:
 - Sarcomatoid keratin-poor carcinoma?
 - Retroperitoneal/ perirenal liposarcoma?
- ❖ Specific sarcoma (osteo! pleomorphic Lipo?): heterologous dediff in RCC?



Thank you for your attention

Seminars in Diagnostic Pathology 38 (2021) 152–162

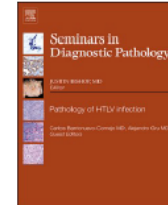


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journal homepage: www.elsevier.com/locate/sem_dp



Undifferentiated and dedifferentiated urological carcinomas: lessons learned from the recent developments

Abbas Agaimy^{a,*}, Arndt Hartmann^a, Kiril Trpkov^b, Ondrej Hes^c

Regrossing is best marker to classify the undifferentiated!!!



Universitätsklinikum
Erlangen

