

# **Biopsy Diagnosis of Renal Mass: BeST Practical Approach**

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# What I learned from Dr. Ro

- Do Your **BeST**
- Work Hard
- Teaching is Learning
- Walk Fast
- Check Pubmed
- Write It Up

# **Renal Mass Biopsy Diagnosis**

## **Outline**

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- **Introduction**
- **Types of renal tumors**
- **Categorization and diagnosis**
- **Use of immunohistochemistry**
- **Case examples**

# Introduction

- **Increased** incidence of renal neoplasm and incidental mass
- **Increased** use of partial nephrectomy
- **Increased** treatment modalities (active surveillance, ablative and targeted therapies)
- **Increase Renal Mass Biopsy (RMB)**

# Indications for RMB

- **Has other primary (r/o mets)**
- **Has prior renal tumor (r/o recurrence)**
- **Multiple synchronous tumors**
- **Suspecting abscess or lymphoma**
- **Candidates for active surveillance**
- **Candidates for ablative therapy**
- **Diagnosis in pts. with disseminated mets or unresectable tumor**

# RMB: Getting Adequate Material

## Insufficient material is common

- **Rate variable: 0-47%**

(Volpe A et al. *Eur Urol* 2012; 62: 491)

- **More frequent in small, cystic or hemorrhagic, and necrotic lesion**

## Approaches to getting material

- **Communicate with radiologist !**
- **Correlate with cytology**
- **Standardized histology protocols**

# RMB Technical Recommendation

- **Image guidance (CT/MRI/US)**
- **At least 2 cores**
- **18G or larger needles**
- **Sampling peripheral & central**
- **Complications: rare, tumor seeding exceedingly rare, minimal morbidity**

# RMB: Objectives

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**To establish the following:**

- **Neoplasm or not**
- **Histologic type**
- **Tumor grade**
- **Other features**

# Diagnostic Accuracy of RMB

**86-100%** Differentiating malignant from benign

**~100%** Specificity

**86-98%** Accuracy histol. subtyping

**46-76%** Accuracy in grading

# Types of Renal Cell Neoplasm Continue to Increase...

1975 (AFIP Fascicle)	2
1997 (UICC/AJCC Consensus)	8
2004 (WHO)	12
2016 (WHO)	16

# Renal Cell Neoplasms (2016 WHO)

- Clear cell RCC
- Papillary RCC
- Chromophobe RCC
- Collecting duct ca
- Renal medullary carcinoma
- Renal cell carcinoma, unclassified
- **Multilocular cystic renal neoplasm of low malignant potential**
- **SDH-deficient RCC**
- **HLRCC-associated RCC**
- **MiT family translocation RCC**
- **Mucinous tubular and spindle cell RCC**
- **Tubulocystic RCC**
- **ACD-associated RCC**
- **Clear cell papillary RCC**
- Papillary adenoma
- Oncocytoma

# Terminology and Its Rationale for Renal Neoplasm is All Over the Place

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**Cytoplasm:** clear cell, chromophobe RCC

**Growth pattern:** papillary RCC

**Cell type:** oncocytoma

**Combinaton pattern & cell:** clear cell papillary RCC

**Embryologic feature:** metanephric adenoma

**Background disease:** ACD-associated RCC

**Anat. location:** collecting duct, medullary carcinoma

**Size:** papillary adenoma

**Molecular changes:** MiT family translocation RCC

**Familial predisposition:** HLRCC-associated, SDH-deficient

# Adult Renal Cell Neoplasm *by Frequency*

- **Clear cell RCC** ~65%
- **Papillary RCC** ~15%
- **Chromophobe RCC** ~6%
- **Oncocytoma** ~5%
- **Clear cell papillary RCC** ~3%
- **MiT family translocation** ~2%
- **Others** ...

# Pattern Categorization

1. Clear cell
2. Papillary
3. Oncocytic
4. Cystic
5. Spindle cell
6. High grade

# **CLEAR CELL Category**

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**Clear cell RCC**

**Chromophobe RCC**

**Clear cell papillary RCC**

**Xp11 translocation RCC**

**Papillary RCC with clear cells**

**Renal urothelial carcinoma**

# Clear Cell RCC

## Morphologic Spectrum

### Growth Patterns

Solid/acinar (classic)

Tubular/Cystic

Pseudopapillary

Hemorrhagic

Hyalinized



### Cytomorphology

Clear cell

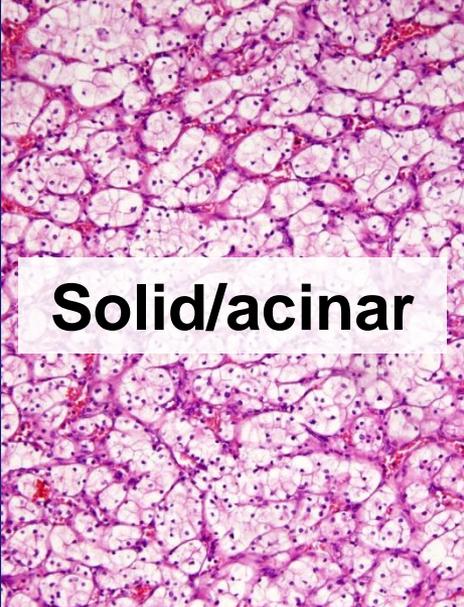
Granular

Epithelioid

Rhabdoid

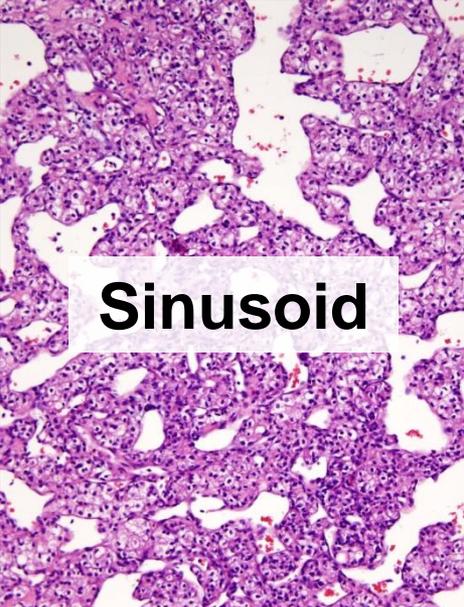
Spindly/sarcomatoid

# Clear Cell RCC Growth Patterns



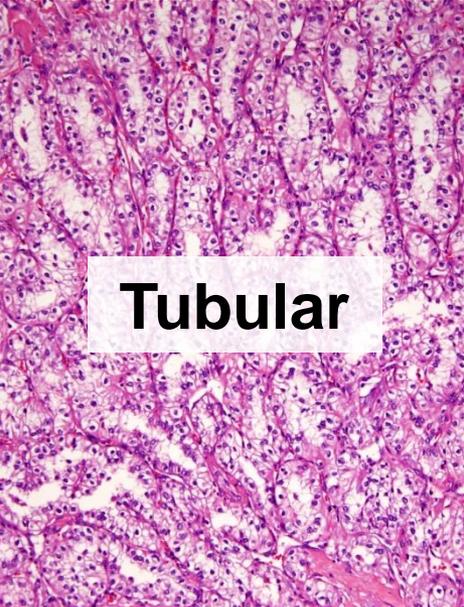
**Solid/acinar**

This micrograph shows a solid growth pattern of clear cell renal cell carcinoma. The tumor cells are arranged in a dense, organized acinar pattern, forming rounded nests or cords. The cells have a characteristic clear cytoplasm and are separated by thin, delicate connective tissue septa.



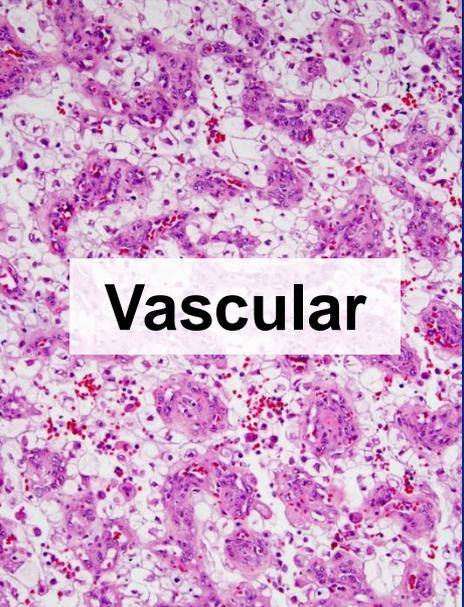
**Sinusoid**

This micrograph illustrates a sinusoidal growth pattern. The tumor cells are organized into cords or nests that are separated by prominent, dilated sinusoidal spaces. These spaces often contain red blood cells, giving the tumor a hemorrhagic appearance.



**Tubular**

This micrograph shows a tubular growth pattern. The tumor cells form irregular, glandular-like tubules of varying sizes. The tubules are lined by a single layer of clear cells and are separated by thin, fibrous connective tissue walls.



**Vascular**

This micrograph depicts a vascular growth pattern. The tumor cells are arranged in nests or cords that are highly vascularized. The surrounding stroma is rich in blood vessels, and the tumor cells often show a foamy or vacuolated appearance due to the presence of intracellular lipids.



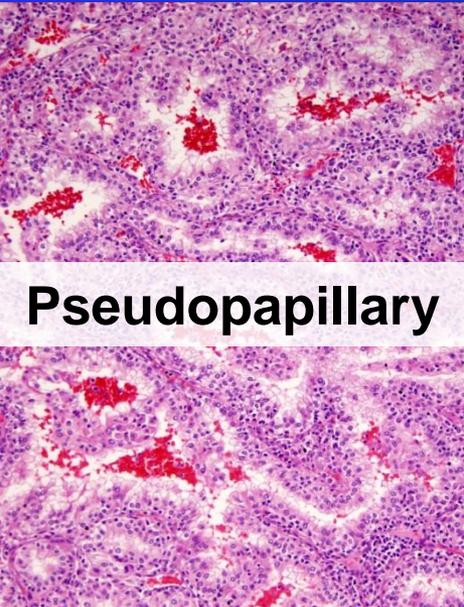
**Hyalinized**

This micrograph shows a hyalinized growth pattern. The tumor cells are arranged in cords or nests that are surrounded by a thick, eosinophilic (pink) hyaline capsule or stroma. The cells themselves have a clear cytoplasm and are separated by thin connective tissue walls.



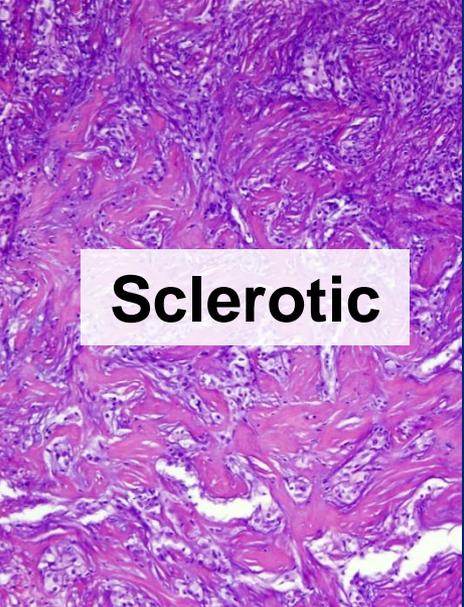
**Hemorrhagic**

This micrograph illustrates a hemorrhagic growth pattern. The tumor cells are arranged in cords or nests that are heavily infiltrated by red blood cells, resulting in a prominent hemorrhagic appearance. The tumor cells have a clear cytoplasm and are separated by thin connective tissue walls.



**Pseudopapillary**

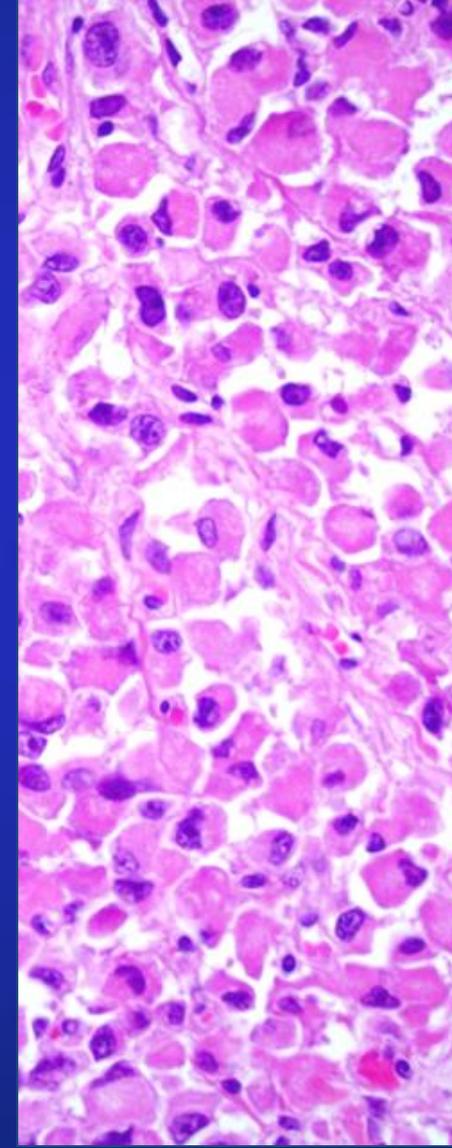
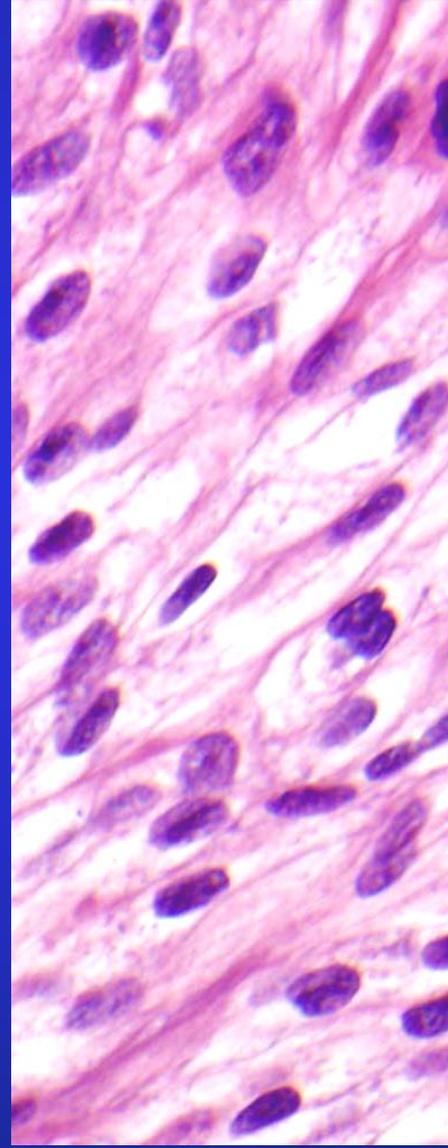
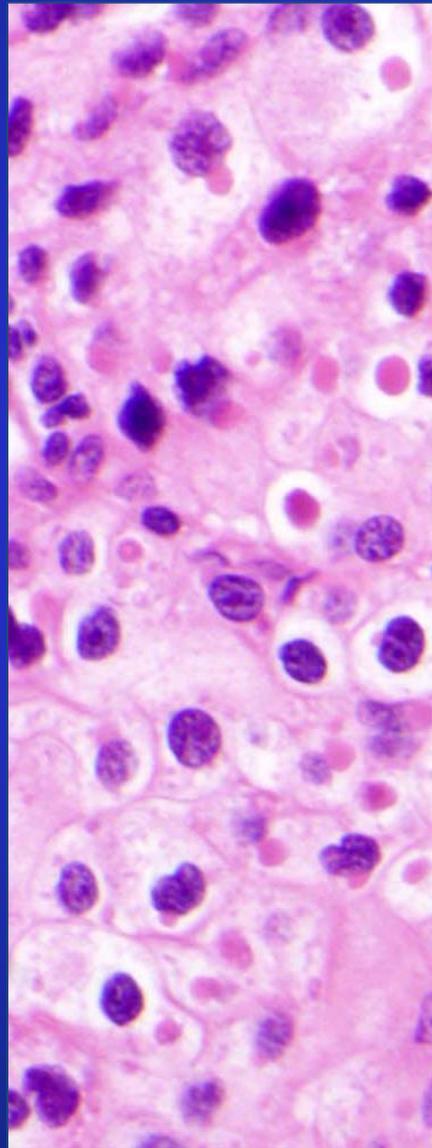
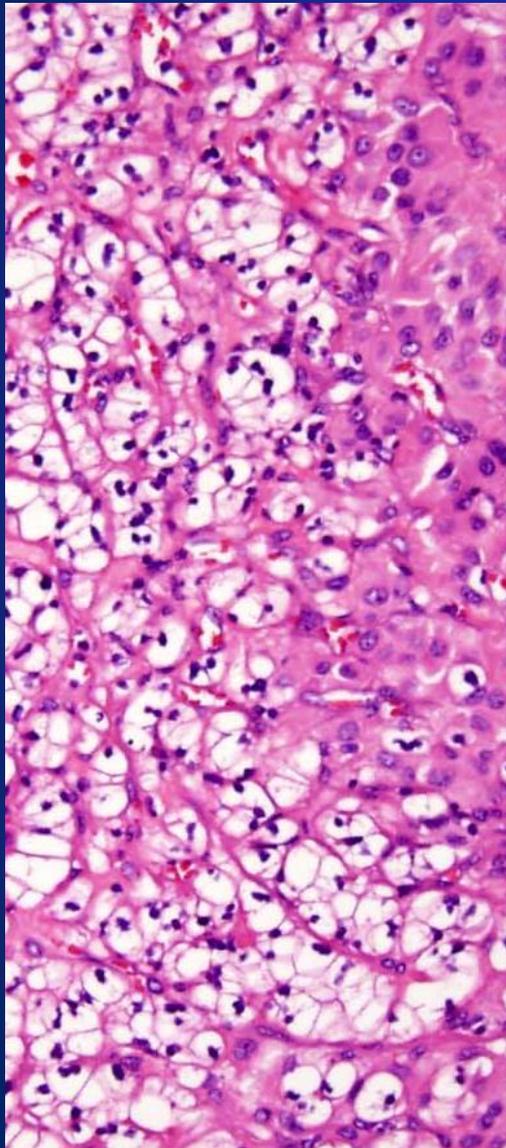
This micrograph shows a pseudopapillary growth pattern. The tumor cells are arranged in cords or nests that are separated by thin connective tissue walls. The overall appearance is that of a papillary structure, but the central cores are not true papillae.



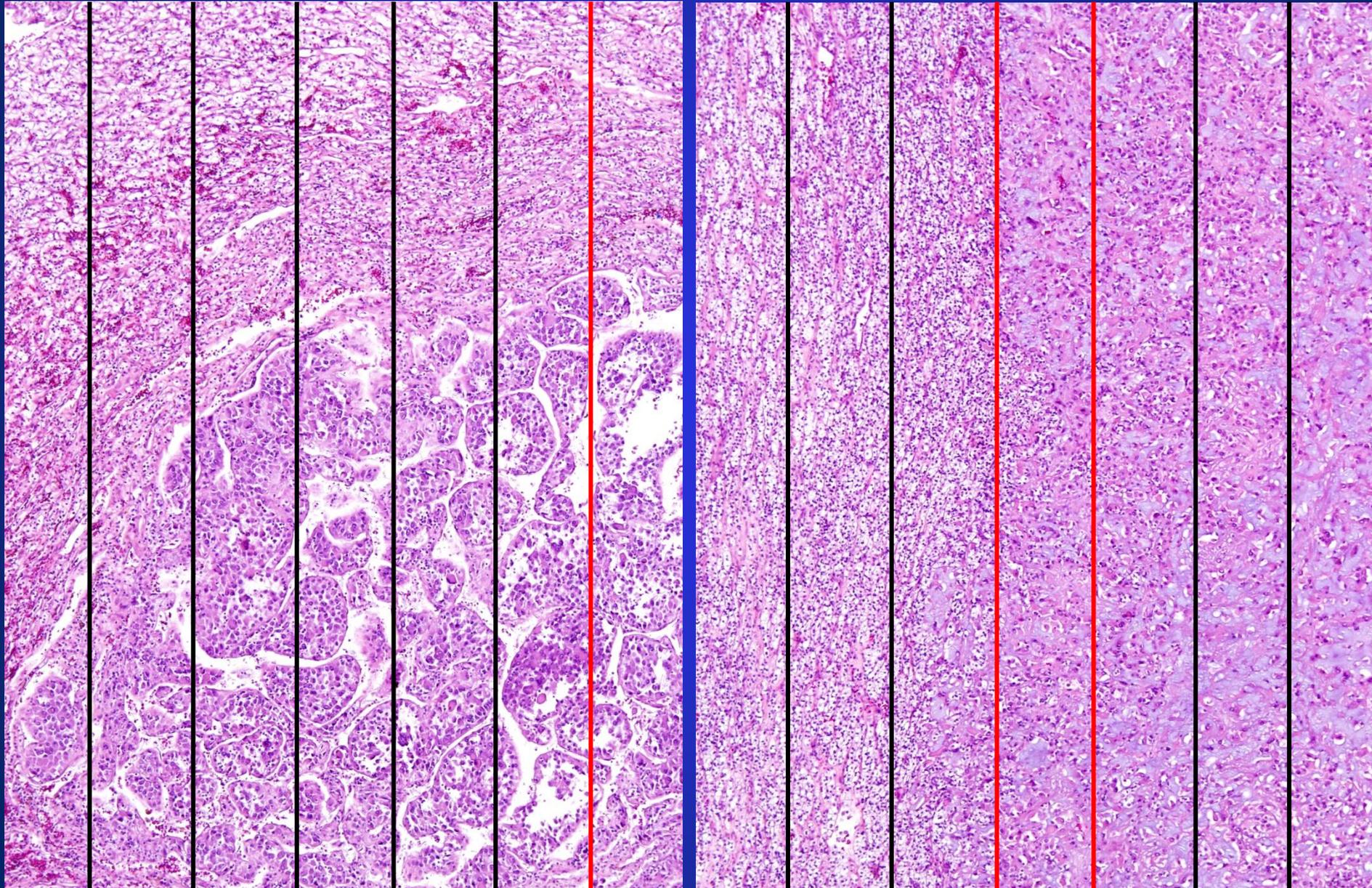
**Sclerotic**

This micrograph depicts a sclerotic growth pattern. The tumor cells are arranged in cords or nests that are surrounded by a thick, dense, eosinophilic (pink) sclerotic capsule or stroma. The cells have a clear cytoplasm and are separated by thin connective tissue walls.

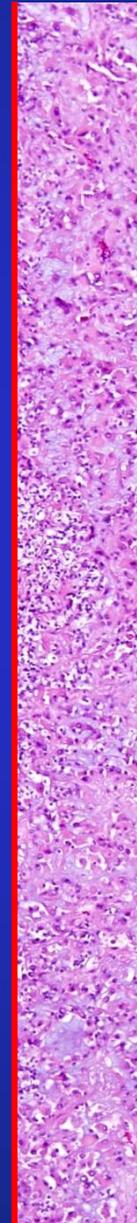
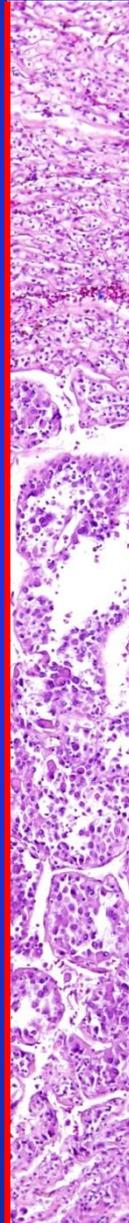
# Clear Cell RCC Cytologic and Nuclear Features



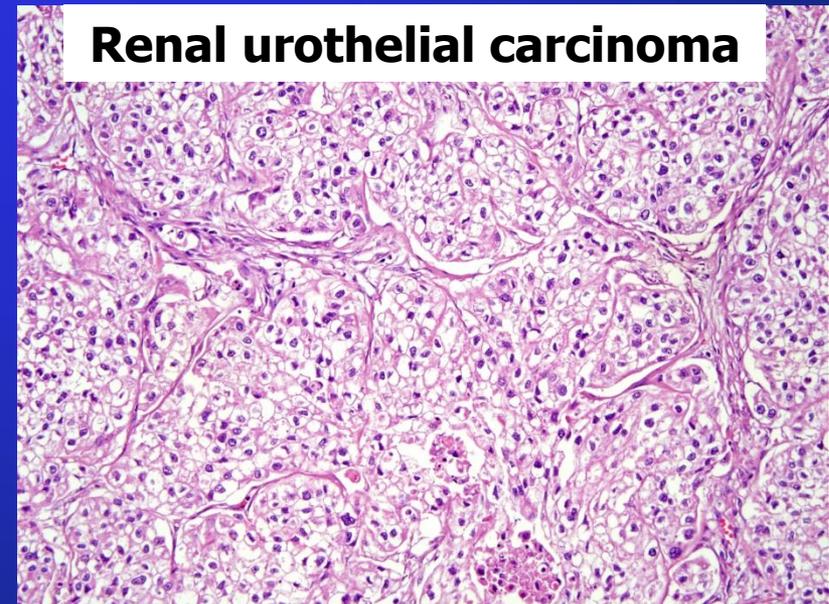
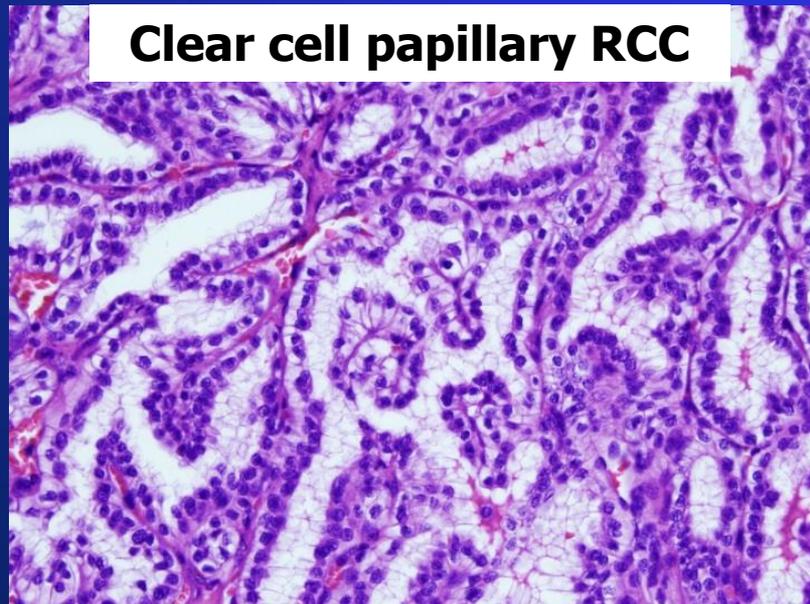
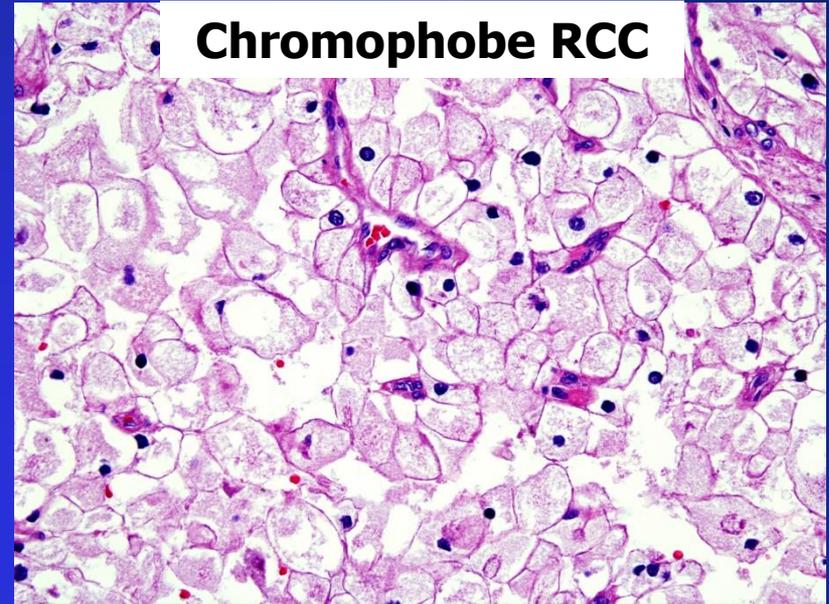
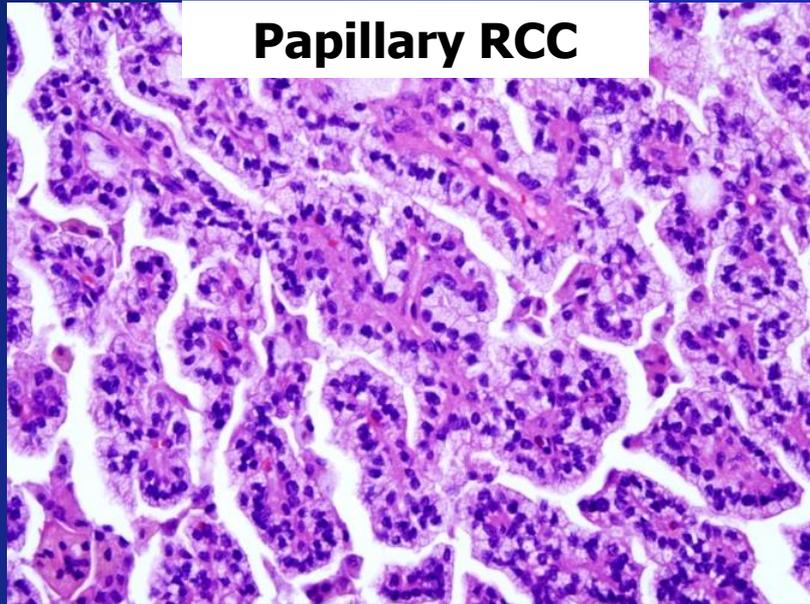
# Clear cell RCC: Heterogenous



# Clear cell RCC: Heterogenous



# Non-clear cell RCC with clear cells



# **PAPILLARY Category**

**Papillary RCC, type 1 and 2**

**Clear cell papillary RCC**

**Clear cell RCC**

**Chromphobe RCC (rarely)**

**Mucinous tubular spindle cell ca**

**Metanephric adenoma**

**Collecting duct carcinoma**

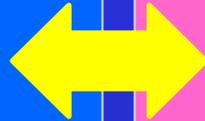
**Metastatic**

# Papillary RCC

## Morphologic Spectrum

### Growth Patterns

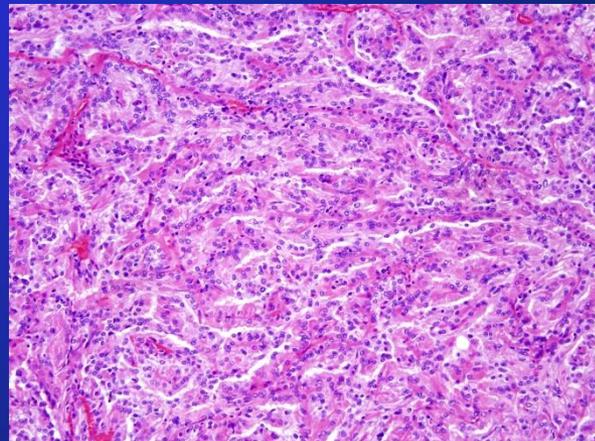
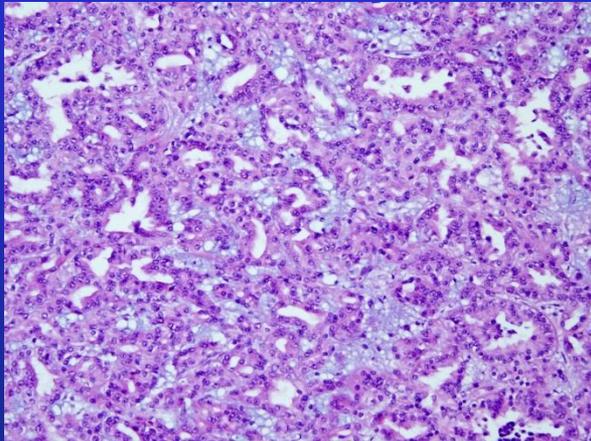
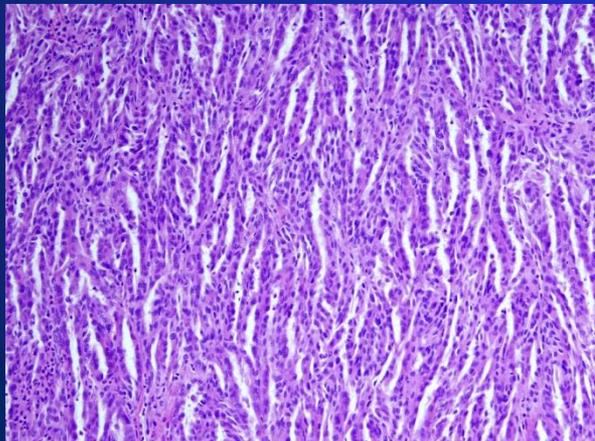
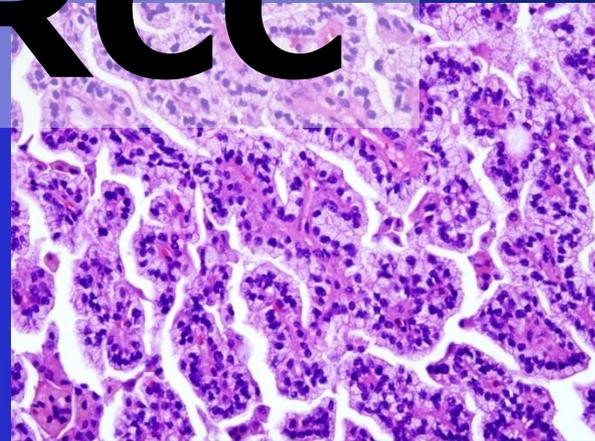
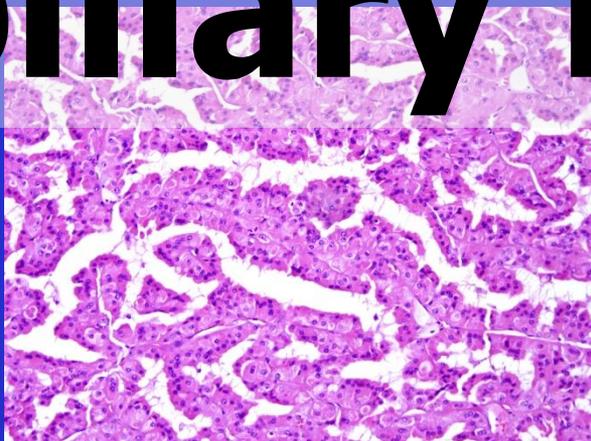
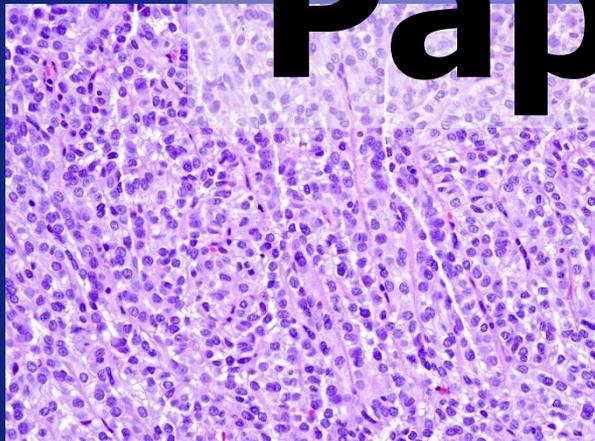
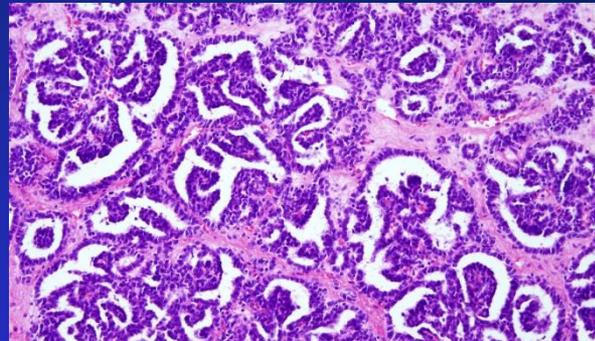
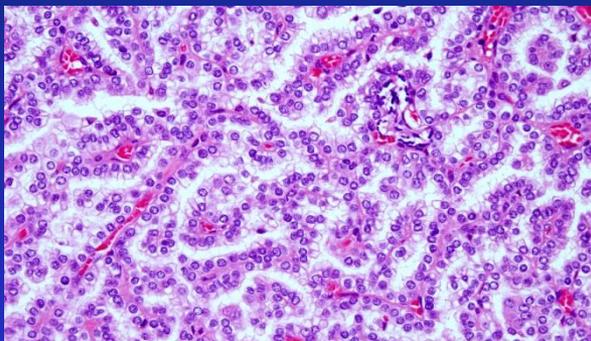
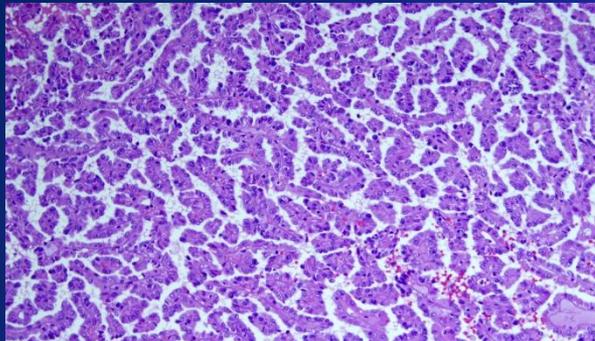
- Papillary
- Tubular
- Glomeruloid
- Solid or cystic



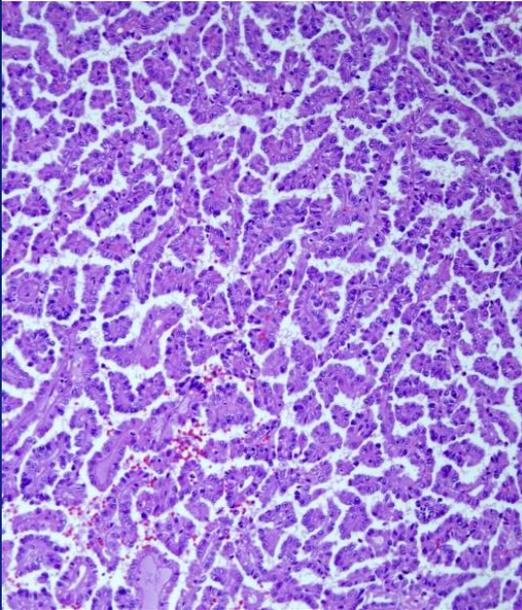
### Cell Types

- Basophilic
- Eosinophilic
- Clear
- Sarcomatoid

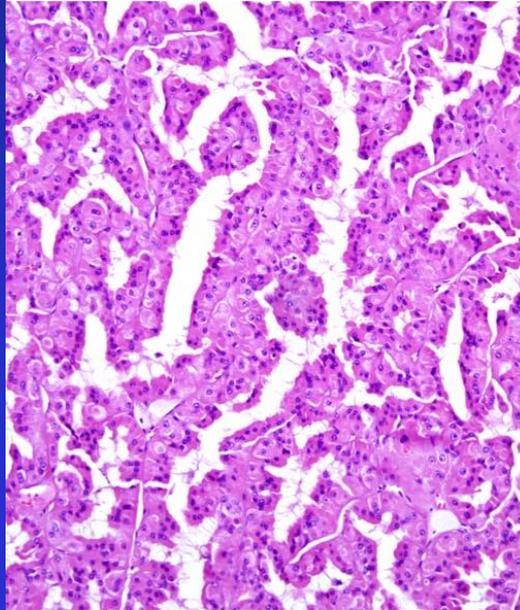
# Papillary RCC



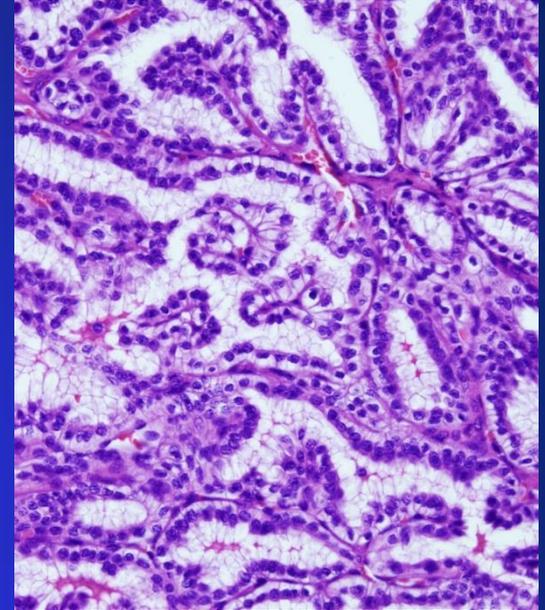
**Papillary Type 1**



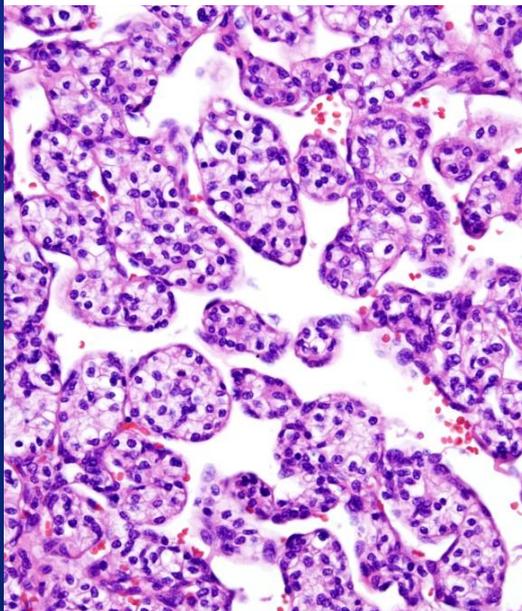
**Papillary Type 2**



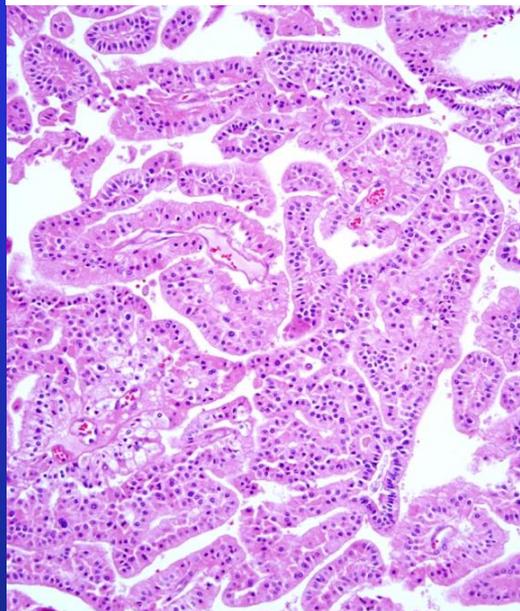
**Clear cell papillary**



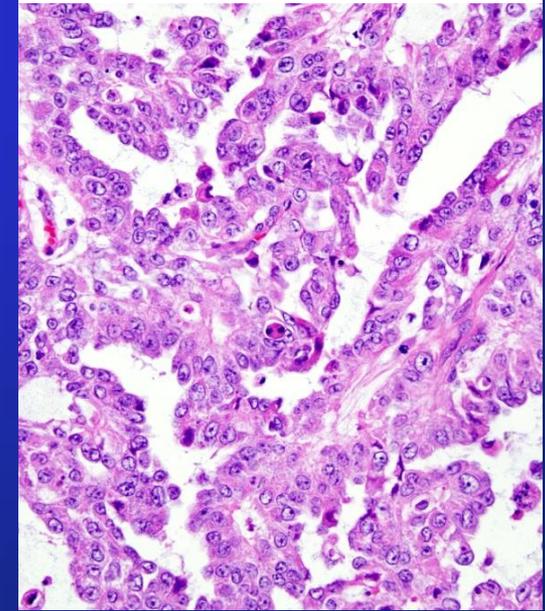
**Clear cell RCC**



**Chromphobe RCC**



**Collecting duct ca**



# ONCOCYTIC Category

Oncocytoma

Chromophobe RCC

Hybrid oncocytic tumor

Clear cell RCC with granular cells

Type 2 papillary or **oncocytic papillary**

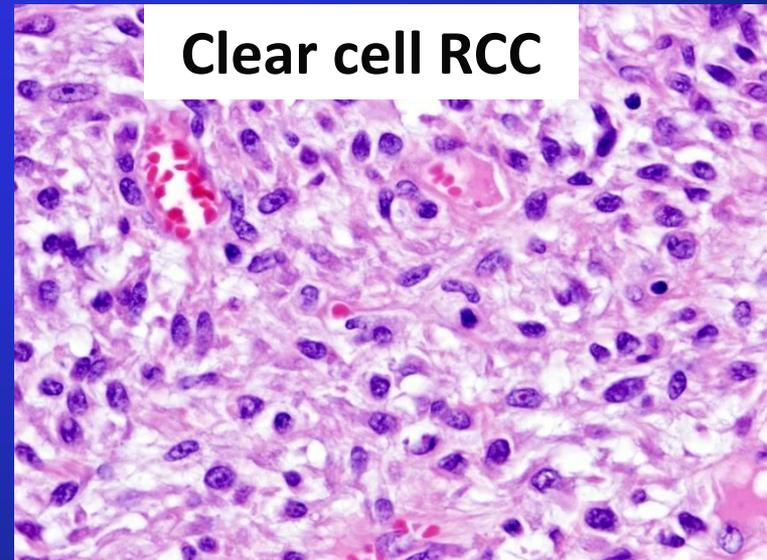
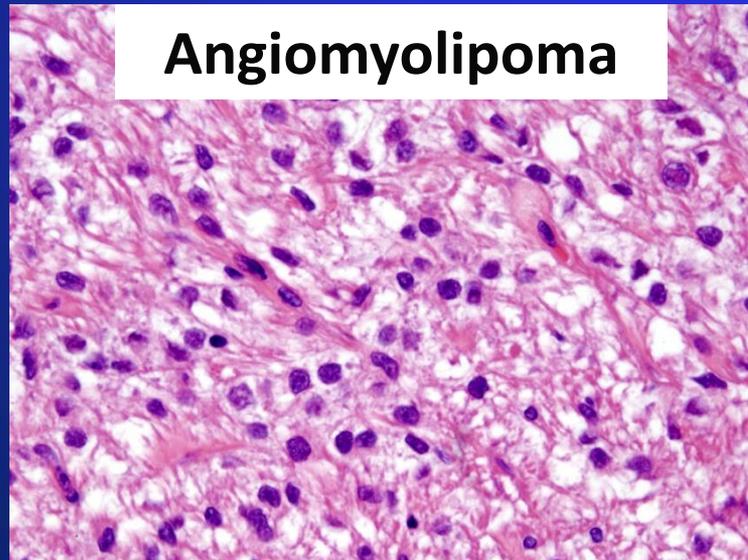
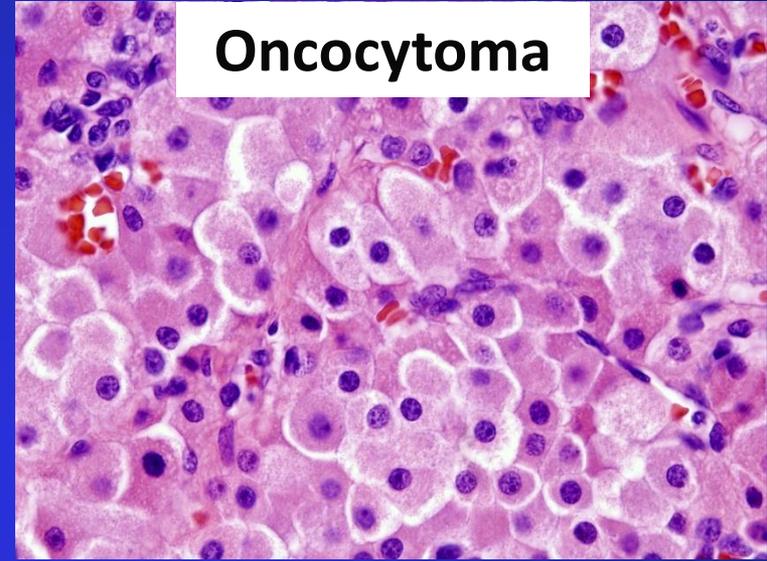
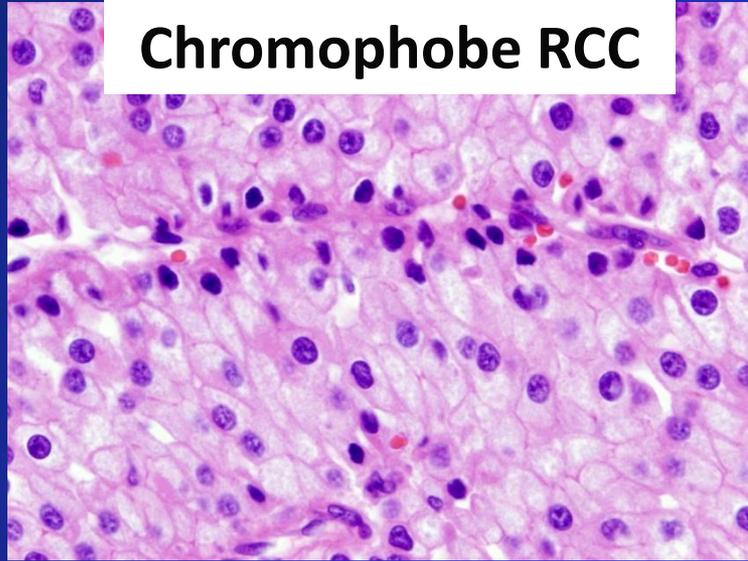
**ACD-associated RCC**

Epithelioid angiomyolipoma

Carcinoid

Adrenal cortical

# Oncocytic Tumor



# **CYSTIC Category**

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**Clear cell RCC**

**Papillary RCC**

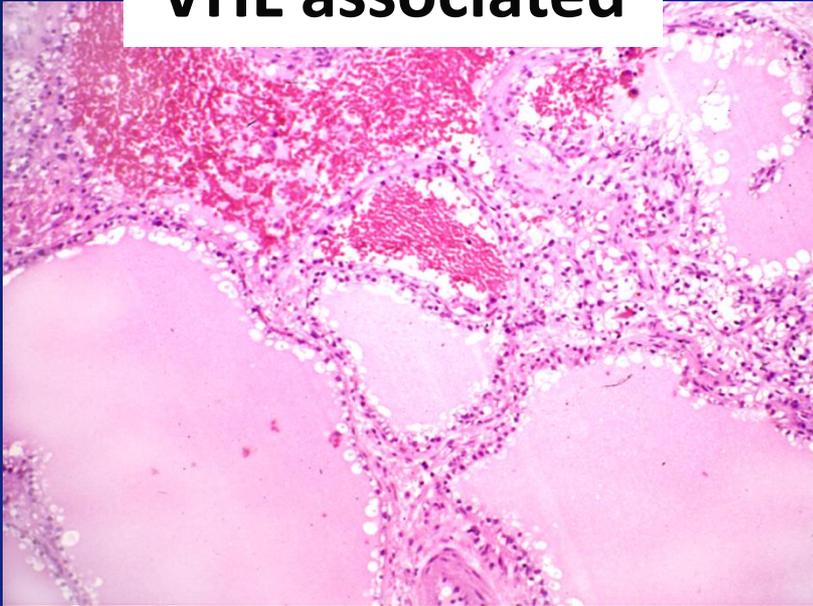
**Clear cell papillary RCC**

**Oncocytoma**

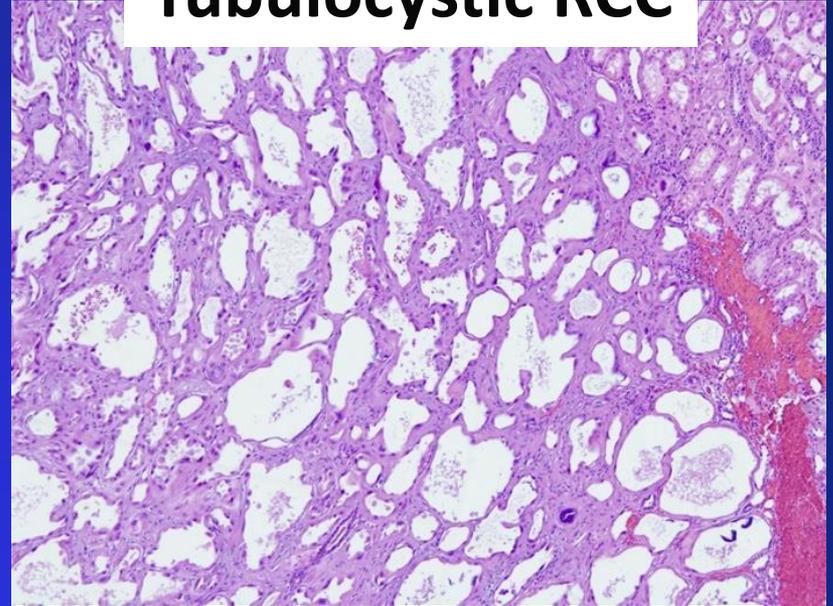
**Cystic nephroma/mixed epithelial  
and stromal tumor of kidney**

**Benign cystic renal disease**

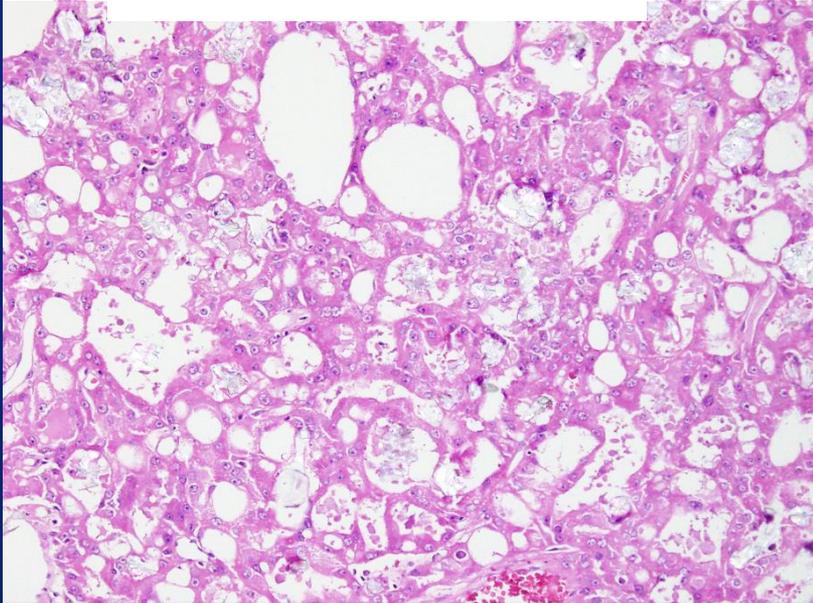
**VHL associated**



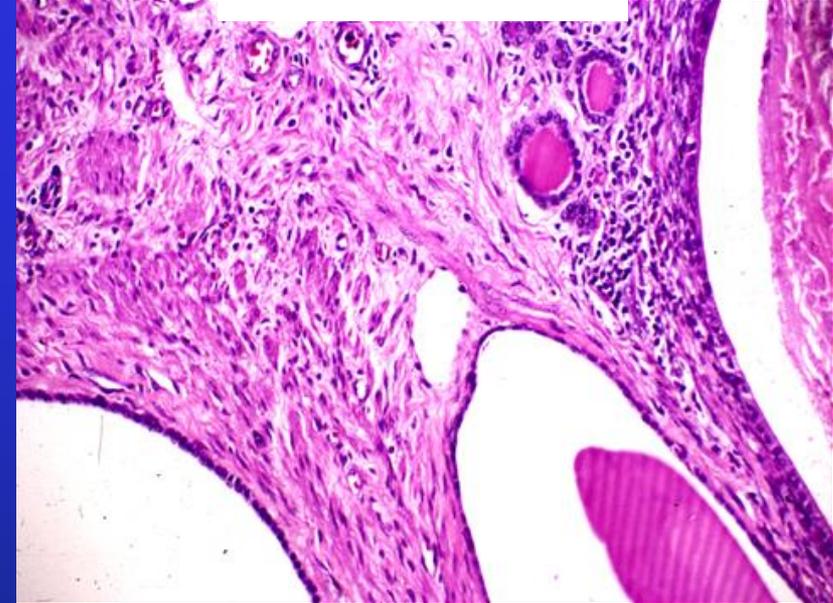
**Tubulocystic RCC**



**ACD associated**



**MESTK**



# **SPINDLE CELL Category**

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**RCC/UCa with sarcomatoid**

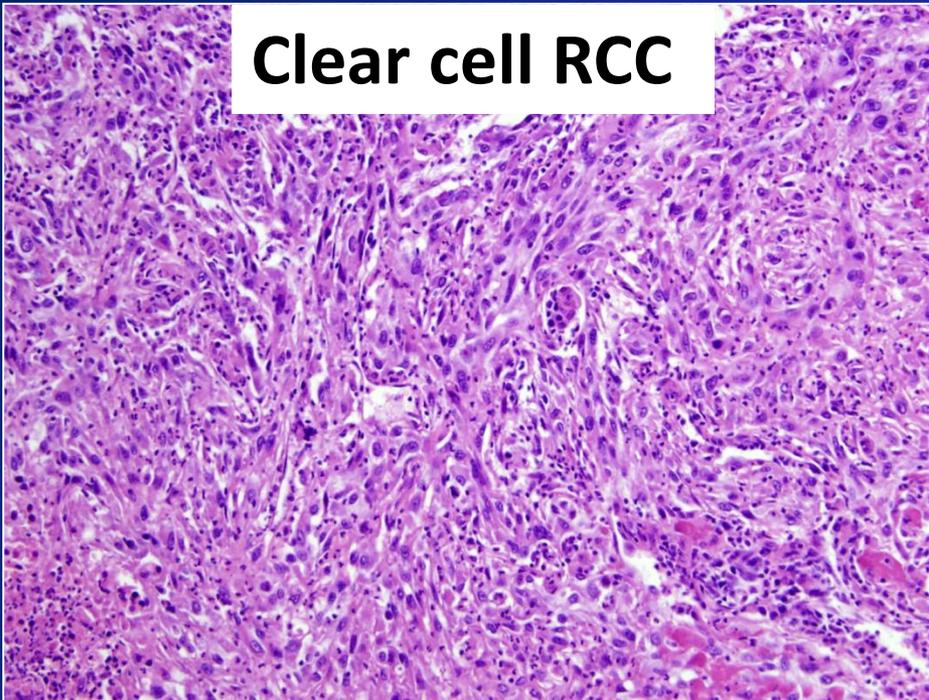
**Mucinous tubular spindle cell RCC**

**Leiomyoma/leiomyosarcoma**

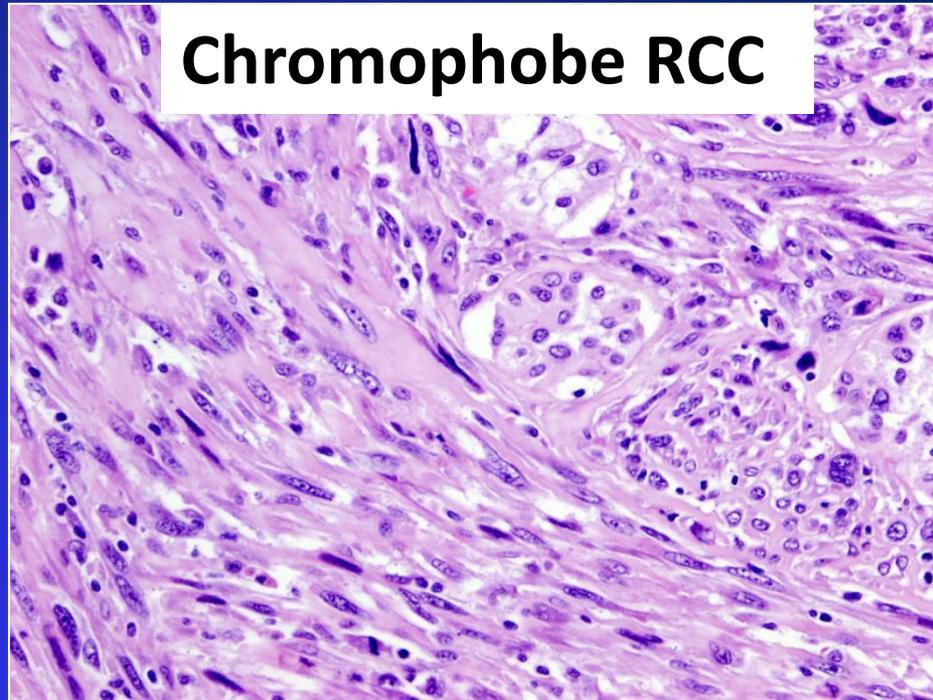
**Angiomyolipoma (fat-poor)**

**Other renal sarcoma**

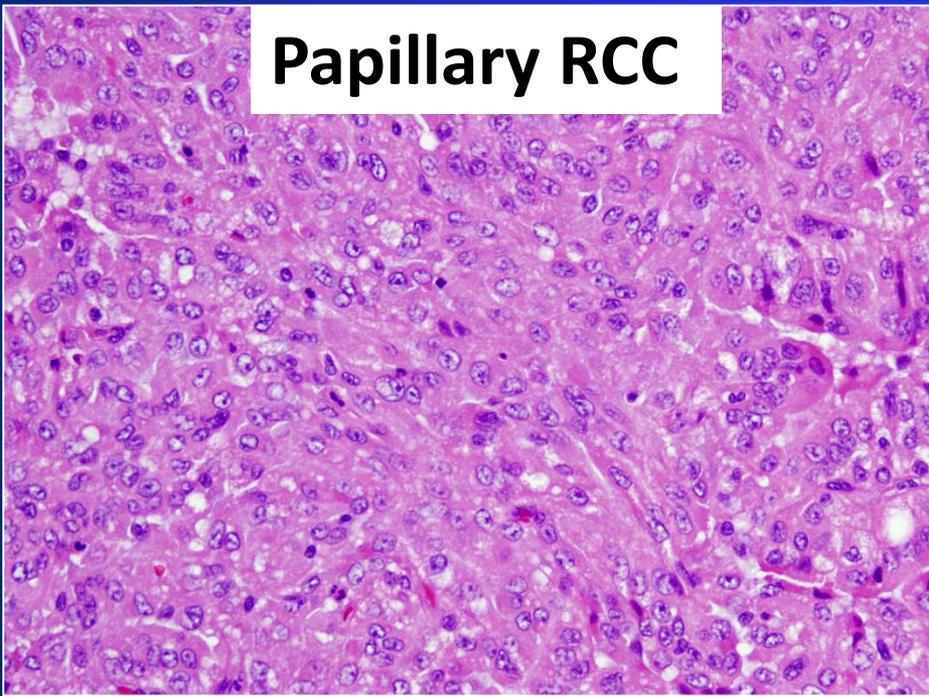
**Clear cell RCC**



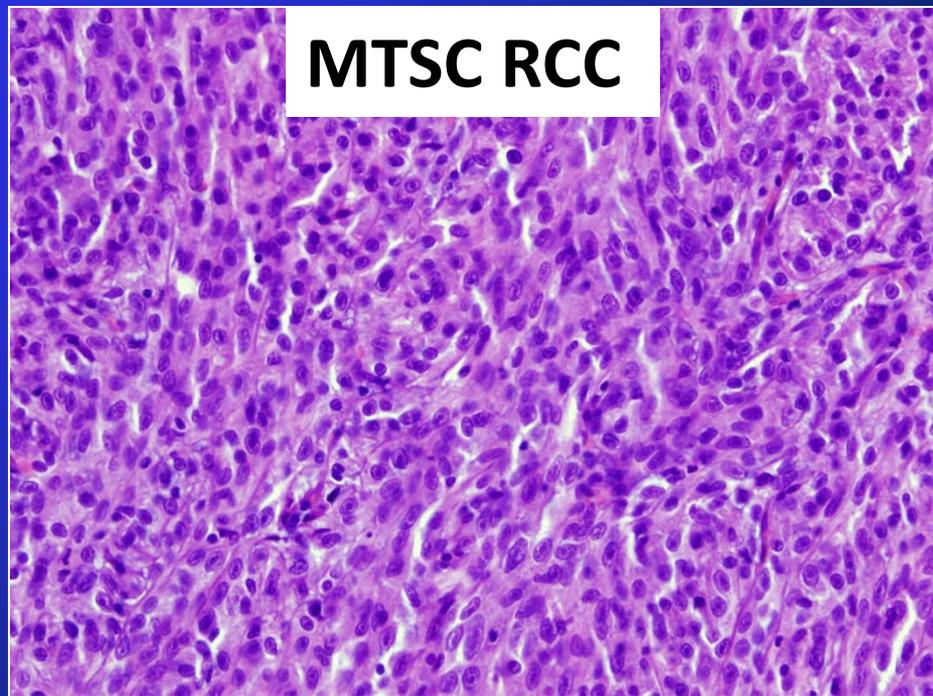
**Chromophobe RCC**



**Papillary RCC**



**MTSC RCC**



# **HIGH GRADE Category**

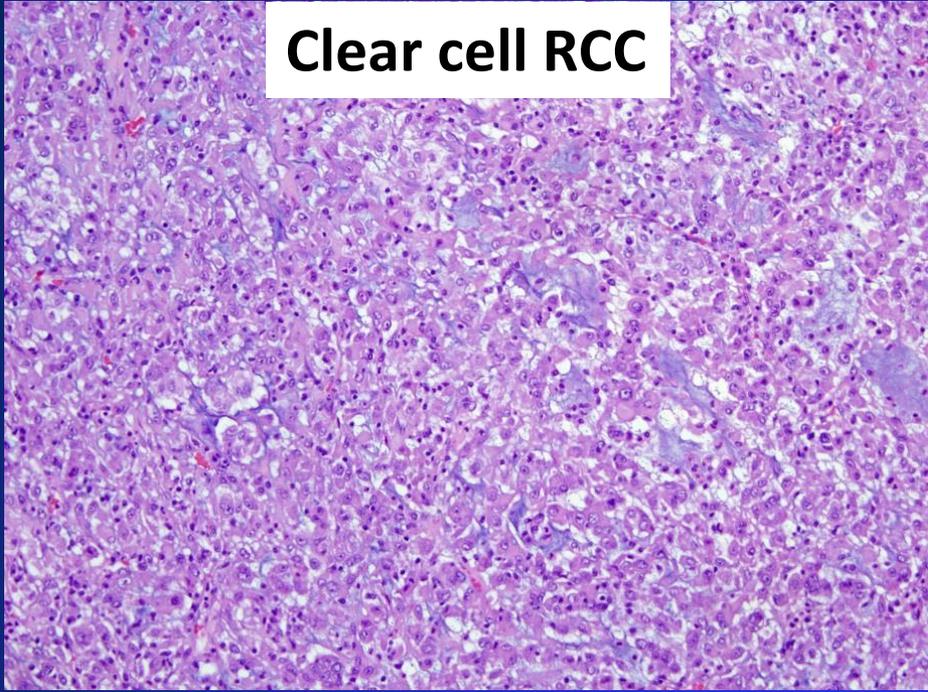
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**RCC: Any type**

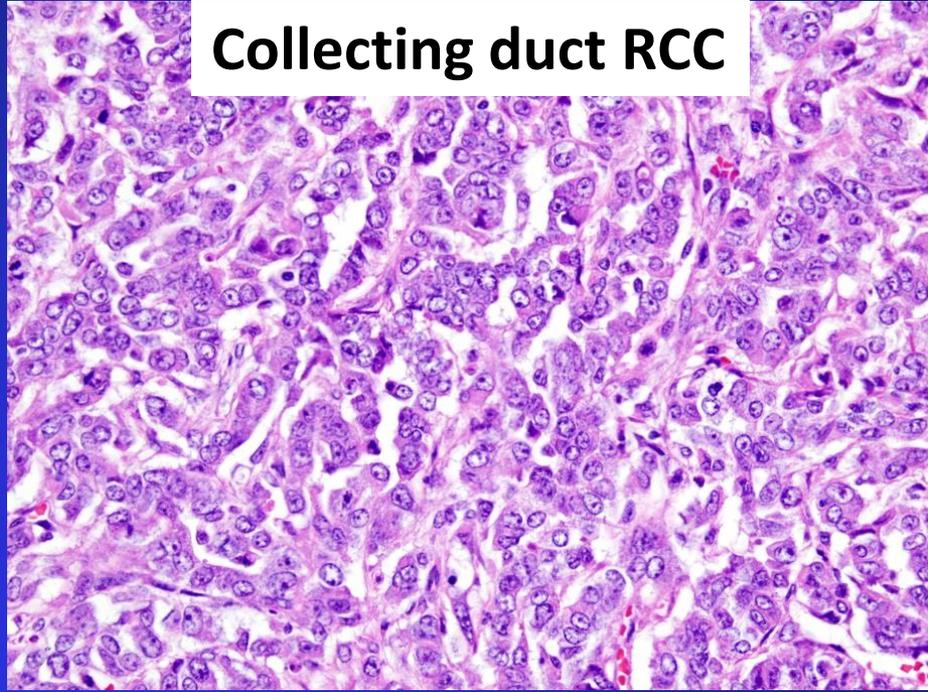
**Urothelial carcinoma**

**Metastatic carcinoma**

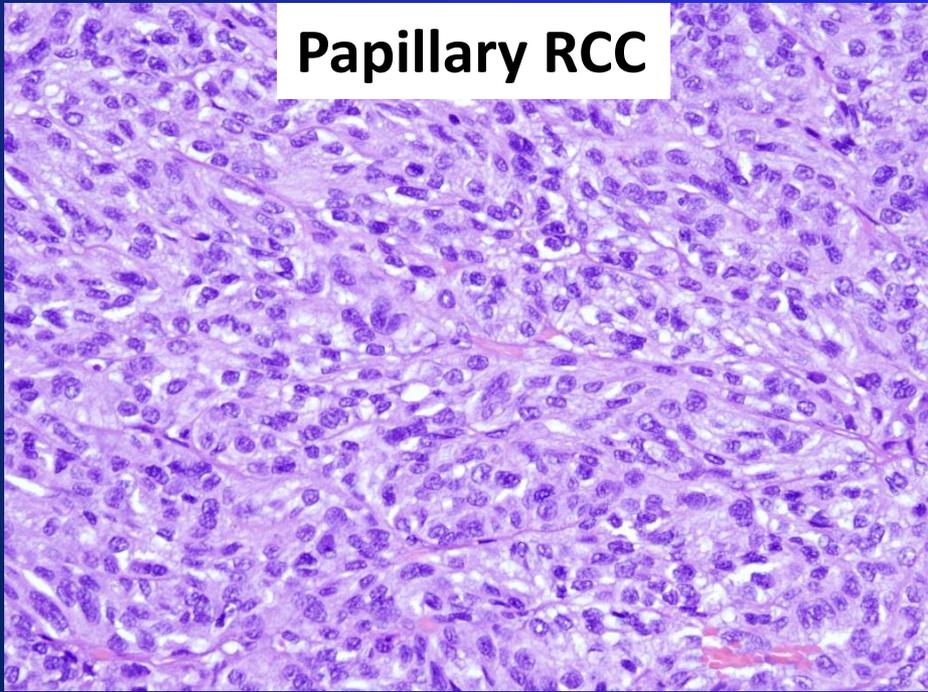
**Clear cell RCC**



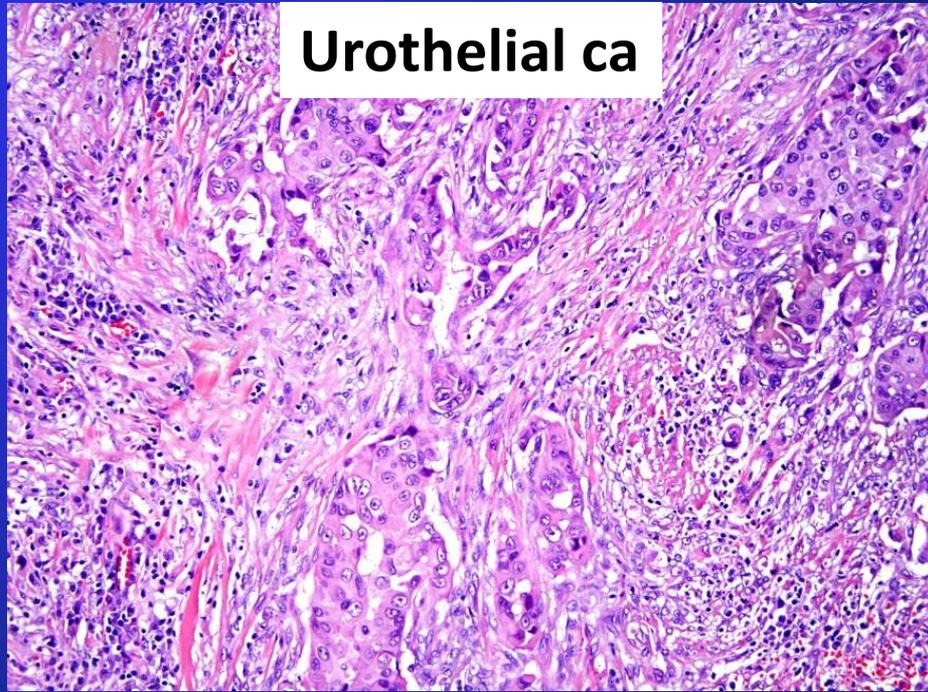
**Collecting duct RCC**



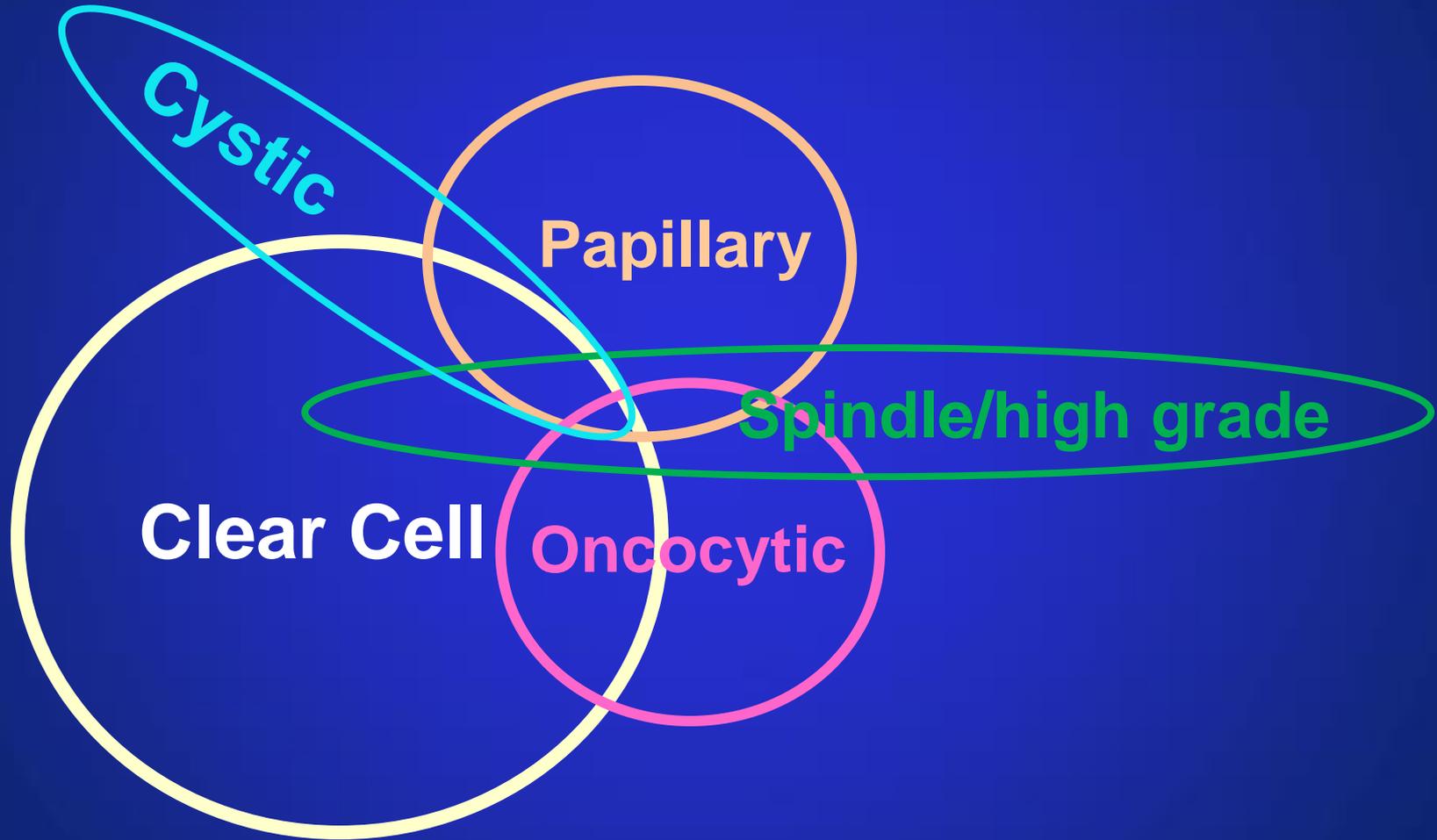
**Papillary RCC**



**Urothelial ca**



# Overall Categorization



# Immunohistochemistry plays an important role in the diagnosis of renal mass biopsy



# Renal Tumors

## *Diagnostic and Prognostic Biomarkers*

*Puay Hoon Tan, MD, FRCPA,\* Liang Cheng, MD,† Nathalie Rioux-Leclercq, MD,‡  
Maria J. Merino, MD,§ George Netto, MD,|| Victor E. Reuter, MD,¶ Steven S. Shen, MD,#  
David J. Grignon, MD,† Rodolfo Montironi, MD, FRCPath,\*\* Lars Egevad, MD,††  
John R. Srigley, MD, FRCPC,‡‡ Brett Delahunt, MD, FRCPA,§§ Holger Moch, MD,|||  
and The ISUP Renal Tumor Panel*

Am J Surg Pathol **2013**;37:1518–1531

## Best Practices Recommendations in the Application of Immunohistochemistry in the Kidney Tumors *Report From the International Society of Urologic Pathology Consensus Conference*

*Victor E. Reuter, MD,\* Pedram Argani, MD,† Ming Zhou, MD, PhD,‡  
Brett Delahunt, MD, FRCPA,§ and Members of the ISUP Immunohistochemistry  
in Diagnostic Urologic Pathology Group*

Am J Surg Pathol **2014**;38:1017–1022, e35-e49

# Establishing Renal Cell Origin

- Recommended marker by ISUP:
  - PAX-8
- Potentially useful markers:
  - CD10
  - RCC marker antigen
  - KSP-cadherin

# IHC for Histologic Subtyping

**Should be based on  
morphologic patterns and  
differential diagnosis**

# Diagnostic Approach

- On-site cytologic evaluation
- Multiple H&E levels (3x)
- Growth patterns
- Cytology (cytoplasm)
- Differential diagnosis
- IHC work-up
- Report and communication

# **Do we need IHC for all cases of renal mass biopsy?**

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**No!**

**For many tumors that have classic morphology, a histologic diagnosis can be made on H&E section**

# Share we see some case examples!

Do I have a good sample?

What's overall category based on patterns/cells?

Do I see features that are classic for a histologic subtype?

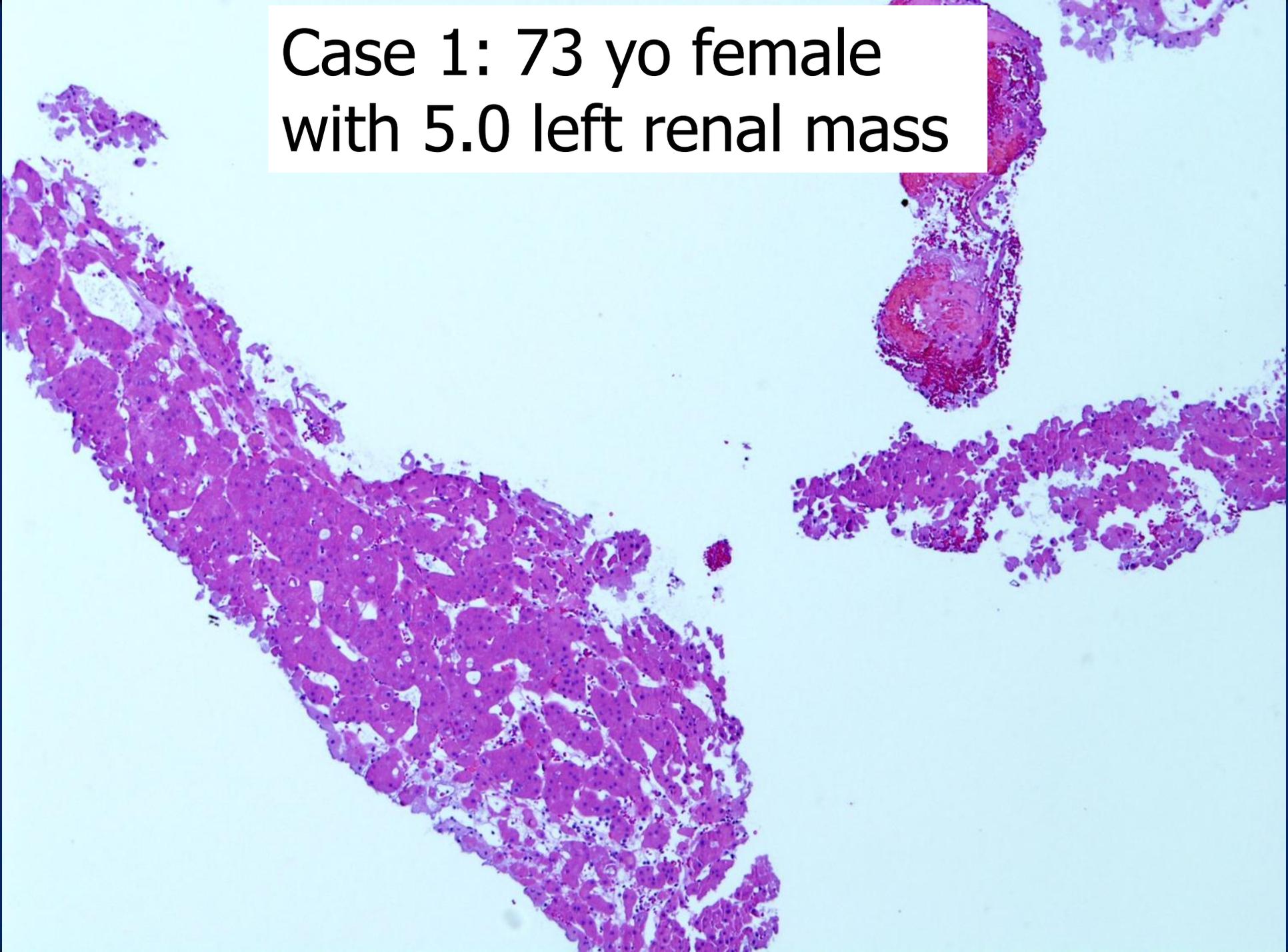
Is it typical enough for a specific diagnosis?

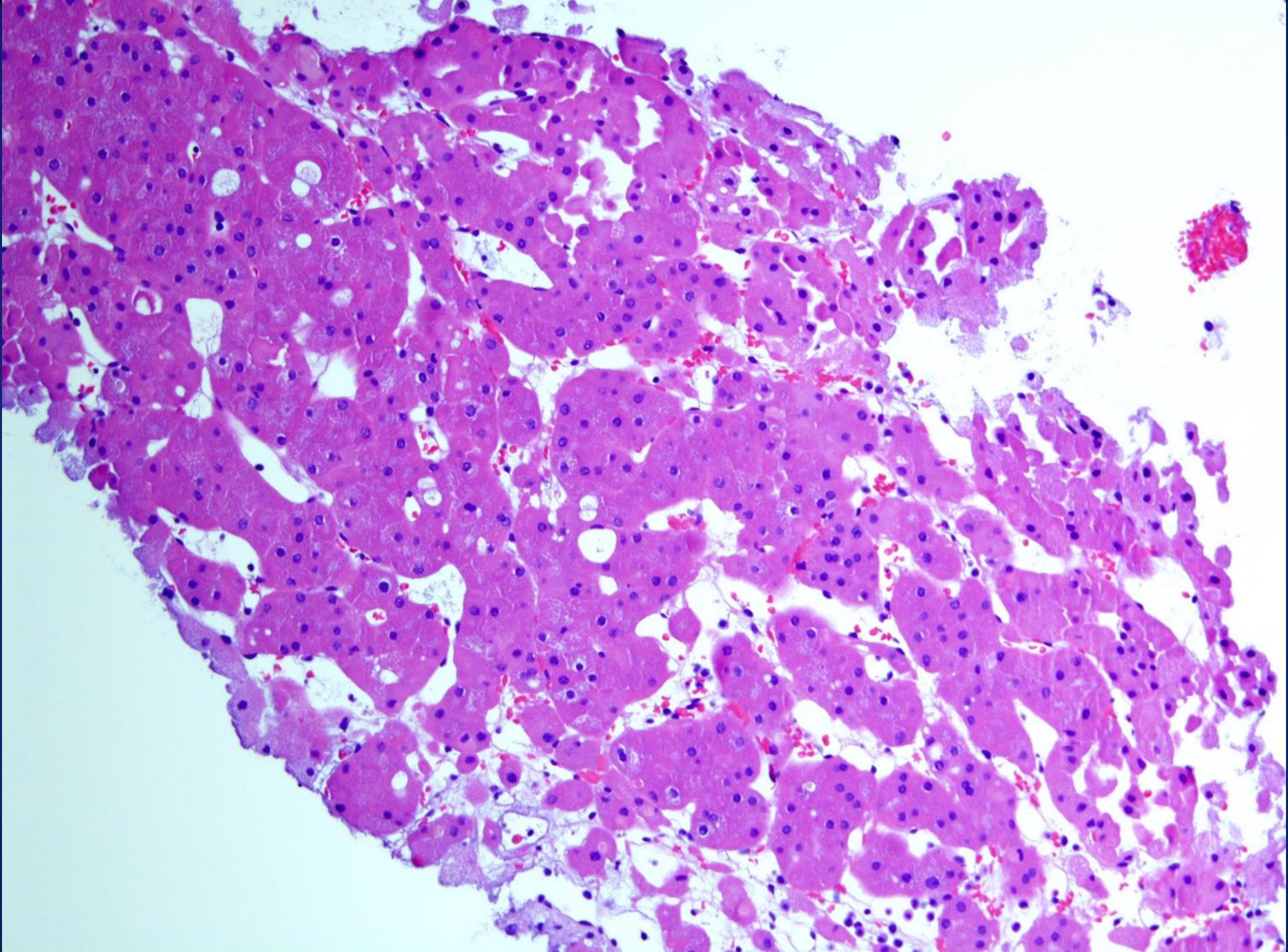
If not, what are my differential?

What are the IHC markers that I may use?

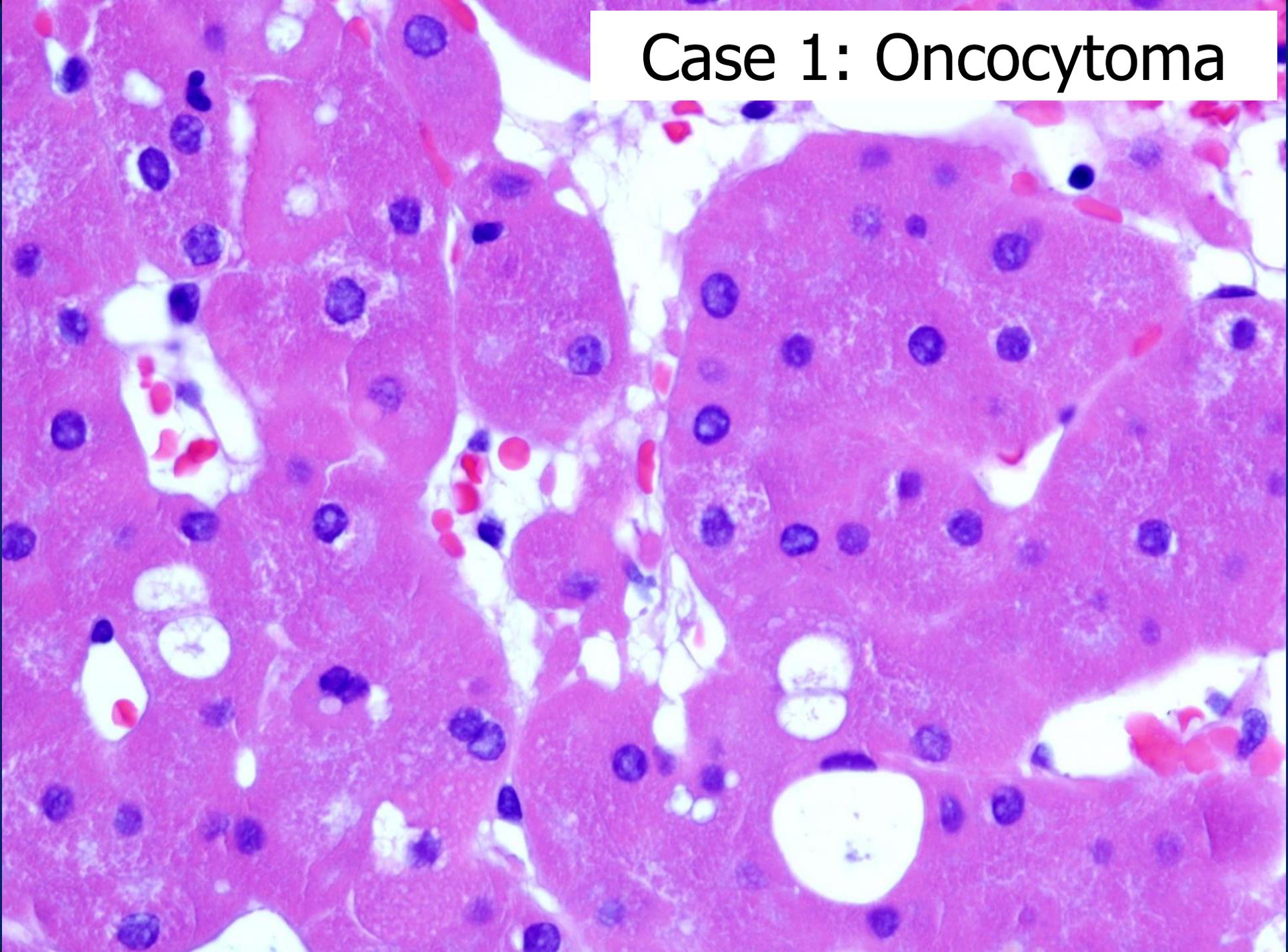
Can I reach a definitive diagnosis?

Case 1: 73 yo female  
with 5.0 left renal mass

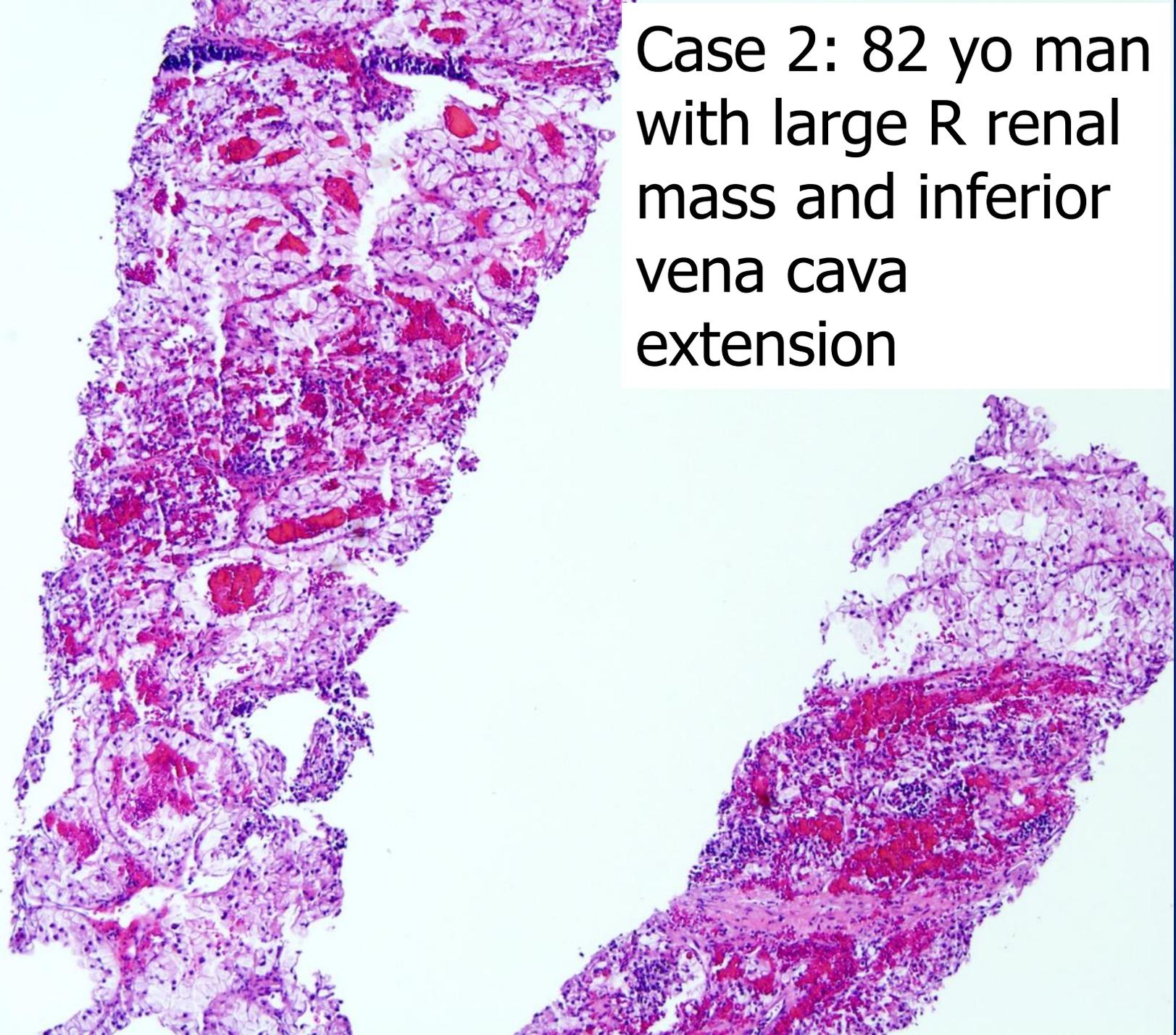




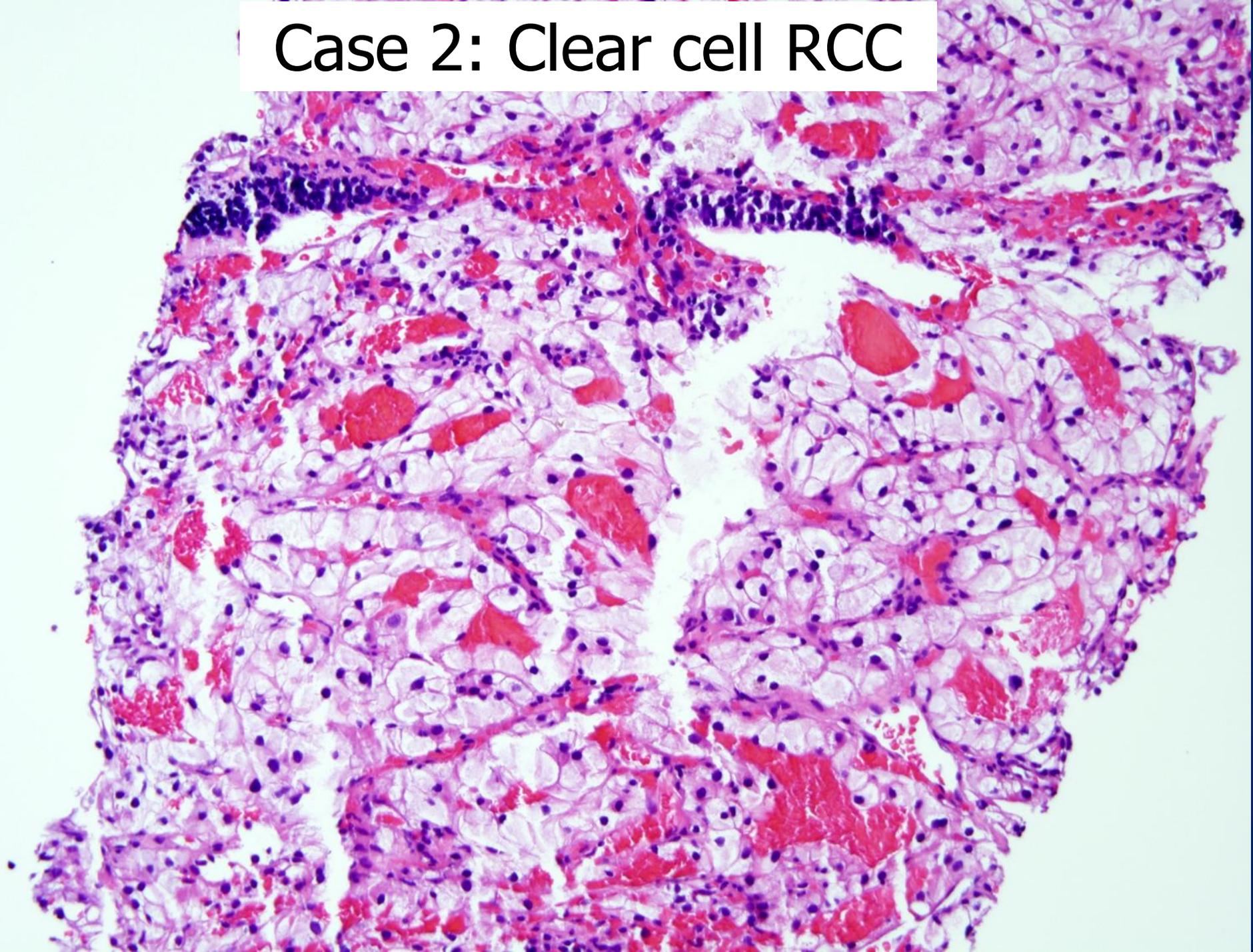
# Case 1: Oncocytoma



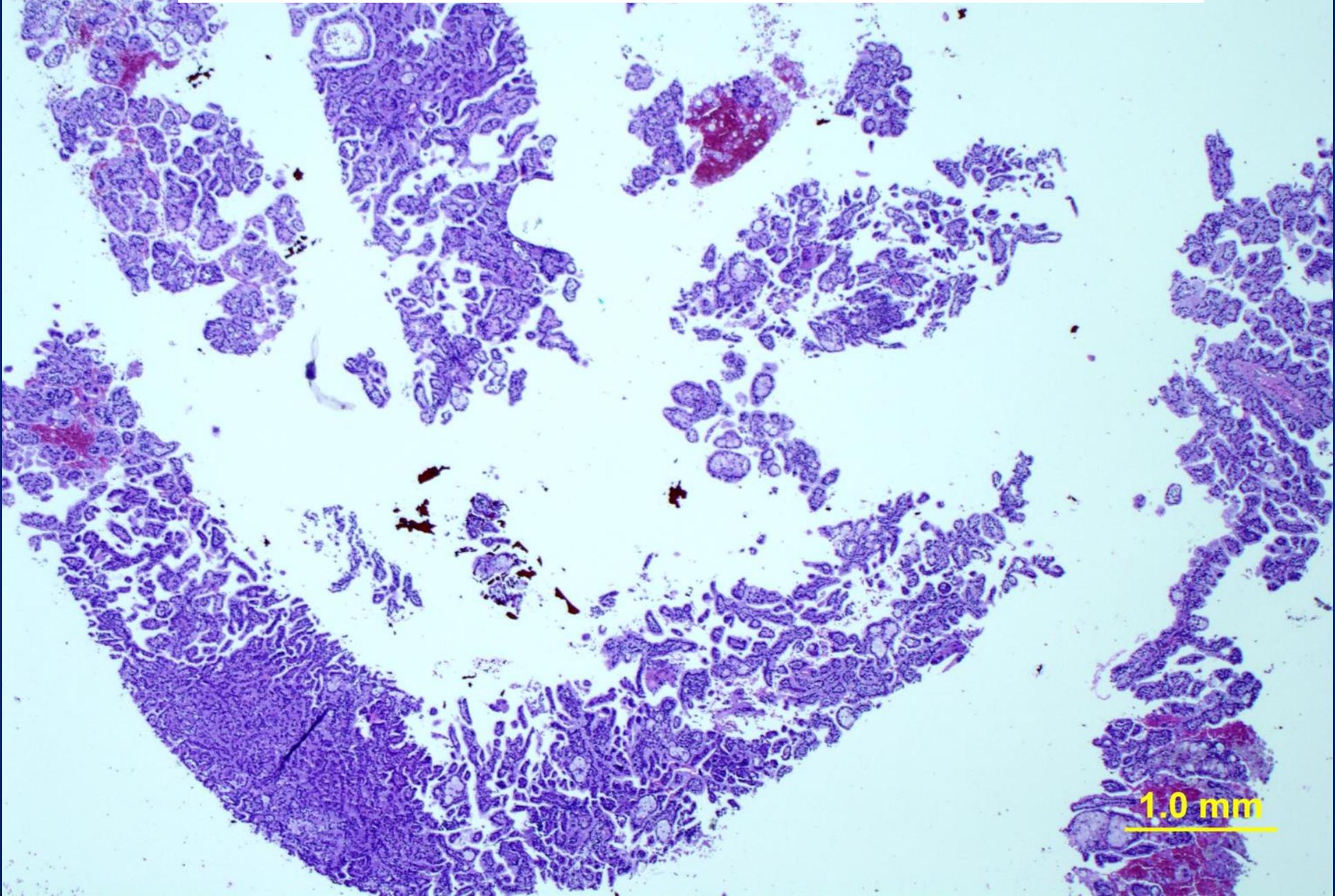
Case 2: 82 yo man  
with large R renal  
mass and inferior  
vena cava  
extension

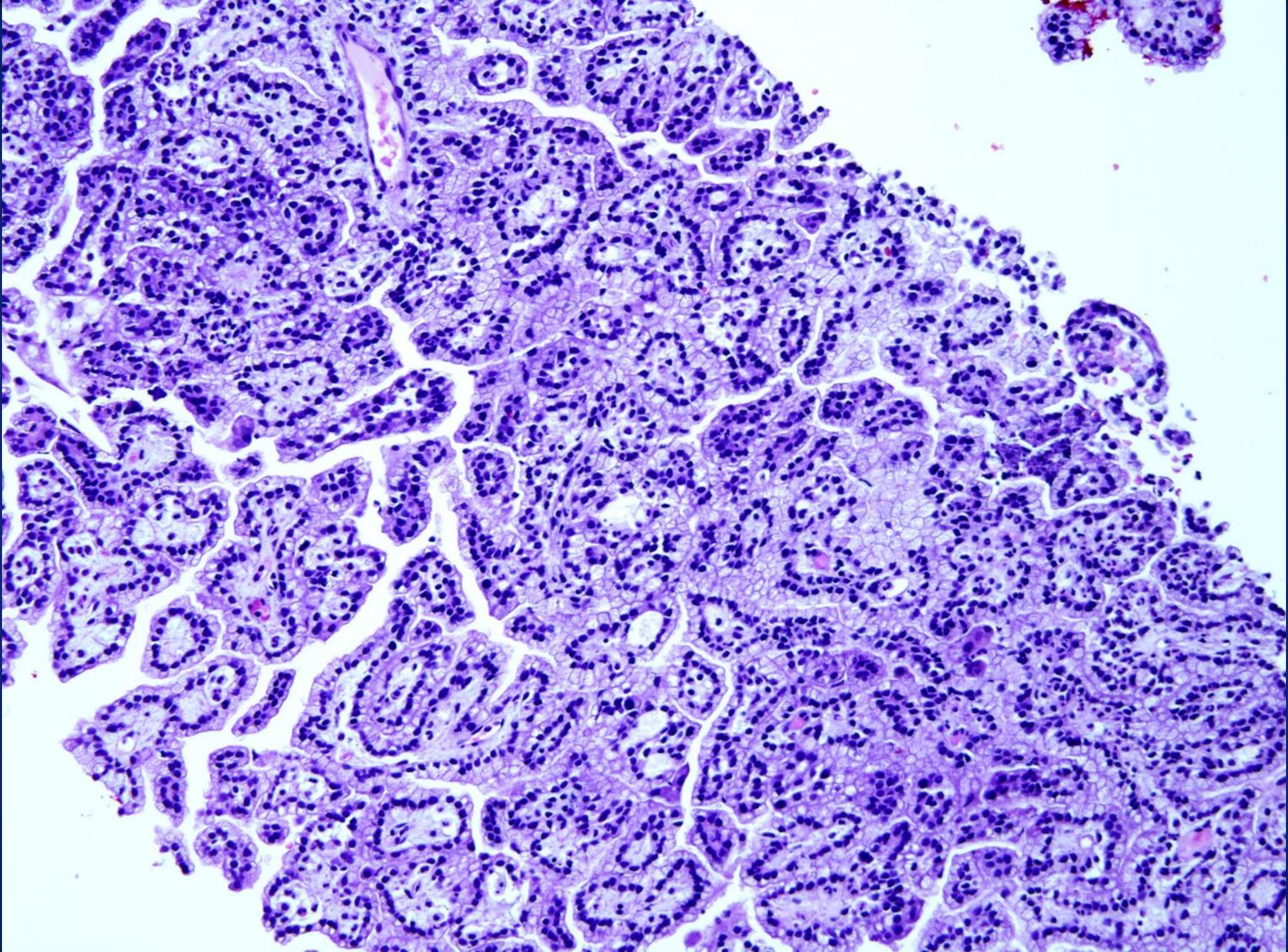


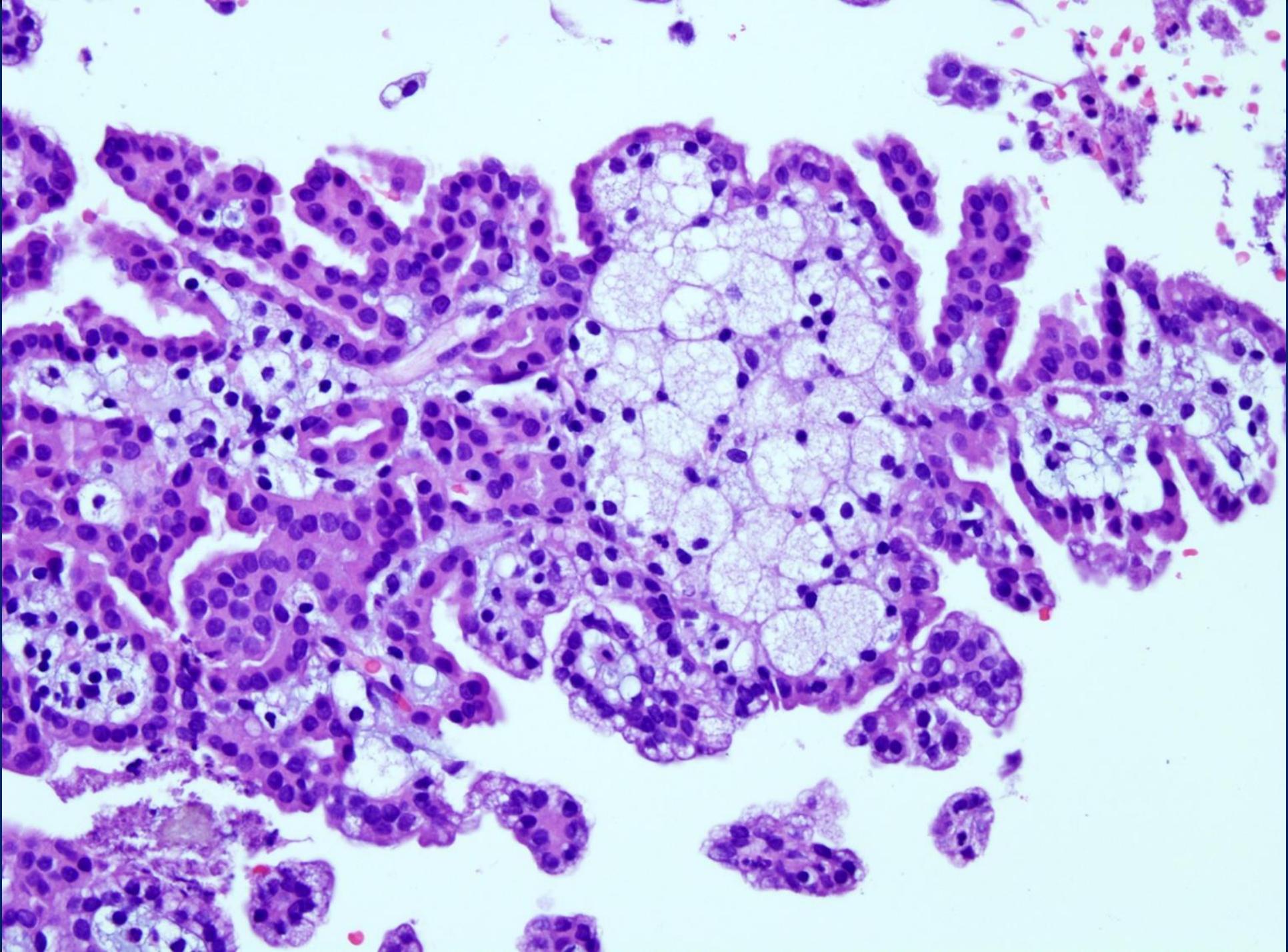
# Case 2: Clear cell RCC



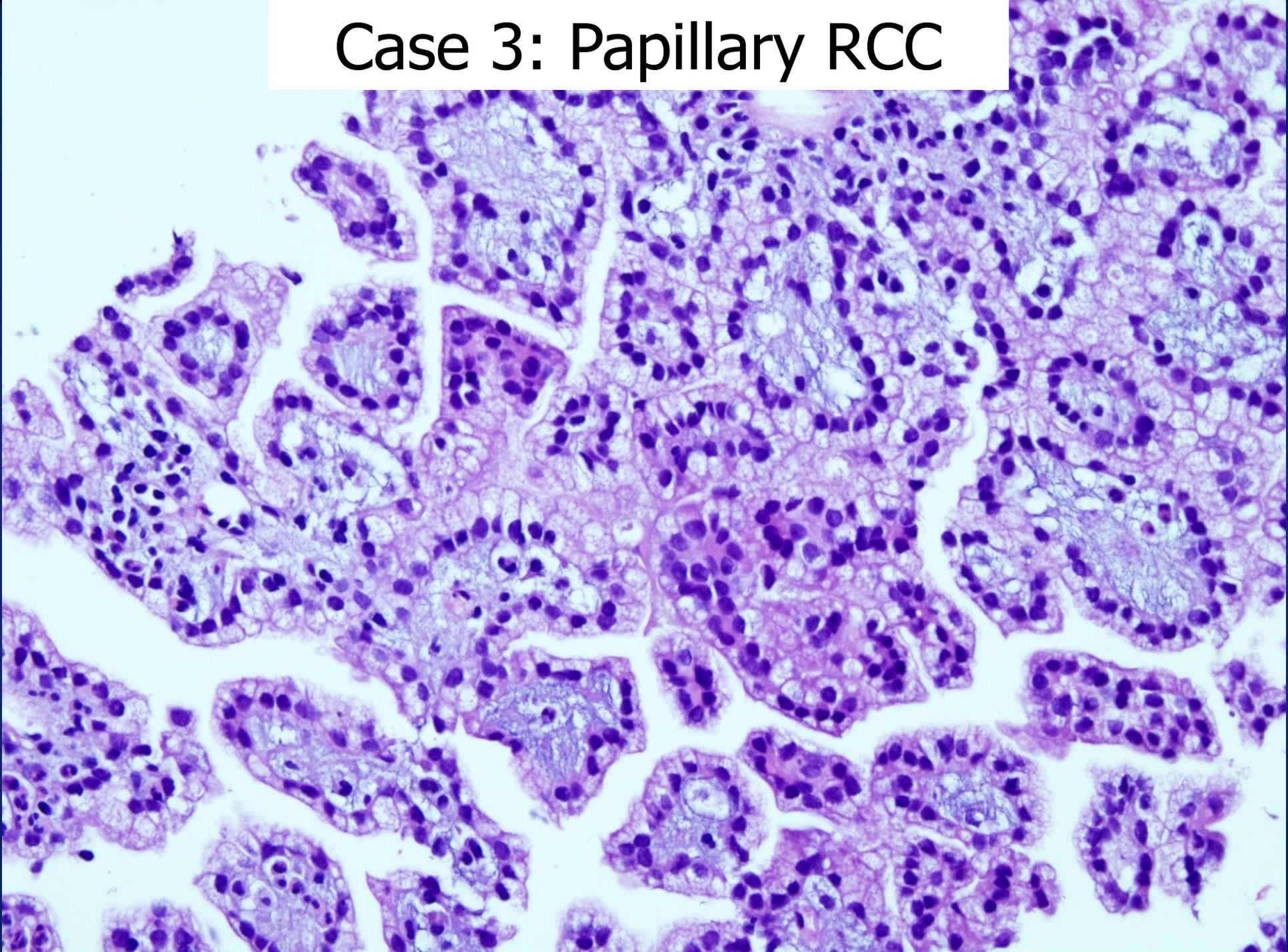
# Case 3: 54M 5.5 cm R renal mass





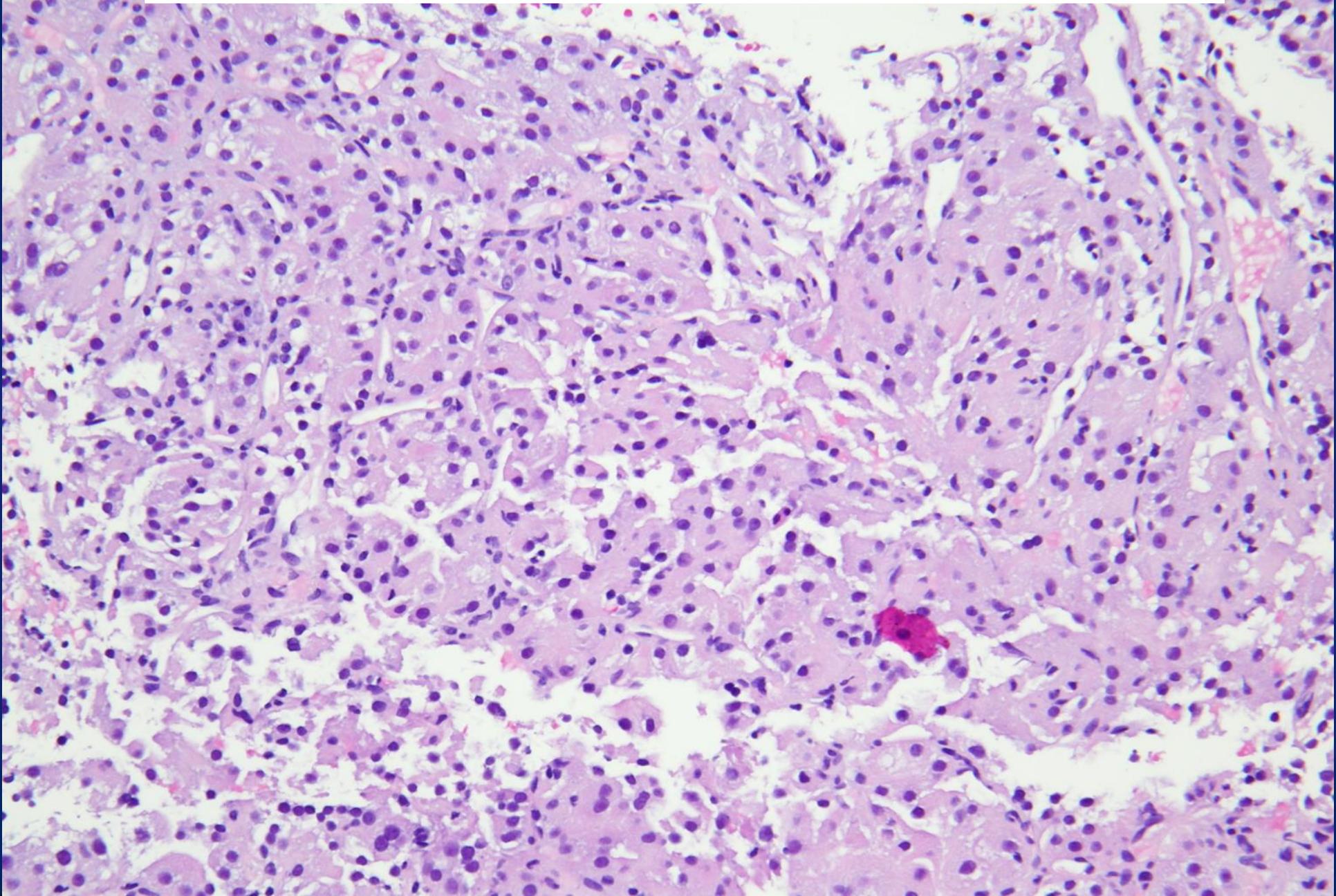


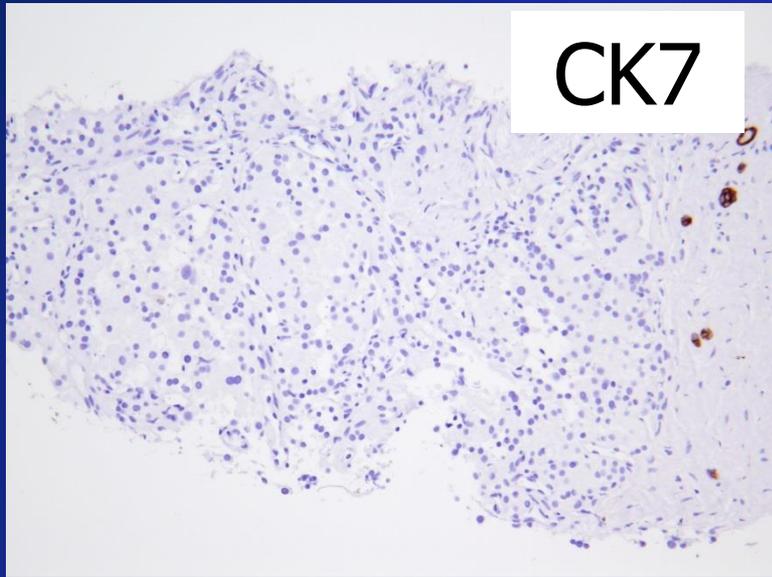
# Case 3: Papillary RCC



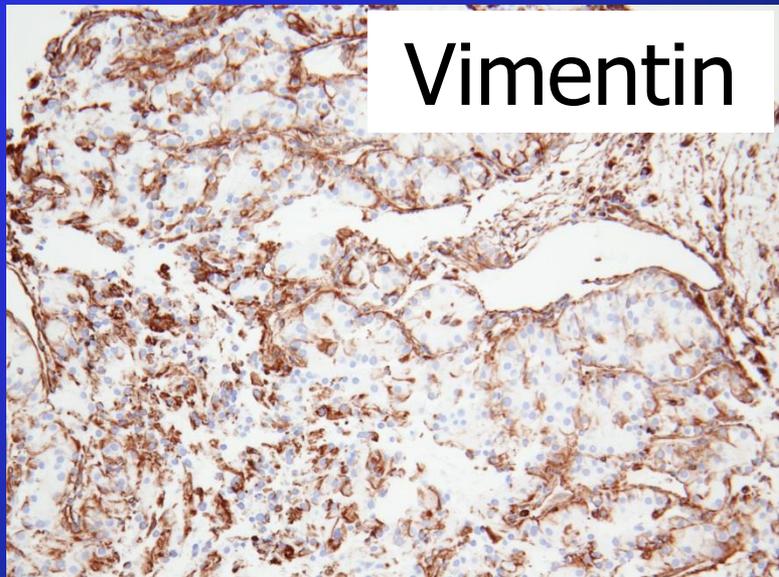
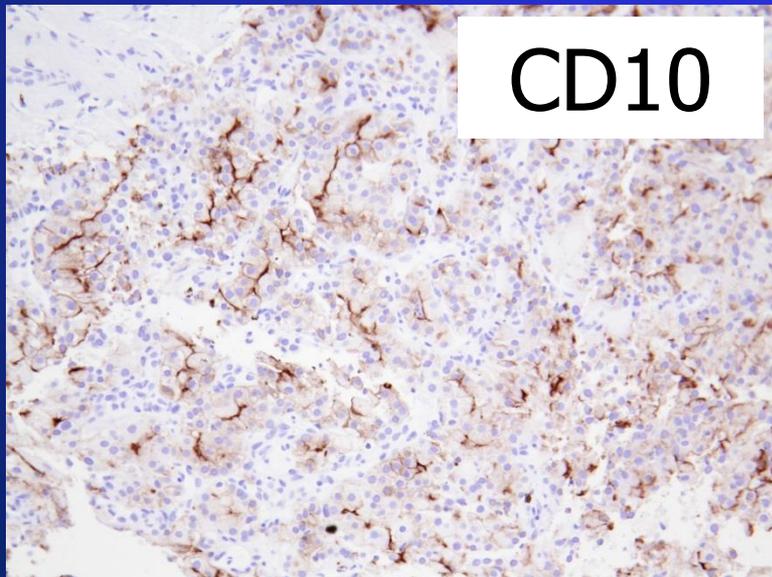


# Case 4: 70M 4.5 cm R renal mass





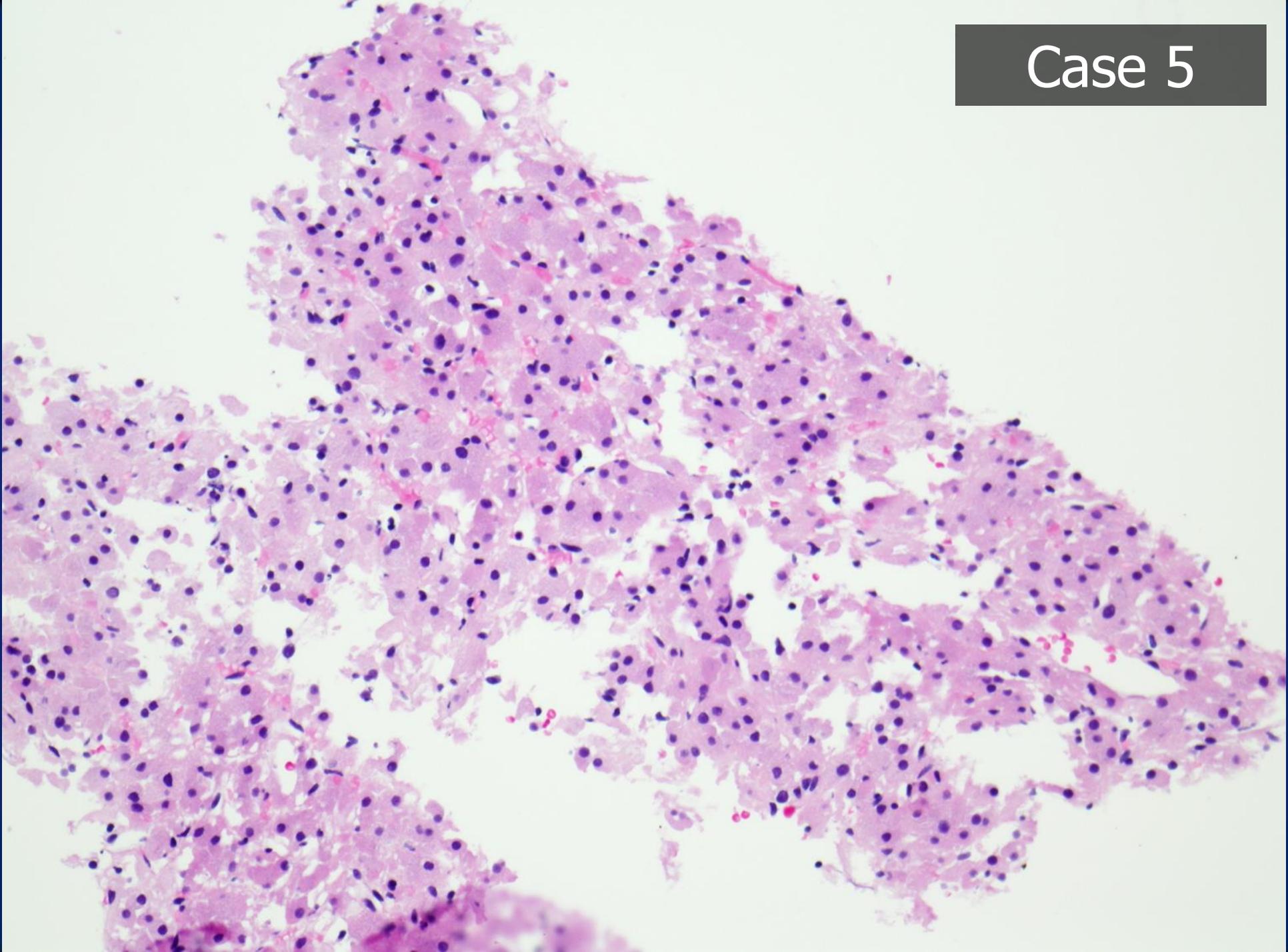
Case 4:  
Clear cell RCC



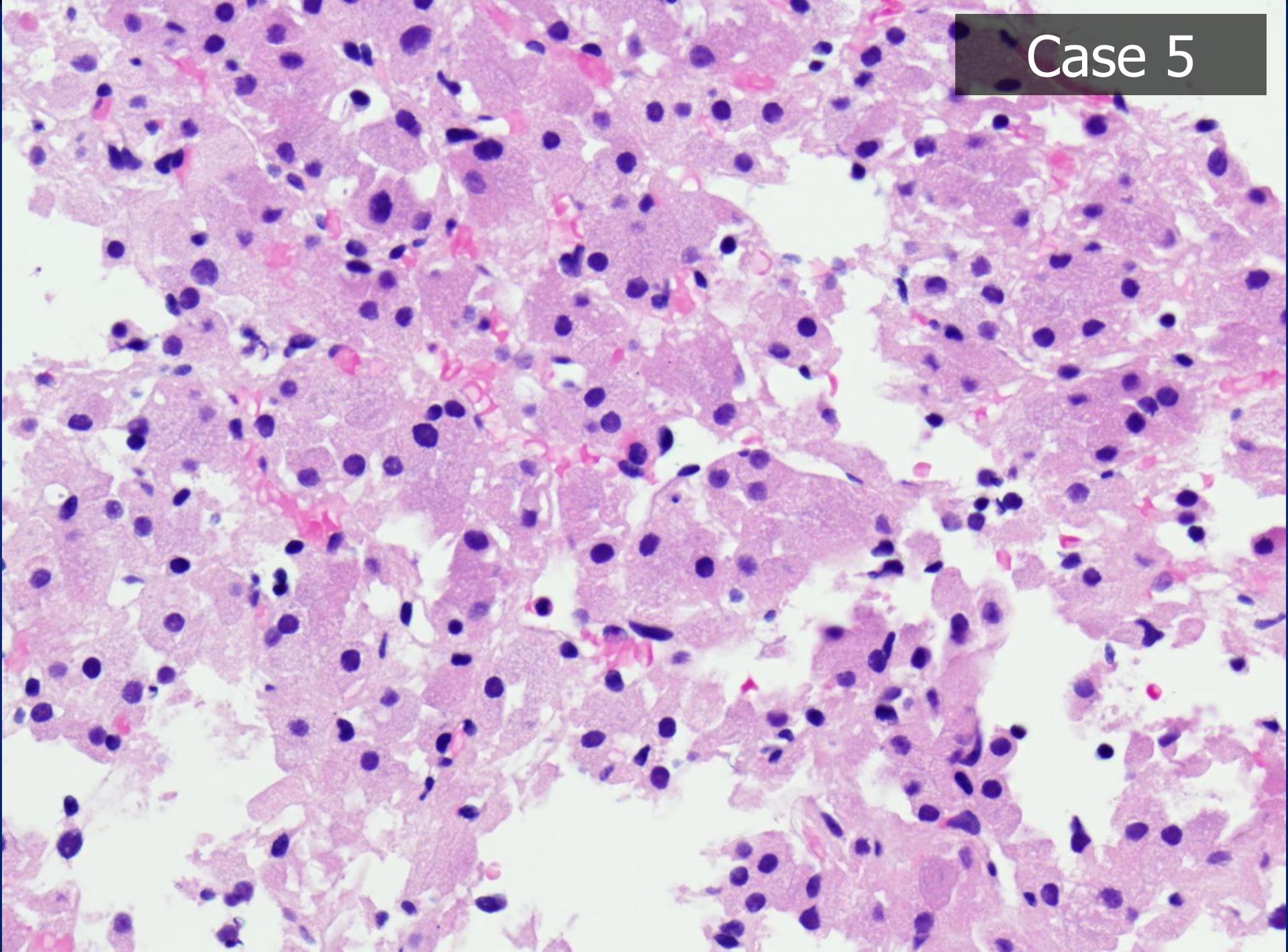
# Common Situations That IHC May Be Helpful

- Clear cell RCC with granular cells
- Chromophobe vs. clear cell RCC
- Chromophobe vs. oncocytoma
- Clear cell pRCC vs. clear or pRCC
- Solid papillary RCC vs. clear cell
- High grade carcinoma
- Confirm AML, urothelial ca, etc.

Case 5

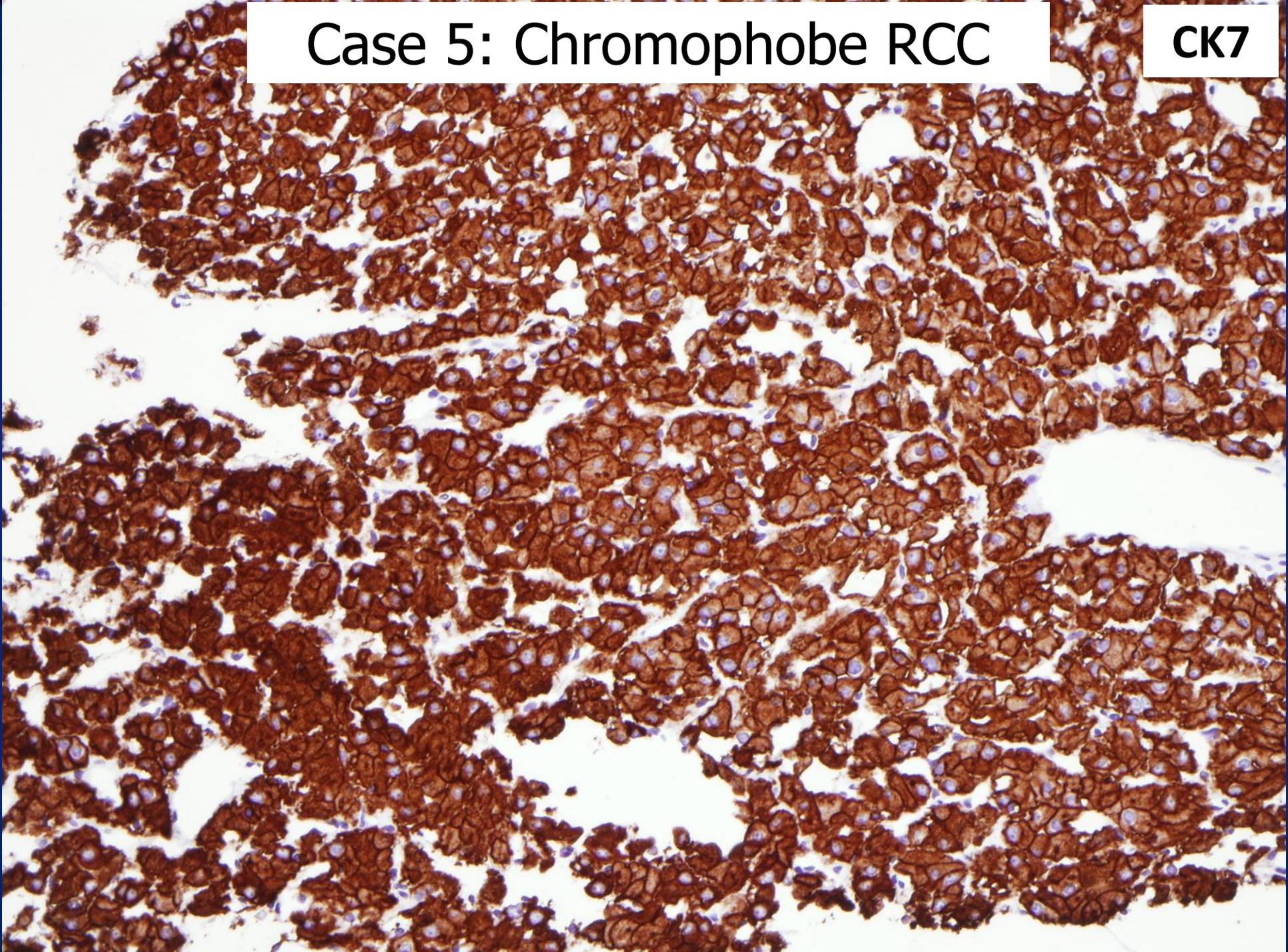


Case 5

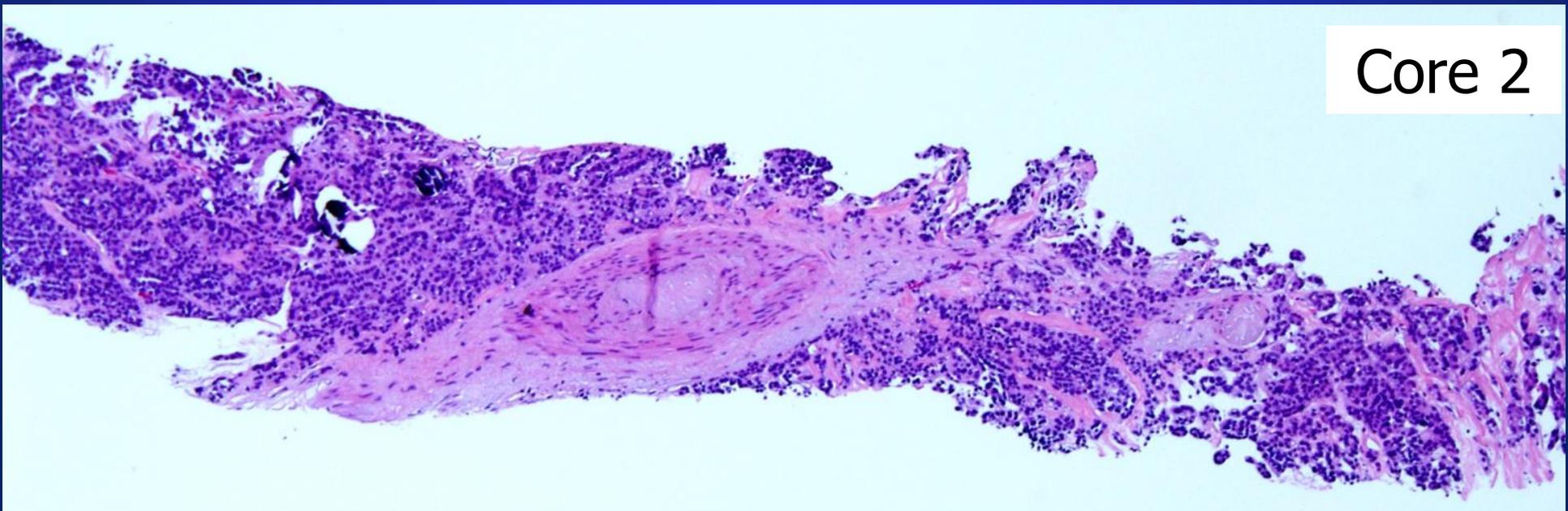
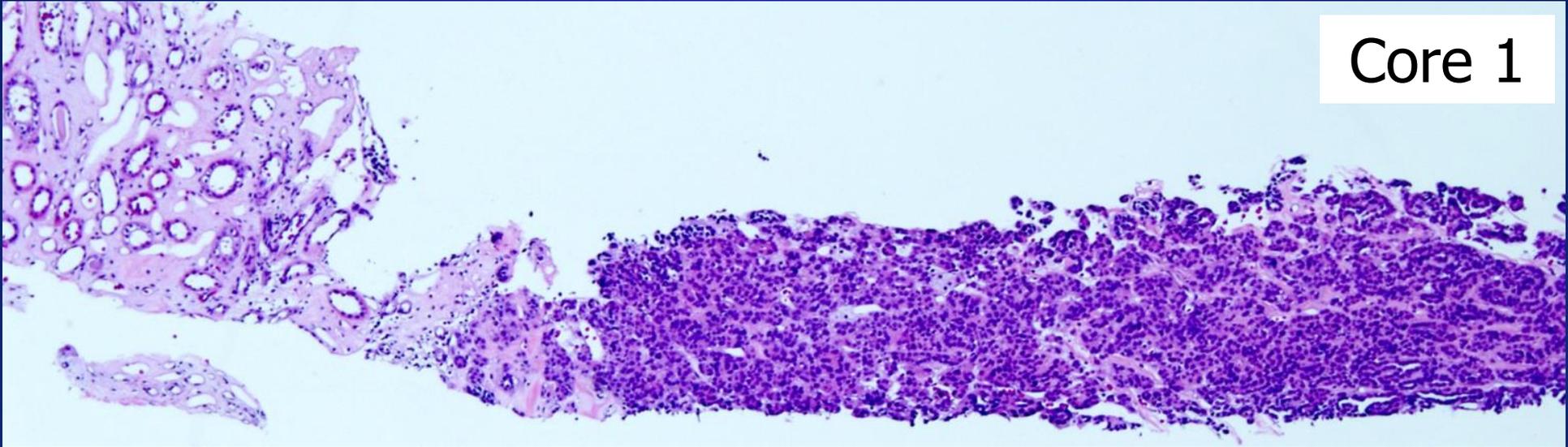


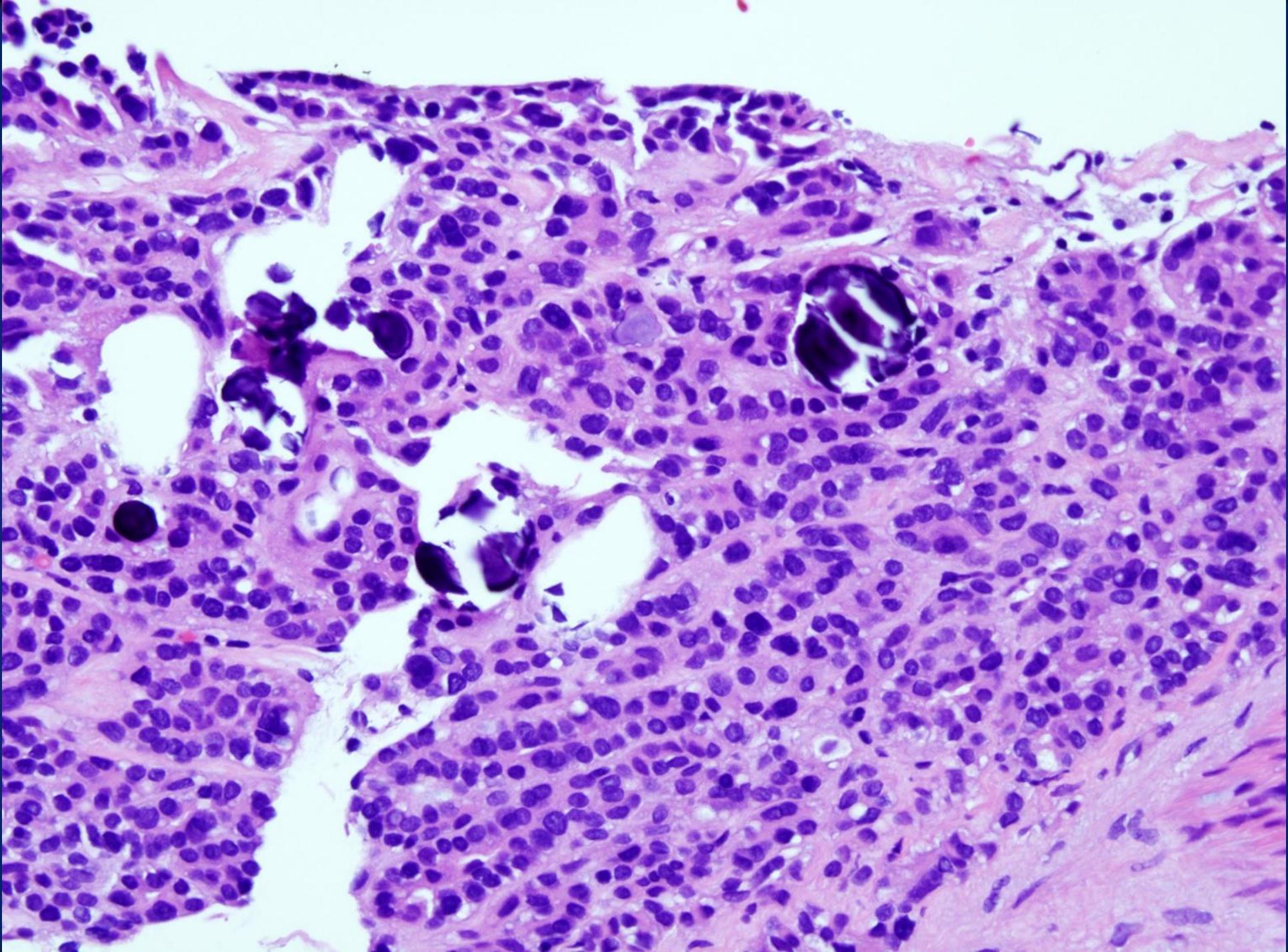
# Case 5: Chromophobe RCC

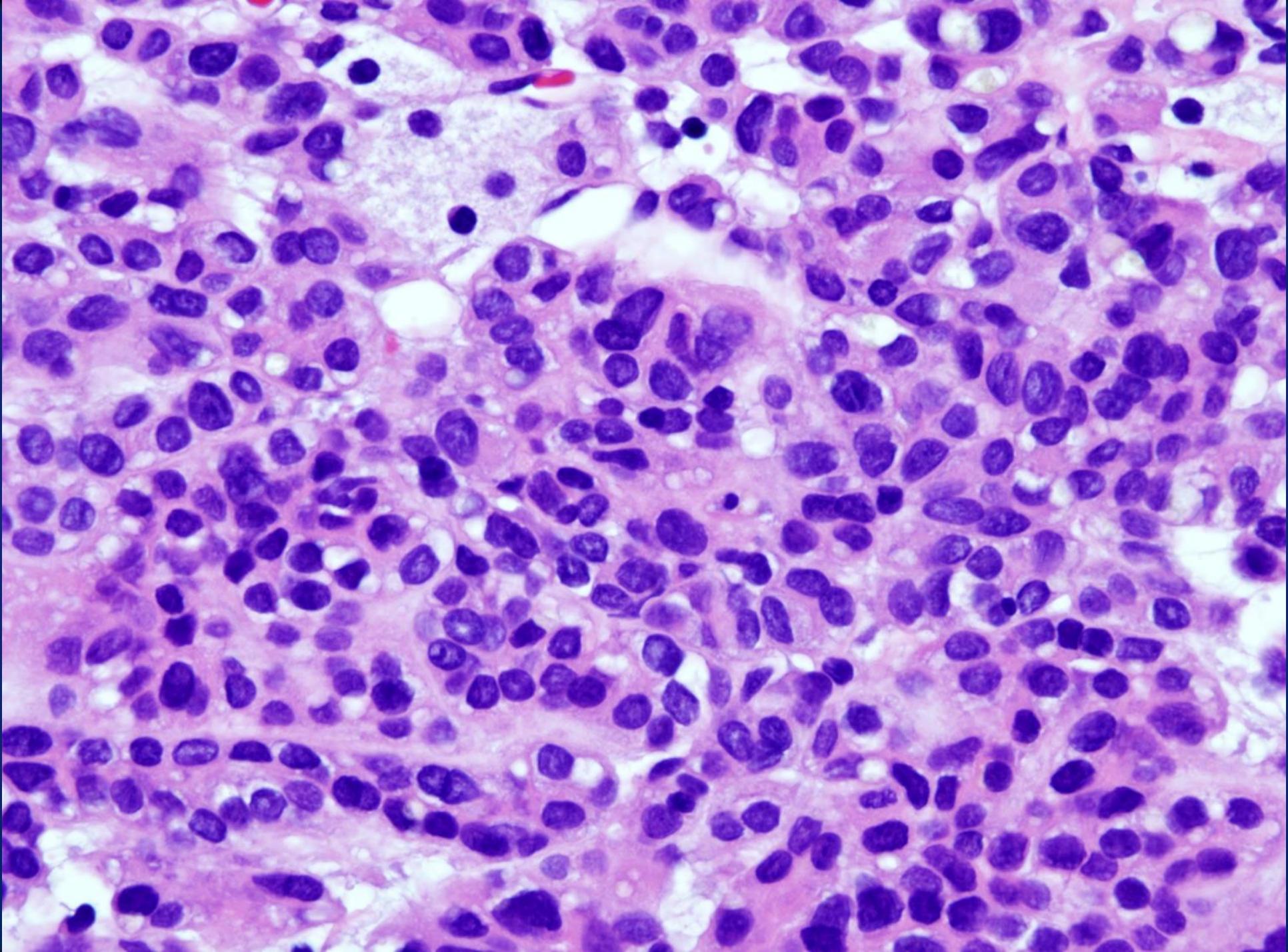
CK7



# Case 6: 52M with 3.5 cm L renal mass

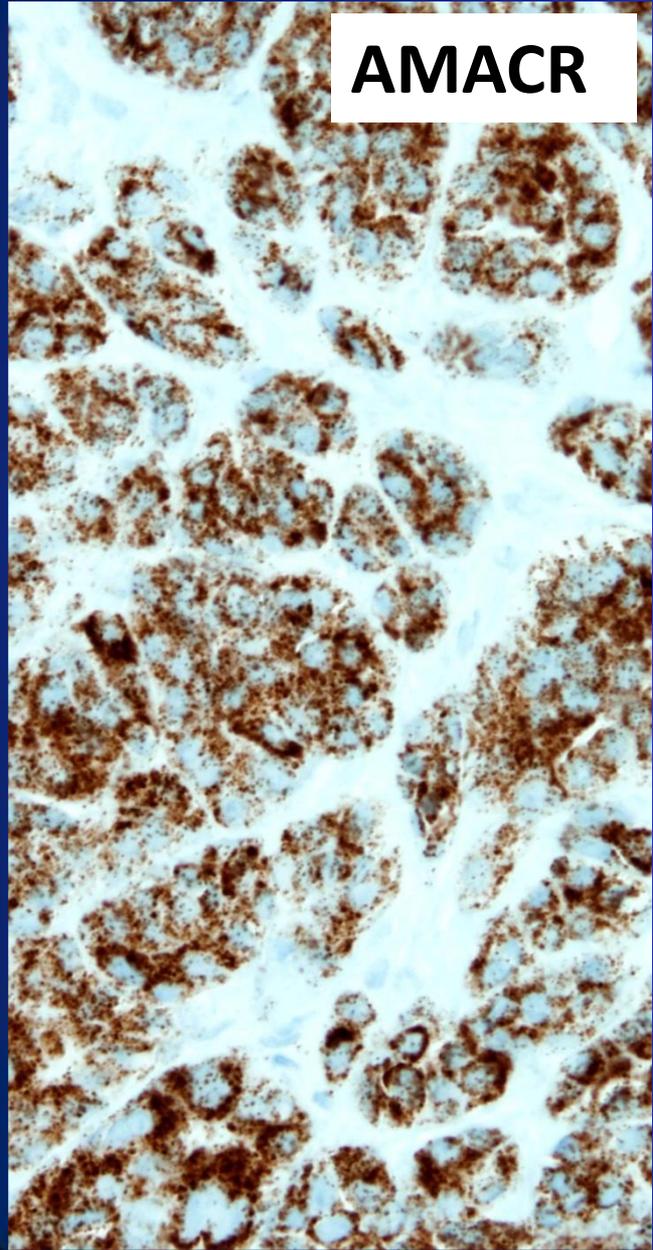




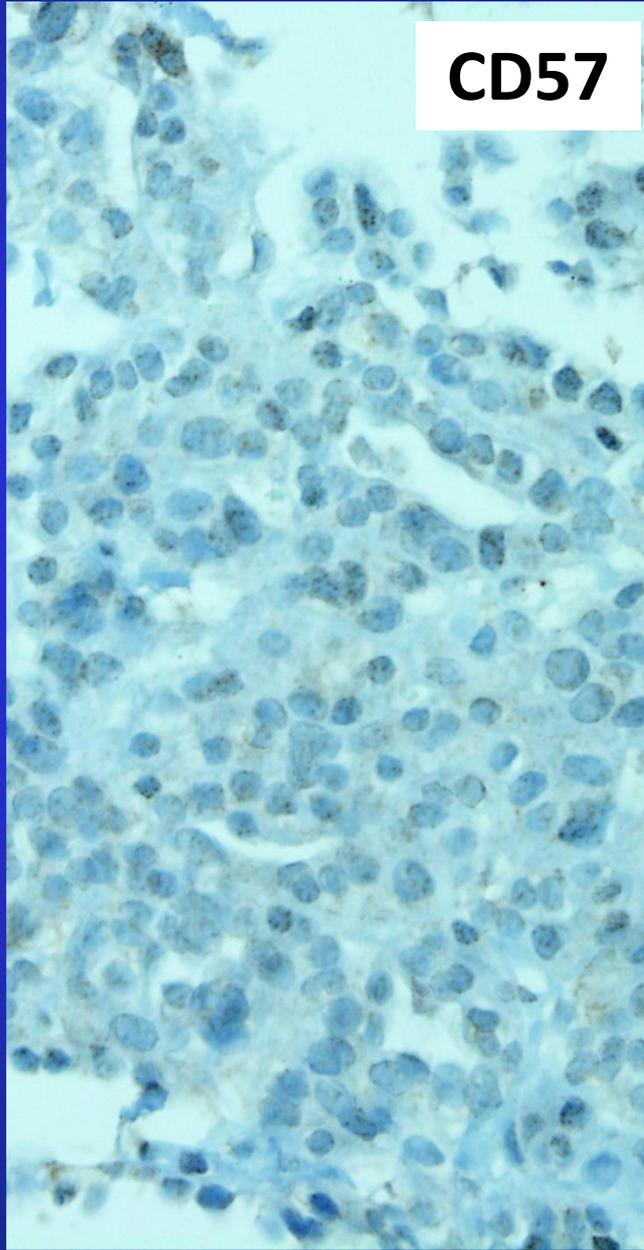


# Case 6: Papillary RCC, type 1

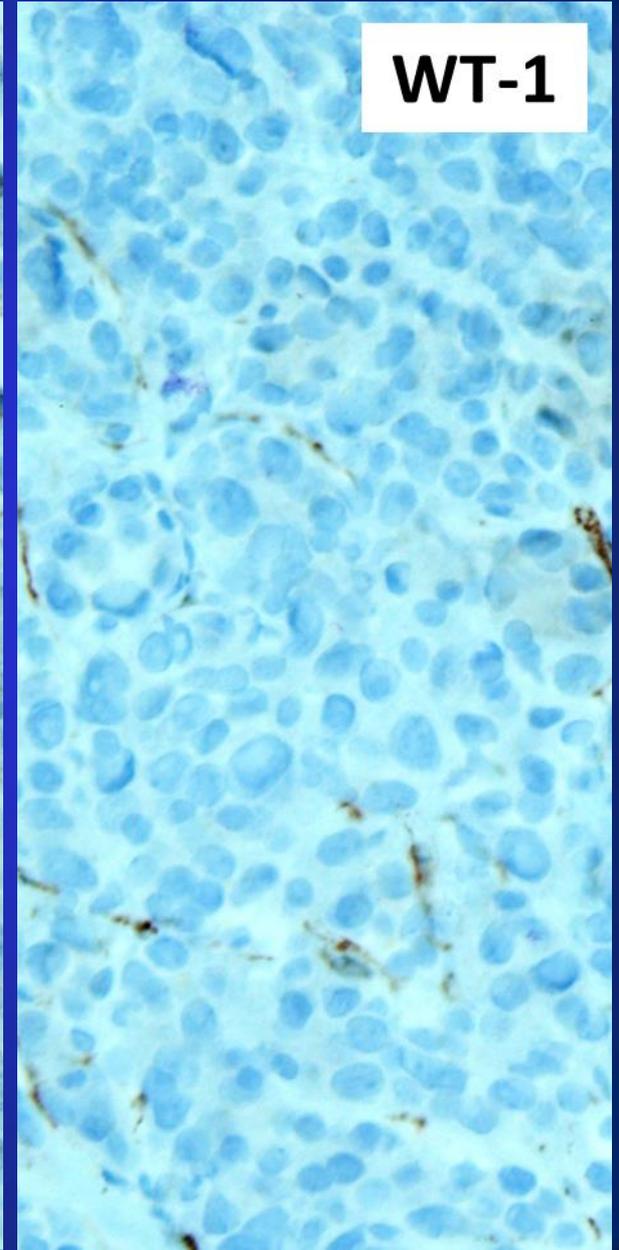
**AMACR**



**CD57**



**WT-1**



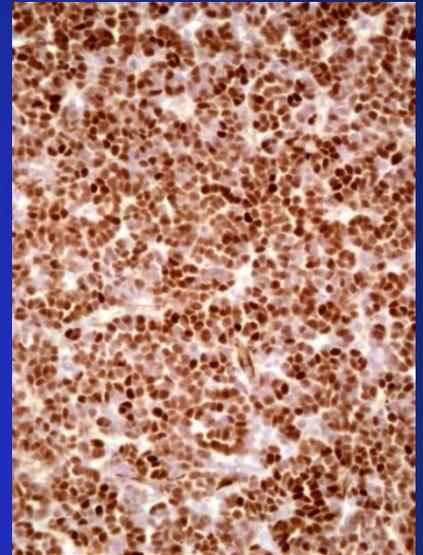
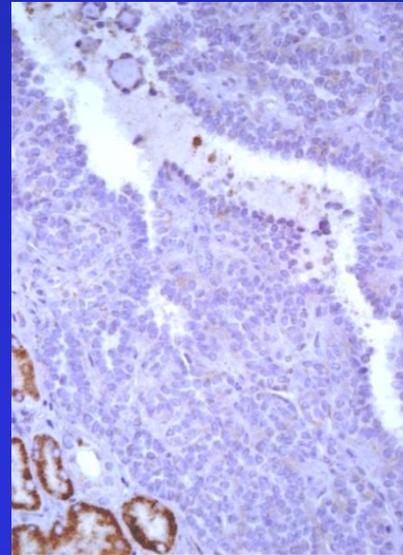
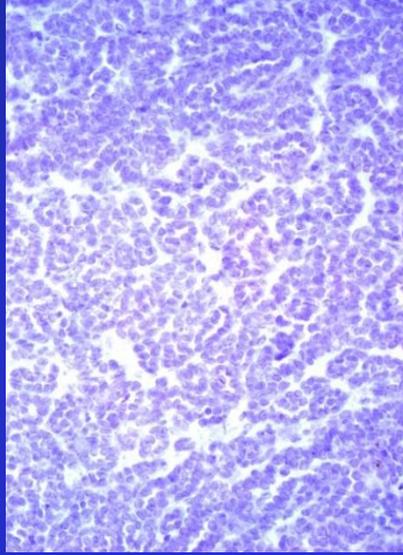
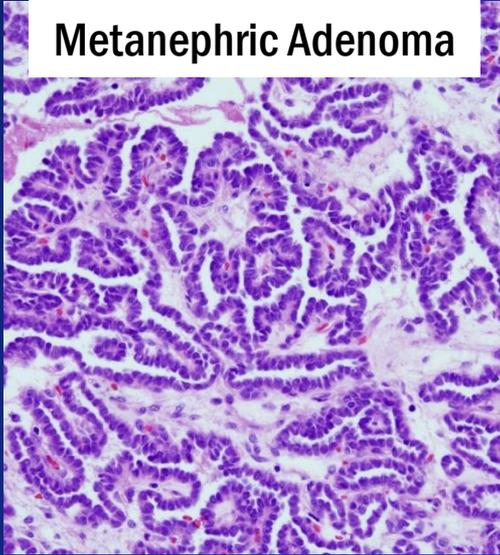
# Metanephric Adenoma vs Papillary RCC

RCCm

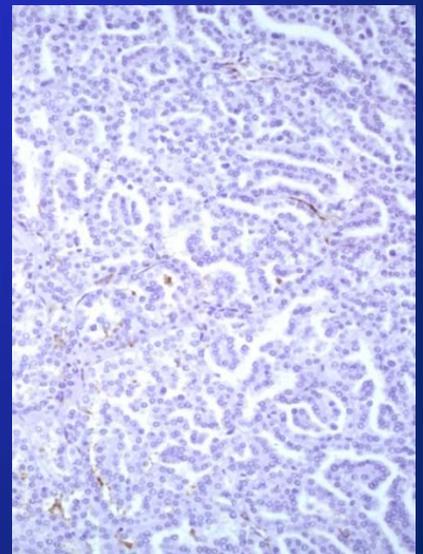
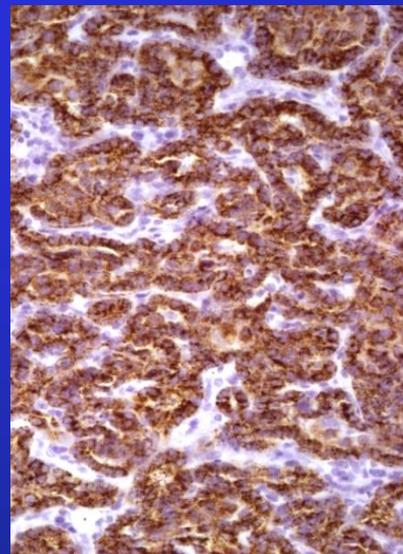
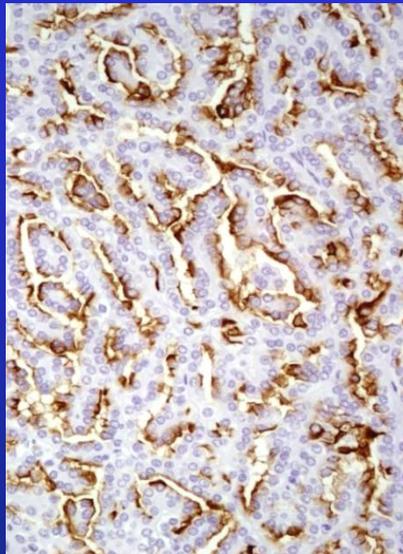
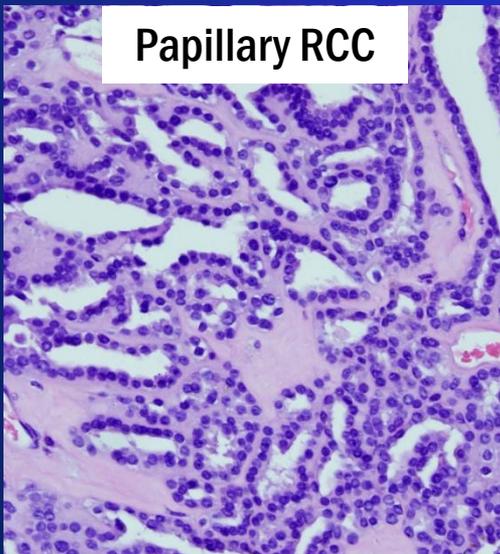
AMACR

WT-1

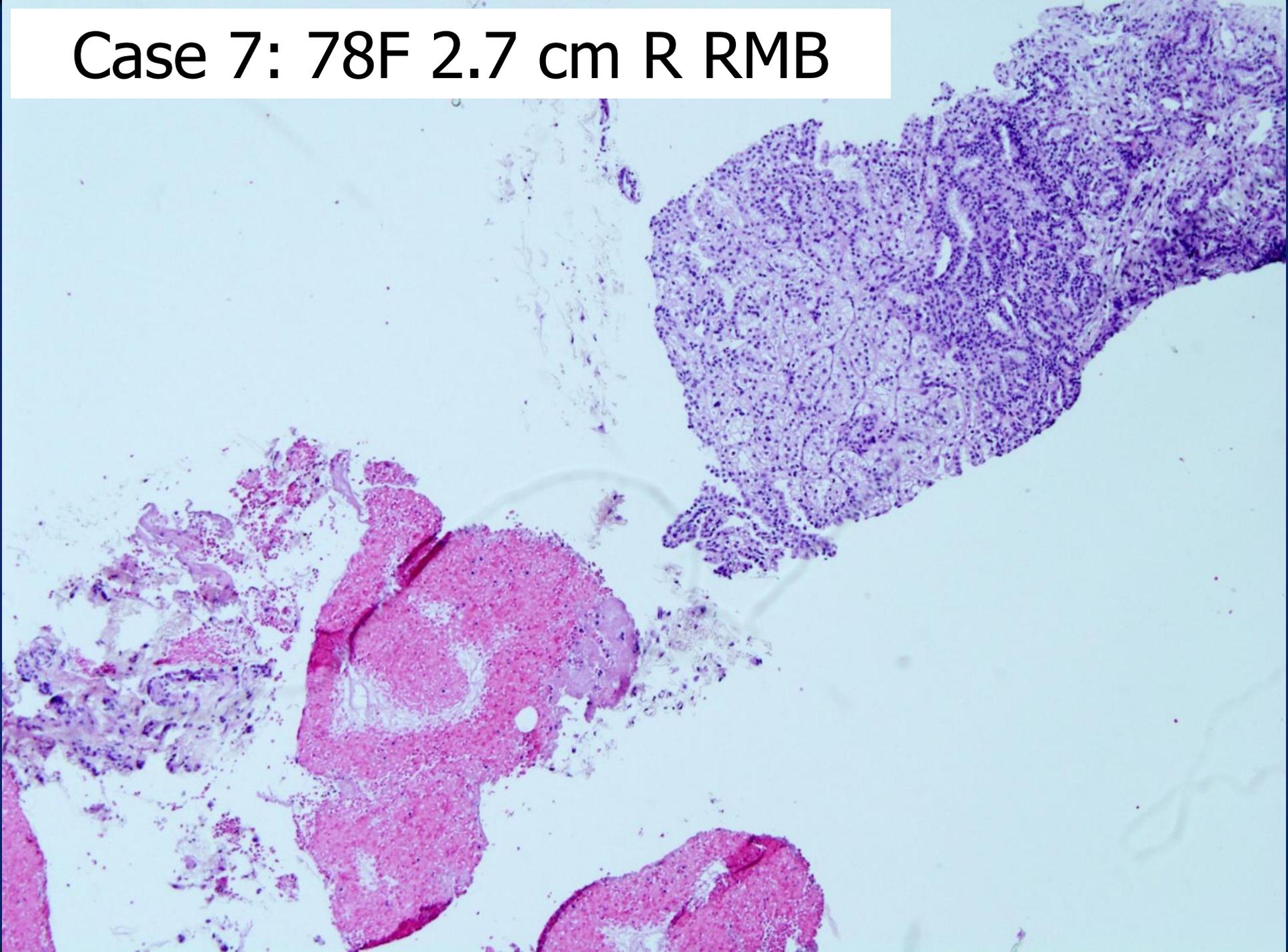
Metanephric Adenoma

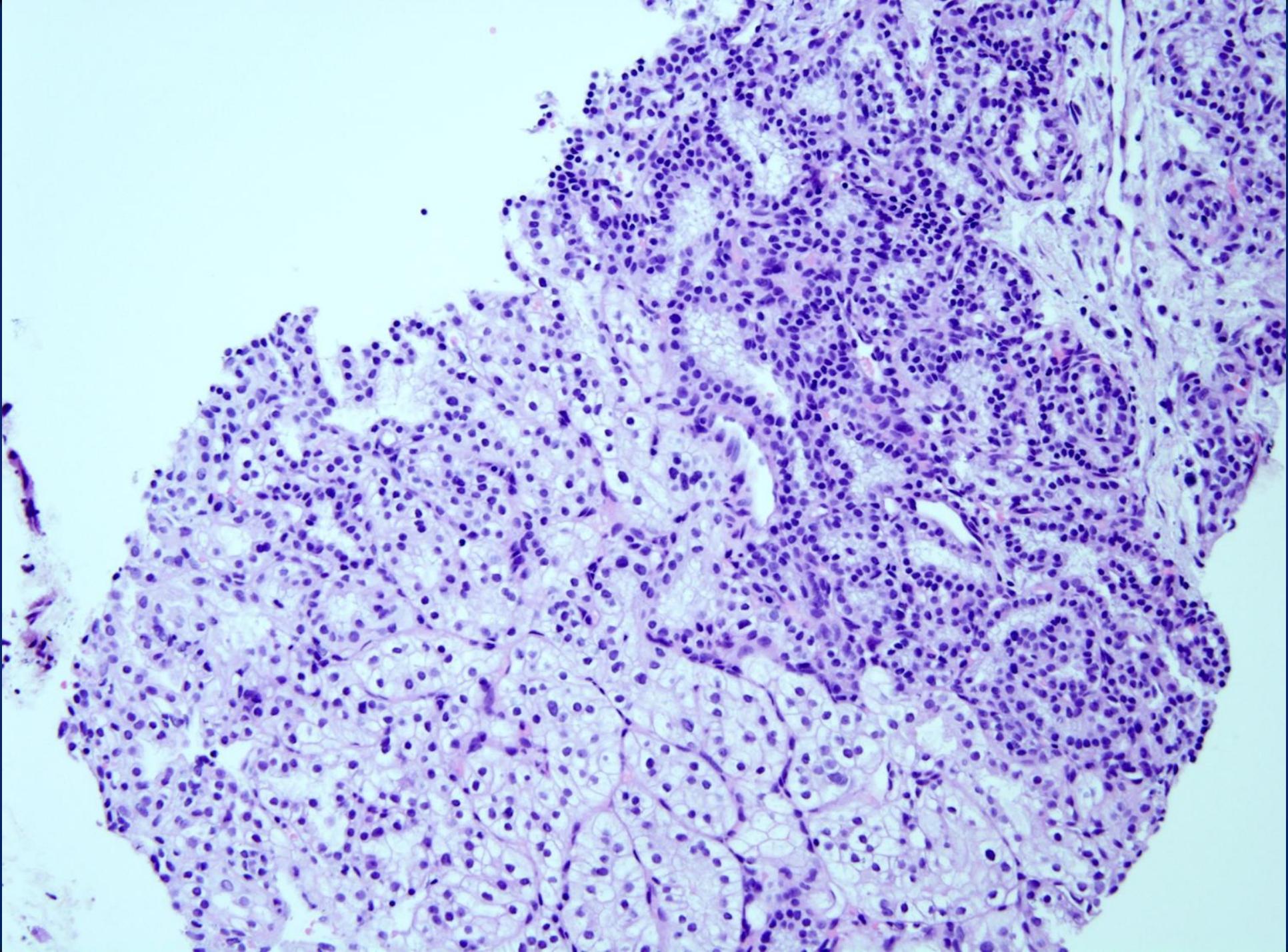


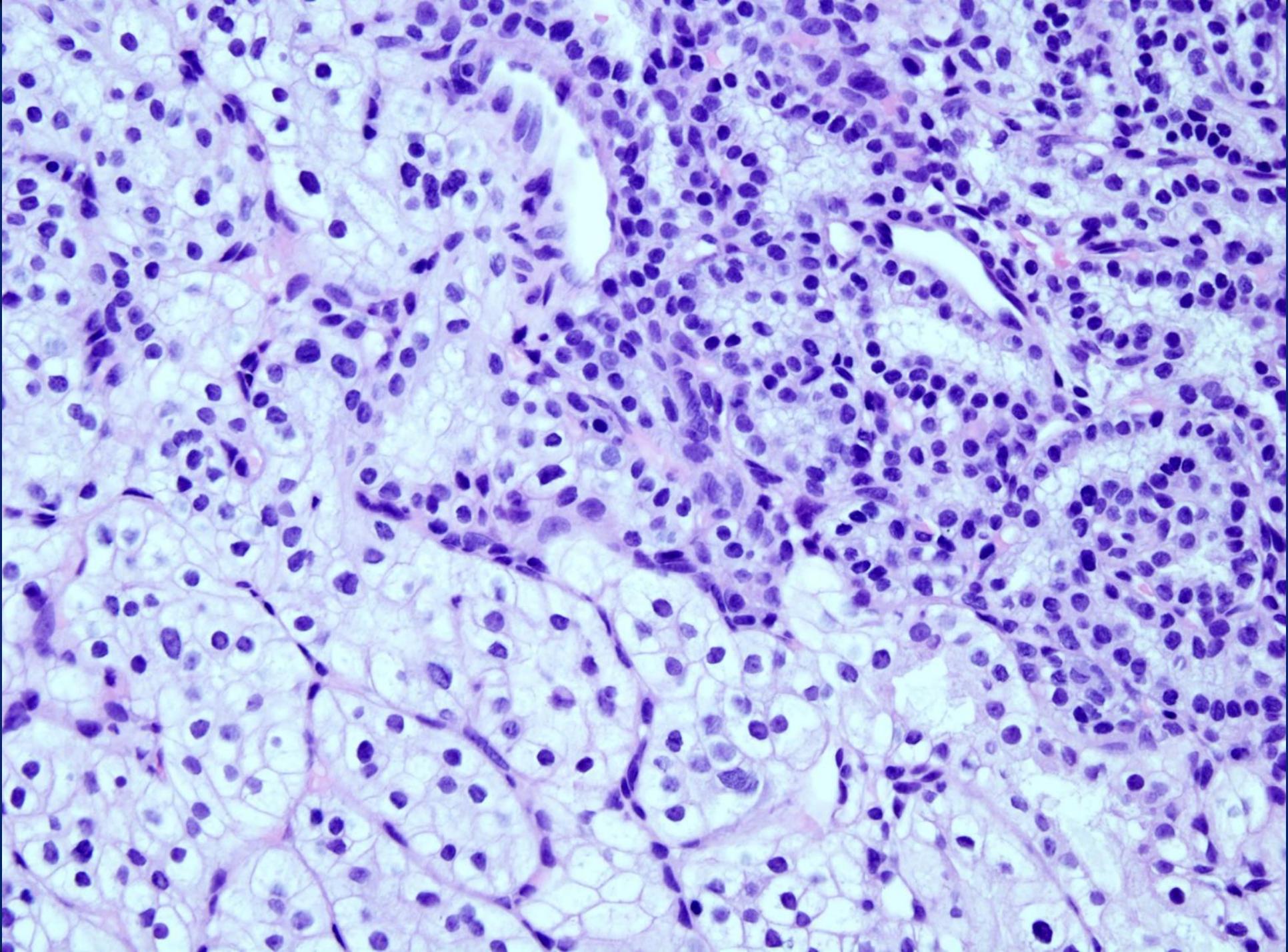
Papillary RCC



Case 7: 78F 2.7 cm R RMB

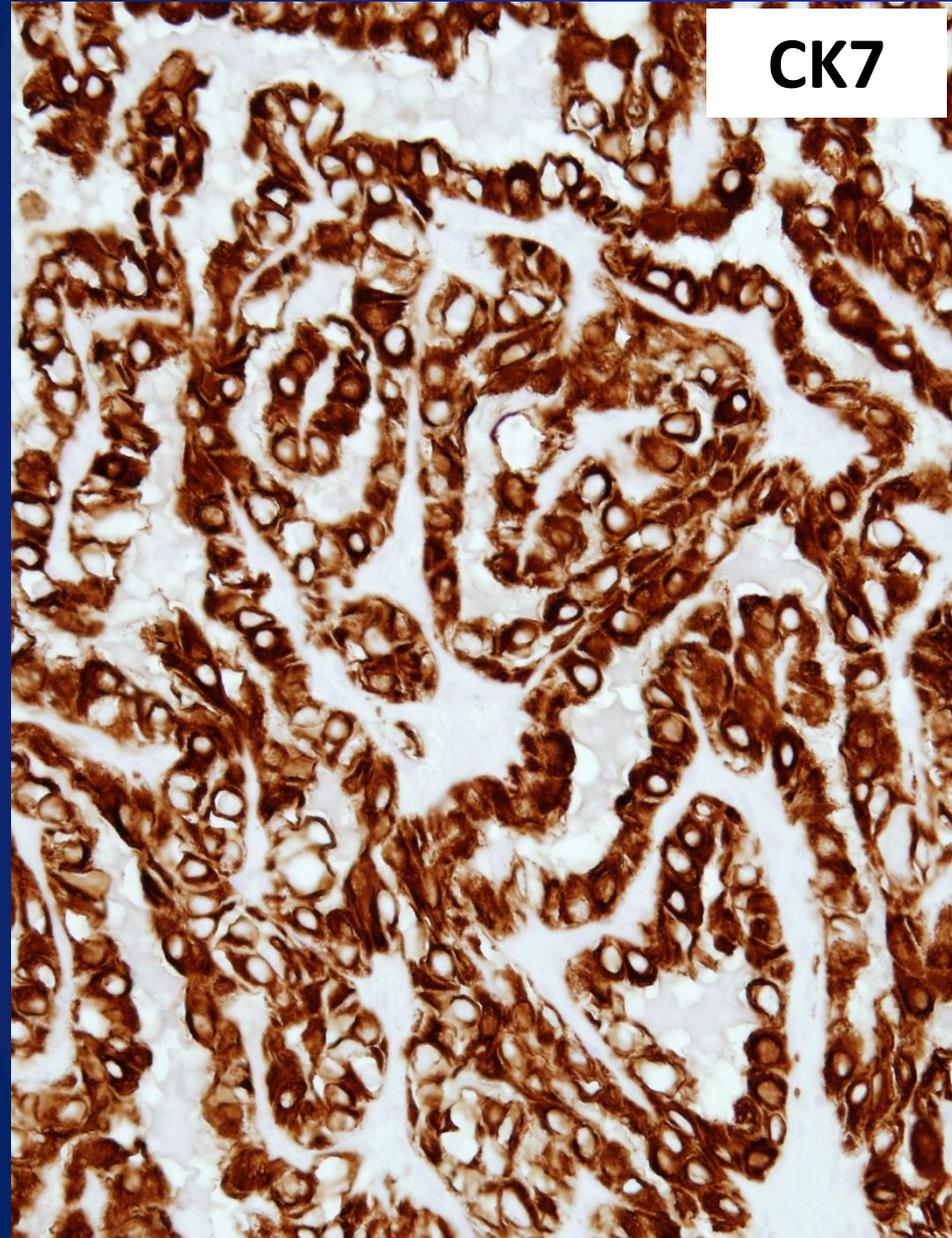




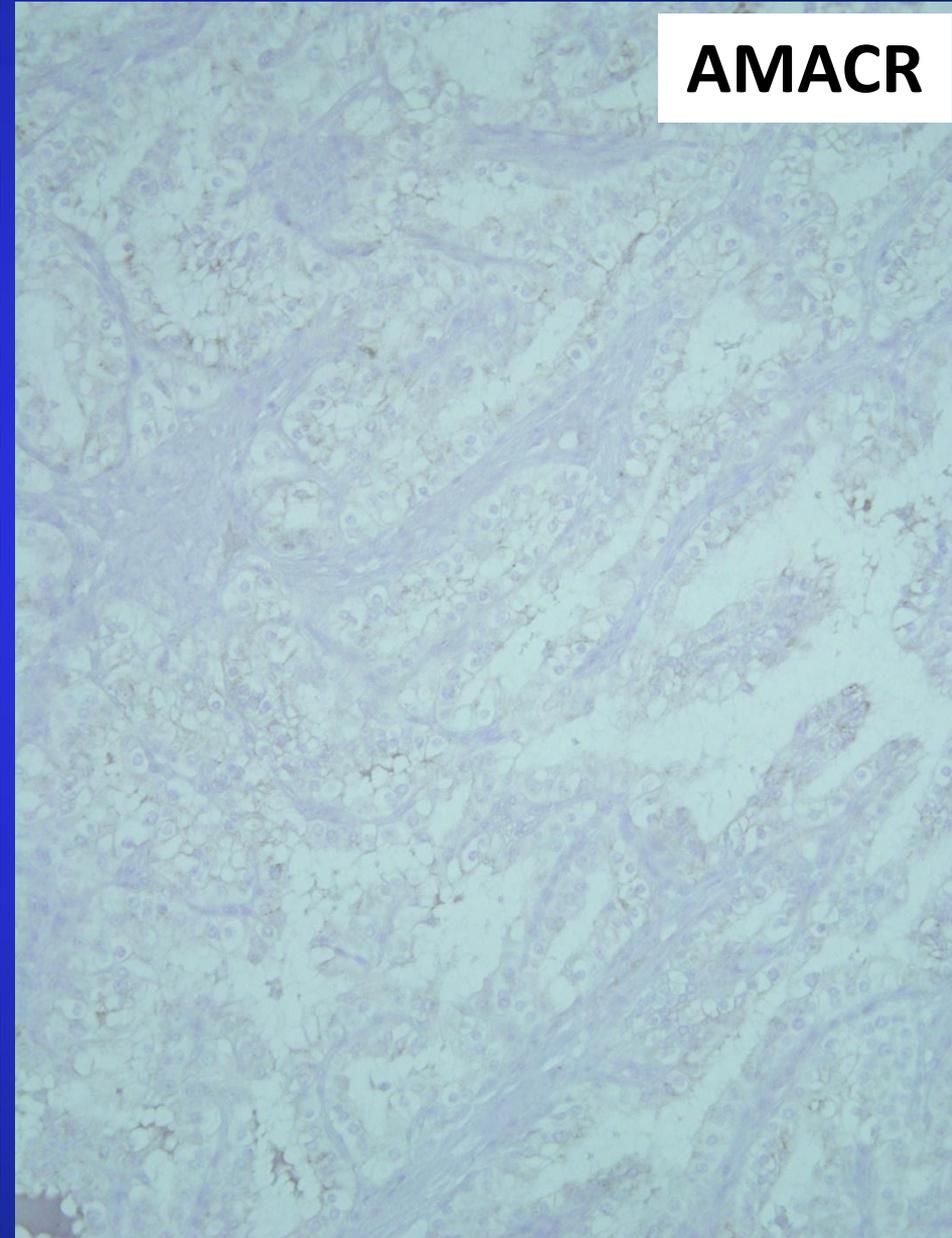


# Case 7: Clear cell papillary RCC

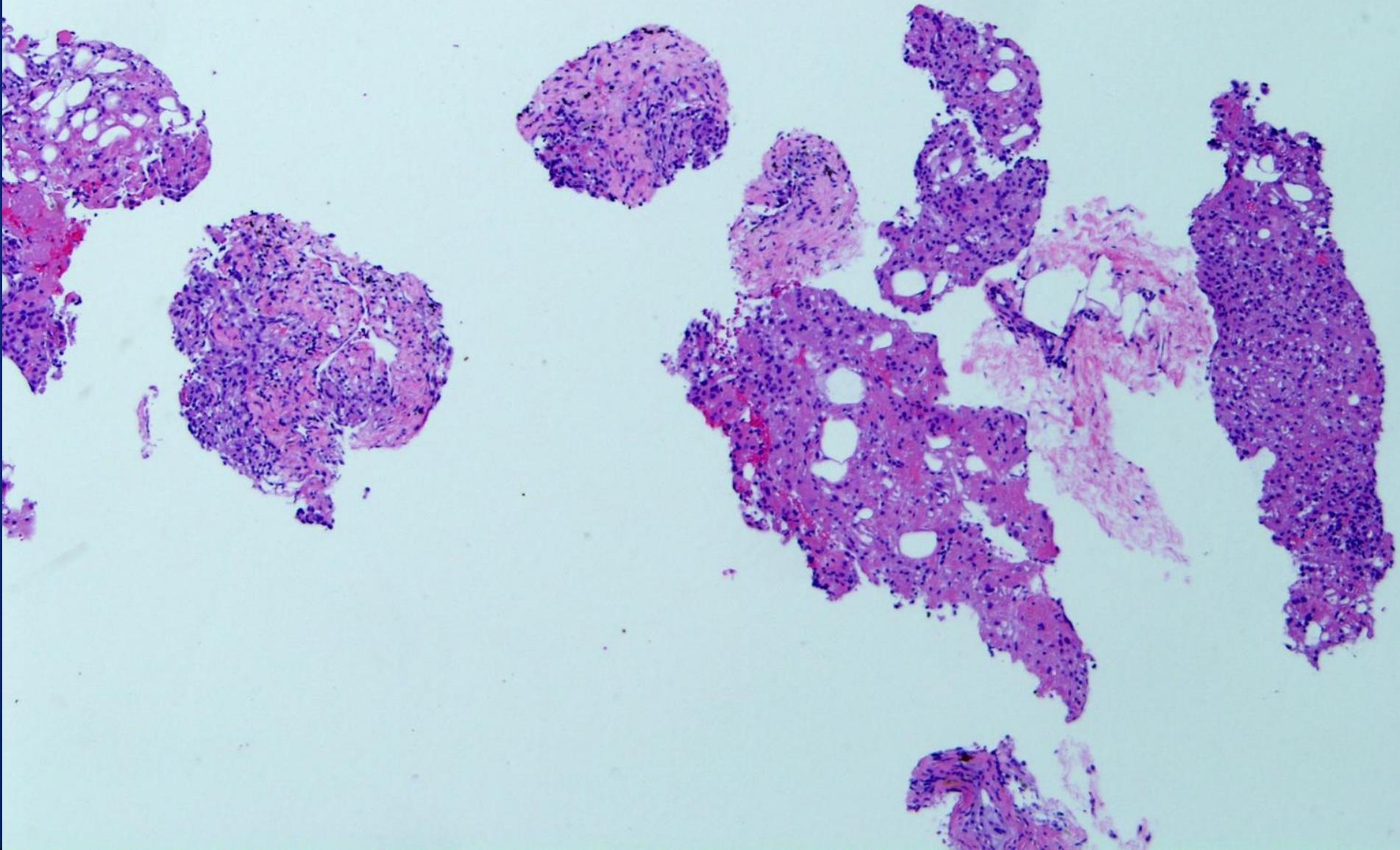
**CK7**

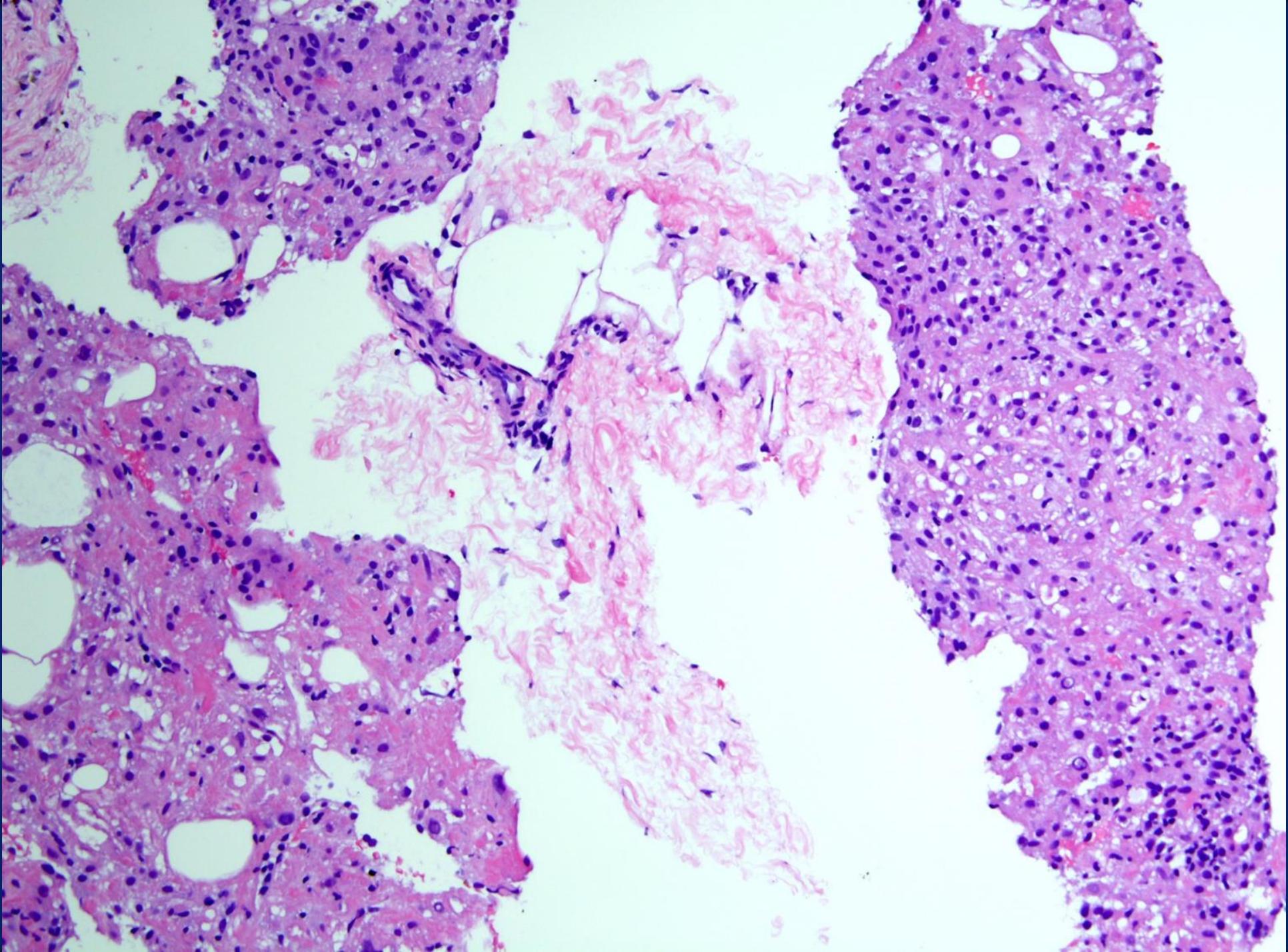


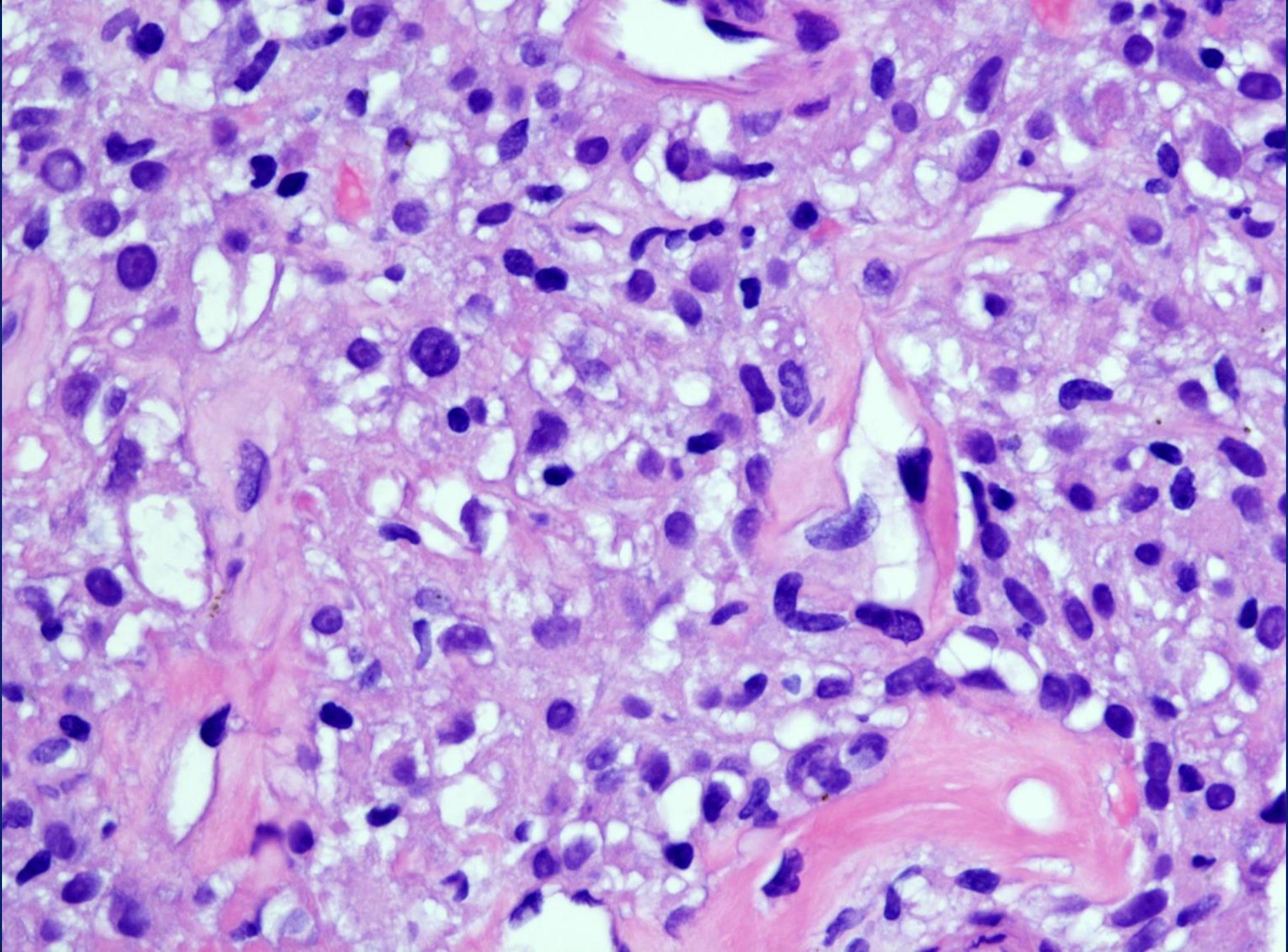
**AMACR**



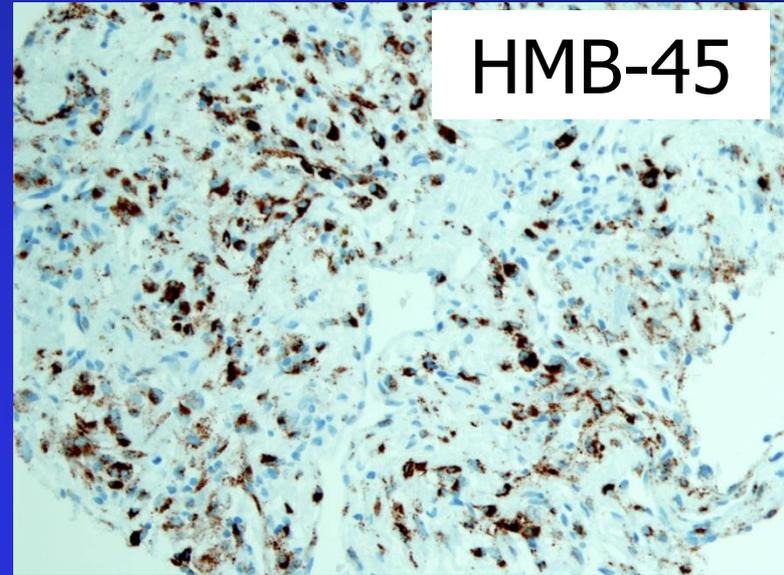
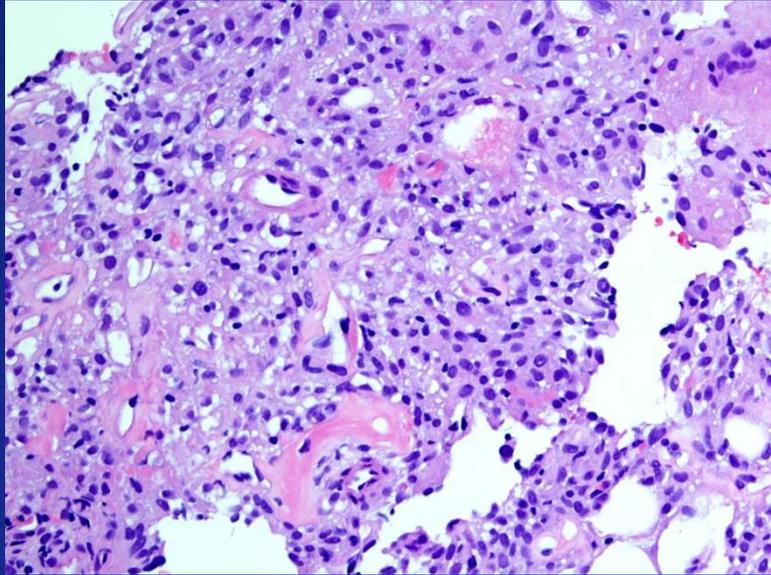
# Case 8: 48F 6.5 cm left renal mass



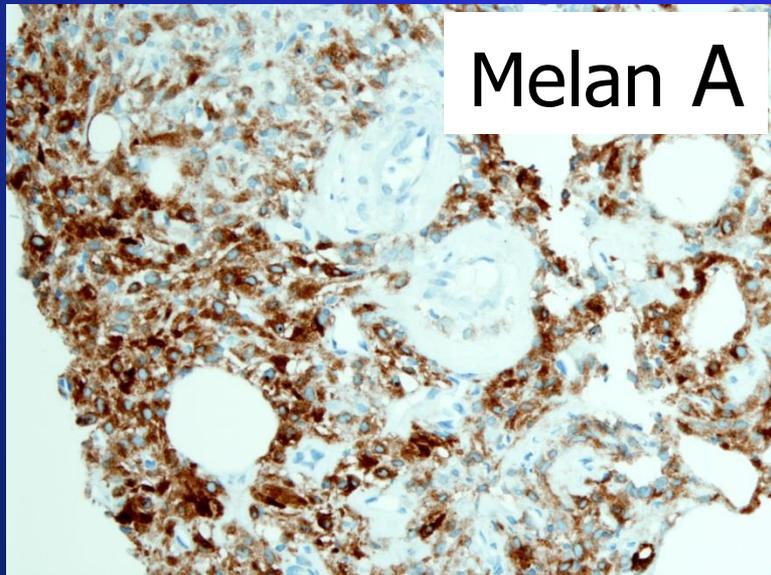




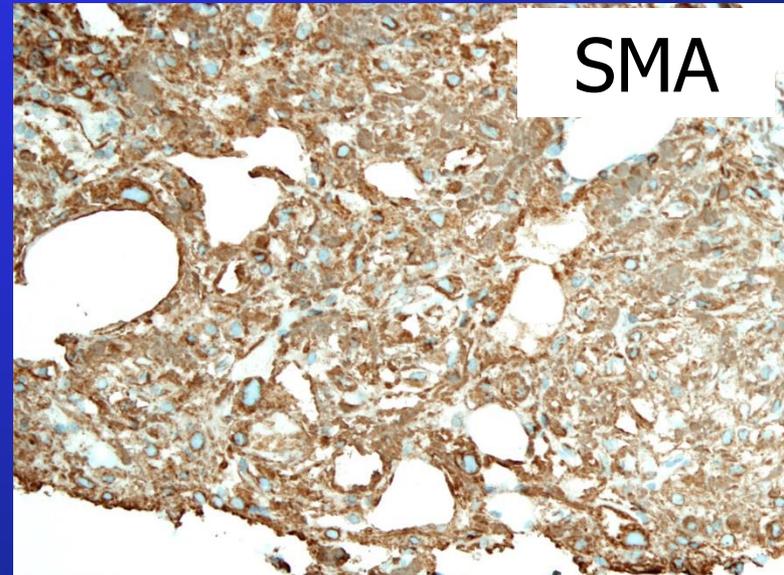
# Case 8: Angiomyolipoma



HMB-45

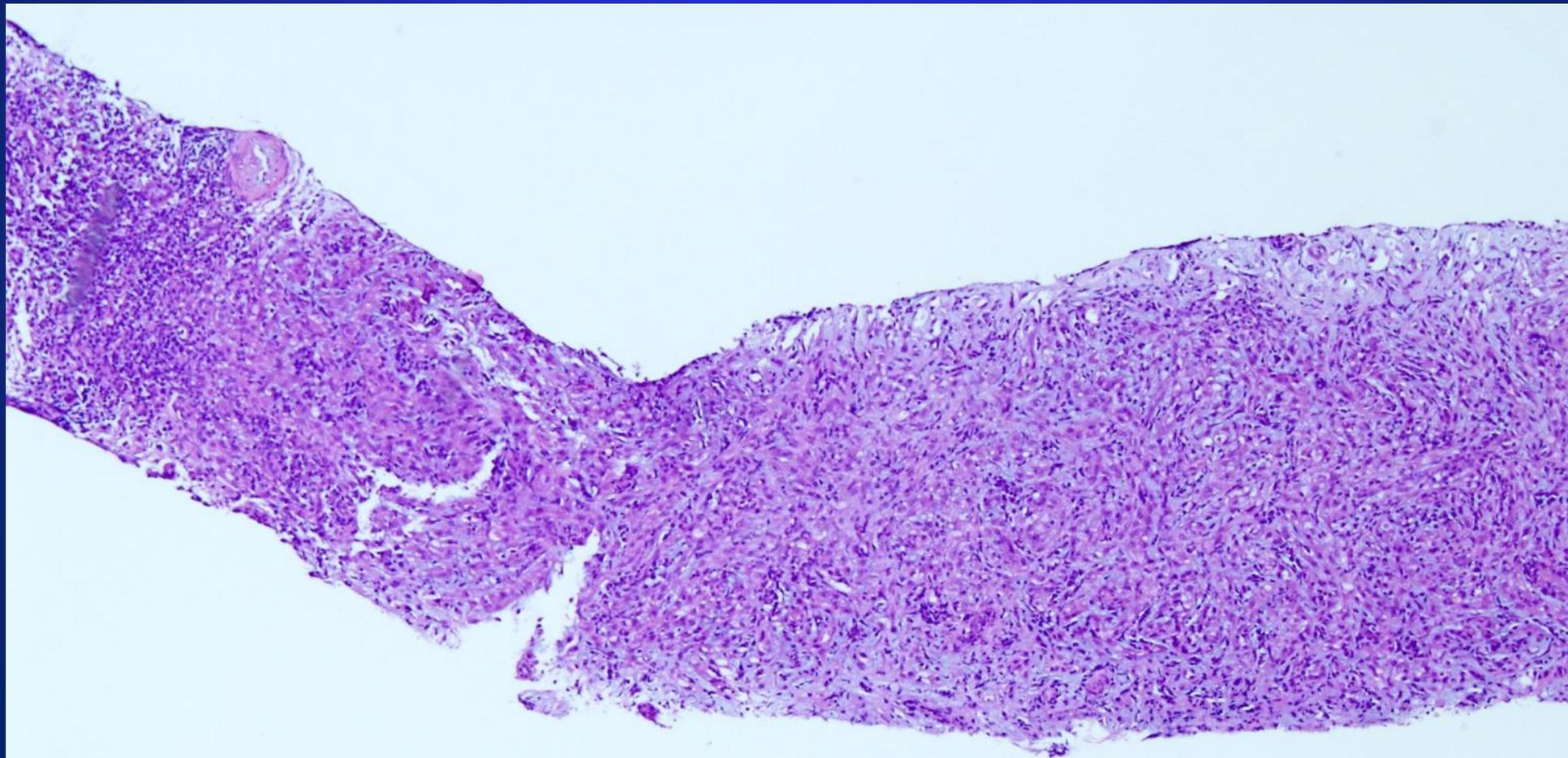


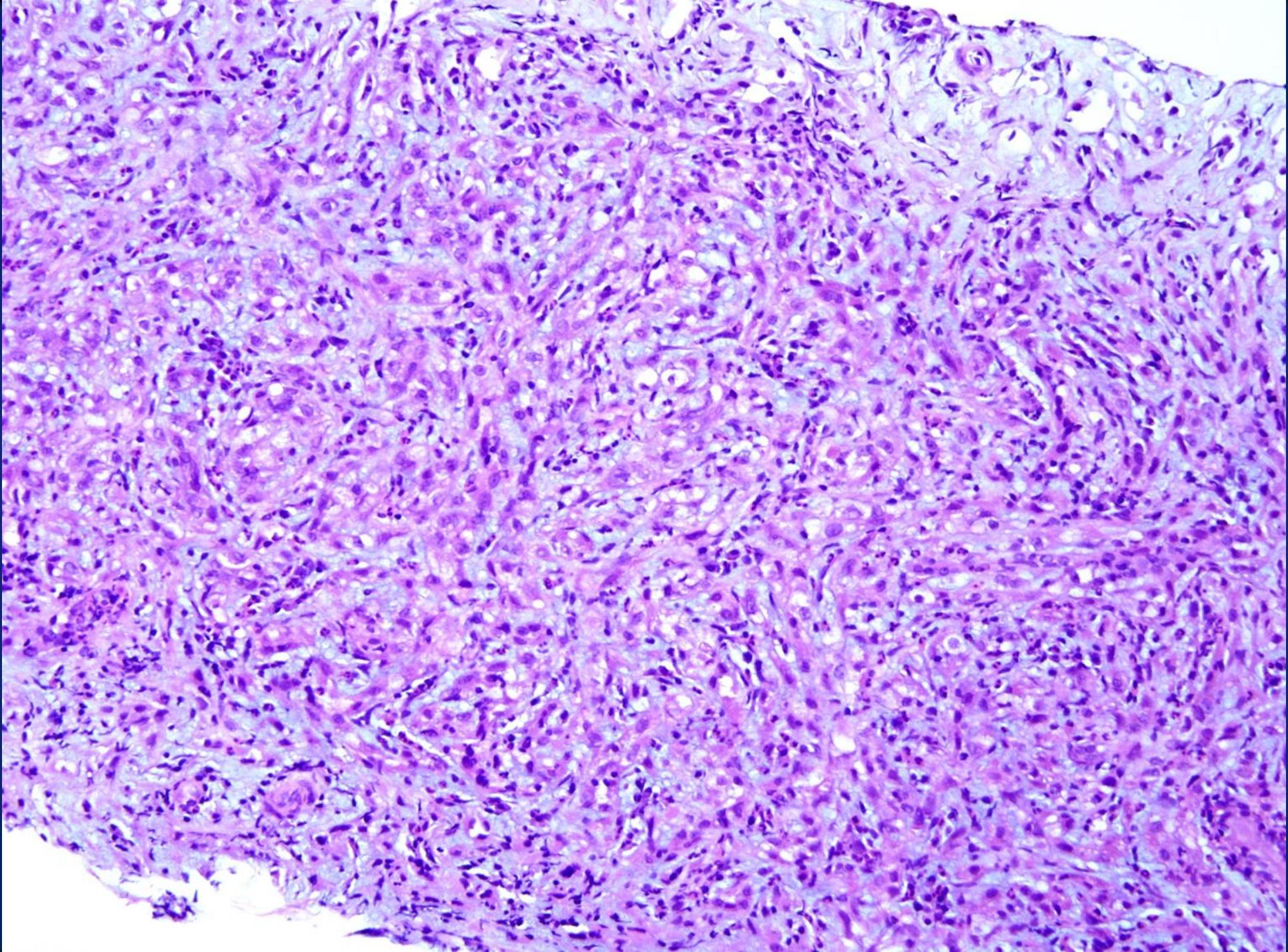
Melan A

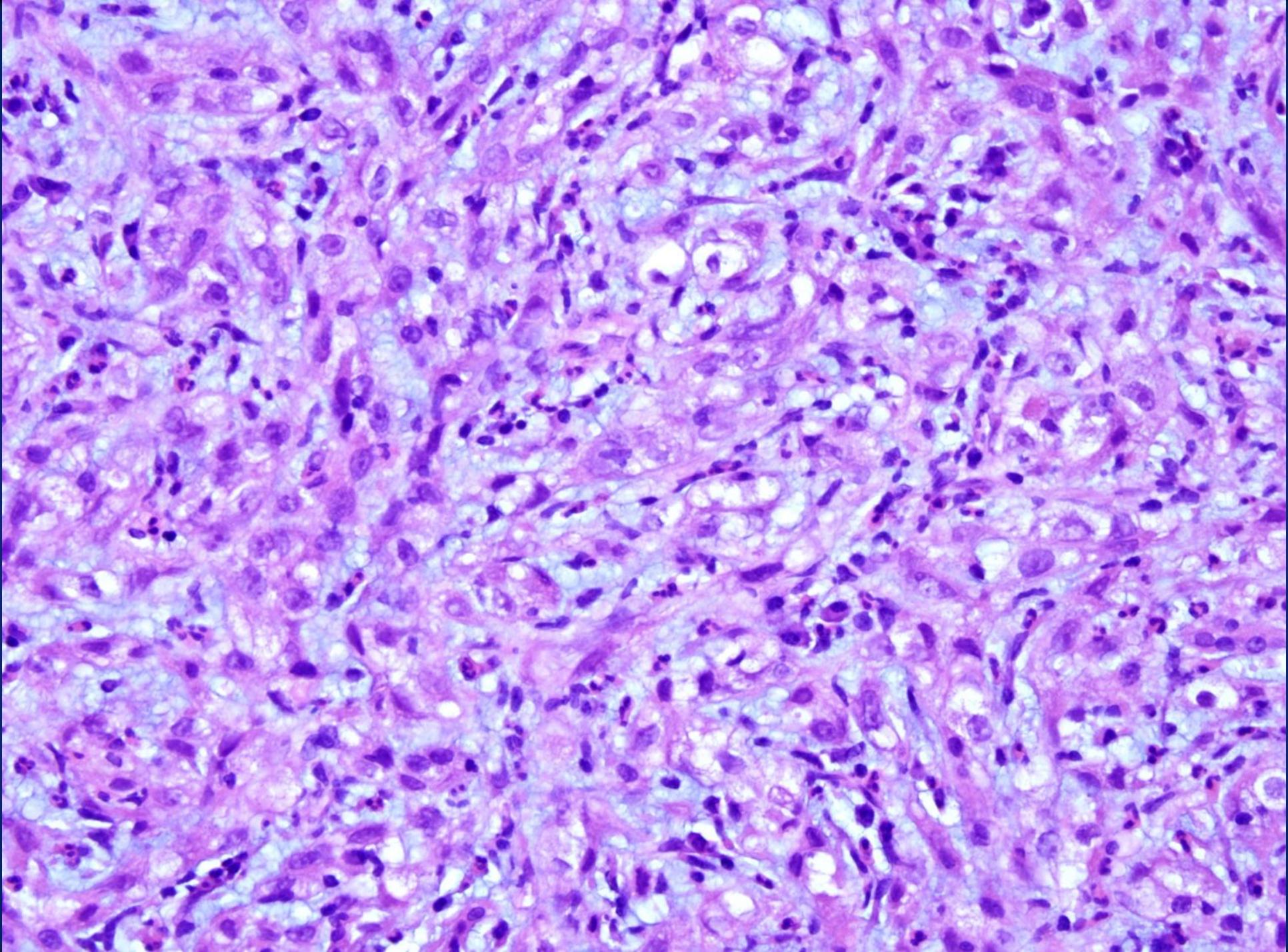


SMA

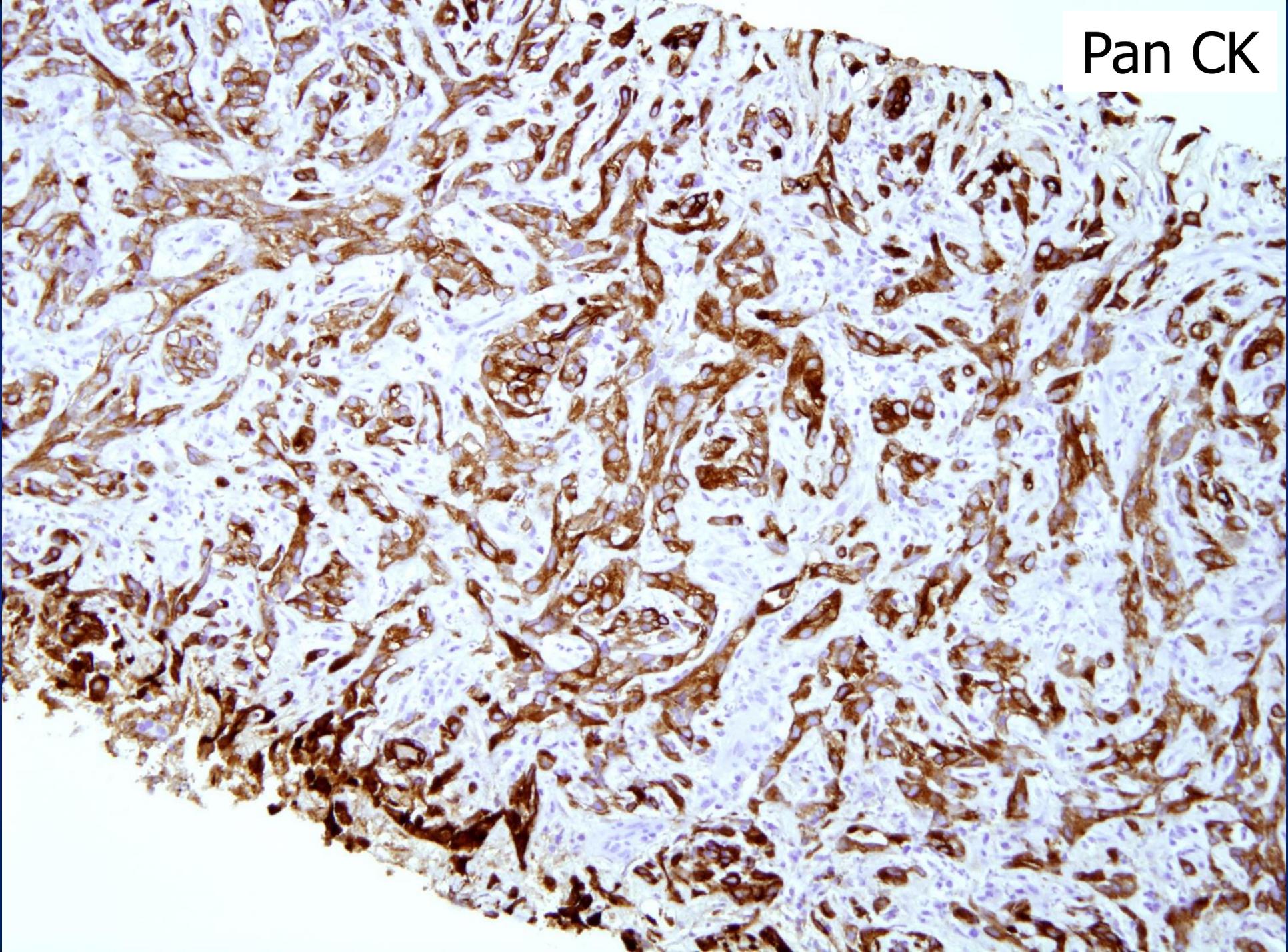
Case 9: 69 F with 6.5 cm right renal mass





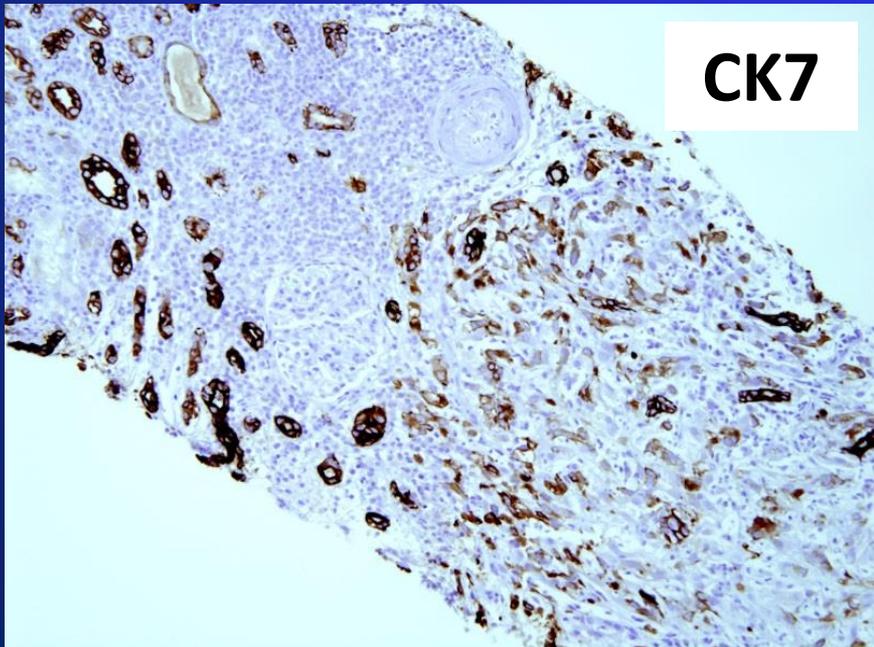
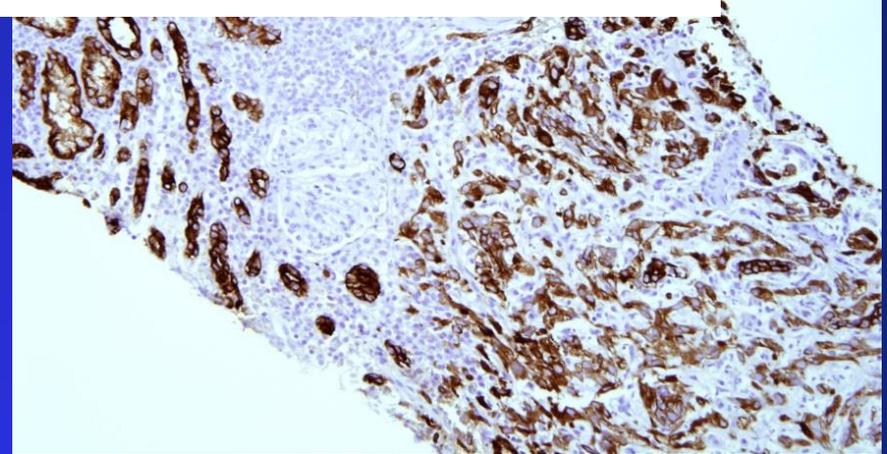
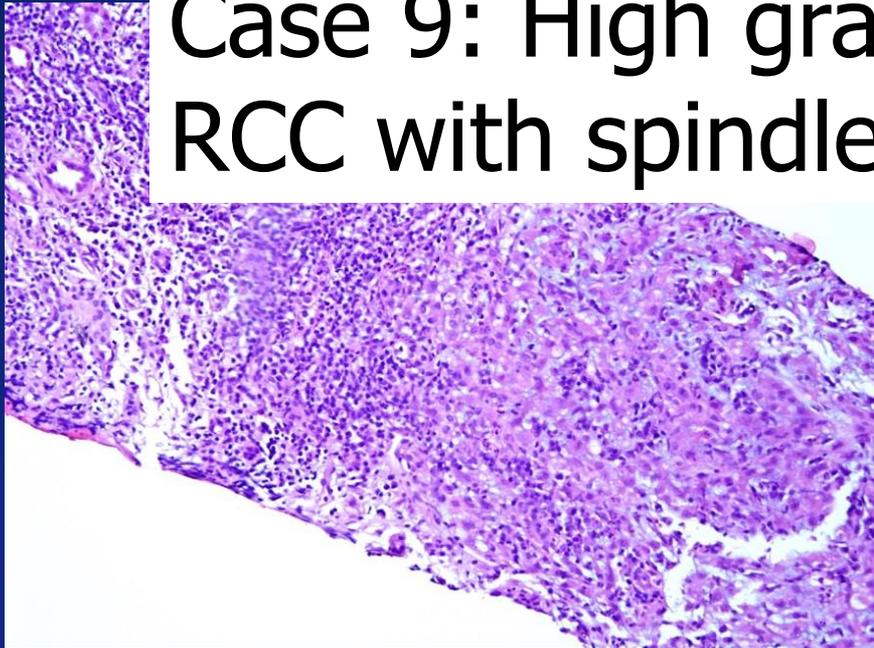


Pan CK

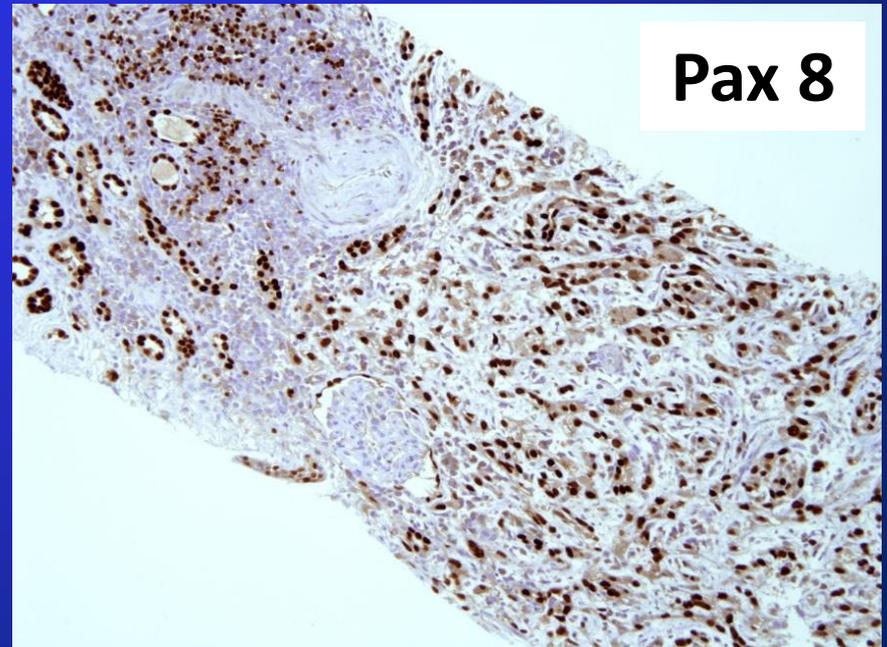


# Case 9: High grade unclassified RCC with spindle cells

CK



CK7

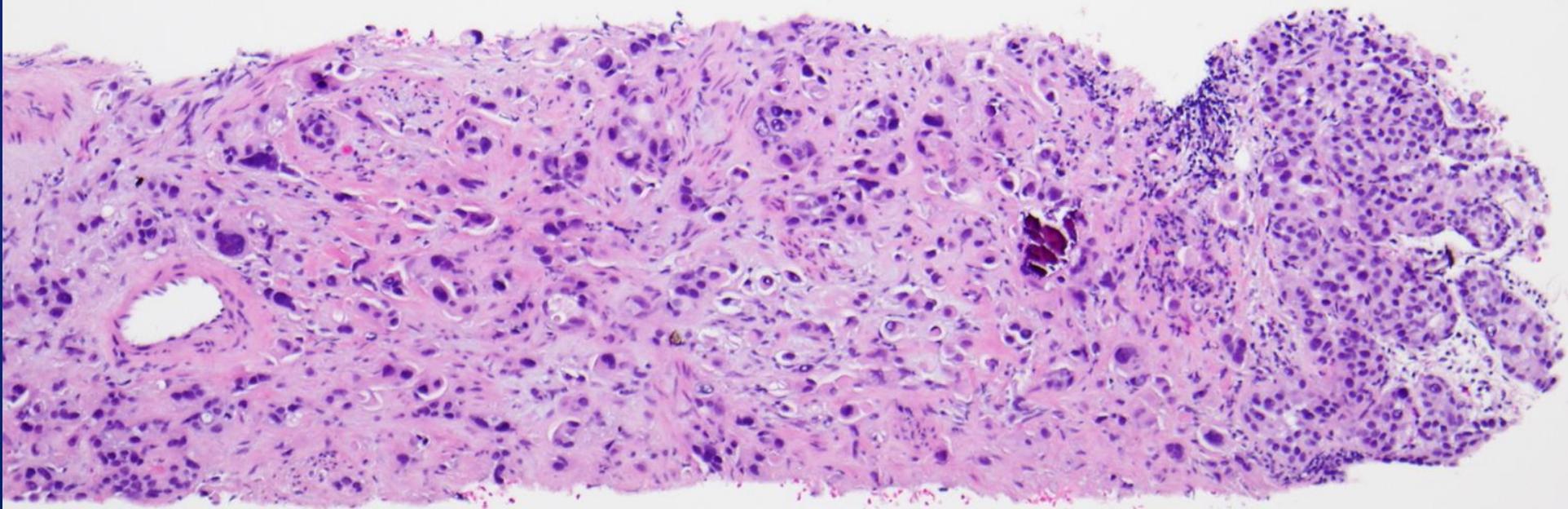


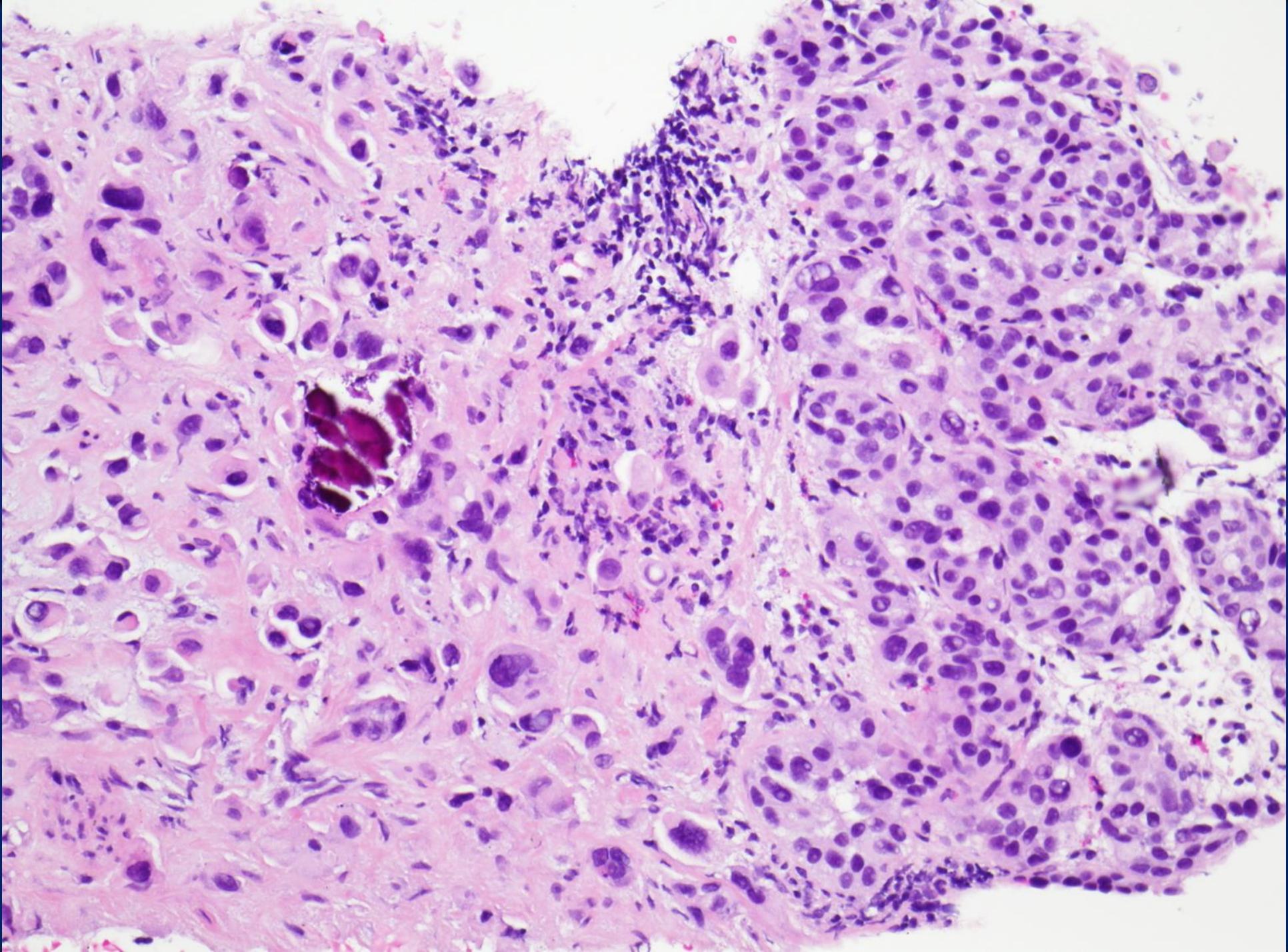
Pax 8

# Radical Nephrectomy

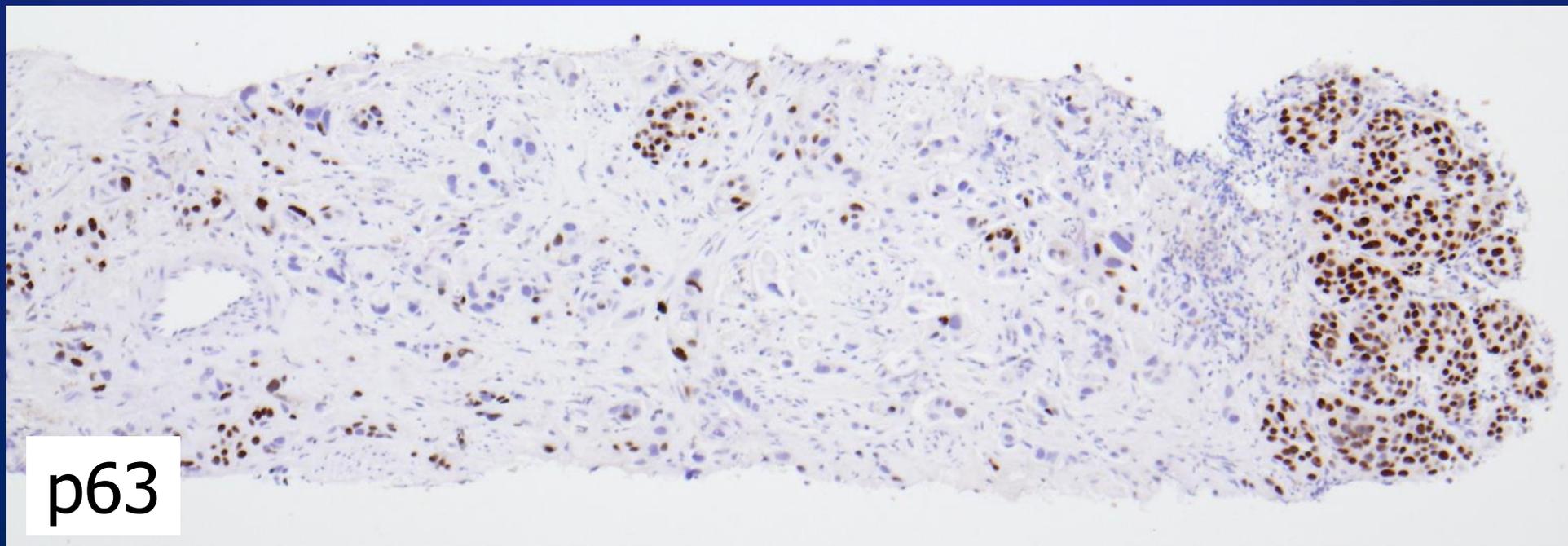
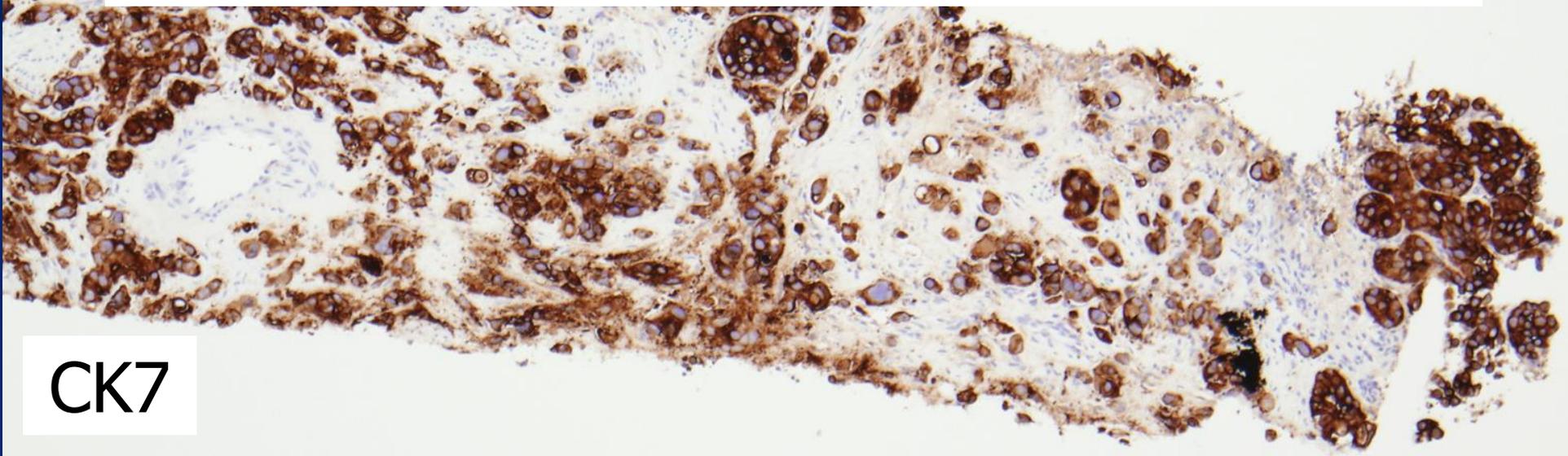
- **Negative: RCCm, AMACR**
- **Positive (focal): CK7, Vim, CD10**
- **Clear cell RCC with sarcomatoid changes**
- **T3aN1 (5/25)**

# Case 10





# Case 10: Invasive urothelial carcinoma



# Summary – Renal Mass Biopsy

- Obtain adequate material
- Get familiar with renal tumor entities
- Adopt a pattern-based histologic evaluation and diagnostic approach
- Use IHC in selective situations
- Acknowledge the limitation

**Thank you!**

