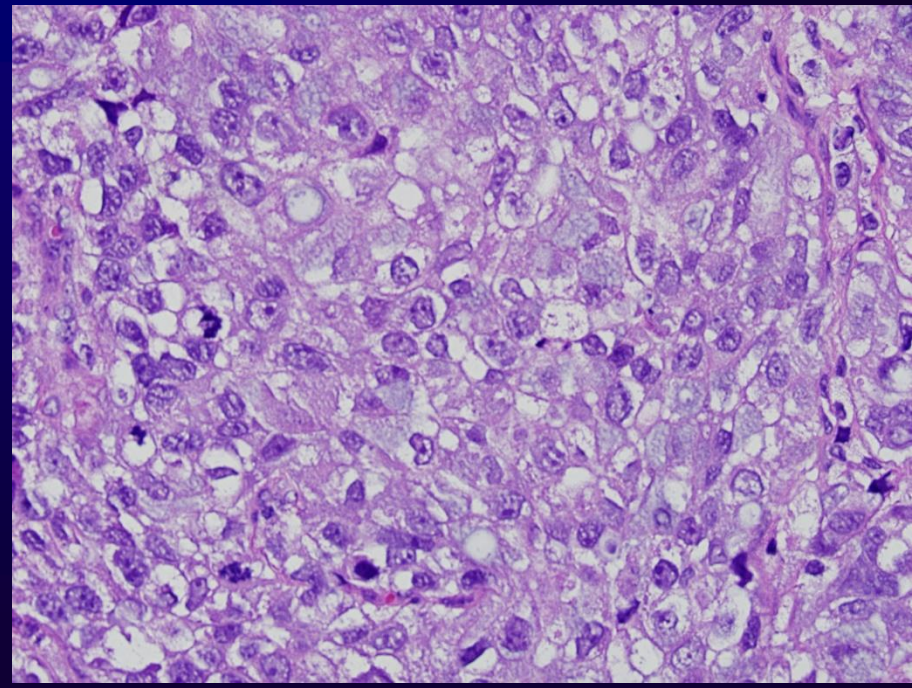
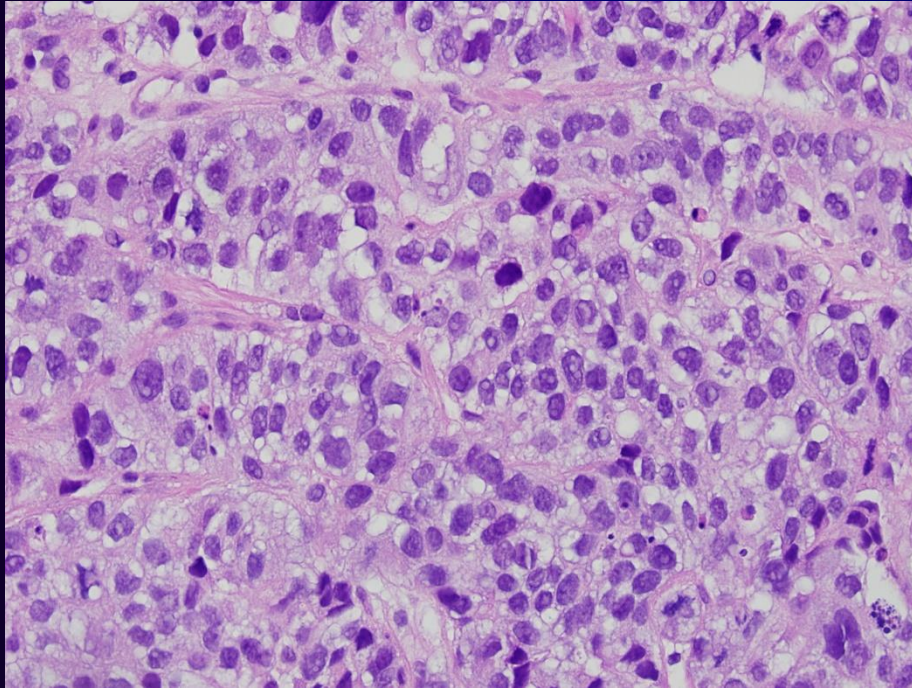


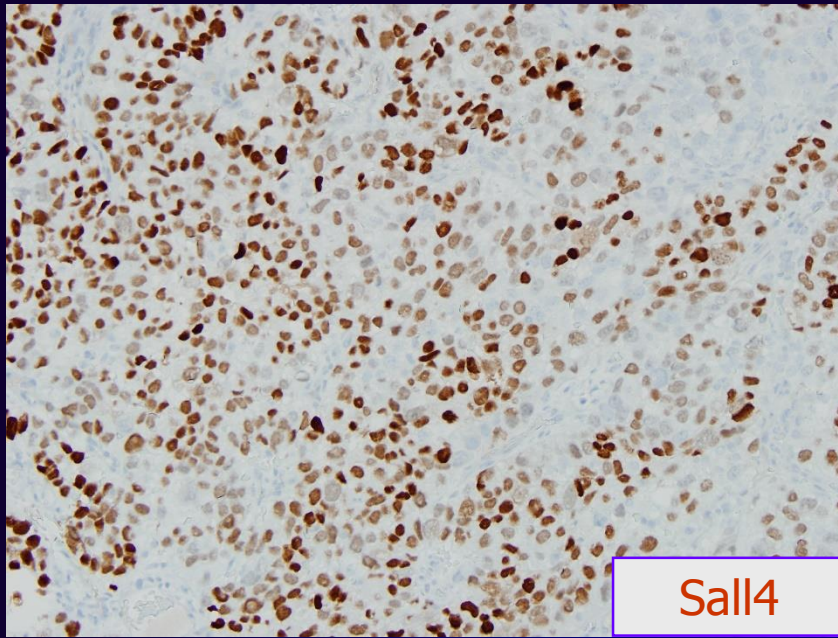
# 10 Challenging GU Pathology Cases

Ximing J. Yang  
M.D., Ph.D.

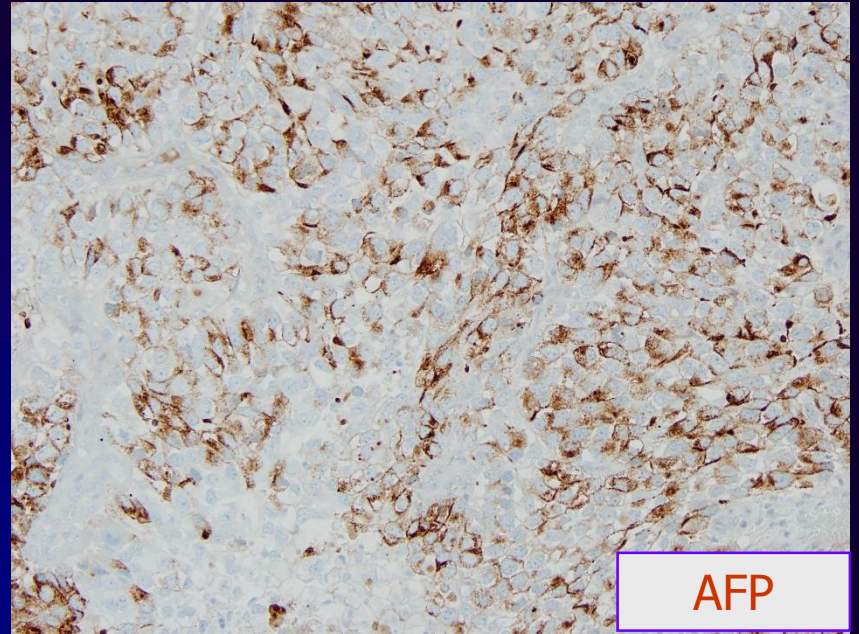
Marie A. Fleming Professor of Pathology  
Chief of Urologic Pathology  
Northwestern University  
Feinberg School of Medicine  
Chicago, USA

# Case 1. Bladder lesion

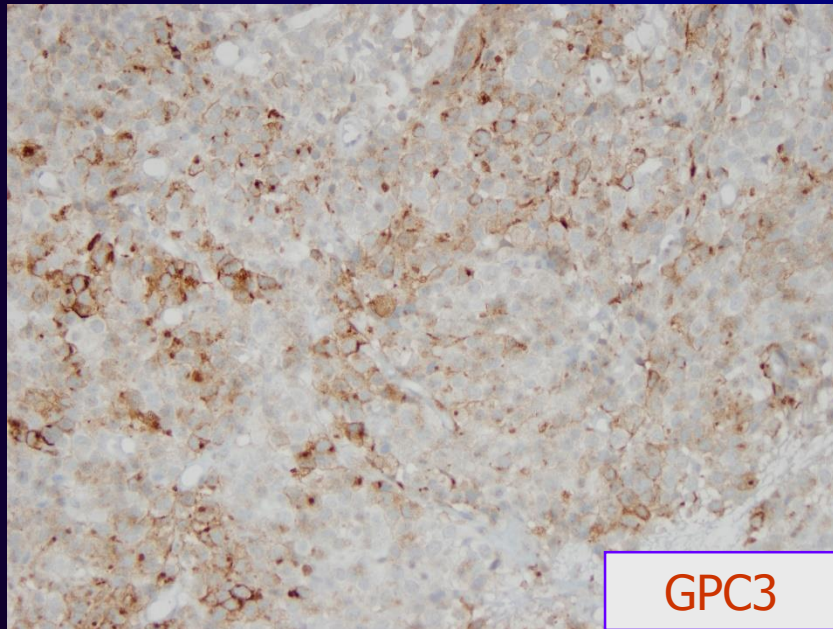




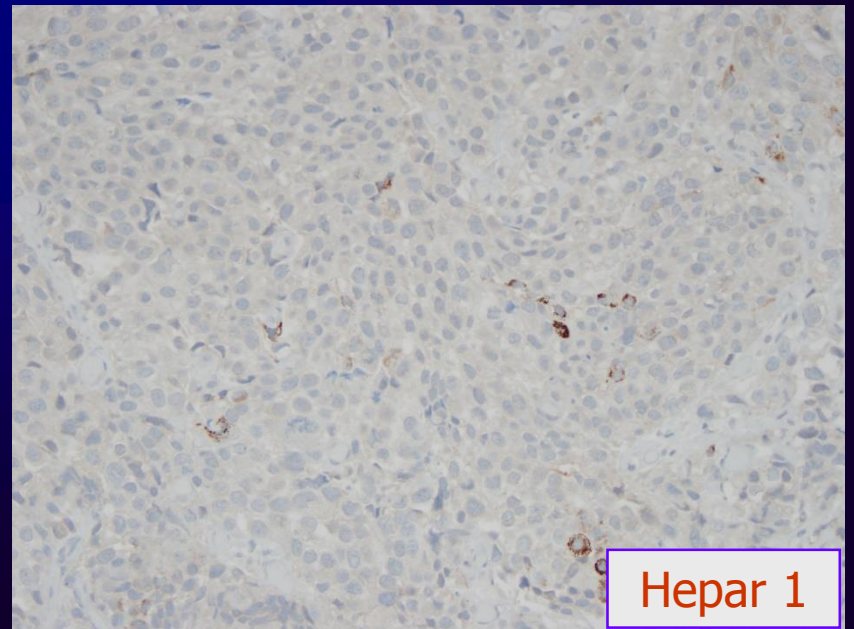
Sall4



AFP

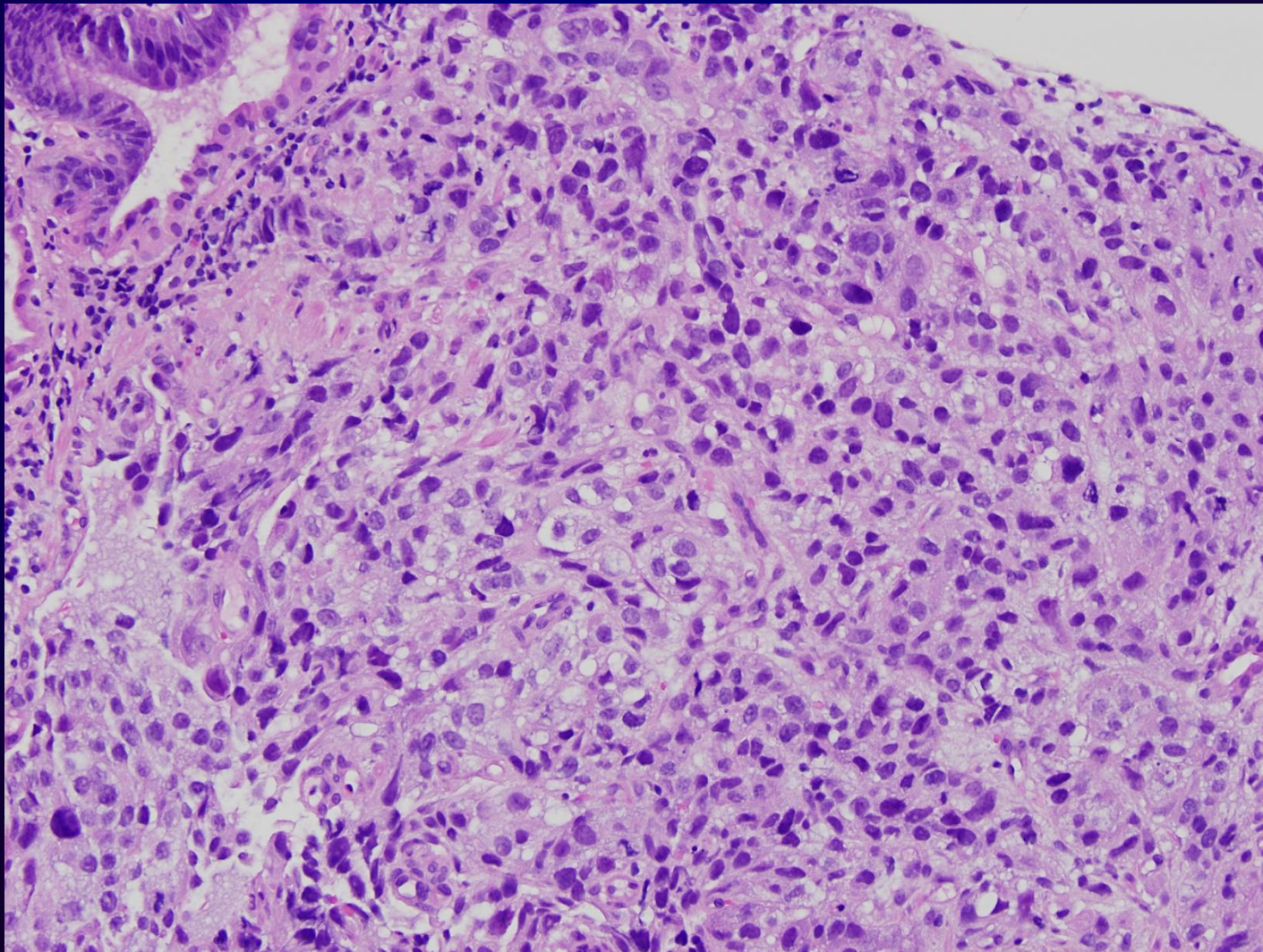


GPC3



Hepar 1

# Previous Gastric Biopsy adenocarcinoma with "signet ring" cells



# Hepatoid adenocarcinoma of the stomach (metastatic)

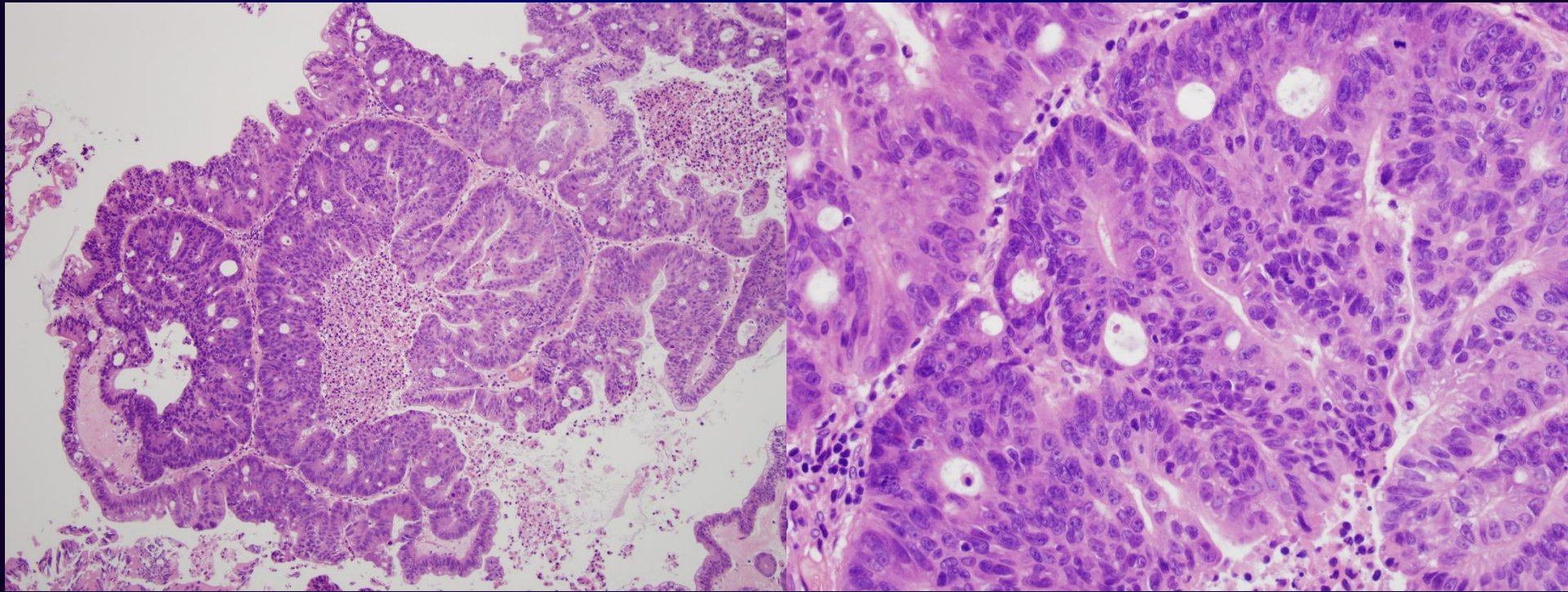
- Rare aggressive variant
- Hepatocellular differentiation
- AFP and Glypican 3 positive
- May have Her2 amp
- P53 CDX2, CEA positive
- Mimic germ cell tumor or HCC

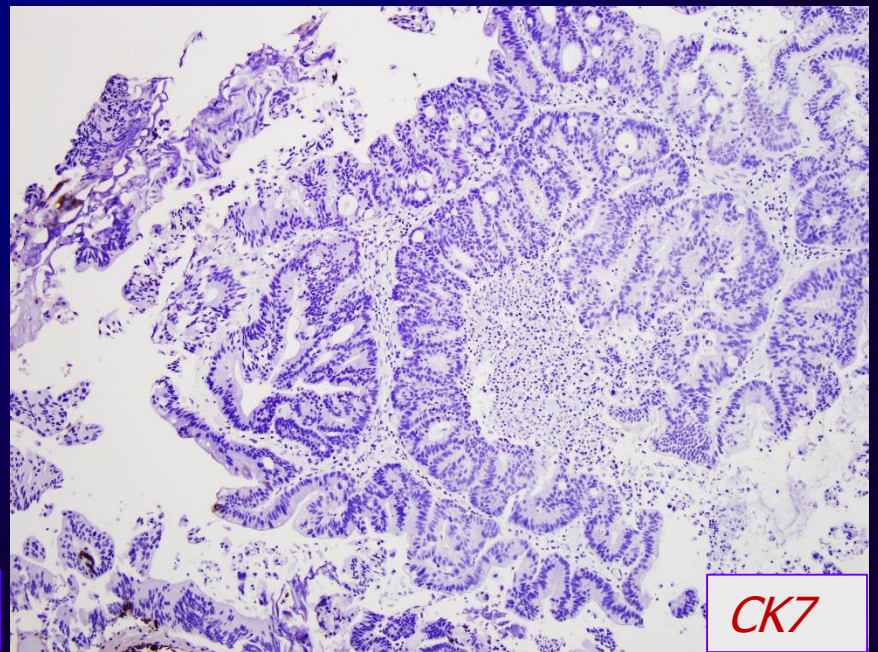
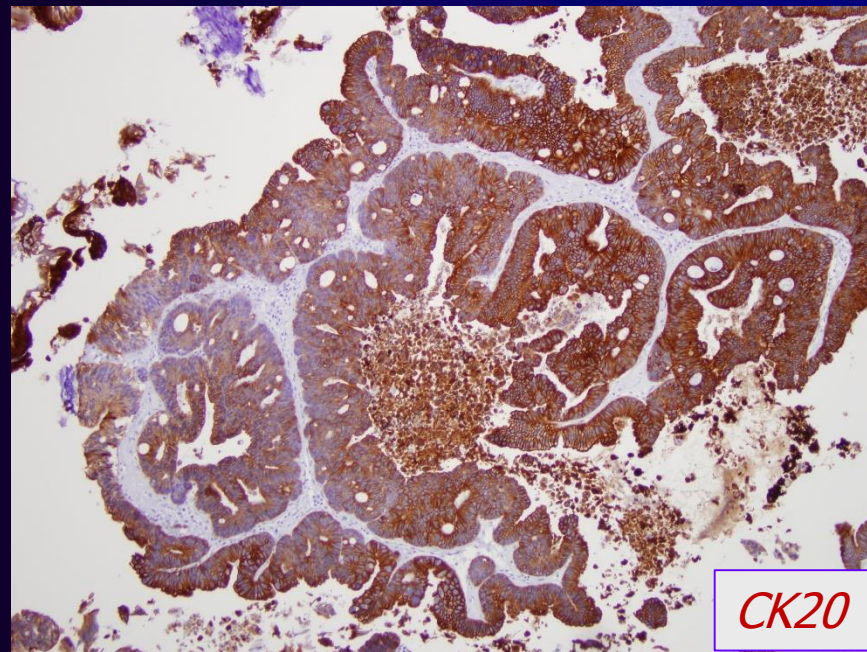
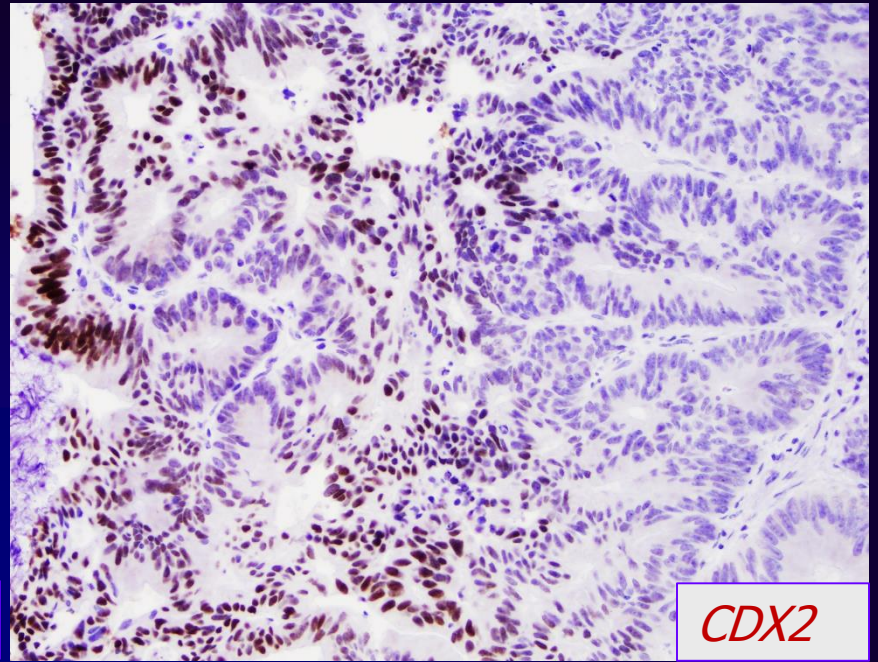
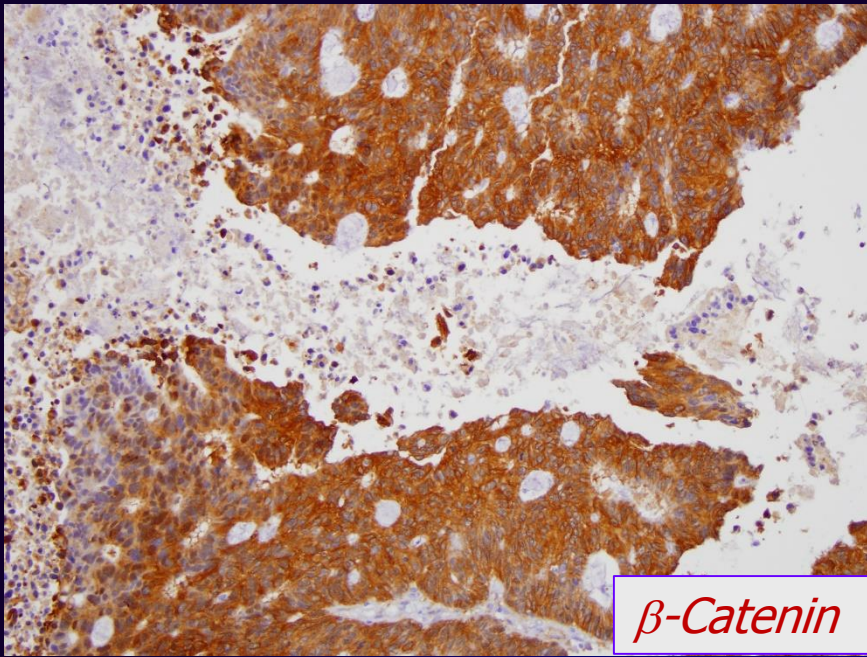
*Secondary adenocarcinoma much more common than primary adenocarcinoma in bladder*

# Our Recent Analysis of 574 cases of bladder carcinoma (NMH 2010-2016)

	Cases		IHC Profile
Primary Adenocarcinoma	9	1.6 %	Beta Catenin 0% (0/9)
Secondary Adenocarcinoma	32	5.6%	
(Prostatic adenocarcinoma)	25	(4.5%)	NKX3.1 100% (25/25) PSA 92% (23/25)
(Colorectal adenocarcinoma)	4	(0.8%)	Beta Catenin 100% (4/4)
Urothelial carcinoma with glandular differentiation	26	4.5%	Gata3 100% (26/26)

# Primary Adenocarcinoma (enteric type)



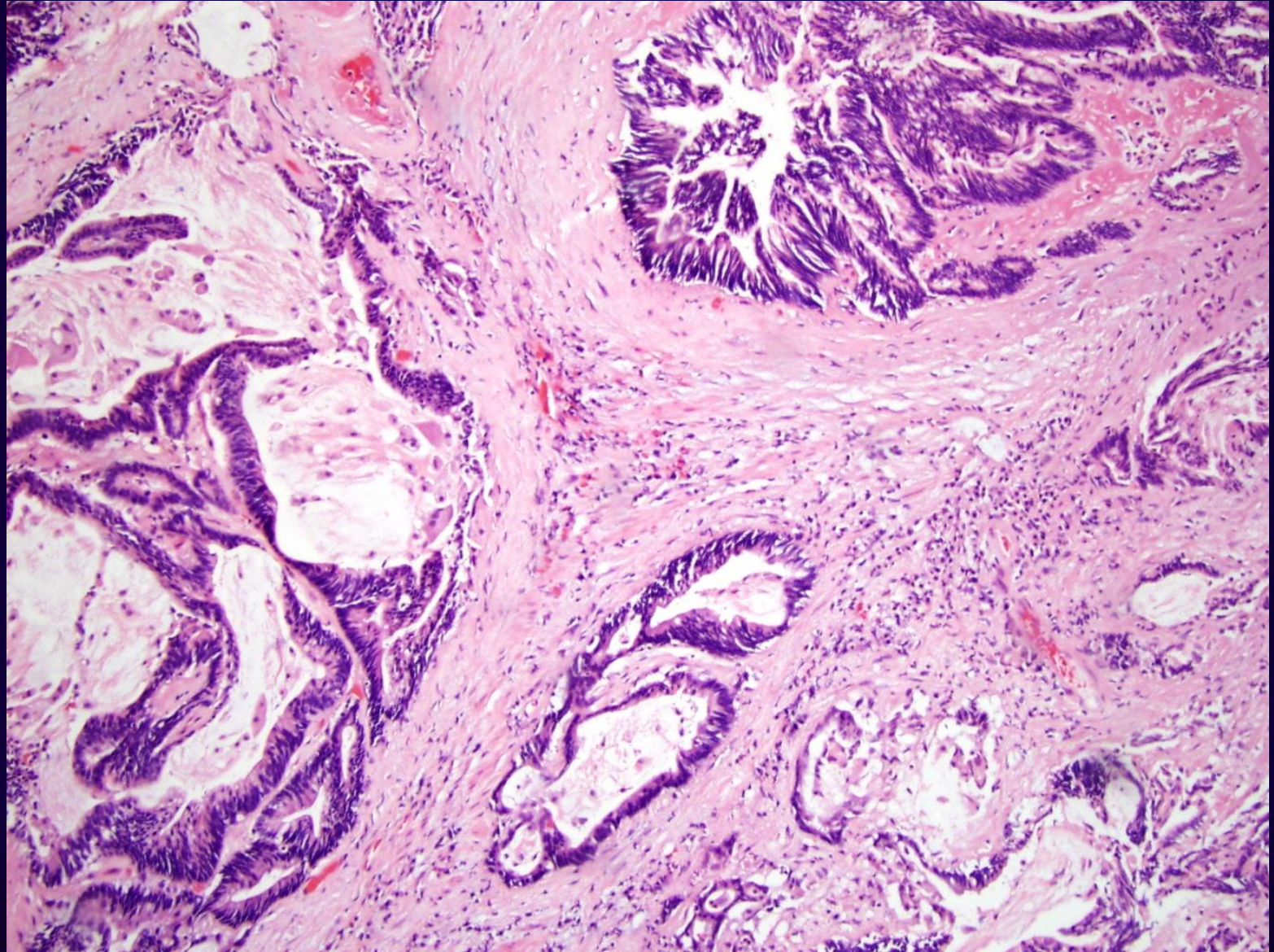




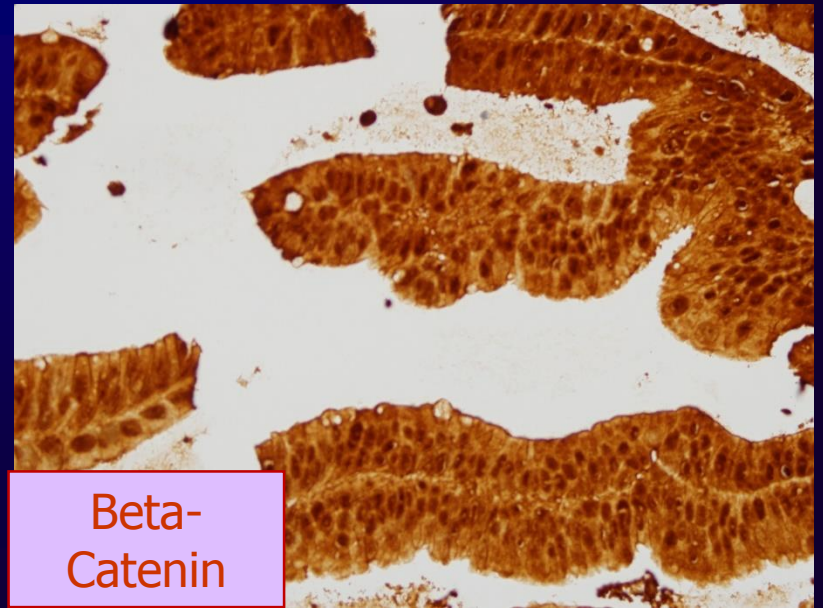
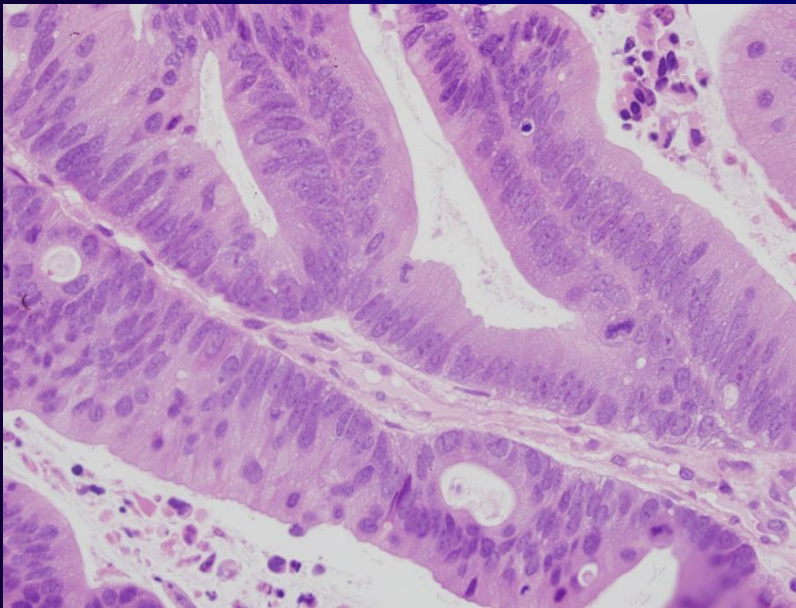
# Secondary Adenocarcinoma metastatic or direct extension

- Colonic adenocarcinoma
- Prostatic adenocarcinoma
- Breast adenocarcinoma
- Endometrial adenocarcinoma
- Clinical history very important
- IHC can be helpful

# Metastatic Adenocarcinoma from Colon



# IHC profile of colonic adenocarcinoma



Beta-Catenin

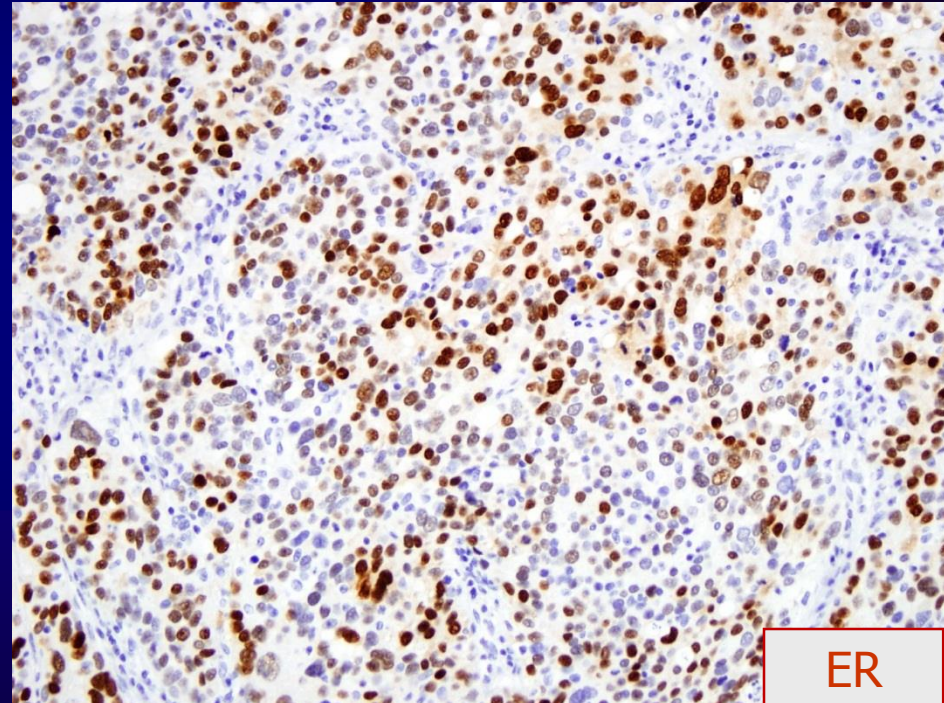
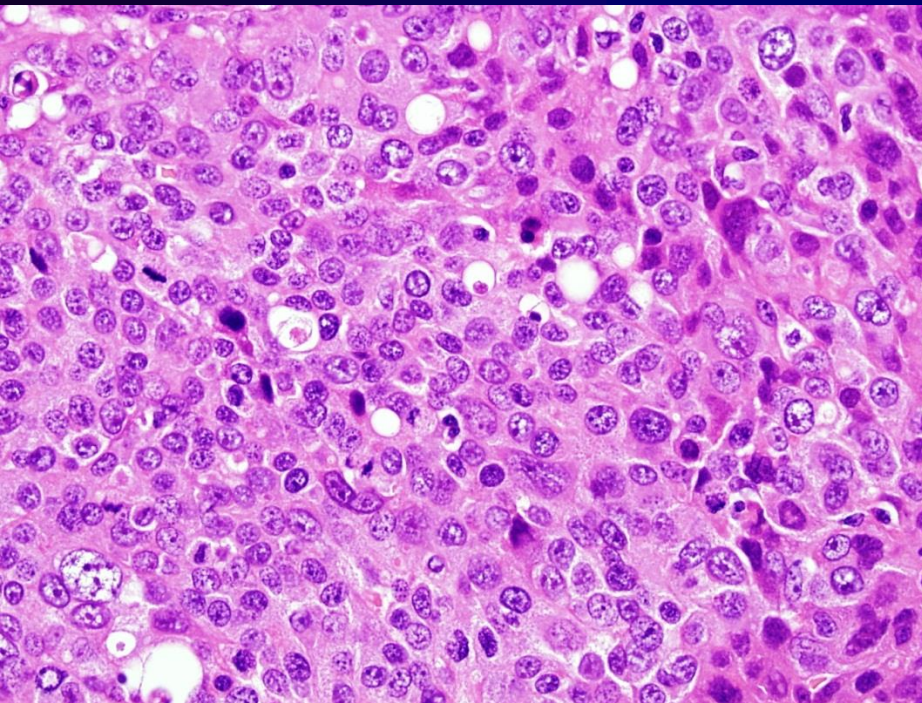
# Primary adenocarcinoma of the urinary bladder is pathogenetically and immunophenotypically distinct from secondary colorectal adenocarcinoma

Wang HL, Lu DW, Yerian LM, Alsikafi N, Steinberg GD, Hart J. Yang XJ.

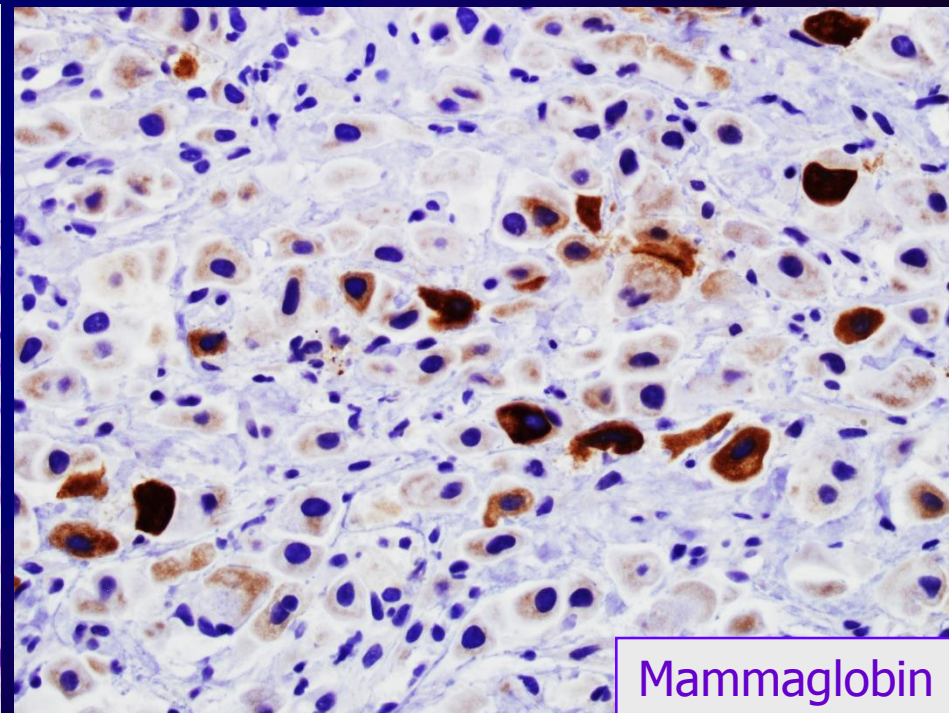
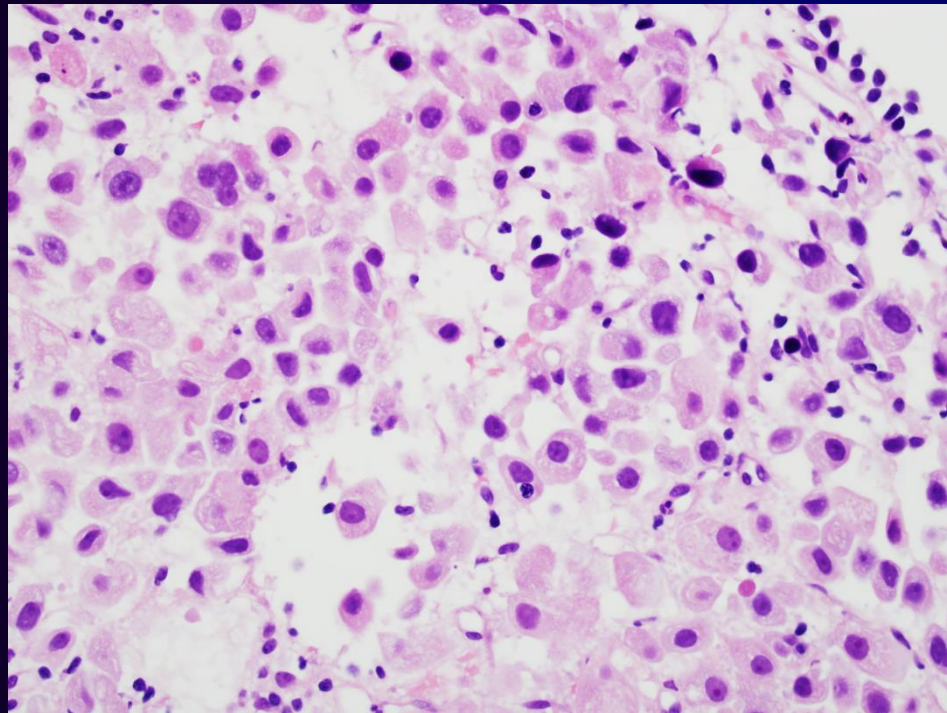
*Am J Surg Pathol.* 25:1380-1387, 2001.

- Utility of beta-Catenin to distinguish primary from secondary adenocarcinoma of the bladder
- Still the best marker after 17 years

# Metastatic Endometrial Adenocarcinoma

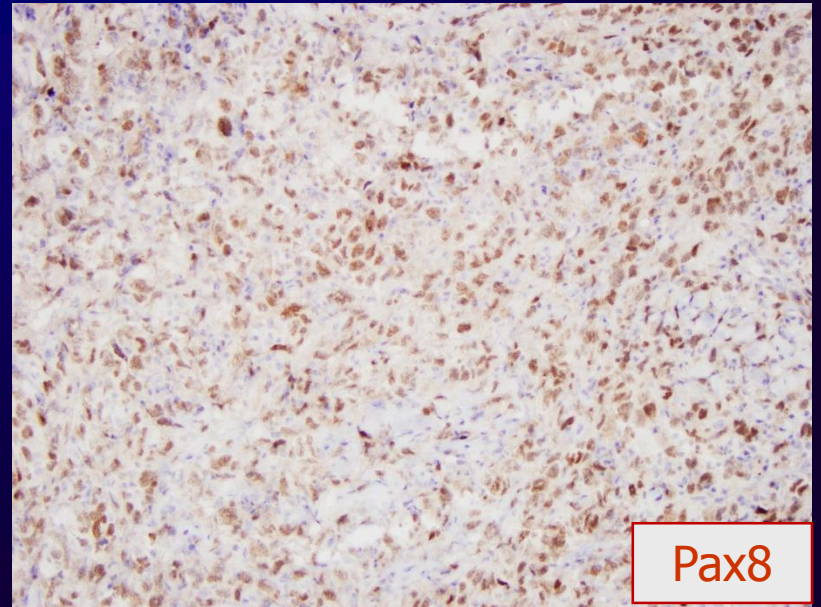
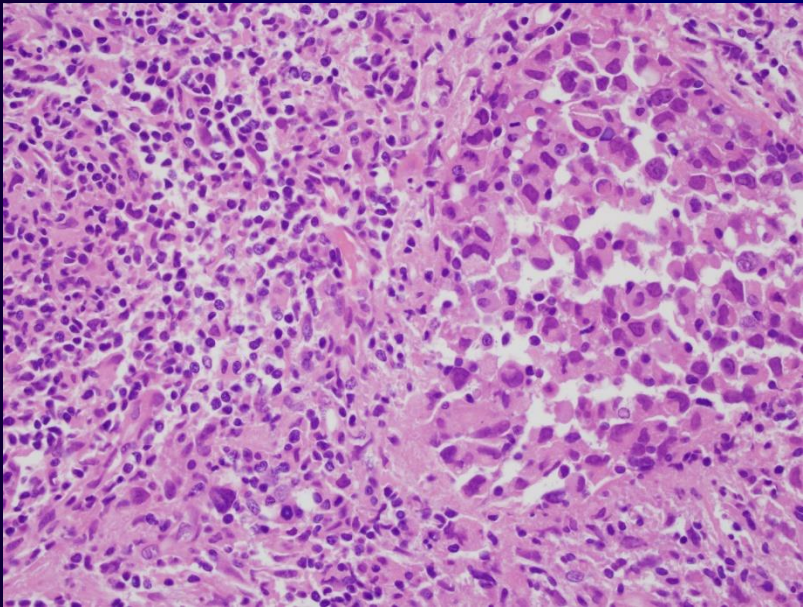


# Metastatic Adenocarcinoma from Breast

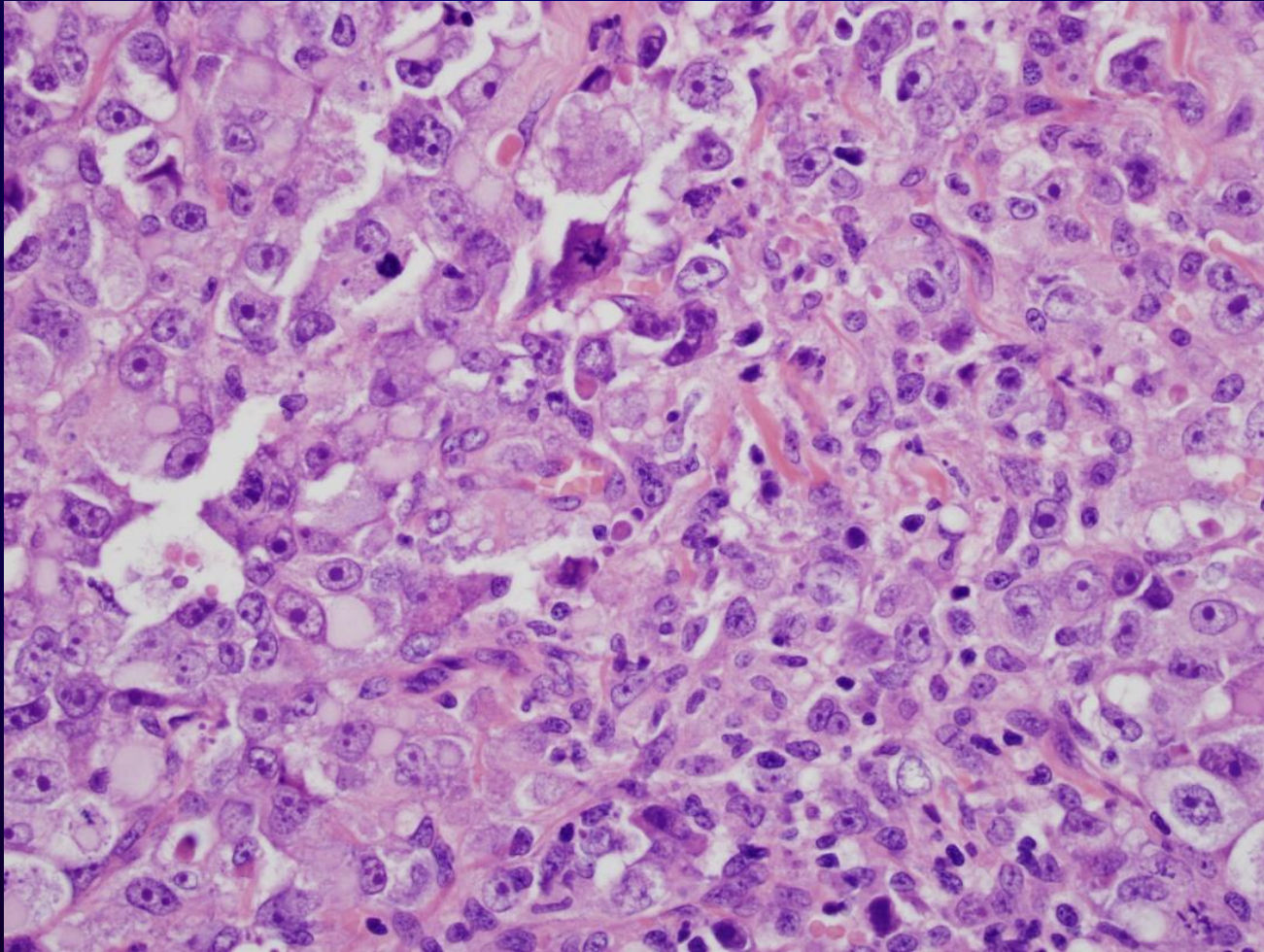


Mammaglobin

# Metastatic ovarian carcinoma

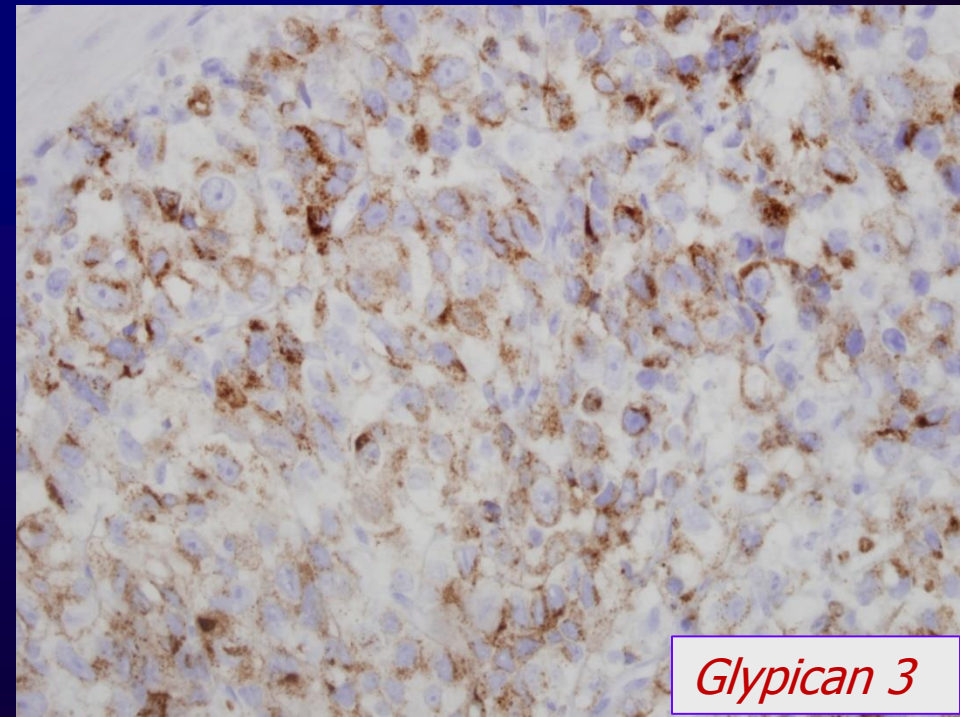
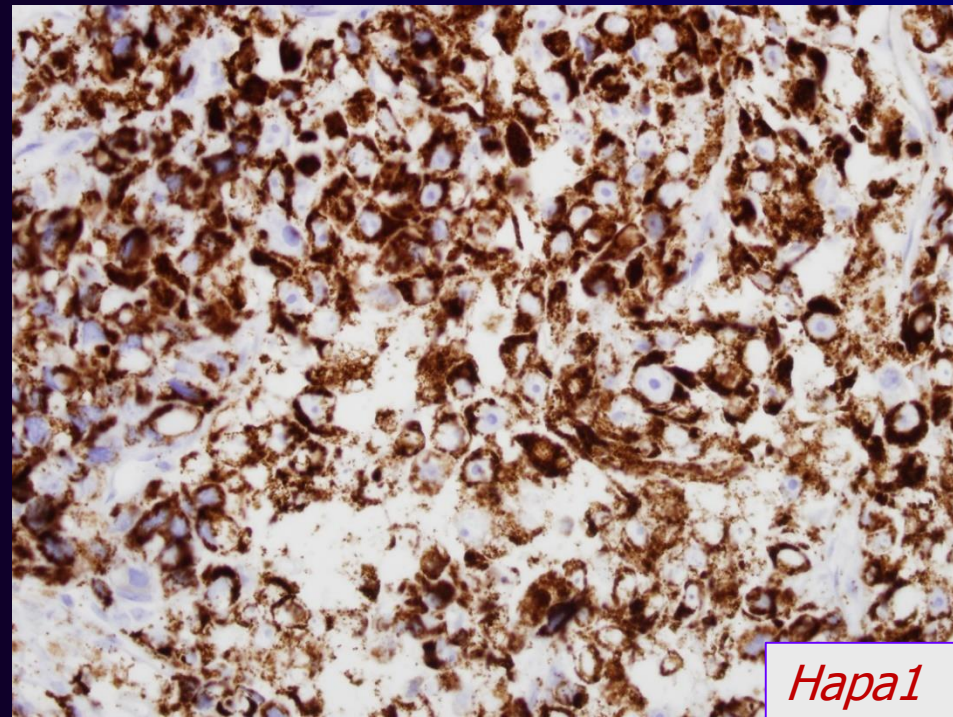


# Metastatic HCC

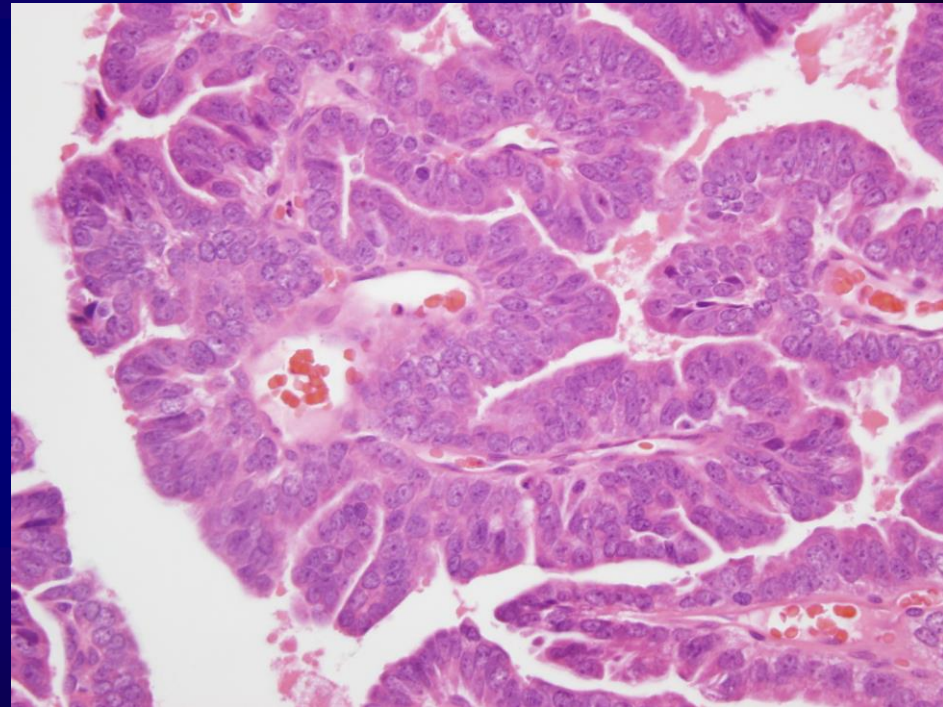
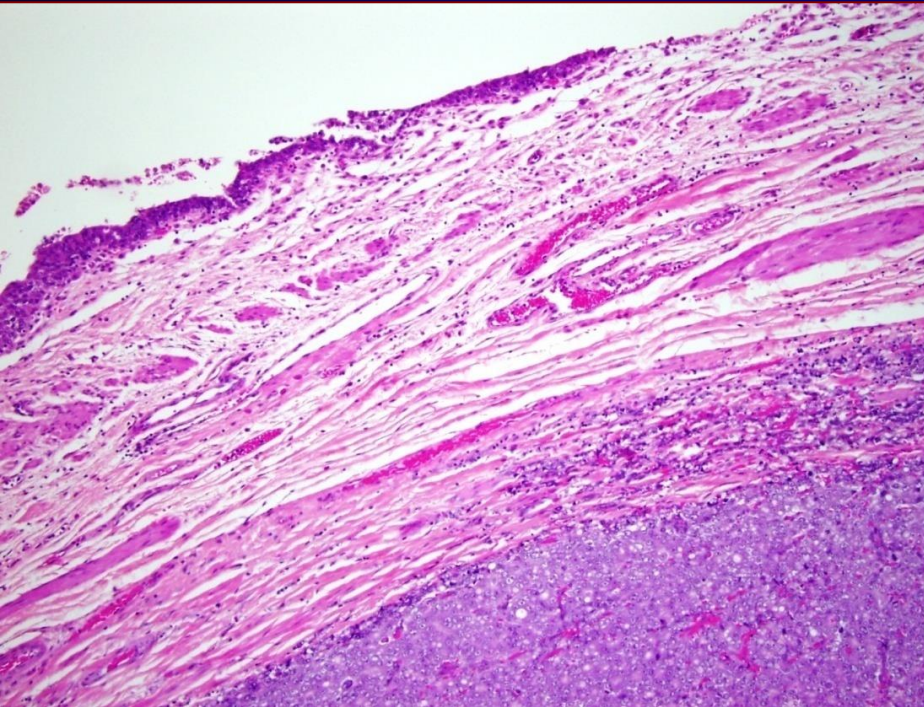




# IHC profile



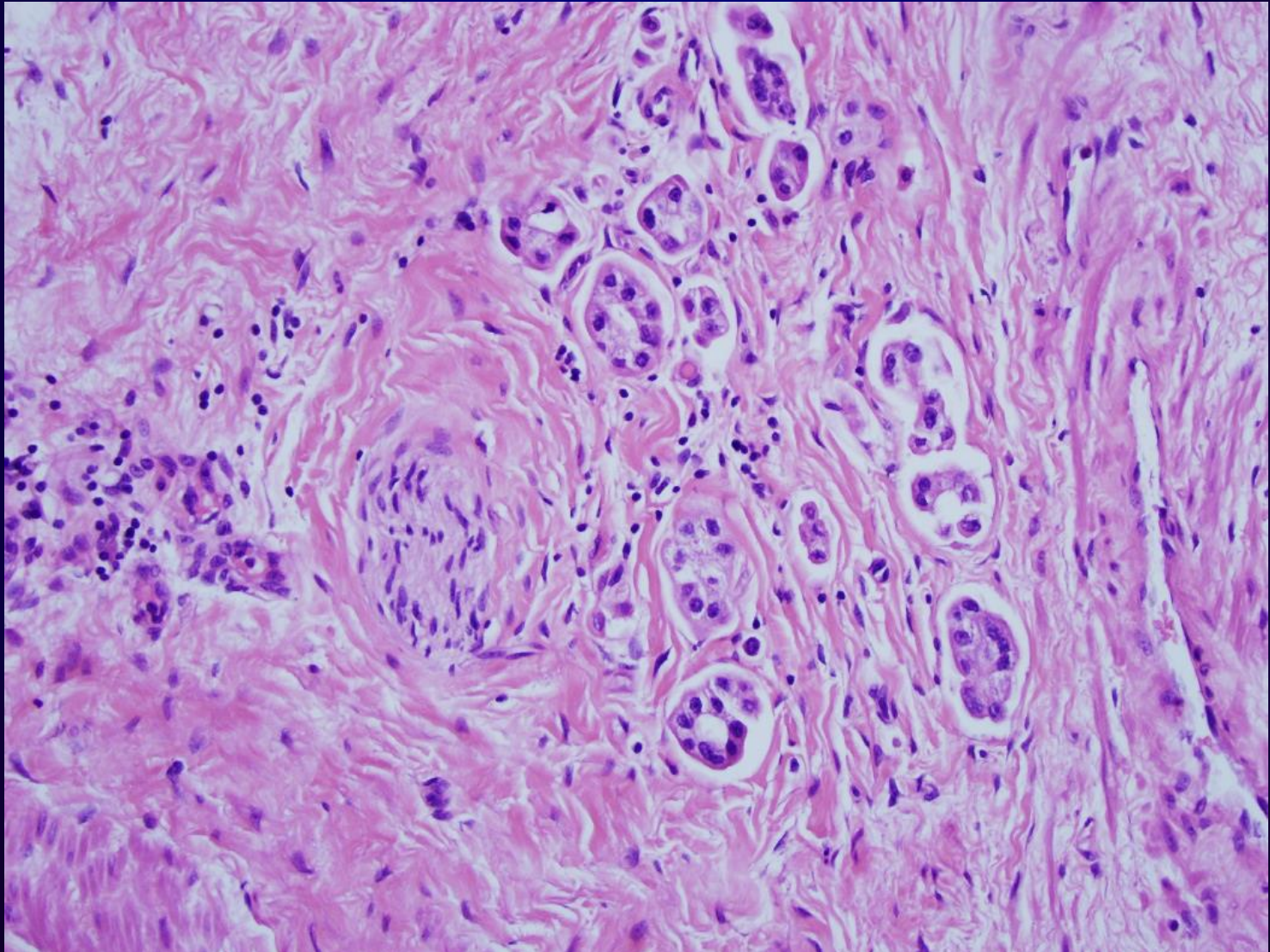
# Metastatic Prostatic Ductal Adenocarcinoma



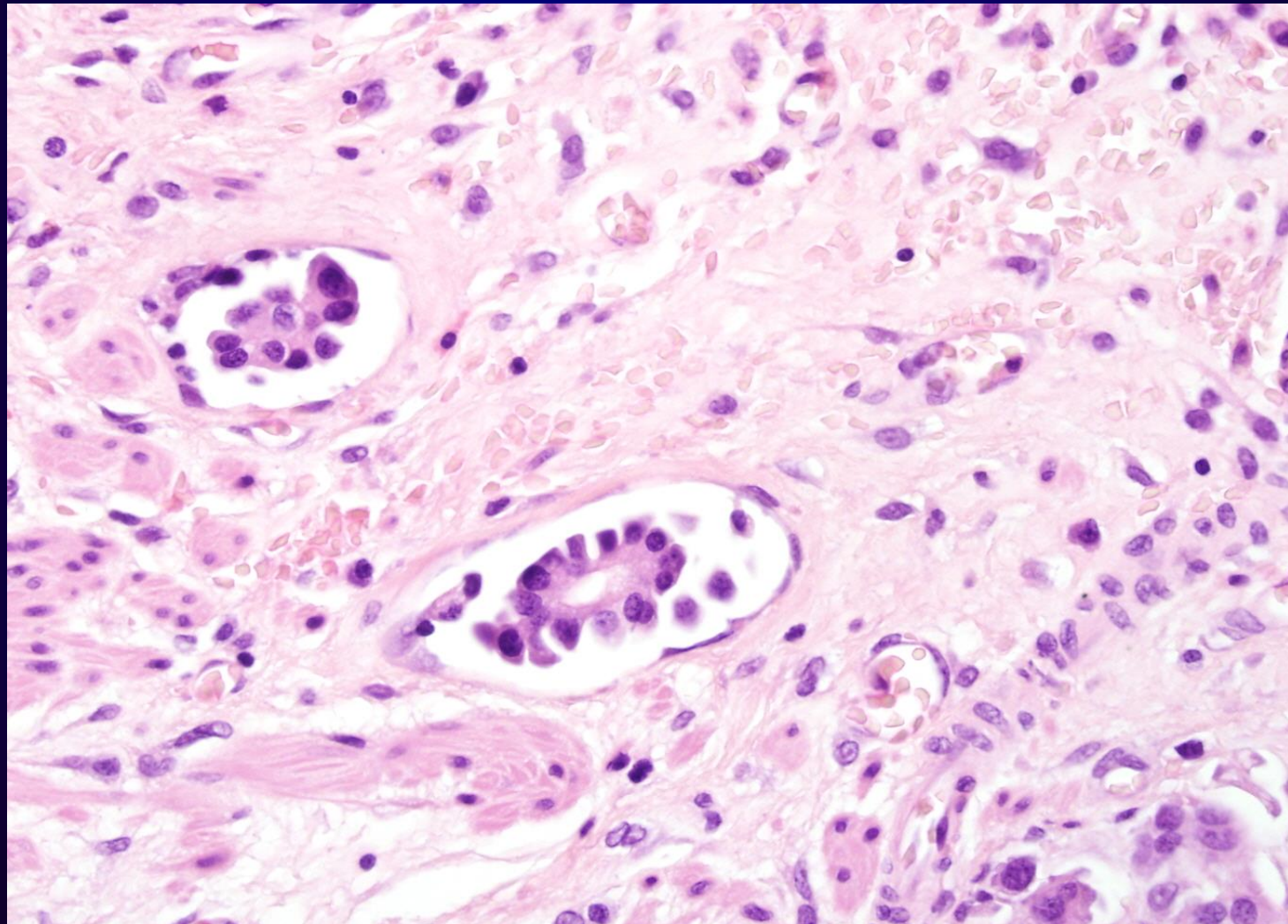
# Immunomarkers for characterization of secondary adenocarcinoma of bladder

Primary site	1 <sup>st</sup> choice	2 <sup>nd</sup> choice
Prostate	NKX3.1	PSA, ERG
Colon	Beta-Catenin	CDX2, CK7/20
Endometrium and ovary	Pax8	ER/PR
HCC	Hapar1	Glypican 3
Breast	Mammaglobin BRST2	Gata3, ER/PR

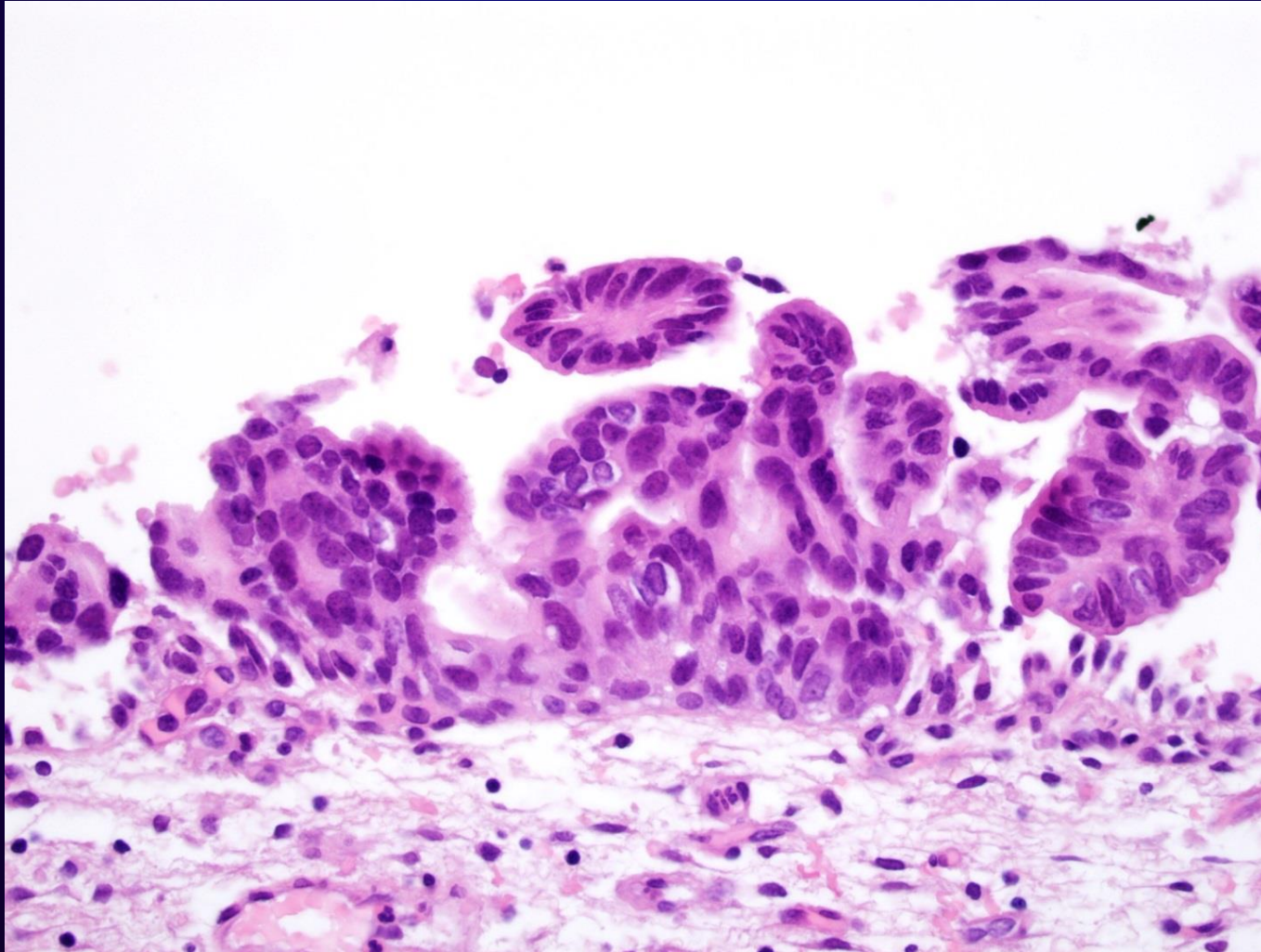
# Case 2. Micropapillary UCa of the bladder involving prostate



# Micropapillary Urothelial Carcinoma

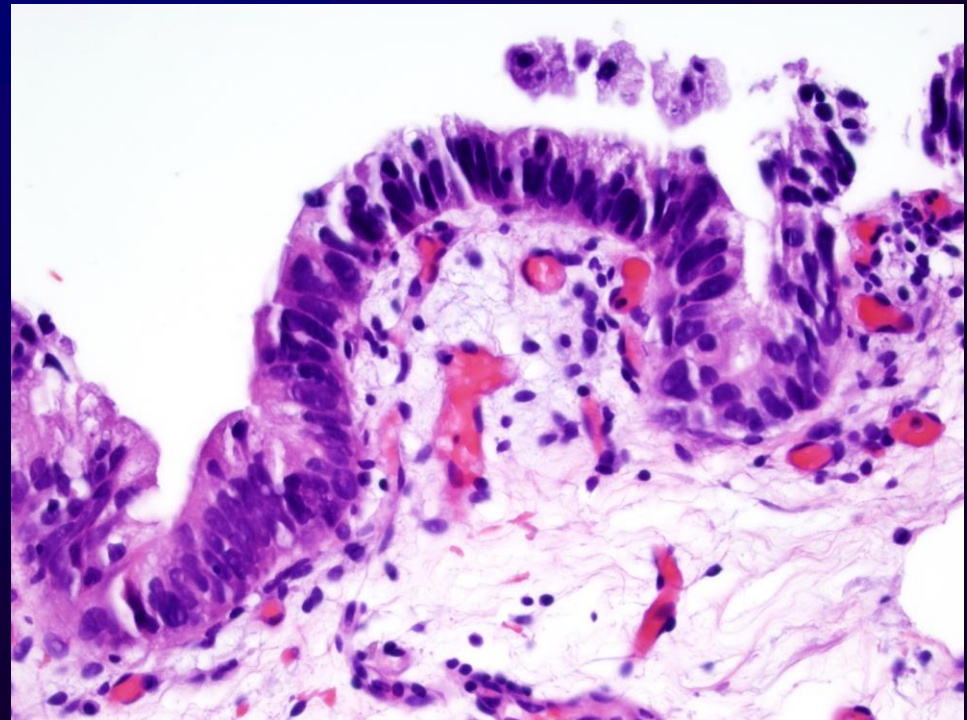


# Micropapillary Urothelial CIS



# Non-invasive urothelial carcinoma with glandular differentiation

- Also known as adenocarcinoma in situ (AIS), morphologically similar to AIS in cervix
- Often associated with high grade urothelial carcinoma



# The utility of p63, p40 and GATA3 in diagnosis of micropapillary urothelial carcinoma

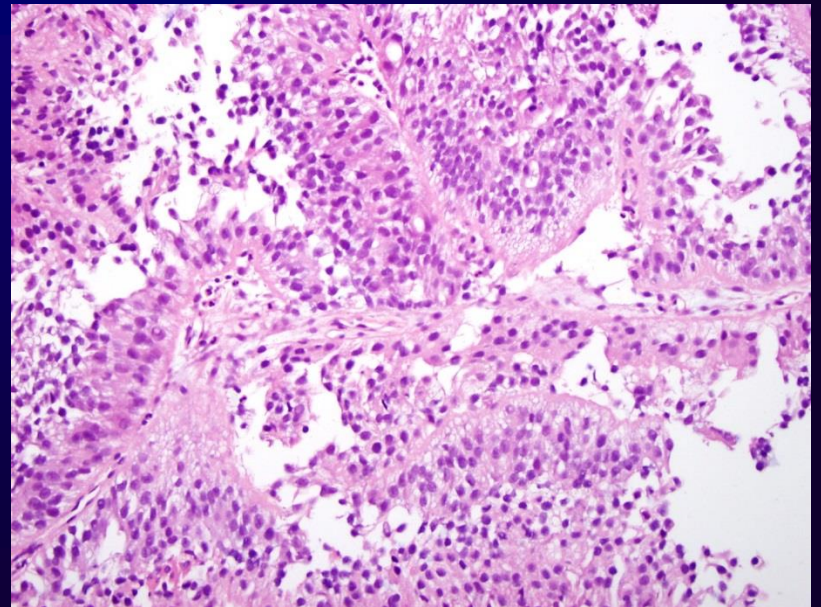
*Lin X, Zhu B, Villa C, Zhong M, Kundu S, Rohan SM, Yang XJ. Hum Pathol. 2014*

- Micropapillary UCA is an aggressive variant of urothelial carcinoma
- They may loss p63, p40 expression, the best marker is GATA3
- Should be included in report because delay treatment will lead to metastasis

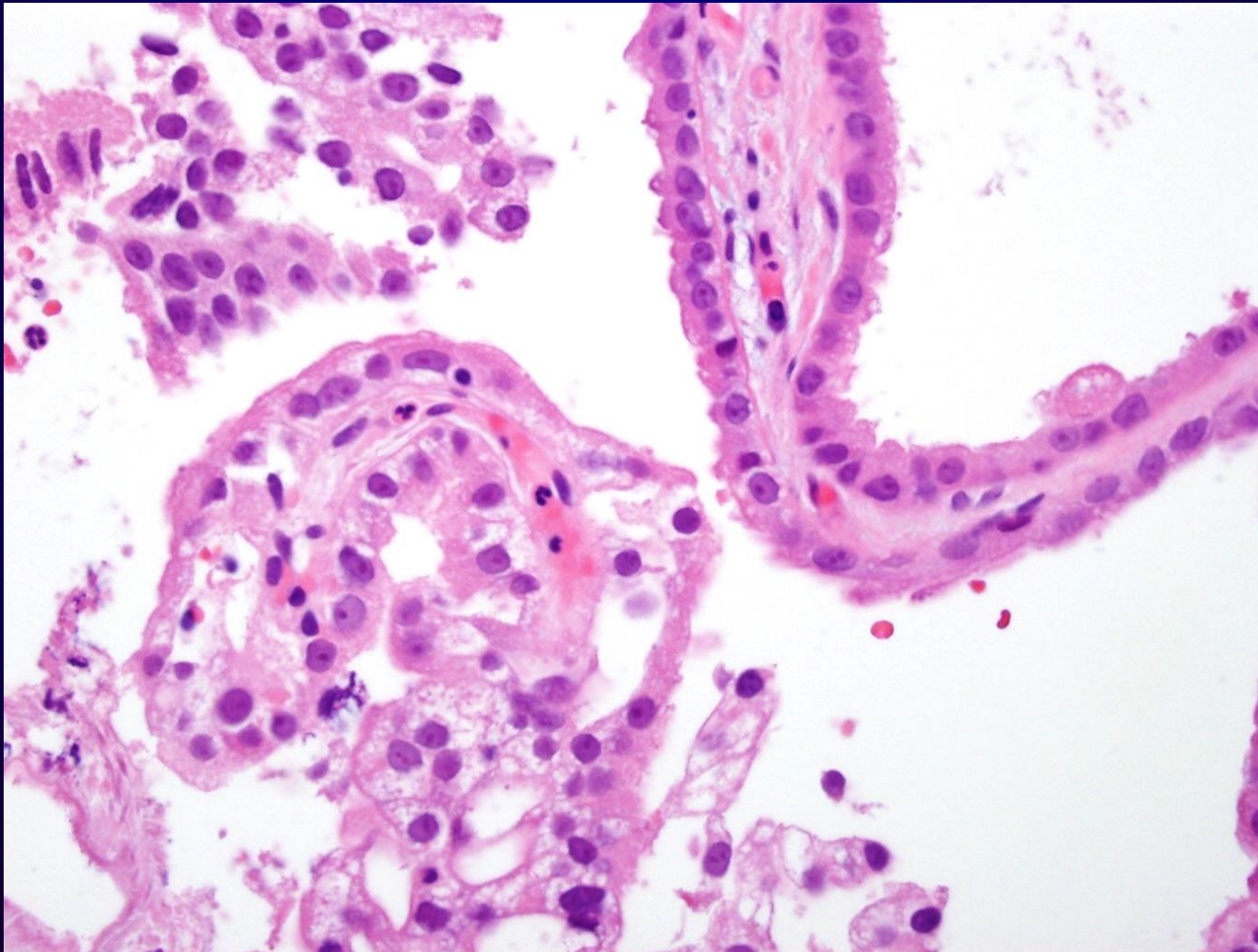


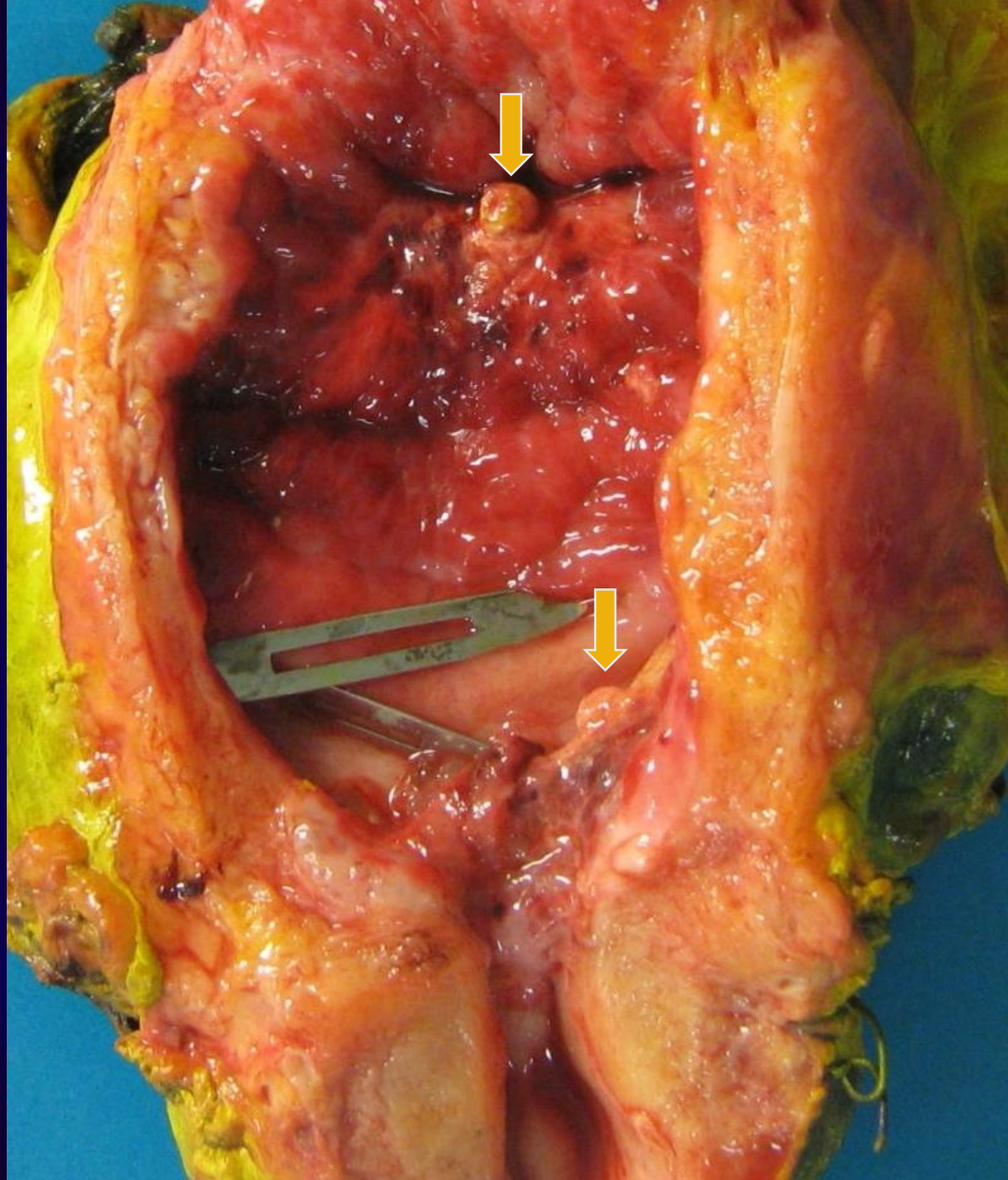
# Case 3. Bladder lesion

- 56 year-old male
- History of renal failure, currently on dialysis
- Developed hematuria
- Cystoscopy showed several small polypoid lesions

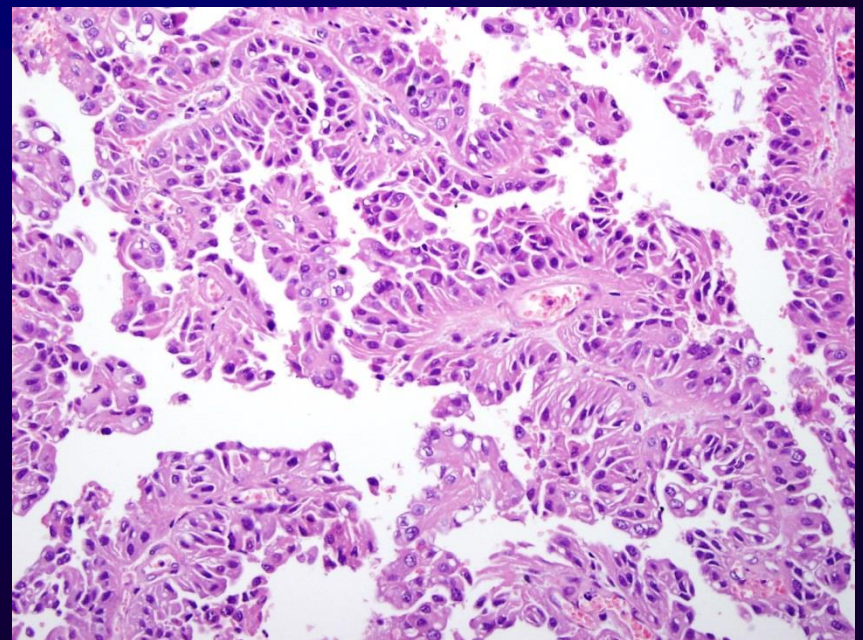
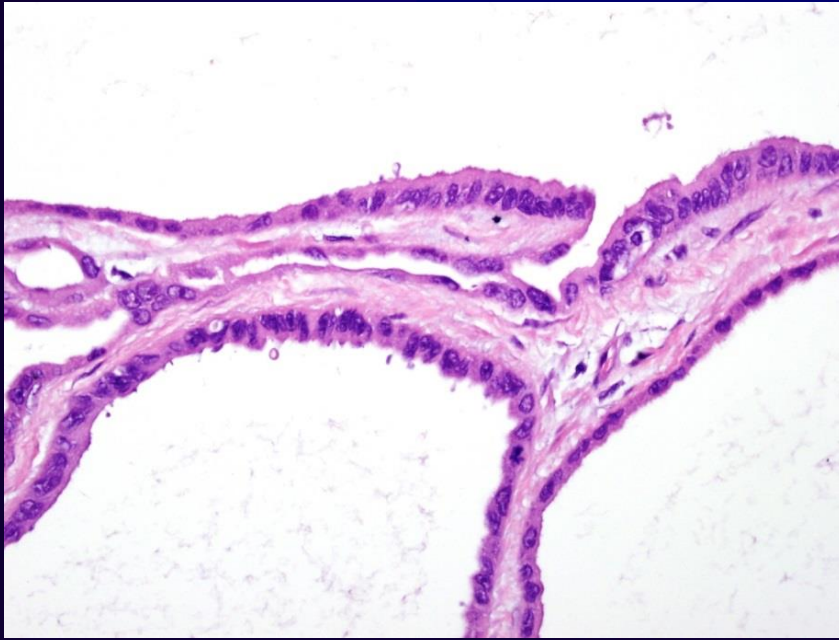


# Other cells in bladder biopsy

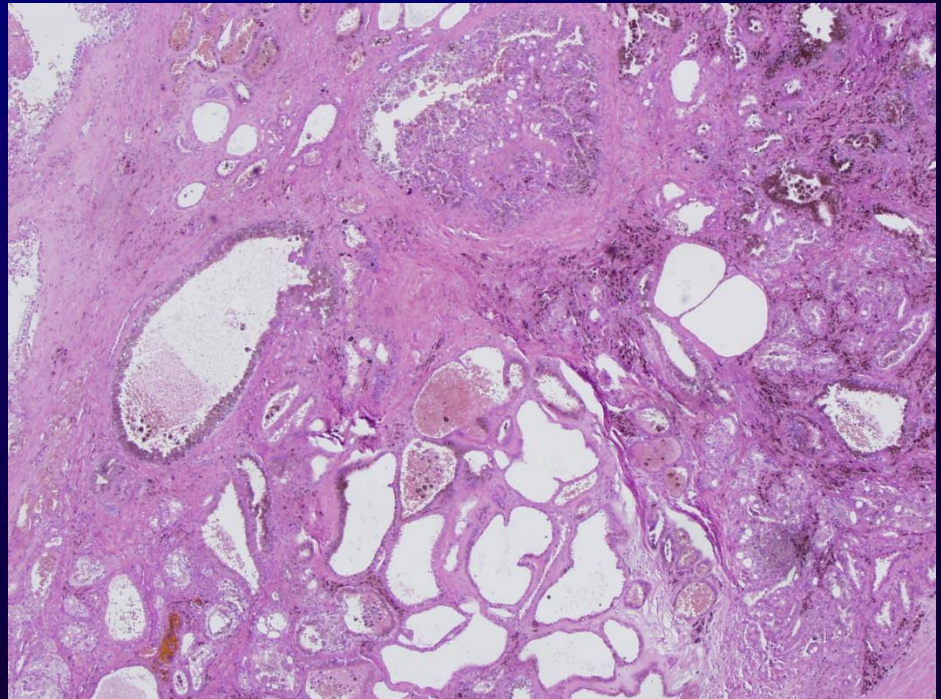




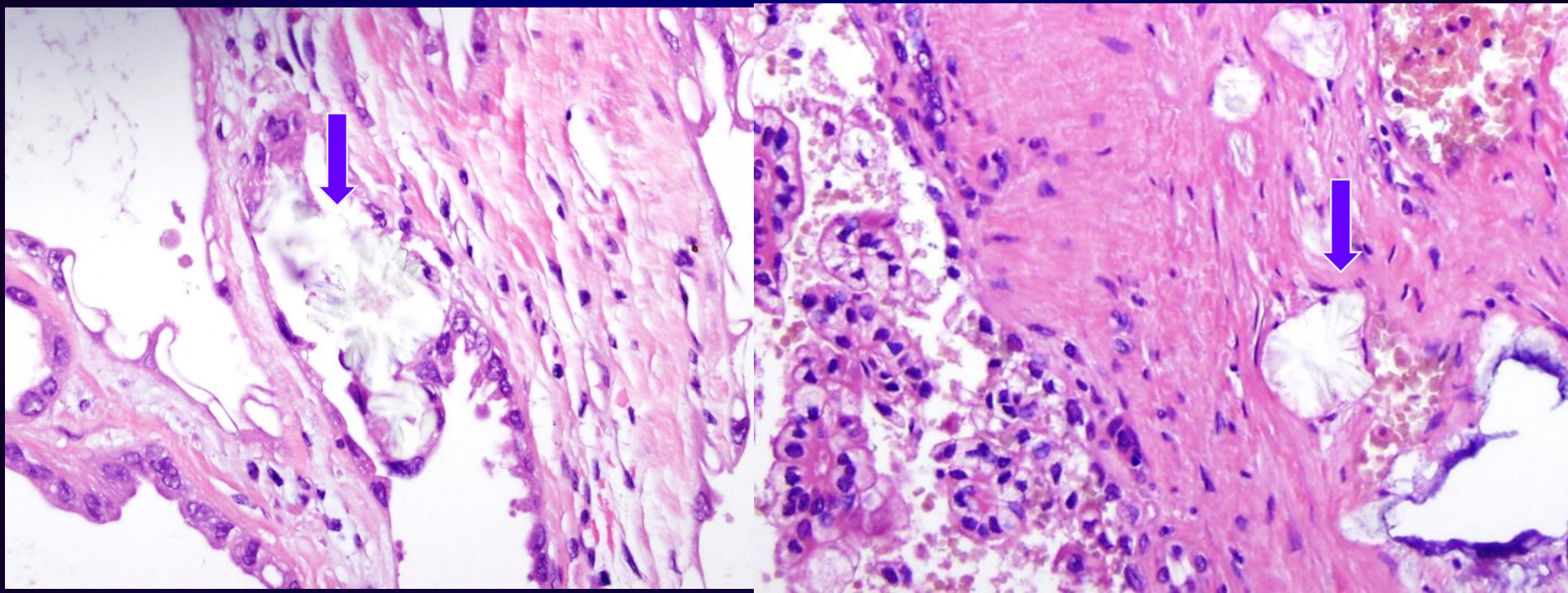
# Two major components: Papillary and tubulocystic



# Kidney Tumors in the Background of Acquired Cystic Disease in this Case



# Calcium Oxalate Crystals



# Case 3. Our Final diagnosis

## Nephrectomies

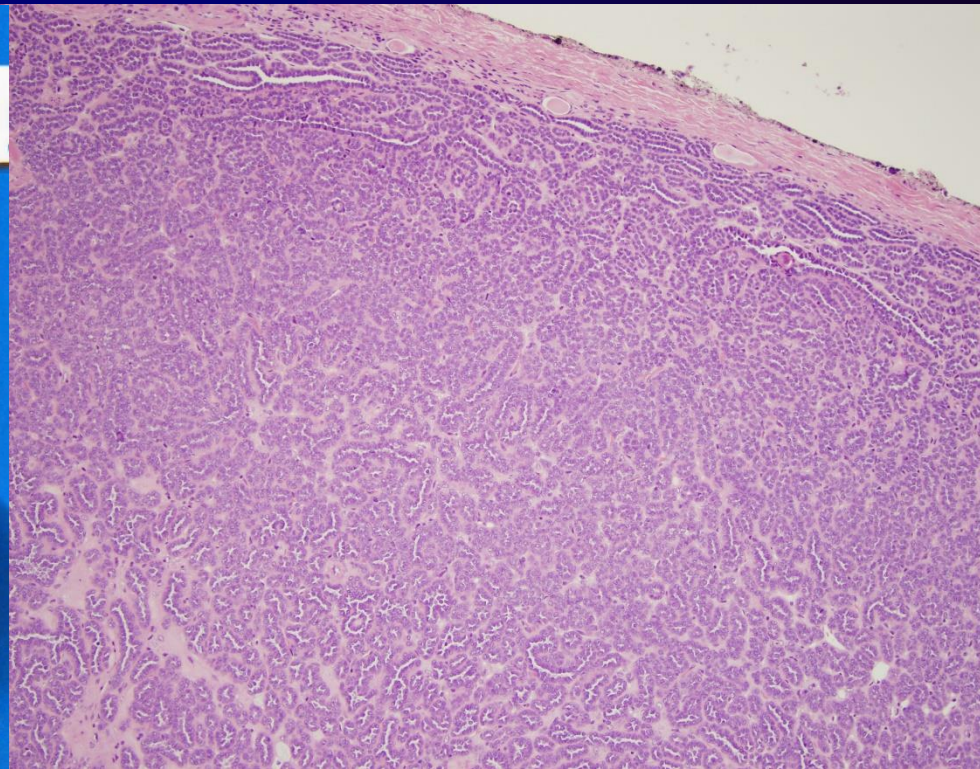
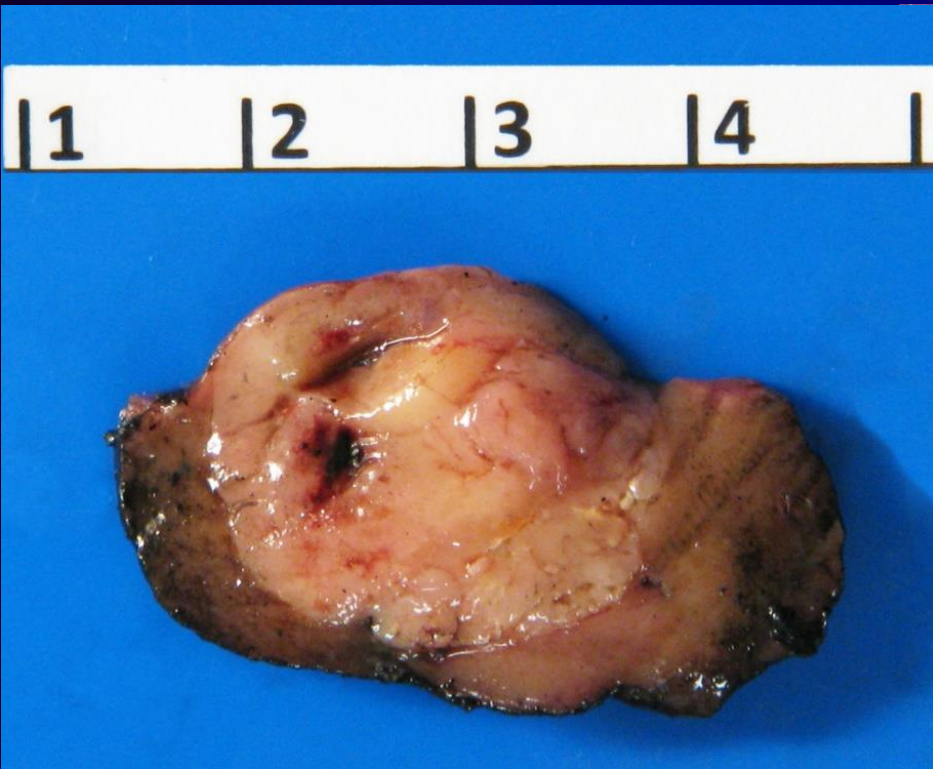
- Acquired cystic disease of the kidney (ACD)
- Bilateral ACD associated RCC

## Cystectomy

- ACD associated renal cell carcinoma involving the bladder
- Mimicking a “nephrogenic adenoma”
- Possibly spread to the bladder as NA
- No residual urothelial carcinoma seen

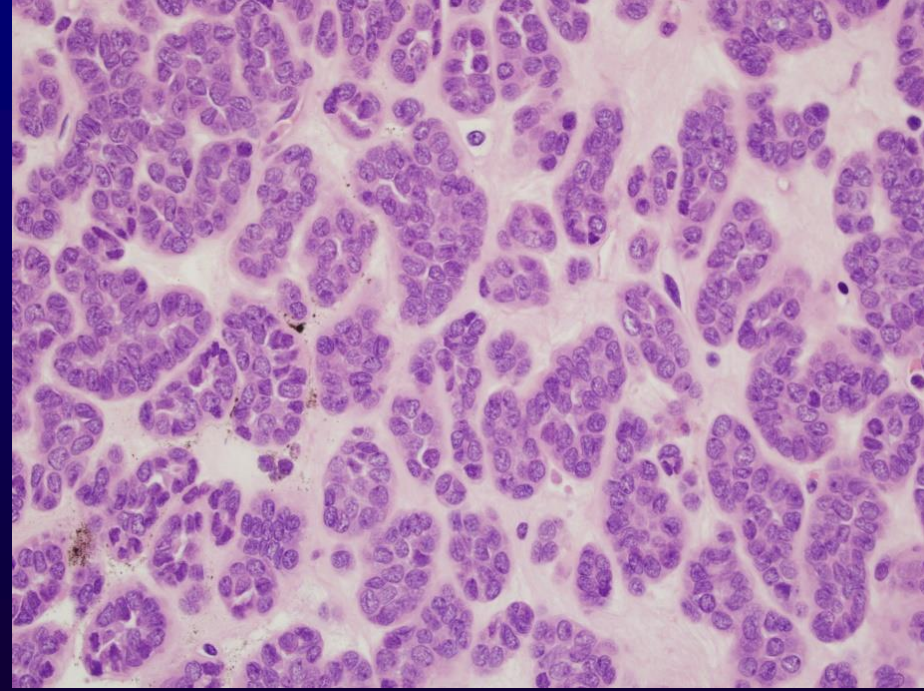
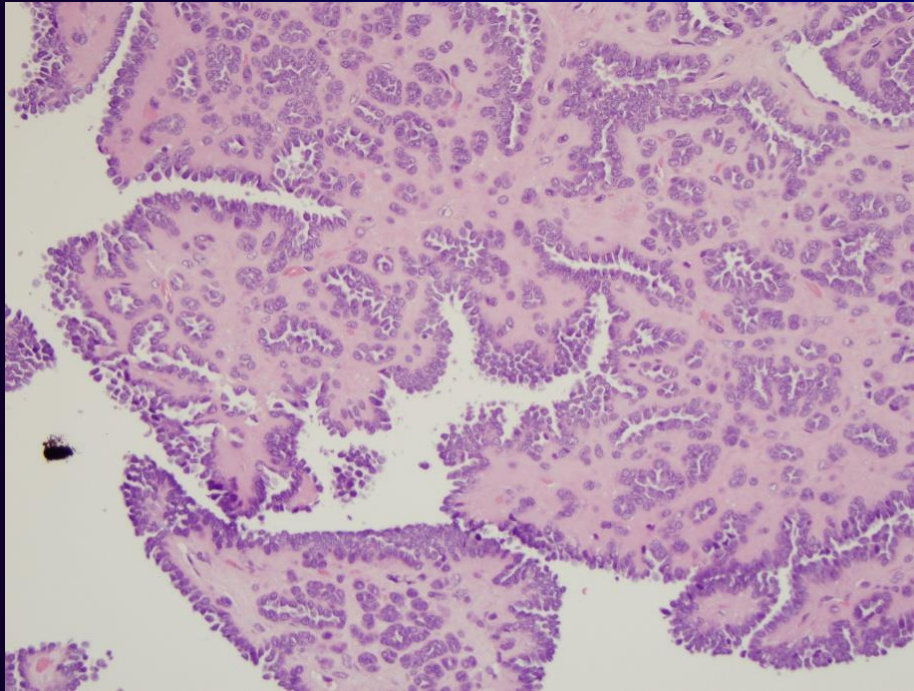
# Case 4.

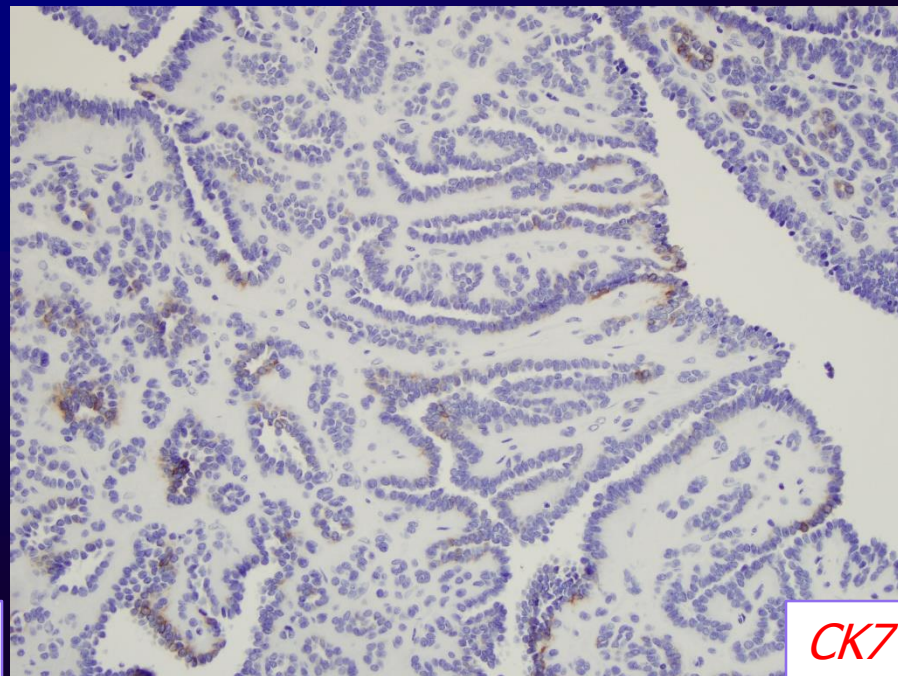
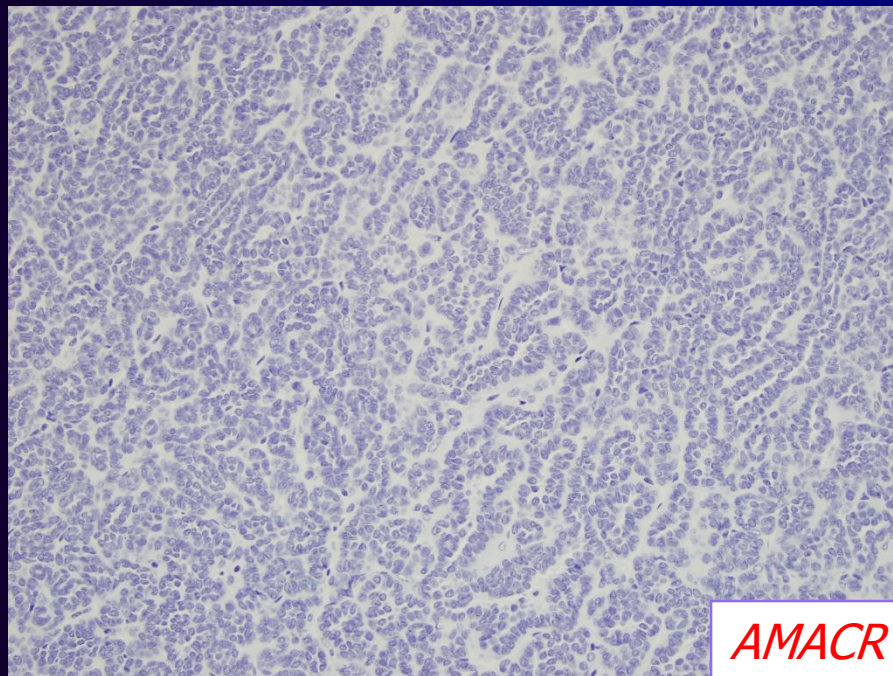
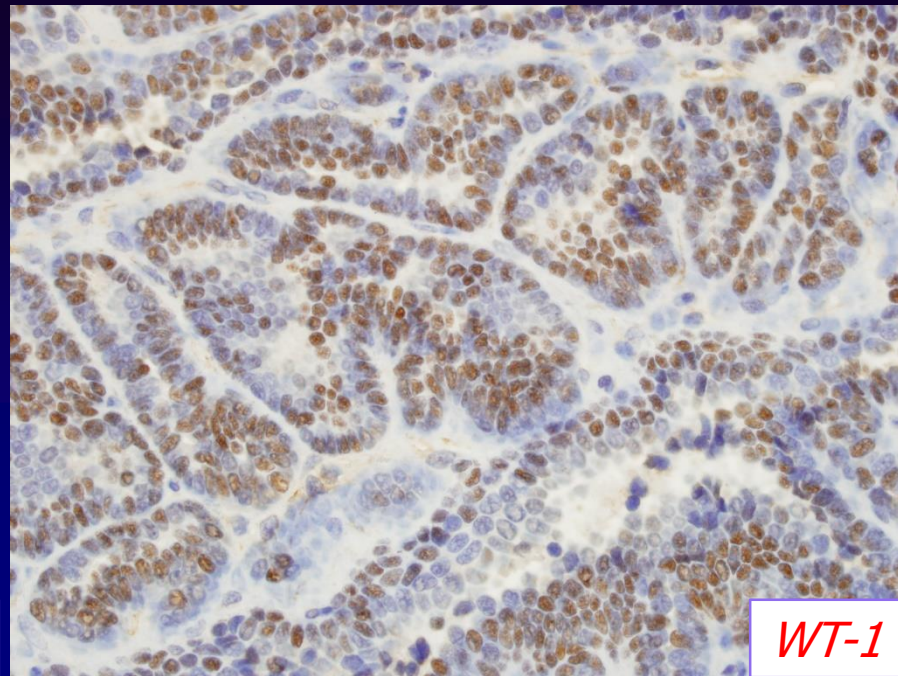
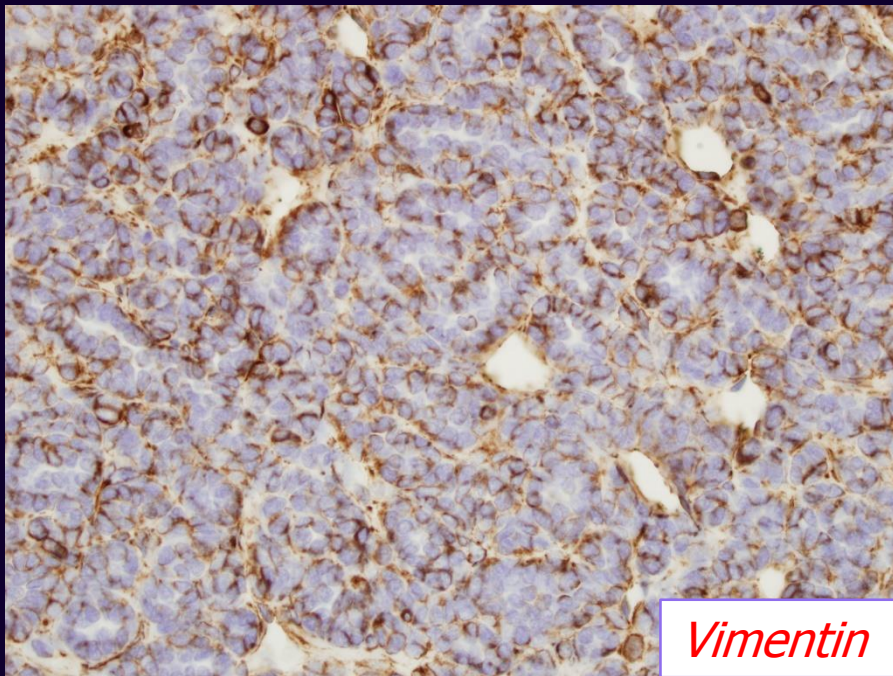
## Renal mass in 65 y-o female





# Metanephric adenoma



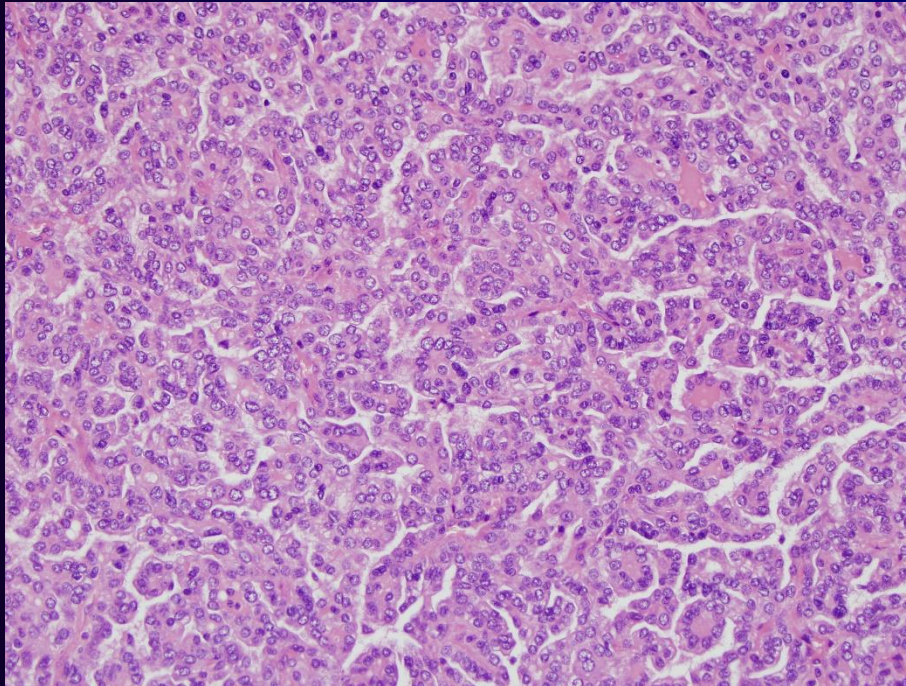


# Differential Diagnosis

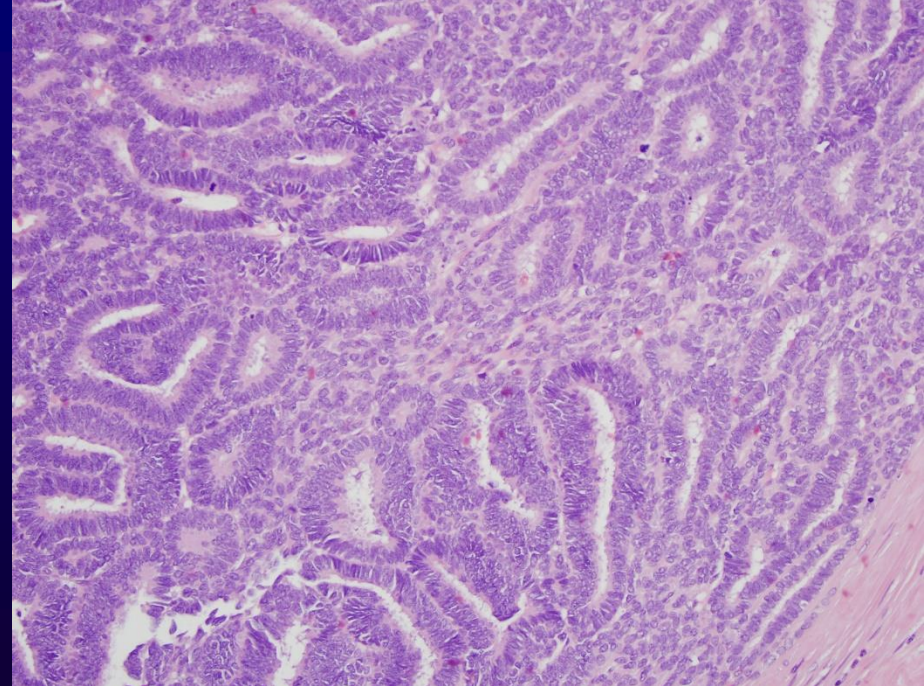
- Papillary adenoma
- Papillary renal cell carcinoma type 1
- Adult Wilms tumor

# Differential Diagnosis

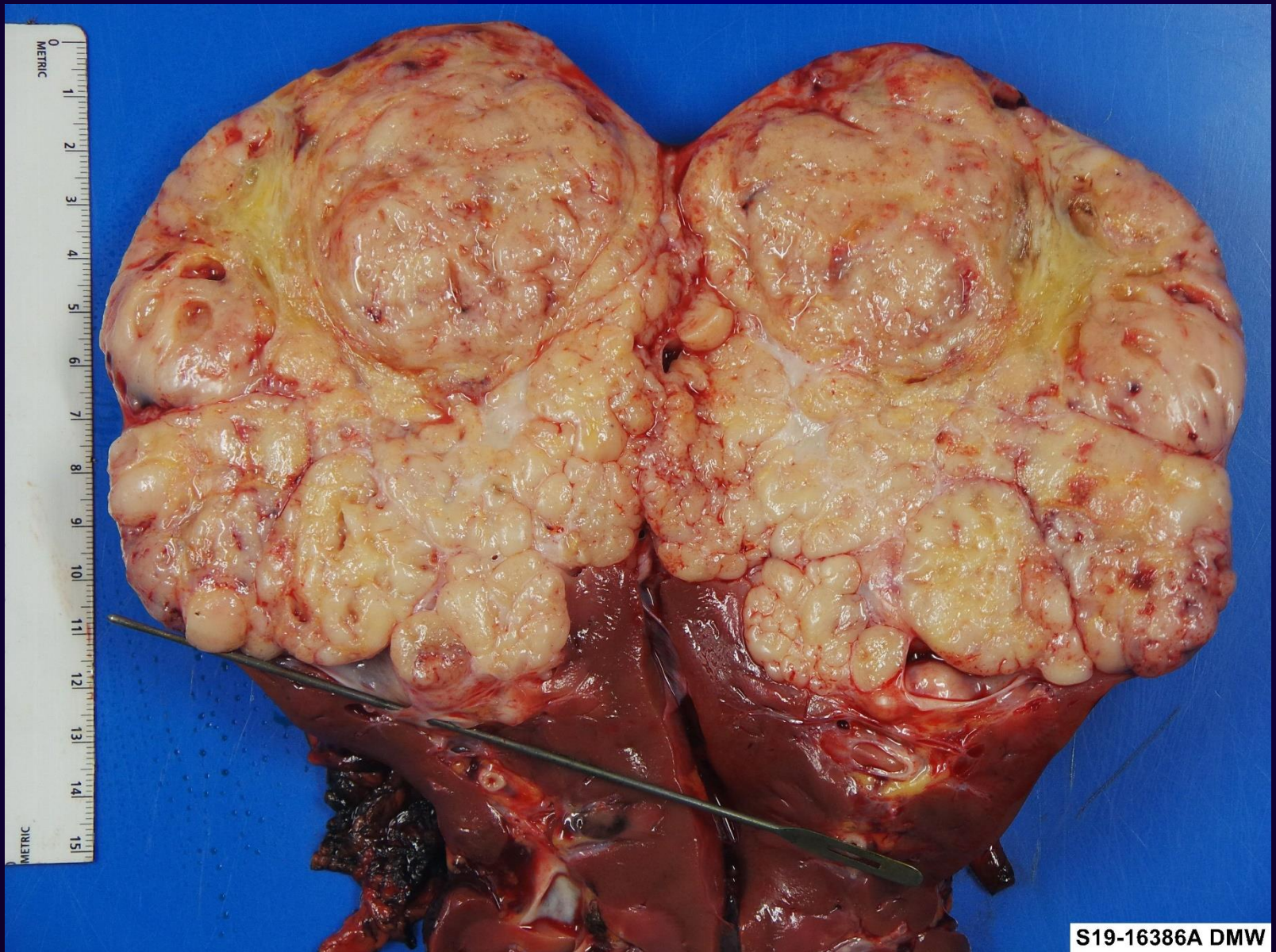
*Papillary RCC Type 1*



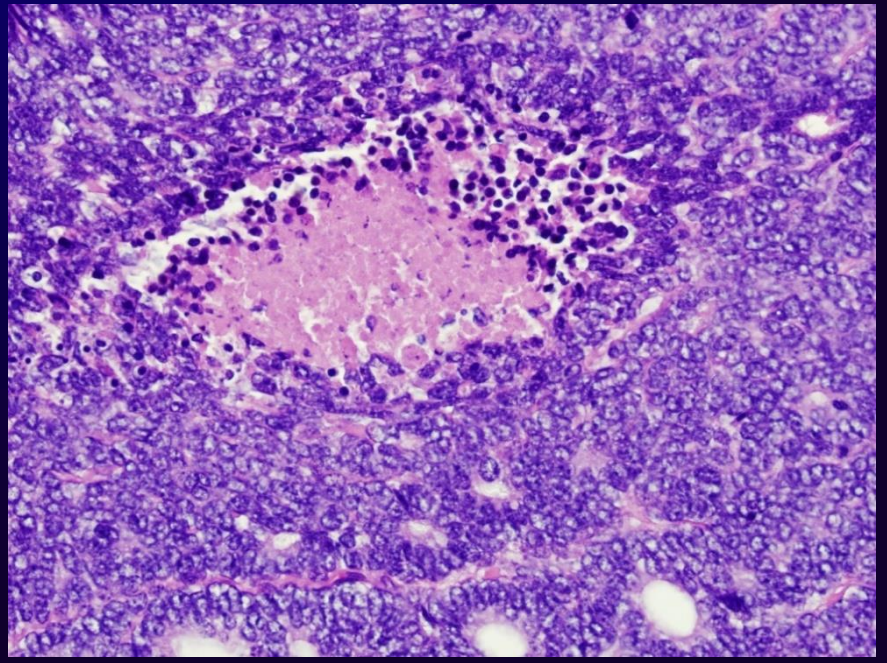
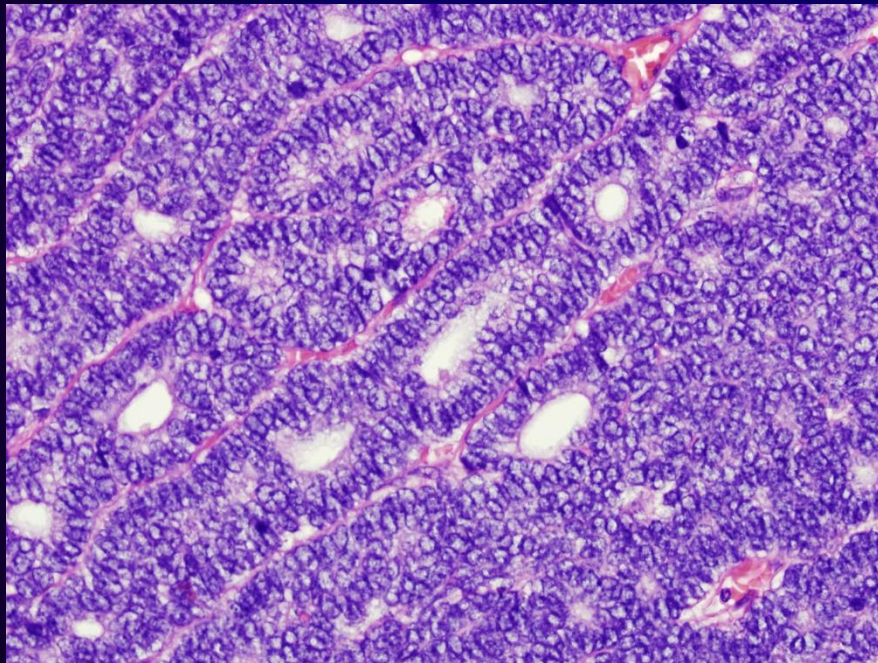
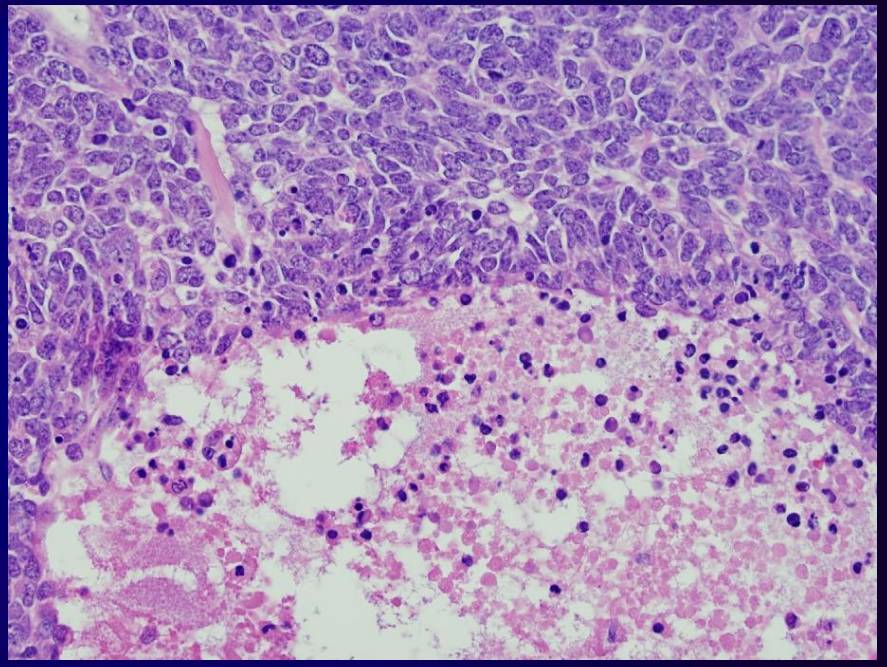
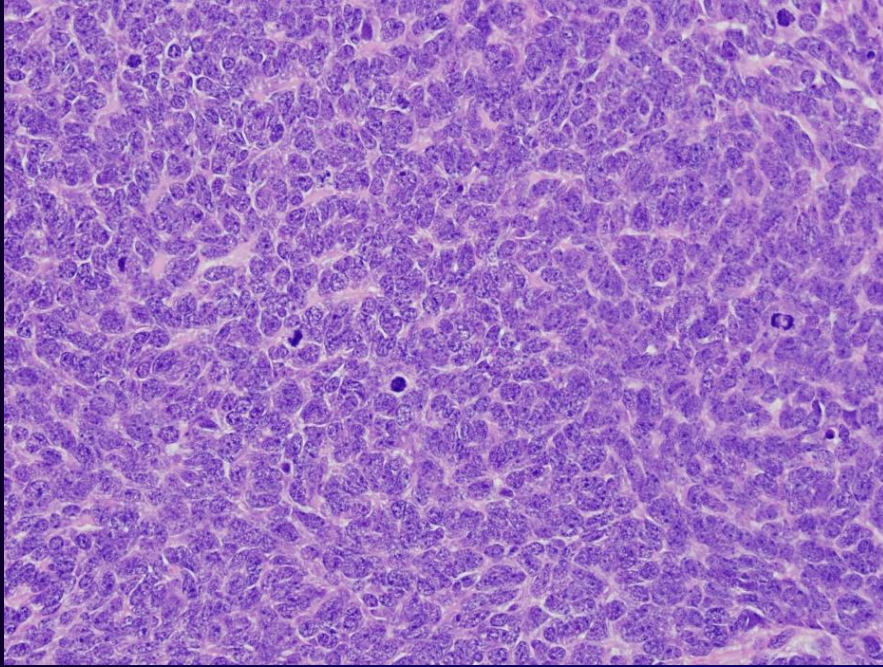
*Adult Wilms tumor*

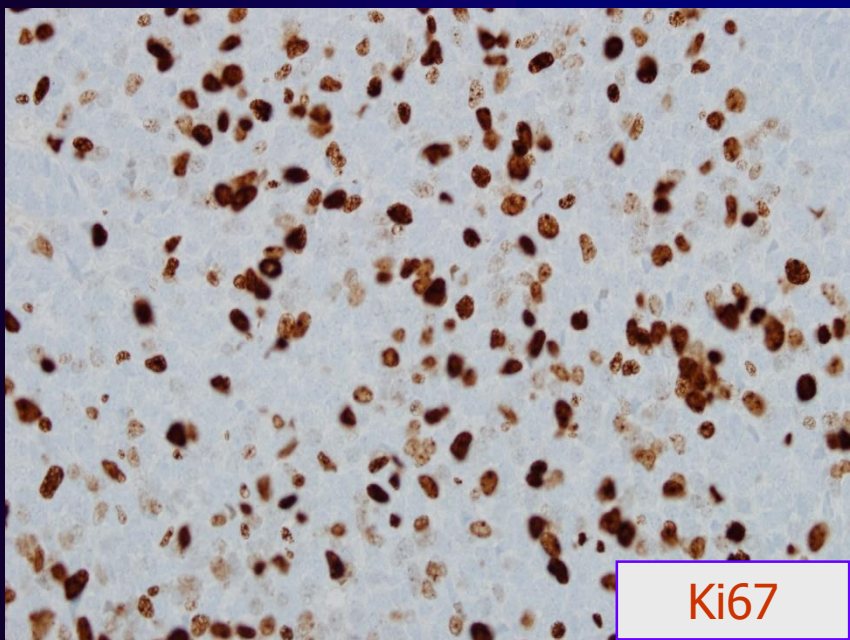
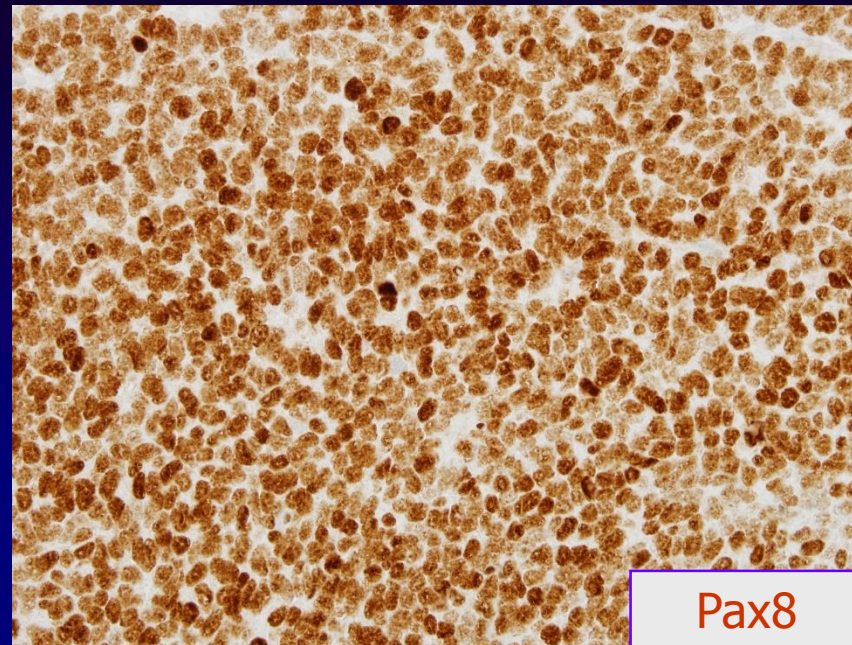
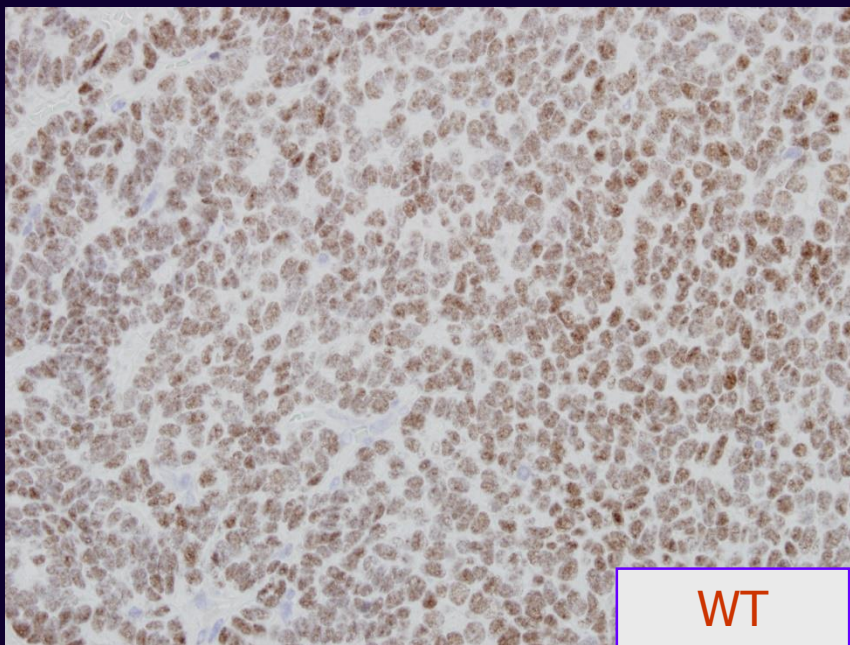


# Case 5. 39-year-old female



S19-16386A DMW





# Wilms tumor (nephroblastoma)

- Wilms tumor is the most common type of renal malignancy in pediatric patients (1/10,000)
- Deletion of WT1 gene (11p3)
- Histology, three components:
  - Blastimal
  - Epithelial
  - Stromal
- Loss of heterozygosity for chromosomes 1p and 16q adverse prognostic factor
- WT rare in adults
- Wilms tumors in adults generally with poor prognosis (35% vs 85% 5 y survival)



# Wilms tumor and syndromes

The syndromes predisposing to WT

1. WAGR (Wilms tumour, aniridia, genitourinary abnormalities and mental retardation)
2. Denys-Drash syndrome (DDS): mesangial sclerosis, male pseudohermaphroditism and Wilms tumours
3. Beckwith-Weideman (BWS): exomphalos, macroglossia, gigantism
4. Simpson Golabi Behemel syndrome (SGBS): overgrowth, mental impairment, craniofacial anomalies

# Iceland



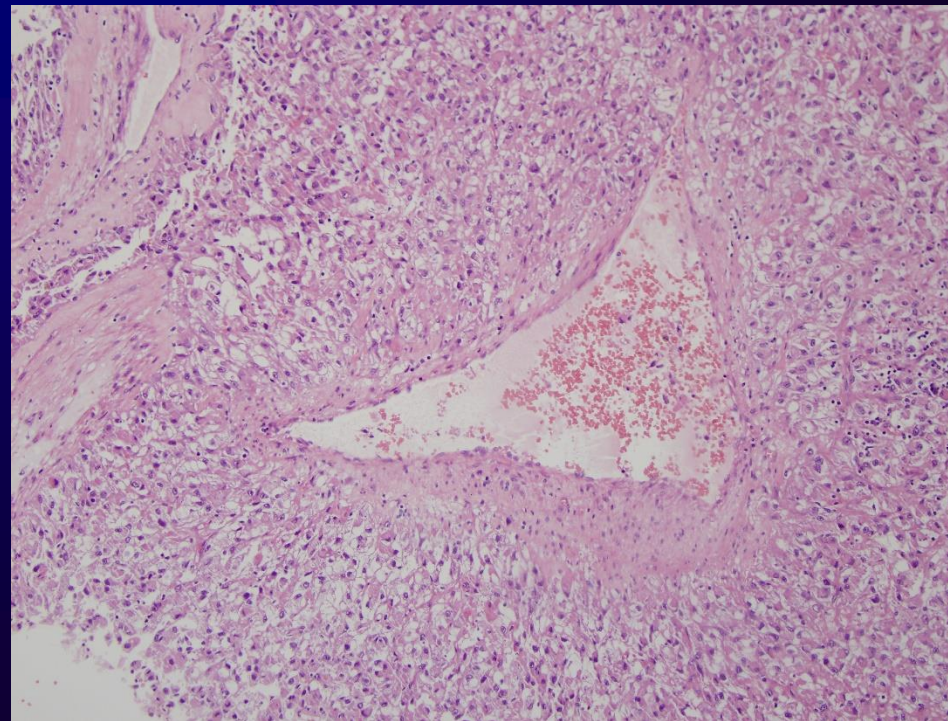
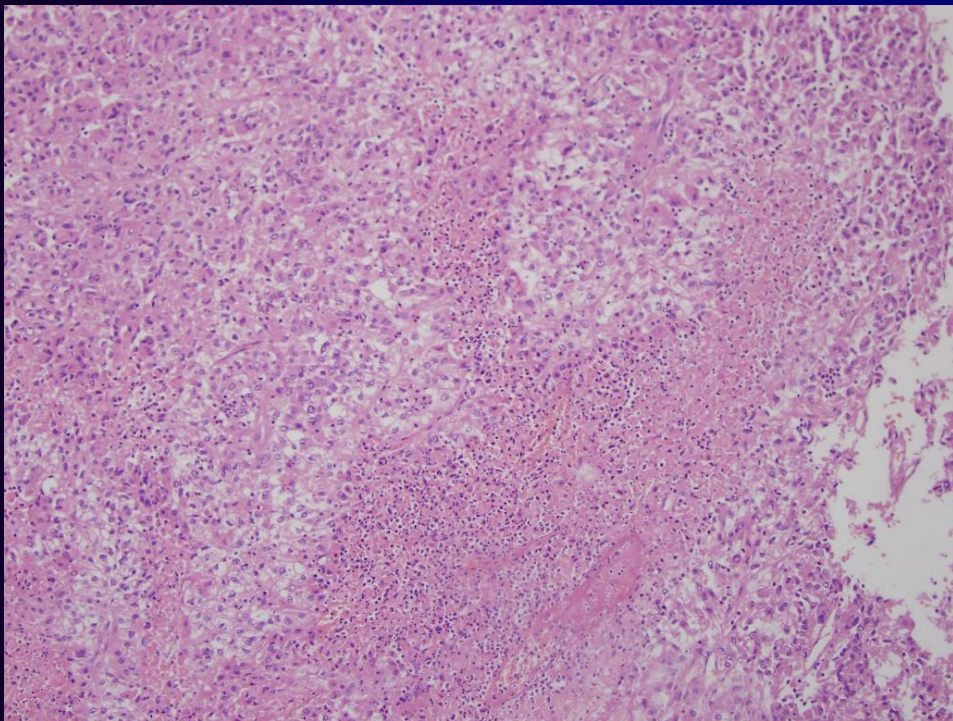
*Jimmy Yang*

# Case 6. Renal Mass

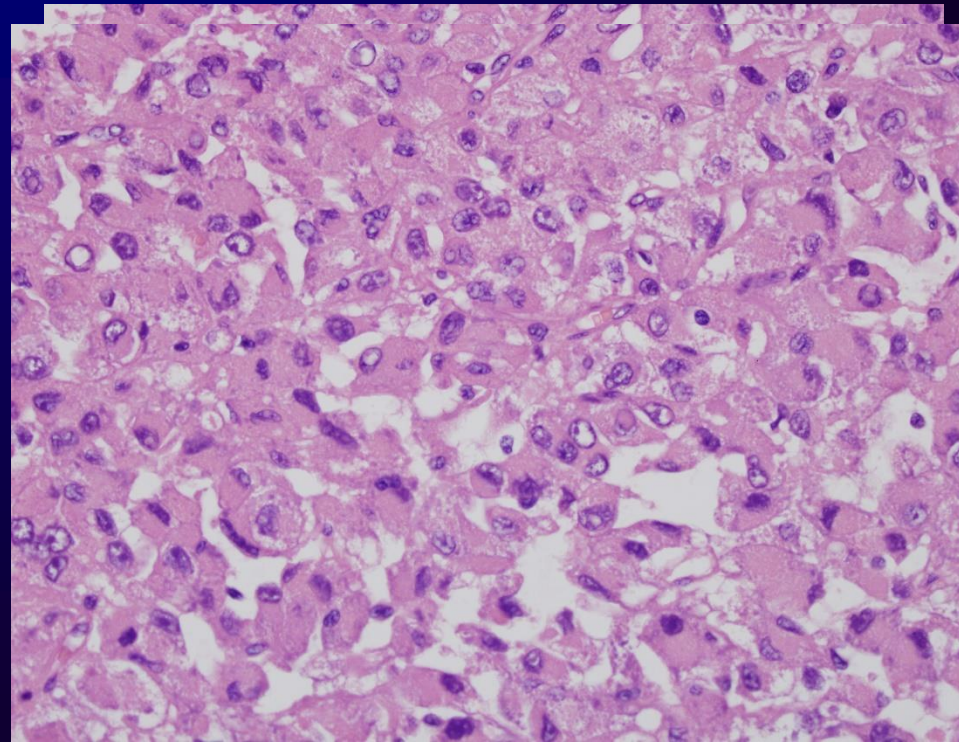
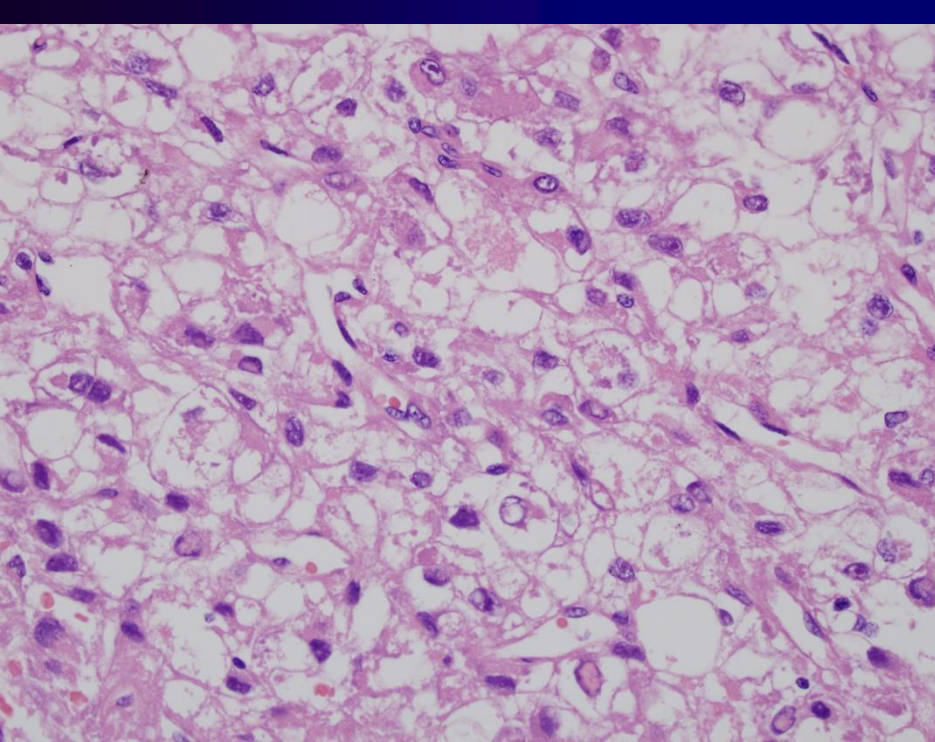
- 37 year old female
- Large renal mass, replacing entire kidney
- Yellow cut surface with hemorrhage and necrosis

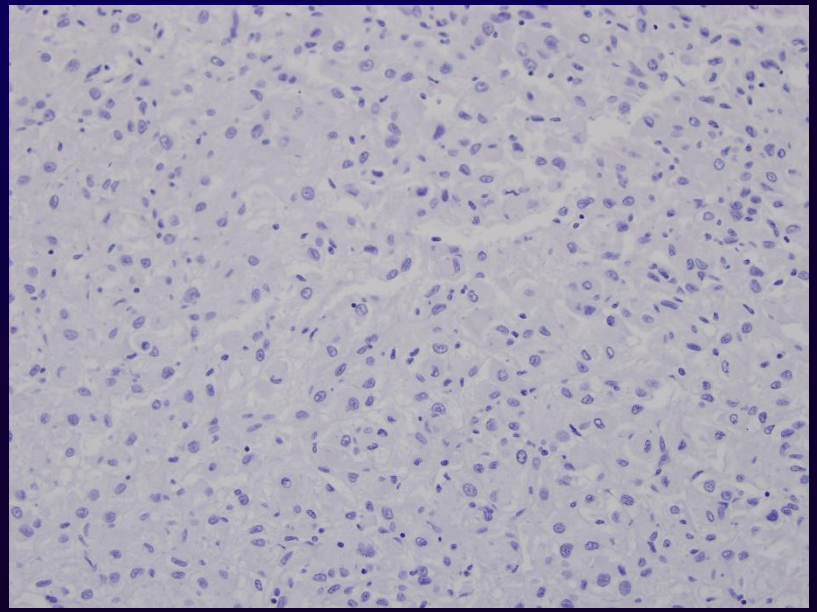
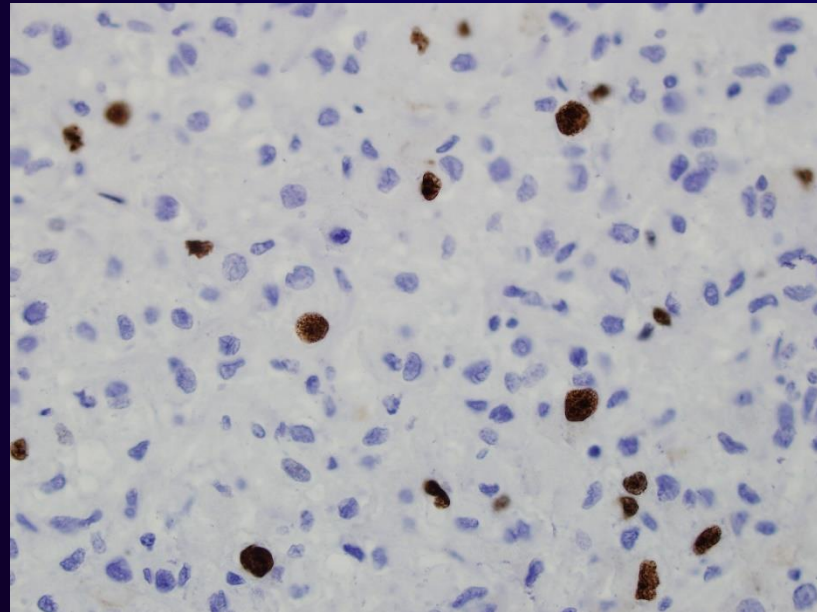
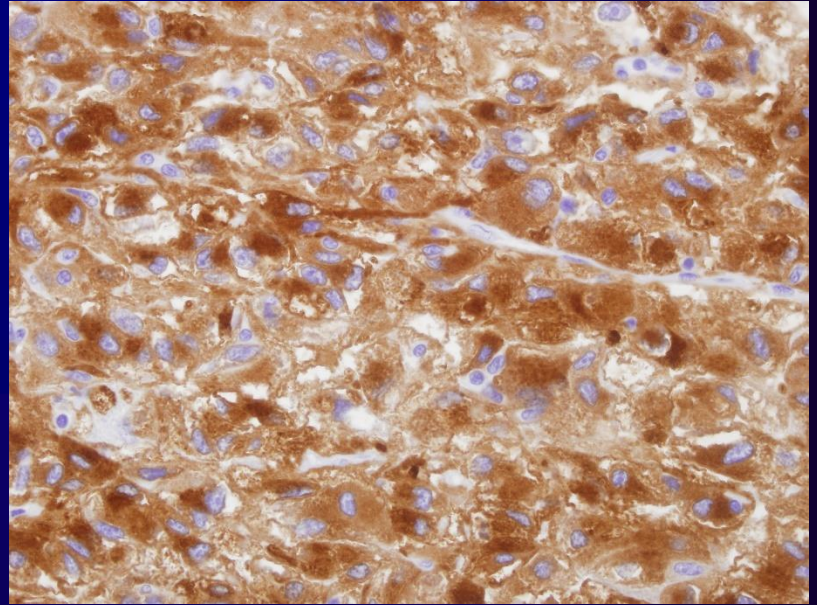
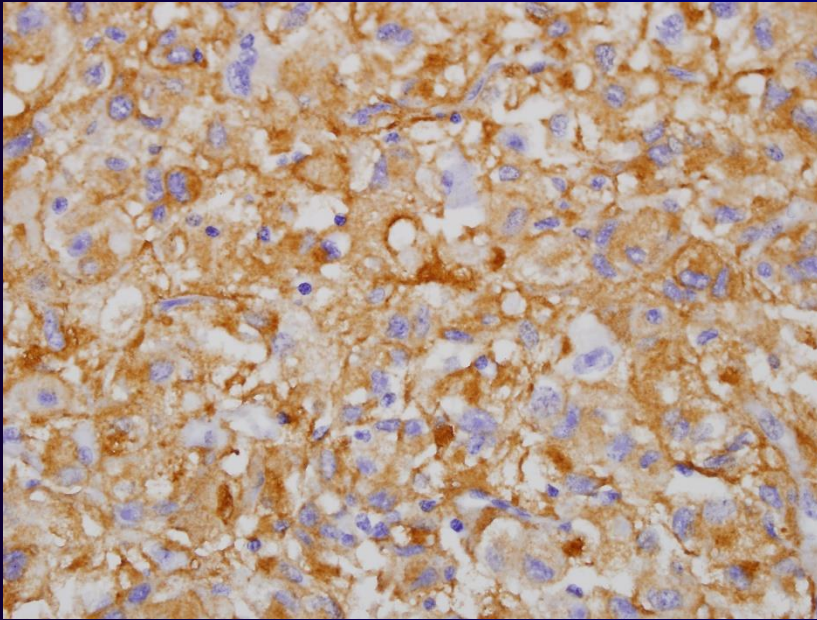


# Close relation to vessels



# Mimicking RCC





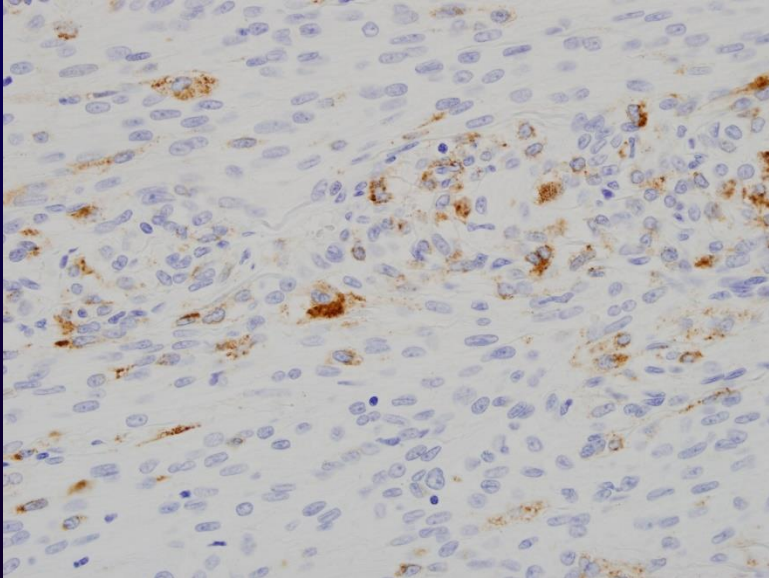
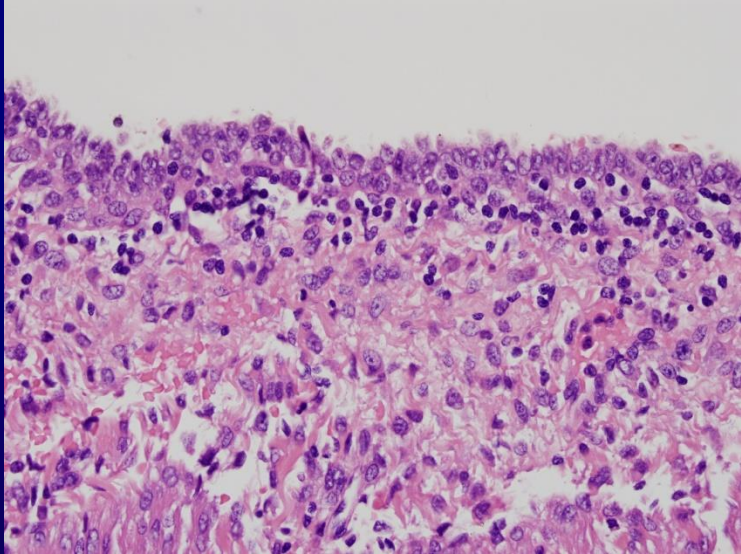
# Diagnosis

## Epithelial Angiomyolipoma

### High risk for aggressive behavior

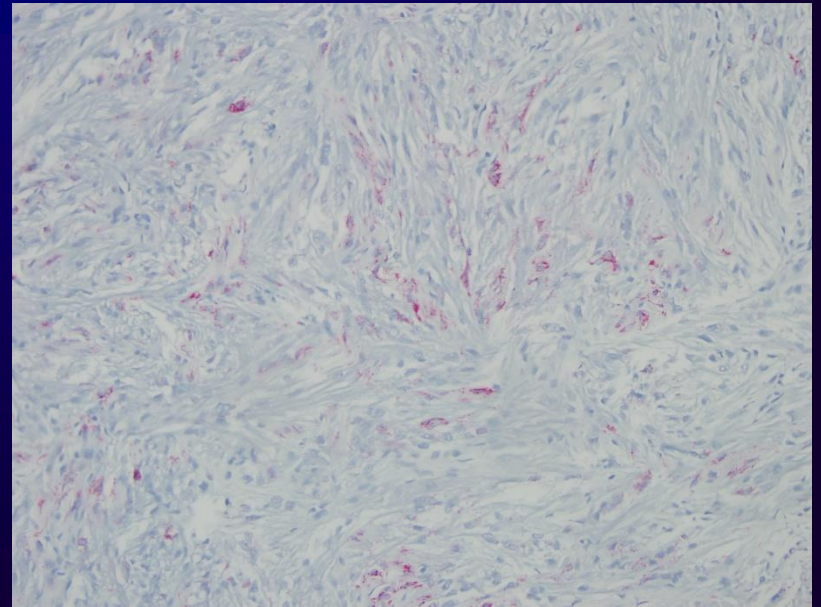
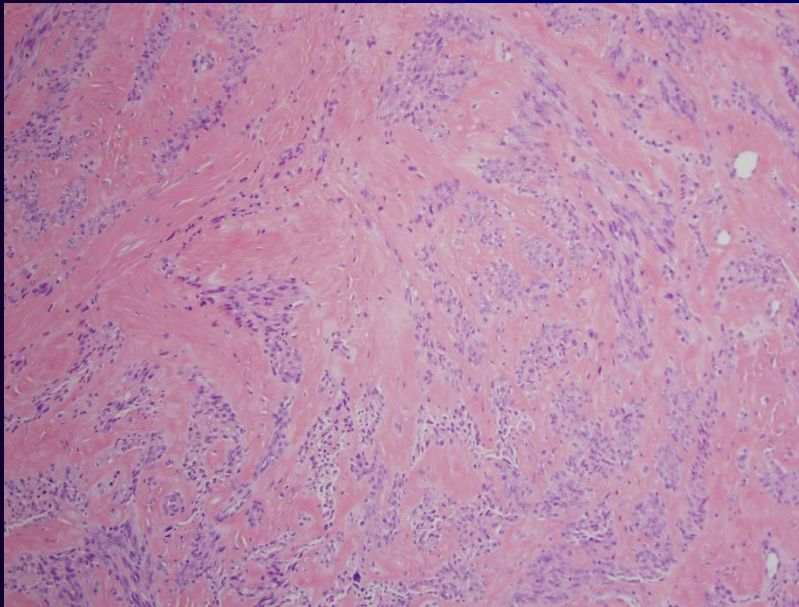
- Greater > 7 cm
- >90% epithelioid tumor cells
- Necrosis
- Invasion
- High mitotic activity

# Cystic AML

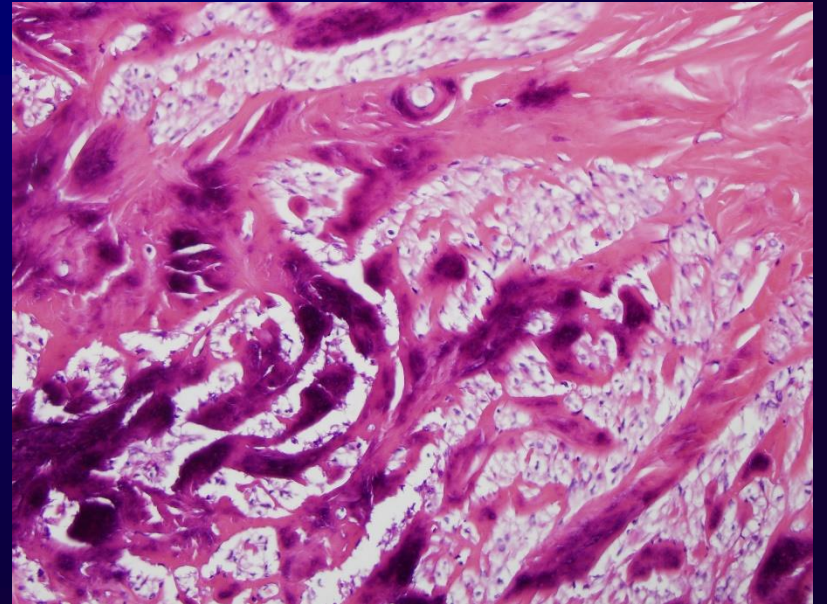
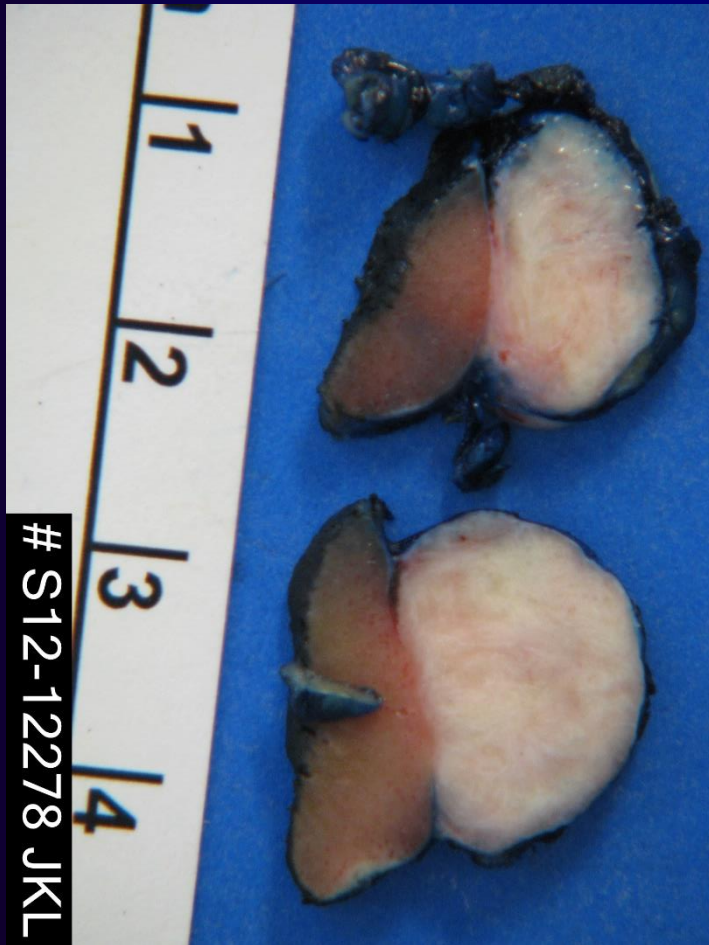




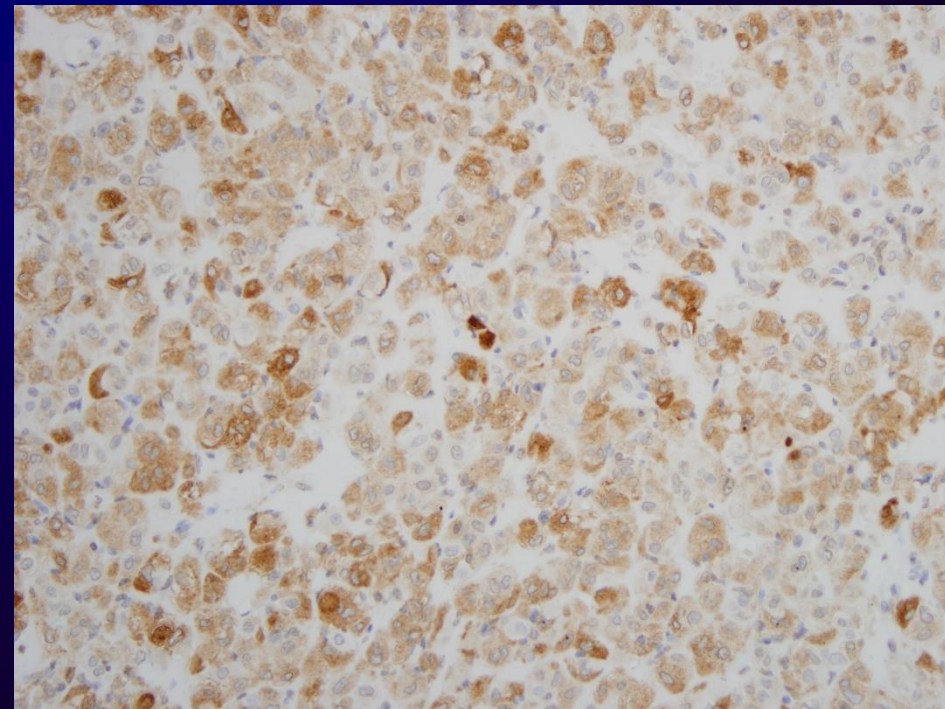
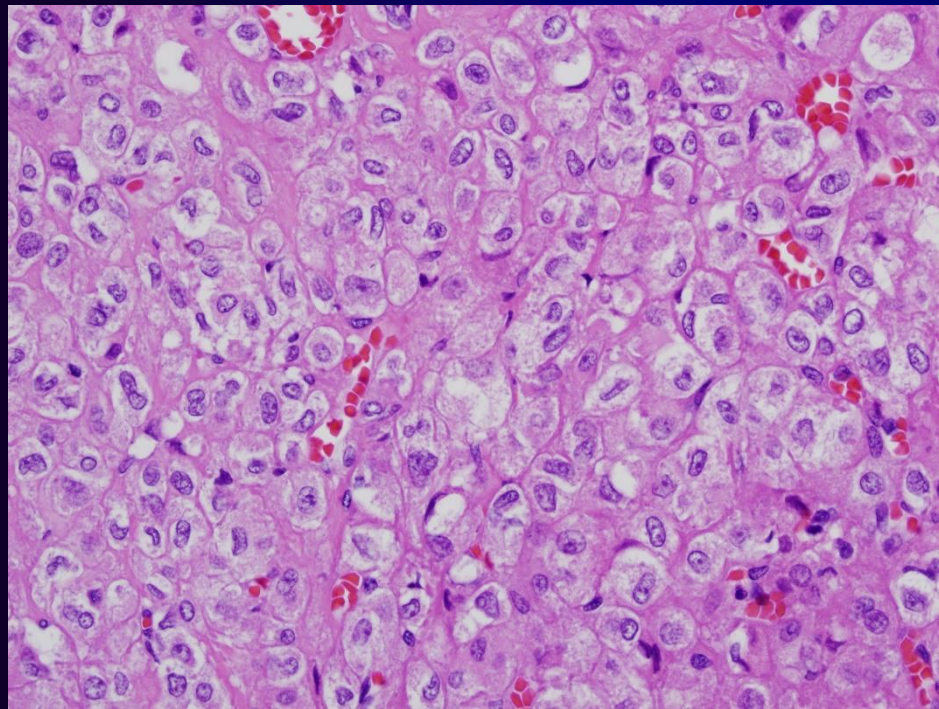
# Monophasic (fat poor) AML



# Hyalinized AML



# Epithelioid AML



# Controversy on Epithelioid AML

- All malignant (AFIP fascicle by Grignon)
- Very low risk for malignancy, 15/194 (7.7%) epithelioid AML, none had recurrence or metastasis – Cleveland
- Very low risk for malignancy, 20/437 epithelioid AML, one develop metastasis –MSK, Mayo and MGH

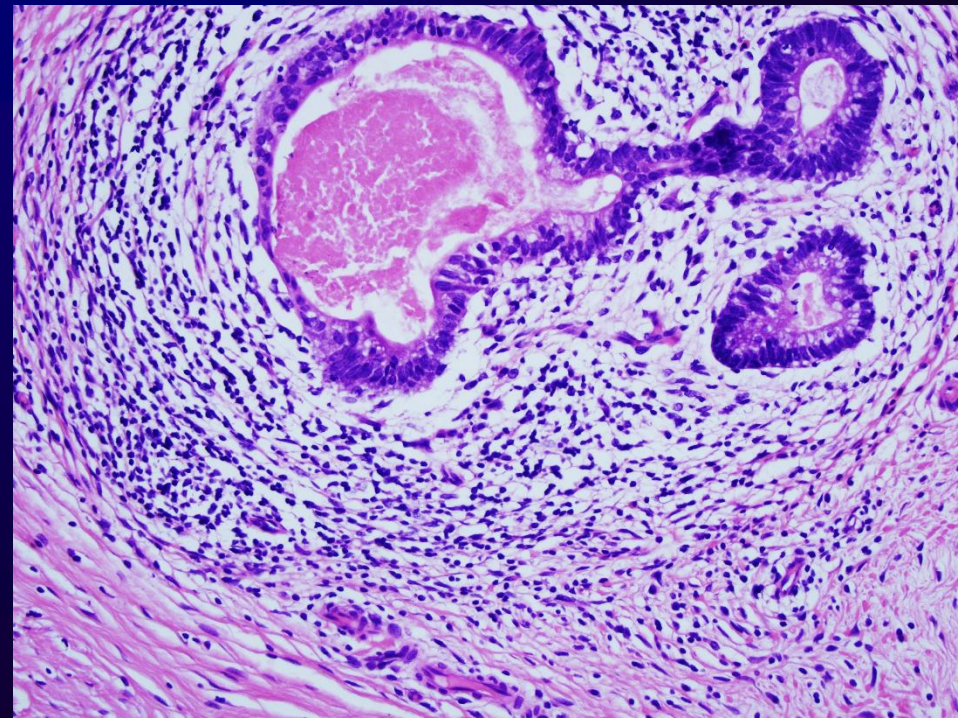
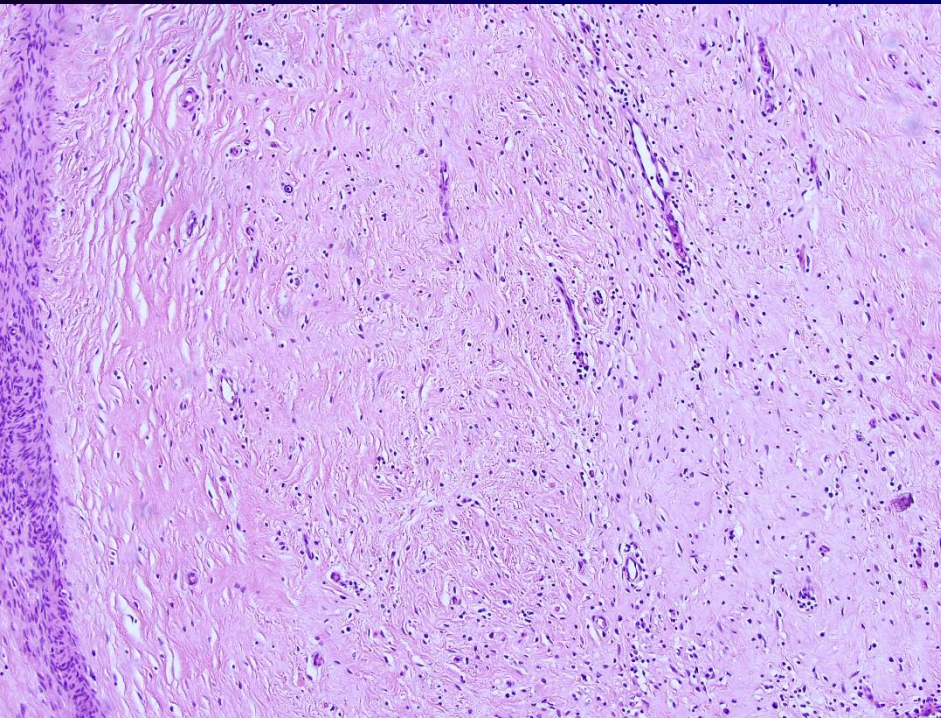
# Pure Epithelioid PEComas

## Epithelioid AML

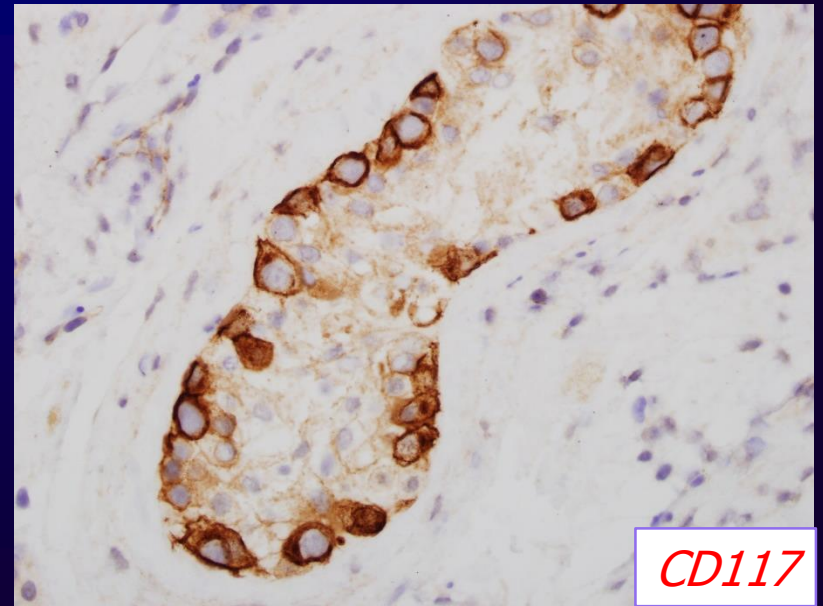
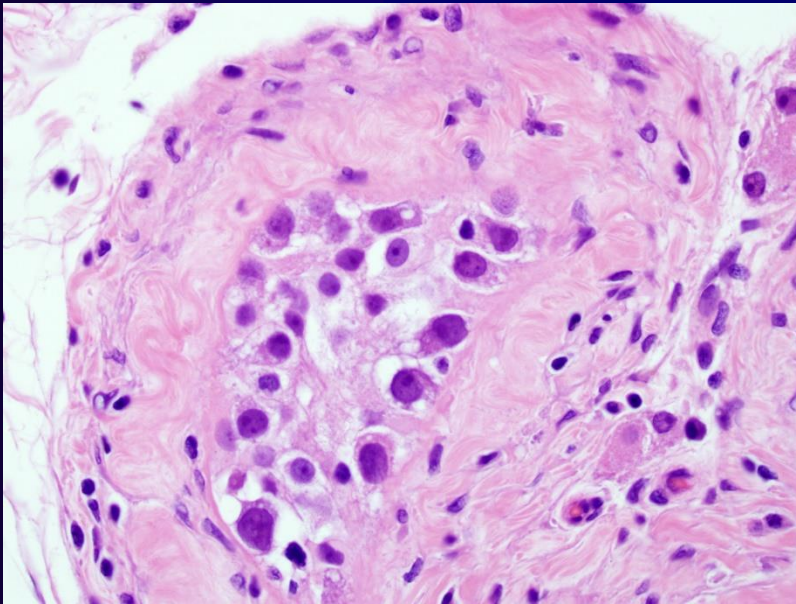
### Amin and others

- 41 Epithelioid AML
- Recurrence 17%
- Metastasis 49%
- Death 33%
- **Risk factors**
  - Necrosis
  - Tumor size > 7 cm
  - Carcinoma like growth pattern
  - Extrarenal or renal vein invasion

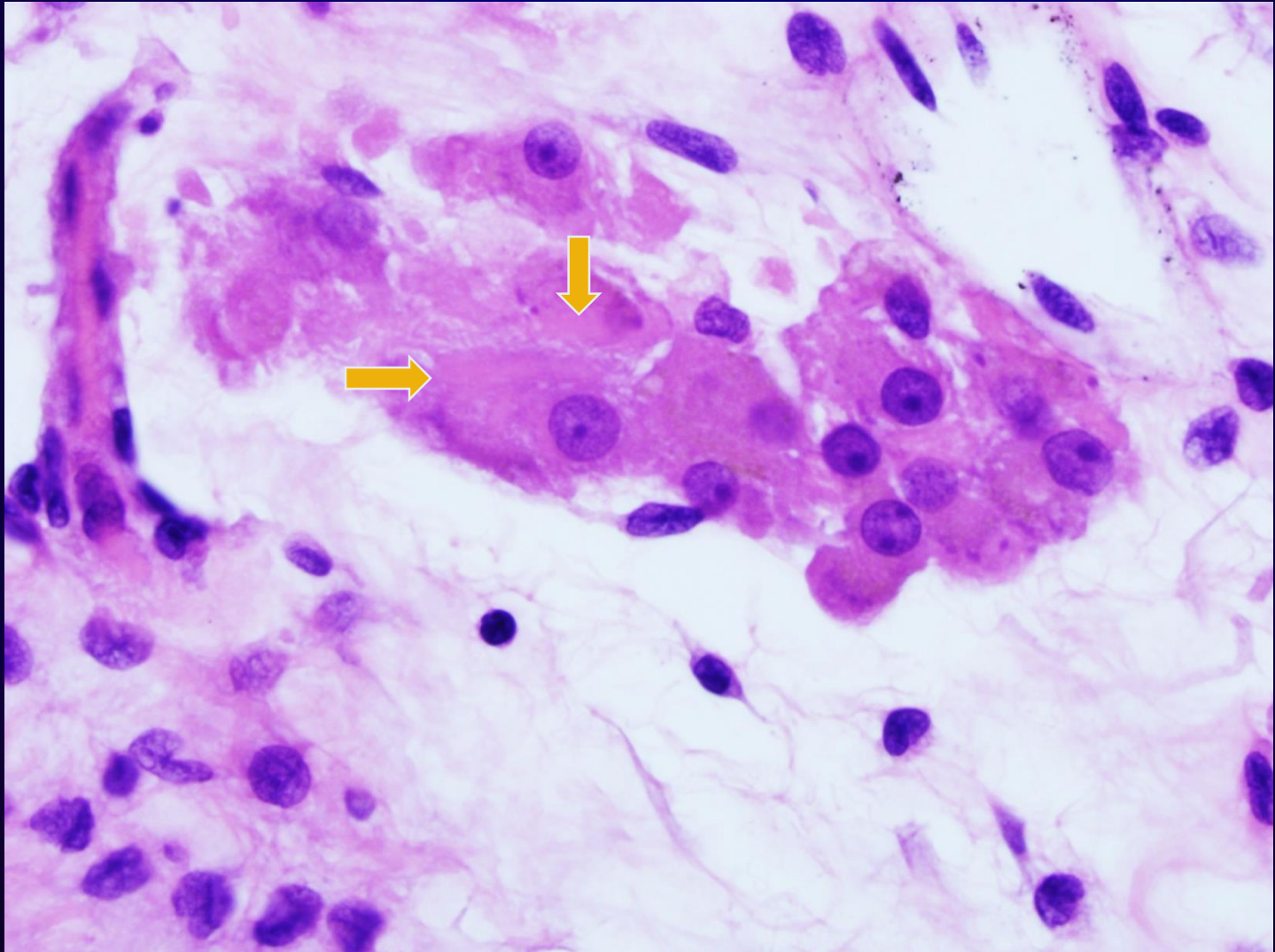
# Case 7. Testicular mass in 37-yo male



# Germ cell neoplasia in situ (Intratubular germ cell neoplasia, unclassified)



# Bonus: Crystals of Reike





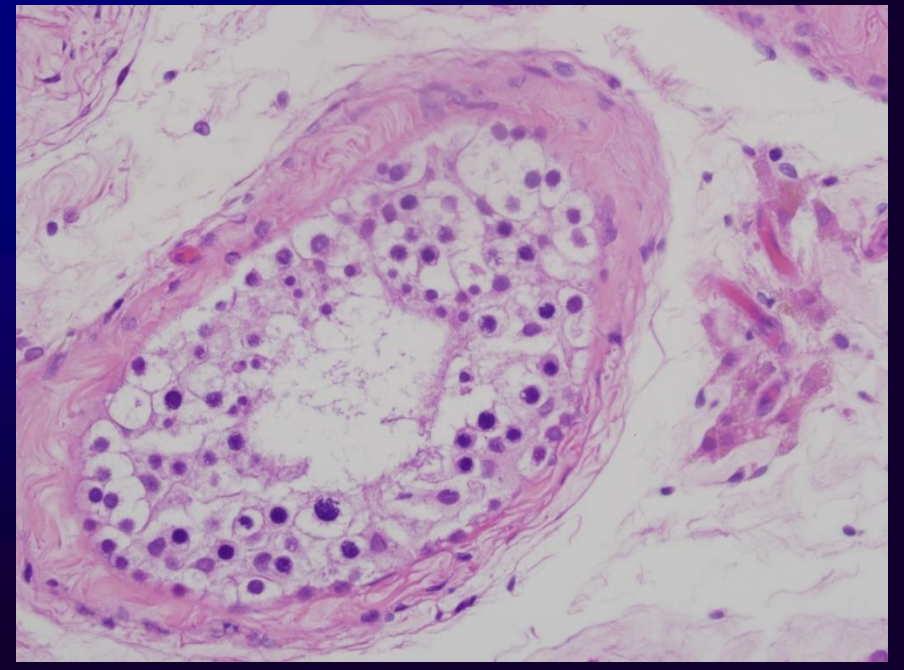
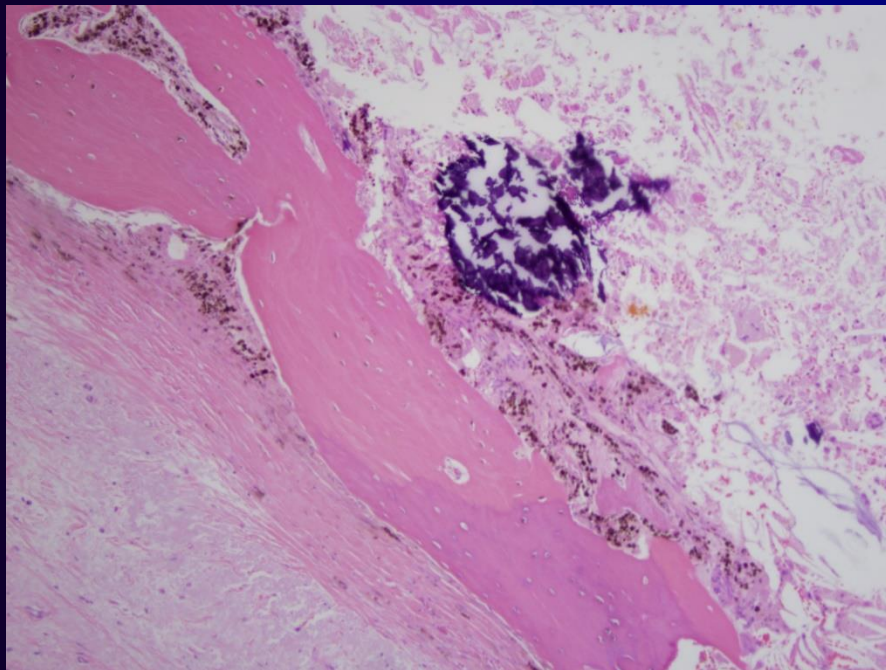
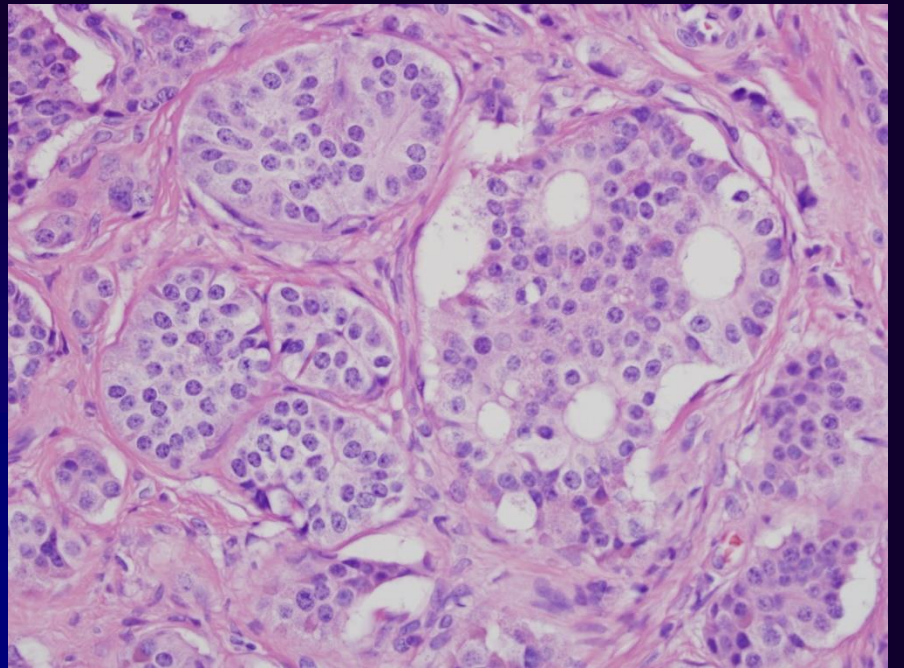
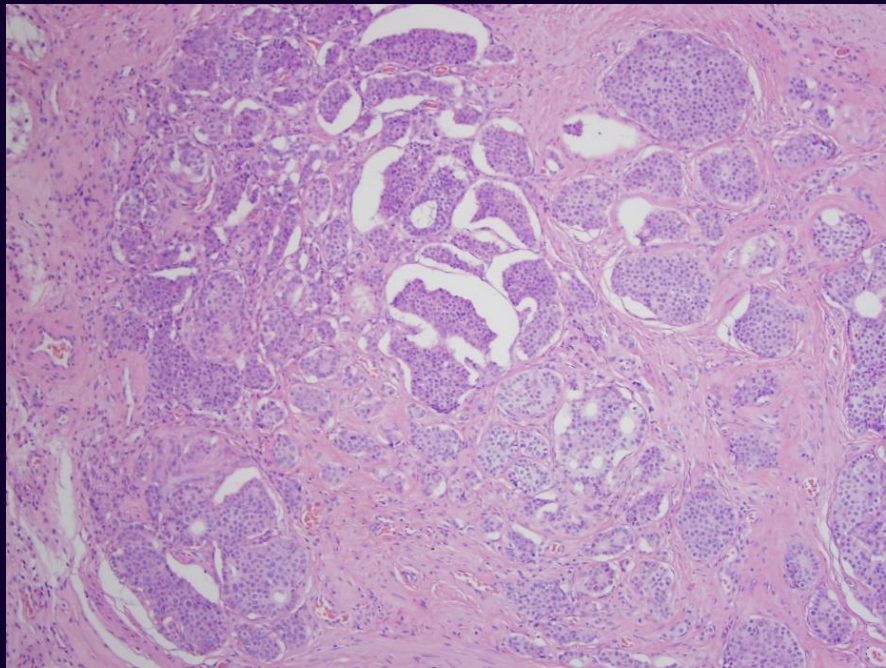
# Case 7. Our Diagnosis

- Malignant germ cell tumor of the testis, composed of mature teratoma (regressed germ cell tumor)
  - Portion of viable teratoma
  - With extensive necrosis and degenerative changes (partially burnt-out)

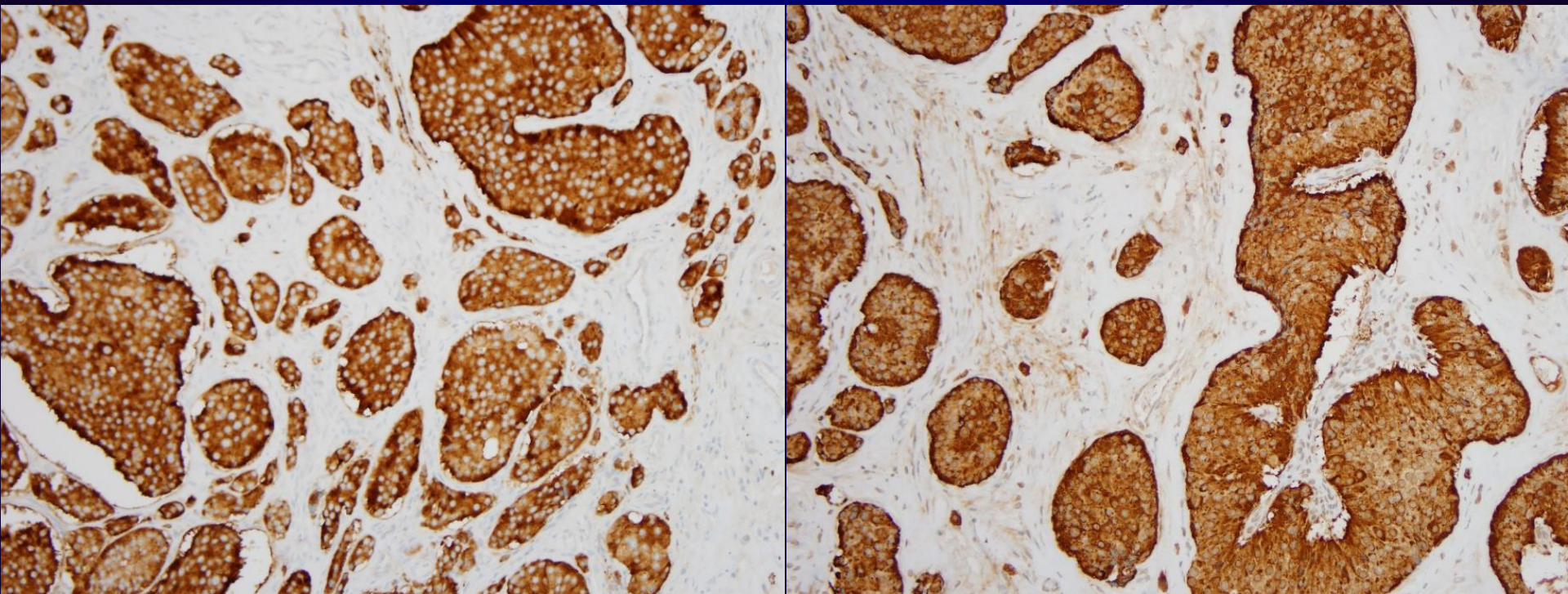
# Case 8. Testicular mass

- 35-year man
- Incidental finding of a testicular mass
- Grossly, a 1.5 cm mass with necrotic areas





# IHC profile



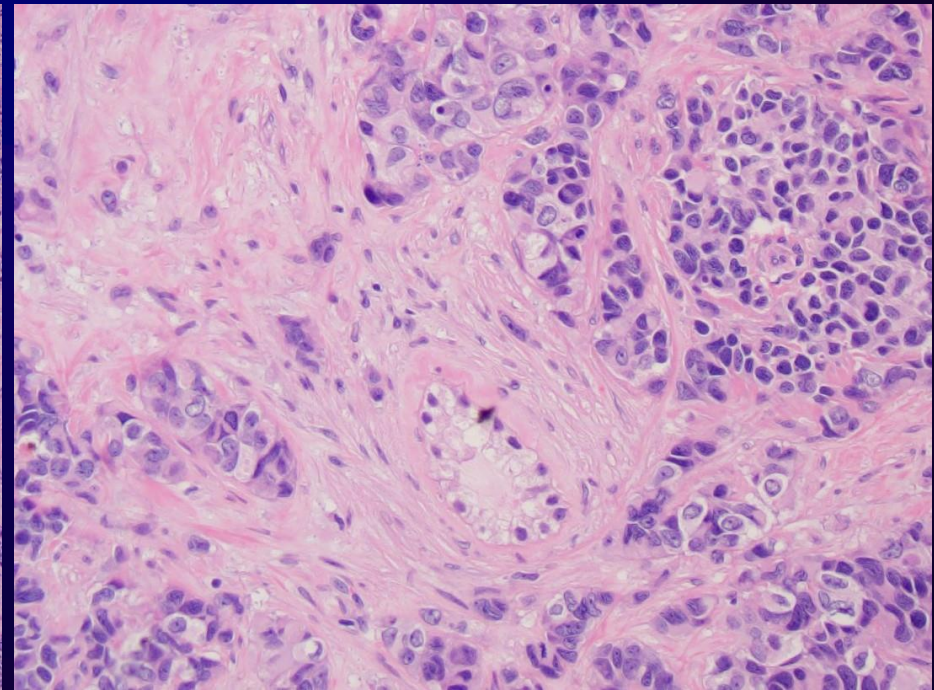
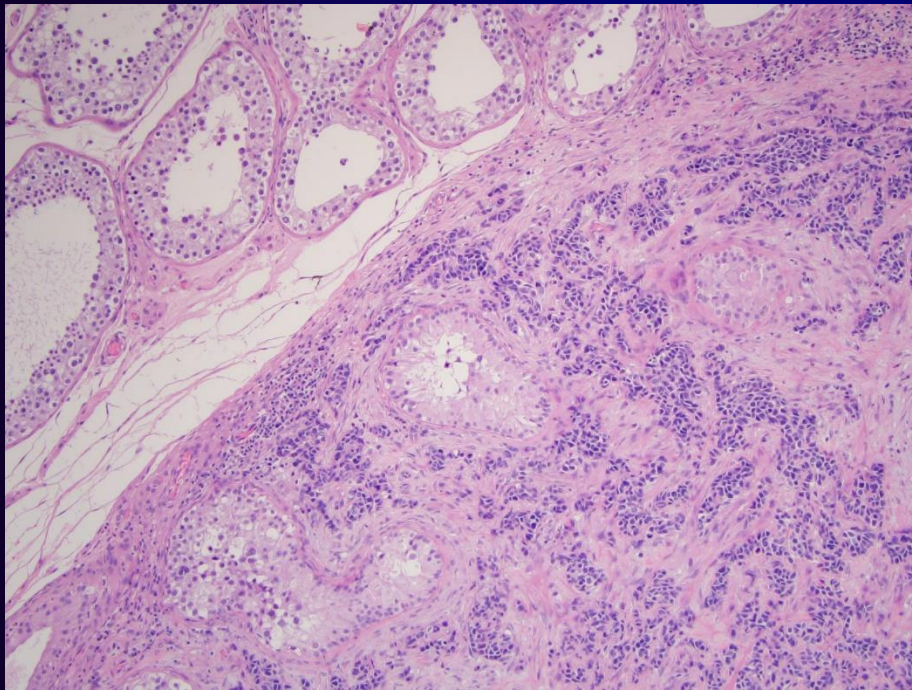
# Our Diagnosis: Well-differentiated neuroendocrine tumor (carcinoid)

- Belongs to teratoma, prepubertal type
- Risk for metastatic disease (10-15%)
- No germ cell neoplasia in situ identified by histology and IHC for OCT-4
- No other viable teratomatous component identified
- Areas of necrosis could be contributed by “burnt out tumor” or dermoid cyst

# Testicular Teratomas (WHO)

	Teratoma, Postpubertal type	Teratoma, Prepubertal type
Definition	Germ cell tumor	Germ cell tumor
GCN in situ	Yes	No
Histology variants	Mature teratoma	Dermoid cyst, Epidermoid cyst
	Immature teratoma	WD neuroendocrine tumor (carcinoid)
Metastatic risk	High 22-37%	Low Minimal for Epi or Dem cysts 10-15% for carcinoma
Prognosis		Dermoid cyst and epidermoid cyst cured by excision Carcinoid with risk of metastasis
Isochromosome 12p	Present	Not identified
Chemotherapy	Not effective for mature Teratoma	
Surgical resection	For primary and mets after chemo	Surgical resection for cure

# Case 9. 21-year man with testicular mass



# Small Blue Cell Tumor

## Differential Diagnosis

- PNET
- Germ cell tumor
- Sarcoma
- Small cell carcinoma
- **Desmoplastic small round cell tumor**
- Prostatic adenocarcinoma, Gleason 5
- Lymphoma
- Melanoma

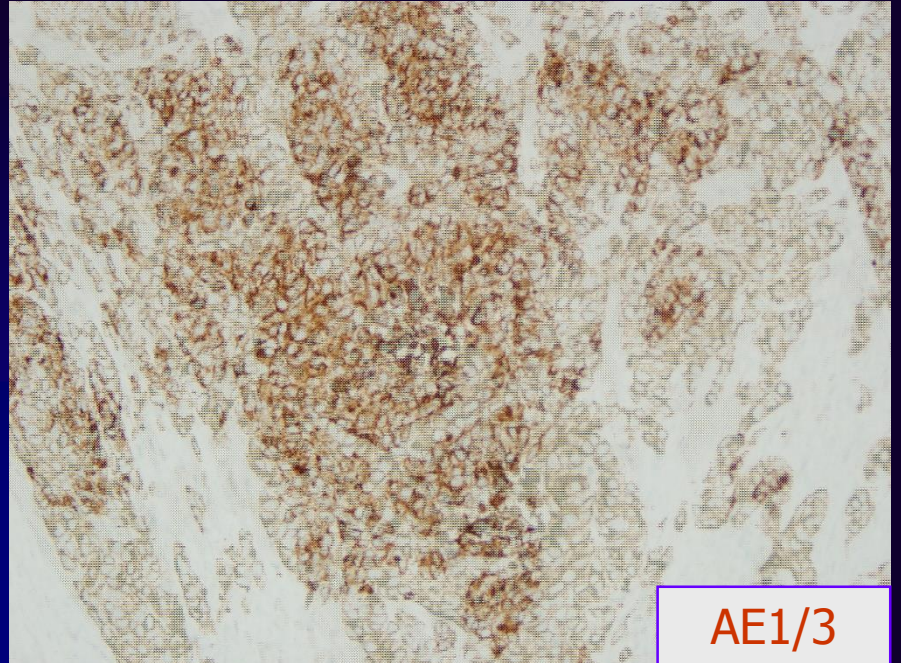
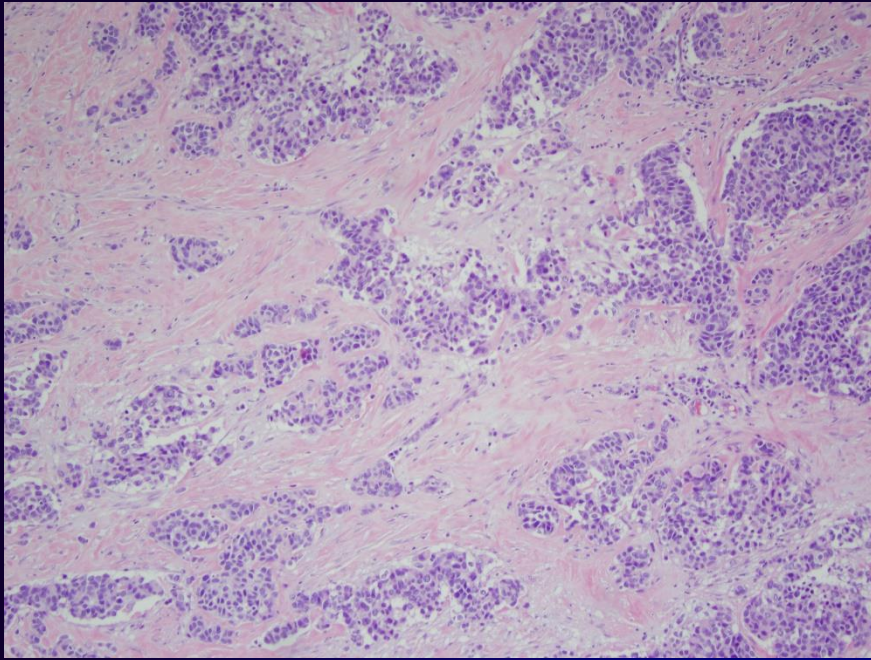


# Case 9. Desmoplastic Small Round Cell Tumor (DSRCT)

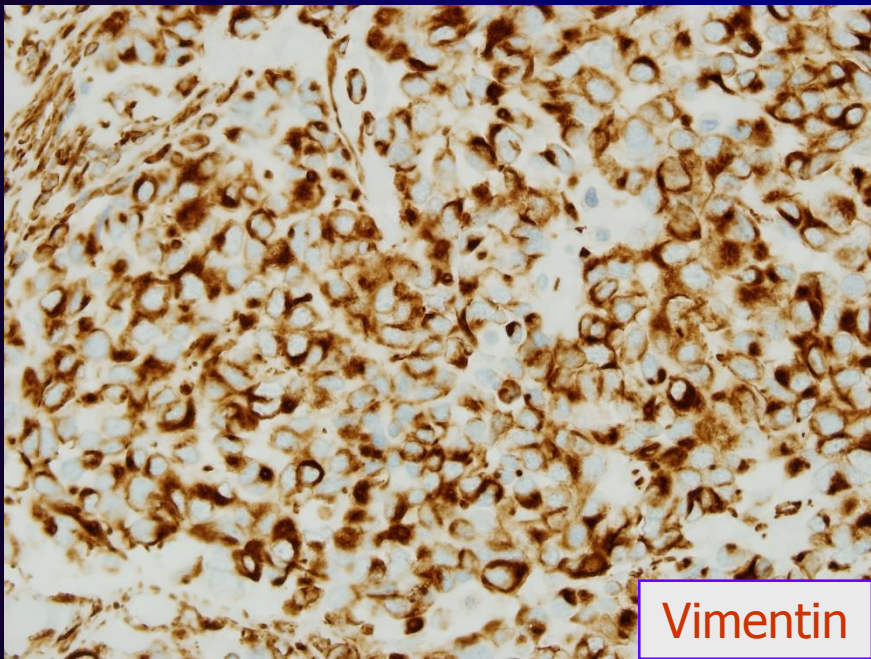
- A primitive malignant tumor with multi-lineage potentials
- Most in patients younger than 22
- First reported by Gerald & Rosai in 1989
- Usually location in abdominal and pelvic cavity
- Rare in extra abdominal sites, only handful cases reported in testis
- Very prognosis, median survival 17-25 months with aggressive treatment

# DSRCT (continued)

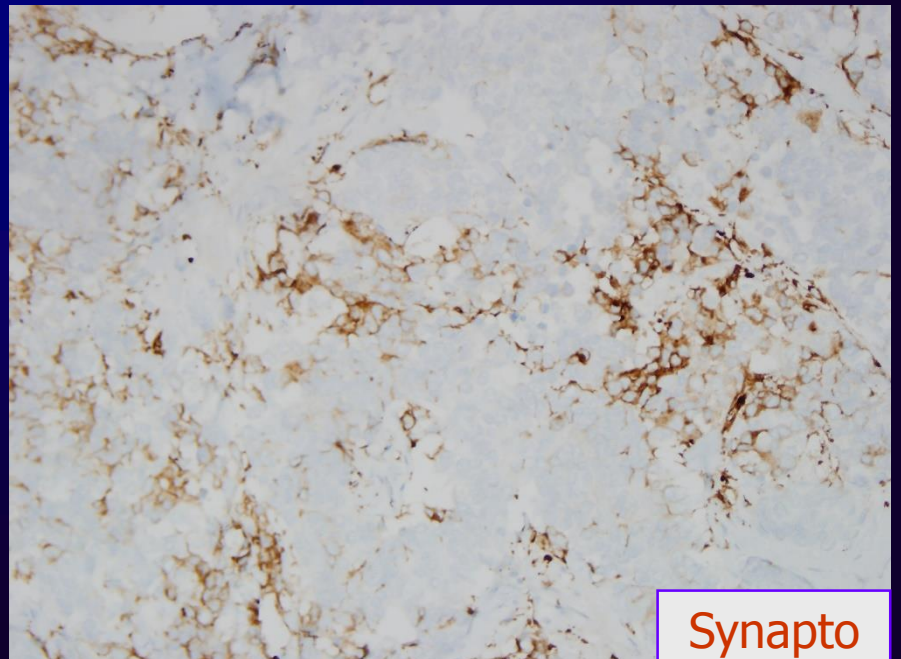
- Histology
  - Small round, ovoid or spindle cells in large or small solid nests
  - Desmoplastic stroma
  - Highly invasive growth
- IHC
  - Epithelial (Keratins), mesenchymal (vimentin), neural (NSE) and
  - Desmin shows distinct punctuate and dots staining
  - WT1 stain positive (focally strong in this case)
- Molecular hallmark EWS-WT1 t (11; 22) (p13; q12) translocation, confirmed in this case



AE1/3



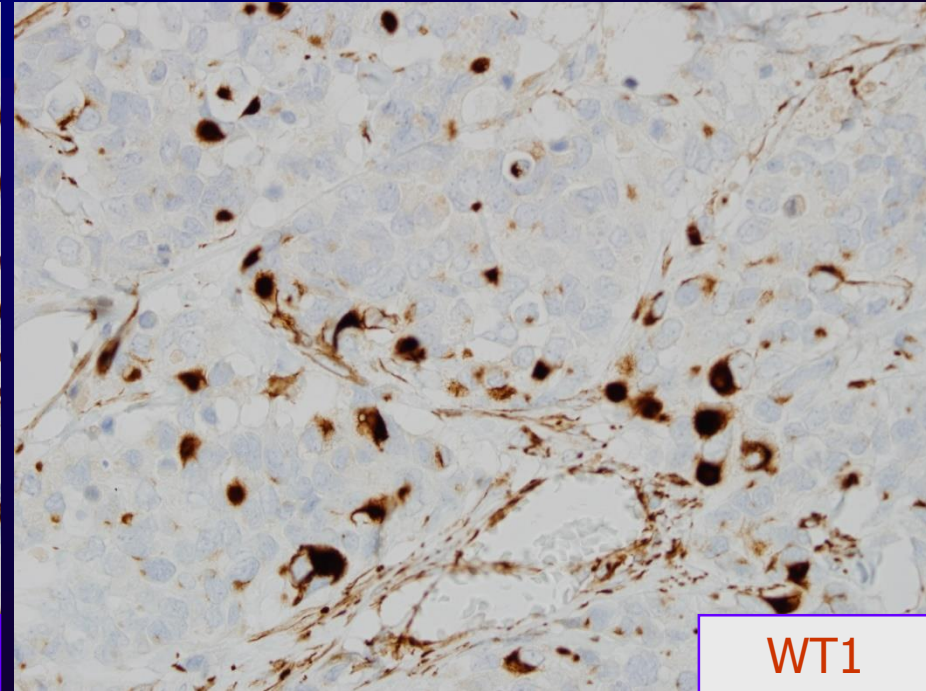
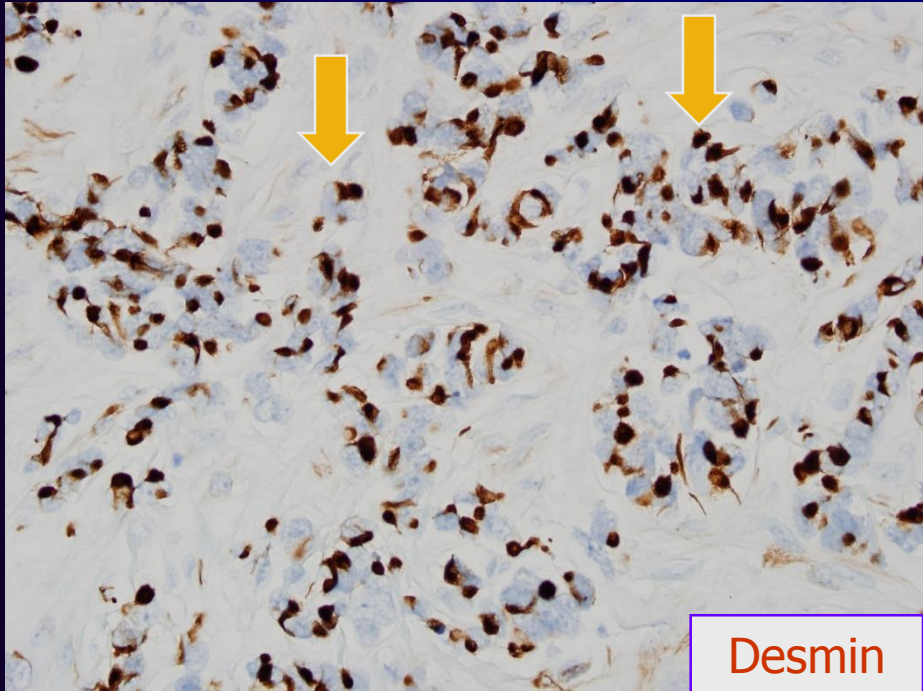
Vimentin



Synapto

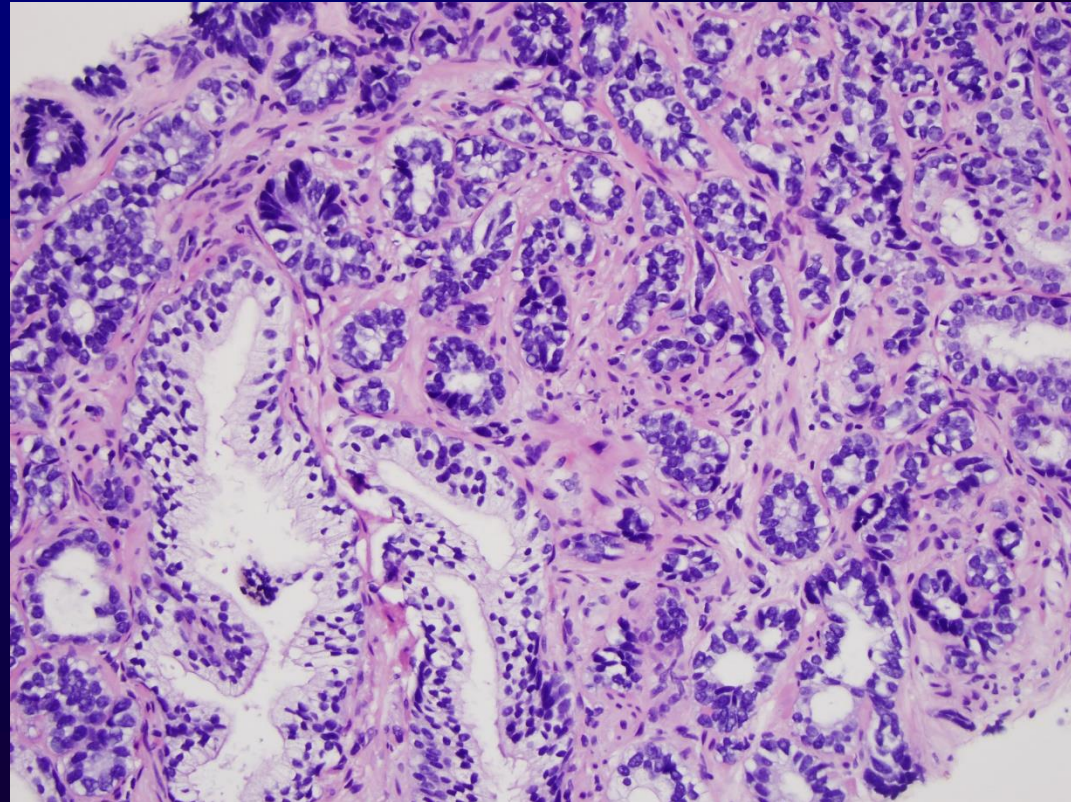
# Special Staining Patterns

*Unique Dotted pattern*



# Case 10. Prostate Lesion

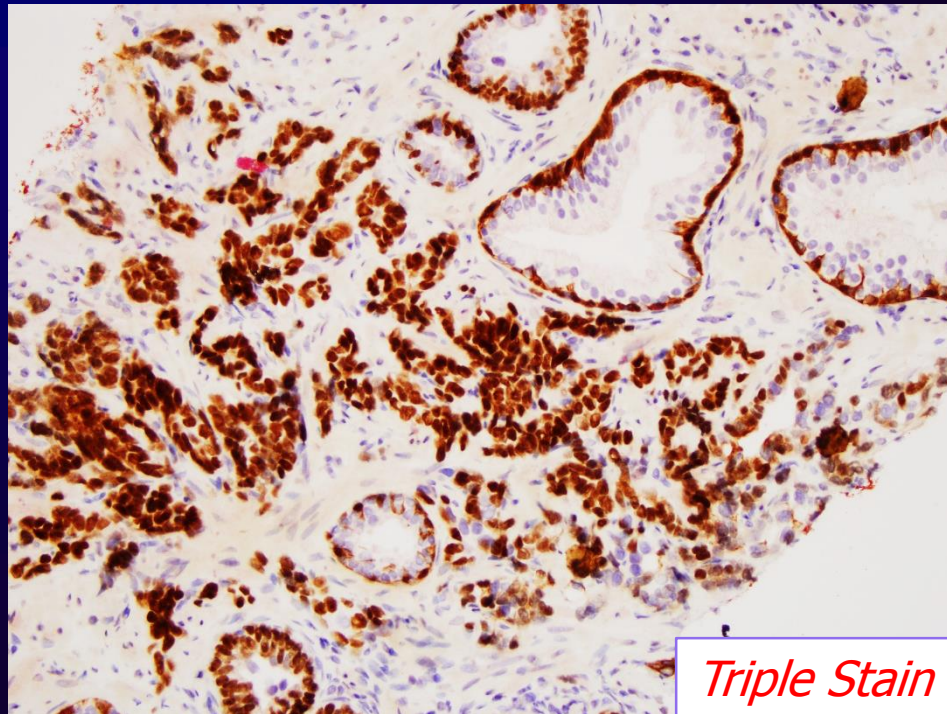
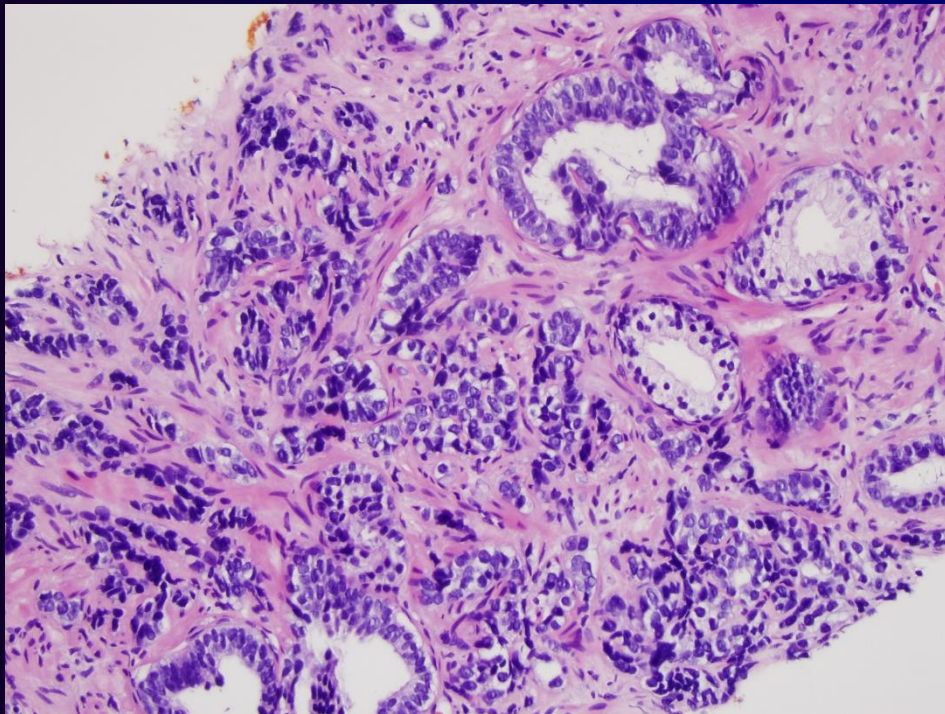
- 65-year-old man
- Mildly elevated serum PSA 5.6
- Underwent needle core biopsy



# Questions

- Your differential diagnosis
- What IHC markers to order?
- A benign, low grade malignancy or high grade malignancy?

# Case 10. Our Diagnosis: Basal cell carcinoma of the prostate

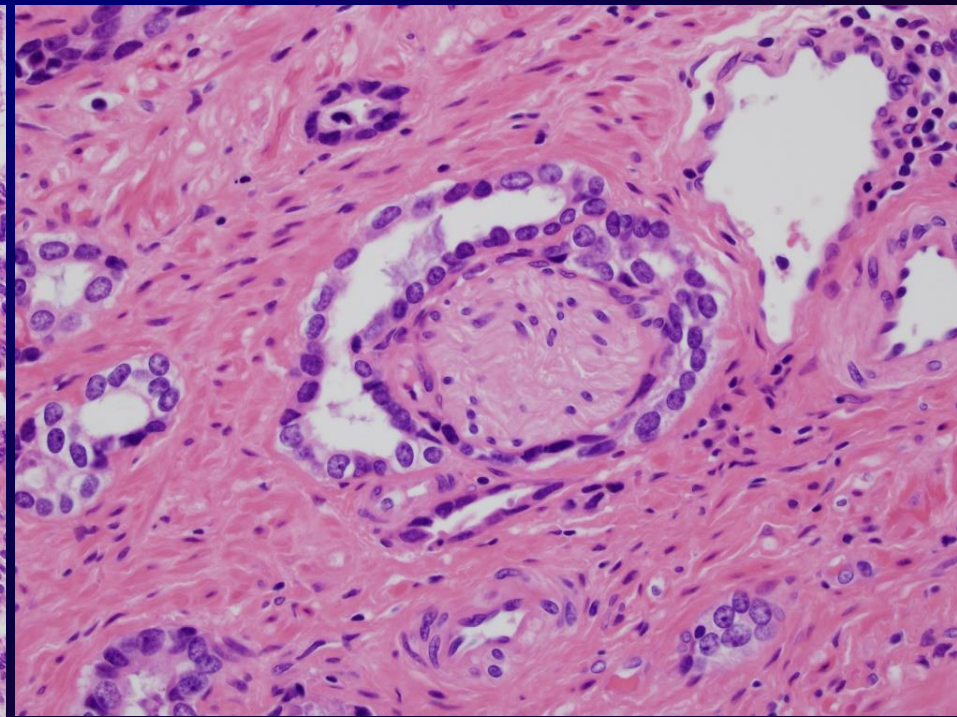
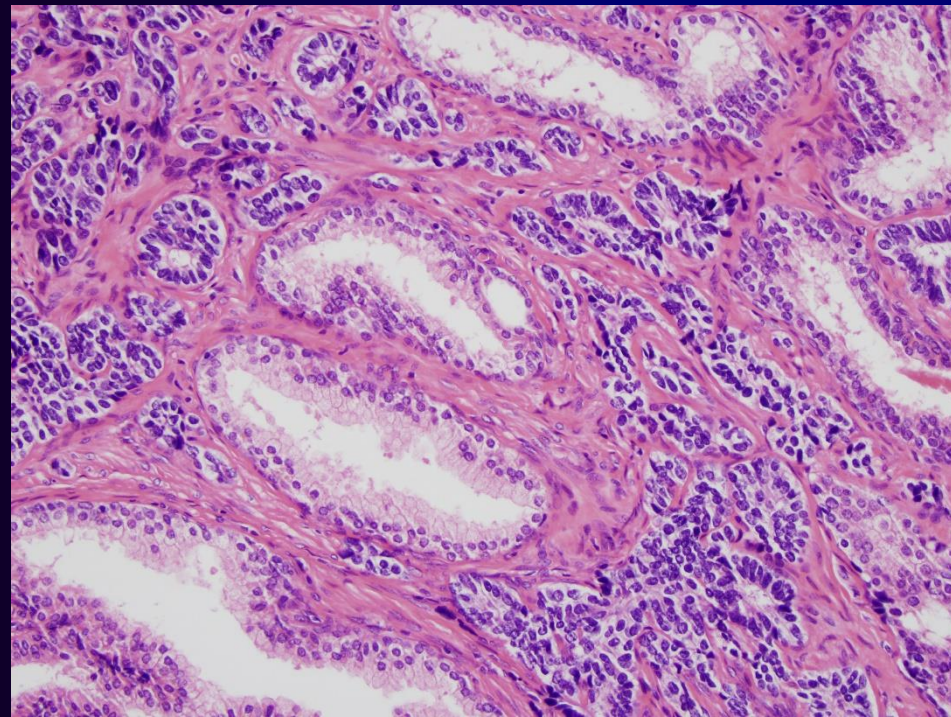


# Clinical course

- Admitted to our hospital
- A bone lesion was identified by bone scan
- Question whether he has metastatic disease in bone
- Eventually metastasis was excluded
- Robotic prostatectomy performed



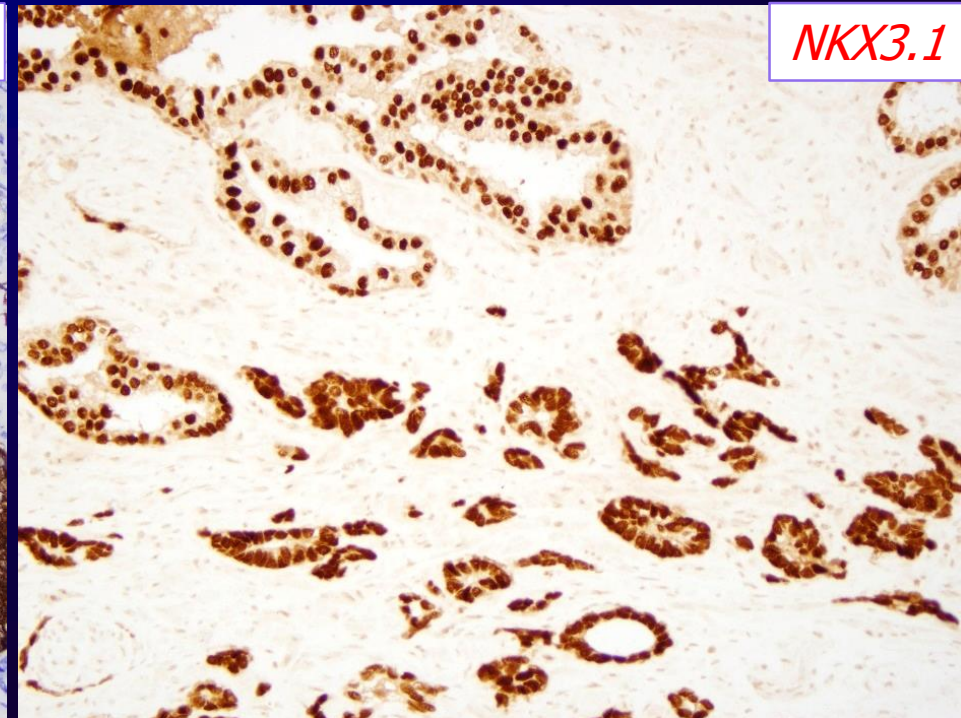
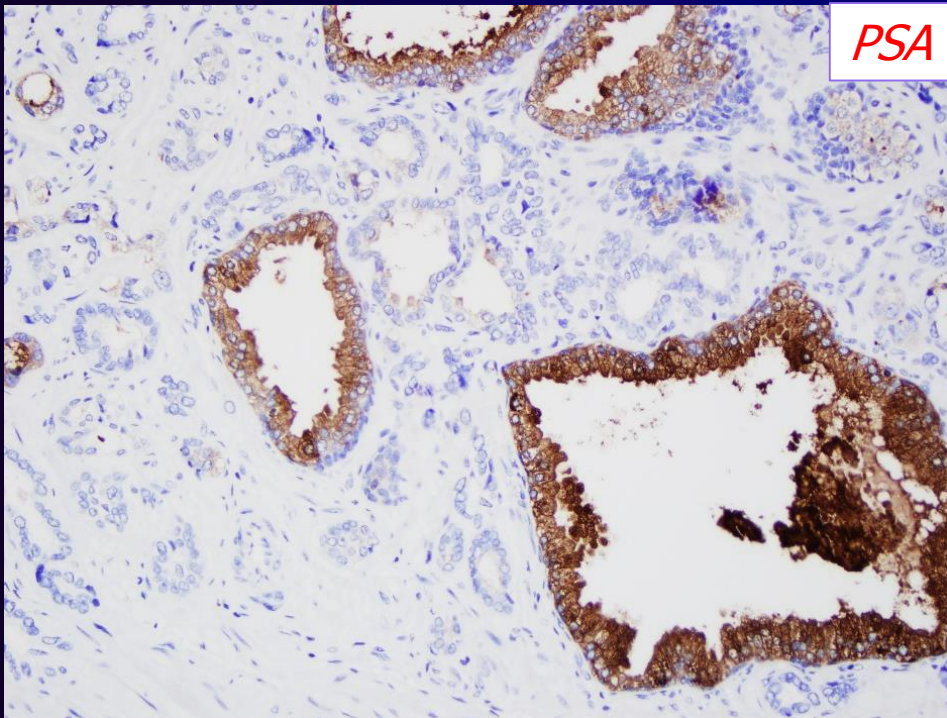
# Case 10. Basal cell carcinoma of the prostate



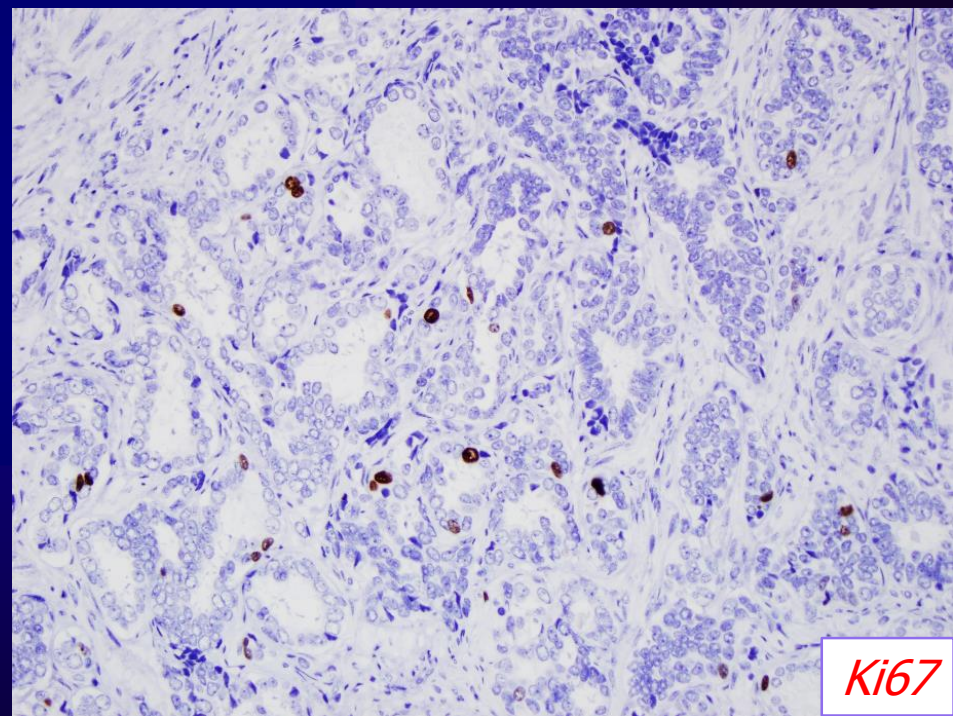
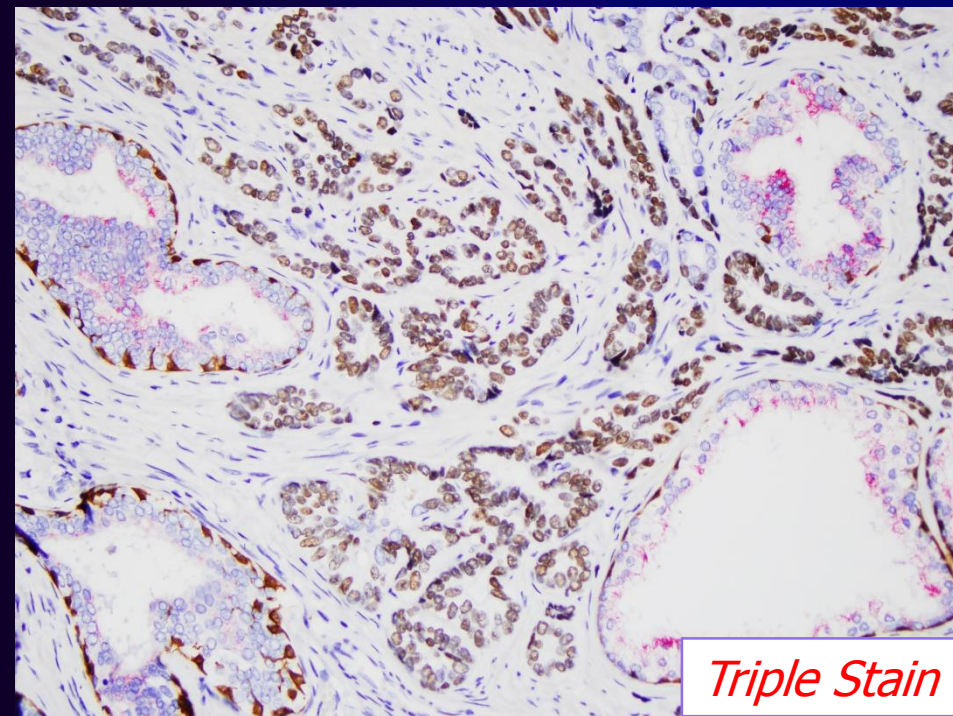
# Immunoprofile

Antibody	Staining in tumor cells
BCL-2	Positive
NKX3.1	Positive
P63	Positive
AMACR	Negative
HMWCK	Negative
Ki67	Mildly increased
PSA	Negative
PSMA	Negative

# IHC Profile



# IHC Profile



# Distinction of basaloid carcinoma of the prostate from benign basal cell lesions by using immunohistochemistry for bcl-2 and Ki-67

*Yang XJ; McEntee M; Epstein JI.  
Human Pathology, 1998 Dec, 29:1447-1450*

- 6 Cases of basaloid carcinoma (BC)
- Bcl-2 positive
- Ki67 increase
- P53 staining and nucleoli size do not correlate with behavior
- No metastasis in 6 cases studied

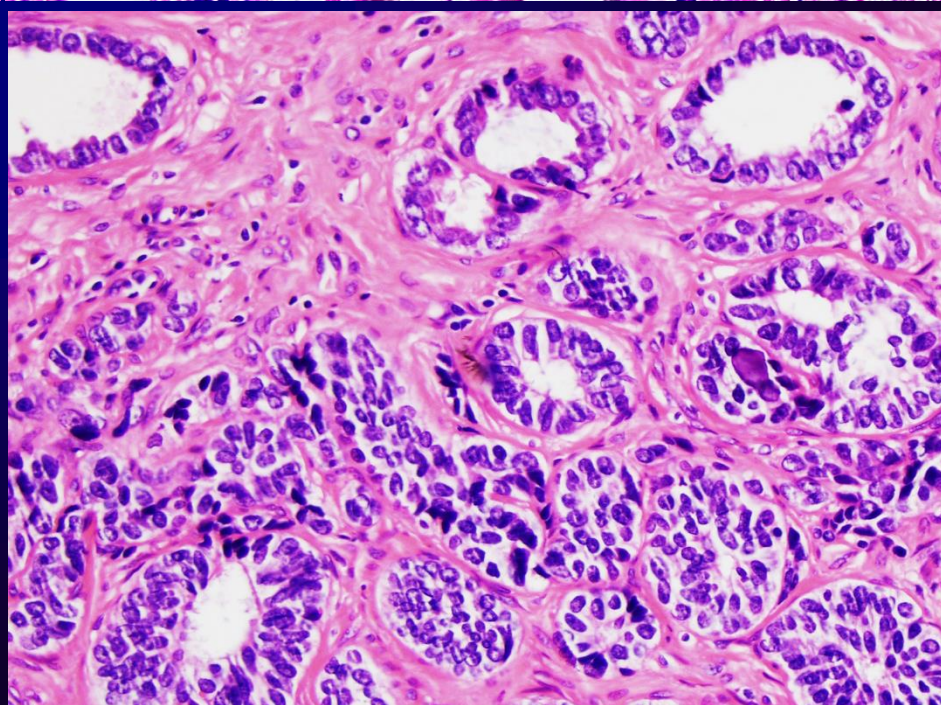
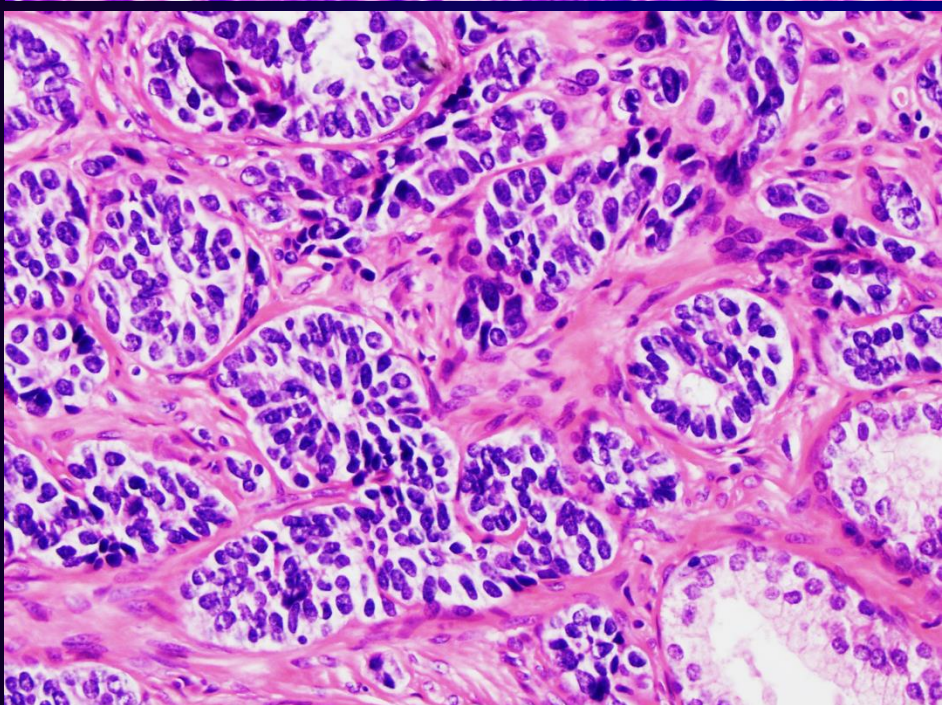
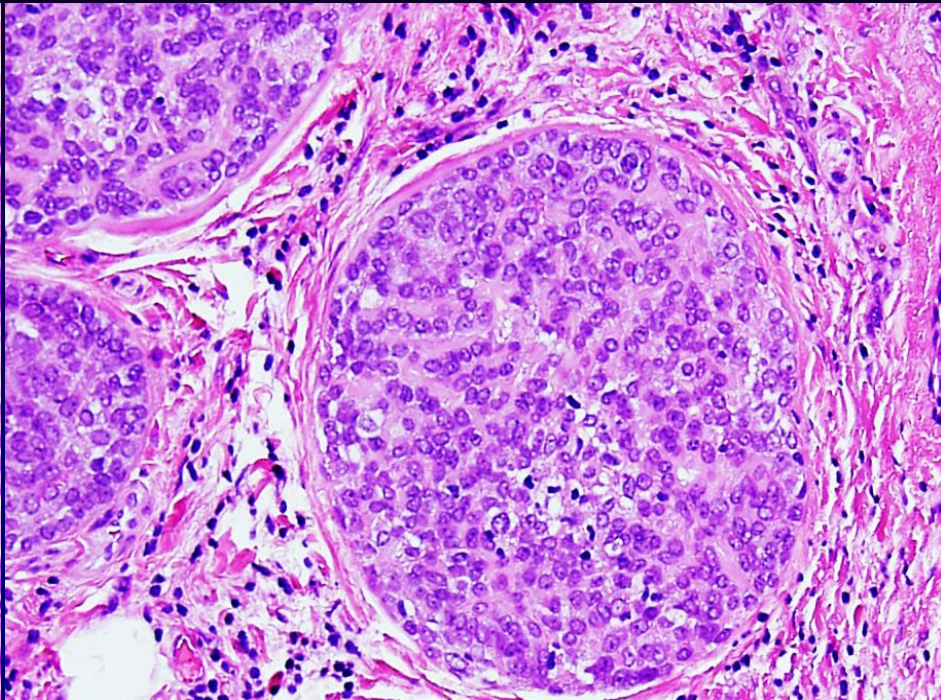
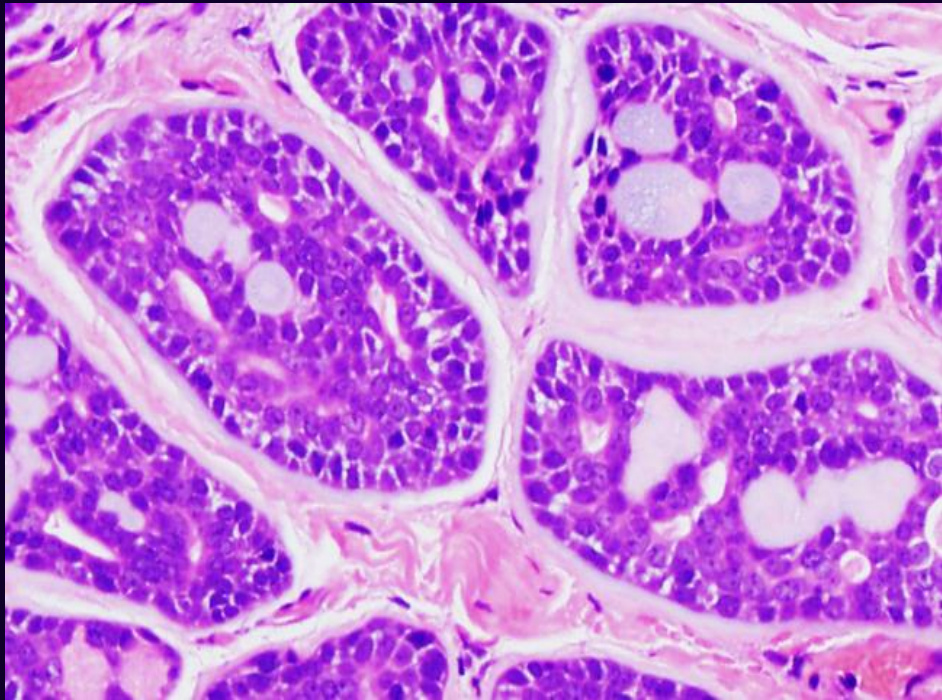
# Basal cell carcinoma of the prostate: a clinicopathologic study of 29 cases

*Ali TZ, Epstein JI, AJSP 2007;31:697-705*

- 29 cases
  - TURP n=29
  - Core Biopsy n=9
- 92% positive for Bcl-2
- Ki67 2-80%
- 5/7 RP ->Extraprostatic extension
- 4/19 with metastasis

# Basal Cell Carcinoma

- Patterns (often mixed)
  - Adenoid cystic (64%)
  - Basal cell hyperplasia-like (32%)
  - Small tubules (32%)
  - Large solid nests (28.5%)
- Infiltrating around benign glands
- Invading muscles
- Perineural invasion





# Basal cell carcinoma

## Summary

### (take home message)

- Basal cell carcinoma of the prostate generally behaves as a low grade malignant neoplasm
- The tumor displays a wide range of patterns
- Most cases are local invasive with indolent course
- A small subset may develop metastatic disease

# Palouse Falls, Washington

