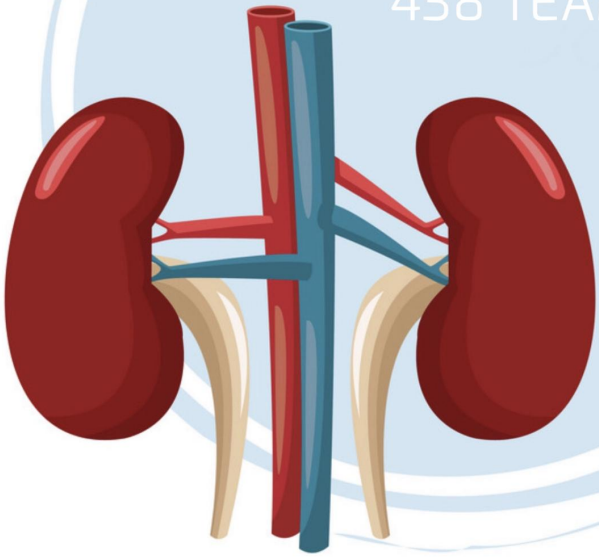
Editing file

Pathology
438 TEAM



Tumors of the renal system

Objectives:

- Recognize the benign tumors of the kidney.
- Describe renal cell carcinoma and Wilm's tumor.
- Recognize transitional cell and squamous carcinoma of the urinary bladder.

Color index:

Black: original content.
Red: Important.
Light Purple: From Robbin's.
Blue: only found in boys slides.

Green: Boy's doctor notes .
Dark orange: Girl's Doctor notes.
Grey: Explanation.
Pink: Only found in girls slides.

Pathology

Reviewed by: Rezan AlRabah & Ibrahim AlBakri

NEOPLASMS OF KIDNEY

TUMORS OF THE KIDNEY

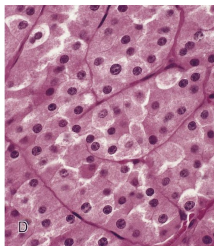
- **Benign Tumors**
  - RENAL ONCOCYTOMA
  - ANGIOMYOLIPOMA
- **Malignant Tumors**
  - RENAL CELL CARCINOMA
  - WILM'S TUMOR

No pleomorphism = benign, except in clear cell type of renal cell carcinoma

ONCOCYTOMA

Definition

Benign tumor of uniform round polygonal cells with abundant, intensely eosinophilic and granular cytoplasm with uniform round and central nuclei.
They arise from the intercalated cells of collecting ducts.
These neoplasms are associated with genetic changes —loss of chromosomes 1 and Y— that distinguish them from other renal neoplasms.



Grossly: well circumscribed mahogany-brown color with a central stellate scar.

Radiologically: they mimic renal cell carcinoma.

Electron microscopy: there are numerous mitochondria in the cytoplasm (gives it the pinkish color).

Complications

spontaneous hemorrhage.

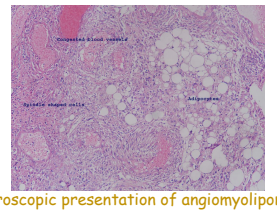
*causing abdominal pain

ANGIOMYOLIPOMA

Definition

Angiomyolipomas benign neoplasm composed of admixture of blood vessels, smooth muscle and adipose tissue.

- The amount of each component is variable.
- usually associated with tuberous sclerosis syndrome (a genetic disorder characterized by the growth of numerous noncancerous (benign) tumors in many parts of the body.).



Microscopic presentation of angiomyolipoma

★ RENAL CELL CARCINOMA (RCC)

Definition

- It is the most common primary cancer of the kidney.
- It accounts for 80% of all renal cancers.
- It arises from renal tubular epithelial cells.
- Seen more in men ranging from 50-60 years of age (affects men more than women).

Types of RCC

- 65% — Clear cell type
- Papillary type — 10-15%
- 5% — Chromophobe type
- Others — 15%

RCC risk factors

- Obesity
- Chronic HTN
- Occupational exposure to cadmium (Silvery white metal)
- Tobacco (smoked or chewed)
- Acquired cystic kidney disease due to end stage renal disease (especially papillary RCC as a complication of chronic dialysis)
- Genetic: about 5% are inherited. Hereditary RCCs tend to be multifocal and bilateral and appear at a younger age than sporadic RCC.

Genetic Risk factor

Hereditary form of clear cell RCC associated with homozygous loss of Von Hippel-Lindau (VHL) tumor-suppressor gene. (VHL syndrome is an autosomal dominant syndrome characterized by cerebellar hemangioblastomas, retinal angiomas, clear cell RCC, pheochromocytoma and cysts in kidney and various organs). The mutation of VHL gene is on chromosome 3.

Hereditary form of papillary RCC shows no association with the VHL gene. Mutations in the c-met proto oncogene (MET) leads to development of hereditary papillary RCC.

Duplications or trisomy of chromosome 7 can also leads to papillary carcinomas

1-inherited disorder characterized by cyst and benign or malignant Tumors in different parts of the body

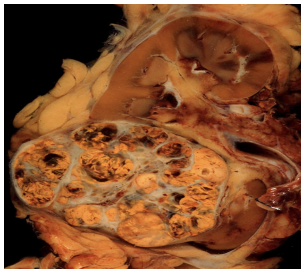
RCC: CLEAR CELL TYPE

Definition

- These are the most common type and arises from proximal tubular epithelial cells.
- The majority of them are sporadic. Uncommonly associated with VHL disease.

Gross

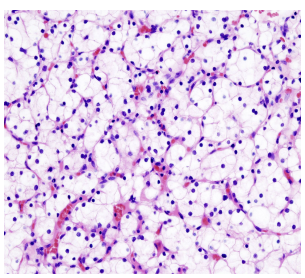
➢ Usually solitary and large.
➢ Cut surface is solid and focally cystic yellow-orange with hemorrhage and necrosis.
➢ The margins of the tumor are well defined.
➢ Tumor commonly invades the renal vein.
➢ There may be direct invasion into the perinephric fat and adrenal gland.



VS

Microscopically

➢ Tumor is made of cells with clear cytoplasm and sharp cell membrane.
➢ The cells are often arranged in sheets or nests.
➢ The stroma is highly vascularized.
➢ The nuclei are usually small and round with little to no pleomorphism.
➢ Some tumors exhibit marked degrees of anaplasia.



RCC: PAPILLARY CELL TYPE

Definition

It is characterized by a papillary growth pattern with fibrovascular stalks.

- These tumors are frequently multifocal and bilateral
- They occur in familial and sporadic forms
- The familial forms show increased expression and mutation in the MET proto-oncogene (located on chromosome 7q).

RCC: CHROMOPHOBE CELL TYPE

Definition

Chromophobe RCC shows a mixture of acidophilic granular cells and clear cells.

- They arise from the intercalated cells of renal collecting ducts.
- These neoplasms are unique in having multiple losses of entire chromosomes leading to extreme hypoploidy.
- Characterized by thick cytoplasmic walls.

Note: papillary and chromophobe RCCs have a better prognosis than the clear cell RCC.

RCC: CLINICAL FEATURES

*sometimes is called silent killer

1. The incidence of RCC peaks in the sixth decade.
2. RCC is twice as frequent in men as in women.
3. Hematuria is the single most common presenting sign.
4. The classic clinical triad: hematuria, flank pain and a palpable abdominal mass.
5. Some patients develop polycythemia.
6. Uncommonly, these tumors produce paraneoplastic syndromes
7. Sometimes it is a silent condition and discovered only after metastasis.
8. The tumor spreads most frequently to the lungs and bones

(e.g. secretion of a parathormone-like substance leads to hyperparathyroidism and hypercalcemia; production of erythropoietin causes erythrocytosis; release of renin results in hypertension. They may present with Cushing syndrome, masculinization).

WILMS TUMOR (NEPHROBLASTOMA)

Definition

It is a malignant neoplasm arising from embryonic nephrogenic elements composed of mixtures of blastemal, stromal , and epithelial tissue.
- Precursor lesions for the wilms tumor are Nephrogenic rests
- Wilms tumor, like retinoblastoma, may arise sporadically or be familial, with the susceptibility to tumorigenesis inherited as an autosomal dominant trait.

It is the most common primary tumor of the kidney in children

In most cases the Wilms tumor is sporadic and unilateral.

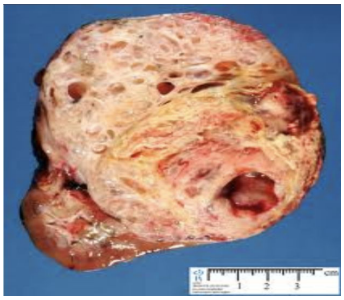
Some cases of Wilms tumor are familial (deletion of WT1 gene on chromosome 11p13)

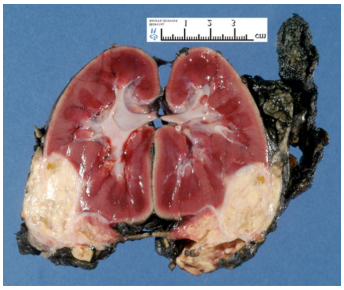
Associated with: WAGR syndrome, Denys Drash syndrome and Beckwith weidmann syndrome.

Morphology

Gross

- Unilateral (10% bilateral), solitary, well circumscribed lesion.
- Wilms tumor tends to be large when detected with a bulging, pale tan
- Cut section uniform, pale gray or tan-pink and soft in consistency (Fish flesh like)
- Tumor is soft, tan with foci of hemorrhage, cystic degeneration and necrosis





Microscopic

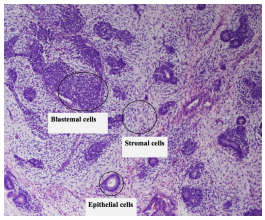
- Tumor is cellular and composed of classical triphasic combination of:

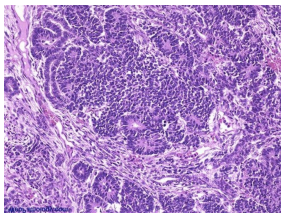
1) Blastemal component: composed of small ovoid cells with scanty cytoplasm and brisk mitosis

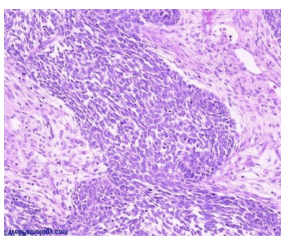
2) Epithelial component: appears as immature primitive tubular structures and immature glomeruli

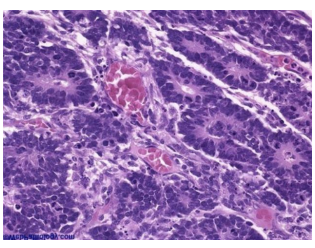
3) Stromal component: loose immature stroma of undifferentiated mesenchymal cells (immature spindle cells and myxoid material).

- Biphasic and monophasic patterns can also occur.
- 5% of tumors contain foci of anaplasia. Anaplasia is an indication of poor prognosis.









WILMS TUMOR (NEPHROBLASTOMA)

Clinical Features

usually presents between 1-3 years of age, and 98% occur before 10 years

*3-4-5 years are asymptomatic

- Abdominal mass (most common sign)
- Hematuria
- Abdominal pain
- Hypertension

Treatment and Prognosis

Chemotherapy and **radiation therapy** combines with **surgical resection** have dramatically improved the outlook of patients with this tumor

The prognosis of Wilms tumor is generally very good

Tumors of the lower urinary tract

Malignant tumor of the bladder are a more cause of death than kidney tumors.

Location of the tumor: it's uncommon in the collecting system above the bladder.

Size of the tumor: a small lesion in the ureter may cause obstruction, while a much larger mass in the bladder will show less clinical significance.

Lower urinary tract neoplasm

urothelial neoplasms

- Benign
  - Papiloma
- between benign and malignant
  - Papillary Urothelial Neoplasm with Low Malignant Potential (PUNLMP)
- Malignant
  1. Low grade papillary urothelial carcinoma
  2. high grade papillary urothelial carcinoma
  3. urothelial carcinoma in situ
  4. invasive urothelial carcinoma

Non-urothelial neoplasm

- Malignant
  1. squamous cell carcinoma
  2. Adenocarcinoma
  3. Neuroendocrine carcinoma
  4. Rhabdomyosarcoma

Rare and all have very poor prognosis.

PAPILLOMA

Definition

- It is a rare benign tumor that is characterized by 0.2 to 0.1 papillary projections lined by transitional epithelium.
- Usually solitary.
- It is noninvasive.
- Rarely recur once removed.

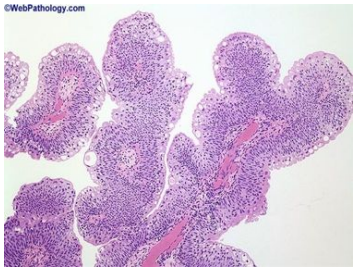
Types

Exophytic

- common
- grows outside the bladder

inverted

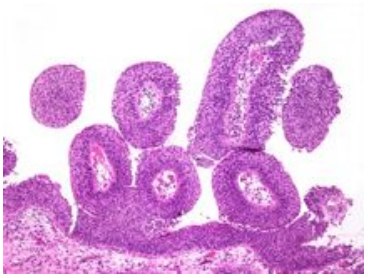
- rare
- grows inside the bladder

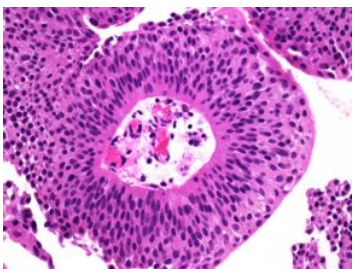


PUNLMP

Definition

- They are uncommon papillary well differentiated urothelial tumors with low malignant potential.
- They are intermediate between benign papillomas and low grade papillary urothelial carcinoma. because it looks like papilloma but it has pleomorphism (very little)
- It differs than benign papilloma because it may recur after removal.

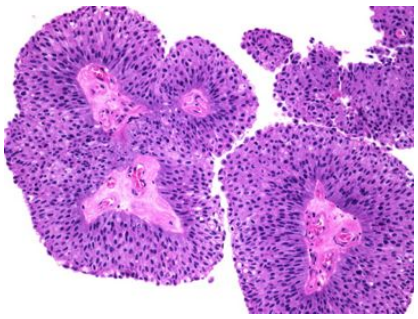




Malignant urothelial neoplasms

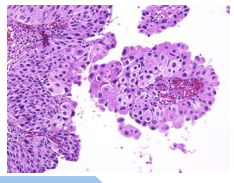
1 Low grade papillary urothelial carcinoma

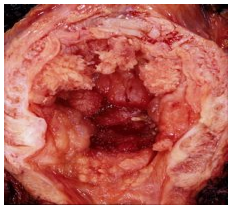
- Papillary projections are lined by neoplastic transitional epithelium
- Minimal pleomorphism
- Minimal mitotic activity.



2 High grade papillary urothelial carcinoma

- Papillary projections that are lined by neoplastic transitional epithelium that is marked by:
  - Hyperchromasia.
  - Pleomorphism.
  - Brisk mitotic activity in all three layers.
- high grade tumors invade to the lamina propria and muscularis propria (invasive carcinoma).

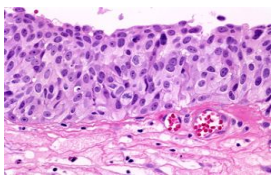


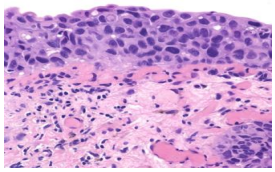


3 urothelial carcinoma in situ

- It's is a Flat-non papillary- lesion with full thickness malignant changes of the urothelium with high cytologic grade (hyperchromatic pleomorphic cells with prominent nuclei)
- Severity:

1- It may extend into the ureters and urethra.
2-Excessive shedding of malignant cells in urine.
3- In about 50% of cases it is associated with subsequent invasive carcinoma.





4 Invasive urothelial carcinoma

- Associated with papillary urothelial cancer (usually of high grade) or CIS (carcinoma in situ) may superficially invade the lamina propria or extend more deeply into underlying muscle.

*(High grade papillary carcinoma + urothelial carcinoma in situ) are both invasive tumors
*tumors in the ureter show the fastest symptoms

Non-urothelial malignant neoplasms

squamous cell carcinoma

- Squamous cell carcinoma of the urinary bladder is a malignant neoplasm derived from bladder urothelium with pure squamous phenotype.
- Develops on foci of squamous metaplasia.
- Usually associated with schistosoma. (chronic inflammation causes irritation of the bladder which will lead to squamous metaplasia then scc)

Clinical Features

- It affects males in the age of 50 to 70 three times more than females.
- They are not familial.

Lesions that invade the ureteral or urethral orifices cause urinary tract obstruction with associated hydronephrosis or pyelonephritis

painless sudden hematuria is the dominant clinical presentation, dysuria is less frequent

- Bladder cancer metastasize to lymph nodes, liver lungs and bones.
- Cystoscopy reveals single or multiple tumors

predisposing factors

1. Bladder tumors are 50 times more common in those exposed to arylamines (B-naphthylamine)
2. Heavy long term exposure to cyclophosphamide
3. Schistosoma haematobium infections in endemic areas & chronic cystitis
4. Cigarette smoking
5. long term use of analgesics
6. previous exposure of the bladder to radiation

Summary

Benign Tumors of The Kidney

Oncocytoma	Angiomyolipoma
Arise from intercalated cells of collecting ducts	Composed of admixture of: ○ Blood vessels ○ Smooth muscle ○ Adipose tissue
They mimic renal cell carcinoma	Associated with Tuberous sclerosis syndrome

Malignant Tumors of The Kidney

Renal Cell Carcinoma Arise from renal tubular epithelial cells			**WILMS Tumor** (Nephroblastoma)
Clear Cell	**Papillary**	**Chromophobe**	Childhood tumor (<10yrs)
Proximal tubular epithelial cells	-	Intercalated cells of collecting ducts	Embryonic nephrogenic elements: ○ Blastemal ○ Stromal ○ Epithelial tissue
Mutation of the VHL gene on chromosome 3	Mutation in c-met proto-oncogene (MET) located on chromosome 7	less common	Deletion of WT1 gene on chromosome 11p13
Hematuria (most common), can spread to the lungs and bones			Abdominal mass (most common)
involves the renal vein	Better prognosis than Clear Cell RCC		Very good prognosis, if anaplasia is indicated → poor prognosis

Tumor of The Lower Urinary Tract

Papilloma	**PUNLMP**	**Low grade papillary urothelial carcinoma**	**High grade papillary urothelial carcinoma**	**Urothelial carcinoma in situ**
Benign	Intermediate	Malignant	Malignant and invasive	Malignant and invasive
Rarely recurs after removal	May recur after removal	Minimal pleomorphism and mitotic activity	Marked hyperchromasia, pleomorphism and rapid mitosis	Lacks cohesiveness → shedding of malignant cells in the urine

Quiz

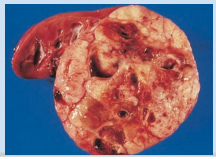
Answer key: Answers Explanation File!

1) D 2) E 3) D 4) E 5) A 6)

1) A 50-year-old man is found to have blood in his urine during a routine checkup. He is otherwise in excellent health, except for a mild microcytic, hypochromic anemia. An enlarged right kidney is found on X-ray examination, and CT scan reveals a renal mass of irregular shape, measuring 6 cm in diameter. Which of the following is the most likely diagnosis?

A	Angiomyolipoma
B	Metastatic carcinoma
C	Nephroblastoma
D	Renal cell carcinoma
E	Wilms tumor

2) The mother of a 12-month-old boy palpates a mass on the right side of the infant's abdomen. The surgical specimen is shown. Microscopically, the tumor is composed of multiple elements, including blastemal, stromal, and epithelial tissues. Which of the following is the most likely diagnosis?

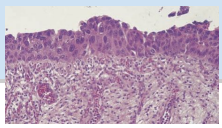


A	Ganglioneuroma
B	Neuroblastoma
C	Renal cell carcinoma
D	Teratocarcinoma
E	Wilms tumor

3) A 65-year-old man presents with a recent episode of painless hematuria. Vital signs are normal. All blood tests and urinalysis are normal, except for the presence of blood in the urine. The patient smokes cigarettes but does not drink alcoholic beverages. Which of the following is the most likely cause of hematuria in this patient?

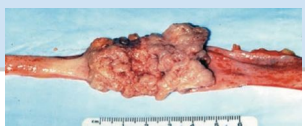
A	Acute cystitis
B	Acute pyelonephritis
C	Bladder calculi
D	Carcinoma of the bladder
E	Prostatic carcinoma

4) A 62-year-old man presents with a 1-month history of intermittent painless hematuria. Cystoscopy reveals multiple,red, velvety flat patches in the bladder mucosa. A biopsy is shown in the image. Which of the following is the appropriate diagnosis?



A	Chronic interstitial cystitis
B	Invasive urothelial cell carcinoma
C	Malakoplakia
D	Urothelial cell carcinoma in situ
E	Urothelial cell papilloma

5) A 50-year-old man presents with painless hematuria. A CT scan of the abdomen reveals a mass in the left ureter, which almost completely obliterates the lumen and has resulted in mild hydronephrosis. The surgical specimen is shown in the image. Which of the following is the most likely histologic diagnosis for this malignant neoplasm



A	Adenocarcinoma
B	Neuroblastoma
C	Pheochromocytoma
D	Renal cell carcinoma
E	Urothelial cell carcinomas

6) A 60-year-old woman with a history of chronic cystitis is referred to a urologist because of hematuria. Cystoscopy reveals a mass in the dome of the bladder. Biopsy shows tumor cells arranged as gland-like structures. Special stains demonstrate mucin in the cytoplasm of the tumor cells. What is the appropriate diagnosis?

A	Adenocarcinoma
B	Inverted papilloma
C	Squamous cell carcinoma
D	Urothelial cell carcinoma
E	Urothelial cell carcinoma in situ

Thank you

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- Alwaleed Alsaleh
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