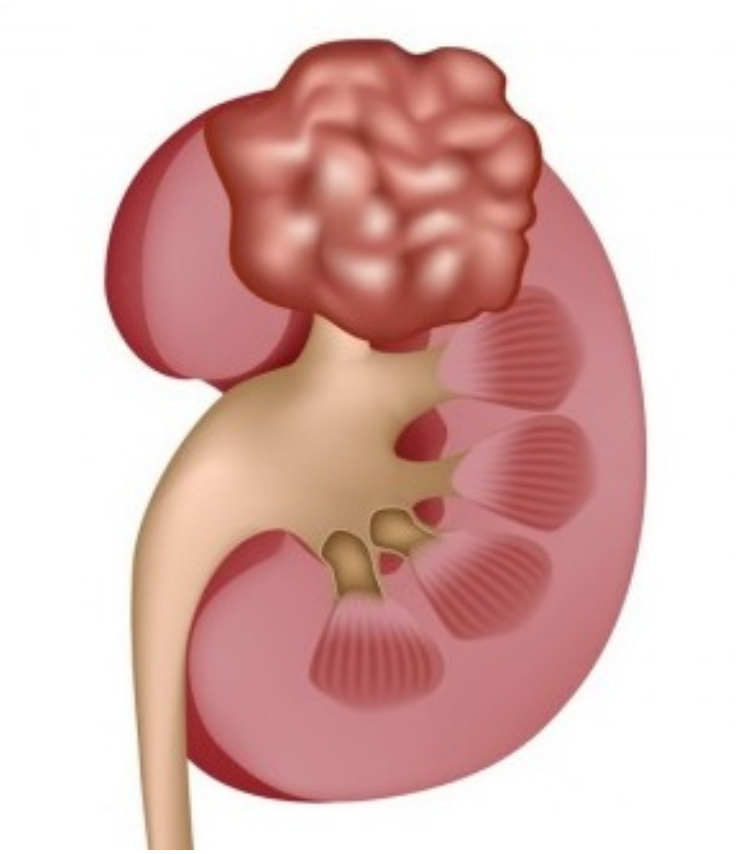
Tumors of urinary tract

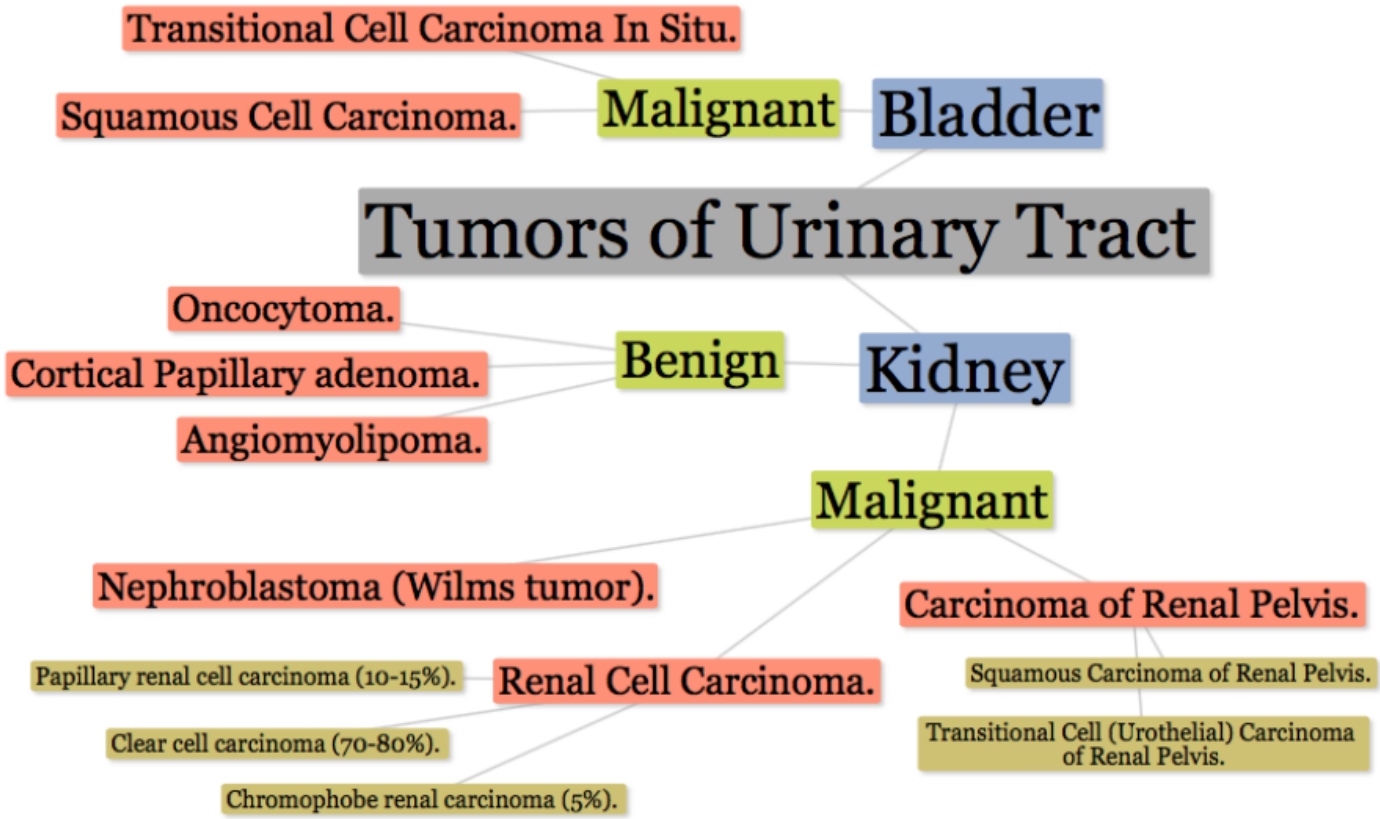


Objectives:

1. Recognize common benign tumors of the kidney.
2. Describe the pathological features of renal cell carcinoma and Wilms tumor.
3. Recognize the predisposing factors and features of transitional cell and squamous carcinoma of the urinary bladder.

Important note: During the previous blocks, we noticed some mistakes just before the exam and we didn't have the time to edit the files. To make sure that all students are aware of any changes, please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all of our work: Pathology Edit.

Introduction.

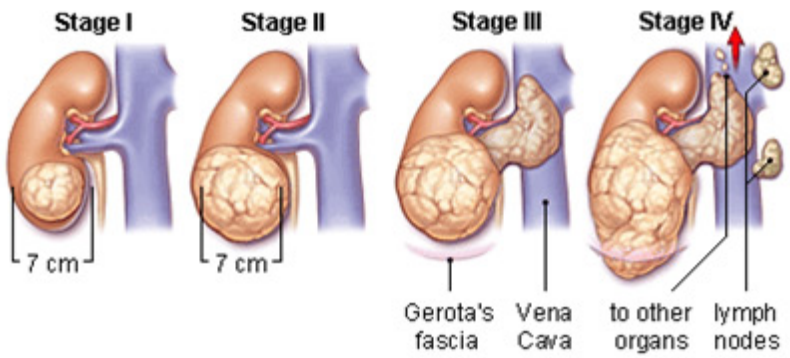


- **Signs & Symptoms of Tumors:** Fever, Malaysia, Rapid loss of weight & appetite.
- **Specific Symptoms of UT Tumors:** Hematuria, Flank pain (kidney), Abdominal mass.

Common Histological Findings for Any Tumor:

- Hyperchromatism.
- Mitosis.
- Necrosis.
- Polymorphism.

*Most important risk factor of cancer is **smoking**.*



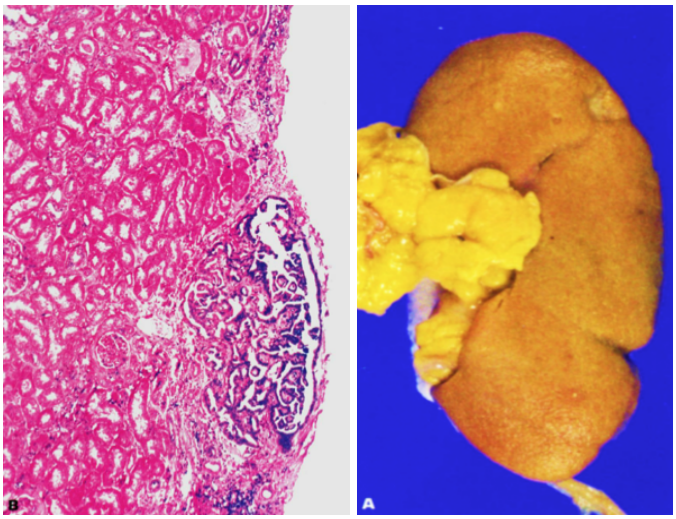
Kidney Tumors.

Benign Tumors.

1. Cortical Papillary adenoma.
2. Angiomyolipoma.
3. Oncocytoma.

1- Cortical (Subcapsular) Papillary Adenoma. Robbins page 547

- **Peripheral**.
- No significant clinical.
- 40% in adults
- Benign tubular cells that can appear as Papilloma.
- Renal adenomas increase in frequency with age, and are **asymptomatic**, usually found at autopsy.
- **Main characteristic:** small Pale nodule on the renal cortex.



A. Kidney with ***ischemic atrophy*** also bears very small subcapsular adenomas near to each pole.
B. Histology of a subcapsular papillary adenoma shows ***tubules arranged in a papillary fashion***.

2- Angiomyolipoma. Goljan Rapid Review Pathology page 525

It is hamartoma composed of blood vessels, smooth muscle, and adipose cells. (Angio = vascular , myo = smooth muscle cells , lipoma = lipomatous lesion)

- It can be large and bilateral compresses the kidney.
- It is very vascular can cause hemorrhage.
- It's a benign tumor that arises from perirenal tissue severe peritoneal **hemorrhage** (can be mistaken for a malignant tumor).
- It is often associated with **tubular sclerosis** (the patient has to be screened for tubular sclerosis, especially if it's bilateral).

3- Oncocytoma. Robbins page 547

- **Main characteristic:** Large tumor with a central scar which could be seen in imaging (radiopaque).
- **Under microscope:** benign cells are called Oncocytes (reddish granular cells which are rich in mitochondria).

Note: It can be mistaken for renal cell carcinoma.

Malignant Tumors.

- Renal Cell Carcinoma.
- Nephroblastoma (Wilms tumor).
- Transitional Cell (Urothelial) Carcinoma of Renal Pelvis.

Renal Cell Carcinoma (RCC). Robbins page 547

- Also known as **hypernephroma**, **Grawitz tumor, renal adenocarcinoma**.
- Represent 85% of all primary malignant tumors of kidney & 2% to 3% of all cancers in adults.
- Most common in men between the age 60-70 years.

Specific Presentation: Microscopic hematuria. (Most common), Flank pain, Abdominal mass.

Risk Factors:

- Smoking, hypertension, obesity.
- Unopposed estrogen Rx[1]. (estrogen treatment enhanced the development of hereditary renal cell tumors)
- Occupational exposure to asbestosis, petroleum products & metals (*cadmium*).
- Acquired polycystic disease[2] as a complication of chronic dialysis (30 fold).
- **Familial:**
  - Von Hippel-Lindau syndrome (**VHL**).
  - Hereditary clear cell carcinoma.
  - Hereditary papillary carcinoma.

Classification:

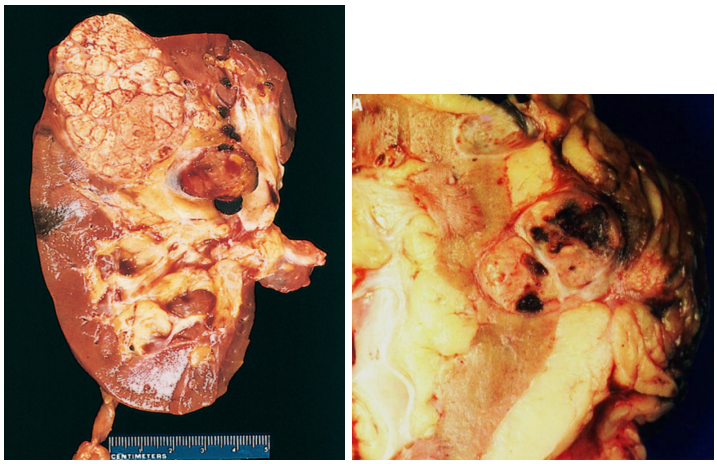
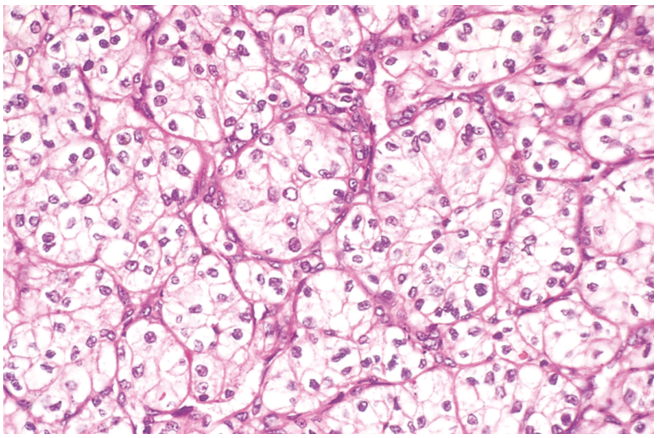
1. Clear cell carcinoma (70-80%).
2. Papillary renal cell carcinoma (10-15%).
3. Chromophobe renal carcinoma (5%).

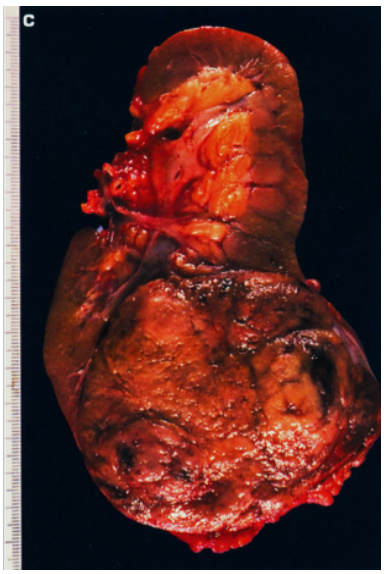
Prognosis: 5 years survival is around 70% in the absence of distant metastases, the figure is reduced to approximately 15-20% with renal vein invasion or extension into the perinephric fat.

[1] Unopposed estrogen is an imbalance of the hormones estrogen and progesterone in a woman's body. Rx =
[2] development of numerous fluid-filled cysts in the kidneys.

1- Clear cell carcinoma. Robbins page 547

Majority are sporadic. VHL syndrome is a risk factor.

Gross	Microscopic
	
- May arise anywhere in the kidney (Mostly **poles**). - **Solitary**[3] unilateral and large lesions (spherical masses). - **Marginated**. - Composed of yellow-gray-white tissues that distorts the renal outline. - Foci of hemorrhagic discoloration. - Grey-white necrosis - Invasion of the renal vein.	- Depending on the amounts of **lipid** and **glycogen** present, the tumor cells may appear almost vacuolated or may be solid. - Nuclei are small and round. - Clear cells with clear or granular pink cytoplasm. (*Clear* renal cell) - Spreading into perirenal adipose tissue.

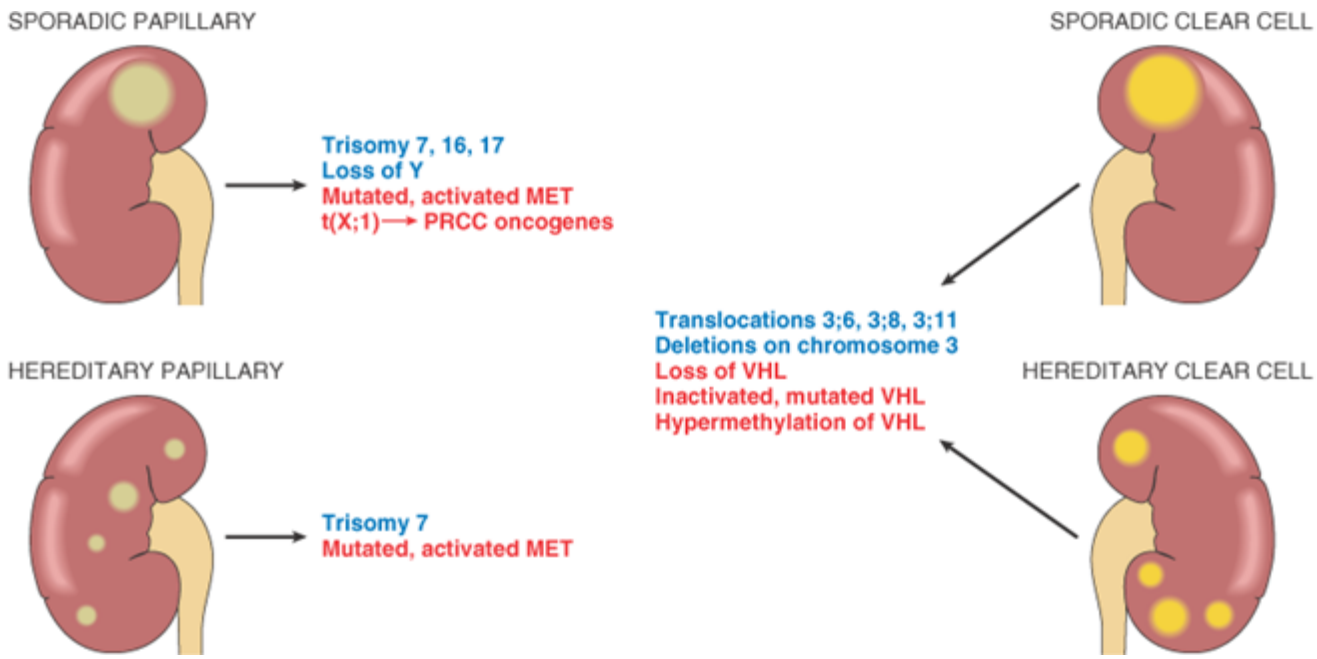


Typical lobulated, whorled[4], tan-colored cut surface of renal cell carcinoma.

[3] arise alone.
[4] helical = spiral

2- Papillary renal cell carcinoma. Robbins page 547

- Papillary growth pattern.
- Frequently multifocal and bilateral.
- Appear as early stage tumor.
- most common cytogenetic abnormalities are **trisomies 7**,**16** and **17**.



SUMMARY

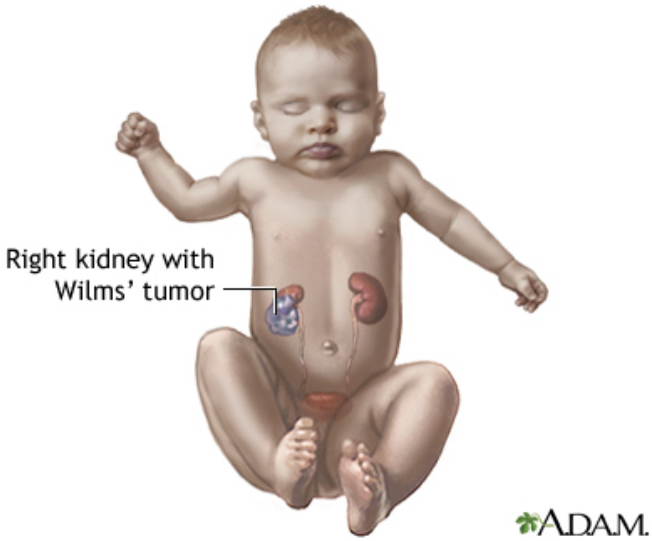
Renal Cell Carcinoma

Renal cell carcinomas account for 2% to 3% of all cancers in adults and are classified into three types:

- *Clear cell carcinomas* are the most common and are associated with homozygous loss of the VHL tumor suppressor protein; tumors frequently invade the renal vein.
- *Papillary renal cell carcinomas* frequently are associated with increased expression and activating mutations of the *MET* oncogene; they tend to be bilateral and multiple and show variable papilla formation.
- *Chromophobe renal cell carcinomas* are less common; tumor cells are not as clear as in the other renal cell carcinomas.

Wilms Tumor (Nephroblastoma). Robbins page 261

Most common primary tumor of the kidney in **children** between 2 and 5 years of age.



Important concepts of childhood tumors:

1. Relationship between *congenital malformation* and increased risk of tumors.
2. Histologic similarity between tumor and developing organ.
3. Remarkable success in the treatment of childhood tumors.

Mutated genes:

- **WAGR syndrome** (i.e., Wilms tumor, aniridia, genital abnormalities, and mental retardation) → Wilms' tumour suppressor gene **WT1** (11p13).
- **Denys-Drash syndrome (DDS)** approximately 90% → **WT1.**
- **Beckwith-Wiedemann syndrome (BWS)**, patients exhibit enlargement of individual body organs → **WT2**.
- **WT3**.

Morphology:

★ Wilms tumor typically is a **large**, solitary[5], well-circumscribed[6] mass.
★ Unilateral or bilateral (10%).
★ The tumor is soft, homogeneous, and tan to gray, with occasional foci of hemorrhage, cystic degeneration, and necrosis.
★ It has the tendency to **metastasize** easily.

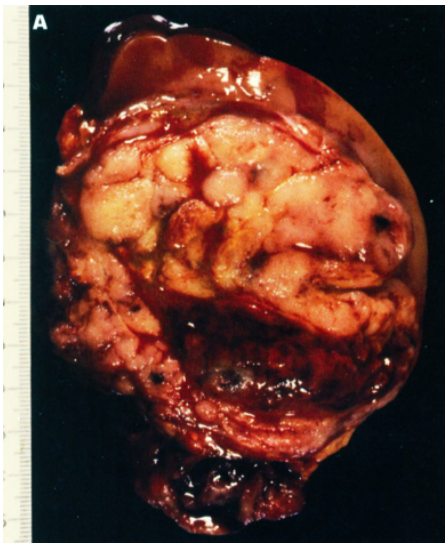
Microscopic examination: Blastemal, stromal & epithelial elements.

Clinical application:

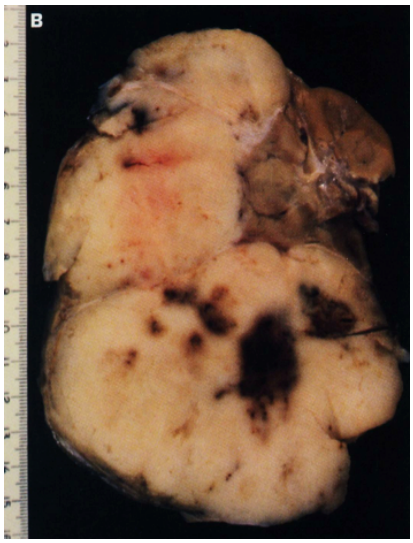
- **Commonly** → Readily **palpable** abdominal mass, which may extend across the midline and down into the pelvis + Hypertension due to renin release.
- **Less often** → fever, abdominal pain, hematuria, intestinal obstruction (uncommon).

Prognosis: 90% generally is very good, and excellent results are obtained with a combination of nephrectomy and chemotherapy.

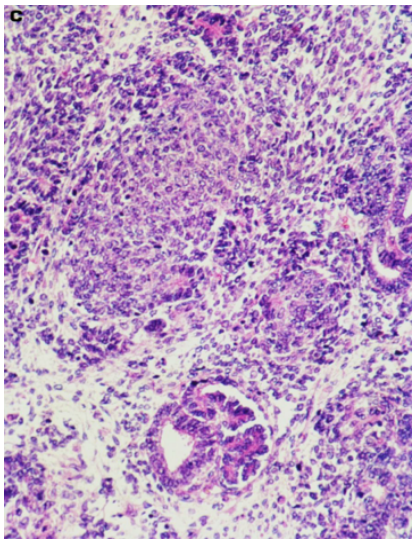
[5] يكون كتلة واحدة
[6] محدد



Solid, bulging, fleshy tan-white, partially necrotic tumor has replaced much of the kidney and is encompassed by a thin rim of renal tissue.



This Wilms' tumor appears whiter due to formalin fixation and has extended beyond the confines of the kidney.



Histology shows hypercellular areas comprising undifferentiated blastema, loose stroma with undifferentiated glomeruloid body.

SUMMARY

Wilms Tumor

- Wilms tumor is the most common renal neoplasm of childhood.
- Patients with three syndromes are at increased risk for Wilms tumors: Denys-Drash, Beckwith-Wiedemann, and Wilms tumor, aniridia, genital abnormalities, and mental retardation syndrome.
- Wilms tumor, aniridia, genital abnormalities, and mental retardation syndrome and Denys-Drash syndrome are associated with *WT1* inactivation, while Beckwith-Wiedemann arises through imprinting abnormalities at the *WT2* locus, principally involving the *IGF2* gene.
- The morphologic components of Wilms tumor include blastema (small, round blue cells) and epithelial and stromal elements.
- Nephrogenic rests are precursor lesions of Wilms tumors.

Renal Pelvis Carcinoma.

- Small.
- Painless hematuria.
- Abdominal pain due to mass caused by hydronephrosis[7].
- Multifocal.
- **Prognosis**: variable depend on stage & grade. Despite removal by nephrectomy: 50% 5 YSR.
- **It has two types:**
    1. Squamous Carcinoma of Renal Pelvis.
    2. Transitional Cell (Urothelial) Carcinoma of Renal Pelvis.

Transitional Cell (Urothelial) Carcinoma of Renal Pelvis.

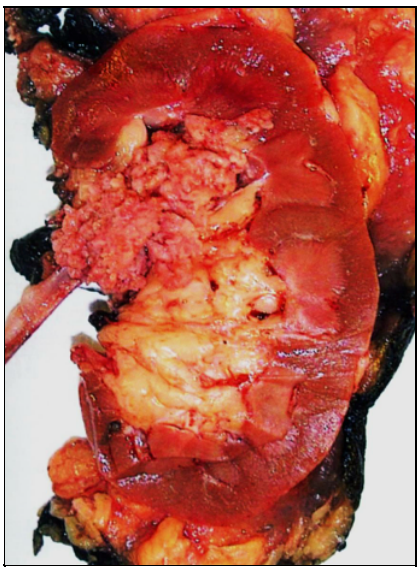
Renal transitional cell carcinoma (TCC), or urothelial carcinoma (UC), is a *malignant* tumor *arising from the **transitional cells*** lining the urinary tract from the renal calyces to the ureteral orifice.

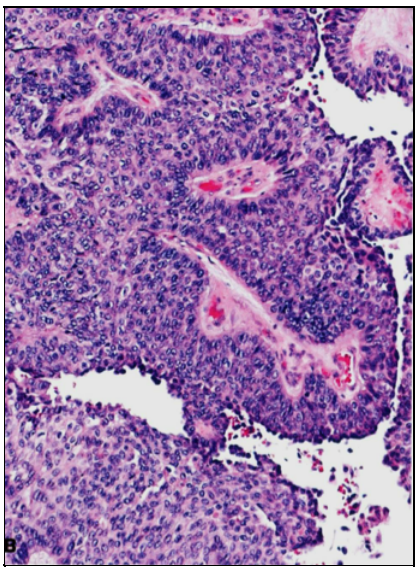
- (TCC) is the most common tumor of the renal pelvis.
- Approximately 50% of patients with TCC have similar tumors elsewhere in the urinary tract.

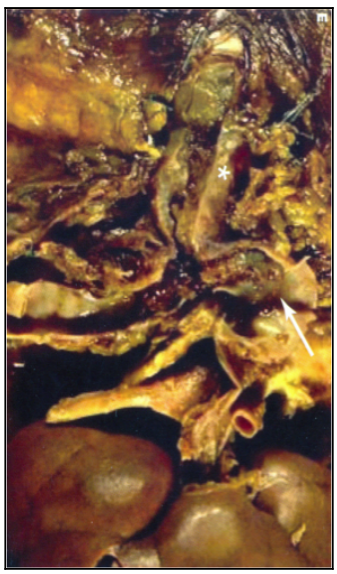
The predominant histologic pattern of TCC is the *exophytic*[8] *"papillary", multi fronded nature of the tumor.*

Risk factors:

1. Smoking (most common).
2. Phenacetin abuse.
3. Aromatic amines (aniline dyes).
4. Cyclophosphamide.







TCC is ***central*** in the kidney

[7] **Hydronephrosis** is the swelling of a kidney due to a build-up of urine.
[8] growing outward.

Bladder Tumors.

Malignant Tumors.

- Transitional Cell Carcinoma In Situ (90%).
- Squamous Cell Carcinoma (3-7%).

Squamous Cell Carcinoma. Robbins page 669

- They typically show extensive *keratinization*.
- Associated with chronic bladder irritation and infection.

Risk factor: *Schistosoma haematobium* infections in areas where it is endemic, such as Egypt.

Transitional Cell Carcinoma In Situ. Robbins page 669

It is more common in men than in women. If untreated, up to 75% of cases go on to invasive cancer.

- Bladder cancer, with rare exceptions, is not familial.

Risk factors of urothelial carcinoma:

- Cigarette *smoking*.
- Various occupational carcinogens.

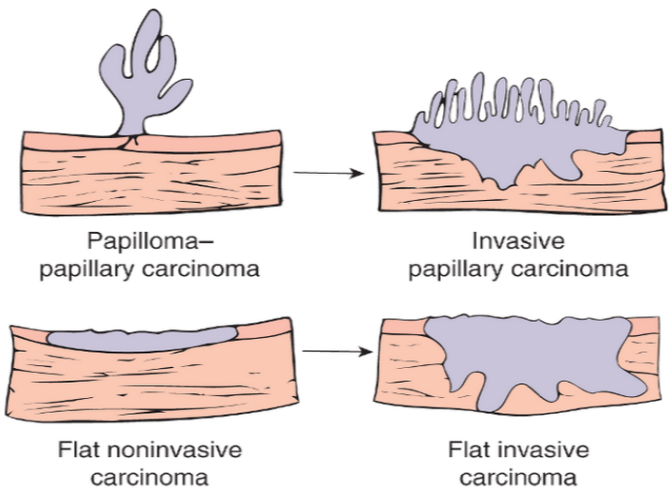
Pathogenesis:

- **first pathway:** The tumor is initiated by deletions of tumor-suppressor genes on 9p and 9q → formation of superficial papillary tumors → may then acquire TP53 mutations → invasion.
- **second pathway:** Initiated by TP53 mutations → carcinoma in situ → loss of chromosome 9 → invasion.

Note: The underlying genetic alterations in superficial tumors include fibroblast growth factor receptor 3 (FGFR3) mutations and activation of the Ras pathway "Ras oncogene".

Morphology:

- Undifferentiated tumor.
- Could be invasive or noninvasive.



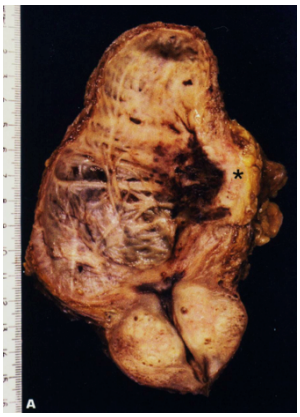
Two distinct precursor lesions to invasive urothelial carcinoma are recognized.

Clinical Features:

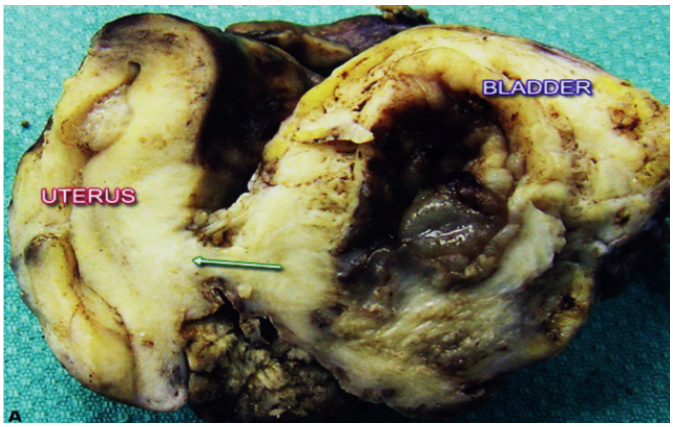
- ***All bladder tumors*** present with **gross painless hematuria.**
- Patients with urothelial tumors, whatever their grade, have a tendency to develop new tumors after excision, and recurrences may exhibit a higher grade.
  - The risk of recurrence is related to several factors, including tumor size, stage, grade, multifocality, mitotic index, and associated dysplasia and/or CIS in the surrounding mucosa.
  - Most recurrent tumors arise at sites different than that of the original lesion, yet share the same clonal abnormalities as those of the initial tumor.

Treatment: Depends on tumor grade and stage and on whether the lesion is flat or papillary.

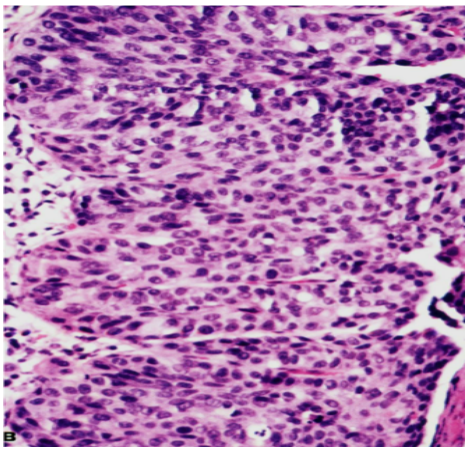
- Small localized papillary tumors → transurethral resection.
- Patients with tumors that are at high risk for recurrence → topical immunotherapy.
- Radical cystectomy.



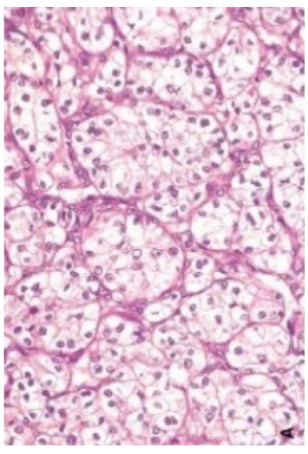
Invasive urothelial carcinoma of the bladder is invading the muscle coat on the right side of the picture.



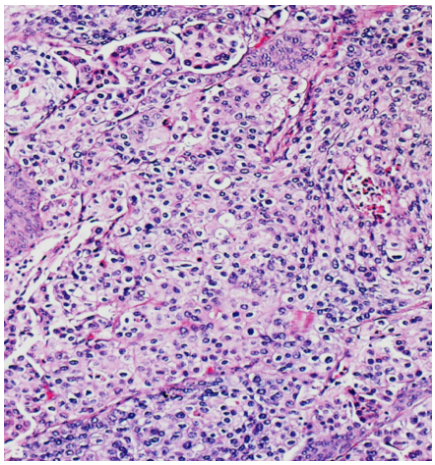
The invasion of the tumor up to the uterus



Histology of carcinoma in situ (surface is to the right).



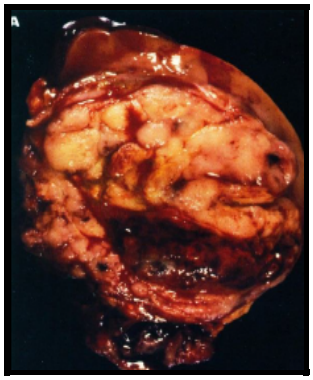
Poorly differentiated urothelial carcinoma.



Summary.

Tumor	Location	Clinical presentations	Etiology	Prognosis	Notes
Cortical (Subcapsular) Papillary Adenoma **Benign Tumor**	**cortical** peripherally (near each pole)	Asymptomatic	-------	Grossly: ischemic atrophy Histology: tubules arranged in papillary fashion.	-------
Angiomyolipoma **Benign Tumor**	Associated with Tubular Sclerosis.	Peritoneal Hemorrhage	-------	**Composed of :** 1- Blood Vessels. 2- Smooth Muscle. 3- Adipose Tissue.	------
Transitional Cell (Papillary Urothelial) Carcinoma of Renal Pelvis **Malignant Tumor**	**Centrally** arise from: transitional cells in Renal Pelvis.	- Small. - Painless hematuria. - hydronephrosis - Multifocal.	-------	Exophytic. Multi Fronded nature.	Most common tumor of renal pelvis
Nephroblastoma (Wilms tumor) **Malignant Tumor**	-------	Readily **palpable** abdominal mass	------	Solid Abdominal mass. Glomeruloid Body. Blastema. loose Stroma. Whitish-Tan. ** Anaplastic Features: 1-Mitosis. 2-Necrosis. 3-Polymorphis.	Most common in children.
Renal Cell Carcinoma (renal adenocarcinoma) (hypernephroma) Grawitz tumor **Malignant Tumor**	peripherally (Poles of the kidney) arise from: Renal tubule cells.	1- Flank pain . 2- Hematuria . 3- Fever . 4- Weight lose . 5- Anemia .	**Sporadic papillary :** Trisomy:7,16,17. activated MET. **Hereditary papillary:** Trisomy : 7 activated MED. **Sporadic & Hereditary Clear cell:** Translocation deletions lose VHL.	Grossly : Hemorrhage & Necrosis Typical lobulated. Tan coloured. Histology : clear cells. papillary carcinoma. (thin vascular background)	Most common in adults . Male more than female. usually Smoker
Transitional Cell (Urothelial) Carcinoma In Situ **Malignant Tumor**	Urinary Bladder	gross painless hematuria	- Smoking. - Occupational carcinogens.	if untreated → invasive Cancer.	------
Squamous Cell Carcinoma **Malignant Tumor**			schistosoma infections	------	South KSA (e.g. Gaizan). Egypt.

MCQ's.



A 4-year-old girl has complained of abdominal pain for the past month. On physical examination, she is febrile, and palpation of the abdomen shows a tender mass on the right. Bowel sounds are present. Laboratory studies show hematuria without proteinuria. Abdominal CT scan shows a 12-cm, circumscribed, solid mass in the right kidney. A right nephrectomy is done; the gross appearance of the mass is shown in the figure. What is the most likely diagnosis?

A. Angiomyolipoma
B. Renal cell carcinoma
C. Transitional cell carcinoma
D. Wilms tumor

Ans:D, Wilms' tumor is the most common renal neoplasm in children.

A 65-year-old man recently retired after many years in a job that involved exposure to aniline dyes, including ßnaphthylamine. One month ago, he had an episode of hematuria that was not accompanied by abdominal pain. On physical examination, there are no abnormal findings. Urinalysis shows 4+ hematuria, and no ketones, glucose, or protein. Microscopic examination of the urine shows RBCs that are too numerous to count, 5 to 10 WBCs per high-power field, and no crystals or casts. The result of a urine culture is negative. What is the most likely diagnosis?

A. Renal cell carcinoma
B. Urothelial carcinoma*
C. Squamous cell carcinoma of the urethra
D. Nephroblastoma

Anc:,B Exposure to arylamines markedly increases the risk of bladder cancer, which can occur decades after the initial exposure.

- a malignant neoplasm derived from transitional epithelium, occurring chiefly in the urinary bladder, ureters, or renal pelvis.

A 3-year-old boy is noted to have absence of the iris bilateral, cryptorchidism*, and mental retardation. His mother has noticed over the past 3 months that the child has an enlarging abdomen. On physical examination, there is a palpable mass. An abdominal CT scan shows bilateral adrenal enlargement and pancreatic enlargement. There is a 6-cm solid mass in the left kidney. Which of the following congenital disorders is the most likely diagnosis?

A. WAGR syndrome
B. McArdle syndrome
C. Klinefelter syndrome
D. Turner syndrome

Anc:A, WAGR syndrome is an uncommon condition that carries an increased risk of development of Wilms tumor, a childhood neoplasm arising in the kidney.

- Cryptorchidism is a genital abnormality in which which one or both of the testes fail to descend from the abdomen into the scrotum.

A patient who was 72 years old, came to the hospital because of flank pain and fever, a urine sample showed presence of RBC's (hematuria), also a palpable mass was present just below the ribs, The surgeon took the patient to the operating room and a mass was removed from the cortex of the kidney, the following characteristics were present in this mass: the kidney was in variegated appearance with a yellowish surface ,hemorrhagic and necrotic areas, present of soft cysts were seen also and the mass was dialated. What is the most likely tumor is present in this case?

A. Adenoma
B. Renal cell carcinoma
C. Oncocytoma
D. Squamous cell carcinoma

Anc:B

In the previous question, which structure in the body must be detected from invasion by this type of tumors?

A. Brain
B. Renal vein
C. Lungs
D. Ureter

Anc:B

What are the chromosomes that may be absent in case of oncocytic cell carcinoma?

A. 11,12,y
B. 4,6,x
C. 5,9,y
D. 1,14,y

Anc:D

SAQs.

What are the of Classifications Renal cell carcinoma?

1- clear cell carcinoma
2- papillary renal cell carcinoma:
3- chromophobe renal carcinoma:

What are the other names of Benign tubular adenoma?

Papillary cortical adenoma and leave me alone lesion

Contact us on: Pathology434@gmail.com
@Pathology434, **Ask us!**

Good Luck!

Done by:

عمر الرهبيني

مها الربيعة
ريما الرشيد
رزان الصبحي
نورة الهلالي
منى المتعب
ريم لبني
ريما الناصر
Najlaa Khalid