



GENITOURINARY SYSTEM

SUBJECT : Pathology

LEC NO. : 7

DONE BY : Sami Alodeh

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GENITOURINARY SYSTEM

Objectives

- Clinical manifestation of kidney disease
- understand the terminology of Renal diseases
- Discussion of Glomerular disease
- Nephrotic syndrome
- Nephritic syndrome
- Disease of blood vessels
- Urinary tract infection
- Analgesic nephropathy
- Acute Tubular Necrosis
- Hemolytic Uremic Syndrome
- Urolithiasis and hydronephrosis
- Renal Tumours RCC
- Bladder Tumours



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Tumors in general :
Primary > arise from the organ itself → can be Benign / Malignant
Secondary > Metastatic Tumor

Classification of renal tumour

Benign	Malignant
Cyst	• RCC most common type
Smooth muscle ← Leiomyoma	• Transitional Cell Ca → arise from renal pelvis ↳ Also called: Urothelial carcinoma
" Fat ← Lipoma	• Oncocytoma
Hemangioma	• Sarcoma
Angiomyolipoma	• Lymphoma
Adenoma	• Metastasis (Lung, Breast, GIT, Prostate, Pancreas, Melanoma)
Juxtaglomerular cell tumour	

* Tumors Can arise from all kidney structures

Renal tumours

Either Benign Tumours arising either from epithelial component of kidney or from mesenchymal tissue

Malignant tumour either epithelial (Renal cell carcinoma) arise from tubules or nephroblastoma arising from Pluripotential stem cells (Children)

❖ The commonest malignant T of the kidney is the

(1) Renal cell carcinoma = **RCC (85%)**, followed by ^{in adults}

(2) Nephroblastoma = **Wilm's tumor (10%)** & by ^{in children}

(3) Carcinoma of the renal calyces & pelvis (5%).

• Benign renal T, such as small (<0.5 cm) **cortical papillary adenomas** or interstitial cell medullary **fibromas** have no clinical significance.

also called urothelial cell carcinoma / transitional cell carcinoma } Name according to the lining

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BENIGN	MALIGNANT
A. EPITHELIAL TUMOURS OF RENAL PARENCHYMA	
Adenoma Oncocytoma	Adenocarcinoma (hypernephroma, renal cell carcinoma)
B. EPITHELIAL TUMOURS OF RENAL PELVIS	
Transitional cell papilloma	Transitional cell carcinoma Others (squamous cell carcinoma, adenocarcinoma of renal pelvis, undifferentiated carcinoma of renal pelvis)
C. EMBRYONAL TUMOURS	
Mesoblastic nephroma Multicystic nephroma	Wilms' tumour (nephroblastoma)
D. NON-EPITHELIAL TUMOURS	
Angiomyolipoma Medullary interstitial tumour (fibroma)	Sarcomas (rare)
E. MISCELLANEOUS	
Juxtaglomerular cell tumour (Reninoma)	
F. METASTATIC TUMOURS	

Classification of kidney tumours

* فيديو Osmosis مفيد

Renal Cell Carcinoma (RCC)

- Renal cell carcinoma (RCC) is the third most common cancer of the genitourinary tract and the most lethal urologic cancer, accounting for approximately 2% of all cancer deaths
- **RCC** are derived from the **renal tubular epithelium**, & hence they are **located** predominantly in the **renal cortex**.
- **RCC** represent **85%** of all primary renal cancers. *Most Common*
- **RCC** are most common from the 6th to 7th decades, & **men are affected about twice as commonly as women**.

→ men : women
2 : 1

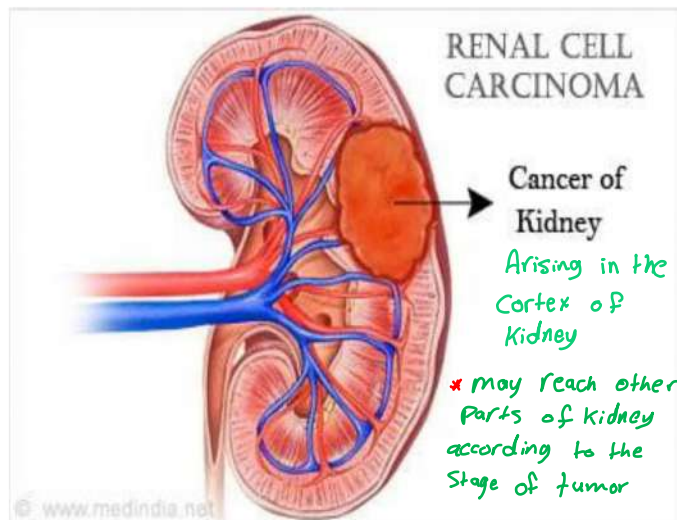
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WHAT IS RENAL CELL CARCINOMA (RCC)?

- Cancer arising from the lining of proximal convoluted tubule.
- The most common type of kidney cancer.
- Also known as Renal Adenocarcinoma or Grawitz's Tumor.
- Most lethal of all the genitourinary tumors.



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- V. imp: الرقم 1/3*
- Approximately one-third of the patients with **RCC** will present with metastases, and many patients will develop metastasis after surgical resection.
 - Traditionally, **RCC** is known to be resistant to chemotherapy. However, there has been tremendous development in effective molecular targeted therapies in the past few years for specific types of RCC with well-defined histology and molecular abnormalities.
 - Therefore, accurate histologic diagnosis and classification is increasingly important
 - **The risk of developing RCC is higher in :**
 - smokers, hypertensive, obese patients, & those who have had occupational exposure to cadmium;

- molecular and genetic studying is important to develop targeted therapy

- targeted therapy for any molecular or genetic abnormality

Metastases (Stage 4) → Can reach lung through : renal vein → IVC → Right side of the heart → Lung

- V. imp: الرقم 30*
- * **30-fold** in individuals who develop **acquired polycystic disease** as a **complication of chronic dialysis**. *due to chronic kidney disease* *Fibrotic kidney*
 - ☐ The role of genetic factors in the causation of RCC is discussed below.
 - Based on their molecular origins, RCC are classified in 3 forms:** *important to develop targeted therapy*
 - **(I) Clear Cell RCC (80%)** *Most common* *contain lipid / glycogen*
 - **(II) Papillary RCC (15%)**
 - **(III) Chromophobe RCC (5%).**

* Patients who undergo chronic dialysis (due to chronic kidney disease / fibrotic kidney) develop Acquired Polycystic disease as a compensatory mechanism

* The incidence of RCC in these patients is known to be higher (30-folds) [V.IMP]

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(I) Clear cell RCC: Clear : contain lipid
 sometime appear eosinophilic due to high glycogen content

- Commonest type, comprises 80% of all RCC, Tumor cells show clear or granular cytoplasm. Majority are sporadic, also occur in familial forms or in association with... An autosomal dominant von Hippel-Lindau (VHL) disease characterized by predisposition to a variety of tumors, but particularly to hemangioblastomas of the cerebellum & retina.
- People who have VHL disease may experience tumors and/or cysts in up to ten parts of the body, including the brain, spine, eyes, kidneys, pancreas, adrenal glands, inner ears, reproductive tract, liver and lung.
- Hundreds of bilateral renal cysts & bilateral, multiple, clear cell RCC develop in 40% to 60% of VHL disease patients.

↑ risk for :
 . renal cancer
 . renal cyst

- Those with VHL syndrome inherit a (germ-line mutation) of the VHL gene on chromosome 3p25 & lose of the second allele by (somatic mutation). / Not only in familial cases / can be found in sporadic cases
- Thus, the loss of both copies of this tumor suppressor gene gives rise to clear cell RCC.

*v. imp / سنوات

The VHL gene is also involved in the majority of sporadic clear cell RCC. Thus, homozygous loss of the VHL gene seems to be the common underlying molecular abnormality in both sporadic & familial forms of clear cell RCC.

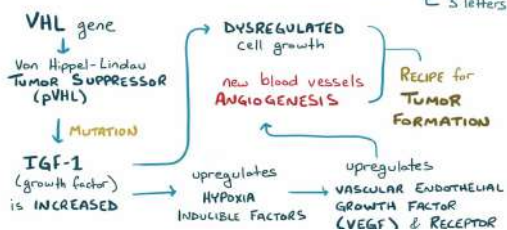
The VHL protein is involved in limiting the angiogenic response to hypoxia; thus, its absence may lead to angiogenesis & tumor growth → by ↑ IGF-1 in familial forms by ↑ VEGF, ↑ PDGF

The mean age of onset of 26 years and 97% of people with a VHL gene mutation have symptoms by the age of 65.

VHL disease affects males and females and all ethnic groups equally, and occurs in all parts of the world.

in sporadic occurs at the 6th and 7th decades

RENAL CELL CARCINOMAS (RCC'S)



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(II) Papillary RCC

- Comprises **15%** of RCC.
- Shows **papillary growth** pattern.
- Are frequently **multifocal & bilateral**;
- Occurs in **familial & sporadic** forms,
- ^{V.I.M.P.} The **cause** is the **MET proto-oncogene**, located on **chromosome 7q31**.^{PS}
- **Trisomy of chromosome 7** is **seen** commonly in **both familial & sporadic cases**, with the addition of an activating mutation of the MET gene in the **familial cases only**.

(III) Chromophobe RCC

- **Rarest (5%)** type of RCC. ^{↳ good prognosis}
- **Arise** from **intercalated cells** of collecting ducts.
- Tumor cells **stain more darkly** (hence the name, i.e., they are **less clear** than cells in clear cell RCC).
- **Unique** in having **multiple losses of entire chromosomes**, including chromosomes **1, 2, 6, 10, 13, 17, & 21**.
- In general, chromophobe RCC have a good prognosis.

^{*}morphologically :
appear like Raisins

Morphology (of all types)

- **Grossly, the clear cell RCC** is usually **solitary, spherical & large** mass, up to 15 cm in \emptyset , arising (anywhere in the cortex) & its cut surface is **yellow orange** with areas of **cystic necrosis** & fresh or old **hemorrhages**.

tend to invade renal capsule

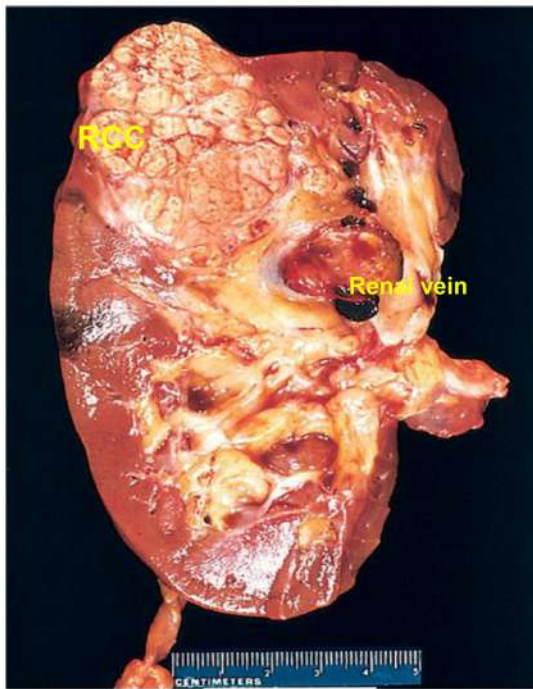
if invasion occur to renal calyces and/or pelvis , patient present with hematuria

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* RCC patients in general presented with one or more of these triad symptoms :
(Renal mass) (Pain) (Hematuria)

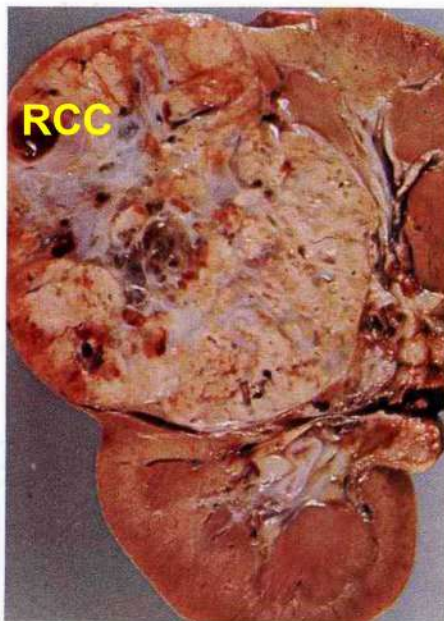


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Renal cell carcinoma (RCC): typical cross-section of ★ yellowish, spherical tumor in the upper pole of the kidney.

★ Note the tumor invasion in the dilated thrombosed renal vein

RCC invade renal vein → Stage 3



10.54 Adenocarcinoma: kidney

Smooth rounded tumor mass in the upper pole of the kidney invading the renal vein (Stage 3)
Yellow cut surface, with greyish fibrous septa, areas of hemorrhage & cystic necrosis

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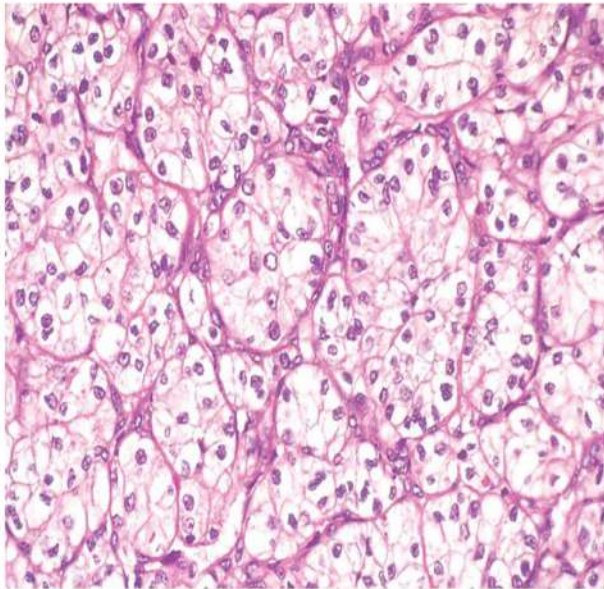
- As the tumor enlarges, it **frequently invades** the
 - ❖ (a) **renal vein** growing as a **solid column** within it, sometimes extending as far as the inferior vena cava & even into the right side of the heart.
 - ❖ Less frequently, it may **invade** through the
 - (b) Walls of the **calyces, pelvis & the ureter**, & **occasionally**,
 - (c) in to the **perinephric fat & adrenal gland**.
- **Histologically**, (*clear cell carcinoma*)
 - Depending on the amounts of lipid & glycogen present, the tumor cells may appear:
 - (a) Classically **vacuolated**, with lipid-laden **clear cells**, with small & round nuclei ,or
 - (b) **Granular cells**, resembling the tubular epithelium, with **granular pink cytoplasm**. (*more glycogen*)

- Some tumors exhibit marked degrees of ^{*Atypia*} **anaplasia**, with **numerous mitotic figures** & markedly **enlarged, hyperchromatic, pleomorphic nuclei**.
- The cellular arrangement, too, varies widely, with **cells** forming **tubules, cords or disorganized masses**. The **stroma** is usually **scant**, but **highly vascularized**



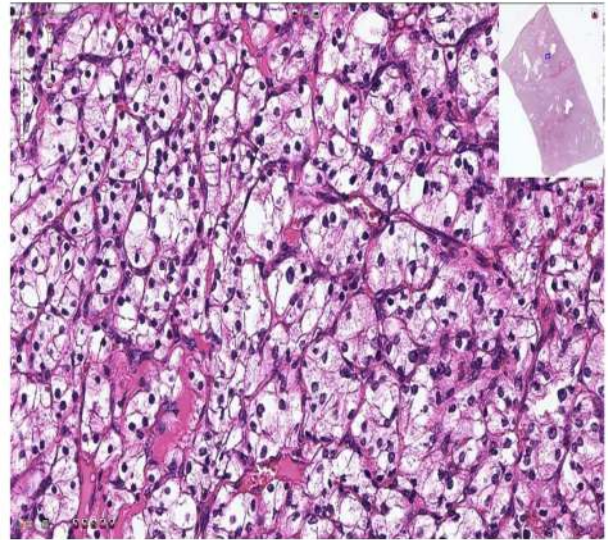
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High power detail of the clear cell pattern of renal cell carcinoma : Arranged in solid pattern of growth



, Tubules
, masses
, cords

RCC



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Grossly:

□ the papillary RCC

- exhibit papillary formation with fibrovascular cores.
- They tend to be bilateral & multiple, & may show gross evidence of cystic degeneration, necrosis & hemorrhage; but because of their lower lipid content, they are less orange-yellow in color.
- The cells can have clear or pink cytoplasm.

□ Chromophobe RCC

or mahogany } Characteristic for this type

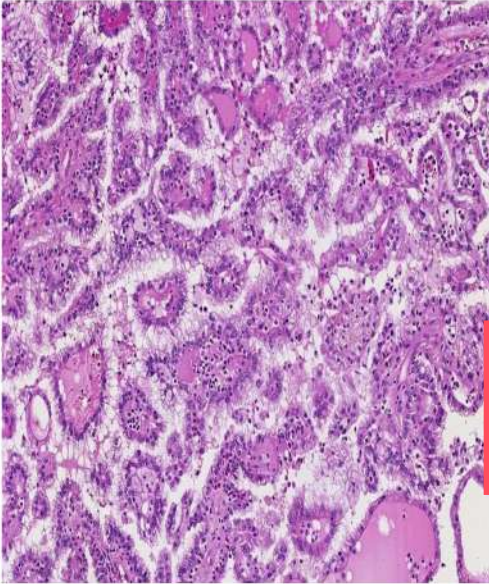
- tends to be tan-brown grossly.
- Their cells usually have clear, flocculent cytoplasm with very prominent, distinct cell membranes.
- * The nuclei are surrounded by halos of cleared cytoplasm.
- By EM, large numbers of characteristic macrovesicles are seen.

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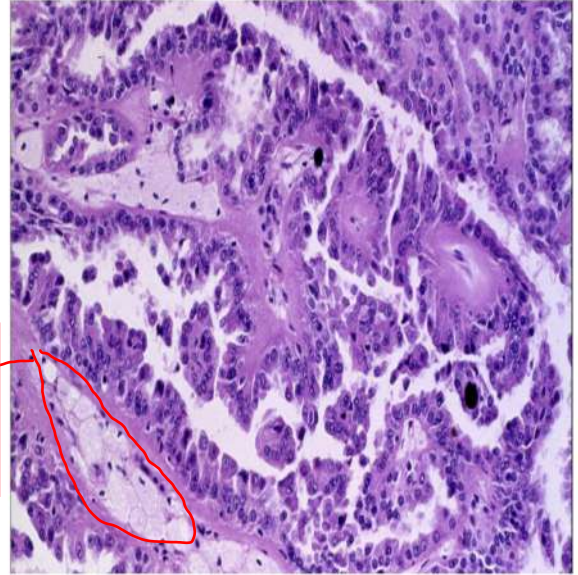


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Papillary RCC



Papillary RCC



benign
histiocytes
in fibrovascular
cord

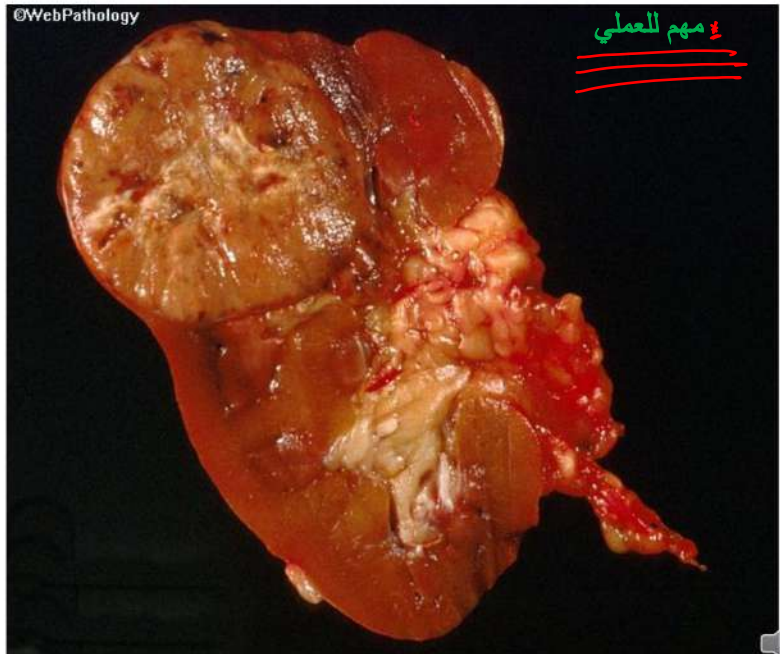
SPOT DIAGNOSIS

Pateint with renal mass , mass shown in the picture , what's your diagnosis?

*V. imp / Lab سنجاش

The upper pole of the kidney shows a well-circumscribed, **mahogany brown tumor with central scar**. The mass bulges the renal capsule but appears to be contained within it. Microscopically, it had classic features of a **chromophobe renal cell carcinoma**.

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مهم للعملي

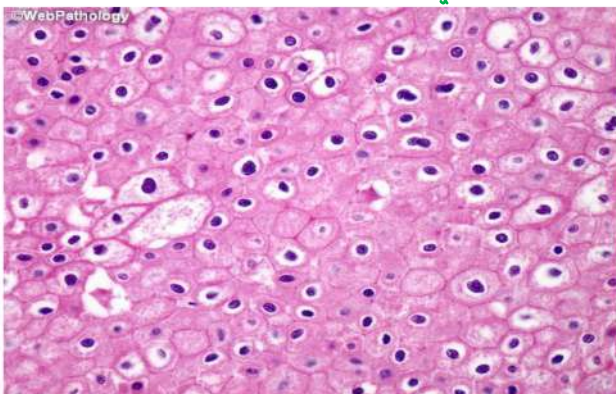
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Chromophobe RCC

مظهر للعلمي



** Look Like Raisins

** Perinuclear halos → due to large numbers of macrovesicles

Patient presented with renal mass , under microscope , it appears as shown in the picture , what's your diagnosis?

Chromophobe RCC

Clinically,

* the most frequent & characteristic presenting manifestation of all RCCs is ((PAIN, HEMATURIA , MASS)):

(I) Hematuria, occurring in more than 50% of cases. due to invading renal pelvis

(Less commonly) as;

(II) painful, palpable flank mass, or may

(III) present with metastases, in which the primary T may remain silent & is discovered only after it metastasizes to other sites, the commonest are the lungs & bones.

imp

* Extra-renal nonspecific effects (manifestation) of RCC are (1) fever, (2)

* polycythemia affecting 5% to 10% of persons with RCC resulting from elaboration of erythropoietin by tumor cells.

* Uncommonly, RCC may cause (3) paraneoplastic syndromes due to their production of a variety of hormone-like substances, resulting in hypercalcemia, hypertension, Cushing syndrome, feminization or masculinization.



Thrombosis +

polycythemia > tumor cells produce EPO

Hypercalcemia > tumor cells produce Parathyroid hormone

Hypertension > tumor cells produce renin

Cushing > tumor cells produce ACTH

Another cancers also produce hormone-like substances:

- Squamous cell carcinoma of the lung

- Small cell carcinoma of the lung

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IMMUNOHISTOCHEMICAL TECHNIQUES IN RENAL NEOPLASMS

• Immunohistochemical techniques with a variety of markers have been applied more frequently in diagnostic pathology of renal neoplasm

• Some of the most important and useful markers for the diagnosis of renal neoplasm include **cytokeratins, vimentin, PAX2, PAX8, RCC marker, CD10**, Each marker has its diagnostic role in a specific diagnostic setting.

• The common diagnostic situations that call for immunohistochemical staining are differential diagnoses of renal versus non renal neoplasms,

F.Y.I
صحت الحقة*

Staging of RCC , V. imp

TNM → T: Size + involvement of renal vein
N: Spread to L.N

STAGING

Based on examination, imaging and biopsy

- AJCC (TNM) staging system:
- T categories for kidney cancer:
 - T0: No evidence of primary tumor
 - T1: The tumor is only in the kidney and is 7cm or less across
 - T1a: The tumor is 4cm across or smaller
 - T1b: The tumor is larger than 4cm but not larger than 7cm
 - T2: The tumor is larger than 7cm across but is still in the kidney
 - T2a: The tumor is more than 7cm but not more than 10
 - T2b: The tumor is more than 10cm across
 - T3: The tumor is growing into a major vein or tissue around the kidney but not into adrenals or beyond Gerota's fascia
 - T3a: The tumor is growing into the main vein or into fatty tissue around the kidney
 - T3b: The tumor is growing into the venacava leading into the heart
 - T3c: The tumor has grown into the part of venacava that is within the chest or growing into the wall of that blood vessel
 - T4: The tumor has spread beyond Gerota's fascia. It may have grown into the adrenal gland

T1: Tumor confined to the kidney and it is 7 cm or less

T2: Tumor still in kidney but larger than 7 cm

T3: Tumor growing into major vein or tissue around the kidney (not adrenals and not beyond Gerota's fascia)

صوات / V. imp

T4: Tumor spread beyond Gerota's fascia or to adjacent structure

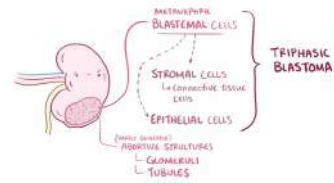


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Nephroblastoma (Wilm's Tumor)

1st common: Neuroblastoma / Rhabdomyosarcoma

- Represent **10%** of all renal cancers.
- The **3rd most common solid cancer in children** younger than 10 years; it occurs rarely in adults,
- A **mixed tumor**, contain a **variety of cell & tissue components** (epithelial & mesenchymal), **all derived from the mesoderm**.
- Triphasic tumour**
 - blastemal tissue** → *embryonal tissue*
 - stromal cells**
 - epithelial cells** (premature tubule and glomeruli)
- Like retinoblastoma, it may arise **sporadically** or be **familial**, inherited as an **autosomal dominant trait**.

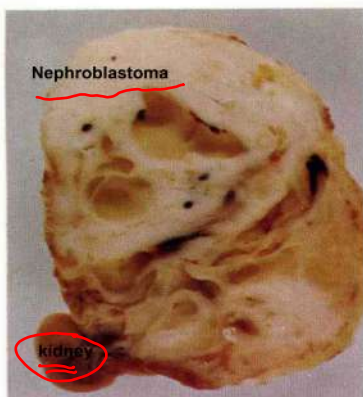


Clinical presentation and diagnosis

mass growth pattern: out of the capsule

- Abdominal mass**, **painless palpable mass**, **non-tender**, **homogenous** or by **incidental finding** of abdominal mass by physician during **routin examination** of healthy child or by mother during bathing.
- (Hematuria)** when tumor ruptures and invades collecting ducts
- (hypertension)** due to renin secretion
- Intestinal **(obstruction)**
- (Fever, anemia)**
- * Diagnosis :**
 - Ultrasound** (initially)
 - CT scan, MRI**

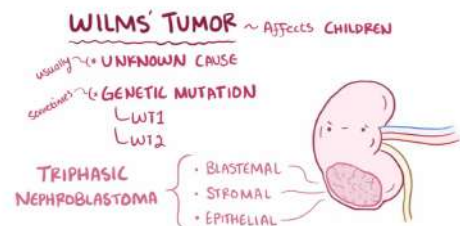
manifest GI symptoms, less likely urological symptoms



10.55 Wilms' tumour (nephroblastoma): kidney

Nephroblastoma (Wilms Tumor).

A **creamy-white tumor** has largely replaced the kidney, a small portion of which is visible at the lower left. Numerous **cysts & focal hemorrhages** are present within the tumor.



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most common

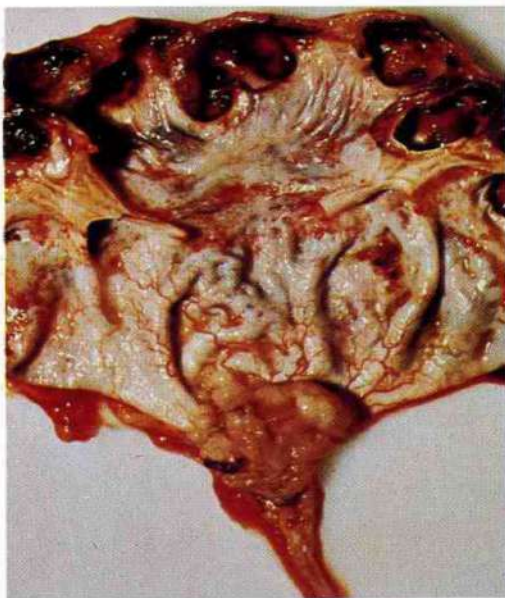
Tumors of the (Renal calyces, Pelvis, Ureter, Urinary Bladder & Urethra)

▪ The entire urinary collecting system, from renal calyces to urethra is lined by transitional epithelium, so its epithelial tumors assume transitional or "urothelial" patterns.

^{imp.} Clinically, the ^{*}most common presentation of all these tumors is (painless terminal hematuria.) → presence of blood in the urine that is visible at the end of urination. / presence of blood in the beginning of urination indicates usually UTIs, stones... rather than tumor

- A small tumor in the ureter may cause urinary outflow obstruction & hydro nephrosis ,
- have greater clinical significance than a much larger mass in the bladder.
- Renal pelvis papillary TCC a carcinomas (comprising 5% of all kidney ca), are much less frequent than bladder ca. Usually causes painless hematuria; but if they cause obstruction, it may result in hydronephrosis and pain in the costovertebral angle.
- Infiltration of the walls of the pelvis, calyces, & renal vein worsens the prognosis

- The reason why the blood appear at the end of urination is that , when the bladder is full there is a pressure on the vessels at bladder wall >> NO BLOOD AT THE BEGINING
- after evacuation, it is followed by terminal hematuria (blood)



10.59 Transitional cell carcinoma: renal pelvis

A sessile papillary yellowish-grey TCCa at the pelvi-ureteric junction lead to obstructing the ureter and producing severe hydronephrosis, with... marked pelvic mucosal congestion & extensive calyceal hemorrhage ^{due to obstruction}



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Bladder cancer *imp.*

Bladder cancer is a disease in which malignant (cancer) cells form in the tissues of the bladder. Smoking can affect the risk of bladder cancer. Signs and symptoms of bladder cancer include blood in the urine and pain during urination. Tests that examine the urine and bladder are used to diagnose bladder cancer.

Bladder ca affect men 3 times as frequently as women. It usually develop in the 50 to 70 years age group.

50 times more common in aniline dye workers, duo to carcinogenic effect of β -naphthylamine. *Plastic Factories*

It is more common in: *(Risk Factors)*

Schistosomiasis of the bladder *[Common in Egypt]*

- Chronic cystitis.
- Cigarette smoking.
- Certain drugs (e.g., cyclophosphamide) are also believed to induce higher rates of bladder cancer



- RISK FACTORS
- AGE
 - CARCINOGENS
 - Phenacetin - a banned analgesic
 - Smoking - #1 risk factor
 - Aniline - rubbers & dyes
 - Cyclophosphamide - medicinal - Treats CANCERS and AUTOIMMUNE diseases

Type of tumor here is squamous because it cause metaplasia (urothelial >> squamous >> squamous cell carcinoma)

Bladder tumors classified into:

(1) Very rare benign papillomas, usually solitary, 0.2-1.0 cm frond like structures having a delicate fibrovascular core covered by multilayered completely normal looking transitional epithelium. They are noninvasive & rarely recur once removed. *to confirm its diagnose -> Should be cautious -> with low-grade papillary ca*

(2) Papillary urothelial tumors of (low malignant potential) *also in ovaries* - growth of the tumor - Papillary growth inside the cavity - Atypia (Little) *قله غير مريح*

(3) Transitional (Urothelial) carcinoma (TCCa) may be papillary or flat, noninvasive or invasive & low or high grade. *but there is no invasion*

- Pathologists divide urothelial carcinoma into two grades - low and high based on how the tumour cells look when examined under the microscope.
- Low-grade tumours are made up of cells that look more like normal urothelial cells while high-grade tumours are made up of more abnormal looking cells that tend to be larger, darker, and less organized than normal urothelial cells.
- The grade is important because high-grade tumours are more likely to re-grow after treatment and spread to other parts of the body.

flat = infiltrative -> growth of the tumor to inside [more invasive] -> may reach muscular wall of bladder
papillary better than flat **(High Staging)*



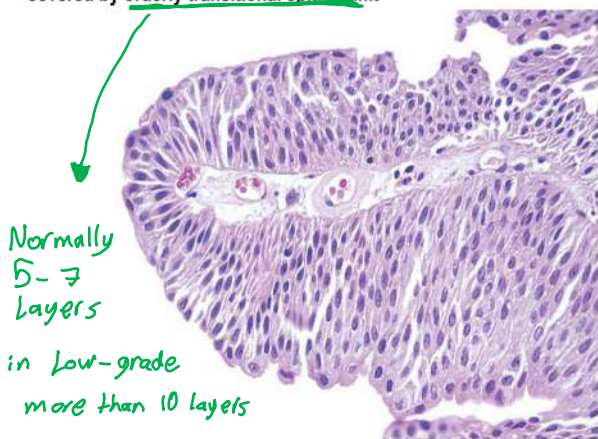
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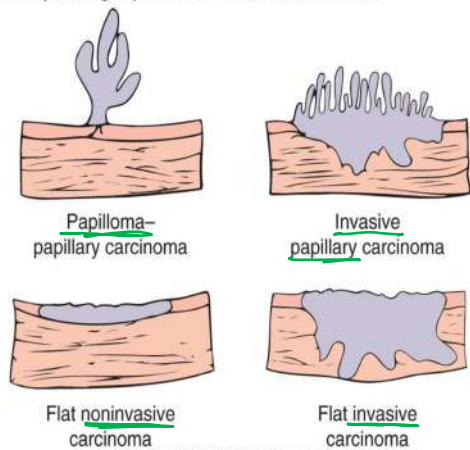
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- **Low-grade (Grade I) ca** :are **always papillary & rarely invasive**, may **recur after removal**. Increasing degrees of cellular atypia & anaplasia are seen in papillary exophytic tumors accompanied by an increase in the size of the tumor & evidence of invasion of the submucosal.
- **High-grade (Grades II & III) ca** can be **papillary or flat** may cover **larger areas** of the mucosa, **invade deeper in the muscular layer**, may ulcerate, & may show foci of squamous differentiation.
- * 5% of bladder ca in US (BUT up 50% else where in world) are usually associated with Schistosomal cystitis are **true squamous cell ca** (metaplasia)
- **Grades II & III ca** infiltrate surrounding structures, spread to regional LNs & occasionally metastasize.
- In addition to overt ca, an in situ (pre-invasive) stage of bladder carcinoma can be recognized, often in individuals with previous or simultaneous papillary or invasive tumors.

Low-grade papillary urothelial carcinoma of the bladder. The delicate papilla is covered by orderly transitional epithelium.



Four morphologic patterns of bladder tumor



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- * The most common genetic abnormalities seen in bladder cancers are mutations, involving several genes, on chromosome 9 (including p16), p53, & FGFR3. *role in blocking apoptosis*
- Bladder tumors prognosis depends most importantly ^① on the depth of the invasion of the ca (muscular invasion usually treated by total cystectomy) & ^② on their histological grade.
- Except for the clearly benign papillomas, *↳ doesn't recur* all bladder tumors tend to recur after removal.
- also can invade prostate* Tumors invading ureteral or urethral orifices cause UT obstruction.
- Prognosis of low-grade shallow bladder tumors, after removal is generally good, but when...
- Deep penetration of the bladder wall muscles has occurred; the prognosis is poor with less than 20% 5-year survival rate



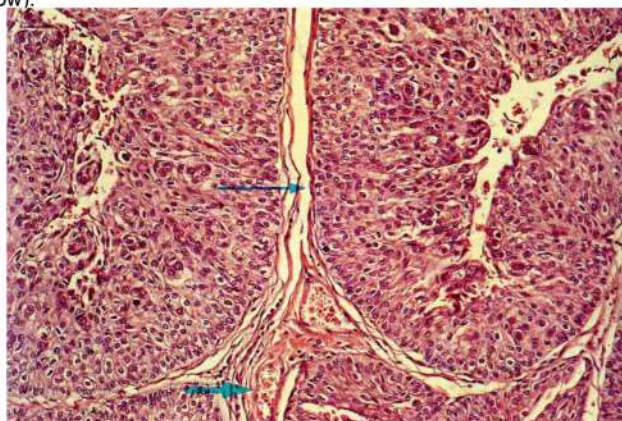
10.63 Papillomas: bladder

Low-grade papillary urothelial carcinoma:
bladder.

- Multiple small sessile papillary tumors, covering large areas of the bladder.

High grade
The patient worked for many years in the rubber industry.

High grade
Transitional cell carcinoma, Grade II X150. Papillae, covered by transitional epithelium, several times thicker than normal (thin arrow) & with a fibrovascular core (thick arrow).



- High stage of*
- Bladder tumor can invade prostate
- Prostate tumors also can invade bladder

to differentiate the origin of the tumor we use specific immunostains (immune panel)

* v.o imp / سنوات ↑

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V imp

V. imp

Staging of urachal tumours
 There is no AJCC staging system for tumors arising in urachal remnants, but they may be staged according to several proposed systems

Urinary bladder staging

- **Tis**: Urothelial carcinoma *in situ* not invading basement membrane
- **Ta**: Noninvasive papillary urothelial carcinoma
- **T1**: Invasive into lamina propria *doesn't reach muscular layer*
- **T2**:
 - * **T2a**: Invasive into inner half of muscularis propria
 - * **T2b**: Invasive into outer half of muscularis propria
- **T3**:
 - * **T3a**: Microscopic invasion in perivesical soft tissue → *can't be seen grossly*
 - * **T3b**: Macroscopic invasion in perivesical soft tissue → *Seen grossly*
- **T4**: Invasion into adjacent organs

Staging of diverticula
 Muscularis propria is absent; thus, there is no T2

Discontinuous involvement of urethra is assigned a separate urethral stage per the urethral staging system

Staging of Urothelial ca of Urinary bladder

STAGES

Stage 0 (Tis)	Flat cancerous cells within the cells lining the bladder
Stage 0 (Ta)	Inner lining of the bladder
Stage 1 (T1)	Into first deep bladder layer
Stage 2 (T2a)	Into bladder muscle
Stage 2 (T2b)	Deeply into bladder muscle
Stage 3 (T3a)	Into bladder fat
Stage 3 (T3b)	Deeply into bladder fat
Stage 4 (T4)	Invading other organs around the bladder (prostate, cervix, vagina)

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GENITOURINARY SYSTEM

Q: A 59-year-old man notes blood in his urine for the past week. On physical examination there are no abnormal findings. A urinalysis confirms the presence of blood, but no proteinuria or glucosuria. A urine culture is negative. A cystoscopy is performed, and a 3 cm exophytic mass is seen in the dome of the bladder. A biopsy of this mass is performed and microscopic examination reveals fibrovascular cores covered by a thick layer of urothelium (transitional cells). Which of the following risk factors is most likely to have led to development of this lesion?

- A Diabetes mellitus
- B Recurrent urinary tract infection
- C Therapy with methicillin
- D Cigarette smoking
- E Tuberos sclerosi
- F Use of NSAIDS

ANS: D

Q: 54 A 60-year-old man has a feeling of fullness in his abdomen and a 5-kg weight loss over the past 6 months. He has a 50 pack-year smoking history. Physical examination is normal. Laboratory studies show hemoglobin of 8.3 g/dL, hematocrit of 24%, and MCV of 70 μm^3 . Urinalysis shows 3+ hematuria, but no protein, glucose, or leukocytes. Abdominal CT scan shows an 11-cm mass in the upper pole of the right kidney. A right-sided nephrectomy is performed, and gross examination reveals that the mass has invaded the renal vein. Microscopic examination of the mass shows cells with abundant clear cytoplasm. Which of the following molecular abnormalities is most likely to be found in tumor cell DNA?

- A) Homozygous loss of the von Hippel–Lind (VHL) gene
- B) Integration of human papillomavirus type 16 (HPV-16)
- C) Microsatellite instability
- D) Mutational activation of the MET proto-oncogene
- E) Trisomy of genes on chromosome 7

ANS: A



GENITOURINARY SYSTEM

Q: A 20-year-old man comes to the clinic due to burning urination for the past 3 weeks. The patient recently returned from a trip to Egypt, where he hiked and swam in freshwater. During that time, the patient developed an itchy rash over some parts of the body, which self-resolved after a few days. Medical history is unremarkable besides a gonorrhea infection 3 years ago, which was successfully treated with antibiotics. Vital signs are within normal limits. Physical examination shows no abnormalities. Complete blood count shows:

Laboratory value	Result
Hemoglobin	12 g/dL
Hematocrit	40%
Leukocyte count	12,100/mm ³
Platelet count	400,000/mm ³
Leukocyte count	16000/mm ³
Neutrophils, segmented	54%
Neutrophils, banded	5%
Eosinophils	12%
Basophils	0%
Lymphocytes	25%
Monocytes	7%

Urine sample is obtained and the specimen under light microscopy is shown below:

- A) Bladder cancer
- B) Aortitis
- C) Swelling in skin
- D) Rapidly fatal meningoencephalitis
- E) Liver abscess



ANS: A

Q: A 3-year-old child has become more irritable over the past two months and does not want to eat much at meals. On physical examination the pediatrician notes an enlarged abdomen and can palpate a mass on the right. An abdominal CT scan reveals a 10 cm solid mass involving the right kidney. The resected mass has a microscopic appearance with sheets of small blue cells along with primitive tubular structures. The child receives chemotherapy and radiation therapy, and there is no recurrence. Which of the following neoplasms is this child most likely to have had?

- A Angiomyolipoma
- B Renal cell carcinoma
- C Urothelial carcinoma
- D Wilms tumor
- E Medullary fibroma

ANS: D

Q: Members of a family with a history of renal cancers undergo ultrasound screening. Two adults are found to have multifocal and bilateral renal mass lesions. Biopsies are obtained, and microscopic examination shows a papillary pattern. A mutation involving which of the following genes is most likely to be found in this family?

- A) RAS
- B) PKD1
- C) MET
- D) TSC1
- E) WT1

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ANS: C



GENITOURINARY SYSTEM

Q: A 60-year-old man has noted a nonproductive cough along with back pain for 4 months. He has passed darker urine for 1 month. He has a 50 pack/year history of smoking. On examination, his blood pressure is 175/110 mm Hg. He has tenderness to percussion of the upper back. Urinalysis shows 3+ blood but no casts or crystals. Chest CT imaging shows a 4-cm solid nodule in the right lower lobe of his lung, as well as 1- to 2-cm lytic lesions in thoracic vertebrae. A neoplasm is most likely to have arisen in which of the following urinary tract locations in this man?

- A) Bladder dome
- B) Calyx
- C) Penile urethra
- D) Renal cortex
- E) Urachus
- F) Ureter

ANS: D

Q: 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 side. 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-sided nephrectomy is performed; the gross appearance of the mass is shown in the figure. What is the most likely diagnosis?

- A) Angiomyolipoma
- B) Interstitial cell tumor
- C) Renal cell carcinoma
- D) Transitional cell carcinoma
- E) Wilms tumor

ANS: E

Q:

A 56-year-old man complains of dull flank pain for the past month. On physical examination he has tenderness to percussion at the right costovertebral angle. Laboratory studies show microscopic hematuria but no proteinuria or glucosuria. A urine cytology shows no atypical cells. A CBC shows WBC count 7800/microliter, Hgb 21.1 g/dL, Hct 63.5%, MCV 94 fL, and platelet count 195,000/microliter. His serum urea nitrogen is 15 mg/dL and creatinine 1 mg/dL. Which of the following radiographic findings is most likely to be present in this man?

- A Hydronephrosis on intravenous pyelogram
- B Renal mass on abdominal CT scan
- C Radiopaque ureteral calculus on an abdominal plain film
- D Enlarged, multicystic kidneys on abdominal ultrasound
- E Pelvic abscess below the bladder on MR imaging

ANS: B

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