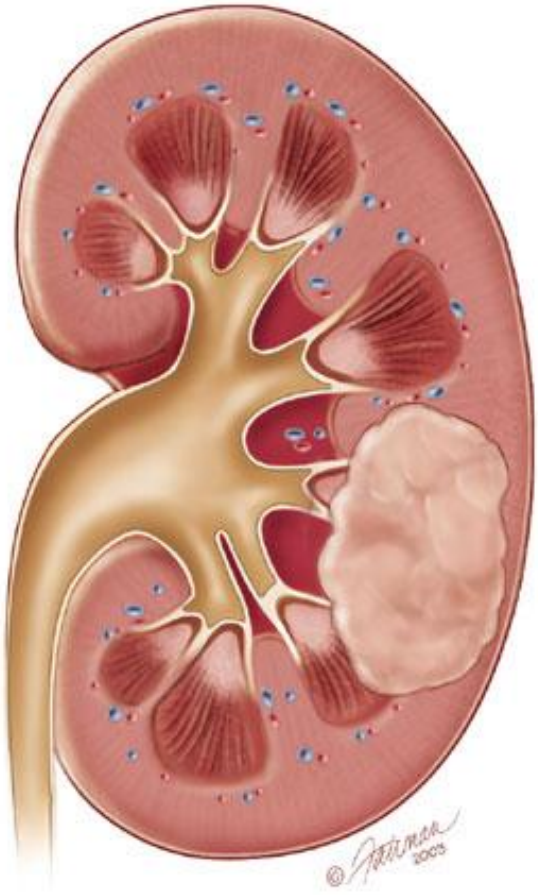
Tumors of The Kidney



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It is Adequate for Studying this Lecture

FULLY REVISED WITH Dr.Hala Kfouri

P.S. What's in the Yellow Box is *General Information* (Read Only).

Introduction:

- The **most common** malignant tumor of the kidney is **Renal Cell Carcinoma > Nephroblastoma (Wilms tumor).**
- Tumors of the lower urinary tract are about twice as common as renal cell carcinoma.

Benign tumors:

1) Renal papillary adenoma:

- small, discrete (usually yellow) tumors are seen in 7% to 22% of autopsies.
- **Histologically**: consist of vacuolated epithelial cells forming tubules and branching papillary structures.

2) Angiomyolipoma:

- **Assiciated with:** Tuberous sclerosis (25% - 50% of patients), these tumors are considered to be **HAMARTOMAS.**

Malignant Tumors:

Renal Cell Carcinoma:

- Most common and men are affected about twice as commonly as women.
- It 85% of all primary malignant tumors of the kidney.
- It arises from the renal tubular epithelium → they are located in the cortex.

Risk Factors

-smoking -hypertension -obesity
-exposure to cadmium -acquired polycystic disease (30-fold increased risk)

Common Forms, Based on Moleculat Origins of these Tumors:

A) Clear Cell Carcinomas:

- The most common type (80% of renal cell cancers).
- They are made up of cells with ***clear or granular cytoplasm***.
- The majority of them are sporadic (not connected)
- They also occur in familial forms or in association with **Von Hippel-Lindau (VHL) disease.**

VHL disease is an autosomal dominant disorder ,
characterized by predisposition to a variety of neoplasms, particularly to ***hemangioblastomas*** of the cerebellum and retina. Those with VHL syndrome inherit a germ-line mutation of the VHL gene on the short arm of chromosome 3 (3p25).

A) Papillary Renal Cell Carcinoma:

- Comprises 10-15% of all renal cancers.
- They show a papillary growth pattern.
- These tumors are frequently *multifocal and bilateral and appear as early-stage tumors*.
- As clear cell carcinoma, they occur in familial and sporadic forms.
- The gene involved is MET proto-oncogene, located on the long arm of chromosome 7.
- This MET gene, which is a tyrosine kinase receptor for hepatocyte growth factor, is expressed in an increased amount, which will result in an abnormal growth in the proximal tubular epithelial cells giving precursors of papillary carcinomas.

B) Chromophope Renal Carcinomas:

- These are the least common, representing 5% of all renal cell carcinomas.
- They arise from intercalated cells of collecting ducts.
- These tumors are unique in having *multiple losses of entire chromosomes* including:1, 2, 6, 10, 13, 17, 21.
- In general, chromophope renal cancers have a good prognosis

Morphology:

A) Clear Cell Cancers

Grossly:

- The most common form, are usually solitary and large when symptomatic (spherical masses 3-15 cm in diameter), They may arise anywhere in the cortex.
- The cut surface is **yellow to orange to gray-white, with prominent areas of cystic softening or of hemorrhage,** either fresh or old.
- The margins of the tumor are well defined.
- Frequently, the **tumor invades the renal vein** and grows as a solid column within this vessel, sometimes extending in serpentine fashion as far as the inferior vena cava and even into the right side of the heart.

Microscopically:

- The tumor cells of clear cell renal cell carcinoma may appear almost vacuolated (full of lipid and glycogen) or may be solid.
- The classic vacuolated (lipid-laden), or clear cells are demarcated only by their cell membranes.
- The nuclei are usually small and round (see the figure). At the other extreme (i.e. solid) are granular cells, resembling the tubular epithelium, which have small, round, regular nuclei enclosed within granular pink cytoplasm.
- Between the extremities of clear cells and solid granular cells, all integrations may be found.
- The Stroma is usually scant but highly vascularized.

B) Papillary renal cell carcinomas

tend to be bilateral and multiple. They may also show gross evidence of necrosis, hemorrhage, and cystic degeneration. The cells can have clear or, more commonly, pink cytoplasm.

C) Chromophobe-type renal cell carcinoma

tends to be grossly tan-brown. Having very prominent, distinct cell membranes. The nuclei are surrounded by halos of cleared cytoplasm.

Clinical course:

- The most frequent presenting manifestation is hematuria, occurring in more than 50% of cases.
- Extra-renal effects are fever and polycythemia, both may be associated with a renal cell carcinoma.
- Polycythemia result from elaboration of erythropoietin by the renal tumor.
- Uncommonly, these tumors can result in paraneoplastic syndromes, some of these are hypercalcemia hypertension, cushing syndrome, feminization or masculinization.
- The prevalent locations for metastases are the lungs and the bones.
- The following triad is characteristic for renal cell carcinoma:
  1) painless hematuria 2) palpable abdominal mass 3) dull flank pain.

Wilm's tumor (nephroblastoma):

- Wilm's tumor is the most common primary kidney tumor in children.
- Most cases occur between the ages of 2 to 5 years
- children that are born with congenital malformations are at high risk of developing Wilm's tumor.

Three malformation syndromes :

1-WAGR (Wilms tumor, Anridia, Genital malformation and Retardation) syndrome:

Associated With abnormalities in the WT1 gene, the abnormality is loss of genetic material (***deletion***).

2-Denys-Drash syndrome (DDS):

Characterized by Gonadal Dysgenesis and Renal malformation.
Patients with this syndrome are at an extremely high risk of developing Wilms' tumor (~90%)
Associated With abnormalities in WT1 gene, but here the abnormality is a ***mutation.***

3-Beckwith-Weidmann syndrome (BWS):

Characterized by enlargement of individual body organs (e.g., tongue, kidneys, or liver) or entire body segments (hemihypertrophy); enlargement of adrenal cortical cells *(adrenal cytomegaly) is a characteristic microscopic feature*

The genetic locus that is involved in these patients is called "WT2" for the second Wilms' tumor locus.
Note :WT1 and WT2 in chromosome 11
Many are now known to be associated with genetic defects on chromosome 11.

Morphology:

Grossly:

Contains a lobulated tan-white mass.

Microscopically:

Triphastic combination of blastemal, stromal, and epithelial cell types, is observed in most lesions (the percentage of each component is variable).

The three types of cells that are present are:

1)Blastemal: appear as Sheets of small blue cells, with few distinctive features.

2)Epithelial: usually takes the form of **abortive tubules or glomeruli.**

Clinical Course:

1. Paitent complaints

Commonly : Palpable abdominal mass that may extend to the pelvis

Rarely: Abdominal pain - Fever - Hematuria - Intestinal obstruction (due to tumor's large size)

2. Progonosis

Nowadays, treatment gives a better than 90% 5 year survival.

Tumors of the Urinary Bladder and Collecting System:

- The entire urinary collecting system from renal pelvis to urethra is lined with transitional epithelium. so its epithelial tumors assume similar morphologic patterns.
- Tumors in the collecting system above the bladder are relatively uncommon.
- In the bladder, however, are an even more frequent cause of death than are kidney tumors.

Classification:

1) Benign papillomas (rare)
2) Urothelial carcinomas

Major clinical problems of urinary bladder

A- Inflammations:

1- interstitial 2- malakoplakia *3- cystitis glandularis*

B- Neoplasms:

Transitional cell carcinoma - Squamus cell carcinoma - Adenocarcenoma (urachal)

Neoplasms risk factors:

1. Industrial exposure to arylamines
2. Schestosomiasis
3. Cigarette smoking
4. Certain drugs
5. Chronic cystitis

Transitional cell carcinoma:

1- papilloma papillary carcinoma toinvasive papillary carcinoma
2- flat non-invasive carcinoma to flat invasive carcinoma

Morphology:

1) Benign papillomas :

The very rare benign **papillomas** are 0.2- to 1.0-cm frondlike structures having a delicate fibrovascular core covered by multilayered, well-differentiated transitional epithelium

2) Urothelial carcinoma :

they range from papillary to flat, noninvasive to invasive, and low grade to high grade.
Occasionally, these cancers show foci of squamous cell differentiation, but **only 5%** of bladder cancers are true **squamous cell carcinomas**.

Clinical course:

Painless hematuria is the dominant clinical presentation of all these tumors.
Tumors of the bladder are more common than those of the collecting system

Urinary bladder tumors:

• They affect men about three times as frequently as women & usually develop between the ages of 50 and 70 years
• The clinical significance of bladder tumors depends on their *Histologic Grade*, *Differentiation* and, most importantly, *On The Depth Of Invasion Of The Lesion.*
• Lesions that invade the ureteral or urethral orifices cause urinary tract obstruction.

AS FOR THE PROGNOSIS :

• **low-grade shallow lesions :** the prognosis is good after removal
• **High-grade with deep penetration of the bladder wall:** the prognosis is bad , the 5-year survival rate is **less than 20%**.

Collecting System (Renal Calyces, Renal Pelvis, Ureter, and Urethra):

Present with:

• Painless hematuria
• Pain in the costovertebral angle as hydronephrosis develops (if the tumor blocks the ureter).
• Infiltration of the walls of the pelvis, calyces, and renal vein worsens the prognosis

Despite removal of the tumor by nephrectomy, fewer than 50% of patients survive for 5 years
Cancer of the ureter is fortunately the rarest of the tumors of the collecting system. The 5-year survival rate is less than 10%.

Wish You All The Best ...
<Pathology Team - 429>