Renal Block

Lecture Six

Tumors of The Kidney

Important Notes & MCQs

Objectives:

- Recognize the benign tumors of the kidney.
- Describe renal cell carcinoma and Wilms tumor.
- Recognize transitional cell and squamous
- Carcinoma of the urinary bladder

- In any tumor, the important thing is to know if it is benign or malignant. *[Differentiation between malignant and benign tumors].*

- There are kidney tumors that occur only to children and the others occur only to adults. For example:
  - **Renal cell carcinoma** usually affect adults.
  - **Wilms's tumor** usually affect children.

- They may affect teenagers who have genetic disorders

- **Let's start with Benign Tumors:**
  - **Adenoma**: *It is a benign tumor forming glands.*
  - **Angiomyolipoma**, which is formed by:

(Angio = blood vessels / myo = muscles "smooth muscles" / lipoma = fats "Adipose tissue")

- **Malignant Tumors:**
  - **Renal cell carcinoma** *(also called Adenocarcinoma or hypernephroma)*
    - Not always we have gland formation that's why we call it Renal cell carcinoma.
    - Depending on where it is coming from, there will be different features.
    - **Mainly in Adults.**
  - **Nephroblastoma (Wilms's tumor):**
    - Blastoma = Blastema

Blastemas are typically found in the early stages of an organism's development such as in embryos, and in the regeneration of tissue, organs and bone. (Extra)

    - **Mainly in children.**
  - **Neoplasms of the Renal Parenchyma:**
    - Renal Parenchyma (Do you remember the four elements that we discussed in the AKI lecture?)
    - **They are:** Glomerulus, blood vessels, interstitium and tubules.

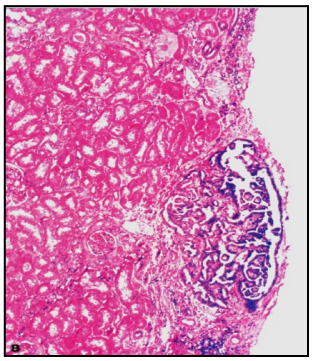
  - Kidney pelvis and calyces are lined by Transitional epithelium, which can be affected, and result in Transitional cell carcinoma.

- **To summarize what we just said:**
- **Kidney tumors:**
  - Adults → Renal cell carcinoma.
  - Children → Nephroblastoma (Wilms's tumor).

- **Histopathology :**
  - **Adenoma :**

    Under the microscope we will see:

    A subcapsular papillary **adenoma** shows tubules arranged in a papillary fashion. *(It has to be small)*



- **Now, we will talk about different types of carcinoma in the kidney:**
  - First, tumors od the Adults:
    - **Renal cell carcinoma:**
      - Depending on what kind of mutation or chromosomal abnormality we have, we will see that there are different types of carcinoma.
      - **Keep in mind** that the most frequent type of carcinoma in adults is **Small clear cell renal cell carcinoma:**

        Small cells with white clear cytoplasm.

        - Sporadic clear cell & Hereditary clear cell:
          - Translocations (3;6 / 3;8 / 3;11)
          - Depletion of Chromosome 3
          - Loss of VHL / Hypermethylation of VHL (von Hippel-Lindau "Tumor suppressor" Mutations of the VHL gene are associated with von Hippel–Lindau disease).
      - In small cell clear carcinoma there are small cells arranged in sheets, In between there is a fine vascular network

- The second most common type is Papillary cell carcinoma: the cells are arranged in papillae, **there are 2 types:**
  - Sporadic papillary:

    There are abnormalities in trisomies 7,16 and 17 or loss of Y.
  - Hereditary papillary:

    Trisomy 7 , mutated and activated MET.

  So, we can say that:

  The chromosome involved in papillary cell carcinoma is Chromosome 7, while in Small clear cell carcinoma it is chromosome 3.

- **Renal cell carcinoma** is usually at the margins *(not central=peripheral)*
- **Grossly, there will be:**
  - Necrosis (caseous yellowish necrosis)
  - Hemorrhage.

- **We started with Benign tumors:**
  1. Adenoma, they are very small and tiny (2-3 ml)
  2. Angiomyolipoma (Blood vessels, smooth muscle and adipose tissues).

- **Then we have discussed malignant tumors:**
  - **Adults:**
    1. **Renal cell carcinoma:**
       - Small clear cell renal cell carcinoma :

         THE MOST FREQUENT TYPE !!
       - Papillary cell carcinoma.
       - Chromophobe renal carcinoma.

    ✓ The most important thing here is to differentiate between sporadic and Hereditary abnormalities :

    2. **Papillary cell carcinoma:**
       - **Sporadic:**

         There are abnormalities in trisomies 7,16and 17 or loss of Y
       - **Hereditary:**

         Trisomy 7 , mutated and activated MET.

3. **Small clear cell renal cell carcinoma :**
    - **Sporadic & Hereditary :**
        - Translocations (3;6 / 3;8 / 3;11)
        - Depletion of Chromosome 3
        - Loss of VHL / Hypermethylation of VHL

          → Usually they have *von Hippel–Lindau disease*

    ✓ Renal Cell Carcinoma is always peripheral. (The renal poles)

    ✓ Gross: We see 2 things: Necrosis & Hemorrhage.

    ✓ Microscopy:

    Small clear cell renal cell carcinoma :

    - There are small cells arranged in sheets, in between there is a fine
    - Vascular network (Thin capillaries).

4. **Transitional cell carcinoma** *(urothelial carcinoma).*

    It is more central.

- **Children:**
    1. **Nephroblastoma (Wilms's tumor):**
        - There are 3 findings under the microscope:
            1) Blastema. *(Immature cells)*
            2) Epithelial elements.
            3) Stroma.

        - **Grossly:**

          Solid / bulgy / fleshy, it could be partially necrotic and it may leave a rim of kidney tissue at the periphery.

        - **There is a criteria to look under the microscope in case of Wilms's tumor:**

          We have to look for certain features that are called as (Anaplasia) which show a lot of polymorphs , mitosis and necrosis > Anaplastic features > HIGH GRADE. High grade means that we have to give the patient much aggressive therapy.

- **Transitional cell carcinoma:** *(urothelial carcinoma).*

  - Can occur in renal calyces, pelvis, ureter, or bladder.

  - Predisposing factors: Smoking.

  - **Carcinoma in situ:**

    It does not cross the basement membrane, they do not invade lamina propria.

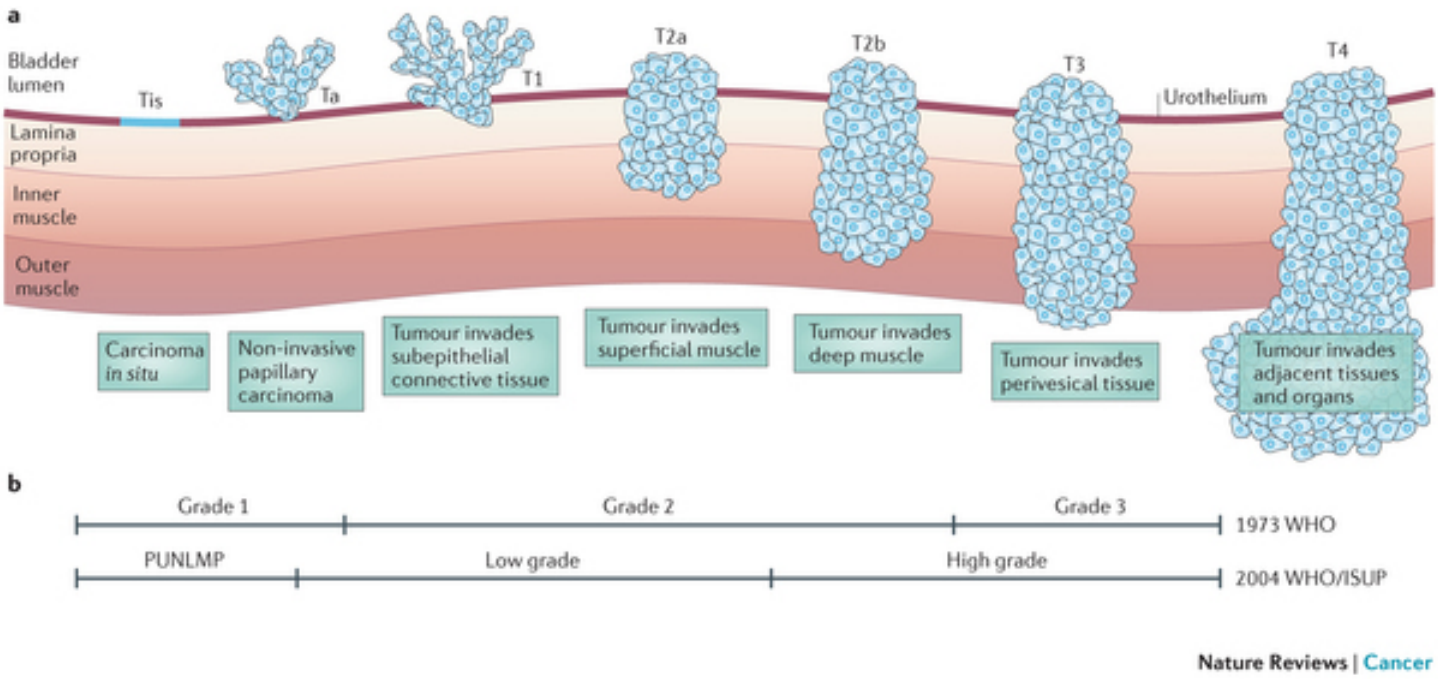
  - **Invasive carcinoma:**

    Infiltrating into the muscles.

  - **The invasion of the muscles** is very important because it may change the whole treatment manner.

  - **Biopsy:**

    We have to consider if it is invasive or not by looking at the muscles : if there is invasion of lamina propria we will say that there is *invasive transitional carcinoma*.



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Summary of 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.
    - Histologically, they are composed of cells with clear cytoplasm.
    - Although most are sporadic, they also occur in familial forms or in association with von Hippel-Lindau (VHL) disease.
    - VHL disease is inherited as an autosomal dominant trait.
    - Those with VHL syndrome inherit a germline mutation of the *VHL* gene on chromosomal band 3p25 and lose the second allele by somatic mutation. Thus, the loss of both copies of this tumor suppressor gene is a key step in the development of clear cell carcinoma.
    - The *VHL* gene is also involved in the majority of sporadic clear cell carcinomas. Cytogenetic abnormalities giving rise to loss of chromosomal segment 3p14 to 3p26 are often seen in sporadic renal cell cancers. This region harbors the *VHL* gene (3p25.3).
    - The VHL protein causes the degradation of hypoxia-induced factors (HIFs), and in the absence of VHL, HIFs are stabilized.
    - HIFs are transcription factors that contribute to carcinogenesis by stimulating the expression of vascular endothelial growth factor (VEGF), an important angiogenic factor, as well as a number of other genes that drive tumor cell growth.
    - An uncommon familial form of clear cell carcinoma unrelated to VHL disease also is associated with cytogenetic abnormalities involving the short arm of chromosome 3 (3p).

- ***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.
    - They show a papillary growth pattern. These tumors are frequently multifocal and bilateral and appear as early-stage tumors.
    - Like clear cell carcinomas, they occur in familial and sporadic forms, but unlike these tumors, papillary renal cancers are not associated with abnormalities of chromosome 3.
    - The culprit in most cases of hereditary papillary renal cell cancers is the *MET* proto-oncogene, located on chromosomal sub-band 7q31.
    - The *MET* gene is a tyrosine kinase receptor for the growth factor called hepatocyte growth factor.

The increased dosage of the *MET* gene due to duplications of chromosome 7 seems to spur abnormal growth in the proximal tubular epithelial cell precursors of papillary carcinomas.

- In familial cases, genetic analysis shows activating mutations of *MET* in the germline, along with increased gene dosage in the cancers. Activating mutations of the *MET* gene also are found in a subset of patients with sporadic forms of papillary renal cell carcinoma.

- *Chromophobe renal cell carcinomas* are less common; tumor cells are not as clear as in the other renal cell carcinomas.

Now Check Your Understanding:

1) Which of the following is the most common malignant tumor of the kidney?

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

2) The risk of developing renal cell carcinoma is higher in……

A. Smokers
B. Hypertensive and obese patients
C. Those who have had occupational exposure to cadmium
D. All of the above

3) All of the following are benign tumors of the kidney EXCEPT …

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

4) The tumors that shows show extreme hypodiploidy are:

A. *Clear cell carcinomas*
B. *Papillary renal cell carcinomas*
C. *Chromophobe renal cell carcinomas*

5) The most frequent presenting manifestation in renal cell carcinoma is:

A. Hematuria
B. Flank pain
C. Polycythemia

6) Wilms tumor is associated with abnormalities of:

A. WT1 and WT2*
B. Trisomy 7
C. Chromosome 3

1. A	2. D	3. A	4. C	5. A	6. A

7) What of the following is a microscopic feature of Wilms tumor?

A. Blastema

B. Necrosis

C. Hemorrahge

8) Hereditary papillary cell carcinoma is caused by:

A. Depletion of chromosome 3

B. Trisomy 7

C. Trisomy 14

D. Deletion of chromosome 3

9) Respectively, what chromosome is involved in papillary cell carcinoma and Small clear cell carcinoma?

A. Chromosome 7, chromosome 3

B. Chromosome 3, Chromosome 7

C. Deletion of 3 and 7

10) Which of these tumors is spreading into the pererenal adipose tissue?

A. Large cell carcinoma

B. Small clear cell carcinoma

C. TTC

11) Which of these carcinomas are related to VHL?

A. Renal cell carcinoma

B. Adenoms

C. Sporadic clear cell

D. Hereditary papillary

12) hereditary clear cell carcinoma is inactivated, mutated _____:

A. Trisomy 7

B. Chromosome 3

C. MET

D. VHL

7. A	8. B	9. A	10. B	11. C	12. D

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