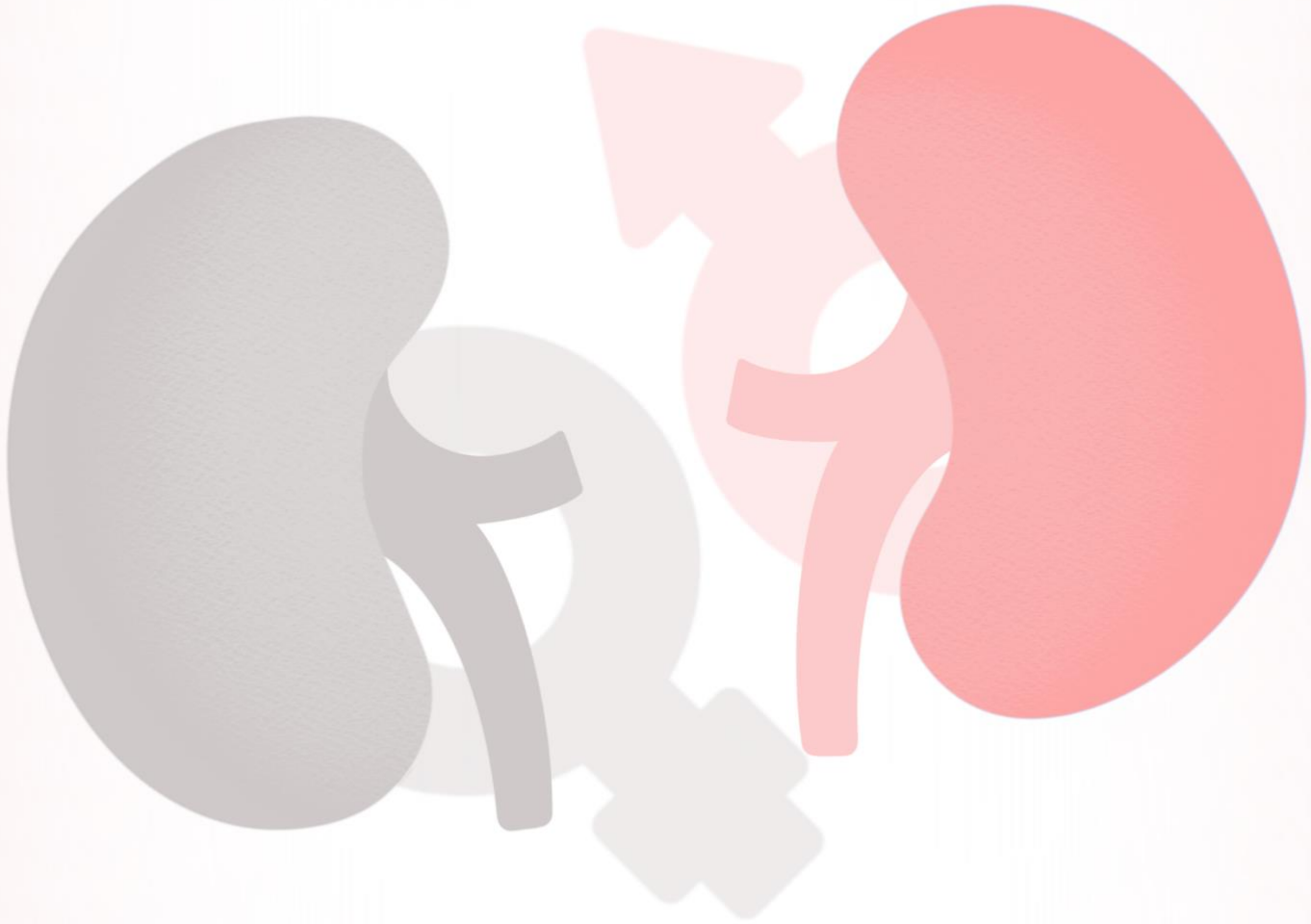
G.U.S.

Pathology

7



Sheet: 7 : Renal Tumors

Writer: Anas Madi

S.corrector: 3omar Ismail o2o

F.corrector: Anas Madi

Doctor: Nisreen Abu Shahin

Renal Tumors

Renal Tumors of Adults are of Two Types:

1. Tumors that target the Kidney itself called **Renal Cell Carcinomas**
2. Tumors that target the Lower Urinary Tract (starting from the Pelvis of the kidney → the Ureters → the Bladder → the Urethra) and these tumors are called **Transitional Cell Carcinomas** or **Urothelial Carcinomas**

• **The Urothelial Carcinomas** (or Transitional Cell Carcinomas) are named so because these tumors involve the hollow structures of the Urinary Tract which are the Pelvis, the Ureters, the Bladder and the Urethra mentioned above; These structures are lined by a certain type of Mucosal Cells (Epithelium) called the **Transitional Mucosa** or Transitional Epithelium (also known as the Urothelium) from which the tumor arise and hence the name

General Facts regarding Renal Tumors:

• **Renal Cell Carcinomas** account for 2-3% of all cancers in adults (not very common)

• The **most common** Malignant Tumor of the Kidney is the **Renal Cell Carcinoma**

• Tumors of The Lower Urinary Tract are **Twice** as common as Renal Cell Carcinoma (so since the Renal Cell Carcinomas account for 2-3% these account for 6-7%)

Renal Cell Carcinomas (RCC)

• Originate from the **Renal Tubular Epithelial Cells** (not the Glomeruli nor the Interstitium)

• Most commonly present in **the Cortex** of the Kidney

• Present 2-3% of all cancers in adults

• Most commonly affects people in their 6^{th} to 7^{th} decade of their life

• More Common in **Males** (Male to Female ratio is 2:1)

• Predisposing factors for RCC:

- ✓ Smoking
- ✓ Hypertension
- ✓ Obesity
- ✓ Occupational exposure to Cadmium (like the Nickel-Cadmium batteries)
- ✓ Chronic Dialysis & Acquired Polycystic disease (Discussed in Lecture 5)

• There is no solid proof or a causality relationship between Hypertension and Obesity with the Renal Cell Carcinoma but they are mentioned as risk factors anyway

• Cadmium is a metal used in the manufacture of Liquid Batteries

• People working with this metal or has an occupational exposure to it were found to have a higher risk of developing RCC than others

Renal Cell Carcinomas are classified based on their Molecular Origin into 3 types: *All forms have Familial and Sporadic cases*

Clear Cell Carcinomas

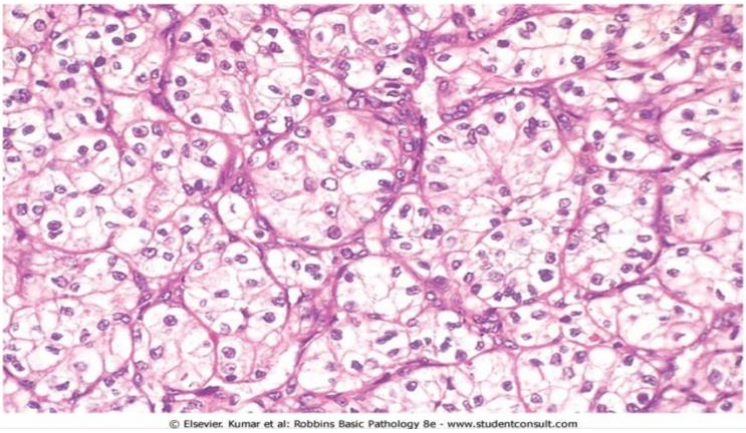
• The most common type (Accounts for 70-80% of RCCs)

• The cells appear to have a **Clear or Granular cytoplasm** (and hence the name)

• Can be Sporadic or Familial

• Both familial and sporadic cases are related to a specific genetic mutation involving a gene located on Chromosome #3 called the **von Hippel-Lindau** gene (VHL gene which is a tumor suppressor gene); a mutation targeting the VHL gene accounts for 60% of Clear Cell Carcinomas cases

• von Hippel-Lindau Disease is a type of the Familial form of Clear Cell Carcinoma



You can notice in this light microscopy image the clear cytoplasm which is a characteristic of Clear Cell Carcinomas

Papillary Renal Cell Carcinomas

• Accounts for 10-15% of cases

• These tumors forms **Papillae** (finger-like projections) which is the growth pattern this tumor follows

• These tumors can be **Multifocal** (multiple masses in the same kidney) and **Bilateral** (multiple masses involving both kidneys)

• Can be Sporadic or Familial

• The genetic abnormality in this tumor involves a gene on Chromosome #7 called **MET proto-oncogene** (proto-oncogenes are natural promoters for cell proliferation and development) and what happens here is that there are **extra copies** of this gene and thus **over-activation** of the MET proto-oncogene resulting in excessive effect on cell growth

• the final effect on the kidney in this case is an increased growth in the **Proximal Tubular Epithelial Cells**

Chromophobe Renal Carcinomas

• The least common type (5% of cases)

• It originates from Tubular Cells and in this case from the **Intercalated Cells of Collecting Ducts**

• Tumor cells appear Less Clear than cells in Clear Cells Carcinomas

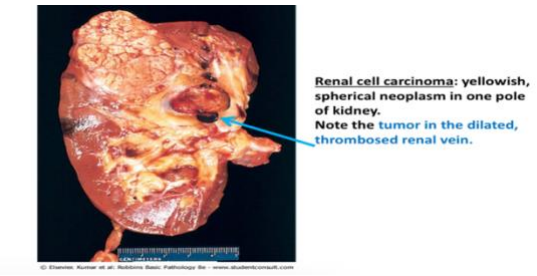
• Chromophobe (Chromo-: color / -Phobe: fear or hate) indicates that cells stain Less Readily and they refuse many staining reactions

• The genetic abnormality here is **Multiple Losses of entire Chromosomes** including 1, 2, 6, 10, 13, 17 and 21

• The result of this of these chromosomes losses is **Extreme Hypoploidy** (Our cells are normally diploid but, in this case, we have lost chromosomes and thus Hypoploidy)

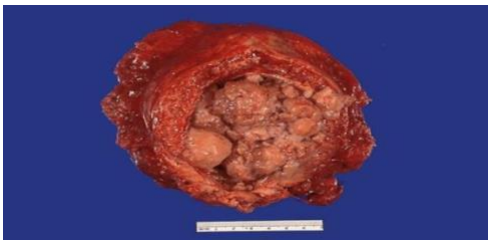
• This tumor has Good Prognosis

Clinical Course of Renal Cell Carcinomas



- ✓ **Painless** Hematuria in 50% of cases
- ✓ **Palpable** Abdominal Mass
- ✓ Dull **Flank** Pain
- ✓ **Fever**
- ✓ **Polycythemia** (5-10%) due to elaboration of **Erythropoietin** by the Tumor
- ✓ **Paraneoplastic Syndromes**: Hypercalcemia / Hypertension / Cushing Syndrome / Feminization or Masculinization (depending on the released hormone)
- ✓ **Metastasis** most commonly to the **Lungs** and **Bones**
- ✓ Vascular Events: Invasion of the **Renal Vein** which may lead to it's Dilation and Thrombosis inside it

Transitional Cell Carcinomas (Urothelial Tumors)



- Classified into 3 Types:

1. Benign Papilloma
2. Papillary Urothelial Neoplasms of Low Grade
3. Papillary Urothelial Carcinoma of High Grade

Papillary Urothelial Carcinoma of Low Grade

• Low Grade means **Well Differentiated** meaning they look similar to the Urothelium

• They are **rarely** invasive and they stay limited to the Mucosa

• Their big issue is that they **Recur** after Removal

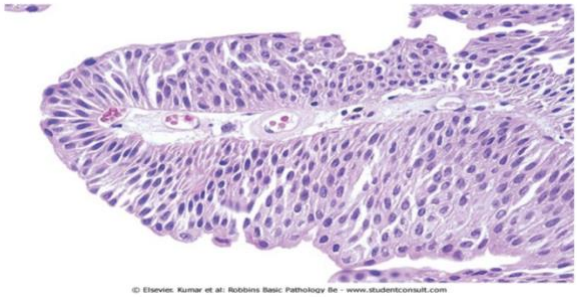
• The most common site for this type of Tumor is the **Urinary Bladder**

• The most prevalent symptom presented is **Painless Hematuria**

• Diagnosis: A **Cystoscopy** is made (Bladder Scope) to make an excision for this tumor which is then sent to the pathology lab to be evaluated Microscopically and Macroscopically to confirm the diagnosis (So the Cystoscopy is both Diagnostic and Therapeutic for this tumor)

• **Remember**: Although the tumor has been remove but recurrence can occur; so a routinely follow-up procedures must be done mainly by **Urine Cytologic Analysis** and using a Cystoscopy every 6 months

• Morphology: Papillary in shape with finger-like projections and present as a Fibrovascular course lined with Urothelium with Low Grade Neoplasms



Bladder Cancers

• Clinical Course of Bladder Cancers:

- ✓ **Painless Hematuria**
- ✓ Male to Female ratio is 3:1
- ✓ Prognosis depends on the Grade (Low Grade = Good Prognosis / High Grade and Deeply Invasive = Bad Prognosis)

• Predisposing Factors of Bladder Cancers:

- ✓ No Familial Cases (Only Sporadic Environmental causes)
- ✓ **β-naphthylamine** (A material found in paint and cigarettes)
- ✓ Smoking
- ✓ Chronic Cystitis and the factors leading up to it
- ✓ **Schistosomiasis** (Bilharziasis)
- ✓ Drugs such as **Cyclophosphamide** (One of it's side effects is that it cause Hemorrhagic Cystitis which increases the risk of Bladder Cancers)

• **Squamous Cell Carcinoma** accounts for 5% of Bladder Cancers and is associated with Schistosomiasis, Chronic Inflammation and Bladder Stones

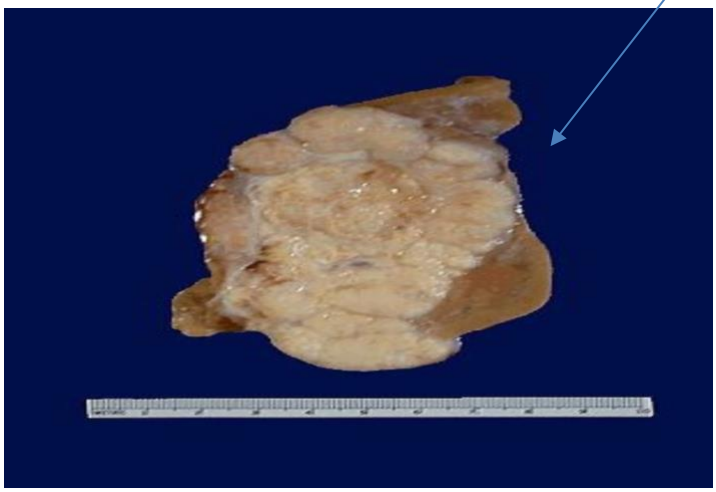
• Treatment of Bladder Cancers:

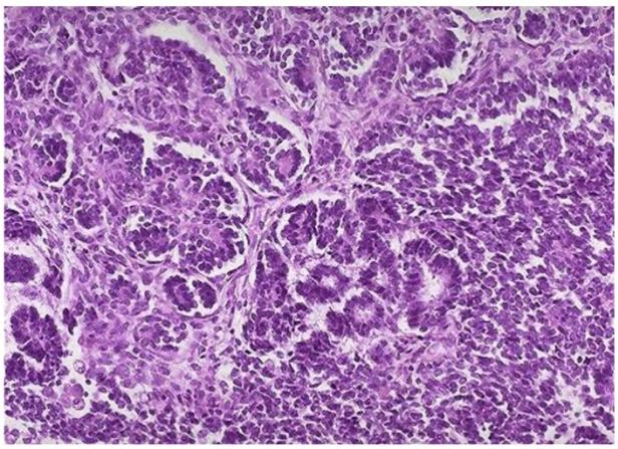
- ➢ Transurethral resection
- ➢ **BCG injections** which induce a Granulomatous reaction leading to an immune response against cancer cells
- ➢ Follow-up for recurrence with Cystoscopy and Urine Cytologic Studies for the rest of the patient's life
- ➢ Radical Cystectomy and chemotherapy for advanced cases

Renal Childhood Tumors

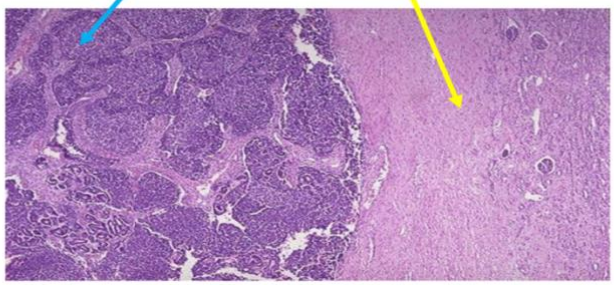
We are only Required with one type which is Wilms Tumor:

- It's the 3rd most common Solid Cancer in children under 10 years (somehow common)
- It is derived from **Primitive Cells** in the Embryo specifically from the **Mesoderm**
- There are Sporadic and Familial cases and the familial form is **Autosomal Dominant**
- Both Sporadic and Familial cases have a genetic abnormality in 2 genes: **WT-1** and **WT-2** genes (WT: Wilms Tumor)
- This Tumor shows attempts to form **Primitive Glomerular and Tubular** structures
- This type of cancer alongside some other forms have their cells form Nests and Sheets of Blue Cells and that's why they are called **Blue Cell Tumors**
- The Gross Appearance of this Tumor appear **Pale** and **Whitish** in color
- Treatment of this cancer is both by **Surgery** and **Chemotherapy**





nests and sheets of dark blue cells at the left with compressed normal renal parenchyma at the right.



Good Luck