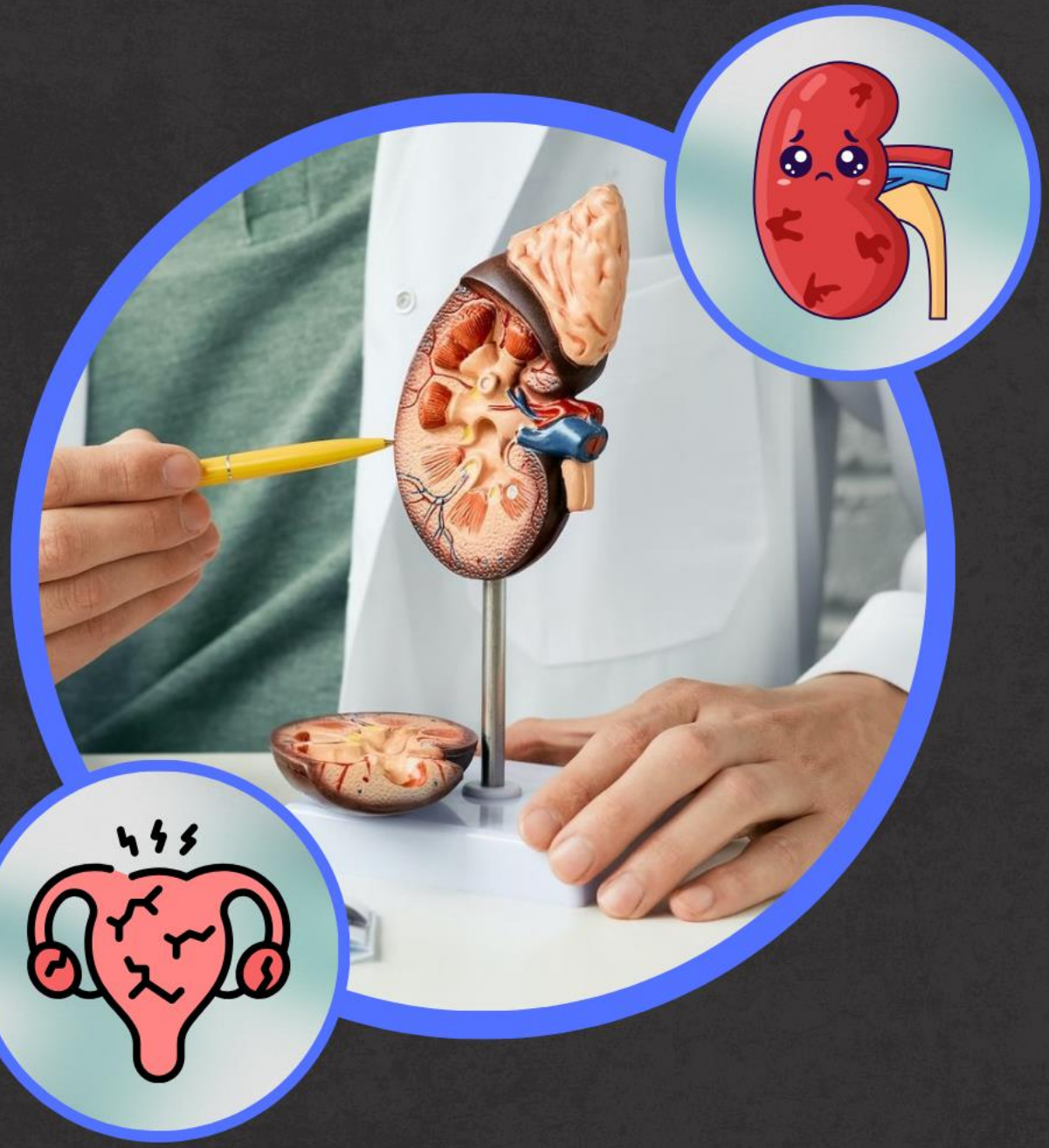

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RENAL TUMORS

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بسم الله الرحمن الرحيم وافضل الصلاة والتسليم على المبعوث رحمة للعالمين سيدنا محمد وعلى اله وصحبه اجمعين

اللهم علمنا ما ينفعنا وانفعنا بما تعلمنا وزدنا بفضلك وكرمك علما وعملا صالحا متقبلا يا أرحم الراحمين

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RENAL TUMORS

All are Adenomas

- **Benign neoplasms such as small cortical papillary adenomas (<0.5 cm in diameter) are found in up to 40% of adults in autopsies.** Usually they are small and Don't cause clinical manifestations so they are unnoticed and found in Post mortem
- **The most common malignant neoplasm of the kidney is renal cell carcinoma.** In adulthood particularly in middle age and beyond
- **Nephroblastoma (Wilms tumor) is the second most common type of tumors.** Occurs in children and young ages

ONCOCYTOMA

- A benign neoplasm that arises from the intercalated cells of collecting ducts.
- It represents about 10% of renal neoplasms.
- It is associated with loss of chromosomes 1 and Y—that is characteristic.

Presents as a cortical mass

It's important because it can mimic malignant neoplasms,
Actually any mass present in the kidney it's significant and must be identified whether malignant or benign

Remember that we previously depend on macroscopic appearance of the tumor for differentiation,
Nowadays It's clear the different types of tumors have a characteristic genetic mutation and sometimes we need to do some genetic studies to reach a correct diagnosis,

A Tumor may show some overlap and a features that can be seen in another one

- **Oncocytomas are characterized by a plethora (Increased) of mitochondria causing tan color and finely granular eosinophilic cytoplasm seen histologically.** Bright pink color
- **A central stellate scar is a characteristic feature of oncocytomas seen on imaging studies.** Stellate =Star shaped

RENAL CELL CARCINOMA

- It is derived from the renal tubular epithelium
- Located predominantly in the cortex.
- Represents 80-85% of all primary malignant neoplasms of the kidney and 2- 3% of all cancers in adults.
- Most common from the 6^{th} -7^{th} Decades age of life
- M:F 2:1

- **Risk factors:**

1. **Smoking**
2. **Hypertension**
3. **Obesity**
4. **Occupational exposure to cadmium** Heavy metals
5. **Acquired polycystic renal disease (30X increase)** E.G. : Stones
6. **Genetic**

Classification

The three most common forms are:

Subtypes

1. Clear cell carcinoma
2. Papillary renal cell carcinoma
3. Chromophobe renalcarcinoma

Classification is dependent on the a appearance of tumor cells

However there is genetic mutation that is a characteristic of each type

CLEAR CELL CARCINOMA

- **It is the most common type**
- **65% of renal cell cancers**

Inherited form is associated with VHL

- **Mostly are sporadic but also occur in familial forms or in association with von Hippel-Lindau (VHL) disease**
- **Histologically they are composed of cells with clear cytoplasm.**

Relatively large with a clear cytoplasm

- **VHL disease is inherited as an autosomal dominant trait**
- **It is characterized by:**

1. **Predisposition to a variety of neoplasms but particularly to hemangioblastomas of the cerebellum and retina**
2. **Bilateral renal cysts and bilateral multiple clear cell carcinomas (in 40-60% of affected individuals**

- **Those with VHL disease inherit a germline mutation of the *VHL* gene on chromosomal band 3p25 and lose the second allele by somatic mutation**

Inevitable occurrence

This will create a condition of homozygosity of gene mutation and presented in younger age

- **The *VHL* gene also is involved in the majority of sporadic clear cell carcinomas**

Presentation takes time because it requires that the two alleles get mutated

- **Loss of a segment on chromosome 3p that harbors the *VHL* gene are often seen in sporadic renal cell cancers**
- **The second, nondeleted allele is inactivated by a somatic mutation or hypermethylation in 60% of sporadic cases**

- **The VHL protein causes the degradation of hypoxia-induced factors (HIFs)**
- **HIFs are transcription factors that contribute to carcinogenesis by stimulating the expression of vascular endothelial growth factor (VEGF) as well as a number of other genes that drive tumor cell growth**

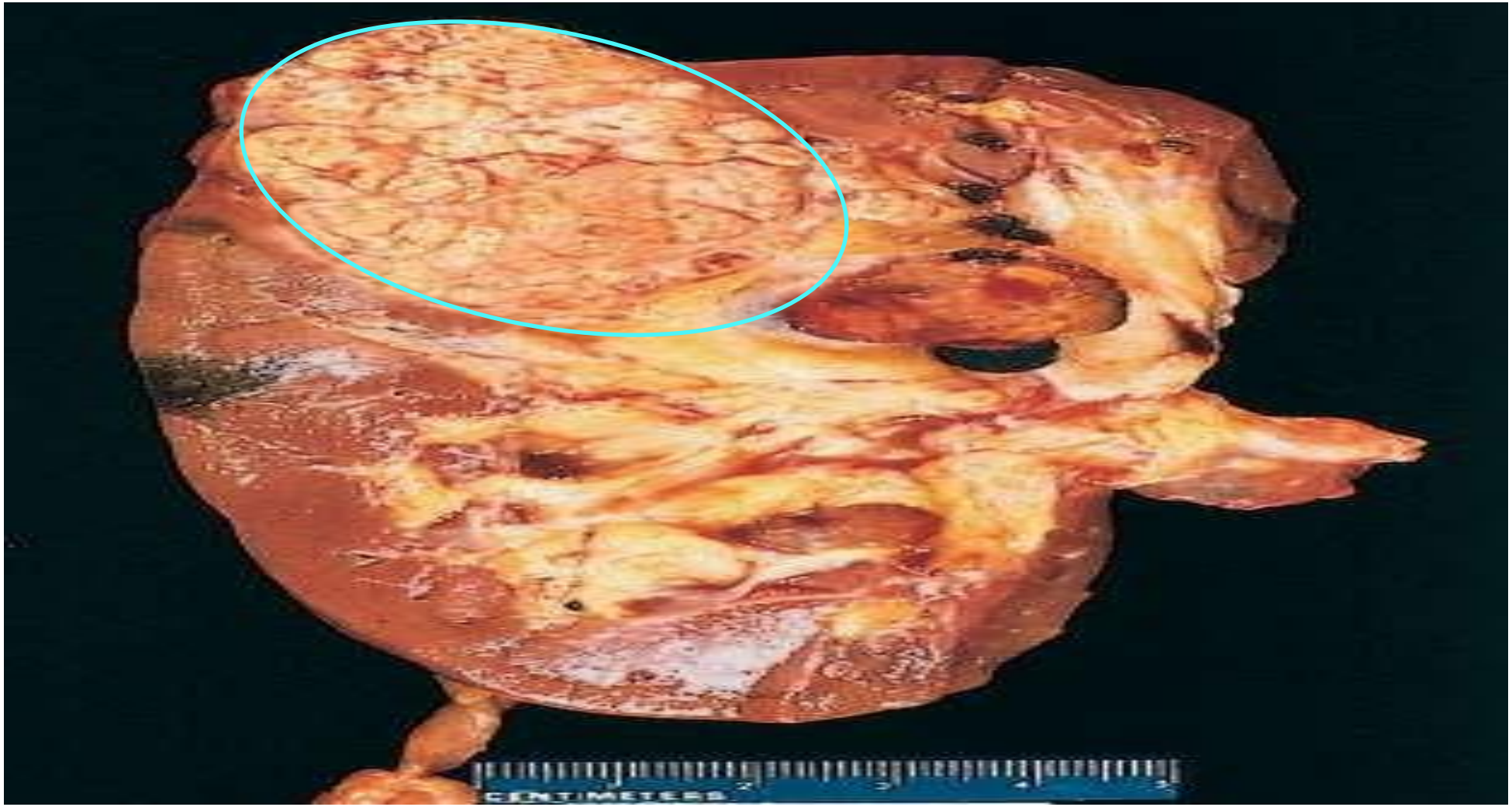
If the VHL gene doesn't degrade the HIF it will lead to accumulation inside the cell which will initiate the process of nuclear signaling and this can be associated with other important growth factors in the carcinogenesis which is the VEGF
This process will continue to give signals for cell division
And this is the mechanism by which the gene mutation Induces the carcinogenesis

- **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).**

It can involve other gene mutations
and chromosomes

Clear cell renal carcinoma

Spherical tumor in the cortex of the kidney



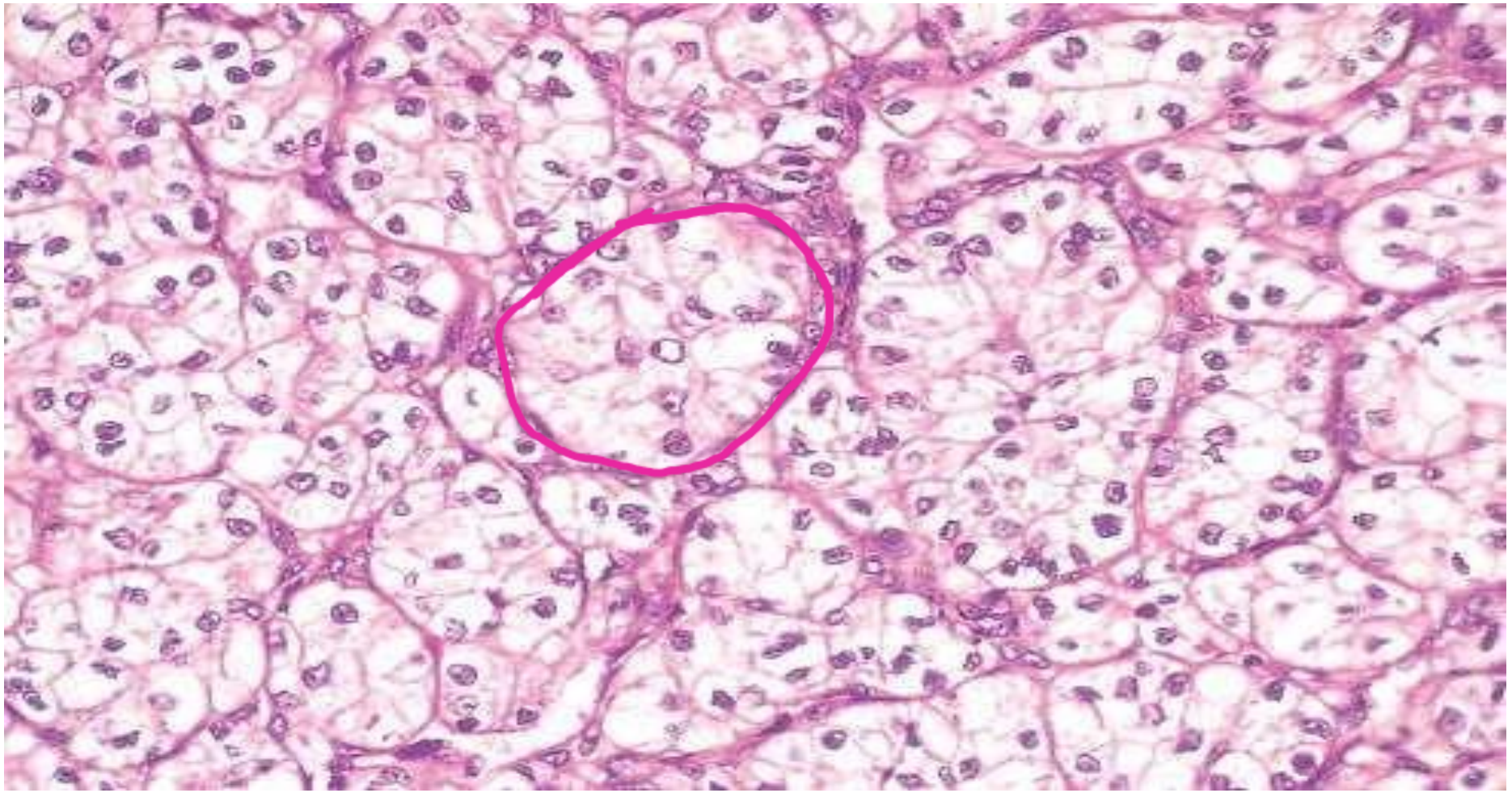
Will demarcated margin of the tumor

However with progression of the tumor this demarcation might be lost due to evolvement of the invasion to the surrounding tissue

The growth of the tumor include the invasion of :
1-the Cortical tissue
2-the kidney capsule (stretched out because of tumor growth)
3-Perinephric fat
4-adrenal gland

Invasion can occur in all directions

Clear cell renal carcinoma



Relatively large due to abundant cytoplasm

Abundant empty cytoplasm (in real life it isn't empty as it is filled with either glycogen or lipid but it is dissolved during processing)
So it appears as a clear cell

Island of the tumor are separated with delicate fibrous tissue

When there is clear cells predominance it's called a clear cells carcinoma, But sometimes there is a mixture with other type of tumor cells

- **Clear cell cancers usually are solitary and large when symptomatic**
- **Spherical masses 3-15 cm in diameter**
- **They may arise anywhere in the cortex.**
- **The cut surface of is yellow to orange to gray-white, with prominent areas of cystic softening or of hemorrhage** With higher grades we can see necrosis
- **The margins of the tumor are well defined.**

- **The margins of the tumor are well defined initially but local invasion is present with tumor progression**
- **The tumor invades the renal vein and grows as a solid column within the vessel sometimes extending in serpentine fashion as far as the inferior vena cava and even into the right side of the heart Occasionally, direct invasion into the perinephric fat and adrenal gland may be seen**

They can invade the draining veins -IVC- and form columns inside it that obstruct or close the,
Leading to complete obstruction sometimes, so the patient suffers from manifestations of that obstruction

- **Depending on the amounts of lipid and glycogen present the neoplastic cells of clear cell renal cell carcinoma may appear almost vacuolated or may be solid**
- **The classic vacuolated (lipid-laden) cells or clear cells are demarcated only by their cell membranes**
- **The nuclei are usually small and round**

The nuclei is very important as helps in grading of the tumor

Collecting ducts

- **The tumor cells can be granular cells resembling the tubular epithelium with small, round, regular nuclei and granular pink cytoplasm** Granular cells are sometimes mixed with Clear cells In Clear cell carcinoma
- **Highly anaplastic tumors show numerous mitotic figures and markedly enlarged, hyperchromatic, pleomorphic nuclei**
- **The stroma is usually scant but highly vascularized**

All aggressive and high grade tumors are highly vascularized

Grading of the tumor is very important ,It reflects the prognosis of the patient and one of the important things to evaluate grading is the nuclei by the degree of the pleomorphism, Hyperchromasia and the precense and the size of the nuclei

- **The tumor invades the renal vein and grows as a solid column within this vessel**
- **It can extend in serpentine fashion as far as the inferior vena cava and even into the right side of the heart**
- **Some neoplasms are highly anaplastic**

Higher grade with different bizarre types of cell and even tumor cells differentiate to other types of cells
And this is called sarcomatoid which is a high grade type of tumor and acts in a very aggressive way
And can show different types of cells like : fibrosarcoma, limasarcoma, rapdomiosarcoma with all types of bizarre cells

PAPILLARY RENAL CELL CARCINOMAS

Finger like projections That show tumor cells overlying a fibrovascular core

- **It accounts for 10-15% of all renal cancers**
- **It is defined in part by their papillary growth pattern**
- **Frequently multifocal and bilateral** Involving both kidneys
- **Appears as early-stage tumors** Or low graded tumors
- **It occurs in familial and sporadic forms**
- **It arises from the proximal tubular epithelial cell**

- **Papillary renal carcinoma is not associated with abnormalities of chromosome 3** In contrast to clear cell carcinoma
- **Characterised by mutation of the *MET* proto-oncogene, located on chromosome 7q** Mutation in this gene will make a continues signals for division leading to an oncogenesis and tumor formation
- ***The MET* gene encodes a tyrosine kinase receptor for hepatocyte growth factor.** Hepatocyte growth factor helps the tumor in metastasis and invasion

- **The tumor exhibits various degrees of papillary formation with fibrovascular cores**
- **They tend to be bilateral and multiple**
- **They also may show gross evidence of necrosis, hemorrhage, and cystic degeneration**
- **The tumor cells are less vibrantly orange-yellow because of their lower lipid content**
- **The cells may have a clear or, more commonly, pink cytoplasm.**

CHROMOPHOBE RENAL CARCINOMA

- **Are the least common form representing 5% of all renal cell carcinomas.**
- **It arises from intercalated cells of collecting ducts**
- **Tumor cells stain more darkly (i.e, they are less clear) than cells in clear cell carcinoma**
- **Characterized by having multiple losses of entire chromosomes leading to extreme hypoploidy**

Less chromosomes than normal

Characterized by ***not*** having a specific gene mutation

- **The tumor appears grossly tan-brown**
- **The cells usually have clear flocculent cytoplasm with very prominent distinct cell membranes**
- **The nuclei are surrounded by halos of clear cytoplasm. Ultrastructurally large numbers of characteristic macrovesicles are seen**

- **Chromophobe renal cancers have a favorable prognosis**

  Have better prognosis than others

CLINICAL FEATURES

- **The most frequent presenting manifestation is hematuria occurring in more than 50% of cases.**
- **Macroscopic hematuria tends to be intermittent and fleeting, superimposed on a steady microscopic hematuria**
- **Less commonly flank pain and a palpable mass** In the posterior aspect mainly

The patient with a proper age presents with a triad of manifestations so we should suspect this cancer and do further more tests (e.g.radiology).
Painless Hematuria causes discoloration of the urine So the patient might himself notice it

- **Extrarenal effects are *fever* and *polycythemia***
- **Polycythemia affects 5-10% of affected individuals and results from production of erythropoietin by the cancer cells**
- **Paraneoplastic syndrome due to tumor production of other hormone-like substances resulting in hypercalcemia, hypertension, Cushing syndrome, or feminization or masculinization.**

Parathyroid » increase release of ca++ from the bones » hypercalcemia

Corticosteroids » masculinization of the females

Androgens » feminization of the males

Urinary bladder

- **Bladder cancer accounts for approximately 5% of cancers**
- **3 types:**

Also called Transitional cell carcinoma

1. The vast majority of bladder cancers is urothelial carcinomas.

2. Squamous cell carcinoma represents about 3-7%

And caused by metaplasia due to chronic irritations

3. Adenocarcinomas of the bladder are rare.

The bladder is lined by epithelium similar to that of Urinary system and part of the urethra so tumors that affect bladder also can arise in other sides

- **M>F**
- **About 80% of patients are between 50-80 years of age.**

Risk factors

1. **Cigarette smoking**
2. **Occupational carcinogens** So we must ask the patient where he works and the environmental exposures so it could explain the cancer and carcinogens
3. **Cyclophosphamide or radiation therapy.**
4. **A family history of bladder cancer**
5. **Squamous cell carcinoma is related to Schistosoma haematobium infections in areas where it is endemic**
6. **Acquired genetic mutations**

- **Two distinct precursor lesions of invasive urothelial carcinoma:**

1. **The most common is a noninvasive papillary tumor**
2. **Carcinoma in situ (CIS)**

A very important aspect in this condition is a precursor lesions and these are found before the development of the invasive carcinoma so we should be aware and follow up the patient

- **The most important prognostic factor in noninvasive papillary urothelial neoplasms is their grade.**
- **The grade is based on both architectural and cytologic features.**

The more likelihood the higher the grade .

The grade depends on the degree of the dysplasia of the epithelium and dysplastic features of the nuclei

- **Grading system subclassifies tumors as follows:**

(1) Papilloma Benign with a Normal lining epithelium having a papillary configuration

(2) Papillary urothelial neoplasm of low malignant potential (PUNLMP) Some nuclear changes Which might indicate a progression of a tumor

(3) Low-grade papillary urothelial carcinoma

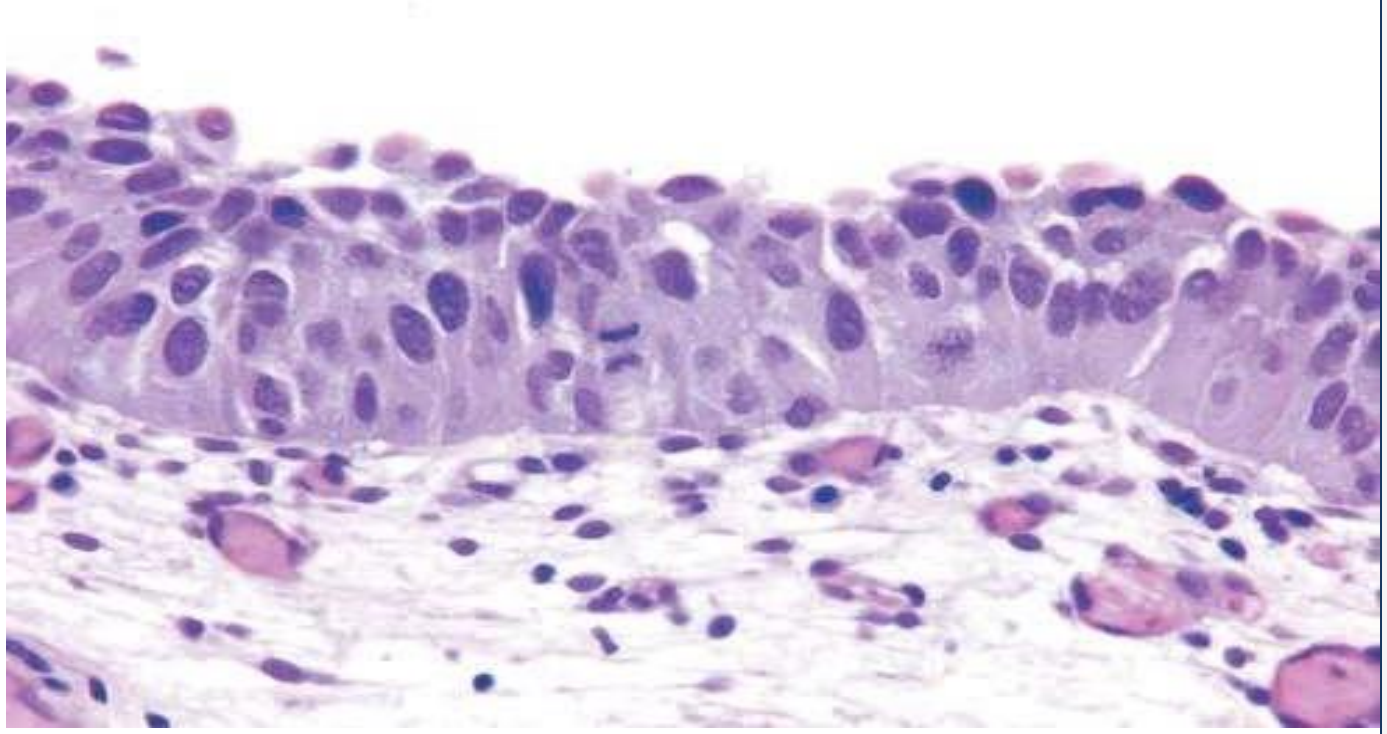
(4) High-grade papillary urothelial carcinoma

Invasive subtypes (Muscular wall / subepithelia)

- **CIS is defined by the presence of overtly malignant appearing cells within a flat urothelium**
- **CIS commonly is multifocal and sometimes involves most of the bladder surface or extends into the ureters and urethra**
- **Without treatment 50-75% of CIS cases progress to invasive cancer**

CIS :No invasion No increased thickness of the epithelia No papillary configuration however it's important In diagnosis and we should know that they can evolve to an invasive cancer

Carcinoma in situ (CIS) with enlarged hyperchromatic nuclei and a mitotic figure



This is a urothelial or transitional epithelium
the urothelial show all nuclear changes involving the full layer (pleomorphic, hyperchromatic nuclei)
And this is the basic definition of CIS

normally the urothelial surface is larger
with abundant cytoplasm showing maturation and we call it umbrella cells
So you can notice the abnormal state here

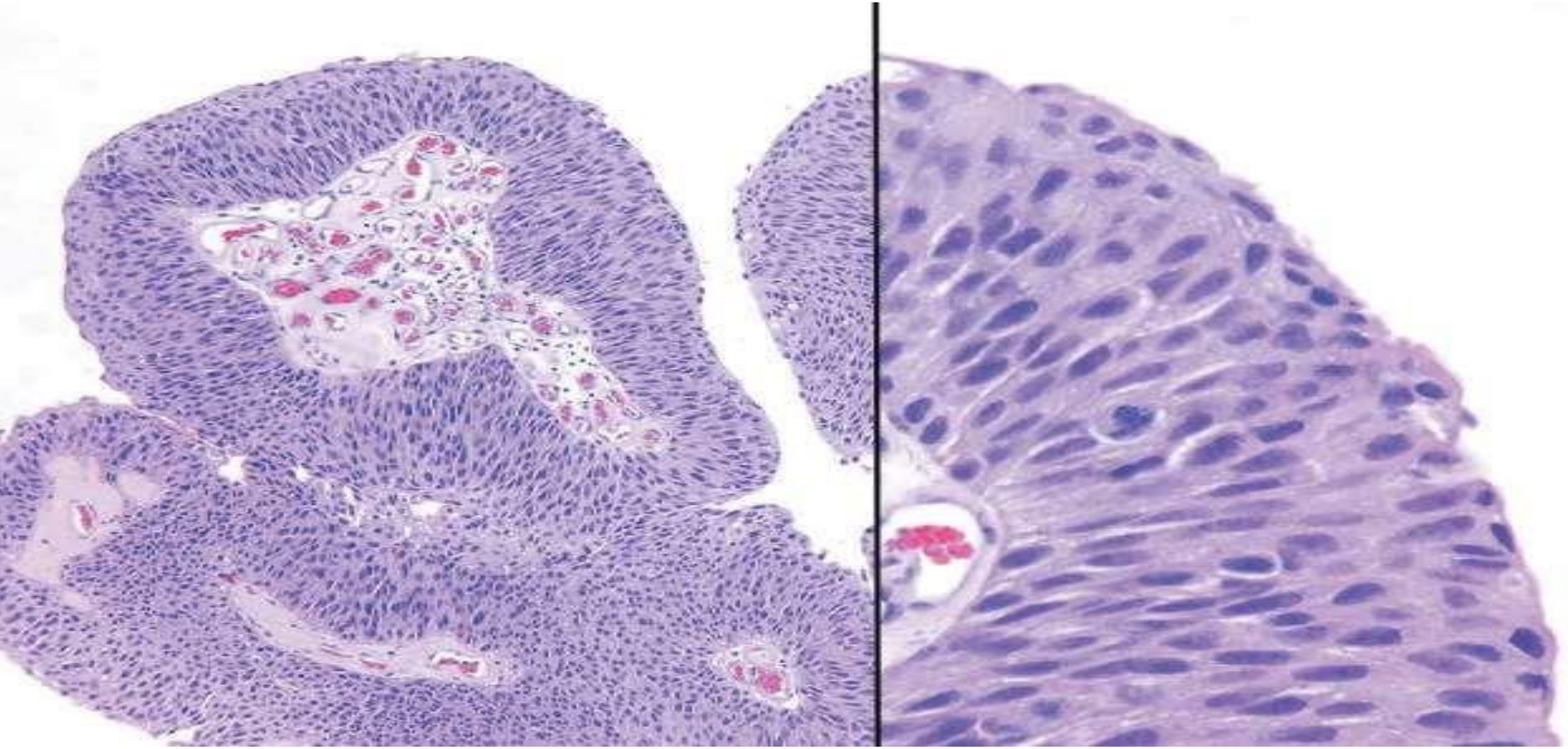
Why it's in situ?

Because the basal membrane over which the epithelium is lying is intact.

Thin flat line with No invasion

- **Invasive urothelial cancer associated with papillary urothelial cancer (usually of high grade) or CIS may superficially invade the lamina propria or extend more deeply into underlying muscle.**
- **The extent of invasion and spread (staging) at the time of initial diagnosis is the most important prognostic factor**
- **Almost all infiltrating urothelial carcinomas are high grade.**

Noninvasive low-grade papillary urothelial carcinoma.
Higher magnification *(right)* shows slightly irregular nuclei with scattered mitotic figures



The core of papilli is formed by fibrous tissue which is vascularized
And if we look at the epithelium which show features of nuclear dysplasia you can see the tumor cells with mitosis

and this depends on the grade of the tumor

Clinical Features

- **Painless hematuria.**

Cells arise from the lining of the bladder
It's an early and a serious manifestation because the bladder is lined with epithelium and can bleed or have necrosis Again
so we must investigate further more and look for a tumor

- **The risk for recurrence is related to several factors:**

1. **Tumor size**
2. **Stage**
3. **Grade**
4. **Multifocality**
5. **Mitotic index**
6. **Associated dysplasia**
7. **CIS in the surrounding mucosa.**

All urothelial carcinomas tend to reoccur frequently and it's so common and the patient will suffer from it to his death

Increasing any factor will increase the risk

يا أرحم الراحمين فرج عن المسلمين

القصيدة المنفرجة للإمام أبي حامد الغزالي

– رحمه الله–

الشدةُ أوْدَتْ بالمُهَجِ ... ياربِّ فعَجِّل بالفرجِ

والأنْفُسُ أمسَتْ في حَرَجٍ ... وبيدِكَ تفريجُ الحَرَجِ

هاجَت لدُعاك خواطِرُنا ... والويلُ لها إن لم تَهِجِ

يا مَن عوَّدْتَ اللُّطفَ أعِدْ ... عاداتِكَ باللطفِ البَهِجِ

واغلِقْ ذا الضِّيقِ وشِدَّتَهُ ... وافتَحْ ما سُدَّ مِن الفَرَجِ

عُجْنَا لجَنَابِك نَقْصِدُهُ ... والأنفس في أَوْجِ الوَهجِ

وإلى إفضالِك يا أَمَلِي ... يا ضَيْعَتَنَا إنْ لَمْ نَعُجِ

مَنْ لِلْمَلْهُوفِ سِواكَ يَغُثْ ... أو للمُضْطَرِّ سِواكَ نَجِي

Additional sources

1. Book pages
2. Youtube videos
3. Webpages…etc

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2			
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!