# Tumors of kidney

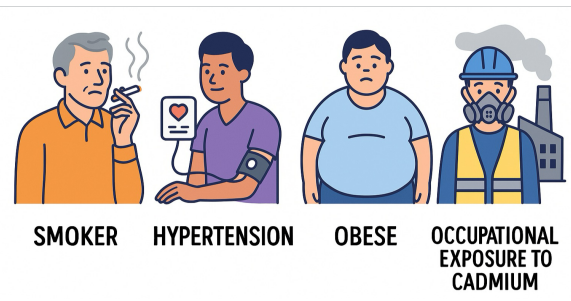
Done by: Kareem obeidallah

- Tumors
  - benign → Small cortical papillary adenoma
    (Precursor lesion for renal cell carcinoma)
    - <0.5 cm in diameter
    - affect 40% of adults in autopsies
    - have limited clinical significance
  - Malignant
    - MC: renal cell carcinoma
    - 2nd MC: Nephroblastoma (Wilms tumor)
    - => followed by tumor of calcyces and pelvis

**Note:**
Neoplasms of the lower urinary tract are about twice as common as renal cell carcinomas
** أي نوع للkidney tumor غير الي ذكرناهم فهو بكون rare

# Renal Cell Carcinoma

- Renal Cell Carcinoma
  - represent: 80% to 85% of all primary malignant neoplasms of the kidney
    ——> 2% to 3% of all cancers in adults
  - derived from renal tubular epithelium
  - Mainly in cortex
  - M:F => (2:1) => MC in 6-7 decades
  - risk factors:
    smokers, hypertension, obese patients, and occupational exposure to cadmium.
    **Risk increased in acquired polycystic disease (complication of chronic dialysis)




## Classification:

In past: classified according morphology and growth pattern

Recently: Molecular origin of tumor

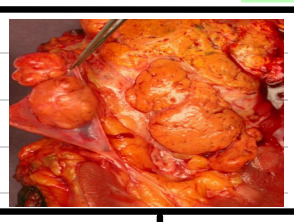
due to advances in understanding genetic basis of RCA

MC to LC

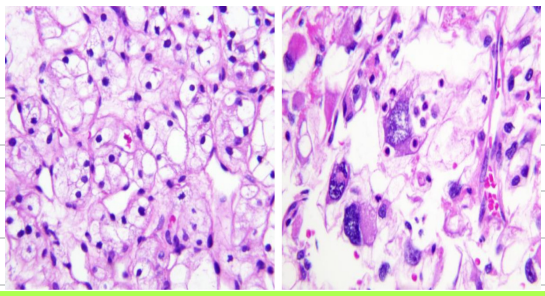
Subtypes:
1) Clear cell carcinoma
2) Papillary renal cell carcinoma
3) Chromophobe renal carcinoma.

Clear cell RCC has worse prognosis than papillary and chromophobe RCC

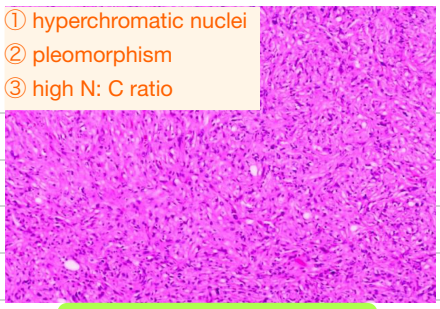
# Clear cell carcinoma



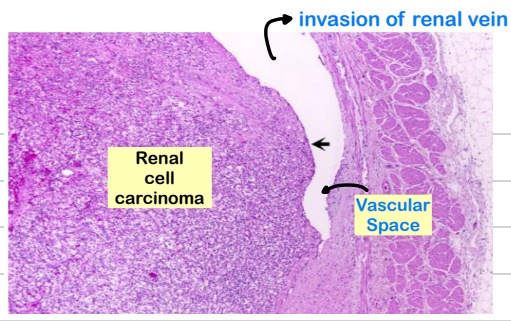
| General features | Histologically | Metastases | Prognosis |
|---|---|---|---|
| 1) most common type<br><br>2) accounting for 65% of renal cell cancers<br><br>3) most are sporadic<br><br>4) familial forms or in association with (von Hippel-Lindau (VHL) disease)<br><br>5) uncommon familial form associated with cytogenetic abnormalities involving the short arm of chromosome 3 (3p) | 1) Arises in epithelial cells lining the proximal convoluted tubule<br><br>2) Cortical mass with golden yellow cut surface<br><br>3) Clear or granular eosinophilic cytoplasm<br><br>4) prominent but delicate capillary network | 1) Hematogenous more common:<br>• lung (most common)<br>• bone<br>• liver<br>• pleura<br>• CNS<br>• head and neck<br><br>2) Lymphatic less common:<br>• hilar<br>• aortic<br>• caval and thoracic lymph nodes<br><br>**Extension into the renal sinus the most common pathway of spread, usually involving extension within the renal vein | Worse prognosis within the same stage:<br>higher histologic grade (M>N>T; بنحكي عليا حسب size of nucleus and nucleolus)<br>sarcomatoid and rhabdoid differentiation<br><br>** If we can see nucleus on low power microscope (it's grade 4 tumor)<br><br>** saromatoid + rhabdrid (it's grade 4 tumor)<br><br>** penetration of renal vein (It's grade 3 tumor)<br><br>T1: <4cm<br>T2: 4-7 cm<br>T3: >7 cm |



Clear cell cytoplasm of Renal cell carcinoma




Sarcomatoid variant




# VHL disease → autosomal dominant trait

( seems to be the common underlying molecular abnormality in both sporadic and familial forms of clear cell carcinomas )

### Cause:

loss or inactivation of both copies of the VHL gene

↓

VHL protein causes the degradation of hypoxia-induced factors (HIFs)

↓

Increase level of "HIFs"

### HIFs

(transcription factors)
contribute to carcinogenesis by:

1) stimulating the expression of vascular endothelial growth factor (VEGF)
( important angiogenic factor )

2) Stimulating number of other genes that drive tumor cell growth

### predispose to a variety of neoplasms:

1) hemangioblastomas
( in cerebellum and retina )

2) Hundreds of bilateral renal cysts

3) bilateral, often multiple, clear cell carcinomas
( develop in 40% to 60% of affected individuals )

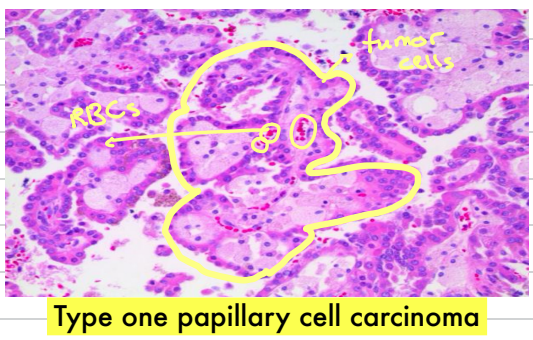
# Papillary renal cell carcinomas → Tumor cells surrounded by fibrovascular core

**( papillary growth pattern )**

### General features:

- account for 10% to 15% of all renal cancers
- These neoplasms are:

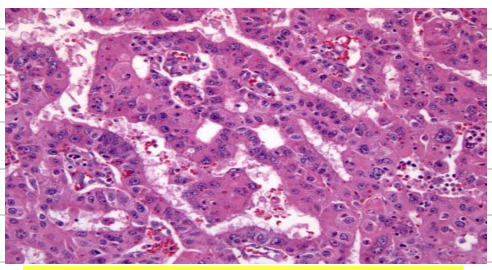
1) frequently multifocal and bilateral
2) appear as early-stage tumors
3) they occur in familial and sporadic forms
( papillary renal cancers are not associated with abnormalities of chromosome 3 )




Type one papillary cell carcinoma

### Cause:

hereditary papillary renal cell cancers
Caused by:
gain of function mutations in MET proto-oncogene
( located on chromosome 7q )



Type two papillary cell carcinoma
( more aggressive )

### Pathogenesis:

The MET gene encodes:
tyrosine kinase receptor for hepatocyte growth factor

↓

increased dosage of the MET gene
( due to duplications of chromosome 7)

↓

abnormal growth in the proximal tubular epithelial cell
" precursors of papillary carcinomas "

# Chromophobe renal carcinomas → when stained cytoplasm will be dark duo to over-activation of mitochondria

**( least common form, representing 5% of all renal cell carcinomas )**

### General features:

1) Their name derives from:
the observation that the tumor cells stain more darkly than cells in clear cell carcinomas
( less clear not as CCC )

2) unique in having multiple losses of entire chromosomes leading to extreme hypoploidy

3) favorable prognosis

### Histological features:

1) Solid tumor composed of:
- granular pale cells
- finely reticular cytoplasm
- prominent cell borders
- perinuclear halos
- wrinkled hyperchromatic nuclei

2) Cell of origin
( intercalated cells of distal convoluted tubules )

3) Solitary kidney mass

4) Most commonly in renal cortex

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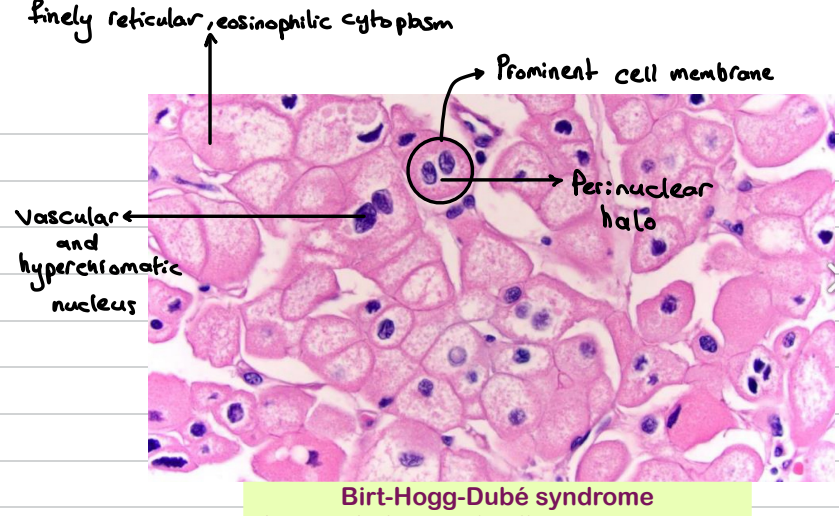
# Birt-Hogg-Dubé syndrome

**Caused by:**
**Mutations in the folliculin gene (FLCN) at 17p11.2**

- Autosomal dominant syndrome
- Patients affected: mean age 51 years at first renal tumor diagnosis
- Patients have: Multiple tumors (mean 5.3)
- Affect MSS by: → small dome shaped papular fibrofolliculomas of : face, neck and upper trunk
- Affect kidney by: → Bilateral multifocal renal tumors
  - Chromophobe renal cell carcinoma
  - oncocytomas
  - hybrid oncocytic chromophobe tumor (HOCT)

  **( may have oncocytosis )**
- Affect lung by: lung cysts and spontaneous pneumothorax




Birt-Hogg-Dubé syndrome
chromophobe renal cell carcinoma بتشبه ال

# Renal Cell Carcinoma

**( clinical features )**

There is variation in signs and symptoms

Characteristics triad of RCC:
- painless hematuria
- palpable abdominal mass
- dull flank pain

**hematuria**
the most frequent presenting manifestation is, occurring in more than 50% of cases
↓
Macroscopic hematuria tends to be intermittent, superimposed on a steady microscopic hematuria

**flank pain and palpable mass**
( Less commonly, when it has grown large enough to produce )

Extrarenal effects are:
**fever and polycythemia**

Polycythemia affects 5% to 10% of affected individuals and results from production of erythropoietin by the cancer cells

Uncommonly may have
**paraneoplastic syndromes**

Uncommonly produce other hormone-like substances resulting in:
- hypercalcemia
- hypertension
- Cushing syndrome
- feminization or masculinization

In some patients, the primary tumor remains silent and is discovered only after metastases produce symptoms
The common locations for metastases are:
- lungs
- the bones

**Note:**
**Because of the widespread use of imaging studies for unrelated conditions, even smaller tumors are detected**

# Wilms Tumor (nephroblastoma)

3rd most common solid (non-hematologic) cancer in children >10 years

**Note:**
** like retinoblastoma, may arise:
- **sporadically** (90%)
- **familial** (10%) ( autosomal dominant trait )

** Rare in adults

Wilms tumor contains a variety of cell and tissue components, all derived from **mesoderm**

**associated with 3 congenital malformations**

**WAGR syndrome**
- Wilms tumor
- Aniridia
- Genital abnormalities
- mental Retardation

↓
approximately one in three (33%) will develop Wilms tumor
↓
loss of genetic material (deletions) of WT1

**Denys-Drash syndrome (DDS)**
characterized by:
- gonadal dysgenesis
- early onset nephropathy

(leading to renal failure )
↓
higher risk (approximately 90%) of Wilms tumor
↓
negative ( inactivating mutation )in WT1

**Beckwith- Wiedemann syndrome (BWS)**
Big baby ( organo + cytomegaley )
exhibit:
- enlargement of individual body organs e.g., tongue, kidneys, or liver)
- or enlargement of entire body segments (hemihypertrophy)
- enlargement of adrenal cortical cells (adrenal cytomegaly) is a characteristic microscopic feature

↓
increased risk for the development of Wilms tumor
↓
BWS is an example of a disorder of genomic imprinting ( just one allele is active ) of WT2

**Note:**
** Wilms tumor 1 (WT1) gene, located on 11p13

** WT2 is in band p15.5 of chromosome 11 distal to the WT1 locus.

## Morphology

- large, solitary
- well-circumscribed mass
- 10% are either bilateral or multicentric at the time of diagnosis

** On cut section, the tumor is:
- soft And homogeneous
- tan to gray
- occasional foci of hemorrhage
- cystic degeneration and necrosis

** The classic triphasic combination of:
( the percentage of each component is variable )

1) blastemal → Sheets of small blue cells, with few distinctive features, characterize the blastemal component

2) stromal → usually fibrocytic or myxoid in nature

3) epithelial cell types → takes the form of abortive tubules or glomeruli

• Approximately 5% of tumors contain foci of anaplasia
(cells with large, hyperchromatic, pleomorphic nuclei and abnormal mitoses)

anaplasia correlates with the presence of acquired TP53 mutations and the emergence of resistance to chemotherapy

The pattern of distribution of anaplastic cells within the primary tumor (focal versus diffuse) has important implications for prognosis

إنه الـ anaplasia يمكن تكون focal or diffuse
لـ هذا رح يجيب مقاومة للعلاج الكيماوي .

## Nephrogenic rests
### ( precursor lesions of Wilms tumors )

** sometimes present in the renal parenchyma adjacent to the tumor

** spectrum of histologic appearances:

- expansile masses (شكلها متعدد) that resemble Wilms tumors

- hyperplastic rests to sclerotic rests consisting predominantly of:

—> fibrous tissue with occasional admixed immature tubules or glomeruli

**Note:**

**presence of nephrogenic rests:**
**increase risk for the development of Wilms tumors in the contralateral kidney**

## Clinical Course of Wilms

- palpable abdominal mass
( may extend across the midline and down into the pelvis )

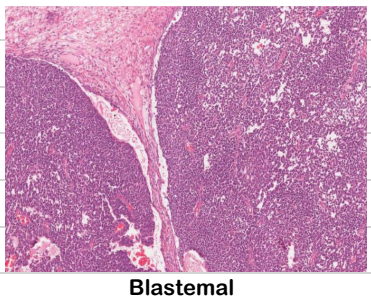
** Less often features are:
- fever
- abdominal pain
- hematuria
- intestinal obstruction as a result of pressure from the tumor

**• The prognosis for Wilms tumor generally is very good**

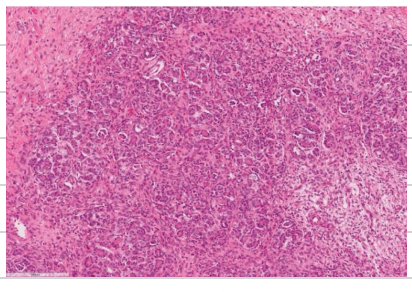
**excellent results are obtained by:**
**** combination of nephrectomy and chemotherapy**

**Anaplasia:**
**( is a harbinger of adverse prognosis, but only if it is diffuse )**

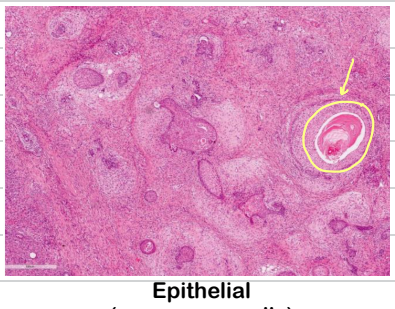
**If the anaplasia is focal and confined within the resected nephrectomy the outcome is no different from that for tumors without evidence of anaplasia**



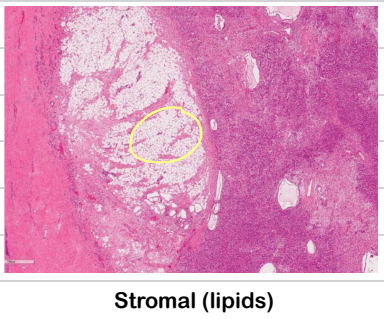
Blastemal
( small round blue cells )



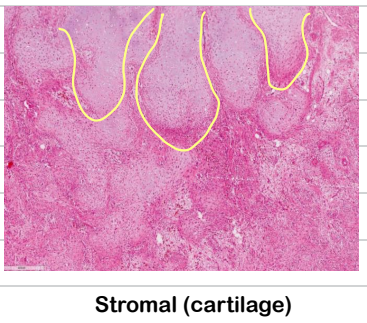
Epithelial ( tubules )



Epithelial
( squamous cells)



Stromal (lipids)



Stromal (cartilage)

# Urinary bladder

**Bladder cancer accounts for approximately 5% of cancers**

**Note:**
**Carcinoma of the bladder is:**
- **more common in men than in women**
- **More in whites than in African- Americans**

**** About 80% of patients are between 50 and 80 years of age**

## Urinary bladder cancers

### Risk factors

**urothelial carcinoma**
( represent vast majority of bladder cancers )
** Environmental risk factors:
- cigarette smoking
- various occupational carcinogens
- prior cyclophosphamide or radiation therapy

** family history of bladder cancer is a known risk factor

**Squamous cell carcinoma**
related to Schistosoma haematobium infections in areas where it is endemic

** Cancers occurring in the setting of schistosoma infections arise in a background of chronic inflammation

** urinary schistosomiasis is endemic

**Note:**
**** Squamous cell carcinomas represent about 3% to 7% of bladder cancers in the United States but are much more common in countries such as Egypt**

**** Adenocarcinomas of the bladder are rare**

### Pathogenesis
**2 possible pathways**

deletions of tumor-suppressor genes on 9p and 9q
↓
leading to the formation of superficial papillary tumors
↓
which may then acquire TP53 mutations and progress to invasive disease

TP53 mutations
↓
leads first to carcinoma in situ
↓
then, with loss of genes from chromosome 9 progresses to invasion

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## Clinical Features:

** **Bladder tumors most commonly present with painless hematuria**

** urothelial tumors (whatever their grade)
have a tendency to develop new tumors after excision, and recurrences may exhibit a higher grade

– The risk for recurrence is related to several factors:
- tumor size
- stage
- grade
- multifocality
- mitotic index
- associated dysplasia and/or CIS in the surrounding mucosa

– high-grade papillary urothelial carcinomas frequently are associated with either concurrent or subsequent invasive urothelial carcinoma

–lower-grade papillary urothelial neoplasms often recur but infrequently invade

**Note:**

**Many recurrent tumors arise at sites different than that of the original lesion, but may be share the same clonal abnormalities as those of the initial tumor**

**these are true recurrences that stem from shedding and implantation of the original tumor cells at new sites**

## Treatment:

–Treatment of bladder cancer depends on:
- tumor grade
- stage
- whether the lesion is flat or papillary

1) For small, localized papillary tumors that are not high-grade:
– Transurethral resection is both diagnostic and therapeutically sufficient

2) Patients with tumors that are at high risk for recurrence or progression typically receive:

– Topical immunotherapy consisting of intravesical instillation of an attenuated strain of the tuberculosis bacillus called Bacillus Calmette-Guérin (BCG)
sometimes followed by intravesical chemotherapy

**Note:**

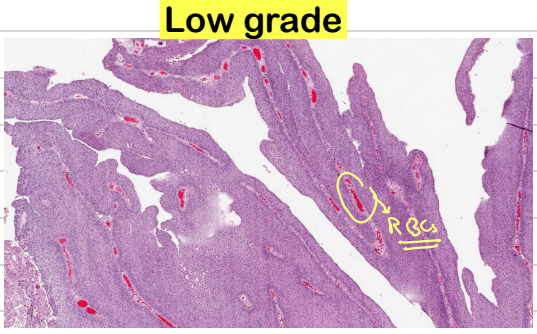
**** BCG elicits a granulomatous reaction that triggers an effective local anti-tumor immune response**

**tumor recurrence is monitored by:**
- **periodic cystoscopy**
- **urine cytologic studies**

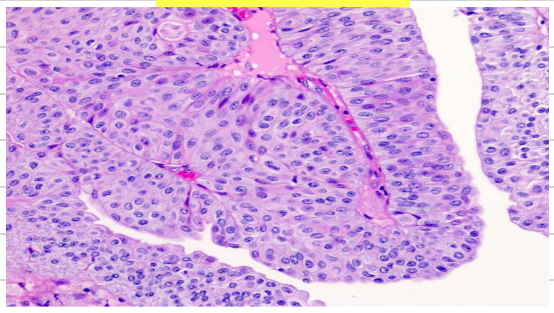
3) Radical cystectomy is reserved for:
A. Tumor invading the muscularis propria ⩾T2
B. CIS or high-grade papillary cancer refractory to BCG.
C. CIS extending into the prostatic urethra and down the prostatic ducts
( where BCG cannot come in contact the neoplastic cells )

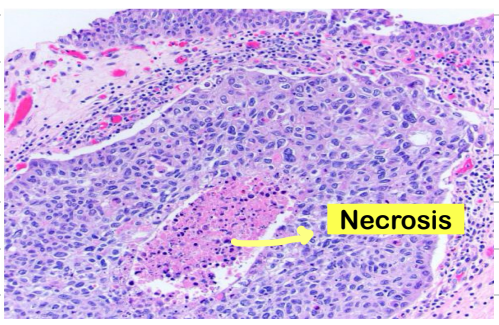
4) Advanced bladder cancer is treated using chemotherapy, which can palliate but is seldom curative

Low grade

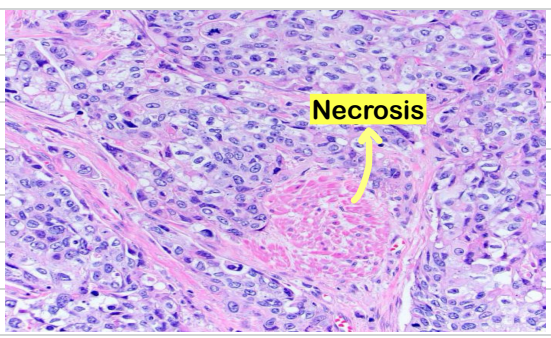


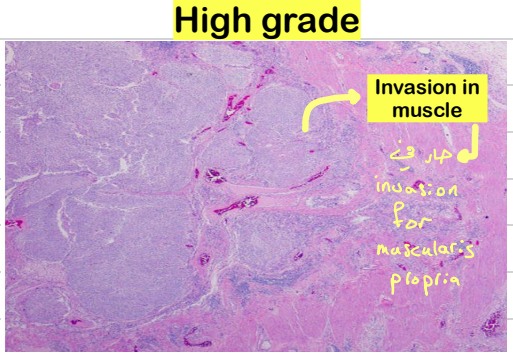

Polarized cells

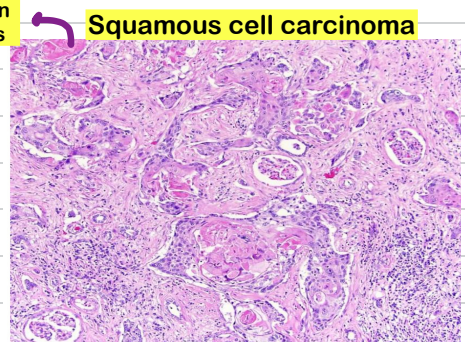




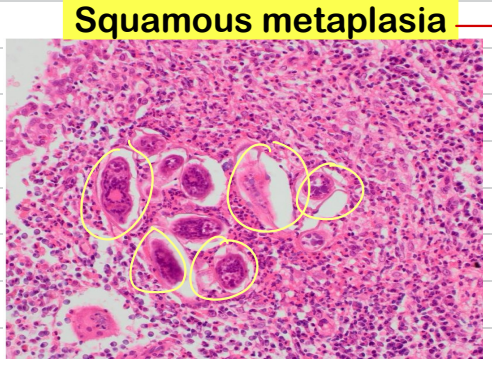

High grade




Squamous metaplasia → due to schistosoma



لأي شخص بدرس من الملف طلب صغير:
تم تشخيص إصابة والدي بوجود كتلة سرطانية، و هو حاليًا عم بعمل فحوصات لاختيار طريقة العلاج المناسبة فلو سمحتم ادعوله بالشفاء العاجل و انه ربنا يخففها عليه، اله و لجميع مرضى المسلمين 🤲🤲

و ما تنسوا أهلنا في غزّة من الدعاء، ربنا ينصرهم و يخفف عنهم و يفرجها عليهم 🤲🤲

نسأل الله لكم التوفيق و السّداد...

**Done by: Kareem obeidallah**