



## **GU Oncology**



**Done By:** Raghad Almutlaq

Reviewed By:
Ibrahim Abunohaiah



# Objectives

1. Not given

## 1. Renal Tumors:

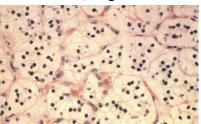
## Pathology:

- Benign tumors of kidney are rare. All renal neoplasms should be regarded as potentially **malignant**.
- Male: Female ratio is approximately 2: 1

#### Types:

- 1. Onchocytoma: the commonest benign type.
- Renal cell carcinoma (RCC): arise from proximal tubule cells. (clear cell carcinoma is the commonest histological subtype) has higher incidence to be seen in VHL syndrome (von Hipple-Lindau)
- 3. Collecting duct carcinoma: arises from collecting duct.
- 4. Papillary cell carcinoma.
- Pathologically may extend into renal vein and inferior vena cava:
  - Could obstruct IVC and cause DVT (Deep Vein Thrombosis)
  - Could reach the heart
- Metastases: Lungs are the commonest site for metastases. Blood born spread can result in 'cannonball' pulmonary metastases. (Looks like a cannonball; large and well circumscribed)

Very clear and impacted cells, dark nuclei with clear cytoplasm: clear cell carcinoma.



#### Clinical features:

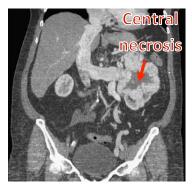
- The commonest presentation is incidental finding.
- **10% only** present with classic trial of gross hematuria, loin pain and a palpable mass (in advanced stage). Others cases discovered before accidentally.
- Other presentations include (Paraneoplastic Syndrome PNS): a unique feature of renal cancer where the tumor starts secreting hormones like ADH (anti-diuretic hormone) or EPO (Erythropoietin: increase RBC production)
  - Systemic manifestations of PNS include pyrexia of unknown origin, hypertension, polycythemia (due to high EPO), Hypercalcaemia (because of high PTH like hormone) and non-metastatic hepatic dysfunction "Stuffer's syndrome" characterized by high liver enzymes without jaundice.
  - **Treatment of PNS:** removal of the underlining cause (tumor) except for Hypercalcaemia could be treated medically.

#### *Note(s):*

VHL syndrome: genetic, autosomal dominant, mutation in tumor suppression gene (chromosome3, short arm), may associate with CNS hemangioblastoma, pheochromocytoma, pancreas and kidney cysts, cyst adenoma in epididymis, renal cell carcinoma, and adrenal gland malignancies. (When having patient with VHL please screen for other tumors!)

## **Investigations:**

- Diagnosis confirmed by renal ultrasound.
- CT scan can be used diagnosis for staging by assessing renal vein and caval spread.
- Echocardiogram (TEE) should be considered if clot in IVC extends (extension **NOT** metastases) above diaphragm.



Huge left RCC, extended to the renal vein → IVC → heart

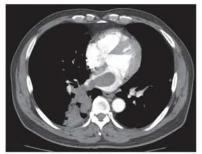


Figure 1: Computed tomography scan of patient's chest when he was first diagnosed with intracardiac extension of disease.



Bilateral tumor → familial syndrome like VHL.

## Management:

- Unless extensive metastatic disease it invariably involves surgical removal.
- Surgical option usually involves a radical nephrectomy (remove the whole kidney)
- Kidney approached through either a trans abdominal or loin incision.
- Renal vein ligated early to reduce tumor propagation.
- Kidney and adjacent tissue (adrenal, perinephric fat) excised.

### Note(s):

- 1) Staging kidney tumor include:
  - 1. Clinical staging by CT.
- 2. Histopathological staging. Grading system for kidney cancer is called: **Fuhrman system**
- 2) Fat can get diposed in malignant cells → golden color grossly.
- 3) Radio, chemo therapy has NO role in RCC management.

Open radical nephrectomy: causes big scar that has to the muscles so patient will suffer with respiration.

Laparoscopic nephrectomy: (Gold standard)
Advantages:

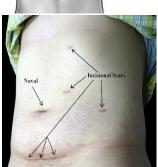
- 1. Shorter hospital stay
- 2. Less pain

Groin incision is used to remove large tumors, so we do not cut muscle. It is a muscle splitting incision.

For Post-menopausal women who have undergone hysterectomy; trans-vaginal approach.







#### If there is metastases:

- Lymph node dissection of no proven benefit (whether you removed them or not patient will have recurrence.)
- Solitary (e.g. lung metastases) can occasionally be resected.
- Radiotherapy and chemotherapy have **No role** (unless in symptomatic bone metastases to reduce pain)
- Immunotherapy can help (for those having good performance status, not a very sick patient):
  - Monoclonal antibodies, interferon, cytokine inhibitors
  - Very cytotoxic
  - Given only to patient with good performance status
  - Not curable but can prolong his life few months

## **Prognosis:**

**Early stage**: 5 years survival 95% / **Metastatic**: 3-6 average survival.

## 2.Bladder Tumors:

## Pathology:

- Of all bladder carcinomas:
  - 90% are transitional cell carcinomas (TCC)
  - 5% are squamous carcinoma (SC)
  - 2% are adenocarcinomas (comes with embryological deformities)
- TCCs should be regarded a 'field change' disease with a spectrum of aggression.
- 80% of TCCs are **superficial** and well differentiated
  - Associated with good prognosis
  - Only 20% progress to muscle invasion
- 20% of TCCs are high-grade and muscle invasive
  - 50% have muscle invasion at time of presentation
  - Associated with poor prognosis

#### Etiology:

- Occupational exposure
  - 20% of transitional cell carcinomas are believed to result from occupational factors.
  - Chemical implicated aniline dyes, chlorinated hydrocarbons.
- Cigarette smoking
- Analgesic abuse e.g. Phenacetin
- Pelvic irradiation for carcinoma of the cervix
- Schistosoma haematobium (Schistosomiasis) (also known as bilharzia, snail fever, and Katayama fever) associated with increased risk of squamous carcinoma.

### Note(s):

Squamous carcinoma (chronic irritations of bladder → SC): The worst prognosis High-risk groups: Smokers Chronic UTI Stones

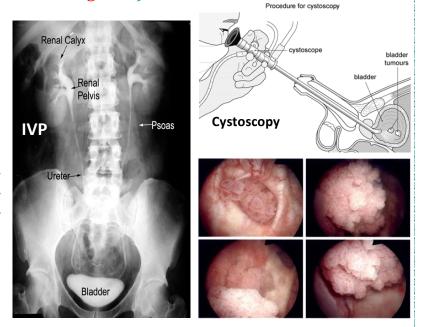
Chronic indwelling catheter Spinal cord injury Schistosomiasis

#### Clinical features:

- 80% present with gross, painless and terminal hematuria.
- Also present with treatment-resistant infection or bladder irritability and sterile pyuria (urine contains pus TB).

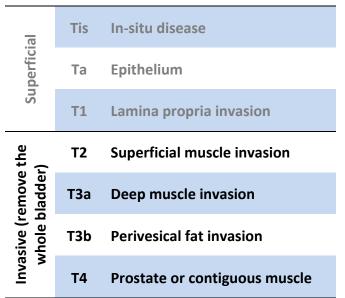
## Investigations: (you have to have full investigation)

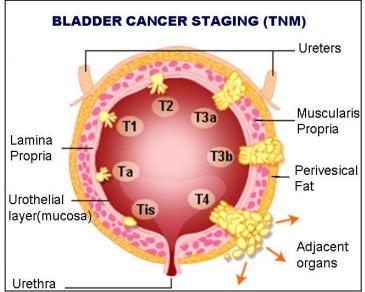
- Urinalysis
- Ultrasound bladder and kidneys
- KUB to exclude urinary tract Calcification
- Cystoscopy (a must in this case)
- Urine Cytology
- Consider IVU- CT scan if no pathology identified (intravenous urogram, other name IVP: shows filling defect, or sometimes hydronephrosis due to obstruction of the ureters).



## Pathological staging:

- Requires bladder muscle to be included in specimen
- Staged according to depth of tumor invasion





## Note(s):

Painless hematuria is considered to be cancer (until proven otherwise). Deep (invasive) metastasize faster.

#### Carcinoma in-situ:

Aggressive disease.

Often associated with positive cytology.

50% of patients progress to muscle invasion.

**Consider immunotherapy** 

If fails, patient may need radical cystectomy.

#### **Grading:**

G1: well differentiated.

G2: moderately well

differentiated.

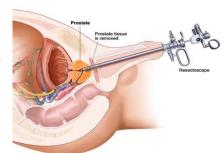
G3: poorly differentiated.

## Treatment of bladder carcinoma (superficial TCC):

- Requires transurethral resection of bladder tumor (TURBT) and regular cystoscopic follow-up (to watch out for recurrence)
- Consider prophylactic chemotherapy if risk factor for recurrence or invasion (e.g. high grade)
  - High risk: multiple tumors, big tumors, carcinoma in situ



- BCG = attenuated strain of Mycobacterium bovis (Stands for: Bacillus Calmette Guérin – vaccine to kill the tumor cells in bladder)
- Reduces risk of recurrence and progression.
- 50-70% response rate recorded.
- Occasionally associated with development of systemic mycobacterial infection.

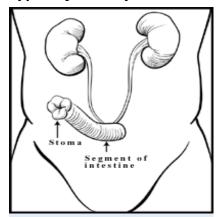




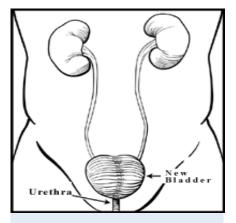
#### Invasive TCC: (confirmed by biopsy)

- Radical Cystectomy has an operative mortality of about 5% (RC: removal of the **whole** bladder, prostate, distal ureter and lymph nodes. In female: + uterus, cervix and anterior vaginal wall)
  - Q: How will the patient excrete urine if bladder is removed?
  - A: Urinary diversion, which is achieved by:
  - Ileal conduit
  - Neo-bladder
- Local recurrence rates after surgery are approximately 15% and after radiotherapy alone 50%.
- Pre-operative radiotherapy is no better than surgery alone.
- Adjuvant chemotherapy may have a role.

### Types of urinary diversion:

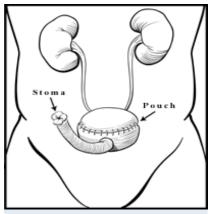


ILEAL CONDUIT (From ileum. Incontinent diversion to skin)



## ORTHOTOPIC NEOBLADDER (Continent diversion to urethra)

- Part taken from GIT → folded and used as new bladder.
- Urine + secretion
- Patient should be followed up because Urine on GI tissue → transition of cells → tumor arises.
- Not preferred for elderly



## CONTINENT CUTANEOUS RESERVOIR

(Continent diversion to skin)
- Same as the 2<sup>nd</sup>, but linked to

- the umbilicus to excrete urine
- Easy for elderly to deal with.

## 3. Prostatic Tumors:

- Commonest malignancy of male urogenital tract.
- Rare before the age of 50 years (screening is recommended at age of 40)
- Found at post-mortem in 50% of men older than 80 years (patient usually dies from other causes, it does not kill the patient).
- 5-10% of operation for benign disease reveal unsuspected prostate cancer.

## Gleason Scale

Well differentiated

Poorly

differentiated

## Pathology:

- The tumors are adenocarcinomas; arise in the peripheral zone of the gland.
- Spread through capsule into peri-neural spaces, bladder neck, pelvic wall and rectum.
- Lymphatic spread is common.
- Hematogenous spread occurs to axial skeleton.
- Tumors are graded by Gleeson classification.

Small, uniform glands

More space between glands

Infiltration of cells from glands at margins

Irregular masses of cells with few glands

Lack of glands, sheets of cells different glands.

Malignant prostate tumors usually arise in the peripheral zone while benign prostate hyperplasia (BPH) in the transitional zone.

### Clinical features:

- Majority these days are picked up by screening.
- 10% are incidental findings at TURP (trans-urethral resection of prostate)
- Remainder present with bone pain, cord compression or leuco-erythroblastic anemia.
- Renal failure can occur due to bilateral ureteric obstruction.

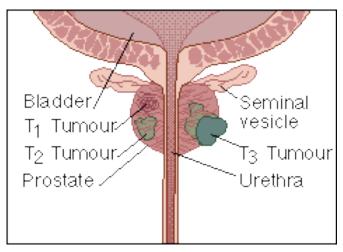
## Diagnosis:

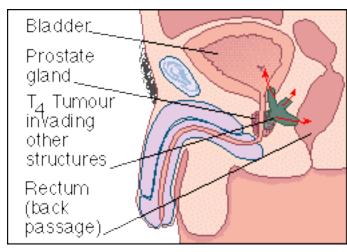
- With locally advanced tumors diagnosis can be confirmed by rectal examination.
- Features include hard nodule or loss of central sulcus.
- Trans-rectal biopsy should be performed.
- Multi-parametric MRI may be useful in the **staging** of the disease.
- Bone scanning may detect the presence of metastases.
- Unlikely to be abnormal if asymptomatic and PSA < 10 ng/ml

#### Serum prostate specific antigen (PSA)

- Kallikrein-like protein produced by prostatic epithelial cells.
- 4 ng/ml is the upper limit of normal.
- >10 ng/ml is highly suggestive of prostatic carcinoma.
- Can be significantly raised in BPH.
- Useful marker for monitoring response to treatment.

## Staging:





- T1: Cannot be felt during a digital rectal exam and cannot be seen in imaging tests.
- T2: Palpable and can be seen by naked eye.
- T3: Cancer has spread beyond the outer layer of the prostate and may have spread to the seminal vesicles.
- T4: has spread beyond the seminal vesicles to nearby tissue or organs, such as the rectum, bladder, or pelvic wall.

(From a website: <a href="http://www.cancer.gov/cancertopics/pdq/treatment/prostate/Patient/page2#Keypoint9">http://www.cancer.gov/cancertopics/pdq/treatment/prostate/Patient/page2#Keypoint9</a>)

#### **Treatment:**

- More men die **with** prostate cancer **than** from prostate cancer (they usually die because of other causes not prostate cancer).
- Treatment depends on stage of disease, patient's age and general fitness.
- Treatment options are for:

#### Local disease:

- Observation (old men older than 80 y.o, it's very slow growing tumor).
- Radical radiotherapy:

(With cord compression → painful. whenever you have patient with prostatic tumor and suffers from lower motor neuron lesions, it is considered as ER case admit him and give him radiotherapy)

Radical prostatectomy

#### Locally advanced disease:

- Radical radiotherapy
- Hormonal therapy
- Metastatic disease
  - Hormonal therapy

#### Hormonal therapy:

- 80-90% of prostate cancers are androgen dependent for their growth.
- Hormonal therapy involves androgen depletion
- Produces good palliation until tumors 'escape' from hormonal control
- Androgen depletion can be achieved by:
- Bilateral orchidectomy
- LHRH agonists goseraline
- Anti-androgens cyproterone acetate, flutamide, Biclutamide
- Complete androgen blockade

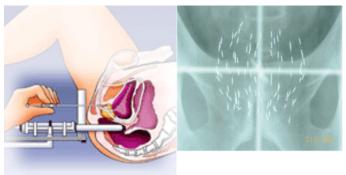
### Open/Laparoscopic/Robotic (respectively)



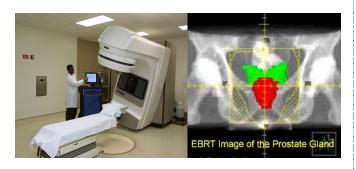




## Brachytherapy: internal radiotherapy in which the radiation source is in the body



EBRT: External beam radiation therapy



## 4. Testicular Tumors:

- Commonest presentation: ipsilateral, painless testicular swelling on the side of the tumor.
- Commonest malignancy in young men
- Highest incidence in Caucasians in northern Europe and USA
- Peak incidence for teratomas is 25 years and seminomas is 35 years
- In those with disease localized to testis more than 95% 5 year survival possible
- Risk factors include cryptorchidism (absence of 1 or more testes), testicular and Klinefelter's syndrome, testicular torsion.

### Classification:

- Seminomas (~50%)
- None- Seminoma (~50%)
  - Teratomas
  - Yolk sac tumors
  - Embryonal
  - Mixed Germ cell tumor

### Note(s):

Klinefelter's syndrome: a genetic disorder in which there is at least one extra X chromosome to a standard human male karyotype or an additional Y chromosome to a standard human female.

## Investigation:

- Diagnosis can often be confirmed by testicular ultrasound.
- Pathological diagnosis made by performing an inguinal orchidectomy.
- Disease can be staged by thoraco-abdominal CT scanning.
- Tumor markers are useful in staging and assessing response to treatment
  - Alpha-fetoprotein (alpha FP)
    - Produced by yolk sac elements
    - Not produced by seminomas
  - Beta-human chorionic gonadotrophin (beta HCG)
    - Produced by trophoblastic elements
    - Elevated levels seen in both teratomas and seminoma
  - LDH (lactate dehydrogenase) test.

## **Stage Definition**

- I : Disease confined to testis
- IM: Rising post-orchidectomy tumor marker
- II: Abdominal lymphadenopathy
  - A) < 2 cm B) 2-5 cm C) > 5 cm
- III: Supra-diaphragmatic disease

### **Treatment:**

#### Seminoma:

- Seminomas are radiosensitive
- The overall cure rate for all stages of seminoma is approximately 90%.
- Stage I and II disease treated by inguinal orchidectomy plus
  - Radiotherapy to ipsilateral abdominal and pelvic nodes ('Dog leg') or
  - Surveillance
- Stage IIC and above treated with chemotherapy

#### Non-Seminoma:

- None-Seminoma are not radiosensitive
- Stage I disease treated by orchidectomy and surveillance Vs RPLVD Vs Chemo
- Chemotherapy (BEP: Bleomycin, Etopiside, Cisplatin) given to:
  - Stage I patients who relapse
  - Metastatic disease at presentation



Seminoma



**Non-Seminoma** 

#### **SUMMARY**

#### 1. Renal tumors:

- Almost all of them are malignant; RCC is the most common type.
- It has higher incidence to be seen in von Hipple-Lindau syndrome.
- Patients come with **loin pain**, painless hematuria, PNS (hypertension, Hypercalcaemia, polycythemia, pyrexia)
- It is chemo and radio resistant so treated surgically: radical nephrectomy (laparoscopic is the gold standard), CT to watch out tumor spread, echocardiogram to asses thrombus formation.

#### 2. Bladder tumors:

- TCC is the most common.
- Patient comes with gross, painless terminal hematuria
- Could be either superficial (80%) or invasive (20%).
- You have to have full investigation
- Stage 2 and higher: removal of the whole bladder.
- Superficial TCC: trans-urethral resection, Invasive TCC: radical cystectomy.
- In squamous carcinoma the major risk factor is chronic irritations of bladder (Bilharzia, stones in the bladder or chronic indwelling catheterization).

#### 3. Prostatic tumors:

- Commonest malignant tumor of male urogenital tracts.
- Might spread to other areas and organs (lymphatic spread is common).
- Can be diagnosed by rectal examination + trans-rectal biopsy + PSA
- Treatment depends on age and stage: radical radiotherapy, prostatectomy, hormonal therapy according to stage.

#### 4. Testicular tumors:

- Ipsilateral painless testicular swelling
- Risk factors include: Cryptorchidism and Klinefelter syndrome
- Classified as: seminoma, non-seminoma
- Investigated by ultrasound and tumor markers
- Seminoma is radiosensitive, non-seminoma treated by orchidectomy.

## Questions

- 1) Which one of the following conditions associated with von Hipple-Lindau syndrome?
  - a. Papillary Cell Carcinoma.
  - b. Renal Cell Carcinoma.
  - c. Squamous Cell Carcinoma.
  - d. Renal oncocytoma.
- 2) Majority of patients with transitional cell carcinoma of the bladder present clinically with:
  - a. Gross hematuria with loin pain.
  - b. Bone pain and leuco-erythroblastic anemia.
  - c. Microscopic, Painful and initial hematuria.
  - d. Macroscopic, Painless and terminal hematuria.
- 3) Which one of the following syndromes is a risk factor of testicular tumors?
  - a. Von Hipple-Lindau syndrome.
  - b. Stuffer's syndrome.
  - c. Klinefelter's syndrome.
  - d. Paraneoplastic Syndrome.



#### Answers:

1st Questions: B

2nd Questions: D

3rd Questions: C