Urinary Tract Tumours

Prof. Nader Salama
Taiba University
Alexandria University
Tumours of the kidney
Pathological classification of renal tumours

- benign tumors
  - oncocytoma
  - angiomyolipoma
  - leiomyoma
  - Lipoma

- malignant tumours
  - renal cell carcinoma (RCC)
  - renal pelvis tumors
  - nephroblastoma (Wilm's tumour)
  - sarcomas
  - metastatic tumours
    - lymphoma
    - others: e.g. lung, breast, stomach
Benign tumors

- **Oncocytoma**
  - 3-5% of all renal tumors
  - cut section: light brown with central stellate scar
  - behaviour: ranging from benign (capsule, no necrosis) to malignant (rare metastases)
  - silent tumor, only in < 20% cause haematuria or flank pain
  - US, CT or MRI: not characteristic
  - Diagnosis: (pathological) large cells with an intensely eosinophilic cytoplasm
  - Treatment: enucleation or nephrectomy (partial or radical - why? – unsure behavior, difficult diagnosis)
Oncocytoma
Angiomyolipoma (hamartoma): 2 types:
- With Tuberous sclerosis: bilateral & asymptomatic, or
- Without Tuberous sclerosis: unilateral & bigger

- Spontaneous rupture: 25% of cases → Retro-peritoneal Hge
- Three major histologic components: mature fat cells, smooth muscle, and blood vessels

Diagnosis: CT (fat density -20 to 80 HU)
Treatment: follow up (US, CT-if asymptomatic), embolisation or nephron sparing surgery (if pain/bleeding).
Renal cell carcinoma (RCC) I.

- 85% of all primary malignant tumors of the kidney
- 58,240 new cases/year (USA, 2010)
- Most common in the 5th-6th decades of life
- Men affected twice as common as women
Renal cell carcinoma (RCC) II.

- **Etiology**
  - smoking
  - chemicals: shoe workers, leather tanners, cadmium, asbestos and petroleum products
  - genetic factors - von Hippel Lindau disease (chromosomal aberration, 3q deletion)
  - acquired cystic renal disease in uremic patients
Renal cell carcinoma (RCC) III.

Pathology

- Cell of origin: proximal renal tubular epithelium
- Colour: yellow (abundance of fat)
- C.S: haemorrhage, necrosis, calcifications
CS in RCC
Renal cell carcinoma (RCC) - History

- asymptomatic: >50% (incidentally with CT screening)
- The classical triad (pain, mass & hematuria): only 7-10%, advanced disease (late).
- Due to metastases: 30%, cough, dyspnea, bone pain
- Organs involved include:
  - Lung (75%)
  - Soft tissues (36%)
  - Bone (20%)
  - Liver (18%)
  - Cutaneous sites (8%)
  - Central nervous system (8%)
• **Paraneoplastic Syndromes**
  - Liver dysfunction (Stauffer’s syndrome), non-metastatic, 3-20%, GMCSF *
  - Hypertension (40%, renin)
  - Erythrocytosis (3-10%, erythropoietin)
  - Hypercalcemia (20%, PTH)

• **Other signs and symptoms**
  - Weight loss
  - Fever
  - Night sweats
  - Varicocele: right-sided, obstruction of rt testicular v.
Diagnosis

- History, physical examination
- Laboratory: anemia, hematuria
- KUB (Mass, Psoas Muscle shadow Obliteration)
- IVU (Filling Defect Area)
- Ultrasonography (Mass, heterogeneous consistency)
- CT scan (staging)
- MRI (IVC involvement)
- Angiography (now decreased after CT advancement)
- Chest radiography
- Radionucleoid bone scan
US and IVU
CT and angiography
Staging

- **The Robson staging system** is as follows:
  - Stage I - Tumor confined within capsule of kidney
  - Stage II - Tumor invading perinephric fat but still contained within the Gerota fascia
  - Stage III - Tumor invading the renal vein or IVC (A), or regional LN involvement (B), or both (C)
  - Stage IV - Tumor invading adjacent viscera or distant metastases

- This system (easy) but does not correlate stage at presentation with prognosis
STAGING OF RENAL CELL CARCINOMA

STAGE I
TUMOR WITHIN CAPSULE

STAGE II
TUMOR INVASION OF PERINEPHRIC FAT (CONFINED TO GEROTA’S FASCIA)

STAGE III
TUMOR INVOLVEMENT OF REGIONAL LYMPH NODES AND/OR RENAL VEIN AND CAVA

STAGE IV
ADJACENT ORGANS OR DISTANT METASTASES

www.icareunit.com
Staging

- The tumor, nodes, and metastases (TNM) classification).
  - **Primary tumor (T)** – tumor size & IVC involvement above/below diaphragm
    - TX - Primary tumor cannot be assessed
    - T0 - No evidence of primary tumor
    - T1 - Tumor 7 cm or smaller in greatest dimension, limited to the kidney (T1a: <4 cm, T1b: 4-7 cm)
    - T2 - Tumor larger than 7 cm in greatest dimension, limited to the kidney (T2a: 7-10 cm, T2b: > 10 cm)
    - T3 - Tumor extends into major veins or perinephric tissues but not adjacent adrenal gland or beyond the Gerota fascia
      - T3a - Tumor invades perinephric tissues or renal v & its branches but not beyond the Gerota fascia
      - T3b - Tumor grossly extends into the IVC below the diaphragm
      - T3c - Tumor grossly extends into the IVC above the diaphragm
    - T4 - Tumor invading beyond the Gerota fascia including adjacent adrenal gland.
• **Regional lymph nodes (N)**
  - NX - Regional lymph nodes cannot be assessed
  - No - No regional lymph node metastasis
  - N1 - Metastasis in a single regional lymph node
  - N2 - Metastasis in more than 1 regional lymph node

• **Distant metastasis (M)**
  - MX - Distant metastasis cannot be assessed
  - Mo - No distant metastasis
  - M1 - Distant metastasis
Treatment

- Surgical therapy
  - radical nephrectomy
    - early control of renal vessels
    - removal of perirenal fat
    - adrenalectomy (if the upper pole is involved)
    - regional lymphadenectomy
  - radical nephrectomy + thrombectomy
  - lung metastases can regress after radical nephrectomy
II- Medical therapy

Indications

- adjuvant therapy of locally invasive disease
- medical therapy of metastatic disease

Types

- Immuno- or combined immuno-chemotherapy
  - Vinblastine + Interferon-alpha
  - 5-FU + Interleukin-2 + Interferon-alpha

- Targeted therapy
  1\textsuperscript{st} line:
  - A combination of bevacizumab (inhibitor of angiogenesis) plus interferon \( \alpha \)
  - Sunitinib (targeting vascular endothelial growth factor)

  2\textsuperscript{nd} line:
  - everolimus (another mTOR* inhibitor)
  - Pazopanib (tyrosine kinase inhibitor)

Radiation therapy

- adjuvant, RCC mostly resistant to radiotherapy
Renal pelvis tumor

- Rare, 4% of all urothelial cancer
- Old age: ≥ 65 y
- Male/female=3/1
- Etiology
  - Smoking
  - analgesics, cyclophosphamid, Balkan nephropathy
  - chemicals
    - petrol and plastic industry, asphalt and tar exposition
  - chronic infections and calculi
  - Thorotrast
- Pathology
  - transitional cell carcinoma (90%)
  - squamous cell carcinoma (10%)
  - adenocarcinoma
Transitional Cell Carcinoma (TCC)

- The vast majority of urothelial tumors arise in the bladder.
- 51:3:1 – UB: renale pelvis: ureteric tumors
- multicentricity
Renal urothelial carcinoma (UC) rarely is reported as an incidental finding.

**Hematuria**
- Gross hematuria is the most common presenting symptom (75-95%).
- Microscopic hematuria occurs in 3-11% of patients.

**Pain**
- Approximately 14-37% of patients report pain.
- Pain is usually _dull and is caused by the gradual obstruction_ of the collecting system.
- Renal colic also may occur with the passage of blood clots.

**Patients are rarely asymptomatic (1-2%).**
Physical Examination

- Physical examination usually is **not informative or specific**, especially in **early** stage disease.

- A palpable **flank mass** may be noted in less than 20% of patients.
Lab Studies

- **Urinalysis and urine culture**
  - The presence of microscopic hematuria suggests urinary tract tumors, which must be ruled out even if the hematuria resolves.
  - The presence of more than 2-5 red blood cells in high-power field is considered enough to warrant further investigation to rule out upper-tract TCC.

- **Cytologic studies**
  - Voided-urine cytology is a convenient and noninvasive method of diagnosis, but it is subjective and lacks the necessary sensitivity for diagnosing upper-tract urothelial tumors, especially low-grade neoplasms.
  - Fluoroscopically guided brush biopsy increases diagnostic accuracy to 80-90%.
Intravenous urography

- Intravenous urography (IVU) was the most commonly used diagnostic method in the evaluation of patients with hematuria in the past.
- Filling defects in the upper urinary tract can be demonstrated in 50-75% of patients. Other common causes of filling defects (eg, nonopaque stones, blood clots, papillary necrosis with sloughing, fungus balls, air bubbles) should be ruled out.
- Nonvisualization of the affected kidney.

CT scan

- CT scan is useful in the diagnosis and staging of renal urothelial tumors. It can distinguish between radiolucent renal stones and upper-tract urothelial tumors, since stones appear opaque on CT scans (>200 HU for uric acid stones against 60-80 HU for tumors).
CT – renal pelvic tumour
Imaging Studies-II

- Cystoscopy with retrograde pyelography
  - Cystoscopy may help to localize bleeding site (left, right) and rule out or confirm concomitant bladder lesions.
  - Retrograde pyelography (RPG) is especially useful when:
    - the kidney cannot be visualized by IVU
    - IVU cannot be performed because of renal insufficiency or severe contrast allergy.

- Ureteroscopy
  - Ureteroscopy is used routinely in the diagnosis of renal pelvic tumors.
Staging

- **Primary tumor (T) (simply, degree of invasion-only)**
  - TX: Primary tumor is occult and cannot be assessed
  - T0: No evidence of primary tumor
  - Ta: Papillary non-invasive carcinoma
  - Tis: Carcinoma in situ
  - T1: Carcinoma involves subepithelial connective tissue
  - T2: Carcinoma invades the muscularis
  - T3: Carcinoma invades beyond muscularis into periureteric or peripelvic fat or into renal parenchyma
  - T4: Carcinoma invades adjacent organs or extends through the kidney into perinephric fat
Regional lymph nodes (N) (size of LN involvement)
- NX: Regional lymph nodes cannot be assessed
- N0: No regional lymph node metastasis
- N1: Metastasis in a single lymph node, 2 cm or less in greatest dimension
- N2: Metastasis in a single lymph node 2 to 5 cm in greatest dimension; or multiple metastatic lymph nodes, none more than 5 cm in greatest dimension
- N3: Metastasis in a lymph node more than 5 cm in greatest dimension

Distant metastasis (M)
- MX: Presence of distant metastasis cannot be assessed
- M0: No distant metastasis
- M1: Distant metastasis
Renal pelvis tumour - Treatment

- Surgical treatment
  - ureteroscopic coagulation with laser*
  - open conservative surgery – excision*
  - (best) nephro-ureterectomy with removal of a bladder cuff - why ??

- Systemic chemotherapy - cisplatin-based chemotherapy (metastatic cases)
Bladder Cancer
Bladder Cancer

- Average age at diagnosis is 68 years, and the incidence increases with age
- Male-to-female ratio is 3:1
- Of bladder tumors, 95% are Transitional Cell Carcinomas (TCC)
- 5% are squamous cell & adenocarcinomas in origin
Presentation

- *painless gross haematuria* (classic presentation), 80-90% of cases.

- Consider all patients with painless gross haematuria to have bladder cancer until proven otherwise.

- 20-30% of patients with bladder cancer experience *irritative bladder symptoms* such as:
  - Dysuria
  - Urgency
  - Frequency

- Patients with *advanced disease* can present with:
  - bony pain,
  - lower-extremity oedema (iliac vessel compression)
  - flank pain (ureteral obstruction)
Risk Factors

• **Smoking**
  ✓ accounts for ~ 50% of all bladder cancers.
  ✓ Tobacco carcinogenics: Nitrosamine, 2-naphthylamine and 4-aminobiphenyl

• Industrial exposure to **aromatic amines**:
  ✓ dyes, paints, solvents, leather dust, inks, combustion products, rubber, and textiles

• **Higher-risk occupations**:
  • painting, driving trucks, and working with metals

• **Medical risk factors**
  • radiation treatment of the pelvis
  • Chemotherapy with cyclophosphamide

• **long-term indwelling catheters**:
  ✓ patients with SCI
Specific Work Up

- **Urinalysis**: hematuria

- **Urine Cytology**: malignant cells

- **CT Abdomen-Pelvis**: imaging, guided biopsy & staging

- **Upper Tract Imaging (IVP/Renal US)**: any multi-centricity, hydronephrosis

- **Cystoscopy (Flexible/Rigid)**: description & biopsy
Bladder Carcinoma - cystogram
Bladder Carcinoma - CT
Papillary TCC of urinary bladder on Cystoscopy
Staging of Bladder Carcinoma

- **Tis (O)**
- **T1**
- **T2a**
- **T2b**
- **T3**
- **T4**

**Region affected:**
- Epithelium
- Lamina propria
- Superficial muscle
- Deep muscle
- Perivesical fat (or peritoneum)
- Prostate (contiguous organs)

**Muscle:**
- Deep longitudinal layers, middle circular and inner longitudinal layers

**Submucosa:**
- Lamina propria
- Epithelium

**Subserosa and perivesical fat**

**Peritoneum**

* **T3a**—microscopic invasion of perivesical tissue

**T3b**—macroscopic invasion of perivesical tissue (extravesical mass)

**T4a**—invasion of prostate, uterus, vagina

**T4b**—invasion of pelvic wall, abdominal wall
Treatment

- **Superficial Bladder Carcinoma**

  T.U.R.B.T ( + deep muscle biopsy) followed by either:
  - Intravesical immunotherapy (Bacillus Calmette-Guérin [BCG])
    * induces nonspecific, cytokine-mediated immune response
  - Intravesical Chemotherapy (Thiotepa/Mitomycin C)

- **Muscle-invasive disease (T2 and greater)**

  - Radical Cystectomy (with urinary diversion) +/- chemotherapy
  - Concomitant chemotherapy & radiotherapy
Benign Prostatic Hypertrophy
Definition (Terminology)

- Benign Prostatic Enlargement (BPE)
  - Clinical Dx

- Benign Prostatic Hyperplasia (BPH)
  - Pathological Dx

- Bladder Outflow Obstruction (BOO)
  - Urodynamic Dx
BPH - Incidence

- The most common benign neoplasm in the aging male
- Usually > 60 years    Rarely < 40 years
- Weight: (prostate) :
  - 12 gm - before the age of 45 years
  - 24 gm - the sixth decade
Epidemiology
Prevalence – clinical

- 26% of men aged 40 to 49 yrs
- 33% of men aged 50 to 59 yrs
- 41% of men aged 60 to 69 yrs
- 46% of men aged 70 to 79 yrs

(Olmstead County study, 1993)

Increases with aging
Epidemiology

Prevalence: Autopsy(pathology)

- 23% of men aged 41 to 50 yrs
- 42% of men aged 51 to 60 yrs
- 71% of men aged 61 to 70 yrs
- 82% of men aged 71 to 80 yrs

Growth rate increase and doubling times gets rapid with age
Etiology

- not completely understood
- **Endocrine controlled**
  - Regression after castration
  - Development with aging (E2 → induction of AR → sensitization of prostate to free T → BPH development)

- **Genetic**
  - \( (T) \ 5\alpha\text{ reductase} \ (\text{DHT}) \ → \text{glandular epith. proliferation} \)
Prostatic Zones

- Bladder / Urethra
- Mushroom = Fibromuscular Zone
- Peas = Periurethral Glandular Zone
- Carrots = Central Zone
- Tomato = Transition Zone
- Potato = Peripheral Zone

Vas Deferens / Seminal Vesicle
Ejaculatory Duct
Pathology

BPH arises from either:

- The transition zone
- Periurethral zone

2 lateral lobes
median lobe

Compression of urethra
- **Microscopy**

  - BPH affects both glandular epithelium and C.T. stroma to variable degree

  If:
  - Mainly glandular------(soft)-*--5α reductase inhibitors
  - Mainly fibrous stroma------(firm)-*--α blockers

- **Macroscopy**

  - Pattern:
    - Monolobar = Median lobe
    - Bilobar = 2 lateral lobes
    - Trilobar = Median + 2 Lateral lobes

* = response
The hyperplastic nodules compress the surrounding zones ➔ **Surgical capsule** with a plane of cleavage in between.
Pathophysiology of BPH-associated obstruction

I- Static component

- The 2 lateral lobes (enlarged) → elongation, compression and angulations of the prostatic urethra
- Middle lobe (enlarged) → obstruction of the bladder neck (ball-valve)
- Bladder stone as a complication → obstruct the bladder neck

II- Dynamic component

- Prostatic smooth muscle & bladder neck are innervated by alpha-adrenergic fibers. The fibers maintain tension (tone) of these structures.
- Atony of detrusor m. by long standing obstruction → chronic retention
Symptoms (LUTS)

A. Obstructive symptoms
   1. Hesitancy
   2. Straining during urination.
   3. Decreased force & caliber of urinary stream
   4. Intermittency
   5. Sense of incomplete emptying
   6. Terminal dribbling

B. Irritative symptoms
   1. Frequency
   2. Nocturia
   3. Urgency
   4. Urge incontinence
<table>
<thead>
<tr>
<th>In the past month:</th>
<th>Not at All</th>
<th>Less than 1 in 5 Times</th>
<th>Less than Half the Time</th>
<th>About Half the Time</th>
<th>More than Half the Time</th>
<th>Almost Always</th>
<th>Your score</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Incomplete Emptying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>How often have you had the sensation of not emptying your bladder?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Frequency</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>How often have you had to urinate less than every two hours?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Intermittency</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>How often have you found you stopped and started again several times when you urinated?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Urgency</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>How often have you found it difficult to postpone urination?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Weak Stream</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>How often have you had a weak urinary stream?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Straining</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>How often have you had to strain to start urination?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Nocturia</td>
<td>None</td>
<td>1 Time</td>
<td>2 Times</td>
<td>3 Times</td>
<td>4 Times</td>
<td>5 Times</td>
<td></td>
</tr>
<tr>
<td>How many times did you typically get up at night to urinate?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Total I-PSS Score**

**Score:** 1-7: Mild       8-19: Moderate       20-35: Severe
Complications

- Hematuria
- Retention
- Infection
- Bladder stone
- Symptoms of renal failure (with chronic retention).
Signs

- Elderly Male
- DRE: size- shape- consistency- symmetry- surface
- Suprapubic Area (urine retention)
- Renal mass (hydronephrosis)
- Hernia orifices (straining)
- Signs of renal failure (late).
Investigations

I- Uroflowmetry

- Simple and non-invasive.
- Normal maximum flow rate (Q-Max) >18 ml/second
- Maximum Flow Rate < 10ml/Sec: indicative of obstruction &/or weak detrusor muscle
II- Laboratory Investigations

- Urine analysis: pus cells, RBC
- Serum creatinine
- Serum PSA (prostatic specific antigen); Normal <4 ng/ml

Before taking test, ensure:

1. No urological instrumentation x 6w (up to)
2. No ejaculation x 48 hrs
3. No Bicycle riding x 48 hrs
4. No current UTI

The most valuable measurement of PSA is its change over time rather than its actual serum level
III - Diagnostic Imaging

A. Ultrasonography

- Trans-rectal (TRUS, best for prostate check-up): size, echogenicity
- Assess:
  - kidneys,
  - post voiding residual (PVR),
  - any incidental pathology (UB stone, diverticulum)
B. Plain KUB and IVU:

**Identify**

- Stones
- Upper tract affection
- Smooth basal filling defect
- Fish hooking of the lower ureters (elevation of the bladder base)
- Bladder trabeculations, cellules, and diverticulae
- Residual urine (post-voiding film)
1. Basal smooth F.D.
2. Fish hook sign
Bladder trabeculations

Bladder diverticulae

Bladder diverticulum
IV - Cystourethroscopy

- Pattern of lobe enlargement (e.g. median, lateral)
- Hematuria
- Bladder stone
- Associated pathology (e.g. tumor)
- Urethral stricture
D.D

- Meatal stenosis
- Urethral stricture
- Prostatic cancer
- Bladder neck fibrosis
- Drugs (parasympatholytic and sympathomimetics)
- Neurologic lesions
Treatment:

- **I- Non-Invasive Therapy (Medical)**
  
  - 1) Watchful waiting
  - 2) Phytotherapy
  - 3) Alpha-blockers
  - 4) 5-alpha reductase inhibitors
1) Watchful waiting (Re-assurance)

- Mild symptoms
- Normal PSA
- Uncomplicated
2) Phytotherapy

(the use of plants or plant extracts for medicinal purposes)

Examples:
- saw palmetto berry (*Serenoa repens*), *(the most well studied)*
- the bark of *Pygeum africanum*,
- the roots of *Echinacea purpurea*
- *Hypoxis rooperi*, pollen extract,
- the leaves of the trembling poplar

Outcome:
- A prospective, randomized *clinical trial* (Bent et al., 2006) & a recent *systematic review* (Wilt et al., 2009) of saw palmetto: *no benefit beyond placebo*
3) Alpha-blockers

- Non-selective
  Phenoxybenzamine

- $\alpha_1$, short acting
  Prazosin

- $\alpha_1$, long acting
  Doxazosin

- $\alpha_1a$-Selective
  - Tamsulosin
  - Alfuzosin

**Advantages**
- Quick action
- Safe
- Selective
- Long lasting

**Side effects**
- Postural hypotension
- Dizziness
- Drowsiness
- Headache
4) 5-alpha reductase inhibitors

✔ Finasteride
✔ Dutasteride

Advantages
✔ Safe
✔ Logical
✔ Reduces prostate volume

Side effects
- reduces libido
- mild ED
- gynecomastia

Combination therapy (3 & 4) has been proven to be superior in treatment and is recommended by AUA
II- Invasive Therapy (Surgical)

A. Endoscopic: Transurethral resection of the prostate (TURP): This is the **Gold standard** option.

B. Open prostatectomy: retropubic, transvesical & perineal approaches

Any removed prostatic tissue (by TURP or open routes) should be subjected to **histopathological examination**.

Other less invasive methods (Still inferior to TURP): hyperthermia, incisions, balloon dilatation, etc.
Prostatic chips after TURP
Indications of surgery

- 1. Repeated attacks of acute urinary retention (AUR)
- 2. Hydronephrosis
- 3. Hematuria
- 4. Recurrent urinary tract infection (UTI)
- 5. Bladder stone
- 6. Severe obstructive symptoms
- 7. Poor response to medical therapy (=failed medical treatment)
Complications of TURP

- Retrograde Ejaculation 70%
- Stricture 2-3%
- Erectile dysfunction 5%
- TUR syndrome <1%
- Redo rate 10%
- Death <1%

Risk factors to develop complications

- Resection time > 90 mins
- Gland volume > 45 mls
- AUR
- Age >80 y
Prostatic carcinoma

- the most common noncutaneous cancer detected among American men.
- More than 200,000 new cases are detected annually.
- Approximately 30,000 men die of the disease annually.
Risk factors

- **Definite**
  - ↑ Age
  - Family history
  - Genetics (BRCA1 or BRCA2 mutations linked to P Ca)
    - Chromosomal rearrangements or copy number abnormalities at 8p, 10q, 11q, 13q, 16q, 17p, and 18q have been described in P Ca).
  - Race (African American > White American)

- **Probable**
  - Dietary fats: high saturated fat
  - Vasectomy
Pathology

- Commonly: adenocarcinoma. 95%
- Other types: 5%
  - TCC
  - Sarcoma

- Usually arises from the peripheral zone
Grading

- **Gleason Grade (Pattern)**
- Depends on glandular differentiation and growth pattern
- Range from 1-5:
  - a primary grade to the pattern of cancer that is most commonly observed.
  - a secondary grade to the second most commonly observed pattern in the specimen.
Gleason Score
- 2 most common patterns displayed
- Ranges from 2-10
- To aid in expecting the prognosis
Spread

- **Direct**
  - bladder, S.V.
- **Lymphatic**
  - Obturator
  - Hypogastric, Ext iliac, others (peri-aortic) LN
- **Distant**
  - 90% to bones (the commonest, osteoblastic, axial bones) → pathological fractures + SC compression
  - Lung, liver
Osteoblastic metastases
Staging TNM

- **T**—Primary tumor
  - **Tx** Cannot be assessed
  - **T0** No evidence of primary tumor
  - **Tis** Carcinoma in situ (PIN)

- **T1** : asymptomatic, no clinical signs
  - **T1a** \( \leq 5\% \) of tissue in resection for benign disease has cancer, normal DRE
  - **T1b** \( >5\% \) of tissue in resection for benign disease has cancer, normal DRE
  - **T1c** : Detected from elevated PSA alone, normal DRE and imaging

- **T2** : palpable, confined to prostate (one/2 lobes)
  - **T2a** : Tumor palpable by DRE or visible by imaging, involving less than half of one lobe of the prostate
  - **T2b** : Tumor palpable by DRE or visible by imaging, involving more than half of one lobe of the prostate
  - **T2c** : Tumor palpable by DRE or visible by imaging, involving both lobes of the prostate
- **T3**: Locally invasive
  - T3a: Extracapsular extension on one or both sides
  - T3b: Seminal vesicle involvement on one or both sides

- **T4**: Tumor spread
  - T4: Tumor directly extends into bladder neck, sphincter, rectum, levator muscles, or into pelvic sidewall
TNM Staging

**Lymph node involvement**
- **NX**: Regional lymph nodes cannot be assessed
- **N\text{0}**: No lymph node metastases
- **N1**: LN metastasis

**Distant metastatic spread**
- **MX**: Distant metastases cannot be assessed
- **M\text{0}**: No evidence of distant metastases
- **M1**: Distant metastasis
Signs & Symptoms

- Often asymptomatic ---- early stage
- Symptoms ------ locally advanced or metastatic disease

  ▶️ LUTS (obstructive / irritative)
  ▶️ Due to metastases
  ➢ Bony pain
  ➢ weakness of the lower extremities (SC compression)

- DRE – hard, nodular prostate (most pathognomonic)
Investigations - radiological - I

- Pelvic / Lumbar spine x-ray
  → suspect osteosclerotic lesions

- IVU/ renal US:
  → kidney ? Hydronephrosis

- TRUS
  → with an elevated serum PSA, abnormal DRE, or a both
  → under its guidance: prost biopsy can be done, 6 pieces per each lobe
Investigations- radiological - II

- **Bone scan**
  - If PSA > 20 ng/mL
  - T2 disease
  - with bony pain

- **Endorectal MRI prostate**
  → accurate staging

- **Axial imaging (CT, MRI)**
  → LN & distant metastases staging
Bone Scan
Investigations - lab

- Anaemia $\rightarrow$ metastases
- Uremia $\rightarrow$ trigonal invasion & ureteral obstruction with hydronephrosis
- Serum markers
  - $\uparrow$ Alk phos $\rightarrow$ bone metastases
  - P.S.A (Normal: 0-4 ng/ml)
PSA 1

- Cheap
- Widely available
- Easy to interpret
- Prostate specific

However

- Not prostate cancer specific
- Normal value does not rule out cancer
- Many patients fall into ‘grey area’, (4-10 ng/mL, 25% possible prost. cancer)
Before taking test, ensure the previous precautions
Many attempts to increase PSA senstivity

- Age adjusted PSA
- PSA density
- PSA velocity / PSA doubling time
- Complexed PSA
- Free/total PSA
### PSA kinetics (suspecious)

#### Standard PSA
- $> 4.0 \text{ ng/ml}$

#### Age adjusted PSA
- 40 - 49 $> 2.5 \text{ ng/ml}$
- 50 - 59 $> 3.5 \text{ ng/ml}$
- 60 - 69 $> 4.5 \text{ ng/ml}$
- 70 - 79 $> 6.5 \text{ ng/ml}$

#### PSA Velocity
- Change $> 0.75 \text{ ng/ml/year}$

#### Free/Total PSA
- $< 0.15$
- May better distinguish BPH from cancer

#### Complexed PSA
- $> 3.75 \text{ ng/ml}$
Treatment options

1- Watchful Waiting
   * Old age- Localized cancer

2- Radical prostatectomy $T_1,T_2$
   * Young patient- Localized cancer
   * Retropubic or perineal approaches
Treatment options

- Radiotherapy
  * Curative = Localized cancer
  * Palliative = Metastatic

- Types:
  - External beam
  - Interstitial irradiation
Treatment options

• 4- Hormonal Therapy
  * Metastatic Tumors

  Types:
  - Anti-androgens (e.g. Flutamide) + 5-alpha reductase inhibitor (e.g. finasteride)
  - LHRH analogues (e.g. leuprolide, Gosereline “Zoladex”)
  - Oestrogens (not used now)
  - Surgical Castration
Emergency Treatment - prostatic cancer complications

- **Cord compression**
  - Laminectomy
  - Ketoconazole
- **Ureteral obstruction**
  - Ureteric catheter (DJ)
  - PCN
  - Ketoconazole
- **Retention**
  - Tunneling
Testicular Cancer
Epidemiology

- 9 new cases /100,000/y (USA)
- Primarily affects young men (20 - 44 y).
Presentation

- **Mostly:** Painless unilateral testicular swelling
- Hydrocoele

- **Endocrinological Effects** –
  - Gynaecomastia / Breast tenderness

- In 10% presenting symptoms due to **metastatic disease:**
  - Neck mass
  - Cough/Dyspnoea
  - Bone pain
Classification

- **Germ Cell Tumours** (95% of all)
  - **Seminomas** (40% of germ cell tumours)
  - **Non Seminomatous** (60% of germ cell tumours)
    - Most nonseminomas contain cells from at least two subtypes, including the following:
      - *Choriocarcinoma* (rare; aggressive; likely to metastasize)
      - *Embryonal carcinoma* (accounts for 20% of cases; likely to metastasize)
      - *Teratoma* (usually benign in children; rarely metastasize)
      - *Yolk sac carcinoma* (most common in young boys; rare in men)

- **Non Germ Cell Tumours** (5% of all)
  - Leydig Cell Tumours
  - Sertoli Cell Tumours

- **Others**:  
  - leukemic infiltration of the testis
  - metastases from prostate (commonest), lung, GIT, melanoma
Risk Factors

- Cryptorchidism
  - 50% of testicular tumors develop in cryptorchidism.
  - (intra-abd testis: 1 in 20 vs inguinal testis: 1 in 80)

- Family History

- Race (Scandinavia vs Japan: 6.7 vs 0.8 new cases/100,000)

- Exogenous estrogen administration during pregnancy
  - associated with an increased relative risk for testicular tumors in the fetus

- ? Trauma ? Orchitis ? Atrophy
  (a causal relationship has not been established)
Work-Up

**Serum tumor markers**
- Serum human chorionic gonadotrophin (βHCG),
- alpha-fetoprotein (AFP),
- lactate dehydrogenase (LDH)

✓ to assess success of treatment
Incidence of elevated tumor markers by histologic type in testis cancer.

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>hCG (%)</th>
<th>AFP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seminoma</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Teratoma</td>
<td>25</td>
<td>38</td>
</tr>
<tr>
<td>Teratocarcinoma</td>
<td>57</td>
<td>64</td>
</tr>
<tr>
<td>Embryonal</td>
<td>60</td>
<td>70</td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td>100</td>
<td>0</td>
</tr>
</tbody>
</table>
Ultrasound

✓ Performed to ensure the correct diagnosis.

(Most tumors are diagnosed based on physical examination finding)
Hypoechoic testicular mass (tumor)
CT scan

- of the abdomen and pelvis: integral to the staging of a testis tumor (LN metastases)
- Of the thorax: for any possible pulmonary metastases

Semen banking
before treatment for future fertility concerns
Metastases from seminoma in para-aortic L.N
Staging

TNM classification

- **T0** no evidence of primary tumour, e.g. histological scar in testis
- **Tis** carcinoma in situ, intra-tubular cancer (CIS, TIN)
- **T1** tumour limited to the testis and epididymis
  - without vascular/lymphatic invasion;
  - tumour may invade into the tunica albug but not the tunica vag
- **T2** tumour limited to the testis and epididymis
  - with vascular/lymphatic invasion or
  - tumour extending through the tunica albug with involvement of the tunica vaginalis
- **T3** tumour invades the spermatic cord with/without vascular/lymphatic invasion
- **T4** tumour invades the scrotum.
N—Regional lymph nodes (size, no of LN)

NX: Cannot be assessed

N0: No regional lymph node metastasis

N1: Lymph node metastasis ≤2 cm, or multiple nodes, none >2 cm and <6 nodes positive

N2: Nodal mass >2 cm and ≤5 cm or ≥6 nodes positive

N3: Nodal mass >5 cm
M—Distant metastasis

MX: Cannot be assessed

M0: No distant metastasis

M1a: Distant metastasis present in nonregional lymph nodes or lungs

M1b: Nonpulmonary visceral metastases
Treatment

- Depends on TNM

- In general –

- Localized Seminoma
  - Inguinal Orchietomy +/- Radiotherapy to L. Nodes

- Seminoma with nodes
  - Inguinal Orchidectomy + Platinum based chemotx

- Nonseminomatous tumour
  - Inguinal Orchidectomy +/- RPLND +/- Chemotx
Inguinal Orchiectomy
Thank You