Pathology of the male genitourinary tract
Pathology of Prostate
Objectives

1. Distinguish acute and chronic prostatitis based on clinical features, etiology and morphology.
2. Distinguish between nodular hyperplasia and carcinoma of the prostate based on clinical features, zones of origin, etiology and morphology.
Objectives

3. Discuss the relationship of racial factors, Prostate Specific Antigen (PSA) and Prostatic Intraepithelial Neoplasia (PIN) to prostatic carcinoma.

4. Explain the basis of grading, scoring and staging of prostate cancer.
Prostate

• ITIS – Prostatitis
  - acute and chronic bacterial and abacterial prostatitis.
  - granulomatous prostatitis
• Nodular hyperplasia (BPH)
• Prostatic adenocarcinoma
Normal Prostate

- CZ – Central zone
- TZ – Transitional zone
- PZ – Peripheral zone
- Region of the anterior fibromuscular stroma

- Normal adult: Prostate weighs 20 gms
Prostatitis

- Acute – E.Coli – intraprostatic reflux of urine.
  - surgical manipulation during catheterization, cystoscopy
- Chronic bacterial prostatitis – difficult to diagnose
  - follows recurrent UTI
- Chronic abacterial prostatitis – most common
  - No h/o recurrent UTI
  - bacterial culture negative.
Prostatitis

- Granulomatous prostatitis – TB, Sarcoidosis, Fungus
- US- Most common cause - BCG instillation within the bladder for the treatment of superficial bladder cancer
Nodular Hyperplasia
(Benign Prostatic Hyperplasia)

• Extremely common disorder in men over age 50
• Hyperplasia of both glandular and stromal components.
• Large, fairly discrete nodules in the periurethral zone
Nomenclature

- BPH – Benign prostatic hypertrophy is a misnomer
- Hypertrophy is always non neoplastic
- Glands undergo hyperplasia not hypertrophy
- Hyperplasia of the prostate is a better term
Etiopathogenesis

- DHT – Dihydrotestosterone
- Autocrine or Paracrine action
- 10 times more potent action than testosterone
- DHT binds to nuclear androgen receptors and signals the transcription of growth factors mitogenic to the stromal and epithelial cells.
- Old age testosterone levels are low
Signs and Symptoms

• Symptoms relate to 2 secondary effects -
  - Compression of the urethra –
    - difficulty in urination (both starting and stopping).
    - frequency
    - dribbling
    - nocturia
    - dysuria (painful micturition)

• Only 10% are symptomatic
Signs and Symptoms

- Urine retention –
  - distension and hypertrophy of bladder,
  - UTIs (retrograde reflux of urine and stasis)
  - Cystitis and Renal infections.
- May be acute requiring catheterization.
Gross Features

- Enlarged prostate (60-100gms) with central zone (periurethral) nodules.
- Slit like urethra.
- Compressed normal tissue separates the nodules – not a true capsule.
Microscopic Features

• Glandular hyperplasia
  - small to large dilated glands with papillary infoldings lined by at least two layers.
Microscopic Features

• Stromal hyperplasia
  - predominates in many cases
  - fibromuscular proliferation
• Corpora amylacea
  - inspissated secretions in the lumen of the glands.
Treatment

- TURP – Transurethral resection
- 5 alpha reductase inhibitors
Prostatic carcinoma

- Most common cancer in men in USA
- 220,900 new cases detected in 2003 of approx. 29,000 lethal
- Incidence has increased 192% since 1973.
Prostatic carcinoma-Risk factors

- Age – incidence increases with age
  - 20% in men in their 50s to approx.
    70% in men b/n ages of 70-80 years.
- Race – More common in Americans (blacks > whites), uncommon in Asians.
  (1-3/100,000 as compared to 50- 60/100,000 among whites in USA.)
- Family history – increased risk
Prostatic carcinoma—Risk factors

• Hereditary form in approx. 9% of all cases and up to 40% of early onset disease.
• Hereditary prostate cancer gene 1 or HPC 1, linked in prostate cancer families to the RNASEL gene.
  - codes for enzyme known as RNase that destroys RNA and can potentially cause tumor cells to die.
Clinical Features

• Often asymptomatic – 50%
• Symptoms may include
  - hematuria
  - bone pain – usually back pain (metastasis)
  - weight loss
• Nodular hyperplasia -like
  - dysuria, weak or interrupted urine flow
Detection of Prostate carcinoma

- Diagnostic triad of
  - Digital rectal examination
  - Serum PSA levels
  - Transrectal ultrasonography.
Screening - DRE

- Practical and efficient method for detection of prostatic carcinoma.
- 70% of the tumors in the peripheral zone, hence easily palpable.
- As a screening test has a yield of < 2% and
- Predictive value ranging from 22-67%.
Transrectal Ultrasound

- Can detect carcinomas as small as 5 mm (appear as hypoechoic lesions)
- Can miss up to 30% of prostatic cancers that are isoechoic.
- Not an efficient tool for screening.
Prostate Specific Antigen

• 33 Kd serine protease
• Normally produced by prostatic glandular epithelium
• Functions in seminal liquefaction
• Secreted by all but most undifferentiated tumors – 75% of prostate cancers have elevated serum PSA levels
PSA - Screening

• PSA is organ specific but not cancer specific antigen.
• The higher the PSA level, the more likely the chance of prostate cancer.
• < 4ng/ml – normal ; >10ng/ml – high
  4-10 ng/ml - ?
PSA

• Serum PSA is elevated in several conditions
  - cancer
  - nodular hyperplasia
  - prostatitis
  - infarct
  - extensive exercise
  - cystoscopy
  - biopsy
PSA - Screening

- Refinements in estimation and interpretation of PSA values have been proposed –
  - PSA Density
  - PSA Velocity
  - Age specific reference range
  - Ratio of free and bound PSA in the serum
PSA Density (PSAd)

- Ratio of the serum PSA to the volume of prostate as determined by TRUS.
- Reflects the PSA produced per gram of prostatic tissue.
- A PSAd of >0.125% is associated with an 80% likelihood of detecting a cancer.
PSA Velocity

• The change in serum PSA over time
  - requires serial sampling
  - high degree of suspicion when the PSA increases more than 0.75ng/ml per year.
  - sensitivity = 72%
  - specificity = 95%
Gross Features

- 70% arise in peripheral zone-posteriorly.
- A firm often non discrete mass,
- Spread by direct extension, lymphatic and hematogenous routes.
Microscopic Features

- Adenocarcinoma
  - crowded small glands
  - scanty intervening stroma
  - single cell layer
Malignant features

• Invasion of
  - capsule
  - perineural
  - lymphatics
Gleason Grading

- 5 grades – glandular patterns and degrees of differentiation
- Grade 1 – well differentiated small glands
- Grade 5 – poorly differentiated sheets and nests
- Most tumors > one pattern
Gleason 1

- Well circumscribed adenocarcinoma
- Hyperplastic glands
Gleason 3

- Most common pattern
- Typically small Irregular glands, often angular
- Often infiltrate b/n adjacent non-neoplastic glands
Gleason 5

- Complete loss of glandular lumina
- Sheets and nests of cells
- Comedonecrosis may be present
Gleason score

- Select the two predominant patterns
- Grade each of them
- Add the 2 numeric figures = Gleason score
- If tumor – same pattern throughout – number is multiplied by 2 (e.g. 1x2=2)
- Gives idea about aggressiveness of tumor
- Patients with score
  - 2-4 – never develop aggressive disease
  - 8-10 – most die of prostatic carcinoma
Gleason score 7(3+4)
Staging

• Based on capsular invasion, nodal and distant metastasis
  - A – microscopic
  - B – palpable disease confined to prostate
  - C – extension outside of the prostate
  - D – distant metastasis
Treatment

• Localized Prostatic carcinoma
  - TURP
  - radical prostatectomy
  - radiation therapy external or internal

• Complications – impotence, incontinence, diarrhea, dysuria, frequency

• Metastatic – chemotherapy, hormonal Rx
Treatment

• Hormonal treatment - lowers androgens
  - orchiectomy
  - estrogen
  - LH-RH analogues suppresses LH-RH synthesis
  - total androgen blockade (flutamide) – inhibits androgen uptake and nuclear binding
Prognosis

• Overall 5 year survival – 92%
• 10 year survival – 67%
• 58% stage A/B – 5 year survival = 100%
• 31% stage C – 5 year survival = 94%
• 11% stage D – 5 year survival = 31%