Some prostatic diseases

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Benign Prostatic Hyperplasia (Nodular Hyperplasia)

• Extremely common

• Present in a significant number of men by the age of 40 & its frequency rises progressively with age, reaching 90% by the eighth decade of life

• Proliferation of both stromal and epithelial elements, with resultant enlargement of the gland and, in some cases, urinary obstruction

• Excessive androgen-dependent growth of stromal and glandular elements has a central role
Benign Prostatic Hyperplasia (Nodular Hyperplasia), pathogenesis

• Dihydrotestosterone (DHT), the ultimate mediator of prostatic growth, is synthesized in the prostate from circulating testosterone by the action of the enzyme 5α-reductase, type 2

• DHT binds to nuclear androgen receptors, which regulate the expression of genes that support the growth and survival of prostatic epithelium and stromal cells

• Although testosterone can also bind to androgen receptors and stimulate growth, DHT is 10 times more potent

• α1-Adrenergic receptor blockers relax prostatic smooth muscle cells and decrease urethral tone
Benign Prostatic Hyperplasia (Nodular Hyperplasia), morphology

• BPH virtually always occurs in the inner, transitional zone of the prostate

• Grossly:
  ...The affected prostate is enlarged, typically weighing between 60 and 100 g
  ...contains many well-circumscribed nodules that bulge from the cut surface

• Microscopically:
  ...the hyperplastic nodules are composed of variable proportions of proliferating glandular elements and fibromuscular stroma

*The hyperplastic glands are lined by tall, columnar epithelial cells and a peripheral layer of flattened basal cells
*The glandular lumina often contain inspissated, proteinaceous secretory material known as corpora amylacea
Benign Prostatic Hyperplasia (Nodular Hyperplasia), morphology...cont’d
Benign Prostatic Hyperplasia (Nodular Hyperplasia), clinical notes

- Clinical manifestations of prostatic hyperplasia occur in only about 10% of men with pathologic evidence of BPH.

- The most common manifestations are related to lower urinary tract obstruction, often in the form of difficulty in starting the stream of urine (hesitancy) and intermittent interruption of the urinary stream while voiding...frequently accompanied by urinary urgency, frequency, and nocturia.

- In some affected men, BPH leads to complete urinary obstruction, with resultant painful distention of the bladder and, in the absence of appropriate treatment, hydronephrosis.

- Treatment: mainly medical...blocking DHT formation or blocking alpha 1 receptors...may be surgical (transurethral resection of prostate (TURP)...etc.)
Carcinoma of the Prostate

...we are talking about adenocarcinoma mainly

...men older than 50 years

...the most common form of cancer in men...not as much common to cause death

...over the past several decades, there has been a significant drop in prostate cancer mortality

...prostate carcinoma commonly is found incidentally at autopsy in men dying of other causes

...many more men die with prostate cancer than of prostate cancer
Carcinoma of the Prostate, pathogenesis

• Androgens
  prostatic carcinoma doesn’t occur in castrated males and castration can be used as a treatment
  some tumors have mutations in androgen receptors so they are resistant to anti-androgen therapy
  while prostate cancer, like normal prostate, is dependent on androgens for its survival, there is no evidence that androgens initiate carcinogenesis

• Heredity
  blacks & Scandinavian countries more than Asians

• Environment

• Acquired somatic mutations...the actual drivers of cellular transformation
  TMPRSS2-ETS fusion genes are the most important (40-50%)
  other common ones: mutations that inactivate the tumor suppressor gene PTEN, which acts as a brake on PI3K activity
Carcinoma of the Prostate, morphology

- Most carcinomas detected clinically are not visible grossly.

- More advanced lesions appear as firm, gray-white lesions with ill-defined margins that infiltrate the adjacent gland.

- Histologically:
  - The glands typically are smaller than benign glands
  - Lined by a single uniform layer of cuboidal or low columnar epithelium
  - Lack the basal cell layer seen in benign
  - Crowded together
  - Lack branching and papillary infolding
  - Nuclei are enlarged and often contain one or more prominent nucleoli
  - In general, pleomorphism is not marked
  - Mitotic figures are uncommon

With increasing grade, irregular or ragged glandular structures, cribriform glands, sheets of cells, or infiltrating individual cells are present.

In approximately 80% of cases, prostatic tissue removed for carcinoma also harbors presumptive precursor lesions, referred to as high-grade prostatic intraepithelial neoplasia (HGPIN).
Carcinoma of the Prostate, morphology

Gleason score is used for grading
...from 1-5
...the grade of the most common pattern + the grade of the second common pattern
...if one pattern is present, the grade is doubled
Carcinoma of the Prostate, clinical features

• A minority of carcinomas are discovered unexpectedly during histologic examination of prostate tissue removed by transurethral resection for BPH

• 70% to 80% of prostate cancers arise in the outer (peripheral) glands and hence may be palpable as irregular hard nodules on digital rectal examination

• Most prostate cancers are small, nonpalpable, asymptomatic lesions discovered on needle biopsy performed to investigate an elevated serum prostate-specific antigen (PSA) level

• Prostate cancer is less likely than BPH to cause urethral obstruction in its initial stages

• Bone metastases, particularly to the axial skeleton, are frequent late in the disease

...typically cause osteoblastic (bone-producing) more than osteolytic
Carcinoma of the Prostate, clinical features

...PSA (Prostate specific antigen)

• a serine protease whose function is to cleave and liquefy the seminal coagulum formed after ejaculation

• The most important test...but:
  ...Although PSA screening can detect prostate cancers early in their course, many prostate cancers are slow-growing and clinically insignificant, requiring no treatment
  ...prostate cancer treatments often cause significant complications, particularly erectile dysfunction and incontinence
  ...can be elevated in BPH, prostatitis, prostatic infarcts, instrumentation of the prostate, and ejaculation
  ...
  20 to 40% of patients with organ-confined prostate cancer have a nonelevated PSA value
Carcinoma of the Prostate, clinical features...PSA (Prostate specific antigen), cont’d

• To better benefit from PSA:
  ...assessment of prostate size is needed (by U/S...etc.)
  ...PR examination
  ...assessment of elevation of PSA over time
  ...using different values as a reference according to age
  ...The percentage of free PSA (the ratio of free PSA to total PSA) is lower in men with prostate cancer than in men with benign prostatic diseases

• Once cancer is diagnosed, serial measurements of PSA are of great value in assessing the response to therapy
Carcinoma of the Prostate, treatment options

• Radical prostatectomy

• Radiotherapy

• Because many prostate cancers follow an indolent course, active surveillance (“watchful waiting”) is an appropriate approach for older men, patients with significant comorbidity, or even some younger men with low serum PSA values and small, low-grade cancers

• Advanced cases: surgical or chemical castration

• Antiandrogen may not be beneficial because androgen-independent clones eventually emerge, leading to rapid disease progression and death
Prostatitis

1- Acute bacterial prostatitis...same bacteria of UTI
2- Chronic bacterial prostatitis...same bacteria of UTI
3- Chronic nonbacterial prostatitis (chronic pelvic pain syndrome)
   90-95% of the cases...no uropathogen is identified
4- Asymptomatic inflammatory prostatitis

*Granulomatous prostatitis:
  -BCG
  -TB
  -Fungal
  -Nonspecific
  -After procedures
Prostatitis, clinical notes

- Acute bacterial prostatitis is associated with fever, chills, and dysuria; it may be complicated by sepsis.  
  ...on rectal examination, the prostate is exquisitely tender and boggy

- Chronic bacterial prostatitis...due to recurrent UTIs  
  ...low back pain, dysuria, and perineal and suprapubic discomfort  
  ...asymptomatic periods in between

- The diagnosis of chronic nonbacterial prostatitis (chronic pelvic pain syndrome) is difficult (PR, urinalysis, prostatic massage...etc.)  
  ...no proven therapy
Thank You