النادي الطبي

GENITOURINARY SYSTEM

SUBJECT : Pathology

LEC NO. : Summary lec 10 (male 3)

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وَقُل رَّبِّ زِدْنِي عِلْمًا

Prostate

Prostatitis

Prostatitis can manifest as either acute or chronic forms

Acute bacterial prostatitis typically arises from common UTI-causing bacteria like E. coli. Patients with acute prostatitis often have concurrent urethral and bladder infections, with bacteria reaching the prostate through direct extension or vascular channels.

Chronic prostatitis may develop after acute episodes or gradually without prior infection. It can be chronic bacterial prostatitis, characterized by increased white blood cells and bacteria in prostatic secretions similar to acute cases, or more commonly chronic abacterial prostatitis, featuring elevated white blood cells but negative bacteriologic findings.

Clinical features Prostatitis presents with dysuria, urinary frequency, lower back pain, and pelvic discomfort. On examination, the prostate may be enlarged and tender, especially in acute cases, often with fever and leukocytosis. **Chronic prostatitis** can lead to recurrent UTIs even without symptoms.

Morphology

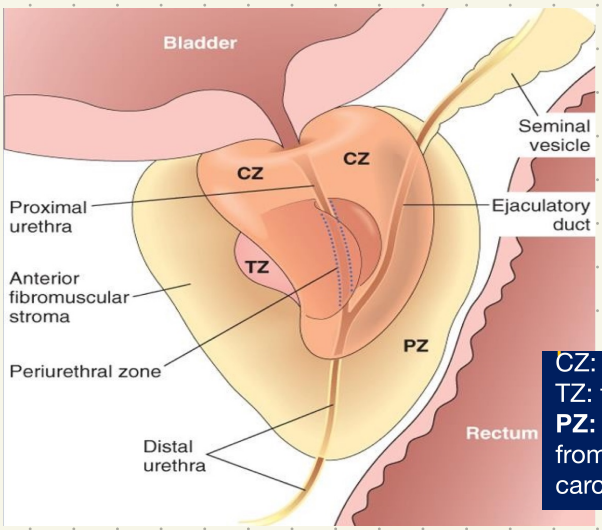
Acute prostatitis is characterized by congestion, edema, and a prominent neutrophilic inflammatory infiltrate, initially within the prostatic glands but later extending into the stroma, leading to microabscess formation. **Grossly** visible abscesses are rare but can occur with severe tissue damage, such as in diabetes mellitus.

Chronic prostatitis presents with nonspecific features including lymphoid infiltrates, glandular injury, fibroblastic proliferation, and often concurrent acute inflammatory changes.

Granulomatous prostatitis can be associated with systemic inflammatory conditions like tuberculosis, sarcoidosis, and fungal infections. Additionally, it may develop as a nonspecific response to thickened prostatic secretions or following transurethral resection (TUR) of prostatic tissue.

Nodular hyperplasia of the prostate

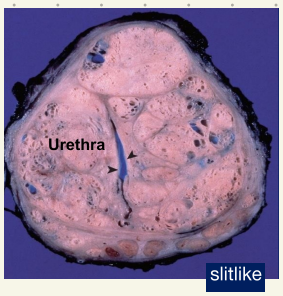
The prostate is comprised of glandular and stromal elements around the urethra, divided into periurethral, central, transitional, and peripheral zones. Carcinomas usually develop in the peripheral zones, while non-cancerous lesions arise in the central and inner transitional zones. Non-cancerous hyperplasia (NH) is common, especially with age reaching 90% by the eighth decade, leading to gland enlargement and potential urinary obstruction.

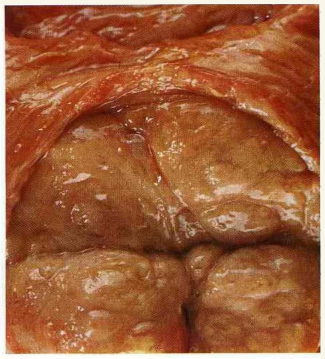


CZ: central: NH, TZ: transitional, **PZ: peripheral** from which most carcinomas arise

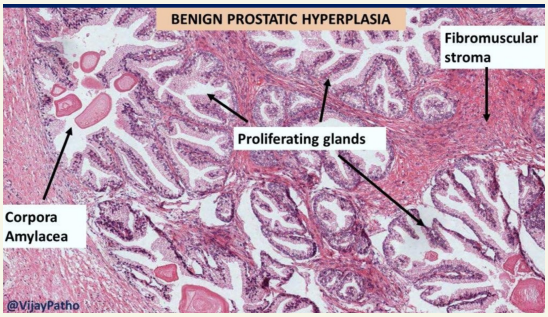
Pathogenesis: The development of NH is influenced by androgens, as evidenced by its absence in castrated males and those with androgen-blocking genetic conditions. Dihydrotestosterone (DHT), a derivative of testosterone, plays a crucial role in stimulating stromal and glandular proliferation. It binds to androgen receptors, prompting DNA, RNA, and protein synthesis, resulting in hyperplasia. This understanding supports the use of 5-alpha-reductase inhibitors in treating symptomatic NH.

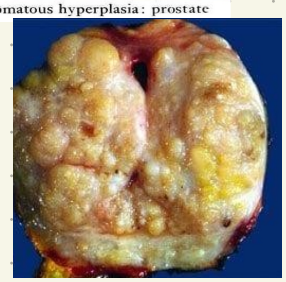
Morphology: NH predominantly affects the inner periurethral glands of the prostate, leading to significant enlargement, with sizes reaching over 300 grams in severe cases. Cross-section reveals multiple well-defined nodules protruding from the surface, especially in the inner region. These nodules may be solid or cystic, and they often compress the urethra, causing a slit-like orifice.



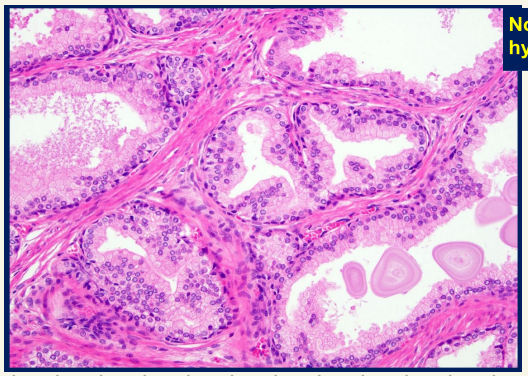

11.6 Adenomatous hyperplasia: prostate

Microscopically, the hyperplastic nodules consist of:
1. Hyperplastic glands with a dual-cell population: tall columnar epithelial cells forming papillary projections, and flattened basal cells at the periphery.
2. Glandular lumina often contain inspissated, proteinaceous secretory material known as corpora amylacea.
3. Proliferating stromal elements surrounding the hyperplastic glands.
4. Some nodules are primarily composed of spindle-shaped stromal cells and connective tissue.





Clinical manifestations of prostatic nodular hyperplasia (NH) affect around 10% of men with the condition. NH mainly affects the inner prostate, leading to symptoms of lower urinary tract obstruction, such as hesitancy and intermittent interruption of urine flow. Severe cases may cause complete urinary obstruction, resulting in painful bladder distention, bilateral hydronephrosis, and renal failure. Other symptoms include urinary urgency, frequency, nocturia, and an increased risk of urinary tract infections.



Prostatic Carcinoma

Prostate carcinoma (Pca) is the most common internal cancer in men, particularly in the Western world. It's the second leading cause (after lung cancer) of cancer-related death in men over 50. Latent Pca is even more prevalent than clinically apparent cases, especially in men over 80.

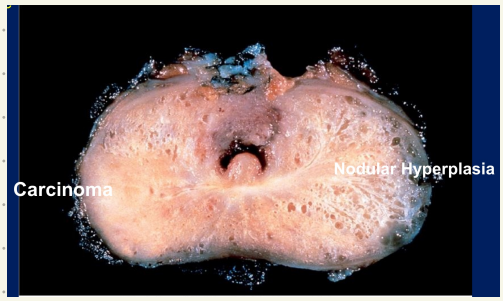
The cause of prostate carcinoma remains unknown, but clinical and experimental evidence indicates that hormones, genes, and environmental factors all play a role in its development.

Hormonal: The role of androgens in the development of prostate carcinoma is indicated by the fact that prostate cancer does not develop in males castrated before puberty and that the growth of many prostate cancers can be inhibited by orchiectomy or estrogen administration such as diethylstilbestrol.

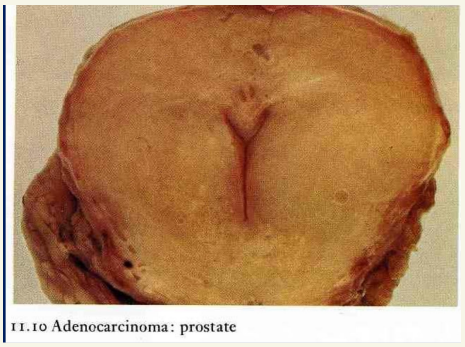
Hereditary: Prostate cancer risk is higher among first-degree relatives of affected individuals and in American blacks, occurring earlier than in other racial groups. Efforts to identify prostate cancer genes have not yielded definitive results, but overexpression of certain ETS family transcription factors and mutations in BRCA1 or BRCA2 genes have been implicated. Men with Lynch syndrome also have an increased risk of prostate cancer due to inherited gene changes.

Environmental influences: on prostate cancer include higher frequencies in certain industrial settings, geographic variations in incidence, and changes in risk with immigration. Males moving from low-risk to high-risk areas initially have lower risks, which increase over generations, indicating environmental factors. **Diets high in animal fat are also considered a risk factor**.

Prostate cancer diagnosis often relies on elevated levels of prostate-specific antigen (PSA) in plasma (above 4 ng/mL). However, since elevated PSA can also occur without cancer, tissue biopsy is necessary to confirm the presence of cancer.

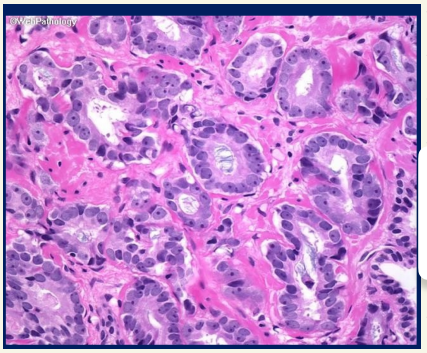


Grossly, 70% to 80% of prostate cancers originate in the peripheral zone, potentially detectable as irregular hard nodules on per-rectal examination. Due to this peripheral location, early prostate cancer is less likely to cause urethral obstruction compared to nodular hyperplasia.
Early prostate cancer typically presents as hard, ill-defined subcapsular masses on cross-section, appearing firm, gray-white to yellow, and infiltrating the adjacent gland.
Microscopically, most prostate cancers are adenocarcinomas, with well-differentiated forms characterized by small glands infiltrating adjacent stroma irregularly.


11.10 Adenocarcinoma: prostate

(1) absence of nodularity, & (2) yellow-orange color, with yellowish areas of necrosis.

Locally advanced prostate cancer often infiltrates the periurethral zones of the prostate, seminal vesicles, and may invade the bladder wall. Typically, Denonvilliers fascia prevents posterior growth towards the rectum, resulting in rare invasion. Metastasis to regional pelvic lymph nodes can occur early.



nuclear enlargement and hyperchromasia, prominent nucleoli, and intraluminal blue mucin.

In contrast to normal and hyperplastic prostate glands, in prostate cancer:
1. Glands appear to dissect sharply through the scant stroma due to a lack of basal cell layer.
2. Glands are lined by a single layer of cuboidal cells without basal cell layer presence.
3. Cell nuclei exhibit conspicuous nucleoli.
With increasing degrees of anaplasia, irregular and ragged glandular structures, papillary or cribriform epithelium, and, in extreme cases, sheets of poorly differentiated cells are present.

PIN (prostatic intraepithelial neoplasia) is considered a likely precursor to prostate cancer due to its frequent coexistence with invasive carcinoma. It is subdivided into high- and low-grade patterns based on the degree of atypia. High-grade PIN shares molecular changes with invasive prostate cancer, suggesting it serves as an intermediate between normal and malignant prostate tissue. Prostate cancer histologic grading commonly employs the Gleason system, which evaluates glandular architecture, differentiation, nuclear anaplasia, and mitotic activity on a scale of 1 to 5 degrees.

Prostate cancer is often **clinically** silent, especially in its early stages. About 10% of localized cases are discovered incidentally during histologic examination of prostate tissue removed for non-neoplastic hyperplasia. Autopsy studies suggest an incidence of around 30% in men aged 30 to 40 years. As most prostate cancers originate in the peripheral regions, they may be detected during routine digital rectal examination.

In advanced stages, prostate cancer can cause "prostatism," leading to local discomfort and evidence of lower urinary tract obstruction. Metastases, though uncommon, may manifest with bone involvement, particularly in the axial skeleton, presenting as osteolytic or more commonly osteoblastic lesions, which strongly suggest advanced disease in older males.

Differentiating between high-grade prostate adenocarcinoma (PAC) and high-grade urothelial carcinoma (UC) invading the prostate is vital for treatment decisions. Using markers like PSA, NKX3.1, p63, thrombomodulin, GATA3, and high molecular weight cytokeratin can help distinguish between the two cancers more accurately.

PSA's diagnostic value is significantly enhanced when used alongside other procedures like PR examination, transrectal sonography, and needle biopsy. While it has limitations as a diagnostic screening test, PSA concentration is invaluable for monitoring patients post-treatment for prostate cancer. Rising levels post-ablative therapy suggest recurrence or metastases.

Prostate-specific antigen (PSA) and prostate acid phosphatase (PAP) are valuable in confirming metastatic carcinoma of unknown origin as prostate-related. However, their effectiveness diminishes in poorly differentiated carcinomas. PSA, produced by normal and neoplastic prostatic epithelium, is commonly used to diagnose early prostate cancer, with a serum level of 4.0 ng/L considered the upper normal limit.

Here's the **table 18-3 TNM** staging of prostatic cancer:

- T1: Clinically Inapparent Lesion By Palpation/Imaging Studies.
  - T1a: Involvement of ≤5% of resected tissue.
  - T1b: Involvement of >5% of resected tissue.
  - T1c: Cancer present on needle biopsy (following elevated PSA).

- T2: Palpable Or Visible Cancer Confined To Prostate.
  - T2a: Involvement of ≤50% of one lobe.
  - T2b: Involvement of >50% of one lobe, but unilateral.
  - T2c: Involvement of both lobes.

- T3: Local Extraprostatic Extension.
  - T3a: Extracapsular extension.
  - T3b: Seminal vesical invasion.

- T4: Invasion of Contiguous Organs And/Or Supporting Structures Including Bladder Neck, Rectum, External Sphincter, Levator Muscles, Or Pelvic Floor.

Here's the status of regional lymph nodes and distant metastases for prostate cancer:

- **Status of Regional Lymph Nodes (N)**
- N0: No Regional LN Metastases
- N1: Metastasis In Regional LN
- **Distant Metastases (M)**
- M0: No Distant Metastases
- M1: Distant metastases present

Anatomic staging of prostate cancer, which includes clinical examination, surgical exploration, radiographic imaging techniques, along with the histologic grade of the tumor and levels of tumor markers, plays a crucial role in evaluation and treatment, and is strongly correlated with prognosis.

Prostate cancer is managed through a combination of surgery, radiation therapy, and hormonal treatments:

- Localized disease often undergoes surgery or radiation therapy.
- Hormonal therapy plays a crucial role in advanced cases, with options including surgical castration, pharmacologic castration, estrogens, and androgen receptor-blocking agents.
- Prognosis is generally favorable for patients with early-stage lesions (T1 or T2), with over 90% surviving 10 years or more. However, the outlook for those with disseminated disease is typically poor.