

**MECHANISMS OF HUMAN DISEASE: LABORATORY SESSION
PATHOLOGY OF THE UROGENITAL TRACT I**

**March 13, 2009
1:00 pm – 2:30pm**

Faculty Copy

GOAL:

1. Describe the basic morphologic and pathophysiologic changes in various diseases of the urogenital tract.
2. Describe and correlate symptoms and signs of a disease with the structural changes in diseased organs.

OBJECTIVES:

1. Describe the morphologic characteristics of malignant tumors of the testicle.
2. Describe the morphologic characteristics of benign prostatic hyperplasia.
3. Describe the morphologic characteristics of prostatic carcinoma.
4. Describe the morphologic characteristics of malignant tumors of the bladder.

CASE 1

HISTORY: A 32-year-old previously healthy man presents with a painless mass in his left testicle. He noticed it about 1 month ago. It was not getting smaller so he sought medical attention.

VITAL SIGNS: 135/80 HR 80 RR 15 T 98°

PHYSICAL EXAMINATION: Palpable, mobile 3 cm non-tender mass is present in the left testicle. Exam is otherwise unremarkable. There is no inguinal lymphadenopathy.

1. What is the main clinical problem?

Testicular mass

2. What is your clinical differential diagnosis?

Testicular tumors (benign/malignant), cyst, granulomatous orchitis, infections

LAB TESTS

Chest X-ray is normal

Serum AFP and HCG are normal

3. Identify organ/describe pathologic changes in the virtual microscopy slide.

Testis; sections of the testicle show a tumor composed of nests of neoplastic cells separated by connective tissue trabeculae containing scattered mononuclear inflammatory cells. The neoplastic cells are uniform, contain abundant clear cytoplasm and large vesicular nuclei with prominent nucleoli.

4. What is your diagnosis?

Seminoma.

Most common type of germ cell tumor; peaks in 30's.

A nearly identical tumor arises in the ovary where it is called dysgerminoma.

Classic seminoma cells do not contain AFP or HCG; the cells stain for placental alkaline phosphatase (PLAP).

15 % of seminomas contains syncytial giant cells which may contain HCG – this subtype may have elevated serum HCG.

Metastasis from seminomas generally involve lymph nodes; hematogenous spread generally occurs late in the disease. Non-seminomatous germ cell tumors metastasize earlier and more frequently hematogenously.

Seminomas are extremely radiosensitive, non-seminomatous germ cell tumors are relatively radioresistant.

HISTORY: 67-year-old male has nocturia, urinary hesitancy (difficulty in starting and stopping urine flow), “weak” urine stream, and dribbling at the end of urination.

PHYSICAL EXAMINATION: On digital rectal exam the prostate gland is enlarged and non-tender. There are no palpable masses.

1. What is the clinical problem?

Voiding problems, nocturia

2. What is your clinical differential diagnosis?

Benign prostatic hyperplasia (BPH), prostatic carcinoma, infection (prostatitis, cystitis)

LAB TESTS:

Prostate specific antigen (PSA) is within normal limits for a man this age.

3. Identify organ/describe pathologic changes in the virtual microscopy slide.

Prostate; sections show multiple nodules composed of hyperplastic glands in which the lining epithelium is thrown up into folds and papillary structures. Some glands are dilated. The glands are lined by two cell layers, an inner columnar and an outer cuboidal layer based on an intact basement membrane. The fibromuscular stroma is similarly hyperplastic.

4. What is your diagnosis?

Benign prostatic hyperplasia (nodular hyperplasia)

5. What complications may occur because of this problem?

**1) Compression of the urethra resulting in difficulty with urination (as in this patient).
2) Retention of urine in the bladder with subsequent distention and hypertrophy of the bladder, infection of the urine, cystitis, kidney infections. Secondary morphologic changes in bladder include hypertrophy, trabeculation, diverticulum formation; hydronephrosis or acute retention with azotemia or uremia may develop in severe cases.**

6. What hormone is related to this process?

Androgens, specifically DHT, a metabolite of testosterone, are the main mediators of prostatic growth. Circulating testosterone is converted to DHT by 5 α reductase, type 2 in the prostate gland. The enzyme is in the stromal cells and DHT can act in an autocrine fashion on the gland. Drugs which inhibit this reductase may be used in treating BPH.

CASE 3

HISTORY: A 72-year-old man presents with back pain. It is constant and exacerbated by movement. The pain often keeps him up at night.

PHYSICAL EXAMINATION: There is tenderness over the lower spine. Neurologic exam is normal. A single, hard prostatic nodule is palpated on digital rectal exam. No lymphadenopathy is noted.

1. What are the main clinical problems?

Back pain
Prostate nodule

2. What diagnostic test(s) are suggested?

RADIOGRAPHY:
Osteoblastic vertebral lesions are noted on x-rays of the spine.

LAB TESTS:
PSA 353.46 H (0.0 - 4.0 NG/ML)

3. Name organ/describe pathologic changes in the virtual microscopy slide.

Prostate; sections of prostate show an infiltrating, well-differentiated adenocarcinoma. The tumor occurs in the background of hyperplasia.

4. What is your diagnosis?

Prostatic adenocarcinoma

5. What is a Gleason grade? What is a Gleason score?

Gleason grade is grading system based on the histologic pattern of the prostatic adenocarcinoma, and is an important predictor of prognosis.

Gleason score (Gleason sum, combined Gleason grade) - the most prevalent morphologic pattern (primary) + the second most prevalent pattern (secondary pattern)

6. Which genetic changes may occur in this process?

10 % white American men have prostate cancer related to germline inheritance of prostate cancer susceptibility genes. In 1/3 of these familial cases, the gene has been mapped to chromosome 1q24-25. In addition, putative cancer-suppressor genes that are lost early in prostate carcinogenesis have been localized to chromosomes 8p, 10q, 12p and 16q.

7. Correlate the clinical and radiographic findings with the pathologic diagnosis.

The patient has prostate cancer which is metastatic to the spine. Osteoblastic bone lesions produce a sclerotic response; very characteristic of metastatic prostatic adenocarcinoma. Osteolytic bone metastases include breast, kidney, lung, and malignant melanoma. Most bone metastases do produce both lytic and blastic responses.

CASE 4

HISTORY: 62-year-old man presents with hematuria. He has no difficulty in voiding and no flank or back pain. He has a history of smoking.

PHYSICAL EXAMINATION: Unremarkable.

LAB TESTS: Urinalysis 4+ blood, protein, 50-100 red blood cells/high power field

1. What is the main clinical problem?

Gross Hematuria

2. What is the clinical differential diagnosis?

Urothelial carcinoma, urinary tract infection, nephrolithiasis, trauma, prostatitis, TB, glomerulopathies/kidney dz

3. Describe/identify organ in the virtual microscopy slide.

Bladder; sections show a papillary structures composed of a fibrovascular core covered by a transitional cell epithelium with an increased number of cell layers and loss of polarity, indicative of urothelial carcinoma. The neoplasm invades the subepithelial stroma but does not appear to invade the muscle.

4. What is your diagnosis?

Urothelial carcinoma

5. What are epidemiologic predisposing factors to this process?

Cigarette smoking is the most important influence, increasing the risk threefold to sevenfold; Industrial exposure to arylamines, schistosoma haematobium infections, long-term use of analgesics, cyclophosphamide;

Genetic factors – molecular and cytogenetic alterations are heterogeneous – chromosome 9 monosomy or deletions of 9p and 9q are most common. 9p21 deletions involve the tumor suppressor gene p16 (MTS1, INK4a)