Male Genital System Pathology

14

PENIS

I. HYPOSPADIAS

A. Opening of urethra on inferior surface of penis
B. Due to failure of the urethral folds to close

II. EPISPADIAS

A. Opening of urethra on superior surface of penis
B. Due to abnormal positioning of the genital tubercle
C. Associated with bladder exstrophy

III. CONDYLOMA ACUMINATUM

A. Benign warty growth on genital skin
B. Due to HPV type 6 or 11; characterized by koilocytic change (Fig. 14.1)

IV. LYMPHOGRANULOMA VENEREUM

A. Necrotizing granulomatous inflammation of the inguinal lymphatics and lymph nodes
B. Sexually transmitted disease caused by ***Chlamydia trachomatis*** (serotypes L1-L3)
C. Eventually heals with fibrosis; perianal involvement may result in rectal stricture.

V. SQUAMOUS CELL CARCINOMA

A. Malignant proliferation of squamous cells of penile skin
B. Risk factors
   1. High risk HPV (2/3 of cases)
   2. Lack of circumcision - Foreskin acts as a nidus for inflammation and irritation if not properly maintained.
C. Precursor in situ lesions
   1. Bowen disease - in situ carcinoma of the penile shaft or scrotum that presents as leukoplakia
   2. Erythroplasia of Queyrat - in situ carcinoma on the glans that presents as erythroplakia
   3. Bowenoid papulosis - in situ carcinoma that presents as multiple reddish papules
      i. Seen in younger patients (40s) relative to Bowen disease and erythroplasia of Queyrat
      ii. Does not progress to invasive carcinoma

TESTICLE

I. CRYPTORCHIDISM

A. Failure of testicle to descend into the scrotal sac
   1. Testicles normally develop in the abdomen and then "descend" into the scrotal sac as the fetus grows.
B. Most common congenital male reproductive abnormality; seen in 1% of male infants

C. Most cases resolve spontaneously; otherwise, orchiopexy is performed before 2 years of age.

D. Complications include testicular atrophy with infertility and increased risk for seminoma.

II. ORCHITIS

A. Inflammation of the testicle

B. Causes

1. *Chlamydia trachomatis* (serotypes D-K) or *Neisseria gonorrhoeae* - Seen in young adults. Increased risk of sterility, but libido is not affected because Leydig cells are spared.
2. *Escherichia coli* and *Pseudomonas* - Seen in older adults; urinary tract infection pathogens spread into the reproductive tract.
3. Mumps virus (teenage males) - increased risk for infertility; testicular inflammation is usually not seen in children < 10 years old.
4. Autoimmune orchitis - characterized by granulomas involving the seminiferous tubules

III. TESTICULAR TORSION

A. Twisting of the spermatic cord; thin-walled veins become obstructed leading to congestion and hemorrhagic infarction (Fig. **14.2**).

B. Usually due to congenital failure of testes to attach to the inner lining of the scrotum (via the processus vaginalis)

C. Presents in adolescents with sudden testicular pain and absent cremasteric reflex

IV. VARICOCELE

A. Dilation of the spermatic vein due to impaired drainage

B. Presents as scrotal swelling with a "bag of worms" appearance

C. Usually left sided; left testicular vein drains into the left renal vein, while the right testicular vein drains directly into the IVC.

1. Associated with left-sided renal cell carcinoma; RCC often invades the renal vein.

D. Seen in a large percentage of infertile males

V. HYDROCELE

A. Fluid collection within the tunica vaginalis

1. Tunica vaginalis is a serous membrane that covers the testicle as well as the internal surface of the scrotum.

B. Associated with incomplete closure of the processus vaginalis leading to communication with the peritoneal cavity (infants) or blockage of lymphatic drainage (adults)

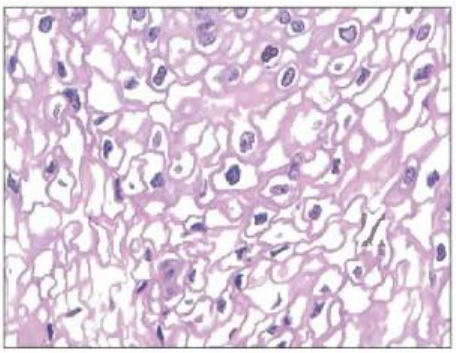

Fig. 14.1 Koilocytic change.

Fig. 14.2 Hemorrhagic infarction of testicle. (Courtesy of humpath.com)

Fig. 14.3 Hydrocele.

C. Presents as scrotal swelling that can be transilluminated (Fig. 14.3)

TESTICULAR TUMORS

I. BASIC PRINCIPLES

A. Arise from germ cells or sex cord-stroma
B. Present as a firm, painless testicular mass that cannot be transilluminated
C. Usually not biopsied due to risk of seeding the scrotum; removed via radical orchiectomy
   1. Most testicular tumors are malignant germ cell tumors.

II. GERM CELL TUMORS

A. Most common type of testicular tumor (> 95% of cases)
B. Usually occur between 15-40 years of age
C. Risk factors include cryptorchidism and Klinefelter syndrome.
D. Divided into seminoma and nonseminoma
   1. Seminomas (55% of cases) are highly responsive to radiotherapy, metastasize late, and have an excellent prognosis.
   2. Nonseminomas (45% of cases) show variable response to treatment and often metastasize early.
E. Seminoma is a malignant tumor comprised of large cells with clear cytoplasm and central nuclei (resemble spermatogonia, Fig. 14.4A); forms a homogeneous mass with no hemorrhage or necrosis (Fig. 14.4B)
   1. Most common testicular tumor; resembles ovarian dysgerminoma
   2. Rare cases may produce β- hCG.
   3. Good prognosis; responds to radiotherapy
F. Embryonal carcinoma is a malignant tumor comprised of immature, primitive cells that may produce glands (Fig. 14.5A); forms a hemorrhagic mass with necrosis (Fig. 14.SB)
   1. Aggressive with early hematogenous spread
   2. Chemotherapy may result in differentiation into another type of germ cell tumor (e.g., teratoma).
   3. Increased AFP or β- hCG may be present.
G. Yolk sac (endodermal sinus) tumor is a malignant tumor that resembles yolk sac elements.
   1. Most common testicular tumor in children
   2. Schiller-Duval bodies (glomerulus-like structures) are seen on histology (Fig. 14.6).
   3. AFP is characteristically elevated.

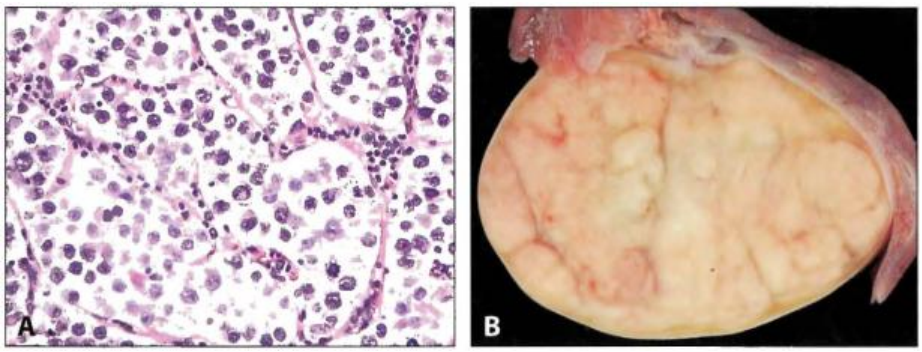

Fig. 14.4 Seminoma. **A,** Microscopic appearance. **B,** Gross appearance. (A, Courtesy of Ed Uthman, MD)

H. Choriocarcinoma is a malignant tumor of syncytiotrophoblasts and cytotrophoblasts (placenta-like tissue, but villi are absent, Fig. 14.7).
   1. Spreads early via blood
   2. β-hCG is characteristically elevated; may lead to hyperthyroidism or gynecomastia (α-subunit of hCG is similar to that of FSH, LH, and TSH)

I. Teratoma is a tumor composed of mature fetal tissue derived from two or three embryonic layers.
   1. Malignant in males (as opposed to females)
   2. AFP or β-hCG may be increased.

J. Mixed germ cell tumors
   1. Germ cell tumors are usually mixed.
   2. Prognosis is based on the worst component.

III. SEX CORD-STROMAL TUMORS

A. Tumors that resemble sex cord-stromal tissues of the testicle (Fig. 14.8); usually benign

B. Leydig cell tumor usually produces androgen, causing precocious puberty in children or gynecomastia in adults.
   1. Characteristic Reinke crystals may be seen on histology.

C. Sertoli cell tumor is comprised of tubules and is usually clinically silent.

IV. LYMPHOMA

A. Most common cause of a testicular mass in males > 60 years old; often bilateral

B. Usually of diffuse large B-cell type

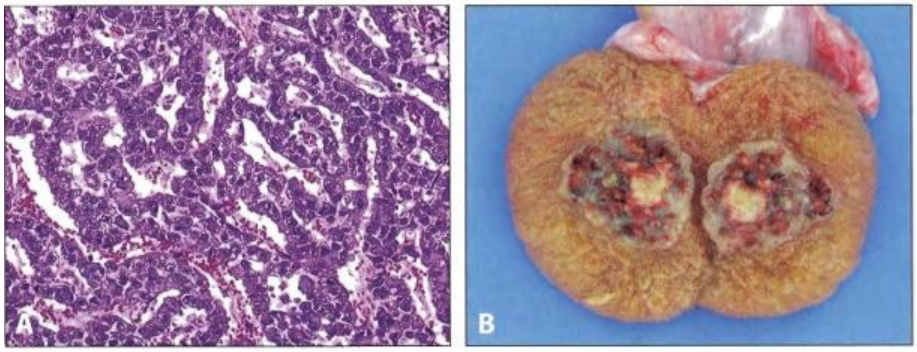

Fig. 14.5 Embryonal carcinoma. **A,** Microscopic appearance. **B,** Gross appearance. (Courtesy of webpathology.com)

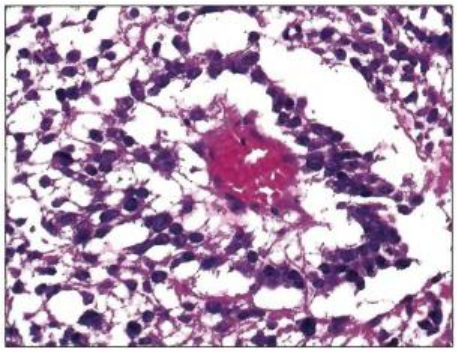

Fig. 14.6 Schiller-Duval body, yolk sac tumor. (Courtesy of webpathology.com)

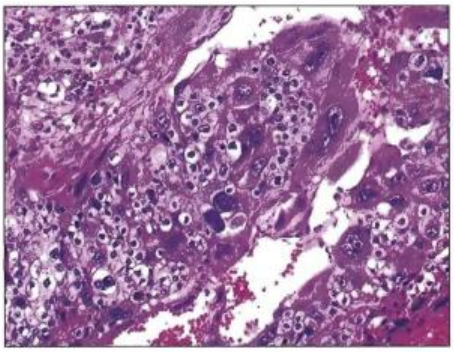

Fig. 14.7 Choriocarcinoma. (Courtesy of webpathology.com)

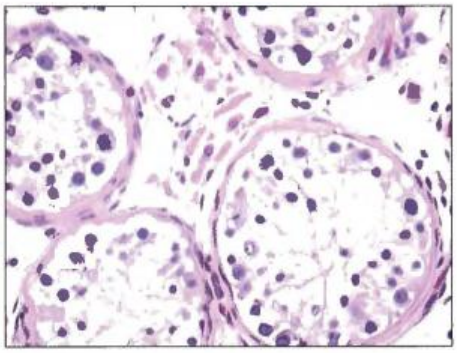

Fig. 14.8 Normal testicle, microscopic appearance.

PROSTATE

I. BASIC PRINCIPLES

A. Small, round organ that lies at the base of the bladder encircling the urethra
B. Sits anterior to the rectum; posterior aspect of prostate is palpable by digital rectal exam (DRE).
C. Consists of glands and stroma (Fig. 14.9)
   1. Glands are composed of an inner layer of luminal cells and an outer layer of basal cells; secrete alkaline, milky fluid that is added to sperm and seminal vesicle fluid to make semen.
   2. Glands and stroma are maintained by androgens.

II. ACUTE PROSTATITIS

A. Acute inflammation of the prostate; usually due to bacteria
   1. *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are common causes in young adults.
   2. *Escherichia coli* and *Pseudomonas* are common causes in older adults.
B. Presents as dysuria with fever and chills
C. Prostate is tender and boggy on digital rectal exam.
D. Prostatic secretions show WBCs; culture reveals bacteria.

III. CHRONIC PROSTATITIS

A. Chronic inflammation of prostate
B. Presents as dysuria with pelvic or low back pain
C. Prostatic secretions show WBCs, but cultures are negative.

IV. BENIGN PROSTATIC HYPERPLASIA (BPH)

A. Hyperplasia of prostatic stroma and glands
B. Age-related change (present in most men by the age of 60 years); no increased risk for cancer
C. Related to dihydrotestosterone (DHT)
   1. Testosterone is converted to DHT by 5α-reductase in stromal cells.
   2. DHT acts on the androgen receptor of stromal and epithelial cells resulting in hyperplastic nodules.
D. Occurs in the central periurethral zone of the prostate
E. Clinical features include
   1. Problems starting and stopping urine stream
   2. Impaired bladder emptying with increased risk for infection and hydronephrosis (Fig. 14.10)
   3. Dribbling

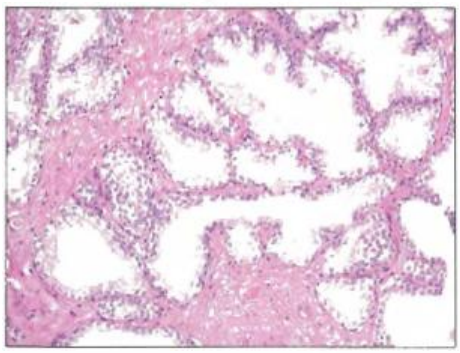

Fig. 14.9 Normal prostate, microscopic appearance.

Fig, 14.10 Hydronephrosis.

4. Hypertrophy of bladder wall smooth muscle; increased risk for bladder diverticula
5. Microscopic hematuria may be present.
6. Prostate-specific antigen (PSA) is often slightly elevated (usually less than 10 ng/mL) due to the increased number of glands; PSA is made by prostatic glands and liquefies semen.

F. Treatment
1. α_1-antagonist (e.g., terazosin) to relax smooth muscle
   i. Also relaxes vascular smooth muscle lowering blood pressure
   ii. Selective α_{1A}-antagonists (e.g., tamsulosin) are used in normotensive individuals to avoid α_{1B} effects on blood vessels.
2. 5α-reductase inhibitor
   i. Blocks conversion of testosterone to DHT
   ii. Takes months to produce results
   iii. Also useful for male pattern baldness
   iv. Side effects are gynecomastia and sexual dysfunction.

V. PROSTATE ADENOCARCINOMA

A. Malignant proliferation of prostatic glands
B. Most common cancer in men; 2nd most common cause of cancer-related death
C. Risk factors include age, race (African Americans > Caucasians > Asians), and diet high in saturated fats.
D. Prostatic carcinoma is most often clinically silent.
1. Usually arises in the peripheral, posterior region of the prostate and, hence, does not produce urinary symptoms early on (Fig. 14.11A)
2. Screening begins at the age of 50 years with DRE and PSA.
   i. Normal serum PSA increases with age due to BPH (2.5 ng/mL for ages 40-49 years vs. 7.5 ng/mL for ages 70-79 years)
   ii. PSA > 10 ng/mL is highly worrisome at any age.
   iii. Decreased % free-PSA is suggestive of cancer (cancer makes bound PSA).

E. Prostatic biopsy is required to confirm the presence of carcinoma.
1. Shows small, invasive glands with prominent nucleoli (Fig. 14.11B)
2. Gleason grading system is based on architecture alone (and not nuclear atypia).
   i. Multiple regions of the tumor are assessed because architecture varies from area to area.
   ii. A score (1-5) is assigned for two distinct areas and then added to produce a final score (2-10).
   iii. Higher score suggests worse prognosis.

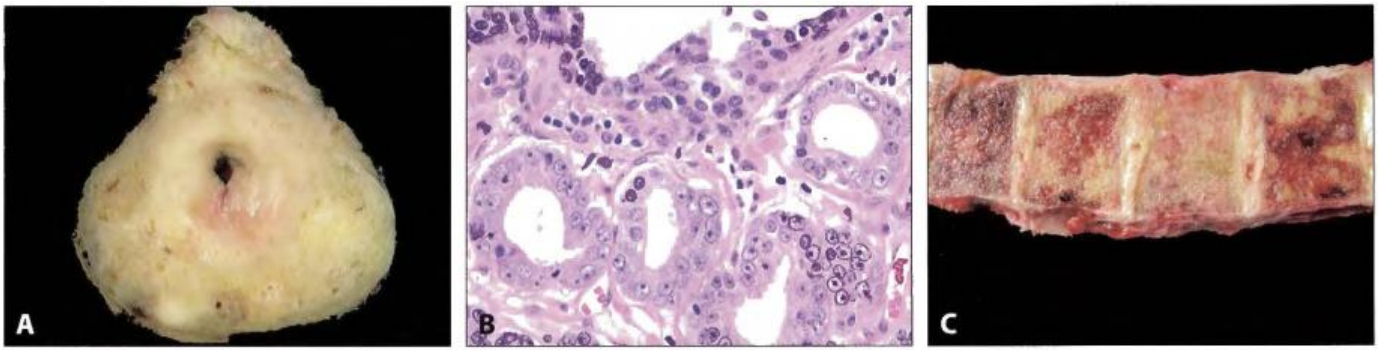

Fig. 14.11 Prostatic adenocarcinoma. **A,** Gross appearance. **B,** Microscopic appearance. **C,** Osteoblastic metastasis involving lumbar spine.

F. Spread to lumbar spine or pelvis is common (Fig. 14.11C); results in osteoblastic metastases that present as low back pain and increased serum alkaline phosphatase, PSA, and prostatic acid phosphatase (PAP)

G. Prostatectomy is performed for localized disease; advanced disease is treated with hormone suppression to reduce testosterone and DHT.

1. Continuous GnRH analogs (e.g., leuprolide) shut down the anterior pituitary gonadotrophs (LH and FSH are reduced).
2. Flutamide acts as a competitive inhibitor at the androgen receptor.