Pathology of the Male Reproductive System

Pathology of the Penis

Congenital Abnormalities

- Hypospadius
  - Urethral opening on ventral surface of penis.
- Epispadius
  - Urethral opening on dorsal surface of penis.
- Both associated with undescended testis

Circumcision, Yes or No

- Maybe helpful in a small number.
- In previous years it did make a difference.
- Phimosis
  - Orifice of the prepuce is too small.
  - Paraphimosis, inflammation and constriction leads to urinary problems.
- ? Risk of cancer

Urethral Cancer
Penile Tumors

- Papillomas
- HPV
  - Some are dangerous serotypes.
  - Cause unregulated epithelial growth

Cancer

- Squamous cell
- HPV 16
- In situ
  - Bowen’s Disease
  - Erythroplasia of Queyrat
  - Bowenoid Papulosis

Squamous Carcinoma

- Invasive
  - Ulcerative
  - HPV
    - 16
    - 18
  - Regional lymph nodes.
  - Metastasizes widely.

Invasive Squamous Cell
Testis and Epididymis

Problems of Migration

Cryptorchid
Cryptorchid

- Increased incidence of tumors
  - Expected rate with no testicular issue is 6/100,000 males
  - 5 to 10X increase
  - Even in the descended testis
  - Still, much less common than hernias (20%)

Testicular Atrophy

- Atherosclerosis
- Inflammation
- Cryptorchid
- Hypopituitarism
- High levels of FSH
  - Exhaustion atrophy
- Malnutrition

Problems Associated with Undescended Testis

Epididymitis

Cryptorchid
Epididmitis

Vascular Related
- Torsion
- Venous compression
- Hemorrhagic infarct
- Young men
- At night
- Very painful
- Can be reduced

Scrotal Masses
- Testicular
  - Tumors (solid)
- Epididymal
  - Inflammatory (rubor, dolor, calor...)
- Peritesticular
  - Hernia
  - Hydrocele (cystic, transilluminates)
  - Vascular in nature

Solid vs. Cystic
Testicular Tumors

- Most are malignant
  - Excellent results with treatment.
  - Must look for ‘markers’ before removal
- Germ line (actual reproductive cells)
  - Seminoma
  - Embryonal
  - Choriocarcinoma
  - Mixed pattern
- Non-germ line
  - Specialized supportive cells
    - Leydig, may be hormonally active

Tumor Markers

- Some tumors produce agents measurable in the blood.
  - Embryonic tissue markers
  - Beta-HCG
    - Placental marker
    - We measure this in pregnancy tests
  - Alpha-feto protein
    - Marker associated with embryonic gut

Seminoma

- Most common type
- Yong men
- Curable
- Arises from sperm producing cells
- Several histologic types.
- Lymphocytes
- No markers

Cell of Origin

- Clonal transformation of something in an embryonic rest
  - One cell goes to the dark side
  - Some differentiation or maturation
  - Maintains appearance

Seminoma

- Little fried egg looking cells.
- Lymphocytes
- No production of Bet-HCG or Alpha-fetoprotein
- Spermatocytic seminoma is different
  - Older mean and is a true mutation of existing cells
Embryonal Carcinoma

- Aggressive tumor
- 20-30 years
- Areas of hemorrhage and necrosis
- Two histologically distinct cell types.
- Markers +/-
- Lance Armstrong

Choriocarcinoma

- Placental elements
  - Syncytiotrophoblasts
  - Make Beta-HCG
- Typically part of a ‘mixed lineage’ tumor.
- Highly aggressive
- This element spreads early.

Embryonal Ca

- Two tissue types
  - Stroma
  - Glands
- Metastasizes widely
- Markers +/-

Trophoblasts

- Testicular Teratoma
Ovarian Teratoma

- Aggressively malignant
- Three germ lines
  - Ectoderm
  - Endoderm
  - Mesoderm
- Makers +/–

Teratoma

- Aggressively malignant
- Three germ lines
  - Ectoderm
  - Endoderm
  - Mesoderm
- Makers +/–

Leydig Cell Tumor

- One of several so-called ‘specialized stromal tumors.’
- Non-germ line
- Benign generally
- Hormonally active
  - Androgens
  - Estrogens
  - Gynecomastia
  - Sometimes even corticosteroids

Leydig Cell Tumors and Hormone Production

Hydrocele
Hydrocele

- Fluid filled scrotal cyst.
- Benign
- Often with inguinal hernia
- Transilluminates
- Fluid will recollect if aspirated.
- Can be large

Prostatic Disease

Prostatitis

- Acute bacterial
  - Ascending
  - E. coli
- Chronic bacterial
  - Low back pain
  - Dysuria
  - Suprapubic pain
  - Common bugs
  - ‘Abacterial’
  - Chlamydia

Benign Prostatic Hyperplasia

- Very common
- Androgen mediated growth (DHT).
- Transitional zone proliferates
  - Stroma 
  - Glands
- Minimal if any increased cancer risk
BPH

- Nodular growth pattern
- Some chronic inflammation
- Glands always have a double layer of epithelium
  - Columnar & Reserve layer

Benign Prostatic Hyperplasia

Prostate Cancer

- Incidence
  - Blacks & Whites
  - Rare in Asians
- Incidence increases with age.
- Peripheral zone
- PSA
- Family history

Prostate Cancer

- Adenocarcinoma
- Single layer of epithelium
- Gland-within-gland
- LN and Bone mets
  - Osteoblastic & Osteolytic
- Treatment
  - Surgery & Hormone manipulation
Distant Mets, Where’s Home?

- Spinal mets ->
- Painful
- May cause lots of reactive bone growth at the site of the met
  - Osteoblastic
  - May cause bone destruction
  - Osteolytic

Osteoblastic (Bone Forming)

Osteolytic (Bone destroying)
Prostate Cancer Can Be
- Either or Both
- Osteolytic or
- Osteoblastic

Sexually Transmitted Diseases
- HPV
- Hepatitis B
- Gonorrhea
- Syphilis
- HIV
- Chlamydia

Age and Demography
- All ages
- All diseases
- HIV in over 45 has risen 94% in past 10 years.
- 20% of over 65 are sexually active.
  - Divorced
  - Widowed
- Child abuse

Old Folks
- All we think of is college-age folks and adolescents.
- Many middle-age and even older folks too.
- Divorced or widowed and pregnancy is not an issue.
  - No condom use.

Viagra
- Developed to lower blood pressure.
  - Vascular dilation
- Reports during clinical trials of penile erections.
  - Dilates vessels into the penis
- Old folks are back in the game.

Meet markets
Gonorrhea

- Neisseria gonorrhoea
  - Gram negative
  - Diplococcus
  - Mucosa
  - Acute inflammation!
  - Scarring
  - Sterility
  - Epididymitis

Neisseria gonorrhoea

Syphilis

- Spirochete
  - Treponema pallidum
  - Arteriole is target
  - Vasculitis
  - Three stages
    - Primary: chancre
    - Secondary: rash
    - Tertiary: systemic
      - CNS
      - Aorta
    - Congenital

Treponema pallidum

- Spirochete
- Infects arterioles
  - Destroys them
  - Rash
  - Vasovasorum of aorta
  - Can’t culture
  - Serology
    - VDRL
    - Specific antibodies

Secondary Syphilis

Tertiary Syphilis
Congenital Syphilis

- Infected during pregnancy
- Third trimester
- Virtually all systems involved
- Periosteal involvement leads to many skeletal deformities

AIDS

- Human immunodeficiency virus
- Several strains
- T-cells infected
- Antibody regulation
- Tumor and cell mediated response

HIV

- Diminished cytoplasmic ability to undergo mitosis
- Reduced T-helper activity
- Reduced Ig production in response to viral antigens

79 YO Woman with hematuria

- Dilated right ureter
- Left shifted diff
- Hematuria
Case 1 Questions

1. What clinical feature is least typical of this patient’s bladder tumor?
   A. Dilated right ureter
   B. Suprapubic fistula
   C. Hematocrit of 39%
   D. Recurrent hematuria
   E. Large suprapubic mass

Case 1 Questions

- Based on the data presented, the immediate cause of death was most likely?
  A. Sepsis
  B. Metastasis to lung
  C. Heart failure
  D. Uremia
  E. Metastasis to liver

Case 1 Questions

A biopsy of the suprapubic fistula would probably NOT have shown what?
   A. Malignant cells
   B. PMN infiltrate
   C. Bacteria
   D. Healthy bladder tissue
   E. All of the above would have been seen in biopsy

Papillary Transitional Cell Ca

72 YO Man with CHF

- Intractable CHF
- Low back pain
- Confused
- Nodular prostate
- High creatinine
- Calcium
- Alk Phos
- PSA
Case 2 Questions

What is least likely to be the etiology of this patient’s pain?
A. Metastatic prostate cancer
B. Aortic aneurysm
C. Herpes zoster infection
D. Osteoarthritis
E. All of the above are possible.

Case 2 Questions

What would be responsible for the elevated alkaline phosphatase and acid phosphatase, respectively?
A. Mets to prostate tissue, mets to bone
B. Mets to liver, mets to bone
C. Mets to bone, mets to prostate tissue
D. Mets to bone, mets to prostate tissue
E. Mets to bone, mets to liver

Case 2 Questions

What is least likely to be a contributing factor to this patient’s confusion?
A. Hypoxia
B. Hemoglobin 11.5
C. Elevated BUN
D. Elevated calcium
E. Age/time spent in hospital

Case 2 Questions

The hepatomegaly may be attributed to what?
A. CHF
B. Mets to liver
C. Thrombosis
D. Liver is normal, only appears enlarged due to cachexia
E. Infection

Case 2 Questions

What histological pattern would you expect to see with this tumor, and what stage does this man’s case represent?
A. Glomerular hypercellularity; stage IV D2
B. Tissue appearing similar to adrenal cortical tissue; stage III
C. Stromal, abortive glomeruli; stage IV D2
D. Single epithelial layer, gland within gland; stage IV D2
E. Glandular and “alveolar” arrangements; stage III
Prostatic Intraepithelial Neoplasia

Hyperplasia or Cancer

Bone Metastases
- Spinal mets -> Painful
- May cause lots of reactive bone growth at the site of the met
  - Osteoblastic
  - May cause bone destruction
  - Osteolytic

Bone Mets

Osteoblastic (Bone Forming)

PSA
PSA

- Age dependent
- Size of gland
- Cancer
- Free or bound
  - Alpha1-antichymotrypsin
    - Free
    - Lower with cancer
    - >25% = low risk of ca

12 YO with Swollen Face

- Incr BP
- RBC casts
- Azotemic

Case 3 Questions

What is the MOST LIKELY cause of this boy’s disease?

A. Juvenile polycystic disease
B. Medullary cystic disease complex (nephronophthisis)
C. Poststreptococcal glomerulonephritis
D. Membranoproliferative glomerulonephritis
E. Membranous glomerulonephritis

Case 3 Questions

The lymphadenopathy reported in this patient’s history is MOST LIKELY do to what?

A. Strep infection
B. Heymann antigen
C. Goodpasture antigen
D. GC infection
E. Mumps infection

Case 3 Questions

Which of the following is the most probable long term outlook for this patient?

A. Sterile, but otherwise healthy
B. Good, complete recovery
C. Chronic decreased renal function from now on
D. Likely complete renal failure before puberty
E. Probable early death

Case 3 Questions

Which laboratory tests would be least helpful (or no help at all) in confirming your suspicions?

A. ASO titer
B. C3 levels
C. IgG/C3 complex levels
D. All would be helpful
E. All would NOT be helpful
RBC Casts

Strep Infections
- Throat
- Skin
  - Toxic changes
  - Direct infection

50 YO Woman with Weight Gain
- How sudden?
- Proteinuria
- Cholesterol = 450
- Serum Alb = 2.1
- Creatinine = 1.3
- Obviously can't be kidney

Case 4 Questions
What best explains the pronounced proteinuria without hematuria?
A. Nephritic syndrome
B. Nephrotic syndrome
C. UTI
D. Pyelonephritis
E. Patient’s recent switch to the Adkin’s diet
Case 4 Questions

Swelling of the legs is most probably due to what?
A. CHF
B. Salt retention
C. Decrease in albumin
D. Patient being on her feet all day
E. Patient’s low activity level

Case 4 Questions

What is NOT a condition in which we see this symptom complex?
A. SLE
B. DM
C. Hep B
D. Tuberculosis
E. RPGN

Case 4 Questions

What laboratory tests would you NOT do to help determine the diagnosis?
A. Hepatitis panel
B. Hgb A1C
C. PPD
D. HIV viral load
E. Renal biopsy

Nephrotic Syndrome

- Differential
  - SLE
  - DM
  - Hep B
  - Tumors
  - TB
  - ...
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HIV

- Decreased response to double antigens
- Decreased symptomatic severity
- Diminished cytotoxic ability
- Memory impairment
- Reduced T-1 invasion
- Poor antigen presentation

Decreased Ig production in response to virus antigens

HIV

- Primary infection
  - Acute-HIV syndrome
    - Wide dissemination of virus
    - Seeding of lymphoid organs
    - Clinical latency

- Opportunistic diseases
- Constitutional symptoms
- Death