Cancer in Men

Bladder Cancer (because we had to put it in somewhere!), Prostate Cancer, Testicular Cancer

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Bladder Cancer

- Most frequent uroepithelial tumor
- About 48,000 cases per year and 10,000 deaths
- Male:Female ratio = 2:1
- Most occur in patients between 50 and 80 years of age
Introduction

- Most common focus is on the posterior and lateral walls.
- **Field cancerization** — the entire bladder is susceptible to toxin exposure and second primaries are frequent.
- Risk of bladder cancer is 2-3 times as high in urbanites.
Carcinogens and Bladder Cancer

- Increased incidence in smokers — most important risk factor in westernized countries; secondhand smoke implicated in women with bladder cancer as well

- Workers in rubber, leather, chemical materials, painters, textile workers, metal workers, and laboratory industries are at increased risk

- *Schistosoma hematobium* — causes squamous carcinomas of the bladder
Pathology of Bladder Cancers

- Transitional cell carcinomas account for 90-95% of all bladder cancers diagnosed in North America.
- Squamous carcinomas and adenocarcinomas account for the bulk of the remainder.
- Leiomyosarcoma is rare, but does occur.
- Current thinking is that all carcinomas begin *in situ* and progress to either papillary or sessile tumors if untreated.
Clinical Presentation

- Hematuria (often painless) is the presenting symptom in 70% of patients with bladder cancer.

- Bladder irritability occurs in 25% of patients.

- At the time they are diagnosed 70% are confined to the bladder and only 7% have clinical evidence of metastases.

- Urinary obstructive symptoms may occur when tumors occur near the urethral ostium.
Diagnosis

- Most often established by cystoscopic biopsy
- In high risk patients, urinary cytology may be an effective screening tool and is helpful for evaluating high grade in situ lesions
- Due to the high incidence of second primaries, visualization of the upper urothelial tract (by contrast urography) is REQUIRED
Staging

- Appropriate studies...
  - Cystoscopic examination of the bladder and biopsy with rectal (vaginal) exam under anesthesia
  - Contrast urography of the upper urinary tract
  - Chest radiograph
  - Baseline biochemical and hematologic studies
  - CT of abdomen/pelvis (to exclude local spread and nodal metastases)
Treatment of Carcinoma *In Situ*

- Frequently a multifocal disease
- Treatment is tailored to the individual
- Initially, many lesions may be managed by intravesical chemotherapy
- If voiding symptoms occur or invasiveness occurs (adverse prognostic signs) the patient is urged to undergo total cystectomy (almost 100% cure rate)
- Close follow-up is required
Treatment of Superficial Low Grade Lesions

- Best managed by transurethral surgery
- Tumor recurrence is the rule and multiple surgeries are the norm
- Total cystectomy for these lesions is rarely required
- Intravesical chemotherapy (thioTEPA, Adriamycin, mitomycin-C, bcg) is of value for patients with frequent recurrences and noninvasive disease
Simple TURB is seldom adequate

Resection of the involved bladder (segmental cystectomy) is an option to total cystectomy

5 year survival rate (Stage II,III) of about 25% with surgery alone

Radiation not of benefit

Some recommend adjuvant chemotherapy as for advanced disease
Treatment of Advanced Disease

- Surgical fulguration and resection for palliative benefit
- Radiation may be of use for local control and relief of urinary irritability in patients who are poor candidates for surgery
- Most patients are managed by combination chemotherapy for palliative intent
# Chemotherapy for Bladder Cancer

- **Single agents**
  - Cisplatin/Carboplatin
  - Methotrexate
  - Adriamycin
  - Cyclophosphamide
  - Ifosfamide
  - Gemcitabine
  - Pemetrexed
  - Paclitaxel
  - Docetaxel
  - Mitomycin C
  - Vinca alkaloids
  - Ixabepilone
Chemotherapy for Bladder Cancer

- Combinations
  - Cisplatin combinations generally favored
  - GC (Gemcitabine, Cisplatin)
    - Less toxic than MVAC though equivalence to MVAC not established
  - MVAC (Methotrexate, Vinblastine, Adriamycin, Cisplatin)
    - Given on a 28 day cycle
    - Response rate is 65% and duration of response averages 8 months
    - Reasonably toxic
Prostate Cancer

- Introduction
- Clinical Presentation
- Diagnosis
- Management of Disease by Stage
Introduction

- The most common cancer in men
- Over 250,000 cases and 28,000 deaths per year
- Median age at onset—70 years, incidence increases exponentially after age 40
- 98% of all prostate cancers are adenocarcinomas, the remainder are sarcomas, transitional carcinomas, and small cell carcinomas
- More common in blacks than whites
Etiology

- Cause is unknown
- Environmental factors appear to play a role (higher in Westernized society)
- Some familial clustering is found
- Autopsy studies have found occult prostate cancer in as much as 40% of males over 75 years of age
Clinical Presentation

- Most often asymptomatic, with a mass found on routine rectal exam.
- Many present with obstructive uropathy, with carcinoma found on TURP specimen.
- If widespread, many men complain of leg edema, leg pain and pelvic fullness from metastases to presacral and iliac lymph nodes.
- Additionally, metastases to bone and lung may occur. Liver metastases are infrequent.
Diagnosis of Prostate Cancer

- A biopsy of every suspicious prostate mass is essential
- Most biopsies are done as a transrectal approach with either direct palpation or guidance by ultrasound
- 80-90% success rate
- Complications (bleeding, abscess formation) are rare
- Limited role for tumor markers in diagnosis of cancer
Tumor Markers and Prostate Cancer

- Prostate specific antigen (PSA)—may be elevated in BPH and prostate cancer
- Level may be increased slightly with manipulation of prostate
- Progressive increases in serum levels of prostatectomized males appear to correlate with amount of tumor present
- Free/Bound PSA and PSA velocity
- Additional strategies to assist detection of disease at early stage
The standard evaluation for prostate carcinoma includes...

- Physical/rectal exam
- PSA
- Chest x-ray
- Prostate nodule biopsy
- Bone scan
- CT of pelvis helpful to assess nodal status
The most favored histologic grading is Gleason score. Tumors are graded 1 (most like normal tissue) to 5 (anaplastic) in each of two features—nuclear differentiation and cellular composition. The two scores are added together to arrive at a final score.
The most favored histologic grading is Gleason score

- 2-4 — well differentiated, closely resemble normal glands
- 5-6 — moderately well differentiated, some glandular appearance
- 7 — moderately poorly differentiated
- 8-10 — poorly differentiated
Tumor Grade and Staging

- More recently, the AJCC has rephrased tumor grading
  - GX — Grade cannot be assessed
  - G1 — Well differentiated (slight anaplasia)
  - G2 — Moderately differentiated (moderate anaplasia)
  - G3 — Poorly differentiated (marked anaplasia)
  - G4 — Undifferentiated
Treatment of Prostate Cancer

- General Principles
  - The roles of surgery and radiation are still not clearly defined.
  - Significant overlap in treatment exists, and treatment for most men can be tailored to meet the needs of the individual.
  - Treatment to maintain urinary patency is required.
  - With current surgical practice, urinary continence is maintained in over 90% of patients.
Treatment of Stage I Disease

- Older patients may be managed by watchful waiting
- Patients over age 70 with histologically aggressive disease can be managed conservatively
- Radiotherapy, brachytherapy (radioactive seed implantation)
- Younger patients usually considered for either RT or prostatectomy
Treatment of Stage II Disease

- Tailor treatment to the age and overall performance status of patient.
- Standard therapy is radical prostatectomy.
- Patients with palpable ($T_2$) disease or with microscopically diffuse disease are at increased risk for metastases and lymphadenectomy is considered.
- External beam XRT and brachytherapy effective and many studies show equivalent results to radical prostatectomy.
Treatment of Stage III Disease

- Radical prostatectomy with lymphadenectomy and XRT are virtually identical.
- Relapse rate is high in this group, but adjuvant chemotherapy not of proven value.
- In some studies, hormonal therapy for 1-2 years may improve disease free interval.
Treatment of Stage IV Disease

- Prostate tissue is hormonally receptive and therefore hormonal manipulation is recommended.
- The use of LHRH agonists (leuprolide, goserelin) will reduce testosterone to near-castrate levels within 3 weeks of administration.
- The addition of a testosterone-receptor blocking agent (flutamide, bicalutamide) further increases the efficacy of LHRH-A.
- Surgery or XRT may still be needed for obstructive symptoms.
Chemotherapy in Prostate Cancer

- Not used for patients other than Stage IV
- No standard therapy
- Active agents include...
  - Docetaxel
  - Paclitaxel
  - Vinca alkaloids
  - Abiraterone
  - Mitoxantrone
  - Estramustine
  - Cabazitaxel
  - Etoposide
  - Adriamycin
  - Gemcitabine
  - Cyclophosphamide
  - Sipuleucel-T
Germ Cell Tumors

- Introduction
- Clinical Presentation
- Pathology
- Diagnosis/Staging
- Treatment of Disease by Stage
Introduction

- Represent only about 1% of all male cancers
- Most common solid tumor in males between ages 29 and 35
- Three peak age groups...
  - Infants—embryonal carcinoma and yolk sack tumors most common
  - Young adults—all types
  - Older adults—seminoma
- Strong association with cryptorchidism and testicular tumors
  Cause of germ cell tumors unknown
Clinical Presentation

- Most complain of scrotal swelling, discomfort, or heaviness
- Pain reported <20% of the time—usually in the scrotum, but back pain from paraaortic node metastases can occur
- Gynecomastia—occurs 10-15% of the time
- Constitutional symptoms...
  - Fatigue, malaise
  - Weight loss
  - Fever
Pathology of Germ Cell Tumors

- For general purposes, germ cell tumors can be divided into two broad categories
  - Seminomas
  - Nonseminomatous germ cell tumors (NGCT)
- Additionally, germ cell tumors can occur in the testis (over 90%) or in primordial germ cell nests in the mediastinum or retroperitoneum which fail to regress in embryonic life (about 5%)
Pathology of Germ Cell Tumors

- Related to respective layers in embryo
- In nonseminomas, tumor marker can be somewhat specific
Seminoma Subtypes

- Classic — most common
- Anaplastic — present with a higher stage when diagnosed
  - 3 mitoses per high power field, very aggressive
  - Treat just like classic seminoma
- Spermatocytic — occurs universally in elderly men
  - Slow growing with excellent prognosis
  - Tends not to metastasize
Nonseminoma Subtypes

- Embryonal carcinoma—highly malignant, anaplastic tumor

- Teratoma
  - Mature—slow growing, least aggressive
  - Immature—more aggressive than the mature type

- Choriocarcinoma—rare, must have both cytotrophoblastic and syncytiotrophoblastic tissue for diagnosis, fairly aggressive

- Yolk sac tumor—very rare but very aggressive tumor
Clinical Course

- The natural history of germ cell tumors is metastases via the retroperitoneal lymph nodes
- Occasionally, hematogenous spread can occur
- These are highly treatable, mostly curable tumors!
Diagnosis and Staging

- Diagnosis depends on biopsy of suspicious testicular mass

- The correct procedure for testicular biopsy is delivery of the testis out of the scrotum—DO NOT DO A TRANSCRROTAL BIOPSY!

- Tumor markers (AFP, βHCG)
  - Often elevated in NGCT but NORMAL in seminoma
  - Levels directly reflect tumor bulk and are valuable in detecting disease recurrence

- LDH
  - LDH-1 may be elevated in seminomas
Diagnosis and Staging

- Required procedures
  - Biopsy and histopathologic review
  - Chest x-ray
  - Tumor markers (βHCG, AFP)
  - CT of abdomen/pelvis for adenopathy
  - US of both testes (overall 15% bilaterality)
Surgery for Germ Cell Tumors

- Radical orchiectomy—removal of affected testis and cord
- Allows for determination of adverse prognostic factors (capsule invasion, direct extension to spermatic cord or vascular structures) and precise pathologic diagnosis
- Retroperitoneal lymph node dissection—gross exoneration of all paraaortic, iliac, and presacral lymph nodes
- Morbidity—lymphedema, ileus, postoperative recovery
Radiation for Germ Cell Tumors

- Usually to the retroperitoneum
- Given for these reasons...
  - Retroperitoneal treatment in patients who are not surgical candidates
  - Residual masses after treatment for seminoma
  - As part of multimodal therapy
Chemotherapy for Germ Cell Tumors

- Cornerstone is a platinum-containing combination regimen
- Both seminomas and NGCT are responsive, usually curable diseases
- Treatment is aggressive and some morbidity occurs in about 75% of cases, mortality from treatment is rare

Complications
- Alopecia
- Pancytopenia—fever, bleeding, anemia (RBC transfusions)
- Nausea/vomiting—minimal to absent
- Pulmonary fibrosis (bleomycin) or cardiomyopathy (Adriamycin)
Treatment of Seminomas

- **Stage I**—radical orchiectomy followed by active surveillance (preferred) or retroperitoneal radiation

- **Stage II**<sub>A</sub> and II<sub>B</sub>—radical orchiectomy followed by radiation; chemotherapy can be used if radiation inappropriate

- **Stage II**<sub>C</sub> and C—radical orchiectomy followed by chemotherapy
Treatment of NGCT

- Stage I—radical orchietomy followed by retroperitoneal node dissection, active surveillance of conscientious patients an option (no difference in survival)
- Stage II\textsubscript{A} and II\textsubscript{B}—radical orchietomy with either retroperitoneal lymph node dissection and/or chemotherapy
- Stage II\textsubscript{C} and III—radical orchietomy and chemotherapy, surgery for debulking of residual tumor