Cancer In Men

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Bladder Cancer

- Most frequent uroepithelial tumor
- About 75,000 cases per year and 15,000 deaths
- Male:Female ratio=3:1
- 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

- Chinese herbs—aristocholic acid causes urothelial cancers (component of Balkan nephropathy)

- *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.
Pathology of Bladder Cancers

- **Low-grade**: recurs after treatment, but rarely invades. Recurrence is common, but metastasis and death are rare.

- **High-grade**: recurs after treatment and has a strong tendency to invade the muscular layer of the bladder and metastasize. Most deaths due to bladder cancer are of this type.
**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
  - CXR
  - 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
Treatment of High Grade High Stage (II or higher) Tumors

- 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
  - PD-1/PD-L1 inhibitors
  - Pemetrexed
  - Paclitaxel
  - Docetaxel
  - Mitomycin C
  - Vinca alkaloids
  - Ixabepilone
  - PD-1/PD-L1 inhibitors
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
The most common cancer in men

- Over 180,000 cases and 26,000 deaths per year
- Median age at onset—66 years, incidence increases exponentially after age 40
- 98% of all prostate cancers are adenocarcinomas, the remainder are sarcomas, transitional carcinomas, and small cell carcinomas

- Prostatic Intraepithelial Neoplasia (PIN)—the high grade form may be a precursor for adenocarcinoma
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
Tumor Grade and Staging

- 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.
Tumor Grade and Staging

- The most favored histologic grading is Gleason score
  - Basically…
    - 2-4—well differentiated, closely resemble normal glands
    - 5-6—moderately well differentiated, some glandular appearance
    - 7—moderately poorly differentiated
    - 8-10—poorly differentiated
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 radical prostatectomy
Treatment of Stage II Disease

- Tailor treatment to the age and overall performance status of patient (watchful waiting is appropriate for older men with indolent tumor)

- 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
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.
- Bisphosphonates can minimize skeletal-related complications.
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 (about 8700 per year)
- 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
  - Present with a higher stage when diagnosed
    - 3 mitoses per high power field, very aggressive
    - Treat just like classic seminoma
- **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 TRANSCROTAL 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 (risk of contralateral disease is ~2%/year for the 15 years post-diagnosis)
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_A and II_B—radical orchiectomy followed by radiation; chemotherapy can be used if radiation inappropriate

- Stage II_C and C—radical orchiectomy followed by chemotherapy
Treatment of NGCT

- Stage I—radical orchiectomy 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 orchiectomy with either retroperitoneal lymph node dissection and/or chemotherapy

- Stage II\textsubscript{C} and III—radical orchiectomy and chemotherapy, surgery for debulking of residual tumor