BLADDER TUMORS

Benign

- Transitional Cell Papilloma 2-3%
- Inverted Papilloma Rare

Malignant

- Transitional (Urothelial) Carcinoma 90%
- Carcinoma In-Situ (By Itself) 5-10%
- Squamous Cell Carcinoma 3-7%
- Adenocarcinoma 1%
- Small Cell Carcinoma Rare
INCIDENCE & PREVALENCE

- 2% of all malignancies
- Male predominance
- Patients usually more than 60 years old
- Recently, there has been an increasing incidence among women and younger persons
UROTHELIAL CARCINOMAS

**Genetic Mutations**

- **Chromosomal Deletions**
  - 9q, 11p, 13q and/or 17p, (p53 locus)
  - Occurrence in 30 to 60% of tumors

- **Increased Oncogene Expression**
  - ras, c-myc, and/or EGF
  - Occurrence is less common and is less well-defined
ETIOLOGIC FACTORS

- Chronic cystitis
- Diverticula
- Chronic irritation (e.g., stone disease)
- Long-standing obstruction with retention
- Cigarette smoking
- Schistosomiasis
- Industrial Exposure to Carcinogens
  - Naphthalamines
  - Benzidine
  - Amino diphenylamines
POOR PROGNOSTIC FACTORS

- High Tumor Grade
- Advanced Tumor Stage
- Squamous or Small Cell Carcinoma
- Loss of Blood Group Antigens
- HCG Expression
- Increased c-myc Expression
- p53 overexpression
- Multiple Chromosomal Mutations
MULTIFOCALITY

- Development of multifocal tumors, either synchronous or metachronous, is common.
- Difficult to manage, even when non-invasive.
- Field effect theory - carcinogens in urine cause independent, genetically dissimilar tumors.
- Monoclonal theory - a single transformed cell proliferates and spreads throughout the urothelium.
- Studies support both theories. Both mechanisms can be operative in a single patient.
Papillary Carcinoma (PTCC +/- Invasion)
- Grade I Shows Uniform Tumor Cells
- Grade II Shows Focal Pleomorphism and Rare Mitoses
- Grade III Shows Moderate Pleomorphism and Occasional Mitoses
- Grade IV is Focally Unrecognizable as Urothelial, and May Show Spindle Cell Features
- Low Grade (I, II) and High Grade (III, IV)

Flat Carcinoma (CIS and Invasive TCC)
- Usually high grade
UROTHELIAL CARCINOMA

- The status of the mucosa away from the tumor is important. Mucosal changes (e.g., CIS) increase the risk of recurrence and invasion.
  - Random bladder biopsies
  - Extensive sectioning and “mapping” of cystectomy specimens
UROTHELIAL CARCINOMA

- Not all CIS is high grade, and can be overlooked. Therefore, underdiagnosis is quite widespread.
<table>
<thead>
<tr>
<th>Depth of Local Invasion</th>
<th>pT</th>
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<tbody>
<tr>
<td>CIS</td>
<td>Tis</td>
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<tr>
<td>Non-invasive Papillary</td>
<td>Ta</td>
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<tr>
<td>Lamina Propria</td>
<td>T1</td>
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<tr>
<td>Superficial 1/2 Muscularis</td>
<td>T2a</td>
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<tr>
<td>Deep 1/2 Muscularis</td>
<td>T2b</td>
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<tr>
<td>Perivesical Fat</td>
<td>T3</td>
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<tr>
<td>Prostatic stroma, Vagina, Uterus</td>
<td>T4a</td>
</tr>
<tr>
<td>Pelvic and/or Abdominal Wall</td>
<td>T4b</td>
</tr>
<tr>
<td>No Evidence of Primary Tumor</td>
<td>T0</td>
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MODE OF INVASION

- Broad Front
- Tentacular
- Lymphatics
- Blood Vessels
- Combination
The majority of invasive carcinomas present initially as invasive carcinomas.

Non-invasive carcinomas can become invasive.

Both tend to be multicentric, and to recur.
THERAPY

- BCG
- Mitomycin-C
- Thiotepa
- Cis-Platinum
- Cyclophosphamide, etc.
- Surgery
- Radiation
SQUAMOUS CARCINOMA

- Associated with:
  - Schistosomiasis
  - Stones
  - Chronic irritation

- About 90% bladder cancers in the Mid-East and Egypt are squamous.

- Tend to be sessile, ulcerated, and invasive at presentation.

- Except for verrucous variant, they are poorly differentiated.
ADENOCARCINOMA
ADENOCARCINOMA

- **Primary**
  - Urachal (dome and anterior wall)
  - Associated with exstrophy
  - Associated with cystitis glandularis, colonic metaplasia, or villous adenoma (usually in trigone)

- **Secondary**
  - Direct extension from elsewhere (e.g., prostate or rectum)

- **Metastasis**
UNCOMMON VARIANTS

- Undifferentiated small cell carcinoma
  - May produce a paraneoplastic syndrome via hormone synthesis (e.g. ACTH)
- Anaplastic Type
- Spindle Cell Type
  - ? metaplasia
  - ? true carcinosarcoma
NON-EPITHELIAL TUMORS

- **Benign**
  - Leiomyoma

- **Malignant**
  - Leiomyosarcoma
  - Rhabdomyosarcoma
    - “Sarcoma Botryoides”
RHABDOMYOSARCOMA
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The pelvic tumors (10-15% of all renal tumors) arise from a) the lining epithelium and are either:

1. TRANSITIONAL (UROTHELIAL) (75%), usually papillary
2. SQUAMOUS (25%), usually solid, ± calculus, infiltrate kidney (silent)
3. ADENOCARCINOMA
4. MIXED (e.g. squamous and transitional)

b) stromal (non-epithelial) tumors are rare lipoma, fibroma, hemangioma, lymphangioma, etc. liposarcoma, fibrosarcoma, myosarcoma, etc.
TESTICULAR TUMORS
GERM CELL TUMORS OF THE TESTIS

- 94% of testicular tumors
  - 38% single histologic type
  - 62% more than one type
- Begin as intratubular malignant germ cells (ITGCN) (“CIS”) and progress to one or more histologic types
INCIDENCE & PREVALENCE
(U.S.)

- 6/100,000 (increasing incidence)
- 11 - 13% of cancer deaths in 15 - 34 year age group
- Commonest cause of death from malignancy in 20 - 34 year groups
- Rare among blacks, in U.S. and Africa
ETIOLOGY: UNKNOWN

Genetic - family history in 16%
Chromosomal abnormalities - isochromosome 12p
Undescended (Cryptorchid) testis
Infection - history of orchitis, especially mumps
Trauma
Abnormal Testis
Endocrine Abnormalities - intersex syndromes
Environmental Factors – isolated cases, no consistent patterns
TUMOR MARKERS

Done pre- and post-operatively

- **BHCG** - beta subunit of Human chronic gonadotropin
- **AFP** - alphafetoprotein
- **HPL** - human placental lactogen
- **SPI** - pregnancy specific beta globulin
- **PLAP** - placental alkaline phosphatase
STAGING (TNM)

- **pTis**: ITGCN
- **pT1**: Limited to testis & epididymis w/o vascular invasion
- **pT2**: Limited to testis & epididymis with **vascular invasion**, or invading tunica vaginalis
- **pT3**: Invades spermatic cord
- **pT4**: Invades scrotum
- **pN**: Based on number and size of involved regional nodes
- **pM**: Distant metastasis
SEMINOMA

- About 50% of tumors in adults, mostly in pure form
- None seen in infants
- Age 30’s - 40’s
- PLAP may be elevated
- Radiosensitive
GROSS

Lobulated, soft pink-tan bulky mass. Rarely, hemorrhage and necrosis.
• Fairly uniform cells typically with clear cytoplasm and well-defined cell borders. Resemble primitive germ cells. Cytoplasm contains glycogen. Large vesicular nucleus with 1-2 nucleoli.

• Cells are arranged in lobules supported by a fibrovascular stroma in which almost invariably a lymphoid infiltration and granulomatous reaction are seen.
SPERMATOCYTIC SEMINOMA
EMBRYONAL CARCINOMA

- In pure form, constitutes 3.1%
- Present in 47% of testicular tumors
- Not seen in infants or children
- AFP may be marginally elevated, but able to be demonstrated in only 13% of cells. (Reported elevations due to overlooked yolk sac tumor elements)
- HPL - more often elevated
Micro

- Primitive epithelial cells form a carcinoma that is usually glandular, but may be papillary, tubular, or reticular.
- No cell borders
- Pleomorphism
- “See-through” nuclei
- Lymphovascular invasion common
YOLK SAC TUMOR

- Endodermal sinus tumor, infantile embryonal carcinoma, orchioblastoma
- 60% of testis tumors in children
- 2.4% of adult tumors in pure form
- Present in 41% of all testis tumors
- **AFP** almost always elevated in serum and present in tumor cells by IHC (93%)
CHORIOCARCINOMA

- Rare (0.3% of testicular tumors) in pure form, but present in 16% of mixed GCTs (usually with embryonal carcinoma or teratoma).
- Primary focus - small and often missed.
- Patients often present with symptoms of metastasis (hematogenous-to brain, lungs).
- Pure form - lethal within 6 weeks
- HCG - very high, AFP negative
- Gynecomastia, thyrotoxicosis
Very small, soft, hemorrhagic mass
MICRO

- Recapitulates placental structures.
- Prominent venous invasion.
- Two cell types must be present:
  - Syncytiotrophoblasts
  - Cytotrophoblasts
- Large choriocarcinomatous component probably worsens prognosis.
TERATOMA

- Tumor showing disorderly arrangement of fetal and adult tissues and structures representing 1 to 3 germ layers:
  - endoderm
  - mesoderm
  - ectoderm
- Subclassified as:
  - mature
  - immature
  - teratoma with malignant areas
    1. adenocarcinoma
    2. squamous carcinoma
    3. Sarcoma
    4. PNET
TERATOMA

- About 40% of testicular germ cell tumors in infants
- In the adult (post-pubertal) testis, all are considered malignant regardless of histology (mature vs. immature)
- Rare epidermoid or dermoid cysts
SEX CORD/ STROMAL TUMORS

- Leydig cell
- Sertoli cell
- Granulosa cell
- Theca cell
- Fibroma
- Mixed/unclassified type
SEX CORD/ STROMAL TUMORS

- All ages
- 5-6% of testicular tumors
- No racial predilection
- Rarely malignant
- Hormone production-gynecomastia, precocious puberty
LEYDIG CELL TUMOR
SERTOLI CELL TUMOR