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

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

Incidence and 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

- 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

Histologic Grading of Transitional Cell Carcinomas

- Papillary, (PTCC) +/- Invasion
  - Grade I Shows Uniform Tumor Cells
  - Grade II Shows Focal Pleomorphism and Rare Mitoses
  - Grade III Shows Moderate Pleomorphism and Occasionally Mitoses
  - Grade IV is Focally Unrecognizable as Urothelium and May Show Spindle Cell Features
  - Low Grade (I,II) and High Grade (III, IV)
- Flat Carcinomas, (CIS and Invasive TCC)
  - Usually Grade III or IV, Rarely Grade II, Never 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.

**Staging (TNM)**

<table>
<thead>
<tr>
<th>Depth of Local Invasion</th>
<th>pT</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIS</td>
<td>TIS</td>
</tr>
<tr>
<td>Non-invasive Papillary</td>
<td>T1</td>
</tr>
<tr>
<td>Lamina Propria</td>
<td>T1</td>
</tr>
<tr>
<td>Superficial 1/2 Muscularis</td>
<td>T2a</td>
</tr>
<tr>
<td>Deep 1/2 Muscularis</td>
<td>T2b</td>
</tr>
<tr>
<td>Pelvic fat</td>
<td>T3</td>
</tr>
<tr>
<td>Prostate, Vagina, Urethra</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>
</tr>
</tbody>
</table>

**Mode of Invasion**

- Broad Front
- Tentacular
- Lymphatics
- Blood Vessels
- Combination
**Invasion**
- 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
- Radiotherapy

**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

- **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 (oat cell)
  - May produce a paraneoplastic syndrome via hormone synthesis
- Anaplastic Type
- Spindle Cell Type
  - ? metaplasia
  - ? true carcinosarcoma

Non-Epithelial Tumors

- Benign
  - Leiomyoma
- Malignant
  - Leiomyosarcoma
  - Rhabdomyosarcoma
    - “Sarcoma Botryoides”

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Tumors of the Renal Pelvis Comprise 10-15% of All Renal Tumors

The Pelvic 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

b) stromal (non-epithelial) tumors are rare: lipoma, fibroma, hemangioma, lymphangioma, etc.
  liposarcoma, fibrosarcoma, myosarcoma, etc.
TESTICULAR TUMORS

Germ Cell Tumors of 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 and 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

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

Micro

- 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.

Gross

Lobulated, soft pink-tan bulky mass. Rarely, hemorrhage and necrosis.
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

Gross

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