PEDIATRIC TESTICULAR TUMORS

Amy Dobberfuhl (U2)
Pediatric Education Conference
Sept. 19, 2012
Testicular Tumors

- 1 to 2 % of all pediatric solid tumors

- Annual incidence 1:100,000 for boys < 15 y/o
  - Bimodal; 2 y/o and after puberty
  - Most commonly Caucasian

- Benign lesions represent greater percentage of cases compared with adults
  - 38 to 74% benign (under-reported ?)
Etiology & Genetics

- **Unknown etiology**
  - Prolonged exposure to carcinogenic stimuli?

- **Increased risk**
  - Disorders of sex development (esp. hypovirilization & gonadal dysgenesis) 6% show intratubular germ cell neoplasia
  - Cryptorchidism (rarely causative in childhood)
Pathology & Theory

- **Cells and origin**
  - Non-germ cell (celomic epithelium)
  - Germ cells (primordial germ cells)

- **Theory**
  - Totipotent germ cells evolve into seminoma or embryonal carcinoma
  - Embryonal carcinoma may differentiate into embryonic structures (mature/immature teratoma) vs. extraembryonic (yolk sac, chorioCA)
  - Seminoma and dysgerminoma is primitive and unable to further differentiate

- Unusual in childhood except in case of gonadal dysgenesis
Symptoms

- Painless testicular mass
- Acute abdominal pain with torsion of abdominal undescended testicle/tumor

Must exclude;
- Epididymitis, hydrocele, hernia, torsion
Evaluation

- Testicular ultrasound with color doppler
  - No reliable sonographic features distinguish benign from malignant

- Anechoic cystic lesions can suggest benign;
  - Simple cyst, cystic dysplasia, teratoma, cystic granulosa cell tumor
Evaluation

- **AFP**
  - Produced by fetal yolk sac, liver and GI tract
  - 5-day half life
  - AFP positive tumors suggest yolk sac elements
  - May be falsely elevated in infant boys and does not always represent malignant tumor or disease
  - Normal adult level (<10 mg/mL) not until 8 months old

- **β-hCG**
  - Embryonal CA and mixed teratoma
  - 24-hour half life
  - Rarely elevated in pre-adolescent tumors
Childrens Oncology Group Staging

- Staging based on tumor markers and pathology

- AFP, checked at diagnosis and after orchiectomy

- CT of retroperitoneum and chest to r/o mets
  - 15 to 20% false negative rate for LN mets
Carcinoma In Situ

- CIS (aka. Intratubular germ cell neoplasia) is common in adults with testiCA.
- Thought to be precursor to development of invasive germ cell tumor.
- Frequent in androgen-insensitivity disorders and dysgenetic gonads.
- Known association between cryptorchidism and development of CIS.
  - Incidence 1.7% in adults s/p orchiopexy.
  - CIS difficult to identify pre-puberty.
    - If found, then re-biopsy after puberty.
## Pediatric Overview

<table>
<thead>
<tr>
<th>Germ Cell</th>
<th>Gonadal Stromal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mature teratoma</td>
<td>Leydig cell</td>
</tr>
<tr>
<td>Epidermoid cyst</td>
<td>Sertoli cell</td>
</tr>
<tr>
<td>Immature teratomas</td>
<td>Gonadoblastoma</td>
</tr>
<tr>
<td>Yolk sac tumor</td>
<td></td>
</tr>
</tbody>
</table>
Mature Teratoma

- 40% of testis tumors in prepubertal children
- Benign clinical course (vs. propensity for adult teratoma to metastasize)
- Ultrasound
  - Complex hypoechoic areas surrounded by highly echogenic signals
- OR
  - Manage with testis sparing procedures through inguinal incision with vascular control
  - Incise tunica and enucleate
  - Frozen section of tumor and tunica closed
  - Close skin if benign
Mature Teratoma

- Heterogeneous mass replacing entire testicle
- Solid and cystic components
Mature Teratoma

- Variety of somatic-type tissues: squamous, enteric, respiratory, cartilaginous
- May have modestly increased AFP
- DDx: epidermoid cyst (squamous lined cyst) or dermoid cyst (squamous lined cyst with sebaceous glands in the wall of the cyst)
Epidermoid Cyst

- 15% of pediatric testicular tumors
- Monodermal teratoma
  - Benign (lack chromosome 12p abnormalities vs. teratoma)
- Ultrasound
  - Heterogeneous with “onion-skin appearance” hypo-hyper echoic layers
  - No flow
- OR
  - Amendable by testis sparing surgery
  - Check frozen section intraop
Immature Teratoma

- Less common tumor of testis
  - Only 10% occur in testes
  - Most common extracranial site is ovary
- Considered to be malignant, however benign in children unless foci of malignant cells
- May observe if resection complete
  - Low risk of relapse
  - Platinum chemotherapy salvage
- Recurrence factors
  - Elevated AFP
  - Foci of yolk sac tumor
Immature Teratoma

- Epithelial component surrounded by immature cellular spindle cell stroma
Yolk Sac Tumor

- 2nd most common prepubertal germ cell tumor
- Usually < 2 y/o
- 90% present with stage 1 disease
- 90% have positive serume levels of AFP
- Initial treatment radical inguinal orchiectomy
  - Usually curative
  - Routine RPLND +/- Chemo not indicated
Yolk Sac Tumor

- Large hyperechoic mass replaces entire testis
- Diffusely increased vascularity around tumor
Yolk Sac Tumor

- A. Reticular microcystic pattern, thin cords and loose spaces
- B. Classic Schiller-Duval boes with central fibrovascular core surrounded by malignant cuboidal columnar cells
Yolk Sac Tumor
Yolk Sac Tumor

- Characteristic hyaline globule in a reticular background of yolk sac tumor
Yolk Sac Tumor

- **Stage 1**
  - May still consider if SCROTAL orchiectomy with negative margins if resected to internal ring
  - Surveillance: CXR, CT or MRI
    - 1, 2, 3, 6 months -- then Q6 months until 3-years
Yolk Sac Tumor

- **Stage 2**
  - Prior scrotal biopsy
  - Complete orchiectomy with removal of all cord structures
  - Hemiscrotectomy not required
  - LN sampling vs. Bx if enlarged nodes on CT
Yolk Sac Tumor

- **Stage 3**
  - Persistent elevated AFP and retroperitoneal adenopathy
  - Chemotherapy (BEP)
    - Cisplatin; Ototoxicity and nephrotoxicity
  - Resect residual masses if present after 12-weeks
Sex cord stromal tumors are the most common non-germ cell tumors in children

- Usually benign
- More common in children than adults
- Arise from common mesenchymal cells
- Secrete hormones
Leydig Cell Tumor

- Most common sex cord tumor
- Peak incidence 4 to 5 y/o
- Produce testosterone
  - May cause precocious puberty
- Also produce corticosterones, progesterone, estrogens
- OR
  - Orchiectomy (most often) vs. Testis sparing/Enucleation
  - Only one report of recurrence
- No reported malignancy
Leydig Cell Tumor

- Large polygonal cells, round nuclei, single prominent nucleolus and abundant eosinophilic cytoplasm.
- Crystals of Reinke
  - Plump rod-shaped intracytoplasmic crystals seen in 40% of cases
Sertoli Cell Tumor

- 2nd most common gonadal stromal tumor in children
- Not as metabolically active as Leydig cell
  - Some gynecomastia reported
- Limited series of reports in children
  - Orchietomy vs. sparing surgery
  - Observation
- Need retroperitoneal evaluation

- Large cell Sertoli cell tumors associated with;
  - Peutz-Jeghers (GI hamartoma and hyperpigment oral)
  - Carney complex (Heart myxoma, skin lentiginosis, endocrine overactive)
Sertoli Cell Tumor

- Groups of cells in chords and trabeculae “beam like”
- Light staining bubbly cytoplasm, Granular chromatin
- Resemble immature seminiferous tubules
Gonadoblastoma

- Most common with disorders of sex differentiation
- Dysgenetic gonads
  - Presence of Y-chromosome in karyotype
  - 25% risk of tumor formation
- Germ cell component prone to malignant degeneration
  - May become Seminoma or NSGCT

- Remove all streak gonads
  - Especially if raised as females or males with mixed dysgenesis and UDT
  - Early gonadectomy before 5 y/o
- Consider observation of scrotal testis in males vs. Bx and evaluation for CIS
Gonadoblastoma

- Mixture of seminoma-like cells (germ cell components) and Sertoli-like cells (sex-cord component)
- Nests of pale seminoma-like cells, clear cytoplasm, well-defined membranes
- At periphery, pallisades of dark angular sex-cord cells, look like Sertoli cell
- Basement membranes can hyalinize and calcify
Leukemia & Lymphoma

- Most common malignancy to spread to testicle
- Relapse of Acute lymphoblastic leukemia
  - None after Chemotherapy
  - 4% if XRT
  - 20% if bulky disease
- Testicular involvement in 4% of Burkitt Lymphoma
Lymphoma

- Diffuse heterogeneous echotecture
- Enlarged testicle
- No discrete mass
- Increased vascularity
Testicular Cystic Dysplasia

- Rare benign lesion in boys
- Multiple small irregular cysts in rete testis
- 50% also have renal agenesis or multicystic renal dysplasia
- Testis sparing surgery vs. Observation (serial u/s)
Testicular Microlithiasis

- Reported in association with testicular tumors
- Present in 5% of healthy young men
- Uncommon in children
  - Observation with u/s until adult
- Cancer risk association
  - Atrophic testicle and infertility
  - Known testis CA and contralateral microlithiasis
Testicular Microlithiasis

- 17 y/o M
  - Diffuse innumerable microliths

- 13 y/o M
  - Punctate echogenic foci
Screening

- Routine self examination
- Advise against routine screening u/s
- If risk factors screening u/s has unclear role given high survival rate
References

- Campbell’s Urology. Chapter 137: Pediatric Urologic Oncology. 11th Ed.
- Webpathology.com