Testicular Tumors
Including Secondary and Unusual Tumors of the Testis

Milton W. Datta
Partner, Hospital Pathology Associates
University of Minnesota
Minneapolis, MN
Topics

- Review Features of Germ Cell Tumors
  - Differential diagnosis
- Discuss staging issues
  - Presence of Lymphatic/vascular invasion
  - Serum markers
- Examine the use of immunohistochemistry
  - Appropriate and judicial use
Testicular Tumors

- Germ Cell Tumors  88%
- Non-Germ Cell Tumors  12%
  - Sertoli Cell Tumor
  - Leydig Cell Tumor
  - Sex Cord Stromal Tumor
  - Spermatiocytic Seminoma
  - Granulosa Cell Tumor
  - Small Cell Carcinoma
  - Carcinoid
  - Lymphoma
  - Secondary Tumors
  - “Other”
Age related

• Younger male
  • Germ cell tumors

• Older Male
  • Lymphoma
  • Secondary tumors
Testis Tumors

- Germ Cell Tumors 88%
  - Seminoma 26%
  - Embryonal Carcinoma 1%
  - Yolk Sac Tumor < 1%
  - Teratoma < 1%
  - Choriocarcinoma < 1%
  - Mixed 60%

- Non-Germ Cell Tumors 12%

M.W. Datta 10/31/14
E.T. Bell Symposium
Germ Cell Tumor Component Percentages

- Poor inter-pathologist agreement in percent of germ cell components
- Key elements that effect prognosis:
  - Predominant Embryonal carcinoma
  - Presence of Choriocarcinoma
  - Presence of mature teratoma
  - Presence of yolk sac tumor
- Pan-staining of tumors to determine percentages in not necessary
Need for Immunohistochemistry

• ISUP Recommendations
• Less than 5% of testicular tumor cases need immunohistochemistry
• Germ cell: SALL4, PLAP
  • Embryonal carcinoma: Oct 3/4, CD30
  • Seminoma: Oct 3/4, CD117
  • Yolk Sac tumor: AFP, Glypican 3
• Choriocarcinoma: bHCG, Glypican 3

Testis Cancer Staging: pT

Key primary tumor staging;
1. Diffuse lymphatic/vascular invasion by tumor
2. Distinction between tunica albuginea and tunica vaginalis
3. Direct extension into spermatic cord
4. Scrotal wall
5. Tumor extension into rete testis (seminoma - radiation oncology)

- pTX Primary tumor cannot be assessed.
- pT0 No evidence of primary tumor (e.g., histologic scar in testis).
- pTis Intratubular germ cell neoplasia (carcinoma in situ).
- pT1 Tumor limited to the testis and epididymis with no vascular/lymphatic invasion; tumor may invade into the tunica albuginea but not the tunica vaginalis.
- pT2 Tumor limited to the testis and epididymis with vascular/lymphatic invasion, or tumor extending through the tunica albuginea with involvement of the tunica vaginalis.
- pT3 Tumor invades the spermatic cord with or without vascular/lymphatic invasion.
- pT4 Tumor invades the scrotum with or without vascular/lymphatic invasion.
Testis Cancer Staging: pN,M

Lymph Node Metastasis determined by number of positive nodes (5 nodes) and metastasis size (2 cm, 5 cm)

- pNX  Regional lymph nodes cannot be assessed.
- pN0  No regional lymph node metastasis.
- pN1  Metastasis with a lymph node mass \( \leq 2 \) cm in greatest dimension and \( \leq 5 \) nodes positive, none \( > 2 \) cm in greatest dimension.
- pN2  Metastasis with a lymph node mass \( > 2 \) cm but not \( > 5 \) cm in greatest dimension; or \( > 5 \) nodes positive, none \( > 5 \) cm; or evidence of extranodal extension of tumor.
- pN3  Metastasis with a lymph node mass \( > 5 \) cm in greatest dimension.

Metastasis determined by site (distant lymph nodes, pulmonary metastasis)

- M0  No distant metastasis.
- M1  Distant metastasis.
- M1a  Nonregional nodal or pulmonary metastasis.
- M1b  Distant metastasis other than to nonregional lymph nodes and lung.
Testis Cancer Staging: pS

- Key focus is residual disease (tumor spread/burden) implied by sustained serum marker elevation
- Need serum marker values 30 days AFTER orchiectomy
  - Serum AFP half life: 4-5 days
  - Serum bHCG half life: 24-36 hours
  - Serum LDH half life: 10 hrs – 3 days (isozymes, LDH-1)
- Stratify into stage 1S (most cases)
  - SX  Marker studies not available or not performed.
  - S0  Marker study levels within normal limits.
  - S1  LDH <1.5 × normal, and hCG (mIu/ml) <5,000 and AFP (ng/ml) <1,000.
  - S2  LDH 1.5–10 × normal or hCG (mIu/ml) 5,000–50,000 or AFP (ng/ml) 1,000–10,000.
  - S3  LDH >10 × normal or hCG (mIu/ml) >50,000 or AFP (ng/ml) >10,000.

Tumors by Histology

• Germ Cell Tumor Histology
  • Seminomatous pattern
  • Embryonal carcinoma pattern
  • Mature Teratoma pattern
• Non-Germ Cell Tumor Histology
  • Leydig pattern
  • Sertoli pattern
  • Granulosa cell pattern
  • Lymphoma pattern
  • Spindle cell pattern
Seminoma

- Mean 40.5 years, wide age range
- Sheets of cells
- Broad fibrous bands
- Lymphocytes, Tumor cells
- Large cells
- Clear to eosinophillic cytoplasm
- Large nuclei, open chromatin
- Prominent pink nucleolus
Variant features

- Pleomorphic “anaplastic” nuclei
- Limited inflammatory components
Seminoma pattern
Secondary tumors of the testicle

- Uncommon, but present, over 350 cases reported.
  - Majority are surgical specimens
  - 2/3 cases this was the only metastasis
  - 21 cases was the presenting finding
    - Long intervals, up to 16 years
- Not always bilateral (5%)
- Wide age range (8 months to 89 years, mean 57.4 years)
  - Colonic (mean 52 years, 18-76)
  - Prostatic (mean 69 years, 47-89)
Melanoma

- 47 years (28-78)
- Cases as presentation
- Many amelanotic.
- Melanospermia
- Outcome up to 12 months

Seminoma Pattern

Renal cell carcinoma
Renal Cell Carcinoma

- Age 35 – 87 yrs.
- Second most common as an initial presentation
- All unilateral
- Clear cell type
- Survival up to 2 years

Metastasis: Tools for Separation

- Seminoma / Melanoma / Renal Cell Carcinoma
- IGCNU
- Any pigment? (Melanoma / Leydig)
- Lace-like vascular network (RCC)
- Stains
  - Oct 3/4, C-kit, PLAP
  - S100, Melan A, MART-1
  - Pax-8 (Renal cell carcinoma)
  - Inhibin (Sertoli)
Embryonal Carcinoma

- Sheets and Glands
- Interspersed loose to embryonic stroma
- Limited inflammatory infiltrate
- Dirty Necrosis
- Large cells, single cell necrosis
- Poorly defined cytoplasmic borders
- Pleomorphic overlapping nuclei
Embryonal Carcinoma Pattern

Gastric CA
Gastric Carcinoma

- 11 cases
- Mean 42 yrs (12-62)
- Grey-white masses
- Fibrotic
- Survival 1-12 months
- Peritoneal carcinomatosis

Carcinomas in Teratoma?

- **Ovary: Dedifferentiation into carcinomas**
  - Squamous cell carcinoma
  - Adenocarcinoma
- **Testis: Dedifferentiation into Carcinomas**
  - Rare
  - 31 cases described (32 year period at Indiana Univ)
  - Poor response to chemotherapy
  - Histology stage, grade did not affect outcome

Embryonal Carcinoma Pattern

Choriocarcinoma
Embryonal Carcinoma Pattern

Angiosarcoma
EC vs Angiosarcoma


M.W. Datta 10/31/14
E.T. Bell Symposium
Sarcomatoid Degeneration

- Present in 3-4 percent of germ cell tumors
- 12-41 years
- Types
  - Rhabdomyosarcoma
  - Chondrosarcoma
  - Osteosarcoma
  - Angiosarcoma
- Clinical: Definitive surgery is the best hope

Rhabdomyosarcoma
Sarcoma: Tools for Separation

- Sarcomatous differentiation
- Defined sarcomatous elements
- Areas of residual mature teratoma, germ cell tumor
- Rhabdomyosarcomatous
  - Desmin
Immature Teratoma?

- **Primitive Neuroectodermal tumor only**
- **Important in the ovary (4 HPF) drops prognosis from 95% to 80% post treatment survival**
- **NOT important in the testis**
  - **Does not affect survival or response to treatment**

Late Recurrence in Germ Cell Tumors

- Indiana University two years after initial treatment (91 cases)
  - 22% teratoma alone (best outcome)
  - 40% teratoma + germ cell tumor
  - 20% pure non-teratoma germ cell components; embryonal carcinoma, yolk sac tumor
  - 18% non-germ cell tumor; sarcoma, carcinoma

- Worse prognosis:
  - Pure non-teratoma, Non-germ cell tumor
  - 83% w/disease, 37% alive at 4.7 years avg

Epidermoid Cyst

- 2nd-4th decades
- Isolated epithelial features
- Epidermal elements
- Fibrous stroma
- No IGCNU – Teratoma
- PLAP, p53, Oct 3/4
Epidermoid Cyst
Mature Teratoma in MMGCT
Leydig Cell Tumor

- 1-3% testis tumors
- Any age
- Gynecomastia (15%)
- Interstitial tumor
- Uniform small cells
- Eosinophillic cytoplasm
- Uniform nuclei
- Small nucleoli
- Inhibin
Leydig pattern
Malignancy in Leydig cell tumors

- No clear-cut indicators of malignancy besides metastatic spread
- Features more often associated with malignancy:
  - Infiltrative tumor borders
  - Vascular invasion by tumor
  - Nuclear atypia
  - Tumor necrosis
  - High mitotic rate
  - Lack of lipofuscin pigment.

Malignant Leydig

15% Prostate cancer
Prostate Cancer

- Most common metastasis to testis
  - Therapeutic orchiectomy
- Mean 69 yrs
- Range 47-89
- 10% bilateral
- Survival 6-18 months
Variant features

- Glandular formation
  - “Gleason progression”
- Nuclear pleomorphism
- Two-cell component
  - Leydig cells – tumor cells
- Nkx3.1, PSA, PAP
- Leydig: Inhibin

Sertoli Cell Tumor (NOS)

- All ages (mean 46 yrs)
- Solid to hollow tubules, nests
- Scant fibrous stroma
  - Sclerosing
  - Large cell Calcifying
- Clear (lipid) to eosinophillic cytoplasm
- Mild nuclear pleomorphism

Sertoli Cell Pattern

Sertoli cell tumor

Carcinoid
Carcinoid Tumor

- 35% teratomatous
- 65% pure
- Mean 36 yrs (12-65)
- Carcinoid syndrome rare
- Overall benign (4.3 yrs f/u)
- NSE, Chromogranin, Synaptophysin

Granulosa Cell Tumor

- Rare, 45 cases
- Mean 40 years (14-87 yrs)
- Gynecomastia
- Microfollicles, Sheets
- Small, uniform cells
- Nuclear grooves
- Minimal cytoplasm
- Discohesive
- 1 sarcomatous degeneration, 1 metastasis (4.1 yr f/u)

Granulosa Cell Pattern

Granulosa cell tumor

Small Cell Carcinoma
Small Cell Carcinoma

- Mean 55 yrs
- Range 47-73 yrs
- Lung, esophagus, stomach, Merkel cell
- Changes chemotherapeutic options

Lymphoma

- 5% of all testis tumors
- Mean 58 yrs (46-76 yrs)
- 38% bilateral
- Diffuse large B-cell type
- Median survival 36 mo

Lymphoma pattern

leukemia
Leukemia

- Associated with Acute (64%) and chronic (22%) leukemias
- Can be a sign of recurrence (ALL)
- Overlaps with plasmacytic tumors

Spermatocytic Seminoma

- Often over 50 yrs, rare under 30
- Lack of uniform cells
- Three cell types large, medium, small
  - Spermatogonia, primary spermatocytes,
- No inflammatory infiltrate (LCA)
- Oct3/4, PLAP, Glypican 3 negative
Splenogonadal Fusion

- Left testis mass, upper pole
- Continuous, discontinuous
- Undescended testis or hernia operation
Spindle Cell Pattern

- Rare in the testis
- Testicular fibroma
- Sex cord stromal tumors
- Fasicles, broad bands
- Spindled morphology
- Mild to moderate nuclear pleomorphism
- Seen in melanoma, renal cell carcinoma
Spindle cell pattern

Spindle sertoli cell

Spindle RCC
Acknowledgements

- Robert Young, Mass. General Hospital
- Tom Ulbright, Indiana Univ
- Mahul Amin, Cedars Sinai Medical Center
  - Michael Whittaker, Community Memorial Hospital
  - Doug Chausow, Community Memorial Hospital