Glandular Lesions and Tumors in Uropathology

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– Videomicroscopy Case #5 –
History

- 64 year-old male patient
- Complaint of unilateral testicular enlargement
- Physical Exam: Swelling of right testis
- Scrotal USG:
  - 6 cm mass lesion occupying right testis
- Past Medical History: Not significant
- Inguinal orchiectomy
  - 5.8 cm tumor in the largest diameter
    - Intratesticular
    - Smooth contoured with pseudocapsule
    - Cream to pale yellow colored
    - Areas of hemorrhage
FISH

(18q11.2) Dual Color, break Apart Rearrangement Probe

break apart of SYT gene
Glandular Lesions of Testis

- **Intratesticular**
  - Sertoli cell lesions (hamartomas or tumors)
  - Germ cell tumors with glandular pattern
    - Yolk sac tm, Embryonal carcinoma, Teratomas
    - Metastases

- **Paratesticular**
  - Rete testis proliferations
  - Epididymal lesions
  - Ovarian type surface epithelial lesions
  - Mesothelial proliferations
  - Metastases
Intratesticular Tumors

**Flowchart:**

1. **Tumour with a glandular and/or tubular pattern**
   - Yes:
     - **IGCNU present?**
     - Yes: Consider embryonal carcinoma (OCT4+/PLAP+/CD30+)
     - No: Consider yolk sac tumour (keratin+/AFP+/OCT4−/PLAP+/CD30−)
   - No: Prominent intertubular and intralymphatic growth?
     - Yes: Consider metastatic adenocarcinoma (keratin+/OCT4−/PLAP−/ inhibin−)
     - No: Consider tubular pattern (keratin usually−/AFP−/OCT4+/PLAP+/CD30−)

2. **Consider Sertoli cell tumour (inhibin+)**
3. **Consider rete testis neoplasm (keratin+/CEA+/EMA+)**
Paratesticular Tumors

Paratesticular tumours with a gland-like, tubular, or papillary pattern

Yes

Expression of mesothelial markers (calretinin, keratin 5/6, vimentin) and absence of expression of epithelial markers (MOC-31, Ber-EP4, CD15)

History of prostatic adenocarcinoma or other carcinoma, prominent intralymphatic tumour

Yes

Consider metastatic adenocarcinoma (PSA, PAP, or other site specific markers may be useful)

No

Consider primary paratesticular mullerian neoplasms and rete testis neoplasms

Tubular pattern with cuboidal to flattened cellular lining, minimal nuclear atypia, densely collagenised stroma?

Yes

Consider adenomatoid tumour

No

Consider mesothelioma
Sarcomas with True Epithelial Differentiation

- Epithelioid Sarcoma
- Synovial Sarcoma
Synovial Sarcoma

• 5% to 10% of all soft tissue sarcomas

• Malignant soft tissue tumor of uncertain type

• Uncertain histogenesis

• No known normal tissue counterpart
Synovial Sarcoma

- **Age:** Newborn to 82 years (mean 34)
- **Most prevalent:** 15 to 40 years of age
- **M/F:** 1.2
- **Palpable, deep seated swelling or mass**
- **Pain or tenderness** ~50% of the cases
Synovial Sarcoma

- Extremely uncommon in joint cavities
- Encountered in areas with no apparent relation to synovial structures
- Extremities: 85-95%
  - primarily in the paraarticular regions, usually in close association with tendon sheaths, bursae, and joint capsules
  - tend to arise in the vicinity of large joints, especially knee
- Head & neck: 10-15%
  - paravertebral connective tissue spaces
- Trunk: 5% (chest wall and abdominal wall)
- Virtually every anatomic site
  - heart, pleuropulmonary region, kidney, prostate, retroperitoneum, GIS, peripheral nerve
<table>
<thead>
<tr>
<th>ANATOMIC LOCATION</th>
<th>NO. OF CASES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Head-Neck</strong></td>
<td>31 (9.0%)</td>
</tr>
<tr>
<td>Neck</td>
<td>12</td>
</tr>
<tr>
<td>Pharynx</td>
<td>7</td>
</tr>
<tr>
<td>Larynx</td>
<td>7</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
</tr>
<tr>
<td><strong>Trunk</strong></td>
<td>28 (8.1%)</td>
</tr>
<tr>
<td>Chest</td>
<td>10</td>
</tr>
<tr>
<td>Abdominal wall</td>
<td>9</td>
</tr>
<tr>
<td>Other</td>
<td>9</td>
</tr>
<tr>
<td><strong>Upper Extremities</strong></td>
<td>80 (23.2%)</td>
</tr>
<tr>
<td>Forearm-wrist</td>
<td>24</td>
</tr>
<tr>
<td>Shoulder</td>
<td>22</td>
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<tr>
<td>Elbow-upper arm</td>
<td>20</td>
</tr>
<tr>
<td>Hand</td>
<td>14</td>
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<tr>
<td><strong>Lower Extremities</strong></td>
<td>206 (59.7%)</td>
</tr>
<tr>
<td>Thigh-knee</td>
<td>102</td>
</tr>
<tr>
<td>Foot</td>
<td>45</td>
</tr>
<tr>
<td>Lower leg-ankle</td>
<td>33</td>
</tr>
<tr>
<td>Hip-groin</td>
<td>22</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>345 (100.0%)</td>
</tr>
</tbody>
</table>

AFIP, Armed Forces Institute of Pathology.

Enzinger and Weiss’s Soft Tissue Tumors
24-year-old man
- Painless left testicular swelling
- Firm mobile mass, 66 × 34 mm
- Normal b-hCG and AFP
- Histology: Monophasic synovial sarcoma, poorly differentiated; grade III
- 1 yr later: recurrent scrotal mass, multiple inguinal l.nodes, pleural met.s
- DOD despite chemo 19 mo.s after diagnosis
SS - Macroscopy

Slowly growing tumors:

- be sharply circumscribed, round, or multilobular
- completely or partially invested by a pseudocapsule
- cyst formation may be prominent, occasional multicystic lesions
- yellow to gray-white
- most 3 and 6 cm

Rapidly growing tumors:

- poorly circumscribed
- variegated, friable or shaggy appearance
- multiple areas of hemorrhage, necrosis, and cyst formation
Histologic Types of SS

• Biphasic
• Monophasic
  – Fibrous type (most common subtype of SS)
  – Epithelial type (difficult to differentiate from adenoca)
• Poorly differentiated (round cell)
Biphasic SS - Microscopy

Coexistence of:

- epithelial cells
  - cuboidal - columnar cells arranged in cords, nests, or glands
  - large, round or oval, vesicular nuclei
  - abundant pale-staining cytoplasm.
  - granular or homogeneous eosinophilic secretions
  - +/- focal squamous metaplasia

- fibroblast-like spindle cells
  - well-oriented, plump, uniform spindle cells
  - narrow indistinct cytoplasm
  - oval dark-staining nuclei
  - solid compact sheets
IHC

- EMA: 97%
- AE1/AE3: 90%
- CK7: 85%
- CK19: 85%
- S-100 protein: 30%
- CD99: 60%
- TLE1: 95%
- β-Catenin: 84%
TLE1 (9q21.32)

- Transducin-like enhancer of split 1
- Nuclear protein
- Transcriptional repressor of wnt/β-catenin signaling
- One of the most consistent synovial sarcoma-associated genes
- Sensitive marker of SS including cytokeratin-negative tumors
Molecular Background

- $t(X;18)(p11.2;q11.2)$
  - $SS18-SSX1$ (65%)
    (Strongly correlates with epithelial differentiation)
  - $SS18-SSX2$ (35%)
  - $SS18-SSX4$ (<1%)
Prognosis of SS

- considered to be a high grade malignancy
- 5-year overall survival: 64% to 76%
  - Lower rates in patients with metastases at the time of diagnosis.
- clinical factors associated with a more favorable clinical outcome
  - age of the patient (15 years or younger)
  - tumor size <5 cm,
  - distal extremity location
- histologic features of prognostic value
  - biphasic synovial sarcomas
  - extensively calcified synovial sarcomas
  - fusion subtype SS18-SSX2
  - poorly differentiated
  - rhabdoid cells
  - extensive tumor necrosis
  - high mitotic index (greater than 10 MF/10 HPF)
  - high nuclear grade
Therapy of SS

• extensive surgery - radical local excision
• adjunctive radiotherapy
• chemotherapy
  – ifosfamide and doxorubicin or epirubicin
• Recurrence rate with adequate excision and adjuvant therapy: <40%
Follow-up

- 4 courses of chemotherapy
  (Ifosfamide/Mesna/Adriamycin)
- Alive without disease for 4 years
Summary

When tumors arising in unusual sites:

• Definitive recognition is more difficult
• Algorithms are useful, but they are not all inclusive
• Spectrum of differential diagnoses needs to be kept broad
• Often confirmation by molecular - genetic techniques is required
Thank you