Pathology Mystery and Surprise

Tim Sloss, MD
Director Anatomic Pathology
Medical University of South Carolina

Disclosures
• No conflicts to declare

Some problem cases
• Kidney tumor
• Scalp tumor
• Bladder tumor
• Kidney tumor
• Shoulder mass
• .
Case 1

• A 64 year old man had a partial nephrectomy for a 3.7 cm. There was also a 5 cm mass in the ipsilateral adrenal gland.
The differential diagnosis for this tumor would include the following choices. Which one is your favorite diagnosis?

a. Papillary renal cell carcinoma
b. Clear cell papillary renal cell carcinoma
c. Sarcomatoid renal cell carcinoma
d. Clear cell renal cell carcinoma
e. Translocation carcinoma
f. Metastatic carcinoma from some other site
g. Melanoma
Translocation carcinomas

- MIT family includes 1) Xp11 [TFE3] and 2) t(6;11) [TFEB]
  - Microphthalmia transcription factor
  - History of cytotoxic chemotherapy

TFE3 translocation carcinoma

- 40% pediatric; 4% adult; few cases described in adults
  - Two possible TFE3 gene fusions: t(x;1) & t(x;17)
  - Adult prognosis similar to CCRCC; children more favorable
  - Micro: slightly different histology, usually high grade; often calcifications
    - IHC: PAX8 +/-, CK, EMA, CA9, HMB45, MART, /p; cathepsin K +/-
  - alveolar soft part sarcoma also have TFE3/ASPSCR1 fusion

TFE3 Translocation carcinoma

- Image of histological slide showing translocation carcinoma.
TFEB translocation carcinoma

- T(6;11) very rare
- Micro: biphasic pattern; large clear epithelioid cells
  - smaller eosinophilic cells
- IHC: PAX 8 +/−, CK, CK7, EMA, CA9 −/p
  - HMB 45, MART, cathepsin K +
- Prognosis good even with local node metastasis
  -

Translocation Renal Cell Carcinomas in Adults: A Single Institution Experience

Menghai Zhang, MD. PhD1, Patricia De Angelis, MSF. Lisa Osborne, MSF. Pascale Mondolli, AE. MD2. Matthew Gruler, DF. Youyi Yang, MSF. W. Marlon Linneman, MSF. Maria J. Marino, MD2. Carla Carden-Cardin, MD. PhD2. and Dongping Cai, MD. PhD2.
Case 2

- This 76 year old woman presented with a 4 cm scalp mass. The lesion had enlarged slowly for at least 12 months. Initial differential included DFSP. Imaging showed at least transcranial dural involvement with suspected underlying brain involvement.

CD 34 negative

What is the best diagnosis for this microscopic appearance?

A. Low grade sarcoma  
B. Dermatofibrosarcoma protuberans  
C. Sarcomatoid glioblastoma  
D. Cutaneous leiomyosarcoma  
E. Spindle cell squamous carcinoma
Case 2

Case 2

Case 2

Case 2
Gliosarcoma

- ~2% of high-grade gliomas
- At least 2 components: GBM and mesenchymal elements
  - Heterologous components: osteosarcoma, chondrosarcoma, rhabdomyosarcoma, angiosarcoma, liposarcoma, leiomyosarcoma, squamous cell adenocarcinoma
- Associated with radiotherapy
- IHC: GFAP+, positivity appropriate for heterologous elements

Case 2

Epithelioid and Pseudopapillary Differentiation in Glioblastoma and Gliosarcoma: A Comparative Morphologic and Molecular Genetic Study

Case 2
Case 2

GFAP
Case 3

- An 82 year old man had hematuria for 18 months. Cystoscopy showed a large fluffy carcinoma occupying the lower half of the bladder and prostatic urethra.
An exophytic lesion such as this in the bladder is likely to be a / an

A. High grade non-invasive urothelial carcinoma
B. High grade invasive urothelial carcinoma
C. Low grade invasive urothelial carcinoma
D. Metastatic germ cell carcinoma
E. Papillary prostate carcinoma
F. Inverted urothelial carcinoma
Case 3

Pseudopapillary Features in Prostatic Adenocarcinoma Mimicking Urothelial Carcinoma

A Diagnostic Pitfall

Jennifer Giordano, MD and Jonathan E. Epstein, MD†
Case 3

Best Practices Recommendations in the Application of Immunohistochemistry in the Prostate
Report From the International Society of Urologic Pathology Consensus Conference
Jonathan J. Epstein, MD; Louis Ignarro, MD; Paul A. Humphrey, MD, PhD;2
Rafael Montironi, MD; and Members of the ISUP Immunohistochemistry
Task Force. Academic Pathology Group

Case 3

<table>
<thead>
<tr>
<th>Protein</th>
<th>Expression/Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>NKX3.1</td>
<td>+ in many PCA and PCa</td>
</tr>
<tr>
<td>AR</td>
<td>Not widely used</td>
</tr>
<tr>
<td>SMARCA5</td>
<td>+ in about 60% of PCa</td>
</tr>
<tr>
<td>TFF1</td>
<td>+ in some PCa</td>
</tr>
<tr>
<td>TP53</td>
<td>57% negative in high-grade PCa</td>
</tr>
<tr>
<td>ERG</td>
<td>Focal positivity; also + in vascular canals; + in 40% of PCa</td>
</tr>
</tbody>
</table>

Case 3

Poorly Differentiated Adenocarcinomas of Prostate Versus High-Grade Urothelial Carcinoma of the Bladder: A Diagnostic Dilemma With Immunohistochemical Evaluation of 2 Cases
Miguel Martínez-Rodríguez, MD, David Ramos, MD, Pilar Soriano, MD, Manish Subramaniam, MD, Naimed Nacarro, MD, and Antonio Llombart-Bosch, MD
Case 3

Case 4

• A 49 year old man was discovered to have a 1.7 cm kidney tumor. It had increased in size from 1.5 cm over a 3 year period. The tumor was discovered incidentally during surveillance for a tonsillar squamous carcinoma 6 years previously. The tumor was removed as a partial nephrectomy.
Immunostains

- TTF-1, CK 7, CK 19, PAX 8 positive
- NAPSIN focal positivity
- TGB, CK20, RACEMASE, RCC negative
- BRAF negative
- RET amplified

The best diagnosis for this tumor is

A. Metastatic papillary thyroid carcinoma
B. Primary papillary renal cell carcinoma
C. Metastatic lung carcinoma
D. Primary thyroid like follicular carcinoma of kidney
E. Metastatic carcinoma from GI tract

Follow up

- No other tumors by imaging
Case 4

- Diagnosis: papillary thyroid carcinoma, maybe metastatic, but where?
- Problem: thyroid-like follicular RCCs
  - Amin et al. "Primary thyroid-like follicular carcinoma of the kidney: report of 6 cases of a histologically distinctive adult renal epithelial neoplasm." AJSF33:393-400, 2009
  - Mimic histology of follicular variant of papillary carcinoma, TTF-1 / TGB –
  - Predominantly women
  - < 30 cases
  - Low grade behavior,
Case 4

• Differential diagnosis
  • Metastatic thyroid carcinoma
  • 16 reported cases
  • End stage kidney thyroidization
  • Metastasis from ovarian teratoma
  • Patient is male
  • Metastasis from other teratoma?

Case 4

• Imaging
  • 1.7 cm LL pole kidney nodule

• IHC
  • TTF, CK7, PAX 8 +
  • TRG, CK20, RCC, P504S –
  • NAPSIN FOCAL
  • BRAF –
  • RET AMPLIFIED
Case 4

A mass on the shoulder of a 48 year old man had been present and growing for about a year. It measured 5.5 cm and was excised with positive margins. The referring diagnosis was sarcoma. The patient and his residual 9 cm mass were referred for re-excision.

Case 5
Case 5

Case 5

Case 5

Case 5
The best diagnosis for this histologic appearance is ........

A. Synovial sarcoma
B. Primitive neuroectodermal tumor
C. Metastatic adult nephroblastoma
D. Metastatic testicular germ cell tumor
E. Primary malignant teratoma of soft tissue
F. Dedifferentiated chondrosarcoma
Case 5

- Diagnosis: teratoma with squamous carcinoma, germ cell tumor and PNET
- Serum markers not elevated
- Imaging of testicles, pineal, mediastinum, midline normal.

- Reported sites for ectopic teratoma: sacrum (a, i), spine (a), kidney, mediastinum (i, t), stomach (i) rarely in soft tissue (a)
Case 5

<table>
<thead>
<tr>
<th>Anatomical Location</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sacrococcygeal</td>
<td>67.0</td>
</tr>
<tr>
<td>Head and neck</td>
<td>9.6</td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>8.3</td>
</tr>
<tr>
<td>Mediastinum</td>
<td>7.6</td>
</tr>
<tr>
<td>Bronchus</td>
<td>9.6</td>
</tr>
<tr>
<td>Liver</td>
<td>1.5</td>
</tr>
<tr>
<td>Abdominal wall/back</td>
<td>1.5</td>
</tr>
</tbody>
</table>

GAP Protocol for the examination of Specimens From Pediatric and Adult Patients with extragonadal Germ cell tumors. Arch Pathol Lab Med. 2011; 135;

Origin of teratomas?

• Germ cell sites
• Must consider undifferentiated cell origin

QUESTIONS