MiT Family Translocation-Associated Renal Cell Carcinoma

A Contemporary Update With Emphasis on Morphologic, Immunophenotypic, and Molecular Mimics

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MiT Family Translocation Renal Cell Carcinomas

- Translocation involving TFE3 (Xp11) or TFEB (t(6;11)).

- Risk factor: exposure to cytotoxic chemotherapy.

- Epidemiology:
  - Xp11 t-RCC: 40% of pediatric RCC → 5 new cases/y
    1,6-5% of adult RCC → 1260 new cases/y
  - t(6;11) t-RCC: 50 reported cases worldwide

- Prognosis:
  - Xp11 t-RCC: in adults similar to ccRCC
    in children more favorable outcome
  - t(6;11) t-RCC: indolent clinical course

Source: Arch Pathol Lab Med—Vol 139, October 2015
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Morphology Xp11 t-RCC:

- Papillary structures and/or nested architecture
- Large, epithelioid cells with abundant clear to eosinophilic cytoplasm
- High grade nuclei
- Psammoma bodies

Source: Arch Pathol Lab Med—Vol 139, October 2015
Morphology Xp11 t-RCC

A

B

Source: Arch Pathol Lab Med—Vol 139, October 2015
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Morphology t(6;11) t-RCC:
- Biphasic pattern:
  - Large, epithelioid cells with clear to eosinophilic cytoplasm.
  - Small cells forming rosette-like structures around basement membrane material.

Source: Arch Pathol Lab Med—Vol 139, October 2015
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Morphology t(6;11) t-RCC
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Immunohistochemistry:

- PAX8 +
- Pancytokeratins, EMA reduced +
- CAIX - or patchy
- TFE3, TFEB +
- Melanocytic markers +
- Cathepsin K +

Source: Arch Pathol Lab Med—Vol 139, October 2015
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DD clear cell RCC

Source: Sternberg's Diagnostic Surgical Pathology, 6th Edition
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Immunohistochemistry ccRCC:

- PAX8, CD10 +
- Pancytokeratin, EMA strong +
- CAIX +
- Negativ: Melanocytic markers, Cathepsin K, TFE3, TFEB

Source: Arch Pathol Lab Med—Vol 139, October 2015
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DD papillary RCC

Source: Sternberg's Diagnostic Surgical Pathology, 6th Edition
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DD papillary RCC
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DD papillary RCC
- PAX8, CD10 +
- Pancytokeratin, EMA strong +
- CK7 + (type 1> type2)
- AMACR +
- CAIX variable
- Negativ: Melanocytic markers, Cathepsin K, TFE3, TFEB

Source: Arch Pathol Lab Med—Vol 139, October 2015
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DD other RCC with clear cells
- TCEB1- mutated RCC
- RCC with angioleiomyoma-like Stroma
- Clear cell papillary RCC

→ IHC: diffuse strong CAIX +

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Other DDs

- Epitheloid Angiomyolipoma
  - HMB-45 +, Melan A +, Cathepsin K +
  - TFE3 may be +
  - PAX8 –
  - Pancytokeratine - and CAIX –
  - SMA +

- Multilocular cystic renal neoplasm of low malignant potential
  - PAX8 +, CAIX +

- Oncozytoma
  - S100A +, KIT +, E-Catherin + and Pancytokeratine +

- Collecting duct carcinoma
  - EMA +, CK7 +
  - CD10 -, CAIX -

Source: Arch Pathol Lab Med—Vol 139, October 2015
WHO Classification of Tumors of the Urinary System and Male Genital Organs, 4th Edition
### Salient Microscopic Features and Ancillary Studies That May Aid in Diagnosis of Translocation-Associated Renal Cell Carcinoma and Its Morphologic, Immunophenotypic, and Molecular Mimics

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Morphologic Features</th>
<th>IHC</th>
<th>Ancillary Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xp11 RCC</td>
<td>Diverse morphologic spectrum: high-grade cells with abundant clear or eosinophilic cytoplasm and papillary/nested architecture; psammomatous calcifications</td>
<td>+/-, /P, /P, /P, /P, /P, /P</td>
<td>TFE3 FISH</td>
</tr>
<tr>
<td>t(6;11) RCC</td>
<td>Classic biphasic appearance: (1) larger epithelioid cells with clear to eosinophilic cytoplasm and (2) small, eosinophilic cells forming rosettelike structures within basement membrane–like material</td>
<td>+/-, /P, /P, /P, +/+, +</td>
<td>TFEB FISH</td>
</tr>
<tr>
<td>CCRCC</td>
<td>Medium cells with clear cytoplasm in nests with delicate fibrovascular septations, or high-grade cells with eosinophilic cytoplasm and papillae/pseudopapillae</td>
<td>+, +, +, +, D, -, -</td>
<td>3p25 FISH</td>
</tr>
<tr>
<td>PRCC</td>
<td>Medium cells with clear to eosinophilic cytoplasm and variably enlarged nuclei; papillae with delicate fibrovascular cores; +/+ foamy macrophages</td>
<td>+, +, +, +, -</td>
<td>7/17 FISH</td>
</tr>
<tr>
<td>TFE3-mutated RCC</td>
<td>Medium cells with clear cytoplasm; tubular and/or papillary architecture; well-circumscribed; thick intervening fibromuscular stromal bands</td>
<td>+, +, +/P, +, D, -</td>
<td>None</td>
</tr>
<tr>
<td>CCRCC</td>
<td>Medium cells with clear cytoplasm with prominent papillary architecture and low-grade, apically oriented nuclei</td>
<td>+, +, +, CL, -</td>
<td>None</td>
</tr>
<tr>
<td>EAML</td>
<td>Tripheic myomelanocytic tumor (smooth muscle, adipose, and vessels) with large epithelioid cells (&gt;80% of cells)</td>
<td>-</td>
<td>Smooth muscle actin IHC</td>
</tr>
<tr>
<td>ASPS</td>
<td>Large cells with eosinophilic cytoplasm and large, eccentric nuclei with macronucleoli; solid nests and/or alveolar-like spaces with intervening fibrous septa</td>
<td>-</td>
<td>TFE3 FISH</td>
</tr>
</tbody>
</table>

**Abbreviations:** ASPS, alveolar soft part sarcoma; CAIX, carbonic anhydrase IX; CCPRCC, clear cell papillary RCC; CCRCC, clear cell RCC; CK7, cytokeratin 7; CL, cuilike membranous staining; D, diffuse membranous staining; EAML, epithelioid angiomylolipoma; EMA, epithelial membrane antigen; FISH, fluorescent in situ hybridization; IHC, immunohistochemistry; P, patchy, predominantly cytoplasmic staining; Pan-CK, pancytokeratins; PRCC, papillary RCC; RCC, renal cell carcinoma; +, positive; -, negative.