SS Soft tissue & bone pathology

Unusual tumors of bone & soft tissue or uncommon presentation of common ones

Case #6

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Disclosure Information

I hereby declare that I have had business or personal interests in the following industrial enterprises since 1 September 2017:

Name of the enterprise / Nature of the interest

Enterprise | Interest
No disclosures.
Clinical history

- A subcutaneous nodule 2.5x2x1.5 was excised from the back of a 12 yo boy.

- No other information or clinical history.
DDx based on stromal pattern

- Myxoid nerve sheath tumor (myxoid epithelioid MPNST).
- Myxoid myoepithelial neoplasm.
- Extraskeletal myxoid chondrosarcoma.
- Low-grade fibromyxoid sarcoma.
- Myxofibrosarcoma
- Myxoid liposarcoma
- Myxoid epithelioid sarcoma
- **Myxoid variant of any entity**
DDx based on cytology

- Myxoid epithelioid MPNST with rhabdoid features.
- Myxoid myoepithelial neoplasm with rhabdoid features
- Myxoid epithelioid sarcoma with rhabdoid pattern
- Myxoid variant of rhabdoid neoplasm
Approach to DDx
Assess:

- **Vascular pattern**: almost avascular stroma
- **Arrangement/architecture**: reticular/chordoid
- **Cytology**: uniformly rhabdoid
- **Nuclear atypia**: enlarged atypical vesicular nuclei
DDx: Absence of curvilinear/arborizing vasculature

- Myxoid nerve sheath tumor (myxoid epithelioid MPNST).
- Myxoid myoepithelial neoplasm
- Extraskeletal myxoid chondrosarcoma.
- Low-grade fibromyxoid sarcoma
- Myxofibrosarcoma
- Myxoid liposarcoma
- Myxoid epithelioid sarcoma
- Myxoid variant of ........
Based on uniform rhabdoid cytology: Does SMARCB1 loss help?
Based on uniform rhabdoid cytology: Does SMARCB1 loss help?

SMARCB1 lost in all of the neoplastic cells
Based on uniform rhabdoid cytology: Does SMARCB1 loss help?

- Myxoid epithelioid MPNST: 50% loss
- Myxoid myoepithelial neoplasm: 10-40% loss
- Extraskeletal myxoid chondrosarcoma: 20%
- Low-grade fibromyxoid sarcoma
- Myxofibrosarcoma
- Myxoid liposarcoma
- Myxoid epithelioid sarcoma: 100%
- Myxoid variant of .......
Epithelioid MPNST: myxoid variant: strongly S100+/SOX10+
Both neg in the current case
Myxoid variant of epithelioid sarcoma

- Pure myxoid variant rare.
- IHC: CK/EMA pos in almost all cases.
- CA125+
- CD34: 50%.
- Others

All neg in the current case
extraskeletal myxoid chondrosarcoma

- S100+
- CD117+
- EWSR1-NR4A3 fusion
Based on uniform rhabdoid cytology: Does SMARCB1 loss help?

- Myxoid epithelioid MPNST: 50% loss
- **Myxoid myoepithelial neoplasm:** 10-40% loss
- Extraskeletal myxoid chondrosarcoma: 20%
- Low-grade fibromyxoid sarcoma
- Myxofibrosarcoma
- Myxoid liposarcoma
- Myxoid epithelioid sarcoma: 100%
- **Myxoid variant of „I don´t knowma“?**
Myxoid myoepithelial neoplasm: example from extremity
Myxoid myoepithelial neoplasm: example from extremity
Plasmacytoid (hyaline cell) myoepithelioma: finger
Our case
### TABLE 2. Anatomic Distribution of 101 Myoepithelial Tumors of Soft Tissue

<table>
<thead>
<tr>
<th>Anatomic Location</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lower limb/limb girdle</strong></td>
<td>41</td>
</tr>
<tr>
<td>Groin/inguinal area</td>
<td>8</td>
</tr>
<tr>
<td>Buttock</td>
<td>5</td>
</tr>
<tr>
<td>Thigh</td>
<td>11</td>
</tr>
<tr>
<td>Knee/popliteal area</td>
<td>2</td>
</tr>
<tr>
<td>Lower leg</td>
<td>4</td>
</tr>
<tr>
<td>Ankle</td>
<td>1</td>
</tr>
<tr>
<td>Foot</td>
<td>5</td>
</tr>
<tr>
<td>Toe</td>
<td>5</td>
</tr>
<tr>
<td><strong>Upper limb/limb girdle</strong></td>
<td>35</td>
</tr>
<tr>
<td>Shoulder</td>
<td>6</td>
</tr>
<tr>
<td>Axilla</td>
<td>3</td>
</tr>
<tr>
<td>Upper arm</td>
<td>3</td>
</tr>
<tr>
<td>Elbow</td>
<td>3</td>
</tr>
<tr>
<td>Forearm</td>
<td>7</td>
</tr>
<tr>
<td>Wrist</td>
<td>5</td>
</tr>
<tr>
<td>Hand</td>
<td>5</td>
</tr>
<tr>
<td>Finger</td>
<td>3</td>
</tr>
<tr>
<td><strong>Head and neck</strong></td>
<td>15</td>
</tr>
<tr>
<td>Scalp</td>
<td>5</td>
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<tr>
<td>Face</td>
<td>1</td>
</tr>
<tr>
<td>Neck</td>
<td>7</td>
</tr>
<tr>
<td>Supraclavicular area</td>
<td>2</td>
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<tr>
<td><strong>Trunk</strong></td>
<td>10</td>
</tr>
<tr>
<td>Back</td>
<td>4</td>
</tr>
<tr>
<td>Chest wall</td>
<td>3</td>
</tr>
<tr>
<td>Abdominal wall</td>
<td>2</td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>101</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Marker</th>
<th>% positive</th>
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</thead>
<tbody>
<tr>
<td>CK or EMA</td>
<td>100%</td>
</tr>
<tr>
<td>S100</td>
<td>87%</td>
</tr>
<tr>
<td>Calponin</td>
<td>86%</td>
</tr>
<tr>
<td>GFAP</td>
<td>46%</td>
</tr>
<tr>
<td>SMA</td>
<td>36%</td>
</tr>
<tr>
<td>p63</td>
<td>23%</td>
</tr>
<tr>
<td>Desmin</td>
<td>14%</td>
</tr>
</tbody>
</table>

**All negative in our case**

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*Myoepithelial Tumors of Soft Tissue: A Clinicopathologic and Immunohistochemical Study of 101 Cases With Evaluation of Prognostic Parameters*

Jason L. Hornick, MD, PhD, and Christopher D. M. Fletcher, MD, FRCPath

Universitätsklinikum Erlangen
Rhabdoid Variant of Myoepithelial Carcinoma, with EWSR1 Rearrangement: Expanding the Spectrum of EWSR1-Rearranged Myoepithelial Tumors

Khin Thway · Nick Bown · Aisha Miah · Rob Turner · Cyril Fisher

+ve: EMA, SMA, calponin, S100
INI1 lost
FISH: unbalanced EWSR1
RT-PCR neg.
Current case highly similar cytologically to Fisher et al case (myxoid variant of same tumor?) but:
lacked myoepithelial marker expression totally
My suggested diagnosis:

Myxoid soft tissue neoplasm with prominent rhabdoid cell features lacking any line of Differentiation (vimentin-only phenotype).

- Myxoid myoepithelial carcinoma, rhabdoid variant?
- Pediatric malignant rhabdoid tumor, myxoid variant?
SMARCB1 loss in myxoid soft tissue neoplasms: Help or problem?

- Epithelioid MPNST: **50%** (occasionally very myxoid)
- Myoepithelial carcinoma: **10-40%** (frequently myxoid)
- Extraskeletal myxoid chondrosarcoma: **20%**
- Epithelioid sarcoma: **100%** (only rarely very myxoid)
- Malignant rhabdoid tumor: **98%** (only rarely very myxoid)
- Other EWSR1-CREB family tumors.
<table>
<thead>
<tr>
<th>Ref</th>
<th>Translocation</th>
<th>Fusion gene</th>
<th>Morphology</th>
<th>IHC</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT1 fusion</td>
<td>Desmoplastic small round cell tumour</td>
<td>5 t(11;22)(p13;q12)</td>
<td>EWSR1-WT1</td>
<td>Small round cells, cellular fibrous stroma</td>
</tr>
<tr>
<td>DDX3 (CHOP) fusion</td>
<td>Myxoid liposarcoma</td>
<td>8 t(12;22)(q13;q12)</td>
<td>EWSR1-DDX3</td>
<td>Spindle/polygonal cells myxoid stroma</td>
</tr>
<tr>
<td>NR4A3 fusion</td>
<td>Extraskelatal myxoid chondrosarcoma</td>
<td>14,53 t(9;22)(q22;q12)</td>
<td>EWSR1-NR4A3</td>
<td>Polygonal cells, myxoid stroma</td>
</tr>
<tr>
<td>CREB1 or ATF1 fusion</td>
<td>Angiomatoid fibrous histiocytoma</td>
<td>23,24 t(2;22)(q33;q12)</td>
<td>EWSR1-CREB1</td>
<td>Clear cells, Osteoclast-like giant cells</td>
</tr>
<tr>
<td>Clear cell sarcoma of soft tissue</td>
<td>25 t(12;22)(q13;q12)</td>
<td>EWSR1-CREB1</td>
<td>Clear cells, Osteoclast-like giant cells</td>
<td>S100pr+, melan-A -HMB45 –</td>
</tr>
<tr>
<td>Clear-cell sarcoma-like tumour of Gl tract</td>
<td>187 t(2;22)(q33;q12)</td>
<td>EWSR1-CREB1</td>
<td>Spindle cells, myxoid stroma</td>
<td>No specific markers</td>
</tr>
<tr>
<td>Primary pulmonary myxoid sarcoma</td>
<td>28 t(2;22)(q33;q12)</td>
<td>EWSR1-CREB1</td>
<td>Spindle cells, myxoid stroma</td>
<td>No specific markers</td>
</tr>
<tr>
<td>Myoepithelial tumour</td>
<td>145 t(12;22)(q13;q12)</td>
<td>EWSR1-ATF1</td>
<td>Epithelioid cell cords, chondromyxoid stroma</td>
<td>S100pr+, EMA+</td>
</tr>
<tr>
<td>Angiosarcoma</td>
<td>146 t(12;22)(q13;q12)</td>
<td>EWSR1-ATF1</td>
<td>Epithelioid and spindle cells</td>
<td>CD31+, FVIIIIRAg+, D2-40+</td>
</tr>
<tr>
<td>Hyalinising clear cell carcinoma of salivary gland</td>
<td>34,35 t(12;22)(q13;q12)</td>
<td>EWSR1-ATF1</td>
<td>Clear cells, hyalinised stroma</td>
<td>S100pr+</td>
</tr>
</tbody>
</table>
Primary Pulmonary Myxoid Sarcoma With EWSR1-CREB1 Fusion: A New Tumor Entity

Khin Thway, FRCPath,* Andrew G. Nicholson, DM, FRCPath,† Kay Lawson, MBBS,‡ David Gonzalez, PhD,§ Alexandra Rice, FRCPath,‡ Bonnie Balzer, MD,§ John Swansbury, FRCPath,∥ Toon Min, PhD,∥ Lisa Thompson, PhD,‡ Kwame Adu-Poku, FRCPath,¶ Anne Campbell, MD, FRCPath,# and Cyril Fisher, MD, DSc, FRCPath*

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EWSR1 Fusions With CREB Family Transcription Factors Define a Novel Myxoid Mesenchymal Tumor With Predilection for Intracranial Location

Yu-Chien Kao, MD,*† Yun-Shao Sung, MSc,† Lei Zhang, MD,† Chun-Liang Chen, MSc,† Sumathi Vaiyapuri, MD,‡ Marc K. Rosenblum, MD,† and Cristina R. Antonescu, MD†

(Am J Surg Pathol 2017;41:482–490)
3 of 4 cases had no EWSR1 fusion by NGS but SMARCB1 loss

The case with EWSR1-CREB fusion had intact SMARCB1
Do SMARCB1 loss and EWSR1 gene fusions coexist? Or are they mutually exclusive?

Molecular and Clinicopathologic Heterogeneity of Intracranial Tumors Mimicking Extraskeletal Myxoid Chondrosarcoma

- 3 of 4 cases had no EWSR1 fusion by NGS but SMARCB1 loss
- The case with EWSR1-CREB fusion had intact SMARCB1
SMARCB1 & EWSR1 are located close to each other on chr 22q.

Four tumors with SMARCB1 loss examined by EWSR1 FISH. (1x epithelioid sarcoma, 1 malignant rhabdoid tumor, 1 myoepithelial carcinoma & 1 poorly diff chordoma).

2 showed unbalanced split signals (bona fide translocation)

2 showed heterozygous deletion mimicking unbalanced transloc.
Small round cell variant of malignant rhabdoid tumor closely mimicking Ewing sarcoma: false + EWSR1 FISH.
Thank you for your attention

It´s the phenotype, stupid!
(comment posted in Dr. David Page´s sign-out area;
(Juan Rosai, Ackermann´s Surgical Pathology)