61st Annual Diagnostic Slide Session 2020

Case 10

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No financial disclosures
Case 10
Clinical summary

- 50-year-old woman
  - Several falls due to syncope with loss of consciousness
Diagnosis?
Desmin negative markers include:

- Myogenin
- MyoD1
- SMA
- STAT6
- Bcl-2
- CD34

Positive markers include:

- S100
- SOX10
- CD138
- AE1/AE3
- CD56
Sarcoma Targeted Gene Fusion Panel

**EWSR1-ATF1 fusion**

*EWSR1*: NM_005243:E7

*ATF1*: NM_005571:E5
Diagnosis:

Angiomatoid fibrous histiocytoma with rhabdoidoid features
Angiomatoid fibrous histiocytoma (AFH)

- Rare, primarily in the extremities of young people
- Encapsulated, with hemorrhagic pseudocystic spaces lacking endothelium
- Variable lymphoplasmocytic inflammation

Thway K et al. Arch Pathol Lab Med. 2015
Chen G et al. Mod Pathol. 2011
Angiomatoid fibrous histiocytoma (AFH)

- Histiocyte-like cells
- Rhabdoid features uncommon
- Variable EMA, desmin, SMA, CD68, and CD99 expression

Recurrent gene fusions involving $EWSR1$ and $FUS$ with members of the cAMP response element binding protein ($CREB$) family ($CREB1$, $ATF1$, and $CREM$)

$EWSR1$-$CREB1$
Intracranial AFH

• Usually in children and young adults
• Intra or extra-axial
• Prominent myxoid features (uncommon in extracranial AFH)
• Overlap with intracranial myxoid mesenchymal tumor
  • AFH-like tumors
Intracranial myxoid mesenchymal tumor (MMT)

- Recently described entity
- Variable myxoid background
- Resembles the myxoid variant of AFH
- Shares genetic alterations with AFH (frequent fusions of *EWSR1* and *CREB* family genes)
## IC AFH, AFH-like and MMT

<table>
<thead>
<tr>
<th>Case #</th>
<th>Reference</th>
<th>Age/Sex</th>
<th>Location</th>
<th>Diagnosis</th>
<th>Molecular fusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dunham et al. (2008)</td>
<td>25/M</td>
<td>Occipital</td>
<td>AFH</td>
<td>EWSR1-ATF1</td>
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<tr>
<td>2</td>
<td>Ochalski et al. (2010)</td>
<td>35/M</td>
<td>Temporal</td>
<td>AFH</td>
<td>EWSR1 rearrangement</td>
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<td>3</td>
<td>Hansen et al. (2015)</td>
<td>17/F</td>
<td>Extra-axial (occipital)</td>
<td>AFH</td>
<td>EWSR1 rearrangement</td>
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<tr>
<td>4</td>
<td>Alshareef et al. (2016)</td>
<td>58/F</td>
<td>CPA/middle cranial fossa</td>
<td>AFH</td>
<td>EWSR1 rearrangement</td>
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<tr>
<td>5</td>
<td>Kao et al. (2017)</td>
<td>15/F</td>
<td>Meningeal</td>
<td>MMT</td>
<td>EWSR1-CREM</td>
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<td>6</td>
<td>Kao et al. (2017)</td>
<td>23/F</td>
<td>Meningeal (occipital)</td>
<td>MMT</td>
<td>EWSR1-CREB1</td>
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<tr>
<td>7</td>
<td>Kao et al. (2017)</td>
<td>20/M</td>
<td>Parenchymal (frontal)</td>
<td>MMT</td>
<td>EWSR1-CREB1</td>
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<td>8</td>
<td>Kao et al. (2017)</td>
<td>12/M</td>
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<td>9</td>
<td>Spatz et al. (2018)</td>
<td>22/F</td>
<td>Right occipital</td>
<td>AFH</td>
<td>Not assessed</td>
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<td>Gareton et al. (2018)</td>
<td>19/M</td>
<td>Intra and extra-axial (CPA)</td>
<td>AFH-like</td>
<td>EWSR1-CREM</td>
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<td>Parenchymal (frontal)</td>
<td>MMT</td>
<td>EWSR1-ATF1</td>
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<tr>
<td>12</td>
<td>Bale et al. (2018)</td>
<td>12/M</td>
<td>Abutting dura (posterior fossa/cerebellar)</td>
<td>MMT</td>
<td>EWSR1-CREB1</td>
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<td>13</td>
<td>Bale et al. (2018)</td>
<td>14/F</td>
<td>Intraventricular (left lateral)</td>
<td>MMT</td>
<td>EWSR1-CREB1</td>
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<td>14</td>
<td>Bale et al. (2018)</td>
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<td>Falcine (frontal)</td>
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<td>Konstantidinis et al. (2019)</td>
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<td>Frontal</td>
<td>AFH</td>
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<td>16</td>
<td>Konstantidinis et al. (2019)</td>
<td>12/F</td>
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<td>9/M</td>
<td>Falcine (frontal)</td>
<td>MMT</td>
<td>EWSR1-CREM</td>
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<td>Komastu et al. (2020)</td>
<td>Middle age/F</td>
<td>Intraventricular (3rd ventricle)</td>
<td>MMT</td>
<td>EWSR1-CREB1</td>
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<td>Ballester et al. (2020)</td>
<td>67/M</td>
<td>Abutting dura (temporal)</td>
<td>MMT</td>
<td>EWSR1-ATF1</td>
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</tbody>
</table>
Conclusions

1. AFH shows a non-specific immunophenotype, but demonstrates recurrent \textit{EWSR1-CREB} gene rearrangements

2. Intracranial AFH frequently shows myxoid change and shares histologic and genetic features with intracranial myxoid mesenchymal tumor

3. Rhabdoid features in AFH are rare and it is important to distinguish it from other mimics, particularly rhabdoid meningioma
Rachael Vaubel, M.D., Ph.D. and Karen Fritchie, M.D.

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