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Clinical Summary

- 5-year-old boy who presented with acute-onset nausea and vomiting
- Initially believed to have appendicitis, but later developed a fixed, dilated right pupil
Imaging

- CT demonstrated right frontal mass with sulcal effacement, midline shift, and early herniation
- DDx: Abscess vs tumor
- Mass was resected
  - Described as gelatinous and friable, non-infiltrating intraparenchymal mass
  - No bony or dural attachment
Differential Diagnosis?

- Immunohistochemical stains?
## Immunohistochemical work-up

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>INI1/BRG (Retained)</td>
<td>GFAP</td>
</tr>
<tr>
<td>CD99 (weak, dot-like)</td>
<td>EMA</td>
</tr>
<tr>
<td>S100 (restricted to chondroid areas)</td>
<td>NKX3.1</td>
</tr>
<tr>
<td>WT-1 (patchy, cytoplasmic)</td>
<td>Synaptophysin</td>
</tr>
<tr>
<td>Mixed CK (AE1/CAM5.2)</td>
<td>SALL4</td>
</tr>
</tbody>
</table>
Molecular testing

- CIC-NUTM1 fusion with rearrangement of exon 17
  - No additional pathogenic/likely pathogenic alterations
- Methylation profiling matched to CIC-rearranged sarcoma
CIC-rearranged Sarcoma

- Recent addition to the WHO; previously described with “Ewing-like sarcomas”
- Rare sarcoma arising in the central nervous system
  - May be bone, dural, or parenchymal-based
  - Identical tumor in peripheral soft tissues and viscera (rarely bone), frequently harboring CIC-DUX4 fusion
- Typically a tumor of adolescents and young adults, though reported age range is wide
Typically described as a poorly-differentiated sarcoma
- Epithelioid to spindled cells with hyperchromatic, irregular nuclei and variable eosinophilic cytoplasm generally arranged as sheets or cords
- Myxoid background is frequently reported
- Numerous mitotic figures and karyorrhectic cells present
- Well-demarcated border with surrounding brain/spinal cord parenchyma

Immunohistochemistry shows no clear line of differentiation
- CD99+ (membranous or dot-like), WT-1 +/-
- ETV4 positivity is reported in most cases
  - ETV3 and ETV5 expression is also present
- Negative for S100, SOX10, PAX7, GFAP, NKX2.2, Synaptophysin

Variety of fusions reported; histology, immunophenotype, and methylation overlap
- CIC-NUTM1
- CIC-NUTM2
- CIC-DUX4
- ATXN1-NUTM1
- ATXN1-DUX4

ETV4 is a useful marker for the diagnosis of CIC-rearranged undifferentiated round-cell sarcomas: a study of 127 cases including mimicking lesions

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### Table 2: Immunohistochemical features of CIC-rearranged round-cell sarcomas

<table>
<thead>
<tr>
<th>Case</th>
<th>CD99</th>
<th>Cyclin B3</th>
<th>Fli1</th>
<th>ERG</th>
<th>WT1 (N-TE1H)</th>
<th>WT1 (L-TE1H)</th>
<th>ETV4</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>(%)</td>
<td>(%), intensity, location</td>
<td>(%)</td>
<td>(%), intensity, location</td>
<td>(%)</td>
<td>(%), intensity, location</td>
<td>(%)</td>
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</table>

Abbreviations: C, cytoplasmic; Pos, m, membranous positivity; N, nuclear; ND, not done.
Chondroid Differentiation

Brain tumor with an ATXN1-NUTM1 fusion gene expands the histologic spectrum of NUTM1-rearranged neoplasia

Aurore Siegfried, Julien Maslah-Planchon, Franck-Emmanuel Roux, Delphine Larrieu-Giron, Gaelle Pierron, Yvan Nicaise, Marion Gambart, Isabelle Catala, Sarah Periant, Charlotte Dubucs, Badreddine Mohand-Oumoussa, Franck Tirode, Franck Bourdeau, and Emmanuelle Uro-Coste

*Adapted from Siegfried et. al. figure 1

*CIC-NUTM1 fusion: A case which expands the spectrum of NUT-rearranged epithelioid malignancies

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*Adapted from Schaefer et. al. figure 2
Differential diagnosis

- Ewing sarcoma-CD99 diffuse membranous expression, ETV4 negative, EWSR1 rearrangement
- Atypical teratoid/rhabdoid tumor-INI1/BRG1 loss
- Mesenchymal chondrosarcoma-HEY1-NCOA2 fusion
- Extraskeletal myxoid chondrosarcoma-INSM1+, EWSR1-NR4A3 rearrangement typical
- High-grade glioma-GFAP, OLIG2+; primitive neuronal component-RB1 loss/MYCN or MYC amplification
References


