New Sarcoma Defined by BCOR-CCNB3 Fusion

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Case History

- 13 year old male
- Left pelvic mass
Pediatric Round cell Sarcomas

- Rhabomyosarcoma
- Ewing sarcoma/PNET
- Neuroblastoma
- Lymphoma/ leukemia
- Small cell osteosarcoma
- Mesenchymal chondrosarcoma

- Sclerosing RMS
- BRD/NUT carcinoma
- Extrarenal rhabdoid tumor
- Desmoplastic small round cell tumor
- Undifferentiated sarcoma
## Immunostains

<table>
<thead>
<tr>
<th>Positive</th>
<th>Negative</th>
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<tbody>
<tr>
<td>CD99 (Weak)</td>
<td>synaptophysin</td>
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<tr>
<td>BCL-2</td>
<td>desmin, myogenin</td>
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<tr>
<td>CD56</td>
<td>S100 protein</td>
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<td>CD31</td>
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<td>EMA and CK-MNF</td>
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<td>FLI-1</td>
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EWSR1 Fusion Partners

- **FLI1** (85%)
- **ERG** (5-10%)
- **FEV**
- **ETV1**
- **E1Af**
Working Diagnosis

Small round blue cell tumor of the bone

- FISH is negative for EWSR1 rearrangement
EWSR1 fusion negative Ewing sarcoma

• Rare
• FUS FISH
• **FUS-ERG** or **FUS-FEV**
Diagnosis?

DX:
Undifferentiated spindle and round cell sarcoma.
Undifferentiated sarcoma

- Fusion negative Ewing-like neoplasms
- CD99: Positive, focal or negative.
- Proportion of cases shows new fusion CIC-DUX4
- t(4;19)
- t(10;19)
Consultation

*CIC-DEX4* gene fusion negative

The tumor instead showed *BCOR-CCNB3* fusion.
Fusion-specific RT-PCR to screen a series of 594 sarcomas.

24 $BCOR$-$CCNB3$–positive tumors were identified
• Gene profiling experiments indicated that $BCOR-CCNB3$–positive cases are biologically distinct from other sarcomas, particularly Ewing sarcoma.

[Birth notice: a new bone sarcoma has been born].

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Comment on
**BCOR-CCNB3 Sarcoma**

- Clinical description is similar to Ewing Sarcoma.
- Median age 13 years
- Male predominance
- Preferentially long bones, the spine and pelvis.

- 20%: soft tissue tumor.
Pathology

- Undifferentiated, small round cell sarcoma, suggestive of the Ewing sarcoma.
- Half lacked strong membrane positivity for CD99.
BCOR and CCNB3 Genes

• Both on the X chromosome
• **BCOR** encodes ubiquitous transcriptional repressor that associates with BCL6 oncoprotein
• **CCNB3** expression is tightly restricted to the testis, with CCNB3 encoding an early meiotic cyclin.
• Ectopic expression of CCNB3 as a result of the BCOR gene fusion may constitute a key oncogenic event.
Undifferentiated/ unclassified Sarcomas

• Introduced a chapter on undifferentiated sarcomas.
• No reproducible immunophenotype.
• Patchy CD99
• CD34+-: No discriminatory value.
• EM: No evidence of differentiation.
Ewing or Ewing look-alike?

Undifferentiated Sarcoma

CIC-DEX4 sarcoma?  BCOR-CCNB3 sarcoma


