Diagnostic Slide Session
2023 Case 9

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Clinical History

• 62-year-old male with a history of mild Hemophilia A who presents with recurrent episodes of syncope
Imaging
Differential diagnosis?
Olig2

GFAP
Immunohistochemical Workup

**Positive**
- GFAP
- Olig2

**Negative**
- P53
- IDH1-R132H
- Synaptophysin
- Chromogranin
- NeuN
- BRAF V600E
- H3 K27M

**Retained**
- H3 K27me3
- ATRX (subset)
Ancillary Studies

- **TERT promoter mutation (TERT promoter -124C>T)**
- FISH for 1p & 19q shows no co-deletions
- FISH for EGFR shows no amplification
- MGMT promoter methylation is ABSENT
Ancillary Studies

- AKT2 & EWSR1-PATZ1 fusions

### NGS TEST: RNA Exome Fusion Panel v1.0

**STRUCTURAL VARIANTS: FUSION**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Transcripts</th>
<th>Genomic Location</th>
<th>Reads</th>
<th>Pathogenicity Assessment</th>
<th>Tier*</th>
</tr>
</thead>
<tbody>
<tr>
<td>EWSR1-PATZ1</td>
<td>e7 : e1</td>
<td>chr22:29885737 - chr22:31740542</td>
<td>54</td>
<td>Likely Pathogenic</td>
<td>Tier 3</td>
</tr>
<tr>
<td>PATZ1-NIPSNAP1</td>
<td>e1 : e4</td>
<td>chr22:31740747 - chr22:29961074</td>
<td>13</td>
<td>Uncertain Significance</td>
<td>Tier 3</td>
</tr>
</tbody>
</table>

*Tier: Actionability Classification

### 1 - FUSION VARIANT INTERPRETATION

**Result:** 1 relevant variant is detected in this study.

**Summary:** EWSR1-PATZ1 fusion was detected with a total of 54 reads, and is consistent with a recent study of 60 predominantly pediatric CNS neoplasms harboring PATZ1 fusions for which DNA methylation profiling defined a biologically distinct molecular class of histologically polyphenotypic neuroepithelial tumors [PMID: 34417833].
Methylation Profile

- Methylation profile on the version 12.5 of Heidelberg classifier matches to neuroepithelial tumor with PATZ1 fusion with a high confidence score
  - EWSR1-PATZ1 fusion found on NGS is consistent with this methylation class
Integrated Diagnosis

- Neuroepithelial tumor with PATZ1 fusion
  - TERT promoter mutation (TERT promoter -124C>T)
  - MGMT promoter methylation ABSENT
  - AKT2 R371H mutation
Neuroepithelial tumor with PATZ1 fusion

- Novel entity
- Histologically heterogenous tumors of different grades
- Varied immunophenotypes
Neuroepithelial tumor with PATZ1 fusion

- Median age at diagnosis 11 years
  - 74% under 18 years
- Located in supratentorial region but rarely in posterior fossa
- Intermediate prognosis
- Currently no therapies available for directly target alterations in EWSR1
Patient Follow-Up

- Completed radiation therapy
- Continues temozolomide
References


