AANP 2021
Diagnostic Slide Session Case 8
Submitted by Drs. Calixto-Hope Lucas, Andrew Bollen, and David Solomon
University of California, San Francisco
Clinical presentation

• Infant boy born at gestational age 37 weeks and 2 days with a vascular brain lesion noted on prenatal imaging.
• MR imaging at 1 week of age showed a 7 cm hyper-vascular right parieto-occipital lesion with significant mass effect on the cerebellum and midbrain.
• He underwent preoperative embolization and subtotal resection at 2 weeks of age.
• Intraoperative findings include a large, white, highly vascular tumor occupying the right parieto-occipital space.
Differential diagnosis?
GFAP

OLIG2

Synaptophysin

Neurofilament

CD34

Ki-67
**Pathogenic or Likely Pathogenic SOMATIC ALTERATIONS**

<table>
<thead>
<tr>
<th>VARIANT</th>
<th>TRANSCRIPT ID</th>
<th>CLASSIFICATION</th>
<th>READS</th>
<th>MUTANT ALLELE FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>LRRFIP1-ALK in-frame gene fusion</td>
<td>NM_001137552, NM_004304</td>
<td>Pathogenic</td>
<td>256 over fusion junction</td>
<td>N/A</td>
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</tbody>
</table>

**LRRFIP1 (chr 2q37)  ALK (chr 2p23)**

*DNA methylation profiling revealed an epigenetic signature aligning with “infantile hemispheric glioma” (DKFZ calibrated score: 0.97)*
Integrated diagnosis: Infant-type hemispheric glioma

*Infant-type hemispheric glioma represents a new tumor entity in the upcoming 5th edition of the CNS WHO 2021

2.1.2.4: Infant-type hemispheric glioma

Definition
A cerebral hemispheric, cellular, high grade astrocytoma presenting in early childhood, typically with receptor tyrosine kinase (RTK) fusions including those in the NTRK family, ROS1, ALK or MET.

Differential diagnosis - imaging

- **DIG/DIA** are solid/cystic with large cystic spaces.
- **IHG** are less well-defined but may be more solid/less cystic.
Differential diagnosis - histology

• **DIG/DIA** typically have:
  • prominent desmoplasia and reticulin deposition
  • low Ki-67 labeling usually
  • scattered foci of primitive-appearing cells in some cases

• **IHG** are less well-defined but often:
  • appear histologically high-grade
  • show an elevated Ki-67 labeling
  • can have palisading necrosis and microvascular proliferation

*This tumor had a mostly circumscribed growth pattern devoid of entrapped axonal processes.

(are infant-type hemispheric gliomas “diffuse/infiltrative” gliomas?)

* This tumor demonstrated dural invasion, mimicking the desmoplasia associated with DIG/DIA.

Ancillary testing:

• Next generation sequencing can help to differentiate DIG/DIA (enriched for \textit{BRAF} mutations, particularly non-p.V600E variants) from IHG (enriched for \textit{ALK}/\textit{ROS}/\textit{MET}/\textit{NTRK} fusions).

• DIG/DIA and IHG have distinct epigenetic signatures and DNA methylation profiling can also be helpful as an ancillary diagnostic tool.
References:


