Clinical History

- 14 mo old twin girl with regression of milestones (loss of “dada” and “mama”) and difficulty in balance (“shaky and takes small steps”)
  - Recent viral gastroenteritis 2 mo prior and viral URI 2 wk prior to presentation

Radiologic Interpretation

- There is a mildly heterogeneous posterior fossa tumor centered in the upper fourth ventricle. The tumor measures 5.5 cm transverse x 5.9 cm AP x 6.9 cm craniocaudal.
  - There is inferior extension of the tumor towards foramen Magendie.
  - There is superior and anterior extension of the tumor over the cerebellar peduncles into the ambient and quadrigeminal plate cisterns, left side worse than right, with compression and deformity of the pons and midbrain with the brainstem displaced anteriorly. The tectum and pineal gland are not identified with tumor in the expected location of the structures.

Imaging Impression

- 6.9 cm minimally enhancing tumor centered in the upper fourth ventricle with associated severe obstructive third and lateral ventricular hydrocephalus with transependymal edema
  - Tumor extends above the tentorium beneath the parasagittal occipital and temporal lobes, left side greater then right with possible involvement of the left occipital lobe
  - Unclear whether the tumor is of superior cerebellar origin or pineal origin given its extensions, but the differential diagnosis includes medulloblastoma, ATRT, and pineoblastoma
  - Note that there is encasement of arteries and veins. There may also be minimal hemorrhage in the lesion.
Immunohistochemistry

What Now?
Biallelic genetic alterations of the \textit{INI-1}/\textit{SMARCBI}/\textit{hSNF5}/\textit{BAF47} gene on 22q11.2

\textit{INI-1} encodes a protein that is a member of the ATP-dependent switching/sucrose non-fermentable (SWI/SNF) complex important in chromatin remodeling and cell cycle regulation.

Studies have shown alterations including large deletions, mutations (in exons 5 and 9) and loss of heterozygosity (LOH).

Recent publication (December 2016), Cancer Cell.

Multi-institutional

191 primary ATRTs and 10 cell lines were analyzed

Three epigenetic subgroups with distinct profiles identified

Differential methylation of a PDGFRB-associated enhancer selective sensitivity to dasatinib and nilotinib
Other Markers for AT/RT and Other Tumors with INI Loss

- **Claudin 6** identified by microarray analysis and reported in AT/RT and not in medulloblastoma/other “PNET”
  - IHC for CLDN6 closely matched the mRNA expression
- **CRINET** (cribriform neuroepithelial tumor) also found to have **INI1 loss** but significantly better prognosis

ATRT “Pearls”

- Consider ATRT in the differential with small round blue cell tumors
  - Especially in the absence of “rhabdoid” cells
- **INI-1 loss** of nuclear expression is diagnostic using multiple methods including immunohistochemistry (BAF-47)
- Other immunohistochemical markers often used include synaptophysin, neurofilament protein, Neu-N and GFAP
- FISH may be useful to separate embryonal tumors (formerly PNETs) and ATRT

Treatment and Outcomes in ATRT

- Chemotherapy (may include intrathecal) and adjuvant radiation
- Gross total resection improves survival, although it generally remains poor (usually less than 2 years even with GTR)
- Youngest children have most aggressive disease
- Cognitive impairment may be sequelae of therapy

References: