Case 2014-5

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Our Case

- 5 year old girl
- Bilateral lower extremity weakness for ~ 2 hours resulting in a fall during walking
- Headache for ~15 minutes with one episode of emesis
- PMH: Developmental delay, macrocephaly, seizure disorder (for 1 year, controlled on Depakote), and cerebellar tonsillar ectopia
  - Periodic radiographic studies to assess for hydrocephalus
    - No masses or hydrocephalus were identified on the most recent CT scan performed 20 months prior
She was placed on steroids and underwent tumor resection a few days after presentation.
Differential Diagnoses?
Differential Diagnoses

• Atypical Teratoid/Rhabdoid Tumor
• Pleomorphic Xanthoastrocytoma
• Ganglioglioma
• Anaplastic large cell lymphoma
• Juvenile xanthogranuloma
• Inflammatory myofibroblastic tumor
• Melanocytic tumor (primary vs. metastasis)
• Meningioma
• Germ cell tumor
Negative Immunohistochemical Stains

- GFAP
- hSNF5/INI-1/SMARCB1 (retained nuclear staining)
- S100
- Synaptophysin
- HMB-45
- CD45, CD2, CD3, CD5, CD30, CD68
- Epithelial membrane antigen
- Myogenin
- Placental alkaline phosphatase
- p53

Cytogenetic studies for Anaplastic Large Cell Lymphoma were negative
Vimentin
Anaplastic Lymphoma Kinase (ALK)
11 cases (10 M, 1 F), all intra-abdominal tumors, 6 multifocal.

Age range: 7 months to 63 years (median=39 years)

Tumor size: 8-26 cm in greatest dimension

Median survival (n=5): 12 months
  - Only one patient with NED at 40 months, on an ALK-inhibitor
Inflammatory Myofibroblastic Tumors

- Median age: 9-10 years, slight female predilection
- Usually occur in the lung or abdomen
- Intracranial IMTs are rare
  - Usually dural-based
  - Spindle cell neoplasms with three common growth patterns:
    - Nodular fasciitis-like
    - Fibromatosis-like
    - Desmoid/scar-like
- Other names for IMT:
  - Inflammatory pseudotumor
  - Plasma cell pseudotumor
  - Plasma cell granuloma
  - Inflammatory myofibrohistiocytic proliferation
  - Omental-mesenteric myxoid hamartoma
  - Inflammatory fibrosarcoma
Inflammatory Myofibroblastic Tumors

• ~50% have clonal rearrangements of ALK gene (2p23)
  • Fused to RANBP2, TPM3, TPM4, CLTC, CARS, ATIC, and SEC31L1
    • Fusion leads to the constitutive, ligand-independent ALK activation

• Tumors of intermediate biological potential
  – Clinical behavior and outcome do not correlate with histologic features
    • Tumor size, mitotic activity, necrosis, nuclear atypia

• Management: Surgical resection
Histologic Features of EIMS

- Epithelioid to round cells with variable amounts of amphophilic or eosinophilic cytoplasm
- Minor spindle cell component (<5% of the tumor)
- Vesicular nuclei with large nucleoli
- Median mitoses = 4/10 HPFs
- Background: myxoid, collagenous, or mixed
- Prominent inflammatory infiltrate
  - Neutrophils >> lymphoplasmacytic >> eosinophils
- Focal necrosis in half of the cases
Immunohistochemistry in EIMS

• All cases are ALK positive
  – Nuclear membranous (9 of 11 cases)
  – Cytoplasmic with perinuclear accentuation (2 of 11 cases)

• Positive markers
  – CD 30 (8 of 8 cases, and not positive in IMTs)
  – SMA (4 of 8 cases)
  – Desmin (10 of 11 cases)

• Negative markers
  – Caldesmon
  – EMA
  – S100
  – Myogenin
  – Cytokeratin
ALK Immunohistochemistry and Molecular Findings

Nuclear Membranous Staining

- \textit{RANBP2/ALK} fusion

Cytoplasmic with Perinuclear Accentuation

- Pattern likely due to normal localization of fusion partner

Our Case: Cytogenetics and Molecular Studies

- ALK FISH: Extra copies of ALK gene and 3’ end of ALK gene, suggestive of clonal rearrangement
- RT-PCR product for RANBP2/ALK fusion was negative
Summary

• Epithelioid Inflammatory Myofibroblastic Sarcoma is an aggressive variant of IMTs
• Have a distinctive clinical course, morphology, immunophenotype, and molecular findings
• This is the first intracranial case
  – Patient had multiple foci of leptomeningeal enhancement within one month surgery
  – She received radiation therapy (ended December 2013)
  – Lost to follow-up
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References


