Case 2014-5

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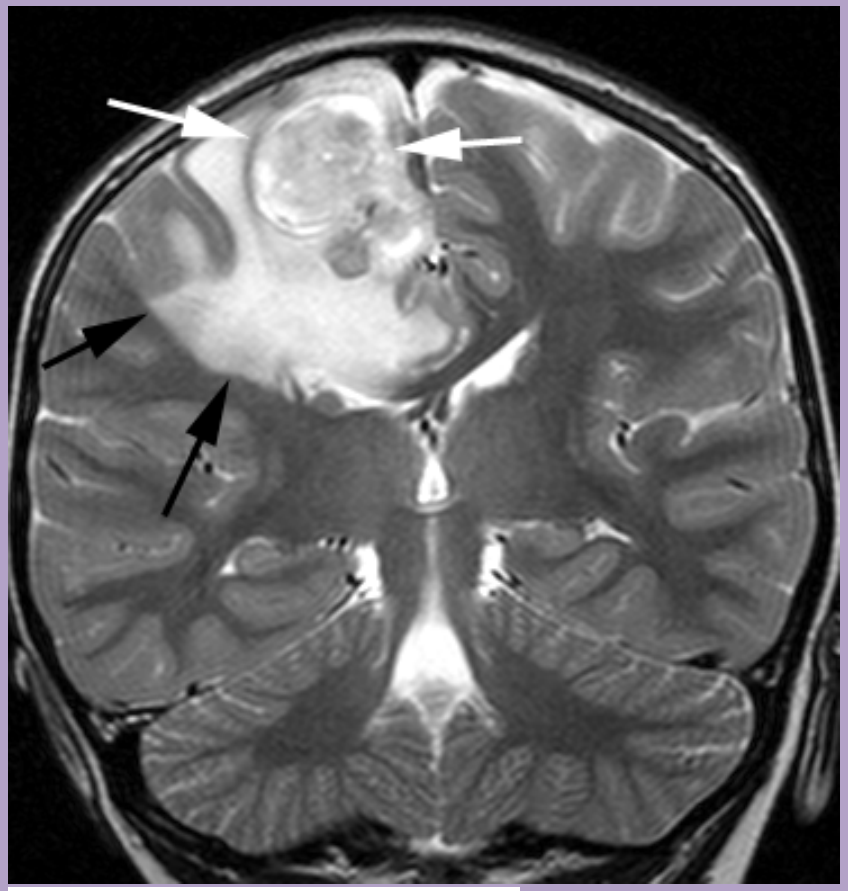
No financial or other disclosures

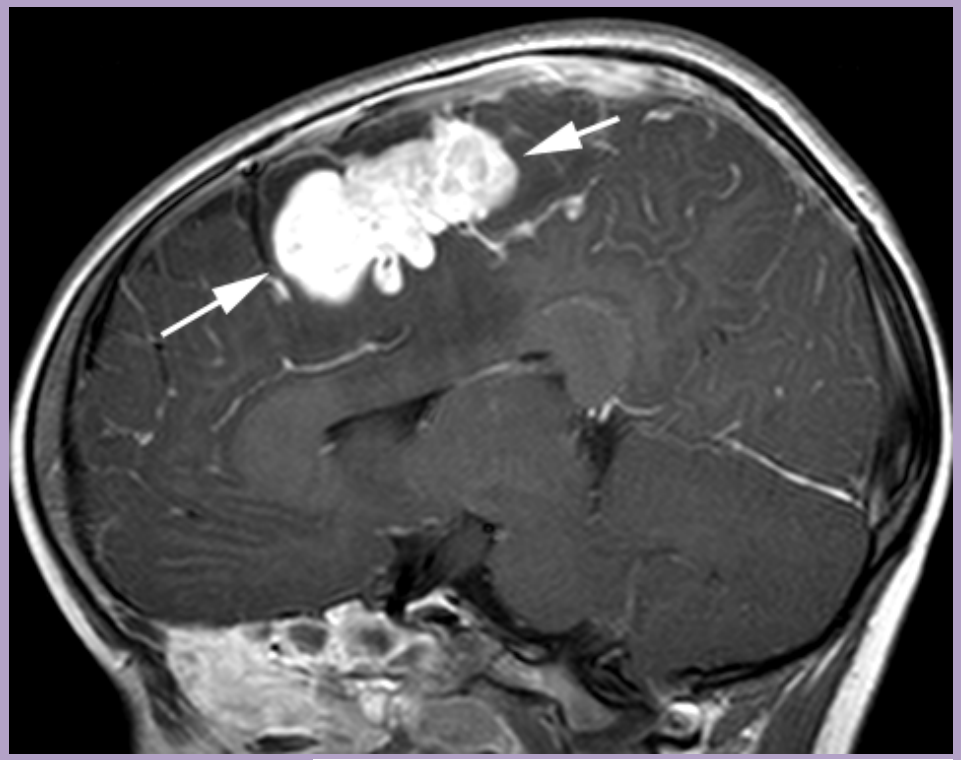
Our Case

- 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

MRI and Plan

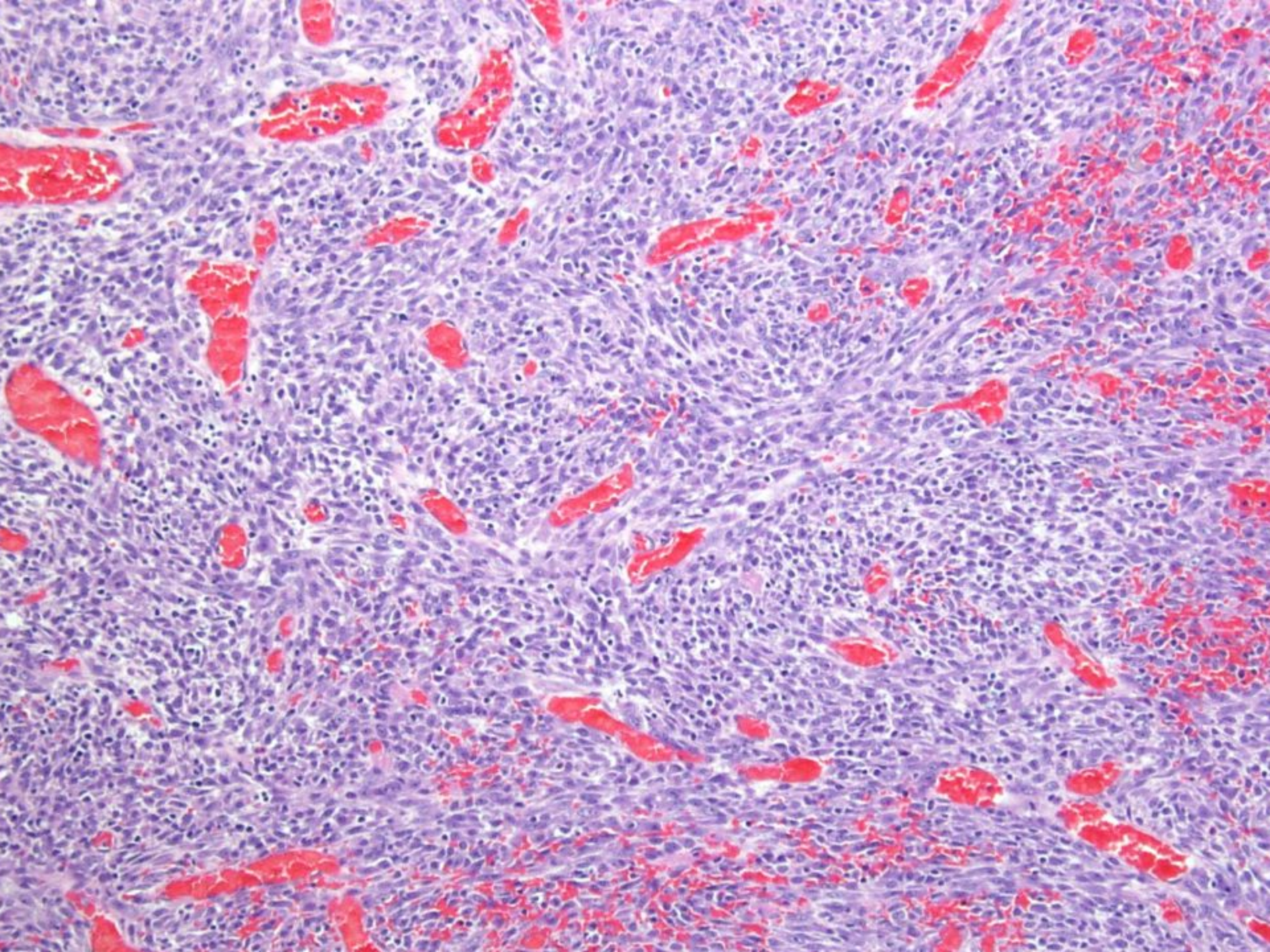


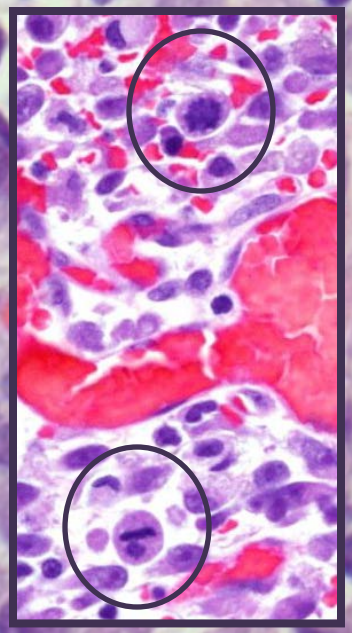
T2 weighted MRI Image



T1 weighted post contrast MRI

- She was placed on steroids and underwent tumor resection a few days after presentation.






Differential Diagnoses?

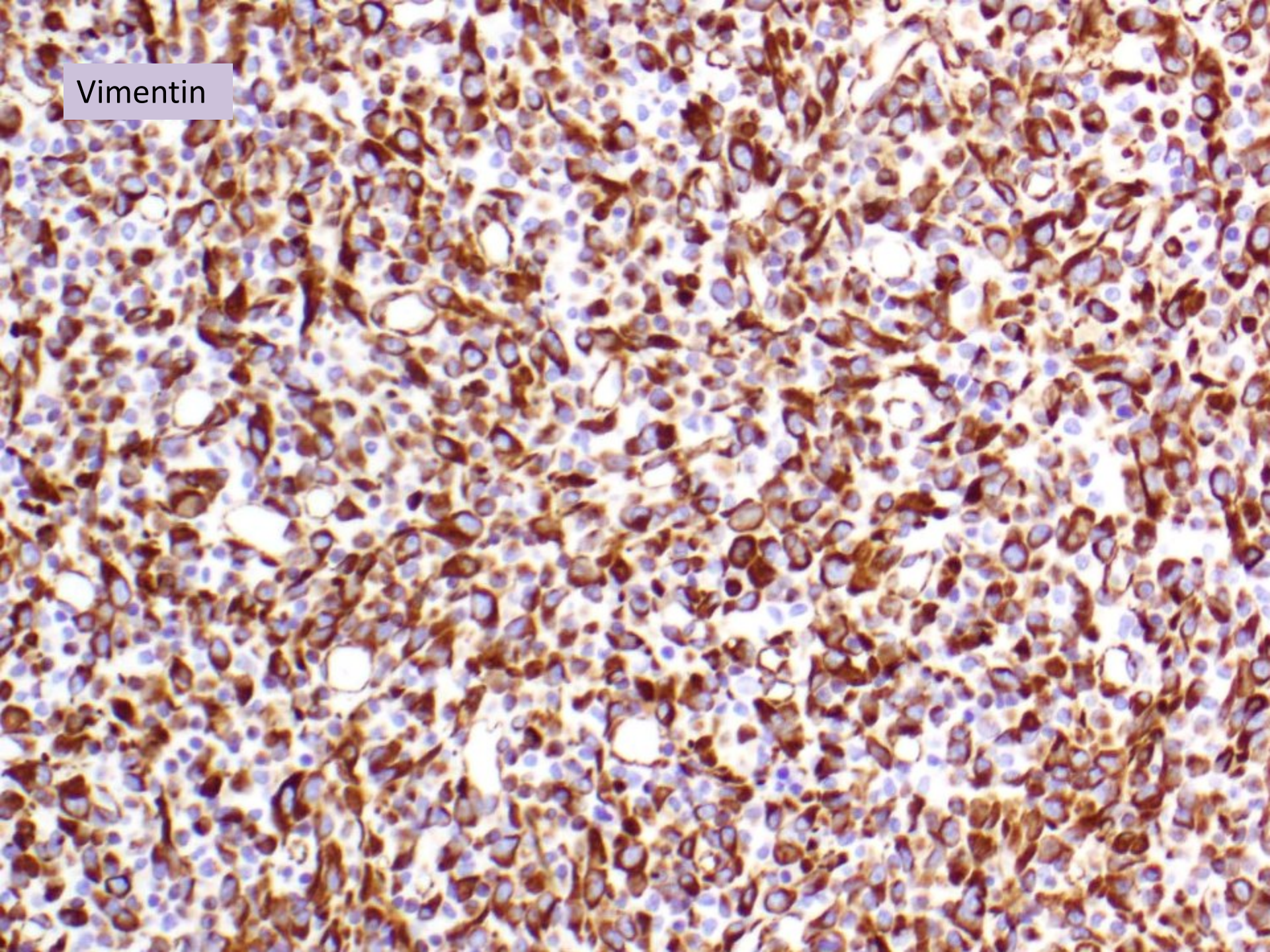
Differential Diagnoses

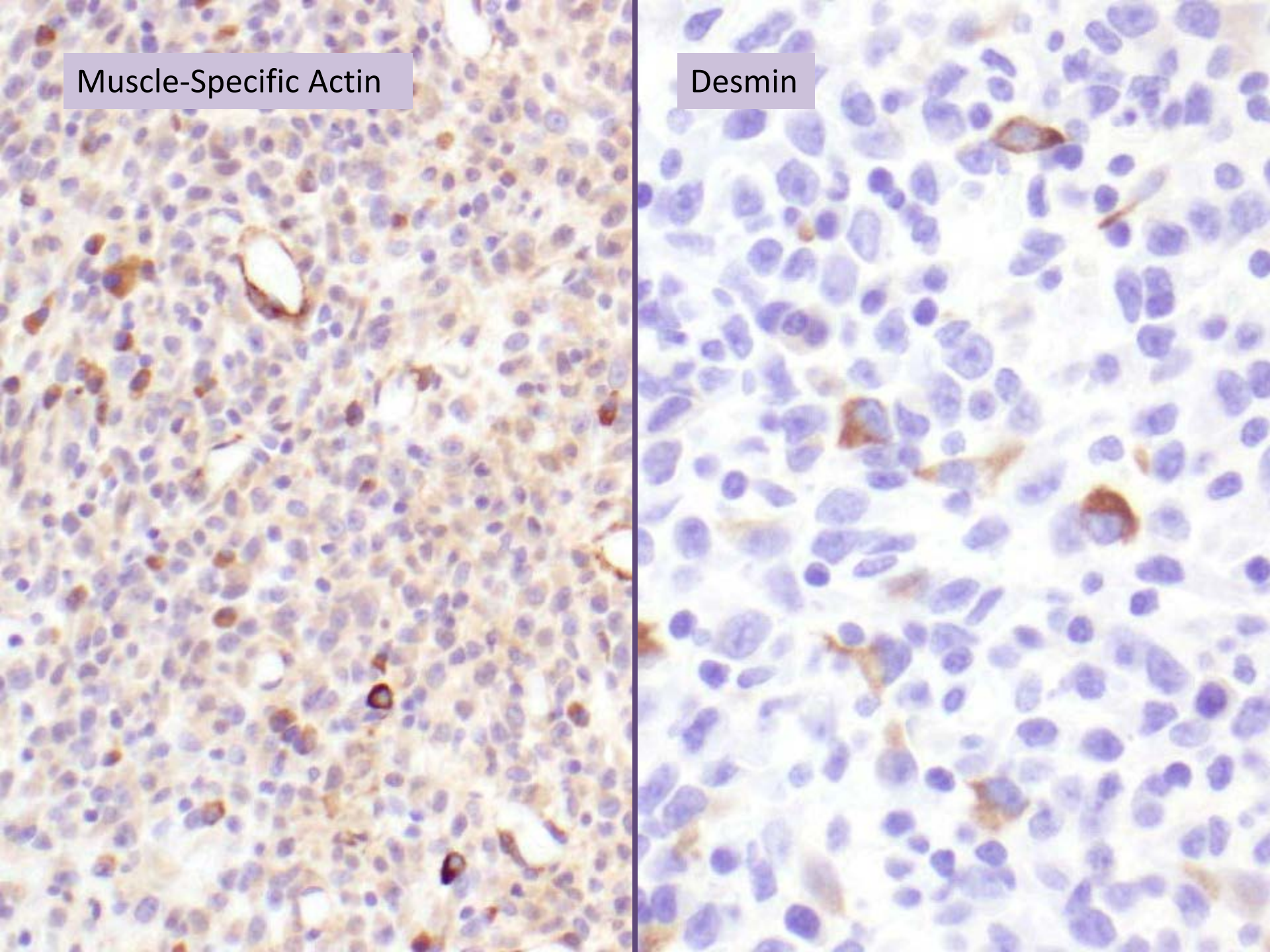
- Atypical Teratoid/Rhabdoid Tumor
- Pleomorphic Xanthoastrocytoma
- Ganglioglioma
- Anaplastic large cell lymphoma
- Juvenile xanthogranuloma
- Inflammatory myofibroblastic tumor
- Melanocytic tumor (primary vs. metastasis)
- Meningioma
- Germ cell tumor

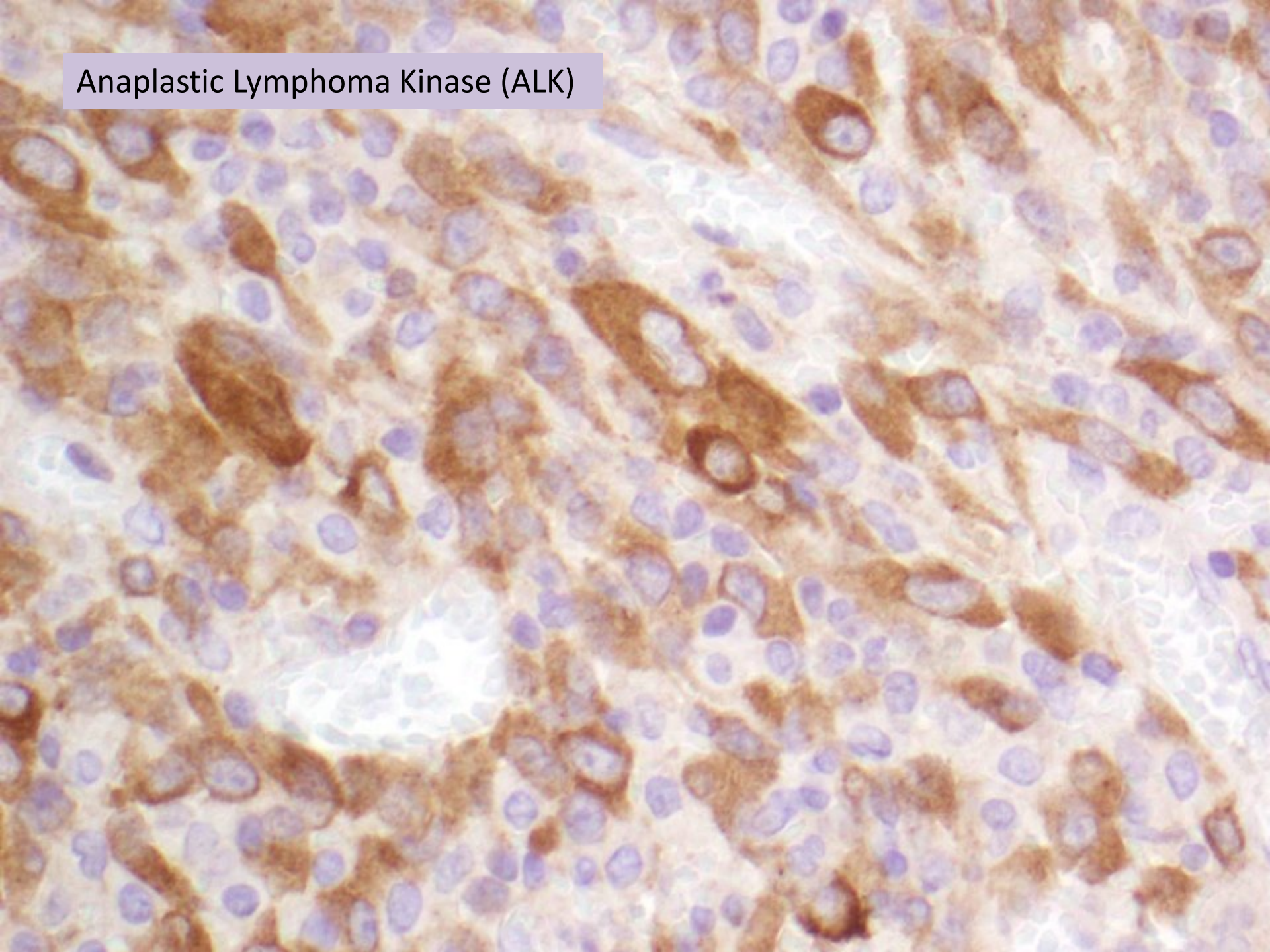
Negative Immunohistochemical Stains

- 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


Muscle-Specific Actin
Desmin


Anaplastic Lymphoma Kinase (ALK)

Epithelioid Inflammatory Myofibroblastic Sarcoma: An Aggressive Intra-abdominal Variant of Inflammatory Myofibroblastic Tumor With Nuclear Membrane or Perinuclear ALK

Adrián Mariño-Enríquez, MD,† Wei-Lien Wang, MD,‡§ Angshumoy Roy, MD, PhD,¶ Dolores Lopez-Terrada, MD, PhD,¶ Alexander J.F. Lazar, MD, PhD,‡§ Christopher D.M. Fletcher, MD, FRCPath,* Cheryl M. Coffin, MD,‖ and Jason L. Hornick, MD, PhD**

Am J Surg Pathol • Volume 35, Number 1, January 2011

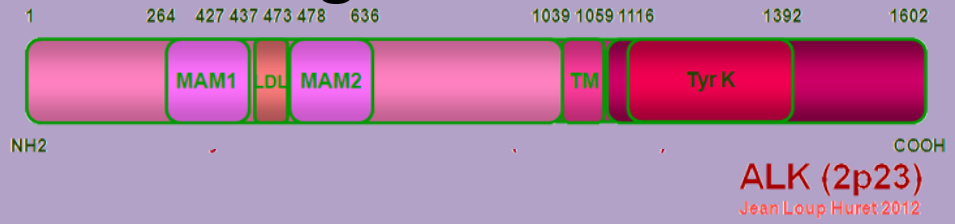
- 11 cases (10 M, 1 F), all intra-abdominal tumors, 6 multifocal
- Age range: 7 months to 63 years (median=39 years)
- Tumor size: 8-26 cm in greatest dimension
- Median survival (n=5): 12 months
    - Only one patient with NED at 40 months, on an ALK-inhibitor

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

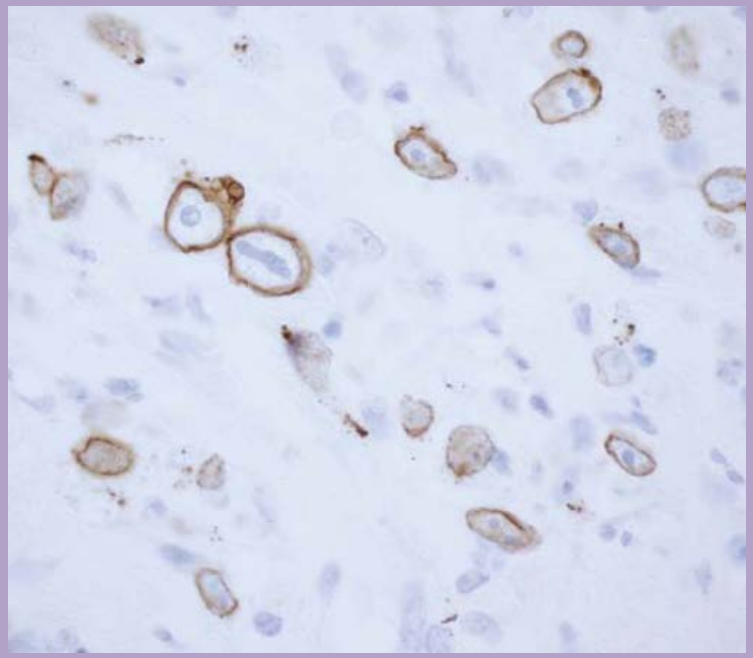
Immunohistochemistry in EIMS

- 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

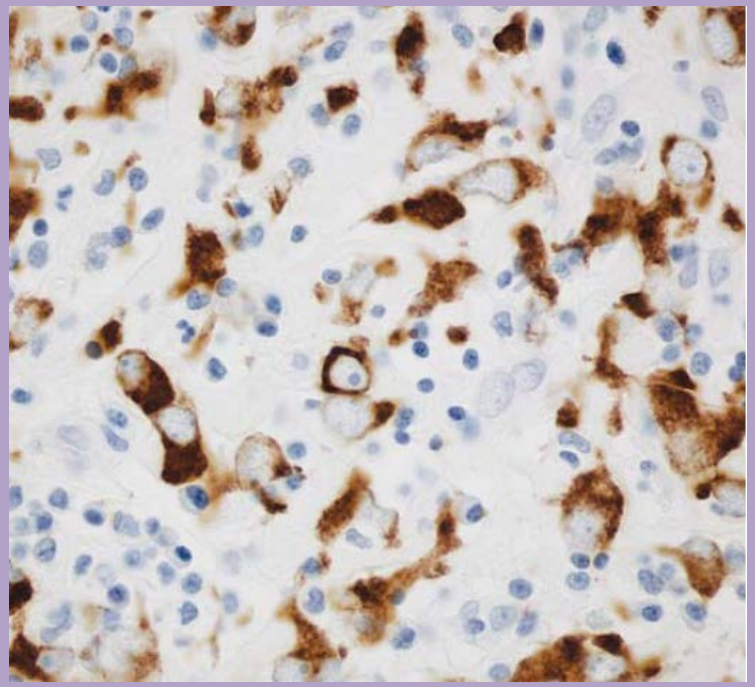
Nuclear Membranous Staining

- *RANBP2/ALK* fusion



Cytoplasmic with Perinuclear Accentuation

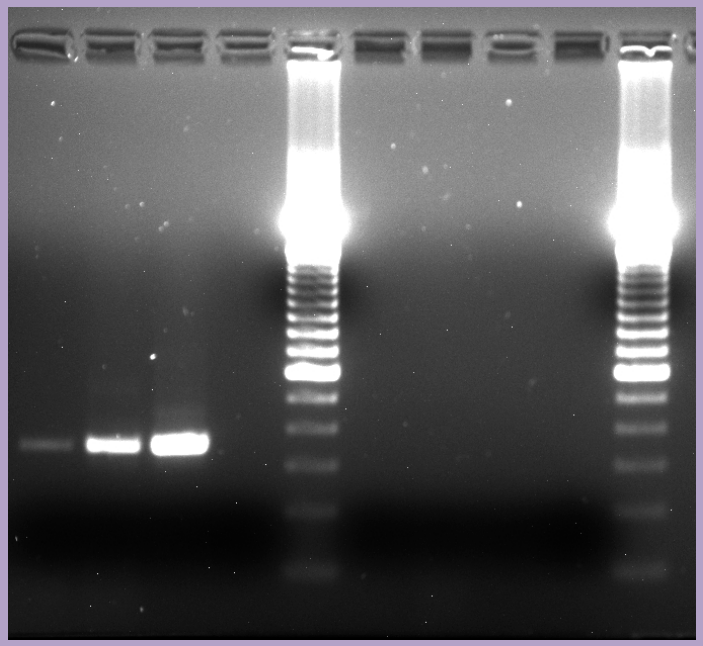
- Pattern likely due to normal localization of fusion partner

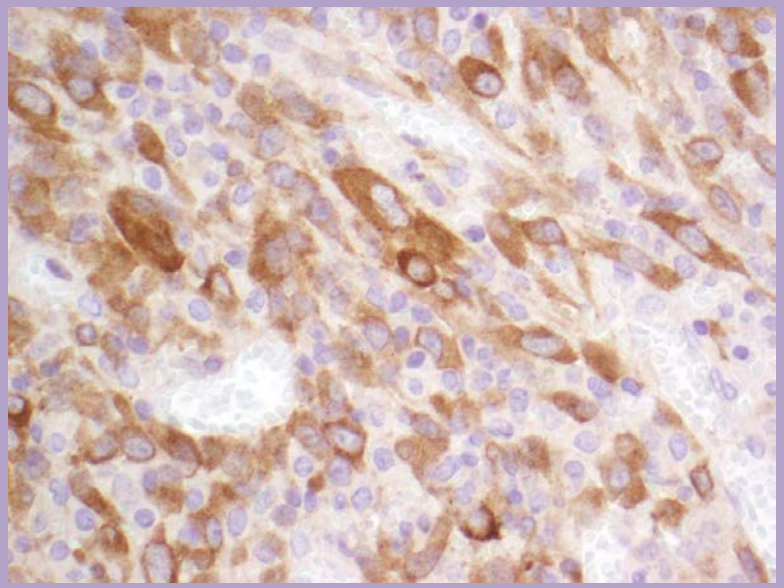


Marino-Enriquez A, et al. *Am J Surg Pathol* 2011;35:135-144.

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

Acknowledgements

- Texas Children's Hospital
  - Dr. Dolores Lopez-Terrada
  - Dr. Stephen F. Sarabia
  - Dr. Angushumoy Roy
- UT Southwestern
  - Dr. Charles White, III
  - Dr. Jack Raisanen
  - Dr. Kimmo Hatanpaa
  - Dr. Dennis Burns
  - Dr. Emily Herndon
- Northwestern University
  - Dr. Eileen Bigio
  - Dr. Qinwen Mao
  - Dr. Warren Tourtellotte

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