



# CIS case presentation

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# Initial presentation

- Presented at 3 years of age with failure to thrive
- Found to have ataxia and developmental delay
- Worsening ulcerated skin lesions
  - Punch biopsy → caseating granulomas



# Evaluation

- Hypogammaglobulinemia
- Poor protective pneumococcal titers post vaccination
  - (3/14 → 6/14 post-vaccination)
- Poor mitogen responses
  - (~30% of control function)
- Low CD4 count
- Elevated AFP
- DNA Sequencing
  - (IVS32+1 G>T) in *ATM* gene - known disease-causing splice site mutation
  - DNA variant of unknown significance in *ATM*

Immunoglobulin	mg/dl
IgG	211 (477-1334)

T cell function	
PHA control (CPM)	75316
PHA patient (CPM)	21174
Control background	212
Patient background	335

Lymphocyte subgroup (absolute)	Cells/ $\mu$ L
CD3+/CD4+ T	456 (500-2400)

	ng/mL
Alpha Fetoprotein	86 (0.6-11)

# Management and interval history

## Management:

- Minimizing exposure to radiation
- Immunoglobulin replacement
- TMP/SMX prophylaxis

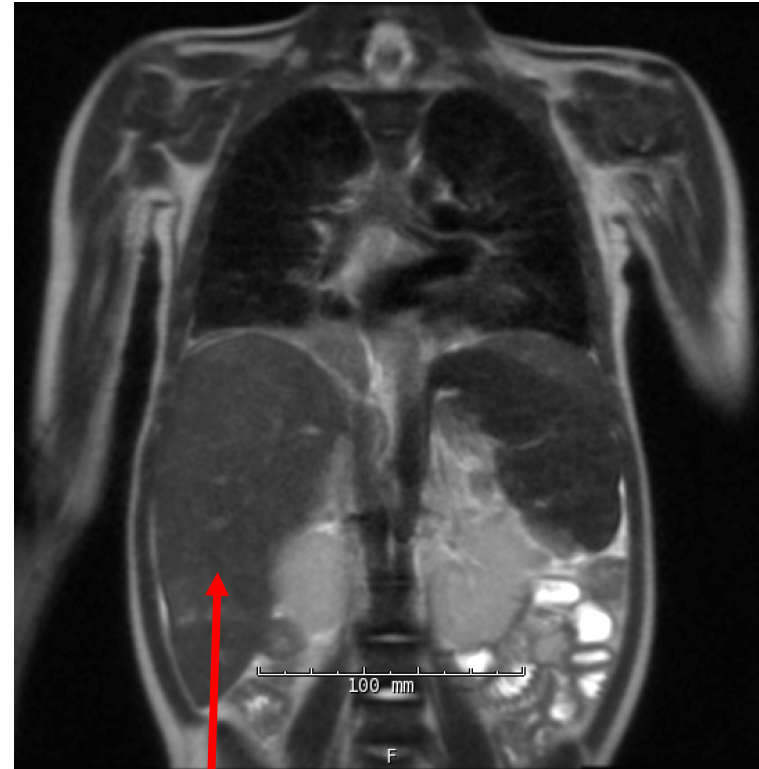
## Interval history:

- Longstanding positive EBV viral load

Virology	Initial presentation (3 years old)	Follow up (5 years old)	Follow up (6 years old)
EBV (copies/mL)	212,254	36,577	195,182

# Presentation 3 years later

- Persistently elevated fevers and hepatomegaly
- Whole body MRI concerning for malignancy in her liver, lungs and abdomen
- Liver biopsy
  - Diffuse large B-cell lymphoma (DLBCL)
  - CD20+ lymphocytes that contained EBV-encoded RNA (EBER)



Enlarged liver measuring 15 cm (normal size in child ~5 cm) with innumerable solid lesions

# Management

- Modified chemotherapy regimens
- Weekly rituximab
- Overall disease progression
- Transferred to MSK and treated with HLA-matched, EBV-specific cytotoxic lymphocytes (CTLs)
- Following therapy - tumors and liver decreased in size
- Seen by Immunology in July 2016 - stable and continues to follow
- This is the first reported case of the use of CTLs in the treatment of DLBCL in a patient with A-T who has been unresponsive to chemotherapy
- Should EBV positive patients with a high-risk of lymphoma be preemptively treated with agents such as Rituximab, prior to the occurrence of EBV-driven disease?

# Thank you!

- Dr. Puck (UCSF)
- Dr. Prockop (MSK)
- Dr. Heimall (CHOP)
- Dr. Sullivan (CHOP)



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Mayan Burial site in Western Belize, known locally as ATM