Mycobacterial Adenitis, Vaccine-strain Varicella, and Pneumonia in a 20 Month Old Girl

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Presentation

20 month old Hispanic female presenting with a several week history of persistent cough and fever.

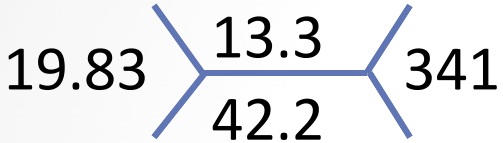
- CXR demonstrating RUL infiltrate
- Cough and fever returned upon completion of antibiotic course, so the patient was admitted to an OSH for IV antibiotics
  - Sputum culture +AFB
  - Bronchoscopy notable for secretions and compression of right main stem bronchus
  - BAL culture normal flora and smear negative on staining
  - Chest CT confirmed RUL infiltrate and showed necrotic lymph node compressing trachea
  - PPD +, quantiferon gold indeterminate

Other Pertinent History

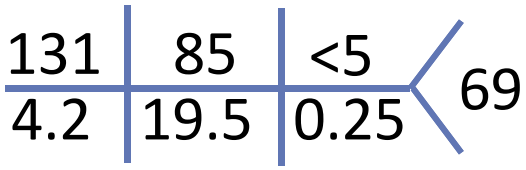
- **Past Medical History**
  - **8 months:** *Mycobacterium fortuitum* cervical adenitis
  - **9 months:** stomatitis x 45 days
  - **12 months:** Varicella zoster infection 10 days after receiving Varivax (VZV DNA by PCR +)
- **Family history**
  - Parents deny consanguinity, but they are from the same town in Brazil
  - No history of miscarriages, early death, immunodeficiency, recurrent infections
- **Social**
  - No pets
  - Travels to Brazil yearly

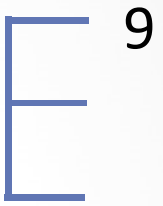
Initial Laboratory Values

CBC and Differential:



Metabolic Panel:





Mono: 595 (180-1750)
Lymph: 3,569 (2820-13475)
Neutro: 14,476 (720-7525)
Eos: 1,190 (0-1050)
Baso: 0 (0-350)

CRP:
13.6

Hepatic function panel:
T. Protein: 7.3
Albumin: 2.8
T. Bili: 0.4
Alk Phos: 371
ALT: 14
AST: 21

Next Steps?

Further Laboratory Evaluation

Immunoglobulins:

IgA: 106

IgG: 898

IgM: 181

Antibody levels:

Tetanus: 0.49

Diphtheria: 0.11

Pneumococcus: +7/14

T- and B-cell Flow Cytometry:

CD3 Absolute: 3433 (2207-8192)

$CD3^+8^+$: 714 (750-3749)

$CD3^+4^+$: 2658 (1089-4552)

$CD3\text{-}16^+56^+$: 109 (182-1581)

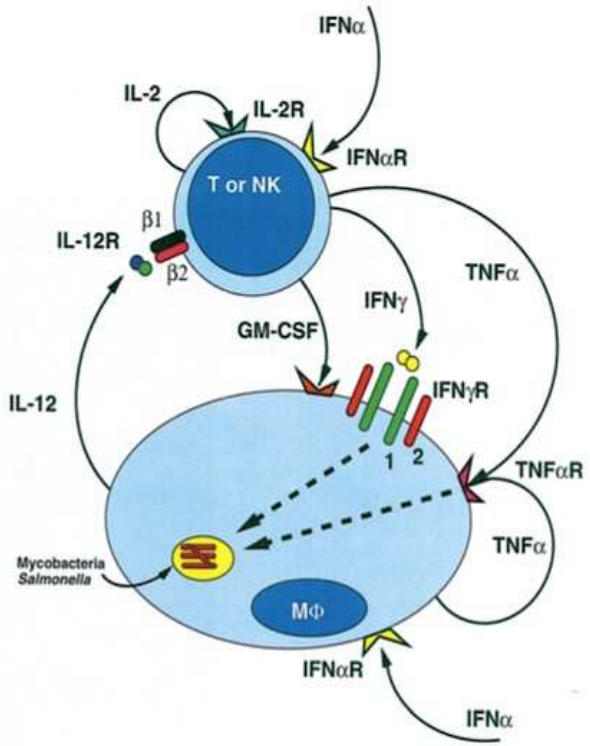
$CD19^+$: 1231 (704-2711)

- **Lymphocyte Blastogenesis to Antigens:** Normal
- **Interferon-γ Production:** >400 (high)
- **Natural Killer Cell Function:** 1.3% (low)

Differential Diagnosis?

- **IFN-ɣ/IL-12 axis defects:**
  - IFN-ɣ R1 or IFN-ɣ R2 deficiencies
  - STAT1 mutation
  - IL-12p40 or IL-12R-B1 deficiencies
  - IRF8 deficiency
  - ISG15 deficiency
  - Anti-IFN-ɣ antibodies
  - NEMO mutations
  - CYBB mutation
  - GATA2 deficiency

IFN-γ/IL-12 axis



Holland,S. 2000.

- B and T cell STAT1 phosphorylation in response to IFN-ɣ absent
- **2 different heterozygous mutations in the IFN-ɣ receptor 1 gene** (c.662T>G p.L221X and c.523delT p.Y175fs) confirming a defect in the IFN-ɣ/IL-12 axis

Treatment

- Started on acyclovir, clarithromycin, ethambutol, rifampin
- Supplemental IFN-ɣ started prior to diagnosis, and continued due to clinical improvement
  - Can supplemental IFN-ɣ augment function?
- Joint pain developed ~2 years into therapies
  - Infection versus drug side effects?
- Prognosis is variable and dependent upon degree of receptor function
  - Compete IFNgR1 deficiency has a poor prognosis
  - 4 survivors of 22 up to the age of 12 years. Of these, 2 (12 and 15 years old) are alive without HPSCT and are still receiving anti-mycobacterial treatment (Roesler et al. J Pediatr 2004).
- Only known curative therapy is HPSCT

Thank you!

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