Fever of Unknown Origin (FUO) in a Healthy Child: A Reminder of an Uncommon Presentation of an Uncommon Disease

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Introduction

- Fever of Unknown Origin (FUO) has a wide variety of differentials to consider
- Nontuberculous mycobacterial (NTM) infection is often associated with lymphadenitis in immunocompetent children and disseminated disease in immunocompromised children.
- We report one immunocompetent pediatric patient who presented with systemic symptoms and mediastinal mass found to have Nontuberculosis mycobacterial species (NTM) on biopsy later identified as Mycobacterium avium complex (MAC).

Case Presentation

4-year-old, who presented with a one-month history of daily fevers

- T max of 103 at home, decrease appetite, and fatigue
- No other symptoms initially
- The week prior to admission pediatrician started amoxicillin empirically for suspected Lyme disease
- Developed bilateral lower extremity pain with joint swelling, generalized blotchy rash, three-days prior to admission
- Refusing to ambulate, unresponsive to anti-inflammatory medications
- Ankles noted to be red, swollen, and painful to touch

Patient history

- No past medical or surgical history
- Streptococcal pharyngitis the year prior
- Mother with history of Hashimoto's thyroiditis; Two sisters, healthy
- ***No recent travel*** or zoonotic exposures
- Lives in a suburban ***wooden*** area in Eastern Pennsylvania. History of ticks found on pets. (Pets include 2 dogs)
- Not known ill contacts

Physical examination

- BP 103/56 mmHg | Pulse **123** | Temp **101.3** °F (38.5 °C, Temporal) Resp 22 | WT 14.5 kg (31 lb. 15.5 oz) | SpO2 100%

Skin Findings

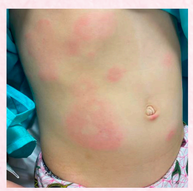


Figure 1a

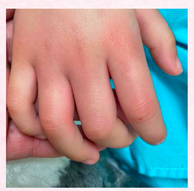


Figure 1b

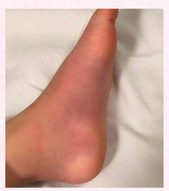
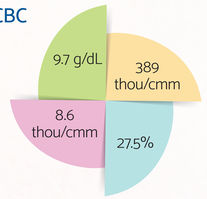


Figure 1c

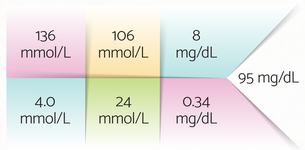
Figure 1a, 1b, 1c: Physical examination findings of the skin revealing a non-blanching macular, raised polymorphous rash with some areas of central clearing on the anterior/ posterior torso, dorsal surfaces of bilateral hands, and bilateral feet.

Laboratory Evaluation

CBC



BMP



OTHER LABS:

CRP **16.4 mg/L** (ref range <7.0)

ESR **20 mm/hr** (ref range 3-13)

EBV VCA IgG ab 345 U/mL (ref range <18.0)

Streptolysin O Ab 68 IU/mL (ref range <105)

CMV IgM & IgM negative

SARS Co V2 IgG Ab negative

M. Pneumoniae IgM & IgG Ab negative

Uric Acid 2.4 mg/dL (ref range 1.8-4.9)

LD **360 U/L** (ref range 192-321)

DNase B Antibody <86 U/mL (ref range 0-250)

Quantiferon plus **negative**

Imaging Findings

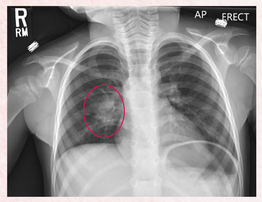


Figure 2a: PA Chest X-ray displaying nonspecific patchy increased density within the right perihilar region which may represent focal consolidation versus right perihilar lymphadenopathy.

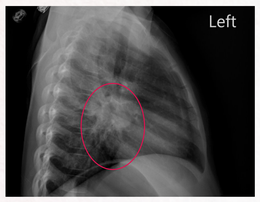


Figure 2b: Lateral Chest X-ray again demonstrating nonspecific patchy increased density within the right perihilar region.

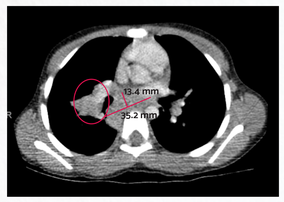


Figure 3a: CT chest showing a right perihilar mass, measuring 3.5 cm X 1.3 cm X 2.4 cm in size, encasing the right pulmonary bronchovascular bundle in continuity with the mediastinum. No satellite pulmonary nodules appreciated.

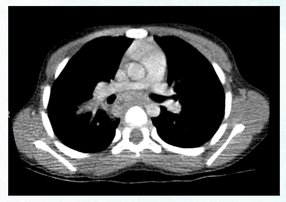


Figure 3b: CT chest again demonstrating this prominent soft tissue mass centered within the subcarinal mediastinum and in continuity with the right perihilar nodal chains. There are no discrete calcifications seen within the mass but areas of low attenuation concerning for necrosis and/or cystic degeneration.

Microbiology

TABLE 1: BONE MARROW ASPIRATE CULTURE RESULTS

	Bone marrow aspirate
Anaerobic/Aerobic culture	**No growth**
Fungal culture	**No growth**
AFB culture	**No growth**

TABLE 2: MEDIASTINAL MASS BIOPSY CULTURE RESULTS

	Mediastinal mass, lung biopsy
Anaerobic/Aerobic culture	**No growth**
Fungal culture	**No growth**
AFB culture	**Culture positive for Mycobacterium avium complex as well as DNA probe. Negative for Mycobacterium tuberculosis complex by DNA probe.**

Histopathology

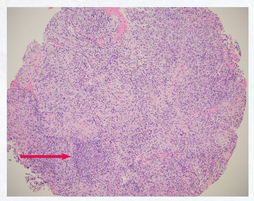


Figure 4a: H & E stain of patient's mediastinum mass resection showing non-caseating granulomas.

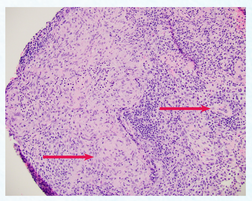


Figure 4b: Redemonstration of H & E stain of the patient's mediastinum mass resection showing non-caseating granulomas.

Clinical Course

- Skin rash and joint pain/swelling consistent with serum sickness secondary to amoxicillin, resolved upon discontinuation of antibiotic.
- Underwent right video-assisted thoracoscopic surgery, biopsy of mediastinal mass
  - Lung tissue with non-caseating granulomas
  - AFB and GMS negative for acid-fast bacilli and fungal elements
  - Molecular testing negative for M. tuberculosis
  - AFB culture from lung tissue identified **Mycobacterium *avium complex***
  - Sensitivities sent to UT Mycology laboratory
- Treatment with triple therapy
  - Azithromycin, Rifampin, Ethambutol
- Follow-up: Outpatient Peds ID clinic. Completed 6 month of triple therapy. No side effects.
- Extensive immune work completed by CHOP Immunology was negative including genetic testing for Mendelian Susceptibility to Mycobacterial Disease (MSMD).

Discussion

- Mycobacterium avium complex (MAC) typically presents with four main clinical syndromes in children including
  - Lymphadenopathy
  - Skin and soft tissue infections
  - Pulmonary disease (in children with pulmonary conditions)
  - Disseminated disease (in immunocompromised children)
- FUO is not a common presentation of MAC pulmonary infection
  - Case reports in the literature suggest few systemic symptoms in an immunocompetent, otherwise healthy child
- Young child may present with new onset wheeze/stridor
- No standardized treatment exists
- Important tool in the work-up of FUO includes Chest X-ray

Conclusion

- FUO is not a common presentation of MAC pulmonary infection
- MAC infection is a rarely recognized cause of pulmonary infection in immunocompetent children with no underlying immune defect.
- Our patient did not present with wheezing or stridor, however MAC should be considered in pediatric patients with prolonged fever and abnormal chest X-ray results with infiltrates/mass or hilar lymphadenopathy with no identifiable risk factors for TB.

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