CGD presenting as Tuberculosis basilar meningitis

Paulina Tran DO[1] Jen Heimall MD [1]

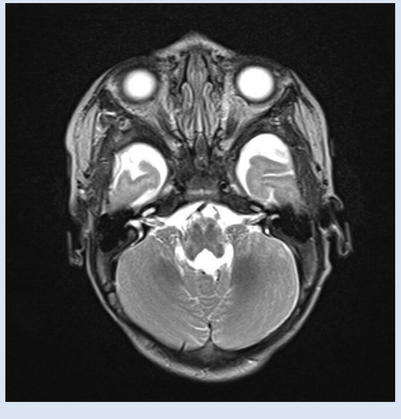
1. Divisions of Allergy and Immunology of The Children's Hospital of Philadelphia, Philadelphia, PA

Introduction

Chronic Granulomatous Disease (CGD): an inherited disorder of the nicotinamide adenine dinucleotide phosphate (NADPH) oxidase complex for superoxide generation

- Increased susceptibility to *Staphylococcus aureus, Serratia marcescens, Burkholderia cepacia, Nocardia, Granulibacter bethesdensis, Actinomyces* and *Aspergillus.*
- Clinical manifestations: liver abscess, pneumonia, skin infections, lymphadenitis, and osteomyelitis
- Mycobacteria, not typically thought of as a sentinel pathogen for CGD, has been increasingly reported in CGD patients.
- CGD should be considered in severe mycobacterial infections

Imaging



- Diffuse leptomeningeal enhancement
- Thick enhancement throughout the basal cisterns and the brainstem

Case Report

A 3-month-old full-term boy who initially presented with acute feeding intolerance, head lag and hypotonia.

- Brain MRI findings were consistent with basilar meningitis
- No mycobacterium was isolated and quantiferon gold negative. Only ⅓ of reported TB cases isolated the organism from CSF
- Infectious disease diagnosed patient with *Tuberculosis* which commonly presents with basilar meningitis
- The patient was initiated on rifampin, isoniazid, pyrazinamide and ethambutol (RIPE) and clinically improved
- He then developed diffuse Candida lusitaniae in urine, CSF fluid and blood and started on Fluconazole
- Immunologic evaluation was initiated and significant for an abnormal dihdrohodamine 123 (DHR) assay. Subsequent genetic testing confirmed chronic granuolomatous disease.

Labs

Relevant Infectious Labs:

PPD - 0 mm; Quantiferon Gold - Negative

Mycobacterium tuberculosis PCR - Negative

Gastric aspirate AFB culture x 2 - Negative

CSF AFB culture x 4- Negative

Immunology Labs:

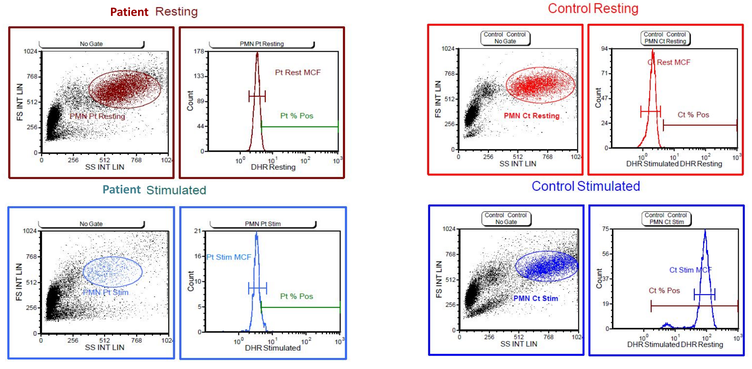
Extended Lymphocyte Panel: Low T Cells (853L cells/µl), B cells (1,334 cells/µl), NK(177 cells/µl), RA:RO(497/36=13:1)

Mitogen Stimulation Test - Normal

DHR - Absent neutrophil oxidative burst

Whole exome - De novo hemizygous variant in the CYBB gene consistent with X-linked CGD. Mother with negative genetic work up.

DHR



DHR Patient Unstimulated %0.2

DHR Patient Stimulated % 5.9

Discussion

- The patient is in stable condition and in the care of a pediatric facility. He has inflammatory bowel disease, hydrocephalus status post VP shunt placement, neurologic issues including vasculitis and epilepsy, and feeding intolerance with GJ-tube and TPN dependence. He is not a BMT candidate given his suboptimal nutritional status and TPN dependence.
- CGD patients can present very early on with severe infectious disease that includes mycobacterial disorders
- Important to prioritize early identification of these patients to prevent devastating outcomes.
- Is there utility to adding a DHR to the newborn screen?

References

1. Chin JH. Tuberculous meningitis: Diagnostic and therapeutic challenges. Neurol Clin Pract. 2014;4(3):199–205.
2. Lee PP, Chan KW, Jiang L, et al. Susceptibility to mycobacterial infections in children with X-linked chronic granulomatous disease: a review of 17 patients living in a region endemic for tuberculosis. Pediatr Infect Dis J. 2008;27:224-30