Extensive Bilateral Cervicofacial Lymphadenitis Caused by Atypical Mycobacterium

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ABSTRACT

Non-tuberculous mycobacterial (NTM) lymphadenitis typically presents as a unilateral, non-tender, slowly enlarging cervical, submandibular, or pre-auricular lymph node in children. Disseminated NTM infection is most often seen in immunocompromised children. Here, we present an unusual case of extensive bilateral cervical and retropharyngeal lymphadenitis caused by Mycobacterium Avium Complex (MAC) in an ostensibly immunocompetent pediatric patient.

KEYWORDS: Disseminated mycobacterium; lymphadenitis; non-tuberculous mycobacterium; pediatric; Castleman disease

INTRODUCTION

Non-tuberculous mycobacterial (NTM) lymphadenitis is a significant cause of cervicofacial lymphadenitis in immunocompetent children ages 1–5.[1] The most common pathogen for this population is Mycobacterium Avium Complex (MAC), acquired through oral mucosa from environmental sources such as contaminated water or soil.[1] Children with NTM lymphadenitis usually present with a non-tender, unilateral, slowly enlarging sub-mandibular, cervical, or pre-auricular node. Infected nodes can become necrotic, suppurate, and fistulize; the indolent presentation can delay proper diagnosis and treatment for NTM lymphadenitis.[2]

Disseminated NTM is uncommon and occurs most frequently in immunocompromised patients. Deficiencies in IL-12 and IFN-γ, which play an important role in cell-mediated immunity, have been increasingly recognized to be associated with disseminated NTM infection.[3] Isolated cases of disseminated NTM in immunocompetent hosts have been reported in the literature.[4,5] Symptomatology in these cases vary, but include spondylitis, skin and soft tissue infection, septic arthritis, and severe pulmonary infection. Such reports are primarily internationally based and involve middle-aged or elderly patients. Scant literature exists describing cases of NTM in immunocompetent children. As such, susceptibility factors for this population are largely unknown. We present an unusual case of extensive disseminated cervical lymphadenitis caused by *Mycobacterium Avium* in an immunocompetent host.

CASE REPORT

An 18-month-old male presented with bronchiolitis and a right-sided neck mass, enlarging over several weeks. Ultrasound demonstrated a four cm right post-auricular complex hypoechoic collection. Computed Tomography (CT) neck scan showed a large fluid filled mass extending from the right to left neck. Intervention was delayed due to bronchiolitis. Two weeks later the patient developed fever of 102° F and an enlarging right-sided neck mass that did not respond to amoxicillin, along with infra-auricular fullness with central fluctuance and overlying erythema and surrounding induration. He did not have night sweats, fatigue, cough, dysphagia, or limited range of motion. C-Reactive protein was 12.8 mg/L, and the Sedimentation Rate was 95 mm/hr.

He was admitted for intravenous ampicillin-sulbactam 200mg/kg/day and interventional radiology guided needle

Figure 1. [**A**] Patient's new left-sided neck mass, and [**B**] right-sided neck mass with fistula.

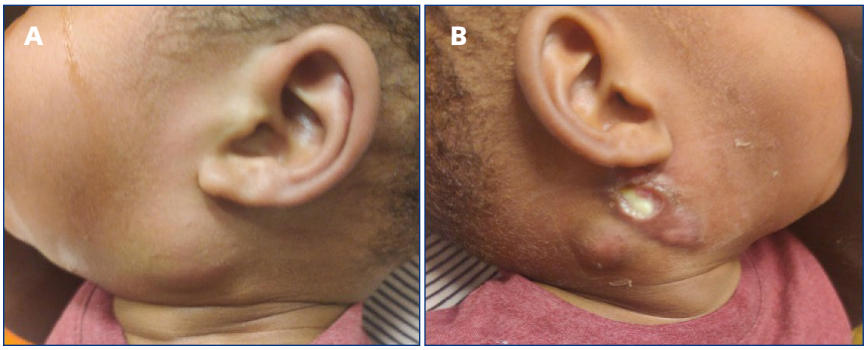
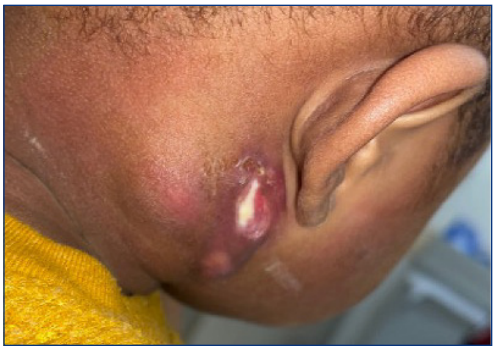


Figure 2. Patient's right-sided neck mass with fistula



drainage. Gram stain of aspirated fluid was negative. A Purified Protein Derivative (PPD) test was positive, and cultures were positive for Mycobacterium Avium Complex (MAC). Shortly after discharge, the patient again developed bronchiolitis, was briefly admitted, and was started on azithromycin 10mg/kg and rifampin 10mg/kg.

Three weeks later, the patient's right-sided neck mass fistulized, and he developed a new left sided neck mass (**Figures 1,2**). Routine immune function tests (IL-12, IL-23, or interferon production. IgM, IgA, and IgG levels and T-cell counts) were normal but an Invitae primary immunodeficiency panel identified a nucleotide-binding oligomerization domain-containing protein 2 (NOD2) variant (c.2104C>T (p.Arg702Trp), that is associated with Crohn's disease. Antibodies to IFN gamma were negative.

He was started on azithromycin, rifampin, and ethambutol. The patient underwent transoral needle aspiration of retropharyngeal fluid collection and selective left-sided neck dissection for debulking. The left-sided neck mass was removed successfully, and the patient was discharged the following day. Surgical pathology was notable for possible Castleman disease.

The patient returned for a right selective neck dissection after six weeks of antibiotics. Multiple inflamed lymph nodes in level IIA, IIB, III, and V were excised. A skin fistula was excised by right superficial parotidectomy, with closure by cervicofacial advancement flap. Antibiotics were discontinued after seven months. There were no complications and the patient recovered well through nine months of follow-up.

DISCUSSION

We describe an unusual case of a disseminated *M. avium* infection in an immunocompetent host. Definitive diagnosis of NTM is via biopsy and culture, although culture yield is only approximately 50%.[2] Acid fast stains and tuberculin skin tests may also suggest NTM. The preferred management strategy for NTM lymphadenitis is surgical excision of the affected node.[6] Other strategies include directed primary or adjuvant antimicrobial therapy, fine needle aspiration, incision and drainage, curettage, and observation; but have lower cure rates and higher recurrence rates.[6] Non-operative management of NTM lymphadenitis may be considered for patients with recurrence or high-risk surgical candidates.

Although the standard of care for NTM lymphadenitis is surgical excision, surgery was delayed due to concern that our patient was not an appropriate surgical candidate given his multiple episodes of bronchiolitis. Due to the delay, the right mass fistulized. Operative removal of the left-sided neck mass was therefore prioritized to prevent fistulization of the left side while attempting to reduce the size of the right neck mass with antibiotics prior to operation.

The patient's episodes of bronchiolitis and diffuse cervical lymphadenitis suggested an immunodeficiency. Disseminated NTM is associated with HIV positivity, or, in HIV negative adults, with anti-IFN-γ IgG autoantibodies.[7] Our patient was negative for HIV and anti-IFN-γ IgG autoantibodies, although his recurrent bronchiolitis suggested possible immunodeficiency, suggesting a possible alterative mechanism of cell-mediated immunodeficiency associated with disseminated NTM.

Gene sequencing for our patient found a heterozygous variant in NOD2, which is involved in immune recognition of mycobacterial antigens.[8] Specific polymorphisms of NOD2 are associated with impaired cytokine production and can lead to susceptibility or resistance to Mycobacterium tuberculum or Mycobacterium leprae.[8] NOD2 variants are also associated with inflammatory and granulomatous disease such as IBD and Blau syndrome.[9] Given the link between NOD2 polymorphisms and other granulomatous diseases, future studies should investigate a possible link between NOD2 polymorphism and reactive skin disease in disseminated NTM.

Surgical pathology for this patient was notable for histology features suggestive of possible Castleman disease, a lymphoproliferative disease of unknown etiology. Common pathological findings of Castleman disease include lymphoid hyperplasia, germinal center formation, capillary proliferation, and endothelial hyperplasia. While this patient had no other clinical features of Castleman's disease, there are case reports that describe Castleman's with a similar presentation to mycobacterial lymphadenitis, or possible overlap between the two conditions. TAFRO syndrome, a multicentric idiopathic form of Castleman's disease, can mimic disseminated mycobacterium.[10] Conversely, there have also been reports of mycobacterial infections mimicking Castleman histologic features, or triggering Castleman's disease.[11]

This unique patient extends our knowledge on clinical presentation of NTM in the pediatric population and highlights the need for further study on mechanisms which predispose HIV and anti-IFN-γ negative patients to disseminated infection. We specifically urge further evaluation on the growing body of literature of both NOD2 polymorphism and Castleman's disease as they pertain to mycobacterium infection.

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