Mycobacterium Avium-Intracellulare: A Rare Cause of Childhood Otitis Media

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Otitis media is a frequent affliction of the pediatric population, with streptococcus pneumonia and nontypeable haeomphilus influenza as the most common bacterial pathogens. Less ordinarily there is an isolated infection of middle ear and mastoid caused by a bacteria of the *Mycobacterium* genus, which are a family of gram positive, aerobic, acid fast bacilli. In the past, *Mycobacterium tuberculosis* was the most frequent culprit, but with much improved antibiotic coverage this has become a known but rare entity in western countries[1]. **Per a 1915 report by Turner titled "Tuberculosis of the Middle Ear Cleft in Children", approximately 50% of children under 1 year of age with chronic suppurative otitis media had disease of tuberculosis origin, and 27% of children under 2 years of age, making it a historically frequently encountered pathogen[2].** Infections from other members of the mycobacterium family, namely the heterogeneous group of nontuberculous mycobacteria, have always been more uncommon and can thus present diagnostic difficulties when they are the cause for isolated disease of the middle ear and mastoid.

Nontuberculous mycobacteria, of which Mycobacterium avium intracellulare (MAI) is the most common disease causing agent in humans, is located throughout the environment in the soil and water but with overall low pathogenicity[3]. The most frequently affected population is the grossly immunocompromised, as a terminal, systemic infection[4]. In the pediatric population, cervical lymphadenitis and pulmonary disease are the most prevalent manifestations of an MAI infection. The topic of this discussion is MAI as a cause of recalcitrant isolated otitis media and mastoiditis, an infrequently seen entity but a diagnostic challenge.

Prior to our case, there were only 12 previously reported cases in the literature[3,5-9]. Without appropriate cognizance, definitive treatment can be difficult. In our instance, an 18-month-old girl who resides on an agricultural farm presented with frequent unilateral left sided otitis media for which initial symptoms started at the age of 4 months.

Prior to presentation, multiple courses of antibiotics had been attempted and failed. An otolaryngologist at an outside facility evaluated and found foul discharge from her ear and biopsied a granuloma in her left ear canal. Biopsy results were inconclusive. Diagnostic imaging was undertaken (**Figure 1**), which showed a middle ear soft tissue density, temporal bone involvement and mass in the bladder. She was subsequently referred to our facility. Repeat imaging

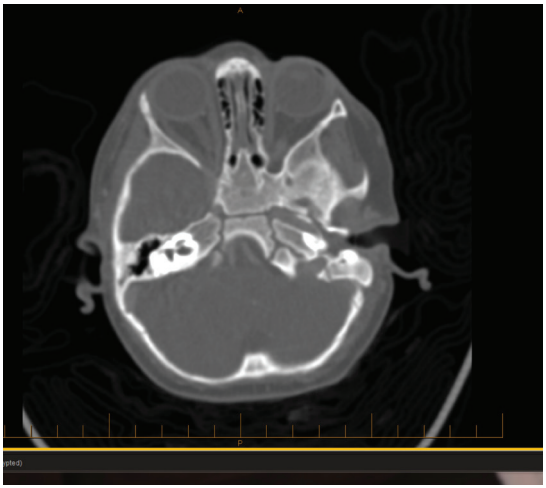

Figure 1. Biopsy results were inconclusive. Diagnostic imaging was undertaken

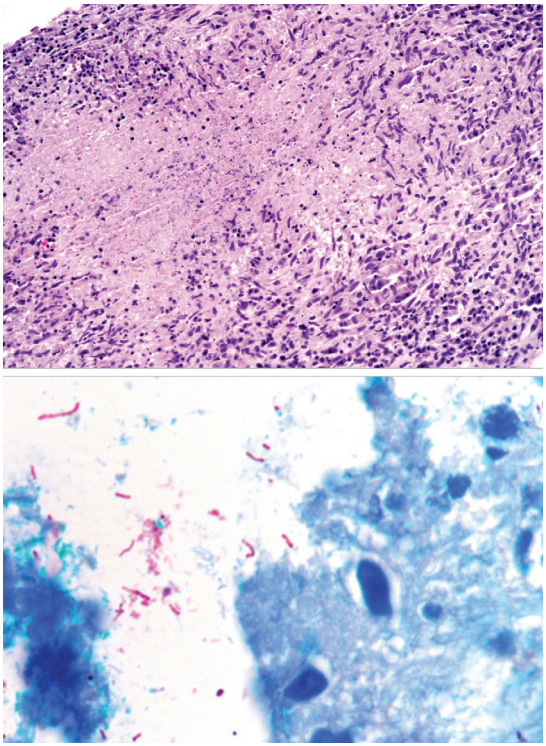

Figure 2. Histology and microbiology were positive for MAI

of the bladder mass showed no evidence of the mass and it was attributed to cystitis, but prior to this result there was concern for metastatic rhabdomyosarcoma.

Persistent middle ear and temporal bone changes led to middle ear exploration with removal of the middle ear mass. The long process of the incus was partially eroded, coupled with a complete obliteration of the tympanic membrane by a granuloma. Histology and microbiology were positive for MAI (**Figure 2**). The patient was started on the appropriate dual antibiotic therapy of azithromycin and rifampin, acknowledging linezolid resistance, with good results and a persistently dry ear. Of note, Purified Protein Derivative (PPD) test for tuberculosis was completed and was negative.

Patient underwent subsequent tympanoplasty with tragal cartilage. Audiogram was completed, hearing thresholds indicated mild hearing loss and appropriate speech thresholds in the better hearing ear by sound field. As the patient gets older, she will need thresholds monitored and to consider ossiculoplasty depending on the longevity of the partially eroded incus in independent ear testing.

It is clear that there was an overall delay in diagnosis in our case as the patient had ear drainage for approximately 14 months. Part of the reason is

the non-specificity of the presentation. The most common signs are secretions, aural polyps, and vigorous granulation tissue[3,6]. Fever is sometimes associated but not the majority of the time, as affected children largely lack evidence of systemic symptoms. Hearing loss is variable and there can be post auricular fluctuance present[9]. There is possible association with perforation of the eardrum as an entry point for infection, be it traumatic, infectious or iatrogenic in nature. Here there is seen some heterogeneity to the group of non-tuberculous mycobacteria as this epidemiological factor may be more common in other strains of mycobacteria than *Mycobacterium avium* intracellulare[3]. The major clue however, pointing to an MAI mastoiditis or middle ear infection would be the chronicity of the drainage and its recalcitrance to topical and systemic antibiotic therapy.

In order to make the diagnosis, the most definitive method is with histology and culture after taking a biopsy of the tissue in the middle ear or ear canal. However, non-tuberculous mycobacteria are fastidious organisms and there is associated lag time as it can take up to 6 weeks for results, if at all, as there can be a ~50% culture recovery rate[10]. For example, the initial biopsy that was taken for our patient returned with an inconclusive result. The second biopsy demonstrated histology and pathology consistent with MAI as there was acid-fast bacilli and necrotizing granulomatous inflammation. There are other options, such as PCR to assist with identification, but these are not necessarily in widespread use and are laboratory dependent. It is important to realize that histopathologically, nontuberculous mycobacteria and *Mycobacterium tuberculosis* can have very similar appearances, which is why further culture testing with bacterial identification and antibiotic susceptibility testing are important[3]. There is evidence of MAI that is macrolide resistant and it is vital to have that information to appropriately treat the patient[11].

In terms of diagnostic imaging, there are no specific features that are unique to MAI otomastoiditis[6]. The CT scan commonly shows bony erosion and soft tissue density in the middle ear and external ear canal. There is possibility of intracranial involvement for which MRI is useful to assess extension. Persistent and progressive bony changes are a reason to keep atypical mycobacterial otomastoiditis in the differential.

A final discussion point on diagnosis is the usefulness of PPD testing. Our patient had a negative PPD. Testing for non-tuberculous mycobacteria is equivocal. There are studies that show usefulness in detection in the setting of chronic lymphadenitis from an atypical mycobacterial source[10], but it is unclear as to the efficacy in terms of isolated non tuberculous otomastoiditis as it is such an uncommon entity.

Early treatment is needed to prevent irreversible damage to hearing function. However, in most of the case reports as well as our own, time to diagnosis is often delayed with multiple empiric courses of antibiotics that do not completely resolve the issue. For adequate treatment, a combination of medical and surgical management is required. This is different than *Mycobacterium tuberculosis,* which can usually be treated without surgical management and solely with appropriate anti-tuberculous antibiotics[7]. For MAI, a full removal of the

granulation tissue is vital followed by a protracted course of multidrug therapy for at least 6 months, based on antibiotic susceptibility data[6,9]. The extent of surgical excision is dependent on the disease, in our case, the tissue could be removed transcanal with an endoscope, but a mastoidectomy was considered. The goal for surgery is to reduce local bacterial load prior to antimicrobial therapy[3]. However, full removal can always be anatomically challenging in the temporal bone. Multiple otologic procedures may be necessary for complete treatment.

Multidrug antibiotic therapy is indicated due to resistance patterns of non-tuberculous mycobacteria. Most frequently recommended is clarithryomycin or azithromycin with rifampin ethambutol or in more severe cases amikacin[3]. Treatment is usually continued for at least 6 months or until 2-3 months after symptom resolution[3,6].

There are complications with this disease profile, some associated with the initial disease, its presentation and clinical course and some that are associated with its definitive treatment. Disease progression and bony erosion can lead to a host of intracranial complications accompanying local infection extension which must be managed with appropriate neurosurgical consultation[3]. The rubbery granulation tissue can also cause tympanic membrane perforation and ossicular erosion, adversely affecting conductive hearing capabilities and requiring secondary tympanoplasties with or without ossiculoplasty[3,6,7]. Much rarer in these cases but also a possible sequelae of the initial surgery, is facial nerve compromise. Medical complications of the antibiotic treatment are also non-trivial and need to be addressed. These patients should be followed by Infectious Disease specialists for management of their long-term therapy and oft associated side effects[8].

Our case is typical within the current literature highlighting a system delay in diagnosis due to rarity of this entity. Early treatment is imperative for hearing preservation. In this case a tympanoplasty was required after surgical removal of the mass with possible plans for an ossiculoplasty in the future depending on independent ear audiometric data. Overall treatment strategy relies on surgical debridement to prevent secondary damage from the infection as well as protracted multidrug antibiotic therapy in setting of significant risk for antibiotic resistance.

Mycobacterium avium intracellulare involvement of the middle ear is extremely rare. With appropriate diagnosis and treatment, a combination of medical and surgical, acceptable outcomes can be obtained as long as medical practitioners remain cognizant of this entity.

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