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Case Report

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Two children with extra-nodal *Mycobacterium avium* complex infection

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Abstract

Mycobacterium avium complex (MAC) is usually considered an opportunistic organism, which infects immunocompromised children or those with structural airway abnormalities. We present two cases of MAC infection affecting immune competent children, likely from hot tubs with primary involvement of pulmonary and urinary systems. These cases highlight the importance of asking about hot tub use in immune competent children with suspected or confirmed MAC infections.

Keywords: *Hot tub; Immune competent; Mycobacterium avium; Pulmonary*

CASE 1

A 3-year-old boy presented with cough, fever, and fatigue. He received treatment with inhaled salbutamol and corticosteroids with no improvement. After 6 weeks, his systemic symptoms resolved, but his non-productive paroxysmal cough persisted. He developed cervical and postauricular red-purple, nontender lesions. These lesions persisted despite treatment with cephalexin, and then trimethoprim-sulfamethoxazole.

Three weeks later, a right supraclavicular lesion was noted (Figure 1). He continued to have a dry cough and dyspnea. Complete blood count showed microcytic anemia. Serology for Epstein-Barr virus, cytomegalovirus, and *Bartonella henselae* were negative. Past history was positive for iron deficiency anemia. Immunizations were up to date. There was no significant family history. Ultrasound of the lesion was suggestive of reactive lymphadenopathy. The lymph node was biopsied and sent for culture. Bacterial, mycobacterial, and fungal cultures were negative. The biopsy suggested a fungal or mycobacterial process.

The C-reactive protein and erythrocyte sedimentation rate were 8.9 mg/L and 33 mm/hour, respectively. Renal and hepatic panels were within normal limits. Plain radiographs of his chest demonstrated two areas of focal airspace disease and suprahilar lymphadenopathy (Figure 2).

Four weeks later, C-reactive protein had decreased to 5.1 mg/L, erythrocyte sedimentation rate to 22 mm/hour, and complete blood count and peripheral blood smear showed microcytic anemia. Immunoglobulin levels, HIV screen, and lymphocyte counts were normal. Mantoux test, *Blastomyces,*

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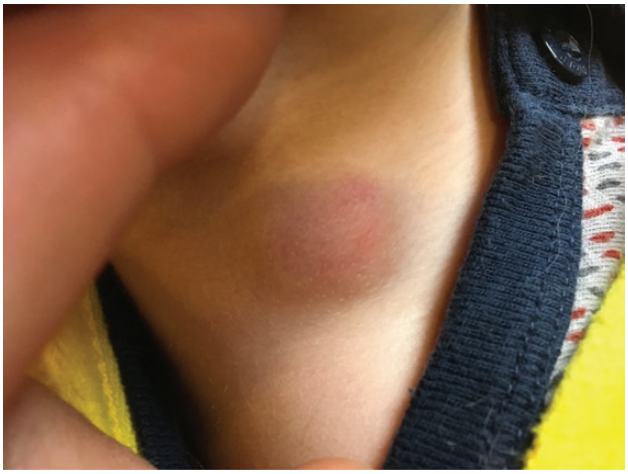

Figure 1. Nontender right sided supraclavicular lymphadenopathy with red-purple discoloration, subsequently drained and biopsied.

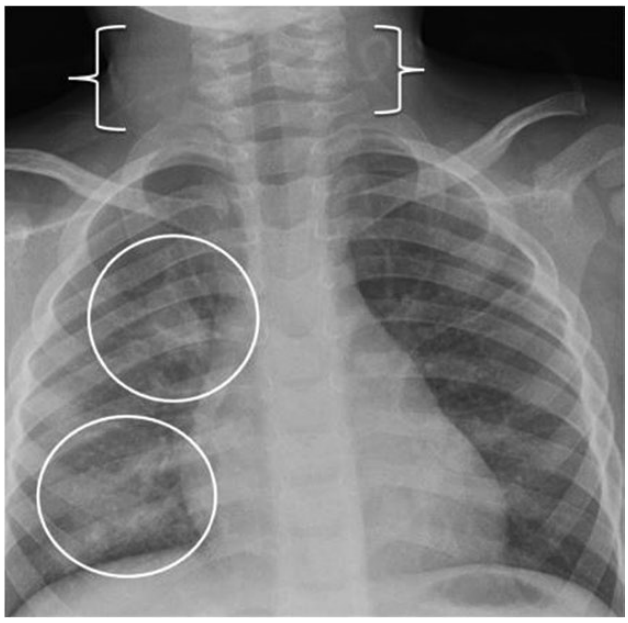

Figure 2. Anterior–posterior view chest radiograph showing patchy airspace disease more obvious on the right with cervical and supra-hilar lymphadenopathy.

and *Histoplasma* IgG serologies were negative. Liver ultrasound showed a lesion, and magnetic resonance imaging (MRI) later confirmed this as a hemangioma. The MRI included the chest and showed dense lesions with areas of necrosis in both lungs (Figure 3).

Because of the MRI, he was referred to Paediatric Respirology and then Infectious Diseases. Further history revealed no out-of-province travel. He did not have any exposure to tuberculosis. They did have an outdoor hot tub, which the family used two to three times per month.

Flexible bronchoscopy and lymph node biopsy were arranged. Samples sent from the lymph node drainage were

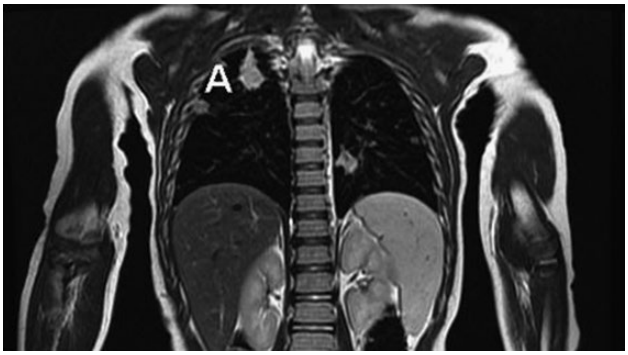

Figure 3. Magnetic resonance imaging sections in phase T2 with enhancing lesions found in bilateral apices and lung parenchyma (demonstrated by A).

negative on gram stain, fungal stain, and auramine-rhodamine stains and cultures were negative. The airways looked mildly inflamed. Bronchoalveolar lavage revealed no growth of bacteria or fungus. Polymerase chain reaction (PCR) from the bronchoalveolar lavage was positive with Mycobacterium primers. Water from the hot tub was collected and centrifuged which showed 4+ fluorescent bacilli with Auramine O stain. MAC was identified using a *Mycobacterium avium* complex DNA probe (AccuProbe). Sequencing and analysis of the hsp65 gene confirmed this identification 4 months later and as such, could not be used on the clinical sample. We cannot confirm if the isolates are indeed the same MAC. After a site visit, inadequate control of pool water alkalinity and pH were suspected as the likely cause of biofilm overgrowth allowing the organism to thrive. The parents were taught to clean and sanitize the filter and hot tub to the current recommended standard for killing highly resistant pathogens (by oxidizing biofilm glycoproteins to destroy pathogenic microbes).

CASE 2

A 9-year-old girl presented to her primary care physician with symptoms of dysuria, increased voiding frequency, urgency, and urinary incontinence. She had a urine culture done which was positive for growth of 10×10^7 cfu/mL of *Escherichia coli*. Despite antibiotic treatment, her symptoms persisted. She was reassessed 6 weeks later with repeat urinalysis and urine culture. The urinalysis was negative for leukocyte esterase, nitrites, glucose, ketones, and hemoglobin. It was positive for protein (0.7 g/L). Microscopy showed 0 to 2 each of leukocytes/high powered field (HPF) and 0 to 2 erythrocytes/HPF. Bacterial culture was negative, prompting PCR analysis. She had a history of urinary tract infections from ages 3 to 6 years, but had been asymptomatic since then. She had no family or personal history to suggest immunodeficiency. She had a normal abdominal ultrasound. She had no history of recent catheterization. Upon reviewing exposure history, they had recently moved to

a new house with an outdoor hot tub, which she used weekly. PCR from the urine sample was positive with Mycobacterium primers. Water from the hot tub was collected and identified MAC using a *Mycobacterium avium* complex DNA probe (AccuProbe), with the same limitations as described above.

DISCUSSION

These cases represent unique manifestations of disease in immune competent children secondary to exposure to MAC from personal hot tubs. MAC is a group of mycobacterial species characterized by slow growth in culture, causing opportunistic infections typically in immunodeficient populations. The organisms are either ingested or inhaled from the environment (e.g., recirculating hot-water systems [1–4]), rather than transmitted between hosts. In case 1, the organisms were likely both ingested and inhaled as the parents described the patient's chin to stand just above the water level in the hot tub and that he would also drink water while trying to swim in it. We postulate that the high number of MAC found in the tub, and the frequency of exposure had contributed to the infection despite immune competence. In case 2, the hot tub did not demonstrate a large number of organisms on staining, so it is more likely that the frequency of exposure and patient's predisposition to urinary tract infections led to the infection. Nontuberculous mycobacteria are known to cause six clinical syndromes: pulmonary, lymphadenitis, skin and soft tissue, skeletal, catheter-related, and disseminated infections (5). MAC is a known culprit of cervical lymphadenitis (6). It also causes pulmonary disease generally in people with structural lung disease or immunodeficiency (1). The American Thoracic Society describes diagnostic criteria of nontuberculous mycobacteria pulmonary disease to require repeated microbiological evidence, chronic respiratory symptoms, and radiological findings consistent with disease (7). One of the clinical contexts described in adults from MAC is known as 'hot tub lung', but reported very rarely in children. Similarly, MAC urinary tract infections are commonly described in adults with AIDS (8), but not in immune competent children. In case 1, the patient's lymphadenopathy was classic for this type of cervical lymphadenitis and was likely due to MAC despite negative PCR from biopsy.

Treatment of pulmonary MAC involves multiple drugs with side effect profiles (8–9). However, hot tub lung secondary to MAC is usually regarded and treated as a hypersensitivity pneumonitis with systemic corticosteroids. Treatment versus watchful-waiting was discussed with both families presented here. Given the persistence of symptoms, case 1 was treated with a 6-month course of clarithromycin 15 mg/kg/day, ethambutol 300 mg daily, and rifampin 300 mg daily. Risk of retinal, hepatic, and renal toxicity were disclosed. He was monitored by bloodwork and ophthalmology without incident. Case 2 was asymptomatic, thought likely to clear the infection independently, and risks of treatment did not outweigh benefit.

TAKE HOME POINTS

MAC infections do occur in immune competent children and in locations other than skin or soft tissue. An exposure history for hot tub use is important. Decision for treatment of MAC infections in children warrants consultation with an infectious disease specialist as the options differ significantly, as illustrated by these cases.

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