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Brief Report

BRIEF REPORT

Pulmonary *Mycobacterium abscessus* Infection in a Patient with Triple A Syndrome

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ABSTRACT

Gastroesophageal disorders such as achalasia can be associated with pulmonary disorders because of non-tuberculous mycobacteria, frequently masquerading as aspiration pneumonia. The optimal therapeutic regimen and duration of treatment for non-tuberculous mycobacteria lung disease is not well established. Here, we present an 11 year old male patient with *Mycobacterium abscessus* pulmonary disease and underlying triple A syndrome, who was successfully treated with 2 months of imipenem, amikacin, clarithromycin and continued for long-term antibiotic treatment.

KEYWORDS: *Mycobacterium abscessus*, achalasia, aspiration pneumonia, non-tuberculous mycobacteria

INTRODUCTION

The incidence of non-tuberculous mycobacteria (NTM) pulmonary infection has been increasing in recent years [1]. *Mycobacterium abscessus (M. abscessus)* is the most common rapidly growing mycobacterium that causes lung disease [2]. Clinically, *M. abscessus* pulmonary infection can range from asymptomatic to severe bronchiectasis and cavitary lung disease, with significant morbidity and mortality [1]. Conditions that have been associated with *M. abscessus* pulmonary disease include achalasia, recurrent vomiting, lipoid pneumonia, coexisting mycobacterial infections, bronchiectasis, cystic fibrosis and lung transplantation [3].

The optimal therapeutic regimen and duration of treatment for *M. abscessus* lung disease has not been established. Here, we present an 11 year old male patient with Triple A syndrome, diagnosed with pulmonary *M. abscessus* infection and treated for long-term antibiotic treatment.

CASE REPORT

An 11 year old male was admitted to the hospital with cough, sputum and fever. He had been

diagnosed with Triple A syndrome, including achalasia, alacrima and adrenal insufficiency, for 7 years. He had a history of cough related with feeding. The child had been hospitalized in another institution because of fever and dyspnea and was diagnosed with tuberculosis about a month ago, which failed to improve despite the use of various antibiotic regimens and Isoniazide, rifampicin, ethambutol and pyrazinamide. He had no contact history of tuberculosis.

Physical examination detected poor weight gain, alacrima and tachypnea, with respiratory rate of 40 breaths/min. Transcutaneous oxygen saturation was 85% in room air, and fine rales were heard on auscultation. Results of full blood counts were as follows: hemoglobin 8.4 g/dl, hematocrit 27.6%, white blood cell count 21.700/mm^3, 78% segmented neutrophils, 4% monocytes, 16% lymphocytes and 2% eosinophils. C-reactive protein and sedimentation rate were elevated, and biochemistry analysis was in the normal range.

Chest radiograph showed bilateral extensive nodular infiltrates, which were coalescing to form an area of consolidation in both lungs; mediastinal and hilar enlargement was consistent with lymphadenopathy (Fig. 1). With a high index of suspicion of multidrug-resistant tuberculosis, bronchoscopy was performed. Bronchoalveolar fluid was negative for acid-fast bacilli (AFB); *Escherichia coli* was detected in the culture. There were no growing fungi in the culture. Tuberculin skin test was 17 mm. Interferon-gamma release assay was performed, which gave a negative result. Contrast-enhanced computed tomography (CT) of the chest revealed multiple pulmonary nodules and consolidation in both lungs and an appearance of tree-in-bud. Enlarged lymph nodes were also detected in the mediastinal and hilar region (Fig. 2). He was treated with broad-spectrum antibiotic treatment and oxygen with 4 l/min; after clinical improvement, he was discharged from the hospital with no oxygen requirement. Heller myotomy had been performed for achalasia by the pediatric surgery department.

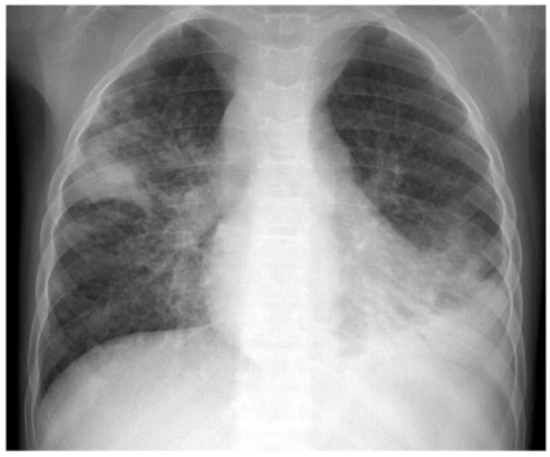

Fig. 1. Chest radiograph shows bilateral extensive nodular infiltrates and area of consolidation in both lungs. Mediastinal and hilar enlargement suggest lymphadenopathy.

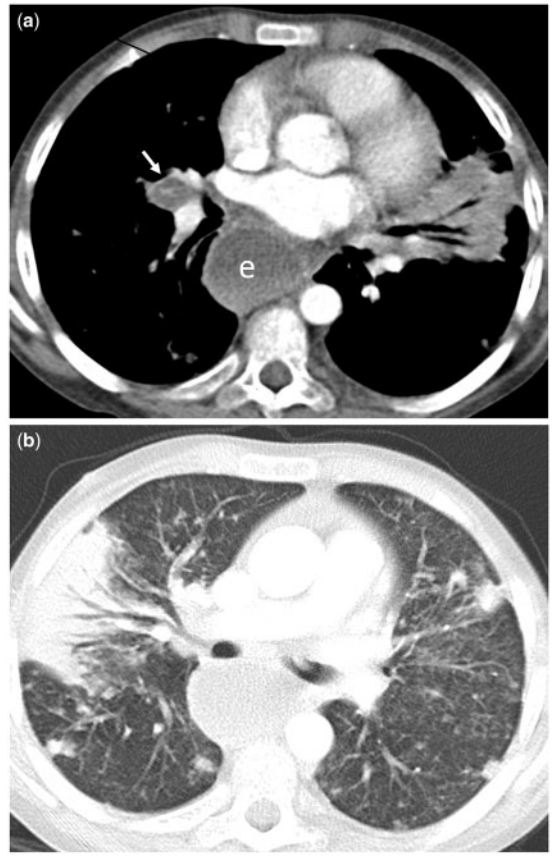

Fig. 2. (A) Contrast-enhanced CT of the chest shows enlarged lymph nodes in the mediastinal and hilar region (short arrow). CT also shows fluid filled dilated esophagus (e) secondary achalasia. **(B)** Multiple pulmonary nodules and consolidation are seen in both lungs.

He was readmitted to the hospital with fever and cough after 1 month of discharge. Fine rales were heard on his physical examination, and chest X-ray revealed bilaterally increasing nodular infiltrates. Inducible sputum was examined, and this time, it was positive for AFB staining; the culture grew *M. abscessus* three times in total. Three subsequent inducible sputum samples were sent to the laboratory. They were positive for AFB. The samples were decontaminated and homogenizated with NaOH and N-acetyl L-cystein [4] and were seeded onto Löwenstein–Jensen slants and into the Mycobacteria Growth Indicator Tube (MGIT; BBL BD Diagnostic Systems, Sparks, MD) system. MGIT results were positive in 4 days for two samples and in 11 days for one sample. Identification of *M. abcessus* was performed with GenoType Mycobacterium CM/AS assay (Hain Lifescience, Germany).

After this assessment, he was started on a 2 month course of imipenem, amikacin and clarithromycin. After initiating treatment, the child began to gain weight; clinical and radiological findings had progressively improved (Fig. 3). Immunological evaluation revealed absence of pathology. Sputum culture converted to negative for *M. abscessus* after the 2 month course of therapy. Treatment is still being continued for a 12 month course of doxycycline, clarithromycin and ciprofloxacin and is planned to stop at the 24th month.

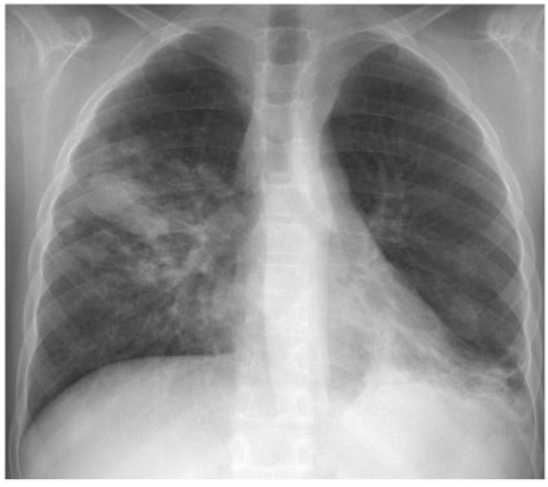

Fig. 3. Control chest radiograph shows regression of nodules and consolidation.

DISCUSSION

Pulmonary infections because of NTM are increasingly recognized worldwide. The diagnosis of NTM pulmonary infection requires the presence of symptoms, radiologic abnormalities and microbiologic cultures in conjunction with the exclusion of other potential etiologies. *Mycobacterium abscessus* accounts for approximately 80% of NTM respiratory disease isolates [1]. The largest group of patients with lung disease are >60 years, with no predisposing conditions or previously recognized lung disease. Underlying disorders that are associated with disease include bronchiectasis, prior mycobacterial infection, gastroesophageal disorders with chronic vomiting, lipoid pneumonia and cystic fibrosis. Almost all patients <40 years have one of the predisposing disorders that cause *M. abscessus* lung disease [5, 6]. Our patient had clinically important achalasia, which is a part of the Triple A syndrome, causing gastroesophageal reflux and aspiration pneumonia. Stasis of food in the esophagus and recurrent aspiration seem to play a primary role in the NTM infection in patients with esophageal dysmotility [7].

The chest radiographs from patients with *M. abscessus* lung disease usually show multilobar, patchy, reticulonodular or mixed interstitial-alveolar opacities. Cavitation occurs in only approximately 15% of cases. Chest CT frequently shows cylindrical bronchiectasis and multiple small nodules. Griffith *et al.* reported that *M. abscessus* most frequently appears radiographically as interstitial (37%), interstitial/alveolar (40%) and reticulonodular shadows (36%), and 77% of patients have bilateral involvement like our patient [5]. In our case, chest CT revealed hilar and mediastinal lymphadenopathies and multiple nodules with an appearance of tree-in-bud.

Mycobacterium abscessus isolates are uniformly resistant to standard antituberculous agents, that is why our patient had no improvement with the four antituberculous drugs, including isoniazide, rifampicin, ethambutol and pyrazinamide [1]. However, the lack of effective therapy for *M. abscessus* and poor tolerability of therapy makes this organism difficult to treat. The 2007 American Thoracic Society (ATS)/ Infectious Diseases Society of America (IDSA) guidelines recommend 2–4 months of intravenous amikacin plus cefoxitin or imipenem, combined with clarithromycin or azithromycin for initial

therapy. Suppressive therapy, including periodic parenteral antibiotics or oral macrolides and fluoroquinolones, may be administered to control the symptoms and progression of *M. abscessus* lung disease [1]. The roles of combined activities of fluoroquinolones with clarithromycin against *M. abscessus* are controversial [8]. Overall, with current antibiotic options, *M. abscessus* is a chronic incurable infection for most patients [9].

One of the most difficult questions regarding the treatment of *M. abscessus* lung disease is when to start antibiotic therapy and how to construct treatment regimens [10]. Here, this patient has been treated with 2 months of imipenem, amikacin, clarithromycin and is being continued with doxycycline, clarithromycin and ciprofloxacilin for 1 year. Negative conversion of sputum was achieved after 2 months of intravenous therapy, and clinical and radiological improvement was the success of this treatment.

In conclusion, *M. abscessus* is a challenging pathogen, causing chronic respiratory infections in patients with underlying diseases, and optimal therapeutic regimens have not been established for *M. abscessus* lung disease. Achalasia and lipoid pneumonia are important risk factors for the development of lung infections caused by rapidly growing mycobacteria; so, mycobacterial culture should be obtained in patients with achalasia and non-resolving aspiration pneumonia despite adequate antibiotic therapy.

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