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CASE REPORT

Fatal pulmonary cavitary disease secondary to *Mycobacterium xenopi* in a patient with sarcoidosis

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ABSTRACT

Introduction: *Mycobacterium xenopi* (*M. xenopi*) has low pathogenicity and usually requires either host immune impairment or structural lung disease to cause clinical disease. Fatal cavitary infection in a patient without immunosuppression is rarely presented.

Case report: A 62-year-old female with history of sarcoidosis and hypertension presented with cough, fever and dyspnea for one week. Chest imaging showed irregular opacification of upper lung zones. The sputum samples tested positive for acid-fast bacilli (AFB) and the subsequent testing identified *M. xenopi*. She was started on rifampin, isoniazid, pyrazinamide and ethambutol along with azithromycin, and was discharged with plans to continue the same. A follow up sputum test was negative for AFB. She was, however, readmitted ten months later with sepsis due to pneumonia. Chest imaging revealed worsening cavitary lung lesions. Despite starting her on intravenous antibiotics while continuing anti-tubercular therapy, she developed severe respiratory distress and had to be intubated. Her condition continued to deteriorate and she expired the following day.

Conclusion: Fatal cavitary infections with M. xenopi have been reported in the absence of established optimal management. Well-designed studies with sufficient power are needed to establish new treatment guidelines.

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KEYWORDS
Mycobacterium xenopi; Sarcoidosis; Nontuberculous mycobacterium

1. Introduction

Non-tuberculous mycobacterium (NTM) displays a large geographic variation in prevalence [1–3]. In the USA, *Mycobacterium avium complex* (MAC) is the most frequent NTM pathogen causing lung disease followed by *Mycobacterium kansasii* [1,2]. *Mycobacterium xenopi* (*M. xenopi*) is a ubiquitous thermophilic bacterium occurring predominantly in water. Its detection in clinical samples is usually associated with contamination and asymptomatic transient colonization [3–6]. However, in recent years an increasing number of clinically relevant *M. xenopi* infections have been reported [7–11].

Clinical and radiological pictures in *M. xenopi* infection are not easily distinguishable from tuberculosis. Pulmonary cavities and nodules are, however, reported to be more common in *M. xenopi* infection as compared to MAC [12].

M. xenopi has low pathogenicity and requires either host impairment or structural lung disease to cause clinical disease. It can occur as an opportunistic infection in immunocompromised individuals with subsequent dissemination and a virulent course or as an indolent infection in immunocompetent adults with structural lung disease like chronic obstructive pulmonary disease.

Here we present a patient without obvious immunosuppression but might have underlying structural lung disease who developed a fatal cavitary infection likely secondary to *M. xenopi*.

2. Case description

A 62-year-old female presented to our Emergency Department in July 2016 with chief complaints of cough, fever, dyspnea of one-week duration and significant unintentional weight loss of 10lbs over a period of 4 months. Medical history was significant for former smoking, sarcoidosis of unknown duration and diet controlled hypertension. Sarcoidosis was under control with PO prednisone 5mg daily, however she discontinued it on her own for the last two years as she didn't have any respiratory symptoms. She has never been on biological therapy for sarcoidosis. She was afebrile and hemodynamically stable. Laboratory testing showed a hemoglobin of 11.5 g/dl, leucocytes 4,300 cells/ul and normal kidney function, electrolytes and liver enzymes. Significantly, C-reactive protein was elevated at 27.3 mg/L, ESR at 52 and ferritin at 235 ng/ml. She tested negative for HIV. Chest X ray showed irregular opacification of

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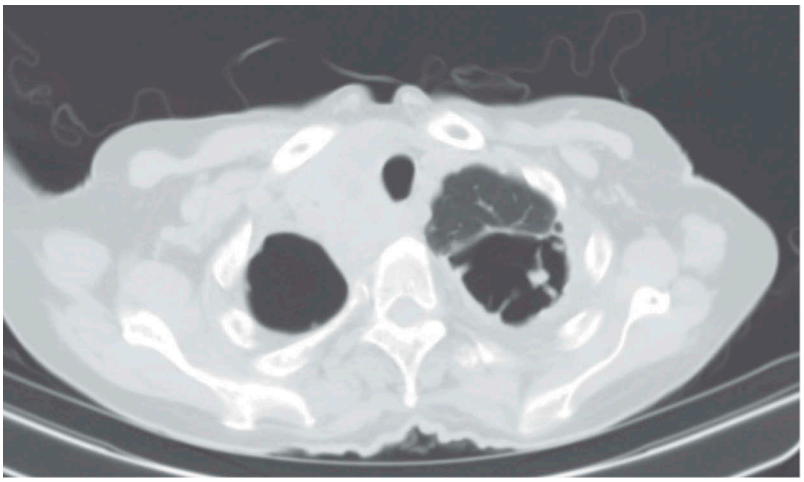
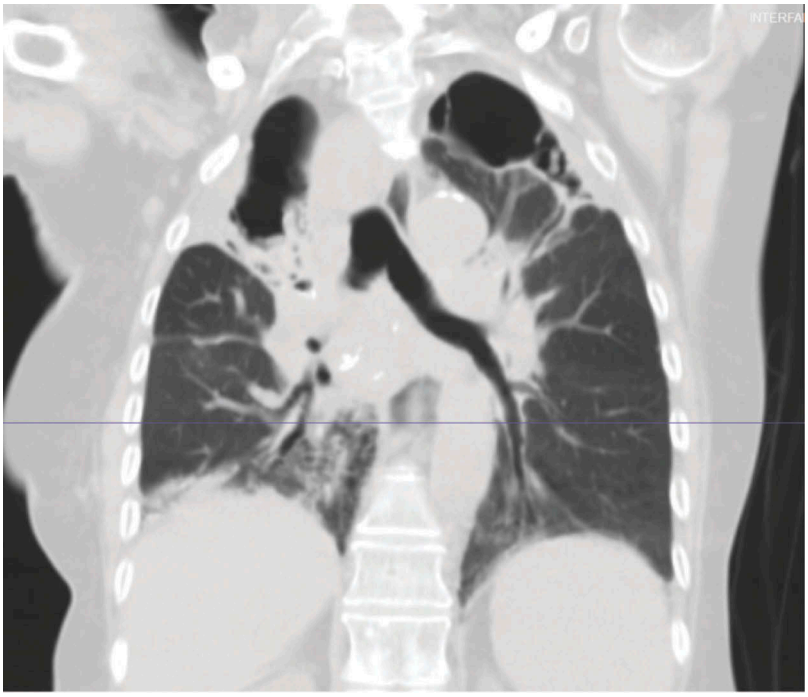
upper lung zones more on the right side, associated with some pleural thickening which was further detailed by the chest CT scan (Figure 1(a,b)) as consolidative volume loss in bilateral upper zones more pronounced on the right lung and bilateral apical cavitary lesions. She was admitted to the medical floor and placed on airborne isolation. Sputum samples were collected 8 h apart, which tested positive for rare acid-fast bacilli in all the three samples. Soon, she was started on anti-tubercular regimen with isoniazid, rifampin, pyrazinamide and ethambutol. Sputum PCR was done which resulted negative for Mycobacterium Tuberculosis. Airborne isolation was discontinued. She was discharged with isoniazid, pyridoxine, rifampin, pyrazinamide, ethambutol and azithromycin. Follow up appointments with Infectious disease and Pulmonary clinic was provided. The patient continued to follow up at the pulmonary clinic every month after hospital discharge, and she was adherent to her medication regimen. Repeated sputum smear and culture for AFB were sent on each visit and were negative for AFB during the entire follow up period.

In September 2016, the organism sequencing result came back and was identified as *M. xenopi* for five sputum samples taken at different times in July 2016. The same medication regimen was planned to continue for 1 year after the last negative sputum sample. The monthly sputum culture was to be continued.

In January 2017, a follow up chest CT scan (Figure 2(a,b)) revealed interval worsening of cavitary lung disease with progressive air space opacities and



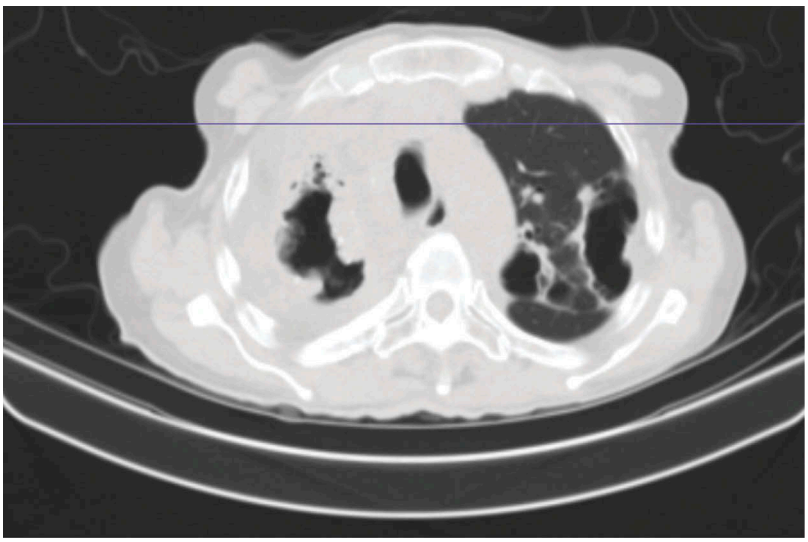
A. Cross section chest CT scan



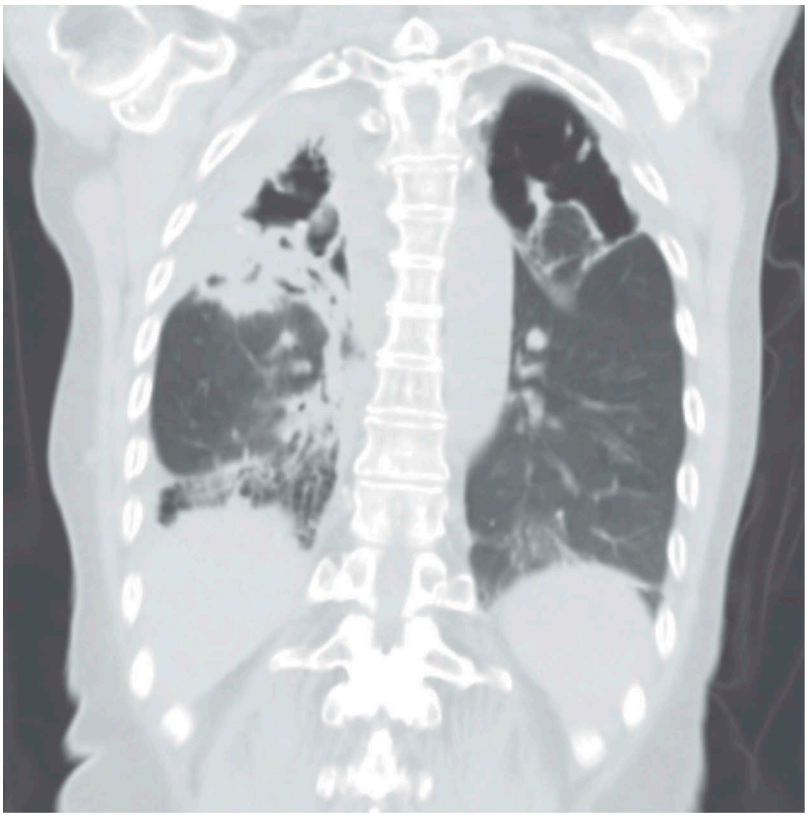
B. Coronal section chest CT scan

Figure 1. (a) Cross section chest CT scan, (b) Coronal section chest CT scan.

Chest CT scan: revealed multifocal cavity lesions, most prominent in the apices, consolidative volume loss greatest in upper zones, right greater than left.



A. Cross section chest CT scan



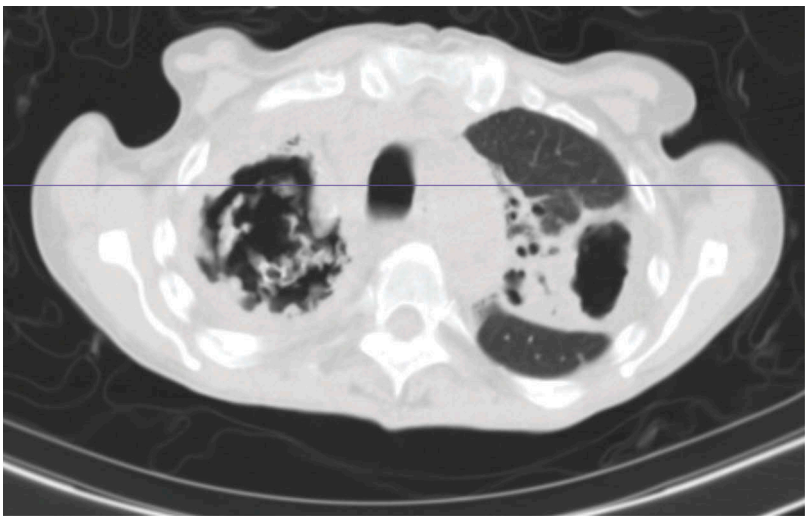
B. Coronal section chest CT scan

Figure 2. (a) Cross section chest CT scan, (b) Coronal section chest CT scan.

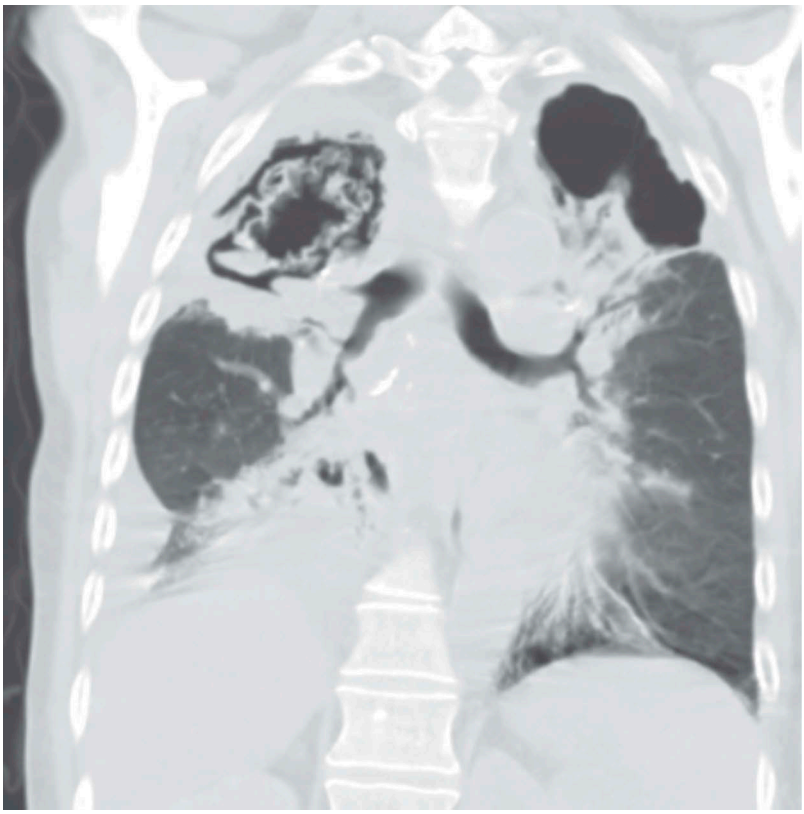
Chest CT scan: revealed progressive airspace opacities and traction bronchiectasis in the right base with small right pleural effusion on the background of severe thick-walled cystic changes in the apices.

traction bronchiectasis on the background of severe thick walled cystic changes in the apices. She was having microbiological response represented by monthly culture was negative for AFB but no radiological response as represented by worsening cavitary lung disease.

In May 2017, the patient was re-admitted to our facility due to sepsis secondary to pneumonia and worsening cavitary lesions seen on the chest X Ray and chest CT scan (Figure 3(a,b)). She was managed with intravenous antibiotics with continuation of anti-tubercular therapy. Blood cultures on admission showed no growth, sputum culture came back positive for *Candida tropicalis* and she was started on Voriconazole. Three days into hospital stay, the patient developed severe respiratory distress with hypoxemia. Upon failure of noninvasive positive pressure ventilation, she was intubated and placed on mechanical ventilation. Bronchoscopy was performed which showed



A. Cross section chest CT scan



B. Coronal section chest CT scan

Figure 3. (a) Cross section chest CT scan, (b) Coronal section chest CT scan.
Chest CT scan: revealed enlarged thick -walled cavities in the bilateral apices, worsening the cavitary lung disease.

edematous mucosa with copious thick purulent secretions. The following day, the patient's condition deteriorated further and she expired. Later on, the result of bronchoalveolar lavage and bronchial washing came back negative for bacterial growth. No autopsy was performed on the case.

3. Discussion

The incidence of *M. xenopi* infections is increasing worldwide. The usual route of infection for pulmonary diseases is inhalation of infected airborne particles. Development of clinical disease requires either immunocompromised host or structural lung disease. Our patient had no clear evidence of immunosuppression, however, she could have had underlying structural lung disease prior to infection. Unfortunately, we don't have any previous imaging prior to the initial presentation. Although she had sarcoidosis, her chest CT scan only revealed hilar and mediastinal lymphadenopathy without reticulonodular infiltrate or fibrosis. It is not clear to what extent sarcoid disease has caused structural lung disease.

Clinically, *M. xenopi* infections can present with cough, malaise, weight loss and hemoptysis. Radiological manifestations can vary according to the patient's immunological status, and can vary from a cavitary form in patients with preexisting pulmonary disease, a solitary nodular form in immunocompetent patients or an acute infiltrate form in immunosuppressed patients [13]. The most common radiological finding, however, is fibro-cavitary apical pulmonary disease as seen in our case [12]. And as with our patient, these pulmonary cavitary lesions can continue to worsen and progress despite sustained microbiological response to treatment. Underlying super-infection with nocardia, *Aspergillus fumigatus, coccidiomycosis, cryptococcosis* and *histoplasmosis* can contribute to worsening cavitary disease. The limitation to our case was the unavailability of prior chest imaging, and autopsy was not performed for further evaluation of demise cause.

The optimal management of patients with pulmonary *M. xenopi* infections has not been well established. Treatment with at least three active drugs against *M. xenopi* is required for 12-18 months. American Thoracic Society has proposed a regimen with clarithromycin, rifampin and ethambutol with the possibility to use moxifloxacin instead of any one of the three drugs. The treatment success rate in patients with pulmonary *M. xenopi* ranged between 8.8%[13–16] and 73%[17] in six different studies, and the all-cause mortality remains very high. Due to a variety of treatment regimens administered in these studies, an optimal multidrug treatment regimen could not be derived. Establishing treatment regimens is further complicated as the published *in vitro* susceptibility results for specific antibiotics may not be predictive of general treatment success with that particular antibiotic [18,19]. Furthermore, susceptibility testing for *M xenopi* may be hampered by the poor growth of that agent *in vitro* [18–20].

Localized surgical resection of the lung represents an important adjunct to chemotherapy for the treatment of *M xenopi* pulmonary disease, and is indicated in patients with medical treatment intolerance, failure, relapse, coexistent aspergilloma with hemoptysis, or lung destruction [21].

Up to the date of writing this case report, there is no study conducted on mortality rate for *M. xenopi* infection. In a recent systemic review and meta-analysis on microbiological and clinical outcomes of treating non-Mycobacterium avium complex nontuberculous mycobacterial pulmonary disease revealed that a sustained microbiological response without surgery is unsatisfactory in treating *Mycobacterium abscessus, M xenopi*, and *Mycobacterium malmoense*. Functional and quality of life aspects should be given more emphasis in the individual evaluation of treatment outcome [22].

In this setting of the absent treatment protocol, well-designed studies with sufficient power are needed to establish new guidelines for the treatment of *M. xenopi*.

Disclosure statement

No potential conflict of interest was reported by the authors.

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