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Mycobacterium kansasaii and *Mycobacterium scrofulaceum* dual pulmonary infection in an immunocompetent male: first report from India

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Abstract

A 57-year-old farmer presented with chronic cough and recurrent hemoptysis, previously treated for sputum-positive pulmonary tuberculosis. Referred to us for evaluation of drug-resistant tuberculosis as his sputum was persistently positive for acid-fast bacilli along with radiological worsening even after 6 months of antitubercular treatment. Bronchoalveolar lavage was performed and he was diagnosed with a rare mixed non-tuberculous mycobacteria (NTM) pulmonary infection despite no immune dysfunction. He was successfully treated with a multidrug regimen of rifampicin, isoniazid, ethambutol and clarithromycin.

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Introduction

Non-tuberculous mycobacteria (NTM) are ubiquitous and are frequently encountered as contaminants in our surroundings. NTM infections are commonly caused by *Mycobacterium* avium complex (MAC), *Mycobacterium kansasii* and rapidly growing mycobacterium (RGM). Mixed infections can occur due to MAC and other RGM, particularly in immunocompromised hosts. Coinfection due to *Mycobacterium kansasaii* and *scrofolaceum* has never been reported before in an immunocompetent host.

Case Report

A 57-year-old gentleman, non-smoker, farmer by occupation, presented to our Outpatient Department with complaints of cough for one year, hemoptysis on and off for the past eight months. Cough was insidious in onset and was not progressive. Cough occurred in bouts, there were no postural or diurnal or seasonal variations. Hemoptysis was scanty and was seen once or twice a month and was associated with minimal whitish sputum production. He had no history of diabetes or hypertension. At the onset of symptoms one year back, he was diagnosed with sputum smear-positive pulmonary tuberculosis. He was treated with anti-tubercular treatment (ATT) consisting of rifampicin (R), isoniazid (H), ethambutol (E), and pyrazinamide (Z) for 2 months and HRE for 4 months as per prevailing guidelines. Even after completion of 6 months of ATT patient had no relief in cough and hemoptysis. For the same he had visited various doctors and had received multiple courses of antibiotics but with no relief along with further deterioration of his general condition. Hence, the patient was referred to us for evaluation of persistent cough and hemoptysis. On examination, his vitals were within normal limits with normal room air saturation. Coarse crepitations were heard in the right infraclavicular area and the rest of the systemic examination was non-contributory. Chest radiograph posterior-anterior view (CXR PA) showed a cavity in the right upper zone with surrounding

patchy consolidation (Figure 1). Later he underwent bronchoscopy with bronchoalveolar lavage (BAL) to rule out drug resistant tuberculosis (DRTB). His BAL, cartridge-based nucleic acid amplification assay (CBNAAT) was negative for mycobacterium tuberculosis. Liquid culture for MTB grew non-tuberculosis mycobacteria (NTM). Repeat BAL was done to rule out contamination and for further speciation, the BAL sample was sent to TB reference laboratory, where liquid culture MTB again showed growth of NTM. The culture specimen was further sent to National Institute for Research in Tuberculosis (NIRT), Chennai, Tamil Nadu, an Indian Council of Medical Research (ICMR) center, a national and also world health organization TB reference center. There the culture was identified as mixed growth of *M. kansasaii* and M. *scrofulaceum* by mycobacterial growth indicator tube (MGIT) liquid culture followed by NTM line probe assay (LPA). Based on the culture report he was started on rifampicin 600 mg once daily (OD), ethambutol 800 mg OD, clarithromycin 500 mg OD. The patient tolerated the regimen well, and no significant adverse reactions were observed. The patient was clinically better by the end of 3 months of treatment, his cough reduced significantly and there was no hemoptysis and his general condition also improved. BAL sample was repeated on 5th and 6th months of treatment and both CBNAAT for MTB and liquid culture for MTB were negative on both occasions. CXR PA View done at 6 months of treatment (Figure 1b) showed resolution of consolidation with a reduction in cavity size, repeated CXR PA view at the completion of treatment (Figure 1c) showed complete healing of the cavity. The REC regimen was further continued to complete a total duration of 18 months with no sequelae.

Discussion

Non-tuberculous mycobacteria (NTM) encompass more than 140 species of mycobacteria other than *M. tuberculosis* complex and *M. leprae* [1]. They are ubiquitous organisms, distributed widely in the environment. NTM are opportunistic pathogens that cause skin and soft tissue infections, lymphadenitis and lung disease in humans in immunocompromised individuals [2-4]. Data regarding NTM infection in India is largely unknown as it is not a reportable disease and also due to lack of identification facilities. The frequency of NTM isolation has increased from 1.0- 3.5% from 2001 to 2020 and 88% of these isolates were clinically significant [5,6]. Most common species isolated from our country are *M. kansasii*, *M. chelonae*, *M. xenopi*, *M. scrofulaceum*, *M. avium*, *M. asiaticum* and *M. fortuitum* [7]. Mixed NTM pulmonary infection due *Mycobaceterium avium complex* and *Mycobacterium abscessus* complex has been reported previously, was associated with nodular bronchiectiasis [8]. Mixed pulmonary infection of *M. kansasii*, *M. avium complex* and *M. abscessus* has also been reported [9]. To the best of our knowledge mixed pulmonary infection due to M. *kansasaii* and *M. scrofulaceum* has never been reported from our country. Both are slow growing NTM, *Mycobacterium*

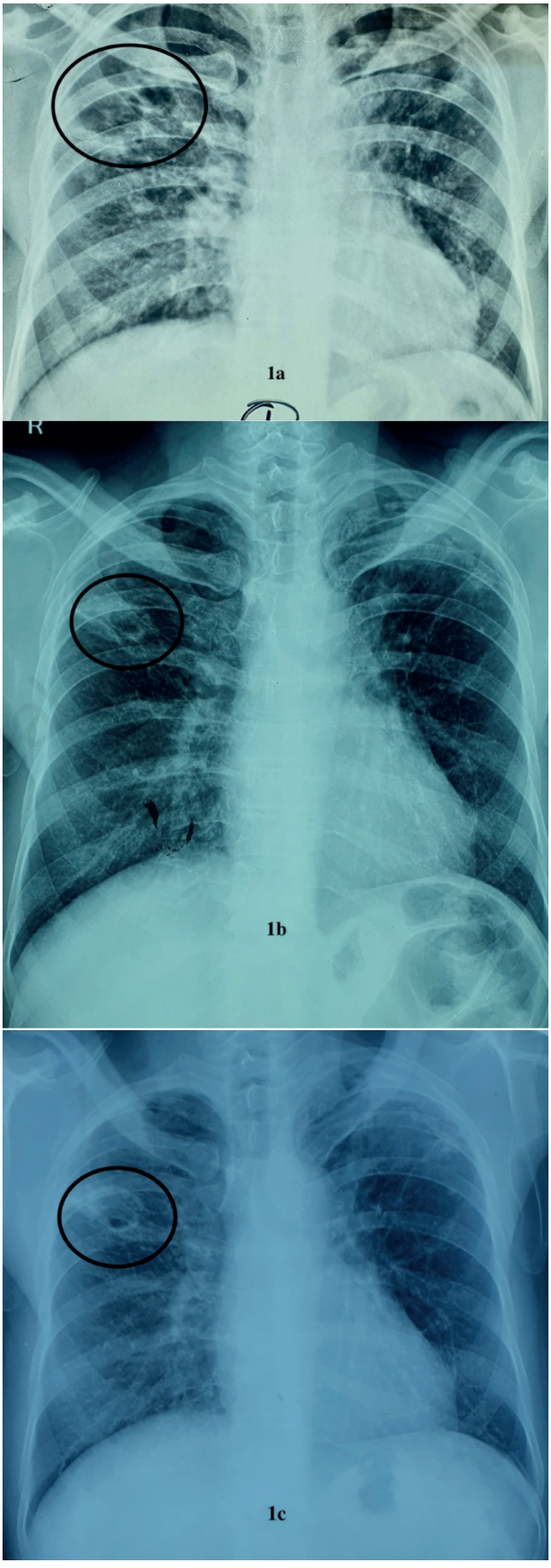

Figure 1. a) CXR-PA view at diagnosis showing cavity in right upper zone. b) CXR-PA view at 6 months of treatment showing reducing in cavity size. c) CXR-PA view at the end of 24 months of treatment showing near total resolution of cavity with fibrosis.

scrofulaceum derived from "scrofula" commonly causes cervicofacial lymphadenitis in preschool children. Lung infection due to *M. scrofulaceum* in immunocompetent adults is very rare. *M scrofulaceum* also exhibits frequent drug resistance to isoniazid. Treatment durations are relatively unknown and clarithromycin is recommended as a preferred agent [10]. *M Kansasaii* is a group I NTM it causes infections in both immunocompromised and immunocompetent hosts, causes chronic pulmonary disease and mimics pulmonary tuberculosis both clinically and radiologically. It is the most frequent NTM isolated in immunocompetent persons and second most common in HIV infected individuals. The recommended treatment of *kansasai* is rifampicin (R), isoniazid (H), ethambutol (E) for at least one year after culture conversions [11]. We encountered the mixed infection for the first time considering the available evidence for treatment, the patient was put on a combination of RHE along with clarithromycin and the patient responded very well both clinically and radiologically. The patient is being followed to date and is asymptomatic for the past year after completion of the treatment.

Conclusions

NTM infection should be suspected in patients remaining persistently sputum smear positive for MTB even in tuberculosis high-burden countries. Confirmation using culture and genotypic methods is essential for starting appropriate and timely treatment to prevent long-term complications like hemoptysis and structural lung disease. Mixed NTM infections are rare in immunocompetent hosts and need to be promptly addressed when diagnosed by reliable laboratory testing.

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