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Case Report

A Rare Case Presentation: Non-Tuberculous *Mycobacteria*

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Received: December 22, 2021; **Published:** February 23, 2022

Abstract

45 years old male; non-smoker; non-alcoholic; presented with complain of shortness of breath, on and off since 2 years aggravated since 1 month, cough with expectoration along with loss of weight and appetite since 1 month and nausea and vomiting since 3 days. The patient was earlier a diagnosed case of *Mycobacterium tuberculosis* microbiologically (sputum) and clinically detected and took treatment for only 2 months. Patient was treated on the lines of non tuberculous *Mycobacteria* both at NITRD (National Institute of Tuberculosis and Respiratory Diseases) Mehrauli, Delhi and at a private hospital in Faridabad, Haryana based on sputum culture reports. Patient further came to SGT Hospital, Gurugram, Haryana as he was not having symptomatic relief. Patient bronchoscopy was done in which BAL (Broncho alveolar lavage) AFB was positive, CBNAAT not detected. BAL culture was positive for NTM (non tuberculous *Mycobacteria*) slow grower *Mycobacterium avium* complex (MAC). Patient was started on tablet rifampicin, tablet ethambutol, tablet azithromycin and injectable amikacin thrice a week and sent home with a plan to repeat sputum culture after 3 months.

Keywords: *Mycobacterium tuberculosis (Mtb); Non-tuberculous Mycobacteria (NTM); Mycobacterium avium Complex (MAC)*

Introduction

From the historic point of view, infections in human species caused due to *Mycobacterium* were most often caused by *Mycobacterium tuberculosis* (TB) and the impact on society of this infection is legendary. Recently, the clinical disease caused by other species of *Mycobacterium* has been discovered and, in many geographical areas, cause greater burden of the disease than TB.

Non-tuberculous *Mycobacteria* (NTM) also been known by several other names which include atypical *Mycobacteria* or anonymous *Mycobacteria*, *Mycobacteria* other than *Mycobacterium tuberculosis* (Mtb) (MOTT) and its close relatives, environmental *Mycobacteria*, *M. africanum, M. canetti, M. caprae, M. pinnipedii, M. bovis*, and *M. leprae* [1].

NTM infections can occur anywhere in the body. The most commonly described attributable human infections are pulmonary infections, lymphadenitis, and skin and soft tissue infections [2]. The susceptibility and manifestations of infection are influenced by host factors and organism characteristics [2].

In countries where the prevalence of TB is high, NTM diagnosis is really difficult due to a lack of awareness among healthcare workers or providers about the NTM diseases. Also, there is inadequate access to adequate laboratory resources for the identification or speciation including mycobacterial culture and molecular methods [3]. So as resources are limited in these settings, there is a heavy dependence on smear microscopy for the diagnosis of TB, and the diagnosis of NTM is frequently being missed and these patients are empirically treated as either drug-sensitive or resistant TB [4].

Till today over 150 different species of NTM have been discovered, most commonly pulmonary infections are due to *Mycobacterium avium* complex (MAC), *Mycobacterium abscessus and Mycobacterium kansasii*. The identification of these organisms in pulmonary infec-

tion does not always co-relate with active disease or infection; supportive clinico- radiological findings are needed to establish the diagnosis. NTM infections are difficult to eradicate. A combination of drugs with a prolonged course of therapy is required.

Case Report

45 years old male; non-smoker; non-alcoholic; presented with complain of shortness of breath, on and off since 2 years aggravated since 1 month, cough with expectoration along with loss of weight and appetite since 1 month and nausea and vomiting since 3 days. The patient earlier visited to a government hospital in Badshahpur, Gurugram, Haryana where Sputum AFB 2+ was detected and was started on anti-tubercular treatment. The patient took treatment for 2 months but discontinued the medication on its own as there was no improvement in symptoms. The patient then went to Civil Hospital Gurugram, Sector 10 where his sputum for Acid fast bacilli (AFB) was negative and he was referred to NITRD (National institute of tuberculosis and respiratory diseases) Mehrauli.

At Mehrauli, patient sputum for CBNAAT (cartridge based nucleic acid amplification test) was negative and patient was diagnosed as a case of suspected NTM (non-tuberculous *Mycobacteria*) and patient was started on tablet rifampicin, ethambutol, clarithromycin and injection amikacin. The patient then itself discontinued the medication after 2 months as there was no improvement in symptoms.

The patient then visited to a private hospital in Faridabad, Haryana where sputum for AFB was positive (1+) and was CBNAAT detected and rifampicin sensitive. Patient was started on full dose ATT (Anti tubercular treatment). The patient then complained of pain in stomach along with loss of appetite and nausea and vomiting after 3 days. His LFT (Liver function test) was done in which Total bilirubin was 2.99 mg/dl, Direct bilirubin 1.40 mg/dl and Indirect bilirubin was 1.59 mg/dl. His SGPT and SGOT was 170 U/L and 175 U/L respectively. Sputum culture was sent and reports were awaited. Patient was planned to be started on modified ATT, injection streptomycin, tablet ethambutol, tablet levofloxacin but streptomycin could not be started as the patient had lean muscle mass (BMI 14). So, the patient was started on tablet ethambutol, tablet levofloxacin, injection amikacin (i.v).

After 2 weeks repeat, LFT showed improvement in Total bilirubin level to 0.6 mg/dl and SGOT and SGPT were 22 U/L and 19 U/L respectively. Meanwhile, Patient sputum culture reports were positive and revealed NTM (non-tuberculous *Mycobacteria*) slow grower *Mycobacterium avium* complex (MAC).

The patient then came to SGT Hospital, Gurugram, Haryana as he was having intermittent episodes of fever along with persistent cough with expectoration for further investigation and treatment. His routine investigations were done in which Hb (hemoglobin) was 11.8 gm/dl and TLC (Total leukocyte count) was 15,900 cmm^3. Liver function test and Kidney function test reports were within normal limits. Chest X-ray (PA view) showed nodular opacities in the bilateral upper zone lung fields. CT chest showed nodular opacities with bilateral upper lobe consolidation.

Patient bronchoscopy was done in which BAL (Bronchoalveolar lavage) AFB was positive, CBNAAT not detected. BAL sample was also sent for culture which was positive and revealed NTM (non tuberculous *Mycobacteria*) slow grower *Mycobacterium avium* complex (MAC). Patient was started on tablet rifampicin, tablet ethambutol, tablet azithromycin and injectable amikacin thrice a week. Patient was planned to do repeat sputum culture after 3 months.

Figure 1: *Anterior view of the patient.*

Figure 2: *Lateral view of the patient.*

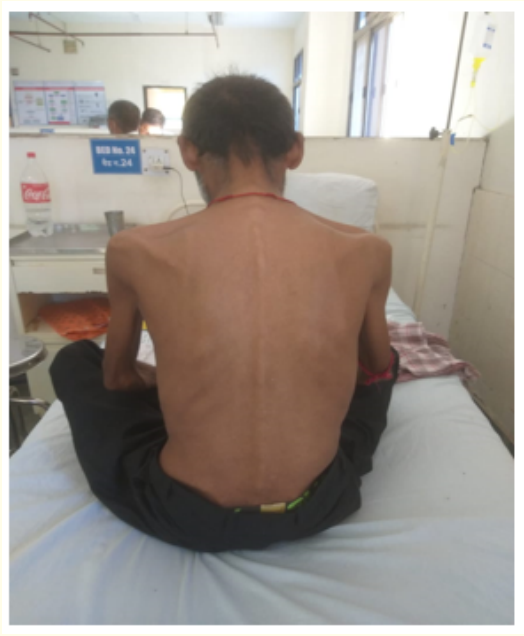

Figure 3: *Posterior view of the patient.*

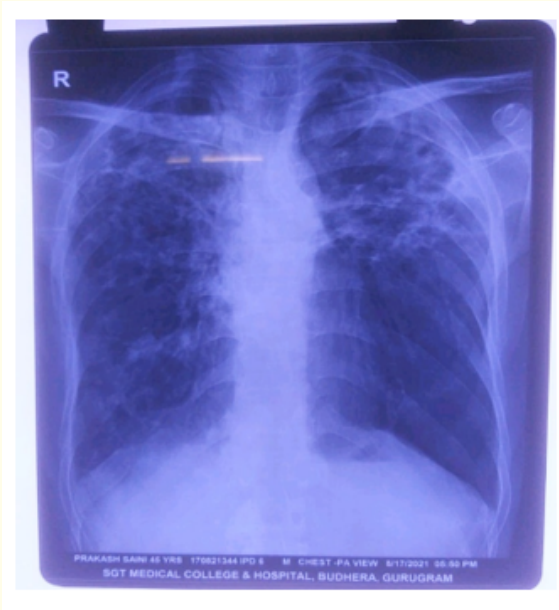

Figure 4: *Chest X ray of patient (PA view).*

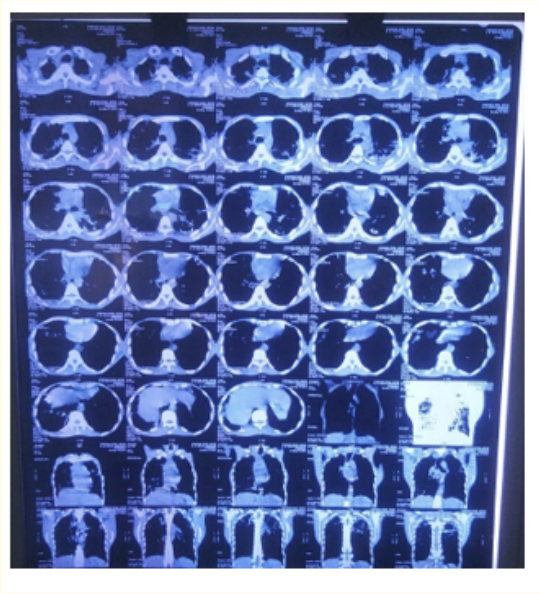

Figure 5: *CT Chest of patient.*

Discussion

Soon after Koch's identification of TB in 1882, *Mycobacterium* organisms other than TB were identified, it was not until the 1950's they were recognized to cause human disease and infection [5]. Different classification systems of the bacteria have been proposed since historic times, but the most common classification of NTM is by growth rate-either slowly growing or rapidly growing. Till now, the most common organism associated with pulmonary disease is a slow-growing NTM, *Mycobacterium avium* complex (MAC), that comprises many subspecies including *avium, hominissuis*, *silvaticum,* and *paratuberculosis,* as well as the species *marseillense, timonense, bouchedur honense, arosiense, intracellulare, chimaera, colombiense,* and *ituriense*. The second most common cause of pulmonary infections or disease is *Mycobacterium kasassii,* also a slow-growing organism [6,7]. The third most common cause of lung disease is *M. abscessus*, the most commonly isolated rapidly growing NTM [6]. Most of the NTM lung infections are caused by these three organisms, it is necessary to identify that many other NTM may cause pulmonary infection in both immunocompetent and immunocompromised hosts. Thus, in the context of a patient's clinical presentation, the pathogenic importance of an NTM specimen must be determined [8,9].

Over the last three decades, it has been suggested that the incidence of both NTM laboratory isolation and disease prevalence is increasing. This change has been attributed, in part, to improved culturing techniques, coupled with greater disease awareness and a true increase in disease prevalence. However, it is challenging to accurately characterize the incidence and prevalence of NTM pulmonary infections since isolation of the organism does not universally indicate clinical infection.

However, not all positive NTM cultures represent infection. A recent analysis showed that approximately half of those with positive NTM respiratory cultures fulfilled clinical criteria for active infection [10].

Women are also more likely to have NTM disease than men [11], the disease prevalence increases with age [12] and it is more common in the West and Southeast [11]. NTM are not visible on routine Gram stain, so the fluorochrome technique for staining is recommended [13].

Cultured NTM should be identified to the species level to guide decisions regarding clinical relevance and appropriate therapy. Speciation of NTM can be achieved with polymerase chain reactions, gene probe assays, and high-performance liquid chromatography [14].

Although the exact route of NTM infection is not established with certainty, based on NTM environmental distribution, it is very likely that the organism is ingested, inhaled, or implanted. Aerosolization of droplets small enough to enter the alveoli is the likely route of acquisition of pulmonary disease.

In an effort to standardize the definition of NTM infection, the American Thoracic Society (ATS) and the Infectious Disease Society of America (IDSA) jointly published guidelines in 2007 [15]. 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. Clinical symptoms vary in scope and intensity but chronic cough, often with purulent sputum, is common. Hemoptysis may also be present. Systemic symptoms including malaise, fatigue, and weight loss may occur often in association with advancing disease.

Fibro cavitary disease is commonly identified on chest roentgenograms. Characteristic findings include thin-walled cavities with an upper lobe distribution and surrounding pleural abnormalities. NTM in conjunction with nodular bronchiectasis may be visible on chest radiograph, but is best appreciated on high resolution chest computed tomography (HRCT). Characteristic findings include clusters of small nodules usually less than 0.5 mm-the so-called tree-in-bud sign. Larger nodules, with or without cavitation, may occur, which are suspicious for malignancy. Uptake of ^{18}F fluorodeoxyglucose (FDG) on PET scan has been described in nodules due to NTM [16]. Infected areas of lung parenchyma may demonstrate atelectasis or cystic or saccular bronchiectasis.

Because NTM are ubiquitous in the environment, especially in water sources, a single positive pulmonary specimen does not fulfill microbiologic criteria for infection. Confirmatory microbiologic findings require culture growth of NTM from either one bronchoalveolar lavage, two sputum samples, or culture from respiratory tissue demonstrating granulomatous histopathology.

Newer macrolide drugs such as azithromycin and clarithromycin are central to drug therapy for MAC lung infections. These agents demonstrate *in vitro* and clinical activity [17] against MAC, and are able to achieve penetration into phagocytes and tissue [18]. It is imperative that these agents not be used in isolation due to the substantial possibility of the development of resistance. Combination drug therapy with a macrolide (azithromycin or clarithromycin), rifampin or rifabutin, and ethambutol with or without an intravenous aminoglycoside are recommended. Therapy should be continued for at least one year after conversion of sputum cultures from positive to negative [19].

For patients with fibrocavitary disease, previously treated disease, or severe disease daily therapy with the inclusion of either streptomycin or amikacin to the fore mentioned agents is recommended.

Prolonged triple drug therapy including isoniazid (INH), rifampin, and ethambutol is recommended for treatment of *M. kansasii* infections. Therapy should be continued for 12 months after sputum conversion to negative. Macrolides such as clarithromycin and the fourth-generation fluoroquinolone moxifloxacin demonstrate very good *in vitro* activity against *M. kansasii* and may be an alternative to INH [20].

Lung infections due to *M. abscessus* are notoriously difficult to treat successfully with drug therapy alone. Chemotherapy in conjunction with surgical resection is often needed in those who can tolerate it.

Summary

The incidence of NTM infections surpasses that of TB infections in developed countries. Although infection may occur in virtually any organ, pulmonary infections are most common. *M. avium, M. kansasii,* and *M. abscessus* are the most frequently identified organisms causing lung disease. The isolation of an NTM organism does not necessarily equate with active infection; clinical, radiologic, and microbiologic parameters are all needed to establish the diagnosis of infection. Eradication of disease with drug therapy requires prolonged combination therapy.

Bibliography

1. Haworth CS., *et al*. "British Thoracic Society Guideline for the management of non-tuberculous mycobacterial pulmonary disease (NTM-PD)". *BMJ Open Respiratory Research* 4 (2017): e000242.

2. Chan ED and Iseman MD. "Underlying host risk factors for nontuberculous mycobacterial lung disease". *Seminars in Respiratory and Critical Care Medicine* 34 (2013): 110-123.

3. Baldwin SL., *et al*. "The complexities and challenges of preventing and treating nontuberculous mycobacterial diseases". *PLOS Neglected Tropical Diseases* 13.2 (2019): e0007083.

4. Sarro YD., *et al*. "Simultaneous diagnosis of tuberculous and non-tuberculous mycobacterial diseases: Time for a better patient management". *Clinical Microbiology and Infectious Diseases* 3.3 (2018): 10.

5. Field SK., *et al*. "Mycobacterium avium complex pulmonary disease in patients without HIV infection". *Chest* 126.2 (2004): 566-581.

6. Griffith DE., *et al*. "An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases". *American Journal of Respiratory and Critical Care Medicine* 175.4 (2007): 367-416.

7. Yates MD., *et al*. "The nature of mycobacterial disease in south east England, 1977-84". *Journal of Epidemiology and Community Health* 40.4 (1986): 295-300.

8. "Pulmonary disease caused by M. malmoense in HIV negative patients: 5-yr follow-up of patients receiving standardised treatment". *European Respiratory Journal* 21.3 (2003): 478-482.

9. Jenkins PA and Campbell IA. "Pulmonary disease caused by Mycobacterium xenopi in HIV-negative patients: five year follow-up of patients receiving standardised treatment". *Respiratory Medicine* 97.4 (2003): 439-444.

10. Winthrop KL., *et al*. "Pulmonary nontuberculous mycobacterial disease prevalence and clinical features: an emerging public health disease". *American Journal of Respiratory and Critical Care Medicine* 182.7 (2010): 977-982.

11. Adjemian J., *et al*. "Prevalence of nontuberculous mycobacterial lung disease in U.S. Medicare beneficiaries". *American Journal of Respiratory and Critical Care Medicine* 185.8 (2012): 881-886.

12. Prevots DR., *et al*. "Nontuberculous mycobacterial lung disease prevalence at four integrated health care delivery systems". *American Journal of Respiratory and Critical Care Medicine* 182.7 (2010): 970-976.

13. Ray CG and Ryan KJ. "Sherris Medical Microbiology, 4th Edition". McGraw-Hill Medical (2004).

14. Herold CD., *et al*. "Current techniques in mycobacterial detection and speciation". *Critical Reviews in Clinical Laboratory Sciences* 33.2 (1996): 83-138.

15. Griffith DE., *et al*. "An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases". *American Journal of Respiratory and Critical Care Medicine* 175.4 (2007): 367-416.

16. Bandoh S., *et al*. "Uptake of fluorine-18-fluorodeoxyglucose in pulmonary Mycobacterium avium complex infection". *Internal Medicine* 42.8 (2003): 726-729.

17. Wallace RJ Jr., *et al*. "Clarithromycin regimens for pulmonary Mycobacterium avium complex. The first 50 patients". *American Journal of Respiratory and Critical Care Medicine* 153.6 (1996): 1766-1772.

18. Eisenberg E and Barza M. "Azithromycin and clarithromycin". *Current Clinical Topics in Infectious Diseases* 14 (1994): 52-79.

19. Griffith DE., *et al*. "ATS Mycobacterial Diseases Subcommittee., American Thoracic Society., Infectious Disease Society of America". *American Journal of Respiratory and Critical Care Medicine* 175.4 (2007): 367-416.

20. Alcaide F., *et al*. "Comparative In Vitro Activities of Linezolid, Telithromycin, Clarithromycin, Levofloxacin, Moxifloxacin, and Four Conventional Antimycobacterial Drugs against *Mycobacterium kansasii*". *Antimicrobial Agents and Chemotherapy* 48.12 (2004): 4562-4565.

Volume 11 Issue 3 March 2022