Case Report

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A Case of Non -Tubercular Mycobacterium - M. *Chimeria* Infection of the Lungs-A Rare and Difficult Entity to Treat

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ABSTRACT

Background

Non tubercular mycobacterium encompasses more than 200 species of ubiquitous environmental pathogens which causes infections in humans. Known mostly to cause disease in debilitated or immunocompromised patients, it has been known to cause diseases in healthy adults also especially if they have any chronic conditions like chronic lung disease or cardiac disease or are immunosuppressed. The possibility of NTM lung infections should be considered in any patient who presents with a long duration of cough, shortness of breath, Fever and Acid fast bacilli in the sputum who tests negative for Gene Xpert or PCR for Mycobacterium tuberculosis. We describe here a case of NTM infection (M. Chimera) of the lungs in a middle age female who presented to our center.

Keywords: NTM; Gene Xpert; PTB; ATT.

INTRODUCTION

NTM are a diverse group of bacteria that are ubiquitous in the environment, often present in soil and water reservoirs.[1] NTM are typically classified into either rapid growing mycobacteria (RGM) or slowly growing mycobacteria (SGM) based on time for mature colony formation in solid growth medium, with Mycobacterium abscessus and Mycobacterium avium-intracellulare complex (MAC) being most common subtypes.[2] With >200 NTM species identified to date, several meta-analyses suggest that the prevalence of NTM infection is increasing across the globe.[3,4] Multiple host and environmental factors are hypothesized to contribute to this rise including the increasing age of the general population, higher prevalence of chronic lung disease, greater use of immunosuppressive medications .[5,6] NTM infections are generally uncommon in immunocompetent hosts as normal immune defense mechanisms are often able to prevent symptomatic infection. However in Cases of transient immune compromise states on background of chronic and structural lung disease, NTM Infections have also been found in immunocompetent host like ours.[6,7]

CASE REPORT

A 45 year old Female, Non smoker and Non alcoholic from Thori, Chitwan presented to our out patient department with complains of Cough for about a year, increased in frequency for about a month associated with shortness of breath, baseline MMRC grade I for the same duration which progressed to Grade II over the past 1 month. She also gave history of low grade fever on and off for the same duration for which she took over the counter paracetamol on regular basis which used to relieve her fever. Her past medical History was remarkable for Pulmonary tuberculosis two times for which she had received Anti tubercular therapy twice- once for 6 months and another for 9 months; the last therapy being a year and half back. However, no formal documents were available. She was initially evaluated at a health post in Thori where her sputum was found to be Acid fast bacilli stain (Z-N stain) 2+ with increased ESR and Mantoux test positive. Considering the diagnosis of pulmonary tuberculosis, she was started on ATT and her Gene Xpert was sent. However, her gene Xpert came out to be negative and thus was referred. At our center her sputum was again repeated in empty stomach with

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morning sample where it was found to be AFB ++. Gene Xpert PTB was negative. Her ESR was found to be 63 and serologic testing for retrovirus was negative. CT scan of chest was done which showed two thick wall cavitary lesion in the left upper lobe along with cystic bronchiectasis in right lung with complete volume loss of right lung and calcification of right mediastinal pleura suggestive of PTB sequel along with mild right sided pleural effusion. In view of her persistent gene Xpert negativity, Considering the possibility of Non tubercular mycobacterial infection her Sputum was sent for NTM culture which yielded growth of Mycobacteria chimera complex- slow grower after 10 weeks of culture. However, the patient was lost to follow up for 2 months where she had continued her ATT despite suboptimal improvement. When she came for Follow up, her symptoms had improved only partially. Her sputum was still AFB positive and she still complained of cough on and off. She was then started on a triple regiment therapy comprising of Rifampicin 600mg daily along with clarithromycin 500mg bd and Ethambutol 600mg once daily. She was closely monitored over the months when she started to show signs of improvement as evident by decreasing cough, shortness of breath and weight gain. She reported no fever over this time and her ESR gradually decreased.

She reverted to sputum negativity after 4 months of treatment with triple regiment therapy. In view of current guidelines and recommendations she is planned for a total of 18-24 months of therapy.

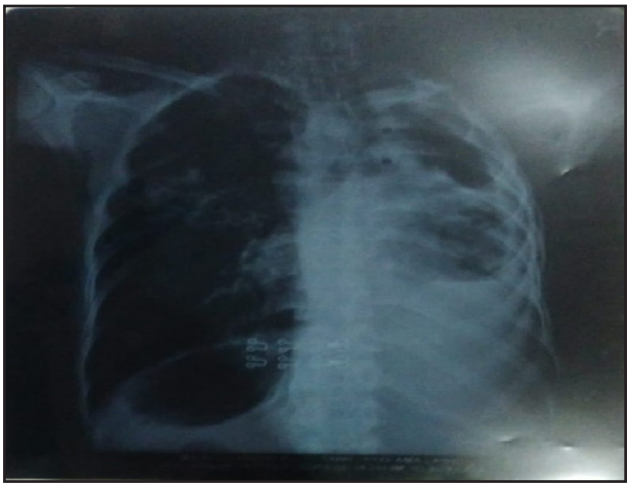


Figure 1. Chest Xray of the patient.

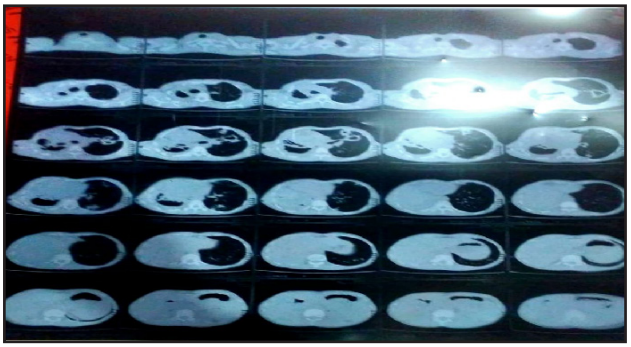


Figure 2. CECT chest of the patient.

Test	Observed Value	Unit	Biological Reference Range	Method
Microbiology				
Sputum For AFB 1st Sample	AFB (++) seen		/HPF	Microscopy
Sputum For AFB 2nd Sample	AFB (++) seen		/HPF	Microscopy

Figure 3. Sputum AFB stain showing Acid Fast Bacilli stain positive.

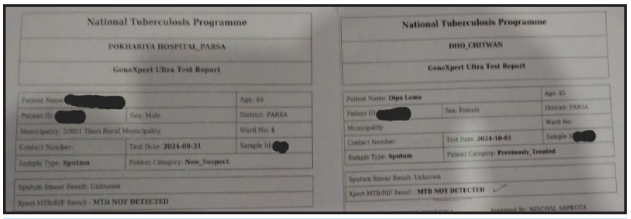
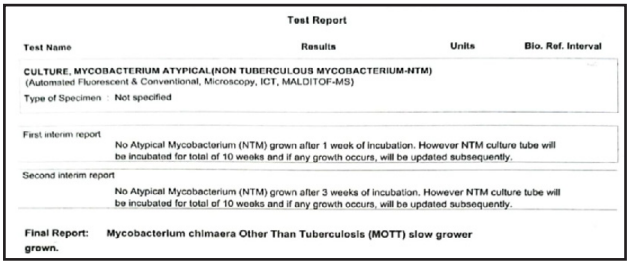


Figure 4. Sputum Gene Xpert showing negative on two samples.



Test Report

Test Name	Results	Units	Bio. Ref. Interval
CULTURE, MYCOBACTERIUM ATYPICAL(NON TUBERCULOUS MYCOBACTERIUM-NTM) (Automated Fluorescent & Conventional, Microscopy, ICT, MALDITOF-MS)			
Type of Specimen : Not specified			
First interim report	No Atypical Mycobacterium (NTM) grown after 1 week of incubation. However NTM culture tube will be incubated for total of 10 weeks and if any growth occurs, will be updated subsequently.		
Second interim report	No Atypical Mycobacterium (NTM) grown after 3 weeks of incubation. However NTM culture tube will be incubated for total of 10 weeks and if any growth occurs, will be updated subsequently.		
Final Report:	Mycobacterium chimaera Other Than Tuberculosis (MOTT) slow grower grown.		

Figure 5. Sputum For NTM culture showing growth of Mycobacteria chimaera other than Tuberculosis- Slow grower.

DISCUSSION

Bacteria of the Mycobacterium avium complex (MAC) play an important role among infections caused by nontuberculous mycobacteria (NTM). MAC consists of the 2 well-established species, M. avium (which has 4 subspecies) and M. intracellulare, Recently, a new species derived from the group of unnamed members of the MAC has been defined which combines features characteristic of different MAC members and has been named M. chimaera sp.[8] It is particularly slow growing; takes 8 weeks or more to obtain visible colonies on solid media.

Known mostly to cause opportunistic infection in immunocompromised hosts, it is defined immensely in literatures as affecting patients undergoing Cardio-pulmonary bypass.[9] However it has been known in cases to cause disseminated respiratory infection in immunocompetent hosts also, especially in patients with preexisting lung disease. Our patient had history of Tuberculosis two times in the past with significant post tubercular sequel (Cavitary lesions, Fibrosis, traction bronchiectasis with volume loss) making her susceptible. Initial M. chimaera infection symptoms are non-specific and often depend on the first body-site or organ involved. Non-specific and indolent symptoms often prompt alternative diagnoses. Common reported symptoms are prolonged intermittent fever, prolonged cough with expectoration, weight loss, generalized malaise and night sweats, with the addition of failure-to-thrive in infants.[10] Diagnosis of Mycobacterium Chimera is complex and relies on growth in culture media. Polymerase Chain reaction is not recommended as it mostly identifies M. chimaera isolate as a member of the M. avium complex (MAC). The complete 16S rDNA gene sequences of MAC species differ by only 6–10 base pairs, and only one base pair discriminates M. chimaera and M. intracellulare.[8] Being slow growers, a sample should not be considered negative until it has been fully incubated at the recommended temperature for about 10 weeks. After growth, it is imperative that the species of NTM be identified. Drug sensitivity is important before initiating the treatment. In our case DST revealed susceptibility to Amikacin, Ciprofloxacin, Clarithromycin, Linezolid, Minocycline, Moxifloxacin, other than the Antitubercular drugs. Thus in accordance with the current ATS/ ERS/ESCMID/IDSA Clinical Practice Guideline we opted for therapy comprising of a Macrolide; Clarithromycin along with Ethambutol and Rifampicin.[11] All patients with NTM-Pulmonary Disease should have a baseline chest radiograph and preferably high-resolution chest CT imaging. There are two broad radiological patterns observed in NTM-PD: fibro cavitary disease, characterized by multiple, thin-walled cavities, usually in the upper lobes of the lungs; and nodular bronchiectasis disease, with nodules, bronchiectasis and bronchial wall thickening. The latter is commonly seen in individuals with no known pre-existing lung disease, but can often be mixed with cavitating nodular change. The optimal duration of treatment is not defined in NTM infection however a consensus statement by various Committee recommends that patients be given therapy for at least 12 months after the sputum conversion to negative. We have planned to repeat her sputum for culture after 6 months of therapy with estimated treatment duration of 18-24 months.

CONCLUSIONS

Although Uncommon, the possibility of Non Tubercular Mycobacterium infection should always be considered in patients with sputum AFB positive but gene Xpert Negative specially if they have an underlying chronic lung condition or cardiac condition which predisposes them to this opportunistic pathogen. Although the duration of treatment is long, with proper counselling, monitoring and treatment regimens, patients will show signs of improvement and start to get better.

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