It Looks Like TB but is not TB

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Abstract

Mycobacterium Abscessus lung infection has a chronic, complicated indolent course with limited treatment options and poor outcomes. We present case of a young female who was treated as a case of pulmonary tuberculosis on the basis of symptoms, radiological findings and positive sputum smears for AFB and negative GeneXpert.

She was declared as treatment failure, sputum cultures were sent which showed growth of NTM. Speciation showed Mycobacterium abscessus, treatment regimen was made according to drug susceptibility testing.

Key Words
Non tuberculosis mycobacteria (NTM), a typical mycobacteria, Mycobacterium abscessus, Mycobacteria other than tuberculosis, Clinical presentation of NTM

Case history
An 18-year-old girl was treated as new acid-fast bacilli (AFB) smear positive pulmonary TB at a private clinic with isoniazid, rifampicin, ethambutol and pyrazinamide for six months. Sputum AFB cultures were not done prior to commencement of ATT. She remained smear positive throughout treatment, without clinical or radiological improvement and was declared treatment failure. She was re-treated with addition of streptomycin but remained symptomatic, with persistent sputum smear positivity for AFB.

She was referred to a specialized TB Center at the Indus Hospital, Karachi with suspicion of drug resistance. Eight sputum specimens yielded positive AFB smears, and four simultaneous GeneXpert tested negative for *M. tuberculosis.*Sputum culture was reported on the fourth day as non-tuberculosis mycobacteria (NTM). A second sample sent four weeks later again rapidly yielded NTM on liquid broth medium, and was speciated as *Mycobacterium abscessus* by Haines test.

Drug sensitivity testing (DST) was performed using brothmicrodilution using RAPMYCO1 Trekdiagnostics sensitivities plates for rapidly growing Mycobacteria. It showed sensitivity to amikacin, cotrimoxazole, linezolid, moxifloxacin and cefoxitin; intermediate sensitivity to imipenem and ciprofloxacin, and resistant to doxycline.

As she was symptomatic with fever and cough and chest X-ray revealed infiltrates it was elected to treat her with amikacin, moxifloxacin and clarithromycin. The patient improved subjectively within two weeks of starting antibiotics, with resolution of cough and fever, however, she complained of hearing difficulty and tinnitus. Audiometry revealed mild to moderate hearing loss, hence amikacin was stopped and substituted with cotrimoxazole. We planned to treat for 6-12 months, with close monitoring. However, after initial clinical improvement she has not returned for follow up visits and remains untraceable.

Discussion
Mycobacteria are divided into two groups namely: *Mycobacterium tuberculosis* (MTB), andnontuberculous mycobacteria (NTM), which do not cause the disease

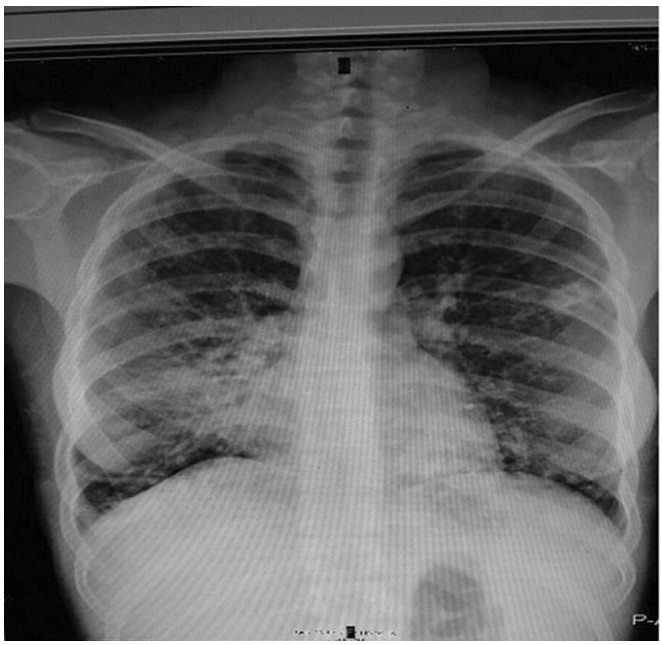

Fig. 1 Chest X Ray, PA view: Areas of bronchiectasis are seen in the left mid zone and periphery; infiltrates are seen in the right middle lobe

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Table 1: Classification of NTM on the basis of growth

Rapidly growing (growth occurring within seven days)	Intermediate growing (growth occurring within 7-10days)	Slow growing (growth occurring in 2-3 weeks)
M abscessus	*M. marinum*	*M. avium* complex (intracellulare)
M chelonae	*M. gordonae*	*M. kansasii*
M. fortutium		*M. Xenopii*
		M. simiae

tuberculosis.[1]

Worldwide, there has been a renewed interest in lung disease caused by NTM, of which *M. intracellulare*, *M. abscessus*, and *M. kansasii*are the most common offenders.[1] *Mycobacterium abscessus* complex is a group of rapidly growing bacilli that is ubiquitous in soil and water, and is known to cause a variety of skin and soft tissue diseases, bacteremia, pulmonary disease, central nervous system and ocular infections.

*M.abscessus*was first described by Moore and Fredric's in 1953.[3] *M. abscessus* complex comprises of 3 sub species on the basis of rpo B sequencing including *M. abscessus*, *M. abscessusmassiliense*, and *M. abscessusBolletii*.[3]

Clinically, it has a wide variety of presentations, ranging from no symptoms to severe bronchiectasis and cavitary lung disease, causing significant morbidity and mortality. Patients with *M. abscessus* pulmonary disease are usually nonsmoking older women, often with no previous lung disease.[2] It causes approximately 65 to 80% of lung disease among rapidly growing mycobacteria.[1]

Our patient did not have apparent risk factors for NTM infection, but given her previous treatment history, it is likely that she had post TB parenchymal lung damage with bronchiectasis. No old chest X-rays were available for comparison.

The conventional method of detecting AFB is through Ziel-Nielsen stain, which does not distinguish MTB from NTM. GeneXpert is a molecular method that detects only MTB DNA, and hence is specific for MTB. Laboratory culture confirms and specialties NTM. DST should be performed to help in adequate treatment of these patients.

Pulmonary infections occur in more densely populated areas, suggesting urban municipal water supply contamination that predisposes individuals to disease.

It manifests as a wide variety of pulmonary disease specifically in hosts with underlying structural lung disease, such as, bronchiectasis, prior tuberculosis and cystic fibrosis.[1] Pulmonary manifestations usually follow an indolent but progressive course, causing debilitating symptoms, worsening of pulmonary function, and poor quality of life; however, the disease can also follow a fulminant course with acute respiratory failure.

According to the 2007 guidelines published by American Thoracic Society/Infectious Diseases Society of America, the diagnosis of *M. abscessus* complex pulmonary disease requires certain clinical and microbiological criteria, such as the presence of clinical symptoms, radiographic evidence of lesions compatible with NTM pulmonary disease and appropriate exclusion of other diseases.[1, 2] Usually positive culture results from at least two separate expectorated sputum samples support the microbiologic diagnosis. Common radiographic findings resemble bronchiolitis, bronchiectasis, nodules, consolidation, and less frequently cavities.

M. abscessus infections are notoriously difficult to treat because they have intrinsic resistance not only to the conventional anti-tuberculous drugs, but also to most conventional antibiotics. Drug related untoward effects are frequently seen, which makes treatment and patient compliance challenging.[1,5] A number of mechanisms are responsible for natural resistance of *M. abscessus*, such as presence of a waxy impermeable cell wall, drug export systems and genetic polymorphism of targeted genes.[3] The mycobacterial cell envelope has a lipid content of approximately 60%, which is primarily responsible for its low permeability to antimicrobials and protects it against toxic extracellular compounds. The existence of the cell wall barrier confers the intrinsic resistance of mycobacterial cells to acids and alkalis and toxic extracellular compounds. In *M. abscessus* complex *erm* (41) gene confers macrolide resistance through methylation of 23S ribosomal RNA. The *erm* (41) gene is present in the *M. abscessus*complex group but absent in *M. chelonae.* Strains of *M. abscessus* sub sp. *massiliense*have a nonfunctional *erm* (41) gene, and as such clarithromycin susceptibility is higher in *M. abscessusmassiliense* than in *M. abscessus*.[1]

The Clinical and Laboratory Standards Institute (CLSI) recommends testing *M. abscessus*mycobacteria for susceptibility to macrolides (clarithromycin and azithromycin), aminoglycosides (amikacin), fluoroquinolones (moxifloxacin, ciprofloxacin), imipenem, doxycycline, tigecycline,cefoxitin,cotrimoxazole, and linezolid.

For effective pulmonary cure, guidelines from the American Thoracic Society/ Infectious Diseases Society of America (ATS/IDSA) recommend multidrug macrolide-based therapy based on susceptibility testing results, along with surgical resection of large cavities or non-resolving parenchymal infiltrates. However, these guidelines also state that there are no effective drug combinations.[1,5] Stout *et al.* recommend using a combination of amikacin plus cefoxitin/imipenem plus clarithromycin/azithromycin, for treating lung disease with *M. abscessus*. Further they report that in vitro assays have shown

that clofazimine, linezolid, bedaquiline, and Tigecycline to act against *M. abscessus*.[2]

According to American Thoracic Society guidelines focal lung disease with *M. abscessus* can be cured with surgical resection along with culture sensitive multi drug chemotherapy. Although surgical resection is curative, associated with improved microbiological and clinical outcomes, surgical complication rate is high, causing increased morbidity and mortality.[2-4]

Conclusion

Our patient had a strong clinical and radiological suspicion of pulmonary TB, along with AFB positive sputum, but failed treatment with antiTb drugs. A positive AFB sputum smear and negative sputum GenExpert is likely to be NTM, and should be confirmed by culture. There are serious limitations for diagnosis and management. Identification and DST of NTM is extremely challenging; *M.abscessus*is a particularly difficult bacterium to cure with antibiotics alone; finally, surgical resection often has to be resorted to, however this option is not easily available in resource-limited countries.

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