

# First case report of chronic pulmonary lung disease caused by *Mycobacterium abscessus* in two immunocompetent patients in Saudi Arabia

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*Mycobacterium abscessus* is a rapidly growing non-tuberculous mycobacterium that is a common water contaminant, and an exclusive opportunistic pathogen in immunosuppressed patients; however, it occasionally causes lung infections in immunocompetent persons as well. We report two cases of chronic pulmonary infection caused by *M. abscessus* in two young migrant workers; they were nonreactive to HIV antigen, without any history of pulmonary disorders and no evidence of any immunocompromized status. Both were initially suspected as having pulmonary tuberculosis, and antituberculosis drugs were administered. The preliminary culture found the isolate as a rapidly growing nontuberculous mycobacteria and later by advanced molecular genotyping of the isolates revealed it as *M. abscessus*. The patients were treated with multiple drugs including clarithromycin. The symptoms resolved slowly, the smears and culture became negative, and they recovered completely. This is the first case of its type to be reported from Saudi Arabia.

**N**ontuberculous mycobacteria (NTM) are increasingly being recognized as pathogens capable of causing pulmonary and extrapulmonary diseases, especially in immunocompromised individuals. The pathogenicity and clinical relevance of many NTM remain poorly understood. Most of the NTM organisms are ubiquitous in nature, and have been isolated from water and soil. Infections are believed to occur from environmental exposures. Person-to-person transmission of NTM is not thought to occur. No reliable estimates of incidence or prevalence of NTM infection are available in Saudi Arabia. A timely diagnosis up to the species level and multidrug therapy is mandatory for a complete cure. We report two rare cases of chronic pulmonary infection found in immunocompetent individuals with the causative agent diagnosed as *Mycobacterium abscessus* by advanced molecular testing methods.

## CASE 1

A 30-year-old malnourished man (by appearance, nature of his work as a laborer in the field, and quality of food) arrived in the hospital in February 2009, citing productive cough, fever, general weakness, and weight loss for 3 months. The patient was nonreactive to HIV antigen, had no relevant transplantation or immunosuppressive drug history, and had never had any episode of tuberculosis or chronic pulmonary disorders. The physical examination showed a patient of average built and the chest examination showed right mid upper zone crackles. However all vital signs were stable, and biochemical and hematological investigations revealed normal results. The erythrocyte sedimentation rate was 34 mm/h. The chest radiograph showed fibronodular infiltration at the right middle zone, and the cardiothoracic ratio was normal. After initial diagnosis, the patient was advised to undergo an early morning sputum analysis

followed by mycobacterial culture. Acid-fast bacilli smear reports evaluated for three consecutive days showed the presence of acid-fast bacilli. He was diagnosed with pulmonary tuberculosis (TB) on 2 February 2009. A Ziehl-Neelsen stain was positive and the sample was sent for TB culture and the patient was isolated after identification of TB. Anti-TB treatment was started on the same day. The two cultures, in the third week, showed heavy confluent growth of beige-colored colonies. The patient was transferred to an isolation ward and the treatment was started with ethambutol (Myambutol) 400 mg, rifampicin 300 mg and isoniazid 150 mg (Rifinah-300), pyrazinamide 1.5 g, and pyridoxine 40 mg. The preliminary culture report showed the presence of rapid-growing nonphotochromogenic NTM, and clarithromycin 500 mg was also started. When the sputum culture showed mycobacteria other than tuberculosis (MOTT) on 24 March 2009, the TB treatment was discontinued and clarithromycin (Klacid) 500 mg twice a day was started for 2 months. The follow up was done on a monthly basis for 6 months. The patient showed improvement clinically and radiologically, and also by sputum smear test. The patient recovered slowly and had a stable smear and the culture was negative at the time of discharge with continuation of the same doses of medicines by April 2009.

## CASE 2

A 40-year-old malnourished man (by appearance, nature of his work as a laborer in the field, and quality of food), was admitted to the hospital in June 2009 with a 2-month history of productive cough, general weakness, intermittent fever, without any chest pain, hemoptysis, and dyspnea. On admission to the hospital his vitals were as follows: temperature, 39°C; pulse, 70 beats/min; blood pressure, 140/90 mm Hg. Chest, abdomen, and extremities were clear and normal. All the vital signs and clinical pathological diagnosis revealed normal results. The repeated chest radiographic examinations showed normal results except a bilateral increased bronchovascular marking. The cardiac size and configuration was normal, and there was no evidence of hilar enlargement. The microscopic examination showed three consecutive smears positive for acid-fast bacilli and two cultures showed heavy rapid growth of mycobacteria. The patient was admitted to the isolation ward and treated with multiple anti-TB drugs (ethambutol [Myambutol] 400 mg, rifampicin 300 mg and isoniazid 150 mg [Rifinah-300], pyrazinamide 1.5 g, and pyridoxine 40 mg); however, the symptoms deteriorated. The culture report showed the presence of rapid-growing nonpigmented NTM, and clarithromycin 500 mg was also added to the drug panel for 2 months. The

isolates were sent for further identification. The patient became stable and negative for smear and culture after 42 days of treatment before discharge. The same doses of drugs were advised during the time of discharge. Follow up was done on a monthly basis for 6 months. The patient showed improvement clinically and radiologically, and also by sputum smear test.

## Microbiology

Sputum samples collected from both the patients were initially cultured on the MGIT 960 automated culture system (Beckton Dickinson, Sparks, NV, USA) and Lowenstein-Jensen's media slants along with a biochemical identification testing, which reported the isolate as rapidly growing, nonpigmented mycobacteria with smooth, beige colored colony morphology. Further investigation to differentiate *M tuberculosis* and NTM by real-time DNA amplification system (Probe-TEC ET, Beckton Dickinson, Sparks, USA) showed the result as NTM. Because of the limited resources, the further identification was not possible in the treatment hospital. Later in a research facility, the DNA was extracted and a polymerase chain reaction (PCR)-based reverse blot hybridization molecular genotyping (Genotype Mycobacterium CM/AS, Hain Life Science, Nehren, Germany) was performed, and the results showed that both the isolates belonged to the same species, *M abscessus*.

## DISCUSSIONS

*M abscessus* belongs to the group of rapid-growing NTM, a heterogenous group of microorganisms that very occasionally cause lung disease, but more commonly affect patients with underlying chronic lung diseases, such as bronchiectasis, pneumoconiosis, emphysema, or cystic fibrosis. *M abscessus* is the most pathogenic and chemotherapy-resistant rapidly growing mycobacterium. It is commonly associated with contaminated traumatic skin wounds and with postsurgical soft tissue infections.<sup>1</sup> Despite the increasing incidence of NTM pulmonary infections, it is often difficult to diagnose this disease because of its insidious and indolent nature. The responsible organism is isolated from sputum or bronchoalveolar lavage fluid intermittently, and a few colonies are generated in culture.<sup>2</sup>

The clinical presentation of the pulmonary disease related to *M abscessus* is quite varied, and the separation of the usually low-grade symptoms from the underlying comorbidity may be difficult. The diagnosis of nontuberculous lung disease is thus a major problem, since the clinical significance of the isolation of NTM has to be established in each case. It requires the integra-

tion of clinical presentation, radiographic findings, and mycobacteriological results. Approximately 40% of patients with the lung disease related to *M. abscessus* have an underlying medical condition, such as previous mycobacterial infections, cystic fibrosis, lipid pneumonia, lung transplantation, achalasia, or other conditions associated with recurrent vomiting.<sup>3,4</sup> These patients often develop the disease at a younger age compared with patients without an underlying illness. In patients without associated medical conditions, the lung disease progresses very slowly, and the chest radiograph usually shows multilobar, patchy, reticulonodular, or mixed interstitial-alveolar infiltrates with an upper lobe predominance.

In both the cases we presented, the late diagnosis and misdiagnosis as TB was noticed. Misdiagnosis of mycobacterial infections can be a life-threatening error especially in the case of immunocompromised patients.<sup>5</sup> The route of transmission of the bacteria could not be traced, and no history of immunosuppression was reported for both the patients. The repeated culturing of sputum samples attained heavy growth of the bacteria and thus colonization could be ruled out. Moreover, the one-time isolation of NTM from the sputum or bronchoalveolar lavage fluid is often caused by contamination or colonization, especially in immunocompetent patients with bronchiectasis.<sup>6</sup> Consequently, according to the American Thoracic Society diagnostic criteria for the NTM pulmonary infection, multiple positive cultures with heavy growth of the infective organism must be demonstrated.<sup>7</sup>

The chest radiographs showed no cavitation in either patient. One patient showed fibronodular infiltration, which is a common radiological manifestation in the NTM-related pulmonary disease. The NTM pulmonary infection in immunocompetent hosts has two distinct radiological manifestations: an upper lobe cavitary form and a nodular bronchiectatic form. The char-

acteristic radiological findings of the upper lobe cavitary form are heterogeneous, nodular with cavitary opacities that are indistinguishable from those seen with the post-primary PTB; however, this form of NTM pulmonary infection usually has a more indolent course.<sup>7-9</sup> Normal chest findings except the slightly exaggerated bronchovascular markings were reported in one patient in three consecutive chest radiographic studies and in concordance with the previous reports.<sup>10</sup>

The final identification of the mycobacterial species was performed by a highly sensitive PCR-based reverse blot hybridization assay.<sup>11,12</sup> The results showed the presence of *M. abscessus*, and finally with the other clinical findings the cases were reported as a true pulmonary infection with partial lung tissue invasion, rather than contamination or colonization. Although the initial misdiagnosis of cases as TB did not affect the treatment, the susceptibility to clarithromycin contributed to a fast recovery in both the cases. The multidrug resistance of *M. abscessus* especially to clarithromycin, which is the key drug for the treatment, is a life-threatening problem in the case of pulmonary as well as disseminated diseases.<sup>5,10</sup>

In conclusion, the pulmonary infection by *M. abscessus* is a rare incident in healthy individuals. Person-to-person transmission of these bacteria is also not yet reported so far. However, characteristics that mimic other mycobacterial diseases make it more difficult to diagnose the condition without molecular identifications. Furthermore, for treating this type of infection, a prolonged combination therapy with the choice of drugs determined by regional susceptibility may be considered, although this requires further research.

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