Nontuberculous Mycobacterial Lung Disease Caused by *Mycobacterium terrae* in a Patient with Bronchiectasis

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We report a rare case of lung disease caused by *Mycobacterium terrae* in a previously healthy woman. A 45-year-old woman was referred to our hospital due to a chronic cough with sputum. A computed tomography scan of the chest revealed bronchiolitis in conjunction with bronchiectasis in both lungs. Nontuberculous mycobacteria were identified and isolated from the bronchoalveolar lavage fluid collected from each lung. All isolates were identified as *M. terrae* by various molecular methods that characterized the rpoB and hsp65 gene sequences. Antibiotic therapy using clarithromycin, rifampin, and ethambutol improved the patient’s condition and successfully resulted in sputum conversion.

**Key Words:** Bronchiectasis; Mycobacterium Infections, Nontuberculous

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**Introduction**

*Mycobacterium terrae* complex is known to comprise multiple species, including *M. terrae, M. non-chromogenicum*, and *M. trivialis*. *M. terrae* is ubiquitous in the environment and generally considered a non-pathogenic nontuberculous mycobacteria (NTM). The most common presentation of *M. terrae* infection is tenosynovitis of the upper extremities, often following trauma. To date, few cases of NTM lung disease caused by *M. terrae* have been reported. Here, we report a very rare case of *M. terrae* lung disease associated with bronchiectasis in an immunocompetent patient.

**Case Report**

In March 2008, a 45-year-old woman was referred to our hospital due to chronic cough and sputum. The patient had been healthy until two months earlier, when cough and purulent sputum developed. She had a history of smoking (10 pack-years), but had stopped 10 years prior. The patient had pectus excavatum, laboratory results were normal with the exception of elevated CA 19-9 (75.32 U/mL, normal range, 0 ~ 37 U/mL). Her height was 161 cm and body weight was 51 kg. A human immunodeficiency virus (HIV) antibody test was negative.

A computed tomography (CT) scan of the chest revealed bronchiectasis and bronchiolitis in both lungs (Figure 1A). The patient also had pectus excavatum in the anterior chest wall. There was no evidence of cystic fibrosis or other common causes of bronchiectasis. NTM were isolated from bronchoalveolar lavage fluid collected from both lungs and cultured *in vitro*.

Polymerase chain reaction (PCR) restriction fragment length polymorphism analysis (PRA) was used to identify the particular mycobacterial species isolated from the
Figure 1. A 45-year-old woman with bronchiectasis and nontuberculous mycobacterial lung disease caused by *Mycobacterium terrae*. (A) A transverse CT scan (2.5-mm-section thickness) obtained on level with the right inferior pulmonary vein at the time of presentation, before treatment, reveals bilateral bronchiectasis (arrows) in the right middle lobe and the lingular segment of the left upper lobe, as well as cellular bronchiolitis with tree-in-bud signs (black arrow heads) in both lungs. Lobular consolidation in the right middle lobe (white arrow heads) was also noted. (B) A CT scan of the same patient after 12 months of antibiotic therapy revealed a decrease in the extent of cellular bronchiolitis and lobular consolidation in both lungs. CT: computed tomography.

Figure 2. Electrophoresis of the PCR restriction enzyme PRA of the *rpoB* and *hsp65* genes from the clinical isolate of the patient. M, size marker; Lane 1, *rpoB* gene PCR product after digestion by *MspI*; Lane 2, *rpoB* gene after digestion by *HaeIII*; Lane 3, *hsp65* gene after digestion by *HaeIII*. PCR: polymerase chain reaction; PRA: polymorphism analysis.

Drug susceptibility testing was performed using a broth microdilution method, as previously described for slow growing mycobacteria, such as *M. kansasii*, according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI). The clinical isolate of *M. terrae* was susceptible to clarithromycin, ethambutol, and amikacin but resistant to ciprofloxacin and rifampin (Table 1).
Table 1. Antimicrobial susceptibility patterns for the Mycobacterium terrae strain isolated from our patient

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC (μg/mL)</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarithromycin</td>
<td>≤0.5</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Rifampin</td>
<td>2</td>
<td>Resistant</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>2</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Amikacin</td>
<td>4</td>
<td>Susceptible</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>8</td>
<td>Resistant</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>2</td>
<td>Intermediate</td>
</tr>
</tbody>
</table>

MIC: minimum inhibitory concentration.

conversion of sputum cultures was achieved and maintained after 12 months of antibiotic therapy (Figure 1B).

Discussion

Despite the prevailing view that M. terrae complex isolates are nonpathogenic, these organisms are occasionally identified in clinical specimens. For example, in our institution, M. terrae complex made up 3% of 1,548 NTM clinical isolates during the 2-year period from 2002 to 2003. Nonetheless, no patient had clinically significant disease caused by M. terrae complex infection during that time.

NTM lung disease caused by M. terrae complex is rarely reported in the literature, and there is no reported case in Korea. Furthermore, previous studies have had difficulty identifying the exact species of clinical isolates, as commercial DNA probes and high performance liquid chromatography (HPLC) are not suitable methods to distinguish between different member species of the M. terrae complex. A recent study analyzing 16S rRNA and hsp65 genes demonstrated genomic heterogeneity among M. terrae complex members. Therefore, we were able to confirm that our patient had M. terrae infection using modern molecular techniques that enabled sequencing of the rpoB and hsp65 genes.

NTM lung disease has two distinct radiographic manifestations: an upper lobe fibrocavitary form and a nodular bronchiectatic form. The nodular bronchiectatic form of the disease occurs predominantly in non-smoking middle-aged or elderly women who have no underlying lung disease. The radiographic features of the nodular bronchiectatic form include bronchiectasis and multiple nodules, which tend to be most severe in the lingular segment of the left lung and in the right middle lobe. These features are well characterized in M. avium complex lung disease, but have also been noted in NTM lung disease caused by other NTM species, such as M. abscessus complex. In addition, women with the nodular bronchiectatic form of NTM lung disease also often have certain medical conditions, including pectus excavatum, scoliosis, and thin body habitus. Our case study presented with typical clinical and radiographic features of the nodular bronchiectatic form of NTM lung disease.

The optimal antimicrobial therapy regimen for M. terrae infection has yet to be established. Some have suggested that drug treatment regimen for M. terrae infection should include macrolide, rifampin, and ethambutol. Our patient received these three drugs and had substantial improvement without significant sequelae. Despite the rifampin resistant that the clinical isolates exhibited in vitro, it was included in the treatment regimen for our patient. It is unclear whether the combination of rifampin and ethambutol proved an additive, or synergistic, effect.

In conclusion, M. terrae should be considered a possible etiologic pathogen of the nodular bronchiectatic form of NTM lung disease, despite the rare occurrence of M. terrae lung disease. Additionally, macrolide-containing antibiotic therapies may be effective in the treatment of M. terrae lung disease.

Acknowledgements

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References