Pulmonary *Mycobacterium intermedium* Disease in an Elderly Man with Healed Pulmonary Tuberculosis

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A 76-year-old man with a history of pulmonary tuberculosis was found to be sputum smear positive for acid-fast bacilli. The 16S rRNA sequence identified the culture isolate as *Mycobacterium intermedium*, the pathogenicity of which has not been confirmed. Chemotherapy with isoniazid, rifampin, and ethambutol resulted in clinical improvement.

CASE REPORT

A 76-year-old man had a routine health checkup in 2002 when his chest radiograph showed thick fibrotic lesions in the apex of both lungs (Fig. 1, left panel). The smear of his sputum for acid-fast bacilli (AFB) was 2+. He was referred to Sapporo Minami National Hospital for suspected pulmonary tuberculosis in October 2002. He denied any symptoms except occasional sputum production.

He remembered being given a diagnosis of pulmonary tuberculosis at about 12 years of age without subsequent chemotherapy. Details of this episode had been lost, along with his *Mycobacterium bovis* BCG status. Medical history was otherwise unremarkable. No risk factors for AIDS were found.

Physical findings were normal. Laboratory data were abnormal in showing an erythrocyte sedimentation rate (ESR) at 1 h of 72 mm and a C-reactive protein (CRP) level of 78.2 mg/liter. A tuberculin skin test resulted in 16 mm of induration. The computed tomography of the thorax showed a cavity with thick, irregular walls at the apex of the left lung abutting caudally the area of severe bronchiectasis. The lesions in the apex of the right lung were mostly thick fibrosis and pleural thickening.

The sputum smear for AFB was repeated on three consecutive days, giving a 3+ result each time. An AMPLICOR nucleic acid amplification test (Roche Diagnostics, Tokyo, Japan) of one sample was all negative for *Mycobacterium tuberculosis* and *Mycobacterium avium* complex (3).

Pending results of the cultures, we started isoniazid, rifampin, and ethambutol on a diagnosis of pulmonary mycobacteriosis possibly due to *Mycobacterium kansasii*, which is the second most prevalent nontuberculous mycobacterium after *M. avium* complex in Japan, considering the negative AMPLICOR result. The clinical course was uneventful. After 2 months of therapy, both smear and culture of the sputum converted to negative, ESR and CRP level were normalized, and a chest radiograph showed clearing of the opacity inside the cavitary lesion of the left upper lobe (Fig. 1, right panel).

The chemotherapy was continued until October 2003, for a total of 12 months. At a follow-up in March 2004, the sputum stayed negative for AFB, and there was no radiographic exacerbation.

Cultures of the initial sputum specimens eventually yielded growth on both mycobacterial growth indicator tubes (BD Diagnostic Systems, Sparks, Md.) and egg-based solid medium (Ogawa medium; Nissui Pharmaceutical Co. Ltd., Tokyo, Japan). The isolated strain showed eugonic growth and photochromogenic character on solid medium. It was positive for urease but negative for nitrate reduction. We were unable to identify the isolate on solid medium by a DNA-DNA hybridization method with a DDH Mycobacteria apparatus (Kyokuto Pharmaceuticals, Tokyo, Japan) (4). Then, the strain was subjected to a 16S rRNA gene sequencing identification method. The bacterial DNA was amplified by PCR with the following primers: primer 264, 5'-TGCACACAGGCCACAAGGGA-3'; primer 285, 5'-GAGAGTTTGATCCTGGCTCAG-3'. The purified DNA amplicon was subjected to direct sequencing with an ABI377 automatic sequencer (Applied Biosystems, Foster City, Calif.) and the dGTP BigDye Terminator Cycle Sequencing FS Ready Reaction kit (Applied Biosystems) according to the manufacturer's instructions. The obtained 16S rRNA sequence data were subjected to Ribosomal Differentiation of Microorganisms (RIDOM) on the website <http://www.ridom-rdna.de/> for homology search. As a result, the strain was identified as *Mycobacterium intermedium*. The MICs of antituberculosis drugs were as follows: isoniazid, 4 µg/ml; rifampin, 0.25 µg/ml; ethambutol, 2 µg/ml; streptomycin, 4 µg/ml; kanamycin, 2 µg/ml; levofloxacin, 0.25 µg/ml; ciprofloxacin, 0.25 µg/ml; clarithromycin, 0.125 µg/ml; ethionamide, 8 µg/ml; amikacin, 2 µg/ml.

M. intermedium is a slowly growing *Mycobacterium* species that was first reported in 1993 (5). Although it was isolated from the sputum of a patient with pulmonary disease, its pathogenic involvement was not formally established (5). To our knowledge, there has been no literature on pulmonary *M. intermedium* disease in humans since then. Regarding our pa-

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FIG. 1. Chest radiographs before (left) and after (right) treatment. The opacity inside the cavitory lesion of the left upper lung diminished after therapy.

tient described in this report, his healed pulmonary tuberculosis lesion seemed to be infected with *M. intermedium*.

Because nontuberculous mycobacteria (NTM) can colonize the airway, one species repeatedly demonstrated in the sputum is considered causative of the lung disease only after clinical and radiographic criteria are also met (1). Although the patient described in this report was nearly asymptomatic, abnormal ESR and CRP level indicated systemic inflammatory reaction. The radiographic abnormalities seen in this case are consistent with healed pulmonary tuberculosis, where NTM infection frequently occurs. Improvement of ESR, CRP level, and the radiographic findings associated with chemotherapy and the resultant disappearance of *M. intermedium* strongly suggest its pathogenic role in our patient's condition. Pathological examination was not done, but the radiographic findings indicate that the infection took place in the wall of the existing cavity and/or dilated bronchi. One might still argue that the present case does not have the symptoms compatible with NTM disease (1). It should be noted, however, that the clinical criteria set by the American Thoracic Society are based on the lung disease caused by *M. avium*, which is more virulent than *M. intermedium*, at least in mice, and hence the latter might cause much more subtle disease (2, 6).

Combination chemotherapy with isoniazid, rifampin, and ethambutol gave a satisfactory result in our patient, although

the MIC of isoniazid for the strain turned out to be high, in keeping with the original report (5). The MIC indicated that the other two drugs were effective. Fluoroquinolones and clarithromycin also had low MICs and might thus have been useful. The optimal regimen, along with the pathogenic potential of *M. intermedium*, remains to be fully established in more cases.

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