Fatal Pulmonary Infection due to Multidrug-Resistant *Mycobacterium kansasii* which Developed in an Immunocompetent Young Man

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A 32-year-old immunocompetent man developed fever and malaise that persisted for three years. As he had no health insurance, he never received any medical treatment. On admission, chest X-ray revealed multiple cavitary lesions and his sputum yielded acid-fast bacilli, that were identified as *Mycobacterium kansasii* with multidrug resistance. Although his general status improved transiently by antituberculoc agents, he died of respiratory insufficiency after four months. The prognosis of *Mycobacterium kansasii* pulmonary disease is reported to be relatively good among non-tuberculous mycobacteriosis, however, physicians must pay careful attention to cases of delayed start of therapy or multidrug resistance, or both.

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**Key words:** nontuberculous mycobacteria, patient’s delay, autopsy

**Introduction**

An increasing number of patients with non-tuberculous pulmonary mycobacteriosis is currently drawing the attention of physicians also in Japan. In this category, *Mycobacterium kansasii* pulmonary disease is known to show a good response to a specific antituberculous regimen. Nevertheless, we encountered a fatal case complicated by both bacteriological and social problems.

For editorial comment, see p 240.

**Case Report**

A formerly healthy 32-year-old man developed fever, productive cough, and general malaise. Because he was uninsured, he did not consult any medical facilities for three years. When he developed exertional dyspnea and weight loss (−10 kg/last 3 months), he was admitted to our hospital. His fingers and toes were clubbed, and bilateral giant cavities in both upper lung fields with mediastinal lymphadenopathy were demonstrated on chest X-ray (Fig. 1) and computed tomography. Elevation of the serum C-reactive protein level of 7.0 mg/ml was detected.

Serum antibody for human immunodeficiency virus was negative. On arterial blood gas analysis, $P_{aO_2}$ was 50.2 Torr in room air. Estimated right ventricle systolic pressure on Doppler echocardiography was 56 Torr. On sputum examination, acid-fast bacilli were detected, then under a tentative diagnosis of pulmonary tuberculosis, combination therapy with isoniazid (INH, 400 mg/day), rifampicin (RFP, 450 mg/day), and ethambutol (EB, 1,000 mg/day) was initiated. Immediately after beginning therapy, smear examinations turned negative, but the results of culture were repeatedly positive. The isolated strain was identified as *Mycobacterium kansasii* by the DNA hybridization method and biochemical analysis, and the drug susceptibility test revealed multidrug resistance (Table 1). The above regimen was continued because his general condition and inflammatory signs were gradually improved.

Four months after the beginning of therapy, new pulmonary infiltrations developed in the bilateral lower lung fields, and he complained of increased exertional dyspnea. Based on a drug susceptibility test, ethionamide (300 mg/day) was co-administered, but he did not respond to any therapeutic modality, and he died of respiratory insufficiency two weeks later.

On autopsy, giant multiple cavities (right $10 \times 9$ cm, left $10 \times 7$ cm) were observed. At the inner lining of the cavity, caseous necrosis with poor granulomatous response was demonstrated.
Multidrug-Resistant *Mycobacterium kansasii*

Table 1. Drug Susceptibility Test

<table>
<thead>
<tr>
<th>Antituberculous agents</th>
<th>Concentration (µg/ml)</th>
<th>Growth</th>
<th>Concentration (µg/ml)</th>
<th>Growth</th>
<th>Concentration (µg/ml)</th>
<th>Growth</th>
<th>Concentration (µg/ml)</th>
<th>Growth</th>
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<tr>
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<td>3+*</td>
<td>0.1</td>
<td>3+</td>
<td>1</td>
<td>3+</td>
<td>5</td>
<td>+§</td>
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<tr>
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<td>3+</td>
<td>10</td>
<td>3+</td>
<td>50</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>SM</td>
<td>0</td>
<td>3+</td>
<td>20</td>
<td>3+</td>
<td>200</td>
<td>+</td>
<td>-</td>
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<td>EB</td>
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<td>3+</td>
<td>2.5</td>
<td>3+</td>
<td>5</td>
<td>3+</td>
<td>-</td>
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<td>3+</td>
<td>1</td>
<td>3+</td>
<td>10</td>
<td>3+</td>
<td>-</td>
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<tr>
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<td>50</td>
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*200–500 colonies, §1–200 colonies, no growth.

Figure 1. Chest X-ray on admission showing giant cavities in the bilateral upper lung fields.

Unlike other non-tuberculous mycobacteria, *Mycobacterium kansasii* frequently affect the respiratory system even in immunocompetent hosts. However, many investigators suggest that *Mycobacterium kansasii* pulmonary disease shows a relatively good response to the conventional antituberculous regimen. Ahn et al (1) reported a 2.5% relapse rate within 6 months after a 12-month regimen with RFP, INH, and EB, plus streptomycin (SM) for the first three months, and according to a study by the British Thoracic Society, a 9.7% relapse rate was calculated after a 9-month course of RFP and EB (2).

In terms of drug susceptibility, previous studies revealed that 19% of strains were resistant to 5 µg/ml of INH, 19% were resistant to 10 µg/ml of SM, and 54% were resistant to 10 µg/ml of paraaminosalicylate in Johanson’s study (3), while 95% were resistant to 1 µg/ml of INH, none were resistant to 1 µg/ml of RFP, 29% were resistant to 2 µg/ml of EB, and 14% were resistant to 2 µg/ml of SM in Ahn’s study (1). In Japan, Nakazono reported that 4.1% of strains were resistant to 1 µg/ml of INH, 2.1% were resistant to 50 µg/ml of RFP, 2.1% were resistant to 5 µg/ml of EB, and 2.1% were resistant to 20 µg/ml of SM (4). In the present case, the isolated strain showed a significantly higher level of resistance than those previously reported, which was one of the major reasons for therapeutic failure, although the drugs of choice were standard and well tolerated. Recent studies demonstrated that non-antituberculous agents such as ofloxacin (5, 6), sparflxacin (6), clarithromycin (1), and sulfamethoxazole-trimethoprim tablets (7) showed bactericidal activity against *Mycobacterium kansasii* at therapeutic doses. These reports suggest the clinical application of these drugs.

Another important factor is that this patient did not have health insurance. This social problem deprived him of the opportunity to receive early treatment, resulting in irreversible and critical pulmonary damage. It goes without saying that physicians must pay attention to social aspects, even in areas where welfare is thought to be well promoted.

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References