Clinical features of eleven cases of *Mycobacterium avium-intracellulare* complex pulmonary disease associated with pneumoconiosis

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**Summary**

The relationship between silicosis and tuberculosis is well known. Also other mycobacteria such as *Mycobacterium kansasii* often occur in association with pneumoconiosis. However, there are few reports describing an association of *M. avium-intracellulare* complex (MAC) lung disease and pneumoconiosis. The purpose of the present study is to describe clinical features of MAC respiratory infection associated with pneumoconiosis. Eleven patients with MAC respiratory infection associated with pneumoconiosis (all men, 6 with silicosis and 5 with welders' pneumoconiosis) were collected. A determination of whether or not MAC caused pulmonary disease was made using the 1997 criteria required by the American Thoracic Society. Radiologically, cavity formation as well as upper lung field predominance of MAC disease were observed in 8 of 11 cases (72.7%). Two of 11 patients died of respiratory failure. Our present study clearly demonstrates that clinical features of MAC respiratory infection associated with pneumoconiosis were different from MAC without underlying diseases.

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**Introduction**

The increased incidence of *Mycobacterium tuberculosis* in silicotic patients is well known.\textsuperscript{1-3} Also, atypical mycobacterial infections appear to be

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**KEYWORDS**

*Mycobacterium avium intracellulare* complex (MAC) infection; Pneumoconiosis; Silicosis; Welders' pneumoconiosis
more frequent in patients with pneumoconiosis, especially *M. kansasii* disease.\(^1\),\(^4\),\(^5\) More recently, Corbett et al. have reported that *M. kansasii* and *M. scrofulaceum* disease are common in HIV-negative South African gold miners and most isolates are associated with new cavitation against a background of silicosis or old tuberculosis scarring.\(^6\)–\(^8\) However, there are few reports describing *M. avium-intracellulare* complex (MAC) disease associated with pneumoconiosis.\(^9\)–\(^11\) In the present study, retrospective cases of MAC respiratory infection in patients with pneumoconiosis were collected and clinical features are described.

### Materials and Methods

#### Patients

A retrospective study was performed in 11 cases of positive sputum cultured for MAC. Patients were collected from 1991 to 2002. The criteria for defining NTM pulmonary disease were those of the American Thoracic Society (1997).\(^12\) Briefly, the diagnosis of lung disease caused by MAC is based on a combination of clinical, radiographic, and bacteriologic criteria. Minimal evaluation should include three or more sputums for acid-fast bacteria and efforts to exclude other confounding disorders such as tuberculosis and lung malignancy.\(^12\) In 4 patients, a diagnosis can be made with histological examination obtained at the operation. Both culture and PCR methods were used to identify mycobacteria and mycobacteria were detected in sputum in all patients. Drug sensitivity test for MAC was performed in none of these patients.

Silicosis was diagnosed by occupational history (tunnel construction work and inhalation of silica dust) and multiple nodules on chest radiography. Welders’ pneumoconiosis was diagnosed by occupational history (arc welding and inhalation of iron dust or fumes) and interstitial changes on chest radiography. In 4 of 5 patients with welder’s pneumoconiosis, diagnosis was confirmed histologically by evaluating operated specimens. Characteristics of these 11 patients are listed in Table 1. Smoking index was calculated as follows; number of cigarettes per day × smoking interval (years). In our report, there were no patients who had AIDS.

### Radiological findings

Chest X-ray and computed tomography (CT) of the chest were performed in all patients. The presence of cavities and the distribution of lesions caused by MAC were classified as upper lung field predominance, upper and lower lung field predominance, and lower lung field predominance.

### Results

Radiological findings of MAC respiratory infection associated with pneumoconiosis are listed in Table 2. Cavity formation was observed in 8 of 11 cases (72.7%). Three cases were determined as upper and lower lung fields predominance, 8 of 11 cases were clearly demonstrated to be upper lung fields predominance. Examples of chest X-ray and chest CT findings are demonstrated in Figs. 1–4 (cases 1 and 4). Chest X-ray and chest CT

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### Table 1 Patient characteristics.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age and sex</th>
<th>Background</th>
<th>Smoking index</th>
<th>WBC</th>
<th>%VC</th>
<th>FEV1%</th>
<th>PaO2</th>
<th>Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65M</td>
<td>Silicosis</td>
<td>900</td>
<td>6300</td>
<td>75.6</td>
<td>65.8</td>
<td>—</td>
<td><em>M. avium</em></td>
</tr>
<tr>
<td>2</td>
<td>73M</td>
<td>Silicosis</td>
<td>1000</td>
<td>8600</td>
<td>—</td>
<td>—</td>
<td>78</td>
<td><em>M. avium</em></td>
</tr>
<tr>
<td>3</td>
<td>75M</td>
<td>Silicosis</td>
<td>200</td>
<td>4900</td>
<td>75.1</td>
<td>36.8</td>
<td>64</td>
<td><em>M. avium</em></td>
</tr>
<tr>
<td>4</td>
<td>64M</td>
<td>Silicosis</td>
<td>1400</td>
<td>7400</td>
<td>95</td>
<td>72.9</td>
<td>87.7</td>
<td><em>M. intracellulare</em></td>
</tr>
<tr>
<td>5</td>
<td>75M</td>
<td>Silicosis</td>
<td>680</td>
<td>5800</td>
<td>77.7</td>
<td>59</td>
<td>78.5</td>
<td><em>M. avium</em></td>
</tr>
<tr>
<td>6</td>
<td>78M</td>
<td>Silicosis</td>
<td>600</td>
<td>5000</td>
<td>107.8</td>
<td>79.3</td>
<td>91.9</td>
<td><em>M. avium</em></td>
</tr>
<tr>
<td>7</td>
<td>47M</td>
<td>Welder's pneumoconiosis</td>
<td>0</td>
<td>7800</td>
<td>92.2</td>
<td>72</td>
<td>86.1</td>
<td><em>M. avium</em></td>
</tr>
<tr>
<td>8</td>
<td>56M</td>
<td>Welder's pneumoconiosis</td>
<td>0</td>
<td>6000</td>
<td>112.7</td>
<td>80.3</td>
<td>81</td>
<td>MAC*</td>
</tr>
<tr>
<td>9</td>
<td>33M</td>
<td>Welder's pneumoconiosis</td>
<td>0</td>
<td>7200</td>
<td>80.6</td>
<td>71.8</td>
<td>78.1</td>
<td>MAC</td>
</tr>
<tr>
<td>10</td>
<td>48M</td>
<td>Welder's pneumoconiosis</td>
<td>80</td>
<td>10900</td>
<td>76.8</td>
<td>75.1</td>
<td>94.7</td>
<td>MAC</td>
</tr>
<tr>
<td>11</td>
<td>59M</td>
<td>Welder's pneumoconiosis</td>
<td>1750</td>
<td>3000</td>
<td>91.9</td>
<td>78.8</td>
<td>94</td>
<td><em>M. avium</em></td>
</tr>
</tbody>
</table>

*Unclassified.*
in these cases clearly demonstrated upper lung field predominance and formations of large cavities especially in the upper lung fields. Anti-mycobacterial chemotherapy was performed in 9 cases, and operation was performed in 4 cases. Despite treatment, 2 of 11 patients died of respiratory failure. 

Table 2 Radiological findings of MAC infection associated with pneumoconiosis.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age and sex</th>
<th>Cavity</th>
<th>Predominant lesion</th>
<th>Therapy</th>
<th>Duration of chemotherapy</th>
<th>Response to chemotherapy</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65M</td>
<td>+</td>
<td>Upper</td>
<td>EB + RFP + CAM</td>
<td>24</td>
<td>No response</td>
<td>Alive</td>
</tr>
<tr>
<td>2</td>
<td>73M</td>
<td>+</td>
<td>Upper</td>
<td>EB + RFP + CAM + SM</td>
<td>12</td>
<td>No response</td>
<td>Dead</td>
</tr>
<tr>
<td>3</td>
<td>75M</td>
<td>–</td>
<td>Upper = lower</td>
<td>None</td>
<td>0</td>
<td>—</td>
<td>Alive</td>
</tr>
<tr>
<td>4</td>
<td>64M</td>
<td>+</td>
<td>Upper</td>
<td>EB + RFP + CAM</td>
<td>22</td>
<td>No response</td>
<td>Dead</td>
</tr>
<tr>
<td>5</td>
<td>75M</td>
<td>+</td>
<td>Upper</td>
<td>EB + RFP + CAM</td>
<td>36</td>
<td>Good</td>
<td>Alive</td>
</tr>
<tr>
<td>6</td>
<td>78M</td>
<td>–</td>
<td>Upper = lower</td>
<td>EB + RFP + CAM</td>
<td>30</td>
<td>Good</td>
<td>Alive</td>
</tr>
<tr>
<td>7</td>
<td>47M</td>
<td>–</td>
<td>Upper = lower</td>
<td>EB + RFP + CAM</td>
<td>18</td>
<td>Good</td>
<td>Alive</td>
</tr>
<tr>
<td>8</td>
<td>56M</td>
<td>+</td>
<td>Upper</td>
<td>Operation</td>
<td>0</td>
<td>—</td>
<td>Alive</td>
</tr>
<tr>
<td>9</td>
<td>33M</td>
<td>+</td>
<td>Upper</td>
<td>INH + RFP → CS + SM → Operation</td>
<td>12</td>
<td>No response</td>
<td>Alive</td>
</tr>
<tr>
<td>10</td>
<td>48M</td>
<td>+</td>
<td>Upper</td>
<td>Operation → INH + RFP + SM + CAM</td>
<td>12</td>
<td>Good</td>
<td>Alive</td>
</tr>
<tr>
<td>11</td>
<td>59M</td>
<td>+</td>
<td>Upper</td>
<td>Operation → CAM</td>
<td>24</td>
<td>No response</td>
<td>Alive</td>
</tr>
</tbody>
</table>

Discussion

In the present study, we describe the clinical features of MAC respiratory infection associated with pneumoconiosis.

Previously, it had been believed that the majority of patients with MAC pulmonary disease have chronic underlying lung disease such as bronchiectasis, chronic bronchitis and emphysema. In these patients, the radiographic pattern may be indistinguishable from post-primary tuberculosis, characterized by nodules, consolidation, and cavities, most often affecting the upper lobes and superior segments of the lower lobes. Radiographic patterns in patients with pneumoconiosis demonstrated in the present study also showed upper lung field predominance and frequent cavity formation.

In contrast, Prince et al. have reported that pulmonary disease caused by MAC can affect persons without predisposing conditions, particularly elderly women. More recently, there have been several reports describing a strong association between bronchiectasis with circumscribed nodules and MAC infection in elderly women in the absence of underlying malignancy or immune compromise. This pattern is characterized by bronchiectasis and nodular densities, particularly affecting the middle lobe and lingua. Therefore, radiological findings are quite different between MAC respiratory infection without underlying diseases in mostly elderly women and MAC with pneumoconiosis in mostly elderly men.

The incidence of mycobacterial infection is 25% in patients with exposure to high concentrations of silica. While half of the mycobacterial infections are caused by *M. tuberculosis*, the other half are caused by atypical organisms such as *M. kansasii* and *M. avium-intracellulare*. There also is an increased incidence of fungal infection in these patients. Some of the infections are caused by opportunistic organisms, such as *Nocardia* and *Cryptococcus*. The primary cause of the increased incidence of mycobacterial and fungal infections is an acquired macrophage dysfunction. It has been shown that *M. tuberculosis* organisms within macrophages multiply more rapidly in the presence of silica. Therefore, in patients with silicosis, the upper lung field predominance of MAC respiratory infection may be explained by the fact that the distribution of nodules caused by silica inhalation is also predominated in the upper lung fields.

In the present study, 2 patients died of respiratory failure despite intensive treatment. Therefore, it seems that MAC associated with pneumoconiosis is more difficult to treat in patients without underlying diseases.

In conclusion, in the present report, we clearly demonstrated clinical features of MAC respiratory infection associated with silicosis.

References