Case Report

Multiple Pulmonary Nodules Caused by Zygomycesis in a Patient without Predisposing Factors

Tomoko KUTSUZAWA, Yoshihumi MATSUURA*, Hideo SAKUMA**, Hiroshi NARIMATSU***, Yasuyo OHTA and Hajime YAMABAYASHI

We report a case of a 61-year-old male without any predisposing factors. His X-ray film showed multiple nodular lesions in bilateral lung fields. Open lung biopsy revealed Zygomyces in the granuloma. The patient was treated with amphotericin B and miconazole, and remains alive more than 32 months later.

Key words: Pulmonary Zygomycesis, Granuloma

The Zygomyces are saprophytic fungi. The family of Zygomyces comprises Mucorales, Entomophthorales, and Zoopagales. They can cause life-threatening infections in patients with depressed immunity (1, 2), including diabetic ketoacidosis, corticosteroid therapy, leukemia, lymphoma, immunosuppressive therapy, neutropenia, and renal failure.

We describe a case of pulmonary zygomycesis with no obvious underlying systemic disease.

CASE REPORT

A 61-year-old Japanese male farmer was referred to the hospital because of multiple nodular shadows on chest X-ray. The chest X-ray taken 2 yr previously was normal. Six months before admission, a chest X-ray for an annual exam disclosed multiple nodular shadows in bilateral lung fields. He was admitted to another hospital for evaluation, but no definite diagnosis was made. On admission, he complained of mild left chest pain. There was no history of dyspnea, cough, hemoptysis, or fever.

The physical exam on admission was unremarkable. The hematocrit was 40%, WBC was 9,200/mm³, with 8% eosinophils. The ESR was 64 mm/h. Serum protein electrophoresis demonstrated elevated gammaglobulins. Complement levels were within normal limits. A 75 g oral glucose tolerance test gave normal results. A sputum culture was negative for bacteria or fungi and sputum cytology showed no atypical cells.

The chest X-ray film (Fig. 1) revealed nodular lesions in the right middle, right lower, left hilum and left upper lung fields. As no pathological diagnosis was made by TBLB, open lung biopsy was elected. A nodule of the left apical-posterior segment showed fibrotic change and hyaline degeneration, in which there were granulomas with Langhans' giant cells and plasma cells. PAS and Grocott stains showed irregular, right-angle branching, non-septate, broad hyphae in the granulomas (Fig. 2). This was identified as a type of Zygomycesis. There was no finding of Zygomyces invasion into the vascular system.

The patient was treated with inspired amphotericin B. Although lab data were improved, the size of the nodules did not change. Four months later, an infiltrative shadow extended to the right middle...
lobe and the CRP increased. He was then re-admitted and treated with miconazole 800 mg/day, in addition to inhalation therapy with amphotericin B. Two months later, the infiltrative shadow was cleared. Similar relapses occurred twice and the same treatment was successful in reducing the inflammation. He remains alive more than 32 months later.

DISCUSSION

Zygomycosis has rarely been reported to be pathogenic in normal people. Only seven cases of primary pulmonary zygomycosis with no predisposing factors have been reported in the literature (Table 1) (3-9).

Table 1. Previous reports of Zygomycosis in patients without Predisposing factors.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Age</th>
<th>Sex</th>
<th>X-ray findings</th>
<th>Diagnostic procedure</th>
<th>Treatment</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Murphy and Bornstein (3)</td>
<td>40</td>
<td>M</td>
<td>Coin lesion (RML)</td>
<td>Thoracotomy</td>
<td>Tumorectomy</td>
<td>alive (3M + *)</td>
</tr>
<tr>
<td>Blankenberg and Verhoeff (4)</td>
<td>23</td>
<td>F</td>
<td>Abscess (RML,RLL)</td>
<td>Lobectomy</td>
<td>Lobectomy</td>
<td>alive (14M +) DM (14M later)</td>
</tr>
<tr>
<td>Record and Ginder (5)</td>
<td>66</td>
<td>M</td>
<td>Infiltrates with cavitation (LUL)</td>
<td>Sputum</td>
<td>Amphotericin B Lobectomy</td>
<td>died (4M) of lung infarction</td>
</tr>
<tr>
<td>Leong (6)</td>
<td>38</td>
<td>F</td>
<td>Bil. hilar mass Paratracheal lymphadenopathy</td>
<td>Thoracotomy</td>
<td>Lugol's iodine</td>
<td>died (3w)</td>
</tr>
<tr>
<td>Matsushima et al (7)</td>
<td>52</td>
<td>M</td>
<td>Coin lesion (RUL)</td>
<td>Lobectomy</td>
<td>Lobectomy</td>
<td>alive (19M +)</td>
</tr>
<tr>
<td>Ferrinho (8)</td>
<td>2M</td>
<td>M</td>
<td>—</td>
<td>Autopsy</td>
<td>—</td>
<td>died (4 day)</td>
</tr>
<tr>
<td>Lake et al (9)</td>
<td>45</td>
<td>M</td>
<td>Cavitation (LUL)</td>
<td>Sputum, Bronchial washing</td>
<td>Amphotericin B 5-FC Ketoconazole Lobectomy</td>
<td>alive (24M +)</td>
</tr>
</tbody>
</table>

* + after number indicates that patient is still alive.
This case is of interest for several reasons. First, the histopathological finding of the nodule was that of a granuloma. Pulmonary zygomycosis typically invades the airway and the pulmonary vascular system which occasionally leads to atelectasis, thrombosis and abscess formation. In the seven reported cases of primary pulmonary zygomycosis, four (4, 5, 8, 9) developed consolidation and/or thrombosis, and three (4, 5, 9) of these four showed cavitary lesions in the lung. These four had infectious symptoms such as fever, productive cough, and hemoptysis. On the other hand, in two of seven cases (3, 7), chest X-ray showed a single nodular lesion which was composed of granuloma. These two cases were asymptomatic. The above instances suggest that there are two types of primary pulmonary zygomycosis: one is an asymptomatic, chronic type which develops granuloma; another is an acute, critical, infectious type which is also seen in the immunocompromised host.

Another interesting point is in the treatment and prognosis of zygomycosis. Since zygomycosis is rarely diagnosed premortem, therapeutic experience is limited. Early diagnosis and resection of the lesion, with or without administration of amphotericin B, may lead to healing (1, 2). In the seven reported cases, five (3–5, 7, 9) received thoracotomy. Two (5, 9) of these five cases were treated with amphotericin B before and/or after lobectomy. In our case, successful remission occurred three times with the combination of amphotericin B and miconazole treatments. Miconazole has been used as an alternative to amphotericin B in patients with coccidioidomycosis and candidiasis (10). Although Zygomycetes have been reported to be relatively resistant to miconazole (10), there has been a report that Zygomycetes isolated from a patient were sensitive to miconazole (9).

REFERENCES